Study Title:

Perioperative chemotherapy with FOLFOX plus Cetuximab versus adjuvant FOLFOX plus Cetuximab for patients with resectable liver metastases of colorectal carcinoma

Open label, multicentre, randomized, parallel 2-arm study. The treatment phase in both arms consists of a total of 12 chemotherapy cycles (cycle duration = 2 weeks):
arm A – 12 postoperative cycles; arm B – 6 cycles before and 6 cycles after the surgery.

Names of the investigational medicinal products
Oxaliplatin
5-Fluorouracil
Folinic acid
Cetuximab

Indication
Colorectal carcinoma with liver metastases

Clinical trial phase II

Short Title / Acronym: PANTER-study
Eudra-CT Number: 2008-005312-41

Study start date – study end date
FSI: August 2011 – early end of treatment: June 2014 – end of follow-up: February 2015

Clinical Study Report

Sponsor of the Clinical Trial:

RWTH Aachen University
Mrs Dipl. Biol. Verena Deserno
Pauwelsstraße 30
52074 Aachen
Germany
Phone: 0049-241-8035849
Fax: 0049-241-803335849

National Coordinating Investigator / Investigator:

Prof. Dr. Ulf Peter Neumann (Germany)
Prof. Dr. Thomas Grünberger (Austria)

Version / Date: Final 1.0 / 22.01.2016

Synopsis

Sponsor:
RWTH Aachen University
represented by the Clinical Trials Centre Aachen (CTC-A) of the Medical Faculty of the RWTH Aachen University,
Mrs Dipl. Biol. Verena Deserno
Phone: 0049-241-8035849
Fax: 0049-241-803335849
E-mail: vdeserno@ukaachen.de
Pauwelsstraße 30, 52074 Aachen, Germany

Investigational medicinal product:
Both Arms: (FOLFOX+Cetuximab): Erbitux®, Oxaliplatin in combination with 5-FU and Folinic acid.

Drug substance: Cetuximab, Oxaliplatin, 5-Fluorouracil, Folinic acid.

Registration: ClinicalTrials.gov registration number: NCT01266187

Study title:
Perioperative chemotherapy with FOLFOX plus Cetuximab versus adjuvant FOLFOX plus Cetuximab for patients with resectable liver metastases of colorectal carcinoma

National Coordinating Investigator in Germany:
Prof. Dr. Ulf Peter Neumann
Department for Surgery
Pauwelsstraße 30
D-52074 Aachen
Germany

National Coordinating Investigator in Austria:
Prof. Dr. Thomas Grünberger
Universität Wien
Abt. für Allg. Chirurgie
Waehringer Guertel 18-20
A- 1090 Wien

Study sites: 27 sites in Germany, 7 sites in Austria

First patient in: August 2011 **Last patient out:** February 2015	**Phase: II**

Study objectives:

To compare the postoperative complication rate according to Clavien score (> grade 1) of a perioperative chemotherapy with FOLFOX and Cetuximab to the postoperative regimen in patients with resectable colorectal liver metastases.
To compare the disease-free survival of the two regimens in the patient subgroup with >3 liver metastases or at least one metastasis ≥ 5 cm in diameter.

The secondary objectives were OS, DFS, surgery rates, resections rates, R0 rates, safety and chemotherapy associated toxicity, number of cycles, dose intensity and dose modification

applied, quality of life, response rate and resected liver mass.

Trial design:

Open label, multicentre, randomized, parallel 2-arm study.
The treatment phase in both arms consisted of a total of 12 chemotherapy cycles (cycle duration = 2 weeks).
Arm A: surgery -> 4-8 weeks rest -> 24 weeks FOLFOX +Cetuximab.
Arm B: 12 weeks FOLFOX + Cetuximab -> 4 weeks rest -> surgery-> 4-8 weeks rest -> 12 weeks FOLFOX + Cetuximab

Number of patients (planned and analysed):

planned 430 (215 each arm); enrolled and analysed 24 (11 in arm A, 13 in arm B)

All patients were enrolled in Germany.

Diagnosis and key inclusion criteria:

K-Ras wildtype patients with colorectal cancer liver metastases

1. Age ≥ 18 years
2. Proven K-RAS wildtype in primary tumour or metastasis tissue
3. Diagnosis of resectable metachronous liver metastases after complete resection (R0) of primary tumour without gross or microscopic evidence of residual disease.
   or
   Diagnosis of resectable synchronous liver metastases after complete resection (R0) of primary tumour more than 1 month before study
   or
   Diagnosis of resectable synchronous liver metastases with sufficient evidence (i.e., CT scan or diagnostic laparoscopy) that both the primary tumour and liver metastases can be completely resected during the same procedure and resection of primary can be delayed 3-4 months.
4. Planned start of study medication between 0 and 3 weeks post randomization
5. ECOG performance status 0 or 1
6. Adequate haematology: neutrophils > 1,5 /nl, platelets > 100/nl, INR < 1,5, aPTT < 1,5 x UNL
7. Adequate biochemistry: total bilirubin < 1,5 x UNL, ASAT and ALAT < 5 x UNL, alkaline phosphatase < 5 x UNL, serum creatinine < 1,5, x UNL.

Duration of treatment:

32-36 weeks: 12 cycles of chemotherapy (2 weeks each), 4-8 weeks recovery from the surgery, 4 weeks pause after the 6^{th} cycle and the surgery in arm B.

Efficacy evaluation:

Due to the premature termination of the study and low number of patients randomized (n=24) no significant results could be obtained. There was no difference in postoperative complications between the two arms. No comparison between the arms was possible for the patients with high tumour burden as only 2 such patients were enrolled and both were randomized to arm A. All treated patients responded to chemotherapy. Of 18 surgeries 14 were R0 resections (77.78 %), 6 of 8 surgeries in Arm A (75 %) and 8 of 10 surgeries in Arm B (80 %). 16 patients entered the follow up period, 13 of whom (81.25 %) showed no recurrent or new metastases until the end of the follow-up period, 3 patients relapsed (distant metastases) 1 from Arm A and 2 from Arm B. There was no difference regarding OS and DFS between the arms. No statement is possible regarding the difference in resected liver mass in both arms. Dose modifications were necessary in both arms.

Safety evaluation:

Adverse events and tolerability were assessed at each visit, at least prior every therapy cycle.

314 adverse events were recorded during the trial, 90 in Arm A and 224 in Arm B. The most common adverse event was 'Rash acneiform' (11.8%). 13 SAEs occurred. Most common were 'Diarrhea' and 'Pulmonary embolism', each with a share of 15.4 %. For 2 patients the treatment had to be discontinued due to intolerable toxicity.

Statistical methods:

Postoperative complications grade > 1 in both treatment arms were compared using the two sided Cochran-Mantel-Haenszel (CMH) test stratified for Fong Score, tumour volume and Study Site at a two-sided significance level of 0.05. The primary analysis for the post-operative complication rate was performed in all patients with surgery for liver resection. An intention-to-treat analysis was also planned in all randomized patients.

In addition to the CMH test, exact 95% confidence intervals for the complication rates and the common odds-ratio were calculated in each arm. Multiple logistic regression analysis were used to further explore the impact of various demographic and disease characteristics on the post-operative complication rates.

DFS in the subgroup of patients with > 3 liver metastases or at least one metastasis ≥ 5 cm in diameter and overall survival (OS) time is presented by means of the Kaplan-Meier curves and associated statistics, i.e. median survival time and two-sided 95% confidence intervals for the median. The hazard ratio (HR) for the time-to-event variables and corresponding 95% confidence intervals for HR was estimated using the Cox proportional hazard models adjusted for the stratification factor Fong Score.

All significance tests were performed two-sided at a significance level of 0.05. Only the two primary objectives were tested sequentially in a confirmatory manner considering the hierarchical order of the two corresponding null hypotheses. The second primary objective could only be tested in a confirmatory manner, if the first null hypothesis has been rejected. This sequential rejecting testing procedure will guarantee a multiple type I error of 0.05.

Descriptive statistics were used to summarize all baseline characteristics and further efficacy and safety variables.

Summary of results:

Efficacy: No difference between the arms could be observed regarding the postoperative complication rate, DFS in patients with high tumour burden, DFS in general, OS or any other secondary endpoint.

Safety: No unexpected safety issues occurred.

Conclusion(s): Due to small sample size no significant result could be obtained in this study.

Date of report: 22.01.2016

Table of Contents

1 List of Acronyms & Abbreviations and Definitions

5-FU	5-fluorouracile
AE	Adverse Event
ALAT	Alanine aminotransferase
AMG	Medicinal Products Act (Arzneimittelgesetz)
ASAT	Aspartase aminotransferase
Ca	Calcium
CEA	Carcinoembryonic antigen
CI	Confidence Interval
CMH	Cochran-Mantel-Haenszel
CRC	Colorectal cancer
CRF	Case report form
CRO	Contract research organisation
CT	Computer tomography
CTC-A	Clinical trial center Aachen
DFS	Disease-free survival
ECOG	Eastern Cooperative Oncology Group
EGF	Epidermal Growth Factor
EGFR	Epidermal Growth Factor Receptor
EORTC	European Organisation for Research and Treatment of Cancer
FOLFOX	Combination of folinic acid, 5-fluorouracile and oxaliplatin
GCP	Good clinical practice
GCP-V	Good clinical practice - Verordnung
G-CSF	Granulocyte-Colony Stimulating Factor
GGT	Gamma-glutamyl transferase
HR	Hazard ratio
INR	International Normalized Ratio
aPTT	activated partial thromboplastin time
ITT	Intent to Treat Population
K	Potassium
Mg	Magnesium
MRI	Magnetic Resonance Imaging
Na	Natrium
OS	Overall survival
PFS	Progression-free survival
SAE	Serious Adverse Events
SAF	Safety Population
SD	Standard deviation
SEM	Standard error of the mean
SP	Surgery population
SUSAR	Suspected Unexpected Serious Adverse Reaction
TGF-α	Transforming Growth Factor α

2 Ethics

2.1 Independent Ethics Committee (IEC) or Institutional Review Board (IRB)

Before the beginning of the study, approvals of the responsible Independent Ethics Committees were obtained for all participating sites.

Amendment No. 1, the only Amendment to the Study Protocol for Germany, was also approved by the Ethics Committee.

The Ethics Committee of the German coordinating investigator was the Ethics Committee of the RWTH Aachen, Pauwelsstraße 30, 52074 Aachen with Prof. Dr. med. G. Schmalzing as Chair.

The study was first approved on 02.05.2011 in Germany and on 21.07.2011 in Austria, the amendment on 24.02.2015.

2.2 Ethical Conduct of the Study

The regulatory basis of the conduct of this study consisted of the Declaration of Helsinki (in its current version), the *AMG* (German and Austrian Medicinal Products Act) in the current versions, and the principles of the proper conduct of clinical trials (ICH GCP).

In accordance with the *AMG*, the sponsor had taken out insurance for all subjects who gave consent to participation in the clinical trial.

2.3 Patient Information and Consent

The subjects' written informed consent was obtained prior to enrolment in the study at the pre-screening visit (i. e., prior to any investigation that is exclusively performed for the study). Informed consent had to be dated and signed personally by both, the subject and the Investigator at the same time.

The Investigator confirmed the provision of consent in the CRF. One original of the signed and dated declaration of informed consent remained at the Investigator's site and was safely archived by the Investigator so that the forms can be retrieved at any time for monitoring, auditing and inspection purposes. A second original of the signed and dated information and consent was provided to the subject prior to participation.

The Investigator provided adequate information to the subject prior to subject signing the informed consent. The Institute provided an information sheet in the local language to the subjects and prepared it in accordance with the Note for Guidance on Good Clinical Practice (ICH, Topic E6, 1995) for the purpose of obtaining informed consent. In addition to this written information, the Investigator informed the subject verbally. In doing so, the wording used will be chosen so that the information can be fully and readily understood by laypersons. The subject information sheet was subject to revision whenever important new information appeared that was relevant to the consent of subjects.

2.4 Funding

Merck Serono GmbH supported the study with a financial grant but had no influence on study design, data collection, analyses and interpretation.

3 Investigators and Study Administrative Structure

This is an investigator-sponsored trial.

Sponsor of the clinical trial:
RWTH Aachen University
represented by the Clinical Trials Center Aachen (CTC-A) of the Medical Faculty of the RWTH Aachen University,
Mrs Dipl. Biol. Verena Deserno
Phone: 0049-241-8035849
fax: 0049-241-803335849
e-mail: vdeserno@ukaachen.de
Pauwelsstraße 30, 52074 Aachen, Germany

Coordinating Investigator in Germany:
Prof. Dr. Ulf P. Neumann
University Hospital Aachen
Department for Surgery
Pauwelsstraße 30
D-52074 Aachen
Tel: +49 241 80-89500
Fax: +49 241 80-82417

Coordinating Investigator in Austria:
Prof. Dr. Thomas Grünberger
Universität Wien
Abt. für Allg. Chirurgie
Waehringer Guertel 18-20
A- 1090 Wien
Tel: +43 1404005621
Fax: +43 1404005641

The coordinating investigators can demonstrate at least 2 years' experience in the clinical testing of medicinal products.

The list of the 14 recruiting German sites and investigators is provided in 6.3.4.

Study monitoring was performed by monitors appointed by the CRO ALCEDIS GmbH. The responsible monitor was allowed on request to inspect the various records of the trial (Case Report Forms and other pertinent data).

At each site an initiation visit was performed and sites which enrolled patients had one monitoring visit and a close out-visit. During each monitoring visit the verification of the source data took place.

4 Introduction

For the past decades CRC has been one of the leading causes of cancer deaths [1] with an

incidence of over million new cases and 340.000 deaths per year [2-7]. CRC is thus an important public health problem in Europe. Effective and sophisticated treatment options are required to meet further increase of CRC incidence in the aging population.

The combination of FOLFOX chemotherapy and Cetuximab has become a safe and effective first-line treatment for patients with colorectal liver metastases after several phase II and phase III studies like CRYSTAL [8], OPUS [9] or CELIM [10] showed improved response rates compared to chemotherapy alone [8, 11-14]. Prior to start of the presented study the combination is regarded the most effective chemotherapy available, with response rates up to 85 %.

However, most combination studies investigated effectiveness in patients with non-resectable liver metastases. There are still not enough trials to evaluate the role of Cetuximab in combination with chemotherapy in patients with resectable colorectal liver metastases. Furthermore, while patients with non-resectable liver metastases profit from perioperative treatment in that the metastases become resectable [10, 15, 16], it is not clear whether perioperative treatment is superior in patients with resectable metastases as well, or whether it leads to increased morbidity and mortality. The only study available prior to the start of the Panter study dealing with preoperative treatment in patients with resectable liver metastases was the EORTC trial by Nordlinger et al. [17]. Here, 364 patients were randomized to receive surgery alone or six respective cycles of FOLFOX regimen given before and after surgery. Although there was a trend in 3-year progression-free survival (28.1% in the surgery group vs. 35.4% in the chemotherapy group), statistical significance was not reached and what is more, the postoperative complications were significantly higher in the chemotherapy arm than in the surgery arm (25 % vs. 16 %).

Although the advantages of perioperative treatment are not proven, this concept has become more and more popular in recent years, mainly due to lack of guidelines. Thus the aim of our study was to compare the complication rate of both therapeutical concepts in K-RAS wildtype patients with resectable colorectal liver metastases. Patients were randomly assigned to either receive six cycles of FOLFOX and Cetuximab before and six cycles after surgery, or to postoperatively receive 12 cycles of FOLFOX and Cetuximab. The treatment duration in adjuvant arm is 34 weeks and in the perioperative arm 32 weeks.
We assumed that the perioperative treatment probably had a better efficacy in patients with high tumour burden (>3 liver metastases or one metastasis ≥ 5 cm in diameter) with effect on disease free survival, which was investigated in a subgroup analysis.
Disease-free survival, overall survival, resection rates, response rates, toxicities and quality of life were used to estimate the efficacy, feasibility, and safety of both regimens.

5 Study Objectives

5.1 Primary objective

The first primary objective of the study was to compare the postoperative complication rate according to Clavien score (> grade 1) of perioperative chemotherapy with a postoperative regimen up to 30th postoperative day or up to the discharge from the hospital.
The second primary objective of the study was to compare the median disease free survival for the patient subgroup with >3 liver metastases or at least one metastasis ≥ 5 cm in diameter to

avoid that the possible benefit of the perioperative treatment is overlooked in this subgroup of patients.

The two primary objectives were investigated using a sequential testing procedure in accordance with their hierarchical order.

5.2 Secondary objectives

The secondary objectives were:

- Overall survival time
- Disease-free survival time
- Surgery rates
- Resection rates
- R0 rates (i.e. proportion of patients with R0 liver resection)
- Safety and chemotherapy-associated toxicity (NCI-CTC V4.0)
- Number of cycles, dose intensity, and dose modification applied
- Quality of life using EORTC QLQ-C30 questionnaire + QLQ-LMC21
- Response rate (RECIST V1.1) after preoperative chemotherapy
- Resected liver mass

6 Investigational Plan

6.1 Overall Study Plan / Study Design

This is an open-label, multicentre, randomized, 2-arm, parallel-group phase II Interventional study with patients with resectable colorectal liver metastases.
Prior to randomization and start of treatment subjects received a multi-slice CT scan or MRI to prove the resectability of the liver metastases. Extrahepatic tumour manifestations had to be excluded, except in patients with synchronous colorectal carcinomas and resectable liver metastases. Eligible patients had to have a proven K-RAS wildtype status in tissue of the primary tumour or metastasis.
Randomization was stratified for centre, tumour volume and Fong Score. We have chosen the FOLFOX plus Cetuximab regimen for the study, since patients with metastatic colorectal cancer assigned to this treatment have previously shown a response rate of up to 85%.

After proof of resectability, patients were randomly assigned in 1:1 allocation ratio to either receive six cycles of FOLFOX and Cetuximab before and six cycles after surgery (arm B), or to receive postoperative therapy of 12 cycles after surgery (arm A) (Fig 1). For doses and dosing instructions see 6.4.2 and 6.4.4. In both arms the first treatment, i.e. surgery for arm A and first cycle of chemotherapy for arm B, began within 3 weeks after randomization.
The assessment for colorectal metastases during the treatment period included chest CT, 4 phase liver CT and CEA/Ca 19-9 measurement. Laboratory evaluations were carried out prior to every chemotherapy cycle. In the perioperative arm B, 4 phase liver CT and CEA/Ca 19-9 were

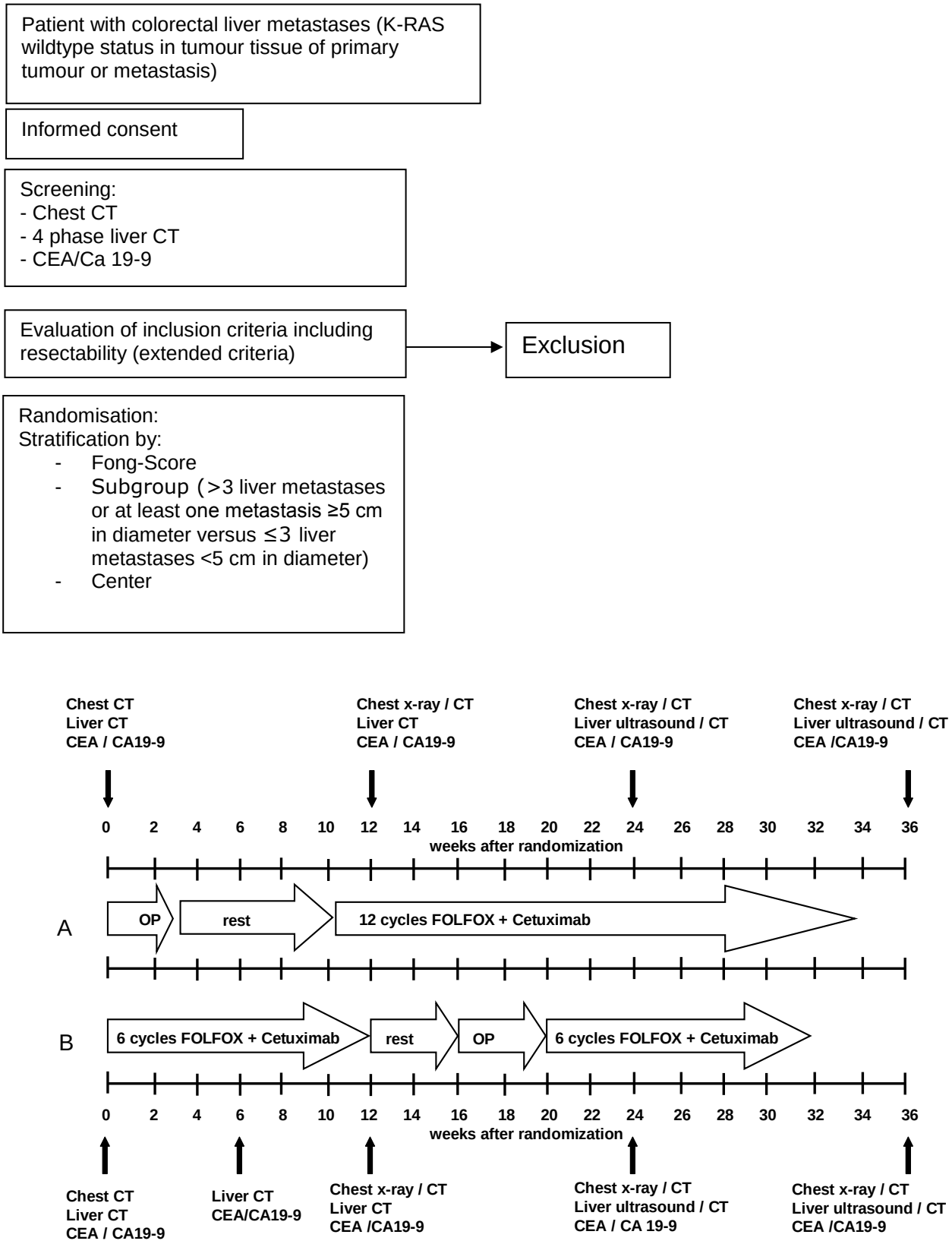
performed after 3 cycles. In both arms, chest x-ray or chest CT, 4 phase liver CT and CEA/Ca 19-9 measurement were performed 12 weeks after randomization. Then chest x-ray or chest CT, 4 phase liver CT or abdominal ultrasound and CEA/Ca 19-9 measurement were performed every 12 weeks after randomization (Fig. 1).

In the perioperative arm surgery was performed 4 weeks after the last cycle of the preoperative phase of treatment, and whenever patients have completely recovered from side-effects of chemotherapy with an ECOG performance status of 0 or 1, and adequate liver function. In both arms postoperative chemotherapy started 4 to 8 weeks after surgery when patients recovered to ECOG performance status 0 or 1.

If during the study a lesion was observed on an X-ray or abdominal ultrasound that was suspicious of metastatic disease, a CT- or MRI-scan were performed to confirm. The evaluation of tumour response according RECIST were based on the CT- or MRI-scan. For response-evaluation, the same investigational method was used throughout. If there was any suspicion of tumour progression, a CT of chest and liver was done earlier. If due to any delay the time from the last CT to surgery was longer than 4 weeks, an additional CT of the liver was done within 4 weeks prior to surgery to confirm resectability.
Further assessment by abdominal ultrasound or CT of the liver and CEA/Ca 19-9 measurements for recurrence/new occurrence of colorectal cancer and survival were performed at the same interval, every 12 weeks, or earlier if there was a clear suspicion of progression/recurrence. The frequency was maintained after the end of study treatment and until the end of the follow-up period in March 2015.
In both arms postoperative complications were recorded daily until the 30th postoperative day or until the day of discharge from hospital according to the complication score published in 2004 by Dindo et al. [18]. Through histological examination of the liver metastases chemotherapy induced toxicity was evaluated.
In total 24 eligible patients were enrolled, 11 in arm A and 13 in arm B.
Patients presenting intolerable severe adverse reactions due to the chemotherapy received no further study medication and were allowed to receive alternative chemotherapy. However, they were not excluded from the study and their follow-up was recorded as mentioned.

In case of a confirmed recurrence/appearance of new colorectal cancer during the primary analysis regarding postoperative morbidity, patients were treated with any subsequent line of chemotherapy, and were also followed-up for survival until the end of the study follow-up period.

Full trial protocol is attached in section 13.1.1 of this report.



This picture is an idealised schedule.
In arm A surgery should be within 3 weeks after randomization and FOLFOX + cetuximab should start 4-8 weeks after surgery. So, end of treatment could range from week 28 to 35 (without delays in the FOLFOX + cetuximab treatment).
In arm B FOLFOX + cetuximab should start as soon as possible within 2 weeks after randomization. Surgery should be performed after a rest of 4 weeks and FOLFOX + cetuximab should start again 4-8 weeks after surgery. So, end of treatment could range from week 32 to 39 (without delays in the FOLFOX + cetuximab treatment). If, during the study a lesion is observed on an X-ray or abdominal ultrasound that is suspicious of metastatic disease, a CT- or MRI-scan must be performed to confirm

Figure 1: Study design

6.2 Discussion of Study Design, Including the Choice of Control Groups

The aim of this study was to compare two approaches of the standard treatment combination of surgery and chemotherapy with FOLFOX and Cetuximab in K-RAS wildtype patients with colorectal liver metastases regarding the post-operative complication rate. One approach is the post-operative adminsitration of 12 chemotherapy cycles (arm A), the other is the peri-operative regimen in which 6 cycles of chemotherapy were given before and 6 after the chemotherapy.
Therefore both arms are investigational and control arm at the same time. Regarding the recent popularity of the perioperative regimen in resectable CRC (see Introduction) the result of this study could justify the perioperative treatment as indeed superior to or at least of equal risk-benefit ratio as the postoperative regimen. In case that the post-operative complication rate is equal in both arms but the resection rate and the R0 resection rate higher for the perioperative regimen (arm B), perioperative treatment can be considered superior. Should the postoperative regimen render higher post-operative complication rate, resection rates, DFS and PFS must be compared between the arms to evaluate superiority.
Furthermore, the study population was stratified for high tumour burden (>3 liver metastases or at least one metastasis ≥ 5 cm in diameter) to avoid that the possible benefit of the perioperative treatment is overlooked in this subgroup of patients.
Patients received recommended doses of the study drug components during recommended treatment duration.
To guarantee patients' safety but also do accurately distinguish treatment complications the surgery and the postoperative chemotherapy were performed only after patients' recovery to ECOG performance status 0 or 1.
In order to assess the efficacy of the both treatment regimens and to compare the postoperative complication rates the physical condition of the patients was assessed prior to every cycle. The tumour burden was assessed prior to surgery and every 12 weeks during the treatment and the follow-up period.

6.3 Selection of Study Population / Study Subjects

430 patients were planned to be enrolled and equally randomized to the 2 treatment arms. Due to very slow recruitment only 24 subjects could be recruited and the study ended prematurely.
There was no specific gender distribution, since no gender specific differences concerning efficacy and safety of the investigational product were expected (see GCP-V § 7 (2) No. 12).

6.3.1 Inclusion Criteria

1) Signed written informed consent obtained prior to any study-specific procedure. (IC 1)
2) Age > 18 years (IC 2)
3) Proven K-RAS wild type in primary tumour or metastasis tissue (IC 3)
4) Diagnosis of resectable metachronous metastases after complete resection (R0) of primary tumour without gross or microscopic evidence of residual disease or diagnosis of resectable synchronous metastases after complete resection (R0) of primary tumour more than 1 month before study or diagnosis of resectable synchronous metastases with sufficient evidence (i.e., CT scan or diagnostic laparoscopy) that both the primary tumour and liver metastases can be completely resected during the same procedure and resection of primary can be delayed 3-4 months. (IC 4)
5) Negative pregnancy test (IC 5)

6) Highly effective contraception during treatment and for at least 3 months thereafter in women (defined as pearl index < 1) and men, if the risk of conception exists (IC 6)
7) Planned start of study medication between 0 and 3 weeks post randomization (IC 7)
8) ECOG performance status 0 or 1 (Appendix 1) (IC 8)
9) Adequate haematology: neutrophils > 1,5 /nl, platelets > 100/nl, INR < 1,5, aPTT < 1,5 x UNL (IC 9)
10) Adequate biochemistry: total bilirubin < 1,5 x UNL, ASAT and ALAT < 5 x UNL, alkaline phosphatase < 5 x UNL, serum creatinine < 1,5, x UNL. (IC 10)

6.3.2 Exclusion Criteria

1) Patients with any relationship of dependence to the sponsor or the investigator (EC 1)
2) Patients committed to an institution (court-ordered or by official orders) (EC 2)
3) Extrahepatic metastatic disease (EC 3)
4) Proven K-RAS mutation or unknown K-RAS mutational status in tumour tissue (EC 4)
5) Oxaliplatin-based adjuvant chemotherapy within 1 year before randomization (EC 5)
6) History of neuropathy ≥ grade 3 (NCI-CTC V4.0) during prior Oxaliplatin-based chemotherapy or currently known peripheral neuropathy, including Oxaliplatin-induced neuropathy ≥ grade 1 (NCI-CTC V4.0). Absence of deep tendon reflexes as the sole neurological abnormality does not render the patient ineligible (EC 6)
7) Any prior chemotherapy for metastatic disease (EC 7)
8) Previous treatment with EGFR antibodies (EC 8)
9) Prior non-colorectal malignancies, except adequately treated basalioma of the skin or carcinoma in situ of the cervix. (EC 9)
10) Bleeding diathesis or coagulation disorders (EC 10)
11) Females with a positive pregnancy test (within 14 days before treatment start) or breast feeding (EC 11)
12) Fertile women (<2 years after last menstruation) and women of childbearing potential not willing to use effective means of contraception (EC 12)
13) History of psychiatric disability judged by the investigator to be clinically significant, precluding informed consent or interfering with compliance for drug intake (EC 13)
14) Clinically significant (i.e. active) cardiovascular disease, e.g. cerebrovascular accidents (<6 months prior to randomization), myocardial infarction (<1 year prior to randomization), Congestive heart failure (NYHA Grades III or IV), uncontrolled hypertension while receiving chronic medication, unstable angina pectoris, significant arrhythmia (EC 14)
15) Known DPD-deficiency (Dihydropyrimidinedehydrogenase) (EC 15)
16) Organ allografts requiring immunosuppressive therapy (EC 16)
17) Serious, non-healing wound, ulcer or bone fracture (EC 17)
18) Serious intercurrent infections (uncontrolled or requiring treatment) (EC 18)
19) Current or recent (within 28 days prior to randomization) treatment with another investigational drug or participation in another investigational study (EC 19)
20) Any contraindications against study medication (including auxiliary substances) (EC 20)
21) Patients unwilling to consent the saving and propagation of pseudonymized medical data for study reasons (EC 21)

6.3.3 Removal of Patients from Therapy or Analysis

The following events could cause premature termination of study treatment of the individual participant:

- Personal wish of the patient
- Pregnancy
- Any other circumstance that makes the Investigator believe that in the patient's own interest he/she should no longer receive study treatment
- A delay of treatment with study medication for more than 4 consecutive weeks
- Tumour progression
- Circumstances which, according to the study protocol, do not allow certain therapeutic interventions / occurrence of new diseases/infections
- Significant violation of the study protocol
- Loss of contact, relocation, change of treating physician
- Subsequent occurrence of exclusion criteria (after enrolment)

If there was a medical reason for withdrawal from study treatment, the patient remained under the supervision of the investigator until the AEs have been resolved or declined to baseline values.

If a patient has failed to attend scheduled assessments in the study, the investigator had to determine the reasons and circumstances as completely and accurately as possible.

In case of premature discontinuation of the study treatment by a patient, the investigations scheduled for the last visit were performed, if possible. In any case, the CRF section entitled "End of Treatment" had to be completed.

Patients excluded during investigations were not replaced.
No patients were removed from the treatment or analysis.

6.3.4 Study Sites and Locations

Data were collected at 14 recruiting sites in Germany. The sites with Principle Investigators and the number of randomized patients are summarized in Table 1.

Table 1. Study sites with Principle Investigators and number of recruited patients.

Org-No.	Site	Country	Number of patients-Arm A	Number of patients-Arm B	Number of patients-Total
0001	Universitätsklinikum der RWTH Aachen, Pauwelsstr. 30, 52074 Aachen	Germany	1	2	3
0002	Universitätsklinikum Jena , Erlanger Allee 101, 07740 Jena	Germany	1	2	3
0003	Klinikum der Otto-von-Guericke Universität Magdeburg , Leipziger Str. 44, 39120 Magdeburg	Germany	.	1	1
0004	Klinikum der J.-W. Goethe-Universität Frankfurt a.M. , Theodor-Stern-Kai 7, 60590 Frankfurt/Main	Germany	1	1	2
0011	Asklepios Klinik Barmbek Rübenkamp 220, 20099 Hamburg	Germany	2	.	2
0014	Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden , Fetscherstraße 74 , 01307 Dresden	Germany	1	3	4
0015	Universitätsklinikum Leipzig , Liebigstraße 20, 04103 Leipzig	Germany	.	1	1
0017	Klinikum der Stadt Ludwigshafen am Rhein gGmbH , Bremser Strasse 79, 67063 Ludwigshafen	Germany	1	1	2
0018	Uniklinikum Würzburg , Oberdürrbacherstr. 6, 97080 Würzburg	Germany	1	.	1
0019	Klinikum rechts der Isar , Ismaninger Straße 22, 81675 München	Germany	.	1	1
0020	Universitätsklinikum Erlangen , Krankenhausstraße 12, 91054 Erlangen	Germany	1	.	1
0023	Medizinische Hochschule Hannover , Carl-Neuberg-Str. 1, 30625 Hannover	Germany	1	.	1
0028	Helios Klinikum Berlin - Klinikum Buch , Schwanebecker Chaussee 50, 13125 Berlin	Germany	.	1	1
0032	Universitätsklinikum Bonn , Siegmund-Freud-Straße 25, 53105 Bonn	Germany	1	.	1
0005	Gemeinschaftspraxis Dr. Tummes, Weinberg, Dr. Guggenberger, Weberstraße 8, 52064 Aachen	Germany	0	0	0
0006	Gemeinschaftspraxis Dr. Maintz / M. Groschek, Mauerfeldchen 72, 52146 Würselen	Germany	0	0	0
0007	Universitätsklinikum Freiburg, Hugstetter Str. 55, 79106 Freiburg	Germany	0	0	0
0010	St. Antonius-Hospital, Dechant-Deckers-Straße 8, 52249 Eschweiler	Germany	0	0	0
0012	Universitätsklinikum Hamburg-Eppendorf, Martinistraße 52, 20246 Hamburg	Germany	0	0	0
0013	Kreiskliniken Altötting, Lehrkrankenhaus der LMU München, Vincenz-von-Paul-Str. 10, 84503 Altötting	Germany	0	0	0
0016	Charité Campus Virchow-Klinikum Universitätsmedizin Berlin, Augustenburger Platz 1, 13351 Berlin	Germany	0	0	0
0024	Praxis Dr. Vehling-Kaiser, Ländgasse 132-135, 84028 Landshut	Germany	0	0	0
0025	Krankenhaus Landshut Achdorf , Achdorferweg 3, 84036 Landshut	Germany	0	0	0
0027	Onco Studies - Onkologische Schwerpunktpraxis, Dr. J. Knoblich / PD Dr. Fischer / Dr. T. Nothhelfer, Röntgenstr. 10, 79539 Lörrach	Germany	0	0	0
0029	Praxis Dr. med. Beyer, Gastroenterologie, Medikamentöse Tumortherapie, Mühldorfer Str. 14, 84503 Altötting	Germany	0	0	0
0033	Klinikum Augsburg, Stenglinstr. 2, 86156 Augsburg	Germany	0	0	0
0034	St. Elisabeth-Krankenhaus Geilenkirchen gGmbH, Martin-Heyden-Straße 32, 52511 Geilenkirchen	Germany	0	0	0
0008	Krankenhaus der Barmherzigen Brüder St. Veit/Glan, Spitalgasse 26, A-9300 St. Veit / Glan	Austria	0	0	0
0009	Universitätsklinikum Innsbruck, Anichstr. 35, A-6020 Innsbruck	Austria	0	0	0
0021	Krankenhaus der Elisabethinen Linz , Fadingerstrasse 1, A-4020 Linz	Austria	0	0	0
0022	Krankenhaus der Barmherzigen Schwestern Linz, BHS Linz, Seilerstätte 4, A-4020 Linz	Austria	0	0	0
0026	SMZ-Ost Donauspital , Langobardenstraße 122, A – 1220 Wien	Austria	0	0	0
0030	LKH-Univ. Klinikum Graz Univ. Klinik für Chirurgie , Auenbruggerplatz 29, A-8036 Graz	Austria	0	0	0
0031	Universität Wien , Waehringer Guertel 18-20, A-1090 Wien	Austria	0	0	0

6.4 Interventions

6.4.1 Investigational Medicinal Products

Study medication utilized in this study was the FOLFOX chemotherapy consisting of Oxaliplatin, 5-Fluorouracil and Folinic acid, along with anti-EGFR antibody Cetuximab.

FOLFOX is given every two weeks and Cetuximab weekly. One cycle is defined as one dose of chemotherapy and Cetuximab on day of chemotherapy until the day before the next chemotherapy. 12 cycles in total were administered in both arms.
Prior to the first Cetuximab infusion, patients must have received premedication with an antihistamine and a corticosteroid. This premedication was administered prior to all subsequent infusions.
All compounds at day 1 (except Cetuximab) were repeated at day 15, day 29, etc. Cetuximab was repeated weekly at day 8, day 15, day 22, day 29 etc.

Methods of administration and dosage is described in 6.4.2 and 6.4.4.

6.4.2 Description of Investigational Medicinal Products

FOLFOX

Combination therapy with Oxaliplatin and infusional 5-FU/FA (FOLFOX) is the standard treatment in metastatic colorectal cancer.

Oxaliplatin

Oxaliplatin is DACH-platin.

Approval: Oxaliplatin is approved in first line therapy of colorectal cancer in combination with 5-FU/FA
Supply of Drug: Commercially available. The drug was purchased through the local pharmacy.
Preparation: After calculation of the 5-FU dose necessary for the individual patient, Oxaliplatin was given as 85 mg/m² infusion (2 h).
Typical toxicity: Peripheral neuropathy with hypesthesia and cold-induced neuropathy. Anaemia, neutropenia, thrombocytopenia, nausea/vomiting, mucositis, liver toxicity
Important interactions: none
Storage: The manufacturer's advice was followed for storage conditions (controlled room temperature (15° to 30° C)).

5-Fluorouracil (5-FU)

5-Fluorouracil is an antimetabolite.

Approval: Among other indications, 5-FU is approved in first-line therapy of colorectal cancer.
Supply of Drug: Commercially available. The drug was purchased through the local pharmacy.
Preparation: After calculation of the 5-FU dose necessary for the individual patient, 5-FU was given as 400 mg/m² i.v. bolus followed by 2400 - 3000 mg/m² continuous infusion (46 h) via a central line or via a port-a-cath attached to a portable pump.

Typical toxicity: Dose limiting toxicity is mucositis, stomatitis and diarrhoea. These side effects as well as marrow suppression (mainly leukopenia and less frequently thrombocytopenia) are dose dependent. Rare side effects are liver toxicity, lung toxicity (bronchial spasm and laryngeal oedema), neurotoxicity and cardiotoxicity. Skin toxicity such as hand-foot-syndrome is often described following continuous infusion schedules.

Important interactions: Allopurinol should not be given concurrently with 5-FU because it may result in reduced efficacy. Also prophylaxis for mucositis should not be performed with Allopurinol mouth washes.

Storage: The manufacturer advice was followed for storage conditions.

Folinic acid

Folinic acid is calcium folinate and was used as the d,l- form in this trial. It enhances the activity of 5-FU by stabilizing the bond between the active metabolite (5-FdUMP) and the enzyme thymidylate synthetase. It is therefore indicated for the treatment of subjects with carcinoma of the colon in combination with 5-FU.

Approval: Among other indications, 5-FU is approved in first line therapy of colorectal cancer.

Supply of Drug: The drug was purchased through the local pharmacy.

Preparation: After calculation of the individually applicable dose, 400 mg/m² Folinic acid was given as 2 h infusion always prior to 5-FU and diluted in isotonic saline. FA is administered at the same time as Irinotecan or Oxaliplatin, but separate lines were used.

Typical toxicity: Possible dose limiting toxicities are gastrointestinal disturbances and rarely allergic reactions.

Important interactions: Interactions with other medication that interfere with Folinic acid are possible (Allopurinol, Trimethroprim, Pyrimetamin).

Storage: The manufacturer advice was followed for storage conditions.

Cetuximab

The targeted therapy with Cetuximab (ERBITUX®, Merck Serono GmbH) is approved and available in over 90 countries worldwide [19]. Cetuximab is a targeted therapeutic agent, a chimeric IgG1 monoclonal antibody that specifically binds to the EGFR with high affinity, internalising the receptor and preventing the ligands EGF and TGF-α from interacting with the receptors, thus effectively blocking ligand-induced EGFR phosphorylation [20]. In addition, Cetuximab has been found to potentiate the effects of chemotherapy and radiotherapy in experimental systems [21, 22]. The dose of Cetuximab (initial dose 400 mg/m^2 and subsequent weekly doses of 250 mg/m^2) has been found to be generally safe and effective in several studies in major tumour types expressing the EGFR. These included colorectal cancer, squamous cell carcinoma of the head and neck, and non-small cell lung cancer. Cetuximab is given either in combination with chemotherapy and/or radiotherapy or as monotherapy. The main side effects of Cetuximab monotherapy are hypersensitivity and acne-like skin reactions.

Approval:

Erbitux (Cetuximab) is indicated for the treatment of patients with epidermal growth factor receptor (EGFR)-expressing, K-RAS wild-type metastatic colorectal cancer

- in combination with chemotherapy

- as a single agent in patients who have failed Oxaliplatin- and Irinotecan-based therapy and who are intolerant to Irinotecan.

Supply of Drug: Commercially available. The drug was purchased through the local pharmacy.
Typical toxicity: Skin reactions mainly present as acne-like rash. Hypomagnesemia and infusion-related reactions.
Storage: Cetuximab was stored under refrigeration at +2ºC to +8ºC without exposure to direct sunlight or heat.

Cetuximab is supplied as an infusion with a concentration of 5 mg/ml in single-use, ready-to-use vials.

Mode of Cetuximab administration:

1st dose:

400 mg/m² Cetuximab administered by i.v. infusion **over 120 minutes**, directly followed by chemotherapy. The maximum infusion rate must not exceed 10 mg/min.

2nd and all subsequent doses:

250 mg/m² Cetuximab administered by i.v. infusion **over 60 minutes**, directly followed by chemotherapy. The maximum infusion rate must not exceed 10 mg/min.

6.4.3 Method of Assigning Subjects to Investigational Medicinal Products / Randomization

After confirmation of resectability in the screening procedure, patients had to be randomized within 2 weeks. In both arms treatment started as soon as possible within 3 weeks after randomization.

Patients are screened to ensure that they meet the eligibility criteria and are enrolled by online registration. All patients, who fulfil all inclusion criteria and do not meet any exclusion criterion, will be randomized to either arm A or arm B.

Stratification factors for randomization are:

- Fong score (≤2 versus >2)
- Study centre
- Subgroup (>3 liver metastases or at least one metastasis ≥5 cm in diameter versus ≤3 liver metastases <5 cm in diameter).

6.4.4 Dose Selection

Cetuximab 400 mg/m²(2.0 h i.v.) as initial infusion in the first week, and
Cetuximab 250 mg/m² (1.0 h i.v.) for all subsequent weekly infusions; 1 h observation after the end of every Cetuximab infusion. In weeks with subsequent chemotherapy, FOLFOX infusion may be started immediately after Cetuximab application. The observation period may occur during chemotherapy.
Oxaliplatin 85 mg/m² (2.0 h i.v.)
Folinic acid (D,L) 400 mg/m² (2.0 h i.v.)

5-FU 400 mg/m² (bolus i.v.)
5-FU 2400 (up to 3000) mg/m² (46 h i.v.)
Oxaliplatin and folinic acid were given at the same time.

Initially 5-FU was given at a dose of 2,400 mg/m². Then the dose was increased to 3,000 mg/m² from cycle 6 if no toxicity ≥ grade 2 occurred. Skin-/nail toxicity and anaphylactoid reaction did not prevent dose increase.

Indicated doses are recommended manufacturers' doses.

Dose modifications

General remarks on dose modifications

The NCI Common Terminology Criteria for Adverse Events v4.0 (CTCAE) (Appendix 3 of the Protocol) were used for the grading of adverse events.

Doses of 5-fluorouracil and Oxaliplatin omitted for toxicity were never replaced or restored. Once the dose has been reduced for any type of toxicity, it was never increased at a later time point, excepting solely dose reductions of Oxaliplatin due to renal impairment. In the event that a single trial drug had to be discontinued (according to the dose modification instructions,) all other trial drugs were still continued according to protocol. If necessary, treatment cycles were delayed for toxicity for a maximum of 4 consecutive weeks.

Dose modifications and treatment alterations for Cetuximab

Patients with any Cetuximab-related grade 4 toxicity (graded according to the NCI-CTCAE version 4.0) were not retreated.

6.4.5 Selection and Timing of Dose for Each Patient

Each patient's dose was calculated according to the body surface. The calculated doses were administered unless therapy induced toxicity occurred. Then the dose was reduced as described in 6.4.4.
In arm A the calculated chemotherapy dose was administered 4-8 weeks after surgery when the patients recovered to ECOG performance status of 0 or 1 and then every two weeks for 12 cycles. The time point of infusion was not dependent on meals or time of day.
In Arm B the first cycle of the chemotherapy was administered within 3 weeks post randomization and then every two weeks for 6 cycles. The second part of the chemotherapy started 4-8 weeks after surgery when the patients recovered to ECOG performance status of 0 or 1 and then again every two weeks for 6 cycles. The time point of infusion was not dependent on meals or time of day.
In case of treatment induced toxicities doses were modified and/or infusions delayed as described in section 6.4.4.

6.4.6 Blinding

This was an open-label study where all enrolled patients in both arms received the same therapy with FOLFOX and Cetuximab. Thus blinding of the investigational medicinal products was not necessary.

6.4.7 Prior and Concomitant Therapy

Premedication

Before Cetuximab:

Prior to the first infusion, patients must have received premedication with an antihistamine (standard H1 blocker, intravenous or oral, at standard dosage) and a corticosteroid (at a dose equivalent to ≥ 8mg dexamethasone intravenous or oral). This premedication is recommended prior to all subsequent infusions.

Before Chemotherapy:

Adequate antiemetic medication was given, preferentially with 5HT3- antagonists and dexamethasone.

Prior randomization

No Oxaliplatin-based adjuvant chemotherapy within 1 year before randomization (EC 5) nor any prior chemotherapy for metastatic disease (EC 7) or treatment with EGFR antibodies (EC 8) were allowed.

Concomitant treatment

No additional investigational products, additional anti-tumour drugs or drugs interacting the EGF-receptor were allowed. Patients with additional radiotherapy were excluded from the study. Simultaneous local ablative therapy was allowed during tumour resection.

Hematopoietic growth factors (G-CSF) could be used to treat neutropenia, but should not be used prophylactically.

6.4.8 Compliance

Study drug was administered by medical study staff at study sites as all used substances were infusions. Due to this controlled way of drug administration no pill counting, patient diaries or measurement of blood drug levels were necessary.

6.5 Efficacy and Safety Variables

6.5.1 Efficacy and Safety Variable Measurements, and Flow Chart

The postoperative complication rate was assessed daily 30 days after surgery or until the discharge from the hospital in the surgery population. These daily examinations included ECG, blood count, biochemistry and coagulation parameters. Liver function was assessed on a daily basis up to day 7, thereafter weekly and at discharge from hospital.

The tumour assessment included chest x-ray or chest CT, 4 phase liver CT and CEA/Ca 19-9 measurement. In both arms chest x-ray and chest CT, 4 phase liver CT and CEA/Ca 19-9 measurement were performed 12 weeks after randomization. Then chest x-ray or chest CT, 4 phase liver CT or abdominal ultrasound and CEA/Ca 19-9 measurement were performed every 12 weeks after randomization. If during the study a lesion was observed on an X-ray or abdominal ultrasound that was suspicious of metastatic disease, a CT- or MRI-scan had to be performed to confirm. The evaluation of tumour response according RECIST must be based on the CT- or MRI-scan. For response-evaluation, the same investigational method must be used

throughout. In the perioperative arm B, 4 phase liver CT and CEA/Ca 19-9 were performed after 6 weeks.

Physical examination including blood pressure, heart ratio and temperature was performed except during the safety follow up at the baseline visit, before every cycle, before surgery and at the end of treatment (Table 2).

Histological evaluation of the liver after surgery assessed chemotherapy induced toxicity.

During the follow-up further assessment by abdominal ultrasound/CT liver, chest x-ray and CEA measurements for recurrence/new occurrence of colorectal cancer and survival were performed every 12 weeks until the end of the follow-up.

Adverse events and tolerability were assessed at each visit, at least prior every therapy cycle in a dialogue with patients. Reported events were then entered into the eCRF.

Table 2. Schedule of visits and assessments

Parameter	Pre-Screening Visit	Baseline Visit	Before every Cycle	Only Arm B: after 3 cycles	Before Surgery	After Surgery	Every 12 weeks until end of treatment	End of treatment cycle 12	Safety follow up 30 days (+/-2) after last study drug	FU*
Written informed consent	X									
Demographics and primary tumour diagnosis	X									
Physical examination including, blood pressure, heart ratio, temperature[6), 7)]		X	X		X			X	X	X
K-ras mutation analysis	X									
Previous and concomitant medication		X								
Randomization		X								
ECG[1), 7)]		X						X	X	
ECOG/ Karnofsky-Index, [7)]		X	X		X			X		
Blood count[2), 6), 7)]		X	X		X			X	X	
Biochemistry[3), 6), 7)]		X	X		X			X	X	
ß-hCG-test (for pre-menopausal females) [7)]		X	X (for Austria)							
Coagulation parameters[4), 6), 7)]		X	X		X			X	x	
Tumour assessment[5)] , [7)] (abdomen and chest,		X		X	X		X	X		X

Parameter	Pre-Screening Visit	Baseline Visit	Before every Cycle	Only Arm B: after 3 cycles	Before Surgery	After Surgery	Every 12 weeks until end of treatment	End of treatment cycle 12	Safety follow up 30 days (+/-2) after last study drug	FU*
CEA/CA-19-9)										
Adverse events		X	X			X		X	X	
Postoperative complications (Clavien Score) [6)]						X				
Concomitant medication		X	X					X		
Quality of life		X			X		X	X		X
Further anti-cancer treatment										X
Survival status										X
Concomitant treatment										X

* Follow-up visits every 12 weeks for the first 2 years after randomization and thereafter every 24 weeks until 5 years post-randomization. An additional safety follow-up visit at 30 (+/- 2) days after last study drug administration has to be done, if this time point is not covered by the scheduled follow-up visits.

1) In case of anomalies more ECGs during therapy

2) Haemoglobin, neutrophils, lymphocytes, monocytes, platelets

3) Na^{+}, K^{+}, Mg^{2+}, Ca^{2+}, ASAT, ALAT, GGT, alkaline phosphatase, urea, total bilirubin, creatinine, if necessary creatinine-clearance

4) INR, aPTT

5) only arm B: 4 phase liver CT and CEA/CA-19-9 after 3 cycles
in both arms chest x-ray or chest CT, 4 phase liver CT and CEA/Ca 19-9 after 12 weeks, then chest x-ray or chest CT, 4 phase liver CT or abdominal ultrasound and CEA/Ca 19-9 every 12 weeks. In case of a suspected metastasis a CT /MRI scan has to be done. The evaluation of tumour response according RECIST must be based on the CT- or MRI-scan. For response-evaluation, the same investigational method must be used throughout.
If due to any delay the time from the last CT to surgery is longer than 4 weeks, an additional CT of the liver will be done within 4 weeks prior to surgery to confirm resectability.

[6] During the first week after surgery, physical and laboratory examination must be assessed daily.
Complication score must be assessed daily until the 30th postoperative day or until the day of discharge from hospital.
[7] All examinations should be performed within 2 weeks before randomisation.

6.5.2 Appropriateness of Outcome Measures

No non-standard efficacy or safety measures were used, nor were there any surrogate markers as endpoints.

6.5.3 Primary Variable(s)

The primary variable is the post-operative complication rate (Clavien score > grade 1) up to the 30th postoperative day or the day of discharge from hospital (for definition of a post-operative complication see Appendix 3 of the protocol).
To avoid that the possible benefit of the perioperative treatment is overlooked in patients with higher tumour burden the median disease free survival was determined for the patient subgroup with >3 liver metastases or at least one metastasis ≥ 5 cm in diameter.
These variables allow determining whether one of the two approaches of the standard therapy of the colorectal liver metastases is superior.

6.5.4 Determination of Study Drug Serum Concentrations

No PK assessments were intended in this study. Thus no study drug serum concentrations were determined.

6.6 Data Quality Assurance

For every participating site initiation was performed at which the study personnel was trained. Study monitoring was undertaken by monitors appointed by ALCEDIS.
Due to the electronic documentation system checks for range and plausibility were performed during data entry. In line with ICH GCP guidelines, monitoring included verification of data entered in the eCRF against original patient records and querying the non-plausible data in the eCRF. Furthermore, manual verification by data management took place. The verification was performed by direct access to the original subject records, and the Sponsor guaranteed that patient confidentiality was respected at all times. Participation in this study was taken as agreement to permit direct source data verification.

6.7 Statistical Methods Planned in the Protocol and Determination of Sample Size

6.7.1 Statistical Analysis Plan

The statistical evaluation was performed under the responsibility of the CRO of this study (Alcedis GmbH). All statistical analysis were performed using the SAS and/or SPSS systems.

The post-operative complication rate (primary endpoint) in both treatment arms were compared using the two sided Cochran-Mantel-Haenszel (CMH) test stratified for Fong Score, tumour volume and Study Site at a two-sided significance level of 0.05.

<u>Hypotheses for the First Primary Endpoint:</u>

The null hypothesis is that the postoperative complication rate (≥ grade I according Dindo et.al.) is equal between the arm treated with perioperative therapy and the arm treated with adjuvant therapy.

The alternative hypothesis is that the postoperative complication rate differs between these two arms.

Hypotheses for the Second Primary Endpoint:

The null hypothesis is that there is no difference in the DFS time of both treatment arms in the subset of ITT patients with > 3 liver metastases or at least on metastasis ≥ 5 cm in diameter.
The alternative hypothesis is that the DFS time is prolonged in the treatment arm with perioperative therapy.

If the null hypotheses can be rejected in favour of Arm A, then the superiority of the adjuvant regimen in comparison to the perioperative regimen regarding post-operative complication rate has been confirmed.

In addition to the CMH test, exact 95% confidence intervals for the complication rates in each arm, and the common odds-ratio (plus associated 95% confidence intervals) will be calculated to assess the treatment difference between both arms. The Breslow-Day test will be used to assess the homogeneity of the odds ratio in the strata mentioned above.
Multiple logistic regression analysis will be used to further explore the impact of various demographic and disease characteristics on the post-operative complication rate.

The second primary endpoint (DFS time in the subgroup of patients with > 3 liver metastases or at least one metastasis ≥ 5 cm in diameter) will be calculated as time from randomization to the date of either progressive or recurrent disease and to the date of surgery if metastases are deemed not resectable, or death of any cause. For patients lost to follow-up, DFS time will be censored at the time the patient was last determined to be disease-free and alive.
DFS time will be presented by means of Kaplan-Meier curves and associated statistics i.e. median DFS time and two-sided 95% confidence intervals for the median. The hazard ratio (HR) for DFS and 95% confidence intervals for HR will be estimated using Cox proportional hazard models adjusted for the stratification factor Fong Score.

Cox proportional hazard models will be also used to investigate the impact of other possible confounding factors on DFS and to test the treatment difference in DFS adjusted for significant confounding factors.

Overall survival time will be calculated for each patient as time from randomization until death. For patients lost to follow-up, survival time will be censored at the time the patient was last determined to be alive.
Overall survival time will be analysed with the same methods specified for DFS time.

For the final statistical analysis a data cut-off was specified in the statistical analysis plan. If for a patient no disease recurrence or progression is reported prior to this clinical cut-off or the death date is beyond the above-mentioned time interval after last tumour assessment, time to progression/death is censored on the date of last tumour assessment or randomization (in case of no post-baseline tumour assessment).

All significance tests will be performed two-sided at a significance level of 0.05. Only the two null hypotheses will be tested sequentially in confirmatory manner considering the hierarchical order of the two hypotheses. If the first null hypothesis cannot be rejected, than the second null hypothesis can only be tested with an explorative manner.

