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Cytomegalovirus (CMV) in allogeneic hematopoietic stem cell transplant patients

Submission date	Recruitment status	[_] Prospectively registered
29/09/2021	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
25/11/2021	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
24/08/2023	Infections and Infestations	

Plain English summary of protocol

Background and study aims
Cytomegalovirus (CMV) is one of the most common infections that affects people with an allogeneic hematopoietic stem cell transplant (HSCT). Allogeneic stem cell transplantation involves transferring stem cells from a healthy person to the patient's body after high-intensity chemotherapy or radiation. The aim of this study is to describe the treatment patterns and outcomes of CMV in about 400 HSCT recipients globally who required treatment for the management of CMV.

Who can participate?
Records from patients who were over 18 years old at the time of their HSCT and who were then treated for a CMV infection

What does the study involve?
The study will use the healthcare information that has already been documented from 1 January 2014 (until no later than determined at site level) related to the HSCT, CMV infections and outcomes including hospital visits, clinic visits, written follow-up notes, drug treatments, tests and procedures. This observational study uses records from routine healthcare, so the results of the study are not expected to be directly or immediately relevant to patient care and will not be shared with each participant.

What are the possible benefits and risks of participating?
This is a retrospective observational study so there are no physical risks that will result from taking part in this study. Taking part in this study has a very low risk of personally identifying information (PII) being accessed by unauthorized people (i.e., individuals who are not part of the study team). To reduce the risk of sharing PII with unauthorized persons, patient identifiers will be removed before being used in research so as to maintain confidentiality and privacy protection. It is expected there will be limited or no direct or immediate benefit to participants.

Where is the study run from?
Shire Human Genetic Therapies, Inc. a wholly-owned subsidiary of Takeda Pharmaceutical Company Ltd (USA)

When is the study starting and how long is it expected to run for?
May 2019 to December 2021

Who is funding the study?
Shire Human Genetic Therapies, Inc. a wholly-owned subsidiary of Takeda Pharmaceutical Company Ltd (USA)

Who is the main contact?
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Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
287712

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
TAK620-5002, IRAS 287712, CPMS 46626

Study information

Scientific Title
Multinational CMV Outcomes, Treatment Patterns and Healthcare Resource Utilization Study following Hematopoietic Stem Cell Transplant (OTUS HSCT)

Acronym
OTUS HSCT

Study objectives
Primary objective:
To evaluate and describe the clinical outcomes with current management patterns

Secondary objectives:
1. To describe the treatment patterns of cytomegalovirus (CMV) management
2. To describe the patient/clinical characteristics of Hematopoietic Stem Cell Transplant (HSCT) recipients
3. To describe the economic burden and healthcare resource utilization

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 11/12/2020, HRA and Health and Care Research Wales (Castlebridge 4, 15 - 19 Cowbridge Rd E, Cardiff, CF11 9AB, UK; +44 (0)2920 230457; HCRW.approvals@wales.nhs.uk); REC ref: 20/LO/1105

Study design
Multinational non-interventional retrospective study

Primary study design
Observational

Secondary study design
Retrospective study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not applicable (retrospective study)

Health condition(s) or problem(s) studied

Cytomegalovirus infection in transplanted patients

Interventions
The study will use the healthcare information that has already been documented from 1 January 2014 (until no later than determined at site level) related to the HSCT, CMV infections and outcomes including hospital visits, clinic visits, written follow-up notes, drug treatments, tests and procedures. This observational study uses records from routine healthcare.

Intervention Type
Other

Primary outcome measure
1. Number of CMV viremia episodes measured using patient records from transplant date until the end of follow-up
2. Time from HSCT to CMV viremia measured using patient records
3. Time to CMV viremia clearance measured using patient records
4. Incidence and time to CMV recurrence measured using patient records from CMV index episode until the end of follow-up
5. Incidence of tissue invasive disease measured using patient records from transplant date until the end of follow-up
6. Incidence of graft rejection measured using patient records from transplant date until the end of follow-up
7. Incidence of post-HSCT non-CMV infections requiring intravenous (IV) treatment or hospitalization, measured using patient records from transplant date to 365 days following the last PRRI CMV episode or until death (whichever occurs first)
8. Incidence of anti-CMV treatment-related myelosuppression, nephrotoxicity or other toxicities, measured using patient records from the first CMV episode until the end of follow-up
9. CMV resistance measured using patient records from the first CMV episode until the end of follow-up
10. CMV-associated mortality measured using patient records
11. All-cause mortality measured using patient records

*Time of follow-up: at least 365 days after being designated as refractory, resistant or intolerant for the first time or until death, whichever comes first.

Secondary outcome measures
1. CMV prophylaxis and pre-emptive therapy, management of CMV reactivation/recurrence, measured from transplant date until the end of follow-up
2. Frequency of first-, second,- and third-line anti-CMV agents, measured using patient records from the first CMV episode until the end of follow-up
3. Time from HSCT to incident CMV-specific anti-viral therapy, measured using patient records
4. Viral load measured using patient records at transplant date and from 14 days prior to the start through the end of CMV episodes or until clearance
5. Medication utilization measured using patient records from transplant date until the end of follow-up
6. Demographics, diagnosis, transplant procedure, clinical, prior transplants, transplant indication, HCT comorbidity index comorbidities and score, prophylactic immunosuppressive regimen, measured using patient records at a pre-transplant time
7. Viral infections and prophylactic/treatment immunosuppressive regimen measured using patient records from transplant date until the end of follow-up
8. Viral infections, incidence and time to acute and chronic graft vs host disease (GVHD) and

immunosuppressive regimen, measured using patient records from transplant date until the end of follow-up
9. Inpatient healthcare utilization, length of hospital stay, cause of hospitalization and number of outpatient clinic visits, measured using patient records from transplant date until the end of follow-up

*Time of follow-up: at least 365 days after being designated as refractory, resistant or intolerant for the first time or until death, whichever comes first.

Overall study start date
20/05/2019

Completion date
06/12/2021

Eligibility

Key inclusion criteria
Cohort 1: Resistant/refractory/intolerant inclusion criteria:
1. Aged ≥18 years at the time of the HSCT
2. Received an HSCT after 1 January 2014
3. Diagnosed with CMV infection any time after the HSCT date
4. Characterized as resistant to currently available treatments, OR refractory to currently available treatments, OR considered intolerant to currently available treatments
5. Follow-up data are available for at least 12 months (1 year) after being characterized in item (4) (above) or until death, whichever occurs first

Cohort 2: Pre-emptive treatment for CMV viremia inclusion criteria:
1. Aged ≥18 years at the time of the HSCT
2. Received an HSCT after 1 January 2017
3. Diagnosed with CMV viremia any time after the HSCT date
4. Received pre-emptive treatment
5. Follow-up data are available for at least 12 months (1 year) after being characterized in item (4) (above) or until death, whichever occurs first

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
400

Total final enrolment

379

Key exclusion criteria
Positive test for HIV before the HSCT

Date of first enrolment
16/10/2020

Date of final enrolment
30/11/2021

Locations

Countries of recruitment
England

France

Germany

Italy

Spain

United Kingdom

United States of America

Wales

Study participating centre
King's College Hospital
United Kingdom
SE5 9RS

Study participating centre
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Study participating centre
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Study participating centre
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02111

Study participating centre
Johns Hopkins University
United States of America
21287

Study participating centre
Weill Cornell Medicine
United States of America
10065

Study participating centre
Memorial Sloan Kettering Cancer Center
United States of America
10065

Study participating centre
University Hospital Mainz
Germany
55131

Study participating centre
University Hospital Dusseldorf
Germany
40225

Sponsor information

Organisation
Takeda (United States)

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Sponsor type
Industry

Website
https://www.takeda.com/

ROR
https://ror.org/03bygaq51

Funder(s)

Funder type
Industry

Funder Name
Takeda Pharmaceuticals U.S.A.

Alternative Name(s)
Takeda, Takeda Pharmaceuticals U.S.A., Inc., Takeda Pharmaceutical Company Limited, Takeda Pharmaceuticals America, Inc., Takeda in the U.S., TPUSA

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
The results of this study are intended to be disseminated through publication in peer-reviewed scientific journals and other publications (i.e. internal reports). The redacted study protocol and redacted statistical analysis plan will be made available.

Intention to publish date
01/02/2023

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the study will be made available upon request to researchers who provide a methodologically sound proposal. The data will be provided after its de-identification, in compliance with applicable privacy laws, data protection and requirements for consent and anonymization.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Other unpublished results	Text-based summary of results	30/07/2023	24/08/2023	No	No