



## Clinical trial results:

**Phase II study, multicenter, prospective, open label, preemptive treatment of cytomegalovirus (CMV) infection driven by virologic monitoring and quantification of T CD8pp65/IE-1-IFNgamma+ lymphocytes in allogeneic hematopoietic transplantation**

### Summary

EudraCT number	2011-001449-34
Trial protocol	ES
Global end of trial date	14 November 2017

### Results information

Result version number	v1 (current)
This version publication date	14 October 2022
First version publication date	14 October 2022

### Trial information

#### Trial identification

Sponsor protocol code	CMV-INMUNOGUIA
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#### Additional study identifiers

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

Notes:

### Sponsors

Sponsor organisation name	Instituto de Investigación Sanitaria INCLIVA
Sponsor organisation address	Avd. Menéndez Pelayo 4, acc, Valencia, Spain, 46010
Public contact	Marta Peiro, Instituto de Investigación Sanitaria INCLIVA, 34 961973536, gestioncientifica@incliva.es
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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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	04 July 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 November 2017
Global end of trial reached?	Yes
Global end of trial date	14 November 2017
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

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Main objective of the trial:

To determine whether a strategy of early treatment of CMV infection post hematopoietic allogeneic transplant, guided by virological monitoring and quantification of T CD8pp65/IE-1-IFNgamma+ lymphocytes is at least the same or more effective than the standard strategy (historical control group).

Protection of trial subjects:

The protocol, informed consent form, participant information sheet and any applicable documents were submitted and approved by an appropriate Ethics Committee.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 December 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	Spain: 117
Worldwide total number of subjects	117
EEA total number of subjects	117

Notes:

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**Subjects enrolled per age group**

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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)	105
From 65 to 84 years	12
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Patients with Cytomegalovirus infection and treated with hematopoietic allogenic transplant. Matched demographic historical control group with CMV infection

### Pre-assignment

Screening details:

Patients who met all inclusion/exclusion criteria were included.

### Pre-assignment period milestones

Number of subjects started	117
Number of subjects completed	117

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Study Group

Arm description:

Valganciclovir, ganciclovir or foscarnet will be used, at the discretion of the site.

Arm type	Experimental
Investigational medicinal product name	GANCICLOVIR
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

10 mg/kg milligram(s)/kilogram

Investigational medicinal product name	FOSCARNET
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

120 mg/kg milligram(s)/kilogram

Investigational medicinal product name	VALGANCICLOVIR
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1800 mg milligram(s)

<b>Arm title</b>	Control Group
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Arm description:

A historical review of patients receiving treatment anticipation of CMV infection guided exclusively by monitoring virological.

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Arm type	No intervention
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No investigational medicinal product assigned in this arm

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<b>Number of subjects in period 1</b>	Study Group	Control Group
Started	61	56
Completed	52	56
Not completed	9	0
Adverse event, serious fatal	3	-
Adverse event, non-fatal	6	-

## Baseline characteristics

### Reporting groups

Reporting group title	Study Group
Reporting group description: Valganciclovir, ganciclovir or foscarnet will be used, at the discretion of the site.	
Reporting group title	Control Group
Reporting group description: A historical review of patients receiving treatment anticipation of CMV infection guided exclusively by monitoring virological.	

Reporting group values	Study Group	Control Group	Total
Number of subjects	61	56	117
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	52	53	105
From 65-84 years	9	3	12
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	28	17	45
Male	33	39	72

## End points

### End points reporting groups

Reporting group title	Study Group
Reporting group description: Valganciclovir, ganciclovir or foscarnet will be used, at the discretion of the site.	
Reporting group title	Control Group
Reporting group description: A historical review of patients receiving treatment anticipation of CMV infection guided exclusively by monitoring virological.	

