Clinical trial results:
IMMULAB – A phase II trial of immunotherapy with pembrolizumab in combination with local ablation for patients with early stage hepatocellular carcinoma (HCC)

Summary

EudraCT number	2018-001381-42
Trial protocol	DE
Global end of trial date	30 April 2024

Results information

Result version number	v1 (current)
This version publication date	15 June 2025
First version publication date	15 June 2025

Trial information

Trial identification

Sponsor protocol code	IMMULAB

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	AIO STUDY NUMBER: AIO-HEP-0417/ass

Notes:

Sponsors

Sponsor organisation name	Frankfurter Institut für Klinische Krebsforschung IKF GmbH
Sponsor organisation address	Steinbacher Hohl 2-26, Frankfurt, Germany, 60488
Public contact	Frankfurter Institut für Klinische Krebsforschung IKF GmbH, Frankfurter Institut für Klinische Krebsforschung IKF GmbH, +49 69 5899 787 19, immulab@ikf-khnw.de
Scientific contact	Frankfurter Institut für Klinische Krebsforschung IKF GmbH, Frankfurter Institut für Klinische Krebsforschung IKF GmbH, +49 69 5899 787 19, immulab@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	28 February 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 April 2024
Global end of trial reached?	Yes
Global end of trial date	30 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was evaluate the objective response rate (ORR) according to RECIST 1.1 criteria after two cycles of treatment with pembrolizumab before conducting radiofrequency ablation (RFA), microwave ablation (MWA), or brachytherapy with or without combination of TACE to assess if this will allow conversion / downstaging of borderline candidates for local ablation.
Secondary objectives were the evaluation of time to recurrence (TTR), recurrence-free survival (RFS) and overall survival (OS), as well as safety and tolerability of peri-interventional treatment with pembrolizumab followed by RFA, MWA, or brachytherapy with or without combination of TACE .

Protection of trial subjects:

This clinical study was designed, 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 could withdraw their participation in the trial at any time without any declaration of reasons, which would 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 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	09 May 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	11
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

30 patients were planned to be recruited into this trial. The recruitment period was from Juli 2019 to November 2021 in 9 centers. 35 patients were screened, 30 were enrolled.

Pre-assignment

Screening details:

Eligible patients had histol. confirmed HCC diagnosis (Child Pugh A) with indication for local ablation via RFA, MWA, brachytherapy with/without TACE, incl. high-risk patients (defined as having ≤ 5 tumor nodules with diameters ≤ 7cm [longest axis] each OR vascular infiltration), and with tumor tissue available for central pathological examination

Period 1

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

Arms

Arm title	Experimental Arm

Arm description:

In this single arm study, all patients received pembrolizumab (200 mg, IV, Q3W on day 1 of cycle 1 and 2) followed by local ablation via RFA, MWA, brachytherapy with/without TACE performed on day 1 of cycle 3 followed by pembrolizumab (200 mg IV, administered 2 days after local ablation, then Q3W for up to 12 months total treatment duration)

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	Keytruda, L01FF02
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Infusion , Intravenous use

Dosage and administration details:

200 mg, IV, Q3W on day 1 of each cycle. Exception: at cycle 3, administered 2 days after local ablation

Number of subjects in period 1	Experimental Arm
Started	30
Completed	11
Not completed	19
Unrelated medical illness or complication	1
Physician decision	3
Consent withdrawn by subject	2
Disease progression	8
Death	2
Unacceptable toxicity	3

Baseline characteristics

Reporting groups

Reporting group title	Experimental Arm

Reporting group description:

In this single arm study, all patients received pembrolizumab (200 mg, IV, Q3W on day 1 of cycle 1 and 2) followed by local ablation via RFA, MWA, brachytherapy with/without TACE performed on day 1 of cycle 3 followed by pembrolizumab (200 mg IV, administered 2 days after local ablation, then Q3W for up to 12 months total treatment duration)

