Clinical trial results:
An Open-label Study Evaluating the Safety, Antiviral Activity, and Pharmacokinetics of IMC-I109V in HLA-A*02:01 Positive Patients with Chronic HBV who are Non-Cirrhotic, Hepatitis B e Antigen-negative, and Virally Suppressed

Summary

EudraCT number	2019-004212-64
Trial protocol	BE GB ES PL RO DK
Global end of trial date	23 December 2024

Results information

Result version number	v1 (current)
This version publication date	08 January 2026
First version publication date	08 January 2026

Trial information

Trial identification

Sponsor protocol code	IMC-I109V-101

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Immunocore, Ltd
Sponsor organisation address	92 Park Drive, Milton Park, Abingdon, Oxon, United Kingdom, OX14 4RY
Public contact	Information Desk, Immunocore Ltd, +44(0) 1235438600, info@immunocore.com
Scientific contact	Regulatory Affairs, Immunocore Ltd, +44(0) 1235438600, Regaffairsgroup@immunocore.com

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 March 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 December 2024
Global end of trial reached?	Yes
Global end of trial date	23 December 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Primary (Part 1 – Single Ascending Dose [SAD])
To evaluate the safety and tolerability of IMC-I109V when administered as a single dose in virally suppressed, Hepatitis B e-antigen (HBeAg)-negative participants
Primary (Part 2 – Multiple Ascending Dose [MAD])
To evaluate the safety and tolerability of IMC-I109V when administered in a multiple dose schedule up to Week 24 in virally suppressed, HBeAg-negative participants
Primary (Part 3 - MAD hepatocellular carcinoma [HCC])
To evaluate the safety and tolerability of IMC-I109V when administered in multiple dose schedule(s) in virally suppressed participants with Hepatitis B virus [HBV]-associated HCC.

Participants were HLA-A*02:01-positive adult male and female participants with chronic HBV (CHB) infection who were virally suppressed and were either non-cirrhotic, HBeAg-negative (Part 1 and Part 2 [not conducted]) or had HBV-associated HCC (Part 3).

Protection of trial subjects:

This trial was conducted in accordance with the ethical principles of Good Clinical Practice, according to the International Conference on Harmonization (ICH) Harmonized Tripartite Guideline, in accordance with local legal and regulatory requirements, and in compliance with the Declaration of Helsinki (with amendments).

Background therapy:

Nucleos(t)ide analogue therapy

Evidence for comparator:

Not applicable

Actual start date of recruitment	01 October 2020
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	Romania: 4
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	Hong Kong: 2
Worldwide total number of subjects	20
EEA total number of subjects	8

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)	19
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Seventeen sites in 8 countries screened participants in Part 1 - SAD. Part 2 - was planned but not conducted for strategic reasons. Part 3 - MAD HCC was initiated and 1 participant was screened but not enrolled due to screen failure.

Pre-assignment

Screening details:

Part 1:
Participants screened: 41
Screen failures: 21
  Failure to meet enrollment criteria: 19
  Physician decision: 1
  Other: 1
Treated: 20

Part 3:
Participants screened: 1
Screen failures: 1
Enrolled: 0

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: IMC-I109V 0.8 mcg

Arm description:

Participants received 1 dose of single-agent IMC-I109V 0.8 mcg on Visit Day 1.

Arm type	Experimental
Investigational medicinal product name	IMC I109V
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dose: from 0.8 mcg to 20 mcg
Strength: 0.20 mg/mL
Frequency: Single dose

Arm title	Part 1: IMC-I109V 2.4 mcg

Arm description:

Participants received 1 dose of single-agent IMC-I109V 2.4 mcg on Visit Day 1.

Arm type	Experimental
Investigational medicinal product name	IMC I109V
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dose: from 0.8 mcg to 20 mcg
Strength: 0.20 mg/mL
Frequency: Single dose

Arm title	Part 1: IMC-I109V 7.0 mcg

Arm description:

Participants received 1 dose of single-agent IMC-I109V 7.0 mcg on Visit Day 1.

Arm type	Experimental
Investigational medicinal product name	IMC I109V
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dose: from 0.8 mcg to 20 mcg
Strength: 0.20 mg/mL
Frequency: Single dose

Arm title	Part 1: IMC-I109V 20.0 mcg

Arm description:

Participants received 1 dose of single-agent IMC-I109V 20.0 mcg on Visit Day 1.

Arm type	Experimental
Investigational medicinal product name	IMC I109V
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dose: from 0.8 mcg to 20 mcg
Strength: 0.20 mg/mL
Frequency: Single dose

Number of subjects in period 1	Part 1: IMC-I109V 0.8 mcg	Part 1: IMC-I109V 2.4 mcg	Part 1: IMC-I109V 7.0 mcg
Started	4	2	6
Completed	4	2	6

Number of subjects in period 1	Part 1: IMC-I109V 20.0 mcg
Started	8
Completed	8

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	20	20	
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)	19	19	
From 65-84 years	1	1	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	47.7		
standard deviation	± 9.73	-	
Gender categorical Units: Subjects			
Female	3	3	
Male	17	17	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	9	9	
Black or African American	2	2	
Native Hawaiian or other Pacific Islander	0	0	
White	8	8	
Not Reported	0	0	
Unknown	0	0	
Other	1	1	
Not Recorded	0	0	
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	20	20	
Not Reported	0	0	
Unknown	0	0	
Other	0	0	
Duration Since HBV Diagnosis Units: Subjects			

<5 years	2	2	
>=5 to <10 years	3	3	
>=10 years	15	15	
HBV Genotype Units: Subjects			
B/C/D	0	0	
Other Genotype	2	2	
Missing	18	18	
Baseline Fibroscan Units: Subjects			
< 7 kPa	18	18	
>= 7 to < 9 kPa	2	2	
Baseline HBsAg Units: IU/mL			
arithmetic mean	1149.3		
standard deviation	± 1181.1	-	
Height Units: cm			
arithmetic mean	174.60		
standard deviation	± 8.17	-	
Baseline Weight Units: kg			
arithmetic mean	77.98		
standard deviation	± 12.04	-	

End points

End points reporting groups

Reporting group title	Part 1: IMC-I109V 0.8 mcg
Reporting group description:	
Participants received 1 dose of single-agent IMC-I109V 0.8 mcg on Visit Day 1.	

Reporting group title	Part 1: IMC-I109V 2.4 mcg
Reporting group description:	
Participants received 1 dose of single-agent IMC-I109V 2.4 mcg on Visit Day 1.	
Reporting group title	Part 1: IMC-I109V 7.0 mcg
Reporting group description:	
Participants received 1 dose of single-agent IMC-I109V 7.0 mcg on Visit Day 1.	
Reporting group title	Part 1: IMC-I109V 20.0 mcg
Reporting group description:	
Participants received 1 dose of single-agent IMC-I109V 20.0 mcg on Visit Day 1.	

Primary: Incidence of dose-limiting toxicities

End point title	Incidence of dose-limiting toxicities[1]
End point description:	
A dose-limiting toxicity (DLT) is defined as an AE that is assessed as having a suspected relationship to IMC-I109V, occurs within the defined observation period up to and including Day 8, is unrelated to the underlying disease, intercurrent illness, or concomitant medication, and meets prespecified DLT criteria.	
End point type	Primary
End point timeframe:	
Up to and Including Day 8	

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: There are no statistical analyses for descriptive data.

End point values	Part 1: IMC-I109V 0.8 mcg	Part 1: IMC-I109V 2.4 mcg	Part 1: IMC-I109V 7.0 mcg	Part 1: IMC-I109V 20.0 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	2	6	8
Units: Participants				
Dose-limiting toxicity	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Incidence and severity of treatment-emergent adverse events (TEAEs)

End point title	Incidence and severity of treatment-emergent adverse events (TEAEs)[2]
End point description:	
A treatment-emergent adverse event (TEAE) is defined as an adverse event (AE) that had an onset	

date, or a worsening in severity from baseline (pre-treatment), on or after the first dose of study drug and up to the 28 days after the last dose of IMC-I109V. Grading of cytokine release syndrome (CRS) is based on the American Society for Transplantation and Cellular Therapy (ASTCT) 2019 consensus grading system. AE severity is graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 5.0.

End point type	Primary

End point timeframe:

On or after the first dose of study drug and up to the 28 days after the last dose of study IMC-I109V

Notes:

[2] - 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: There are no statistical analyses for descriptive data.

End point values	Part 1: IMC-I109V 0.8 mcg	Part 1: IMC-I109V 2.4 mcg	Part 1: IMC-I109V 7.0 mcg	Part 1: IMC-I109V 20.0 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	2	6	8
Units: Participants				
Any treatment-emergent adverse event (TEAE)	1	0	2	4
Any TEAE Grade ≥3	0	0	1	1
Any serious adverse event (SAE)	0	0	0	1
Any TEAE leading to death	0	0	0	0
Any AE leading to treatment discontinuation	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Changes in safety parameters

End point title	Changes in safety parameters[3]

End point description:

Clinically significant abnormal laboratory findings are those which are not associated with the underlying disease, unless judged by the Investigator to be more severe than expected for the participant's condition. Other safety variables and evaluations include vital signs and electrocardiogram findings.

