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Cost-Effectiveness of Dostarlimab Monotherapy for the Second-Line Treatment of Advanced or Recurrent dMMR/MSI-H Endometrial Cancer Patients Previously Treated With Platinum-Based Chemotherapy in Spain

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Context and aim

- The majority of endometrial cancers (EC) are detected at an early stage. However, around 20% of cases are diagnosed at an advanced stage, when their five-year survival rate is only 20%[1].
- In these cases, first-line treatment is a combination of carboplatin and paclitaxel, and, as of the study date, no designated second-line (2L) treatment exists.
  - Clinical outcomes for 2L chemotherapy generally showed an objective response rate of less than 20%, progression-free survival (PFS) less than 4 months, and overall survival (OS) less than 12 months, regardless of the chemotherapy used [2, 3, 4, 5, 6].
- For mismatch repair deficient (dMMR) / microsatellite instability-high (MSI-H) EC patients, dostarlimab addresses this gap, supported by the efficacy results from the GARNET study[7].
- Dostarlimab is an anti-programmed cell death ligand-1 (PD-L1) therapy that binds to the PD-1 receptor and blocks interactions with its ligands for patients with advanced or recurrent EC.
- The objective of this study is to evaluate the cost-effectiveness of dostarlimab compared to the historic 2L standard of care (SoC) treatment (weighted basket of all therapies currently used in practice) for the population of interest from the perspective of the Spanish National Health System (NHS).

Population

- Adult women with advanced or recurrent dMMR / MSI-H EC.
- Previously treated with platinum-based chemotherapy and PD-L1 inhibitor naïve.

Study design

- A cost-effectiveness model was developed using a partitioned survival model structure with three mutually exclusive states: 1) PFS, 2) post-progression survival (PPS), and 3) death. Individual patient data were used to model the survival curves and fitted to parametric survival models:
  - The efficacy of 2L dostarlimab was modeled using individual patient data extracted from the GARNET trial[7].
  - The efficacy of 2L SoC treatment for patients similar to those in the GARNET trial was modeled using individual patient data from the UK National Cancer Registration and Analysis Services[14] (NCRAS) (closest country to Spain with available data) by digitizing their Kaplan-Meier curves.
  - The survival extrapolation curve was chosen based on model fit and input from clinical experts.
- Costs (€2023) and resource use associated with screening, pharmacological treatments, disease management, monitoring, subsequent treatments, and adverse events (AE, grade ≥3, ≥5% patients[7, 4]) were considered. Resource use was obtained from expert validation or literature sources, while cost data were obtained from national databases[8, 11]. Utilities for health states[4, 7] and the costs and disutilities for adverse events were extracted from the literature and national databases[8, 9, 12, 13].
- Deterministic costs and quality-adjusted life years (QALYs) were calculated over a 40-year time horizon, which effectively covered the entire lifetime of the patients, and the incremental cost-effectiveness ratio (ICER) was calculated. The model cycles were 3 weeks long, and costs and QALYs were discounted at 3% per year.
- Univariate and probabilistic sensitivity analysis was performed.