Reporting group values	Experimental Arm	Total	
Number of subjects	30	30	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	11	11	
From 65-84 years	19	19	
85 years and over	0	0	
Age continuous Units: years			
median	70		
full range (min-max)	40 to 80	-	
Gender categorical Units: Subjects			
Female	8	8	
Male	22	22	
ECOG Units: Subjects			
ECOG PS 0	27	27	
ECOG PS 1	3	3	
Child-Pugh classification score Units: Subjects			
Score 5	25	25	
Score 6	5	5	
Tumor histology Units: Subjects			
Trabecular	10	10	
Pseudoglandular	1	1	
Solid	10	10	
Other	7	7	
Unknown	2	2	
BCLC (Barcelona Clinic Liver Cancer) stage			

Units: Subjects			
Stage 0	2	2	
Stage A	15	15	
Stage B	11	11	
Stage C	2	2	
T stage Units: Subjects			
T1a/b	16	16	
T2	11	11	
T3/3a	3	3	
N stage Units: Subjects			
Nx	2	2	
N0	28	28	
M stage Units: Subjects			
M1	1	1	
M0	29	29	
Histopathological grade Units: Subjects			
Gx	7	7	
G1	3	3	
G2	15	15	
G3	5	5	
Has HCC advanced since initial diagnosis Units: Subjects			
Yes	15	15	
No	15	15	
Previous treatment for HCC Units: Subjects			
Yes	16	16	
No	14	14	
BMI Units: BMI			
median	28		
full range (min-max)	20 to 40	-	
ALBI score Units: ALBI score			
median	-2.8		
full range (min-max)	-3.8 to -1.6	-	
Number of target lesions Units: countable unit(s)			
median	1		
full range (min-max)	1 to 2	-	

End points

End points reporting groups

Reporting group title	Experimental Arm

Reporting group description:

In this single arm study, all patients received pembrolizumab (200 mg, IV, Q3W on day 1 of cycle 1 and 2) followed by local ablation via RFA, MWA, brachytherapy with/without TACE performed on day 1 of cycle 3 followed by pembrolizumab (200 mg IV, administered 2 days after local ablation, then Q3W for up to 12 months total treatment duration)

Primary: Objective response rate (ORR)

End point title	Objective response rate (ORR)[1]

End point description:

ORR, defined as achieving complete response (CR) or patial response (PR) according to RECIST 1.1 criteria (measured after two cycles of treatment, but before RFA, MWA, brachytherapy or combination of TACE with RFA, MWA or brachytherapy, compared to baseline)

End point type	Primary

End point timeframe:

from baseline to 6-8 weeks after first treatment

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 explorative nature of this trial and the small number of patients only descriptive statistics was performed.

End point values	Experimental Arm			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Subject				
Yes	4			
No	26			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to recurrence (TTR)

End point title	Time to recurrence (TTR)

End point description:

End point type	Secondary

End point timeframe:

from enrollment to end of study

End point values	Experimental Arm			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: months				
median (confidence interval 95%)	16.4 (8.31 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Recurrence-free survival (RFS)

End point title	Recurrence-free survival (RFS)

End point description:

End point type	Secondary

End point timeframe:

from enrollment to end of study

End point values	Experimental Arm			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: month				
median (confidence interval 95%)	12.4 (2.99 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

End point type	Secondary

End point timeframe:

from enrollment to end of study

End point values	Experimental Arm			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: month				
median (confidence interval 95%)	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: 2-year OS rate

End point title	2-year OS rate

End point description:

End point type	Secondary

End point timeframe:

from enrollment to end of study

End point values	Experimental Arm			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: %	76			

Statistical analyses

No statistical analyses for this end point

Secondary: 3-year OS rate

End point title	3-year OS rate

End point description:

End point type	Secondary

End point timeframe:

from enrollment to end of study

End point values	Experimental Arm			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: %	66			

Statistical analyses

No statistical analyses for this end point

Secondary: 4-year OS rate

End point title	4-year OS rate

End point description:

End point type	Secondary

End point timeframe:

from enrollment to end of study

End point values	Experimental Arm			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: %	56			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Patients were closely monitored for adverse events (AEs) from date of inclusion until at least 30 days after last dose of study treatment for AEs, and for at least 110 days for serious AEs, events of clinical interest, and pembrolizumab-associated AEs

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	Experimental Arm

Reporting group description: -

Serious adverse events	Experimental Arm		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 30 (46.67%)		
number of deaths (all causes)	11		
number of deaths resulting from adverse events	4		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Other, specify	Additional description: following MWA unchanged vital HCC lesion S 5		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Thromboembolic event			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Other, specify	Additional description: Sedation during ERCP		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
General disorders and administration site conditions			
Other, specify	Additional description: Worsening of general condition		

subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood bilirubin increased			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Encephalopathy			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	2 / 30 (6.67%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Colonic obstruction				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colonic perforation				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Esophageal hemorrhage				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric hemorrhage				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Other, specify	Additional description: Varices ligature			
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Hepatic failure				
subjects affected / exposed	2 / 30 (6.67%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	1 / 1			
Portal vein thrombosis				

subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Chronic kidney disease			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal colic			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abdominal infection			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Enterocolitis infectious			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Experimental Arm		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 30 (93.33%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Thromboembolic event			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
General disorders and administration site conditions			
Edema limbs			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Fatigue			
subjects affected / exposed	8 / 30 (26.67%)		
occurrences (all)	8		
Flu like symptoms			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Localized edema			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Pain			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Dyspnea			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	6 / 30 (20.00%)		
occurrences (all)	6		
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 30 (23.33%)		
occurrences (all)	7		
Blood bilirubin increased			
subjects affected / exposed	6 / 30 (20.00%)		
occurrences (all)	8		
Platelet count decreased			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Nervous system disorders			
Encephalopathy			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	4		
Headache			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	3		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	7 / 30 (23.33%)		
occurrences (all)	7		
Ascites			

subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 4		
Colitis subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2		
Diarrhea subjects affected / exposed occurrences (all)	4 / 30 (13.33%) 5		
Dry mouth subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 3		
Gastritis subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2		
Gastroesophageal reflux disease subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2		
Mucositis oral subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2		
Hepatobiliary disorders Hepatic failure subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 3		
Portal vein thrombosis subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	8 / 30 (26.67%) 8		
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 4		
Endocrine disorders			

Hyperthyroidism subjects affected / exposed occurrences (all) Hypothyroidism subjects affected / exposed occurrences (all)	 6 / 30 (20.00%) 6 3 / 30 (10.00%) 3		
Musculoskeletal and connective tissue disorders Arthritis subjects affected / exposed occurrences (all)	 2 / 30 (6.67%) 2		
Infections and infestations Bronchial infection subjects affected / exposed occurrences (all)	 2 / 30 (6.67%) 2		
Metabolism and nutrition disorders Anorexia subjects affected / exposed occurrences (all) Hyperglycemia subjects affected / exposed occurrences (all) Hyponatremia subjects affected / exposed occurrences (all)	 2 / 30 (6.67%) 2 3 / 30 (10.00%) 3 2 / 30 (6.67%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 May 2019	Main changes of the study protocol: • "Patients with child-pugh classification score ≤ 6, including high risk candidates for local ablation (defined as patient is having ≤ 5 tumor nodules with diameters ≤ 5cm [longest axis] each OR patient with vascular infiltration) will be included in the study" • Inclusion criterion #4: "High risk patient, i.e. presence of ≤ 5 tumor nodules with diameters ≤ 5cm [longest axis] each OR vascular infiltration" – IEC: 03 Jul 2019, PEI: 13 Jun 2019
12 February 2020	Main change: Expansion of local ablation options to include brachytherapy as well as the possibility of combining local ablation with TACE

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported