IGCS 2022 Abstracts: Oral Abstract Presentations (Seminal Abstracts)

The IGCS 2022 program includes five seminal abstracts to be presented in the below session.

The session will be live-streamed in real-time on the Meeting Portal and recorded for on-demand viewing from 24 hours after the session ends until December 28, 2022.

Plenary 04: Surviving PARPs – Separating between Opinions and Facts

- **Friday, September 14, 2022**
- **02:45 PM - 03:55 PM**
- **Hall 501**

S001 / #1608

Plenary Session
PLENARY 04: SURVIVING PARPS – SEPARATING BETWEEN OPINIONS AND FACTS
30-09-2022 2:45 PM - 3:55 PM

SEMINAL ABSTRACT PRESENTATION: ATHENA–MONO (GOG-3020/ENGOT-OV45): A RANDOMIZED, DOUBLE-BLIND, PHASE 3 TRIAL EVALUATING RUCAPARIB MONOTHERAPY VS PLACEBO AS MAINTENANCE TREATMENT FOLLOWING RESPONSE TO FIRST-LINE PLATINUM-BASED CHEMOTHERAPY IN OVARIAN CANCER

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Objectives: While PARP inhibitors have shown efficacy as first-line (1L) maintenance treatment for patients (pts) with ovarian cancer (OC), questions remain about the pt population that may benefit from their use. ATHENA (NCT03522246) was designed to test if rucaparib may be effective as 1L maintenance treatment in a broad pt population, including those without BRCA mutations or other evidence of homologous recombination deficiency (HRD), or high-risk clinical characteristics such as residual disease. Here we report results from the ATHENA–MONO comparison of rucaparib vs placebo.

Methods: Pts with stage III–IV high-grade OC who had completed cytoreductive surgery (R0 permitted) and 4–8 cycles of 1L platinum-doublet (bevacizumab allowed with chemotherapy) with a response were randomized 4:1 to oral rucaparib 600 mg BID or placebo. Pts were stratified by HRD status (as determined by FoundationOne CDx), residual disease status after chemotherapy, and timing of surgery. The primary endpoint of investigator-assessed PFS per RECIST was assessed in a step-down procedure first in the HRD population (BRCA mutant or BRCA wild-type/loss of heterozygosity [LOH] high carcinoma) and then in the intent-to-treat (ITT) population. Blinded independent central review (BICR)–assessed PFS was a stand-alone, secondary endpoint. PFS in BRCA mutant and HRD-negative pts (BRCA wild-type/LOH low) were exploratory endpoints.

Results: As of Mar 23, 2022 (visit cutoff), 427 and 111 pts were randomized to rucaparib monotherapy or placebo (median time on treatment, 14.7 and 9.9 mo). PFS data are shown in the Table. Most common grade ≥3 TEAEs were anemia (rucaparib, 28.7% vs placebo, 0%), neutropenia (14.6% vs 0.9%), and ALT/AST increased (10.6% vs 0.9%). Rucaparib dose reduction, interruption, and discontinuation due to TEAEs occurred in 49.4%, 60.7%, and 11.8% of pts.

Conclusions: Rucaparib monotherapy is effective as 1L maintenance with significant benefit vs placebo observed in the ITT and HRD populations, as well as the non-nested subgroup of pts without known HRD.

	Rucaparib, n (%)	Placebo, n (%)	Median investigator-assessed PFS, mo; log-rank *P* value	HR (95% CI); *P* value	Median BICR-assessed PFS, mo; log-rank *P* value	HR (95% CI); *P* value
Primary analyses						
HRD	185 (43%)	49 (44%)	28.7 vs 11.3; *P*=.0004	0.47 (0.31–0.72); *P*=.0005	NR vs 9.9; *P*=.0004	0.44 (0.28–0.70); *P*=.0005
ITT	427 (100%)	111 (100%)	20.2 vs 9.2; *P*<.0001	0.52 (0.40–0.68); *P*<.0001	25.9 vs 9.1; *P*<.0001	0.47 (0.36–0.63); *P*<.0001
Exploratory analyses (*P* values are nominal, not adjusted for multiplicity)						
BRCA mutant	91 (21%)	24 (22%)	NR vs 14.7; *P*=.0041	0.40 (0.21–0.75); *P*=.0045	NR vs NR; *P*=.0566	0.48 (0.23–1.00); *P*=.0512
HRD-negative	189 (44%)	49 (44%)	12.1 vs 9.1; *P*=.0284	0.65 (0.45–0.95); *P*=.0260	12.0 vs 6.4; *P*=.0119	0.60 (0.40–0.89); *P*=.0113

S002 / #1609

Plenary Session
PLENARY 04: SURVIVING PARPS – SEPARATING BETWEEN OPINIONS AND FACTS
30-09-2022 2:45 PM - 3:55 PM

SEMINAL ABSTRACT PRESENTATION: FINAL OVERALL SURVIVAL (OS) RESULTS FROM THE PHASE III PAOLA-1/ENGOT-OV25 TRIAL EVALUATING MAINTENANCE OLAPARIB (OLA) PLUS BEVACIZUMAB (BEV) IN PATIENTS (PTS) WITH NEWLY DIAGNOSED ADVANCED OVARIAN CANCER (AOC)

Isabelle Ray-Coquard[1], Alexandra Leary[2], Sandro Pignata[3], Claire Cropet[4], Antonio Gonzalez-Martin[5], Gerhard Bogner[6], Hiroyuki Yoshida[7], Ignace Vergote[8], Nicoletta Colombo[9], Johanna Mäenpää[10], Frédéric Selle[11], Barbara Schmalfeldt[12], Giovanni Scambia[13], Eva Guerra Alia[14], Claudia Lefeuvre-Plesse[15], Antje Belau[16], Alain Lortholary[17], Martina Gropp-Meier[18], Eric Pujade-Lauraine[19], Philipp Harter[20]
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Objectives: In the PAOLA-1/ENGOT-ov25 (NCT02477644) primary analysis, adding ola to maintenance bev after first-line (1L) platinum-based chemotherapy (PBC) + bev led to a significant progression-free survival (PFS) benefit in AOC (HR 0.59, 95% CI 0.49–0.72; *P*<0.001), particularly in pts with homologous recombination deficiency (HRD+; *BRCA1/2* mutation [BRCAm] and/or genomic instability; Ray-Coquard *et al NEJM* 2019). Here, we report the prespecified final OS analysis.

Methods: Pts with high-grade AOC, in response after PBC + bev, were randomized 2:1 to ola tablets (300 mg bid; up to 24 months [mo]) + bev (15 mg/kg q3w; 15 mo total) or placebo [pbo] + bev. OS (intent-to-treat [ITT] population) was a key secondary endpoint, with analysis planned for 3 years after the primary analysis as part of hierarchical testing.

Results: 537 pts were randomized to ola + bev and 269 to pbo + bev (median follow-up 61.7 and 61.9 mo, respectively; OS data maturity: 55.3%). Median OS in the ITT population was 56.5 mo with ola + bev vs 51.6 mo with pbo + bev (HR 0.92, 95% CI 0.76–1.12; *P*=0.4118; OS at 5 y, 47.3 vs 41.5%). In HRD+ pts, OS was prolonged with ola + bev (HR 0.62, 95% CI 0.45–0.85; OS at 5 y, 65.5 vs 48.4%), with benefit in HRD+ pts with or without a tumour BRCAm (tBRCAm; Table). No benefit was seen in HRD- pts (HR 1.19, 95% CI 0.88–1.63). Subsequent PARP inhibitor therapy was received by 105 (19.6%) ola + bev pts vs 123 (45.7%) pbo + bev pts. Myelodysplastic syndrome, acute myeloid leukaemia and aplastic anaemia incidence, and new primary malignancy incidence, was respectively: ola + bev, 9 pts [1.6%] and 22 pts [4.1%]; pbo + bev, 6 pts [2.2%]) and 8 pts [2.9%]).

Table.

OS*	No. of events/ no. of pts (%)		5 y OS rate, % (95% CI)		HR (95% CI)
	Ola + bev	Pbo + bev	Ola + bev	Pbo + bev	
ITT	288/537 (53.6)	158/269 (58.7)	47.3	41.5	0.92 (0.76–1.12)
HRD+§	93/255 (36.5)	69/132 (52.3)	65.5	48.4	0.62 (0.45–0.85)
tBRCAm§	48/157 (30.6)	37/80 (46.3)	73.2	53.8	0.60 (0.39–0.93)
HRD+ excluding tBRCAm§	44/97 (45.4)	32/55 (58.2)	54.7	44.2	0.71 (0.45–1.13)
HRD-/unknown§	195/282 (69.1)	89/137 (65.0)	30.6	34.9	1.14 (0.89–1.48)
HRD-§	140/192 (72.9)	58/85 (68.2)	25.7	32.3	1.19 (0.88–1.63)

*tBRCAm status by central labs; HRD status by Myriad myChoice HRD Plus

§Preplanned exploratory analysis

Conclusions: Despite a high proportion of pts in the control arm receiving a PARP inhibitor post-progression, ola + bev provided a clinically meaningful improvement in OS for 1L HRD+ pts with and without a tBRCAm, confirming ola + bev as standard of care in this setting.

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S003 / #1610

Plenary Session
PLENARY 04: SURVIVING PARPS – SEPARATING BETWEEN OPINIONS AND FACTS
30-09-2022 2:45 PM - 3:55 PM

SEMINAL ABSTRACT PRESENTATION: OVERALL SURVIVAL (OS) AT 7-YEAR (Y) FOLLOW-UP (F/U) IN PATIENTS (PTS) WITH NEWLY DIAGNOSED ADVANCED OVARIAN CANCER (OC) AND A BRCA MUTATION (BRCAM) WHO RECEIVED MAINTENANCE OLAPARIB IN THE SOLO1/GOG-3004 TRIAL

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Objectives: In the Phase III SOLO1/GOG-3004 trial (NCT01844986), maintenance olaparib provided sustained benefit beyond the end of treatment in pts with newly diagnosed advanced OC and a BRCAm. At 5-y f/u, median progression-free survival was 56.0 months [m] with olaparib vs 13.8m with placebo (pbo) (HR 0.33; 95% CI 0.25–0.43); 48% vs 21% of pts, respectively, were progression-free (KM estimates) (Banerjee *et al. Lancet Oncol* 2021). Given that most OC deaths occur 5–10y after diagnosis, we report OS in SOLO1 at 7-y f/u, a clinically relevant timepoint.

Methods: Pts who were in response to first-line platinum-based chemotherapy received maintenance olaparib tablets 300 mg bid or pbo for up to 2y or until progression. A descriptive analysis of OS, a secondary endpoint, was performed 7y after the last pt was randomized; prespecified final analysis of OS is planned at 60% data maturity.

Results: 260 pts were randomized to olaparib and 131 to pbo (median treatment duration 24.6 vs 13.9m, respectively). At OS data maturity of 38.1% (data cut-off 7 Mar 2022), median OS was not reached in olaparib pts vs 75.2m in pbo pts, with an OS HR of 0.55 (95% CI 0.40–0.76; unadjusted for crossover; 44.3% of pbo pts received a PARP inhibitor in a subsequent line of therapy) (Table). At 7y, 45.3% of

olaparib pts vs 20.6% of pbo pts were alive and had still not received a first subsequent treatment (KM estimates). The incidence of MDS/AML remained low and new primary malignancies remained balanced between arms (Table).

Table.

