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A pharmacokinetic and pharmacodynamic study of valganciclovir in solid organ transplant patients

Submission date	Recruitment status	[_] Prospectively registered
11/12/2006	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
14/02/2007	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
19/07/2021	Infections and Infestations	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title

A pharmacokinetic and pharmacodynamic study of valganciclovir in solid organ transplant patients

Study objectives
Valganciclovir is a prodrug of ganciclovir with improved oral bioavailability, potentially useful for the treatment of Cytomegalovirus (CMV) infection in organ transplant recipients and for the prophylaxis of CMV infection in liver and lung transplant patients, two indications currently not validated. Our hypothesis is that valganciclovir produces drug levels and virological responses similar to those obtained with intravenous ganciclovir. This would provide indirect evidence for the use of oral valganciclovir instead of intravenous ganciclovir within the settings mentioned above.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval received by the local ethics committee (Commission déthique de la recherche clinique, Faculté de Médecine et Biologie, Université de Lausanne) on the 20th September 2005 (ref: 94 /05).

Study design
Prospective observational trial with historical controls

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Cytomegalovirus (CMV) infection

Interventions
Patients will receive valganciclovir (900 mg once daily [QD], adjusted to their renal function according to the information provided by the manufacturer), over three months, for primary prophylaxis. During such period, blood samples will be collected monthly to determine ganciclovir plasma levels (immediately before and three hours after oral administration) and CMV blood viral loads will be measured by real time quantitative Polymerase Chain Reaction (PCR). Upon the initial prophylaxis termination, and over the following three months, universal blood monitoring for CMV infection will continue on a fortnightly basis.

In case of detection of high viremia level (more than 10,000 - 100,000 copies of CMV Deoxyribonucleic Acid [DNA]/million leukocytes) and/or symptomatic CMV disease, patients will receive therapeutic dosages of valganciclovir (900 mg twice daily [bid], adjusted to renal function) until they achieve a clinical response or their viral load drops. Throughout such treatment phase, ganciclovir plasma level and CMV viral load assays will be performed weekly. Treated subjects will then receive secondary prophylaxis (half the therapeutic dose of valganciclovir, 900 mg QD, adjusted to renal function) for one month, with fortnightly

ganciclovir plasma levels and CMV viral load assays. In selected patients, treating physicians may opt at their discretion for intravenous ganciclovir rather than oral valganciclovir, based on their clinical judgement. Any such patients will have plasma levels and CMV viral load tested weekly.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Valganciclovir

Primary outcome(s)
1. To determine whether the average ganciclovir blood levels following the oral administration of valganciclovir are comparable to the known therapeutic range associated with the use of intravenous ganciclovir
2. To assess the variability of ganciclovir blood levels attained with oral valganciclovir, to evaluate its potential repercussions on therapeutic response, and to identify influential factors which modulate valganciclovir absorption and disposition

Key secondary outcome(s))
1. To evaluate the relationship between ganciclovir blood levels and anti-CMV efficacy using a pharmacokinetic-pharmacodynamic model incorporating the relevant pharmacokinetic, virological and clinical response parameters
2. To determine the impact of specific clinical conditions (malabsorption, cystic fibrosis, kidney failure), concomitant medications (drugs inhibiting organic anion transport) and possibly genetic traits (drug transporters polymorphisms) on ganciclovir and valganciclovir pharmacokinetics and dose requirements
3. To further assess the safety and tolerability of oral valganciclovir

Completion date
31/12/2007

Eligibility

Key inclusion criteria
1. Solid organ transplant recipient
2. More than or equal to 18 years old
3. At risk for CMV disease (D+/R-, D+/R+ or D-/R+)
4. Written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Not Specified

Key exclusion criteria
1. Failure to give written informed consent
2. Known intolerance to ganciclovir or valganciclovir

Date of first enrolment
15/11/2005

Date of final enrolment
31/12/2007

Locations

Countries of recruitment
Switzerland

Study participating centre
Division de Pharmacologie et Toxicologie Cliniques
Lausanne
Switzerland
1011

Sponsor information

Organisation
University Hospital Complex of Vaud (Centre Hospitalier Universitaire Vaudois [CHUV]) (Switzerland)

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
University Hospital Complex of Vaud (Centre Hospitalier Universitaire Vaudois [CHUV]) (Switzerland)

Funder Name
Roche (Switzerland) - unrestricted grant

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Thesis results		26/05/2008	19/07/2021	No	No