

# Cost comparison of adverse event management with poly(ADP-ribose) polymerase (PARP) inhibitors or chemotherapy in gBRCAm, HER2-negative advanced breast cancer (ABC) – a US and German healthcare perspective

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## Background

- gBRCAm advanced breast cancer (locally advanced or metastatic cancer, ABC) represents ~5% of the overall breast cancer population and is associated with younger age at diagnosis and aggressive disease characteristics[1,2]
- Until recently, no targeted therapeutic options were approved for patients with gBRCAm, HER2-negative ABC – cytotoxic chemotherapy was the mainstay treatment and prognosis was generally poor
- PARP inhibitors olaparib and talazoparib have been shown to significantly improve progression-free survival and delay deterioration in quality of life in patients with gBRCAm, HER2-negative ABC vs chemotherapy[3–5]
- Treatment decisions are based on multiple factors including effectiveness, safety profile, treatment costs, ease of administration and quality of life impact

## Objectives

- The aim of this study is to describe and compare the adverse event (AE) profiles of three treatment strategies in gBRCAm, HER2-negative ABC: the licensed PARP inhibitors olaparib and talazoparib, and chemotherapy
- The associated management costs are explored from a USA and German healthcare system perspective

## Methods

### Systematic literature review and network meta-analysis

- A systematic literature review (SLR) following the guidelines published by the Cochrane Collaboration was conducted to identify clinical trials that reported data on the incidence of AEs with olaparib, talazoparib and chemotherapy in ABC
- A Bayesian network meta-analysis (NMA) was performed using data from PARP inhibitor clinical trials to determine the odds ratios (OR) for Grade 3–4 AEs in each treatment arm versus a pooled chemotherapy arm

### Adverse event incidence

- AE incidence was compared in two separate analyses: firstly, a within-study comparison, with AE incidence expressed as the percentage of patients in the trial arm experiencing the selected AE; secondly, a cross-study comparison, using the relative treatment effects captured by the ORs from the NMA
- The formula used to calculate the AE incidence (p<sub>j</sub>) in the cross-study comparison is:

$$p_j = ([OR]_{ij} * p_i) / (1 + p_i ([OR]_{ij} - 1))$$

p<sub>i</sub> = Pooled incidence of selected AE for TPC

p<sub>j</sub> = Adjusted incidence of selected AE for the PARP inhibitor

[OR]<sub>ij</sub> = Odds Ratio of observing selected AE for the PARP inhibitor relative to TPC

### Calculation of costs

- The average per-patient costs of AE management for olaparib, talazoparib and chemotherapy were generated by multiplying the AE incidence data by a weighted average of inpatient and outpatient costs for each AE
- Costs covering the timeframe of the trials were calculated from both a German and USA healthcare system perspective
- Unit costs (per event) were obtained via systematically reviewing the literature and inflated to 2018 price levels[6–9]
- The proportion of events managed in the inpatient/outpatient setting were identified through a targeted literature review and validated through expert medical opinion

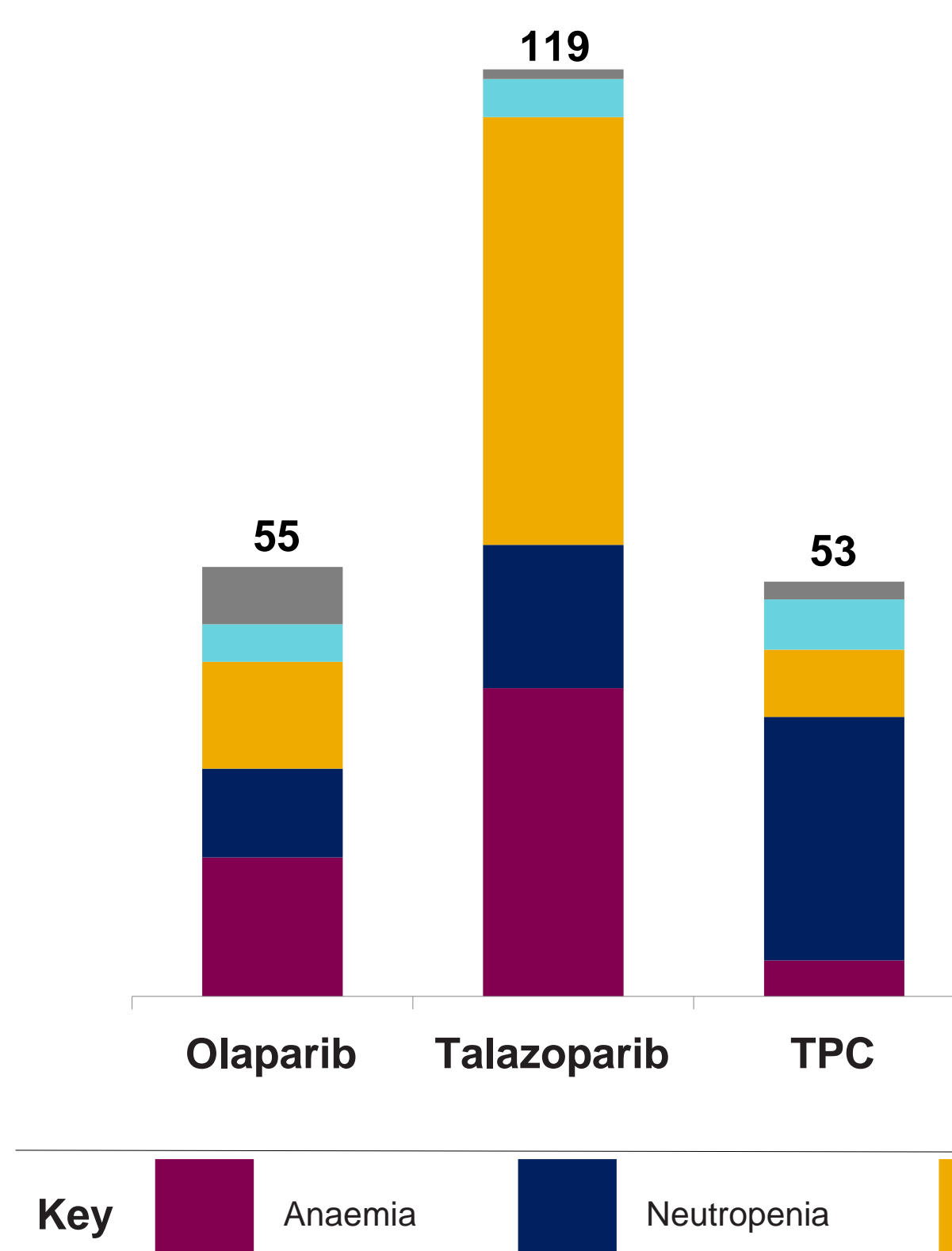
## Results

- The SLR identified OlympiAD (NCT02000622) and EMBRACA (NCT01945775) trials of PARP inhibitors in gBRCAm, HER2-negative ABC, comparing olaparib and talazoparib with chemotherapy of physician choice (TPC, consisting of capecitabine, vinorelbine, gemcitabine or eribulin)[3,4]
- Trial design and patient population were analysed and deemed sufficiently similar to carry out cross-study comparison for a sub-set of Grade 3–4 AEs that were consistently defined across the trials
- AEs included covered the main drivers of AE profile for comparators: four haematological AEs (anaemia, thrombocytopenia, neutropenia and leukopenia) and one non-haematological AE (fatigue)
- In within-study comparisons, olaparib was estimated to have lower AE costs than TPC in both the USA and Germany. Talazoparib was estimated to have higher AE costs than TPC. Total AE costs for TPC were comparable across OlympiAD and EMBRACA (Table 1)
- Olaparib had a favourable safety profile vs talazoparib in the cross-study comparison; this difference was driven by lower haematological Grade 3 or 4 AE incidence (Figure 1)

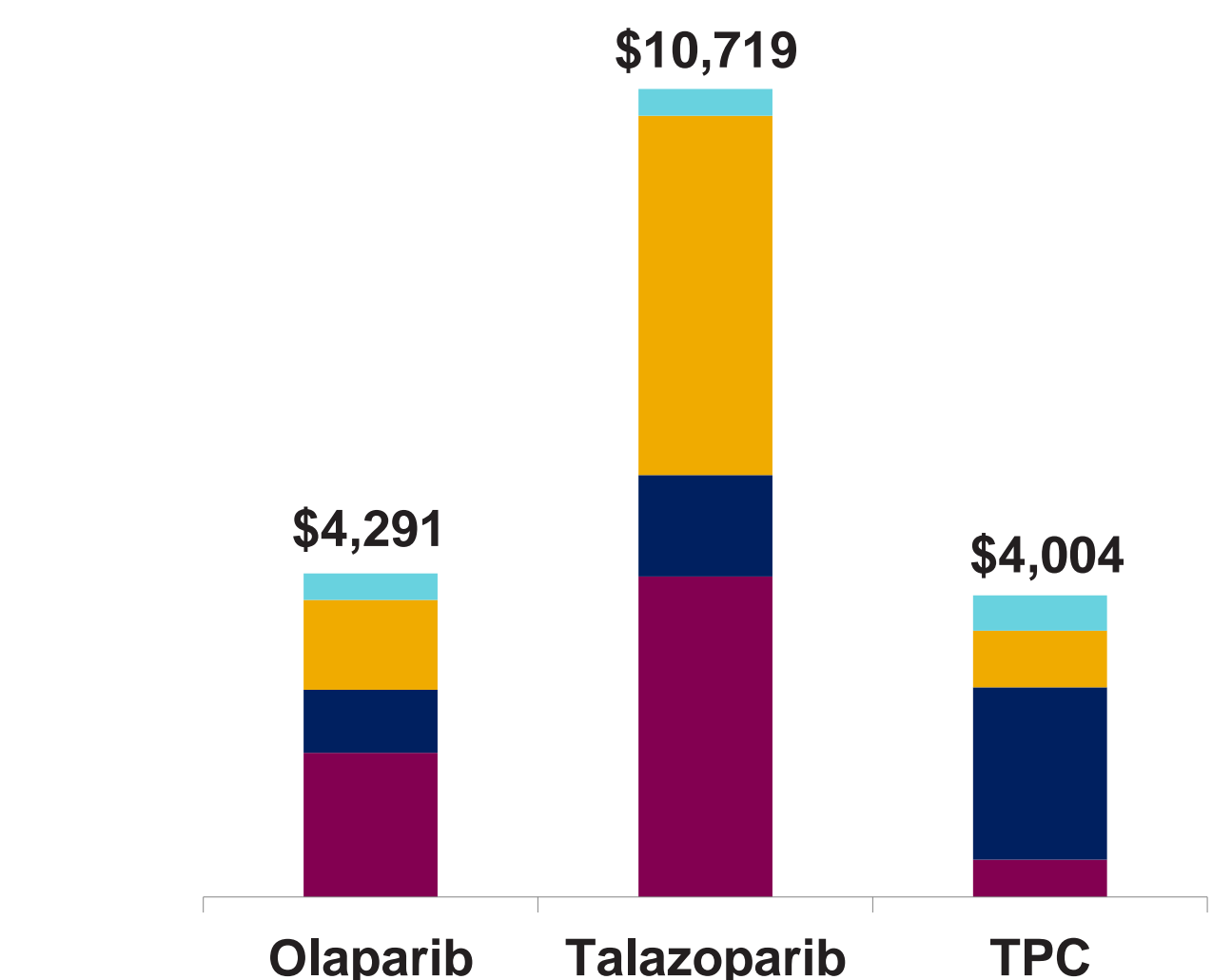
**Table 1:** Management costs (per patient, by AE category, rounded down to the nearest \$/€) – within-study analysis

	OlympiAD		EMBRACA	
	Olaparib	TPC	Talazoparib	TPC
<b>USA (\$)</b>				
Anaemia	1726	471	4200	510
Neutropenia	677	1925	1531	2549
Thrombocytopenia	562	1598	1271	137
Leukopenia	178	240	485	637
<b>Total</b>	<b>3143</b>	<b>4236</b>	<b>7489</b>	<b>3835</b>
<b>Germany (€)</b>				
Anaemia	207	56	505	61
Neutropenia	67	191	152	253
Thrombocytopenia	26	75	60	6
Leukopenia	18	23	48	63
<b>Total</b>	<b>318</b>	<b>347</b>	<b>765</b>	<b>384</b>

**Figure 1:** Mean number of Grade ≥3 AEs per 100 patients by AE category – cross-study analysis

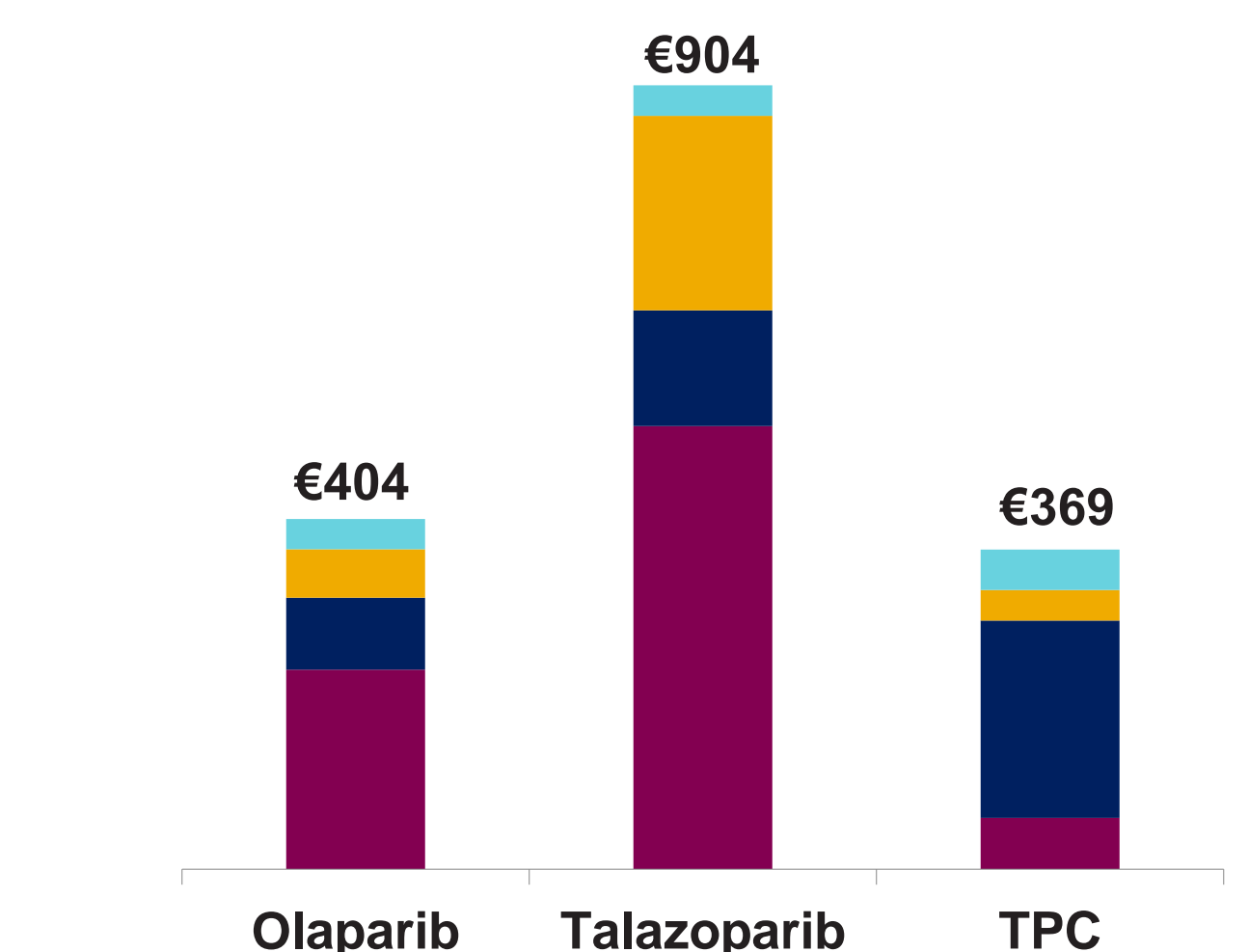


**Figure 2:** Management costs per patient by AE category – USA, cross-study analysis



- Similar AE management costs were estimated for olaparib and TPC in both the USA and Germany (Figures 2 and 3)
- An increased incidence of anaemia, thrombocytopenia and neutropenia resulted in greater AE management costs for talazoparib vs olaparib
- Uncertainty in the base case is driven by absolute costs selected and inpatient:outpatient weighting – varying costs simultaneously ±20%, and setting inpatient management to 100% for all included AEs did not change the base case conclusions

**Figure 3:** Management costs per patient by AE category – Germany, cross-study analysis



## Conclusions

- Based on RCT evidence, olaparib appears to have a favourable safety profile compared with talazoparib and TPC, which translates to cost savings in managing Grade ≥3 AEs
- Despite additional time on therapy, olaparib had lower AE management costs than TPC in the OlympiAD study; the adjusted comparison indicates similar costs to TPC based on pooled OlympiAD/EMBRACA data
- This conclusion must be interpreted with caution due to uncertainty in AE costing/management setting, and heterogeneity in AE reporting between studies
- Real-world studies are required to capture the resource use associated with AE management in this patient population

## References

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**Key** Anaemia Neutropenia Thrombocytopenia Leukopenia Fatigue (no cost applied)