	Olaparib	Pbo
OS	**N=260**	**N=131**
Median f/u, m	88.9	87.4
Events, n (%)	84 (32.3)	65 (49.6)
Median OS, m	NR	75.2
HR (95% CI)	0.55 (0.40–0.76)	
P value	0.0004*	
7-y OS rate,† %	67.0	46.5
AEs of special interest, n (%)	**N=260**	**N=130‡**
MDS/AML	4 (1.5)	1 (0.8)
New primary malignancies	14 (5.4)	8 (6.2)
Pneumonitis	5 (1.9)	0

*$P<0.0001$ required for statistical significance; †KM estimates; ‡1 pt randomized to pbo did not receive treatment. AE, adverse event; AML, acute myeloid leukaemia; CI, confidence interval; HR, hazard ratio; KM, Kaplan–Meier; MDS, myelodysplastic syndrome; NR, not reached

Conclusions: 2y of maintenance olaparib provided a clinically meaningful improvement in OS over pbo in pts with newly diagnosed advanced OC and a BRCAm. At 7y, 67.0% of olaparib pts vs 46.5% of pbo pts were alive; no new safety signals were detected. These data provide the longest f/u for any PARP inhibitor in this setting and support use of maintenance olaparib to achieve long-term remission and enhance the potential for cure.

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S004 / #461

Plenary Session
PLENARY 04: SURVIVING PARPS – SEPARATING BETWEEN OPINIONS AND FACTS
30-09-2022 2:45 PM - 3:55 PM

SEMINAL ABSTRACT PRESENTATION: OVERALL SURVIVAL RESULTS FROM THE PHASE 3 ARIEL4 STUDY OF RUCAPARIB VS CHEMOTHERAPY IN PATIENTS WITH ADVANCED, RELAPSED OVARIAN CARCINOMA AND A DELETERIOUS BRCA1/2 MUTATION

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Objectives: Rucaparib significantly improved progression-free survival (PFS) vs chemotherapy (CT) in patients with relapsed, heavily pretreated, BRCA1/2-mutated ovarian carcinoma in ARIEL4 (NCT02855944; Kristeleit et al. Lancet Oncol. 2022;23:465-78). We present final overall survival (OS) and PFS on the subsequent line of therapy (PFS2) data.

Methods: Patients were randomized 2:1 to oral rucaparib 600 mg BID or CT. In the CT group, patients with platinum-resistant (progression-free interval [PFI] ≥1 to <6 months) or partially platinum-sensitive (PFI ≥6 to <12 months) disease received weekly paclitaxel; those with fully platinum-sensitive disease (PFI ≥12 months) received investigator's choice of platinum-based CT (single-agent platinum or platinum doublet). Patients allocated to CT could cross over to receive rucaparib upon confirmed radiographic progression per RECIST. OS was a standalone secondary endpoint; PFS2 was exploratory.

Results: As of data cutoff, 14/233 (6%) rucaparib-group and 0/116 CT-group patients were ongoing on assigned study treatment; 80 (69%) patients crossed over to receive rucaparib. Overall, 313/349 (90%) patients received rucaparib from randomization or after crossover. Death events have occurred in 244 (70%) patients. Efficacy endpoints are presented in the Table. Rucaparib safety was consistent with previous

reports.

	ITT population		ITT, excluding pts who crossed over to rucaparib		ITT, censoring pts who crossed over to rucaparib		Platinum-sensitive		Platinum-resistant	
	Rucaparib (n=233)	CT (n=116)	Rucaparib (n=233)	CT (n=36)	Rucaparib (n=233)	CT (n=116)	Rucaparib (n=113)	CT (n=57)	Rucaparib (n=120)	CT (n=59)
PFS HR (95% CI)*	0.665 (0.516–0.858); *P*=0.002		NA		NA		0.502 (0.343–0.733); *P*=0.0004		0.821 (0.583–1.155); *P*=0.257	
PFS2 HR (95% CI)†	0.860 (0.674–1.098)		NA		NA		0.737 (0.512–1.060)		0.968 (0.697–1.344)	
Median OS, mo†	19.4	25.4	19.4	9.1	19.4	26.2	29.4	27.6	14.2	22.2
OS HR (95% CI)†	1.313 (0.999–1.725)		0.423 (0.276–0.650)		1.059 (0.688–1.630)		1.071 (0.709–1.618)		1.511 (1.053–2.170)	

HR, hazard ratio; NA, not analyzed; pts; patients.
*Data cutoff: Sep 30, 2020; †Data cutoff: Apr 10, 2022.

Conclusions: PFS2 did not significantly differ between treatment groups, while OS favored CT in the intent-to-treat (ITT) population. OS was similar between treatment groups amongst patients with platinum-sensitive disease; the difference in OS in the ITT population was driven by the platinum-resistant subgroup. The high rate of crossover confounded OS, highlighting important questions about PARP inhibitor sequencing in the treatment of advanced ovarian carcinomas.

S005 / #1753

Plenary Session
PLENARY 04: SURVIVING PARPS – SEPARATING BETWEEN OPINIONS AND FACTS
30-09-2022 2:45 PM - 3:55 PM

SEMINAL ABSTRACT PRESENTATION: PRIMA/ENGOT-OV26/GOG-3012 STUDY: UPDATED LONG-TERM PFS AND SAFETY

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Objectives: Niraparib (nir) has shown PFS benefit as a first-line (1L) maintenance therapy (MT) in the primary analysis of PRIMA (data cut 17 May 2019) in all subgroups regardless of biomarker status. These results were the basis for approval of nir as MT after response to 1L platinum-based chemo (CT). Here we report updated long-term efficacy and safety in the PRIMA study.

Methods: This double-blind, placebo (PBO)-controlled phase 3 trial evaluated nir in pts with newly diagnosed advanced high-grade serous or endometrioid ovarian, primary peritoneal, or fallopian tube cancer (OC) with a complete or partial response (CR or PR) to 1L platinum-based CT. Stratification factors were best response to 1L CT regimen (CR/PR), receipt of neoadjuvant CT (NACT; yes/no), and homologous recombination deficiency (HRD) status (HRd/HRp/HRnd) per Myriad myChoice HRD test. Pts received nir or PBO QD (2:1 ratio). The primary endpoint of PFS by blinded independent central review was concordant with investigator assessment (INV). Updated (ad hoc) data are by INV, as of 17 Nov 2021.

Results: Of 733 randomized pts (nir, 487; PBO, 246), 373 (51%) were HRd (nir, 247; PBO, 126), and 249 (34%) were HRp (nir, 169; PBO, 80). Overall, 35% had stage IV disease, 67% received NACT, and 33% had a PR to 1L CT. As of 17 Nov 2021, median PFS follow-up time was 3.5 y. Nir-treated pts (HRd/HRp/overall) received continued PFS benefit vs PBO (Table). All subgroups showed a sustained and durable treatment effect. The most common grade ≥3 adverse events in the nir arm were thrombocytopenia (40%), anemia (32%), and neutropenia (21%). No related ontreatment deaths occurred. MDS/AML were reported at the same incidence in nir 6/484 (1.2%) and PBO 3/244 (1.2%) arms. OS remains immature at 41% for the overall population; 33% of PBO vs 9% of nir pts received subsequent PARPi.

	Primary efficacy analysis 17 May 2019		Updated efficacy analysis (INV) 17 Nov 2021
	BICR	INV	
Median PFS, mo			
Overall Nir vs PBO HR (95% CI) *p*	13.8 vs 8.2 0.62 (0.50–0.76) <0.0001	13.8 vs 8.2 0.63 (0.51–0.76) <0.0001	13.8 vs 8.2 0.66 (0.56–0.79) <0.0001
HRd Nir vs PBO HR (95% CI) *p*	21.9 vs 10.4 0.43 (0.31–0.59) <0.0001	21.9 vs 11.2 0.46 (0.34–0.63) <0.0001	24.5 vs 11.2 0.52 (0.40–0.68) <0.0001
HRp Nir vs PBO HR (95% CI) *p*	8.1 vs 5.4 0.68 (0.49–0.94) 0.0203	8.3 vs 5.4 0.62 (0.45–0.85) 0.0025	8.4 vs 5.4 0.65 (0.49–0.87) 0.0038
Estimated probability of no progressive disease or death for ≥4y			**Overall** Nir: 24% PBO: 14% **HRd** Nir: 38% PBO: 17%
BICR, blinded independent central review; INV, investigator assessed.			

Conclusions: Nir maintained clinically significant improvement in PFS with 3.5 y of follow-up in pts with newly diagnosed advanced OC at high risk of progression irrespective of HRD status. No new safety signals were identified.

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