



Clinical trial results:

A Randomized, Double-Blind, Double-Dummy Phase II Study of Single Dose HDIT101 versus Standard of Care Valaciclovir in Patients with Chronic Recurrent Anogenital HSV-2 Infection

Summary

EudraCT number	2019-000880-26
Trial protocol	DE
Global end of trial date	25 August 2021

Results information

Result version number	v1 (current)
This version publication date	10 September 2022
First version publication date	10 September 2022

Trial information

Trial identification

Sponsor protocol code	HTX101-02G
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04165122
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Heidelberg ImmunoTherapeutics GmbH
Sponsor organisation address	Max-Jarecki-Str. 21, Heidelberg, Germany,
Public contact	Stefan Schöffel, Heidelberg ImmunoTherapeutics GmbH, +49 6221391938, stefan.schoeffel@hditx.de
Scientific contact	Prof. Dr. Jürgen Krauss, Heidelberg ImmunoTherapeutics GmbH, +49 622139190, juergen.krauss@hditx.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	22 March 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	25 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of single dose of HDIT101 versus episodic standard of care treatment with Valaciclovir in patients with chronic recurrent anogenital HSV-2 infection as measured by the percentage of days with lesion(s) during the study (calculated as number of days with lesion, except the lesion episode at randomization, divided by the number of days in the study after IMP infusion).

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki, Good Clinical Practice (GCP) guidelines and local law requirements. Patients were allowed to be treated symptomatically with 1 gram paracetamol taken orally for flu-like symptoms that might occur due to the mode of action of HDIT101

Background therapy:

There were restrictions on the use of concomitant medications/therapies during the trial. The following medications/therapies were not permitted: immunosuppressive or immunomodulatory therapy (topical, oral, parenteral and/or inhaling steroids), hepatotoxic drugs, any herpes simplex virus therapy different than the investigational medicinal product, nephrotoxic medicinal products, and medicinal products that compete with or inhibit active tubular secretion due to their potential influence on the outcome measures of the study.

Evidence for comparator:

Valaciclovir 500 mg tablets twice daily for 3 days was used as standard of care therapy of HSV-2 lesions occurrence during the trial. Treatment with Valaciclovir is one of the available options for treatment of HSV-2 mediated anogenital infections that has shown efficacy in reducing clinical symptoms in patients with chronic recurrent anogenital HSV-2 infection. Valaciclovir-placebo was used in patients receiving the test drug (HDIT101 group) to ensure treatment blinding and reduce potential bias during data collection.

Actual start date of recruitment	18 November 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: 122
Worldwide total number of subjects	122
EEA total number of subjects	122

Notes:

Subjects enrolled per age group

In utero	0
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Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	111
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

261 patients (≥ 18 years of age) were screened for eligibility in 8 trial sites in Germany. Of these, 122 patients were randomized: 81 to HDIT101 and Valaciclovir-placebo; 41 to Valaciclovir and HDIT101-placebo. The remaining 139 patients were screening failures.

Pre-assignment

Screening details:

261 patients with history of chronic recurrent anogenital HSV-2 infection ≥ 4 outbreaks in the last year (≥ 2 lesions under standard suppressive antiviral therapy), and no active lesion at enrolment were screened. Screening failures (139) including patients who did not develop lesion within 4 months after enrolment were withdrawn.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

Study treatments were blinded and the allocation to treatment groups was not known to the investigator or other persons involved in the conduct of the study until completion of the study, except the site pharmacies personnel and in cases of emergency. To ensure that the double-blind design of the study was maintained, HDIT101 and Valaciclovir were identical in appearance with the respective placebos matching the intravenous (IV) infusion and oral treatments.

Arms

Are arms mutually exclusive?	Yes
Arm title	HDIT101

Arm description:

Patients receiving single intravenous infusion of HDIT101 on Day 1 and episodic standard of care treatment with Valaciclovir-placebo starting at Day 1 and in case of recurrences during the trial.

Arm type	Experimental
Investigational medicinal product name	HDIT101
Investigational medicinal product code	HDIT101
Other name	Humanized IgG1 monoclonal antibody
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Day 1: Single intravenous infusion of HDIT101 2 grams flat over 1 hour and Valaciclovir-placebo (1 capsule twice daily for 3 days). Starting at Day 1 and until end of study: episodic treatment with Valaciclovir-placebo, 1 capsule twice daily for 3 days, in case of new recurrences during the trial.

Arm title	Valaciclovir
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Arm description:

Patients receiving single IV infusion of HDIT101-placebo on Day 1 and episodic standard of care treatment with Valaciclovir starting at Day1 and in case of recurrences during the trial.

Arm type	Active comparator
Investigational medicinal product name	Valaciclovir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Day 1: Single intravenous infusion of HDI101-placebo flat over 1 hour and Valaciclovir 500 mg (1 capsule twice daily for 3 days). Starting at Day 1 and until end of study: episodic treatment with Valaciclovir 500 mg, 1 capsule twice daily for 3 days, in case of new recurrences during the trial.

Number of subjects in period 1	HDIT101	Valaciclovir
Started	81	41
Completed	61	35
Not completed	20	6
Physician decision	4	-
Consent withdrawn by subject	11	5
Other	1	1
Lost to follow-up	4	-

Baseline characteristics

Reporting groups

Reporting group title	HDIT101
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Reporting group description:

Patients receiving single intravenous infusion of HDIT101 on Day 1 and episodic standard of care treatment with Valaciclovir-placebo starting at Day 1 and in case of recurrences during the trial.

Reporting group title	Valaciclovir
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Reporting group description:

Patients receiving single IV infusion of HDIT101-placebo on Day 1 and episodic standard of care treatment with Valaciclovir starting at Day1 and in case of recurrences during the trial.

Reporting group values	HDIT101	Valaciclovir	Total
Number of subjects	81	41	122
Age categorical			
Units: Subjects			
Adults (18-64 years)	73	38	111
From 65-84 years	8	3	11
Age continuous			
Units: years			
arithmetic mean	44.4	43.3	
standard deviation	± 13.66	± 13.42	-
Gender categorical			
Units: Subjects			
Female	42	22	64
Male	39	19	58
HSV-1 seropositivity test			
Herpes simplex virus-1 seropositivity test			
Units: Subjects			
Positive	42	22	64
Negative	39	19	58
Episodes of anogenital herpes			
Number of episodes of anogenital herpes in the last year			
Units: Subjects			
3 episodes	1	1	2
4 episodes	12	6	18
5 episodes	9	3	12
more than 5 episodes	59	31	90
Ethnicity			
Units: Subjects			
Hispanic or Latino	2	1	3
Not-Hispanic or Latino	79	40	119
Smoking habits			
Units: Subjects			
Current smoker	22	11	33
Ex-smoker	22	10	32
Non-smoker	37	20	57
Post hoc: Subgroups based on number of episodes of anogenital herpes in the			

last year			
Subgroups were defined for a post hoc analysis of time to first recurrence.			
Units: Subjects			
3-4	13	7	20
5-9	40	21	61
10-14	23	10	33
15 or more	5	3	8
Time since first diagnosis			
Time since first diagnosis/symptoms of genital herpes			
Units: years			
median	4.731	4.709	
full range (min-max)	0.74 to 45.77	0.29 to 39.95	-
Weight			
Units: kilogram(s)			
arithmetic mean	72.9	72.7	
standard deviation	± 12.95	± 15.35	-
Body mass index			
Units: kilogram(s)/square metre			
arithmetic mean	24.016	23.938	
standard deviation	± 3.2904	± 3.5120	-

End points

End points reporting groups

Reporting group title	HDIT101
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Reporting group description:

Patients receiving single intravenous infusion of HDIT101 on Day 1 and episodic standard of care treatment with Valaciclovir-placebo starting at Day 1 and in case of recurrences during the trial.

Reporting group title	Valaciclovir
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Reporting group description:

Patients receiving single IV infusion of HDIT101-placebo on Day 1 and episodic standard of care treatment with Valaciclovir starting at Day1 and in case of recurrences during the trial.

Subject analysis set title	Safety analysis set
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Subject analysis set type	Safety analysis
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Subject analysis set description:

All patients in the FAS who received at least one dose of IMP (i.e., "treated population") and had at least one post-baseline safety assessment (where the statement that a patient had no AE on the AE eCRF constitutes a safety assessment). The assignment of patients to the treatment groups was as actually treated.

Subject analysis set title	Pharmacokinetic set
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

All patients who received a single dose of HDIT101 and had at least one post-dose PK assessment. Of note, one patient with a positive HDIT101 concentration pre-dose was excluded from the PK analysis as it could not be ruled out that the PK samples of this patient were mixed up

Subject analysis set title	Immunogenicity set
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

All patients who received a single dose of HDIT101 and had at least one post-dose immunogenicity assessment

Subject analysis set title	Full analysis set
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Subject analysis set type	Full analysis
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Subject analysis set description:

All randomized patients; following the intent-to-treat principle, patients were analyzed as randomized.

Primary: Percentage of days with lesion(s)

End point title	Percentage of days with lesion(s)
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End point description:

End point type	Primary
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End point timeframe:

Number of days with lesion (except the lesion episode at randomization) divided by the number of study days after the investigational medicinal product infusion.

End point values	HDIT101	Valaciclovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	41		
Units: Percentage				
median (full range (min-max))	11.926 (0 to 77.78)	12.000 (0 to 33.51)		

Statistical analyses

Statistical analysis title	Treatment contrast
Statistical analysis description: The primary alternative hypothesis (H1) was that the percentage of days with lesions relative to the days in the study after initial treatment was lower with HDIT101 treatment than with Valaciclovir treatment. H1 was tested against the null hypothesis (H0, one-sided) that the percentage of days with lesions in the HDIT101 arm was equal or larger than in the valaciclovir arm.	
Comparison groups	HDIT101 v Valaciclovir
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5772
Method	Wald statistics
Parameter estimate	event rate ratio
Point estimate	1.037
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.718
upper limit	1.498

Secondary: Key Secondary: 1_Time to first recurrence

End point title	Key Secondary: 1_Time to first recurrence
End point description: Time to first recurrence of lesion was defined as time from HDIT101/HDIT101-placebo infusion to the day with presence of a new recurrence with HSV score 2-7	
End point type	Secondary
End point timeframe: Time from initial IMP infusion until the first day of a new recurrence with HSV score 2-7 as reported by the patient and verified by the investigator.	

End point values	HDIT101	Valaciclovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	41		
Units: days				
arithmetic mean (standard deviation)	57.5 (± 53.61)	44.3 (± 44.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Key secondary: 2_Recurrence rate

End point title	Key secondary: 2_Recurrence rate
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End point description:

A right censoring was made after study day 187 (upper limit of visit 7 window). Recurrence rates were calculated for each subject and standardised to a period of 180 days by $180 \times (\text{number of recurrences} / \text{days in the study after start of initial IMP infusion})$

End point type	Secondary
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End point timeframe:

Number of recurrences divided by the total number of study days after IMP infusion

End point values	HDIT101	Valaciclovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	41		
Units: percent				
arithmetic mean (standard deviation)	3.173 (\pm 2.7719)	3.764 (\pm 2.5850)		

Statistical analyses

Statistical analysis title	Treatment contrast
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Comparison groups	HDIT101 v Valaciclovir
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Number of subjects included in analysis	118
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Analysis specification	Pre-specified
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Analysis type	superiority
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P-value	= 0.0658
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Method	van Elteren test
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Secondary: Key secondary: 3_Duration of recurrent lesion

End point title	Key secondary: 3_Duration of recurrent lesion
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End point description:

Total number of consecutive days with lesions of HSV score 2-7 divided by the number of recurrences

End point type	Secondary
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End point timeframe:

Recurrence duration was defined as the accumulated duration of all recurrences after clearance from symptoms after initial treatment as reported by patient divided by the number of recurrences.

End point values	HDIT101	Valaciclovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	41		
Units: day				
arithmetic mean (standard deviation)	8.5 (\pm 5.25)	6.1 (\pm 3.86)		

Statistical analyses

Statistical analysis title	Treatment contrast
Comparison groups	HDIT101 v Valaciclovir
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9943
Method	van Elteren test

Secondary: Key secondary: 4_Disease-specific symptoms

End point title	Key secondary: 4_Disease-specific symptoms
End point description:	Average Herpes Symptom Checklist (HSC) total score as measure of the disease-specific symptoms severity assessed by the patient and documented in the patient's diary on daily basis.
End point type	Secondary
End point timeframe:	Daily basis from the first to the last day of disease-specific symptoms during the study

End point values	HDIT101	Valaciclovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	40		
Units: Average total score				
arithmetic mean (standard deviation)	6.827 (\pm 4.4939)	6.958 (\pm 5.3335)		

Statistical analyses

Statistical analysis title	Treatment contrast
Comparison groups	HDIT101 v Valaciclovir

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6902
Method	van Elteren test

Secondary: Key secondary: 5_Herpes outbreak impact

End point title	Key secondary: 5_Herpes outbreak impact
End point description: Average Herpes Outbreak Impact Questionnaire (HOIQ) total score as measure of the daily impact specific to herpes outbreaks on patient's emotional, self-care, social, sexual, and work-related functioning	
End point type	Secondary
End point timeframe: Daily basis from the first to the last day of symptoms per lesion episode during the study	

End point values	HDIT101	Valaciclovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	40		
Units: Total score				
arithmetic mean (standard deviation)	10.390 (\pm 7.4588)	10.246 (\pm 6.7861)		

Statistical analyses

Statistical analysis title	Treatment contrast
Comparison groups	HDIT101 v Valaciclovir
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5005
Method	van Elteren test

Secondary: Key secondary: 6_Changes in patients' quality of life

End point title	Key secondary: 6_Changes in patients' quality of life
End point description: Change in Recurrent Genital Herpes Quality of Life (RGHQoL) total score from baseline to end of the study	
End point type	Secondary
End point timeframe: From baseline (Day 1, Visit 1) to end of study (Visit 7)	

End point values	HDIT101	Valaciclovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	9		
Units: Total score				
arithmetic mean (standard deviation)	5.3 (± 8.16)	6.1 (± 12.19)		

Statistical analyses

Statistical analysis title	Treatment contrast
Comparison groups	HDIT101 v Valaciclovir
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5854
Method	van Elteren test

Secondary: Immunogenicity: Number of patients with positive ADA

End point title	Immunogenicity: Number of patients with positive ADA
End point description:	
Serum titers of ADA against HDIT101	
End point type	Secondary
End point timeframe:	
From baseline (Day 1, Visit 1) to end of study (Visit 7)	

End point values	Immunogenicity set			
Subject group type	Subject analysis set			
Number of subjects analysed	49			
Units: Number of patients				
Visit 1 (Baseline)	5			
Visit 2	0			
Visit 4	0			
Visit 6	5			
Visit 7	6			
Overall post baseline	8			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Secondary: Number of lesion episodes

End point title	Secondary: Number of lesion episodes
End point description: Number of lesion episodes (i.e. lesion with HSV score 2-7 after initial treatment) using right censored data after Day 187	
End point type	Other pre-specified
End point timeframe: Lesion episodes after initial treatment to Day 187	

End point values	HDIT101	Valaciclovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	41		
Units: Number				
arithmetic mean (standard deviation)	2.4 (\pm 1.96)	3.4 (\pm 2.43)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Secondary: Mean log number of HSV-2 DNA Copies in positive samples

End point title	Secondary: Mean log number of HSV-2 DNA Copies in positive samples
End point description: Mean log number of HSV-2 DNA copies in HSV-2 positive swabs collected during Screening, Visit 1 and Visit 6 periods	
End point type	Other pre-specified
End point timeframe: The number of HSV-2 DNA copies was determined in all HSV-2 positive swabs of the swabbing periods, i.e., collected during a 28-day swabbing period after IMP infusion (Visit 1 [Day 1]) and during a 28-day swabbing period after Visit 6 (Day 150).	

End point values	HDIT101	Valaciclovir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	41		
Units: Log number				
arithmetic mean (standard deviation)				
Screening	4.889 (\pm 1.2459)	5.305 (\pm 1.0146)		
Visit 1	4.954 (\pm 0.9168)	4.854 (\pm 0.7783)		

Visit 6	4.759 (\pm 0.9988)	4.236 (\pm 1.1298)		
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Statistical analyses

Statistical analysis title	Treatment contrast
Comparison groups	HDIT101 v Valaciclovir
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6438
Method	Wald statistics

Other pre-specified: PK: AUC0-inf

End point title	PK: AUC0-inf
End point description:	Total exposure - area under the serum concentration-time curve from administration until infinity
End point type	Other pre-specified
End point timeframe:	Scheduled sampling time point (Pre-dose, End of infusion, Visit 2 (Day 15), Visit 4 (Day 60), Visit 6 (Day 150) and Visit 7 (Day 180))

End point values	Pharmacokinetic set			
Subject group type	Subject analysis set			
Number of subjects analysed	44			
Units: day*ng/mL				
geometric mean (geometric coefficient of variation)	10447685.2 (\pm 21.72)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: PK: Cmax

End point title	PK: Cmax
End point description:	Concentration maximum until the end of the 180 days pharmacokinetics period
End point type	Other pre-specified

End point timeframe:

Scheduled sampling time point (Pre-dose, End of infusion, Visit 2 (Day 15), Visit 4 (Day 60), Visit 6 (Day 150) and Visit 7 (Day 180))

End point values	Pharmacokinetic set			
Subject group type	Subject analysis set			
Number of subjects analysed	45			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	590771.74 (\pm 16.526)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: PK: Tmax

End point title	PK: Tmax
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End point description:

Time when concentration maximum is observed

End point type	Other pre-specified
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End point timeframe:

Scheduled sampling time point (Pre-dose, End of infusion, Visit 2 (Day 15), Visit 4 (Day 60), Visit 6 (Day 150) and Visit 7 (Day 180))

