The Cost-Effectiveness of Maribavir for Post-Transplant Refractory Cytomegalovirus Infection in France

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INTRODUCTION

- Cytomegalovirus (CMV) is a common human herpesvirus that infects people of all ages worldwide and can lead to severe complications in immunocompromised patients who have undergone a hematopoietic stem cell transplant (HSCT) or solid organ transplant (SOT).
- Maribavir (MBV) is a therapeutic option for the treatment of post-transplant patients with refractory CMV infection. It is used in patients whose CMV illness had inadequate response to at least one other treatment, including ganciclovir, valganciclovir, cidofovir or foscarnet. Its European marketing authorization was granted in November 2022 and its launch in France is still ongoing.
- This study aimed to estimate the cost-effectiveness of MBV versus investigator-assigned therapy (IAT; valganciclovir/ganciclovir, foscarnet, or cidofovir) which is the current standard of care for the treatment of refractory CMV infection post-transplant in France.

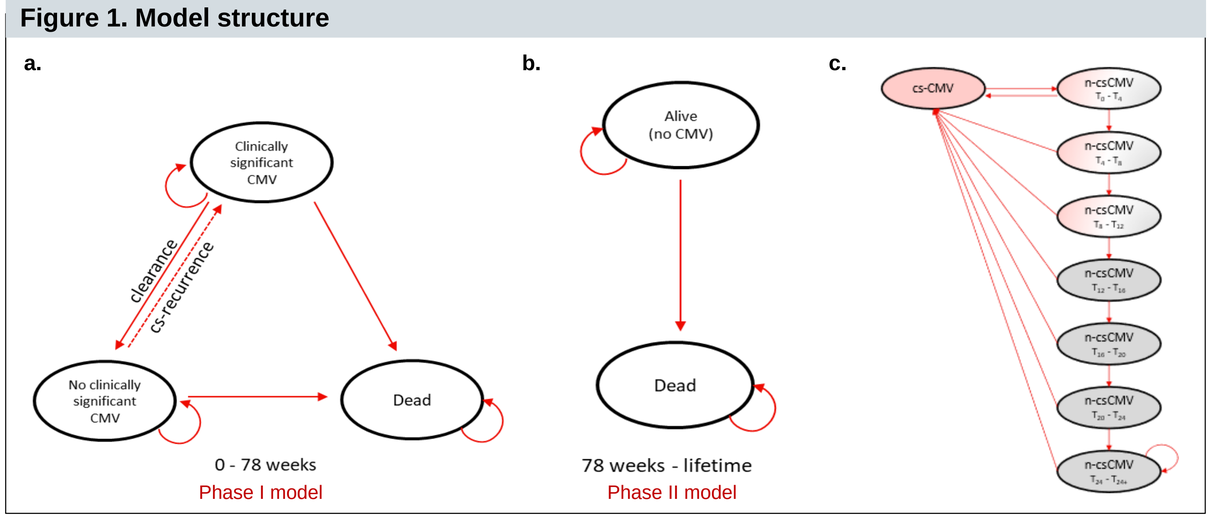
METHODS

This cost-effectiveness analysis was developed using two consecutive Markov models to capture the post-transplant journey for SOT and HSCT patients with R/R CMV.

1) Phase I: a 3-state CMV Markov was used for 78 weeks, capturing transitions between clinically significant CMV (cs-CMV), non-clinically significant CMV (n-cs-CMV), and dead health states (**Figure 1.a**).
2) Phase II: from 78 weeks until the lifetime horizon, patients moved to a 2-state, alive/dead model (**Figure 1.b**).

- Transitions between the cs-CMV state and n-csCMV state were time dependent with tunnel states used to track time since clearance as displayed on **Figure 1.c**.
- Transition probabilities and other relevant clinical outcomes related to MBV and its comparators were derived from the Phase 3 SOLSTICE study[1] and from the OTUS observational study.
- The price of MBV was set to €45,000 for an 8-week treatment regimen. Costs (€) were measured in 2021 and effects measured in quality-adjusted life years (QALYs). These were evaluated with a discount rate of 2.5% per year according to French guidelines.
- To assess the impact of the different model parameters (e.g costs, mortality, graft loss, etc.) on the results, deterministic/probabilistic sensitivity analyses were performed.

Figure 1. Model structure



RESULTS

- Over a lifetime horizon, MBV versus IAT is associated with 0.4173 QALYs gained at a total incremental cost of 18,286€, resulting in an incremental cost-effectiveness ratio (ICER) of 43,824€/QALY as exhibited in **Table 1**.
- In terms of QALY gained, **Table 2** shows that MBV generates higher QALYs by keeping patients in the non-clinically significant CMV health state longer. Similarly, MBV has a positive impact on mortality as suggested by the incremental QALY in the alive state of the Phase II model.

Table 1. Cost-effectiveness results (per patient)

	Maribavir	IAT	Incremental
Costs	82,331.66 €	64,045.93 €	18,285.72 €
Life years	11.53	11.19	0.34
QALYs total	10.41	9.99	0.42
ICER (€/Life year)			**53,076**
ICER (€/QALY)			**43,824**

Table 2. QALY breakdown (per patient)

	Maribavir	IAT	Incremental
Clinically significant CMV (0-78 wks)	**0.3392**	**0.4594**	**-0.1202**
Non-clinically significant CMV (0-78 wks)	**0.7977**	**0.6463**	**0.1515**
Part 2-model	**9.3706**	**9.0601**	**0.3105**
Adverse Events	**-0.0477**	**-0.1184**	**0.0707**
Treatment	-0.0094	-0.0648	0.0554
Retreatment	-0.0383	-0.0536	0.0153
Graft loss	**-0.0477**	**-0.0525**	**0.0048**
Total	**10.4121**	**9.9949**	**0.4173**

- When considering all cost except acquisition ones, **Table 3** shows that administration costs have a greater impact on the total incremental costs than any other costs. This result is confirmed by the tornado diagram (**Figure 2**) where the administration cost of foscarnet appears to be the most impactful parameter on the ICER.
- Other key drivers of the deterministic sensitivity analysis are the efficacy, the risk of graft loss and the recurrence rate.
- Regarding the probabilistic sensitivity analysis, the scatterplot displayed on **Figure 3** shows that it generated a minimal deviation of the deterministic ICER (+1.26%). The majority of iterations falls in the north-east quadrant indicating MBV provides more QALYs at a higher cost than IAT.
- In the end, MBV has an 88.7% probability of being cost-effective based on a willingness to pay of 147,093€/QALY as estimated as final value of statistical QALY in Téhard et al.[2]

Table 3. Cost breakdown (per patient)

	Maribavir	IAT	Incremental
Treatment costs	**42,497 €**	**11,763 €**	**30,734 €**
Total acquisition costs	42,197 €	422 €	41,775 €
Total administration costs	0 €	10,947 €	-10,947 €
Total monitoring costs	300 €	393 €	-94 €
Re-treatment with IAT costs	**22,480 €**	**31,477 €**	**-8,997 €**
Total acquisition costs	807 €	1,130 €	-323 €
Total administration costs	20,916 €	29 289 €	-8,373 €
Total monitoring costs	757 €	1,058 €	-301 €
Total health resource utilisation	**7,631 €**	**10,124 €**	**-2,493 €**
Total adverse events	**653 €**	**1,640 €**	**-987 €**
Treatment	158 €	934 €	-776 €
Retreatment with IAT	495 €	706 €	-211 €
Total graft loss	**2,334 €**	**2,607 €**	**-274 €**
Total monitoring costs of transplant	**3,581 €**	**3,235 €**	**346 €**
Total end of life costs	**3,156 €**	**3,199 €**	**-43 €**
Total	**82,332 €**	**64,046 €**	**18,286 €**

Footnotes

Figure 2. Tornado diagram

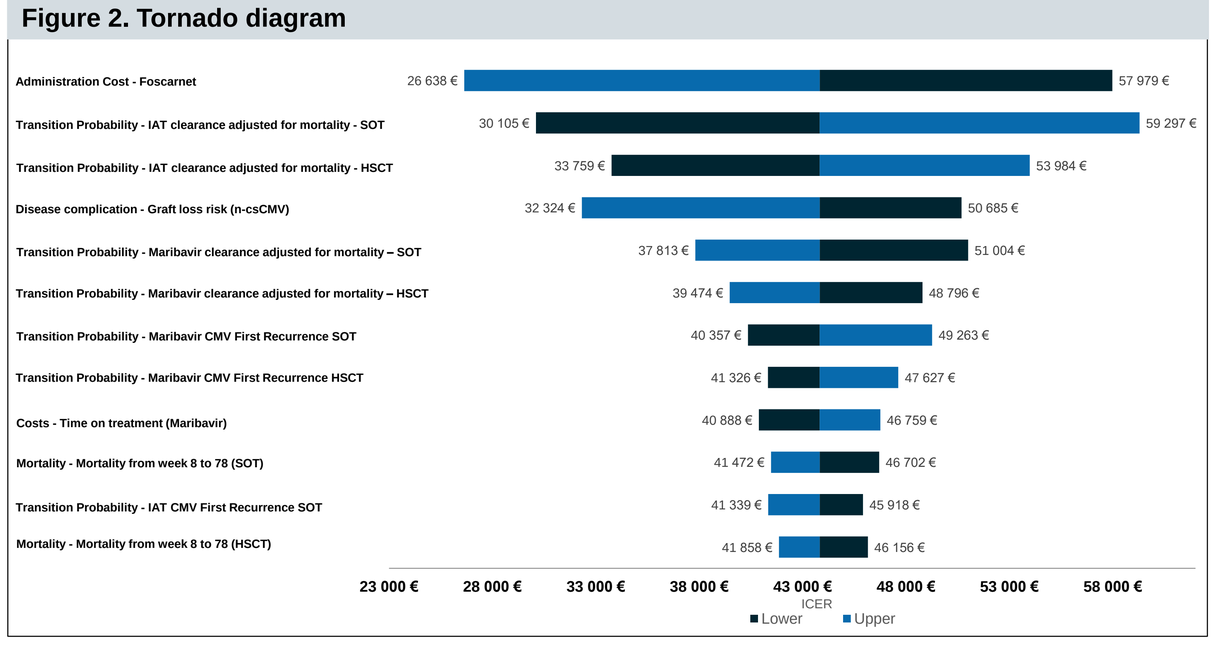
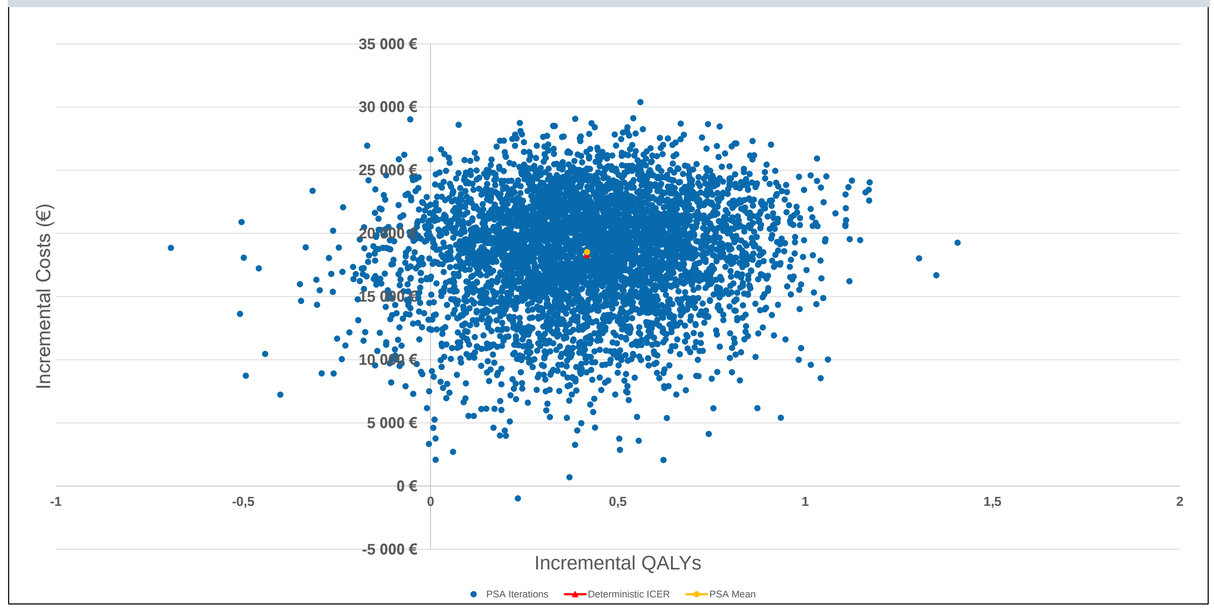


Figure 3. Incremental cost-effectiveness scatterplot



CONCLUSIONS

- This cost-effectiveness analysis indicates that MBV is a cost-effective strategy in France compared to alternative anti-CMV therapies for the treatment of patients with post transplant refractory CMV infection.
- The ICER of MBV versus IAT is 43,824 €/QALY for an incremental costs of 18,286 € and an incremental QALY of 0.42.
- Sensitivity analyses demonstrated a limited deviation from the ICER (+1.26%) ensuring the robustness of this cost-effectiveness analysis.
- The robustness of the model will help to understand the potential impact of MBV in terms of externalities and savings, and on benefit of drug beyond clinical value.

DISCLOSURES: AN, CL and MM: employees of Takeda France SAS. SLA: employees of Takeda Development Center Americas. SL and LM: employees of stève consultants who were supported by Takeda France SAS for their contributions to this work.

Disclaimer: *This poster is intended for healthcare professionals only.*

ACKNOWLEDGMENTS: This study was sponsored by Takeda France SAS.

REFERENCES: [1]Maribavir for Refractory Cytomegalovirus Infections With or Without Resistance Post-Transplant: Results From a Phase 3 Randomized Clinical Trial
[2]Téhard et al. (2020). Value of a QALY for France: A New Approach to Propose Acceptable Reference Values. Value in Health, 23(8)

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