



## Clinical trial results:

**Transarterial chemoembolization (TACE) with Irinotecan and Mitomycin C versus TACE with Doxorubicin in patients with Hepatocellular carcinoma not amenable to curative treatment - IRITACE- a randomized multicenter phase 2 trial. A trial of the German Alliance for Liver Cancer (GALC)**

### Summary

EudraCT number	2019-000922-23
Trial protocol	DE
Global end of trial date	22 November 2023

### Results information

Result version number	v1 (current)
This version publication date	10 August 2024
First version publication date	10 August 2024

### Trial information

#### Trial identification

Sponsor protocol code	IRITACE
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	AIO study number: AIO-HEP-0220/ass

Notes:

### Sponsors

Sponsor organisation name	Goethe University Frankfurt
Sponsor organisation address	Theodor-W.-Adorno-Platz 1, Frankfurt am Main, Germany, 60629
Public contact	Project Management, Frankfurter Institut für Klinische Krebsforschung IKF GmbH, iritace@ikf-khnw.de
Scientific contact	Project Management, Frankfurter Institut für Klinische Krebsforschung IKF GmbH, iritace@ikf-khnw.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	11 January 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 November 2023
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

The main scope of the trial was to evaluate the efficacy and safety of TACE with irinotecan and mitomycin C compared with TACE with doxorubicin in patients with non-curable intermediate-stage hepatocellular carcinoma (HCC). The primary endpoint was the determination of progression free survival (PFS) time.

Protection of trial subjects:

This clinical study was designed and shall be implemented and reported in accordance with the protocol, the AMG (Arzneimittelgesetz), the ICH Harmonized Tripartite Guidelines for Good Clinical Practice, with applicable local regulations (including European Directive 2001/20/EC), and with the ethical principles laid down in the Declaration of Helsinki. The trial was authorized/approved by the competent authority (Paul-Ehrlich-Institut, PEI) and the competent ethics committee responsible for the trial ("federführende Ethikkommission").

Before recruitment into the clinical trial, each patient was informed that participation in the study is completely voluntary, and that he or she may withdraw his or her participation in the trial at any time without any declaration of reasons, which will not lead to any disadvantage for the respective patient. The eligibility of a new patient was determined by the local investigator during regular clinical visits. The examinations for the study and the inclusion of the patient were done after detailed written and oral education about aims, methods, anticipated benefits and potential hazards of the study by use of the informed consent forms and after given written consent of the patient.

Safety of study treatment was monitored continuously by careful monitoring of all adverse events (AEs) and serious adverse events (SAEs) reported.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 June 2020
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: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

Notes:

### Subjects enrolled per age group

In utero	0
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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)	7
From 65 to 84 years	12
85 years and over	1

## Subject disposition

### Recruitment

Recruitment details:

104 patients for were planned. Due to slow recruitment and changes in the therapy landscape the trial was prematurely terminated.

The recruitment period was 26 months, June 2020 - August 2022 and took place in 8 centers in Germany.

### Pre-assignment

Screening details:

Patients with histologically confirmed HCC primarily not suitable for resection, ablation alone or liver transplantation, without extra-hepatic spread. A combined therapy with TACE and subsequent ablation was possible.

25 patients were screened, 5 were ineligible (inclusion/exclusion criteria), 3 did not start trial treatment

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Experimental arm

Arm description:

Patients received Mitomycin C and Irinotecan via TACE

Arm type	Experimental
Investigational medicinal product name	Mitomycin C
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Injection

Dosage and administration details:

For transarterial chemoembolization, 4 ml of 70-150 µm drug-eluting beads loaded with 10 mg Mitomycin C were injected every 8 weeks for up to 18 months. Mitomycin C had to be administered before Irinotecan.

Investigational medicinal product name	Irinotecan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

For transarterial chemoembolization, 4 ml of 70-150 µm drug-eluting beads loaded with 200 mg Irinotecan were injected every 8 weeks for up to 18 months. Irinotecan had to be administered after Mitomycin C.

<b>Arm title</b>	Standard arm
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Arm description:

Patients received Doxorubicin monotherapy via TACE

Arm type	Active comparator
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Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Injection

Dosage and administration details:

For transarterial chemoembolization, 4 ml of 70-150 µm drug-eluting beads loaded with 150 mg Doxorubicin were injected every 8 weeks for up to 18 months.

Number of subjects in period 1 <sup>[1]</sup>	Experimental arm	Standard arm
Started	9	8
Completed	0	0
Not completed	9	8
Physician decision	3	3
Death	1	1
Minor residual finding/TACE not reasonable	-	1
Complete response	1	2
Decision for ablation in tumor board	1	-
Progressive disease	3	-
Patients wish	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 3 of the patients enrolled in the Standard Arm did not start treatment.

These patients were, according to the prespecified definition, excluded from all analysis population.

## Baseline characteristics

### Reporting groups

Reporting group title	Experimental arm
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Reporting group description:

Patients received Mitomycin C and Irinotecan via TACE

Reporting group title	Standard arm
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Reporting group description:

Patients received Doxorubicin monotherapy via TACE

Reporting group values	Experimental arm	Standard arm	Total
Number of subjects	9	8	17
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
median	66	73	
full range (min-max)	57 to 75	59 to 90	-
Gender categorical			
Units: Subjects			
Female	1	1	2
Male	8	7	15
ECOG Performance			
Units: Subjects			
Status 0	9	7	16
Status 1	0	1	1
Type of tumor			
Units: Subjects			
trabecular	7	6	13
pseudoglandular	1	0	1
solid	1	1	2
not determinable	0	1	1
T-stage			
Tumor stage and nodal stage assessed at first diagnosis			
Units: Subjects			
T1	2	2	4
T2	3	3	6
T3	1	1	2

T3a	3	2	5
N-stage			
Tumor stage and nodal stage assessed at first diagnosis			
Units: Subjects			
N0	8	7	15
Nx	1	1	2
Histopathological grade			
Units: Subjects			
G1	0	2	2
G2	9	6	15
Presentation of tumor in intermediate stage			
Units: Subjects			
Solitary large HCC	3	1	4
Multinodular HCC	4	5	9
Missing	2	2	4

## End points

### End points reporting groups

Reporting group title	Experimental arm
Reporting group description: Patients received Mitomycin C and Irinotecan via TACE	
Reporting group title	Standard arm
Reporting group description: Patients received Doxorubicin monotherapy via TACE	

### Primary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS) <sup>[1]</sup>
End point description: Patients in the intention-to-treat population without any documentation of events are censored at their date of end of study respectively at the last date known to be progression-free.	
End point type	Primary
End point timeframe: from randomization to the first documented evidence of disease progression or death	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Due to the premature recruitment stop of this trial and the resulting small number of patients and explorative nature of the trial, only descriptive statistics were performed.

End point values	Experimental arm	Standard arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: month				
median (confidence interval 90%)	9.2 (4.0 to 99.99)	21.1 (4.3 to 99.99)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Tumor response acc. to RECIST 1.1

End point title	Tumor response acc. to RECIST 1.1
End point description:	
End point type	Secondary
End point timeframe: from randomization to end of study	



End point values	Experimental arm	Standard arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: Subject				
Complete response (CR)	1	2		
Partial response (PR)	3	3		
Stable disease (SD)	3	1		
Progressive disease (PD)	1	0		
Missing	1	2		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Overall survival

End point title	Overall survival
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End point description:

Patients without any documentation of events are censored at their date of end of study respectively at the last date known to be alive. Median overall survival was not reached in the Standard arm.

End point type	Secondary
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End point timeframe:

from randomization to death from any cause

End point values	Experimental arm	Standard arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: month				
median (confidence interval 90%)	28.8 (4.8 to 99.99)	99.99 (99.99 to 99.99)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Tumor response rates

End point title	Tumor response rates
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End point description:

End point type	Secondary
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End point timeframe:

from randomization to end of study

<b>End point values</b>	Experimental arm	Standard arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: percent				
number (confidence interval 90%)				
Objective response rate (ORR)	44 (17 to 75)	63 (29 to 89)		
Disease control rate (DCR)	78 (45 to 96)	75 (40 to 95)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to progression (TTP)

End point title	Time to progression (TTP)
End point description:	
End point type	Secondary
End point timeframe: from randomization to end of study	

<b>End point values</b>	Experimental arm	Standard arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: month				
median (confidence interval 90%)				
Time to progression	9.2 (7.8 to 9999)	21.1 (8.9 to 9999)		

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

from signing of informed consent up to 30 days after last dose of study treatment

Assessment type	Systematic
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### Dictionary used

Dictionary name	CTCAE
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Dictionary version	5
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### Reporting groups

Reporting group title	Experimental arm
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Reporting group description:

Patients received Mitomycin C and Irinotecan via TACE

Reporting group title	Standard arm
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Reporting group description:

Patients received Doxorubicin monotherapy via TACE

Serious adverse events	Experimental arm	Standard arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 9 (33.33%)	2 / 8 (25.00%)	
number of deaths (all causes)	4	2	
number of deaths resulting from adverse events	1	0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Esophageal varices hemorrhage			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (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	1 / 9 (11.11%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Infections and infestations</b>			
Biliary tract infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	Experimental arm	Standard arm	
<b>Total subjects affected by non-serious adverse events</b>			
subjects affected / exposed	7 / 9 (77.78%)	5 / 8 (62.50%)	
<b>Investigations</b>			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Blood bilirubin increased			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Platelet count decreased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
<b>Blood and lymphatic system disorders</b>			
Anaemia			
subjects affected / exposed	2 / 9 (22.22%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Leukocytosis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
<b>General disorders and administration site conditions</b>			

Chills			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Oedema	Additional description: limbs		
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Fever			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 9 (33.33%)	1 / 8 (12.50%)	
occurrences (all)	4	1	
Ascites			
subjects affected / exposed	2 / 9 (22.22%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Constipation			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Duodenal ulcer			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Portal vein thrombosis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	
occurrences (all)	1	0	

Productive cough subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 8 (0.00%) 0	
Skin and subcutaneous tissue disorders			
Alopecia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 8 (0.00%) 0	
Pruritus subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 8 (0.00%) 0	
Worsening of psoriasis subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 8 (12.50%) 1	
Infections and infestations			
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 8 (0.00%) 0	
Infection subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 2	0 / 8 (0.00%) 0	
Metabolism and nutrition disorders			
Anorexia subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 8 (12.50%) 1	
Hyponatraemia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 8 (0.00%) 0	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 January 2021	<ul style="list-style-type: none"><li>- Change of inclusion criterion 2 from "Patients with histologically fissured HCC that cannot be treated by resection, ablation or liver transplantation (&gt; 3 tumors &gt;3 cm or 1 tumor &gt; 5 cm)" to "Patients with histologically confirmed HCC primarily not suitable for resection, ablation alone or liver transplantation. A combined therapy with TACE and subsequent ablation is possible"</li><li>- Minor adaptations of inclusion criteria 3 and 10</li><li>- Actualization of the treatment schedule</li></ul>

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported