STUDY REPORT SYNOPSIS

C-PATROL

A single arm, prospective non-interventional study to collect Clinical and Patient Reported outcome data in an Olaparib treated *BRCA*m+ PSR ovarian cancer population

Milestones:	First patient in (or database start date)	13OCT2015
	Last patient last visit	01DEC2022
Phase of development:	Non-interventional	
Sponsor:	AstraZeneca GmbH	
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This study was performed in compliance with Good Clinical Practice (GCP) and Good Pharmacoepidemiology Practice (GPP), including the archiving of essential documents.

Background/rationale: Maintenance therapy with poly(ADP-ribose) polymerase (PARP) inhibitors has achieved significant clinical efficacy in the treatment of platinum-sensitive relapsed ovarian cancer (PSR OC). The approval of olaparib maintenance treatment was based on two randomized clinical trials (study 19 and SOLO2) that showed significant improvements in progression-free survival (PFS) versus placebo in patients with PSR *high-grade* epithelial OC who are in response (complete or partial) to retreatment with platinum-based chemotherapy (PBC). This prospective non-interventional study was designed to generate real-world clinical and patient-reported outcome (PRO) data on olaparib maintenance monotherapy in this patient population with a confirmed *BRCA1/2* mutation who are treated according to label in Germany.

Objectives: The primary objective is to determine the effectiveness of olaparib maintenance monotherapy through determining investigator-assessed PFS according to evaluation criteria used in routine clinical practice. Relevant secondary objectives are to determine overall survival (OS) and safety.

Study design: This is a German prospective, non-interventional study (pursuant to § 67 (6) German Medicines Act [AMG]) to collect real-world clinical and patient-reported outcome (PRO) data in PSR OC patients with a *BRCA1/2* mutation (germline and/or somatic) treated with olaparib maintenance monotherapy according to label (hard capsules (HC) and since August 2018 also film-coated tablets (FT).

Data source: Patients were recruited in a consecutive manner by 68 hospital or practice-based oncologists or gynaecologists in Germany who regularly treat patients with OC. Data of 277 enrolled patients were collected over a period of up to 7 years. The patients' data that were collected during routine visits were transferred into an eCRF. In addition, patients completed paper PRO questionnaires during routine visits (during follow-up the questionnaires could also be completed at home) that were sent to the CRO and entered in the eCRF by double data entry.

Study population: Adult patients with *BRCA1/2*m PSR *high-grade* epithelial OC who were in response (complete or partial) to PBC were included in the study in a consecutive manner. Patients had to be eligible and planned for olaparib maintenance monotherapy. Between October 13th, 2015, and September 30th, 2019, 277 patients gave their written informed consent and were enrolled in the study. Last patient last visit (LPLV) was on December 1st, 2022. Of the 274 patients that received at least one dose of olaparib (safety set), 7 violated inclusion or exclusion criteria. Thus, 267 patients were included in the intention-to-treat set (ITT).

Inclusion criteria: Patients observed in this study had to fulfil all of the following criteria:

(1) First or further recurrence of platinum-sensitive *high-grade* serous epithelial ovarian, fallopian tube, or primary peritoneal cancer confirmed by biopsy.
Platinum-sensitivity defined as disease progression ≥ 6 months after completion of last PBC.

(2) In response to PBC of current relapse.

(3) (Likely) pathogenic *BRCA1/2* mutation (germline and/or somatic) according to *BRCA1/2* test result.

(4) Eligible for treatment with olaparib according to SmPC.

(5) Able to read and understand German, English, Turkish or Arabic.

(6) Aged ≥ 18 years.

(7) Signed written informed consent.

Exclusion criteria: Patients observed in this study must not fulfil any of the following criteria:

(1) Known hypersensitivity to olaparib or any of the excipients of the drug.

(2) Start of olaparib monotherapy more than 14 days before signed written informed consent.

(3) Pregnancy or breast feeding (women of childbearing potential must use reliable contraception according to standard of care).