The sample size of the study is not sufficient to establish equivalence between the two treatment arms. However, an equivalent efficacy of both treatment arms is also very unlikely, if no significant effect can be observed with respect to the second primary objective, but there is a statistically significant difference ($p < 0.05$) for DFS and / or OS) in the ITT population.
If no significant difference is detected, then the point estimations for DFS and OS will be used to assess, whether a similar efficacy in both treatment arms might be present.
Descriptive statistics will be used to summarize all further continuous and categorical outcome variables. The number of subjects (N), mean, standard deviation (SD), standard error of the mean (SEM), median, minimum, and maximum values will be provided for continuous variables. If appropriate, 95 % confidence intervals for the estimates of these variables will be presented. In general, the denominator for the percentage calculation will be based on the total number of subjects in the treatment arm and analysis population concerned, unless otherwise specified.

Demographic and baseline disease characteristics (e.g. age, height, weight, body mass index, race, blood pressure smoking status or ECOG performance score) as well as concomitant diseases and treatment will be summarized descriptively by treatment arm and overall (i.e. both treatment arms combined).

Assumptions of the key analyses will be explored and, if necessary, appropriate transformations or non-parametric analysis techniques will be used.

Missing values will not be replaced unless otherwise stated in the statistical analysis plan. Where appropriate the last available value for a variable will be summarized in addition to the summaries for the various time points. The calculation of absolute and relative change from baseline will be based on the number of subjects whose data is available at the specific study time.

To test the robustness of the results, sensitivity analyses will be performed.

A more detailed description of the analysis is presented in the statistical analysis plan.

6.7.2 Sample Size

In treatment Arm A (adjuvant regimen) a post-operative complication rate (grade > 1) of 15% is expected in comparison to a rate of 26.5% in patients receiving the perioperative regimen (treatment Arm B). In total 430 patients are necessary (2 x 215) to detect a reduction from 26.5% to 15% with 80% power at a two-sided significance level of 0.05 considering that in approximately 10% of the randomized patients no surgery will be performed.
If the perioperative regimen has an advantage with respect to efficacy, then it is expected that especially patients with a higher tumour burden will benefit from a preoperative FOLFOX plus Cetuximab treatment. This hypothesis was evaluated by comparing the disease free

survival time between both treatment arms in the subgroup of patients with > 3 liver metastases or at least one metastasis ≥ 5 cm in diameter. A two-sided log-rank test with an sample size of 2 x 86 patients and 158 target events will provide a power of 80% to detect an increase from 7.0 to 11.0 months for the perioperative chemotherapy arm in comparison to the postoperative chemotherapy arm at a significance level of 0.05 (Hazard Ratio = 0.636). It was furthermore assumed, that the enrolment period was 36 months, the total follow-up time 60 months and that the proportion of patients dropping out per months would be 0.25%.

6.8 Changes in the Conduct of the Study or Planned Analytical Methods

Neither study design, nor the statistical analysis plan was subject to changes. However, since the trial was stopped prematurely, only some selected data were descriptively analysed. After 36 months of recruitment only 24 patients could be randomized, which led to premature ending of the study. The 24 enrolled patients were treated and analysed as stated in the study protocol and the statistical analysis plan. Fisher's Exact Test was used for comparison of postoperative complication rate.

7 Study Population

7.1 Disposition of Study Patients

24 Patients were randomized, 11 in Arm A and 13 in Arm B.
In Arm A 8 patients underwent surgery, 7 patients completed 3 cycles, 5 patients completed 5 cycles, 4 patients completed 11 cycles, 3 completed 12, and 1 completed 13 cycles of chemotherapy.
In Arm B 12 patients started with the pre-operative part of the chemotherapy, 11 of which completed the pre-operative 6 cycles. 10 patients underwent surgery and 8 started and completed the post-operative part of the chemotherapy (cycles 6-12).

4 patients from Arm A and 1 from Arm B did not receive the allocated intervention, 2 out of these 5 patients due to withdrawal of the informed consent before start of treatment, 3 patients due to violation of the inclusion-/ exclusion-criteria (no colorectal metastases, urgent suspicion of breast cancer, primarily not resectable).
4 patients from arm A and 4 from arm B discontinued the treatment. 3 discontinuations were due to tumour progression, 3 due to the personal wish of the patient, 2 due to non-tolerable treatment-related toxicity (Listing 12 in section 13.2.5).

Study termination

11 patients (45.8%) were documented with premature study termination. 3 patients are known to have died (12.5%), 2 because of disease progression. There was no known autopsy performed. None of the patients was lost to follow-up and 4 patients withdrew their informed consent one of them after the end of treatment.

7.2 Recruitment

Recruitment period:	April 2011 – March 2014
End of the treatment phase:	November 2014
End of Follow Up:	QI 2015

During the three years of recruitment only 24 instead of 430 eligible patients could be enrolled into the study. The study was then prematurely stopped due to very low recruitment rate.

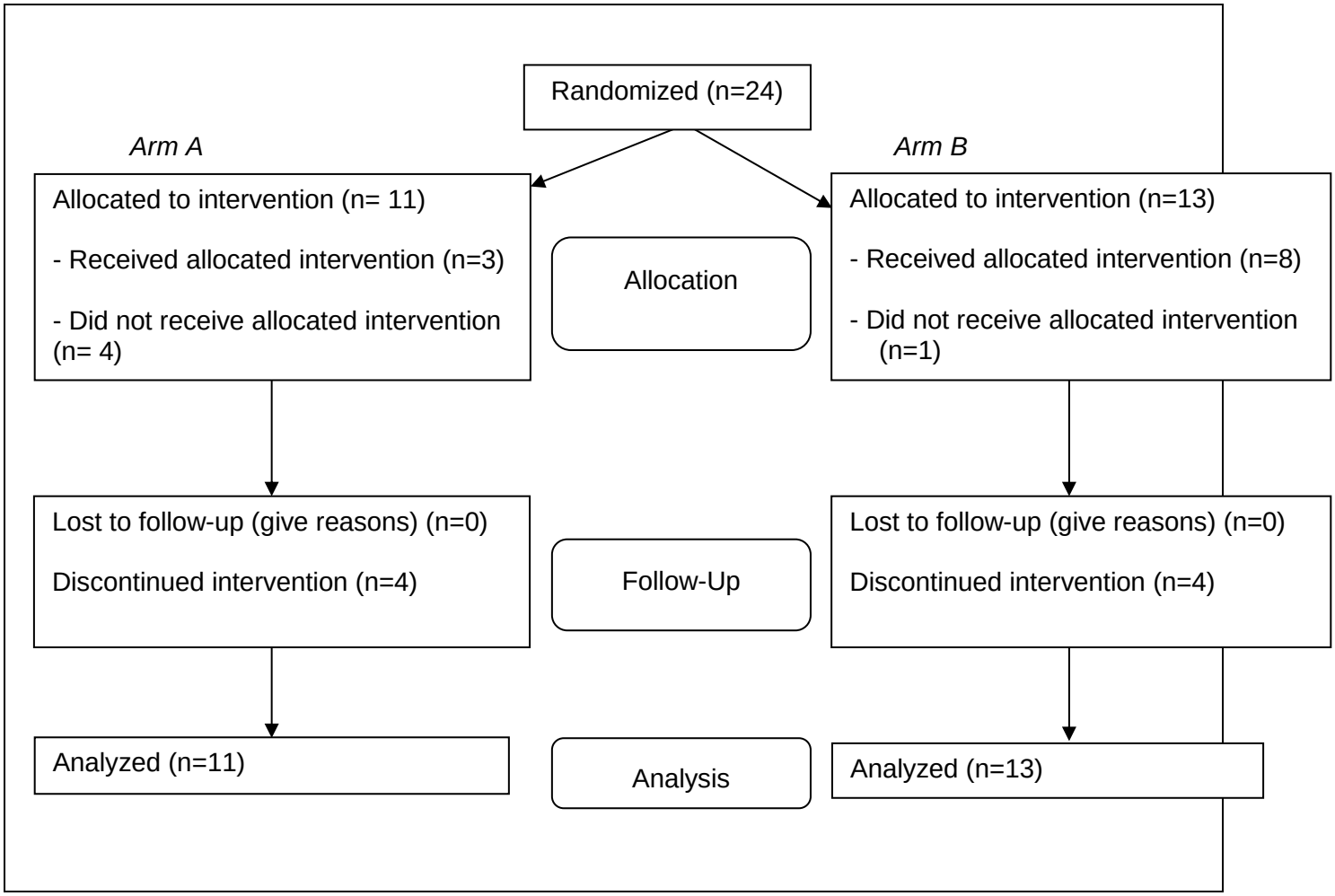


Figure 2. Flow chart from CONSORT for presentation of the disposition of trial subjects

8 Efficacy Evaluation

8.1 Data Sets Analysed

Intention-to-treat Population (ITT): The ITT population for the efficacy analysis consisted of subjects who were randomized. In the ITT analysis patients were analysed in the treatment arm as randomized.

Surgery Population (SP): The surgery population consisted of all subjects randomized, for whom the surgery for liver resection was started, even if the resection was not successful. All patients were analysed in the treatment arm as randomized.

Safety Population (SAF): With regard to the safety analysis, the evaluable analysis population consists of subjects who received at least one dose of the trial medication (Arm B) or for whom the surgery for liver resection was started (Arm A).

Table 3. Analysis data sets

Number of screened patients:		24
	ITT-Set	24
	SP Set	18
	SAF Set	20
Number of recruiting sites		14

The following aspects were documented:

- Patient characteristics (e.g., sex, age, oncology data)
- Therapy data (e.g. surgery, chemotherapy)
- End of therapy, follow-up and study termination
- Laboratory
- (Serious) Adverse events and quality of life

Since the study was stopped prematurely, all analyses were done for the ITT-set, except the safety analyses, which were done for the safety population and the primary endpoint analysis, which was done for the surgery population.
Results will be presented overall and according to the following treatment arms
Arm A: Surgery → 4-8 weeks rest → 24 weeks FOLFOX + Cetuximab
Arm B: 12 weeks FOLFOX + Cetuximab → 4 weeks rest → surgery → 4-8 weeks rest → 12 weeks FOLFOX + Cetuximab

The primary analysis for the post-operative complication rate was performed in all patients with surgery for liver resection (surgery population). An ITT analysis in all patients randomized was also planned for the primary endpoint. The primary analysis for the second primary endpoint disease-free survival time was performed in those patients of the ITT population who have > 3 liver metastases or at least one metastasis ≥ 5 cm in diameter.

8.2 Demographic and Other Baseline Characteristics

Baseline

The median age of patients in this study was 65.0 years. 8 women and 16 men were included in the study. The median height was 172.0 cm and median BSA 1.93 m². Regarding the inclusion criteria 2 patients violated criterion 4 and regarding the exclusion criteria criterion 9 was not fulfilled by 1 patient. Anyhow, the patients were randomized and therefore included in the analyses according to the ITT-Set definition. 7 patients fulfilled the translational research program 1 and 4 patients program 2. For all patients participation was possible.

Anamnesis

14 patients were documented with ‘Colon’ as their primary tumour localization, 9 with ‘Rectum’ and 1 with ‘Sigma’, (c)TNM stadium was summarized in Listing 1 (section 11.1). Information about the Fong score was calculated in Table 4. 5 patients had more than 3 metastases, 8 patients had a tumour larger than 5 cm in diameter.

Table 4. Individual tumour burden and Fong Score

Patient No.	Treatment Arm	Disease free interval	Number of tumor burden	Tumor size >= 5cm	Fong score
0002	Arm A	No	4	No	2
0083	Arm A	Yes	2	No	2
0085	Arm A	No	2	No	1
0086	Arm A	Yes	2	No	2
0087	Arm A	No	1	No	1
0089	Arm A	No	1	No	2
0090	Arm A	No	3	No	1
0161	Arm A	Yes	1	Yes	4
0163	Arm A	Yes	2	Yes	3
0166	Arm A	Yes	6	Yes	4
0402	Arm A	Unknown	2	No	Unknown
0001	Arm B	No	1	Yes	2
0003	Arm B	No	1	Yes	2
0081	Arm B	No	5	No	1
0082	Arm B	Yes	1	No	2
0084	Arm B	Yes	3	No	2
0088	Arm B	No	2	No	2
0162	Arm B	Yes	5	No	3
0164	Arm B	Yes	2	Yes	3
0165	Arm B	No	6	Yes	3
0167	Arm B	Yes	1	Yes	3
0241	Arm B	Yes	2	No	3
0242	Arm B	Yes	1	No	3
0401	Arm B	Unknown	1	No	Unknown

Table 5 and Table 6 summarize the Fong Score and the tumour burden in surgery population.

Table 5. Fong-Score in the surgery population

Fong score	Arm A		Arm B		Total	
	N	%	N	%	N	%
1	3	37.50	.	.	3	16.67
2	3	37.50	4	40.00	7	38.89
3	1	12.50	5	50.00	6	33.33
4	1	12.50	.	.	1	5.56
Unknown	.	.	1	10.00	1	5.56
Total	8	100.00	10	100.00	18	100.00

Table 6. Tumour burden in the surgery population

Tumor burden	Arm A		Arm B		Total	
	N	%	N	%	N	%
1	3	37.50	5	50.00	8	44.44
2	4	50.00	2	20.00	6	33.33
3	1	12.50	1	10.00	2	11.11
5	.	.	1	10.00	1	5.56
6	.	.	1	10.00	1	5.56
Total	8	100.00	10	100.00	18	100.00

For details on concomitant disease and pre-treatment see Listing 2 in section 11.1. 21 patients had previous surgeries, 4 had previous radiotherapy 3 of which also had previous chemotherapy for metastatic disease.
The most common previous relevant diseases were obesity, diabetes, hypertension and diseases of the GI tract.

Tumor assessment

Tumour location and size were determined by CT-Scan. At the beginning of the study, all patients had liver metastases and none had extrahepatic metastases. 10 patients had metachronous (41.7%) and 14 had synchronous metastases (58.3%). Regarding the best response, 10 patients (41.7%) had CR as their best response, 4 patients (16.7%) had PR and 2 patients (8.3%) had PD (Table 7).

Table 7. Tumour assessment- Best response

Best response	Arm A		Arm B		Total	
	N	%	N	%	N	%
CR	4	36.36	6	46.15	10	41.67
PR	1	9.09	3	23.08	4	16.67
PD	2	18.18	.	.	2	8.33
Missing	4	36.36	4	30.77	8	33.33
Total	11	100.00	13	100.00	24	100.00

8.3 Efficacy Analysis Results and Tabulations of Individual Patient Data

8.3.1 Efficacy Analysis

The primary trial endpoint was the postoperative complication rate (>grade I) measured by the Clavien score.
A total of 24 patients from 14 clinics in Germany were included in the analyses. 11 patients in arm A and 13 patients in arm B (Figure 2 in section 7.2). 18 patients underwent surgery. In the context of the primary endpoint, the postoperative complication rate > grade I occurred with 44.4 % with no differences between arm A and arm B (p=1.0, Fisher's Exact Test; Table 8). 4 patients from each arm reached this endpoint. Furthermore, a Cochran-Mantel-Haenszel test (Table 26 in section 11.2) was performed, but there was neither a strong association between treatment arm and postoperative complications after adjusting for Fong Score, nor after adjusting for tumour burden or for study site (stratification factors). In addition, no test of independence showed significance. In this context should be noted, that

there were strata with single observation, e.g. site. Moreover, a logistic regression (Tables 27 and 28, section 11.2) was performed, but no predictor could be found.
Of 8 patients falling under this primary endpoint two showed a Clavian score grade II complication rate and one patient showed grade IV (arm A). The other 5 patients were all classified as grade I (Fig. 3 and Listing 3 in section 11.2).

Table 8. Surgery population- Postoperative complication rate

Postoperative complication rate	N	Number of patients with Clavien score > grade 1	Rate	CI 95%
Arm A	8	4	50.00	15.70-84.30
Arm B	10	4	40.00	12.16-73.76
Total	18	8	44.44	21.53-69.24

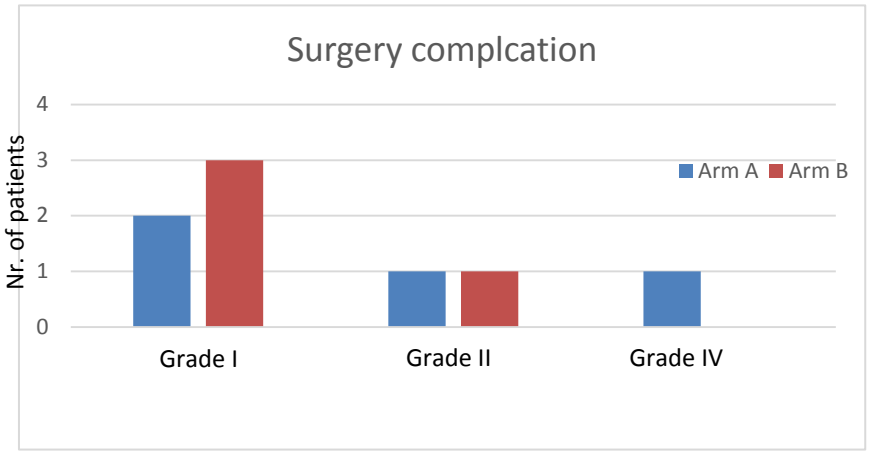


Figure 3. Postoperative complication rate according to Clavian score.

Further primary endpoint was disease free survival (DFS) in the trial population with high tumour burden, i. e. with >3 liver metastases or at least one metastasis larger than 5 cm in diameter. DFS is calculated as the time from randomization to the date of either progressive or recurrent disease, or death of any cause (whatever occurs earlier).
Median disease-free survival amounted to 21.0 months for patients with >3 liver metastases or at least one metastasis ≥5 cm in diameter. It should be noted, that only two events occurred, both in Arm A, and that there was no evidence for a difference between Arm A and Arm B (p=0.09, Log-Rank Test; Table 9).

Table 9. Disease- free survival for patients with > 3 liver metastases or at least one metastasis ≥5 cm in diameter [months]

Disease-free survival	N	Disease	Censored	Mean	Standard error	Median	CI 95%
Arm A	2	2	0	10.74	10.28	10.74	0.46- 21.02
Arm B	4	0	4	.	.	.	.- .
Total	6	2	4	17.59	4.42	21.02	0.46- .

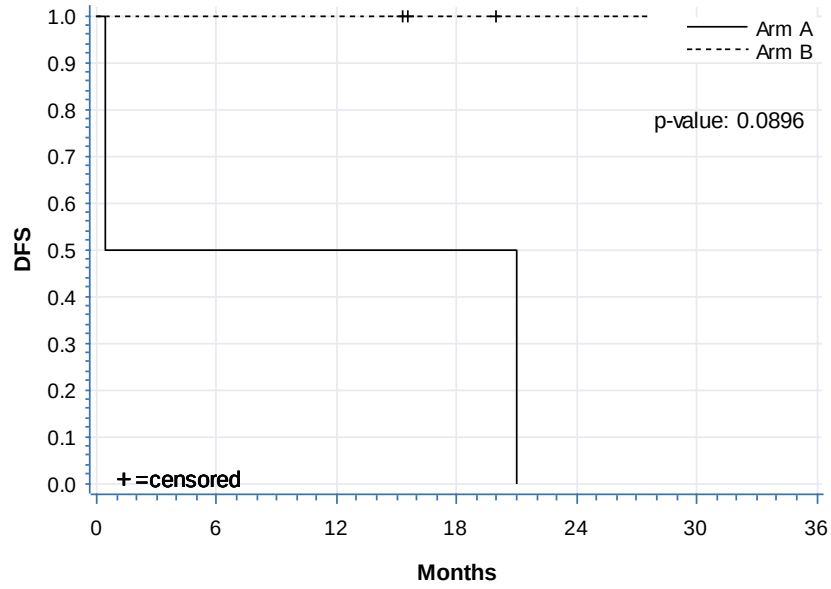


Figure 4: DFS for patients with > 3 liver metastases or at least one metastasis ≥5 cm in diameter [months]

Overall survival (OS), disease-free survival (DFS), surgery rate, resection rate, and R0 rate, safety and toxicity, quality of life, number of applied cycles, dose intensity, dose modifications, response rate after preoperative chemotherapy, and resected liver mass were secondary endpoints.

Overall survival time:

Mean overall survival amounted to 22.5 months with no differences between Arm A and Arm B (p=0.80, Log-Rank Test) and a Cox regression was performed (Table 10), showing no statistical significance between the 2 arms.

Table 10. Overall survival [months]

OS	N	Death	Censored	Mean	Standard error	Median	CI 95%
Arm A	10	1	9	21.02	.	.	21.02- .
Arm B	13	2	11	22.55	0.31	.	21.35- .
Total	23	3	20	22.50	0.23	.	21.35- .

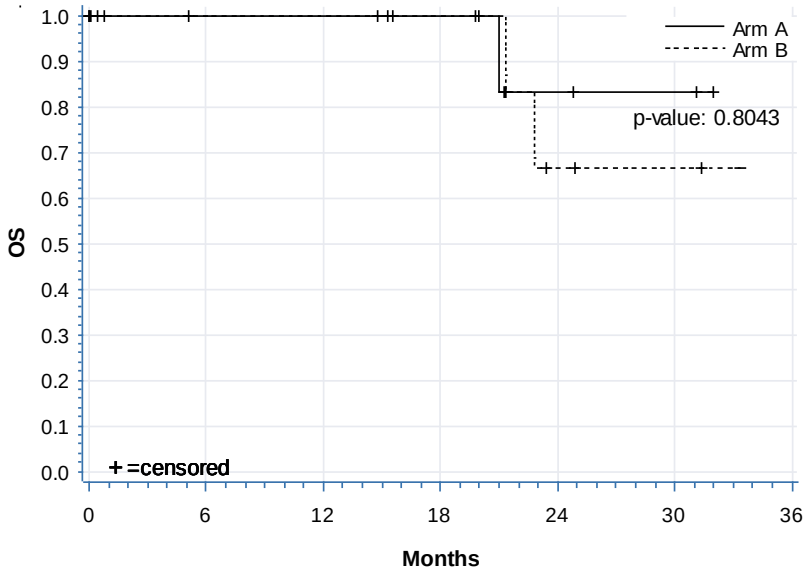


Figure 5: Overall Survival - OS [months]

Disease free survival:

The mean disease-free survival for all patients amounted to 16.98 months with no differences between Arm A and Arm B (p=0.75, Log-Rank Test; Table 11). In addition, for disease-free survival, hazard ratios for Fong score were calculated (HR=1.031 (Fong 1-2 vs. Fong 3-5); Table 30, section 11.2) and adjusted Cox regression was performed, but no predictor could be found (Table 31, section 11.2). The hazard ratio comparing the study arms was 2.0 (Arm A vs. Arm B).

Table 11: Disease- free survival [months]

Disease-free survival	N	Disease	Censored	Mean	Standard error	Median	CI 95%
Arm A	10	3	7	16.16	3.65	.	0.46- .
Arm B	13	3	10	12.62	1.26	.	6.12- .
Total	23	6	17	16.98	1.79	.	14.24- .

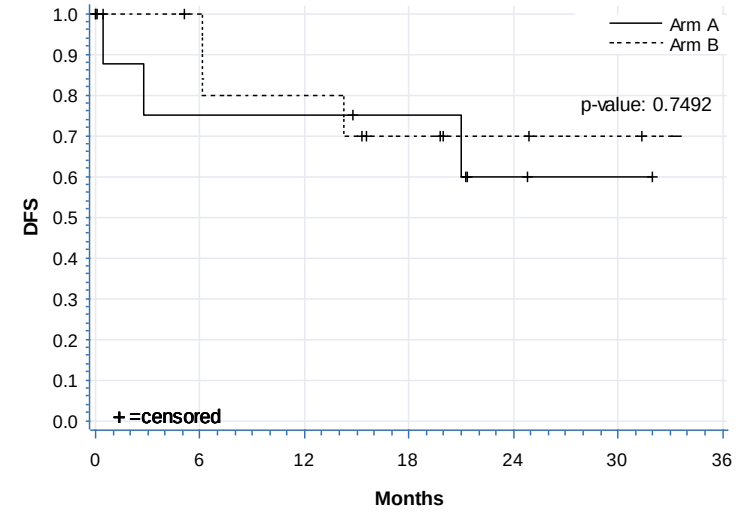


Figure 6: Disease Free Survival - DFS [months]

Surgery, resection and R0 rates:

18 of 24 patients underwent surgery, which corresponds to a resection rate of 75 %. 3 of 11 patients in Arm A were not operated although this was the first treatment in this arm (2 out of these 3 patients due to withdrawal of the informed consent, 1 patient due to violation of the inclusion-/ exclusion-criteria: urgent suspicion of breast cancer). The proportion of patients with R0 liver resection was 62.5 % (Table 12).
Individual patient data are depicted in Table 32 in section 11.2 together with belonging liver resection mass.

Table 12. Surgery, Resection and R0 rate of metastasis

Response rate		N	Number of patients with resection/R0	Rate	CI 95%	p-Value (Fisher's Exact Test)
Resection	Arm A	11	8	72.73	39.03-93.98	1.0
	Arm B	13	10	76.92	46.19-94.96	
	Total	24	18	75.00	53.29-90.23	
R0	Arm A	11	6	54.55	23.38-83.25	0.6752
	Arm B	13	9	69.23	38.57-90.91	
	Total	24	15	62.50	40.59-81.20	

Number of cycles, dose intensity, and dose modification applied:

19 patients received chemotherapy. Median number of cycles was 12, median of applied dose modifications of Cetuximab was 1 and of chemotherapy 2 (Table 13). Dose intensity of Cetuximab is given for each cycle in Table 33 (section 11.2). The median duration of treatment with FOLFOX + Cetuximab amounted to 173 weeks (Table 34, section 11.2).

Table 13. Patients with chemotherapy- Number of cycles and applied dose modifications

Number of...		N	Mean	STD	SEM	Median	Min	Max	NMiss	p-Value (Wilcoxon Two-Sample Test)
Cycles	Arm A	7	8.43	4.54	1.72	11.00	3.00	13.00	0	0.5515
	Arm B	12	9.58	3.80	1.10	12.00	1.00	12.00	0	
	Total	19	9.16	4.00	0.92	12.00	1.00	13.00	0	
Cetuximab- Applied dose modifications	Arm A	7	2.29	2.93	1.11	1.00	0.00	7.00	0	0.7239
	Arm B	12	2.33	2.67	0.77	1.00	0.00	9.00	0	
	Total	19	2.32	2.69	0.62	1.00	0.00	9.00	0	
Chemotherapy- Applied dose modifications	Arm A	7	3.57	3.05	1.15	4.00	0.00	8.00	0	0.3830
	Arm B	12	2.17	2.52	0.73	1.50	0.00	6.00	0	
	Total	19	2.68	2.73	0.63	2.00	0.00	8.00	0	

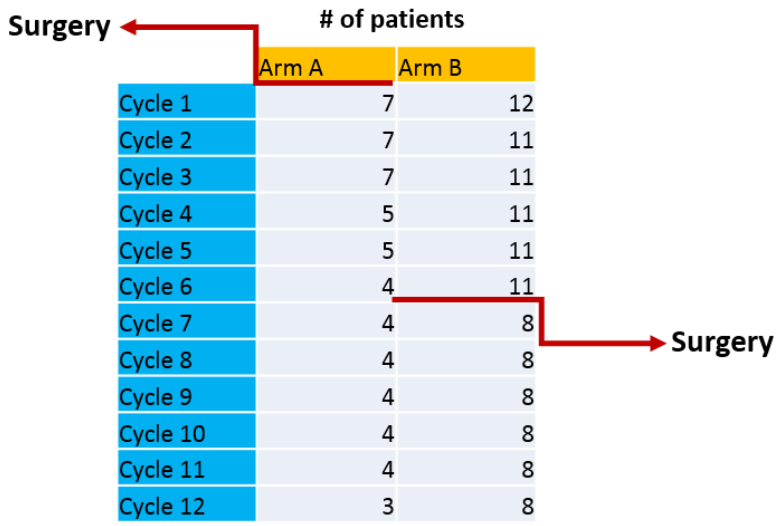


Figure 7. Number of patients receiving indicated number of chemotherapy cycle.

Quality of life using EORTC QLQ-C30 questionnaire + QLQ-LMC21:

Scores of EORTC QLQ-C30 and LMC21 were summarized in listings 9 through 11 in section 13.2.5.

The quality of life could not be evaluated as change over time because the quality of life was not assessed at each planned time point and each patient. Thus, there were too few overlapping questionnaires.

Response rate (RECIST V1.1) after preoperative chemotherapy:

The response rate after preoperative chemotherapy in arm B according to RECIST was 100% (Table 14).

Table 14. Response rate according to RECIST V1.1 after preoperative chemotherapy

Response rate	N	Number of patients with CR+PR as best response	Rate	CI 95%
Arm B	9	9	100.00	66.37-100.00

Resected liver mass:

Median resected liver mass was 261g (Table 15). Median resected liver mass in Arm A was 362 g while 229 g were resected in median in Arm B. However, of 18 resections only 9 resected liver masses were determined. The masses ranged from 43 g to 900 g (Table 32 section 11.2).

Table 15. Resected liver mass [g]

Resected liver weight	N	Mean	STD	SEM	Median	Min	Max	NMiss	p-Value (Wilcoxon Two-Sample Test)
Arm A	5	369.00	259.04	115.85	362.00	67.00	670.00	3	0.9025
Arm B	4	350.25	377.75	188.87	229.00	43.00	900.00	6	

Resected liver weight	N	Mean	STD	SEM	Median	Min	Max	NMiss	p-Value (Wilcoxon Two-Sample Test)
Patients with surgery	9	360.67	295.23	98.41	261.00	43.00	900.00	9	

Follow-up

No patients were lost to follow-up. For 4 out of 24 patients the follow-up was not performed. One of them discontinued treatment before follow up, one was subject to screening failure, one had no colorectal tumour and one was not available at the point of the first follow-up visit due to holiday (Listing 13, 13.2.5).

14 patients were under current treatment during the follow up period of which 12 have received chemotherapy and 2 underwent an additional surgery with a R0 resection. One of the patients receiving subsequent chemotherapy received parallel radiotherapy, 4 patients received parallel immunotherapy, and one underwent additional surgery with R0 resection immunotherapy (Listing 13, section 13.2.5).

3 of 24 patients relapsed during the follow-up period, 1 in arm A and 2 in Arm B, all of whom developed liver metastases (Listing 13, Appendix 13.2.5).

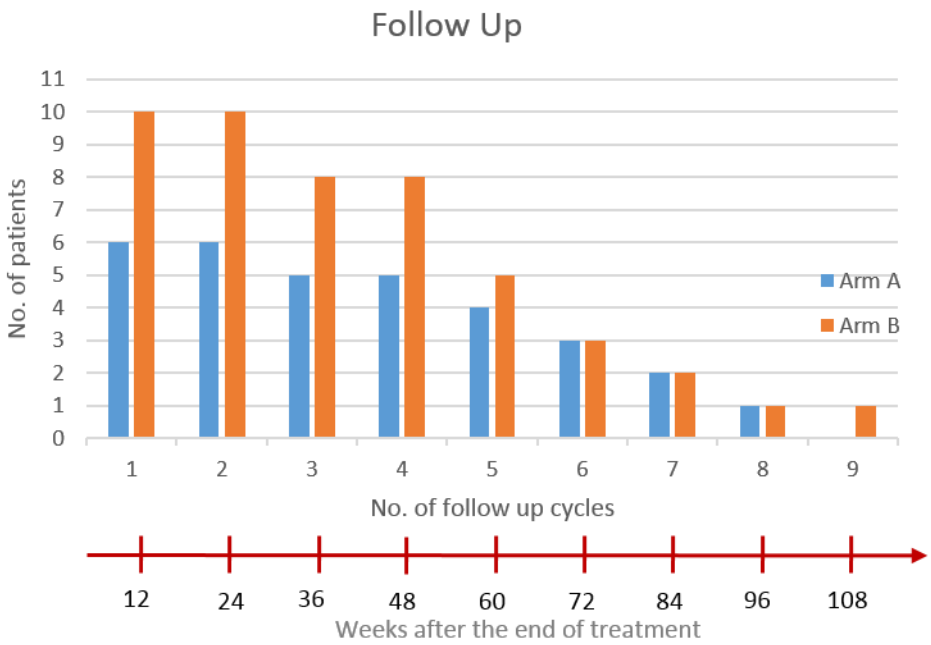


Figure 8. Follow up participation until the end of the study.

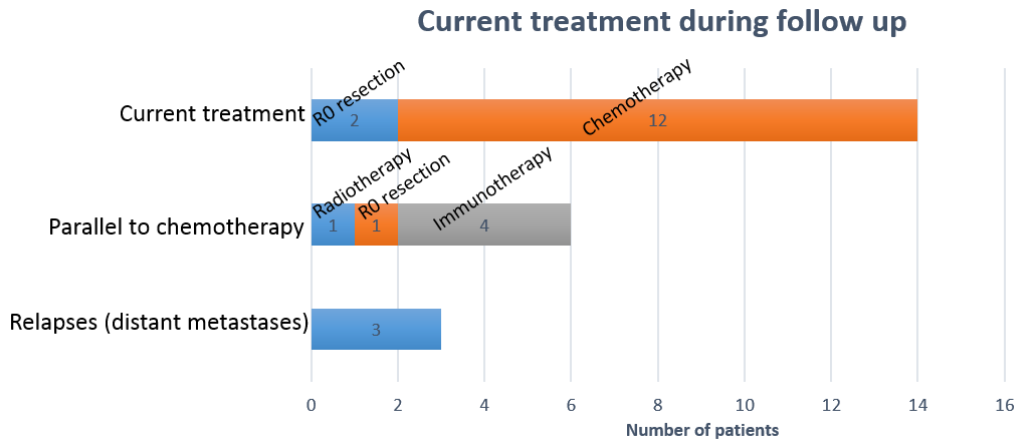


Figure 9. Current treatment during the follow up and the number of relapses.

8.3.2 Statistical Methods

Hypotheses for the First Primary Endpoint:
The null hypothesis is that the postoperative complication rate (≥ grade I according Dindo et.al.) is equal between the arm treated with perioperative therapy and the arm treated with adjuvant therapy.
The alternative hypothesis is that the postoperative complication rate differs between these two arms.

Hypotheses for the Second Primary Endpoint
The null hypothesis is that there is no difference in the DFS time of both treatment arms in the subset of ITT patients with > 3 liver metastases or at least on metastasis ≥ 5 cm in diameter.
The alternative hypothesis is that the DFS time is prolonged in the treatment arm with perioperative therapy.

Since the study was recruiting insufficiently, it was stopped prematurely. Therefore, only some selected data were descriptively analysed (e.g. safety). The other data are given in listings. For categorical variables, summary tabulations of the number and percentage within each category (with a category for missing data) of the parameter are presented. In general, the denominator for the percentage calculation will be presented by the total number of subjects in the treatment arm and analysis population concerned, unless otherwise specified. For continuous variables, the mean, median, standard deviation, standard error of the mean (SEM), minimum and maximum values are given as well as the number of missing values. If appropriate, 95% confidence intervals for the estimates of these variables will be presented.
The calculations of absolute and relative change from baseline are based on the number of subjects whose data was available at the specific study time.
All analyses, except the analysis of the primary endpoint, are explorative.
Randomization to the two arms was performed with the stratification factors Fong-Score (≤2, >2, unknown), metastases (>3 liver metastases or at least one metastasis ≥5 cm, ≤3 liver metastases <5 cm in diameter) and site. The block size was 4.

The two null hypotheses were tested by confirmatory statistics in hierarchical order, so that no alpha adjustment was necessary. This means, the second null hypothesis was only tested with a confirmatory claim if the first null hypothesis was rejected at a significance level of 0.05. This sequential rejecting testing procedure guaranteed a multiple type I error of 0.05. If the first null hypothesis could not be rejected, then the second null hypothesis was only tested in an explorative manner.
The null hypothesis for the first primary endpoint was that the postoperative complication rate was equal between the arm treated with perioperative therapy and the arm treated with adjuvant therapy. The alternative hypothesis was that the postoperative complication rate differs between these two arms.
The null hypothesis for the second primary endpoint was that there was no difference in the DFS of both treatment arms in the subset of ITT patients with > 3 liver metastases or at least one metastasis ≥ 5 cm in diameter. The alternative hypothesis was that the DFS was prolonged in the treatment arm with perioperative therapy.

8.3.3 Tabulation of Individual Data

Individual data on quality of life, current treatment during the follow-up and the status at the end of treatment are provided in the Appendix 13.2.6

8.3.4 Patient Profiles

n.a.

8.3.5 Efficacy Analysis Conclusion(s)

Considering primary and secondary endpoints no differences between the two arms could be observed. There were no significant differences between the postoperative and perioperative treatment regimen in the complication rate, DFS in patients with a high tumour burden and DFS in general, OS, R0 resection rates and quality of life, which were the efficacy variables.
Having the small sample size in mind (11 patients in Arm A and 13 in Arm B) no conclusion, however, can be drawn that the two treatments are equally efficient.

9 Safety Analysis

9.1 Extent of Exposure

Patients were exposed either to 12 postoperative cycles of chemotherapy with FOLFOX and Cetuximab (Arm A) or to 6 pre-operative and 6 postoperative cycles of the same treatment (Arm B). Single and total doses of the chemotherapy for the whole duration of 12 cycles are depicted for both arms in Tables 36 and 37 of the Statistical Report. Absolute doses for each administered substance were determined according to the body surface area of each individual patient.

9.2 Adverse Events

9.2.1 Brief Summary of Adverse Events

A total of 314 adverse events (AEs) occurred in 19 patients, who received chemotherapy in both arms (Listing 14, section 13.2.6). 90 AEs occurred in Arm A and 224 in Arm B. 6 of the 19 patients showed SAEs, 4 in Arm A and 2 in Arm B (Table 16).

The most common adverse event was ‘Rash acneiform’ (11.8 %, Table 17). Other common adverse events were nausea (6.69 %), decreased neutrophil count (6.05 %) and peripheral sensory neuropathy (6.05 %). Diarrhoea was accountable for 3.82 % of adverse events.
The maximum grade per patient is shown in Table 18. The outcome was mostly ‘recovered’ in 76.4% of the cases (Table 19). Only 1.59% of the events were previous diseases (Table 49 of the statistical report). Regarding the relation to study medication, 26.8% were related to Cetuximab, 49.0% to Oxaliplatin, 11.5% to Folinic acid and 45.2% to 5-FU (Table 20). In 15.0% of the cases an action was taken regarding the study medication. The actions are summarized in Table 21. In 2 cases (0.6%) the event was the reason for end of treatment (Table 53 of the statistical report).
1 adverse event was an intraoperative complication (Table 54 of the statistical report) of the kind ‘Hypertension’ (Table 55 of the statistical report), which was related to general anaesthesia (Table 57 of the statistical report). 8 events were postoperative complications (Table 58 of the statistical report), 2 were other surgical untoward events (Table 59 of the statistical report) and 8 were non-surgical untoward events (Table 60 of the statistical report).

9.2.2 Presentation of Adverse Events

All 19 patients who received chemotherapy showed adverse events, which occurred during the treatment. 6 patients even displayed SAEs.

Table 16: Adverse events- Number of patients with…

Number of patients...	Arm A		Arm B		Total	
	N	%	N	%	N	%
with AE	7	87.50	12	100.00	19	95.00
with SAE	4	50.00	2	16.67	6	30.00
with treatment-emergent AE	7	87.50	12	100.00	19	95.00
with drug-related TEAE	7	87.50	12	100.00	19	95.00
with serious TEAE	4	50.00	2	16.67	6	30.00
with AEs leading to study termination	1	12.50	.	.	1	5.00
Number of patients in SAF	8	100.00	12	100.00	20	100.00

Adverse events stated as most common in the „Fachinformationen“ were also most common in this study. The most common adverse events are marked red in the Table 17.

Table 17: Common adverse events according to NCI

Adverse event	Arm A		Arm B		Total	
	N	%	N	%	N	%
Abdominal pain	3	3.33	3	1.34	6	1.91
Alopecia	.	.	4	1.79	4	1.27
Anaemia	2	2.22	4	1.79	6	1.91
Blood and lymphatic system disorders - Other, specify	3	3.33	2	0.89	5	1.59
Constipation	1	1.11	3	1.34	4	1.27
Diarrhoea	7	7.78	5	2.23	12	3.82
Dry skin	.	.	5	2.23	5	1.59
Fatigue	.	.	9	4.02	9	2.87
Fever	4	4.44	1	0.45	5	1.59

Adverse event	Arm A		Arm B		Total	
	N	%	N	%	N	%
Hypertension	.	.	7	3.13	7	2.23
Mucositis oral	3	3.33	10	4.46	13	4.14
Nausea	3	3.33	18	8.04	21	6.69
Neutrophil count decreased	3	3.33	16	7.14	19	6.05
Pain	2	2.22	4	1.79	6	1.91
Palmar-plantar erythrodysesthesia syndrome	1	1.11	3	1.34	4	1.27
Paresthesia	2	2.22	4	1.79	6	1.91
Peripheral sensory neuropathy	1	1.11	18	8.04	19	6.05
Platelet count decreased	6	6.67	5	2.23	11	3.50
Pleural effusion	3	3.33	1	0.45	4	1.27
Rash acneiform	5	5.56	32	14.29	37	11.78
Skin and subcutaneous tissue disorders - Other, specify	1	1.11	7	3.13	8	2.55
Thromboembolic event	4	4.44	1	0.45	5	1.59
White blood cell decreased	.	.	15	6.70	15	4.78

9.2.3 Analysis of Adverse Events

For two patients adverse events were reason for treatment discontinuation.
Most adverse events were grade 1: 34 of 72 in Arm A (47.22 %) and 51 of 110 in Arm B (46.36 %). Of grade 2 events there were 22 in Arm A (30.55 %) and 40 in Arm B (36.36 %). 14 events (19.44 %) were classified as grade 3 in Arm A and 19 (17.27 %) such events were recorded in Arm B. While no grade 4 adverse events occurred in Arm B there were 2 grade 4 events in Arm A (2.78 %).

Table 18: Adverse events- Maximum NCI grade per patient

Adverse event- Maximum grade		Grade 1		Grade 2		Grade 3		Grade 4		Total	
		N	%	N	%	N	%	N	%	N	%
Arm A	Abdominal infection	.	.	.	.	1	7.14	.	.	1	1.39
	Abdominal pain	2	5.88	.	.	.	.	.	.	2	2.78
	Allergic reaction	.	.	2	9.09	.	.	.	.	2	2.78
	Anemia	.	.	2	9.09	.	.	.	.	2	2.78
	Aphonia	.	.	.	.	1	7.14	.	.	1	1.39
	Biliary anastomotic leak	1	2.94	.	.	.	.	.	.	1	1.39
	Blood and lymphatic system disorders - Other, specify	.	.	2	9.09	.	.	.	.	2	2.78
	Bone marrow hypocellular	1	2.94	.	.	.	.	.	.	1	1.39
	Bronchial infection	.	.	.	.	.	.	1	50.00	1	1.39
	Cardiac disorders - Other, specify	.	.	.	.	1	7.14	.	.	1	1.39
	Constipation	1	2.94	.	.	.	.	.	.	1	1.39
	Diarrhea	2	5.88	.	.	2	14.29	.	.	4	5.56
	Dyspnea	1	2.94	.	.	.	.	.	.	1	1.39
	Edema trunk	1	2.94	.	.	.	.	.	.	1	1.39
	Febrile neutropenia	.	.	.	.	1	7.14	.	.	1	1.39
	Fever	2	5.88	1	4.55	.	.	.	.	3	4.17
	Gastrointestinal disorders - Other, specify	2	5.88	.	.	1	7.14	.	.	3	4.17
	Gum infection	1	2.94	.	.	.	.	.	.	1	1.39
	Hallucinations	1	2.94	.	.	.	.	.	.	1	1.39
	Hepatobiliary disorders - Other, specify	1	2.94	.	.	.	.	.	.	1	1.39

	Adverse event- Maximum grade	Grade 1		Grade 2		Grade 3		Grade 4		Total	
		N	%	N	%	N	%	N	%	N	%
	Hypocalcemia	1	2.94	.	.	.	.	.	.	1	1.39
	Hypotension	1	2.94	.	.	.	.	.	.	1	1.39
	Hypoxia	.	.	.	.	.	.	1	50.00	1	1.39
	Infections and infestations - Other, specify	.	.	.	.	1	7.14	.	.	1	1.39
	Infusion related reaction	.	.	1	4.55	.	.	.	.	1	1.39
	Leukocytosis	.	.	.	.	1	7.14	.	.	1	1.39
	Mucositis oral	2	5.88	.	.	1	7.14	.	.	3	4.17
	Nausea	3	8.82	.	.	.	.	.	.	3	4.17
	Neoplasms benign, malignant and unspecified (incl cysts and polyps) - Other, specify	1	2.94	.	.	.	.	.	.	1	1.39
	Neutrophil count decreased	.	.	.	.	1	7.14	.	.	1	1.39
	Pain	.	.	2	9.09	.	.	.	.	2	2.78
	Palmar-plantar erythrodysesthesia syndrome	1	2.94	.	.	.	.	.	.	1	1.39
	Papulopustular rash	.	.	1	4.55	.	.	.	.	1	1.39
	Paresthesia	2	5.88	.	.	.	.	.	.	2	2.78
	Peripheral sensory neuropathy	1	2.94	.	.	.	.	.	.	1	1.39
	Platelet count decreased	1	2.94	2	9.09	.	.	.	.	3	4.17
	Pleural effusion	.	.	2	9.09	.	.	.	.	2	2.78
	Pneumothorax	.	.	1	4.55	.	.	.	.	1	1.39
	Rash acneiform	.	.	3	13.64	1	7.14	.	.	4	5.56
	Skin and subcutaneous tissue disorders - Other, specify	1	2.94	.	.	.	.	.	.	1	1.39
	Thromboembolic event	.	.	1	4.55	2	14.29	.	.	3	4.17
	Thrombotic thrombocytopenic purpura	2	5.88	.	.	.	.	.	.	2	2.78
	Vascular disorders - Other, specify	1	2.94	.	.	.	.	.	.	1	1.39
	Visceral arterial ischemia	.	.	1	4.55	.	.	.	.	1	1.39
	Vomiting	1	2.94	.	.	.	.	.	.	1	1.39
	Wound infection	.	.	1	4.55	.	.	.	.	1	1.39
	Total	34	100.00	22	100.00	14	100.00	2	100.00	72	100.00
Arm B	**Abdominal infection**	.	.	.	.	1	5.26	.	.	1	0.91
	Abdominal pain	3	5.88	.	.	.	.	.	.	3	2.73
	Alanine aminotransferase increased	1	1.96	.	.	.	.	.	.	1	0.91
	Alopecia	2	3.92	1	2.50	.	.	.	.	3	2.73
	Anemia	.	.	1	2.50	.	.	.	.	1	0.91
	Anorexia	1	1.96	.	.	.	.	.	.	1	0.91
	Aspartate aminotransferase increased	1	1.96	.	.	.	.	.	.	1	0.91
	Blood and lymphatic system disorders - Other, specify	1	1.96	1	2.50	.	.	.	.	2	1.82
	Blood bilirubin increased	1	1.96	.	.	.	.	.	.	1	0.91
	Breast infection	.	.	1	2.50	.	.	.	.	1	0.91
	Bruising	1	1.96	.	.	.	.	.	.	1	0.91
	Chest pain - cardiac	.	.	1	2.50	.	.	.	.	1	0.91
	Conjunctivitis	1	1.96	.	.	.	.	.	.	1	0.91
	Constipation	2	3.92	1	2.50	.	.	.	.	3	2.73
	Dehydration	1	1.96	.	.	.	.	.	.	1	0.91
	Delirium	.	.	.	.	1	5.26	.	.	1	0.91
	Diarrhea	3	5.88	1	2.50	1	5.26	.	.	5	4.55
	Dizziness	1	1.96	.	.	.	.	.	.	1	0.91
	Dry skin	1	1.96	1	2.50	.	.	.	.	2	1.82
	Dysgeusia	1	1.96	.	.	.	.	.	.	1	0.91
	Dyspnea	.	.	.	.	1	5.26	.	.	1	0.91

	Adverse event- Maximum grade	Grade 1		Grade 2		Grade 3		Grade 4		Total	
		N	%	N	%	N	%	N	%	N	%
	Fatigue	.	.	3	7.50	.	.	.	.	3	2.73
	Fever	1	1.96	.	.	.	.	.	.	1	0.91
	GGT increased	1	1.96	.	.	.	.	.	.	1	0.91
	General disorders and administration site conditions - Other, specify	.	.	1	2.50	.	.	.	.	1	0.91
	Gynecomastia	1	1.96	.	.	.	.	.	.	1	0.91
	Hematoma	.	.	1	2.50	.	.	.	.	1	0.91
	Hepatic hemorrhage	.	.	1	2.50	.	.	.	.	1	0.91
	Hepatobiliary disorders - Other, specify	.	.	1	2.50	.	.	.	.	1	0.91
	Hoarseness	1	1.96	.	.	.	.	.	.	1	0.91
	Hyperglycemia	.	.	.	.	1	5.26	.	.	1	0.91
	Hyperkalemia	.	.	1	2.50	.	.	.	.	1	0.91
	Hypertension	.	.	1	2.50	1	5.26	.	.	2	1.82
	Hypokalemia	1	1.96	.	.	.	.	.	.	1	0.91
	Infections and infestations - Other, specify	.	.	1	2.50	.	.	.	.	1	0.91
	Insomnia	1	1.96	.	.	.	.	.	.	1	0.91
	Investigations - Other, specify	.	.	1	2.50	1	5.26	.	.	2	1.82
	Lung infection	.	.	.	.	1	5.26	.	.	1	0.91
	Mucositis oral	1	1.96	4	10.00	.	.	.	.	5	4.55
	Nausea	5	9.80	1	2.50	.	.	.	.	6	5.45
	Nervous system disorders - Other, specify	.	.	1	2.50	.	.	.	.	1	0.91
	Neutrophil count decreased	.	.	1	2.50	2	10.53	.	.	3	2.73
	Pain	1	1.96	.	.	1	5.26	.	.	2	1.82
	Pain in extremity	1	1.96	.	.	.	.	.	.	1	0.91
	Palmar-plantar erythrodysesthesia syndrome	.	.	2	5.00	.	.	.	.	2	1.82
	Paresthesia	1	1.96	1	2.50	.	.	.	.	2	1.82
	Peripheral sensory neuropathy	2	3.92	.	.	2	10.53	.	.	4	3.64
	Platelet count decreased	3	5.88	.	.	.	.	.	.	3	2.73
	Pleural effusion	.	.	.	.	1	5.26	.	.	1	0.91
	Productive cough	1	1.96	.	.	.	.	.	.	1	0.91
	Prostatic obstruction	1	1.96	.	.	.	.	.	.	1	0.91
	Pruritus	.	.	1	2.50	.	.	.	.	1	0.91
	Rash acneiform	1	1.96	4	10.00	4	21.05	.	.	9	8.18
	Rash maculo-papular	.	.	1	2.50	.	.	.	.	1	0.91
	Rectal obstruction	1	1.96	.	.	.	.	.	.	1	0.91
	Seroma	1	1.96	.	.	.	.	.	.	1	0.91
	Skin and subcutaneous tissue disorders - Other, specify	2	3.92	2	5.00	.	.	.	.	4	3.64
	Thromboembolic event	.	.	.	.	1	5.26	.	.	1	0.91
	Vascular disorders - Other, specify	.	.	1	2.50	.	.	.	.	1	0.91
	Vertigo	1	1.96	.	.	.	.	.	.	1	0.91
	Vomiting	.	.	1	2.50	.	.	.	.	1	0.91
	White blood cell decreased	2	3.92	1	2.50	.	.	.	.	3	2.73
	Total	51	100.00	40	100.00	19	100.00	.	.	110	100.00
Total	**Abdominal infection**	.	.	.	.	2	6.06	.	.	2	1.10
	Abdominal pain	5	5.88	.	.	.	.	.	.	5	2.75
	Alanine aminotransferase increased	1	1.18	.	.	.	.	.	.	1	0.55
	Allergic reaction	.	.	2	3.23	.	.	.	.	2	1.10
	Alopecia	2	2.35	1	1.61	.	.	.	.	3	1.65
	Anemia	.	.	3	4.84	.	.	.	.	3	1.65

Adverse event- Maximum grade	Grade 1		Grade 2		Grade 3		Grade 4		Total	
	N	%	N	%	N	%	N	%	N	%
Anorexia	1	1.18	.	.	.	.	.	.	1	0.55
Aphonia	.	.	.	.	1	3.03	.	.	1	0.55
Aspartate aminotransferase increased	1	1.18	.	.	.	.	.	.	1	0.55
Biliary anastomotic leak	1	1.18	.	.	.	.	.	.	1	0.55
Blood and lymphatic system disorders - Other, specify	1	1.18	3	4.84	.	.	.	.	4	2.20
Blood bilirubin increased	1	1.18	.	.	.	.	.	.	1	0.55
Bone marrow hypocellular	1	1.18	.	.	.	.	.	.	1	0.55
Breast infection	.	.	1	1.61	.	.	.	.	1	0.55
Bronchial infection	.	.	.	.	.	.	1	50.00	1	0.55
Bruising	1	1.18	.	.	.	.	.	.	1	0.55
Cardiac disorders - Other, specify	.	.	.	.	1	3.03	.	.	1	0.55
Chest pain - cardiac	.	.	1	1.61	.	.	.	.	1	0.55
Conjunctivitis	1	1.18	.	.	.	.	.	.	1	0.55
Constipation	3	3.53	1	1.61	.	.	.	.	4	2.20
Dehydration	1	1.18	.	.	.	.	.	.	1	0.55
Delirium	.	.	.	.	1	3.03	.	.	1	0.55
Diarrhea	5	5.88	1	1.61	3	9.09	.	.	9	4.95
Dizziness	1	1.18	.	.	.	.	.	.	1	0.55
Dry skin	1	1.18	1	1.61	.	.	.	.	2	1.10
Dysgeusia	1	1.18	.	.	.	.	.	.	1	0.55
Dyspnea	1	1.18	.	.	1	3.03	.	.	2	1.10
Edema trunk	1	1.18	.	.	.	.	.	.	1	0.55
Fatigue	.	.	3	4.84	.	.	.	.	3	1.65
Febrile neutropenia	.	.	.	.	1	3.03	.	.	1	0.55
Fever	3	3.53	1	1.61	.	.	.	.	4	2.20
GGT increased	1	1.18	.	.	.	.	.	.	1	0.55
Gastrointestinal disorders - Other, specify	2	2.35	.	.	1	3.03	.	.	3	1.65
General disorders and administration site conditions - Other, specify	.	.	1	1.61	.	.	.	.	1	0.55
Gum infection	1	1.18	.	.	.	.	.	.	1	0.55
Gynecomastia	1	1.18	.	.	.	.	.	.	1	0.55
Hallucinations	1	1.18	.	.	.	.	.	.	1	0.55
Hematoma	.	.	1	1.61	.	.	.	.	1	0.55
Hepatic hemorrhage	.	.	1	1.61	.	.	.	.	1	0.55
Hepatobiliary disorders - Other, specify	1	1.18	1	1.61	.	.	.	.	2	1.10
Hoarseness	1	1.18	.	.	.	.	.	.	1	0.55
Hyperglycemia	.	.	.	.	1	3.03	.	.	1	0.55
Hyperkalemia	.	.	1	1.61	.	.	.	.	1	0.55
Hypertension	.	.	1	1.61	1	3.03	.	.	2	1.10
Hypocalcemia	1	1.18	.	.	.	.	.	.	1	0.55
Hypokalemia	1	1.18	.	.	.	.	.	.	1	0.55
Hypotension	1	1.18	.	.	.	.	.	.	1	0.55
Hypoxia	.	.	.	.	.	.	1	50.00	1	0.55
Infections and infestations - Other, specify	.	.	1	1.61	1	3.03	.	.	2	1.10
Infusion related reaction	.	.	1	1.61	.	.	.	.	1	0.55
Insomnia	1	1.18	.	.	.	.	.	.	1	0.55
Investigations - Other, specify	.	.	1	1.61	1	3.03	.	.	2	1.10
Leukocytosis	.	.	.	.	1	3.03	.	.	1	0.55
Lung infection	.	.	.	.	1	3.03	.	.	1	0.55
Mucositis oral	3	3.53	4	6.45	1	3.03	.	.	8	4.40

Adverse event- Maximum grade	Grade 1		Grade 2		Grade 3		Grade 4		Total	
	N	%	N	%	N	%	N	%	N	%
Nausea	8	9.41	1	1.61	.	.	.	.	9	4.95
Neoplasms benign, malignant and unspecified (incl cysts and polyps) - Other, specify	1	1.18	.	.	.	.	.	.	1	0.55
Nervous system disorders - Other, specify	.	.	1	1.61	.	.	.	.	1	0.55
Neutrophil count decreased	.	.	1	1.61	3	9.09	.	.	4	2.20
Pain	1	1.18	2	3.23	1	3.03	.	.	4	2.20
Pain in extremity	1	1.18	.	.	.	.	.	.	1	0.55
Palmar-plantar erythrodysesthesia syndrome	1	1.18	2	3.23	.	.	.	.	3	1.65
Papulopustular rash	.	.	1	1.61	.	.	.	.	1	0.55
Paresthesia	3	3.53	1	1.61	.	.	.	.	4	2.20
Peripheral sensory neuropathy	3	3.53	.	.	2	6.06	.	.	5	2.75
Platelet count decreased	4	4.71	2	3.23	.	.	.	.	6	3.30
Pleural effusion	.	.	2	3.23	1	3.03	.	.	3	1.65
Pneumothorax	.	.	1	1.61	.	.	.	.	1	0.55
Productive cough	1	1.18	.	.	.	.	.	.	1	0.55
Prostatic obstruction	1	1.18	.	.	.	.	.	.	1	0.55
Pruritus	.	.	1	1.61	.	.	.	.	1	0.55
Rash acneiform	1	1.18	7	11.29	5	15.15	.	.	13	7.14
Rash maculo-papular	.	.	1	1.61	.	.	.	.	1	0.55
Rectal obstruction	1	1.18	.	.	.	.	.	.	1	0.55
Seroma	1	1.18	.	.	.	.	.	.	1	0.55
Skin and subcutaneous tissue disorders - Other, specify	3	3.53	2	3.23	.	.	.	.	5	2.75
Thromboembolic event	.	.	1	1.61	3	9.09	.	.	4	2.20
Thrombotic thrombocytopenic purpura	2	2.35	.	.	.	.	.	.	2	1.10
Vascular disorders - Other, specify	1	1.18	1	1.61	.	.	.	.	2	1.10
Vertigo	1	1.18	.	.	.	.	.	.	1	0.55
Visceral arterial ischemia	.	.	1	1.61	.	.	.	.	1	0.55
Vomiting	1	1.18	1	1.61	.	.	.	.	2	1.10
White blood cell decreased	2	2.35	1	1.61	.	.	.	.	3	1.65
Wound infection	.	.	1	1.61	.	.	.	.	1	0.55
Total	85	100.00	62	100.00	33	100.00	2	100.00	182	100.00

Table 19. Adverse events outcome

Adverse event- Outcome	Arm A		Arm B		Total	
	N	%	N	%	N	%
Recovered (AE disappeared)	75	83.33	165	73.66	240	76.43
Recovered with sequelae	1	1.11	.	.	1	0.32
Not yet recovered	4	4.44	10	4.46	14	4.46
Change in toxicity garde/sensitivy or seriousness	3	3.33	31	13.84	34	10.83
Not yet recovered at end of study	1	1.11	16	7.14	17	5.41
Unknown at end of study	6	6.67	2	0.89	8	2.55
Total	90	100.00	224	100.00	314	100.00

Table 20. Adverse events- Causality related to study medication (multiple answers possible)

Adverse event- Causality	Arm A		Arm B		Total	
	N	%	N	%	N	%
Cetuximab	22	24.44	62	27.68	84	26.75

Adverse event- Causality	Arm A		Arm B		Total	
	N	%	N	%	N	%
Oxaliplatin	32	35.56	122	54.46	154	49.04
Folinic acid	17	18.89	19	8.48	36	11.46
5-FU	31	34.44	111	49.55	142	45.22
Number of AE	90	100.00	224	100.00	314	100.00

Table 21. Adverse events- Which action was taken concerning which study medication

Adverse event- Which action taken		Arm A		Arm B		Total	
		N	%	N	%	N	%
Cetuximab	**No change**	6	33.33	16	55.17	22	46.81
	Reduction of infusion rate	.	.	2	6.90	2	4.26
	Dose reduction	4	22.22	.	.	4	8.51
	Temporary discontinuation	3	16.67	6	20.69	9	19.15
	Permanent discontinuation	4	22.22	4	13.79	8	17.02
	Other	1	5.56	1	3.45	2	4.26
	Total	18	100.00	29	100.00	47	100.00
Oxaliplatin	**No change**	7	38.89	17	58.62	24	51.06
	Reduction of infusion rate	.	.	2	6.90	2	4.26
	Dose reduction	2	11.11	2	6.90	4	8.51
	Temporary discontinuation	2	11.11	7	24.14	9	19.15
	Permanent discontinuation	3	16.67	1	3.45	4	8.51
	Other	4	22.22	.	.	4	8.51
	Total	18	100.00	29	100.00	47	100.00
Folinic acid	**No change**	8	44.44	18	62.07	26	55.32
	Reduction of infusion rate	.	.	1	3.45	1	2.13
	Dose reduction	1	5.56	1	3.45	2	4.26
	Temporary discontinuation	2	11.11	6	20.69	8	17.02
	Permanent discontinuation	3	16.67	2	6.90	5	10.64
	Other	4	22.22	1	3.45	5	10.64
	Total	18	100.00	29	100.00	47	100.00
5-FU	**No change**	7	38.89	15	51.72	22	46.81
	Reduction of infusion rate	.	.	1	3.45	1	2.13
	Dose reduction	2	11.11	5	17.24	7	14.89
	Temporary discontinuation	2	11.11	6	20.69	8	17.02
	Permanent discontinuation	3	16.67	2	6.90	5	10.64
	Other	4	22.22	.	.	4	8.51
	Total	18	100.00	29	100.00	47	100.00

9.2.4 Listing of Adverse Events by Patient

All adverse events are listed in section 13.2.6.

9.3 Deaths, Other Serious Adverse Events, and Other Significant Adverse Events

9.3.1 Listing of Deaths, Other Serious Adverse Events, and Other Significant Adverse Events

9.3.1.1 Deaths

3 patients died (12.5%), 2 because of disease progression. There was no known autopsy performed.

Table 22. Overall survival [months]

OS	N	Death	Censored	Mean	Standard error	Median	CI 95%
Arm A	10	1	9	21.02	.	.	21.02- .
Arm B	13	2	11	22.55	0.31	.	21.35- .
Total	23	3	20	22.50	0.23	.	21.35- .

9.3.1.2 Other SAEs

Serious adverse events

Median weight was 92 kg (Table 23). The most common SAEs were ‘Diarrhoea’ and ‘Pulmonary embolism‘, each with a share of 15.4% (Table 24). Reason for seriousness was ‘Hospitalization’ in 12 cases and ‘life-threatening’ in 1 case (Table 25). 76.9% of the serious adverse events were recovered. Furthermore, 1 event was probably related to Cetuximab (7.7%) and 1 possibly, 1 probably and also 1 certainly (7.7%) related to chemotherapy (Table 65, statistical report). 5 events were moderate (38.5%), 7 were severe (53.9%) and 1 was life-threatening (7.7%, Table 66 in the statistical report). The cause of SAE was ‘basic disease’ in 2 cases and ‘other’ in 8 (Table 67, statistical report). In addition, the study therapy had not yet been started for 4 events (30.8%; Table 68, statistical report). The status of Cetuximab was not changed in 66.7% and of Fluorouracil in 55.6% (Table 69, statistical report).

Table 23. Serious adverse event- Weight [kg]

Weight	N	Mean	STD	SEM	Median	Min	Max	NMiss
Arm A	11	81.13	16.53	4.98	92.00	61.30	98.00	0
Arm B	2	101.00	2.83	2.00	101.00	99.00	103.00	0
Total	13	84.18	16.85	4.67	92.00	61.30	103.00	0

Table 24. Serious adverse events according to MedDRA-SOC and PT

Serious adverse events		Arm A		Arm B		Total	
		N	%	N	%	N	%
Gastrointestinal disorders	**Diarrhoea**	2	18.18	.	.	2	15.38
	Gastrointestinal disorder	1	9.09	.	.	1	7.69
	Intestinal ischaemia	1	9.09	.	.	1	7.69
General disorders and administration site conditions	**Pyrexia**	1	9.09	.	.	1	7.69
Infections and infestations	**Abdominal infection**	.	.	1	50.00	1	7.69
	Bronchopneumonia	1	9.09	.	.	1	7.69
Metabolism and nutrition disorders	**Hyperglycaemia**	.	.	1	50.00	1	7.69
Respiratory, thoracic and mediastinal disorders	**Hypoxia**	1	9.09	.	.	1	7.69

Serious adverse events		Arm A		Arm B		Total	
		N	%	N	%	N	%
	Pleural effusion	1	9.09	.	.	1	7.69
	Pulmonary embolism	2	18.18	.	.	2	15.38
Vascular disorders	Jugular vein thrombosis	1	9.09	.	.	1	7.69
Total		11	100.00	2	100.00	13	100.00

Table 25. Serious adverse event- Reason for seriousness (multiple answers possible)

Serious adverse events- Reason	Arm A		Arm B		Total	
	N	%	N	%	N	%
Life-threatening	1	9.09	.	.	1	7.69
In-patient hospitalization or prolongation	10	90.91	2	100.00	12	92.31
Number of SAE	11	100.00	2	100.00	13	100.00

9.3.1.3 Other Significant AEs

n.a.

9.4 Evaluation of Clinical Laboratory Tests

9.4.1 Listing of Laboratory Tests by Individual Patient and by Each Abnormal Laboratory Value

The laboratory tests were ideally performed at the pre-examination visit, prior to surgery, prior to every treatment cycle and at the end of treatment.
The complete lists of laboratory tests for each individual patient over time can be found in section 13.2.7 Listings 15-27 Statistical Report.

9.4.2 Evaluation of Each Laboratory Parameter

n.a.

9.4.2.1 Laboratory Values Over Time

n.a.

9.4.2.2 Individual Patient Changes

n.a.

9.4.2.3 Individual Clinically Significant Abnormalities

n.a.

9.5 Vital Signs, Physical Findings, and Other Observations Related to Safety

n.a.

9.6 Safety Analysis Conclusion(s)

No unexpected safety issues occurred during the trial. All adverse events occurred as expected and described in the “Fachinformation” of each substance.
71.34 % of all AEs appeared in the study arm B (224 of 314), however, there were 114 chemotherapy cycles in total performed in Arm B compared to 58 cycles in Arm A. Therefore it cannot be concluded that postoperative administration of chemotherapy is of better

tolerability. Also, 11 of 13 severe adverse events occurred in in Arm A. Furthermore, the sample size was too small to draw any conclusions.
Due to adverse events Cetuximab had to be permanently discontinued in 8 patients, Oxaliplatin in 4 and 5-FU and Folinic acid in 5, respectively. The distribution of patients with discontinued therapy was equal between the arms.
3 patients died during the trial, 2 of which due to the progression of disease and were not a SUSAR consequence.

10 Discussion and Overall Conclusions

Despite lack of guidelines perioperative chemotherapy treatment of resectable colorectal liver metastases has gained on popularity during the past years without any evidence of superiority for this approach towards the adjuvant treatment.
In this trial we wanted to compare the two approaches with regards to the post-operative complication rate (Clavian Score), DFS, OS, R0 resections rates with resected liver masses, quality of life and safety.
The study had to be terminated prematurely due to very slow recruitment. Instead of planned 430 patients only 24 could be enrolled during the 3-years-recruitment period.
All 24 patients were recruited in Germany. 11 Patients were allocated to Arm A (adjuvant regimen) and 13 to Arm B (peri-operative treatment). Due to small sample size no significant results could be obtained.

In context of baseline data, median age amounted to 65.0 years, which is expected as colorectal cancer rarely occurs under the age of 40 years. 8 women and 16 men were included in the study, which mirrors, despite the small sample size, the trend of higher incidence in man than in women. Median height was 172.0 cm and median BSA 1.93 m^2. Regarding the inclusion criteria, 2 patients violated criterion and regarding the exclusion criteria, criterion 9 was not fulfilled by 1 patient. Anyhow, the patients were randomized and therefore included in the analyses according to the ITT-Set definition.

14 patients were documented with ‘Colon’ as their primary tumour localization, 9 with ‘Rectum’, 1 with ‘Sigma’ and all patients were diagnosed with ‘wild type K-RAS, no mutation’.

At the beginning of the study, all patients had liver metastases and none had extrahepatic metastases. Furthermore, 10 patients had metachronous (41.7%) and 14 patients had synchronous metastases (58.3%).

There was no difference between arms either in primary, or in secondary endpoint. In context of the primary endpoint, the postoperative complication rate was 44.4% with no differences between Arm A and Arm B. Most of the complication rates were Grade I (Clavien Score). Only 2 were Grade II (requiring pharmacological treatment with drugs other than such allowed for grade I complications) and one Grade IV (Life-threatening complication including CNS complications, requiring IC/ICU management). It must be said, that the two patients with Grade II also had a Fong Score of 2. Further, the treatment of both these patients had to be disrupted. For one patient the reason for discontinuation was non-tolerable treatment-related toxicity and for the other patient the reason was tumour progression. Patients were from both arms. The patient with Grade IV belonged to Arm A and suffered in the past from

hepatitis A and several other relevant dieses like diverse allergies and had already a surgery and radiotherapy as treatment. Patient's questionnaires also indicate a suboptimal condition of the patient, which may have led to complications mentioned, although ECOG performance status was 0 until the 4th cycle when it jumped to 4 but returned to 0 again at the 5th cycle. Nevertheless, an R0 resection was performed. The treatment of the patient was discontinued after cycle 5 due to intolerable treatment related toxicities.

Median disease-free survival amounted to 21.0 months for patients with >3 liver metastases or at least one metastasis ≥5 cm in diameter. It should be noted, that only two events occurred, both in Arm A, and that there was no evidence for a difference between Arm A and Arm B (p=0.09, Log-Rank Test). It would have been relevant to see whether the population with a high tumour burden indeed benefited from the perioperative treatment in terms of DFS.

Regarding the secondary endpoints, mean disease-free survival for all patients amounted to 17 months with no differences between Arm A and Arm B (p=0.75, Log-Rank Test). In addition, for disease-free survival, hazard ratios for Fong score were calculated (HR=1.031 (Fong 1-2 vs. Fong 3-5)) and adjusted Cox regression was performed, but no predictor could be found. The hazard ratio comparing the study arms was 2.0 (Arm A vs. Arm B).
Further on, mean overall survival amounted to 22.5 months with no differences between Arm A and Arm B (p=0.80, Log-Rank Test) and a Cox regression was performed, again with no findings. 22.5 months are rather short compared to the literature value of 3.6 years (43.2 months, [23]. Again, due to the small sample size the result in this trial can only be regarded as arbitrary.

18 of 24 patient underwent surgery (75 %) and 62.5 % had a R0 resection. Also in this respect there was no difference between arms.
Median resected liver mass was 261g, with somewhat larger median in the postoperative Arm A (362 g) than in the perioperative Arm B (229 g), which could be due to the downsizing effect of the chemotherapy but could not be confirmed with significance even though the response rate according to RECIST after preoperative treatment part in arm B was 100 %. Furthermore, the largest resection of 900 g tumour tissue occurred in Arm B.

19 patients received chemotherapy. Median number of cycles was 12, median of applied dose modification of Cetuximab was 1 and of chemotherapy 2. The median duration of treatment with FOLFOX + Cetuximab amounted to 173 weeks.

In context of the safety analysis, a total of 314 adverse events occurred in 19 patients, 6 patients showed SAEs. The most common adverse event was 'Rash acneiform' (11.8%), which is also the most frequent adverse event of Cetuximab according to "Fachinformation". The outcome of all adverse events was mostly 'recovered', 76.4% of the cases, and only 1.59% of the events were previous diseases. Regarding the relation to study medication, 26.8% were related to Cetuximab, 49.0% to Oxaliplatin, 11.5% to Folinic acid and 45.2% to 5-FU. In 15% of the cases, an action was taken regarding the study medication. Moreover, in 2 cases (0.6%) the event was the reason for end of treatment, 1 adverse event was an intraoperative complication of the kind 'Hypertension', which was related to general anaesthesia and 8 events were postoperative complications, together 2 surgical untoward events and 8 non-surgical untoward events. In addition to the adverse events, 13 serious adverse events were documented in 6 patients, mostly 'Diarrhoea' or 'Pulmonary embolism',

each with a share of 15.4%. Reasons for seriousness were ‘Hospitalization’ in 12 cases and ‘life-threatening’ in 1 case. Moreover, 76.9% of the serious adverse events were recovered, 1 event was probably related to Cetuximab (7.7%) and each 1 event was possibly, probably or certainly related to chemotherapy. Further on, 5 events were moderate (38.5%), 7 were severe (53.9%) and 1 was life-threatening (7.7%). The cause of SAE was ‘basic disease’ in 2 cases or other causes. Finally, the study therapy had not yet been started for 4 events (30.8%) and the status of Cetuximab was not changed in 66.7% of the cases and the status of Fluorouracil was not changed in 55.6% of the cases.
In summary, no unexpected safety issues have occurred.

11 patients (45.8%) were documented with premature study termination and 3 patients were known to have died (12.5%), 2 because of disease progression. There was no known autopsy performed. In addition, none of the patients was lost to follow-up and 4 patients withdrew their informed consent.

No significant conclusions can be drawn from this trial as there was no difference in any of the study variables between the two arms.
Before the start of the Panter study only one study tried to assess the benefit of the perioperative treatment for resectable liver metastases compared to surgery alone (EORTC trial by Nordlinger et al. [17]) but neither this study rendered significant results. There was no difference between the arms.

But what could be the benefit of the perioperative treatment of resectable liver metastases?
In case of non-resectable liver metastases the neoadjuvant treatment was shown to successfully deem 12.5 % of the metastases resectable [15] enabling surgery and thus the best opportunity for survival.
Direct surgery treatment of resectable hepatic metastases not only prevents dissemination of the disease from the liver to other sites but also has shown the best overall survival results [24]. The postoperative chemotherapy with novel combinations like FOLFOX supported by immunotherapy are promising in prolonging the time until the timer of disease recurrence [25, 26]. Pre-operative chemotherapy could downsize the tumour burden but on the other hand, it could lead to more post-operative complications. Unfortunately, we were not able to clarify this dilemma in our study. A recent study by Primrose et al [27] surprisingly indicated that addition of Cetuximab to the perioperative chemotherapy treatment even reduces the progression free survival. In this trial 128 patients with resectable colorectal metastases were randomized to be perioperatively treated with chemotherapy alone (Oxaliplatin 85 mg/m2 intravenously over 2 h and fluorouracil bolus 400 mg/m2 intravenously over 5 min, followed by a 46 h infusion of Fluorouracil 2400 mg/m2 repeated every 2 weeks (regimen one) or Oxaliplatin 130 mg/m2 intravenously over 2 h and oral Capecitabine 1000 mg/m2 twice daily on days 1–14 repeated every 3 weeks (regimen two)) or with perioperative chemotherapy with addition of Cetuximab.
With an overall median follow-up of 20.7 months (95% CI 17・9–25.6) and 123 (58%) of 212 required events observed, progression-free survival was significantly shorter in the chemotherapy plus Cetuximab group than in the chemotherapy alone group (14.1 months [95% CI 11.8–15.9] *vs* 20.5 months [95% CI 16.8–26.7], hazard ratio 1.48, 95% CI 1.04–2.12, p=0.030).
However, this study initiated a vivid controversy due to suspected unreliability of the data [28, 29].

At present, there is a number of studies started or ongoing to elaborate the benefit of the perioperative chemotherapy treatment with or without immunotherapy for the patients with colorectal liver metastases (e.g. Combination Chemotherapy With or Without Cetuximab Before and After Surgery in Treating Patients With Resectable Liver Metastases Caused By Colorectal Cancer (NCT00482222), Compare FOFLOX4 in Preoperative and Postoperative and Postoperative in Resectable Liver Metastasis Colorectal Cancer (MCC) (NCT01035385), Perioperative vs Postoperative Chemotherapy + Bevacizumab in Colorectal Cancer, Liver Mets (NCT01632722) examples). None of these studies have delivered results yet, though. Interestingly, not few studies are struggling with the low recruitment rate, which was the reason for termination for some studies (e.g. Combination Chemotherapy Before or After Surgery in Treating Patients With Colorectal Cancer With Liver Metastases That Could Be Removed By Surgery. NCT01189227).

11 Tables, Graphs, and Lists Cited but not Included in the Text

11.1 Demographic Data

Listing 1: Primary tumor and stadium TNM classification

Patient No.	Treatment Arm	Localization of primary tumor	T stadium	N stadium	M stadium	cT stadium	cN stadium	cM stadium	Histology
0002	Arm A	Colon	T3	N1b	M1				Adenocarcinoma (tubular, azinar, papillary)
0083	Arm A	Colon	T3	N0	M0				Adenocarcinoma (tubular, azinar, papillary)
0085	Arm A	Rectum	T3	N0	MX				Adenocarcinoma (tubular, azinar, papillary)
0086	Arm A	Rectum	T3	N0	M1				Adenocarcinoma (tubular, azinar, papillary)
0087	Arm A	Rectum	T1	N0	MX				Adenocarcinoma (tubular, azinar, papillary)
0089	Arm A	Colon	T3	N1b	M1				Adenocarcinoma (tubular, azinar, papillary)
0090	Arm A	Rectum	T3	N0	M0				Adenocarcinoma (tubular, azinar, papillary)
0161	Arm A	Colon	T4a	N1b	M1				Adenocarcinoma (tubular, azinar, papillary)
0163	Arm A	Rectum	T1	N0	M1				Adenocarcinoma (tubular, azinar, papillary)
0166	Arm A	Rectum	T3	N2a	M1				Adenocarcinoma (tubular, azinar, papillary)
0402	Arm A	Other- sigma	T3	N2a	M1				Adenocarcinoma (tubular, azinar, papillary)
0001	Arm B	Colon				Tis	N0	M1	Adenocarcinoma (tubular, azinar, papillary)
0003	Arm B	Rectum	T2	N0	M0				Adenocarcinoma (tubular, azinar, papillary)
0081	Arm B	Colon				T3	N0	M1	Adenocarcinoma (tubular, azinar, papillary)
0082	Arm B	Colon	T4	N0	M1				Adenocarcinoma (tubular, azinar, papillary)
0084	Arm B	Colon	T3	N0	M1				Adenocarcinoma (tubular, azinar, papillary)
0088	Arm B	Colon	T4b	N2b	M1				Adenocarcinoma (tubular, azinar, papillary)
0162	Arm B	Colon	T3	N1a	M1				Adenocarcinoma (tubular, azinar, papillary)
0164	Arm B	Colon	T3	N0	M0				Adenocarcinoma (tubular, azinar, papillary)
0165	Arm B	Rectum	T3	N1a	M1				Adenocarcinoma (tubular, azinar, papillary)
0167	Arm B	Colon	T3	N0	MX				Adenocarcinoma (tubular, azinar, papillary)
0241	Arm B	Rectum	T3	N2b	M0				Adenocarcinoma (tubular, azinar, papillary)
0242	Arm B	Colon	T3	N1b	M1				Adenocarcinoma (tubular, azinar, papillary)
0401	Arm B	Colon	T3	N1a	M0				Adenocarcinoma (tubular, azinar, papillary)

Listing 2: Previous treatments and relevant diseases

Patient No.	Treatment Arm	Surgery	Radiotherapy	Adjuvant chemotherapy	Chemotherapy for metastatic disease	Any previous relevant diseases	Previous relevant diseases
0002	Arm A	Yes	No	No	No	No	
0083	Arm A	Yes	No	No	No	No	
0085	Arm A	Yes	Yes	Yes	No	Yes	Hepatitis A without hepatic coma ; Allergic rhinitis due to pollen ; Predominantly allergic asthma ; Bilateral inguinal hernia, without obstruction or gangrene ; Allergic urticaria ; Low back pain
0086	Arm A	No	No	No	No	Yes	Non-insulin-dependent diabetes mellitus: With renal complications ; Other obesity ; Essential (primary) hypertension ; Other psoriasis ; Arthropathic psoriasis ; Cyst of kidney, acquired
0087	Arm A	Yes	Yes	Yes	No	Yes	Disorders of acoustic nerve ; Pulmonary embolism without mention of acute cor pulmonale ; Phlebitis and thrombophlebitis of femoral vein
0089	Arm A	Yes	No	No	No	No	
0090	Arm A	Yes	No	No	No	Yes	Essential (primary) hypertension
0161	Arm A	Yes	No	No	No	No	
0163	Arm A	Yes	Yes	No	No	No	
0166	Arm A	Yes	No	No	No	Yes	Essential (primary) hypertension ; Chronic ischaemic heart disease, unspecified ; Diverticular disease of large intestine without perforation or abscess ; Post-traumatic wound infection, not elsewhere classified ; Acquired absence of genital organ(s)
0402	Arm A	Yes	No	No	No	No	
0001	Arm B	No	No	No	No	No	
0003	Arm B	Yes	No	No	No	Yes	Obesity, unspecified ; Essential (primary) hypertension ; Hypertensive heart disease without (congestive) heart failure
0081	Arm B	No	No	No	No	No	
0082	Arm B	Yes	No	No	No	No	
0084	Arm B	Yes	No	No	No	No	
0088	Arm B	Yes	No	No	No	No	
0162	Arm B	Yes	No	No	No	No	
0164	Arm B	Yes	No	No	No	Yes	Non-insulin-dependent diabetes mellitus: With renal complications ; Obesity, unspecified ; Hyperlipidaemia, unspecified ; Hyperuricaemia without signs of inflammatory arthritis and tophaceous disease ; Essential (primary) hypertension ; Fatty (change of) liver, not elsewhere classified ; Glomerular disorders in diabetes mellitus ; Chronic kidney disease, unspecified ; Acquired absence of genital organ(s) ; Acquired absence of other parts of digestive tract
0165	Arm B	Yes	No	No	No	No	
0167	Arm B	Yes	No	No	No	Yes	Atherosclerosis of arteries of extremities
0241	Arm B	Yes	Yes	Yes	No	No	
0242	Arm B	Yes	No	No	No	Yes	Iron deficiency anaemia secondary to blood loss (chronic) ; Obesity, unspecified ; Essential (primary) hypertension ; Atrial fibrillation and flutter ; Unspecified haemorrhoids without complication ; Cellulitis, unspecified ; Other complications of procedures, not elsewhere classified
0401	Arm B	Yes	No	No	No	Yes	Essential (primary) hypertension

11.2 EfficacyData

Table 26. Surgery population- Postoperative complication rate- Cochran-Mantel-Haenszel test and cross-tabulations with study arm

Cochran-Mantel-Haenszel	Number of strata	p-Value (General association)	Probability of postoperative complications (Arm A vs. Arm B)	CI 95%	Breslow-Day test (p-value)
Fong Score	5	0.6517	1.50	0.25-8.99	0.2168
Tumor burden	5	0.8220	1.15	0.35-3.75	0.5573
Study site	12	1.0000	1.00	0.06-15.99	0.0455

Table 27. Surgery population- Postoperative complication rate- Logistic regression

Postoperative complication rate- Logistic regression- Type III Effect	Univariate (p-Value)
Arm	0.6719
Fong Score	0.9296
Age at randomization	0.7377
Gender	0.9557
ECOG at baseline	.
Pre-existing diseases	0.1765
Prior surgery	0.9778
Prior chemotherapy for metastatic disease	.
K-RAS-Mutation	.
Metastases status	0.1172

Table 28. Surgery population- Postoperative complication rate- Logistic regression- Stepwise selection

Multivariate logistic regression- Stepwise selection	Effect entered	Effect removed	p-Value
Step 1	Metastases status		0.0935
Step 2		Metastases status	0.1172

*Pre-existing diseases and metastases status were considered for the stepwise selection. The first effect entered was metastases status. Because this effect was also removed, model building was terminated.

Listing 3: Surgery

Patient No.	Treatment Arm	Surgery performed	Synchronous resected colorectal carcinoma	Synchronous resected colorectal carcinoma- Location	Type of surgery	Vascular resection	Vascular graft	Intraoperative/postoperative complication	Clavien score
0002	Arm A	No							
0083	Arm A	Yes	No			No	No	Postoperative complications	Grade II
0085	Arm A	Yes	No			Yes	No	Postoperative complications	Grade IV
0086	Arm A	Yes	No			No	No	None	Grade I
0087	Arm A	Yes	No			No	No	None	Grade I
0089	Arm A	Yes	No			No	No	None	No deviation from the normal postoperative course
0090	Arm A	Yes	No			No	No	None	No deviation from the normal postoperative course
0161	Arm A	Yes	No			No	No	None	No deviation from the normal postoperative course
0163	Arm A	Yes	No			No	No	None	No deviation from the normal postoperative course
0166	Arm A	No							
0402	Arm A	No							
0001	Arm B	No							
0003	Arm B	Yes	No			No	No	None	No deviation from the normal postoperative course
0081	Arm B	No							
0082	Arm B	Yes	No			No	No	None	No deviation from the normal postoperative course
0084	Arm B	Yes	No			No	No	None	No deviation from the normal postoperative course
0088	Arm B	Yes	No			No	No	None	Grade II
0162	Arm B	Yes	No			No	No	None	No deviation from the normal postoperative course
0164	Arm B	No							
0165	Arm B	Yes	No			No	No	None	Grade I
0167	Arm B	Yes	No			No	No	None	No deviation from the normal postoperative course
0241	Arm B	Yes	No			No	No	None	No deviation from the normal postoperative course
0242	Arm B	Yes	No			No	No	None	Grade I
0401	Arm B	Yes	No			Yes	No	Intra- and postoperative complications	Grade I

Table 29. Overall survival- Adjusted univariate Cox regression

Overall survival- Adjusted Cox regression	Parameter vs. Reference value	Estimate (Parameter)	Standard error	p-Value	Hazard ratio	CI 95% (Wald)
Arm	Arm A vs. Arm B	0.14208	1.37329	0.9176	1.153	0.078- 17.008
Age at randomization [linear]	Linear	0.02165	0.09628	0.8221	1.022	0.846- 1.234
Gender	Female vs. male	-18.18888	7021	0.9979	<0.001	0- .
Preexisting disease	No vs. yes	17.15483	5563	0.9975	28199856	0- .
Prior surgery	No vs. yes	-16.20704	6036	0.9979	<0.001	0- .

Table 30. Disease- free survival- Hazard ratio for Fong Score

Fong Score- Hazard Ratio	Parameter vs. Reference value	Estimate (Parameter)	Standard error	p-Value	Hazard ratio	CI 95% (Wald)
Fong score	1-2 vs 3-5	0.0302	0.9135	0.9736	1.031	0.172-6.176
Fong score (linear)	Unit=1	0.0970	0.5455	0.8589	1.102	0.378-3.210

Table 31. Disease-free survival- Adjusted univariate Cox regression

Disease-free survival- Adjusted Cox regression	Parameter vs. reference value	Estimate	Standard error	p-Value	Hazard ratio	CI 95% (Wald)
Arm	Arm A vs. Arm B	0.6954	0.9489	0.4637	2.004	0.312-12.874
Age at randomization [linear]	Unit=1	-0.02277	0.07273	0.7542	0.977	0.848- 1.127
Gender	Female vs male	-17.64990	4494	0.9969	<0.001	0- .
Pre-existing diseases	No. vs. yes	1.0545	1.20292	0.3807	2.871	0.272- 30.332
Prior surgery	No. vs. yes	-15.13918	2849	0.9958	<0.001	0- .

Table 32. Resection rate and resected liver mass (g)

Patient No.	Treatment Arm	Surgery performed	Segment	Resection	Atypical/wedge resection	Atypical/wedge resection- Number of areas	Weight of resected liver tissue [g]
0002	Arm A	No				.	.
0083	Arm A	Yes	Segment V – inferior subsegment of the anterior segment	R0	No	.	670
0085	Arm A	Yes	Segment IV – Lobus quadratus	R0	Yes	5	581
0086	Arm A	Yes	Segment IVb – inferior subsegment of the medial segment	R1	Yes	4	165
0087	Arm A	Yes	Segment VI – inferior subsegment of the posterior segment	R0	Yes	3	67
0089	Arm A	Yes	Segment VII – superior subsegment of the posterior segment	R0	No	.	.
0090	Arm A	Yes	Segment VIII – superior subsegment of the anterior segment	R0	No	.	.
0090	Arm A	Yes	Segment III – inferior subsegment of the lateral segment	R0	Yes	1	.

Patient No.	Treatment Arm	Surgery performed	Segment	Resection	Atypical/wedge resection	Atypical/wedge resection- Number of areas	Weight of resected liver tissue [g]
0090	Arm A	Yes	Segment IVa – superior subsegment of the medial segment	R0	Yes	1	.
0161	Arm A	Yes	Segment VII – superior subsegment of the posterior segment	R0	Yes	1	362
0163	Arm A	Yes	Segment II – superior subsegment of the lateral segment	RX	No	.	.
0166	Arm A	No				.	.
0402	Arm A	No				.	.
0001	Arm B	No				.	.
0003	Arm B	Yes	Segment II – superior subsegment of the lateral segment	R0	No	.	.
0003	Arm B	Yes	Segment III – inferior subsegment of the lateral segment	R0	No	.	197
0081	Arm B	No				.	.
0082	Arm B	Yes	Segment V – inferior subsegment of the anterior segment	R0	No	.	.
0084	Arm B	Yes	Segment III – inferior subsegment of the lateral segment	R0	Yes	1	.
0088	Arm B	Yes	Segment III – inferior subsegment of the lateral segment	RX	No	.	.
0088	Arm B	Yes	Segment II – superior subsegment of the lateral segment	RX	No	.	261
0162	Arm B	Yes	Segment II – superior subsegment of the lateral segment	R0	Yes	1	.
0162	Arm B	Yes	Segment IVa – superior subsegment of the medial segment	R0	Yes	1	.
0162	Arm B	Yes	Segment VI – inferior subsegment of the posterior segment	R0	Yes	1	.
0162	Arm B	Yes	Segment VIII – superior subsegment of the anterior segment	R0	Yes	1	.
0162	Arm B	Yes	Segment VII – superior subsegment of the posterior segment	R0	No	.	.
0164	Arm B	No				.	.
0165	Arm B	Yes	Other -Segment V; VI and VII	R0	No	.	.

Patient No.	Treatment Arm	Surgery performed	Segment	Resection	Atypical/wedge resection	Atypical/wedge resection- Number of areas	Weight of resected liver tissue [g]
0167	Arm B	Yes	Other -partially segment IVa, IVb	R0	No	.	.
0167	Arm B	Yes	Segment II – superior subsegment of the lateral segment	R0	No	.	.
0167	Arm B	Yes	Segment III – inferior subsegment of the lateral segment	R0	No	.	.
0241	Arm B	Yes	Segment VII – superior subsegment of the posterior segment	R0	No	.	.
0241	Arm B	Yes	Segment VI – inferior subsegment of the posterior segment	R0	No	.	.
0242	Arm B	Yes	Segment VI – inferior subsegment of the posterior segment	R0	Yes	1	43
0401	Arm B	Yes	Segment I – Lobus caudatus	R0	Yes	1	.
0401	Arm B	Yes	Segment II – superior subsegment of the lateral segment	R0	Yes	1	.
0401	Arm B	Yes	Segment VIII – superior subsegment of the anterior segment	R0	No	.	.
0401	Arm B	Yes	Segment V – inferior subsegment of the anterior segment	R0	No	.	.
0401	Arm B	Yes	Segment VII – superior subsegment of the posterior segment	R0	No	.	.
0401	Arm B	Yes	Segment IVb – inferior subsegment of the medial segment	R0	Yes	1	.
0401	Arm B	Yes	Segment VI – inferior subsegment of the posterior segment	R0	No	.	900

Table 33. Patients with chemotherapy- Dose intensity of cetuximab- Applied total dose [mg]

Applied total dose		N	Mean	Changes from baseline (Mean)	STD	SEM	Median	Min	Max	NMiss	Changes from baseline- p-Value (Wilcoxon Two-Sample Test)
Cycle 1	Arm A	7	603.36	0.00	95.00	35.91	617.50	467.50	716.00	0	-
	Arm B	12	611.34	0.00	97.02	28.01	618.50	507.00	868.00	0	
	Total	19	608.40	0.00	93.68	21.49	617.50	467.50	868.00	0	
Cycle 2	Arm A	7	460.79	-142.57	88.27	33.36	475.00	287.50	548.00	0	0.7166
	Arm B	11	408.28	-207.50	144.04	43.43	465.00	0.00	500.00	0	
	Total	18	428.70	-182.25	125.10	29.49	470.00	0.00	548.00	0	

Applied total dose		N	Mean	Changes from baseline (Mean)	STD	SEM	Median	Min	Max	NMiss	Changes from baseline-p-Value (Wilcoxon Two-Sample Test)
Cycle 3	Arm A	7	475.36	-128.00	127.90	48.34	475.00	240.00	650.00	0	0.7511
	Arm B	11	426.80	-188.99	158.84	47.89	466.25	0.00	650.00	0	
	Total	18	445.68	-165.27	145.63	34.33	470.63	0.00	650.00	0	
Cycle 4	Arm A	5	449.20	-162.00	97.94	43.80	475.00	287.50	543.50	0	0.8650
	Arm B	11	381.34	-234.44	148.62	44.81	407.50	0.00	500.00	0	
	Total	16	402.55	-211.80	135.42	33.86	452.50	0.00	543.50	0	
Cycle 5	Arm A	5	440.40	-170.80	118.61	53.04	475.00	240.00	547.00	0	0.8650
	Arm B	11	349.30	-266.49	190.30	57.38	407.50	0.00	500.00	0	
	Total	16	377.77	-236.58	172.61	43.15	453.13	0.00	547.00	0	
Cycle 6	Arm A	4	295.63	-325.88	246.04	123.02	331.25	0.00	520.00	0	0.6477
	Arm B	11	354.40	-261.38	187.39	56.50	407.50	0.00	500.00	0	
	Total	15	338.73	-278.58	196.92	50.84	407.50	0.00	520.00	0	
Cycle 7	Arm A	4	295.75	-325.75	244.46	122.23	341.50	0.00	500.00	0	0.1066
	Arm B	8	447.16	-133.98	109.10	38.57	452.13	250.00	611.00	0	
	Total	12	396.69	-197.90	171.55	49.52	452.13	0.00	611.00	0	
Cycle 8	Arm A	4	300.75	-320.75	250.16	125.08	341.50	0.00	520.00	0	0.4962
	Arm B	8	391.50	-189.64	163.69	57.87	437.50	0.00	500.00	0	
	Total	12	361.25	-233.34	190.04	54.86	437.50	0.00	520.00	0	
Cycle 9	Arm A	4	301.38	-320.13	250.90	125.45	341.50	0.00	522.50	0	0.6098
	Arm B	8	360.44	-220.70	163.92	57.95	412.50	0.00	485.00	0	
	Total	12	340.75	-253.84	187.38	54.09	412.50	0.00	522.50	0	
Cycle 10	Arm A	4	300.75	-320.75	250.16	125.08	341.50	0.00	520.00	0	0.3949
	Arm B	8	430.77	-150.37	63.43	22.43	439.00	312.38	500.00	0	
	Total	12	387.43	-207.16	154.03	44.47	439.00	0.00	520.00	0	
Cycle 11	Arm A	4	296.63	-324.88	245.40	122.70	343.25	0.00	500.00	0	0.6098
	Arm B	8	330.47	-250.67	207.83	73.48	413.13	0.00	500.00	0	
	Total	12	319.19	-275.40	210.21	60.68	413.13	0.00	500.00	0	
Cycle 12	Arm A	3	332.17	-329.00	287.67	166.09	496.50	0.00	500.00	0	0.8379
	Arm B	8	392.58	-188.56	124.49	44.01	415.00	104.13	500.00	0	
	Total	11	376.10	-226.86	167.91	50.63	420.00	0.00	500.00	0	
Cycle 13	Arm A	1	250.00	-367.50	.	.	250.00	250.00	250.00	0	
	Total	1	250.00	-367.50	.	.	250.00	250.00	250.00	0	

Table 34. Patients with chemotherapy- Duration of treatment with FOLFOX + cetuximab [weeks]

Duration of treatment	N	Mean	STD	SEM	Median	Min	Max	NMiss	p-Value (Wilcoxon Two-Sample Test)
Arm A	7	114.57	65.03	24.58	147.00	35.00	175.00	0	0.0572
Arm B	12	179.17	90.64	26.16	229.50	1.00	253.00	0	
Total	19	155.37	86.34	19.81	173.00	1.00	253.00	0	

11.3 Safety Data

11.3.1 Presentations of AEs

Table 35. Adverse events according to NCI

Adverse event	Arm A		Arm B		Total	
	N	%	N	%	N	%
Abdominal infection	1	1.11	1	0.45	2	0.64
Abdominal pain	3	3.33	3	1.34	6	1.91
Alanine aminotransferase increased	.	.	1	0.45	1	0.32
Allergic reaction	2	2.22	.	.	2	0.64
Alopecia	.	.	4	1.79	4	1.27
Anemia	2	2.22	4	1.79	6	1.91
Anorexia	.	.	3	1.34	3	0.96
Aphonia	1	1.11	.	.	1	0.32
Aspartate aminotransferase increased	.	.	1	0.45	1	0.32
Biliary anastomotic leak	1	1.11	.	.	1	0.32
Blood and lymphatic system disorders - Other, specify	3	3.33	2	0.89	5	1.59
Blood bilirubin increased	.	.	1	0.45	1	0.32
Bone marrow hypocellular	1	1.11	.	.	1	0.32
Breast infection	.	.	1	0.45	1	0.32
Bronchial infection	1	1.11	.	.	1	0.32
Bruising	.	.	1	0.45	1	0.32
Cardiac disorders - Other, specify	1	1.11	.	.	1	0.32
Chest pain - cardiac	.	.	2	0.89	2	0.64
Conjunctivitis	.	.	1	0.45	1	0.32
Constipation	1	1.11	3	1.34	4	1.27
Dehydration	.	.	1	0.45	1	0.32
Delirium	.	.	1	0.45	1	0.32
Diarrhea	7	7.78	5	2.23	12	3.82
Dizziness	.	.	1	0.45	1	0.32
Dry skin	.	.	5	2.23	5	1.59
Dysgeusia	.	.	2	0.89	2	0.64
Dyspnea	1	1.11	1	0.45	2	0.64
Edema trunk	1	1.11	.	.	1	0.32
Fatiguep0üß	.	.	9	4.02	9	2.87
Febrile neutropenia	1	1.11	.	.	1	0.32
Fever	4	4.44	1	0.45	5	1.59
GGT increased	.	.	1	0.45	1	0.32
Gastrointestinal disorders - Other, specify	3	3.33	.	.	3	0.96
General disorders and administration site conditions - Other, specify	.	.	1	0.45	1	0.32
Gum infection	1	1.11	.	.	1	0.32
Gynecomastia	.	.	1	0.45	1	0.32
Hallucinations	1	1.11	.	.	1	0.32
Hematoma	.	.	1	0.45	1	0.32
Hepatic hemorrhage	.	.	1	0.45	1	0.32
Hepatobiliary disorders - Other, specify	2	2.22	1	0.45	3	0.96
Hoarseness	.	.	1	0.45	1	0.32
Hyperglycemia	.	.	1	0.45	1	0.32
Hyperkalemia	.	.	1	0.45	1	0.32
Hypertension	.	.	7	3.13	7	2.23
Hypocalcemia	1	1.11	.	.	1	0.32
Hypokalemia	.	.	1	0.45	1	0.32
Hypotension	1	1.11	.	.	1	0.32
Hypoxia	1	1.11	.	.	1	0.32

Adverse event	Arm A		Arm B		Total	
	N	%	N	%	N	%
Infections and infestations - Other, specify	2	2.22	1	0.45	3	0.96
Infusion related reaction	1	1.11	.	.	1	0.32
Insomnia	.	.	1	0.45	1	0.32
Investigations - Other, specify	.	.	2	0.89	2	0.64
Leukocytosis	1	1.11	.	.	1	0.32
Lung infection	.	.	1	0.45	1	0.32
Mucositis oral	3	3.33	10	4.46	13	4.14
Nausea	3	3.33	18	8.04	21	6.69
Neoplasms benign, malignant and unspecified (incl cysts and polyps) - Other, specify	1	1.11	.	.	1	0.32
Nervous system disorders - Other, specify	.	.	1	0.45	1	0.32
Neutrophil count decreased	3	3.33	16	7.14	19	6.05
Pain	2	2.22	4	1.79	6	1.91
Pain in extremity	.	.	1	0.45	1	0.32
Palmar-plantar erythrodysesthesia syndrome	1	1.11	3	1.34	4	1.27
Papulopustular rash	3	3.33	.	.	3	0.96
Paresthesia	2	2.22	4	1.79	6	1.91
Peripheral sensory neuropathy	1	1.11	18	8.04	19	6.05
Platelet count decreased	6	6.67	5	2.23	11	3.50
Pleural effusion	3	3.33	1	0.45	4	1.27
Pneumothorax	1	1.11	.	.	1	0.32
Productive cough	.	.	1	0.45	1	0.32
Prostatic obstruction	.	.	1	0.45	1	0.32
Pruritus	.	.	1	0.45	1	0.32
Rash acneiform	5	5.56	32	14.29	37	11.78
Rash maculo-papular	.	.	2	0.89	2	0.64
Rectal obstruction	.	.	3	1.34	3	0.96
Seroma	.	.	1	0.45	1	0.32
Skin and subcutaneous tissue disorders - Other, specify	1	1.11	7	3.13	8	2.55
Thromboembolic event	4	4.44	1	0.45	5	1.59
Thrombotic thrombocytopenic purpura	2	2.22	.	.	2	0.64
Vascular disorders - Other, specify	1	1.11	1	0.45	2	0.64
Vertigo	.	.	1	0.45	1	0.32
Visceral arterial ischemia	1	1.11	.	.	1	0.32
Vomiting	1	1.11	1	0.45	2	0.64
White blood cell decreased	.	.	15	6.70	15	4.78
Wound infection	1	1.11	.	.	1	0.32
Total	90	100.00	224	100.00	314	100.00

11.3.2 Listings of Deaths, SAEs, Other Significant AEs

Listing 4: Serious adverse events

Site	Patient -No.	Treatment Arm	Age [years]	Gender	Event	PT term	Serious TEAE	Start of SAE	End of SAE	Severity	Relation to cetuximab	Relation to chemotherapy	Outcome	Reason for SAE
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Hypoxia	Hypoxia	Yes	03JAN2013	04JAN2013	Life threatening or disabling	Not related	Not related	Recovered without sequelae	Life-threatening
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Pleura effusion	Pleural effusion	Yes	16JAN2013	21JAN2013	Moderate	Not related	Not related	Change in toxicity grade / severity	In-patient hospitalization or prolongation
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	pulmonary embolism	Pulmonary embolism	Yes	11FEB2013	27FEB2013	Severe	Not related	Not related	Recovered without sequelae	In-patient hospitalization or prolongation
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0090	Arm A	58	Male	Diarrhea	Diarrhoea	Yes	01MAR2014	03MAR2014	Severe	Probable	Possible	Recovered without sequelae	In-patient hospitalization or prolongation
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0090	Arm A	58	Male	jugular vein thrombosis	Jugular vein thrombosis	Yes	05MAR2014	24MAR2014	Severe	Not related	Not related	Recovered without sequelae	In-patient hospitalization or prolongation
Universitätsklinikum Erlangen ,Erlangen	0083	Arm A	71	Male	Diarrhea	Diarrhoea	Yes	12OCT2012	26OCT2012	Severe	Not related	Probable	Recovered without sequelae	In-patient hospitalization or prolongation
Universitätsklinikum Erlangen ,Erlangen	0083	Arm A	71	Male	Broncho-pulmonal infection	Bronchopneumonia	Yes	27NOV2012	22DEC2012	Severe	Not likely	Certain / definite	Recovered without sequelae	In-patient hospitalization or prolongation
Universitätsklinikum Jena ,Jena	0086	Arm A	64	Male	pulmonary embolism	Pulmonary embolism	Yes	18FEB2013	.	Severe	Not related	Not related	Ongoing, no therapy	In-patient hospitalization or prolongation
Universitätsklinikum Jena ,Jena	0086	Arm A	64	Male	Fever unknown genesis	Pyrexia	Yes	19APR2013	23APR2013	Moderate	Not likely	Not likely	Recovered without sequelae	In-patient hospitalization or prolongation
Universitätsklinikum Jena ,Jena	0086	Arm A	64	Male	suspiction of thickening intestinal wall at cecum	Gastrointestinal disorder	Yes	23MAY2013	27MAY2013	Moderate	Not related	Not related	Recovered without sequelae	In-patient hospitalization or prolongation
Universitätsklinikum Jena ,Jena	0086	Arm A	64	Male	ischaemia of the distal 9 cm upstream of the colon	Intestinal ischaemia	Yes	30AUG2013	08NOV2013	Moderate	Not related	Not related	Recovered with sequelae	In-patient hospitalization or prolongation

Site	Patient -No.	Treatment Arm	Age [years]	Gender	Event	PT term	Serious TEAE	Start of SAE	End of SAE	Severity	Relation to cetuximab	Relation to chemotherapy	Outcome	Reason for SAE
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0084	Arm B	69	Male	Hyper-glycaemia	Hyperglycaemia	Yes	08NOV2012	12NOV2012	Severe	Not related	Not related	Recovered without sequelae	In-patient hospitalization or prolongation
Universitätsklinikum Jena ,Jena	0003	Arm B	60	Male	abdominal infection-Grade 3(Norovirus positiv)	Abdominal infection	Yes	20FEB2014	25FEB2014	Moderate	Not related	Not related	Recovered without sequelae	In-patient hospitalization or prolongation

11.3.3 Narratives of Deaths, SAEs, Other Significant AEs

n.a.

11.3.4 Abnormal Laboratory Values (by-patient listing)

n.a.

12 List of References

1. de Martel, C., et al., *Global burden of cancers attributable to infections in 2008: a review and synthetic analysis.* Lancet Oncol, 2012. **13**(6): p. 607-15.

2. Haggar, F.A. and R.P. Boushey, *Colorectal cancer epidemiology: incidence, mortality, survival, and risk factors.* Clin Colon Rectal Surg, 2009. **22**(4): p. 191-7.

3. Organization, W.H., *Cancer Incidence in Five Continents*, in *The World Health Organization and the International Agency for Research on Cancer*. 2002: Lyon.

4. Boyle, P. and J.S. Langman, *ABC of colorectal cancer: Epidemiology.* BMJ, 2000. **321**(7264): p. 805-8.

5. Boyle, P. and J. Ferlay, *Mortality and survival in breast and colorectal cancer.* Nat Clin Pract Oncol, 2005. **2**(9): p. 424-5.

6. Parkin, D.M. and L.M. Fernandez, *Use of statistics to assess the global burden of breast cancer.* Breast J, 2006. **12 Suppl 1**: p. S70-80.

7. Janout, V. and H. Kollarova, *Epidemiology of colorectal cancer.* Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub, 2001. **145**(1): p. 5-10.

8. Van Cutsem, E., Nowacki M, Lang I, Cascinu S, Shchepotin I, Maurel J, and C.D. Rougier P, Nippgen J, Kohne C., *Randomized phase III study of irnitecan and 5-FU/FA with or without cetuximab in the first-line treatment of patients with metastatic colorectal cancer: the crystal trial.* J Clin Oncol 2007, 2007. **ASCO Annual Meeting Proceedings Part I 2007; 25: 1**.

9. Bokemeyer, B., *#3004 für OPUS.* ECCO 2007.

10. Folprecht, G., et al., *Tumour response and secondary resectability of colorectal liver metastases following neoadjuvant chemotherapy with cetuximab: the CELIM randomised phase 2 trial.* Lancet Oncol, 2010. **11**(1): p. 38-47.

11. Cunningham, D., et al., *Cetuximab monotherapy and cetuximab plus irinotecan in irinotecan-refractory metastatic colorectal cancer.* N Engl J Med, 2004. **351**(4): p. 337-45.

12. Saltz, L.B., et al., *Phase II trial of cetuximab in patients with refractory colorectal cancer that expresses the epidermal growth factor receptor.* J Clin Oncol, 2004. **22**(7): p. 1201-8.

13. Folprecht, G., et al., *Cetuximab and irinotecan/5-fluorouracil/folinic acid is a safe combination for the first-line treatment of patients with epidermal growth factor receptor expressing metastatic colorectal carcinoma.* Ann Oncol, 2006. **17**(3): p. 450-6.

14. Min, B.S., et al., *Cetuximab in combination with 5-fluorouracil, leucovorin and irinotecan as a neoadjuvant chemotherapy in patients with initially unresectable colorectal liver metastases.* Onkologie, 2007. **30**(12): p. 637-43.

15. Adam, R., et al., *Rescue surgery for unresectable colorectal liver metastases downstaged by chemotherapy: a model to predict long-term survival.* Ann Surg, 2004. **240**(4): p. 644-57; discussion 657-8.

16. Schmiegel W, R.-S.A., Arnold D, et al., *S3-Leitlinie „Kolorektales Karzinom"-Aktualisierung 2008. Ergebnis einer evidenzbasierten Konsensuskonferenz. (Manuskript in Vorbereitung).*

17. Nordlinger, B., et al., *Perioperative chemotherapy with FOLFOX4 and surgery versus surgery alone for resectable liver metastases from colorectal cancer (EORTC Intergroup trial 40983): a randomised controlled trial.* Lancet, 2008. **371**(9617): p. 1007-16.

18. Dindo, D., N. Demartines, and P.A. Clavien, *Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey.* Ann Surg, 2004. **240**(2): p. 205-13.

19. http://www.merck.de/de/presse/extNewsDetail.html?newsId=F4B2469FBCFEB82BC1257C470077F73B&newsType=1. 2013.

20. Baselga, J., *The EGFR as a target for anticancer therapy--focus on cetuximab.* Eur J Cancer, 2001. **37 Suppl 4**: p. S16-22.

21. Fan, Z., et al., *Antitumor effect of anti-epidermal growth factor receptor monoclonal antibodies plus cis-diamminedichloroplatinum on well established A431 cell xenografts.* Cancer Res, 1993. **53**(19): p. 4637-42.

22. Milas, L., et al., *In vivo enhancement of tumor radioresponse by C225 antiepidermal growth factor receptor antibody.* Clin Cancer Res, 2000. **6**(2): p. 701-8.

23. Kanas, G.P., et al., *Survival after liver resection in metastatic colorectal cancer: review and meta-analysis of prognostic factors.* Clin Epidemiol, 2012. **4**: p. 283-301.

24. Weiss, L., et al., *Haematogenous metastatic patterns in colonic carcinoma: an analysis of 1541 necropsies.* J Pathol, 1986. **150**(3): p. 195-203.

25. Jones, O.M., et al., *Biopsy of resectable colorectal liver metastases causes tumour dissemination and adversely affects survival after liver resection.* Br J Surg, 2005. **92**(9): p. 1165-8.

26. Portier, G., et al., *Multicenter randomized trial of adjuvant fluorouracil and folinic acid compared with surgery alone after resection of colorectal liver metastases: FFCD ACHBTH AURC 9002 trial.* J Clin Oncol, 2006. **24**(31): p. 4976-82.

27. Primrose, J., et al., *Systemic chemotherapy with or without cetuximab in patients with resectable colorectal liver metastasis: the New EPOC randomised controlled trial.* Lancet Oncol, 2014. **15**(6): p. 601-11.

28. Hasegawa, K., M. Oba, and N. Kokudo, *Cetuximab for resectable colorectal liver metastasis: new EPOC trial.* Lancet Oncol, 2014. **15**(8): p. e305-6.

29. Primrose, J.N., *Cetuximab for resectable colorectal liver metastasis: new EPOC trial--author's reply.* Lancet Oncol, 2014. **15**(8): p. e306.