End point type	Primary

End point timeframe:

On or after the first dose of study drug and up to the 28 days after the last dose of study IMC-I109

Notes:

[3] - 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: There are no statistical analyses for descriptive data.

End point values	Part 1: IMC-I109V 0.8 mcg	Part 1: IMC-I109V 2.4 mcg	Part 1: IMC-I109V 7.0 mcg	Part 1: IMC-I109V 20.0 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	2	6	8
Units: Participants				
Clinically significant safety laboratory changes	0	0	2	3
Clinically significant vital sign changes	0	0	0	1

Clinically significant electrocardiogram changes	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of anti-IMCI109V antibody formation

End point title	Incidence of anti-IMCI109V antibody formation

End point description:

Overall anti-drug antibody (ADA) incidence equaled subjects with a treatment-induced or treatment-boosted ADA response or with positive post-baseline ADA result but no baseline ADA sample divided by the number of evaluable subjects. Evaluable subjects were subjects with ADA results after first dose.

End point type	Secondary

End point timeframe:

Following administration of 1 dose of study drug, with sample collections occurring pre-dose and 4 weeks post dose

End point values	Part 1: IMC-I109V 0.8 mcg	Part 1: IMC-I109V 2.4 mcg	Part 1: IMC-I109V 7.0 mcg	Part 1: IMC-I109V 20.0 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	2[4]	6	8[5]
Units: Participants	0	0	1	0

Notes:

[4] - 1 participant had a positive ADA result at baseline, that did not increase on trial.

[5] - 3 participants had a positive ADA result at baseline, that did not increase on trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Hepatitis B surface antigen (HBsAg) change from baseline

End point title	Hepatitis B surface antigen (HBsAg) change from baseline

End point description:

End point type	Secondary

End point timeframe:

From Baseline through end of trial

End point values	Part 1: IMC-I109V 0.8 mcg	Part 1: IMC-I109V 2.4 mcg	Part 1: IMC-I109V 7.0 mcg	Part 1: IMC-I109V 20.0 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	2	6	8
Units: IU/mL				
log mean (standard deviation)				
Week 1 Day 3 - Log Change from Baseline	-0.028 (± 0.0333)	-0.034 (± 0.0367)	-0.074 (± 0.1406)	-0.209 (± 0.3436)
Week 2 Day 1 - Log Change from Baseline	-0.000 (± 0.0487)	-0.043 (± 0.0005)	-0.051 (± 0.1589)	-0.121 (± 0.2633)
Week 3 Day 1 - Log Change from Baseline	0.001 (± 0.0399)	-0.068 (± 0.0529)	-0.051 (± 0.1298)	-0.102 (± 0.2435)
Week 4 Day 1 - Log Change from Baseline	0.024 (± 0.0484)	-0.073 (± 0.0765)	0.005 (± 0.1458)	-0.106 (± 0.2419)
Week 5 Day 1 - Log Change from Baseline	0.013 (± 0.0314)	-0.054 (± 0.0578)	-0.056 (± 0.1232)	-0.109 (± 0.2068)

Statistical analyses

No statistical analyses for this end point

Secondary: Hepatitis B core-related antigen (HBcrAg) change from baseline

End point title	Hepatitis B core-related antigen (HBcrAg) change from baseline

End point description:

End point type	Secondary

End point timeframe:

From Baseline through end of trial

End point values	Part 1: IMC-I109V 0.8 mcg	Part 1: IMC-I109V 2.4 mcg	Part 1: IMC-I109V 7.0 mcg	Part 1: IMC-I109V 20.0 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	2	3	4
Units: IU/mL				
log mean (standard deviation)				
Week 1 Day 3 - Log Change from Baseline	-0.008 (± 0.0073)	-0.005 (± 0.0074)	-0.003 (± 0.0139)	-0.018 (± 0.0154)
Week 2 Day 1 - Log Change from Baseline	-0.013 (± 0.0010)	-0.004 (± 0.0247)	-0.005 (± 0.0203)	-0.014 (± 0.0210)
Week 3 Day 1 - Log Change from Baseline	-0.004 (± 0.0073)	-0.005 (± 0.0074)	0.004 (± 0.0194)	-0.017 (± 0.0155)
Week 4 Day 1 - Log Change from Baseline	-0.004 (± 0.0073)	-0.018 (± 0.0049)	0.007 (± 0.0065)	-0.006 (± 0.0215)
Week 5 Day 1 - Log Change from Baseline	-0.008 (± 0.0073)	-0.012 (± 0.0027)	0.004 (± 0.0194)	-0.006 (± 0.0215)

Statistical analyses

No statistical analyses for this end point

Secondary: HBV RNA change from baseline

End point title	HBV RNA change from baseline

End point description:

End point type	Secondary

End point timeframe:

From Baseline through end of trial

End point values	Part 1: IMC-I109V 0.8 mcg	Part 1: IMC-I109V 2.4 mcg	Part 1: IMC-I109V 7.0 mcg	Part 1: IMC-I109V 20.0 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[6]	1[7]	2[8]	0[9]
Units: IU/mL				
log mean (standard deviation)				
Week 1 Day 3 - Log Change from Baseline	()	-0.013 (± 0)	0.007 (± 0.0275)	()
Week 2 Day 1 - Log Change from Baseline	()	0.000 (± 0)	0.006 (± 0.0307)	()
Week 3 Day 1 - Log Change from Baseline	()	0.008 (± 0)	0.011 (± 0.0095)	()
Week 4 Day 1 - Log Change from Baseline (n=1, n=1)	()	0.018 (± 0)	0.000 (± 0)	()
Week 5 Day 1 - Log Change from Baseline (n=1, n=0)	()	-0.035 (± 0)	0 (± 0)	()

Notes:

[6] - All values for participants in this arm were below the limit of detection.

[7] - Note: "0" was used when a value was not available or when standard deviation was not calculable.

[8] - Note: "0" was used when a value was not available or when standard deviation was not calculable.

[9] - All values for participants in this arm were below the limit of detection.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum plasma concentration (Cmax) for IMC-I109V

End point title	Maximum plasma concentration (Cmax) for IMC-I109V

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, end of infusion (EOI), 2 hours post-EOI, 4 hours post-EOI, 8 hours post-EOI, 12 hours post-EOI, 24 hours post-EOI, 48 hours post-EOI, and 72 hours post-EOI

End point values	Part 1: IMC-I109V 0.8 mcg	Part 1: IMC-I109V 2.4 mcg	Part 1: IMC-I109V 7.0 mcg	Part 1: IMC-I109V 20.0 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	2	6	8
Units: pg/mL				
arithmetic mean (full range (min-max))	133 (102 to 136)	694 (610 to 778)	1400 (1060 to 1930)	3380 (2020 to 5060)

Statistical analyses

No statistical analyses for this end point

Secondary: Half-life (t1/2) for IMC-I109V

End point title	Half-life (t1/2) for IMC-I109V

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, end of infusion (EOI), 2 hours post-EOI, 4 hours post-EOI, 8 hours post-EOI, 12 hours post-EOI, 24 hours post-EOI, 48 hours post-EOI, and 72 hours post-EOI

End point values	Part 1: IMC-I109V 0.8 mcg	Part 1: IMC-I109V 2.4 mcg	Part 1: IMC-I109V 7.0 mcg	Part 1: IMC-I109V 20.0 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[10]	2	6	8
Units: Hours				
arithmetic mean (full range (min-max))	(to)	9.40 (9.28 to 9.52)	11.0 (9.43 to 13.2)	14.0 (9.21 to 20.7)

Notes:

[10] - Due to insufficient data in the elimination phase after dosing, t1/2 could not be estimated.

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the concentration curve from time zero to the last measurable concentration sampling time (AUClast) for IMC-I109V

End point title	Area under the concentration curve from time zero to the last measurable concentration sampling time (AUClast) for IMC-I109V

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, end of infusion (EOI), 2 hours post-EOI, 4 hours post-EOI, 8 hours post-EOI, 12 hours post-EOI, 24 hours post-EOI, 48 hours post-EOI, and 72 hours post-EOI

End point values	Part 1: IMC-I109V 0.8 mcg	Part 1: IMC-I109V 2.4 mcg	Part 1: IMC-I109V 7.0 mcg	Part 1: IMC-I109V 20.0 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	2	6	8
Units: h*pg/mL				
arithmetic mean (full range (min-max))	455 (115 to 720)	7100 (6280 to 7910)	15500 (12700 to 23900)	40500 (29900 to 55900)

Statistical analyses

No statistical analyses for this end point

Secondary: Total body clearance of drug from the plasma (CL) for IMC-I109V

End point title	Total body clearance of drug from the plasma (CL) for IMC-I109V

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, end of infusion (EOI), 2 hours post-EOI, 4 hours post-EOI, 8 hours post-EOI, 12 hours post-EOI, 24 hours post-EOI, 48 hours post-EOI, and 72 hours post-EOI

End point values	Part 1: IMC-I109V 0.8 mcg	Part 1: IMC-I109V 2.4 mcg	Part 1: IMC-I109V 7.0 mcg	Part 1: IMC-I109V 20.0 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[11]	2	6	8
Units: L/h				
arithmetic mean (full range (min-max))	(to)	0.280 (0.246 to 0.314)	0.362 (0.237 to 0.452)	0.437 (0.293 to 0.578)

Notes:

[11] - Due to insufficient data in the elimination phase after dosing, CL could not be estimated.

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the concentration curve from time zero to infinity (AUCinf) for IMC-I109V

End point title	Area under the concentration curve from time zero to infinity (AUCinf) for IMC-I109V

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, end of infusion (EOI), 2 hours post-EOI, 4 hours post-EOI, 8 hours post-EOI, 12 hours post-EOI, 24 hours post-EOI, 48 hours post-EOI, and 72 hours post-EOI

End point values	Part 1: IMC-I109V 0.8 mcg	Part 1: IMC-I109V 2.4 mcg	Part 1: IMC-I109V 7.0 mcg	Part 1: IMC-I109V 20.0 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[12]	2	6	8
Units: h*pg/mL				
arithmetic mean (full range (min-max))	(to)	8700 (7630 to 9770)	20200 (15500 to 29500)	47900 (34600 to 68200)

Notes:

[12] - Due to insufficient data in the elimination phase after dosing, AUCinf could not be estimated.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
On or after the first dose of study drug and up to the 28 days after the last dose of study IMC-I109	
Adverse event reporting additional description:	
The safety analysis set consists of all participants who receive at least one dose of investigational product, IMC-I109V.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups	
Reporting group title	Part 1: IMC-I109V 0.8 mcg
Reporting group description:	
Participants received 1 dose of single-agent IMC-I109V 0.8 mcg on Visit Day 1	
Reporting group title	Part 1: IMC-I109V 2.4 mcg
Reporting group description:	
Participants received 1 dose of single-agent IMC-I109V 2.4 mcg on Visit Day 1.	
Reporting group title	Part 1: IMC-I109V 7.0 mcg
Reporting group description:	
Participants received 1 dose of single-agent IMC-I109V 7.0 mcg on Visit Day 1.	
Reporting group title	Part 1: IMC-I109V 20.0 mcg
Reporting group description:	
Participants received 1 dose of single-agent IMC-I109V 20.0 mcg on Visit Day 1.	

Serious adverse events	Part 1: IMC-I109V 0.8 mcg	Part 1: IMC-I109V 2.4 mcg	Part 1: IMC-I109V 7.0 mcg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Shock			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 1: IMC-I109V 20.0 mcg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Vascular disorders			
Shock			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part 1: IMC-I109V 0.8 mcg	Part 1: IMC-I109V 2.4 mcg	Part 1: IMC-I109V 7.0 mcg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	2 / 6 (33.33%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Amylase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Ventricular extrasystoles			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Injection site reaction			

subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash pruritic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Oliguria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 1: IMC-I109V 20.0 mcg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 8 (50.00%)		

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Amylase increased			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Lymphocyte count decreased			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	2		
Cardiac disorders			
Ventricular extrasystoles			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Injection site reaction			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			

subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Respiratory, thoracic and mediastinal disorders Hypoxia subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1		
Skin and subcutaneous tissue disorders Rash pruritic subjects affected / exposed occurrences (all)	 0 / 8 (0.00%) 0		
Renal and urinary disorders Oliguria subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1		
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	 2 / 8 (25.00%) 2		
Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 May 2020	Version 2.0 includes revisions in response to Medicines and Healthcare products Regulatory Agency (MHRA) and Investigator feedback, as well as administrative changes. Main changes to Version 2.0: - Indicated that the proposed 28-day follow-up period for Part 1 – SAD will serve to fully characterize the HBV biomarker kinetics and to confirm that all laboratory abnormalities have resolved - Indicated that the proposed 24-week follow up period for Part 2 – MAD will serve to evaluate criteria for HBV functional cure, fully characterize the HBV biomarker kinetics, assess durability of response, and continue to monitor safety signals - Added a new section for infusion duration justification and clarified that based on the anticipated pharmacokinetic (PK) profile of IMC-I109V, there is no significant impact on Cmax for a variety of infusion durations within the range permitted by dosing formulation stability. - Revised duration of contraception (from 6 to 3 months) and prohibited egg donation - Provided guidance regarding the use of live and non-live vaccines before and after administration of IMC-I109V administration - Specified the all participants receiving the lead-in doses and the first target dose of IMC-I109V in Part 2 – MAD should be observed for 24 hours from the end of infusion. - Clarified that 2 additional cohorts may be enrolled in Part 1 at higher (rather than intermediate) doses after Cohort 5: 120 mcg (2-fold from 60 mcg) and 180 mcg (0.5-fold from 120 mcg). - Clarified that study participants in Part 1 – SAD may be considered for inclusion in Part 2 – MAD (number of participants from Part 1 participating in any given Part 2 cohort would be limited to 30%) and expansion cohort in Part 2 if they meet all of the retreatment criteria
03 March 2021	Version 3.0 includes revisions in response to changes requested by MHRA Health Authorities and administrative changes. Main changes in Version 3.0: - Added ibuprofen as a possible non-steroidal anti-inflammatory agent for premedication - Added HBeAg assessment at screening - Updated the schedule of activities to ensure that vital signs are collected during the 2-hour infusion in the Part 1 - SAD and the first 3 doses in Part 2 - MAD - Provided clarification on the justification of the proposed maximum dose of 180 mcg for Part 1 - SAD - Changed the maximum age for inclusion from 55 to 65 years - Allowed patients with HCC Stage 0 to participate in the study - Clarified that participants must receive entecavir and/or tenofovir (including tenofovir alafenamide) as indicated by the Principal Investigator during their participation in the study - Added additional non-mandatory premedication - Clarified the rules during dose escalation in Part 1 - SAD and lead-in doses in Part 2 - MAD - Added reasons for early study termination

09 May 2022	Version 4.0 includes revisions to reduce participant burden and address slow accrual of study participants. Main changes in Version 4.0: - Removed the Week 1 Day 5 visit - Corrected the number and timing of vital signs and samples to be taken for PK, peripheral blood mononuclear cells (PBMC), whole blood messenger RNA (mRNA) and plasma - Amended SAD cohort size to 2-4 participants - Amended Inclusion/Exclusion Criteria regarding quantitative HBsAg (qHBsAg) and thresholds for alanine aminotransferase (ALT) and platelet counts - Amended clinically active dose definition with respect to ALT change post-dosing and futility criteria for consistency with change to clinically active dose definition - Updated ALT criteria for dose modification
03 April 2023	Version 5.0 includes Part 3 - MAD in participants with HBV-associated HCC who are virally suppressed. In addition to the inclusion of Part 3, revisions to Version 5.0: - Added HBV Genotyping to enable determination of benefit / risk for any patient identified as having genotypes other than B, C, D or E - Changed pregnancy test changed from serum to urine - Added severe acute respiratory coronavirus 2 (SAR-COV-2) antigen testing pre-dose - Changed PK sample 48 hours post EOI to optional sample on Day 3 - Removed serum sample collection 4 hours post EOI - Updated summary data of patients dosed with Immune-mobilizing monoclonal T-cell receptor against virus (ImmTAC) molecules - Added option for additional cohorts evaluating dosing less frequently than every week - Clarified contraindications to intra-patient dose escalation - Allowed people with treated HIV to be considered for enrollment - Allowed people in observational studies to be permitted with approval of the Medical Monitor - Updated criteria for steroid premedication; changed preferred corticosteroid from intravenous (IV) methylprednisolone to oral prednisolone and reduction in recommended dose of corticosteroid - Provided for overnight monitoring to be discontinued for any dose that has been deemed to be safe and tolerable in ≥ 10 patients - Reduced infusion time to 1 hour - Changed preferred corticosteroid for premedication from dexamethasone to prednisolone and use of mandatory corticosteroid premedication for any participants not receiving extended monitoring - Modified definition of Grade 3 events that will be considered a DLT - Removed cap on proportion of participants in Part 2 who have also participated in Part 1 - Added provision for unscheduled visits to collect additional blood samples if needed

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
23 December 2024	Following portfolio review, the study was terminated early (prior to treating subjects in Part 2) by the Sponsor as a strategic decision (not based on any safety signal).	-

Notes:

Limitations and caveats

None reported