Clinical trial results:
A randomized phase II trial of nal-IRI and 5-Fluorouracil compared to 5-Fluorouracil in patients with cholangio- and gallbladder carcinoma previously treated with gemcitabine-based therapies

Summary

EudraCT number	2016-003709-33
Trial protocol	DE
Global end of trial date	08 March 2022

Results information

Result version number	v1 (current)
This version publication date	09 May 2026
First version publication date	09 May 2026

Trial information

Trial identification

Sponsor protocol code	AIO-HEP-0116

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AIO-Studien-gGmbH
Sponsor organisation address	Kuno-Fischer-Str. 8, Berlin, Germany, 14057
Public contact	info@aio-studien-ggmbh.de, AIO-Studien-gGmbH, 0049 30814534431, info@aio-studien-ggmbh.de
Scientific contact	info@aio-studien-ggmbh.de, AIO-Studien-gGmbH, 0049 30814534431, info@aio-studien-ggmbh.de

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 March 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 March 2022
Global end of trial reached?	Yes
Global end of trial date	08 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of nal-IRI in gemcitabine pre-treated patients with cholangiocarcinoma.

Protection of trial subjects:

This study was planned, analyzed and conducted according to the study protocol and in accordance with the International Conference on Harmonization (ICH) ‚Guideline for Good Clinical Practice E6(R2)', CPMP/ICH/135/95, based on the principles of the Declaration of Helsinki (1964) and its October 2013 amendment (Fortaleza,Brazil). The study was duly conducted in compliance with the German Arzneimittelgesetz (AMG; German Drug Law), and the corresponding EU Directive 2001/20/EC. Subjects were fully informed regarding all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 December 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 100
Worldwide total number of subjects	100
EEA total number of subjects	100

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	48
From 65 to 84 years	50

85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Between December 2017 and August 2021, 100 patients were screened and randomized at 17 German study sites.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Nal-IRI + 5-FU/LV

Arm description:

Patients in the experimental treatment group received 70 mg/m² nanoliposomal irinotecan anhydrous free base as a 90-min infusion, followed by leucovorin at 400 mg/m² in a 30-min infusion and fluorouracil at 2400 mg/m² as a 46-h infusion on day 1 of every 2-week cycle.

Arm type	Experimental
Investigational medicinal product name	5-Fluorouracil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5-FU was administered at 2400 mg/ m2 every two weeks.

Investigational medicinal product name	Leucovorin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Leucovorin (folinic acid) was co-administered with 5-FU at 400 mg/ m2 every two weeks.

Investigational medicinal product name	Nal-IRI
Investigational medicinal product code	
Other name	Onivyde
Pharmaceutical forms	Concentrate for dispersion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Nal-IRI (pegylated liposomal irinotecan) was administered at 70 mg/m2 (anhydrous free base) every two weeks.

Arm title	5-FU/LV

Arm description:

Patients in the control group received leucovorin at 400 mg/m² in a 30-min infusion and fluorouracil at 2400 mg/m² as a 46-h infusion on day 1 of every 2-week cycle.

Arm type	Active comparator

Investigational medicinal product name	5-Fluorouracil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5-FU was administered at 2400 mg/ m2 every two weeks.

Investigational medicinal product name	Leucovorin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Leucovorin (folinic acid) was co-administered with 5-FU at 400 mg/ m2 every two weeks.

Number of subjects in period 1	Nal-IRI + 5-FU/LV	5-FU/LV
Started	49	51
Completed	49	51

Baseline characteristics

Reporting groups	
Reporting group title	Nal-IRI + 5-FU/LV
Reporting group description:	
Patients in the experimental treatment group received 70 mg/m² nanoliposomal irinotecan anhydrous free base as a 90-min infusion, followed by leucovorin at 400 mg/m² in a 30-min infusion and fluorouracil at 2400 mg/m² as a 46-h infusion on day 1 of every 2-week cycle.	
Reporting group title	5-FU/LV
Reporting group description:	
Patients in the control group received leucovorin at 400 mg/m² in a 30-min infusion and fluorouracil at 2400 mg/m² as a 46-h infusion on day 1 of every 2-week cycle.	