Statistical methods: In accordance with the descriptive nature of the study, the analyses were of purely descriptive and explorative character. Variables are summarized by the appropriate methods: categorical variables by frequency tables and continuous variables by sample statistics (i.e. n, mean, standard deviation, minimum, Q1, median, Q3, maximum, nmiss). Time-to-event endpoints are analyzed by Kaplan-Meier methods. The median survival time is presented as well as the 95% confidence interval (CI). Safety analyses were performed for the SAF (all patients who signed the informed consent and received at least one dose of olaparib). All other analyses were performed for the ITT (all patients from the SAF who fulfilled all inclusion and exclusion criteria).

Results: This final analysis was performed with database lock on April 01st, 2023, comprising 277 patients enrolled between October 28th, 2015, and October 17th, 2019, and observed over a period of up to 7 years. The median duration of follow-up was 23.5 months (range 0.0–80.5).

Median age at enrolment was 60 years. The patients' performance status was generally good (ECOG ≤ 1: 93%), at least one concomitant disease was documented for 49% of patients. As required by the protocol, all patients had a confirmed (germline and/or somatic) mutation in *BRCA1*, *BRCA2* or both (*BRCA1/2*). Two-thirds (65.92%) of patients were detected with *BRCA1* mutations, 30.71% with *BRCA2* mutations, and 3.37% with both.

32% of patients underwent surgery for their current relapse and 78% of these had no macroscopic residual disease as outcome of surgery.

71.2% received two, 22.8% three and 6.0% received four or more prior lines of PBC. Neoadjuvant chemotherapy (NACT) was documented for 7.9% of patients. Most patients (97.8%) received carboplatin as their last PBC. On average, six cycles of PBC were administered. Most patients (69%) had a partial response to their most recent PBC.

67% of patients received prior targeted therapy, 98% of whom received bevacizumab. Prior radiotherapy was documented for 7.1% of patients.

More than two-thirds (68%) received olaparib at their first relapse. Most patients (83%) started olaparib treatment with HC, of whom 31% switched to FT; 17% started with FT. Median olaparib treatment duration was 13.6 months (0.1–80.9). 27 patients (10%) received olaparib for ≥ 5 years. 41 patients (15%) were still receiving olaparib at the end of the study.

Effectiveness: Median PFS, measured as date of first documented dose of olaparib until date of first progression as assessed by the investigator or death (of any cause), was 14.47 months (95% CI 12.40–18.03).

Median OS, defined as time between date of first documented dose of olaparib until death of any cause, was 35.36 months (95% CI 29.18–49.93).

Safety: Adverse events (AEs) were collected from first olaparib intake until at least 30 days after last intake of olaparib or, if AE was olaparib-related, until it resolved during complete follow-up period. AEs independent of severity (all CTCAE grade) were reported for 261 patients (95.26%) of the SAF. Most commonly documented non-haematologic AEs were nausea (45.99%), fatigue (39.05%) and vomiting (17.15%). Most common haematologic AE were anaemia (31.4%). CTCAE grade ≥ 3 AEs were reported for 110 patients (40.15%), most commonly anaemia (14.23%). Nine patients (3.28%) had an AE with the outcome of death. AEs were mainly managed by interrupting olaparib treatment

(32.85%) or changing its dose (21.90%); treatment was discontinued due to AEs for 11.31% of patients. AEs mainly occurred within the first 3 months of olaparib treatment.

The FACT-O TOI and total score as well as the FACIT-Fatigue score remained stable over time. The impact of nausea and vomiting on patients' daily lifes as measured by the FLIE questionnaire slightly increased during the first week of therapy with scores remaining stable afterwards.

Conclusion: This observational study shows that olaparib maintenance monotherapy is effective and safe in the real word setting in patients with PSR *BRCA1/2*m (germline and/or somatic) *high-grade* epithelial OC who are in response (complete or partial) to PBC. Thus, the findings support the use of olaparib in this patient group.

Publications: Several full publications are in preparation and are planned to be submitted during 2024.