End point values	Pharmacokinetic set			
Subject group type	Subject analysis set			
Number of subjects analysed	45			
Units: day				
geometric mean (geometric coefficient of variation)	0.00745 (\pm 47.130644)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: PK: T1/2

End point title	PK: T1/2
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End point description:

Apparent elimination half-life

End point type	Other pre-specified
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End point timeframe:

Scheduled sampling time point (Pre-dose, End of infusion, Visit 2 (Day 15), Visit 4 (Day 60), Visit 6 (Day 150) and Visit 7 (Day 180))

End point values	Pharmacokinetic set			
Subject group type	Subject analysis set			
Number of subjects analysed	44			
Units: day				
geometric mean (geometric coefficient of variation)	20.64 (\pm 21.135)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: PK: Clearance

End point title PK: Clearance

End point description:

Pharmacokinetic measurement of the volume of plasma from which study treatment was completely removed per unit time (mL/day)

End point type Other pre-specified

End point timeframe:

Scheduled sampling time point (Pre-dose, End of infusion, Visit 2 (Day 15), Visit 4 (Day 60), Visit 6 (Day 150) and Visit 7 (Day 180))

End point values	Pharmacokinetic set			
Subject group type	Subject analysis set			
Number of subjects analysed	44			
Units: mL/day				
geometric mean (geometric coefficient of variation)	189.93 (\pm 21.794)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: PK: Volume of distribution

End point title PK: Volume of distribution

End point description:

Individual drug's propensity to either remain in the plasma or redistribute to other tissue compartments.

End point type Other pre-specified

End point timeframe:

Scheduled sampling time point (Pre-dose, End of infusion, Visit 2 (Day 15), Visit 4 (Day 60), Visit 6 (Day 150) and Visit 7 (Day 180))

End point values	Pharmacokinetic set			
Subject group type	Subject analysis set			
Number of subjects analysed	44			
Units: millilitre(s)				
geometric mean (geometric coefficient of variation)	5655.27 (\pm 21.859)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Immunogenicity: ADA titer

End point title	Immunogenicity: ADA titer
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End point description:

Serum titers of ADA against HDIT101

End point type	Other pre-specified
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End point timeframe:

Blood sampling for ADA titer assessments was performed at all on-site visits except screening as well as at all unscheduled visits (UV) except an UV prior to Day 15

End point values	Immunogenicity set			
Subject group type	Subject analysis set			
Number of subjects analysed	49			
Units: serum titer				
arithmetic mean (standard deviation)				
Visit 1 (Baseline)	2.2 (\pm 1.1)			
Visit 2	0 (\pm 0)			
Visit 4	0 (\pm 0)			
Visit 6	9.0 (\pm 13.15)			
Visit 7	8.5 (\pm 14.07)			
Overall post baseline	0 (\pm 0)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline to end of the study (Day 180)

Adverse event reporting additional description:

Patients were expected to volunteer information about adverse events that they experienced. In addition, the investigator or designee questioned the patient at each visit about adverse events and recorded these as well as other adverse events at the visit

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	HDIT101
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Reporting group description: -

Reporting group title	Valaciclovir
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Reporting group description: -

Serious adverse events	HDIT101	Valaciclovir	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 80 (1.25%)	0 / 41 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 80 (1.25%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	HDIT101	Valaciclovir	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 80 (56.25%)	19 / 41 (46.34%)	
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 80 (10.00%)	6 / 41 (14.63%)	
occurrences (all)	10	8	
Migraine			

subjects affected / exposed occurrences (all)	1 / 80 (1.25%) 1	2 / 41 (4.88%) 2	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	7 / 80 (8.75%) 8	0 / 41 (0.00%) 0	
Eye disorders Photopsia subjects affected / exposed occurrences (all)	4 / 80 (5.00%) 4	0 / 41 (0.00%) 0	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	3 / 80 (3.75%) 3	1 / 41 (2.44%) 1	
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	1 / 80 (1.25%) 2 3 / 80 (3.75%) 3 3 / 80 (3.75%) 4	3 / 41 (7.32%) 4 1 / 41 (2.44%) 1 0 / 41 (0.00%) 0	
Infections and infestations Oral herpes subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	8 / 80 (10.00%) 12 7 / 80 (8.75%) 8	5 / 41 (12.20%) 6 1 / 41 (2.44%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 August 2020	Main changes included in protocol v3.0 were adaptations with regard to adaptations for the COVID-19 pandemic, further clarifications, and minor changes. Note: The study was approved with protocol v2.0 - therefore no changes are listed for protocol v1.0 to v2.0

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported