NCT
NATIONALES CENTRUM FÜR TUMORERKRANKUNGEN HEIDELBERG

getragen von:
Deutsches Krebsforschungszentrum
Universitätsklinikum Heidelberg
Thoraxklinik-Heidelberg
Deutsche Krebshilfe

Ergebnisbericht nach §42b Arzneimittelgesetz (AMG)

Name of Sponsor/Company: University Hospital Heidelberg represented in law by its commercial Director Irmtraut Gürkan Im Neuenheimer Feld 672 69120 Heidelberg Germany
Name of Finished Product: Oxaliplatin Winthrop®
Name of Active Ingredient: Oxaliplatin
Title of Study: *identify version of protocol and amendments* Phase II study on curative resectability of not optimally resectable liver and/or lung metastases from colorectal carcinoma (CRC) under intensified chemotherapy (FOLFOXIRI/ Bevacizumab) – APRIORI Protocol No. NCT-2007-11-02-1003, Version 1.0 final vom 15.11.2007: Initial submission Protocol No. NCT-2007-11-02-1003, Version 1.1 final vom 28.05.2009: First Amendment concerning the change of formulation of Oxaliplatin Winthrop® from powder to liquid concentrate for preparation of infusions by the marketing authorization holder Winthrop Arzneimittel GmbH, Germany
Study centre(s) and Principle Investigator(s): University Hospital Heidelberg, Medical Oncology National Center for Tumor Diseases (NCT) Prof. Dr. med. Dirk Jäger (Coordinating Investigator) PD Dr. med. Thomas Hermann (Principle Investigator till 16. March 2010) Dr. Stefan Bauer (Principle Investigator from 17. March 2010) Im Neuenheimer Feld 460 69120 Heidelberg Zentrum Fuxius und Karcher Dr. med. Stefan Fuxius Kurfürstenanlage 34 69115 Heidelberg Gemeinschaftspraxis für Hämatologie, Onkologie und Infektiologie Dr. med. Maria Procaccianti Kriegstr. 236 76135 Karlsruhe

SLK Kliniken Heilbronn GmbH
Innere Med. Hämatologie/Onkologie/Gastroenterologie
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Publication (reference):

Not applicable

Studied period (years):
incl. interruptions, early terminations and discontinuations

25. January 2010 (First patient in)

17. August 2010 (Last patient out)

16. March 2011 Premature closure of trial

Phase of development:

Phase 2

Objectives:

The primary objective was to evaluate the proportion of patients who achieve surgically complete resectability (SCR) of metastases after preoperative chemotherapy.

Secondary objectives were to evaluate the acute and perioperative toxicity of preoperative chemotherapy and to evaluate the survival rate (OS) and the progression free survival (PFS).

In addition, the prognostic values of baseline parameters for SCR have been analyzed.

Methodology:

This study had a two-stage design according to Simon, more specifically, an optimal design minimizing the expected sample size if the true S-CR rate r equals the "uninteresting" rate r_0. "Uninteresting" S-CR rate: r_0=10%, corresponding to the null hypothesis H_0; "interesting" S-CR rate r_1=30%, corresponding to the alternative hypothesis H1; α=10%, β=10%.
The decision rules of this design were as follows:

- Stage 1: n_1=12; reject the treatment as "not interesting" and terminate the trial if no more than one S-CR has been observed among the first 12 patients. Otherwise proceed to stage two.
- Stage 2: n_2=23 patients; reject the treatment as "not interesting" if no more than 5 S-CR have been observed up to the end of stage two.

The total sample size implied by this design is less or equal to 35.

Number of patients (planned and analysed):

Planned No.: 35

Analyzed No.: 3

Diagnosis and main criteria for inclusion:

Advanced colorectal carcinoma of UICC stage IV, liver and/or lung metastases only, not optimally resectable.

Inclusion criteria (in brief):

- Histologically confirmed advanced colorectal carcinoma of UICC Stages IV with liver and/or lung only metastases which are not optimally resectable
- Measurable disease according to RECIST criteria
- Adequate lab parameters

Exclusion criteria (in brief):

- Previous chemotherapy
- History or evidence upon physical examination of CNS disease unless adequately treated
- Serious, non-healing wound, ulcer, or bone fracture.
- Clinically significant (i.e. active) cardiovascular disease
- Hemapoetic diseases

Test product, dose and mode of administration, batch number:

Oxaliplatin Winthrop®, Winthrop Arzneimittel GmbH, Germany,

Concentrate for formulation of an infusion, 85 mg/m2 as a 2-h IV infusion (in 500 mL 5% glucose solution)

Marketable good

Duration of treatment:

Treatment duration depended on the individual subject's tolerance to the dosing prescribed in the trial protocol (dose-limiting toxicity of the trial medication). It was anticipated that the preoperative chemotherapy would continue until 2-4 weeks prior to surgery (last application of bevacizumab 4 weeks before surgery). The maximum treatment duration for candidates not eligible for surgery was to be 16 cycles (approximately 7-8 months) in total.

Reference therapy, dose and mode of administration, batch number:

Not applicable

Criteria for evaluation:

Efficacy:

Primary efficacy parameter: S-CR, which is defined as histologically confirmed tumor free resection margins (R0-resection).

Secondary efficacy parameter: Progression free overall survival.

Safety:

Serious adverse events according to ICH (NCI CTCAE) criteria in terms of all chemotherapy related acute and perioperative toxicities as well as peri- and postsurgical complications.

Statistical methods:

Considering the premature close of this trial - after the inclusion of merely 3 patients - any statistical analyses were deemed inappropriate. Tabulations were confined to basic patient characteristics, adverse events as well as laboratory parameters.

SUMMARY - CONCLUSIONS

EFFICACY RESULTS:

Not applicable

SAFETY RESULTS:

Tables of adverse events were produced. No descriptive or confirmatory statistical analyses were done. The APRIORI trial was stopped prematurely. The decision to stop this trial was not the result of a planned interim analysis or an accumulation of SAEs or deaths.

CONCLUSION:

Not applicable

Substantial amendments / interruptions or early termination: Amendments see above: "*Title of Study*"
Date of the report: 2. May 2012