Table 1: **Main parameters**

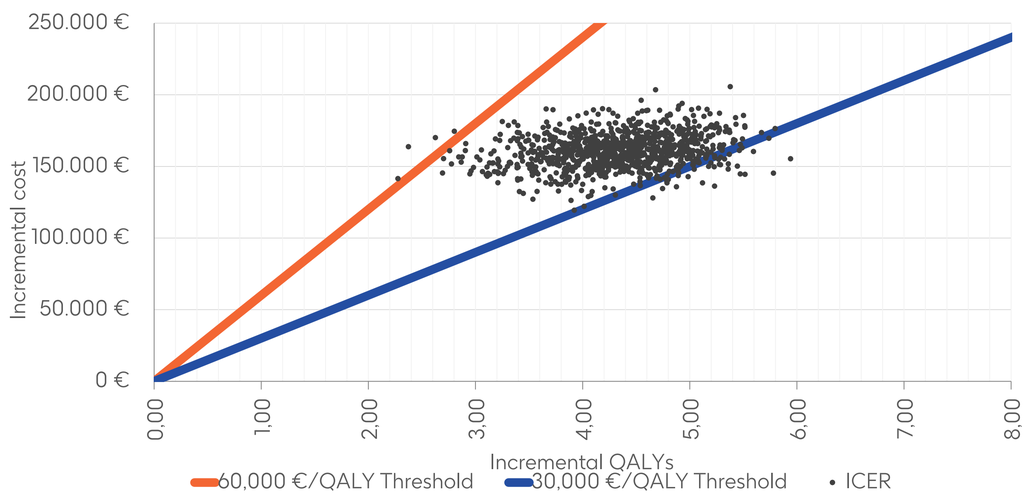
Item	Value	Source
Screening and follow-up unit costs, €		
Screening	123,93	(8)
Follow-up visit, first	180,59	(8)
Follow-up visit, subs.	176,31	(8)
Blood test	75,29	(8)
Computed tomography	202,82	(8)
Specialist nurse visit	71,17	(8)
End of life and AE unit costs, €		
End of life care	2 912,90	(10)
Abdominal pain	334,82	(8)
Other AE*	528,95	(8)
Pharmacological costs (per cycle), €		
Dostarlimab 500 mg‡	5 588,23	(11)
Standard of care	645,92	(11)
Utilities		
PFS, ≤ 5y pre-death	0,60	(7)
PFS, > 5y pre-death	0,72	(7)
PPS, ≤ 5y pre-death	0,55	(7)
PPS, > 5y pre-death	0,66	(7)
Disutilities per adverse event		
Abdominal pain	-0,07	(9)
Anemia	-0,12	(9)
Fatigue	-0,07	(9)
Nausea	-0,05	(12)
Neutropenia	-0,09	(9, 12)
Thrombocytopenia	-0,0001	(12)
Vomiting	-0,23	(13)
Leukopenia	-0,09	(9)

*The cost for all other adverse events is standardized to the hospitalization cost without an overnight stay. This cost is then multiplied by the incidence of AEs in each treatment arm.
‡During the first 4 cycles, a dose of 500 mg was administered every 21 days. From the fifth cycle on, a dose of 1000 mg was administered every 42 days.

Results

- Patients treated with SoC had 0.9 QALYs with a cost of 15 278 €.
- Patients treated with dostarlimab had 5.3 QALYs with a cost of 176 446 €.
- The incremental QALYs were +4.4, while the incremental costs were 161 168 €. The deterministic ICER was 36 403 €/QALY.
- At a cost-effectiveness threshold of 30 000 €/QALY, 3.5% of simulations are cost-effective, and this percentage increases to 99.6% at a threshold of 60 000 €. The mean probabilistic ICER was 37 187 €/QALY
- One-way sensitivity analysis demonstrated that patient utility at diagnosis had the greatest impact on the final outcome, while the other variables did not change the ICER significantly.

Figure 1: **Probabilistic SA: cost-effectiveness**



SA: sensitivity analysis

Conclusions

2L dostarlimab provides nearly six-times more QALYs than historic SoC at an acceptable incremental cost.

The treatment is cost-effective at a threshold of 60 000 €/QALY, which has previously been used for oncology treatments in Spain from an NHS perspective.[15, 16]

Dostarlimab is a valuable treatment option for 2L dMMR/MSI-H EC patients in terms of efficacy and economic viability.

Abbreviations

AE: adverse events. EC: endometrial cancer. ICER: incremental cost-effectiveness ratio. MSI-H: high microsatellite instability. NHS: National Health System. PD-L1: anti-Programmed cell death ligand-1. PFS: progression-free survival. QALY: quality-adjusted life years. PPS: post-progression survival. WTP: willingess-to-pay. SoC: standard of care. 2L: second line. dMMR: deficient mismatch repair.

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