Cost-Effectiveness of Olaparib Plus Bevacizumab First-Line Maintenance in Ovarian Cancer Alongside the PAOLA-1 Trial

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Objective

PAOLA-1 trial demonstrated a clinically meaningful progression-free survival *(PFS)* and overall survival *(OS)* benefit when maintenance olaparib was added to bevacizumab in newly diagnosed advanced ovarian cancer patients with a positive tumor homologous recombination deficiency *(HRD)* test, leading to a U.S. Food and Drug Administration *(FDA)* / European Medicines Agency *(EMA)* label in 2020. The aim of this study was to conduct a cost-effectiveness analysis *(CEA)* from the French National Health perspective and based on patient-level data from the PAOLA-1 trial in the HRD positive population *(n = 387/806)*.

Methods

Study population

- The CEA was preplanned as a secondary objective of the randomized, double-blind, PAOLA-1 phase III trial run in 11 countries *(NCT02477644) [1]*.
- Patients aged ≥18 years with newly diagnosed advanced stage [International Federation of Gynecology and Obstetrics *(FIGO)* stage III or IV] high-grade serous or endometrioid ovarian cancer, and complete or partial response or no evidence of disease following first line platinum-based chemotherapy plus bevacizumab were randomized 2:1 to olaparib *(300 mg twice daily)* plus bevacizumab or placebo plus bevacizumab.
- Prespecified tumor HRD status was determined retrospectively before the primary analysis by MyChoice® HRD Plus assay *(Myriad Genetic Laboratories, Inc., Salt Lake City, UT)*.

Cost data

- Individual healthcare consumptions, including subsequent therapies, were drawn from the case report.
- Costs *(in 2022 euros)* were assessed from the French National Health perspective with a 60 month time horizon, and by distinguishing two periods ≤ 24 and >24 months. A 2.5% discount rate was applied.
- *Hospital stays*: the reasons for hospitalization were used to characterize diagnosis related groups *(DRGs)*. The costs were then valued using the national cost studies *(ENC 2019 V2021) [2]*. Costs for ambulance services were also included. Costs were inflated in 2022 euros.
- *Bevacizumab, olaparib, and subsequent therapies*: the quantities administered were multiplied by their prices *[3]*.
- *HRD status test*: price was derived from Elsea D et al. *[4]*.

Effectiveness and incremental Cost-Effectiveness Ratios (ICERs)

- Survival was based on the last data cut-off (March 2022) and calculated using restricted mean survival time *(RMST)*.
- ICERs were expressed in cost per progression free life year gained *(PF-LYG)* and in cost per life year gained *(LYG)*.
- Uncertainty was handled by bootstrapping *(1,000 replications)* and cost-effectiveness acceptability curves *(CEAC)* were generated.

Results

Patient characteristics

- From July 2015 through September 2017, 806 patients were randomized on the intent-to-treat population *(ITT)*. N = 387/806 were HRD-positive. Patients' characteristics are provided in *Table 1*.

Costs and incremental cost-effectiveness ratios (ICERs)

- Total mean costs per patient at 5 years were €112,510 *(SD: 50,519)* in the olaparib plus bevacizumab group and €70,517 *(SD: 62,312)* in the placebo plus bevacizumab group *(cf. Table 2)*.
- Mean progression free survival were 3.375 and 2.058 years respectively, leading to an ICER of €31,885 per PF-LYG.
- Mean overall survival were 4.20 in the olaparib plus bevacizumab group *(255/387)* and 3.875 years in the placebo plus bevacizumab group *(132/387)*. The corresponding ICER was €129,209 per LYG. Cost-effectiveness plans *(scatter of points and confidence ellipses)* and acceptability curves are presented in *Figures 1 and 2*.

HRD positive population	Olaparib (n = 255)		Placebo (n = 132)		Subtotal (n = 387)	
Age (years)						
N	255		132		387	
Mean (Std)	58.5 (9.2)		57.3 (9.6)		58.1 (9.3)	
Median (min; max)	58.0 (32.0; 77.0)		58.0 (35.0; 82.0)		58.0 (32.0; 82.0)	
ECOG-PS						
0	190	(74.5%)	100	(75.8%)	290	(74.9%)
1	61	(23.9%)	31	(23.5%)	92	(23.8%)
Missing	4	(1.6%)	1	(0.8%)	5	(1.3%)
FIGO staging						
III B	25	(9.8%)	9	(6.8%)	34	(8.8%)
III C	157	(61.6%)	81	(61.4%)	238	(61.5%)
IV	73	(28.6%)	42	(31.8%)	115	(29.7%)

Table 1: Patient's characteristics

HRD positive population Costs *(in €, 2022)*	Olaparib *(n = 255)* *Mean (SD)*	Placebo *(n = 132)* *Mean (SD)*
Period 1 (≤ 24 months)		
Hospitalisation	€5,924 *(8,990)*	€10,554 (12,251)
Transportation	€436 *(701)*	€730 (784)
Olaparib	€69,542 *(43,583)*	€0 (0)
Myriad MyChoice Plus HRD test	€3,725 *(0)*	€0 (0)
Bevacizumab	€21,131 *(6,926)*	€19,989 *(7,852)*
Total cost at 2 years	€100,758 *(44,250)*	€31,273 *(13,446)*
Period 2 (>24 months)		
Hospitalisations	€4,847 *(7,356)*	€8,635 *(10,024)*
Transportation	€358 *(574)*	€598 *(642)*
Olaparib	€5,064 *(27,128)*	€21,736 *(51,171)*
Subsequent therapies	€1,483 *(10,140)*	€8,275 *(33,056)*
Total cost at 60 months	€112,510 *(50,519)*	€70,517 *(62,312)*

Table 2: Mean costs per patient

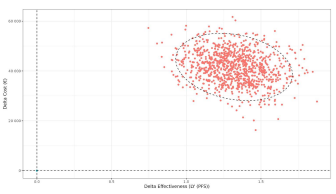

Figure 1a: Cost-effectiveness plan (PF-LYG)

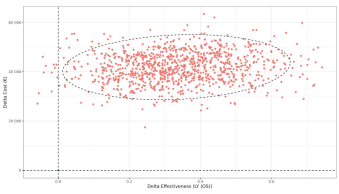

Figure 2a: Cost-effectiveness plan (LYG)

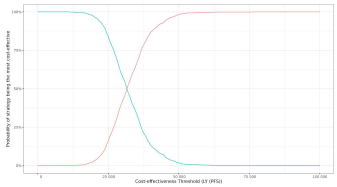

Figure 1b: Acceptability curve (PF-LYG)

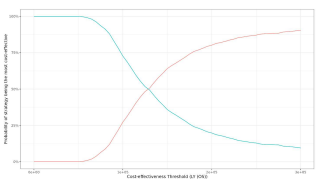

Figure 2b: Acceptability curve (LYG)

Conclusions

- The probability of olaparib plus bevacizumab being cost effective compared with placebo plus bevacizumab was 28% at €100,000 level of willingness to pay per LYG.
- The 60 month time horizon is a limitation of the current analysis. ICER is expected to reduce with further follow-up as the long-term benefit on overall survival is expected to increase. ICER calculated using overall survival endpoint should be taken with caution, as crossover adjustment methods have not yet been applied.

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[3] https://www.atih.sante.fr/unites-communes-de-dispensation-prises-en-charge-en-sus; https://base-donnees-publique.medicaments.gouv.fr/extrait.php?specid=60059820#.
[4] Elsea D et al. Cost-Effectiveness Analysis of Olaparib in Combination with Bevacizumab Compared with Bevacizumab Monotherapy for the First-Line Maintenance Treatment of Homologous Recombination Deficiency-Positive Advanced Ovarian Cancer. Pharmacoecon Open. 2022 Nov;6(6):811-822.

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