### Primary: Percentage of patients with negative CMV in blood

End point title	Percentage of patients with negative CMV in blood
End point description:	
End point type	Primary
End point timeframe: Day 7, 14, 21 or 28	

End point values	Study Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	56		
Units: % patients	87	62		

### Statistical analyses

Statistical analysis title	McNemar x2
Comparison groups	Study Group v Control Group
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	Chi-squared

### Primary: Percentage of patient who develop nephrotoxicity

End point title	Percentage of patient who develop nephrotoxicity
End point description:	
End point type	Primary

End point timeframe:  
During 100 days of the study

End point values	Study Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	56		
Units: unit(s)				
number (not applicable)	53	0		

### Statistical analyses

Statistical analysis title	Descriptive
Comparison groups	Study Group v Control Group
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	Descriptive

### Secondary: Percentage of patients who, after achieving hematological recovery, develop neutropenia of $<1.0 \times 10^9 / L$ and $<0.5 \times 10^9 / L$

End point title	Percentage of patients who, after achieving hematological recovery, develop neutropenia of $<1.0 \times 10^9 / L$ and $<0.5 \times 10^9 / L$
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End point description:

End point type	Secondary
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End point timeframe:

During the first 100 days of TPH.

End point values	Study Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	56		
Units: % patients	43	36		

### Statistical analyses

No statistical analyses for this end point

**Secondary: Percentage of patients who develop CMV disease**

End point title	Percentage of patients who develop CMV disease
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End point description:

End point type	Secondary
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End point timeframe:

During treatment and 2 months after treatment

End point values	Study Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	56		
Units: % patients	3	2		

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Frequency and type of infections**

End point title	Frequency and type of infections
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End point description:

End point type	Secondary
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End point timeframe:

During treatment and 2 months of follow-up.

End point values	Study Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	56		
Units: number of infections	61	56		

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Total days of antiviral treatment**

End point title	Total days of antiviral treatment
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End point description:

End point type	Secondary
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End point timeframe:

End of treatment

End point values	Study Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	56		
Units: days	28	31		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Consumables: drug used, number of drug administrations / day, use of central / peripheral catheter.

End point title	Consumables: drug used, number of drug administrations / day, use of central / peripheral catheter.
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End point description:

End point type	Secondary
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End point timeframe:

During treatment

End point values	Study Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	56		
Units: days	61	56		

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

Adverse events occurred during treatment or within 28 days after the end of treatment.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	4.0
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### Reporting groups

Reporting group title	Study Group
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Reporting group description:

Valganciclovir, ganciclovir or foscarnet will be used, at the discretion of the site.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Non serious adverse events occur usually in all patients postrasplant

Serious adverse events	Study Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	43 / 61 (70.49%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events			
Vascular disorders			
Haemorrhage			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Stomatitis			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lumbar pain			

subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	3 / 61 (4.92%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
hemoperitoneum			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac arrest			

subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aplasia			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	7 / 61 (11.48%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Graft versus host disease			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	6 / 61 (9.84%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peritonitis			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute Gastroenteritis			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic failure			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatomegaly			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal fa			
subjects affected / exposed	4 / 61 (6.56%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dysuria			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Cystitis haemorrhagic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	3 / 61 (4.92%) 0 / 0 0 / 0		
Endocrine disorders Hyperbilirubinaemia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 61 (1.64%) 0 / 0 0 / 0		
Musculoskeletal and connective tissue disorders Intermittent claudication subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 61 (1.64%) 0 / 0 0 / 0		
Infections and infestations Septic shock subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 61 (1.64%) 0 / 0 0 / 0		
Staphylococcal bacteraemia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 61 (1.64%) 0 / 0 0 / 0	Additional description: Staphylococcus epidermis	
Fever subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	8 / 61 (13.11%) 0 / 0 0 / 0		
Cytomegalovirus infection reactivation subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 61 (1.64%) 0 / 0 0 / 0		

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

<b>Non-serious adverse events</b>	Study Group		
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 61 (0.00%)		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 May 2014	Changes in sections: Name and description of the investigational product; principal objective and randomization process
30 December 2014	Summary of changes: To add a clinical report form specific for data collection of the control group

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported