Olaparib not cost-effective as maintenance therapy for platinum-sensitive, BRCA1/2 germline-mutated metastatic pancreatic cancer

Authors: Tarun Mehra[1], Judith E. Lupatsch[2], Thibaud Kössler[3], Konstantin Dedes[4], Alexander R. Siebenhüner[5], Roger von Moos[6], Andreas Wicki[1], Matthias E. Schwenkglenks[2]

Affiliations: 1) Department of Medical Oncology and Hematology, University Hospital of Zurich, Rämistrasse 100, CH-8091 Zurich. 2) Institute of Pharmaceutical Medicine (ECPM) and Health Economics Facility, Department of Public Health, University of Basel, Basel. 3) Service d'oncologie, Hôpitaux Universitaires Genève, Geneva. 4) Breast Cancer Center Zürichsee, Zurich. 5) Onkozentrum Hirslanden Zurich AG and University of Zurich, Zurich. 6) Department of Medical Oncology and Hematology, Cantonal Hospital of Graubünden, Chur

Objective: To assess the cost-effectiveness and budget impact of olaparib as a maintenance therapy in platinum-responsive, metastatic pancreatic cancer patients harboring a germline BRCA1/2 mutation, using the Swiss context as a model.

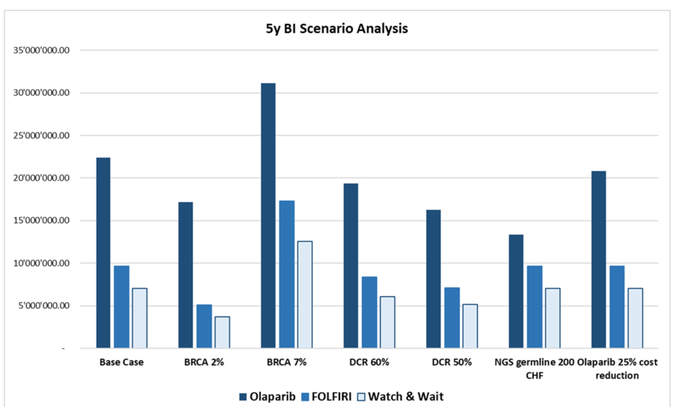
Methods: Based on data from the POLO trial, published literature and local cost data, we developed a partitioned survival model of olaparib maintenance including full costs for BRCA1/2 germline testing compared to FOLFIRI maintenance chemotherapy and watch-and-wait. We calculated the incremental cost-effectiveness ratio (ICER) for the base case and several scenario analyses and estimated 5-year budget impact.

Table 1. Results from cost-effectives analysis

Strategy	Cost	Incr Cost	Eff	Incr Eff	ICER[3]	ICER without BRCA cohort testing
Base Case						
Observation	110,445	141,212	1.43	0.05	2,711,716	814,167
Maintenance	136,252	115,405	1.43	0.05	2,217,083	318,732
Olaparib	251,657		1.48			
Scenarios						
1 Olaparib - 25%	231,330	120,884	1.48	0.05	2,322,345	432,815
2 Olaparib OS curve	279,133	168,688	1.79	0.36	468,605	195,491
3 Different PD QALY[1]						
Observation	110,445		1.22			
Olaparib	251,657	141,212	1.37	0.15	943,604	283,188
4 Different PD QALY[1] + Olap OS curve						
Olaparib	279,133	168,688	1.61	0.39	429,973	195,492
5 Disutility for Adverse Events[2]						
Observation	110,445		1.08			
Olaparib	251,657	141,212	1.16	0.07	1,916,845	575,514
6 BRCA test USD 200 (180 CHF)						
Olaparib	153,043	42,598	1.48	0.05	818,007	

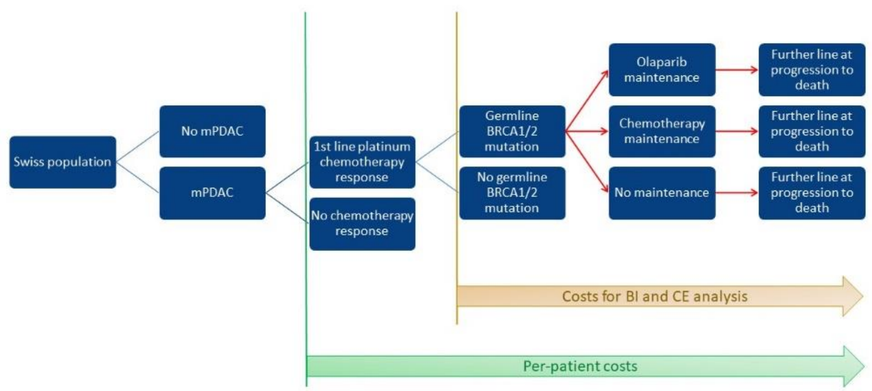
gBRCA1/2: germline BRCA1 and BRCA2. All costs in CHF.
1) Progressive disease utility: 0.58 [15], instead of 0.73 [29]
2) Disutility of – 0.2
3)Considering gBRCA1/2 testing costs of all eligible patients
The olaparib maintenance strategy included costs for gBRCA1/2 testing of all pancreatic cancer patients evaluated for eligibility.

Figure 3. 5-year Budget Impact



DCR: disease control rate; NGS: next generation sequencing. All costs in CHF
Scenario analysis of the 5-year total costs for the treatment of platinum-sensitive germline BRCA 1/2 mutated pancreatic cancer in Switzerland with either olaparib maintenance, FOLFIRI maintenance or watch and wait strategy (accounting for costs for germline BRCA 1/2 companion diagnostics for screening failures) (yearly incidence of n=23). Costs include maintenance therapy, 2nd line chemotherapy with gemcitabine and nab-paclitaxel, as well as palliative end of life care, including costs of side-effects, routine medical visits and laboratory testing as well as imaging costs. Costs for standard care first line platinum-based chemotherapy and routine somatic genetic testing not included.

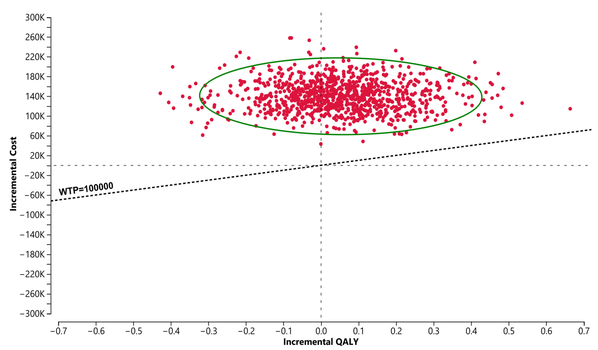
Fig 1. Clinical pathway model



mPDAC: metastatic pancreatic ductal adeno-carcinoma. 1st line platinum chemotherapy: FOLFIRINOX. Chemotherapy maintenance: FOLFIRI. Further line chemotherapy: gemcitabine & nab-paclitaxel. All pathways assume 1.5 months of palliative end-of-life care.

Results: Comparing olaparib with watch-and wait and maintenance chemotherapy resulted in incremental cost-effectiveness ratios of CHF 2,711,716 and CHF 2,217,083 per QALY gained, respectively. The 5-year costs for the olaparib strategy in Switzerland would be CHF 22.4 million, of which CHF 11.4 million would be accounted for by germline BRCA1/2 screening of the potentially eligible population. This would amount to a budget impact of CHF 15.4 million (USD 16.9 million) versus watch-and-wait

Figure 2. Probabilistic Sensitivity Analysis Olaparib versus Observation – Base Case



QALY: quality-adjusted life-year. WTP: willingness-to-pay threshold (CHF).

Conclusion: Olaparib is not a cost-effective maintenance treatment option. Companion diagnostics are an equally important cost driver as the drug itself.

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Contact information:
Dr. med. Tarun Mehra
tarun.mehra@usz.ch