



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 occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 2 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Malaise subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Pain subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Hypoxia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Rash pruritic subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Renal and urinary disorders Oliguria subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 6 (0.00%) 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 occurrences (all) | 2 / 8 (25.00%) 2 | | |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Amylase increased subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | | |
| Lymphocyte count decreased subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 2 | | |
| Cardiac disorders | | | |
| Ventricular extrasystoles subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| General disorders and administration site conditions | | | |
| Chills subjects affected / exposed occurrences (all) | 2 / 8 (25.00%) 2 | | |
| Pyrexia subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Injection site reaction subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | | |
| Malaise subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Pain subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 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 | <p>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:</p> <ul style="list-style-type: none">- 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 C_{max} 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 | <p>Version 3.0 includes revisions in response to changes requested by MHRA Health Authorities and administrative changes. Main changes in Version 3.0:</p> <ul style="list-style-type: none">- 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 | <p>Version 4.0 includes revisions to reduce participant burden and address slow accrual of study participants. Main changes in Version 4.0:</p> <ul style="list-style-type: none"> - 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 | <p>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:</p> <ul style="list-style-type: none"> - 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