13 Appendices

13.1 Study Information

13.1.1 Study Protocol and Amendments


Panter_Protocol_V 7.9_26012015_incl A


Panter_Protocol_V 8.0_19042011_2011-

13.1.2 Sample CRF


ecrf.pdf

13.1.3 List of Ethics Committees and Sample Patient Information Sheet and Informed Consent Form

Ethikkommission (EK)	Strasse	PLZ	Ort	Ihr Zeichen
Ethikkommission der RWTH Aachen (federführend)	Pauwelstraße 30	52074	Aachen	EK 009/11
Landesamt für Gesundheit und Soziales	Fehrbelliner Platz 1	10707	Berlin	11/0460-ZS EK 11
Ethikkommission Rheinische Friedrich-Wilhelms-Universtiät Bonn	Siegmund-Freud-Str. 25	53105	Bonn	085/12
Ethikkommission der Medizinischen Fakultät der der Technischen Universität Dresden	Fetscherstraße 74	01307	Dresden	EK162052011
Ethikkommission bei der Landesärztekammer Nordrhein	Tersteegenstraße 9	40474	Düsseldorf	2011344
Medizinische Fakultät der Friedrich-Alexander-Universität Erlangen-Nürnberg	Krankenhausstr. 12	91054	Erlangen	
Ethikkommission des Fachbereichs Medizin der Johann Wolfgang Goethe-Universität	Theodor-Stern-Kai 7	60590	Frankfurt/Main	5/11

Ethikkommission (EK)	Strasse	PLZ	Ort	Ihr Zeichen
Ethikkommission der Albert-Ludwigs-Universität Freiburg	Engelberger Straße 21	79106	Freiburg	5/11_120280
Ethikkommission der Medizinischen Fakultät Göttingen	Robert-Koch-Straße 40	37075	Göttingen	22.01.2011
Ethikkommission bei der Landesärztekammer Hamburg	Weidestraße 122 b	22083	Hamburg	MC-002/11
Ethikkommission der Medizinischen Hochschule Hannover	Carl-Neuberg-Str. 1	30625	Hannover	5817NM
Friedrich-Schiller Universität Jena Medizinische Fakultät Ethik-Kommission	Bachstraße 18	07743	Jena	11.01.3012
Ethikkommission an der Medizinischen Fakultät der Universität Leipzig	Käthe-Kollwitz-Str. 82	04109	Leipzig	
Ethik-Kommission an der Medizinischen Fakultät der Otto-von-Guericke-Universität Magdeburg	Leipziger Str. 44	39120	Magdeburg	
Ethikkommission bei der Landesärztekammer Rheinland-Pfalz	Deutschhausplatz 3	55116	Mainz	837.410.11(7952)
Ethikkommission der Medizinischen Fakultät Mannheim der Uni Heidelberg, Medizinische Ethik-Kommission II, Haus 42 - Ebene 3	Theodor-Kutzer-Ufer 1-3	68167	Mannheim	2011-001B-MA
Ethikkommission bei der Landesärztekammer Bayern	Mühlbaurstr. 16	81677	München	7/11003
Ethikkommission der Medizinische Fakultät der TU München	Ismaninger Str. 22	81675	München	
Ethikkommission des Fachbereichs Medizin, LMU München	Pettenkoferstr. 8 a	80336	München	
Ethikkommission der Landesärztekammer Westfalen-Lippe	Pavillon Alte Rechtsmedizin - Von-Esmarch-Str. 62	48149	Münster	2001-002-b-A
Ethikkommission bei der Landesärztekammer Baden-Württemberg	Jahnstraße 40	70597	Stuttgart	B-AM-2012-059#N1
Ethik-Kommission bei der Medizinischen Fakultät der Universität Würzburg Institut für Pharmakologie und Toxikologie	Versbacher Str. 9	97078	Würzburg	12/11_b
Ethikkommission der Med.Universität Graz	Auenbruggerplatz 2	A-8036	Graz	
Ethikkommission der Medizinischen Universität Innsbruck	Innrain 43	A-6020	Innsbruck	
Ethikkommission KH Barmh.Schwestern	Seilerstätte 4	A-4020	Linz	

Ethikkommission (EK)	Strasse	PLZ	Ort	Ihr Zeichen
Ethikkommission KH Elisabethinen	Fadingerstrasse 1	A-4020	Linz	
Ethikkommission des Landes Kärnten	St.-Veiter-Strasse 45-47	A-9020	Klagenfurt	
Ethikkommission der Medizinischen Universität Wien	Borschkegasse 8b/E06	A-1090	Wien	087-2011
Ethikkommission der Stadt Wien	TownTown, Thomas-Klestil-Platz 8	A-1030	Wien	EK-11-001-LOKAL

Sample Patient Information and Informed Consent Form

Germany:


Panter_Patinfo_V 7.1_31082011_Germa


Panter_Einv_V 7.1_31082011_Germa

Austria:


Panter_Patinfo_V 8.1_05092011_+ûst_


Panter_Einv_V 8.1_05092011_+ûst_

List of Signatures of the *LKP* [National Coordinating Investigator], the Sponsor, and the Biostatistician, and, if applicable, of Other Authors

By signing this Clinical Study Report, the undersigned authors agree with the contents of this Clinical Study Report. The clinical trial reported here was conducted in accordance with the principles of the Declaration of Helsinki, Good Clinical Practice (GCP), and applicable legislation.

Sponsor (Representative)	Dipl. Biol. Verena Deserno	14 Apr 2016 Aachen, date
National Coordinating Investigator / Investigator (Germany)	Prof. Dr. Ulf Peter Neumann	18.4.16 Aachen, date
Biostatistician	Dr. Christine Windemuth Kieselbach	14.04.2016 Giessen, date
Author of the Report	Dr. Marija Vukajlovic	13.04.2016 Hamburg, date

13.1.4 Listing of Patients by Study Drug Batch

n.a.

13.1.5 Randomization Scheme and Codes

All patients, who fulfilled all inclusion criteria and did not meet any exclusion criterion, were randomized to either arm A or arm B.
Stratification factors for randomization were:

- Fong score (≤2 versus >2)
- Subgroup (>3 liver metastases or at least one metastasis ≥5 cm in diameter versus ≤3 liver metastases <5 cm in diameter)

Online randomization was possible 24 hours a day.

13.1.6 Publications Based on the Clinical Trial

n.a.

13.2 Patient Data Listings

13.2.1 Protocol Deviations

n.a.

13.2.2 Subjects Excluded from the Efficacy Analysis

n.a.

13.2.3 Demographic Data

Table 36. Age at registration [Years]

Age	N	Mean	STD	SEM	Median	Min	Max	NMiss
Arm A	11	61.64	8.02	2.42	63.00	50.00	72.00	0
Arm B	13	65.77	7.12	1.97	68.00	53.00	76.00	0
Total	24	63.88	7.67	1.57	65.00	50.00	76.00	0

Table 37. Gender

Gender	Arm A		Arm B		Total	
	N	%	N	%	N	%
Female	3	27.27	5	38.46	8	33.33
Male	8	72.73	8	61.54	16	66.67
Total	11	100.00	13	100.00	24	100.00

Table 38. Height [cm]

Height	N	Mean	STD	SEM	Median	Min	Max	NMiss
Arm A	11	174.91	9.57	2.88	174.00	160.00	195.00	0
Arm B	13	171.08	7.94	2.20	168.00	157.00	185.00	0
Total	24	172.83	8.75	1.79	172.00	157.00	195.00	0

Table 39. Body surface area (BSA) [m²]

BSA	N	Mean	STD	SEM	Median	Min	Max	NMiss
Arm A	11	1.96	0.22	0.07	1.95	1.60	2.35	0
Arm B	13	1.91	0.24	0.07	1.92	1.54	2.35	0
Total	24	1.93	0.23	0.05	1.93	1.54	2.35	0

Listing 5: Primary tumor and stadium TNM classification

Patient No.	Treatment Arm	Localization of primary tumor	T stadium	N stadium	M stadium	cT stadium	cN stadium	cM stadium	Histology
0002	Arm A	Colon	T3	N1b	M1				Adenocarcinoma (tubular, azinar, papillary)
0083	Arm A	Colon	T3	N0	M0				Adenocarcinoma (tubular, azinar, papillary)
0085	Arm A	Rectum	T3	N0	MX				Adenocarcinoma (tubular, azinar, papillary)
0086	Arm A	Rectum	T3	N0	M1				Adenocarcinoma (tubular, azinar, papillary)
0087	Arm A	Rectum	T1	N0	MX				Adenocarcinoma (tubular, azinar, papillary)
0089	Arm A	Colon	T3	N1b	M1				Adenocarcinoma (tubular, azinar, papillary)
0090	Arm A	Rectum	T3	N0	M0				Adenocarcinoma (tubular, azinar, papillary)
0161	Arm A	Colon	T4a	N1b	M1				Adenocarcinoma (tubular, azinar, papillary)
0163	Arm A	Rectum	T1	N0	M1				Adenocarcinoma (tubular, azinar, papillary)
0166	Arm A	Rectum	T3	N2a	M1				Adenocarcinoma (tubular, azinar, papillary)
0402	Arm A	Other- sigma	T3	N2a	M1				Adenocarcinoma (tubular, azinar, papillary)
0001	Arm B	Colon				Tis	N0	M1	Adenocarcinoma (tubular, azinar, papillary)
0003	Arm B	Rectum	T2	N0	M0				Adenocarcinoma (tubular, azinar, papillary)
0081	Arm B	Colon				T3	N0	M1	Adenocarcinoma (tubular, azinar, papillary)
0082	Arm B	Colon	T4	N0	M1				Adenocarcinoma (tubular, azinar, papillary)
0084	Arm B	Colon	T3	N0	M1				Adenocarcinoma (tubular, azinar, papillary)
0088	Arm B	Colon	T4b	N2b	M1				Adenocarcinoma (tubular, azinar, papillary)
0162	Arm B	Colon	T3	N1a	M1				Adenocarcinoma (tubular, azinar, papillary)
0164	Arm B	Colon	T3	N0	M0				Adenocarcinoma (tubular, azinar, papillary)
0165	Arm B	Rectum	T3	N1a	M1				Adenocarcinoma (tubular, azinar, papillary)
0167	Arm B	Colon	T3	N0	MX				Adenocarcinoma (tubular, azinar, papillary)
0241	Arm B	Rectum	T3	N2b	M0				Adenocarcinoma (tubular, azinar, papillary)
0242	Arm B	Colon	T3	N1b	M1				Adenocarcinoma (tubular, azinar, papillary)
0401	Arm B	Colon	T3	N1a	M0				Adenocarcinoma (tubular, azinar, papillary)

Listing 6: Fong score

Patient No.	Treatment Arm	Disease free interval	Number of tumor burden	Tumor size >= 5cm	Fong score
0002	Arm A	No	4	No	2
0083	Arm A	Yes	2	No	2
0085	Arm A	No	2	No	1
0086	Arm A	Yes	2	No	2
0087	Arm A	No	1	No	1
0089	Arm A	No	1	No	2
0090	Arm A	No	3	No	1
0161	Arm A	Yes	1	Yes	4
0163	Arm A	Yes	2	Yes	3
0166	Arm A	Yes	6	Yes	4
0402	Arm A	Unknown	2	No	Unknown
0001	Arm B	No	1	Yes	2
0003	Arm B	No	1	Yes	2
0081	Arm B	No	5	No	1
0082	Arm B	Yes	1	No	2
0084	Arm B	Yes	3	No	2
0088	Arm B	No	2	No	2
0162	Arm B	Yes	5	No	3
0164	Arm B	Yes	2	Yes	3
0165	Arm B	No	6	Yes	3
0167	Arm B	Yes	1	Yes	3
0241	Arm B	Yes	2	No	3
0242	Arm B	Yes	1	No	3
0401	Arm B	Unknown	1	No	Unknown

Listing 7: Previous treatments and relevant diseases

Patient No.	Treatment Arm	Surgery	Radiotherapy	Adjuvant chemotherapy	Chemotherapy for metastatic disease	Any previous relevant diseases	Previous relevant diseases
0002	Arm A	Yes	No	No	No	No	
0083	Arm A	Yes	No	No	No	No	
0085	Arm A	Yes	Yes	Yes	No	Yes	Hepatitis A without hepatic coma ; Allergic rhinitis due to pollen ; Predominantly allergic asthma ; Bilateral inguinal hernia, without obstruction or gangrene ; Allergic urticaria ; Low back pain
0086	Arm A	No	No	No	No	Yes	Non-insulin-dependent diabetes mellitus: With renal complications ; Other obesity ; Essential (primary) hypertension ; Other psoriasis ; Arthropathic psoriasis ; Cyst of kidney, acquired
0087	Arm A	Yes	Yes	Yes	No	Yes	Disorders of acoustic nerve ; Pulmonary embolism without mention of acute cor pulmonale ; Phlebitis and thrombophlebitis of femoral vein
0089	Arm A	Yes	No	No	No	No	
0090	Arm A	Yes	No	No	No	Yes	Essential (primary) hypertension
0161	Arm A	Yes	No	No	No	No	
0163	Arm A	Yes	Yes	No	No	No	
0166	Arm A	Yes	No	No	No	Yes	Essential (primary) hypertension ; Chronic ischaemic heart disease, unspecified ; Diverticular disease of large intestine without perforation or abscess ; Post-traumatic wound infection, not elsewhere classified ; Acquired absence of genital organ(s)
0402	Arm A	Yes	No	No	No	No	
0001	Arm B	No	No	No	No	No	
0003	Arm B	Yes	No	No	No	Yes	Obesity, unspecified ; Essential (primary) hypertension ; Hypertensive heart disease without (congestive) heart failure
0081	Arm B	No	No	No	No	No	
0082	Arm B	Yes	No	No	No	No	
0084	Arm B	Yes	No	No	No	No	
0088	Arm B	Yes	No	No	No	No	
0162	Arm B	Yes	No	No	No	No	
0164	Arm B	Yes	No	No	No	Yes	Non-insulin-dependent diabetes mellitus: With renal complications ; Obesity, unspecified ; Hyperlipidaemia, unspecified ; Hyperuricaemia without signs of inflammatory arthritis and tophaceous disease ; Essential (primary) hypertension ; Fatty (change of) liver, not elsewhere classified ; Glomerular disorders in diabetes mellitus ; Chronic kidney disease, unspecified ; Acquired absence of genital organ(s) ; Acquired absence of other parts of digestive tract
0165	Arm B	Yes	No	No	No	No	
0167	Arm B	Yes	No	No	No	Yes	Atherosclerosis of arteries of extremities
0241	Arm B	Yes	Yes	Yes	No	No	
0242	Arm B	Yes	No	No	No	Yes	Iron deficiency anaemia secondary to blood loss (chronic) ; Obesity, unspecified ; Essential (primary) hypertension ; Atrial fibrillation and flutter ; Unspecified haemorrhoids without complication ; Cellulitis, unspecified ; Other complications of procedures, not elsewhere classified
0401	Arm B	Yes	No	No	No	Yes	Essential (primary) hypertension

Listing 8: Tumor assessment

Patient No.	Treatment Arm	Staging No.	Measurable?	Location	Method	Measurable lesions- Size [mm]	Non-measurable lesions- Tumor type	Overall assessment
0002	Arm A	0	Yes	Liver - Leason S8 + S1	CT scan	36		
0002	Arm A	0	No	Liver - Leason S6 + S2/3	CT scan	.	Present	
0083	Arm A	0	Yes	Liver - Segment 6	CT scan	20		
0083	Arm A	0	Yes	Liver - Segment 8	CT scan	10		
0083	Arm A	1	Yes	Liver - Segment 8	CT scan	0		
0083	Arm A	1	Yes	Liver - Segment 6	CT scan	.		CR
0085	Arm A	0	Yes	Liver - Segment 6	CT scan	25		
0085	Arm A	0	Yes	Liver - Segment 7	CT scan	14		
0085	Arm A	1	Yes	Liver - Segment 6	CT scan	0		
0085	Arm A	1	Yes	Liver - Segment 7	CT scan	0		CR
0085	Arm A	2	Yes	Liver - Segment 7	CT scan	0		
0085	Arm A	2	Yes	Liver - Segment 6	CT scan	0		CR
0085	Arm A	3	Yes	Liver - Segment 6	CT scan	0		
0085	Arm A	3	Yes	Liver - Segment 7	CT scan	0		CR
0086	Arm A	0	Yes	Liver - Segment IV B	CT scan	13		
0086	Arm A	0	No	Liver - Segment V	CT scan	.	Present	
0086	Arm A	0	No	Liver - Segment VI	CT scan	.	Present	
0086	Arm A	1	No	Liver - Segment VI	CT scan	.	Absent	
0086	Arm A	1	No	Liver - Segment V	CT scan	.	Absent	
0086	Arm A	1	Yes	Liver - Segment IV B	CT scan	0		CR
0086	Arm A	2	No	Liver - Segment VI	CT scan	.	Absent	
0086	Arm A	2	Yes	Liver - Segment IV B	CT scan	0		
0086	Arm A	2	No	Liver - Segment V	CT scan	.	Absent	CR
0086	Arm A	3	No	Liver - Segment VI	CT scan	.	Absent	
0086	Arm A	3	No	Liver - Segment V	CT scan	.	Absent	
0086	Arm A	3	Yes	Liver - Segment IV B	CT scan	0		CR
0087	Arm A	0	Yes	Liver - S6	CT scan	27		
0087	Arm A	1	Yes	Liver - S6	CT scan	.		
0087	Arm A	1	Yes	Liver - Segment3	CT scan	23		PD
0087	Arm A	2	Yes	Liver - Segment3	CT scan	16		
0087	Arm A	2	Yes	Liver - S6	CT scan	.		
0087	Arm A	3	Yes	Liver - Segment3	CT scan	.		
0087	Arm A	3	Yes	Liver - S6	CT scan	.		

Patient No.	Treatment Arm	Staging No.	Measurable?	Location	Method	Measurable lesions- Size [mm]	Non-measurable lesions- Tumor type	Overall assessment
0089	Arm A	0	Yes	Liver - 8. segment	CT scan	35		
0089	Arm A	1	Yes	Liver - 8. segment	CT scan	0		
0089	Arm A	1	Yes	Liver - 2. segment	CT scan	15		PD
0089	Arm A	2	Yes	Liver - 8. segment	CT scan	.		
0089	Arm A	2	Yes	Liver - 2. segment	CT scan	10		
0089	Arm A	3	Yes	Liver - 2. segment	CT scan	.		
0089	Arm A	3	Yes	Vagina - Excatio rectouterina	CT scan	91		
0089	Arm A	3	Yes	Liver - 8. segment	CT scan	.		
0089	Arm A	4	Yes	Liver - 2. segment	CT scan	.		
0089	Arm A	4	Yes	Vagina - Excatio rectouterina	CT scan	91		
0089	Arm A	4	Yes	Liver - 8. segment	CT scan	.		
0089	Arm A	5	Yes	Liver - 2. segment	CT scan	.		
0089	Arm A	5	Yes	Vagina - Excatio rectouterina	CT scan	91		
0089	Arm A	5	Yes	Liver - 8. segment	CT scan	.		
0090	Arm A	0	Yes	Liver - Segment IV/V	CT scan	36		
0090	Arm A	0	Yes	Liver - Segment VIII	CT scan	20		
0090	Arm A	0	Yes	Liver - Segment II/III	CT scan	30		
0090	Arm A	1	Yes	Liver - Segment IV/V	CT scan	0		
0090	Arm A	1	Yes	Liver - Segment VIII	CT scan	0		
0090	Arm A	1	Yes	Liver - Segment II/III	CT scan	0		CR
0161	Arm A	0	Yes	Liver - Segment 6/7	CT scan	69		
0161	Arm A	0	No	Liver - Segment VIII	CT scan	.	Present	
0161	Arm A	1	No	Liver - Segment VIII	CT scan	.	Present	
0161	Arm A	1	Yes	Liver - Segment 6/7	CT scan	0		PR
0161	Arm A	2	No	Liver - Segment VIII	CT scan	.	Present	
0161	Arm A	2	Yes	Liver - Segment 6/7	CT scan	0		PR
0161	Arm A	3	No	Liver - Segment VIII	CT scan	.	Present	
0161	Arm A	3	Yes	Liver - Segment 6/7	CT scan	0		PR
0161	Arm A	4	No	Lung intrapulmonary - Upperlobe right left	CT scan	.	Present	
0161	Arm A	4	Yes	Liver - Segment 6/7	CT scan	0		
0161	Arm A	4	No	Liver - Segment VIII	CT scan	.	Present	PD
0161	Arm A	5	No	Liver - Segment VIII	CT scan	.	Present	
0161	Arm A	5	No	Lung intrapulmonary - Upperlobe right left	CT scan	.	Present	
0161	Arm A	5	Yes	Liver - Segment 6/7	CT scan	0		
0163	Arm A	0	No	Liver - Segment 3	MRI scan	.	Present	

Patient No.	Treatment Arm	Staging No.	Measurable?	Location	Method	Measurable lesions- Size [mm]	Non-measurable lesions- Tumor type	Overall assessment
0166	Arm A	0	Yes	Liver - Right lobe of the liver	Spiral-CT	80		
0166	Arm A	0	No	Lymph nodes mesenterial - Fatty tissue	Clinical lesions	.	Present	
0402	Arm A	0	Yes	Liver - Liver segment IVa and VIII	CT scan	71		
0402	Arm A	0	Yes	Liver - Liver segment V, VI, VII and VIII	CT scan	90		
0001	Arm B	0	Yes	Liver - Seg. 5	CT scan	65		
0003	Arm B	0	Yes	Liver - Segment II/III	CT scan	102		
0003	Arm B	1	Yes	Liver - Segment II/III	CT scan	59		PR
0003	Arm B	2	Yes	Liver - Segment II/III	CT scan	41		PR
0081	Arm B	0	Yes	Liver - Segment 7	CT scan	12		
0081	Arm B	0	Yes	Liver - Segment 2	CT scan	22		
0082	Arm B	0	Yes	Liver - Segment 5	Spiral-CT	22		
0082	Arm B	0	No	Liver - Segment 6	PET scan	.	Present	
0082	Arm B	1	Yes	Liver - Segment 5	Spiral-CT	9		
0082	Arm B	1	No	Liver - Segment 6	PET scan	.	Present	PR
0084	Arm B	No staging						
0088	Arm B	0	Yes	Liver - Segment 6	Spiral-CT	29		
0088	Arm B	0	Yes	Liver - Segment 2	Spiral-CT	33		
0088	Arm B	1	Yes	Liver - Segment 2	Spiral-CT	25		
0088	Arm B	1	Yes	Liver - Segment 6	Spiral-CT	23		SD
0088	Arm B	2	Yes	Liver - Segment 2	Spiral-CT	12		
0088	Arm B	2	Yes	Liver - Segment 6	Spiral-CT	6		PR
0088	Arm B	3	Yes	Liver - Segm 6/7	CT scan	9		
0088	Arm B	3	Yes	Liver - Segm 6	CT scan	6		
0088	Arm B	3	Yes	Liver - Segment 2	Spiral-CT	.		
0088	Arm B	3	Yes	Liver - Segment 6	Spiral-CT	13		PD
0162	Arm B	0	No	Liver - Segment 2	Spiral-CT	.	Present	
0162	Arm B	0	Yes	Liver - Segment 8	Spiral-CT	26		
0162	Arm B	1	Yes	Liver - Segment 8	Spiral-CT	11		
0162	Arm B	1	No	Liver - Segment 2	Spiral-CT	.	Present	PR
0162	Arm B	2	Yes	Liver - Segment 8	Spiral-CT	.		
0162	Arm B	2	No	Liver - Segment 2	Spiral-CT	.	Absent	CR
0162	Arm B	3	Yes	Liver - Segment 8	Spiral-CT	.		
0162	Arm B	3	No	Liver - Segment 2	Spiral-CT	.	Absent	CR
0162	Arm B	4	Yes	Liver - Segment 8	Spiral-CT	.		
0162	Arm B	4	No	Liver - Segment 2	Spiral-CT	.	Absent	CR

Patient No.	Treatment Arm	Staging No.	Measurable?	Location	Method	Measurable lesions- Size [mm]	Non-measurable lesions- Tumor type	Overall assessment
0162	Arm B	5	No	Liver - Segment 2	Spiral-CT	.	Absent	
0162	Arm B	5	Yes	Liver - Segment 8	Spiral-CT	.		CR
0162	Arm B	6	No	Liver - Segment 2	Spiral-CT	.	Absent	
0162	Arm B	6	Yes	Liver - Segment 8	Spiral-CT	.		CR
0164	Arm B	0	Yes	Liver - Segment VII	CT scan	20		
0164	Arm B	0	Yes	Liver - SegmentVI	CT scan	14		
0165	Arm B	0	Yes	Liver - Segment VII	MRI scan	23		
0165	Arm B	0	Yes	Liver - Segment VIIb	MRI scan	18		
0165	Arm B	1	Yes	Liver - Segment VIIb	MRI scan	6		
0165	Arm B	1	Yes	Liver - Segment VII	MRI scan	6		PR
0165	Arm B	2	Yes	Liver - Segment VIIb	MRI scan	.		
0165	Arm B	2	Yes	Liver - Segment VII	MRI scan	.		CR
0165	Arm B	3	Yes	Liver - Segment VIIb	MRI scan	.		
0165	Arm B	3	Yes	Liver - Segment VII	MRI scan	.		CR
0165	Arm B	4	Yes	Liver - Segment VIIb	MRI scan	.		
0165	Arm B	4	Yes	Liver - Segment VII	MRI scan	.		CR
0165	Arm B	5	Yes	Liver - Segment VII	MRI scan	.		
0165	Arm B	5	Yes	Liver - Segment VIIb	MRI scan	.		CR
0165	Arm B	6	Yes	Liver - Segment VII	MRI scan	.		
0165	Arm B	6	Yes	Liver - Segment VIIb	MRI scan	.		CR
0167	Arm B	0	Yes	Liver - Segment II, III, IVa, IVb	CT scan	74		
0167	Arm B	1	Yes	Liver - Segment II, III, IVa, IVb	CT scan	56		SD
0167	Arm B	2	Yes	Liver - Segment II, III, IVa, IVb	CT scan	40		PR
0167	Arm B	3	Yes	Liver - Segment II, III, IVa, IVb	CT scan	.		CR
0241	Arm B	0	Yes	Liver - Segment 7	CT scan	44		
0241	Arm B	0	Yes	Liver - Segment 6	CT scan	39		
0241	Arm B	1	Yes	Liver - Segment 6	CT scan	27		
0241	Arm B	1	Yes	Liver - Segment 7	CT scan	24		PR
0241	Arm B	2	Yes	Liver - Segment 7	CT scan	18		
0241	Arm B	2	Yes	Liver - Segment 6	CT scan	24		PR
0241	Arm B	3	Yes	Liver - Segment 6	CT scan	0		
0241	Arm B	3	Yes	Liver - Segment 7	CT scan	0		CR
0241	Arm B	4	Yes	Liver - Segment 6	CT scan	0		
0241	Arm B	4	Yes	Liver - Segment 7	CT scan	0		CR
0242	Arm B	0	Yes	Liver - Segment 8	CT scan	34		

Patient No.	Treatment Arm	Staging No.	Measurable?	Location	Method	Measurable lesions- Size [mm]	Non-measurable lesions- Tumor type	Overall assessment
0242	Arm B	1	Yes	Liver - Segment 8	CT scan	23		PR
0242	Arm B	2	Yes	Liver - Segment 8	CT scan	17		PR
0242	Arm B	3	Yes	Liver - Segment 8	CT scan	0		CR
0242	Arm B	4	Yes	Liver - Segment 8	CT scan	0		CR
0242	Arm B	5	Yes	Liver - Segment 8	CT scan	0		CR
0401	Arm B	0	No	Liver - Segment II of liver	CT scan	.	Present	
0401	Arm B	0	No	Liver - Segment IIIa of liver	CT scan	.	Present	
0401	Arm B	0	No	Liver - Segment IVa of liver	CT scan	.	Present	
0401	Arm B	0	No	Liver - Boundary of segment IVa/IVb of liver	CT scan	.	Present	
0401	Arm B	0	Yes	Liver - Dorsal edge of liver	CT scan	12		
0401	Arm B	1	No	Liver - Segment II of liver	CT scan	.	Absent	
0401	Arm B	1	No	Liver - Segment IVa of liver	CT scan	.	Absent	
0401	Arm B	1	No	Liver - Boundary of segment IVa/IVb of liver	CT scan	.	Absent	
0401	Arm B	1	Yes	Liver - Dorsal edge of liver	CT scan	0		
0401	Arm B	1	No	Liver - Segment IIIa of liver	CT scan	.	Absent	CR
0401	Arm B	2	No	Liver - Boundary of segment IVa/IVb of liver	CT scan	.	Absent	
0401	Arm B	2	No	Liver - Segment IIIa of liver	CT scan	.	Absent	
0401	Arm B	2	No	Liver - Segment IVa of liver	CT scan	.	Absent	
0401	Arm B	2	No	Liver - Segment II of liver	CT scan	.	Absent	
0401	Arm B	2	Yes	Liver - Dorsal edge of liver	CT scan	0		CR
0401	Arm B	3	No	Liver - Segment IVa of liver	CT scan	.	Absent	
0401	Arm B	3	Yes	Liver - Dorsal edge of liver	CT scan	17		
0401	Arm B	3	No	Liver - Boundary of segment IVa/IVb of liver	CT scan	.	Absent	
0401	Arm B	3	No	Liver - Segment II of liver	CT scan	.	Absent	
0401	Arm B	3	No	Liver - Segment IIIa of liver	CT scan	.	Absent	PD

13.2.4 Compliance Data and/or Serum Levels

n.a.

13.2.5 Individual Efficacy and Response Data

Listing 9: EORTC QLQ-C30- Functional scales

Patient-No.	Treatment Arm	Visit	Physical Functioning (PF)	Role Functioning (RF)	Emotional Functioning (EF)	Cognitive Functioning (CF)	Social Functioning (SF)	Global health status / QoL (QL)
0002	Arm A	Before surgery	100.00	83.33	58.33	100.00	100.00	58.33
0083	Arm A	Before surgery	86.67	100.00	66.67	66.67	50.00	83.33
0083	Arm A	Follow-up 2	100.00	100.00	100.00	66.67	83.33	83.33
0083	Arm A	Follow-up 3	100.00	100.00	100.00	66.67	100.00	83.33
0085	Arm A	Preexamination	91.67	100.00	83.33	66.67	66.67	75.00
0085	Arm A	Before surgery	86.67	50.00	75.00	66.67	66.67	66.67
0085	Arm A	Follow-up 1	60.00	16.67	66.67	66.67	66.67	25.00
0085	Arm A	Follow-up 4	73.33	33.33	75.00	50.00	66.67	41.67
0085	Arm A	Follow-up 7	80.00	66.67	75.00	66.67	100.00	58.33
0085	Arm A	Follow-up 10	80.00	66.67	83.33	83.33	100.00	83.33
0085	Arm A	Follow-up 13	86.67	66.67	91.67	66.67	66.67	83.33
0086	Arm A	Preexamination	100.00	100.00	91.67	100.00	100.00	100.00
0086	Arm A	Before surgery	100.00	100.00	91.67	100.00	100.00	100.00
0087	Arm A	Preexamination	80.00	100.00	75.00	100.00	100.00	83.33
0087	Arm A	Follow-up 3	66.67	50.00	58.33	100.00	83.33	66.67
0087	Arm A	Follow-up 6	80.00	66.67	75.00	100.00	100.00	83.33
0087	Arm A	Follow-up 9	86.67	100.00	91.67	100.00	100.00	91.67
0087	Arm A	Follow-up 12	86.67	100.00	91.67	100.00	83.33	91.67
0087	Arm A	Follow-up 14	100.00	100.00	83.33	100.00	100.00	83.33
0089	Arm A	Preexamination	80.00	33.33	83.33	100.00	83.33	58.33
0089	Arm A	Before surgery	86.67	33.33	8.33	100.00	50.00	66.67
0089	Arm A	Cycle 6	86.67	50.00	41.67	66.67	33.33	50.00
0089	Arm A	Cycle 12	80.00	50.00	50.00	100.00	50.00	58.33
0090	Arm A	Preexamination	80.00	33.33	66.67	100.00	100.00	33.33
0090	Arm A	Before surgery	100.00	100.00	33.33	66.67	100.00	83.33
0090	Arm A	Cycle 6	66.67	66.67	41.67	100.00	66.67	33.33
0090	Arm A	Cycle 12	93.33	83.33	50.00	100.00	66.67	50.00
0090	Arm A	Follow-up 4	93.33	83.33	75.00	100.00	100.00	66.67
0090	Arm A	Follow-up 7	100.00	100.00	91.67	100.00	100.00	66.67
0161	Arm A	Before surgery	93.33	33.33	25.00	100.00	50.00	50.00
0163	Arm A	Before surgery	80.00	66.67	44.44	100.00	33.33	66.67
0166	Arm A	Preexamination	86.67	50.00	100.00	100.00	100.00	83.33
0402	Arm A	No questionnaire	.	.	.	.	.	.
0001	Arm B	No questionnaire	.	.	.	.	.	.

Patient-No.	Treatment Arm	Visit	Physical Functioning (PF)	Role Functioning (RF)	Emotional Functioning (EF)	Cognitive Functioning (CF)	Social Functioning (SF)	Global health status / QoL (QL)
0003	Arm B	Preexamination	100.00	100.00	66.67	100.00	100.00	91.67
0003	Arm B	Before surgery	80.00	16.67	41.67	66.67	33.33	58.33
0081	Arm B	Preexamination	100.00	100.00	75.00	100.00	50.00	58.33
0082	Arm B	Preexamination	86.67	100.00	50.00	100.00	100.00	66.67
0082	Arm B	Before surgery	73.33	66.67	66.67	83.33	100.00	75.00
0082	Arm B	Cycle 6	73.33	66.67	75.00	100.00	66.67	58.33
0082	Arm B	Cycle 12	73.33	33.33	66.67	66.67	50.00	58.33
0082	Arm B	Follow-up 3	86.67	100.00	100.00	66.67	100.00	91.67
0082	Arm B	Follow-up 11	100.00	100.00	100.00	100.00	100.00	83.33
0084	Arm B	Before surgery	66.67	33.33	66.67	66.67	33.33	33.33
0088	Arm B	Preexamination	73.33	33.33	100.00	83.33	50.00	50.00
0162	Arm B	No questionnaire	.	.	.	.	.	.
0164	Arm B	Preexamination	86.67	100.00	66.67	100.00	100.00	66.67
0164	Arm B	Cycle 6	86.67	66.67	66.67	100.00	100.00	58.33
0165	Arm B	Preexamination	100.00	100.00	91.67	100.00	83.33	83.33
0167	Arm B	Preexamination	86.67	100.00	66.67	100.00	100.00	83.33
0167	Arm B	Before surgery	86.67	83.33	91.67	100.00	100.00	66.67
0167	Arm B	Cycle 6	86.67	66.67	83.33	100.00	100.00	41.67
0241	Arm B	Preexamination	100.00	100.00	91.67	100.00	100.00	75.00
0241	Arm B	Before surgery	100.00	100.00	83.33	100.00	83.33	83.33
0241	Arm B	Cycle 6	100.00	66.67	83.33	100.00	66.67	83.33
0241	Arm B	Follow-up 6	100.00	100.00	91.67	100.00	100.00	83.33
0241	Arm B	Follow-up 9	100.00	83.33	91.67	100.00	83.33	91.67
0241	Arm B	Follow-up 12	100.00	100.00	100.00	100.00	100.00	83.33
0241	Arm B	Follow-up 14	100.00	83.33	83.33	100.00	100.00	83.33
0242	Arm B	Preexamination	60.00	50.00	75.00	100.00	100.00	50.00
0242	Arm B	Before surgery	46.67	66.67	75.00	83.33	100.00	58.33
0242	Arm B	Cycle 12	33.33	33.33	75.00	66.67	100.00	66.67
0242	Arm B	Follow-up 3	26.67	50.00	66.67	66.67	66.67	50.00
0242	Arm B	Follow-up 6	33.33	33.33	66.67	66.67	83.33	58.33
0242	Arm B	Follow-up 8	53.33	50.00	83.33	66.67	100.00	58.33
0401	Arm B	Preexamination	40.00	50.00	66.67	50.00	66.67	33.33
0401	Arm B	Before surgery	66.67	66.67	58.33	50.00	100.00	33.33

Listing 10: EORTC QLQ-C30- Symptoms scales

Patient-No.	Treatment Arm	Visit	Fatigue (FA)	Nausea / Vomiting (NV)	Pain (PA)	Dyspnoea (DY)	Sleep disturbance (SL)	Constipation (CO)	Diarhoea (DI)	Financial Problems (FI)
0002	Arm A	Before surgery	11.11	0.00	16.67	0.00	66.67	0.00	66.67	0.00
0083	Arm A	Before surgery	33.33	0.00	0.00	33.33	33.33	33.33	0.00	0.00
0083	Arm A	Follow-up 2	33.33	0.00	0.00	33.33	66.67	0.00	33.33	0.00
0083	Arm A	Follow-up 3	0.00	0.00	0.00	33.33	0.00	0.00	0.00	0.00
0085	Arm A	Preexamination	33.33	0.00	16.67	0.00	0.00	0.00	0.00	66.67
0085	Arm A	Before surgery	55.56	0.00	33.33	0.00	33.33	0.00	0.00	100.00
0085	Arm A	Follow-up 1	77.78	0.00	83.33	66.67	0.00	0.00	0.00	66.67
0085	Arm A	Follow-up 4	66.67	0.00	33.33	33.33	0.00	0.00	0.00	66.67
0085	Arm A	Follow-up 7	33.33	0.00	33.33	33.33	0.00	0.00	0.00	33.33
0085	Arm A	Follow-up 10	22.22	0.00	16.67	33.33	0.00	0.00	0.00	33.33
0085	Arm A	Follow-up 13	44.44	0.00	16.67	33.33	0.00	0.00	0.00	33.33
0086	Arm A	Preexamination	0.00	0.00	0.00	0.00	33.33	0.00	33.33	0.00
0086	Arm A	Before surgery	0.00	0.00	0.00	0.00	33.33	0.00	33.33	0.00
0087	Arm A	Preexamination	22.22	0.00	0.00	33.33	0.00	0.00	0.00	0.00
0087	Arm A	Follow-up 3	66.67	16.67	0.00	33.33	33.33	0.00	33.33	33.33
0087	Arm A	Follow-up 6	33.33	0.00	0.00	33.33	33.33	0.00	33.33	0.00
0087	Arm A	Follow-up 9	11.11	0.00	0.00	33.33	0.00	0.00	0.00	0.00
0087	Arm A	Follow-up 12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	33.33
0087	Arm A	Follow-up 14	0.00	0.00	16.67	33.33	0.00	0.00	0.00	0.00
0089	Arm A	Preexamination	33.33	0.00	0.00	0.00	33.33	0.00	0.00	33.33
0089	Arm A	Before surgery	22.22	0.00	16.67	0.00	33.33	0.00	0.00	0.00
0089	Arm A	Cycle 6	33.33	0.00	0.00	0.00	0.00	33.33	100.00	33.33
0089	Arm A	Cycle 12	22.22	0.00	0.00	33.33	0.00	33.33	33.33	33.33
0090	Arm A	Preexamination	44.44	0.00	50.00	66.67	66.67	0.00	0.00	100.00
0090	Arm A	Before surgery	22.22	0.00	0.00	0.00	66.67	0.00	0.00	0.00
0090	Arm A	Cycle 6	66.67	0.00	50.00	66.67	66.67	0.00	100.00	66.67
0090	Arm A	Cycle 12	11.11	0.00	0.00	33.33	66.67	0.00	0.00	100.00
0090	Arm A	Follow-up 4	33.33	50.00	33.33	0.00	33.33	0.00	100.00	100.00
0090	Arm A	Follow-up 7	0.00	0.00	16.67	33.33	33.33	0.00	33.33	100.00
0161	Arm A	Before surgery	55.56	0.00	50.00	0.00	0.00	0.00	0.00	0.00
0163	Arm A	Before surgery	22.22	0.00	0.00	0.00	33.33	0.00	0.00	0.00
0166	Arm A	Preexamination	11.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0402	Arm A	No questionnaire	.	.	.	.	.	.	.	.
0001	Arm B	No questionnaire	.	.	.	.	.	.	.	.

Patient-No.	Treatment Arm	Visit	Fatigue (FA)	Nausea / Vomiting (NV)	Pain (PA)	Dyspnoea (DY)	Sleep disturbance (SL)	Constipation (CO)	Diarhoea (DI)	Financial Problems (FI)
0003	Arm B	Preexamination	0.00	0.00	0.00	0.00	33.33	33.33	0.00	0.00
0003	Arm B	Before surgery	66.67	16.67	33.33	33.33	0.00	0.00	66.67	0.00
0081	Arm B	Preexamination	33.33	0.00	16.67	0.00	33.33	0.00	0.00	0.00
0082	Arm B	Preexamination	11.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0082	Arm B	Before surgery	33.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0082	Arm B	Cycle 6	33.33	16.67	0.00	0.00	0.00	33.33	33.33	0.00
0082	Arm B	Cycle 12	55.56	16.67	0.00	0.00	33.33	33.33	0.00	0.00
0082	Arm B	Follow-up 3	22.22	0.00	0.00	0.00	0.00	33.33	0.00	0.00
0082	Arm B	Follow-up 11	11.11	0.00	0.00	0.00	33.33	0.00	0.00	0.00
0084	Arm B	Before surgery	33.33	0.00	0.00	66.67	66.67	0.00	0.00	0.00
0088	Arm B	Preexamination	44.44	0.00	33.33	0.00	0.00	0.00	0.00	33.33
0162	Arm B	No questionnaire	.	.	.	.	.	.	.	.
0164	Arm B	Preexamination	0.00	0.00	0.00	0.00	33.33	0.00	0.00	0.00
0164	Arm B	Cycle 6	0.00	0.00	0.00	0.00	66.67	0.00	0.00	0.00
0165	Arm B	Preexamination	0.00	0.00	0.00	0.00	0.00	0.00	0.00	33.33
0167	Arm B	Preexamination	11.11	0.00	16.67	33.33	0.00	0.00	33.33	0.00
0167	Arm B	Before surgery	33.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0167	Arm B	Cycle 6	33.33	0.00	0.00	33.33	0.00	0.00	0.00	0.00
0241	Arm B	Preexamination	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0241	Arm B	Before surgery	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0241	Arm B	Cycle 6	0.00	0.00	16.67	0.00	0.00	0.00	33.33	0.00
0241	Arm B	Follow-up 6	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0241	Arm B	Follow-up 9	0.00	0.00	0.00	0.00	0.00	33.33	33.33	0.00
0241	Arm B	Follow-up 12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0241	Arm B	Follow-up 14	0.00	0.00	0.00	0.00	0.00	33.33	33.33	0.00
0242	Arm B	Preexamination	44.44	0.00	16.67	66.67	33.33	0.00	0.00	0.00
0242	Arm B	Before surgery	55.56	0.00	0.00	33.33	33.33	0.00	0.00	0.00
0242	Arm B	Cycle 12	66.67	0.00	0.00	66.67	.	0.00	0.00	0.00
0242	Arm B	Follow-up 3	66.67	0.00	83.33	66.67	66.67	0.00	0.00	0.00
0242	Arm B	Follow-up 6	44.44	0.00	66.67	66.67	66.67	0.00	0.00	0.00
0242	Arm B	Follow-up 8	44.44	0.00	50.00	33.33	33.33	0.00	0.00	0.00
0401	Arm B	Preexamination	66.67	33.33	33.33	0.00	33.33	100.00	0.00	0.00
0401	Arm B	Before surgery	55.56	0.00	16.67	0.00	66.67	33.33	0.00	0.00

Listing 11: EORTC QLQ-LMC21

Patient-No.	Treatment Arm	Visit	Eating	Actibity/Vigour	Pain	Emotional problems	Weight loss	Taste	Dry mouth	Sore mouth/tongue	Peripheral neuropathy	Jaundice	Contact with friends	Talking about feelings	Sex life
0002	Arm A	Before surgery	0.00	0.00	33.33	33.33	33.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0083	Arm A	Before surgery	0.00	55.56	11.11	58.33	0.00	0.00	33.33	0.00	0.00	0.00	33.33	0.00	0.00
0083	Arm A	Follow-up 2	0.00	44.44	33.33	8.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0083	Arm A	Follow-up 3	0.00	33.33	11.11	16.67	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0085	Arm A	Preexamination	0.00	22.22	0.00	33.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	33.33	0.00
0085	Arm A	Before surgery	0.00	44.44	33.33	25.00	0.00	0.00	0.00	0.00	0.00	33.33	0.00	33.33	33.33
0085	Arm A	Follow-up 1	16.67	66.67	0.00	50.00	33.33	100.00	33.33	66.67	66.67	0.00	66.67	66.67	66.67
0085	Arm A	Follow-up 4	0.00	33.33	22.22	41.67	33.33	66.67	33.33	33.33	100.00	0.00	33.33	33.33	33.33
0085	Arm A	Follow-up 7	0.00	33.33	11.11	33.33	0.00	33.33	33.33	0.00	66.67	0.00	0.00	33.33	33.33
0085	Arm A	Follow-up 10	0.00	22.22	0.00	25.00	0.00	33.33	0.00	0.00	0.00	0.00	0.00	33.33	33.33
0085	Arm A	Follow-up 13	0.00	33.33	11.11	33.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	66.67
0086	Arm A	Preexamination	0.00	0.00	0.00	16.67	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0086	Arm A	Before surgery	0.00	0.00	0.00	16.67	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0087	Arm A	Preexamination	0.00	0.00	0.00	8.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0087	Arm A	Follow-up 3	0.00	11.11	0.00	25.00	0.00	0.00	0.00	33.33	0.00	0.00	0.00	0.00	0.00
0087	Arm A	Follow-up 6	0.00	22.22	0.00	25.00	0.00	0.00	0.00	33.33	33.33	0.00	0.00	0.00	0.00
0087	Arm A	Follow-up 9	0.00	22.22	0.00	25.00	0.00	0.00	0.00	0.00	33.33	0.00	0.00	0.00	0.00
0087	Arm A	Follow-up 12	0.00	22.22	0.00	25.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0087	Arm A	Follow-up 14	0.00	0.00	0.00	25.00	0.00	0.00	0.00	0.00	33.33	0.00	0.00	0.00	0.00
0089	Arm A	Preexamination	50.00	44.44	0.00	33.33	66.67	0.00	0.00	0.00	0.00	0.00	0.00	0.00	100.00
0089	Arm A	Before surgery	66.67	77.78	0.00	91.67	100.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	100.00
0089	Arm A	Cycle 6	16.67	44.44	11.11	50.00	0.00	66.67	66.67	66.67	33.33	0.00	0.00	0.00	100.00
0089	Arm A	Cycle 12	50.00	33.33	11.11	50.00	0.00	66.67	66.67	66.67	33.33	0.00	33.33	33.33	100.00
0090	Arm A	Preexamination	0.00	66.67	55.56	66.67	0.00	0.00	0.00	0.00	33.33	0.00	0.00	0.00	100.00
0090	Arm A	Before surgery	16.67	0.00	33.33	66.67	33.33	0.00	0.00	0.00	0.00	0.00	0.00	66.67	100.00
0090	Arm A	Cycle 6	50.00	77.78	66.67	83.33	100.00	66.67	100.00	100.00	100.00	0.00	33.33	33.33	100.00
0090	Arm A	Cycle 12	0.00	33.33	22.22	75.00	0.00	100.00	0.00	0.00	66.67	0.00	0.00	0.00	100.00
0090	Arm A	Follow-up 4	16.67	11.11	44.44	41.67	0.00	100.00	33.33	100.00	100.00	0.00	0.00	0.00	100.00
0090	Arm A	Follow-up 7	0.00	0.00	22.22	33.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	100.00
0161	Arm A	Before surgery	33.33	100.00	0.00	83.33	66.67	0.00	66.67	0.00	0.00	0.00	33.33	0.00	100.00
0163	Arm A	Before surgery	0.00	22.22	0.00	66.67	0.00	0.00	0.00	0.00	0.00	0.00	33.33	33.33	100.00
0166	Arm A	Preexamination	16.67	33.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0402	Arm A	No questionnaire	.	.	.	.	.	.	.	.	.	.	.	.	.
0001	Arm B	No questionnaire	.	.	.	.	.	.	.	.	.	.	.	.	.

Patient-No.	Treatment Arm	Visit	Eating	Actibity/Vigour	Pain	Emotional problems	Weight loss	Taste	Dry mouth	Sore mouth/tongue	Peripheral neuropathy	Jaundice	Contact with friends	Talking about feelings	Sex life
0003	Arm B	Preexamination	33.33	22.22	22.22	33.33	0.00	0.00	33.33	0.00	33.33	0.00	0.00	0.00	0.00
0003	Arm B	Before surgery	16.67	44.44	33.33	50.00	0.00	66.67	0.00	0.00	66.67	0.00	33.33	0.00	33.33
0081	Arm B	Preexamination	.	33.33	33.33	50.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0082	Arm B	Preexamination	0.00	33.33	0.00	58.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0082	Arm B	Before surgery	0.00	22.22	0.00	33.33	0.00	33.33	0.00	33.33	33.33	0.00	0.00	0.00	0.00
0082	Arm B	Cycle 6	33.33	55.56	0.00	33.33	0.00	33.33	0.00	33.33	66.67	0.00	0.00	0.00	0.00
0082	Arm B	Cycle 12	33.33	77.78	22.22	58.33	0.00	33.33	0.00	33.33	33.33	0.00	33.33	66.67	0.00
0082	Arm B	Follow-up 3	0.00	22.22	0.00	8.33	0.00	0.00	0.00	0.00	33.33	0.00	0.00	0.00	0.00
0082	Arm B	Follow-up 11	0.00	11.11	0.00	16.67	0.00	0.00	0.00	0.00	33.33	0.00	0.00	0.00	0.00
0084	Arm B	Before surgery	16.67	77.78	0.00	66.67	0.00	100.00	66.67	66.67	100.00	0.00	33.33	0.00	66.67
0088	Arm B	Preexamination	0.00	55.56	0.00	16.67	33.33	0.00	0.00	0.00	0.00	0.00	33.33	0.00	66.67
0162	Arm B	No questionnaire	.	.	.	.	.	.	.	.	.	.	.	.	.
0164	Arm B	Preexamination	0.00	0.00	0.00	16.67	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0164	Arm B	Cycle 6	0.00	0.00	0.00	33.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0165	Arm B	Preexamination	0.00	0.00	0.00	16.67	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0167	Arm B	Preexamination	0.00	0.00	0.00	83.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0167	Arm B	Before surgery	16.67	33.33	0.00	16.67	0.00	0.00	0.00	0.00	33.33	0.00	0.00	0.00	0.00
0167	Arm B	Cycle 6	0.00	44.44	0.00	41.67	0.00	0.00	33.33	0.00	66.67	0.00	0.00	0.00	0.00
0241	Arm B	Preexamination	0.00	0.00	0.00	16.67	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0241	Arm B	Before surgery	0.00	0.00	0.00	16.67	0.00	0.00	0.00	0.00	33.33	0.00	0.00	0.00	0.00
0241	Arm B	Cycle 6	16.67	11.11	33.33	16.67	33.33	0.00	0.00	66.67	66.67	0.00	0.00	33.33	0.00
0241	Arm B	Follow-up 6	0.00	0.00	0.00	8.33	0.00	0.00	0.00	0.00	33.33	0.00	0.00	0.00	0.00
0241	Arm B	Follow-up 9	0.00	0.00	0.00	8.33	0.00	0.00	0.00	0.00	33.33	0.00	0.00	0.00	0.00
0241	Arm B	Follow-up 12	0.00	0.00	0.00	8.33	0.00	0.00	0.00	0.00	33.33	0.00	0.00	0.00	0.00
0241	Arm B	Follow-up 14	0.00	0.00	0.00	25.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0242	Arm B	Preexamination	16.67	44.44	0.00	16.67	0.00	0.00	0.00	33.33	0.00	0.00	0.00	0.00	33.33
0242	Arm B	Before surgery	16.67	77.78	0.00	25.00	33.33	66.67	0.00	33.33	100.00	0.00	0.00	0.00	66.67
0242	Arm B	Follow-up 3	16.67	66.67	22.22	41.67	0.00	0.00	33.33	0.00	66.67	0.00	0.00	0.00	66.67
0242	Arm B	Follow-up 6	0.00	66.67	22.22	41.67	0.00	0.00	33.33	0.00	33.33	0.00	0.00	0.00	100.00
0242	Arm B	Follow-up 8	16.67	66.67	11.11	41.67	0.00	0.00	33.33	0.00	66.67	0.00	0.00	0.00	100.00
0401	Arm B	Preexamination	50.00	66.67	55.56	33.33	66.67	33.33	100.00	33.33	0.00	0.00	0.00	0.00	0.00
0401	Arm B	Before surgery	0.00	44.44	33.33	58.33	33.33	33.33	33.33	0.00	0.00	0.00	0.00	33.33	0.00

Listing 12: End of treatment

Patient No.	Treatment Arm	Study treatment performed	Premature termination of study therapy (< cycle 12)	Reason for premature termination	Progression	Progression distant metastasis- Organ
0002	Arm A	No				
0083	Arm A	Yes	Yes	Non-tolerable treatment-related toxicity		
0085	Arm A	Yes	Yes	Delay of therapy for more than 4 consecutive weeks caused by treatment-related toxicities		
0086	Arm A	Yes	No			
0087	Arm A	Yes	Yes	Tumor progression	Local	
0089	Arm A	Yes	No			
0090	Arm A	Yes	No			
0161	Arm A	Yes	Yes	Personal wish of the patient		
0163	Arm A	No				
0402	Arm A	No				
0001	Arm B	Yes	Yes	Personal wish of the patient		
0003	Arm B	Yes	No			
0081	Arm B	No				
0082	Arm B	Yes	No			
0084	Arm B	Yes	Yes	Tumor progression	Distant metastasis	Other- Peritoneum
0088	Arm B	Yes	Yes	Tumor progression	Distant metastasis	Other- Liver
0162	Arm B	Yes	No			
0164	Arm B	Yes	Yes	Personal wish of the patient		
0165	Arm B	Yes	No			
0167	Arm B	Yes	No			
0241	Arm B	Yes	No			
0242	Arm B	Yes	No			
0401	Arm B	Yes	No			

Listing 13: Follow-up- Current treatment

Patient No.	Treatment Arm	FU number	Follow-up done	Reason for no FU	Current treatment	Which current treatment	Surgery/Resection result	Relapse or progression	Local/Distant metastases	Progression distant metastasis-Organ
0002	Arm A	Follow-up 1	No	No study patient anymore						
0083	Arm A	Follow-up 1	Yes		No			No		
0083	Arm A	Follow-up 2	Yes		No			No		
0083	Arm A	Follow-up 3	Yes		No			No		
0083	Arm A	Follow-up 4	Yes		No			No		
0083	Arm A	Follow-up 5	Yes		No			No		
0085	Arm A	Follow-up 1	Yes		Yes	Chemotherapy		No		
0085	Arm A	Follow-up 2	Yes		No			No		
0085	Arm A	Follow-up 3	Yes		No			No		
0085	Arm A	Follow-up 4	Yes		No			No		
0085	Arm A	Follow-up 5	Yes		No			No		
0085	Arm A	Follow-up 6	Yes		No			No		
0085	Arm A	Follow-up 7	Yes		No			No		
0085	Arm A	Follow-up 8	Yes		No			No		
0086	Arm A	Follow-up 1	Yes		No			No		
0086	Arm A	Follow-up 2	Yes		Yes	Chemotherapy , Radiotherapy		No		
0086	Arm A	Follow-up 3	Yes		No			No		
0086	Arm A	Follow-up 4	Yes		No			No		

Patient No.	Treatment Arm	FU number	Follow-up done	Reason for no FU	Current treatment	Which current treatment	Surgery/Resection result	Relapse or progression	Local/Distant metastases	Progression distant metastasis-Organ
0086	Arm A	Follow-up 5	Yes		No			No		
0086	Arm A	Follow-up 6	Yes		No			No		
0087	Arm A	Follow-up 1	Yes		Yes	Chemotherapy		No		
0087	Arm A	Follow-up 2	Yes		Yes	Resection of metastasis	R0	No		
0087	Arm A	Follow-up 3	Yes		No			No		
0087	Arm A	Follow-up 4	Yes		No			No		
0087	Arm A	Follow-up 5	Yes		No			No		
0087	Arm A	Follow-up 6	Yes		No			No		
0087	Arm A	Follow-up 7	Yes		No			Yes	Distant metastasis	Other- Hepatic
0089	Arm A	Follow-up 1	Yes		No			No		
0089	Arm A	Follow-up 2	Yes		No			No		
0089	Arm A	Follow-up 3	Yes		No			No		
0089	Arm A	Follow-up 4	Yes		No			No		
0090	Arm A	Follow-up 1	Yes		No			No		
0090	Arm A	Follow-up 2	Yes		No			No		
0161	Arm A	Follow-up 1	No	Due to patient vacation						
0163	Arm A	Follow-up 1	No	The patien has not colorectal metastase. See screening block						
0402	Arm A	Follow-up 1	No	Screen Failure						
0003	Arm B	Follow-up 1	Yes		No			No		

Patient No.	Treatment Arm	FU number	Follow-up done	Reason for no FU	Current treatment	Which current treatment	Surgery/Resection result	Relapse or progression	Local/Distant metastases	Progression distant metastasis-Organ
0003	Arm B	Follow-up 2	Yes		No			No		
0082	Arm B	Follow-up 1	Yes		No			No		
0082	Arm B	Follow-up 2	Yes		No			No		
0082	Arm B	Follow-up 3	Yes		No			No		
0082	Arm B	Follow-up 4	Yes		No			No		
0082	Arm B	Follow-up 5	Yes		No			No		
0082	Arm B	Follow-up 6	Yes		No			No		
0082	Arm B	Follow-up 7	Yes		No			No		
0082	Arm B	Follow-up 8	Yes		No			No		
0082	Arm B	Follow-up 9	Yes		No			No		
0084	Arm B	Follow-up 1	Yes		Yes	Chemotherapy		No		
0084	Arm B	Follow-up 2	Yes		Yes	Chemotherapy		No		
0084	Arm B	Follow-up 3	Yes		Yes	Chemotherapy , Bevacizumab		No		
0084	Arm B	Follow-up 4	Yes		Yes	Chemotherapy , Immunotherapy - Panitumumab		No		
0084	Arm B	Follow-up 5	Yes		Yes	Chemotherapy , Immunotherapy - Panitumumab		No		
0084	Arm B	Follow-up 6	Yes		No			No		
0088	Arm B	Follow-up 1	Yes		Yes	Chemotherapy , Cetuximab		No		
0088	Arm B	Follow-up 2	Yes		Yes	Chemotherapy		No		
0088	Arm B	Follow-up 3	Yes		No			Yes	Distant metastasis	Other- Liver

Patient No.	Treatment Arm	FU number	Follow-up done	Reason for no FU	Current treatment	Which current treatment	Surgery/Resection result	Relapse or progression	Local/Distant metastases	Progression distant metastasis-Organ
0088	Arm B	Follow-up 4	Yes		Yes	Chemotherapy		No		
0162	Arm B	Follow-up 1	Yes		No			No		
0162	Arm B	Follow-up 2	Yes		No			No		
0162	Arm B	Follow-up 3	Yes		No			No		
0162	Arm B	Follow-up 4	Yes		No			No		
0162	Arm B	Follow-up 5	Yes		Yes	Resection of metastasis	R0	No		
0162	Arm B	Follow-up 6	Yes		No			No		
0162	Arm B	Follow-up 7	Yes		No			No		
0165	Arm B	Follow-up 1	Yes		No			No		
0165	Arm B	Follow-up 2	Yes		No			No		
0165	Arm B	Follow-up 3	Yes		No			No		
0165	Arm B	Follow-up 4	Yes		No			No		
0165	Arm B	Follow-up 5	Yes		No			No		
0167	Arm B	Follow-up 1	Yes		No			No		
0167	Arm B	Follow-up 2	Yes		No			No		
0241	Arm B	Follow-up 1	Yes		No			No		
0241	Arm B	Follow-up 2	Yes		No			No		
0241	Arm B	Follow-up 3	Yes		No			No		
0241	Arm B	Follow-up 4	Yes		No			No		
0241	Arm B	Follow-up 5	Yes		No			No		

Patient No.	Treatment Arm	FU number	Follow-up done	Reason for no FU	Current treatment	Which current treatment	Surgery/Resection result	Relapse or progression	Local/Distant metastases	Progression distant metastasis-Organ
0242	Arm B	Follow-up 1	Yes		No			No		
0242	Arm B	Follow-up 2	Yes		No			No		
0242	Arm B	Follow-up 3	Yes		No			No		
0242	Arm B	Follow-up 4	Yes		No			No		
0401	Arm B	Follow-up 1	Yes		Yes	Chemotherapy		No		
0401	Arm B	Follow-up 2	Yes		No			Yes	Distant metastasis	Other- Liver
0401	Arm B	Follow-up 3	Yes		No			No		
0401	Arm B	Follow-up 4	Yes		No			No		

13.2.6 AE Listings (by patient)

Listing 14: Adverse events

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Infusion related reaction	Yes	04MAR2013	04MAR2013	2	Cetuximab	Yes	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Peripheral sensory neuropathy	Yes	01APR2013	15MAY2014	1	Oxaliplatin	No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Platelet count decreased	Yes	11MAR2013	25MAR2013	1	Oxaliplatin , Folinic acid , 5-FU	No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Papulopustular rash	Yes	25MAR2013	09APR2013	2	Cetuximab	No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Hypoxia	Yes	03JAN2013	04JAN2013	4		No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Papulopustular rash	Yes	06MAR2013	25MAR2013	1	Cetuximab	No	Change in toxicity garde/sensitivy or seriousness	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Neutrophil count decreased	Yes	11MAR2013	17MAR2013	2	Oxaliplatin , Folinic acid , 5-FU	No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Nausea	Yes	05MAR2013	08MAR2013	1	Oxaliplatin , Folinic acid , 5-FU	No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Allergic reaction	Yes	04MAR2013	04MAR2013	2	Cetuximab	Yes	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Anemia	Yes	02JAN2013	03JAN2013	2		No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Palmar-plantar erythrodysesthesia syndrome	Yes	25MAR2013	09APR2013	1	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Neutrophil count decreased	Yes	18MAR2013	25MAR2013	3	Oxaliplatin , Folinic acid , 5-FU	Yes	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Platelet count decreased	Yes	02APR2013	22MAY2013	1	Oxaliplatin , Folinic acid , 5-FU	Yes	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Pneumothorax	Yes	04JAN2013	27FEB2013	2		No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Mucositis oral	Yes	25MAR2013	09APR2013	1	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	No	Recovered (AE disappeared)	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Infections and infestations - Other, specify	No	01JAN2013	31JAN2013	1		No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Infections and infestations - Other, specify	Yes	11FEB2013	27FEB2013	3		No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Hallucinations	Yes	03JAN2013	04JAN2013	1		No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Bone marrow hypocellular	Yes	02APR2013	15APR2013	1	Oxaliplatin , 5-FU	Yes	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Vascular disorders - Other, specify	Yes	04JAN2013	05JAN2013	1		No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Gastrointestinal disorders - Other, specify	Yes	02JAN2013	06JAN2013	3		No	Recovered (AE disappeared)	Postoperative complication
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Abdominal pain	No	05JAN2012	15JAN2013	1		No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Aphonia	Yes	06JAN2013	15JAN2013	3		No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Fever	Yes	15JAN2013	09FEB2013	1		No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Platelet count decreased	Yes	02JAN2013	09JAN2013	2		No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Pleural effusion	Yes	16JAN2013	21JAN2013	2		No	Change in toxicity garde/sensitivy or seriousness	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Thromboembolic event	Yes	11FEB2013	27FEB2013	3		No	Recovered (AE disappeared)	Postoperative complication
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Pleural effusion	Yes	21JAN2013	03JUN2013	1		No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Neutrophil count decreased	Yes	06MAY2013	13MAY2013	2	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	Yes	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Papulopustular rash	Yes	29APR2013	22MAY2013	2	Cetuximab	No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Platelet count decreased	Yes	09APR2013	15APR2013	2	Oxaliplatin , Folinic acid , 5-FU	Yes	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0085	Arm A	58	Male	Fever	Yes	04JAN2013	05JAN2013	1		No	Recovered (AE disappeared)	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Asklepios Klinik Barmbek ,Hamburg	0087	Arm A	54	Male	Vomiting	Yes	26JAN2013	26JAN2013	1		No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0087	Arm A	54	Male	Nausea	Yes	26JAN2013	26JAN2013	1		No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0087	Arm A	54	Male	Skin and subcutaneous tissue disorders - Other, specify	Yes	05MAR2013	02JUL2013	1	Cetuximab	No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0087	Arm A	54	Male	Diarrhea	Yes	05MAR2013	06MAR2013	1	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0087	Arm A	54	Male	Gastrointestinal disorders - Other, specify	Yes	26FEB2013	01MAR2013	1		No	Recovered (AE disappeared)	None
Asklepios Klinik Barmbek ,Hamburg	0087	Arm A	54	Male	Hypotension	Yes	26JAN2013	26JAN2013	1		No	Recovered (AE disappeared)	None
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0090	Arm A	58	Male	Diarrhea	Yes	01MAR2014	05MAR2014	3	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	Yes	Recovered (AE disappeared)	None
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0090	Arm A	58	Male	Abdominal pain	Yes	26FEB2014	28FEB2014	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0090	Arm A	58	Male	Thromboembolic event	Yes	05MAR2014	24MAR2014	2		No	Recovered (AE disappeared)	None
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0090	Arm A	58	Male	Abdominal pain	Yes	01MAR2014	01MAR2014	1		No	Recovered (AE disappeared)	None
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0090	Arm A	58	Male	Constipation	Yes	27FEB2014	28FEB2014	1		No	Recovered (AE disappeared)	None
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0090	Arm A	58	Male	Pain	Yes	14NOV2013	21NOV2013	2		No	Recovered (AE disappeared)	None
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0090	Arm A	58	Male	Platelet count decreased	Yes	24JAN2014	31JAN2014	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0090	Arm A	58	Male	Diarrhea	Yes	14JAN2014	30JAN2014	2	5-FU	Yes	Recovered (AE disappeared)	None
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0090	Arm A	58	Male	Diarrhea	Yes	17DEC2013	17DEC2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0090	Arm A	58	Male	Nausea	Yes	17DEC2013	17DEC2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0090	Arm A	58	Male	Rash acneiform	Yes	23DEC2013	01MAR2014	2	Cetuximab	No	Recovered (AE disappeared)	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0090	Arm A	58	Male	Paresthesia	Yes	30DEC2013	29JAN2015	1	Oxaliplatin	Yes	Recovered (AE disappeared)	None
Universitätsklinikum Bonn ,Bonn	0089	Arm A	50	Female	Gum infection	Yes	05NOV2013	.	1	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	No	Not yet recovered	None
Universitätsklinikum Bonn ,Bonn	0089	Arm A	50	Female	Neoplasms benign, malignant and unspecified (incl cysts and polyps) - Other, specify	Yes	15NOV2013	.	1		No	Not yet recovered	None
Universitätsklinikum Bonn ,Bonn	0089	Arm A	50	Female	Fever	Yes	22MAY2013	23MAY2013	1		No	Recovered (AE disappeared)	None
Universitätsklinikum Bonn ,Bonn	0089	Arm A	50	Female	Pain	Yes	21MAY2013	27MAY2013	2		No	Recovered (AE disappeared)	None
Universitätsklinikum Bonn ,Bonn	0089	Arm A	50	Female	Dyspnea	Yes	01JUN2013	05JUN2013	1		No	Recovered (AE disappeared)	None
Universitätsklinikum Bonn ,Bonn	0089	Arm A	50	Female	Wound infection	Yes	24MAY2013	02JUL2013	2		No	Recovered (AE disappeared)	None
Universitätsklinikum Bonn ,Bonn	0089	Arm A	50	Female	Rash acneiform	Yes	04JUL2013	.	1	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	No	Not yet recovered	None
Universitätsklinikum Bonn ,Bonn	0089	Arm A	50	Female	Hepatobiliary disorders - Other, specify	Yes	21MAY2013	05JUN2013	1		No	Recovered (AE disappeared)	None
Universitätsklinikum Bonn ,Bonn	0089	Arm A	50	Female	Hepatobiliary disorders - Other, specify	Yes	28MAY2013	02JUL2013	1		No	Recovered (AE disappeared)	None
Universitätsklinikum Bonn ,Bonn	0089	Arm A	50	Female	Leukocytosis	Yes	21MAY2013	22MAY2013	3		No	Recovered (AE disappeared)	None
Universitätsklinikum Bonn ,Bonn	0089	Arm A	50	Female	Platelet count decreased	Yes	27MAY2013	09JUL2013	2		No	Recovered (AE disappeared)	None
Universitätsklinikum Bonn ,Bonn	0089	Arm A	50	Female	Anemia	No	02APR2013	06AUG2013	2	Oxaliplatin , Folinic acid , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinikum Bonn ,Bonn	0089	Arm A	50	Female	Diarrhea	Yes	15AUG2013	18AUG2013	1	Oxaliplatin , Folinic acid , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinikum Bonn ,Bonn	0089	Arm A	50	Female	Rash acneiform	Yes	27AUG2013	.	2	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	No	Not yet recovered	None
Universitätsklinikum Erlangen ,Erlangen	0083	Arm A	71	Male	Abdominal infection	Yes	18OCT2012	26OCT2012	3	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Universitätsklinikum Erlangen ,Erlangen	0083	Arm A	71	Male	Diarrhea	Yes	27NOV2012	22DEC2012	3	Oxaliplatin , 5-FU	Yes	Recovered (AE disappeared)	None
Universitätsklinikum Erlangen ,Erlangen	0083	Arm A	71	Male	Blood and lymphatic system disorders - Other, specify	Yes	18OCT2012	19OCT2012	2	Cetuximab , Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinikum Erlangen ,Erlangen	0083	Arm A	71	Male	Allergic reaction	Yes	04OCT2012	04OCT2012	2	Cetuximab	Yes	Recovered (AE disappeared)	None
Universitätsklinikum Erlangen ,Erlangen	0083	Arm A	71	Male	Diarrhea	Yes	12OCT2012	26OCT2012	3	Oxaliplatin , 5-FU	Yes	Recovered (AE disappeared)	None
Universitätsklinikum Erlangen ,Erlangen	0083	Arm A	71	Male	Blood and lymphatic system disorders - Other, specify	Yes	15OCT2012	18OCT2012	1	Cetuximab , Oxaliplatin , 5-FU	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinikum Erlangen ,Erlangen	0083	Arm A	71	Male	Pleural effusion	Yes	07AUG2012	09AUG2012	2		No	Recovered (AE disappeared)	Postoperative complication
Universitätsklinikum Erlangen ,Erlangen	0083	Arm A	71	Male	Bronchial infection	Yes	27NOV2012	22DEC2012	4	Oxaliplatin , 5-FU	Yes	Recovered (AE disappeared)	None
Universitätsklinikum Erlangen ,Erlangen	0083	Arm A	71	Male	Mucositis oral	Yes	27NOV2012	22DEC2012	1	Oxaliplatin , 5-FU	Yes	Recovered (AE disappeared)	None
Universitätsklinikum Erlangen ,Erlangen	0083	Arm A	71	Male	Thrombotic thrombocytopenic purpura	Yes	21NOV2012	27NOV2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinikum Erlangen ,Erlangen	0083	Arm A	71	Male	Edema trunk	Yes	07AUG2012	09AUG2012	1		No	Recovered (AE disappeared)	Postoperative complication
Universitätsklinikum Jena ,Jena	0086	Arm A	64	Male	Biliary anastomotic leak	Yes	18FEB2013	.	1		No	Unknown at end of study	None
Universitätsklinikum Jena ,Jena	0086	Arm A	64	Male	Cardiac disorders - Other, specify	Yes	01MAR2013	.	3		No	Not yet recovered at end of study	None
Universitätsklinikum Jena ,Jena	0086	Arm A	64	Male	Thromboembolic event	Yes	19FEB2013	.	1		No	Unknown at end of study	None
Universitätsklinikum Jena ,Jena	0086	Arm A	64	Male	Fever	Yes	19APR2013	23APR2013	2		No	Recovered (AE disappeared)	None
Universitätsklinikum Jena ,Jena	0086	Arm A	64	Male	Gastrointestinal disorders - Other, specify	Yes	10MAY2013	27MAY2014	1		No	Recovered (AE disappeared)	None
Universitätsklinikum Jena ,Jena	0086	Arm A	64	Male	Thromboembolic event	Yes	18FEB2013	.	3		No	Unknown at end of study	Postoperative complication
Universitätsklinikum Jena ,Jena	0086	Arm A	64	Male	Visceral arterial ischemia	Yes	30AUG2013	08NOV2013	2		No	Recovered with sequelae	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Universitätsklinikum Jena ,Jena	0086	Arm A	64	Male	Febrile neutropenia	Yes	23APR2013	25APR2013	3		No	Recovered (AE disappeared)	None
Universitätsklinikum Jena ,Jena	0086	Arm A	64	Male	Blood and lymphatic system disorders - Other, specify	Yes	10MAY2013	.	2		No	Unknown at end of study	None
Universitätsklinikum Jena ,Jena	0086	Arm A	64	Male	Hypocalcemia	Yes	02APR2013	19APR2013	1		No	Recovered (AE disappeared)	None
Universitätsklinikum Jena ,Jena	0086	Arm A	64	Male	Paresthesia	Yes	07JUN2013	.	1		No	Unknown at end of study	None
Universitätsklinikum Jena ,Jena	0086	Arm A	64	Male	Rash acneiform	Yes	06FEB2013	.	2	Cetuximab	No	Unknown at end of study	None
Universitätsklinikum der RWTH Aachen ,Aachen	0161	Arm A	72	Male	Mucositis oral	Yes	30NOV2011	11JAN2012	3	Cetuximab	Yes	Recovered (AE disappeared)	None
Universitätsklinikum der RWTH Aachen ,Aachen	0161	Arm A	72	Male	Rash acneiform	Yes	09NOV2011	29FEB2012	3	Cetuximab	Yes	Recovered (AE disappeared)	None
Universitätsklinikum der RWTH Aachen ,Aachen	0161	Arm A	72	Male	Thrombotic thrombocytopenic purpura	Yes	14DEC2011	18JAN2012	1	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	Yes	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Peripheral sensory neuropathy	Yes	16AUG2013	20OCT2013	1	Oxaliplatin	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Alopecia	Yes	27AUG2013	05MAR2014	2	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Pain	Yes	13AUG2013	26AUG2013	1		No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Peripheral sensory neuropathy	Yes	16DEC2013	27APR2014	3	Oxaliplatin	Yes	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Dysgeusia	Yes	28OCT2013	03NOV2013	1	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Rash acneiform	Yes	28OCT2013	01DEC2013	2	Cetuximab	No	Change in toxicity garde/sensitivy or seriousness	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Skin and subcutaneous tissue disorders - Other, specify	Yes	28OCT2013	03NOV2013	1	Oxaliplatin	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Hematoma	Yes	29OCT2013	18NOV2013	2		No	Recovered (AE disappeared)	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Bruising	Yes	29OCT2013	10NOV2013	1		No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Hypertension	Yes	18NOV2013	21NOV2013	3	5-FU	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Peripheral sensory neuropathy	Yes	18NOV2013	15DEC2013	1	Oxaliplatin	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Pain	Yes	15NOV2013	24NOV2013	3		No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Hypertension	Yes	16DEC2013	05JAN2014	3	5-FU	Yes	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Rash acneiform	Yes	02DEC2013	15DEC2013	3	Cetuximab	No	Change in toxicity garde/sensitivy or seriousness	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Rash acneiform	Yes	16DEC2013	05JAN2014	2	Cetuximab	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Palmar-plantar erythrodysesthesia syndrome	Yes	16DEC2013	22DEC2013	2	Oxaliplatin	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Fatigue	Yes	25NOV2013	28NOV2013	2	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Hypertension	Yes	20JAN2014	05MAR2014	3	5-FU	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Rash acneiform	Yes	06JAN2014	19JAN2014	3	Cetuximab	Yes	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Fatigue	Yes	19DEC2013	05JAN2014	1	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Palmar-plantar erythrodysesthesia syndrome	Yes	13JAN2014	26JAN2014	2	Oxaliplatin	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Rash acneiform	Yes	20JAN2014	05MAR2014	2	Cetuximab	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Pruritus	Yes	20JAN2014	26JAN2014	2	Cetuximab	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Nausea	Yes	01JUN2013	01JUN2013	1	Cetuximab , Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Hypertension	Yes	05JUN2013	06JUN2013	3		No	Recovered (AE disappeared)	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Fatigue	Yes	06JUN2013	14AUG2013	1	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Peripheral sensory neuropathy	Yes	29MAY2013	31MAY2013	1	Oxaliplatin	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Rash acneiform	Yes	08JUN2013	03JUL2013	2	Cetuximab	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Hypertension	Yes	07JUN2013	15JUN2013	3		No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Hypertension	Yes	21JUN2013	03JUL2013	3		No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Dysgeusia	Yes	14JUN2013	24AUG2013	1	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Peripheral sensory neuropathy	Yes	14JUN2013	26JUL2013	1	Oxaliplatin	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Rash acneiform	Yes	04JUL2013	24JUL2013	1	Oxaliplatin	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Skin and subcutaneous tissue disorders - Other, specify	Yes	11JUL2013	01SEP2013	1	Cetuximab	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Rash acneiform	Yes	25JUL2013	07AUG2013	2	Cetuximab	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Skin and subcutaneous tissue disorders - Other, specify	Yes	25JUL2013	01SEP2013	1	Cetuximab	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Peripheral sensory neuropathy	Yes	27JUL2013	30JUL2013	2	Oxaliplatin	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Mucositis oral	Yes	01AUG2013	07AUG2013	2	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Peripheral sensory neuropathy	Yes	01AUG2013	07AUG2013	1	Oxaliplatin	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Rash acneiform	Yes	08AUG2013	26AUG2013	1	Cetuximab	No	Recovered (AE disappeared)	None
Helios Klinikum Berlin - Klinikum Buch ,Berlin	0242	Arm B	70	Male	Rash acneiform	Yes	27AUG2013	15SEP2013	2	Cetuximab	No	Recovered (AE disappeared)	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Klinikum der J.-W. Goethe-Universität Frankfurt a.M. ,Frankfurt/Main	0165	Arm B	68	Male	Nervous system disorders - Other, specify	Yes	10FEB2014	.	2	Oxaliplatin	Yes	Unknown at end of study	None
Klinikum der J.-W. Goethe-Universität Frankfurt a.M. ,Frankfurt/Main	0165	Arm B	68	Male	Rash acneiform	Yes	16DEC2013	06JAN2014	2	Cetuximab	Yes	Recovered (AE disappeared)	None
Klinikum der J.-W. Goethe-Universität Frankfurt a.M. ,Frankfurt/Main	0165	Arm B	68	Male	Nausea	Yes	16JUL2013	21AUG2013	1	5-FU	Yes	Recovered (AE disappeared)	None
Klinikum der J.-W. Goethe-Universität Frankfurt a.M. ,Frankfurt/Main	0165	Arm B	68	Male	Chest pain - cardiac	Yes	19JUL2013	19JUL2013	2	Folinic acid , 5-FU	Yes	Recovered (AE disappeared)	None
Klinikum der J.-W. Goethe-Universität Frankfurt a.M. ,Frankfurt/Main	0165	Arm B	68	Male	Rash acneiform	Yes	27AUG2013	03SEP2013	2	Cetuximab	Yes	Recovered (AE disappeared)	None
Klinikum der J.-W. Goethe-Universität Frankfurt a.M. ,Frankfurt/Main	0165	Arm B	68	Male	Chest pain - cardiac	Yes	24JUL2013	07AUG2013	2	Folinic acid , 5-FU	Yes	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Rectal obstruction	Yes	25APR2013	04MAY2013	1		No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Mucositis oral	Yes	06APR2013	12APR2013	1	Oxaliplatin , 5-FU	No	Change in toxicity garde/sensitivy or seriousness	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Alanine aminotransferase increased	Yes	07MAY2013	28AUG2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Rectal obstruction	Yes	06JUN2013	10JUN2013	1		No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Nausea	Yes	30MAY2013	31MAY2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Nausea	Yes	04JUN2013	06JUN2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Rash acneiform	Yes	10APR2013	16APR2013	2	Cetuximab	No	Change in toxicity garde/sensitivy or seriousness	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Diarrhea	Yes	15APR2013	16APR2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Infections and infestations - Other, specify	Yes	08APR2013	16APR2013	2		No	Recovered (AE disappeared)	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Platelet count decreased	Yes	04JUN2013	08JUL2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Anorexia	Yes	03APR2013	16APR2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Nausea	Yes	23APR2013	02MAY2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Anorexia	Yes	25APR2013	13MAY2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Aspartate aminotransferase increased	Yes	07MAY2013	28AUG2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	GGT increased	Yes	07MAY2013	.	1	Oxaliplatin , 5-FU	No	Not yet recovered at end of study	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	White blood cell decreased	Yes	14MAY2013	28MAY2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Neutrophil count decreased	Yes	14MAY2013	04JUN2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Nausea	Yes	03APR2013	06APR2013	2	Oxaliplatin , 5-FU	No	Change in toxicity garde/sensitivy or seriousness	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Anorexia	Yes	29MAY2013	.	1	Oxaliplatin , 5-FU	No	Not yet recovered at end of study	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Rectal obstruction	Yes	11MAY2013	15MAY2013	1		No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Nausea	Yes	16JUN2013	20JUN2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	White blood cell decreased	Yes	01JUL2013	08JUL2013	1	Oxaliplatin , 5-FU	Yes	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Blood bilirubin increased	Yes	18JUN2013	26AUG2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Nausea	Yes	14JUN2013	15JUN2013	2	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Nausea	Yes	09MAY2013	13MAY2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Mucositis oral	Yes	18APR2013	06MAY2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Nausea	Yes	12JUN2013	13JUN2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Neutrophil count decreased	Yes	01JUL2013	08JUL2013	2	Oxaliplatin , 5-FU	Yes	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Fever	Yes	25AUG2013	29AUG2013	1		No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Rash acneiform	Yes	17APR2013	15JUL2013	1	Cetuximab	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Nausea	Yes	01JUN2013	03JUN2013	2	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Mucositis oral	Yes	15JUN2013	28JUN2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Mucositis oral	Yes	05JUN2013	08JUN2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Mucositis oral	Yes	10MAY2013	28MAY2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Abdominal pain	Yes	05APR2013	10APR2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Mucositis oral	Yes	13APR2013	17APR2013	2	Oxaliplatin , 5-FU	No	Change in toxicity garde/sensitivy or seriousness	None
Klinikum der Otto-von-Guericke Universität Magdeburg ,Magdeburg	0088	Arm B	53	Male	Nausea	Yes	07APR2013	10APR2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0241	Arm B	69	Male	Breast infection	Yes	16JUL2012	19JUL2012	2		No	Recovered (AE disappeared)	None
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0241	Arm B	69	Male	Rash acneiform	Yes	22JUN2012	20SEP2012	2	Cetuximab	No	Recovered (AE disappeared)	None
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0241	Arm B	69	Male	Productive cough	Yes	30JUN2012	15JUL2012	1		No	Recovered (AE disappeared)	None
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0241	Arm B	69	Male	Rash acneiform	Yes	13DEC2012	13MAR2013	2	Cetuximab	No	Recovered (AE disappeared)	None
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0241	Arm B	69	Male	Mucositis oral	Yes	19DEC2012	30JAN2013	2	5-FU	No	Recovered (AE disappeared)	None
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0241	Arm B	69	Male	Blood and lymphatic system disorders - Other, specify	Yes	11JUL2012	18JUL2012	2	Oxaliplatin , 5-FU	Yes	Recovered (AE disappeared)	None
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0241	Arm B	69	Male	Conjunctivitis	Yes	15JAN2013	21JAN2013	1	Cetuximab	No	Recovered (AE disappeared)	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Klinikum der Stadt Ludwigshafen am Rhein gGmbH ,Ludwigshafen	0241	Arm B	69	Male	Diarrhea	Yes	16JUL2012	17JUL2012	1	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	No	Recovered (AE disappeared)	None
Klinikum rechts der Isar ,München	0167	Arm B	64	Female	Pain in extremity	No	.	.	1	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	No	Not yet recovered at end of study	None
Klinikum rechts der Isar ,München	0167	Arm B	64	Female	Abdominal pain	No	.	20JUN2014	1	Cetuximab , Folinic acid , 5-FU	No	Recovered (AE disappeared)	None
Klinikum rechts der Isar ,München	0167	Arm B	64	Female	Investigations - Other, specify	Yes	01OCT2013	19SEP2014	2		No	Recovered (AE disappeared)	None
Klinikum rechts der Isar ,München	0167	Arm B	64	Female	Skin and subcutaneous tissue disorders - Other, specify	Yes	28OCT2013	20JUN2014	2	Cetuximab	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Alopecia	Yes	05JUN2012	08JAN2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Rash acneiform	Yes	29OCT2012	12NOV2012	2	Cetuximab	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Neutrophil count decreased	Yes	12JUN2012	19JUN2012	2	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Peripheral sensory neuropathy	Yes	02JAN2013	15APR2013	2	Oxaliplatin	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Rash acneiform	Yes	16MAY2012	21MAY2012	1	Cetuximab	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Nausea	No	02MAY2012	02MAY2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Peripheral sensory neuropathy	Yes	20NOV2012	01JAN2013	3	Oxaliplatin	Yes	Change in toxicity garde/sensitivy or seriousness	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Rash acneiform	Yes	12JUN2012	16JUL2012	2	Cetuximab	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Nausea	Yes	23OCT2012	19NOV2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Neutrophil count decreased	Yes	05JUN2012	12JUN2012	3	Oxaliplatin , 5-FU	Yes	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Mucositis oral	Yes	30MAY2012	04JUN2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Nausea	Yes	24JUL2012	.	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Neutrophil count decreased	Yes	13NOV2012	19NOV2012	3	Oxaliplatin , 5-FU	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Fatigue	Yes	06NOV2012	11NOV2012	2	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Peripheral sensory neuropathy	Yes	17OCT2012	28OCT2012	1	Oxaliplatin	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Dizziness	Yes	17JUL2012	.	1		No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Fatigue	Yes	30OCT2012	03NOV2012	2	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Diarrhea	Yes	28MAY2012	04JUN2012	3	Oxaliplatin , 5-FU	Yes	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Peripheral sensory neuropathy	Yes	05JUN2012	11JUN2012	1	Oxaliplatin	No	Recovered (AE disappeared)	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Rash acneiform	Yes	22MAY2012	29MAY2012	2	Cetuximab	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Dry skin	Yes	08JAN2013	.	2	Cetuximab	No	Not yet recovered at end of study	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Fatigue	Yes	03JUL2012	23JUL2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Fatigue	Yes	04DEC2012	09DEC2012	2	5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Neutrophil count decreased	Yes	11DEC2012	17DEC2012	1	5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Peripheral sensory neuropathy	Yes	13NOV2012	19NOV2012	1	Oxaliplatin	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Neutrophil count decreased	Yes	20NOV2012	25NOV2012	2	5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Rash acneiform	Yes	13NOV2012	.	1	Cetuximab	No	Not yet recovered	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Neutrophil count decreased	Yes	05NOV2012	12NOV2012	3	Oxaliplatin , Folinic acid , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Rash acneiform	Yes	17JUL2012	.	1	Cetuximab	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Dry skin	Yes	10JUL2012	.	2	Cetuximab	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Neutrophil count decreased	Yes	03JUL2012	09JUL2012	2	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Rash acneiform	Yes	30MAY2012	11JUN2012	1	Cetuximab	No	Change in toxicity garde/sensitivy or seriousness	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	White blood cell decreased	Yes	05NOV2012	19NOV2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Peripheral sensory neuropathy	Yes	29OCT2012	12NOV2012	2	Oxaliplatin	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Nausea	Yes	11JUL2012	15JUL2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	White blood cell decreased	Yes	05JUN2012	11JUN2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0082	Arm B	67	Female	Constipation	Yes	04DEC2012	10DEC2012	1	5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0084	Arm B	69	Male	Hyperglycemia	Yes	07NOV2012	12NOV2012	3		No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0084	Arm B	69	Male	Investigations - Other, specify	Yes	30AUG2012	30AUG2012	3	Cetuximab	Yes	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0084	Arm B	69	Male	Peripheral sensory neuropathy	Yes	06SEP2012	11SEP2012	1	Oxaliplatin	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0084	Arm B	69	Male	Peripheral sensory neuropathy	Yes	19SEP2012	25SEP2012	1	Oxaliplatin	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0084	Arm B	69	Male	Skin and subcutaneous tissue disorders - Other, specify	Yes	19SEP2012	25SEP2012	1	Cetuximab	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0084	Arm B	69	Male	Platelet count decreased	Yes	26SEP2012	.	1	Oxaliplatin , Folinic acid	No	Not yet recovered	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0084	Arm B	69	Male	Thromboembolic event	Yes	04OCT2012	.	3	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	No	Not yet recovered	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Neutrophil count decreased	Yes	27JUN2012	03JUL2012	2	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Peripheral sensory neuropathy	Yes	05JUL2012	08JUL2012	1	Oxaliplatin	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Skin and subcutaneous tissue disorders - Other, specify	Yes	25JUL2012	31JUL2012	1	Cetuximab	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Dry skin	Yes	04JUL2012	10JUL2012	1	Cetuximab	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Rash acneiform	Yes	06JUN2012	10JUL2012	1	Cetuximab	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	White blood cell decreased	Yes	01AUG2012	07AUG2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Blood and lymphatic system disorders - Other, specify	Yes	27JUN2012	03JUL2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Peripheral sensory neuropathy	Yes	24OCT2012	.	1	Oxaliplatin	No	Not yet recovered	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Neutrophil count decreased	Yes	01AUG2012	27AUG2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Alopecia	Yes	17OCT2012	.	1	Oxaliplatin , 5-FU	No	Not yet recovered	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Anemia	Yes	08SEP2012	03OCT2012	2		No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	White blood cell decreased	Yes	11JUL2012	17JUL2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Anemia	Yes	23MAY2012	29MAY2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	White blood cell decreased	Yes	07NOV2012	13NOV2012	2	Oxaliplatin , 5-FU	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	White blood cell decreased	Yes	25JUL2012	31JUL2012	2	Oxaliplatin , 5-FU	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Alopecia	Yes	18JUL2012	07AUG2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Platelet count decreased	Yes	23MAY2012	29MAY2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Neutrophil count decreased	Yes	11JUL2012	17JUL2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Constipation	Yes	04OCT2012	16OCT2012	1		No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Anemia	Yes	06SEP2012	07SEP2012	1		No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Anemia	Yes	04OCT2012	.	1	Oxaliplatin , 5-FU	No	Not yet recovered	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Rash acneiform	Yes	24OCT2012	.	1	Oxaliplatin , 5-FU	No	Not yet recovered	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	White blood cell decreased	Yes	30MAY2012	06JUN2012	2	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	White blood cell decreased	Yes	17OCT2012	23OCT2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Skin and subcutaneous tissue disorders - Other, specify	Yes	20NOV2012	.	2	Cetuximab	No	Not yet recovered	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Neutrophil count decreased	Yes	25JUL2012	31JUL2012	2	Oxaliplatin , 5-FU	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	White blood cell decreased	Yes	28NOV2012	05DEC2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Neutrophil count decreased	Yes	06JUN2012	12JUN2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	White blood cell decreased	Yes	14NOV2012	19NOV2012	1	Oxaliplatin , 5-FU	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	White blood cell decreased	Yes	20NOV2012	27NOV2012	2	Oxaliplatin , 5-FU	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Neutrophil count decreased	Yes	30MAY2012	05JUN2012	3	Oxaliplatin , 5-FU	Yes	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Dry skin	Yes	07NOV2012	.	1	Cetuximab	No	Not yet recovered	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Peripheral sensory neuropathy	Yes	07JUN2012	10JUN2012	1	Oxaliplatin	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	White blood cell decreased	Yes	27JUN2012	03JUL2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Neutrophil count decreased	Yes	24OCT2012	.	1	Oxaliplatin , 5-FU	No	Not yet recovered	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Platelet count decreased	Yes	28NOV2012	05DEC2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Dry skin	Yes	18JUL2012	07AUG2012	1	Cetuximab	No	Recovered (AE disappeared)	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	White blood cell decreased	Yes	01NOV2012	07NOV2012	1	Oxaliplatin , 5-FU	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinik Carl Gustav Carus der Technischen Universität Dresden ,Dresden	0162	Arm B	56	Female	Platelet count decreased	Yes	04JUL2012	07AUG2012	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinikum Jena ,Jena	0003	Arm B	60	Male	Paresthesia	Yes	30OCT2013	06MAR2014	1	Oxaliplatin , 5-FU	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinikum Jena ,Jena	0003	Arm B	60	Male	Rash acneiform	Yes	02APR2014	.	1	Cetuximab	No	Not yet recovered at end of study	None
Universitätsklinikum Jena ,Jena	0003	Arm B	60	Male	Abdominal infection	Yes	20FEB2014	25FEB2014	3		No	Recovered (AE disappeared)	None
Universitätsklinikum Jena ,Jena	0003	Arm B	60	Male	Diarrhea	Yes	15FEB2014	28FEB2014	2	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	Yes	Recovered (AE disappeared)	None
Universitätsklinikum Jena ,Jena	0003	Arm B	60	Male	Nausea	Yes	15FEB2014	28FEB2014	1	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	Yes	Recovered (AE disappeared)	None
Universitätsklinikum Jena ,Jena	0003	Arm B	60	Male	Hoarseness	Yes	02OCT2013	.	1	5-FU	No	Not yet recovered at end of study	None
Universitätsklinikum Jena ,Jena	0003	Arm B	60	Male	Paresthesia	Yes	07MAR2014	24MAR2014	2	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinikum Jena ,Jena	0003	Arm B	60	Male	Paresthesia	Yes	02APR2014	.	1	Oxaliplatin , 5-FU	No	Not yet recovered at end of study	None
Universitätsklinikum Jena ,Jena	0003	Arm B	60	Male	Rash acneiform	Yes	22NOV2013	17MAR2014	2	5-FU	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinikum Jena ,Jena	0003	Arm B	60	Male	Rash acneiform	Yes	25MAR2014	01APR2014	2	Cetuximab	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinikum Jena ,Jena	0003	Arm B	60	Male	Rash acneiform	Yes	18MAR2014	24MAR2014	3	Cetuximab	Yes	Change in toxicity garde/sensitivy or seriousness	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Universitätsklinikum Jena ,Jena	0164	Arm B	70	Female	Mucositis oral	Yes	21JUN2013	.	2	Folinic acid	Yes	Not yet recovered at end of study	None
Universitätsklinikum Jena ,Jena	0164	Arm B	70	Female	Palmar-plantar erythrodysesthesia syndrome	Yes	02AUG2013	.	2	5-FU	Yes	Unknown at end of study	None
Universitätsklinikum Jena ,Jena	0164	Arm B	70	Female	Nausea	Yes	14JUN2013	21JUN2013	1	Cetuximab , Oxaliplatin	No	Recovered (AE disappeared)	None
Universitätsklinikum Jena ,Jena	0164	Arm B	70	Female	Diarrhea	Yes	16AUG2013	01SEP2013	1	5-FU	No	Recovered (AE disappeared)	None
Universitätsklinikum Jena ,Jena	0164	Arm B	70	Female	Hepatobiliary disorders - Other, specify	Yes	06SEP2013	.	2		No	Not yet recovered at end of study	None
Universitätsklinikum Jena ,Jena	0164	Arm B	70	Female	Fatigue	Yes	16AUG2013	01SEP2013	2	Cetuximab , Oxaliplatin	Yes	Recovered (AE disappeared)	None
Universitätsklinikum Jena ,Jena	0164	Arm B	70	Female	Paresthesia	Yes	21JUN2013	.	1	Oxaliplatin	No	Not yet recovered at end of study	None
Universitätsklinikum Jena ,Jena	0164	Arm B	70	Female	Dehydration	Yes	02AUG2013	05SEP2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinikum Jena ,Jena	0164	Arm B	70	Female	Rash acneiform	Yes	02AUG2013	.	3	5-FU	Yes	Not yet recovered at end of study	None
Universitätsklinikum Jena ,Jena	0164	Arm B	70	Female	Vascular disorders - Other, specify	Yes	18JUL2013	.	2		No	Not yet recovered at end of study	None
Universitätsklinikum Jena ,Jena	0164	Arm B	70	Female	Fatigue	Yes	25JUL2013	30JUL2013	2	Cetuximab	Yes	Recovered (AE disappeared)	None
Universitätsklinikum Jena ,Jena	0164	Arm B	70	Female	Rash acneiform	Yes	21JUN2013	01AUG2013	1	Cetuximab , Oxaliplatin	No	Change in toxicity garde/sensitivy or seriousness	None
Universitätsklinikum Jena ,Jena	0164	Arm B	70	Female	Vertigo	Yes	21JUN2013	28JUN2013	1	Oxaliplatin , 5-FU	No	Recovered (AE disappeared)	None
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	Pain	Yes	06DEC2012	06DEC2012	1		No	Recovered (AE disappeared)	None
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	Constipation	Yes	05DEC2012	22JAN2013	2		No	Recovered (AE disappeared)	None
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	Abdominal pain	Yes	06NOV2012	.	1		No	Recovered (AE disappeared)	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	Gynecomastia	Yes	06NOV2012	.	1		No	Not yet recovered at end of study	None
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	Hypertension	Yes	07NOV2012	07NOV2012	2		No	Recovered (AE disappeared)	Intraoperative complication
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	General disorders and administration site conditions - Other, specify	Yes	12DEC2012	.	2	Cetuximab , Oxaliplatin , Folinic acid , 5-FU	Yes	Not yet recovered at end of study	None
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	Pain	Yes	07NOV2012	19NOV2012	1		No	Recovered (AE disappeared)	None
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	Dyspnea	Yes	07NOV2012	11NOV2012	3		No	Recovered (AE disappeared)	None
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	Delirium	Yes	07NOV2012	08NOV2012	3		No	Recovered (AE disappeared)	Postoperative complication
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	Hepatic hemorrhage	Yes	08NOV2012	16NOV2012	2		No	Recovered (AE disappeared)	Postoperative complication
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	Hyperkalemia	Yes	08NOV2012	12NOV2012	2		No	Recovered (AE disappeared)	None
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	Pleural effusion	Yes	10NOV2012	13NOV2012	3		No	Recovered (AE disappeared)	None
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	Hypokalemia	Yes	13NOV2012	13NOV2012	1		No	Recovered (AE disappeared)	None
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	Seroma	Yes	12NOV2012	10DEC2012	1		No	Recovered (AE disappeared)	None
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	Prostatic obstruction	Yes	12NOV2012	.	1		No	Not yet recovered at end of study	None
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	Rash acneiform	Yes	12JUN2012	.	3	Cetuximab	Yes	Not yet recovered at end of study	None
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	Insomnia	Yes	12NOV2012	12NOV2012	1		No	Recovered (AE disappeared)	None
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	Lung infection	Yes	12NOV2012	19NOV2012	3		No	Recovered (AE disappeared)	Postoperative complication
Universitätsklinikum Leipzig ,Leipzig	0401	Arm B	75	Male	Vomiting	Yes	13NOV2012	13NOV2012	2		No	Recovered (AE disappeared)	None
Universitätsklinikum der RWTH Aachen ,Aachen	0001	Arm B	58	Female	Rash maculo-papular	Yes	20AUG2012	20AUG2012	2	Cetuximab	Yes	Recovered (AE disappeared)	None

Site	Patient-No.	Treatment Arm	Age [years]	Gender	Event	TEAE	Start of AE	End of AE	NCI grade	Relation to	Action taken	Outcome	Intra-/Postoperartive complications
Universitätsklinikum der RWTH Aachen ,Aachen	0001	Arm B	58	Female	Rash maculo-papular	Yes	21AUG2012	21AUG2012	2	Cetuximab	Yes	Recovered (AE disappeared)	None

13.2.7 Listing of Individual Laboratory Measurements (by patient), if required by regulatory authorities

Listing 15: Laboratory- Blood chemistry

Patient No.	Treatment Arm	Point in time	Calcium	Sodium	Potassium	Magnesium	Bilirubin (total)	Creatinine	Ceratinine clearance	GOT (ASAT)	GPT (ALAT)	Gamma-GT	Urea	Alkaline phosphatase
0002	Arm A	Pre-examination		138 mmol/l	4.3 mmol/l	0.72 mmol/l	0.4 mg/dl	0.78 mg/dl		20.3 U/l	25.4 U/l	80.6 U/l	26.2 mg/dl	76 U/l
0083	Arm A	Pre-examination	2.4 mmol/l	139 mmol/l	4.9 mmol/l	0.8 mmol/l	0.5 mg/dl	0.72 mg/dl	60 ml/min	23 U/l	14 U/l	32 U/l		96 U/l
0083	Arm A	Surgery	2.4 mmol/l	138 mmol/l	4.1 mmol/l	0.8 mmol/l	0.6 mg/dl	0.69 mg/dl	60 ml/min	22 U/l	15 U/l	36 U/l	35 mg/dl	101 U/l
0083	Arm A	Surgery	2.3 mmol/l	136 mmol/l	4.1 mmol/l			0.67 mg/dl	60 ml/min					
0083	Arm A	Surgery	2.2 mmol/l	139 mmol/l	4.5 mmol/l	0.9 mmol/l	1.2 mg/dl	0.81 mg/dl	60 ml/min	110 U/l	121 U/l	54 U/l	54 mg/dl	100 U/l
0083	Arm A	Surgery	2.2 mmol/l	138 mmol/l	3.8 mmol/l	1 mmol/l	1.1 mg/dl	0.96 mg/dl	60 ml/min	160 U/l	160 U/l	46 U/l	56 mg/dl	94 U/l
0083	Arm A	Surgery	2.1 mmol/l	141 mmol/l	4.1 mmol/l	0.5 mmol/l	1.1 mg/dl	0.74 mg/dl	60 ml/min	56 U/l	69 U/l	57 U/l	46 mg/dl	90 U/l
0083	Arm A	Cycle 1- Other timepoints	2.2 mmol/l	140 mmol/l	4.4 mmol/l	0.8 mmol/l	0.7 mg/dl	0.84 mg/dl		31 U/l	12 U/l	56 U/l	31 mg/dl	96 U/l
0083	Arm A	Cycle 2- Day 1/ before cycle	2.2 mmol/l	138 mmol/l	4.5 mmol/l	0.8 mmol/l	0.3 mg/dl	0.61 mg/dl		56 U/l	44 U/l	122 U/l	44 mg/dl	114 U/l
0083	Arm A	Cycle 3- Other timepoints		134 mmol/l	3.7 mmol/l		0.9 mg/dl	0.66 mg/dl		32 U/l	22 U/l	65 U/l		100 U/l
0085	Arm A	Pre-examination	2.33 mmol/l	146 mmol/l	3.75 mmol/l	0.91 mmol/l	0.8 mg/dl	0.8 mg/dl		28 U/l	31 U/l	35 U/l	24 mg/dl	61 U/l
0085	Arm A	Surgery	2.3 mmol/l	135 mmol/l	3.26 mmol/l	0.89 mmol/l	1.5 mg/dl	1.1 mg/dl		139 U/l	164 U/l	450 U/l	41 mg/dl	288 U/l
0085	Arm A	Surgery	2.44 mmol/l	143 mmol/l	3.87 mmol/l	0.9 mmol/l	0.8 mg/dl	0.8 mg/dl		31 U/l	37 U/l	38 U/l	24 mg/dl	58 U/l
0085	Arm A	Surgery	2.03 mmol/l	140 mmol/l	4.22 mmol/l	0.91 mmol/l	3.2 mg/dl	0.8 mg/dl		453 U/l	499 U/l	48 U/l	46 mg/dl	44 U/l
0085	Arm A	Surgery	2.06 mmol/l	136 mmol/l	3.61 mmol/l	0.84 mmol/l	3.8 mg/dl	0.8 mg/dl		300 U/l	398 U/l	39 U/l	49 mg/dl	48 U/l
0085	Arm A	Surgery	2.1 mmol/l	138 mmol/l	3.83 mmol/l		5.6 mg/dl	0.8 mg/dl		178 U/l	293 U/l			49 U/l
0085	Arm A	Surgery	2.08 mmol/l	139 mmol/l	4.26 mmol/l		2.9 mg/dl	0.8 mg/dl		100 U/l	210 U/l	56 U/l	41 mg/dl	50 U/l

Patient No.	Treatment Arm	Point in time	Calcium	Sodium	Potassium	Magnesium	Bilirubin (total)	Creatinine	Ceratinine clearance	GOT (ASAT)	GPT (ALAT)	Gamma-GT	Urea	Alkaline phosphatase
0085	Arm A	Surgery	2.14 mmol/l	139 mmol/l	3.77 mmol/l		2.2 mg/dl	0.8 mg/dl		92 U/l	184 U/l	92 U/l	33 mg/dl	62 U/l
0085	Arm A	Surgery	2.1 mmol/l	138 mmol/l	2.96 mmol/l		2.5 mg/dl	0.8 mg/dl			183 U/l	180 U/l		89 U/l
0085	Arm A	Surgery	2.16 mmol/l	138 mmol/l	3.28 mmol/l	0.87 mmol/l	2.4 mg/dl	1.1 mg/dl		80 U/l	100 U/l	479 U/l	39 mg/dl	206 U/l
0085	Arm A	Surgery	2.14 mmol/l	139 mmol/l	3.39 mmol/l	0.89 mmol/l	2.1 mg/dl	0.8 mg/dl		162 U/l	234 U/l	241 U/l		120 U/l
0085	Arm A	Surgery	1.9 mmol/l	141 mmol/l	4.24 mmol/l		1.1 mg/dl	0.9 mg/dl		375 U/l	390 U/l	29 U/l	37 mg/dl	32 U/l
0085	Arm A	Cycle 1- Other timepoints	2.4 mmol/l	139 mmol/l	3.78 mmol/l	1.02 mmol/l	0.8 mg/dl	0.8 mg/dl		30 U/l	26 U/l	129 U/l	26 mg/dl	129 U/l
0085	Arm A	Cycle 2- Other timepoints	2.26 mmol/l	139 mmol/l	3.59 mmol/l	0.84 mmol/l	0.6 mg/dl	0.8 mg/dl		38 U/l	38 U/l	124 U/l	25 mg/dl	84 U/l
0085	Arm A	Cycle 3- Day 1/ before cycle	2.36 mmol/l	140 mmol/l	3.49 mmol/l	0.75 mmol/l	1 mg/dl	0.8 mg/dl		40 U/l	38 U/l	139 U/l	36 mg/dl	97 U/l
0085	Arm A	Cycle 4- Day 1/ before cycle	2.36 mmol/l	141 mmol/l	3.53 mmol/l	0.79 mmol/l	0.9 mg/dl	0.8 mg/dl		42 U/l	38 U/l	116 U/l	30 mg/dl	109 U/l
0085	Arm A	Cycle 5- Day 1/ before cycle	2.22 mmol/l	143 mmol/l	3.63 mmol/l	0.78 mmol/l	0.6 mg/dl	0.8 mg/dl		47 U/l	35 U/l	118 U/l	24 mg/dl	110 U/l
0085	Arm A	End of treatment	2.41 mmol/l	141 mmol/l	3.81 mmol/l	0.79 mmol/l	1.2 mg/dl	0.6 mg/dl		36 U/l	20 U/l	90 U/l	31 mg/dl	90 U/l
0086	Arm A	Pre-examination	2.38 mmol/l	137 mmol/l	5.51 mmol/l	0.93 mmol/l	5 µmol/l	85 µmol/l		0.94 µmol/sl	1.58 µmol/sl	13.19 µmol/sl	3.6 mmol/l	1.14 µmol/sl
0086	Arm A	Surgery	2.54 mmol/l	140 mmol/l	4.77 mmol/l	0.92 mmol/l	12 µmol/l	94 µmol/l		0.71 µmol/sl	1.08 µmol/sl	10.79 µmol/sl	5 mmol/l	1.19 µmol/sl
0086	Arm A	Surgery	1.22 mmol/l	137 mmol/l	4.8 mmol/l		20 µmol/l	112 µmol/l		4.94 µmol/sl	2.92 µmol/sl	8.12 µmol/sl	6.4 mmol/l	0.9 µmol/sl
0086	Arm A	Surgery	2.18 mmol/l	146 mmol/l	3.62 mmol/l		9 µmol/l	102 µmol/l		1.44 µmol/sl	2.57 µmol/sl	6.82 µmol/sl	6.6 mmol/l	1.42 µmol/sl
0086	Arm A	Surgery	2.29 mmol/l	143 mmol/l	3.71 mmol/l		9 µmol/l	112 µmol/l		1.88 µmol/sl	3.45 µmol/sl	6.86 µmol/sl	7.1 mmol/l	1.34 µmol/sl
0086	Arm A	Surgery	1.2 mmol/l	137 mmol/l	4.7 mmol/l		17 µmol/l	104 µmol/l		8.85 µmol/sl	6.2 µmol/sl	6.32 µmol/sl	7 mmol/l	0.7 µmol/sl
0086	Arm A	Cycle 1- Day 1/ before cycle	2.36 mmol/l	135 mmol/l	4.27 mmol/l		8 µmol/l	98 µmol/l		0.59 µmol/sl	0.45 µmol/sl	2.87 µmol/sl	2.9 mmol/l	1.57 µmol/sl
0086	Arm A	Cycle 2- Day 1/ before cycle	2.29 mmol/l	135 mmol/l	3.78 mmol/l		8 µmol/l	82 µmol/l			0.55 µmol/sl			1.52 µmol/sl
0086	Arm A	Cycle 3- Day 1/ before cycle	2.25 mmol/l	138 mmol/l	3.39 mmol/l		6 µmol/l	85 µmol/l		0.63 µmol/sl	0.84 µmol/sl	2.19 µmol/sl	3.8 mmol/l	1.33 µmol/sl
0086	Arm A	Cycle 4- Day 1/ before cycle	2.27 mmol/l	140 mmol/l	3.92 mmol/l		6 µmol/l	77 µmol/l		0.73 µmol/sl	0.62 µmol/sl	2.13 µmol/sl	4.7 mmol/l	1.31 µmol/sl

Patient No.	Treatment Arm	Point in time	Calcium	Sodium	Potassium	Magnesium	Bilirubin (total)	Creatinine	Ceratinine clearance	GOT (ASAT)	GPT (ALAT)	Gamma-GT	Urea	Alkaline phosphatase
0086	Arm A	Cycle 5- Day 1/ before cycle	2.11 mmol/l	138 mmol/l	4.36 mmol/l		4 µmol/l	79 µmol/l		0.94 µmol/sl	0.72 µmol/sl	2.32 µmol/sl	5.1 mmol/l	1.87 µmol/sl
0086	Arm A	Cycle 6- Day 1/ before cycle	2.18 mmol/l	139 mmol/l	4.45 mmol/l		6 µmol/l	76 µmol/l			6.1 µmol/sl			1.47 µmol/sl
0086	Arm A	Cycle 7- Day 1/ before cycle	2.19 mmol/l	137 mmol/l	4.47 mmol/l		5 µmol/l	81 µmol/l			0.62 µmol/sl			1.48 µmol/sl
0086	Arm A	Cycle 8- Day 1/ before cycle	2.3 mmol/l	144 mmol/l	4.54 mmol/l		4 µmol/l	86 µmol/l		0.77 µmol/sl	0.65 µmol/sl	3.48 µmol/sl	5.4 mmol/l	1.48 µmol/sl
0086	Arm A	Cycle 9- Day 1/ before cycle	2.38 mmol/l	143 mmol/l	4.61 mmol/l		9 µmol/l	84 µmol/l			0.65 µmol/sl			1.52 µmol/sl
0086	Arm A	Cycle 10- Day 1/ before cycle	2.13 mmol/l	139 mmol/l	3.99 mmol/l		6 µmol/l	74 µmol/l		0.82 µmol/sl	0.69 µmol/sl	4.21 µmol/sl	4.2 mmol/l	1.52 µmol/sl
0086	Arm A	Cycle 11- Day 1/ before cycle	2.38 mmol/l	139 mmol/l	4.45 mmol/l		4 µmol/l	81 µmol/l		0.78 µmol/sl	0.67 µmol/sl	4.56 µmol/sl	3.4 mmol/l	1.48 µmol/sl
0086	Arm A	Cycle 12- Day 1/ before cycle	2.29 mmol/l	138 mmol/l	4.1 mmol/l	0.76 mmol/l	8 µmol/l	82 µmol/l		1 µmol/sl	0.82 µmol/sl	5.06 µmol/sl	3.7 mmol/l	1.73 µmol/sl
0086	Arm A	End of treatment	2.29 mmol/l	139 mmol/l	4.69 mmol/l		8 µmol/l	87 µmol/l		1 µmol/sl	0.87 µmol/sl	10.19 µmol/sl		2.09 µmol/sl
0087	Arm A	Pre-examination	2.41 mmol/l	138 mmol/l	4.57 mmol/l	0.85 mmol/l	0.6 mg/dl	1 mg/dl		43 U/l	66 U/l	45 U/l	25 mg/dl	90 U/l
0087	Arm A	Surgery	2.08 mmol/l	142 mmol/l	3.32 mmol/l	0.68 mmol/l	0.3 mg/dl	0.8 mg/dl		62 U/l	194 U/l	43 U/l	16 mg/dl	68 U/l
0087	Arm A	Surgery	2.33 mmol/l	143 mmol/l	3.42 mmol/l	0.7 mmol/l	0.4 mg/dl	0.8 mg/dl		95 U/l	171 U/l	67 U/l	9 mg/dl	79 U/l
0087	Arm A	Surgery	2.31 mmol/l	141 mmol/l	3.63 mmol/l		0.4 mg/dl	0.9 mg/dl		51 U/l	126 U/l	71 U/l	11 mg/dl	84 U/l
0087	Arm A	Surgery	2.09 mmol/l	141 mmol/l	4.15 mmol/l		0.6 mg/dl	0.8 mg/dl		298 U/l	391 U/l	35 U/l	17 mg/dl	56 U/l
0087	Arm A	Surgery	2.42 mmol/l	142 mmol/l	3.88 mmol/l	0.82 mmol/l	0.7 mg/dl	1 mg/dl		33 U/l	68 U/l	51 U/l	17 mg/dl	88 U/l
0087	Arm A	Surgery	2.12 mmol/l	139 mmol/l	3.94 mmol/l	0.74 mmol/l	0.4 mg/dl	0.9 mg/dl		133 U/l	295 U/l	38 U/l	23 mg/dl	66 U/l
0087	Arm A	Surgery	2.06 mmol/l	139 mmol/l	3.93 mmol/l		1 mg/dl	0.8 mg/dl		291 U/l	303 U/l	37 U/l	19 mg/dl	56 U/l
0087	Arm A	Surgery	2.27 mmol/l	143 mmol/l	3.54 mmol/l	0.71 mmol/l	0.3 mg/dl	0.8 mg/dl		89 U/l	188 U/l	54 U/l	14 mg/dl	75 U/l
0087	Arm A	Cycle 1- Day 1/ before cycle	2.43 mmol/l	140 mmol/l	3.87 mmol/l	0.83 mmol/l	0.5 mg/dl	1 mg/dl		28 U/l	97 U/l	49 U/l	24 mg/dl	97 U/l
0087	Arm A	Cycle 2- Day 1/ before cycle	2.4 mmol/l	139 mmol/l	3.83 mmol/l	0.78 mmol/l	0.6 mg/dl	0.9 mg/dl		37 U/l	79 U/l	50 U/l	16 mg/dl	105 U/l

Patient No.	Treatment Arm	Point in time	Calcium	Sodium	Potassium	Magnesium	Bilirubin (total)	Creatinine	Ceratinine clearance	GOT (ASAT)	GPT (ALAT)	Gamma-GT	Urea	Alkaline phosphatase
0087	Arm A	Cycle 3- Day 1/ before cycle	2.39 mmol/l	139 mmol/l	3.78 mmol/l	0.76 mmol/l	0.7 mg/dl	0.9 mg/dl		35 U/l	70 U/l	59 U/l	17 mg/dl	113 U/l
0087	Arm A	End of treatment	2.45 mmol/l	140 mmol/l	3.78 mmol/l		0.6 mg/dl	0.9 mg/dl		48 U/l	70 U/l	66 U/l	14 mg/dl	116 U/l
0089	Arm A	Pre-examination	2.23 mmol/l	142 mmol/l	4.58 mmol/l	0.8 mmol/l	0.32 mg/dl	0.51 mg/dl		15 U/l	19 U/l	43 U/l	17 mg/dl	83 U/l
0089	Arm A	Surgery	2.07 mmol/l	141 mmol/l	4.27 mmol/l	0.79 mmol/l	0.66 mg/dl	0.5 mg/dl		128 U/l	81 U/l	24 U/l	15 mg/dl	62 U/l
0089	Arm A	Surgery	2 mmol/l	142 mmol/l	4.5 mmol/l	0.69 mmol/l	0.74 mg/dl	0.53 mg/dl		125 U/l	125 U/l	22 U/l	19 mg/dl	
0089	Arm A	Surgery		147 mmol/l	4.11 mmol/l		1.1 mg/dl	0.59 mg/dl			119 U/l	22 U/l		58 U/l
0089	Arm A	Surgery		141 mmol/l	3.79 mmol/l		0.37 mg/dl	0.39 mg/dl			153 U/l			
0089	Arm A	Surgery			4.05 mmol/l			0.4 mg/dl		24 U/l				
0089	Arm A	Surgery	2.16 mmol/l	141 mmol/l	4.44 mmol/l		0.19 mg/dl	0.55 mg/dl			56 U/l	96 U/l		
0089	Arm A	Cycle 1- Day 1/ before cycle	2.16 mmol/l	140 mmol/l	4.22 mmol/l	0.78 mmol/l	0.24 mg/dl	0.49 mg/dl		17 U/l	18 U/l	37 U/l	23 mg/dl	102 U/l
0089	Arm A	Cycle 2- Day 1/ before cycle	2.22 mmol/l	141 mmol/l	3.98 mmol/l	0.86 mmol/l	0.29 mg/dl	0.57 mg/dl		16 U/l	24 U/l	37 U/l	20 mg/dl	84 U/l
0089	Arm A	Cycle 3- Day 1/ before cycle	2.09 mmol/l	142 mmol/l	3.85 mmol/l	0.84 mmol/l	0.17 mg/dl	0.41 mg/dl		12 U/l	21 U/l	45 U/l	15 mg/dl	
0089	Arm A	Cycle 4- Day 1/ before cycle	2.05 mmol/l	141 mmol/l	3.82 mmol/l	0.72 mmol/l	0.3 mg/dl	0.45 mg/dl		14 U/l	22 U/l	43 U/l	17 mg/dl	83 U/l
0089	Arm A	Cycle 5- Day 1/ before cycle	2.09 mmol/l	141 mmol/l	3.92 mmol/l		0.21 mg/dl	0.47 mg/dl		15 U/l		63 U/l		
0089	Arm A	Cycle 6- Day 1/ before cycle	2.03 mmol/l	140 mmol/l	3.74 mmol/l		0.22 mg/dl	0.46 mg/dl		15 U/l		48 U/l		
0089	Arm A	Cycle 7- Day 1/ before cycle	2.14 mmol/l	143 mmol/l	3.83 mmol/l	0.69 mmol/l	0.19 mg/dl	0.62 mg/dl		18 U/l	38 U/l	75 U/l	13 mg/dl	96 U/l
0089	Arm A	Cycle 8- Day 1/ before cycle	2.14 mmol/l	144 mmol/l	3.5 mmol/l	0.64 mmol/l	0.28 mg/dl	0.45 mg/dl		17 U/l	24 U/l	61 U/l	14 mg/dl	86 U/l
0089	Arm A	Cycle 9- Day 1/ before cycle	2.13 mmol/l	142 mmol/l	3.97 mmol/l	0.7 mmol/l	0.32 mg/dl	0.55 mg/dl		21 U/l	33 U/l	71 U/l	10 mg/dl	93 U/l
0089	Arm A	Cycle 10- Day 1/ before cycle	2.2 mmol/l	139 mmol/l	3.71 mmol/l	0.65 mmol/l	0.25 mg/dl	0.48 mg/dl		26 U/l	55 U/l	93 U/l	16 mg/dl	99 U/l
0089	Arm A	Cycle 11- Day 1/ before cycle	2.22 mmol/l	140 mmol/l	3.91 mmol/l		0.32 mg/dl	0.41 mg/dl		28 U/l	58 U/l	102 U/l	18 mg/dl	117 U/l
0089	Arm A	Cycle 11- Other timepoints	2.18 mmol/l	144 mmol/l	4.06 mmol/l	0.68 mmol/l	0.21 mg/dl	0.44 mg/dl		19 U/l	42 U/l	121 U/l	17 mg/dl	117 U/l
0089	Arm A	Cycle 12- Day 1/ before cycle	2.2 mmol/l	143 mmol/l	4.3 mmol/l		0.26 mg/dl	0.48 mg/dl		30 U/l		122 U/l		

Patient No.	Treatment Arm	Point in time	Calcium	Sodium	Potassium	Magnesium	Bilirubin (total)	Creatinine	Ceratinine clearance	GOT (ASAT)	GPT (ALAT)	Gamma-GT	Urea	Alkaline phosphatase
0089	Arm A	Cycle 13- Day 1/ before cycle	2.02 mmol/l	143 mmol/l	3.87 mmol/l	0.62 mmol/l	0.2 mg/dl	0.5 mg/dl		27 U/l	43 U/l	125 U/l	15 mg/dl	117 U/l
0089	Arm A	End of treatment	2.39 mmol/l	141 mmol/l	4.87 mmol/l		0.18 mg/dl	0.59 mg/dl			29 U/l	57 U/l		
0090	Arm A	Pre-examination	2.35 mmol/l	138 mmol/l	4.6 mmol/l	0.79 mmol/l	0.33 mg/dl	1.02 mg/dl	81 ml/min	32 U/l	28 U/l	21 U/l	46 mg/dl	76 U/l
0090	Arm A	Surgery	2.2 mmol/l	137 mmol/l	4.2 mmol/l	0.86 mmol/l	0.25 mg/dl	0.86 mg/dl	90 ml/min	28 U/l	100 U/l	229 U/l	37 mg/dl	177 U/l
0090	Arm A	Surgery				0.74 mmol/l	0.73 mg/dl	0.82 mg/dl	90 ml/min	317 U/l	639 U/l	28 U/l	23 mg/dl	50 U/l
0090	Arm A	Surgery	2.28 mmol/l	137 mmol/l	4.3 mmol/l	0.84 mmol/l	0.34 mg/dl	0.87 mg/dl	90 ml/min	44 U/l	42 U/l	21 U/l	38 mg/dl	66 U/l
0090	Arm A	Surgery					0.68 mg/dl	0.86 mg/dl	90 ml/min	187 U/l	278 U/l	14 U/l	36 mg/dl	25 U/l
0090	Arm A	Surgery					0.76 mg/dl	0.88 mg/dl	90 ml/min	462 U/l	699 U/l	16 U/l	36 mg/dl	27 U/l
0090	Arm A	Surgery	2.11 mmol/l	134 mmol/l	3.8 mmol/l	0.82 mmol/l	0.59 mg/dl	0.88 mg/dl	90 ml/min	150 U/l	446 U/l	77 U/l	26 mg/dl	101 U/l
0090	Arm A	Surgery	2.12 mmol/l	140 mmol/l	4 mmol/l	0.86 mmol/l	0.38 mg/dl	0.79 mg/dl	90 ml/min	88 U/l	352 U/l	143 U/l	32 mg/dl	152 U/l
0090	Arm A	Surgery	2.2 mmol/l	138 mmol/l	4.3 mmol/l	0.82 mmol/l	0.42 mg/dl	0.84 mg/dl	90 ml/min	66 U/l	292 U/l	197 U/l	33 mg/dl	187 U/l
0090	Arm A	Surgery	2.21 mmol/l	137 mmol/l	4.2 mmol/l	0.87 mmol/l	0.27 mg/dl	0.96 mg/dl	87 ml/min	43 U/l	182 U/l	194 U/l	35 mg/dl	168 U/l
0090	Arm A	Surgery	2.14 mmol/l	137 mmol/l	4.2 mmol/l	0.83 mmol/l	0.27 mg/dl	0.92 mg/dl	90 ml/min	41 U/l	147 U/l	224 U/l	36 mg/dl	166 U/l
0090	Arm A	Surgery	2.18 mmol/l	137 mmol/l	4 mmol/l		0.29 mg/dl	0.88 mg/dl	90 ml/min	38 U/l	131 U/l	243 U/l	37 mg/dl	187 U/l
0090	Arm A	Cycle 1- Day 1/ before cycle	2.27 mmol/l	137 mmol/l	4.5 mmol/l	0.82 mmol/l	0.25 mg/dl	0.97 mg/dl	86 ml/min	42 U/l	53 U/l	206 U/l	44 mg/dl	103 U/l
0090	Arm A	Cycle 1- Day 1/ before cycle	2.09 mmol/l	135 mmol/l	4.4 mmol/l		0.22 mg/dl	0.83 mg/dl	90 ml/min	33 U/l	52 U/l	146 U/l	45 mg/dl	85 U/l
0090	Arm A	Cycle 2- Day 1/ before cycle	2.26 mmol/l	136 mmol/l	4.4 mmol/l	0.77 mmol/l	0.21 mg/dl	0.98 mg/dl	85 ml/min	32 U/l	39 U/l	107 U/l	42 mg/dl	99 U/l
0090	Arm A	Cycle 2- Day 1/ before cycle	2.12 mmol/l	134 mmol/l	4.2 mmol/l		0.3 mg/dl	0.78 mg/dl	90 ml/min	34 U/l	51 U/l	78 U/l	39 mg/dl	87 U/l
0090	Arm A	Cycle 3- Day 1/ before cycle	2.2 mmol/l	133 mmol/l	4.1 mmol/l	0.7 mmol/l	0.33 mg/dl	0.88 mg/dl	90 ml/min	41 U/l	48 U/l	57 U/l	36 mg/dl	100 U/l
0090	Arm A	Cycle 3- Day 1/ before cycle	2.03 mmol/l	133 mmol/l	4 mmol/l		0.69 mg/dl	0.81 mg/dl	90 ml/min	36 U/l	37 U/l	55 U/l	35 mg/dl	66 U/l
0090	Arm A	Cycle 3- Other timepoints	1.98 mmol/l	137 mmol/l	3.6 mmol/l	0.66 mmol/l	0.36 mg/dl	0.8 mg/dl	90 ml/min	40 U/l	42 U/l	43 U/l	32 mg/dl	87 U/l
0090	Arm A	Cycle 3- Other timepoints	2.37 mmol/l	135 mmol/l	4.4 mmol/l	0.78 mmol/l	0.38 mg/dl	0.9 mg/dl	90 ml/min	70 U/l	72 U/l	50 U/l	36 mg/dl	134 U/l

Patient No.	Treatment Arm	Point in time	Calcium	Sodium	Potassium	Magnesium	Bilirubin (total)	Creatinine	Ceratinine clearance	GOT (ASAT)	GPT (ALAT)	Gamma-GT	Urea	Alkaline phosphatase
0090	Arm A	Cycle 4- Day 1/ before cycle	2.35 mmol/l	137 mmol/l	4.6 mmol/l	0.78 mmol/l	0.5 mg/dl	0.98 mg/dl	85 ml/min	51 U/l	57 U/l	49 U/l	41 mg/dl	106 U/l
0090	Arm A	Cycle 4- Day 1/ before cycle	2.2 mmol/l	135 mmol/l	4.1 mmol/l	0.78 mmol/l	0.63 mg/dl	0.87 mg/dl	90 ml/min	31 U/l	36 U/l	67 U/l	29 mg/dl	82 U/l
0090	Arm A	Cycle 5- Day 1/ before cycle	2.19 mmol/l	135 mmol/l	3.7 mmol/l	0.68 mmol/l	0.38 mg/dl	0.83 mg/dl	90 ml/min	52 U/l	36 U/l	53 U/l	27 mg/dl	89 U/l
0090	Arm A	Cycle 5- Day 1/ before cycle	2.03 mmol/l	133 mmol/l	4 mmol/l		0.48 mg/dl	0.86 mg/dl	90 ml/min	30 U/l	46 U/l	73 U/l		90 U/l
0090	Arm A	Cycle 6- Day 1/ before cycle	2.17 mmol/l	136 mmol/l	3.7 mmol/l	0.73 mmol/l	0.44 mg/dl	0.87 mg/dl	90 ml/min	50 U/l	48 U/l	90 U/l	17 mg/dl	101 U/l
0090	Arm A	Cycle 7- Day 1/ before cycle	2.27 mmol/l	137 mmol/l	3.9 mmol/l	0.72 mmol/l	0.43 mg/dl	0.83 mg/dl	90 ml/min	43 U/l	50 U/l	70 U/l	23 mg/dl	97 U/l
0090	Arm A	Cycle 8- Day 1/ before cycle	2.26 mmol/l	136 mmol/l	3.8 mmol/l	0.82 mmol/l	0.49 mg/dl	0.89 mg/dl	90 ml/min	50 U/l	42 U/l	73 U/l	44 mg/dl	95 U/l
0090	Arm A	Cycle 9- Day 1/ before cycle	2.33 mmol/l	140 mmol/l	3.9 mmol/l	0.86 mmol/l	0.42 mg/dl	0.98 mg/dl	85 ml/min	49 U/l	34 U/l	78 U/l	27 mg/dl	84 U/l
0090	Arm A	Cycle 10- Day 1/ before cycle	2.31 mmol/l	136 mmol/l	4.1 mmol/l	0.77 mmol/l	0.54 mg/dl	1.03 mg/dl	80 ml/min	40 U/l	30 U/l	80 U/l	34 mg/dl	82 U/l
0090	Arm A	Cycle 11- Day 1/ before cycle	2.29 mmol/l	137 mmol/l	4.6 mmol/l	0.81 mmol/l	0.37 mg/dl	0.93 mg/dl	90 ml/min	37 U/l	34 U/l	86 U/l	32 mg/dl	86 U/l
0090	Arm A	Cycle 12- Day 1/ before cycle	2.29 mmol/l	140 mmol/l	3.9 mmol/l	0.75 mmol/l	0.38 mg/dl	0.94 mg/dl	88 ml/min	45 U/l	39 U/l	86 U/l	35 mg/dl	87 U/l
0090	Arm A	End of treatment	2.21 mmol/l	139 mmol/l	4.4 mmol/l		0.28 mg/dl	0.93 mg/dl	90 ml/min	45 U/l	34 U/l	69 U/l	35 mg/dl	96 U/l
0161	Arm A	Pre-examination	2.37 mmol/l	139 mmol/l	4.9 mmol/l	0.8 mmol/l	0.5 mg/dl	0.9 mg/dl	60 ml/min	44 U/l	37 U/l	111 U/l	28 mg/dl	120 U/l
0161	Arm A	Surgery	2 mmol/l	141 mmol/l	3.6 mmol/l	0.6 mmol/l	1.3 mg/dl	0.7 mg/dl		257 U/l	183 U/l	46 U/l	29 mg/dl	173 U/l
0161	Arm A	Surgery	2.2 mmol/l	140 mmol/l	3.7 mmol/l		0.9 mg/dl	1.2 mg/dl		132 U/l	288 U/l	106 U/l	27 mg/dl	110 U/l
0161	Arm A	Surgery	2.1 mmol/l	143 mmol/l	4.4 mmol/l	0.75 mmol/l	0.9 mg/dl	0.8 mg/dl		388 U/l	450 U/l	65 U/l	48 mg/dl	81 U/l
0161	Arm A	Surgery	2 mmol/l	138 mmol/l	4.1 mmol/l	0.65 mmol/l	0.7 mg/dl	0.7 mg/dl		208 U/l	344 U/l	67 U/l	38 mg/dl	84 U/l
0161	Arm A	Surgery	2.24 mmol/l	142 mmol/l	3.5 mmol/l	0.79 mmol/l	0.7 mg/dl	0.9 mg/dl		77 U/l	161 U/l	161 U/l	35 mg/dl	121 U/l
0161	Arm A	Surgery	2.41 mmol/l	140 mmol/l	4.4 mmol/l	0.76 mmol/l	0.4 mg/dl	0.8 mg/dl		35 U/l	17 U/l	72 U/l	34 mg/dl	116 U/l
0161	Arm A	Cycle 1- Day 1/ before cycle	2.27 mmol/l	138 mmol/l	4.5 mmol/l		0.4 mg/dl	0.8 mg/dl		27 U/l	20 U/l	89 U/l	38 mg/dl	107 U/l
0161	Arm A	Cycle 2- Day 1/ before cycle	2.15 mmol/l	137 mmol/l	4 mmol/l	1 mmol/l	0.5 mg/dl	0.7 mg/dl		27 U/l	18 U/l	62 U/l		95 U/l
0161	Arm A	Cycle 3- Day 1/ before cycle	2.18 mmol/l	137 mmol/l	3.9 mmol/l		0.4 mg/dl	0.7 mg/dl		39 U/l	26 U/l	53 U/l	20 mg/dl	98 U/l

Patient No.	Treatment Arm	Point in time	Calcium	Sodium	Potassium	Magnesium	Bilirubin (total)	Creatinine	Ceratinine clearance	GOT (ASAT)	GPT (ALAT)	Gamma-GT	Urea	Alkaline phosphatase
0161	Arm A	Cycle 4- Day 1/ before cycle	2.16 mmol/l	143 mmol/l	3.4 mmol/l		0.4 mg/dl	0.6 mg/dl		40 U/l	26 U/l	49 U/l	20 mg/dl	77 U/l
0161	Arm A	Cycle 5- Day 1/ before cycle	2.18 mmol/l	141 mmol/l	3.7 mmol/l		0.5 mg/dl	0.7 mg/dl		40 U/l	26 U/l	45 U/l	22 mg/dl	81 U/l
0161	Arm A	Cycle 6- Day 1/ before cycle	2.07 mmol/l	139 mmol/l	3.3 mmol/l		0.4 mg/dl	0.7 mg/dl		35 U/l	21 U/l	43 U/l	23 mg/dl	80 U/l
0161	Arm A	Cycle 7- Day 1/ before cycle	2.22 mmol/l	139 mmol/l	3.6 mmol/l		0.4 mg/dl	0.7 mg/dl		39 U/l	32 U/l	61 U/l	28 mg/dl	90 U/l
0161	Arm A	Cycle 8- Day 1/ before cycle	2.14 mmol/l	141 mmol/l	3.7 mmol/l		0.4 mg/dl	0.7 mg/dl		37 U/l	25 U/l	82 U/l	22 mg/dl	98 U/l
0161	Arm A	Cycle 9- Day 1/ before cycle	2.29 mmol/l	144 mmol/l	3.9 mmol/l		0.4 mg/dl	0.7 mg/dl		38 U/l	21 U/l	75 U/l	19 mg/dl	100 U/l
0161	Arm A	Cycle 10- Day 1/ before cycle	2.33 mmol/l	139 mmol/l	3.9 mmol/l		0.4 mg/dl	0.7 mg/dl		38 U/l	26 U/l	65 U/l	22 mg/dl	106 U/l
0161	Arm A	Cycle 11- Day 1/ before cycle	3.27 mmol/l	139 mmol/l	3.7 mmol/l		0.4 mg/dl	0.7 mg/dl		41 U/l	26 U/l	59 U/l	19 mg/dl	99 U/l
0161	Arm A	End of treatment	2.36 mmol/l	139 mmol/l	3.9 mmol/l		0.5 mg/dl	0.8 mg/dl		40 U/l	24 U/l	60 U/l	24 mg/dl	114 U/l
0163	Arm A	Pre-examination		143 mmol/l	4.17 mmol/l		0.6 mg/dl	1.03 mg/dl		21 U/l	15 U/l	24 U/l		57 U/l
0163	Arm A	Surgery	2.24 mmol/l	140 mmol/l	3.85 mmol/l	0.87 mmol/l	0.6 mg/dl	0.97 mg/dl		22 U/l	14 U/l	20 U/l	7.2 mg/dl	52 U/l
0163	Arm A	End of treatment	2.14 mmol/l	137 mmol/l	3.95 mmol/l	0.79 mmol/l	0.4 mg/dl	0.89 mg/dl		17 U/l	31 U/l	68 U/l	15 mg/dl	60 U/l
0166	Arm A	Pre-examination	2.36 mmol/l	138 mmol/l	5.1 mmol/l		4 µmol/l	71 µmol/l	70.4 ml/min	46 U/l	134 U/l	593 U/l	7.5 mmol/l	196 U/l
0402	Arm A	Pre-examination	2.33 mmol/l	136.6 mmol/l	4.2 mmol/l	0.74 mmol/l	12 µmol/l	64 µmol/l	84.9 ml/min	0.56 µmol/sl	0.27 µmol/sl	1.16 µmol/sl	3.6 mmol/l	1.42 µmol/sl
0001	Arm B	Pre-examination	2.36 mmol/l	141 mmol/l	5.2 mmol/l	0.79 mmol/l	0.2 mg/dl	0.6 mg/dl	60 ml/min	19 U/l	9 U/l	45 U/l	22 mg/dl	86 U/l
0001	Arm B	Cycle 1- Day 1/ before cycle	2.29 mmol/l	137.2 mmol/l	4.3 mmol/l		0.33 mg/dl	0.46 mg/dl	140 ml/min	16 U/l	11 U/l	66 U/l	31.2 mg/dl	97 U/l
0003	Arm B	Pre-examination	2.4 mmol/l	140 mmol/l	4.54 mmol/l		23 µmol/l	94 µmol/l		0.46 µmol/sl	0.54 µmol/sl	1.84 µmol/sl		1.84 µmol/sl
0003	Arm B	Surgery	2.28 mmol/l	144 mmol/l	3.88 mmol/l		7 µmol/l	71 µmol/l		0.5 µmol/sl	1.52 µmol/sl	1.59 µmol/sl		1.58 µmol/sl
0003	Arm B	Surgery	2.2 mmol/l	140 mmol/l	3.39 mmol/l		12 µmol/l	70 µmol/l		1.01 µmol/sl	4.18 µmol/sl	1.21 µmol/sl		1.47 µmol/sl
0003	Arm B	Surgery					28 µmol/l	81 µmol/l		13.92 µmol/sl	14.74 µmol/sl	0.77 µmol/sl	5.9 mmol/l	1.09 µmol/sl
0003	Arm B	Surgery	2.19 mmol/l	142 mmol/l	3.11 mmol/l		14 µmol/l	75 µmol/l		2.56 µmol/sl	7.69 µmol/sl	1.04 µmol/sl		1.4 µmol/sl

Patient No.	Treatment Arm	Point in time	Calcium	Sodium	Potassium	Magnesium	Bilirubin (total)	Creatinine	Ceratinine clearance	GOT (ASAT)	GPT (ALAT)	Gamma-GT	Urea	Alkaline phosphatase
0003	Arm B	Surgery	2.23 mmol/l	142 mmol/l	3.56 mmol/l		11 µmol/l	69 µmol/l		0.76 µmol/sl	3.29 µmol/sl	1.46 µmol/sl		1.55 µmol/sl
0003	Arm B	Surgery	2.04 mmol/l	139 mmol/l	3.51 mmol/l		27 µmol/l	76 µmol/l		11.23 µmol/sl	15.98 µmol/sl	0.67 µmol/sl		1.09 µmol/sl
0003	Arm B	Surgery	2.38 mmol/l	143 mmol/l	3.97 mmol/l		20 µmol/l	73 µmol/l		0.49 µmol/sl	0.72 µmol/sl	1.03 µmol/sl		1.68 µmol/sl
0003	Arm B	Surgery	2.26 mmol/l	144 mmol/l	3.63 mmol/l		12 µmol/l	71 µmol/l		1.47 µmol/sl	5.56 µmol/sl	1.15 µmol/sl		1.42 µmol/sl
0003	Arm B	Surgery	2.1 mmol/l	143 mmol/l	3.51 mmol/l		17 µmol/l	78 µmol/l		4.83 µmol/sl	9.95 µmol/sl	0.73 µmol/sl		1.17 µmol/sl
0003	Arm B	Surgery					31 µmol/l	73 µmol/l		2.22 µmol/sl	2.15 µmol/sl	0.78 µmol/sl	3.7 mmol/l	1.27 µmol/sl
0003	Arm B	Cycle 1- Day 1/ before cycle	2.34 mmol/l	139 mmol/l	3.82 mmol/l	0.81 mmol/l	14 µmol/l	79 µmol/l		0.38 µmol/sl	0.44 µmol/sl	1.73 µmol/sl	5.7 mmol/l	1.74 µmol/sl
0003	Arm B	Cycle 2- Day 1/ before cycle	2.35 mmol/l	135 mmol/l	3.86 mmol/l	0.83 mmol/l	17 µmol/l	74 µmol/l		0.43 µmol/sl	0.61 µmol/sl	1.47 µmol/sl		1.84 µmol/sl
0003	Arm B	Cycle 3- Day 1/ before cycle	2.3 mmol/l	136 mmol/l	3.85 mmol/l	0.83 mmol/l	18 µmol/l	73 µmol/l		0.49 µmol/sl	0.78 µmol/sl	1.13 µmol/sl	4.9 mmol/l	1.8 µmol/sl
0003	Arm B	Cycle 4- Day 1/ before cycle	2.3 mmol/l	140 mmol/l	3.84 mmol/l	0.77 mmol/l	24 µmol/l	77 µmol/l		0.54 µmol/sl	1.06 µmol/sl	1.06 µmol/sl	4.3 mmol/l	1.81 µmol/sl
0003	Arm B	Cycle 5- Day 1/ before cycle	2.31 mmol/l	138 mmol/l	3.72 mmol/l	0.75 mmol/l	25 µmol/l	74 µmol/l		0.84 µmol/sl	1.41 µmol/sl	1.03 µmol/sl	4 mmol/l	1.77 µmol/sl
0003	Arm B	Cycle 6- Day 1/ before cycle	2.35 mmol/l	137 mmol/l	3.69 mmol/l	0.76 mmol/l	30 µmol/l	74 µmol/l		0.74 µmol/sl	1.19 µmol/sl	1.05 µmol/sl	4.4 mmol/l	1.8 µmol/sl
0003	Arm B	Cycle 7- Day 1/ before cycle	2.28 mmol/l	141 mmol/l	3.67 mmol/l		16 µmol/l	71 µmol/l		0.39 µmol/sl	0.47 µmol/sl	1.16 µmol/sl	4.1 mmol/l	1.67 µmol/sl
0003	Arm B	Cycle 8- Day 1/ before cycle	2.18 mmol/l	143 mmol/l	2.26 mmol/l		14 µmol/l	71 µmol/l		0.51 µmol/sl	0.77 µmol/sl	0.67 µmol/sl		
0003	Arm B	Cycle 9- Day 1/ before cycle	2.21 mmol/l	141 mmol/l	3.47 mmol/l			68 µmol/l						
0003	Arm B	Cycle 10- Day 1/ before cycle	2.3 mmol/l	140 mmol/l	3.49 mmol/l		19 µmol/l	72 µmol/l		0.61 µmol/sl	0.67 µmol/sl	0.76 µmol/sl		
0003	Arm B	Cycle 11- Day 1/ before cycle	2.33 mmol/l	139 mmol/l	3.73 mmol/l			69 µmol/l						
0003	Arm B	Cycle 12- Day 1/ before cycle	2.34 mmol/l	140 mmol/l	3.68 mmol/l			68 µmol/l						
0003	Arm B	End of treatment	2.32 mmol/l	141 mmol/l	4.43 mmol/l		25 µmol/l	76 µmol/l		0.55 µmol/sl	0.57 µmol/sl	0.8 µmol/sl		
0081	Arm B	Pre-examination	2.19 mmol/l	139 mmol/l	4.8 mmol/l	0.97 mmol/l	0.4 mg/dl	1.2 mg/dl	80 ml/min	24 U/l	21 U/l	27 U/l	43 mg/dl	64 U/l

Patient No.	Treatment Arm	Point in time	Calcium	Sodium	Potassium	Magnesium	Bilirubin (total)	Creatinine	Ceratinine clearance	GOT (ASAT)	GPT (ALAT)	Gamma-GT	Urea	Alkaline phosphatase
0081	Arm B	End of treatment	2.19 mmol/l	139 mmol/l	4.8 mmol/l	0.97 mmol/l	0.4 mg/dl	1.2 mg/dl	80 ml/min	24 U/l	21 U/l	27 U/l	43 mg/dl	64 U/l
0082	Arm B	Pre-examination	2.37 mmol/l	143.7 mmol/l	4.22 mmol/l	0.8 mmol/l	8.6 µmol/l	68 µmol/l	80 ml/min	0.32 µmol/sl	0.32 µmol/sl	0.47 µmol/sl	3.4 mmol/l	1.42 µmol/sl
0082	Arm B	Surgery	2.08 mmol/l	149.3 mmol/l	4.14 mmol/l		12.9 µmol/l	57 µmol/l	90 ml/min	2.91 µmol/sl	2.39 µmol/sl	0.24 µmol/sl	4.5 mmol/l	0.87 µmol/sl
0082	Arm B	Cycle 1- Day 1/ before cycle	2.05 mmol/l	134.7 mmol/l	4.02 mmol/l	0.74 mmol/l	6.8 µmol/l	66 µmol/l	83 ml/min	0.35 µmol/sl	0.15 µmol/sl	0.36 µmol/sl	4.5 mmol/l	1.33 µmol/sl
0082	Arm B	Cycle 1- Other timepoints	2.23 mmol/l	140 mmol/l	3.97 mmol/l	0.82 mmol/l	8 µmol/l	69 µmol/l	62.5 ml/min	0.26 µmol/sl	0.2 µmol/sl	0.38 µmol/sl	4.6 mmol/l	1.35 µmol/sl
0082	Arm B	Cycle 2- Day 1/ before cycle	2.11 mmol/l	140.9 mmol/l	4.04 mmol/l		3.9 µmol/l	64 µmol/l	86 ml/min		0.22 µmol/sl	0.32 µmol/sl	4 mmol/l	1.4 µmol/sl
0082	Arm B	Cycle 2- Other timepoints	2.36 mmol/l	141.4 mmol/l	3.88 mmol/l	0.73 mmol/l	7.7 µmol/l	72 µmol/l	75 ml/min	0.46 µmol/sl	0.39 µmol/sl	0.37 µmol/sl	4.1 mmol/l	1.42 µmol/sl
0082	Arm B	Cycle 3- Day 1/ before cycle	2.39 mmol/l	146.9 mmol/l	4.59 mmol/l		7.6 µmol/l	79 µmol/l	54.6 ml/min	0.4 µmol/sl	0.59 µmol/sl	0.37 µmol/sl	3.8 mmol/l	1.78 µmol/sl
0082	Arm B	Cycle 3- Other timepoints	2.22 mmol/l	142.6 mmol/l	4.43 mmol/l		7.8 µmol/l	66 µmol/l	83 ml/min		0.28 µmol/sl	0.36 µmol/sl	3.6 mmol/l	1.48 µmol/sl
0082	Arm B	Cycle 4- Day 1/ before cycle	2.35 mmol/l	141 mmol/l	4.75 mmol/l		7.8 µmol/l	76 µmol/l	70 ml/min		0.28 µmol/sl	0.29 µmol/sl	5.1 mmol/l	1.6 µmol/sl
0082	Arm B	Cycle 4- Other timepoints	2.32 mmol/l	144.6 mmol/l	4.05 mmol/l		7.5 µmol/l	77 µmol/l	69 ml/min		0.2 µmol/sl	0.31 µmol/sl	4.1 mmol/l	1.43 µmol/sl
0082	Arm B	Cycle 5- Day 1/ before cycle	2.3 mmol/l	140.3 mmol/l	5.36 mmol/l	0.79 mmol/l	7.2 µmol/l	72 µmol/l	75 ml/min	0.69 µmol/sl	0.33 µmol/sl	0.31 µmol/sl	3.7 mmol/l	1.62 µmol/sl
0082	Arm B	Cycle 5- Other timepoints	2.37 mmol/l	137.4 mmol/l	4.07 mmol/l	0.78 mmol/l	7.6 µmol/l	74 µmol/l	73 ml/min	0.34 µmol/sl	0.28 µmol/sl	0.38 µmol/sl	5 mmol/l	1.8 µmol/sl
0082	Arm B	Cycle 6- Day 1/ before cycle	2.33 mmol/l	139.1 mmol/l	6 mmol/l	0.79 mmol/l	13.4 µmol/l	70 µmol/l	78 ml/min	0.97 µmol/sl	0.23 µmol/sl	0.32 µmol/sl	3.5 mmol/l	1.44 µmol/sl
0082	Arm B	Cycle 7- Day 1/ before cycle	2.31 mmol/l	138.1 mmol/l	4.44 mmol/l	0.81 mmol/l	6.8 µmol/l	73 µmol/l	74 ml/min	0.34 µmol/sl	0.2 µmol/sl	0.91 µmol/sl	5.8 mmol/l	2.17 µmol/sl
0082	Arm B	Cycle 7- Other timepoints	2.26 mmol/l	138.2 mmol/l	4.46 mmol/l	0.83 mmol/l	6 µmol/l	73 µmol/l	74 ml/min		0.24 µmol/sl	0.88 µmol/sl	4.5 mmol/l	2.04 µmol/sl
0082	Arm B	Cycle 8- Day 1/ before cycle	2.3 mmol/l	141.4 mmol/l	4.48 mmol/l	0.8 mmol/l	6.6 µmol/l	65 µmol/l	69.8 ml/min	0.31 µmol/sl	0.22 µmol/sl	0.81 µmol/sl	4.5 mmol/l	2.15 µmol/sl
0082	Arm B	Cycle 8- Other timepoints	2.2 mmol/l	139.3 mmol/l	4.45 mmol/l	0.79 mmol/l	5.3 µmol/l	68 µmol/l			0.17 µmol/sl	0.82 µmol/sl	3.8 mmol/l	2.11 µmol/sl
0082	Arm B	Cycle 9- Day 1/ before cycle	2.2 mmol/l	141.1 mmol/l	4.54 mmol/l		9.5 µmol/l	65 µmol/l	83.8 ml/min		0.28 µmol/sl	0.73 µmol/sl	4.7 mmol/l	2.15 µmol/sl
0082	Arm B	Cycle 10- Day 1/ before cycle	2.23 mmol/l	142 mmol/l	4.64 mmol/l	0.83 mmol/l	5 µmol/l	73 µmol/l	73.3 ml/min	0.32 µmol/sl	0.21 µmol/sl	0.68 µmol/sl	4.1 mmol/l	2.06 µmol/sl

Patient No.	Treatment Arm	Point in time	Calcium	Sodium	Potassium	Magnesium	Bilirubin (total)	Creatinine	Ceratinine clearance	GOT (ASAT)	GPT (ALAT)	Gamma-GT	Urea	Alkaline phosphatase
0082	Arm B	Cycle 10- Other timepoints	2.27 mmol/l	141.6 mmol/l	4.19 mmol/l		5.2 µmol/l	69 µmol/l	78.2 ml/min		0.16 µmol/sl	0.67 µmol/sl	4.8 mmol/l	2.11 µmol/sl
0082	Arm B	Cycle 11- Day 1/ before cycle	2.3 mmol/l	141.8 mmol/l	4.09 mmol/l		9.8 µmol/l	75 µmol/l	61.97 ml/min		0.24 µmol/sl	0.67 µmol/sl	4.5 mmol/l	2.33 µmol/sl
0082	Arm B	Cycle 12- Day 1/ before cycle	2.37 mmol/l	141.7 mmol/l	4.53 mmol/l		7.4 µmol/l	76 µmol/l	61.16 ml/min		0.2 µmol/sl	0.6 µmol/sl	3.7 mmol/l	2.29 µmol/sl
0082	Arm B	Cycle 12- Other timepoints	2.32 mmol/l	142.9 mmol/l	4.64 mmol/l	0.78 mmol/l	8.9 µmol/l	69 µmol/l	67.36 ml/min	0.2 µmol/sl	0.15 µmol/sl	0.63 µmol/sl	3.6 mmol/l	2.35 µmol/sl
0082	Arm B	End of treatment	2.32 mmol/l	142.9 mmol/l	4.64 mmol/l	0.78 mmol/l	8.9 µmol/l	69 µmol/l	67.36 ml/min	0.2 µmol/sl	0.15 µmol/sl	0.63 µmol/sl	3.6 mmol/l	2.35 µmol/sl
0084	Arm B	Pre-examination	2.41 mmol/l	140.5 mmol/l	4.44 mmol/l	0.73 mmol/l	7.2 µmol/l	107 µmol/l	61 ml/min	0.26 µmol/sl	0.25 µmol/sl	1.24 µmol/sl	7.8 mmol/l	1.78 µmol/sl
0084	Arm B	Surgery	2.1 mmol/l				8.9 µmol/l	100 µmol/l	64.3 ml/min	1.75 µmol/sl	0.8 µmol/sl	1.54 µmol/sl	5.4 mmol/l	1.84 µmol/sl
0084	Arm B	Cycle 1- Day 1/ before cycle	2.42 mmol/l	140.3 mmol/l	4.57 mmol/l	0.75 mmol/l	5 µmol/l	105 µmol/l	62 ml/min	0.23 µmol/sl	0.15 µmol/sl	0.91 µmol/sl	6.4 mmol/l	1.67 µmol/sl
0084	Arm B	Cycle 1- Other timepoints	2.22 mmol/l	138.5 mmol/l	4.67 mmol/l	0.77 mmol/l	5.3 µmol/l	102 µmol/l	64 ml/min	0.33 µmol/sl	0.18 µmol/sl	0.77 µmol/sl	8.5 mmol/l	1.61 µmol/sl
0084	Arm B	Cycle 2- Day 1/ before cycle	2.38 mmol/l	137.7 mmol/l	4.71 mmol/l	0.73 mmol/l	6.1 µmol/l	105 µmol/l	62 ml/min	0.25 µmol/sl	0.24 µmol/sl	0.77 µmol/sl	7.5 mmol/l	1.89 µmol/sl
0084	Arm B	Cycle 2- Other timepoints	2.31 mmol/l	136.5 mmol/l	4.51 mmol/l	0.74 mmol/l	5.4 µmol/l	98 µmol/l	68 ml/min	0.49 µmol/sl	0.38 µmol/sl	0.86 µmol/sl	7.6 mmol/l	1.75 µmol/sl
0084	Arm B	Cycle 3- Day 1/ before cycle	2.3 mmol/l	138.1 mmol/l	4.19 mmol/l	0.8 mmol/l	8.7 µmol/l	109 µmol/l	59 ml/min	0.34 µmol/sl	0.36 µmol/sl	0.78 µmol/sl	9.6 mmol/l	1.87 µmol/sl
0084	Arm B	Cycle 4- Day 1/ before cycle	2.37 mmol/l	136 mmol/l	4.1 mmol/l	0.72 mmol/l	6.2 µmol/l	105 µmol/l	62 ml/min	1.09 µmol/sl	1.17 µmol/sl	1.39 µmol/sl	6.5 mmol/l	2.32 µmol/sl
0084	Arm B	Cycle 5- Day 1/ before cycle	2.3 mmol/l	137.4 mmol/l	3.92 mmol/l	0.7 mmol/l	8 µmol/l	107 µmol/l	61 ml/min		0.82 µmol/sl	2.05 µmol/sl	5.5 mmol/l	2.49 µmol/sl
0084	Arm B	Cycle 6- Day 1/ before cycle	2.41 mmol/l	134.7 mmol/l	4.15 mmol/l	0.8 mmol/l	6.5 µmol/l	102 µmol/l	64 ml/min	0.63 µmol/sl	0.52 µmol/sl	2.56 µmol/sl	8.6 mmol/l	2.74 µmol/sl
0084	Arm B	End of treatment	2.15 mmol/l	138.8 mmol/l	4.55 mmol/l		4.8 µmol/l	126 µmol/l	49.1 ml/min	0.62 µmol/sl	0.41 µmol/sl	1.87 µmol/sl	9 mmol/l	3.15 µmol/sl
0088	Arm B	Pre-examination	2.33 mmol/l	140 mmol/l	4.31 mmol/l		14.3 µmol/l	82 µmol/l	1.6 ml/s	0.43 µmol/sl	0.39 µmol/sl	0.74 µmol/sl	3.7 mmol/l	1.35 µmol/sl
0088	Arm B	Surgery	2.33 mmol/l	142 mmol/l	4.03 mmol/l		29.7 µmol/l	79 µmol/l		0.9 µmol/sl	0.88 µmol/sl	3 µmol/sl	4.9 mmol/l	3.13 µmol/sl
0088	Arm B	Cycle 1- Day 1/ before cycle	2.26 mmol/l	143 mmol/l	4.29 mmol/l	0.9 mmol/l	16.2 µmol/l	80 µmol/l		0.4 µmol/sl	0.3 µmol/sl	0.56 µmol/sl	4.3 mmol/l	1.46 µmol/sl
0088	Arm B	Cycle 2- Day 1/ before cycle	2.44 mmol/l	135 mmol/l	4.92 mmol/l	1.08 mmol/l	13.7 µmol/l	52 µmol/l		0.65 µmol/sl	0.64 µmol/sl	0.61 µmol/sl	3.4 mmol/l	1.74 µmol/sl

Patient No.	Treatment Arm	Point in time	Calcium	Sodium	Potassium	Magnesium	Bilirubin (total)	Creatinine	Ceratinine clearance	GOT (ASAT)	GPT (ALAT)	Gamma-GT	Urea	Alkaline phosphatase
0088	Arm B	Cycle 3- Day 1/ before cycle	2.28 mmol/l	139 mmol/l	4.22 mmol/l	0.87 mmol/l	22.7 µmol/l	73 µmol/l		1.47 µmol/sl	2.13 µmol/sl	0.84 µmol/sl	4.5 mmol/l	1.93 µmol/sl
0088	Arm B	Cycle 4- Day 1/ before cycle	2.29 mmol/l	140 mmol/l	4.16 mmol/l	0.88 mmol/l	12.3 µmol/l	74 µmol/l		1.24 µmol/sl	1.89 µmol/sl	1.26 µmol/sl	4.1 mmol/l	2.36 µmol/sl
0088	Arm B	Cycle 5- Other timepoints	2.3 mmol/l	135 mmol/l	3.97 mmol/l	0.83 mmol/l	25.6 µmol/l	69 µmol/l		1.12 µmol/sl	1.66 µmol/sl	1.91 µmol/sl	5 mmol/l	2.46 µmol/sl
0088	Arm B	Cycle 6- Day 1/ before cycle	2.24 mmol/l	141 mmol/l	3.74 mmol/l	0.93 mmol/l	23.4 µmol/l	66 µmol/l		1 µmol/sl	1.24 µmol/sl	2.39 µmol/sl	4.8 mmol/l	2.8 µmol/sl
0162	Arm B	Pre-examination	2.3 mmol/l	138.6 mmol/l	4.02 mmol/l	0.83 mmol/l	8.7 µmol/l	63 µmol/l	90 ml/min	0.26 µmol/sl	0.15 µmol/sl	0.99 µmol/sl	4.4 mmol/l	1.47 µmol/sl
0162	Arm B	Surgery					13.4 µmol/l	51 µmol/l		4.43 µmol/sl	3.26 µmol/sl	0.57 µmol/sl	4.8 mmol/l	1.32 µmol/sl
0162	Arm B	Cycle 1- Day 1/ before cycle	2.41 mmol/l	141.2 mmol/l	4.28 mmol/l	0.81 mmol/l	6.5 µmol/l	64 µmol/l	90 ml/min	0.33 µmol/sl	0.21 µmol/sl	1.03 µmol/sl	4.3 mmol/l	1.48 µmol/sl
0162	Arm B	Cycle 1- Other timepoints	2.25 mmol/l	143.6 mmol/l	4.01 mmol/l	0.79 mmol/l	6.3 µmol/l	57 µmol/l	90 ml/min	0.26 µmol/sl	0.17 µmol/sl	0.85 µmol/sl	3.5 mmol/l	1.39 µmol/sl
0162	Arm B	Cycle 2- Day 1/ before cycle	2.38 mmol/l	143.5 mmol/l	4.78 mmol/l	0.89 mmol/l	4.6 µmol/l	61 µmol/l	90 ml/min	0.33 µmol/sl	0.31 µmol/sl	0.79 µmol/sl	4 mmol/l	1.91 µmol/sl
0162	Arm B	Cycle 2- Other timepoints	2.31 mmol/l	144 mmol/l	6.39 mmol/l	0.87 mmol/l	6.3 µmol/l	65 µmol/l	91 ml/min	0.75 µmol/sl	0.25 µmol/sl	0.74 µmol/sl	3.8 mmol/l	1.67 µmol/sl
0162	Arm B	Cycle 3- Day 1/ before cycle	2.28 mmol/l	139 mmol/l	4.02 mmol/l	0.82 mmol/l	7.5 µmol/l	60 µmol/l	90 ml/min	0.53 µmol/sl	0.34 µmol/sl	0.73 µmol/sl	3.2 mmol/l	1.81 µmol/sl
0162	Arm B	Cycle 3- Other timepoints	2.32 mmol/l	140.1 mmol/l	4.16 mmol/l	0.78 mmol/l	6 µmol/l	60 µmol/l	90 ml/min	0.57 µmol/sl	0.5 µmol/sl	0.72 µmol/sl	4.7 mmol/l	1.8 µmol/sl
0162	Arm B	Cycle 4- Day 1/ before cycle	2.29 mmol/l	144.6 mmol/l	4.2 mmol/l	0.81 mmol/l	8.2 µmol/l	57 µmol/l	90 ml/min	0.75 µmol/sl	0.86 µmol/sl	0.8 µmol/sl	3.9 mmol/l	1.96 µmol/sl
0162	Arm B	Cycle 4- Other timepoints	2.35 mmol/l	140.5 mmol/l	3.93 mmol/l	0.76 mmol/l	7.8 µmol/l	55 µmol/l	90 ml/min	0.39 µmol/sl	0.53 µmol/sl	0.82 µmol/sl	3.8 mmol/l	1.89 µmol/sl
0162	Arm B	Cycle 5- Day 1/ before cycle	2.35 mmol/l	141.4 mmol/l	4.05 mmol/l	0.8 mmol/l	12.7 µmol/l	65 µmol/l	90 ml/min	0.76 µmol/sl	0.86 µmol/sl	0.88 µmol/sl	4.9 mmol/l	1.9 µmol/sl
0162	Arm B	Cycle 5- Other timepoints	2.28 mmol/l	142.1 mmol/l	4.25 mmol/l	0.8 mmol/l	8.1 µmol/l	56 µmol/l	90 ml/min	0.5 µmol/sl	0.4 µmol/sl	0.81 µmol/sl	3.4 mmol/l	1.8 µmol/sl
0162	Arm B	Cycle 6- Day 1/ before cycle	2.28 mmol/l	143.8 mmol/l	4.16 mmol/l	0.79 mmol/l	6.9 µmol/l	57 µmol/l	90 ml/min	0.61 µmol/sl	0.58 µmol/sl	0.84 µmol/sl	3.8 mmol/l	125 µmol/sl
0162	Arm B	Cycle 7- Day 1/ before cycle	2.53 mmol/l	138.8 mmol/l	4.85 mmol/l	0.81 mmol/l	4.8 µmol/l	61 µmol/l	93.5 ml/min	0.39 µmol/sl	0.22 µmol/sl	2.04 µmol/sl	4.7 mmol/l	2.53 µmol/sl
0162	Arm B	Cycle 7- Other timepoints	2.33 mmol/l	134.5 mmol/l	4.17 mmol/l	0.78 mmol/l	4.6 µmol/l	53 µmol/l	110 ml/min	0.45 µmol/sl	0.24 µmol/sl	1.79 µmol/sl	4.5 mmol/l	2.36 µmol/sl
0162	Arm B	Cycle 8- Day 1/ before cycle	2.19 mmol/l	141.5 mmol/l	4.14 mmol/l	0.82 mmol/l	6.6 µmol/l	52 µmol/l	112.5 ml/min	0.43 µmol/sl	0.19 µmol/sl	1.28 µmol/sl	3.6 mmol/l	2.35 µmol/sl

Patient No.	Treatment Arm	Point in time	Calcium	Sodium	Potassium	Magnesium	Bilirubin (total)	Creatinine	Ceratinine clearance	GOT (ASAT)	GPT (ALAT)	Gamma-GT	Urea	Alkaline phosphatase
0162	Arm B	Cycle 8- Other timepoints	2.23 mmol/l		3.91 mmol/l		8.9 µmol/l	59 µmol/l	90 ml/min		0.19 µmol/sl	1.23 µmol/sl	2.5 mmol/l	2.31 µmol/sl
0162	Arm B	Cycle 9- Day 1/ before cycle	2.36 mmol/l	139.2 mmol/l	4.46 mmol/l	0.79 mmol/l	5.4 µmol/l	49 µmol/l	101.3 ml/min	0.47 µmol/sl	0.2 µmol/sl	1.13 µmol/sl	3.7 mmol/l	2.48 µmol/sl
0162	Arm B	Cycle 10- Day 1/ before cycle	2.39 mmol/l	140.8 mmol/l	4.52 mmol/l	0.85 mmol/l	9.2 µmol/l	55 µmol/l	105.4 ml/min	0.49 µmol/sl	0.23 µmol/sl	1.13 µmol/sl	4.3 mmol/l	2.63 µmol/sl
0162	Arm B	Cycle 10- Other timepoints	2.29 mmol/l	142.7 mmol/l	4.48 mmol/l	0.75 mmol/l	9.1 µmol/l	52 µmol/l	90 ml/min	0.32 µmol/sl	0.23 µmol/sl	1.07 µmol/sl	3.4 mmol/l	2.56 µmol/sl
0162	Arm B	Cycle 11- Day 1/ before cycle	2.27 mmol/l	142.6 mmol/l	4.22 mmol/l		12 µmol/l	60 µmol/l	95.3 ml/min		0.25 µmol/sl	1.01 µmol/sl	2.2 mmol/l	2.61 µmol/sl
0162	Arm B	Cycle 11- Other timepoints	2.41 mmol/l	140.7 mmol/l	4.44 mmol/l	0.75 mmol/l	7.6 µmol/l	56 µmol/l	90 ml/min		0.19 µmol/sl	1.07 µmol/sl	3.6 mmol/l	2.76 µmol/sl
0162	Arm B	Cycle 12- Day 1/ before cycle	2.35 mmol/l	143.5 mmol/l	4.2 mmol/l		8.2 µmol/l	55 µmol/l	90 ml/min		0.21 µmol/sl	1.01 µmol/sl	3.6 mmol/l	2.62 µmol/sl
0162	Arm B	Cycle 12- Other timepoints	2.33 mmol/l	139.7 mmol/l	4.27 mmol/l	0.76 mmol/l	7.6 µmol/l	62 µmol/l	91.8 ml/min	0.63 µmol/sl	0.29 µmol/sl	1.02 µmol/sl	3.8 mmol/l	2.62 µmol/sl
0162	Arm B	End of treatment	2.33 mmol/l	138.8 mmol/l	4.06 mmol/l	0.73 mmol/l	12.5 µmol/l	62 µmol/l	82.02 ml/min	0.34 µmol/sl	0.35 µmol/sl	0.9 µmol/sl	3.9 mmol/l	2.58 µmol/sl
0164	Arm B	Pre-examination	2.51 mmol/l	137 mmol/l	4.02 mmol/l		17 µmol/l	78 µmol/l		0.69 µmol/sl	1 µmol/sl	0.91 µmol/sl		1.16 µmol/sl
0164	Arm B	Cycle 1- Day 1/ before cycle	2.44 mmol/l	136 mmol/l	3.8 mmol/l	0.72 mmol/l	14 µmol/l	90 µmol/l		0.51 µmol/sl	0.78 µmol/sl	0.79 µmol/sl	7.1 mmol/l	1.37 µmol/sl
0164	Arm B	Cycle 2- Day 1/ before cycle	2.4 mmol/l	139 mmol/l	3.01 mmol/l		13 µmol/l	77 µmol/l		0.59 µmol/sl	0.87 µmol/sl			1.27 µmol/sl
0164	Arm B	Cycle 3- Day 1/ before cycle	2.48 mmol/l	138 mmol/l	3.03 mmol/l		22 µmol/l	85 µmol/l			1.08 µmol/sl			1.13 µmol/sl
0164	Arm B	Cycle 4- Day 1/ before cycle	2.42 mmol/l	138 mmol/l	3.03 mmol/l	0.57 mmol/l	16 µmol/l	79 µmol/l		0.62 µmol/sl	0.85 µmol/sl	0.68 µmol/sl	5.6 mmol/l	1.16 µmol/sl
0164	Arm B	Cycle 5- Day 1/ before cycle	2.44 mmol/l	136 mmol/l	3.13 mmol/l	0.65 mmol/l	18 µmol/l	83 µmol/l			0.6 µmol/sl		8.4 mmol/l	1.11 µmol/sl
0164	Arm B	Cycle 6- Day 1/ before cycle	2.35 mmol/l	138 mmol/l	3.58 mmol/l	0.64 mmol/l	9 µmol/l	112 µmol/l		0.6 µmol/sl	0.64 µmol/sl	1.19 µmol/sl	7.8 mmol/l	1.2 µmol/sl
0164	Arm B	End of treatment	2.52 mmol/l	140 mmol/l	3.6 mmol/l		13 µmol/l	95 µmol/l		0.56 µmol/sl	0.55 µmol/sl	1.12 µmol/sl		1.24 µmol/sl
0165	Arm B	Pre-examination	4.89 mmol/l	144 mmol/l	4.89 mmol/l	0.85 mmol/l	0.3 mg/dl	0.95 mg/dl	67.37 ml/min	28 U/l	40 U/l	45 U/l	38 mg/dl	68 U/l
0165	Arm B	Surgery	2.33 mmol/l	144 mmol/l	4.34 mmol/l		0.4 mg/dl	0.83 mg/dl	92.1 ml/min		38 U/l	46 U/l		76 U/l
0165	Arm B	Cycle 1- Day 1/ before cycle		142 mmol/l	4.7 mmol/l		0.3 mg/dl	0.87 mg/dl		25 U/l	31 U/l	39 U/l		71 U/l

Patient No.	Treatment Arm	Point in time	Calcium	Sodium	Potassium	Magnesium	Bilirubin (total)	Creatinine	Ceratinine clearance	GOT (ASAT)	GPT (ALAT)	Gamma-GT	Urea	Alkaline phosphatase
0165	Arm B	Cycle 2- Day 1/ before cycle	2.19 mmol/l	142 mmol/l	4.52 mmol/l	0.77 mmol/l	0.3 mg/dl	0.82 mg/dl	93.4 ml/min	22 U/l	28 U/l	34 U/l	22 mg/dl	
0165	Arm B	Cycle 3- Day 1/ before cycle	2.35 mmol/l	143 mmol/l	5.05 mmol/l	0.78 mmol/l	0.3 mg/dl	1 mg/dl	74.3 ml/min	26 U/l	25 U/l	34 U/l	25 mg/dl	
0165	Arm B	Cycle 4- Day 1/ before cycle	2.39 mmol/l	142 mmol/l	4.91 mmol/l	0.69 mmol/l	0.2 mg/dl	0.81 mg/dl	94.8 ml/min	32 U/l	28 U/l	44 U/l	27 mg/dl	
0165	Arm B	Cycle 5- Day 1/ before cycle	2.36 mmol/l	146 mmol/l	4.65 mmol/l	0.78 mmol/l	0.2 mg/dl	0.82 mg/dl	93.4 ml/min	38 U/l	28 U/l	42 U/l	20 mg/dl	
0165	Arm B	Cycle 6- Day 1/ before cycle	2.35 mmol/l	142 mmol/l	4.89 mmol/l	0.67 mmol/l	0.2 mg/dl	0.79 mg/dl	97.5 ml/min	43 U/l	39 U/l	48 U/l	23 mg/dl	
0165	Arm B	Cycle 7- Day 1/ before cycle		142 mmol/l	4.25 mmol/l		0.3 mg/dl	0.85 mg/dl	89.6 ml/min	21 U/l	16 U/l	127 U/l		97 U/l
0165	Arm B	Cycle 8- Day 1/ before cycle	0.73 mmol/l	141 mmol/l	4.42 mmol/l	0.73 mmol/l		0.82 mg/dl	93.4 ml/min	29 U/l	29 U/l	159 U/l	21 mg/dl	
0165	Arm B	Cycle 9- Day 1/ before cycle	2.34 mmol/l	141 mmol/l	4.43 mmol/l	0.72 mmol/l	0.5 mg/dl	0.72 mg/dl	108.6 ml/min	38 U/l	34 U/l	124 U/l		
0165	Arm B	Cycle 10- Day 1/ before cycle	2.34 mmol/l	144 mmol/l	4.91 mmol/l	0.73 mmol/l	0.2 mg/dl	0.73 mg/dl	106.8 ml/min	38 U/l	35 U/l	127 U/l	30 mg/dl	
0165	Arm B	Cycle 11- Day 1/ before cycle	2.3 mmol/l	140 mmol/l	4.56 mmol/l	0.7 mmol/l	0.2 mg/dl	0.76 mg/dl	102 ml/min	33 U/l	31 U/l	102 U/l	26 mg/dl	
0165	Arm B	Cycle 12- Day 1/ before cycle	2.27 mmol/l	147 mmol/l	5.13 mmol/l	0.71 mmol/l	0.2 mg/dl	0.79 mg/dl	97.5 ml/min	36 U/l	32 U/l	119 U/l	30 mg/dl	
0165	Arm B	End of treatment	2.27 mmol/l	147 mmol/l	5.13 mmol/l	0.71 mmol/l	0.2 mg/dl	0.79 mg/dl	97.5 ml/min	36 U/l	32 U/l	119 U/l	30 mg/dl	
0167	Arm B	Pre-examination	2.58 mmol/l	138 mmol/l	4.6 mmol/l		0.8 mg/100ml	0.6 mg/dl		42 U/l	23 U/l	102 U/l		220 U/l
0167	Arm B	Surgery	2.51 mmol/l	144 mmol/l	4.7 mmol/l		0.6 mg/100ml	0.5 mg/dl		50 U/l	34 U/l	52 U/l	7 mg/dl	162 U/l
0167	Arm B	Cycle 1- Day 1/ before cycle	2.35 mmol/l	141 mmol/l	4.3 mmol/l	0.81 mmol/l	0.3 mg/100ml	0.6 mg/dl		39 U/l		148 U/l		217 U/l
0167	Arm B	Cycle 2- Day 1/ before cycle	2.42 mmol/l	138 mmol/l	4.7 mmol/l		0.5 mg/100ml	0.6 mg/dl		43 U/l		119 U/l		186 U/l
0167	Arm B	Cycle 3- Day 1/ before cycle	2.42 mmol/l	139 mmol/l	4.5 mmol/l	0.72 mmol/l	0.7 mg/100ml	0.7 mg/dl		34 U/l	31 U/l	84 U/l		189 U/l
0167	Arm B	Cycle 4- Day 1/ before cycle	2.37 mmol/l	139 mmol/l	4.7 mmol/l	0.72 mmol/l	0.2 mg/100ml	0.6 mg/dl		40 U/l		63 U/l		170 U/l
0167	Arm B	Cycle 5- Day 1/ before cycle	2.26 mmol/l	139 mmol/l	4.3 mmol/l		0.3 mg/100ml	0.5 mg/dl		38 U/l	36 U/l	52 U/l		155 U/l
0167	Arm B	Cycle 6- Day 1/ before cycle	2.31 mmol/l	141 mmol/l	4.7 mmol/l	0.72 mmol/l	0.4 mg/100ml	0.5 mg/dl		55 U/l		50 U/l		153 U/l

Patient No.	Treatment Arm	Point in time	Calcium	Sodium	Potassium	Magnesium	Bilirubin (total)	Creatinine	Ceratinine clearance	GOT (ASAT)	GPT (ALAT)	Gamma-GT	Urea	Alkaline phosphatase
0167	Arm B	Cycle 7- Day 1/ before cycle	2.3 mmol/l	138 mmol/l	5 mmol/l	0.79 mmol/l	0.3 mg/100ml	0.5 mg/dl		32 U/l	19 U/l	141 U/l		235 U/l
0167	Arm B	Cycle 8- Day 1/ before cycle	2.3 mmol/l	141 mmol/l	4.1 mmol/l	0.77 mmol/l	0.3 mg/100ml	0.4 mg/dl		22 U/l		146 U/l		268 U/l
0167	Arm B	Cycle 9- Day 1/ before cycle	2.23 mmol/l	139 mmol/l	4.7 mmol/l	0.75 mmol/l	0.3 mg/100ml	0.5 mg/dl		31 U/l		103 U/l		257 U/l
0167	Arm B	Cycle 10- Day 1/ before cycle	2.3 mmol/l	141 mmol/l	3.8 mmol/l	0.69 mmol/l	0.4 mg/100ml	0.5 mg/dl		25 U/l		83 U/l		247 U/l
0167	Arm B	Cycle 11- Day 1/ before cycle	2.3 mmol/l	139 mmol/l	4.4 mmol/l		0.4 mg/100ml	0.5 mg/dl		37 U/l	22 U/l	100 U/l		245 U/l
0167	Arm B	Cycle 12- Day 1/ before cycle	2.35 mmol/l	143 mmol/l	4.7 mmol/l	0.73 mmol/l	0.5 mg/100ml	0.5 mg/dl		48 U/l	25 U/l	99 U/l		254 U/l
0167	Arm B	End of treatment	2.51 mmol/l	143 mmol/l	5 mmol/l	0.68 mmol/l	0.5 mg/100ml	0.5 mg/dl		38 U/l	24 U/l	121 U/l	9 mg/dl	268 U/l
0241	Arm B	Pre-examination	2.28 mmol/l	140 mmol/l	4.8 mmol/l	0.8 mmol/l	0.86 mg/dl	0.85 mg/dl	89 ml/min	25 U/l	16 U/l	59 U/l	36 mg/dl	108 U/l
0241	Arm B	Surgery	2.16 mmol/l	138 mmol/l	4.5 mmol/l	0.9 mmol/l	0.57 mg/dl	0.61 mg/dl	90 ml/min	26 U/l	48 U/l	98 U/l	18 mg/dl	129 U/l
0241	Arm B	Surgery	2.24 mmol/l	142 mmol/l	5.4 mmol/l	0.84 mmol/l	0.31 mg/dl	0.63 mg/dl	90 ml/min	23 U/l	21 U/l	85 U/l	18 mg/dl	137 U/l
0241	Arm B	Surgery	2.16 mmol/l	149 mmol/l	4.5 mmol/l	0.79 mmol/l	0.93 mg/dl	0.62 mg/dl	90 ml/min	249 U/l	186 U/l	35 U/l	17 mg/dl	95 U/l
0241	Arm B	Surgery	2.36 mmol/l	141 mmol/l	4.3 mmol/l	0.82 mmol/l	0.93 mg/dl	0.67 mg/dl	90 ml/min	29 U/l	25 U/l	54 U/l		131 U/l
0241	Arm B	Surgery	2.14 mmol/l	140 mmol/l	4.7 mmol/l	0.74 mmol/l	1.08 mg/dl	0.62 mg/dl	90 ml/min	270 U/l	228 U/l	29 U/l	17 mg/dl	78 U/l
0241	Arm B	Surgery	2.12 mmol/l	139 mmol/l	4.8 mmol/l	0.88 mmol/l	0.6 mg/dl	0.59 mg/dl	90 ml/min	29 U/l	57 U/l	89 U/l	20 mg/dl	117 U/l
0241	Arm B	Surgery	2.05 mmol/l	139 mmol/l	4.6 mmol/l	0.81 mmol/l	1.03 mg/dl	0.58 mg/dl	90 ml/min	40 U/l	86 U/l	68 U/l	12 mg/dl	93 U/l
0241	Arm B	Surgery	2.03 mmol/l	139 mmol/l	4.6 mmol/l	0.81 mmol/l	0.67 mg/dl	0.51 mg/dl	90 ml/min	30 U/l	66 U/l	86 U/l	16 mg/dl	105 U/l
0241	Arm B	Surgery	2.12 mmol/l	138 mmol/l	4.5 mmol/l	0.72 mmol/l	1.19 mg/dl	0.62 mg/dl	90 ml/min	68 U/l	138 U/l	43 U/l	11 mg/dl	96 U/l
0241	Arm B	Cycle 1- Day 1/ before cycle	2.29 mmol/l	139 mmol/l	4.6 mmol/l	0.85 mmol/l	0.69 mg/dl	0.76 mg/dl	90 ml/min	25 U/l	18 U/l	58 U/l	41 mg/dl	106 U/l
0241	Arm B	Cycle 2- Day 1/ before cycle	2.23 mmol/l	137 mmol/l	4.7 mmol/l	0.88 mmol/l	1.03 mg/dl	0.75 mg/dl	90 ml/min	28 U/l	29 U/l	38 U/l	26 mg/dl	127 U/l
0241	Arm B	Cycle 3- Day 1/ before cycle	2.31 mmol/l	138 mmol/l	5.1 mmol/l	0.81 mmol/l	0.49 mg/dl	0.77 mg/dl	90 ml/min	27 U/l	31 U/l	25 U/l	32 mg/dl	117 U/l

Patient No.	Treatment Arm	Point in time	Calcium	Sodium	Potassium	Magnesium	Bilirubin (total)	Creatinine	Ceratinine clearance	GOT (ASAT)	GPT (ALAT)	Gamma-GT	Urea	Alkaline phosphatase
0241	Arm B	Cycle 4- Day 1/ before cycle	2.2 mmol/l	141 mmol/l	4.8 mmol/l	0.78 mmol/l	0.69 mg/dl	0.7 mg/dl	90 ml/min	29 U/l	28 U/l	28 U/l	29 mg/dl	102 U/l
0241	Arm B	Cycle 5- Day 1/ before cycle	2.34 mmol/l	137 mmol/l	4.4 mmol/l	0.67 mmol/l	1.14 mg/dl	0.77 mg/dl	90 ml/min	42 U/l	50 U/l	33 U/l	27 mg/dl	125 U/l
0241	Arm B	Cycle 6- Day 1/ before cycle	2.25 mmol/l	139 mmol/l	4.6 mmol/l	0.74 mmol/l	0.83 mg/dl	0.7 mg/dl	90 ml/min	43 U/l	47 U/l	30 U/l	19 mg/dl	118 U/l
0241	Arm B	Cycle 7- Day 1/ before cycle	2.3 mmol/l	142 mmol/l	4.9 mmol/l	0.85 mmol/l	0.5 mg/dl	0.7 mg/dl		16 U/l	11 U/l	45 U/l	26 mg/dl	114 U/l
0241	Arm B	Cycle 8- Day 1/ before cycle	2.3 mmol/l	137 mmol/l	4.5 mmol/l	0.84 mmol/l	0.6 mg/dl	0.6 mg/dl		21 U/l	19 U/l	39 U/l	25 mg/dl	132 U/l
0241	Arm B	Cycle 9- Day 1/ before cycle		139 mmol/l	4.41 mmol/l			0.66 mg/dl					23 mg/dl	
0241	Arm B	Cycle 10- Day 1/ before cycle	2.4 mmol/l	141 mmol/l	4.2 mmol/l	0.86 mmol/l	0.9 mg/dl	0.6 mg/dl		34 U/l	34 U/l	45 U/l	22 mg/dl	157 U/l
0241	Arm B	Cycle 11- Day 1/ before cycle	2.3 mmol/l	138 mmol/l	3.9 mmol/l	0.81 mmol/l	0.9 mg/dl	0.6 mg/dl		39 U/l	36 U/l	43 U/l	21 mg/dl	131 U/l
0241	Arm B	Cycle 12- Day 1/ before cycle	2.2 mmol/l	139 mmol/l	4.1 mmol/l	0.69 mmol/l	1 mg/dl	0.6 mg/dl		39 U/l	39 U/l	41 U/l	23 mg/dl	140 U/l
0241	Arm B	End of treatment	2.4 mmol/l	136 mmol/l	4.4 mmol/l	0.88 mmol/l	0.6 mg/dl	0.7 mg/dl		47 U/l	38 U/l	66 U/l	18 mg/dl	178 U/l
0242	Arm B	Pre-examination	2.64 mmol/l	136 mmol/l	4.96 mmol/l	0.83 mmol/l	6.3 µmol/l	96 mmol/l		19 U/l	12 U/l	40 U/l	5.7 mmol/l	74 U/l
0242	Arm B	Surgery		139 mmol/l	4.66 mmol/l		8.1 µmol/l	96 µmol/l			18 U/l	37 U/l		
0242	Arm B	Surgery					11.3 µmol/l	121 µmol/l			129 U/l	30 U/l	10.1 mmol/l	
0242	Arm B	Surgery		140 mmol/l	4.12 mmol/l			91 µmol/l						
0242	Arm B	Surgery		140 mmol/l	4.23 mmol/l			86 µmol/l						
0242	Arm B	Cycle 1- Other timepoints	2.35 mmol/l	139 mmol/l	3.78 mmol/l	0.68 mmol/l	5.9 µmol/l	83 µmol/l		17 U/l	12 U/l	26 U/l	4.2 mmol/l	69 U/l
0242	Arm B	Cycle 2- Day 1/ before cycle	2.42 mmol/l	139 mmol/l	4.19 mmol/l	0.74 mmol/l	8.2 µmol/l	84 µmol/l		22 U/l	15 U/l	35 U/l	5 mmol/l	78 U/l
0242	Arm B	Cycle 2- Other timepoints	2.4 mmol/l	139 mmol/l	3.82 mmol/l	0.72 mmol/l	12.5 µmol/l	82 µmol/l		19 U/l	14 U/l	32 U/l	5.6 mmol/l	76 U/l
0242	Arm B	Cycle 3- Day 1/ before cycle	2.37 mmol/l	138 mmol/l	4.3 mmol/l	0.76 mmol/l	8.2 µmol/l	83 µmol/l		21 U/l	19 U/l	44 U/l	5.2 mmol/l	89 U/l
0242	Arm B	Cycle 3- Other timepoints	2.3 mmol/l	139 mmol/l	3.99 mmol/l	0.73 mmol/l	5.4 µmol/l	83 µmol/l		17 U/l	17 U/l	31 U/l	5.8 mmol/l	81 U/l
0242	Arm B	Cycle 4- Day 1/ before cycle	2.41 mmol/l	139 mmol/l	3.92 mmol/l	0.66 mmol/l	8.9 µmol/l	88 µmol/l		17 U/l	20 U/l	35 U/l	5.3 mmol/l	89 U/l
0242	Arm B	Cycle 5- Day 1/ before cycle	2.46 mmol/l	140 mmol/l	3.91 mmol/l	0.66 mmol/l	5.3 µmol/l	95 µmol/l		17 U/l	15 U/l	30 U/l	5.7 mmol/l	86 U/l

Patient No.	Treatment Arm	Point in time	Calcium	Sodium	Potassium	Magnesium	Bilirubin (total)	Creatinine	Ceratinine clearance	GOT (ASAT)	GPT (ALAT)	Gamma-GT	Urea	Alkaline phosphatase
0242	Arm B	Cycle 5- Other timepoints	2.38 mmol/l	138 mmol/l	3.79 mmol/l	0.73 mmol/l	10.9 µmol/l	81 µmol/l		20 U/l	15 U/l	26 U/l	6.3 mmol/l	84 U/l
0242	Arm B	Cycle 6- Day 1/ before cycle	2.41 mmol/l	138 mmol/l	3.87 mmol/l		7 µmol/l	98 µmol/l		21 U/l	17 U/l		4.6 mmol/l	88 U/l
0242	Arm B	Cycle 6- Other timepoints	2.47 mmol/l	138 mmol/l	4.64 mmol/l	0.65 mmol/l	9.3 µmol/l	93 µmol/l		19 U/l	20 U/l	29 U/l	5.8 mmol/l	88 U/l
0242	Arm B	Cycle 7- Day 1/ before cycle	2.45 mmol/l	140 mmol/l	3.97 mmol/l	0.72 mmol/l	10.1 µmol/l	81 µmol/l		20 U/l	14 U/l		5.9 mmol/l	85 U/l
0242	Arm B	Cycle 7- Other timepoints	2.37 mmol/l	140 mmol/l	4.06 mmol/l	0.77 mmol/l	8.2 µmol/l	74 µmol/l		21 U/l	16 U/l		5.2 mmol/l	101 U/l
0242	Arm B	Cycle 8- Day 1/ before cycle	2.38 mmol/l	139 mmol/l	3.96 mmol/l	0.7 mmol/l	8.4 µmol/l	81 µmol/l		22 U/l	18 U/l		5.3 mmol/l	95 U/l
0242	Arm B	Cycle 8- Other timepoints	2.36 mmol/l	142 mmol/l	3.68 mmol/l	0.66 mmol/l	8.6 µmol/l	84 µmol/l		26 U/l	18 U/l		6 mmol/l	104 U/l
0242	Arm B	Cycle 9- Day 1/ before cycle	2.32 mmol/l	139 mmol/l	3.8 mmol/l	0.69 mmol/l	7 µmol/l	80 µmol/l		19 U/l	18 U/l		5.5 mmol/l	108 U/l
0242	Arm B	Cycle 10- Day 1/ before cycle	2.43 mmol/l	140 mmol/l	3.59 mmol/l	0.62 mmol/l	6.6 µmol/l	88 µmol/l		26 U/l	25 U/l	44 U/l	5.8 mmol/l	135 U/l
0242	Arm B	Cycle 11- Day 1/ before cycle	2.36 mmol/l	140 mmol/l	3.58 mmol/l		7.8 µmol/l	82 µmol/l		21 U/l	18 U/l		4.4 mmol/l	148 U/l
0242	Arm B	Cycle 12- Day 1/ before cycle	2.41 mmol/l	138 mmol/l	3.72 mmol/l	0.59 mmol/l	12.7 µmol/l	92 µmol/l		29 U/l	19 U/l	40 U/l	5.7 mmol/l	110 U/l
0242	Arm B	Cycle 12- Other timepoints	2.35 mmol/l	136 mmol/l	3.74 mmol/l	0.63 mmol/l	9.9 µmol/l	86 µmol/l		21 U/l	21 U/l	38 U/l	6.7 mmol/l	99 U/l
0242	Arm B	End of treatment	2.51 mmol/l	139 mmol/l	3.74 mmol/l	0.69 mmol/l	9.5 µmol/l	90 µmol/l		28 U/l	20 U/l		4.5 mmol/l	
0401	Arm B	Pre-examination	2.24 mmol/l	137.6 mmol/l	4.76 mmol/l	0.94 mmol/l	5.1 µmol/l	82 µmol/l		0.36 µkatal/l	0.51 µkatal/l	0.47 µkatal/l	4.88 mmol/l	0.96 µkatal/l
0401	Arm B	Surgery	2.19 mmol/l	142.5 mmol/l	5.95 mmol/l	0.84 mmol/l	36.3 µmol/l	72 µmol/l		4.34 µkatal/l	4.66 µkatal/l	0.66 µkatal/l	6.09 mmol/l	1.09 µkatal/l
0401	Arm B	Surgery					28 µmol/l	56 µmol/l			2.42 µkatal/l		4.35 mmol/l	1.63 µkatal/l
0401	Arm B	Surgery	2.14 mmol/l	139.6 mmol/l	3.38 mmol/l	0.79 mmol/l	38.2 µmol/l	66 µmol/l		0.49 µkatal/l	1.04 µkatal/l	2.01 µkatal/l	6.6 mmol/l	1.86 µkatal/l
0401	Arm B	Surgery	2.17 mmol/l	138.5 mmol/l	3.85 mmol/l	0.78 mmol/l	39.8 µmol/l	64 µmol/l		0.78 µkatal/l	1.6 µkatal/l	2.13 µkatal/l	5.3 mmol/l	1.95 µkatal/l
0401	Arm B	Surgery	2.11 mmol/l	139.9 mmol/l	3.76 mmol/l		43.2 µmol/l	75 µmol/l		0.48 µkatal/l	0.71 µkatal/l	2.41 µkatal/l	7.8 mmol/l	1.89 µkatal/l
0401	Arm B	Surgery	2.41 mmol/l	141.7 mmol/l	5.05 mmol/l	0.87 mmol/l	5.6 µmol/l	85 µmol/l		0.37 µkatal/l	0.39 µkatal/l	0.35 µkatal/l	5.89 mmol/l	1.13 µkatal/l

Patient No.	Treatment Arm	Point in time	Calcium	Sodium	Potassium	Magnesium	Bilirubin (total)	Creatinine	Ceratinine clearance	GOT (ASAT)	GPT (ALAT)	Gamma-GT	Urea	Alkaline phosphatase
0401	Arm B	Surgery	2.17 mmol/l	142 mmol/l	5.17 mmol/l	0.89 mmol/l	34.4 µmol/l	73 µmol/l		3.25 µkatal/l	3.6 µkatal/l	0.54 µkatal/l	7.71 mmol/l	1.06 µkatal/l
0401	Arm B	Surgery					29.3 µmol/l	66 µmol/l					6.86 mmol/l	
0401	Arm B	Surgery					16.3 µmol/l	76 µmol/l		3.88 µkatal/l	3.78 µkatal/l	0.53 µkatal/l	5.77 mmol/l	0.92 µkatal/l
0401	Arm B	Cycle 1- Day 1/ before cycle	2.36 mmol/l	136.5 mmol/l	4.52 mmol/l	0.95 mmol/l	5.7 µmol/l	82 µmol/l		0.34 µkatal/l	0.32 µkatal/l	0.32 µkatal/l	4.1 mmol/l	1.04 µkatal/l
0401	Arm B	Cycle 2- Day 1/ before cycle	2.18 mmol/l	138.2 mmol/l	4.4 mmol/l	0.91 mmol/l	3 µmol/l	65 µmol/l		0.37 µkatal/l	0.22 µkatal/l	0.3 µkatal/l	4.83 mmol/l	1.18 µkatal/l
0401	Arm B	Cycle 3- Day 1/ before cycle	2.19 mmol/l	141 mmol/l	4.29 mmol/l	0.85 mmol/l	6.1 µmol/l	65 µmol/l		0.42 µkatal/l	0.28 µkatal/l	0.36 µkatal/l	4.96 mmol/l	0.91 µkatal/l
0401	Arm B	Cycle 4- Day 1/ before cycle	2.22 mmol/l	141.4 mmol/l	4.16 mmol/l	0.96 mmol/l	7.9 µmol/l	66 µmol/l		0.35 µkatal/l	0.31 µkatal/l		4.79 mmol/l	1.18 µkatal/l
0401	Arm B	Cycle 5- Day 1/ before cycle	2.26 mmol/l	141.7 mmol/l	4.04 mmol/l	0.74 mmol/l	6.3 µmol/l	66 µmol/l		0.43 µkatal/l	0.46 µkatal/l	0.25 µkatal/l	4.7 mmol/l	0.97 µkatal/l
0401	Arm B	Cycle 6- Day 1/ before cycle	2.21 mmol/l	141.9 mmol/l	4.03 mmol/l	0.8 mmol/l	8.3 µmol/l	65 µmol/l		0.46 µkatal/l	0.45 µkatal/l	0.29 µkatal/l	4.03 mmol/l	0.96 µkatal/l
0401	Arm B	Cycle 7- Day 1/ before cycle	2.2 mmol/l	134.5 mmol/l	4.64 mmol/l	0.87 mmol/l	11.3 µmol/l	76 µmol/l		0.61 µkatal/l	0.36 µkatal/l		4.64 mmol/l	
0401	Arm B	Cycle 10- Day 1/ before cycle	2.24 mmol/l	138 mmol/l	4.17 mmol/l	0.82 mmol/l	8.4 µmol/l	74 µmol/l		0.47 µkatal/l	0.39 µkatal/l		5.8 mmol/l	
0401	Arm B	Cycle 11- Day 1/ before cycle	2.19 mmol/l	135.1 mmol/l	4.07 mmol/l	0.92 mmol/l	10.7 µmol/l	81 µmol/l		0.62 µkatal/l	0.74 µkatal/l		4.3 mmol/l	
0401	Arm B	Cycle 12- Day 1/ before cycle	2.22 mmol/l	138 mmol/l	4.48 mmol/l	0.82 mmol/l	8.6 µmol/l	86 µmol/l		0.57 µkatal/l	0.5 µkatal/l		5.1 mmol/l	
0401	Arm B	End of treatment	2.16 mmol/l	136.7 mmol/l	4.41 mmol/l	0.89 mmol/l		74 µmol/l		0.7 µkatal/l	0.44 µkatal/l			

Listing 16: Laboratory- Hematology

Patient No.	Treatment Arm	Point in time	Hemoglobin	Lymphocytes (total)	Neutrophils (total)	Platelets	Monocytes	Leukocytes
0002	Arm A	Pre-examination	13.3 g/dl	17.1 nx1000/µl	3.72 nx1000/µl	216 nx1000/µl	0.6 nx1000/µl	5.6 nx1000/µl
0083	Arm A	Pre-examination	13.1 g/dl	3.04 nx1000/µl	2.84 nx1000/µl	256 nx1000/µl	1 nx1000/µl	7.1 nx1000/µl
0083	Arm A	Surgery	10.1 g/dl	1.47 nx1000/µl		215 nx1000/µl	1.39 nx1000/µl	7.36 nx1000/µl
0083	Arm A	Surgery	11 g/dl	2.41 nx1000/µl		218 nx1000/µl	1.52 nx1000/µl	8.23 nx1000/µl
0083	Arm A	Surgery	13.5 g/dl	1.87 nx1000/µl	3.95 nx1000/µl	251 nx1000/µl	0.85 nx1000/µl	6.82 nx1000/µl
0083	Arm A	Surgery	10.5 g/dl	1.3 nx1000/µl		177 nx1000/µl	1.47 nx1000/µl	8.08 nx1000/µl

Patient No.	Treatment Arm	Point in time	Hemoglobin	Lymphocytes (total)	Neutrophils (total)	Platelets	Monocytes	Leukocytes
0083	Arm A	Surgery	10.5 g/dl	1.1 nx1000/µl		207 nx1000/µl	1.57 nx1000/µl	9.9 nx1000/µl
0083	Arm A	Cycle 1- Other timepoints	11.8 g/dl	2.47 nx1000/µl	3.22 nx1000/µl	153 nx1000/µl	1.15 nx1000/µl	7.13 nx1000/µl
0083	Arm A	Cycle 2- Day 1/ before cycle	11.1 g/dl	2.44 nx1000/µl	5.59 nx1000/µl	154 nx1000/µl	1.52 nx1000/µl	9.85 nx1000/µl
0083	Arm A	Cycle 3- Other timepoints	12.3 g/dl	1.92 nx1000/µl	3.58 nx1000/µl		1.47 nx1000/µl	7.82 nx1000/µl
0085	Arm A	Pre-examination	14.7 g/dl	1.1 pt/nl	2.9 pt/nl	187 pt/nl	0.3 pt/nl	4.7 pt/nl
0085	Arm A	Surgery	8.1 g/dl			69 pt/nl		5.1 pt/nl
0085	Arm A	Surgery	14.6 g/dl	1.2 pt/nl	4.3 pt/nl	216 pt/nl	0.4 pt/nl	6.1 pt/nl
0085	Arm A	Surgery	8.5 g/dl	0.4 pt/nl	7.7 pt/nl	89 pt/nl	0.7 pt/nl	8.8 pt/nl
0085	Arm A	Surgery	10.7 g/dl			73 pt/nl		6.9 pt/nl
0085	Arm A	Surgery	9.4 g/dl	0.6 pt/nl	3.7 pt/nl	73 pt/nl	0.5 pt/nl	4.9 pt/nl
0085	Arm A	Surgery	9.8 g/dl			80 pt/nl		5.1 pt/nl
0085	Arm A	Surgery	10.2 g/dl			90 pt/nl		5 pt/nl
0085	Arm A	Surgery	10.9 g/dl	1.2 pt/nl	5.3 pt/nl	111 pt/nl	1 pt/nl	8.3 pt/nl
0085	Arm A	Surgery	10.6 g/dl	0.9 pt/nl	7.1 pt/nl	223 pt/nl	0.9 pt/nl	9.5 pt/nl
0085	Arm A	Surgery	10 g/dl	0.8 pt/nl	6.7 pt/nl	71 pt/nl	0.7 pt/nl	8.4 pt/nl
0085	Arm A	Surgery	11.4 g/dl	1.2 pt/nl	7.1 pt/nl	251 pt/nl	1.3 pt/nl	10.3 pt/nl
0085	Arm A	Cycle 1- Other timepoints	12.6 g/dl	1.2 pt/nl	2.9 pt/nl	235 pt/nl	0.4 pt/nl	4.7 pt/nl
0085	Arm A	Cycle 2- Other timepoints	11.5 g/dl	0.9 pt/nl	0.8 pt/nl	119 pt/nl	0.3 pt/nl	2.3 pt/nl
0085	Arm A	Cycle 3- Day 1/ before cycle	12.9 g/dl	1.3 pt/nl	6.2 pt/nl	93 pt/nl		7.9 pt/nl
0085	Arm A	Cycle 4- Day 1/ before cycle	12 g/dl	0.8 pt/nl	1.5 pt/nl	164 pt/nl	0.6 pt/nl	3.2 pt/nl
0085	Arm A	Cycle 5- Day 1/ before cycle	10.7 g/dl	0.9 pt/nl	2.6 pt/nl	89 pt/nl		4.2 pt/nl
0085	Arm A	End of treatment	11.1 g/dl	1.1 pt/nl	3.2 pt/nl	149 pt/nl	0.5 pt/nl	5.4 pt/nl
0086	Arm A	Pre-examination	8.8 mmol/l	1.27 Gpt/l	2.93 Gpt/l	189 Gpt/l	0.72 Gpt/l	5 Gpt/l
0086	Arm A	Surgery	6 mmol/l			208 Gpt/l		8.7 Gpt/l
0086	Arm A	Surgery	5.5 mmol/l			217 Gpt/l		5.8 Gpt/l
0086	Arm A	Surgery	8.1 mmol/l			174 Gpt/l		17.2 Gpt/l
0086	Arm A	Surgery	8.9 mmol/l	1.64 Gpt/l	7.02 Gpt/l	170 Gpt/l	1.26 Gpt/l	10 Gpt/l
0086	Arm A	Cycle 1- Other timepoints	6.5 mmol/l	1.77 Gpt/l	5.63 Gpt/l	310 Gpt/l	1.21 Gpt/l	8.9 Gpt/l
0086	Arm A	Cycle 2- Day 1/ before cycle	6.5 mmol/l		6.17 Gpt/l	176 Gpt/l		9 Gpt/l
0086	Arm A	Cycle 3- Day 1/ before cycle	6.4 mmol/l		1.85 Gpt/l	180 Gpt/l		4.2 Gpt/l
0086	Arm A	Cycle 4- Day 1/ before cycle	6.4 mmol/l	1.41 Gpt/l	3.52 Gpt/l	124 Gpt/l	0.73 Gpt/l	5.7 Gpt/l
0086	Arm A	Cycle 5- Day 1/ before cycle	6.6 mmol/l	1.37 Gpt/l	2.44 Gpt/l	179 Gpt/l	1.14 Gpt/l	5 Gpt/l
0086	Arm A	Cycle 6- Day 1/ before cycle	6.3 mmol/l		5.12 Gpt/l	149 Gpt/l		7.4 Gpt/l
0086	Arm A	Cycle 7- Day 1/ before cycle	6.3 mmol/l		2.4 Gpt/l	197 Gpt/l		4.4 Gpt/l
0086	Arm A	Cycle 8- Day 1/ before cycle	6.2 mmol/l	1.59 Gpt/l	1.54 Gpt/l	218 Gpt/l	1.04 Gpt/l	4.2 Gpt/l

Patient No.	Treatment Arm	Point in time	Hemoglobin	Lymphocytes (total)	Neutrophils (total)	Platelets	Monocytes	Leukocytes
0086	Arm A	Cycle 9- Day 1/ before cycle	6.2 mmol/l		4.02 Gpt/l	145 Gpt/l		6.3 Gpt/l
0086	Arm A	Cycle 10- Day 1/ before cycle	6.2 mmol/l	1.85 Gpt/l		158 Gpt/l	1.67 Gpt/l	12.6 Gpt/l
0086	Arm A	Cycle 11- Day 1/ before cycle	6.2 mmol/l	1.4 Gpt/l	2.9 Gpt/l	213 Gpt/l	1.1 Gpt/l	5.6 Gpt/l
0086	Arm A	Cycle 12- Day 1/ before cycle	6.2 mmol/l	1.3 Gpt/l	4.9 Gpt/l	137 Gpt/l	1.2 Gpt/l	7.5 Gpt/l
0086	Arm A	End of treatment	6.1 mmol/l			162 Gpt/l		7 Gpt/l
0087	Arm A	Pre-examination	15 g/dl	1.1 pt/nl	4.8 pt/nl	211 pt/nl	0.5 pt/nl	6.7 pt/nl
0087	Arm A	Surgery	11.8 g/dl	0.7 pt/nl	5.4 pt/nl	225 pt/nl	0.5 pt/nl	7 pt/nl
0087	Arm A	Surgery	11.1 g/dl			188 pt/nl		7.2 pt/nl
0087	Arm A	Surgery	13.9 g/dl	1.2 pt/nl	5.4 pt/nl	324 pt/nl	0.7 pt/nl	7.6 pt/nl
0087	Arm A	Surgery	15.2 g/dl	1.1 pt/nl	3.4 pt/nl	252 pt/nl	0.2 pt/nl	5.3 pt/nl
0087	Arm A	Surgery	11.4 g/dl	0.9 pt/nl	5.5 pt/nl	219 pt/nl	0.4 pt/nl	7.6 pt/nl
0087	Arm A	Surgery	12.9 g/dl	1.2 pt/nl	3.9 pt/nl	290 pt/nl	0.6 pt/nl	6.2 pt/nl
0087	Arm A	Surgery	11.9 g/dl	0.6 pt/nl	3.8 pt/nl	232 pt/nl	0.4 pt/nl	5 pt/nl
0087	Arm A	Surgery	12.9 g/dl	0.6 pt/nl	3.7 pt/nl	254 pt/nl	0.5 pt/nl	5.2 pt/nl
0087	Arm A	Cycle 1- Day 1/ before cycle	14.2 g/dl	1.1 pt/nl	3.8 pt/nl	315 pt/nl	0.4 pt/nl	5.5 pt/nl
0087	Arm A	Cycle 2- Day 1/ before cycle	14.3 g/dl	1 pt/nl	2 pt/nl	179 pt/nl	0.2 pt/nl	3.4 pt/nl
0087	Arm A	Cycle 3- Day 1/ before cycle	14.4 g/dl	1 pt/nl	1.7 pt/nl	190 pt/nl		3.2 pt/nl
0087	Arm A	End of treatment	15.1 g/dl	1 pt/nl	1.6 pt/nl	274 pt/nl	0.9 pt/nl	3.8 pt/nl
0089	Arm A	Pre-examination	9.3 g/dl	1.14 Gpt/l	3.34 Gpt/l	339 Gpt/l	9.4 %	5.09 Gpt/l
0089	Arm A	Surgery	9.1 g/dl			321 Gpt/l		13.69 Gpt/l
0089	Arm A	Surgery	9.1 g/dl			347 Gpt/l		9.93 Gpt/l
0089	Arm A	Surgery	9.3 g/dl			475 Gpt/l		8.09 Gpt/l
0089	Arm A	Surgery	8.7 g/dl	0.89 Gpt/l	7.12 Gpt/l	538 Gpt/l	8.3 %	8.88 Gpt/l
0089	Arm A	Surgery	9.8 g/dl	5.7 %	89.5 %	347 Gpt/l	4.1 %	11.8 Gpt/l
0089	Arm A	Cycle 1- Day 1/ before cycle	9.5 g/dl	11.5 %	82 %	380 Gpt/l	4.7 %	6.17 Gpt/l
0089	Arm A	Cycle 2- Day 1/ before cycle	9.1 g/dl	1.01 Gpt/l	4.8 Gpt/l	363 Gpt/l	10.7 %	6.29 Gpt/l
0089	Arm A	Cycle 3- Day 1/ before cycle	8.5 g/dl	21.1 %	58.7 %	297 Gpt/l	12.6 %	4.84 Gpt/l
0089	Arm A	Cycle 4- Day 1/ before cycle	10.7 g/dl	19.8 %	55.8 %	228 Gpt/l	14.1 %	5.05 Gpt/l
0089	Arm A	Cycle 5- Day 1/ before cycle	10.3 g/dl	20.8 %	56.5 %	204 Gpt/l	12.3 %	5.68 Gpt/l
0089	Arm A	Cycle 6- Day 1/ before cycle	9.8 g/dl	20.2 %	55.7 %	154 Gpt/l	14 %	4.56 Gpt/l
0089	Arm A	Cycle 7- Day 1/ before cycle	10.6 g/dl	26.6 %	54 %	211 Gpt/l	14.8 %	4.13 Gpt/l
0089	Arm A	Cycle 8- Day 1/ before cycle	10.6 g/dl	23.9 %	57.9 %	205 Gpt/l	13.6 %	4.72 Gpt/l
0089	Arm A	Cycle 9- Day 1/ before cycle	10.3 g/dl	26.4 %	51.4 %	178 Gpt/l	15.4 %	4.28 Gpt/l
0089	Arm A	Cycle 10- Day 1/ before cycle	10.6 g/dl	28.7 %	51.9 %	173 Gpt/l	14.4 %	4.25 Gpt/l
0089	Arm A	Cycle 11- Day 1/ before cycle	10.2 g/dl	20 %	60.8 %	145 Gpt/l	15.4 %	4.74 Gpt/l

Patient No.	Treatment Arm	Point in time	Hemoglobin	Lymphocytes (total)	Neutrophils (total)	Platelets	Monocytes	Leukocytes
0089	Arm A	Cycle 11- Other timepoints	11.2 g/dl	35.1 %	47.1 %	234 Gpt/l	13.1 %	3.88 Gpt/l
0089	Arm A	Cycle 12- Day 1/ before cycle	10 g/dl	25.9 %	50.5 %	153 Gpt/l	17.7 %	4.17 Gpt/l
0089	Arm A	Cycle 13- Day 1/ before cycle	10.5 g/dl	24 %	54.2 %	151 Gpt/l	15.6 %	4.54 Gpt/l
0089	Arm A	End of treatment	11.6 g/dl	28.8 %	57.6 %	248 Gpt/l	19.1 %	3.96 Gpt/l
0090	Arm A	Pre-examination	13.9 g/dl	28.1 %	54.2 %	310 10?/l	9.7 %	8 10?/l
0090	Arm A	Surgery	9.1 g/dl			467 10?/l		
0090	Arm A	Surgery	13.5 g/dl	27.2 %	55.4 %	271 10?/l	9.5 %	7 10?/l
0090	Arm A	Surgery	9.5 g/dl			226 10?/l		15.3 10?/l
0090	Arm A	Surgery	9.3 g/dl			210 10?/l		11.2 10?/l
0090	Arm A	Surgery	8.7 g/dl			203 10?/l		12.4 10?/l
0090	Arm A	Surgery	9.1 g/dl	10.2 %	75.7 %	246 10?/l	11.9 %	12.1 10?/l
0090	Arm A	Surgery	9.3 g/dl	14.7 %	70.8 %	304 10?/l	9.7 %	9.2 10?/l
0090	Arm A	Surgery	9.5 g/dl	18.1 %	62.2 %	372 10?/l	14.1 %	9.6 10?/l
0090	Arm A	Surgery	10 g/dl	13 %	62.2 %	477 10?/l	10 %	12 10?/l
0090	Arm A	Surgery	9.1 g/dl	11.3 %	73.8 %	452 10?/l	8 %	15.1 10?/l
0090	Arm A	Surgery	9.1 g/dl	15 %		533 10?/l	4 %	9.5 10?/l
0090	Arm A	Cycle 1- Day 1/ before cycle	11.4 g/dl	26.1 %	56.1 %	299 10?/l	10.1 %	7.6 10?/l
0090	Arm A	Cycle 1- Day 1/ before cycle	11.7 g/dl	14.7 %	73.3 %	251 10?/l	3.8 %	7.4 10?/l
0090	Arm A	Cycle 2- Day 1/ before cycle	12 g/dl	23.5 %	60.6 %	249 10?/l	12 %	6 10?/l
0090	Arm A	Cycle 2- Day 1/ before cycle	12.3 g/dl	59 %	22.3 %	303 10?/l	10 %	2.8 10?/l
0090	Arm A	Cycle 3- Day 1/ before cycle	11.9 g/dl	35 %	41.1 %	192 10?/l	19.6 %	5.4 10?/l
0090	Arm A	Cycle 3- Day 1/ before cycle	12.9 g/dl	46.2 %	36.5 %	207 10?/l	7.6 %	3.4 10?/l
0090	Arm A	Cycle 3- Other timepoints	11.9 g/dl	22.9 %	57.7 %	90 10?/l	16.3 %	5.3 10?/l
0090	Arm A	Cycle 3- Other timepoints	12.7 g/dl	26 %	44 %	222 10?/l	18 %	4.4 10?/l
0090	Arm A	Cycle 4- Day 1/ before cycle	12.8 g/dl	32.2 %	50.9 %	236 10?/l	12.8 %	6.2 10?/l
0090	Arm A	Cycle 4- Day 1/ before cycle	12.9 g/dl	22.6 %	67.9 %	201 10?/l	4.4 %	8.6 10?/l
0090	Arm A	Cycle 5- Day 1/ before cycle	11.2 g/dl	25.3 %	55.6 %	124 10?/l	15.7 %	5.9 10?/l
0090	Arm A	Cycle 5- Day 1/ before cycle	14.2 g/dl	16.6 %	75.2 %	202 10?/l	6.4 %	5.6 10?/l
0090	Arm A	Cycle 6- Day 1/ before cycle	12.5 g/dl	37.3 %	36.5 %	170 10?/l	22.7 %	4.6 10?/l
0090	Arm A	Cycle 7- Day 1/ before cycle	12 g/dl	34.6 %	37.5 %	137 10?/l	23.9 %	4 10?/l
0090	Arm A	Cycle 8- Day 1/ before cycle	11.3 g/dl	31 %	46.1 %	161 10?/l	21.4 %	6 10?/l
0090	Arm A	Cycle 9- Day 1/ before cycle	11.2 g/dl	43 %	32.4 %	215 10?/l	21.1 %	5.6 10?/l
0090	Arm A	Cycle 10- Day 1/ before cycle	11.8 g/dl	33.6 %	46.1 %	196 10?/l	18.4 %	4.5 10?/l
0090	Arm A	Cycle 11- Day 1/ before cycle	11.6 g/dl	19 %		158 10?/l	18 %	5.5 10?/l
0090	Arm A	Cycle 12- Day 1/ before cycle	11.3 g/dl	28.7 %	52.4 %	142 10?/l	17.5 %	5.8 10?/l

Patient No.	Treatment Arm	Point in time	Hemoglobin	Lymphocytes (total)	Neutrophils (total)	Platelets	Monocytes	Leukocytes
0090	Arm A	End of treatment	11.9 g/dl	30.2 %	52.8 %	204 10?/l	13.7 %	5.3 10?/l
0161	Arm A	Pre-examination	131 g/l	22 %	70 %	567 Gpt/l	7 %	9.4 Gpt/l
0161	Arm A	Surgery	120 g/l	15 %	78 %	365 Gpt/l	7 %	10.3 Gpt/l
0161	Arm A	Surgery	135 g/l			249 Gpt/l		9.6 Gpt/l
0161	Arm A	Surgery	120 g/l	14 %	80 %	225 Gpt/l	6 %	13.9 Gpt/l
0161	Arm A	Surgery	140 g/l	17 %	74 %	242 Gpt/l	8 %	9.9 Gpt/l
0161	Arm A	Surgery	117 g/l			235 Gpt/l		21.7 Gpt/l
0161	Arm A	Cycle 1- Day 1/ before cycle	124 g/l	27 %	63 %	388 Gpt/l	9 %	7.6 Gpt/l
0161	Arm A	Cycle 2- Day 1/ before cycle	119 g/l			301 Gpt/l		4.6 Gpt/l
0161	Arm A	Cycle 3- Day 1/ before cycle	126 g/l	30 %	51 %	174 Gpt/l	17 %	4.8 Gpt/l
0161	Arm A	Cycle 4- Day 1/ before cycle	125 g/l	26 %	57 %	102 Gpt/l	15 %	4.4 Gpt/l
0161	Arm A	Cycle 5- Day 1/ before cycle	119 g/l	30 %	53 %	116 Gpt/l	14 %	4.8 Gpt/l
0161	Arm A	Cycle 6- Day 1/ before cycle	122 g/l	27 %	59 %	91 Gpt/l	13 %	5.8 Gpt/l
0161	Arm A	Cycle 7- Day 1/ before cycle	121 g/l	21 %	66 %	134 Gpt/l	11 %	7.2 Gpt/l
0161	Arm A	Cycle 8- Day 1/ before cycle	125 g/l	21 %	66 %	341 Gpt/l	11 %	7.8 Gpt/l
0161	Arm A	Cycle 9- Day 1/ before cycle	123 g/l	23 %	64 %	346 Gpt/l	11 %	6.9 Gpt/l
0161	Arm A	Cycle 10- Day 1/ before cycle	123 g/l	19 %	69 %	191 Gpt/l	10 %	7.7 Gpt/l
0161	Arm A	Cycle 11- Day 1/ before cycle	124 g/l	19 %	68 %	188 Gpt/l	11 %	7.4 Gpt/l
0161	Arm A	End of treatment	125 g/l	23 %	67 %	218 Gpt/l	9 %	6.4 Gpt/l
0163	Arm A	Pre-examination	13.8 g/dl	22.7 %	64.2 %	202 pt/nl	9.7 %	5.55 pt/nl
0163	Arm A	Surgery	12.6 g/dl			136 pt/nl		8.61 pt/nl
0163	Arm A	End of treatment	11.4 g/dl					6.78 pt/nl
0166	Arm A	Pre-examination	10.6 g/dl	1.6 Tsd/µl	5.3 Tsd/µl	428 Tsd/µl	0.8 Tsd/µl	8 Tsd/µl
0402	Arm A	Pre-examination	7.7 mmol/l	2.01 Gpt/l	6.45 Gpt/l	334 Gpt/l		9.2 Gpt/l
0001	Arm B	Pre-examination	117 g/l	20 %	70 %	415 Gpt/l	9 %	7.2 Gpt/l
0001	Arm B	Cycle 1- Day 1/ before cycle	11.2 g/dl			385 $10^3/mm^3$		7.6 $10^3/mm^3$
0003	Arm B	Pre-examination	8.4 mmol/l	1.12 Gpt/l	4.36 Gpt/l	231 Gpt/l	0.5 Gpt/l	6.1 Gpt/l
0003	Arm B	Surgery	6.5 mmol/l	0.74 Gpt/l	6.79 Gpt/l	151 Gpt/l	0.92 Gpt/l	8.5 Gpt/l
0003	Arm B	Surgery	7.3 mmol/l	1.19 Gpt/l	10.41 Gpt/l	171 Gpt/l	0.96 Gpt/l	12.4 Gpt/l
0003	Arm B	Surgery	6.8 mmol/l	1.05 Gpt/l	6.87 Gpt/l	260 Gpt/l	0.7 Gpt/l	8.7 Gpt/l
0003	Arm B	Surgery	8.7 mmol/l			221 Gpt/l		6 Gpt/l
0003	Arm B	Surgery	7.8 mmol/l			191 Gpt/l		14.4 Gpt/l
0003	Arm B	Surgery	6.8 mmol/l			356 Gpt/l		5.2 Gpt/l
0003	Arm B	Surgery	7 mmol/l	1.21 Gpt/l	4.52 Gpt/l	182 Gpt/l	0.66 Gpt/l	6.5 Gpt/l
0003	Arm B	Surgery	6.7 mmol/l	0.74 Gpt/l	4.11 Gpt/l	220 Gpt/l	0.51 Gpt/l	5.4 Gpt/l

Patient No.	Treatment Arm	Point in time	Hemoglobin	Lymphocytes (total)	Neutrophils (total)	Platelets	Monocytes	Leukocytes
0003	Arm B	Surgery	6.6 mmol/l	1.19 Gpt/l	7.88 Gpt/l	152 Gpt/l	0.88 Gpt/l	10 Gpt/l
0003	Arm B	Surgery	6.5 mmol/l	0.9 Gpt/l	3.49 Gpt/l	218 Gpt/l	0.47 Gpt/l	5 Gpt/l
0003	Arm B	Cycle 1- Day 1/ before cycle	8.1 mmol/l	1.3 Gpt/l	5.1 Gpt/l	251 Gpt/l	0.6 Gpt/l	7.1 Gpt/l
0003	Arm B	Cycle 2- Day 1/ before cycle	8.7 mmol/l	1 Gpt/l	4.4 Gpt/l	271 Gpt/l	0.4 Gpt/l	5.9 Gpt/l
0003	Arm B	Cycle 3- Day 1/ before cycle	8.5 mmol/l	1.1 Gpt/l	4.6 Gpt/l	209 Gpt/l	0.7 Gpt/l	6.5 Gpt/l
0003	Arm B	Cycle 4- Day 1/ before cycle	8.7 mmol/l	1 Gpt/l	4.4 Gpt/l	169 Gpt/l	0.6 Gpt/l	6.1 Gpt/l
0003	Arm B	Cycle 5- Day 1/ before cycle	8.9 mmol/l	1 Gpt/l	3.9 Gpt/l	148 Gpt/l	0.6 Gpt/l	5.7 Gpt/l
0003	Arm B	Cycle 6- Day 1/ before cycle	9.2 mmol/l	1.2 Gpt/l	4.9 Gpt/l	148 Gpt/l	0.8 Gpt/l	7.1 Gpt/l
0003	Arm B	Cycle 7- Day 1/ before cycle	7.4 mmol/l	1 Gpt/l	3.8 Gpt/l	243 Gpt/l	0.5 Gpt/l	5.5 Gpt/l
0003	Arm B	Cycle 8- Day 1/ before cycle	7.7 mmol/l		3 Gpt/l	202 Gpt/l		4.6 Gpt/l
0003	Arm B	Cycle 9- Day 1/ before cycle	8.1 mmol/l	4.5 Gpt/l	2.8 Gpt/l	178 Gpt/l		
0003	Arm B	Cycle 10- Day 1/ before cycle	8.4 mmol/l		2.9 Gpt/l	141 Gpt/l		4.5 Gpt/l
0003	Arm B	Cycle 11- Day 1/ before cycle	8.7 mmol/l		3.5 Gpt/l	130 Gpt/l		5.2 Gpt/l
0003	Arm B	Cycle 12- Day 1/ before cycle	8.7 mmol/l		3.8 Gpt/l	112 Gpt/l		5.4 Gpt/l
0003	Arm B	End of treatment	9.1 mmol/l		4.73 Gpt/l	163 Gpt/l		6.6 Gpt/l
0081	Arm B	Pre-examination	146 g/l	21 %	66 %	220 Gpt/l	8 %	6.3 Gpt/l
0081	Arm B	End of treatment	146 g/l	21 %	66 %	220 Gpt/l	8 %	6.3 Gpt/l
0082	Arm B	Pre-examination	8.6 mmol/l	2.11 Gpt/l	3.74 Gpt/l	340 Gpt/l	0.46 Gpt/l	6.39 Gpt/l
0082	Arm B	Surgery	6.8 mmol/l			162 Gpt/l		9.9 Gpt/l
0082	Arm B	Cycle 1- Day 1/ before cycle	7.8 mmol/l	1.93 Gpt/l	3.25 Gpt/l	304 Gpt/l		5.7 Gpt/l
0082	Arm B	Cycle 1- Other timepoints	8.5 mmol/l	1.61 Gpt/l	2.81 Gpt/l	304 Gpt/l	0.28 Gpt/l	5.2 Gpt/l
0082	Arm B	Cycle 2- Day 1/ before cycle	8.5 mmol/l	1.4 Gpt/l	3.31 Gpt/l	248 Gpt/l		5.4 Gpt/l
0082	Arm B	Cycle 2- Other timepoints	9.4 mmol/l	1.79 Gpt/l	1.25 Gpt/l	301 Gpt/l	0.52 Gpt/l	3.72 Gpt/l
0082	Arm B	Cycle 3- Day 1/ before cycle	9.5 mmol/l	2.33 Gpt/l	1.42 Gpt/l	335 Gpt/l		4.8 Gpt/l
0082	Arm B	Cycle 3- Other timepoints	8.9 mmol/l	2.39 Gpt/l	2.71 Gpt/l	244 Gpt/l		5.7 Gpt/l
0082	Arm B	Cycle 4- Day 1/ before cycle	9 mmol/l	1.89 Gpt/l	2.92 Gpt/l	203 Gpt/l		5.7 Gpt/l
0082	Arm B	Cycle 4- Other timepoints	8.7 mmol/l	2.34 Gpt/l	1.46 Gpt/l	300 Gpt/l		4.6 Gpt/l
0082	Arm B	Cycle 5- Day 1/ before cycle	9.1 mmol/l	1.79 Gpt/l	2.26 Gpt/l	249 Gpt/l	0.63 Gpt/l	5.07 Gpt/l
0082	Arm B	Cycle 5- Other timepoints	9.5 mmol/l	2.09 Gpt/l	2.07 Gpt/l	219 Gpt/l	0.57 Gpt/l	5 Gpt/l
0082	Arm B	Cycle 6- Day 1/ before cycle	9.1 mmol/l	1.86 Gpt/l	2.94 Gpt/l	192 Gpt/l	0.82 Gpt/l	6.03 Gpt/l
0082	Arm B	Cycle 7- Day 1/ before cycle	7.9 mmol/l	2.14 Gpt/l	2.27 Gpt/l	330 Gpt/l	0.58 Gpt/l	5.23 Gpt/l
0082	Arm B	Cycle 7- Other timepoints	7.9 mmol/l	1.96 Gpt/l	2.38 Gpt/l	300 Gpt/l	0.41 Gpt/l	4.91 Gpt/l
0082	Arm B	Cycle 8- Day 1/ before cycle	7.9 mmol/l	1.44 Gpt/l	2.6 Gpt/l	266 Gpt/l		4.6 Gpt/l
0082	Arm B	Cycle 8- Other timepoints	8 mmol/l	1.95 Gpt/l	0.82 Gpt/l	288 Gpt/l	0.43 Gpt/l	3.35 Gpt/l
0082	Arm B	Cycle 9- Day 1/ before cycle	8.3 mmol/l	2.26 Gpt/l	1.04 Gpt/l	304 Gpt/l		4.2 Gpt/l

Patient No.	Treatment Arm	Point in time	Hemoglobin	Lymphocytes (total)	Neutrophils (total)	Platelets	Monocytes	Leukocytes
0082	Arm B	Cycle 10- Day 1/ before cycle	8.3 mmol/l	1.6 Gpt/l	2.41 Gpt/l	217 Gpt/l	0.46 Gpt/l	4.68 Gpt/l
0082	Arm B	Cycle 10- Other timepoints	8.1 mmol/l	1.96 Gpt/l	1.35 Gpt/l	260 Gpt/l		3.7 Gpt/l
0082	Arm B	Cycle 11- Day 1/ before cycle	8.5 mmol/l	1.48 Gpt/l	2.93 Gpt/l	274 Gpt/l		4.8 Gpt/l
0082	Arm B	Cycle 12- Day 1/ before cycle	8.7 mmol/l	2.25 Gpt/l	2.49 Gpt/l	2.49 Gpt/l		2.49 Gpt/l
0082	Arm B	Cycle 12- Other timepoints	8.9 mmol/l	1.95 Gpt/l	2.3 Gpt/l	292 Gpt/l	0.39 Gpt/l	4.79 Gpt/l
0082	Arm B	End of treatment	8.9 mmol/l	1.95 Gpt/l	2.3 Gpt/l	292 Gpt/l	0.39 Gpt/l	4.79 Gpt/l
0084	Arm B	Pre-examination	7.4 mmol/l	1.39 Gpt/l	4.54 Gpt/l	256 Gpt/l	0.83 Gpt/l	7.11 Gpt/l
0084	Arm B	Surgery	6.7 mmol/l			144 Gpt/l		14.66 Gpt/l
0084	Arm B	Cycle 1- Day 1/ before cycle	7.3 mmol/l	0.97 Gpt/l	6.5 Gpt/l	293 Gpt/l	0.93 Gpt/l	8.79 Gpt/l
0084	Arm B	Cycle 1- Other timepoints	7.2 mmol/l	0.94 Gpt/l	5.02 Gpt/l	256 Gpt/l	0.53 Gpt/l	7.07 Gpt/l
0084	Arm B	Cycle 2- Day 1/ before cycle	6.9 mmol/l	0.65 Gpt/l	5.28 Gpt/l	190 Gpt/l	0.34 Gpt/l	6.28 Gpt/l
0084	Arm B	Cycle 2- Other timepoints	7.5 mmol/l	1.19 Gpt/l	2.67 Gpt/l	228 Gpt/l	0.72 Gpt/l	4.91 Gpt/l
0084	Arm B	Cycle 3- Day 1/ before cycle	7.4 mmol/l	0.82 Gpt/l	3.86 Gpt/l	119 Gpt/l	0.77 Gpt/l	5.96 Gpt/l
0084	Arm B	Cycle 4- Day 1/ before cycle	7.2 mmol/l	0.96 Gpt/l	2.94 Gpt/l	100 Gpt/l		4.9 Gpt/l
0084	Arm B	Cycle 5- Day 1/ before cycle	7.3 mmol/l	0.92 Gpt/l	2.41 Gpt/l	103 Gpt/l		4 Gpt/l
0084	Arm B	Cycle 6- Day 1/ before cycle	8 mmol/l	0.99 Gpt/l	2.98 Gpt/l	109 Gpt/l	0.84 Gpt/l	4.87 Gpt/l
0084	Arm B	End of treatment	6.1 mmol/l	0.88 Gpt/l	4.58 Gpt/l	206 Gpt/l		7 Gpt/l
0088	Arm B	Pre-examination	8.9 mmol/l	38 %	47 %	251 Gpt/l	7 %	5.1 Gpt/l
0088	Arm B	Surgery	8.9 mmol/l			135 Gpt/l		7 Gpt/l
0088	Arm B	Cycle 1- Day 1/ before cycle	9.3 mmol/l	27 %	56 %	250 Gpt/l	6 %	6.14 Gpt/l
0088	Arm B	Cycle 1- Other timepoints	10.6 mmol/l	21 %	68 %	235 Gpt/l	4 %	8.02 Gpt/l
0088	Arm B	Cycle 2- Day 1/ before cycle	15.5 g/dl	2.24 $10^3/mm^3$	2.07 $10^3/mm^3$	314 $10^3/mm^3$	0.84 $10^3/mm^3$	5.5 $10^3/mm^3$
0088	Arm B	Cycle 2- Other timepoints	10.1 mmol/l	32 %	58 %	176 Gpt/l	3 %	6.01 Gpt/l
0088	Arm B	Cycle 3- Day 1/ before cycle	15.2 g/dl	1.76 $10^3/mm^3$	2.27 $10^3/mm^3$	182 $10^3/mm^3$	0.61 $10^3/mm^3$	4.9 $10^3/mm^3$
0088	Arm B	Cycle 3- Other timepoints	9.8 mmol/l	38 %	50 %	134 Gpt/l	4 %	3.99 Gpt/l
0088	Arm B	Cycle 4- Day 1/ before cycle	16 g/dl	2.05 Gpt/l	1.85 Gpt/l	246 Gpt/l	0.9 Gpt/l	5 Gpt/l
0088	Arm B	Cycle 4- Other timepoints	10.7 mmol/l	1.482 %	68 %	118 Gpt/l	0.114 %	5.7 Gpt/l
0088	Arm B	Cycle 5- Day 1/ before cycle	15.5 g/dl	1.83 $10^3/mm^3$	2.4 $10^3/mm^3$	139 $10^3/mm^3$	0.82 $10^3/mm^3$	5.4 $10^3/mm^3$
0088	Arm B	Cycle 5- Other timepoints	10 mmol/l	41 %	46 %	148 Gpt/l	5 %	4.02 Gpt/l
0088	Arm B	Cycle 6- Day 1/ before cycle	15.8 g/dl	2.15 $10^3/mm^3$	2.51 $10^3/mm^3$	187 $10^3/mm^3$	0.73 $10^3/mm^3$	5.6 $10^3/mm^3$
0088	Arm B	Cycle 6- Other timepoints	9.9 mmol/l	32 %	57 %	115 Gpt/l	3 %	4.72 Gpt/l
0162	Arm B	Pre-examination	7.8 mmol/l	2.04 Gpt/l	4.75 Gpt/l	222 Gpt/l	0.66 Gpt/l	7.62 Gpt/l
0162	Arm B	Surgery	6.2 mmol/l			100 Gpt/l		10.96 Gpt/l
0162	Arm B	Cycle 1- Day 1/ before cycle	8 mmol/l	1.36 Gpt/l	2.85 Gpt/l	166 Gpt/l	0.45 Gpt/l	4.9 Gpt/l
0162	Arm B	Cycle 1- Other timepoints	7.3 mmol/l	1.32 Gpt/l	3.24 Gpt/l	128 Gpt/l	0.3 Gpt/l	4.95 Gpt/l

Patient No.	Treatment Arm	Point in time	Hemoglobin	Lymphocytes (total)	Neutrophils (total)	Platelets	Monocytes	Leukocytes
0162	Arm B	Cycle 2- Day 1/ before cycle	8.3 mmol/l	1.91 Gpt/l	1.79 Gpt/l	228 Gpt/l	0.82 Gpt/l	4.68 Gpt/l
0162	Arm B	Cycle 2- Other timepoints	8.1 mmol/l	1.48 Gpt/l	2.96 Gpt/l	158 Gpt/l	0.49 Gpt/l	5 Gpt/l
0162	Arm B	Cycle 3- Day 1/ before cycle	8 mmol/l	1.44 Gpt/l	2.18 Gpt/l	150 Gpt/l	0.66 Gpt/l	4.45 Gpt/l
0162	Arm B	Cycle 3- Other timepoints	7.9 mmol/l	1.55 Gpt/l	1.34 Gpt/l	159 Gpt/l	0.52 Gpt/l	3.53 Gpt/l
0162	Arm B	Cycle 4- Day 1/ before cycle	8.1 mmol/l	1.55 Gpt/l	2.31 Gpt/l	119 Gpt/l	0.66 Gpt/l	4.64 Gpt/l
0162	Arm B	Cycle 4- Other timepoints	8 mmol/l	1.09 Gpt/l	1.62 Gpt/l	130 Gpt/l	0.49 Gpt/l	3.28 Gpt/l
0162	Arm B	Cycle 5- Day 1/ before cycle	8.3 mmol/l	1.63 Gpt/l	2.37 Gpt/l	115 Gpt/l		4.6 Gpt/l
0162	Arm B	Cycle 5- Other timepoints	7.7 mmol/l	1.16 Gpt/l	1.01 Gpt/l	104 Gpt/l	0.21 Gpt/l	2.47 Gpt/l
0162	Arm B	Cycle 6- Day 1/ before cycle	7.8 mmol/l	1.02 Gpt/l	1.6 Gpt/l	86 Gpt/l	0.53 Gpt/l	3.19 Gpt/l
0162	Arm B	Cycle 7- Day 1/ before cycle	6.2 mmol/l	1.28 Gpt/l	2.71 Gpt/l	228 Gpt/l	0.54 Gpt/l	4.98 Gpt/l
0162	Arm B	Cycle 7- Other timepoints	6.2 mmol/l	1.39 Gpt/l	2.89 Gpt/l	224 Gpt/l	0.41 Gpt/l	4.86 Gpt/l
0162	Arm B	Cycle 8- Day 1/ before cycle	6.4 mmol/l	0.94 Gpt/l	1.96 Gpt/l	179 Gpt/l	0.53 Gpt/l	3.54 Gpt/l
0162	Arm B	Cycle 8- Other timepoints	6.3 mmol/l	1.43 Gpt/l	1.79 Gpt/l	199 Gpt/l		3.5 Gpt/l
0162	Arm B	Cycle 9- Day 1/ before cycle	6.5 mmol/l	1.19 Gpt/l	1.59 Gpt/l	211 Gpt/l	0.54 Gpt/l	3.41 Gpt/l
0162	Arm B	Cycle 10- Day 1/ before cycle	6.6 mmol/l	0.9 Gpt/l	1.99 Gpt/l	154 Gpt/l	0.65 Gpt/l	3.62 Gpt/l
0162	Arm B	Cycle 10- Other timepoints	6.3 mmol/l	1.02 Gpt/l	0.87 Gpt/l	154 Gpt/l		2.1 Gpt/l
0162	Arm B	Cycle 11- Day 1/ before cycle	6.4 mmol/l	0.98 Gpt/l	2.02 Gpt/l	136 Gpt/l		3.7 Gpt/l
0162	Arm B	Cycle 11- Other timepoints	6.9 mmol/l	1.53 Gpt/l	1.88 Gpt/l	207 Gpt/l	0.67 Gpt/l	4.16 Gpt/l
0162	Arm B	Cycle 12- Day 1/ before cycle	6.9 mmol/l	1.53 Gpt/l	1.88 Gpt/l	207 Gpt/l	0.67 Gpt/l	4.16 Gpt/l
0162	Arm B	Cycle 12- Other timepoints	6.6 mmol/l	1.73 Gpt/l	1.72 Gpt/l	143 Gpt/l	0.4 Gpt/l	3.91 Gpt/l
0162	Arm B	End of treatment	6.7 mmol/l	1.31 Gpt/l	5.25 Gpt/l	189 Gpt/l	0.47 Gpt/l	7.06 Gpt/l
0164	Arm B	Pre-examination	9.7 mmol/l		5.72 Gpt/l	209 Gpt/l		7.6 Gpt/l
0164	Arm B	Cycle 1- Day 1/ before cycle	9.7 mmol/l	1.4 Gpt/l	5.3 Gpt/l	205 Gpt/l	0.4 Gpt/l	7.3 Gpt/l
0164	Arm B	Cycle 2- Day 1/ before cycle	9.1 mmol/l		4.5 Gpt/l	162 Gpt/l		7.1 Gpt/l
0164	Arm B	Cycle 3- Day 1/ before cycle	9.5 mmol/l		6.1 Gpt/l	152 Gpt/l		9.5 Gpt/l
0164	Arm B	Cycle 4- Day 1/ before cycle	9 mmol/l	1.9 Gpt/l	4.6 Gpt/l	125 Gpt/l	0.9 Gpt/l	7.5 Gpt/l
0164	Arm B	Cycle 5- Day 1/ before cycle	8.4 mmol/l	1.6 Gpt/l	2.8 Gpt/l	189 Gpt/l	0.9 Gpt/l	5.4 Gpt/l
0164	Arm B	Cycle 6- Day 1/ before cycle	7.9 mmol/l	1.5 Gpt/l	3.27 Gpt/l	129 Gpt/l	0.6 Gpt/l	5.2 Gpt/l
0164	Arm B	End of treatment	8.1 mmol/l			230 Gpt/l		4.6 Gpt/l
0165	Arm B	Pre-examination	13.6 g/dl	30.4 %	59.5 %	227 pt/nl	8 %	6.87 pt/nl
0165	Arm B	Surgery	15.1 g/dl			212 pt/nl		6.04 pt/nl
0165	Arm B	Cycle 1- Day 1/ before cycle	14.7 g/dl	31.4 %	58.3 %	233 pt/nl	8.2 %	6.12 pt/nl
0165	Arm B	Cycle 2- Day 1/ before cycle	14.5 g/dl	18.5 %	63.9 %	192 pt/nl	15.6 %	7.1 pt/nl
0165	Arm B	Cycle 3- Day 1/ before cycle	14.4 g/dl	21.9 %	62.2 %	123 pt/nl	13.8 %	8.02 pt/nl
0165	Arm B	Cycle 4- Day 1/ before cycle	15.2 g/dl	25.8 %	60.2 %	153 pt/nl	12 %	7.9 pt/nl

Patient No.	Treatment Arm	Point in time	Hemoglobin	Lymphocytes (total)	Neutrophils (total)	Platelets	Monocytes	Leukocytes
0165	Arm B	Cycle 5- Day 1/ before cycle	14.2 g/dl	27.3 %	59.8 %	129 pt/nl	9.7 %	7.35 pt/nl
0165	Arm B	Cycle 6- Day 1/ before cycle	14.6 g/dl	31.6 %	53.9 %	154 pt/nl	12.4 %	7.18 pt/nl
0165	Arm B	Cycle 7- Day 1/ before cycle	13.4 g/dl	37.9 %	48.6 %	181 pt/nl	11.2 %	8.28 pt/nl
0165	Arm B	Cycle 8- Day 1/ before cycle	14.2 g/dl	19 %	68.4 %	199 pt/nl	10.5 %	11.62 pt/nl
0165	Arm B	Cycle 9- Day 1/ before cycle	14.8 g/dl	38.6 %	41.7 %	189 pt/nl	17.7 %	6.84 pt/nl
0165	Arm B	Cycle 10- Day 1/ before cycle	15.3 g/dl	31.4 %	55 %	181 pt/nl	11.8 %	8 pt/nl
0165	Arm B	Cycle 11- Day 1/ before cycle	14.8 g/dl	28.2 %	54.1 %	164 pt/nl	14.6 %	6.77 pt/nl
0165	Arm B	Cycle 12- Day 1/ before cycle	14.9 g/dl	29.3 %	53.7 %	149 pt/nl	14.9 %	7.5 pt/nl
0165	Arm B	End of treatment	14.9 g/dl	29.3 %	53.7 %	149 pt/nl	14.9 %	7.5 pt/nl
0167	Arm B	Pre-examination	14.8 g/dl	20 %	71 %	465 Gpt/l	6 %	11.03 Tpt/l
0167	Arm B	Surgery	15.6 g/dl			244 Gpt/l		9.64 Tpt/l
0167	Arm B	Cycle 1- Day 1/ before cycle	14.5 g/dl	12 %	78 %	375 Gpt/l	6 %	11.1 Tpt/l
0167	Arm B	Cycle 2- Day 1/ before cycle	14.3 g/dl			290 Gpt/l		8.44 Tpt/l
0167	Arm B	Cycle 3- Day 1/ before cycle	14.9 g/dl	9 %	80 %	280 Gpt/l	9 %	12.12 Tpt/l
0167	Arm B	Cycle 4- Day 1/ before cycle	14.1 g/dl	13 %	71 %	216 Gpt/l	11 %	7.08 Tpt/l
0167	Arm B	Cycle 5- Day 1/ before cycle	14.4 g/dl	17 %	67 %	171 Gpt/l	12 %	5.67 Tpt/l
0167	Arm B	Cycle 6- Day 1/ before cycle	14.5 g/dl	15 %	71 %	149 Gpt/l	11 %	5.8 Tpt/l
0167	Arm B	Cycle 7- Day 1/ before cycle	13.5 g/dl	14 %	47 %	388 Gpt/l	6 %	10.93 Tpt/l
0167	Arm B	Cycle 8- Day 1/ before cycle	13.3 g/dl	9 %	76 %	246 Gpt/l	7 %	11.45 Tpt/l
0167	Arm B	Cycle 9- Day 1/ before cycle	13 g/dl	11 %	75 %	249 Gpt/l	7 %	8.4 Tpt/l
0167	Arm B	Cycle 10- Day 1/ before cycle	12.9 g/dl	13 %	75 %	247 Gpt/l	8 %	7.66 Tpt/l
0167	Arm B	Cycle 11- Day 1/ before cycle	14.3 g/dl	18 %	65 %	249 Gpt/l	9 %	8.98 Tpt/l
0167	Arm B	Cycle 12- Day 1/ before cycle	13.6 g/dl	15 %	68 %	177 Gpt/l	9 %	6.54 Tpt/l
0167	Arm B	End of treatment	13.9 g/dl			235 Gpt/l		7.56 Tpt/l
0241	Arm B	Pre-examination	14.2 g/dl	17.4 %	71.5 %	277 10?/l	8.8 %	6.5 10?/l
0241	Arm B	Surgery	11 g/dl	10.3 %	76.2 %	248 10?/l	10.8 %	10 10?/l
0241	Arm B	Surgery	11.1 g/dl	14.3 %	69.9 %	376 10?/l	8.1 %	9.1 10?/l
0241	Arm B	Surgery	11 g/dl	25.8 %	61.8 %	601 10?/l	12.4 %	7.2 10?/l
0241	Arm B	Surgery	11.8 g/dl			224 10?/l		12.8 10?/l
0241	Arm B	Surgery	11.2 g/dl	9.4 %	73.7 %	344 10?/l	9.9 %	9.6 10?/l
0241	Arm B	Surgery	13.9 g/dl			255 10?/l		8.4 10?/l
0241	Arm B	Surgery	10.5 g/dl	8.2 %	82.9 %	214 10?/l	86 %	12.7 10?/l
0241	Arm B	Surgery	12.4 g/dl	12.4 %	80.2 %	259 10?/l	4.7 %	1.4 10?/l
0241	Arm B	Surgery	11 g/dl	11.6 %	72.9 %	300 10?/l	10 %	8.4 10?/l
0241	Arm B	Cycle 1- Day 1/ before cycle	14.2 g/dl	19.8 %	65.3 %	291 10?/l	13.1 %	7.2 10?/l

Patient No.	Treatment Arm	Point in time	Hemoglobin	Lymphocytes (total)	Neutrophils (total)	Platelets	Monocytes	Leukocytes
0241	Arm B	Cycle 2- Day 1/ before cycle	13.7 g/dl	20.7 %	57.3 %	242 10?/l	18.4 %	5.3 10?/l
0241	Arm B	Cycle 3- Day 1/ before cycle	14.6 g/dl	29 %	46 %	374 10?/l	22 %	5.4 10?/l
0241	Arm B	Cycle 4- Day 1/ before cycle	14.4 g/dl	19.9 %	60.7 %	149 10?/l	15.9 %	4 10?/l
0241	Arm B	Cycle 5- Day 1/ before cycle	15.2 g/dl	25.4 %	53.8 %	197 10?/l	19 %	5.6 10?/l
0241	Arm B	Cycle 6- Day 1/ before cycle	13.9 g/dl	20 %	62.4 %	156 10?/l	8 %	4.4 10?/l
0241	Arm B	Cycle 7- Day 1/ before cycle	12 g/dl	22 %	63 %	357 Gpt/l	10 %	5.8 Gpt/l
0241	Arm B	Cycle 8- Day 1/ before cycle	12.6 g/dl	21 %	62 %	307 Gpt/l	12 %	6.4 Gpt/l
0241	Arm B	Cycle 9- Day 1/ before cycle	13.3 g/dl	28.8 %	52 %	193 Gpt/l	17 %	5.9 Gpt/l
0241	Arm B	Cycle 10- Day 1/ before cycle	14.1 g/dl	29 %	51 %	172 Gpt/l	14 %	5.7 Gpt/l
0241	Arm B	Cycle 11- Day 1/ before cycle	13.4 g/dl	30 %	48 %	148 Gpt/l	16 %	4.7 Gpt/l
0241	Arm B	Cycle 12- Day 1/ before cycle	13.1 g/dl	27 %	51 %	149 Gpt/l	16 %	4.8 Gpt/l
0241	Arm B	End of treatment	14.5 g/dl	26 %	59 %	294 Gpt/l	14 %	8.5 Gpt/l
0242	Arm B	Pre-examination	11.7 g/dl	1.3 Gpt/l	3.83 Gpt/l	315 Gpt/l	0.65 Gpt/l	5.9 Gpt/l
0242	Arm B	Surgery	14 g/dl			196 Gpt/l		8.2 Gpt/l
0242	Arm B	Surgery	11.4 g/dl			171 Gpt/l		11.1 Gpt/l
0242	Arm B	Surgery	12.3 g/dl			195 Gpt/l		9.4 Gpt/l
0242	Arm B	Surgery	12 g/dl			209 Gpt/l		8.6 Gpt/l
0242	Arm B	Cycle 1- Other timepoints	11.1 g/dl	1.07 Gpt/l	2.58 Gpt/l	151 Gpt/l	0.43 Gpt/l	4.3 Gpt/l
0242	Arm B	Cycle 2- Day 1/ before cycle	11 g/dl	1.12 Gpt/l	3.91 Gpt/l	128 Gpt/l	0.99 Gpt/l	6.2 Gpt/l
0242	Arm B	Cycle 2- Other timepoints	11.3 g/dl	1.03 Gpt/l	3.48 Gpt/l	224 Gpt/l	0.29 Gpt/l	4.9 Gpt/l
0242	Arm B	Cycle 3- Day 1/ before cycle	11.9 g/dl	1.08 Gpt/l	2.94 Gpt/l	138 Gpt/l	0.78 Gpt/l	4.9 Gpt/l
0242	Arm B	Cycle 3- Other timepoints	13.4 g/dl	1.39 Gpt/l	1.82 Gpt/l	199 Gpt/l	0.43 Gpt/l	3.8 Gpt/l
0242	Arm B	Cycle 4- Day 1/ before cycle	12.2 g/dl	1 Gpt/l	4.07 Gpt/l	112 Gpt/l	11 Gpt/l	5.9 Gpt/l
0242	Arm B	Cycle 5- Day 1/ before cycle	11.9 g/dl	1.14 Gpt/l	4.76 Gpt/l	126 Gpt/l	0.74 Gpt/l	6.7 Gpt/l
0242	Arm B	Cycle 5- Other timepoints	13.6 g/dl	1.28 Gpt/l	2.18 Gpt/l	144 Gpt/l	0.22 Gpt/l	3.9 Gpt/l
0242	Arm B	Cycle 6- Day 1/ before cycle	12.1 g/dl	1.19 Gpt/l	3.46 Gpt/l	118 Gpt/l	0.7 Gpt/l	5.4 Gpt/l
0242	Arm B	Cycle 6- Other timepoints	13.1 g/dl	1.11 Gpt/l	2.8 Gpt/l	133 Gpt/l	0.38 Gpt/l	4.4 Gpt/l
0242	Arm B	Cycle 7- Day 1/ before cycle	13.1 g/dl	1.64 Gpt/l	4.99 Gpt/l	193 Gpt/l	0.86 Gpt/l	7.8 Gpt/l
0242	Arm B	Cycle 7- Other timepoints	12.8 g/dl	1.45 Gpt/l	4.76 Gpt/l	157 Gpt/l	0.48 Gpt/l	6.9 Gpt/l
0242	Arm B	Cycle 8- Day 1/ before cycle	12.4 g/dl	1.03 Gpt/l	4.97 Gpt/l	150 Gpt/l	0.69 Gpt/l	6.9 Gpt/l
0242	Arm B	Cycle 8- Other timepoints	13.7 g/dl	1.05 Gpt/l	3.22 Gpt/l	194 Gpt/l	0.4 Gpt/l	4.8 Gpt/l
0242	Arm B	Cycle 9- Day 1/ before cycle	12.2 g/dl	1.12 Gpt/l	4.69 Gpt/l	142 Gpt/l	0.98 Gpt/l	7 Gpt/l
0242	Arm B	Cycle 9- Other timepoints	13.9 g/dl	1.21 Gpt/l	3.26 Gpt/l	174 Gpt/l	0.41 Gpt/l	5 Gpt/l
0242	Arm B	Cycle 10- Day 1/ before cycle	14 g/dl	1.22 Gpt/l	4.29 Gpt/l	198 Gpt/l	0.7 Gpt/l	6.4 Gpt/l
0242	Arm B	Cycle 10- Other timepoints	14.8 g/dl	1.77 Gpt/l	5.59 Gpt/l	140 Gpt/l	0.6 Gpt/l	8.2 Gpt/l

Patient No.	Treatment Arm	Point in time	Hemoglobin	Lymphocytes (total)	Neutrophils (total)	Platelets	Monocytes	Leukocytes
0242	Arm B	Cycle 11- Day 1/ before cycle	13.3 g/dl	1.04 Gpt/l	4.75 Gpt/l	210 Gpt/l	0.52 Gpt/l	6.5 Gpt/l
0242	Arm B	Cycle 12- Day 1/ before cycle	13.2 g/dl	1.24 Gpt/l	4.96 Gpt/l	156 Gpt/l	0.88 Gpt/l	7.3 Gpt/l
0242	Arm B	Cycle 12- Other timepoints	15.1 g/dl	1.07 Gpt/l	3.23 Gpt/l	185 Gpt/l	0.6 Gpt/l	5.1 Gpt/l
0242	Arm B	End of treatment	14.5 g/dl	1.56 Gpt/l	3.91 Gpt/l	209 Gpt/l	0.74 Gpt/l	6.4 Gpt/l
0401	Arm B	Pre-examination	6.3 mmol/l	0.79 Gpt/l	2.34 Gpt/l	323 Gpt/l	0.33 Gpt/l	3.6 Gpt/l
0401	Arm B	Surgery	5.5 mmol/l	0.49 Gpt/l	26.2 Gpt/l	113 Gpt/l	3.53 Gpt/l	28.7 Gpt/l
0401	Arm B	Surgery	5.1 mmol/l	1.52 Gpt/l	20.47 Gpt/l	110 Gpt/l	2.06 Gpt/l	23.5 Gpt/l
0401	Arm B	Surgery	5.5 mmol/l			121 Gpt/l		10.1 Gpt/l
0401	Arm B	Surgery	4.9 mmol/l			122 Gpt/l		7.2 Gpt/l
0401	Arm B	Surgery	7 mmol/l	1.35 Gpt/l	4.06 Gpt/l	250 Gpt/l	0.66 Gpt/l	6.3 Gpt/l
0401	Arm B	Surgery	5.4 mmol/l	0.78 Gpt/l	10.08 Gpt/l	105 Gpt/l	1.15 Gpt/l	12.2 Gpt/l
0401	Arm B	Surgery	5.8 mmol/l	0.36 Gpt/l	13.4 Gpt/l	149 Gpt/l	0.94 Gpt/l	14 Gpt/l
0401	Arm B	Surgery	5.7 mmol/l			157 Gpt/l		8.5 Gpt/l
0401	Arm B	Surgery	4.9 mmol/l			135 Gpt/l		13 Gpt/l
0401	Arm B	Cycle 1- Day 1/ before cycle	6.6 mmol/l	0.86 Gpt/l	2.67 Gpt/l	175 Gpt/l	0.28 Gpt/l	4.3 Gpt/l
0401	Arm B	Cycle 2- Day 1/ before cycle	6.4 mmol/l	0.92 Gpt/l	1.91 Gpt/l	288 Gpt/l	0.47 Gpt/l	3.5 Gpt/l
0401	Arm B	Cycle 3- Day 1/ before cycle	6.5 mmol/l	0.79 Gpt/l	3.16 Gpt/l	200 Gpt/l	0.36 Gpt/l	4.5 Gpt/l
0401	Arm B	Cycle 4- Day 1/ before cycle	6.83 mmol/l	0.73 Gpt/l	2.03 Gpt/l	163 Gpt/l	0.39 Gpt/l	3.5 Gpt/l
0401	Arm B	Cycle 5- Day 1/ before cycle	6.5 mmol/l	0.77 Gpt/l	2.19 Gpt/l	188 Gpt/l	0.33 Gpt/l	3.5 Gpt/l
0401	Arm B	Cycle 6- Day 1/ before cycle	6.8 mmol/l	0.94 Gpt/l	2.51 Gpt/l	156 Gpt/l	0.49 Gpt/l	4.2 Gpt/l
0401	Arm B	Cycle 7- Day 1/ before cycle	5.6 mmol/l	0.57 Gpt/l	1.69 Gpt/l	299 Gpt/l	0.51 Gpt/l	2.9 Gpt/l
0401	Arm B	Cycle 10- Day 1/ before cycle	6 mmol/l	0.88 Gpt/l	2.62 Gpt/l	145 Gpt/l	0.35 Gpt/l	4 Gpt/l
0401	Arm B	Cycle 11- Day 1/ before cycle	6.2 mmol/l	0.7 Gpt/l	4.5 Gpt/l	116 Gpt/l	0.91 Gpt/l	6.3 Gpt/l
0401	Arm B	Cycle 12- Day 1/ before cycle	6 mmol/l	0.88 Gpt/l	1.18 Gpt/l	126 Gpt/l	0.35 Gpt/l	2.5 Gpt/l
0401	Arm B	End of treatment	5.9 mmol/l	0.64 Gpt/l	0.75 Gpt/l	125 Gpt/l	0.54 Gpt/l	2 Gpt/l

Listing 17: Laboratory coagulation and tumor marker

Patient No.	Treatment Arm	Point in time	PTT	INR	CEA	Ca 19-9
0002	Arm A	Pre-examination	28.3 s	0.97	16.9 µg/l	13.2 U/ml
0083	Arm A	Pre-examination	32.7 s	0.99	8.5 ng/ml	621 U/ml
0083	Arm A	Surgery	37.1 s	.		
0083	Arm A	Surgery	40 s	.		
0083	Arm A	Surgery	34 s	0.96		
0083	Arm A	Surgery	33.9 s	.		
0083	Arm A	Cycle 1- Other timepoints	36.3 s	.		
0083	Arm A	Cycle 2- Day 1/ before cycle	30.8 s	.		
0083	Arm A	Cycle 2- Other timepoints		.	1.9 ng/ml	38 U/ml
0083	Arm A	Cycle 3- Other timepoints	32.3 s	.		
0085	Arm A	Pre-examination	30 s	0.90	3.92 µg/l	2 kU/l
0085	Arm A	Surgery	33 s	1.25		
0085	Arm A	Surgery	29 s	1.11		
0085	Arm A	Surgery	31 s	1.17		
0085	Arm A	Surgery	30 s	0.93		
0085	Arm A	Surgery	25 s	1.03		
0085	Arm A	Surgery	96 s	1.10		
0085	Arm A	Surgery	26 s	1.00		
0085	Arm A	Surgery	24 s	1.06		
0085	Arm A	Surgery	25 s	0.99		
0085	Arm A	Surgery	27 s	1.01		
0085	Arm A	Surgery	45 s	1.15		
0085	Arm A	Cycle 1- Other timepoints	41 s	1.00		
0085	Arm A	Cycle 2- Other timepoints	34 s	1.00		
0085	Arm A	Cycle 3- Day 1/ before cycle	36 s	2.65		
0085	Arm A	Cycle 4- Day 1/ before cycle	33 s	3.04		
0085	Arm A	Cycle 5- Day 1/ before cycle		2.86		
0085	Arm A	End of treatment	32 s	2.12		
0086	Arm A	Pre-examination	26.8 s	0.90	9.9 ng/ml	58 U/ml
0086	Arm A	Surgery	27.7 s	0.90		
0086	Arm A	Surgery	21.1 s	1.00		
0086	Arm A	Surgery	25.1 s	1.00		
0086	Arm A	Surgery	25.6 s	0.90		
0086	Arm A	Surgery	24.7 s	0.90		
0086	Arm A	Cycle 1- Other timepoints	26.1 s	1.00	55.2 ng/ml	2.4 U/ml
0086	Arm A	Cycle 2- Day 1/ before cycle	33.4 s	1.00	3 ng/ml	33.2 U/ml
0086	Arm A	Cycle 3- Day 1/ before cycle	30.1 s	0.90		
0086	Arm A	Cycle 4- Day 1/ before cycle	36.5 s	1.00		
0086	Arm A	Cycle 5- Day 1/ before cycle	39.2 s	0.90		
0086	Arm A	Cycle 7- Other timepoints		.	1.3 ng/ml	13 U/ml
0086	Arm A	Cycle 8- Day 1/ before cycle	34.4 s	1.00		
0086	Arm A	Cycle 10- Day 1/ before cycle	57.9 s	1.10		
0086	Arm A	Cycle 11- Day 1/ before cycle	39.7 s	0.90		
0086	Arm A	Cycle 12- Day 1/ before cycle	39.8 s	1.00		
0086	Arm A	End of treatment	31.7 s	0.90	2.2 ng/ml	34.8 U/ml
0087	Arm A	Pre-examination	36 s	0.98	1.17 µg/l	4 kU/l
0087	Arm A	Surgery	34 s	1.10		
0087	Arm A	Surgery	31 s	1.04		
0087	Arm A	Surgery	34 s	1.09		
0087	Arm A	Surgery	36 s	1.20		
0087	Arm A	Surgery	41 s	1.01		
0087	Arm A	Surgery	32 s	1.03		

Patient No.	Treatment Arm	Point in time	PTT	INR	CEA	Ca 19-9
0087	Arm A	Surgery	38 s	1.30		
0087	Arm A	Surgery	34 s	1.15		
0087	Arm A	Cycle 1- Day 1/ before cycle	28 s	57.00		
0087	Arm A	Cycle 2- Day 1/ before cycle	34 s	1.60		
0087	Arm A	Cycle 3- Day 1/ before cycle	32 s	1.25		
0087	Arm A	End of treatment	32 s	1.26	1.2 µg/l	5 kU/l
0089	Arm A	Pre-examination	26 s	0.90	20.4 ng/ml	43.2 U/ml
0089	Arm A	Surgery	27 s	0.90		
0089	Arm A	Surgery	30 s	0.90		
0089	Arm A	Surgery	27.6 s	1.00		
0089	Arm A	Surgery	31 s	1.10		
0089	Arm A	Surgery	26 s	0.90		
0089	Arm A	Cycle 1- Day 1/ before cycle	26 s	0.90	2.3 ng/ml	3.5 U/ml
0089	Arm A	Cycle 2- Day 1/ before cycle	24 s	0.90		
0089	Arm A	Cycle 3- Day 1/ before cycle	23 s	0.90	1.2 ng/ml	
0089	Arm A	Cycle 4- Day 1/ before cycle	25 s	0.90		
0089	Arm A	Cycle 5- Day 1/ before cycle	24 s	0.90		
0089	Arm A	Cycle 6- Day 1/ before cycle	22 s	1.00		
0089	Arm A	Cycle 7- Day 1/ before cycle	25 s	0.90		
0089	Arm A	Cycle 8- Day 1/ before cycle	24 s	0.90		
0089	Arm A	Cycle 9- Day 1/ before cycle	24 s	1.00		
0089	Arm A	Cycle 10- Day 1/ before cycle	24 s	0.90		
0089	Arm A	Cycle 11- Day 1/ before cycle	22 s	0.90		
0089	Arm A	Cycle 11- Other timepoints	22 s	0.90	1.4 ng/ml	6.9 U/ml
0089	Arm A	Cycle 12- Day 1/ before cycle	25 s	0.90		
0089	Arm A	Cycle 13- Day 1/ before cycle	25 s	0.90		
0089	Arm A	End of treatment	26 s	0.90	1.1 ng/ml	2.4 U/ml
0090	Arm A	Pre-examination	30.3 s	0.92	2.2 ng/ml	7 U/ml
0090	Arm A	Surgery	30.1 s	1.18		
0090	Arm A	Surgery	26.8 s	1.02		
0090	Arm A	Surgery	29.1 s	1.15		
0090	Arm A	Surgery	30 s	0.90		
0090	Arm A	Surgery	28 s	0.99		
0090	Arm A	Surgery	28.4 s	1.01		
0090	Arm A	Surgery	28.4 s	1.07		
0090	Arm A	Surgery	26.9 s	0.99		
0090	Arm A	Surgery	29.2 s	1.01		
0090	Arm A	Surgery	29.6 s	1.19		
0090	Arm A	Surgery	29.5 s	0.98		
0090	Arm A	Cycle 1- Day 1/ before cycle	24.7 s	1.04		
0090	Arm A	Cycle 1- Day 1/ before cycle	28.8 s	0.92		
0090	Arm A	Cycle 1- Other timepoints		.	0.7 ng/ml	6 U/ml
0090	Arm A	Cycle 2- Day 1/ before cycle	26.4 s	1.02		
0090	Arm A	Cycle 2- Other timepoints		.	0.7 ng/ml	6 U/ml
0090	Arm A	Cycle 3- Day 1/ before cycle	26.9 s	1.02		
0090	Arm A	Cycle 3- Other timepoints	27.9 s	0.96	0.7 ng/ml	6 U/ml
0090	Arm A	Cycle 3- Other timepoints	28 s	1.08	0.7 ng/ml	6 U/ml
0090	Arm A	Cycle 4- Day 1/ before cycle	26 s	1.04		
0090	Arm A	Cycle 4- Day 1/ before cycle	27.2 s	0.88		
0090	Arm A	Cycle 4- Other timepoints		.	0.7 ng/ml	6 U/ml
0090	Arm A	Cycle 5- Day 1/ before cycle	28 s	1.03		
0090	Arm A	Cycle 5- Other timepoints		.	0.7 ng/ml	6 U/ml
0090	Arm A	Cycle 6- Day 1/ before cycle	38.1 s	1.08		
0090	Arm A	Cycle 6- Other timepoints		.	0.7 ng/ml	6 U/ml

Patient No.	Treatment Arm	Point in time	PTT	INR	CEA	Ca 19-9
0090	Arm A	Cycle 7- Day 1/ before cycle	29.3 s	0.99	2.2 ng/ml	4 U/ml
0090	Arm A	Cycle 8- Day 1/ before cycle	36.5 s	0.93		
0090	Arm A	Cycle 8- Other timepoints		.	2.2 ng/ml	4 U/ml
0090	Arm A	Cycle 9- Day 1/ before cycle	38.3 s	0.87		
0090	Arm A	Cycle 9- Other timepoints		.	2.2 ng/ml	4 U/ml
0090	Arm A	Cycle 10- Day 1/ before cycle	42.5 s	1.03		
0090	Arm A	Cycle 10- Other timepoints		.	2.2 ng/ml	4 U/ml
0090	Arm A	Cycle 11- Day 1/ before cycle	42.2 s	0.94		
0090	Arm A	Cycle 11- Other timepoints		.	2.2 ng/ml	4 U/ml
0090	Arm A	Cycle 12- Day 1/ before cycle	30.8 s	0.90	2.4 ng/ml	5 U/ml
0090	Arm A	End of treatment	39 s	0.89	2.4 ng/ml	5 U/ml
0161	Arm A	Pre-examination	23 s	1.11	147 µg/l	893 kU/l
0161	Arm A	Surgery	27 s	1.40		
0161	Arm A	Surgery	24 s	1.20		
0161	Arm A	Surgery	24 s	1.12		
0161	Arm A	Surgery	26 s	1.40		
0161	Arm A	Cycle 1- Day 1/ before cycle	24 s	1.09	5 µg/l	
0161	Arm A	Cycle 2- Day 1/ before cycle	26 s	1.16	3 µg/l	
0161	Arm A	Cycle 3- Day 1/ before cycle	28 s	1.12	3 µg/l	
0161	Arm A	Cycle 4- Day 1/ before cycle	51 s	1.13	4 µg/l	
0161	Arm A	Cycle 5- Day 1/ before cycle		.	4 µg/l	
0161	Arm A	Cycle 6- Day 1/ before cycle	46 s	1.18	5 µg/l	
0161	Arm A	Cycle 7- Day 1/ before cycle	30 s	1.07	5 µg/l	
0161	Arm A	Cycle 8- Day 1/ before cycle	52 s	1.13	5 µg/l	
0161	Arm A	Cycle 9- Day 1/ before cycle	41 s	1.10	6 µg/l	
0161	Arm A	Cycle 10- Day 1/ before cycle	51 s	1.07	6 µg/l	
0161	Arm A	Cycle 11- Day 1/ before cycle	51 s	1.07	5.2 µg/l	
0161	Arm A	End of treatment	39 s	1.13	5.4 µg/l	
0163	Arm A	Pre-examination	32 s	1.05	2.3 ng/ml	24 U/ml
0163	Arm A	Surgery	31 s	1.31		
0166	Arm A	Pre-examination	24 s	0.95	53.3 µg/l	147.4 kU/l
0402	Arm A	Pre-examination	30 s	1.06	747.6 ng/ml	1346 U/ml
0001	Arm B	Pre-examination	31 s	1.00	12 µg/l	12 kU/l
0001	Arm B	Cycle 1- Other timepoints		.	6.4 µg/l	
0003	Arm B	Pre-examination	29.1 s	0.90	157.7 ng/ml	884.2 U/ml
0003	Arm B	Surgery	30 s	0.90		
0003	Arm B	Surgery	27.3 s	1.00		
0003	Arm B	Surgery	28.5 s	1.00		
0003	Arm B	Surgery	27.5 s	1.10		
0003	Arm B	Surgery	28 s	1.00		
0003	Arm B	Surgery	26.9 s	1.10		
0003	Arm B	Surgery	27.9 s	1.00		
0003	Arm B	Surgery	29.9 s	1.00		
0003	Arm B	Surgery	27.3 s	1.00		
0003	Arm B	Surgery	28.5 s	1.00		
0003	Arm B	Cycle 1- Day 1/ before cycle	29.9 s	1.00	114.2 ng/ml	759.6 U/ml
0003	Arm B	Cycle 2- Day 1/ before cycle	43.3 s	1.00	152.7 ng/ml	759.4 U/ml
0003	Arm B	Cycle 3- Day 1/ before cycle	37.7 s	1.00	51.3 ng/ml	301.7 U/ml
0003	Arm B	Cycle 4- Day 1/ before cycle	28.7 s	1.00	16.1 ng/ml	131.7 U/ml
0003	Arm B	Cycle 5- Day 1/ before cycle	32.6 s	1.00		
0003	Arm B	Cycle 6- Day 1/ before cycle	33.5 s	1.00	4 ng/ml	35.2 U/ml
0003	Arm B	Cycle 7- Day 1/ before cycle	29.7 s	1.00	1 ng/ml	20.9 U/ml
0003	Arm B	Cycle 8- Day 1/ before cycle	30.4 s	1.00		
0003	Arm B	Cycle 9- Day 1/ before cycle		.	1.3 ng/ml	13 U/ml

Patient No.	Treatment Arm	Point in time	PTT	INR	CEA	Ca 19-9
0003	Arm B	Cycle 10- Day 1/ before cycle	28.8 s	1.00		
0003	Arm B	End of treatment	32.1 s	1.00	1.8 ng/ml	13 U/ml
0081	Arm B	Pre-examination	24 s	1.01	2.7 µg/l	27 kU/l
0081	Arm B	End of treatment	24 s	1.01	3 µg/l	27 kU/l
0082	Arm B	Pre-examination	27 s	0.90	0.7 ng/ml	9.9 U/ml
0082	Arm B	Surgery	30 s	1.19		
0082	Arm B	Cycle 1- Day 1/ before cycle		.	0.7 ng/ml	9.9 U/ml
0082	Arm B	Cycle 1- Other timepoints	25 s	1.01		
0082	Arm B	Cycle 2- Other timepoints	24 s	0.97		
0082	Arm B	Cycle 3- Day 1/ before cycle	32 s	1.12		
0082	Arm B	Cycle 5- Other timepoints	24 s	0.98		
0082	Arm B	Cycle 7- Day 1/ before cycle	27 s	0.97		
0082	Arm B	Cycle 7- Other timepoints	26 s	1.03		
0082	Arm B	Cycle 8- Other timepoints	26 s	0.99		
0082	Arm B	Cycle 10- Day 1/ before cycle	25 s	0.95		
0082	Arm B	Cycle 12- Other timepoints	25 s	0.96	1 ng/ml	5.8 U/ml
0082	Arm B	End of treatment	25 s	0.96	1 ng/ml	5.8 U/ml
0084	Arm B	Pre-examination	31 s	1.12	1.6 ng/ml	13.7 U/ml
0084	Arm B	Surgery	36 s	1.19		
0084	Arm B	Cycle 1- Day 1/ before cycle	30 s	1.09	1.67 ng/ml	13.7 U/ml
0084	Arm B	Cycle 1- Other timepoints	29 s	1.12		
0084	Arm B	Cycle 2- Day 1/ before cycle	30 s	1.11		
0084	Arm B	Cycle 2- Other timepoints	28 s	1.13		
0084	Arm B	Cycle 3- Day 1/ before cycle	30 s	1.12		
0084	Arm B	Cycle 4- Day 1/ before cycle	36 s	1.10		
0084	Arm B	Cycle 5- Day 1/ before cycle	30 s	1.05		
0084	Arm B	Cycle 6- Day 1/ before cycle	31 s	1.08		
0084	Arm B	End of treatment	34 s	1.16		
0088	Arm B	Pre-examination	29.9 s	0.95	6.7 ng/ml	17.4 U/ml
0088	Arm B	Surgery	30.7 s	1.00		
0088	Arm B	Cycle 1- Day 1/ before cycle	29.6 s	0.94	8 ng/ml	27.3 U/ml
0088	Arm B	Cycle 2- Day 1/ before cycle	22.2 s	0.94		
0088	Arm B	Cycle 3- Day 1/ before cycle	26.7 s	0.94		
0088	Arm B	Cycle 4- Day 1/ before cycle	36.8 s	0.94		8.2 U/ml
0088	Arm B	Cycle 5- Other timepoints	35.5 s	0.94	3.1 ng/ml	7.1 U/ml
0088	Arm B	Cycle 6- Day 1/ before cycle	28.4 s	0.95	2.8 ng/ml	6.7 U/ml
0162	Arm B	Pre-examination	27 s	1.10	2 ng/ml	2.1 U/ml
0162	Arm B	Surgery	27 s	1.34		
0162	Arm B	Cycle 1- Day 1/ before cycle	27 s	1.00		
0162	Arm B	Cycle 1- Other timepoints	26 s	1.10		
0162	Arm B	Cycle 2- Day 1/ before cycle	26 s	0.94		
0162	Arm B	Cycle 2- Other timepoints	27 s	1.00		
0162	Arm B	Cycle 3- Day 1/ before cycle	26 s	0.96		
0162	Arm B	Cycle 3- Other timepoints	27 s	0.98		
0162	Arm B	Cycle 4- Day 1/ before cycle	26 s	0.94		
0162	Arm B	Cycle 4- Other timepoints	25 s	0.99	2.2 ng/ml	4.9 U/ml
0162	Arm B	Cycle 5- Day 1/ before cycle	25 s	0.94		
0162	Arm B	Cycle 5- Other timepoints	26 s	1.00		
0162	Arm B	Cycle 6- Day 1/ before cycle	26 s	0.99		
0162	Arm B	Cycle 7- Day 1/ before cycle	28 s	1.04	2.9 ng/ml	5.6 U/ml
0162	Arm B	Cycle 7- Other timepoints	26 s	1.05		
0162	Arm B	Cycle 8- Day 1/ before cycle	26 s	1.08		
0162	Arm B	Cycle 9- Day 1/ before cycle	26 s	0.98		
0162	Arm B	Cycle 10- Other timepoints	25 s	1.05		

Patient No.	Treatment Arm	Point in time	PTT	INR	CEA	Ca 19-9
0162	Arm B	Cycle 11- Other timepoints	27 s	1.05		
0162	Arm B	Cycle 12- Other timepoints	26 s	1.10		
0162	Arm B	End of treatment	27 s	1.09	2.2 ng/ml	5.5 U/ml
0164	Arm B	Pre-examination	33 s	1.10	3.6 ng/ml	16.4 U/ml
0164	Arm B	Cycle 1- Day 1/ before cycle	32.7 s	1.10	3 ng/ml	13.2 U/ml
0164	Arm B	Cycle 2- Day 1/ before cycle	47.1 s	1.20		
0164	Arm B	Cycle 3- Day 1/ before cycle		.	2.1 ng/ml	13 U/ml
0164	Arm B	Cycle 4- Day 1/ before cycle	32.5 s	1.10		
0164	Arm B	Cycle 5- Day 1/ before cycle	36.9 s	1.20		
0164	Arm B	Cycle 6- Day 1/ before cycle	49.4 s	1.10		
0164	Arm B	Cycle 6- Other timepoints		.	3.4 ng/ml	19.2 U/ml
0164	Arm B	End of treatment	31.5 s	1.10	2.6 ng/ml	13 U/ml
0165	Arm B	Pre-examination	32 s	0.90	1.5 ng/ml	7 U/ml
0165	Arm B	Surgery	32 s	0.95		
0165	Arm B	Cycle 1- Day 1/ before cycle	32 s	1.01		
0165	Arm B	Cycle 1- Other timepoints		.	1.5 ng/ml	7 U/ml
0165	Arm B	Cycle 6- Other timepoints		.	2.7 ng/ml	7 U/ml
0165	Arm B	Cycle 7- Day 1/ before cycle	31 s	0.96		
0167	Arm B	Pre-examination	38 s	1.00	16.46 ng/ml	
0167	Arm B	Surgery	35 s	1.00		
0167	Arm B	Cycle 1- Day 1/ before cycle	36 s	1.00	12.62 ng/ml	17 U/ml
0167	Arm B	Cycle 4- Day 1/ before cycle	36 s	1.00		
0167	Arm B	Cycle 4- Other timepoints		.	14.73 ng/ml	7 U/ml
0167	Arm B	Cycle 5- Day 1/ before cycle	33 s	1.00		
0167	Arm B	Cycle 6- Day 1/ before cycle	34 s	1.10		
0167	Arm B	Cycle 7- Day 1/ before cycle	36 s	1.00	4.34 ng/ml	
0167	Arm B	Cycle 8- Day 1/ before cycle	37 s	1.10		
0167	Arm B	Cycle 9- Day 1/ before cycle	41 s	1.10		
0167	Arm B	Cycle 10- Day 1/ before cycle	39 s	1.10	4.95 ng/ml	13 U/ml
0167	Arm B	Cycle 11- Day 1/ before cycle	33 s	1.10		
0167	Arm B	Cycle 12- Day 1/ before cycle	34 s	1.10		
0167	Arm B	End of treatment	36 s	1.00	6.68 ng/ml	24 U/ml
0241	Arm B	Pre-examination	33.6 s	1.00	12.4 ng/ml	265 U/ml
0241	Arm B	Surgery	31.4 s	1.02		
0241	Arm B	Surgery	30.7 s	1.06		
0241	Arm B	Surgery	31.6 s	1.05		
0241	Arm B	Surgery	31.6 s	1.07		
0241	Arm B	Surgery	31.1 s	1.31		
0241	Arm B	Surgery	34 s	0.96		
0241	Arm B	Surgery	28.4 s	1.13		
0241	Arm B	Surgery	30.9 s	1.04		
0241	Arm B	Cycle 1- Day 1/ before cycle	35.5 s	0.97		
0241	Arm B	Cycle 1- Other timepoints		.	12.4 ng/ml	265 U/ml
0241	Arm B	Cycle 2- Day 1/ before cycle	33.4 s	1.04		
0241	Arm B	Cycle 3- Day 1/ before cycle	33.3 s	1.00		
0241	Arm B	Cycle 4- Day 1/ before cycle	33.4 s	1.01	2 ng/ml	50 U/ml
0241	Arm B	Cycle 5- Day 1/ before cycle	33 s	1.04		
0241	Arm B	Cycle 6- Day 1/ before cycle	33.6 s	0.96		
0241	Arm B	Cycle 6- Other timepoints		.	4.3 ng/ml	51 U/ml
0241	Arm B	Cycle 7- Day 1/ before cycle	36 s	.	1.3 µg/l	22.8 U/ml
0241	Arm B	Cycle 8- Other timepoints	37 s	.		
0241	Arm B	Cycle 10- Day 1/ before cycle	60 s	.		
0241	Arm B	Cycle 11- Day 1/ before cycle	36 s	.		
0241	Arm B	Cycle 12- Other timepoints	37 s	.		

Patient No.	Treatment Arm	Point in time	PTT	INR	CEA	Ca 19-9
0241	Arm B	End of treatment	41 s	.	3.5 µg/l	50.3 U/ml
0242	Arm B	Pre-examination	32.8 s	1.06	6.6 µg/l	8.7 kU/l
0242	Arm B	Surgery	34.2 s	1.00		
0242	Arm B	Surgery	37.2 s	1.23		
0242	Arm B	Cycle 1- Other timepoints	33.8 s	1.14		
0242	Arm B	Cycle 2- Day 1/ before cycle	32.4 s	1.07		
0242	Arm B	Cycle 2- Other timepoints	34.9 s	1.13		
0242	Arm B	Cycle 3- Day 1/ before cycle	30.4 s	1.07		
0242	Arm B	Cycle 3- Other timepoints	32.2 s	1.01		
0242	Arm B	Cycle 4- Day 1/ before cycle	31 s	1.05	0.9 µg/l	6.7 kU/l
0242	Arm B	Cycle 5- Day 1/ before cycle	31.5 s	1.10		
0242	Arm B	Cycle 5- Other timepoints	32.1 s	1.06		
0242	Arm B	Cycle 6- Day 1/ before cycle	32.4 s	1.04		
0242	Arm B	Cycle 6- Other timepoints	32.4 s	1.05	0.9 µg/l	7.2 kU/l
0242	Arm B	Cycle 7- Day 1/ before cycle	46.6 s	2.54	0.9 µg/l	
0242	Arm B	Cycle 7- Other timepoints	44.8 s	2.71		
0242	Arm B	Cycle 8- Day 1/ before cycle	47.7 s	3.17		
0242	Arm B	Cycle 8- Other timepoints	37.7 s	2.94	0.7 µg/l	7.3 kU/l
0242	Arm B	Cycle 9- Day 1/ before cycle	55.6 s	3.54		
0242	Arm B	Cycle 10- Day 1/ before cycle	40.5 s	2.22	1 µg/l	
0242	Arm B	Cycle 11- Day 1/ before cycle	40.8 s	2.29		
0242	Arm B	Cycle 12- Day 1/ before cycle	40.6 s	2.28		
0242	Arm B	Cycle 12- Other timepoints	44.6 s	2.55		
0242	Arm B	End of treatment	45.1 s	2.33	0.7 µg/l	
0401	Arm B	Pre-examination	29.8 s	1.00	1.21 ng/ml	5.63 U/ml
0401	Arm B	Surgery	24.6 s	.		
0401	Arm B	Surgery	31 s	1.40		
0401	Arm B	Surgery	29.9 s	.		
0401	Arm B	Surgery	27 s	1.80		
0401	Arm B	Surgery	30.4 s	1.30		
0401	Arm B	Surgery	28.9 s	1.00		
0401	Arm B	Surgery	30.9 s	1.80		
0401	Arm B	Surgery	28.9 s	1.40		
0401	Arm B	Surgery	29.6 s	.		
0401	Arm B	Cycle 1- Day 1/ before cycle	30.7 s	1.10		
0401	Arm B	Cycle 2- Day 1/ before cycle	28.3 s	1.00		
0401	Arm B	Cycle 3- Day 1/ before cycle	24.9 s	1.00		
0401	Arm B	Cycle 4- Day 1/ before cycle	30.5 s	1.10		
0401	Arm B	Cycle 6- Day 1/ before cycle	33.2 s	1.00	3.31 ng/ml	10.75 U/ml