UK COST-EFFECTIVENESS ANALYSIS FOR MANAGEMENT OF CMV DISEASE IN PATIENTS POST ALLOGENEIC STEM CELL TRANSPLANTATION WITH A NOVEL ADOPTIVE T CELL THERAPY

Mark Nuijten1, Sybille Dihanich2, Holger Müller3, Karl Peggs3
1 A2M Ars Accessus Medica, Dorpsstraat 75, 1546 LG Jisp, Rotterdam, The Netherlands
2 Cell Medica Ltd., 8-14 St. Pancras Way, London NW1 0QG, United Kingdom
3 UCL Hospitals NHS Foundation Trust and UCL Medical School, Department of Haematology, Euston Road, London, United Kingdom

BACKGROUND
Viral infections, predominantly from latent viruses, are a well known complication of hematopoietic stem cell transplantations (HSCTs) with potentially life threatening outcomes. The cytomegalovirus (CMV) is one of the most frequent culprits and it is estimated that up to 80% of transplants recipients develop a CMV infection and historically between 20-35% of transplants recipients develop CMV disease. The current standard of care is treatment with antiviral drugs which demonstrate efficacy in suppressing the viral replication, but do not address the root cause of the infection: a compromised immune system. Directly selected CMV-specific T cell therapy presents a novel treatment option that may lead to improved patient outcomes and cost savings for the health economic system.

OBJECTIVES
The aim of this study was to assess the cost-effectiveness of Streptamer®-selected CMV-specific T cells for the management of CMV disease in patients following a HSCT in the UK.

METHODS
A Markov model, reflecting current clinical guidelines2, was developed. TreeAge Pro (Williamstown, Mass) was used for model design and all analyses. Data sources used included clinical trials, published literature, national costs, tariff lists, and a Delphi panel. The model simulated the clinical and economic outcomes associated with Streptamer-selected CMV-specific T cells and standard antiviral drug treatment (ganciclovir, foscarnet and cidofovir). Analysis was performed for a hypothetical cohort of patients after allogeneic HSCT. The clinical characteristics of these patients were representative of patients in the clinical trials used as the main source of efficacy data. Effectiveness was expressed as quality-adjusted life years (QALYs). The model uses efficacy data from recurring CMV infections, EQ-5D outcome data3, and mortality rates from the two clinical trials ASPECT and IMPACT together with other mortality and utility values sourced from a literature search in order to estimate the QALY that apply to each health state. Extensive sensitivity and scenario analyses were conducted.

MODEL DESIGN
Figure 1 shows the general structure of the model, assuming ganciclovir as first-line (1-line) therapy, in-line with current standard of care in the UK2.

The transitions between the different model states were based on CMV viral load as determined by weekly quantitative PCR testing and shown in Figure 2.

RESULTS
In the base case scenario the use of the cellular therapy as 2-line treatment leads to an incremental cost-effectiveness ration (ICER) of £ 12,902/QALY whereas the ICER for 3-line increases to £ 24,710/QALY. Figure 3 shows the results of a probabilistic sensitivity analysis for the 2-line CMV disease treatment which demonstrates that the probability is 79% that the ICER remains below the threshold of £ 30,000/QALY.

DISCUSSION
The primary objective of this study was to assess the cost-effectiveness of Streptamer-selected T cells. The analyses show that Streptamer-selected T cells are cost effective in both 2-line and 3-line setting, with health economic benefits from this therapy diminishing with later line use. The principle driver for the observed cost-effectiveness is the reduction in recurring infections as demonstrated in the IMPACT clinical trial. Pooling data from both ASPECT and IMPACT for the presented health economic calculations should be considered with caution. However, extensive sensitivity and scenario modelling has been conducted to compensate for this uncertainty. The fact that probability is 79% that the ICER remains below the NICE threshold of £ 30,000/QALY supports the robustness of this assumption.

CONCLUSION
This study showed that the use of Streptamer-selected CMV-specific T cells for the treatment of CMV disease can be considered cost-effective if the NICE threshold of £ 30,000/QALY is considered. Intervention in 2nd-line setting leads to lower cost (and higher cost savings) for the health care society than delayed intervention.

REFERENCES
3 unpublished data (Cell Medica Ltd, Company Core Data Sheet)