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Cost-Effectiveness Analysis of Dostarlimab Plus Carboplatin-Paclitaxel in Primary Advanced or Recurrent Endometrial Cancer With Deficient Mismatch Repair (dMMR) and High Microsatellite Instability (MSI-H) in France

Dostarlimab + CP is cost-effective compared to CP alone in the treatment of patients with pA/R EC dMMR/MSI-H in France leading to an ICER of 43k€/QALY as base case, and 72k€/QALY with additional conservative assumptions made per HAS.

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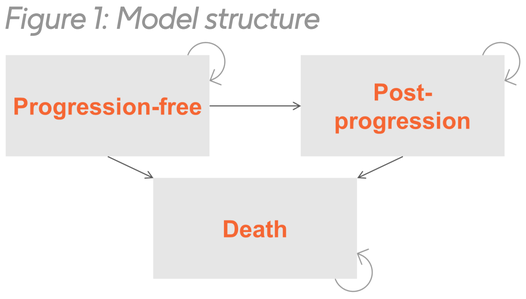
Aims

We assessed the cost-effectiveness of dostarlimab plus carboplatin-paclitaxel (D+CP) versus CP alone in primary advanced or recurrent endometrial cancer (pA/R EC) with deficient mismatch repair (dMMR) and high microsatellite instability (MSI-H) according to French HTA requirements.

Methods

A partitioned survival model (progression-free, post-progression, and death) comparing dostarlimab plus CP (D+CP) versus CP was developed (Figure 1).

Figure 1: Model structure



A time horizon of 20 years in the base case analysis was considered.

A collective perspective restricted to the health system was retained.

Costs of treatment acquisition and administration, disease monitoring, management of adverse events, subsequent treatments post-progression, transportation, and end-of-life care were considered and based on public French data.

Subsequent treatment distribution was based on RUBY trial and confirmed by expert opinion and a retrospective study of women with EC identified in the French National Health Insurance database from 2016–2021 (MOONBEAM).[1]

Utility scores were estimated from RUBY trial, adjusting for French population[2] at 0.896 in the progression-free state, and 0.853 in the post-progression state.

The efficacy curves (OS and PFS) were extrapolated according to the AIC and BIC criteria.

The treatment duration was extrapolated based on a maximum treatment period of 3 years.

All causes grade ≥3 adverse events with an incidence of ≥5% in RUBY trial were considered in the analysis.

A dossier was initially submitted and then amended following technical discussions with the HAS. Here, we presented the initial model submitted to HAS, and the conservative scenarios requested by HAS aimed at limiting model uncertainty as evaluated per HAS guidelines.

Results

In the dossier initially submitted, the average survival of patients treated with D+CP was 8,65 years, corresponding to 6,98 QALY. Dostarlimab was associated with an incremental survival gain of 4,88 years (+129%) and 3,91 QALY (+127%) *versus* CP alone. The total cost of patients treated with CP was €45,864. Treatment with dostarlimab was associated with an additional cost of €171,708. D+CP leads to an ICER of €43,956/QALY compared to CP alone.

During the technical exchange, the HAS made several requests with varying impacts on the ICER, as detailed in Table 1.

Table 1: Impact on ICER of HAS requested choices

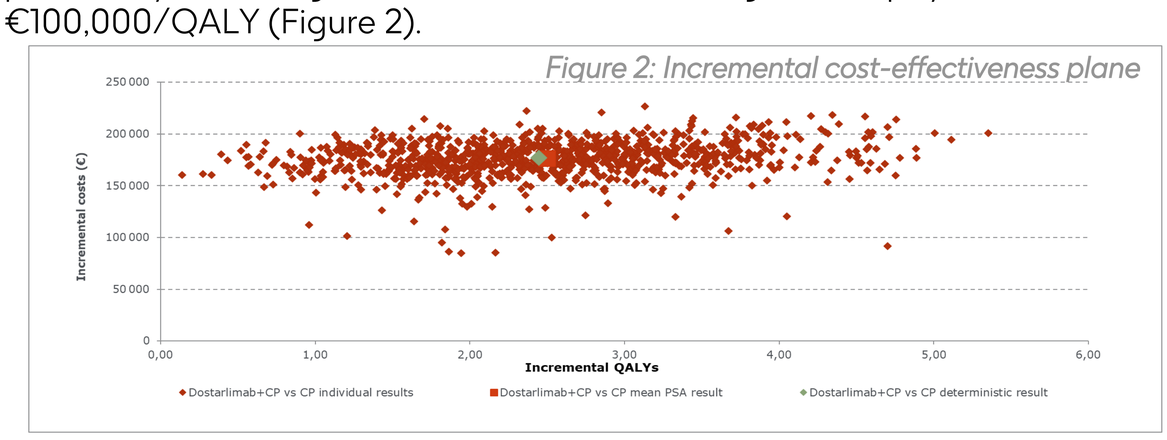
Criteria		ICER (€/QALY)	% of variation vs first submission
Initial ICER submitted		43 956	-
Final ICER		72 256	+ 57%
Conservative scenarii	Shorter time horizon (20 years → 15 years)	51 935	+ 18%
	Immediate waning effect on PFS after treatment	47 672	+8%
	Gradual waning effect on OS after treatment*	63 640	+45%

*extremely conservative assumption given the consistent plateau seen in RUBY IA1 and IA2 datacuts in dMMR, which indicates a potential curative intent [10].

Over a restricted 15-years time horizon, the average survival of patients treated with D+CP was 7.41 years, corresponding to 5.98 QALY. Dostarlimab was associated with an incremental survival gain of 3.05 years (+70%) and 2.45 QALY (+69%) *versus* CP alone The total cost of patients treated with CP was €40,391. Treatment with dostarlimab was associated with an additional cost of €176,745. This is explained by the treatment duration (maximum of 3 years). In parallel, patients treated with dostarlimab progressed more slowly, resulting in lower post-progression costs and therefore generating savings. Thus, D+CP leads to an ICER of €72,256/QALY compared to CP.

Probabilistic sensitivity analyses (1,000 iterations) based on HAS case confirmed the cost-effectiveness results of dostarlimab, with 80% probability to being cost-effective at a willingness-to-pay threshold of €100,000/QALY (Figure 2).

Figure 2: Incremental cost-effectiveness plane



Background

Deficient mismatch repair (dMMR) and high microsatellite instability (MSI-H) accounts for 15% to 33% of endometrial cancer (EC).[3,4,5,6,7,8]

Marketing Authorization was granted in Europe in December 2023 based on part 1 of the RUBY clinical trial.[9]

Conclusions

Despite a strict conservative approach required by the HAS, dostarlimab + CP in the treatment of patients with dMMR/MSI-H pA/R EC is a cost-effective strategy in France.

This outcome is attributed to the substantial improvement of PFS (HR=0.28) and OS (HR=0.30) in RUBY trial, the maintenance of patients as progression-free that is associated with better utility value, and the reduced subsequent treatment cost.

Abbreviations

EC, endometrial cancer
pA/R, primary advanced/recurrent
CP, carboplatin-paclitaxel
D + CP, dostarlimab + carboplatin-paclitaxel
dMMR, deficient mismatch repair
MSI-H, high microsatellite instability
OS, overall survival
PFS, progression-free survival
HAS, Haut Autorité de Santé
QALY, quality-adjusted life-year
ICER, incremental cost-effectiveness ratio
AIC, Akaike information criterion
BIC, Bayesian information criterion

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Authors disclosure

Thibault de la Motte Rouge and Jean-Sebastien Frenel have no conflicts to declare.
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