Reporting group values	Nal-IRI + 5-FU/LV	5-FU/LV	Total
Number of subjects	49	51	100
Age categorical			
Units: Subjects			
Adults (18-64 years)	19	29	48
From 65-84 years	30	20	50
85 years and over	0	2	2
Age continuous			
Units: years			
median	66	63	
full range (min-max)	43 to 80	33 to 87	-
Gender categorical			
Units: Subjects			
Female	23	22	45
Male	26	29	55
ECOG performance status			
Units: Subjects			
ECOG 0	33	36	69
ECOG 1	16	14	30
ECOG 2	0	1	1

End points

End points reporting groups

Reporting group title	Nal-IRI + 5-FU/LV
Reporting group description:	
Patients in the experimental treatment group received 70 mg/m² nanoliposomal irinotecan anhydrous free base as a 90-min infusion, followed by leucovorin at 400 mg/m² in a 30-min infusion and fluorouracil at 2400 mg/m² as a 46-h infusion on day 1 of every 2-week cycle.	
Reporting group title	5-FU/LV
Reporting group description:	
Patients in the control group received leucovorin at 400 mg/m² in a 30-min infusion and fluorouracil at 2400 mg/m² as a 46-h infusion on day 1 of every 2-week cycle.	

Primary: Progression-free survival

End point title	Progression-free survival
End point description:	
Subjects who died without reported progression were considered to have progressed on the date of their death. If neither death nor progression were observed during the study, PFS data was censored at the last valid tumor assessment. Subjects who did not have any on-study tumor assessments and did not die were censored on the date they were randomized. Subjects who started any subsequent anticancer therapy without prior reported progression were censored at the last evaluable tumor assessment prior to or on the date of initiation of the subsequent anticancer therapy.	
End point type	Primary
End point timeframe:	
PFS was defined as the number of months from the date of randomization to the date of progression per RECIST v1.1 or death by any cause, whichever occurred earlier.	

End point values	Nal-IRI + 5-FU/LV	5-FU/LV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	51		
Units: Months				
median (confidence interval 95%)	2.6 (1.7 to 3.6)	2.3 (1.6 to 3.4)		

Statistical analyses

Statistical analysis title	Statistical analysis primary endpoint - mPFS
Comparison groups	Nal-IRI + 5-FU/LV v 5-FU/LV
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.521
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.867

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.559
upper limit	1.345

Secondary: Overall survival

End point title	Overall survival

End point description:

End point type	Secondary

End point timeframe:

Overall survival (OS) was calculated from the date of subject randomization until the date of death from any cause. If no event was reported, OS was censored at the day of last subject contact.

End point values	Nal-IRI + 5-FU/LV	5-FU/LV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	51		
Units: Months				
median (confidence interval 95%)	6.9 (5.3 to 10.6)	8.2 (5.4 to 11.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective tumor response rate (ORR)

End point title	Objective tumor response rate (ORR)

End point description:

BOR was determined by the best response designation recorded between the date of subject randomization and the date of objectively documented progression. For subjects without documented progression, all available response designations were contributed to the BOR determination.

End point type	Secondary

End point timeframe:

ORR was defined as the proportion of all randomized subjects in each treatment arm whose best overall response (BOR) from baseline was either complete remission (CR) or partial remission (PR) per RECIST v1.1 criteria.

End point values	Nal-IRI + 5-FU/LV	5-FU/LV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	51		
Units: Patients	7	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Patients were monitored for occurrence of adverse events from the time of signing the informed consent until 30 days after last dose of study treatment.

Assessment type	Non-systematic

Dictionary used

Dictionary name	NCI CTCAE
Dictionary version	4.01

Reporting groups

Reporting group title	Nal-IRI + 5-FU/LV

Reporting group description:

Total number of deaths is reported for all enrolled subjects (N=49 for Nal-IRI/5-FU/LV and N=51 for 5-FU/LV) and until end of follow-up.

Reporting group title	5-FU/LV

Reporting group description:

Total number of deaths is reported for all enrolled subjects (N=49 for Nal-IRI/5-FU/LV and N=51 for 5-FU/LV) and until end of follow-up.

Serious adverse events	Nal-IRI + 5-FU/LV	5-FU/LV	
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 48 (56.25%)	19 / 48 (39.58%)	
number of deaths (all causes)	36	39	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Thromboembolic event			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fall			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fever			
subjects affected / exposed	0 / 48 (0.00%)	2 / 48 (4.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Other - Worsening of general			

condition			
subjects affected / exposed	2 / 48 (4.17%)	2 / 48 (4.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Psychosis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral motor neuropathy			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Other - Pancytopenia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	1 / 48 (2.08%)	2 / 48 (4.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	3 / 48 (6.25%)	2 / 48 (4.17%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	6 / 48 (12.50%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	5 / 7	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal stenosis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal ulcer			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric stenosis			

subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Other - Cholangitis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Other - Suspected Clostridium difficile infection			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jejunal ulcer			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malabsorption			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucositis oral			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			

subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	3 / 48 (6.25%)	5 / 48 (10.42%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Other - Cholangitis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 48 (2.08%)	3 / 48 (6.25%)	
occurrences causally related to treatment / all	1 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Fracture			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle weakness lower limb			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Other - Coxarthrosis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal infection			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary tract infection			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis infectious			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Other - Unknown infection			
subjects affected / exposed	1 / 48 (2.08%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Other - Cholangitis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Other - Infection			

subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal infection			
subjects affected / exposed	2 / 48 (4.17%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 48 (4.17%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 48 (0.00%)	3 / 48 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 48 (4.17%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Nal-IRI + 5-FU/LV	5-FU/LV	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 48 (95.83%)	47 / 48 (97.92%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 48 (2.08%)	2 / 48 (4.17%)	
occurrences (all)	1	2	
Thromboembolic event			
subjects affected / exposed	1 / 48 (2.08%)	2 / 48 (4.17%)	
occurrences (all)	2	2	
General disorders and administration site conditions			

Chills			
subjects affected / exposed	2 / 48 (4.17%)	1 / 48 (2.08%)	
occurrences (all)	2	1	
Edema limbs			
subjects affected / exposed	6 / 48 (12.50%)	4 / 48 (8.33%)	
occurrences (all)	6	4	
Fatigue			
subjects affected / exposed	18 / 48 (37.50%)	13 / 48 (27.08%)	
occurrences (all)	27	22	
Fever			
subjects affected / exposed	2 / 48 (4.17%)	7 / 48 (14.58%)	
occurrences (all)	9	13	
General disorders and administration site conditions - other			
subjects affected / exposed	7 / 48 (14.58%)	4 / 48 (8.33%)	
occurrences (all)	11	4	
Pain			
subjects affected / exposed	6 / 48 (12.50%)	7 / 48 (14.58%)	
occurrences (all)	9	10	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 48 (4.17%)	5 / 48 (10.42%)	
occurrences (all)	2	5	
Dyspnoea			
subjects affected / exposed	3 / 48 (6.25%)	4 / 48 (8.33%)	
occurrences (all)	3	4	
Epistaxis			
subjects affected / exposed	3 / 48 (6.25%)	4 / 48 (8.33%)	
occurrences (all)	3	4	
Hoarseness			
subjects affected / exposed	2 / 48 (4.17%)	1 / 48 (2.08%)	
occurrences (all)	2	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 48 (8.33%)	1 / 48 (2.08%)	
occurrences (all)	4	2	
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	3 / 48 (6.25%)	2 / 48 (4.17%)	
occurrences (all)	3	3	
Alkaline phosphatase increased			
subjects affected / exposed	2 / 48 (4.17%)	2 / 48 (4.17%)	
occurrences (all)	2	3	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 48 (4.17%)	2 / 48 (4.17%)	
occurrences (all)	2	2	
Blood bilirubin increased			
subjects affected / exposed	2 / 48 (4.17%)	1 / 48 (2.08%)	
occurrences (all)	7	1	
Creatinine increased			
subjects affected / exposed	2 / 48 (4.17%)	2 / 48 (4.17%)	
occurrences (all)	2	4	
GGT increased			
subjects affected / exposed	3 / 48 (6.25%)	3 / 48 (6.25%)	
occurrences (all)	4	10	
Lymphocyte count decreased			
subjects affected / exposed	3 / 48 (6.25%)	2 / 48 (4.17%)	
occurrences (all)	3	2	
Platelet count decreased			
subjects affected / exposed	1 / 48 (2.08%)	3 / 48 (6.25%)	
occurrences (all)	1	4	
Weight loss			
subjects affected / exposed	4 / 48 (8.33%)	3 / 48 (6.25%)	
occurrences (all)	6	3	
Neutrophil count decreased			
subjects affected / exposed	13 / 48 (27.08%)	1 / 48 (2.08%)	
occurrences (all)	23	1	
White blood cell decreased			
subjects affected / exposed	7 / 48 (14.58%)	2 / 48 (4.17%)	
occurrences (all)	13	5	
Cardiac disorders			

Cardiac disorders - other			
subjects affected / exposed	0 / 48 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 48 (8.33%)	4 / 48 (8.33%)	
occurrences (all)	5	5	
Dysgeusia			
subjects affected / exposed	0 / 48 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
Headache			
subjects affected / exposed	3 / 48 (6.25%)	1 / 48 (2.08%)	
occurrences (all)	3	1	
Paresthesia			
subjects affected / exposed	2 / 48 (4.17%)	3 / 48 (6.25%)	
occurrences (all)	2	3	
Peripheral motor neuropathy			
subjects affected / exposed	0 / 48 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
Peripheral sensory neuropathy			
subjects affected / exposed	3 / 48 (6.25%)	7 / 48 (14.58%)	
occurrences (all)	4	7	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	9 / 48 (18.75%)	6 / 48 (12.50%)	
occurrences (all)	12	16	
Blood and lymphatic system disorders - other			
subjects affected / exposed	1 / 48 (2.08%)	2 / 48 (4.17%)	
occurrences (all)	1	3	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 48 (4.17%)	1 / 48 (2.08%)	
occurrences (all)	2	3	
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	7 / 48 (14.58%)	8 / 48 (16.67%)	
occurrences (all)	7	8	
Ascites			
subjects affected / exposed	4 / 48 (8.33%)	6 / 48 (12.50%)	
occurrences (all)	7	7	
Constipation			
subjects affected / exposed	16 / 48 (33.33%)	7 / 48 (14.58%)	
occurrences (all)	20	8	
Diarrhoea			
subjects affected / exposed	25 / 48 (52.08%)	9 / 48 (18.75%)	
occurrences (all)	50	11	
Dysphagia			
subjects affected / exposed	2 / 48 (4.17%)	0 / 48 (0.00%)	
occurrences (all)	2	0	
Flatulence			
subjects affected / exposed	2 / 48 (4.17%)	2 / 48 (4.17%)	
occurrences (all)	2	3	
Gastroesophageal reflux disease			
subjects affected / exposed	3 / 48 (6.25%)	1 / 48 (2.08%)	
occurrences (all)	3	3	
Gastrointestinal disorders - other			
subjects affected / exposed	5 / 48 (10.42%)	3 / 48 (6.25%)	
occurrences (all)	7	3	
Mucositis oral			
subjects affected / exposed	11 / 48 (22.92%)	8 / 48 (16.67%)	
occurrences (all)	15	11	
Nausea			
subjects affected / exposed	28 / 48 (58.33%)	15 / 48 (31.25%)	
occurrences (all)	48	25	
Obstruction gastric			
subjects affected / exposed	0 / 48 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
Vomiting			
subjects affected / exposed	17 / 48 (35.42%)	4 / 48 (8.33%)	
occurrences (all)	26	4	
Hepatobiliary disorders			

Hepatobiliary disorders - other			
subjects affected / exposed	1 / 48 (2.08%)	2 / 48 (4.17%)	
occurrences (all)	3	3	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	7 / 48 (14.58%)	4 / 48 (8.33%)	
occurrences (all)	9	4	
Dry skin			
subjects affected / exposed	8 / 48 (16.67%)	5 / 48 (10.42%)	
occurrences (all)	10	5	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	2 / 48 (4.17%)	1 / 48 (2.08%)	
occurrences (all)	4	1	
Pruritus			
subjects affected / exposed	1 / 48 (2.08%)	4 / 48 (8.33%)	
occurrences (all)	1	6	
Rash acneiform			
subjects affected / exposed	2 / 48 (4.17%)	2 / 48 (4.17%)	
occurrences (all)	2	2	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 48 (4.17%)	0 / 48 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 48 (6.25%)	4 / 48 (8.33%)	
occurrences (all)	3	4	
Flank pain			
subjects affected / exposed	0 / 48 (0.00%)	3 / 48 (6.25%)	
occurrences (all)	0	4	
Pain			
subjects affected / exposed	2 / 48 (4.17%)	0 / 48 (0.00%)	
occurrences (all)	2	0	
Pain in extremity			
subjects affected / exposed	2 / 48 (4.17%)	1 / 48 (2.08%)	
occurrences (all)	2	1	

Infections and infestations			
Lung infection			
subjects affected / exposed	2 / 48 (4.17%)	0 / 48 (0.00%)	
occurrences (all)	2	0	
Urinary tract infection			
subjects affected / exposed	2 / 48 (4.17%)	2 / 48 (4.17%)	
occurrences (all)	2	2	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	15 / 48 (31.25%)	8 / 48 (16.67%)	
occurrences (all)	29	11	
Dehydration			
subjects affected / exposed	4 / 48 (8.33%)	0 / 48 (0.00%)	
occurrences (all)	4	0	
Hypoalbuminaemia			
subjects affected / exposed	3 / 48 (6.25%)	1 / 48 (2.08%)	
occurrences (all)	4	1	
Hypokalaemia			
subjects affected / exposed	3 / 48 (6.25%)	3 / 48 (6.25%)	
occurrences (all)	5	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 July 2020	With this amemdment, the nominal dose of nal-IRI was changed from 80 mg/m2 to 70 mg/m2. The context of this amendment was that the nal-IRI standard dose had always been given as 70 mg/m2 in the US, which describes the dose of active substance as anhydrous free base. By contrast, for the EU, the standard dose had been described as 80 mg/m2 irinotecan hydrochloride. In 2020, the MAH aligned the wording of the dosing information globally to 70 mg/m2 anhydrous free base, and updated all prescribing information accordingly. The amendment of the study's protocol was neccessary to align the protocol with up to date prescribing information.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported