ESMO 2020: UPDATE

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Primary results from IMagyn050/GOG 3015/ENGOT-OV39, a double-blind placebo-controlled randomised phase 3 trial of bevacizumab-containing therapy ± atezolizumab for newly diagnosed stage III/IV ovarian cancer

K Moore[1], M Bookman[2], J Sehouli[3], A Miller[4], C Anderson[5], G Scambia[6], T Myers[7], C Taskiran[8], K Robison[9], J Maenpaa[10], L Willmott[11], N Colombo[12], J Thomes-Pepin[13], MA Gold[14], C Aghajanian[15], F Wu[16], L Molinero[16], V Khor[16], YG Lin[16], S Pignata[17]

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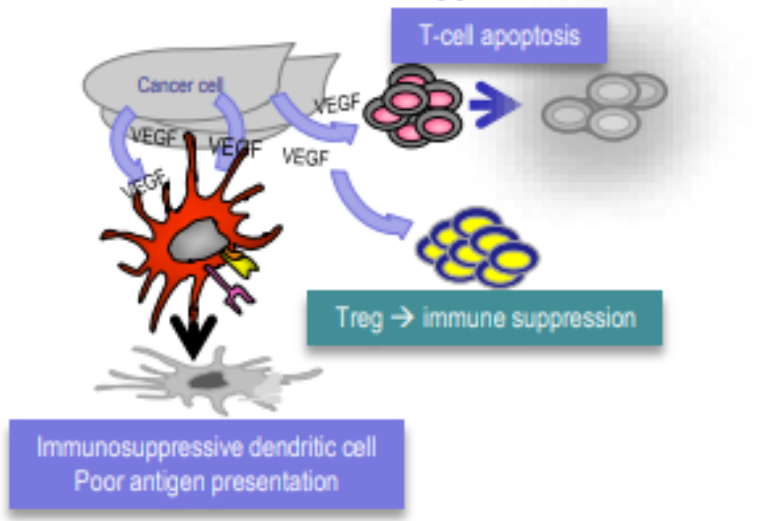
Rationale

- Atezolizumab, which targets PD-L1, has demonstrated efficacy in several cancers[1–6]
  - Immune cell PD-L1 expression is associated with greater atezolizumab effect in some tumours[1]
- Platinum–taxane chemotherapy combination with bevacizumab is an established front-line regimen for ovarian cancer (GOG-0218,[7] ICON7[8])
- Blocking tumour-associated VEGF may promote T-cell infiltration into the tumour bed and boost anti-tumour immune response, providing the rationale for combining atezolizumab with the anti-angiogenic agent bevacizumab[9,10]
- Combining anti-angiogenic approaches with PD-1/PD-L1 pathway blockade has shown clear anti-tumour efficacy in metastatic non-small-cell lung cancer,[2] unresectable hepatocellular cancer[5] and advanced endometrial cancer[13]

VEGF-associated immune suppression[11,12]



PD-1 = programmed death-1;
PD-L1 = programmed death-ligand 1;
Treg = regulatory T cell;
VEGF = vascular endothelial growth factor

[1]Schmid P et al. NEJM 2018; [2]Socinski MA et al. NEJM 2018; [3]Horn L et al. NEJM 2018; [4]Rittmeyer A et al. Lancet 2017; [5]Finn RS et al. NEJM 2020; [6]Powles T et al. Lancet 2018; [7]Burger RA et al. NEJM 2011; [8]Perren TJ et al. NEJM 2011; [9]Motz GT et al. Nat Med 2014; [10]Wallin J et al. Nat Commun 2016; [11]Coukos G et al. Adv Exp Med Biol 2007; [12]Shrimali RK et al. Cancer Res 2010; [13]Makker V et al. J Clin Oncol 2020

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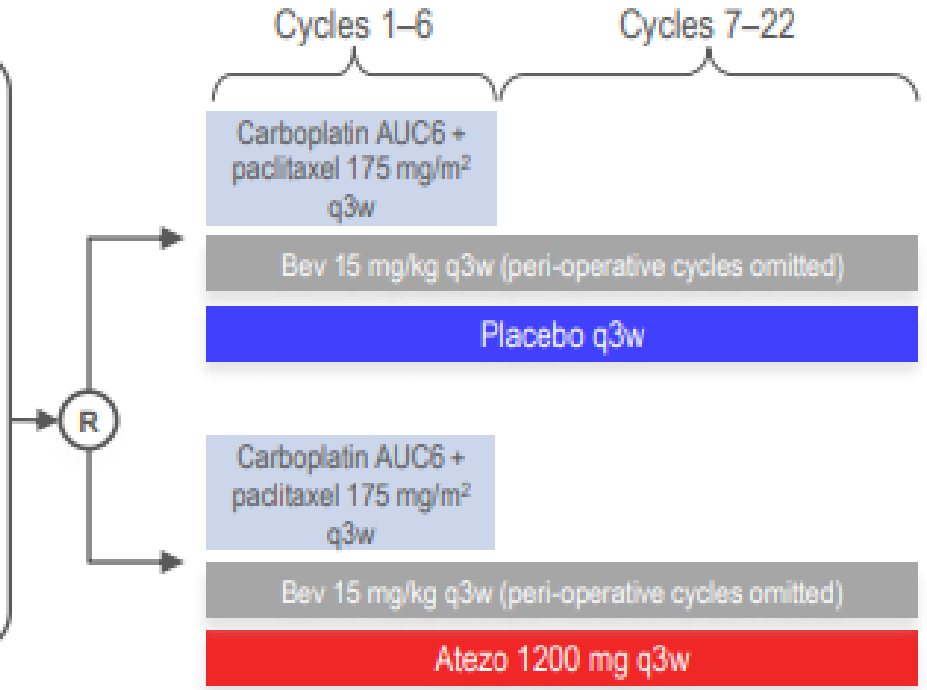
Trial design

- Previously untreated epithelial ovarian, primary peritoneal or fallopian tube cancer
- Post-operative stage III with macroscopic residual disease or stage IV or neoadjuvant candidate with planned interval surgery
- ECOG PS 0–2



Co-primary endpoints

- **PFS** (per RECIST v1.1)
  (PD-L1+ and ITT populations tested simultaneously; p≤0.002 considered positive)
- **OS**
  (hierarchical testing, PD-L1+ then ITT)

Stratification factors

- Stage (III vs IV)
- ECOG PS (0 vs 1/2)
- Treatment approach (adjuvant vs neoadjuvant)
- PD-L1 status (IC <1% vs ≥1%; VENTANA SP142 assay)

NCT03038100

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Atezo = atezolizumab; AUC = area under the curve; bev = bevacizumab; ECOG PS = Eastern Cooperative Oncology performance status; IC = immune cell; ITT = intent to treat; OS = overall survival; PFS = progression-free survival; q3w = every 3 weeks; RECIST = Response Evaluation Criteria in Solid Tumours

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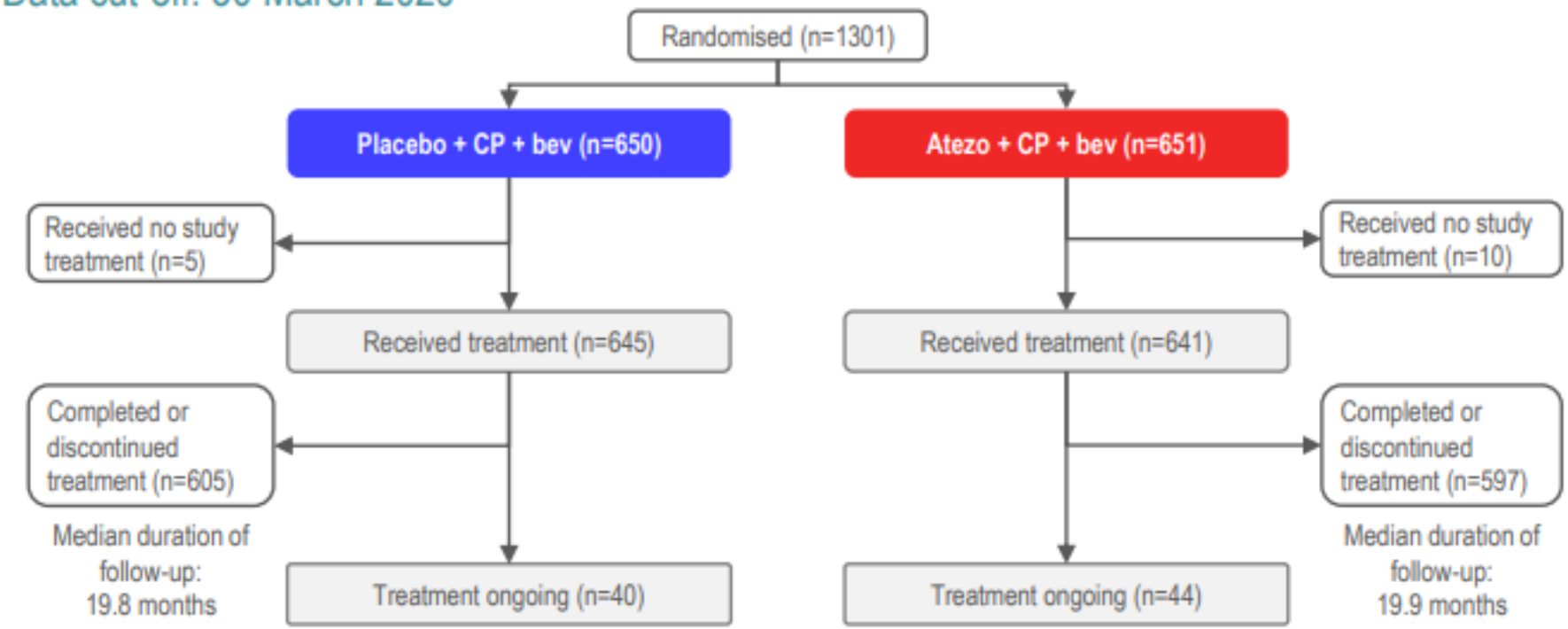
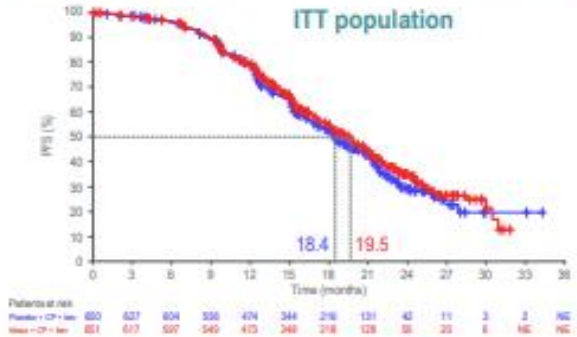
Patient flow

Data cut-off: 30 March 2020



CP = carboplatin + paclitaxel

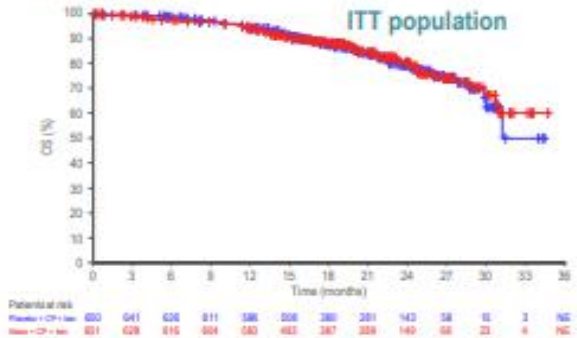
Progression-free survival

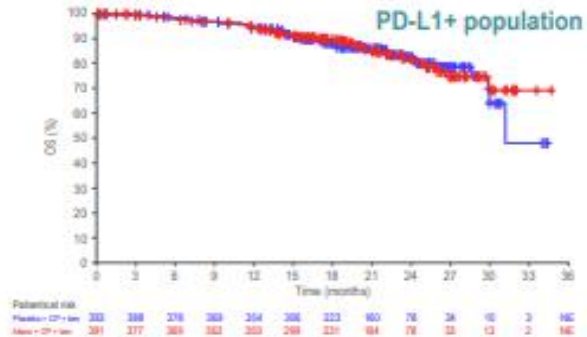


PFS	ITT population		PD-L1+ population	
	Placebo + CP + bev (n=650)	Atezo + CP + bev (n=651)	Placebo + CP + bev (n=393)	Atezo + CP + bev (n=391)
Patients with events, n (%)	341 (52.5)	323 (49.6)	199 (50.6)	167 (42.7)
Median PFS, months (95% CI)	18.4 (17.2–19.8)	19.5 (18.1–20.8)	18.5 (16.6–21.4)	20.8 (19.1–24.2)
Stratified HR (95% CI)	0.92 (0.79–1.07)		0.80 (0.65–0.99)	
Stratified log-rank p-value	0.2785		0.0376	
2-year event-free rate (95% CI)	29.1 (23.9–34.3)	35.1 (30.0–40.3)	32.2 (25.4–39.0)	43.9 (37.2–50.5)

CI = confidence interval; HR = hazard ratio

Overall survival: first interim analysis[a]





OS	ITT population		PD-L1+ population	
	Placebo + CP + bev (n=650)	Atezo + CP + bev (n=651)	Placebo + CP + bev (n=393)	Atezo + CP + bev (n=391)
Patients with events, n (%)	110 (16.9)	109 (16.7)	59 (15.0)	57 (14.6)
Median OS, months (95% CI)	NE	NE	31.2 (30.0–NE)	NE
Stratified HR (95% CI)	0.96 (0.74–1.26)		0.98 (0.68–1.41)	
Stratified log-rank p-value	0.7887		0.9083	
2-year event-free rate (95% CI)	79.4 (75.4–83.3)	80.6 (76.8–84.5)	82.5 (77.8–87.3)	82.1 (77.2–87.0)

[a]Information fraction: 41% (ITT population) and 37% (PD-L1+ population). NE = not estimable

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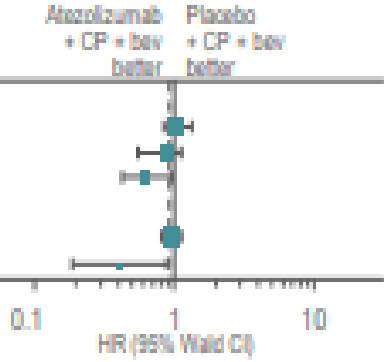
Subgroup analyses of PFS by PD-L1 status

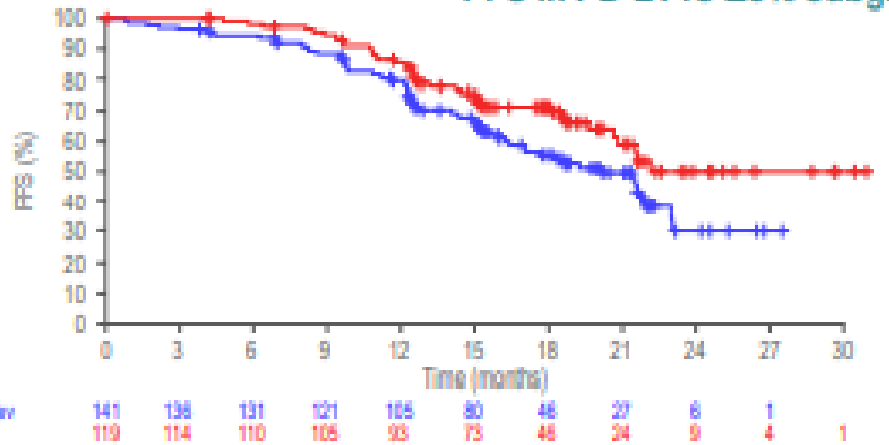
ITT population

PD-L1 status	Total n	Placebo + CP + bev (n=650) n	Placebo + CP + bev (n=650) Median (months)	Atezolizumab + CP + bev (n=651) n	Atezolizumab + CP + bev (n=651) Median (months)	HR (95% Wald CI)
PD-L1 IC status						
IC <1%	517 (40%)	257	18.3	260	17.4	1.06 (0.84–1.33)
IC ≥1% to <5%	524 (40%)	252	18.2	272	19.3	0.89 (0.55–1.13)
IC ≥5%	260 (20%)	141	20.2	119	NE	0.64 (0.43–0.96)
PD-L1 TC status						
TC <1%	1228 (94%)	610	18.4	618	19.2	0.96 (0.82–1.12)
TC ≥1%[a]	73 (6%)	40	15.0	33	NE	0.41 (0.19–0.90)

[a]PD-L1 TC ≥1% and IC ≥1%: n=67. PD-L1 TC ≥1% and IC <1%: n=6



PFS in PD-L1 IC ≥5% subgroup



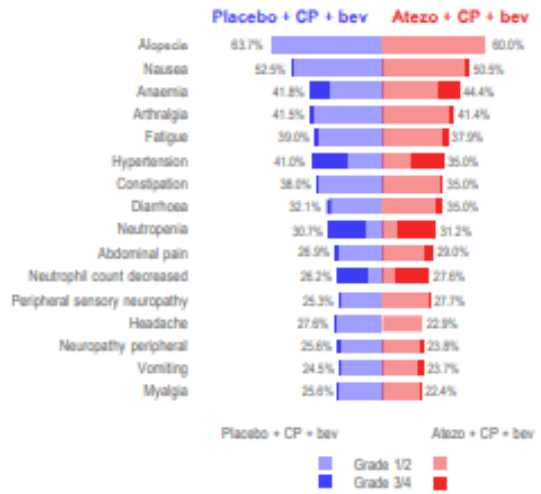
Patients at risk

Placebo + CP + bev	141	138	131	121	105	80	46	27	6	1
Atezo + CP + bev	119	114	110	105	93	73	48	24	9	4	1

	Placebo + CP + bev (n=141)	Atezo + CP + bev (n=119)
Patients with events, n (%)	66 (46.8)	30 (32.8)
Median PFS, months	20.2	NE
(95% CI)	(17.1–21.9)	(20.8–NE)
Unstratified HR (95% CI)	0.64 (0.43–0.96)	
Unstratified log-rank p-value	0.0278	

Most common AEs

Most common AEs (≥25% in either arm)



SAEs with ≥2% incidence in either arm

SAEs	Placebo + CP + bev (n=644)	Atezo + CP + bev (n=642)
Febrile neutropenia	3.7%	8.4%
Pyrexia	1.2%	4.0%

AEs of special interest for atezolizumab (>2 patients in either arm)

Immune-mediated AEs by medical concept, n (%)	Placebo + CP + bev (n=644)		Atezo + CP + bev (n=642)	
	Any grade	Grade 3/4[a]	Any grade	Grade 3/4[a]
Hepatitis	14 (2.2)	4 (0.6)	17 (2.6)	7 (1.1)
Pneumonitis	4 (0.6)	0	12 (1.9)	1 (0.2)
Hypothyroidism	83 (12.9)	1 (0.2)	166 (25.9)	3 (0.5)
Hyperthyroidism	23 (3.6)	0	51 (7.9)	0
Adrenal insufficiency	2 (0.3)	0	5 (0.8)	1 (0.2)
Infusion-related reactions	49 (7.6)	2 (0.3)	78 (12.1)	5 (0.8)
Colitis	11 (1.7)	7 (1.1)	21 (3.3)	11 (1.7)
Rash	165 (25.6)	6 (0.9)	265 (41.3)	41 (6.4)
Severe cutaneous reactions	3 (0.5)	0	15 (2.3)	8 (1.2)
Myositis	5 (0.8)	0	4 (0.6)	2 (0.3)
Meningoencephalitis[b]	3 (0.5)	0	3 (0.5)	1 (0.2)
Pancreatitis	0	0	5 (0.8)	4 (0.6)

[a]Grade 3/4 AE refers to highest grade experienced. [b]No cases of meningitis, 1 patient with encephalitis, remaining events were photophobia. In the atezo arm there was one (fatal) case of myasthenia gravis and two cases of systemic immune activation (one grade 4; both resolved). Diabetes mellitus and rhabdomyolysis each occurred in 2 patients (0.3%) in the atezo arm (grade 3/4 in 1 patient; 0.2%) and there were three cases of diabetes mellitus (0.5%) in the placebo arm (no grade 3/4). Myocarditis and Guillain–Barré syndrome each occurred in 1 patient (0.2%) in each arm, all grade 3/4 in all cases except for myocarditis in the atezo arm. There were no cases of haemophagocytic lymphohistiocytosis or hypophysitis in either arm

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Conclusions

- IMagyn050/GOG 3015/ENGOT-OV39 is a global randomised phase III trial powered to assess treatment effect in PD-L1+ ovarian cancer
- The addition of atezolizumab to a chemotherapy + bevacizumab backbone did not significantly improve PFS vs chemotherapy + bevacizumab alone in the ITT or PD-L1+ (IC ≥1%) populations
  - ITT population: HR = 0.92 (95% CI 0.79–1.07); median PFS: 19.5 vs 18.4 months
  - PD-L1+ population: HR = 0.80 (95% CI 0.65–0.99); median PFS 20.8 vs 18.5 months
  - Exploratory PFS analyses in the PD-L1 IC ≥5% subgroup showed a trend favouring atezolizumab
- First interim OS analysis did not show a significant OS benefit with the addition of atezolizumab to chemotherapy + bevacizumab
  - Final OS results are expected in 2023
- Safety of atezolizumab in combination with bevacizumab and chemotherapy was consistent with the known safety profile of individual drugs and their combination

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ICON8: Overall survival results in a GCIG phase III randomised controlled trial of weekly dose-dense chemotherapy in first line epithelial ovarian, fallopian tube or primary peritoneal carcinoma treatment

Andrew Clamp[1], Elizabeth James[2], Iain McNeish[3], Andrew Dean[4], Jae-Weon Kim[5], Dearbhaile O'Donnell[6], Jane Hook[7], Dolores Gallardo-Rincon[8], Christopher Coyle[2], Sarah Blagden[9], James Brenton[10], Raj Naik[11], Tim Perren[7], Sudha Sundar[12], Adrian Cook[2], Jonathan Badrock[2], Anne Marie Swart[13], Max Parmar[2], Rick Kaplan[2], Jonathan Ledermann[14]

[1]The Christie NHS Foundation Trust and University of Manchester, Manchester, UK, [2]MRC Clinical Trials Unit at UCL, London, UK, [3]Imperial College London - Hammersmith Hospital, London, UK, [4]St John of God Subiaco Hospital, Sydney, Australia, [5]Seoul National University Hospital, Seoul, Korea, Republic of, [6]St James's Hospital, Dublin, Ireland, [7]St James' University Hospital- Leeds Teaching Hospitals NHS Trust, Leeds, UK, [8]Instituto Nacional de Cancerologia, Mexico City, Mexico, [9]Churchill Hospital - Oxford University Hospitals NHS Foundation Trust, Oxford, UK, [10]Cancer Research UK Cambridge Institute, Cambridge, UK, [11]Queen Elizabeth Hospital, Gateshead, UK, [12]University of Birmingham, Birmingham, UK, [13]Norwich Medical School, University of East Anglia, Norwich, UK, [14]University College London Cancer Institute, London, UK

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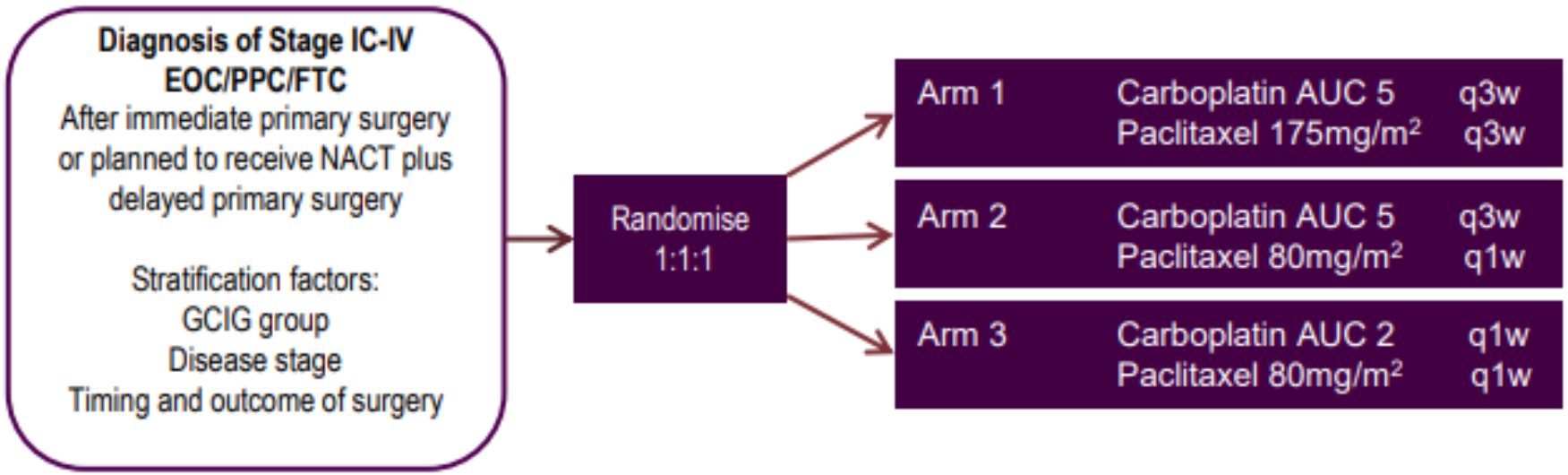
ICON8 Trial Schema



- Six cycles chemotherapy mandated

Delayed Primary Surgery cohort

- Cytoreductive surgery strongly advised after 3 cycles of chemotherapy
- Cycle 3 day 15 treatment omitted in arms 2 and 3

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ICON8 Statistical Design

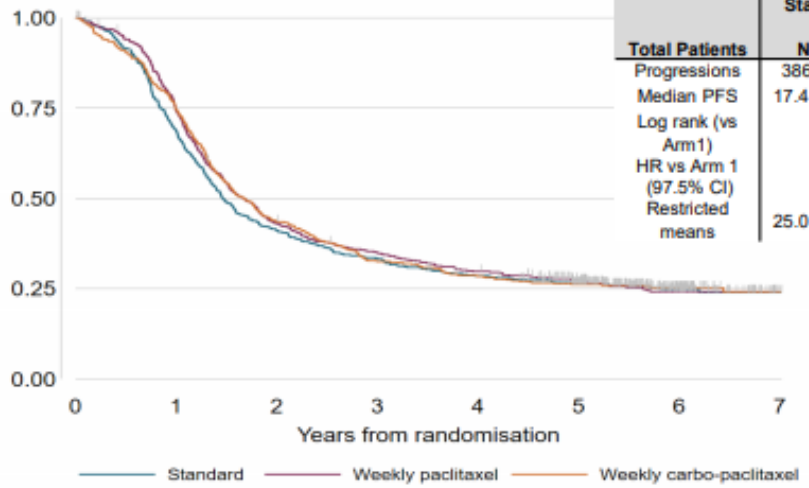
- Co-primary outcomes – **Progression-Free Survival and Overall Survival**
- Estimated median PFS = 16 months, median OS = 34 months
- **Target HR = 0.75** with 2-sided significance level of 0.025 (due to multiple comparisons – weekly paclitaxel vs standard & weekly carbo-paclitaxel vs standard)
- **Require 602 events** in each comparison for PFS and OS.
- **Sample size = 1485 women**

ACCRUAL

- Jun 2011 – Nov 2014
- 1566 women recruited

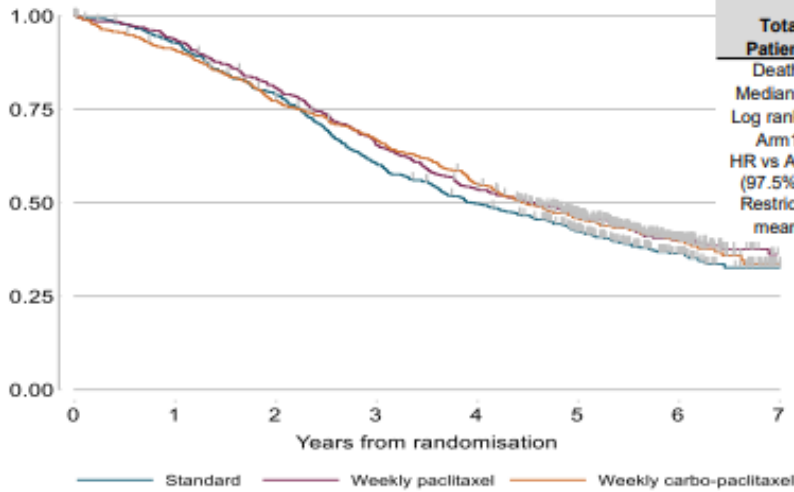
Country	Patients recruited
UK	1397 (89%)
Australia/New Zealand	70 (4%)
Mexico	43 (3%)
Korea	32 (2%)
Republic of Ireland	24 (2%)
Total	**1566 (100%)**

ICON8 Progression Free Survival (updated 2020)



Total Patients	Arm 1 Standard N=522	Arm 2 Weekly paclitaxel N=523	Arm 3 Weekly carbo-paclitaxel N=521
Progressions	386 (74%)	386 (74%)	384 (74%)
Median PFS	17.4 months	20.1 months	20.1 months
Log rank (vs Arm1)		p=0.37	p=0.48
HR vs Arm 1 (97.5% CI)		0.94 (0.80, 1.10)	0.95 (0.81, 1.11)
Restricted means	25.0 months	25.5 months	25.9 months

ICON8 Overall Survival



Total Patients	Arm 1 Standard N=522	Arm 2 Weekly paclitaxel N=523	Arm 3 Weekly carbo-paclitaxel N=521
Deaths	319 (61%)	300 (57%)	304 (58%)
Median OS	47.4 mths	54.1 mths	53.4 mths
Log rank (vs Arm1)		p=0.14	p=0.27
HR vs Arm 1 (97.5% CI)		0.89 (0.74, 1.06)	0.91 (0.76, 1.09)
Restricted means	46.5 mths	47.2 mths	48.0 mths

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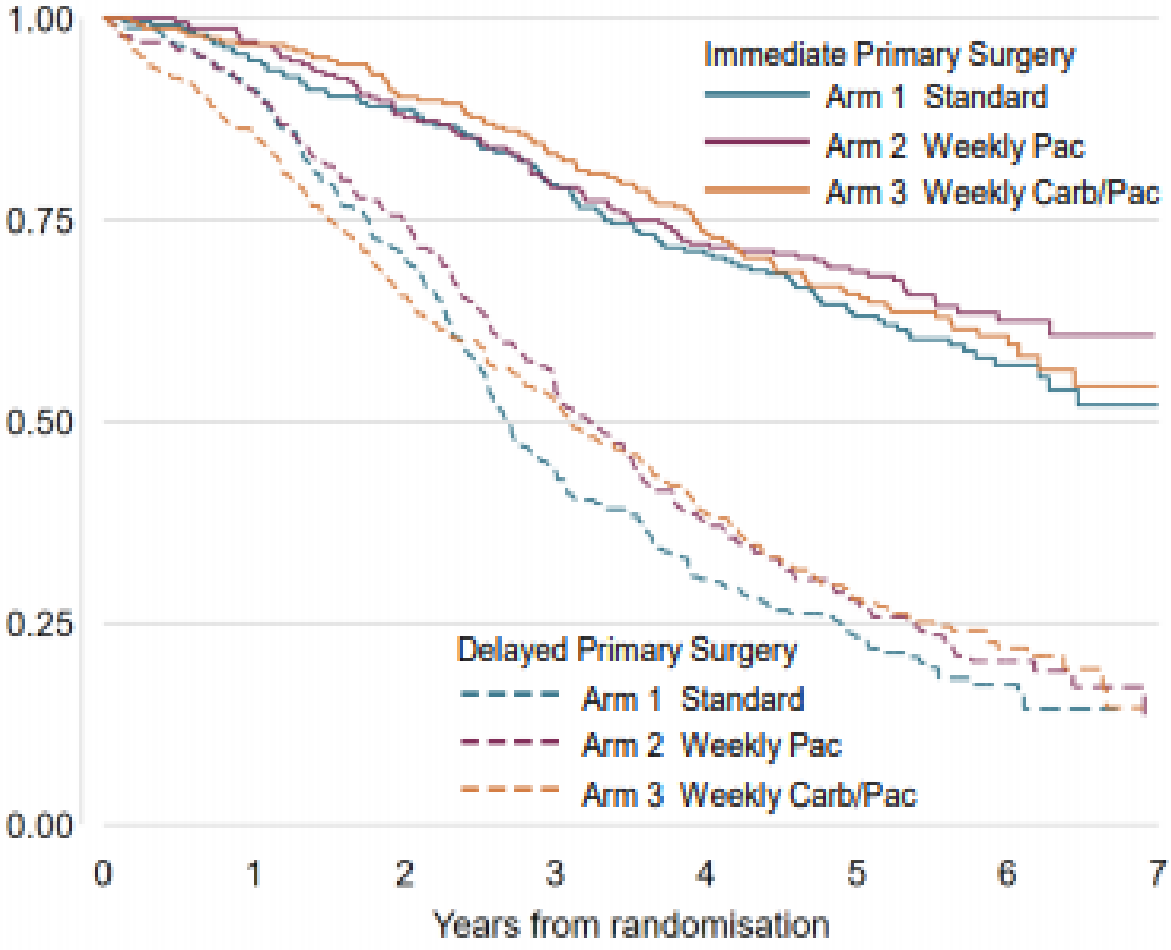
ICON8 Conclusions

- Weekly dose-dense chemotherapy regimens are safe and well-tolerated in European patient group
  - Adjuvant treatment
  - Primary therapy with interval cytoreductive surgery
- Incorporation of weekly dose-dense chemotherapy regimens into first-line treatment for women with epithelial ovarian cancer does not improve PFS or OS
- 3-weekly carboplatin-paclitaxel remains the standard-of-care chemotherapy component of first-line ovarian cancer treatment
  - Further hypothesis-generating analyses underway in DPS patient cohort

ICON8 OS, by timing of surgery



Immediate Primary Surgery			
	Arm 1	Arm 2	Arm 3
HR	-	0.88	0.93
(97.5% CI)	-	(0.63,1.23)	(0.67,1.29)
p		0.40	0.60
Median survival	-	86 mths	-

Delayed Primary Surgery			
	Arm 1	Arm 2	Arm 3
HR	-	0.86	0.88
(97.5% CI)	-	(0.69,1.07)	(0.71,1.10)
p	-	0.13	0.20
Median survival	32 mths	39 mths	37 mths

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Maintenance olaparib for patients with newly diagnosed advanced ovarian cancer and a BRCA mutation: 5-year follow-up from SOLO1

Susana Banerjee,[1] Kathleen Moore,[2] Nicoletta Colombo,[3] Giovanni Scambia,[4] Byoung-Gie Kim,[5] Ana Oaknin,[6] Michael Friedlander,[7] Alla Lisyanskaya,[8] Anne Floquet,[9] Alexandra Leary,[10] Gabe S Sonke,[11] Charlie Gourley,[12] Amit Oza,[13] Antonio González-Martín,[14] Carol Aghajanian,[15] William Bradley,[16] Eileen Holmes,[17] Elizabeth S Lowe,[18] Paul DiSilvestro[19]

[1]The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, UK; [2]Stephenson Oklahoma Cancer Center, Oklahoma City, OK, USA; [3]University of Milan-Bicocca and Istituto Europeo di Oncologia, Milan, Italy; [4]Università Cattolica del Sacro Cuore-Fondazione Policlinico A. Gemelli, IRCCS, Rome, Italy; [5]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; [6]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [7]University of New South Wales Clinical School, Prince of Wales Hospital, Randwick, Australia; [8]St Petersburg City Oncology Dispensary, St Petersburg, Russia; [9]Institut Bergonié, Comprehensive Cancer Centre, Bordeaux, and Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens, France; [10]Institut Gustave-Roussy, Villejuif, and Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens, France; [11]The Netherlands Cancer Institute, Amsterdam, The Netherlands; [12]Cancer Research UK Edinburgh Centre, University of Edinburgh, Edinburgh, UK; [13]Princess Margaret Cancer Centre, Toronto, ON, Canada; [14]Clínica Universidad de Navarra, Madrid, Spain; [15]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [16]Froedtert and the Medical College of Wisconsin, Milwaukee, WI, USA; [17]AstraZeneca, Cambridge, UK; [18]AstraZeneca, Gaithersburg, MD, USA; [19]Women & Infants Hospital, Providence, RI, USA

Conducted in partnership with the Gynecologic Oncology Group (GOG-3004)
ClinicalTrials.gov identifier: NCT01844986. This study was sponsored by AstraZeneca and is part of an alliance between AstraZeneca and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA

Mobile-friendly infographic

ATION: 16-18 OCTOBER 2020

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The SOLO1 trial[1]

5-year survival for newly diagnosed advanced ovarian cancer is 30-50% and patients are at high risk of relapse;[2,3] treatment goals in this setting include delay of recurrence and, for some patients, increased chance of cure

- Newly diagnosed, FIGO stage III–IV, high-grade serous or endometrioid ovarian, primary peritoneal or fallopian tube cancer
- BRCAm
- ECOG performance status 0–1
- Cytoreductive surgery*
- In clinical complete response or partial response after platinum-based chemotherapy

Olaparib 300 mg bid (N=260)

For up to **2 years** or until disease progression

Placebo (N=131)

Primary endpoint[1]

- PFS (investigator-assessed)

Secondary endpoints included:

- PFS2
- TSST
- Safety

*Upfront or interval attempt at optimal cytoreductive surgery for stage III disease and either biopsy and/or upfront or interval cytoreductive surgery for stage IV disease.
BRCAm, deleterious or suspected deleterious germline or somatic mutation on *BRCA1* and/or *BRCA2*; ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics; PFS, progression-free survival; PFS2, time to second progression or death; TSST, time to second subsequent therapy or death

1. Moore *et al. N Engl J Med* 2018;379:2495–505; 2. Tewari *et al. J Clin Oncol* 2019;37:2317–28; 3. Ledermann *et al. Ann Oncol* 2013;24 vi24–vi32

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PFS benefit of maintenance olaparib was sustained beyond the end of treatment

	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	118 (45)	100 (76)
Median PFS, months	**56.0**	**13.8**
Difference, months	42.2	
	HR 0.33 (95% CI 0.25–0.43)	

Median treatment duration:
Olaparib, 24.6 months
Placebo†, 13.9 months

No. at risk

Olaparib	260	229	212	194	173	140	129	115	101	91	58	30	2	0
Placebo	131	103	65	53	41	38	30	24	23	22	16	3	0	

*13 patients, all in the olaparib arm, continued study treatment past 2 years; †n=130 (safety analysis set)
Investigator-assessed by modified RECIST v1.1. DCO: 5 March 2020

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Conclusions

- We present data from the SOLO1 trial after the longest duration of follow-up for any PARP inhibitor in the newly diagnosed advanced ovarian cancer setting
- The benefit derived from maintenance olaparib was sustained substantially beyond the end of treatment
  - Median PFS was 56 months, whereas median treatment duration was only 25 months
- More than half of women in complete response at baseline who received maintenance olaparib for 2 years remained free from relapse 5 years later
- No new safety signals were observed with long-term follow-up
  - No new cases of MDS/AML were reported and incidence of new primary malignancies remained balanced between arms
- These results provide further evidence to support the use of maintenance olaparib as a standard of care for women with newly diagnosed advanced ovarian cancer and a BRCA mutation, and suggest the possibility of long-term remission or even cure for some patients

Mobile-friendly infographic

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Maintenance olaparib plus bevacizumab in patients with newly diagnosed, advanced high-grade ovarian carcinoma: final analysis of second progression-free survival (PFS2) in the Phase III PAOLA-1/ENGOT-ov25 trial

Antonio González Martin,[1] Youssef Tazi,[2] Florian Heitz,[3] Laure Montane,[4] Piera Gargiulo,[5] Regina Berger,[6] Kan Yonemori,[7] Ignace Vergote,[8] Alessandra Bologna,[9] Johanna Mäenpää,[10] Cristina Costan,[11] Ulrich Canzler,[12] Claudio Zamagni,[13] Eva Maria Guerra-Alia,[14] Charles Briac Levaché,[15] Frederik Marmé,[16] Elsa Kalbacher,[17] Nikolaus de Gregorio,[18] Nadine Dohollou,[19] Isabelle Ray-Coquard[20]

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ClinicalTrials.gov identifier: NCT02477644 | This study was sponsored by ARCAGY Research.

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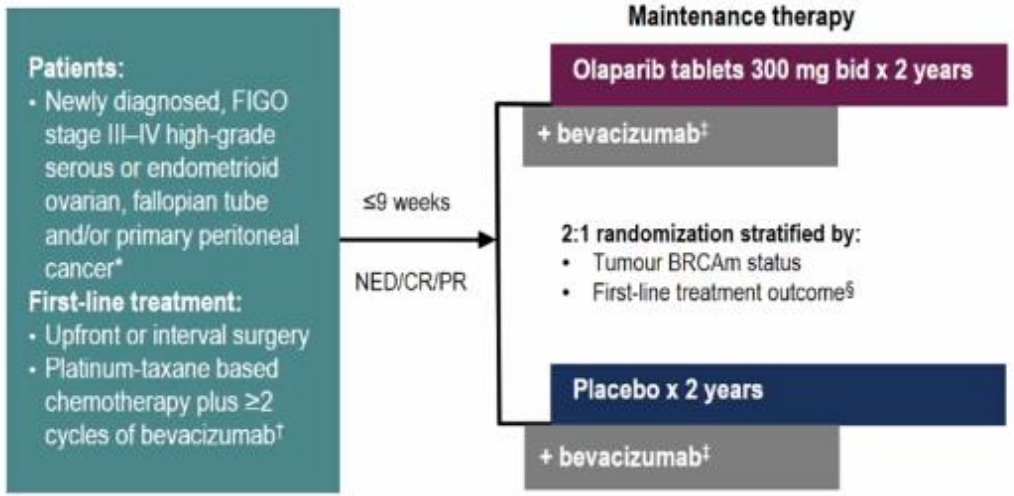
PAOLA-1/ENGOT-ov25 trial design



- Primary endpoint: investigator-assessed PFS (RECIST v1.1)
- In the primary analysis, a statistically significant PFS benefit was observed[1]

Primary PFS analysis (DCO 22 March 2019)

	Olaparib + bev (N=537)	Placebo + bev (N=269)
Median PFS, months	22.1	16.6
HR (95% CI); *P* value	0.59 (0.49–0.72) *P*<0.001	

*Patients with other epithelial non-mucinous ovarian cancer were eligible if they had a germline *BRCA1* and/or *BRCA2* mutation; †Patients must have received ≥3 cycles of bevacizumab with the last 3 cycles of chemotherapy, apart from patients undergoing interval surgery who were permitted to receive only 2 cycles of bevacizumab with the last 3 cycles of chemotherapy; ‡Bevacizumab 15 mg/kg, every 3 weeks for a total of 15 months, including when administered with chemotherapy; §According to timing of surgery and NED/CR/PR

bid, twice daily; BRCAm, BRCA mutation; CI, confidence interval; CR, complete response; DCO, data cut-off; FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio; NED, no evidence of disease; PFS, time from randomization to progression or death; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours;

1. Ray-Coquard I *et al. N Engl J Med* 2019;381:2416–28

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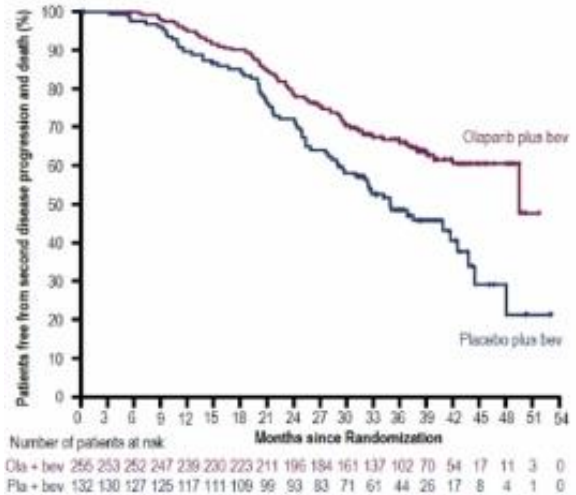
PFS2 subgroup analysis by HRD status

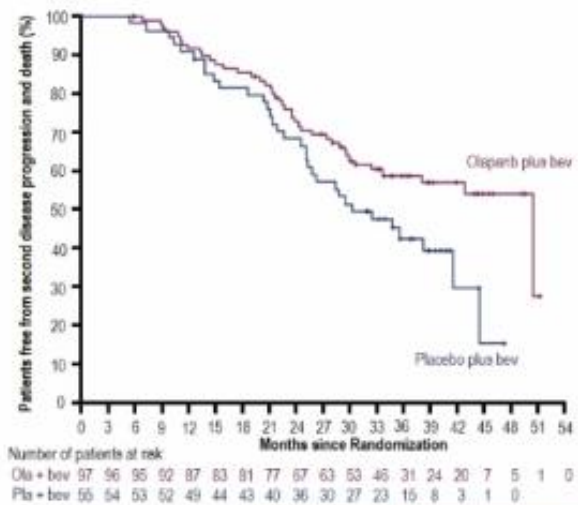
HRD positive,* including tumour BRCAm



	Olaparib + bev (n=255)	Placebo + bev (n=132)
Events, n (%)	85 (33)	70 (53)
Median PFS2, months	**50.3†**	**35.3**

HR 0.56 (95% CI 0.41–0.77)

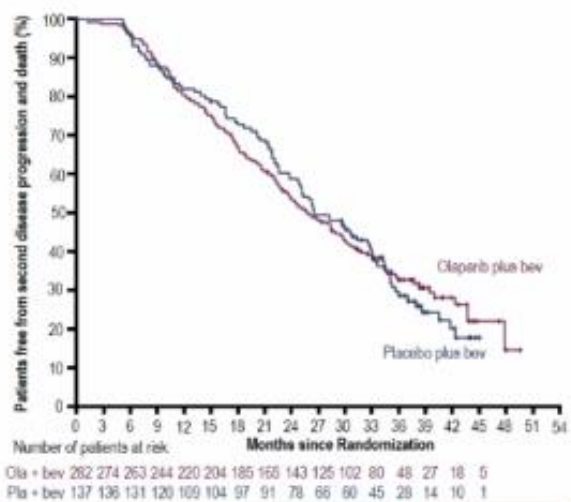
HRD positive,* excluding tumour BRCAm



	Olaparib + bev (n=97)	Placebo + bev (n=55)
Events, n (%)	41 (42)	33 (60)
Median PFS2, months	**50.3†**	**30.1**

HR 0.60 (95% CI 0.38–0.96)

HRD negative/unknown



	Olaparib + bev (n=282)	Placebo + bev (n=137)
Events, n (%)	175 (62)	94 (69)
Median PFS2, months	**26.3**	**28.1**

HR 0.98 (95% CI 0.77–1.27)

*HRD positive defined as a tumour BRCAm and/or genomic instability score of ≥42 on the Myriad myChoice CDx® assay; †Unstable median due to lack of events

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Conclusions

- In PAOLA-1/ENGOT-ov25, the addition of maintenance olaparib to bevacizumab provided continued benefit beyond first progression, with a statistically significant improvement in PFS2:
  - A substantial PFS2 benefit was seen in patients who were HRD positive, regardless of tumour BRCAm status
- The significant PFS2 improvement was supported by a significant delay in TSST
- No new safety signals were observed with longer-term follow-up
- OS data are still immature

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Maintenance olaparib + bevacizumab in patients with newly diagnosed advanced high-grade ovarian cancer: RECIST and/or CA-125 objective response rate in the Phase III PAOLA-1 trial

Nicoletta Colombo, Justine Gantzer, Beyhan Ataseven, Claire Cropet, Giovanni Scambia, Ana Herrero, Paul Sevelda, Hiroaki Kobayashi, Peter Vuylsteke, Mansoor Raza Mirza, Franck Priou, Paul Buderath, Carmela Pisano, Nuria Lainez, Cécile Guillemet, Alexander Burges, Robert Sverdlin, Ahmed El-Balat, Nadia Raban, Isabelle Ray-Coquard

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ClinicalTrials.gov identifier: NCT02477644 | This study was sponsored by ARCAGY Research.

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Conclusions

- In PAOLA-1/ENGOT-ov25, first-line maintenance bevacizumab alone had an overall RECIST ORR of 25%
  - ORR was higher in patients with a BRCAm and HRD-positive patients (BRCAm, 42%; HRD-positive, 31%; HRD-negative, 15%)
- The addition of olaparib maintenance to bevacizumab improved RECIST ORR and CR in the ITT population
  - Substantial ORR benefits were observed, particularly in patients with a BRCAm (64 vs 42%) and in HRD-positive patients (53% vs 31%)
  - In particular, higher CR rates were seen in patients with a BRCAm (57% vs 26%) and in HRD-positive patients (43% vs 22%)
- Together with the previously reported significant PFS improvement,[1] these data further support the addition of maintenance olaparib to bevacizumab for women with newly diagnosed advanced ovarian cancer

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1. Ray-Coquard I *et al. N Engl J Med* 2019;381:2416–28.

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Patient-Reported Outcomes in Patients Receiving Niraparib in the PRIMA/ENGOT-OV26/GOG-3012 Trial

Bhavana Pothuri

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GOG FOUNDATION

ENGOT European Network of Gynaecological Oncological Trial groups

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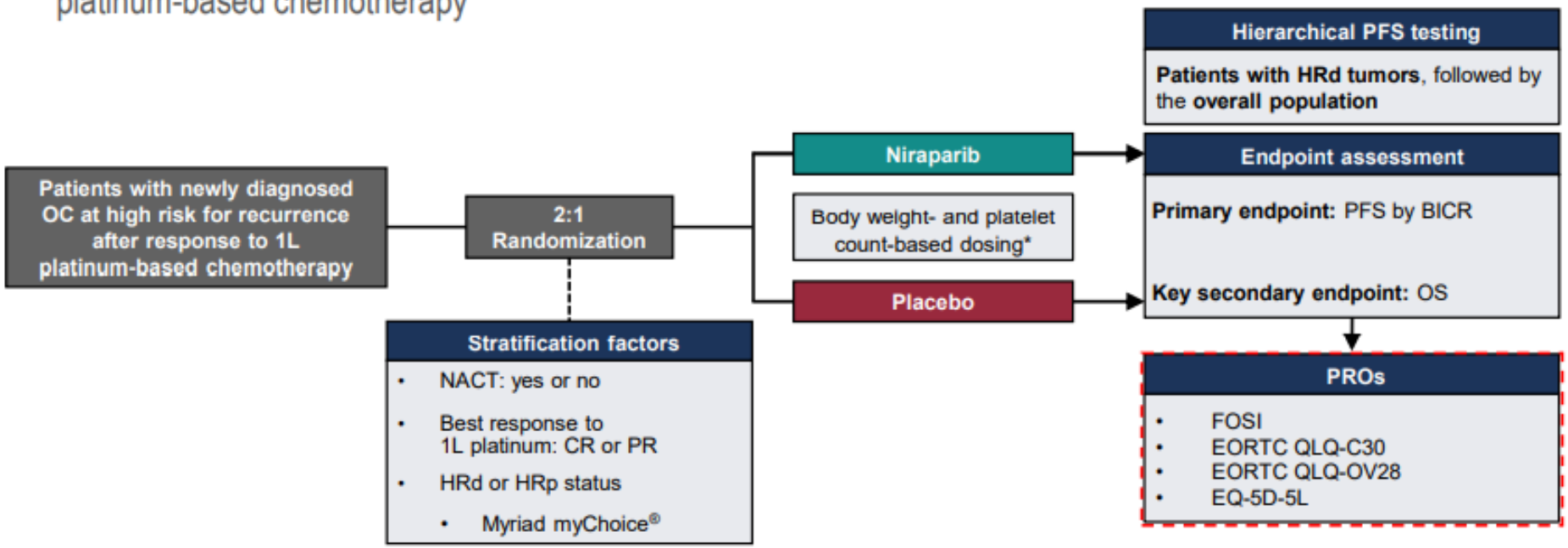
PRIMA Trial Design

- PRIMA is a randomized, double-blind, placebo-controlled phase 3 trial of niraparib vs placebo in patients with newly diagnosed advanced ovarian, primary peritoneal, or fallopian tube cancer with a CR or PR to 1L platinum-based chemotherapy



Patients received treatment until disease progression or a maximum of 36 months.
*After November 27, 2017, patients with baseline body weight <77 kg and/or platelet count <150,000/µL started at 200 mg QD; all other patients started at 300 mg QD. 1L, first-line; BICR, blinded independent central review; CR, complete response; EORTC QLQ-C30/OV28, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire/Ovarian Cancer Module; EQ-5D-5L, EuroQol 5-Dimension 5-Level; FOSI, Functional Ovarian Symptom Index; HRd, homologous recombination deficient; NACT, neoadjuvant chemotherapy; OC, ovarian cancer; OS, overall survival; PFS, progression-free survival; PFS2, progression-free survival 2; PR, partial response; PRO, patient-reported outcome; QD, once daily; TFST, time to first subsequent therapy.

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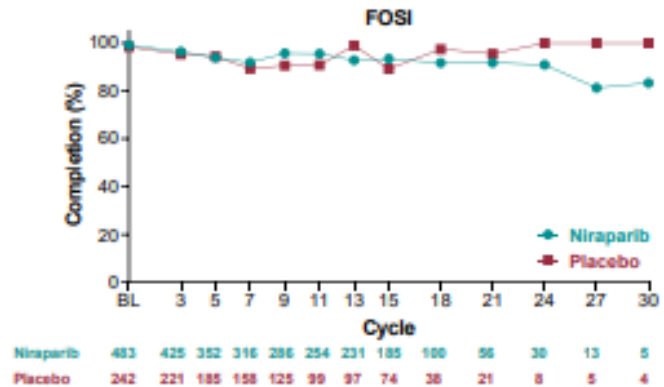
PRO Instruments

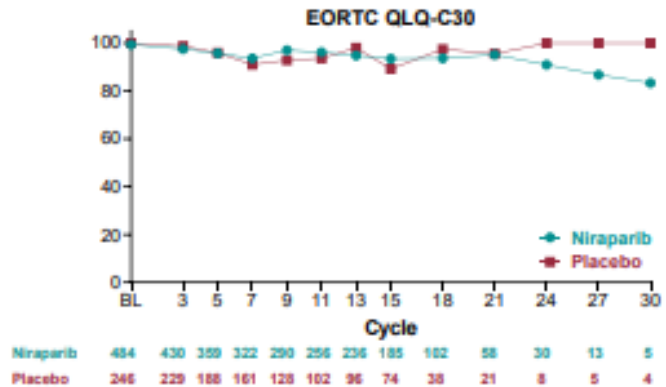
Instrument	Domains assessed	Score	Higher score indicates	Clinically meaningful change from baseline
FOSI Functional Ovarian Symptom Index	**Symptoms**: Fatigue, nausea, bloating, worry, pain, vomiting, cramping, QoL	Total 0–32	Better symptoms/HUI	± 2
EORTC QLQ-C30 European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire	**Functional scale**: Physical, role, emotional, cognitive, social function	0–100	Better functioning	± 10
	Symptoms: Fatigue, nausea & vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, financial difficulties	0–100	Worse symptoms	
	Global health status/QoL	0–100	Better QoL	
EORTC QLQ-OV28 European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Ovarian Cancer Module	**Functional scale**: Body image, sexuality, attitude toward disease/treatment	0–100	Better functioning	± 10
	Symptoms: Abdominal/GI symptoms, peripheral neuropathy, hormonal/menopausal symptoms, other chemotherapy side effects, hair loss	0–100	Worse symptoms	
EQ-5D-5L EuroQol 5-Dimension 5-Level	**Health state for five domains**: Mobility, self-care, usual activities, pain/discomfort, anxiety/depression	HUI 0–1	Better QoL	-
	Visual analog scale (VAS)	VAS 0–100	Better QoL	

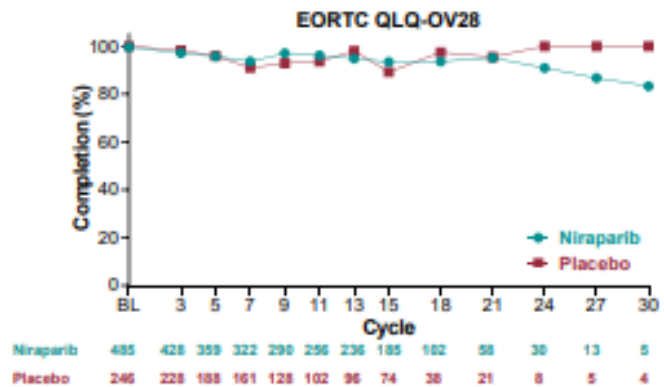
EOT, end of treatment; GI, gastrointestinal; HUI, health utility index; PRO, patient-reported outcome; QoL, quality of life; VAS, visual analog scale.

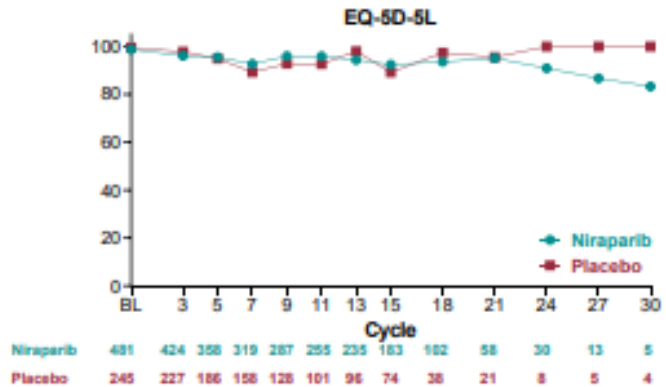
High Compliance Rates by PRO Instrument

- Patient compliance rates remained consistently high (>80%) across all PRO instruments throughout the trial









BL, baseline; EORTC QLQ-C30/OV28, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire/Ovarian Cancer Module; EQ-5D-5L, EuroQol 5-Dimension 5-Level; FOSI, Functional Ovarian Symptom Index; PRO, patient-reported outcome.

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Conclusions

- Patient compliance rates were high across all PRO instruments (>80%)
- FOSI scores between niraparib and placebo were comparable
  - Percentages of patients reporting lethargy, nausea, vomiting, and abdominal cramps were similar in niraparib and placebo arms
- QoL were comparable between niraparib and placebo, as indicated by the EORTC QLQ-C30 instrument
- Abdominal/GI symptoms and other CT effects were comparable in both arms, as assessed by the EORTC QLQ-OV28 instrument
- Overall QoL was similar in patients receiving niraparib compared with those receiving placebo, as assessed by the EQ-5D-5L instrument
- Consistent with PRO results in the NOVA study, patients receiving niraparib in the PRIMA trial did not experience a decrement in QoL compared with placebo during their treatment, despite AEs including grade ≥3 hematologic toxicity

AE, adverse event; CT, chemotherapy; EORTC QLQ-C30/OV28, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire/Ovarian Cancer Module; EQ-5D-5L, EuroQol 5-Dimension 5-Level; FOSI, Functional Ovarian Symptom Index; GI, gastrointestinal; PRO, patient-reported outcome; QoL, quality of life.

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#938 Health-related quality of life in patients with newly diagnosed stage III or IV ovarian cancer treated with veliparib + chemotherapy followed by veliparib maintenance

David Cella

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Northwestern University, Chicago, IL,
United States

ON: 16-18 OCTOBER 2020

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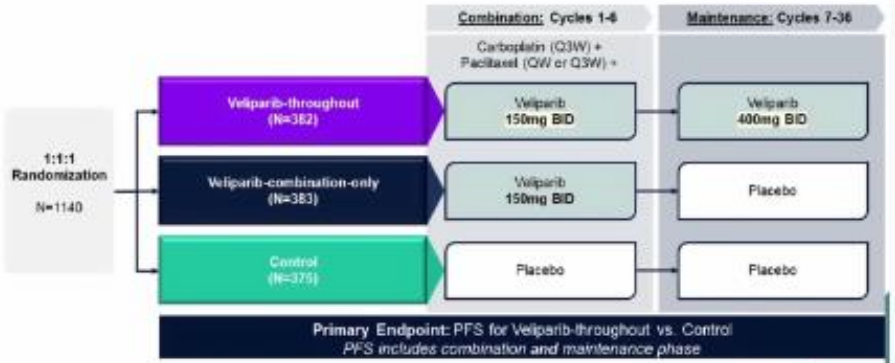
Background, Objective, and Methodology

- We investigated the effect of veliparib, an oral poly (ADP-ribose) polymerase inhibitor, on HRQoL in a Phase 3 study (NCT02470585) in women with advanced-stage ovarian cancer
- All patients were to receive carboplatin and paclitaxel (CP) for 6 cycles. Veliparib (or placebo) was to be administered together with CP followed by maintenance monotherapy (30 additional cycles)



- HRQoL measures were the NCCN Functional Assessment of Cancer Therapy Ovarian Symptom Index-18 and the EuroQoL-5D-5L
- Analyses included on-treatment comparisons of mean change from baseline in HRQoL scores and median time to symptom worsening
- Baseline demographics were similar between treatment arms with study compliance >90%

ADP, adenosine diphosphate; BID, twice a day; CP, carboplatin/paclitaxel; EQ-5D-5L, EuroQol 5-Dimensions 5-Levels; HRQoL, health-related quality of life; NCCN, National Comprehensive Cancer Network; PFS, progression-free survival; QW, once a week; Q3W, once every 3 weeks.

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Conclusions

- Compared with placebo+CP followed by placebo maintenance, addition of veliparib to CP followed by veliparib maintenance showed smaller improvements in HRQoL scores from baseline
- For both study arms, while early declines in treatment side effect scores were noted, improvements were observed in later cycles
- Time to symptom worsening for HRQoL domains were similar across study arms
- There were no clinically meaningful differences observed between the veliparib+ CP/veliparib and the placebo+CP/placebo arms for any HRQoL domain
- Thus, the addition of veliparib to CP followed by veliparib maintenance does not substantially increase treatment burden as measured by HRQoL, compared with chemotherapy alone in women with newly diagnosed stage high-grade serous epithelial ovarian cancer

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INOVATYON study

INternational OVArian cancer patients Trial with YONdelis

Randomized phase III international study comparing trabectedin/PLD followed by platinum at progression vs Carboplatin/PLD in patients with recurrent ovarian cancer progressing within 6-12 months after last platinum line.

N. Colombo[1], A. Gadducci[2], J. Sehouli[3], E. Biagioli[4], G.-B. Nyvang[5], S. Riniker[6], A. Montes[7], N. Ottevanger[8], A. G. Zeimet[9], I. Vergote[10], G. Funari[4], A. Baldoni[11], G. Tognon[12], A. De Censi[13], C. Churruca Galaz[14], R. Chekerov[3], J. Maenpaa[15], E. Rulli[4], R. Fossati[4], A. Poveda[16]

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Abstract #2694

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Individualized Starting Dose of Niraparib in Patients with Platinum-Sensitive Recurrent Ovarian Cancer (NORA) : A Randomized, Double-Blind, Placebo-Controlled, Phase III Trial

Xiaohua Wu[1], Jianqing Zhu[2], Rutie Yin[3], Jiaxin Yang[4], Jihong Liu[5], Jing Wang[6], Lingying Wu[7], Ziling Liu[8], Yunong Gao[9], Danbo Wang[10], Ge Lou[11], Hongying Yang[12], Qi Zhou[13], Beihua Kong[14], Yi Huang[15], Lipai Chen[16], Guiling Li[17], Ruifang An[18], Ke Wang[19], Yu Zhang[20]

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NORA Study Design

Main Inclusion Criteria

- Platinum-sensitive, recurrent ovarian cancer;
- High grade serous or high grade predominantly serous histology or known to have g*BRCA*mut;
- Completed at least 2 previous lines of platinum-containing therapy;
- Partial or complete response to the last platinum-based chemotherapy.

Stratification Factor

- g*BRCA* mutation: Yes or No
- Response to last chemotherapy: CR or PR
- Time to progression after penultimate platinum-based regimen: 6-12 months or ≥ 12 months

Randomization 2:1

- Niraparib# (n=160)
- Placebo (n=80)

Until disease progression or unacceptable toxicity

Primary Endpoint

- Progression-free survival (PFS) determined by BICR

Secondary Endpoints

- Safety
- Chemotherapy-free interval (CFI)
- Time to first subsequent therapy (TFST)
- Overall survival (OS)

Primary analysis of PFS

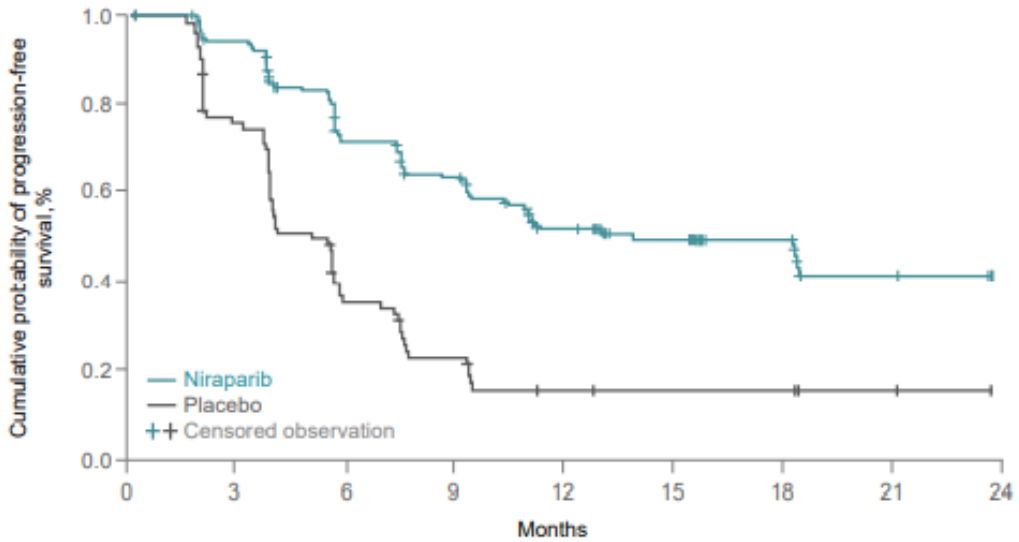
- **ITT population**
- Statistical assumption: PFS hazard ratio of 0.54, two-sided type I error of 0.05, power >90%

#After initial fixed dose of 300mg (n=16), adopted ISD in protocol amendment:

- **200 mg QD** for Patients with baseline body weight <77 kg or platelets count <150,000/μL;
- **300 mg QD** for Patients with baseline body weight ≥77 kg and platelets count ≥150,000/μL.

g*BRCA*mut, germline *BRCA* mutation; ITT, intention to treat; CR, complete response; PR, partial response; BICR: blinded independent central review

NORA Primary Endpoint: PFS (BICR) in ITT Population



Niraparib	177	160	116	100	70	43	25	8	0
Placebo	88	63	28	18	11	8	8	2	0

68% reduction of hazard for relapse or death with niraparib

	Niraparib (n=177)	Placebo (n=88)
Median PFS		
Months (95% CI)	18.3 (10.9–NE)	5.4 (3.7–5.7)
Hazard ratio (95% CI)	0.32 (0.23-0.45)	
p-value[1]	<0.0001	

- Niraparib resulted in significantly longer mPFS than placebo in ITT population of all-comer patients

ITT, intention to treat; BICR: blinded independent central review; CI, confidence interval; NE, not estimable; PFS, progression-free survival
[1]p-value is from stratified log-rank test.

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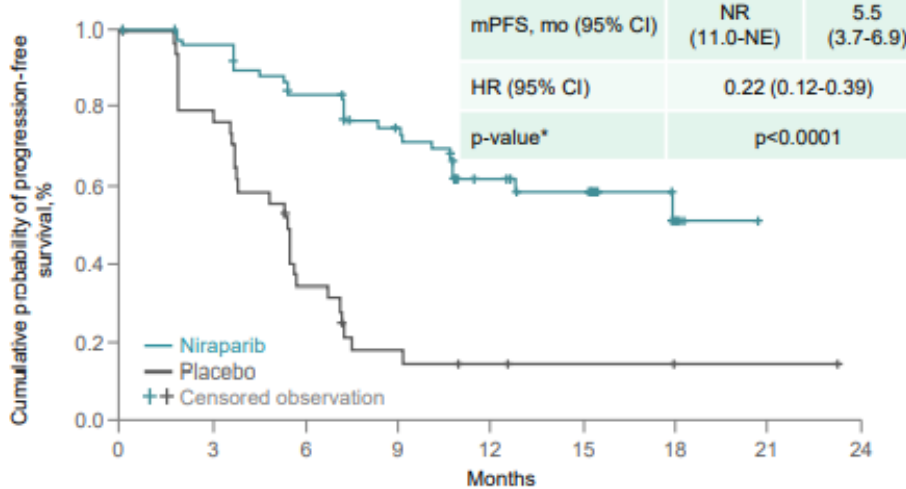
PFS (BICR) in Biomarker Subgroups

g*BRCA*mut subgroups

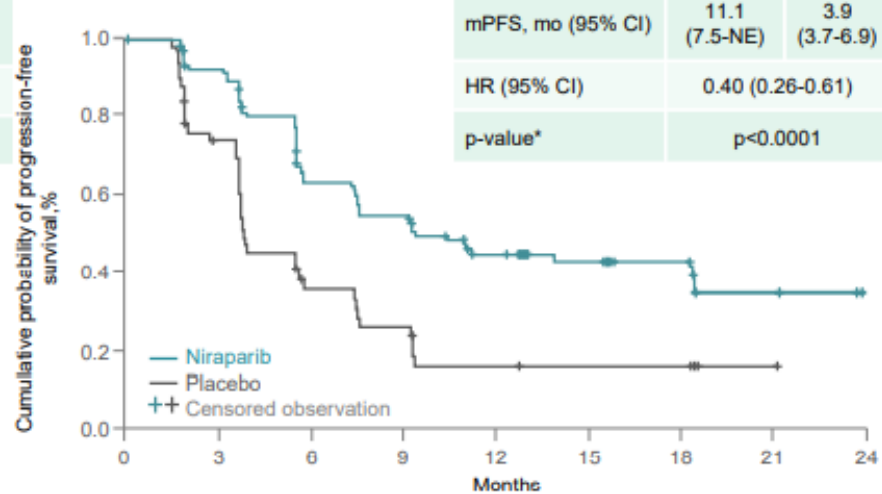
	Niraparib (n=65)	Placebo (n=35)
mPFS, mo (95% CI)	NR (11.0-NE)	5.5 (3.7-6.9)
HR (95% CI)	0.22 (0.12-0.39)	
p-value*	p<0.0001	



Niraparib	65	61	51	43	29	18	9	1	0
Placebo	35	27	11	5	3	2	2	1	0

Non-g*BRCA*mut subgroups

	Niraparib (n=112)	Placebo (n=53)
mPFS, mo (95% CI)	11.1 (7.5-NE)	3.9 (3.7-6.9)
HR (95% CI)	0.40 (0.26-0.61)	
p-value*	p<0.0001	



Niraparib	112	99	65	57	41	25	16	7	0
Placebo	53	36	17	13	8	6	6	1	0

- Niraparib provided clinical benefit regardless of g*BRCA* mutation status

PFS, progression-free survival; BICR: blinded independent central review; g*BRCA*mut, germline *BRCA* mutation; CI, confidence interval; NE, not estimable; NR, not reached.

* p-value is from stratified log-rank test, descriptive only

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Summary of the Efficacy (PFS) of NORA vs NOVA

	NORA	NOVA [1]
Number of Patients	265	553
Overall Population, HR (95% CI)	0.32 (0.23 to 0.45)	NA
g*BRCA*mut, HR (95% CI)	0.22 (0.12 to 0.39)	0.27 (0.17 to 0.41)
Non-g*BRCA*mut, HR (95% CI)	0.40 (0.26 to 0.61)	0.45 (0.34 to 0.61)

HR, hazard ratio, CI, confidence interval, NA, not available, g*BRCA*mut, germline *BRCA* mutation, PFS, progression-free survival

1. Mirza MR, et al. N Engl J Med, 2016, 375(22): 2154-2164

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Selective Grade 3/4 TEAEs by PT in NORA and NOVA

NORA

	Niraparib (N=177) n (%)	Placebo (N=88) n (%)
Neutrophil count decreased[a]	36 (20.3)	7 (8.0)
Anaemia[b]	26 (14.7)	2 (2.3)
Platelet count decreased[c]	20 (11.3)	1 (1.1)
Hypertension	2 (1.1)	0

NOVA

	Niraparib (N=367) n (%)	Placebo (N=179) n (%)
Thrombocytopenia[d]	124 (33.8)	1 (0.6)
Anaemia[b]	93 (25.3)	0
Neutropenia[e]	72 (19.6)	3 (1.7)
Hypertension	30 (8.2)	4 (2.2)

[a]The category of neutrophil count decreased includes reports of neutrophil count decreased and neutropenia. No febrile neutropenia reported in NORA.
[b]The category of anaemia includes reports of anaemia and decreased hemoglobin count.
[c]The category of platelet count decreased includes reports of platelet count decreased and thrombocytopenia.
[d]The category of thrombocytopenia includes reports of thrombocytopenia and decreased platelet count.
[e]The category of neutropenia includes reports of neutropenia, decreased neutrophil count, and febrile neutropenia.

TEAEs, treatment emergent adverse events.; PT, preferred term

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Conclusions

- NORA is the first fully powered phase III RCT evaluating a PARP inhibitor in Chinese patients with ovarian cancer.
- NORA met its primary endpoint, demonstrating that niraparib administered with an ISD regimen significantly improves the outcome in the patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.
  - PFS overall population: HR 0.32 ($p<0.0001$)
    - PFS in g*BRCA* mutation subgroup: HR 0.22 ($p<0.0001$)
    - PFS in non-g*BRCA* mutation subgroup: HR 0.40 ($p<0.0001$)
- Prospective evaluation of ISD in NORA validated the NOVA retrospective analysis. ISD of niraparib demonstrated consistent PFS benefit compared to NOVA with improved safety profile, especially the hematological toxicities.
- ISD of niraparib is effective and safe and should be considered the standard clinical practice for the maintenance therapy of patients with ovarian cancer.

g*BRCA*, germline *BRCA*; PFS, progression-free survival; RCT, Randomized Clinical Trial

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Efficacy of subsequent chemotherapy for patients with BRCA1/2 mutated platinum-sensitive recurrent epithelial ovarian cancer progressing on olaparib vs placebo

Post-hoc analyses of the SOLO2/ENGOT Ov-21 trial.

JS Frenel, J-W Kim, D Berton, R Asher, L Vidal, P Pautier, J-A. Ledermann, R T. Penson, A M. Oza, J Korach, T Huzarski, S Pignata, N Colombo, T-W Park-Simon, K Tamura, G S. Sonke, AE. Freimund, C K Lee, E Pujade-Lauraine

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Institut de Cancérologie de L'Ouest/ GINECO group

ON: 16-18 OCTOBER 2020

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Background and objectives

- SOLO 2 trial if the first Phase 3 trial of maintenance therapy with PARP inhibitor showing a clinically meaningful prolongation of:
  - ✓ PFS1 by 13.6 months over placebo
  - ✓ PFS2 (median not reached for patients in the olaparib arm)
  - ✓ and of OS by 12.9 months
- Optimal management of patients after progression is still to be determined

We conducted a post-hoc analysis of patients in the SOLO2 trial who had a RECIST progression and explored the

- ✓ Type of treatment that the patients received after first disease progression
- ✓ Time to second progression defined as the time between RECIST first progression to second progression or death

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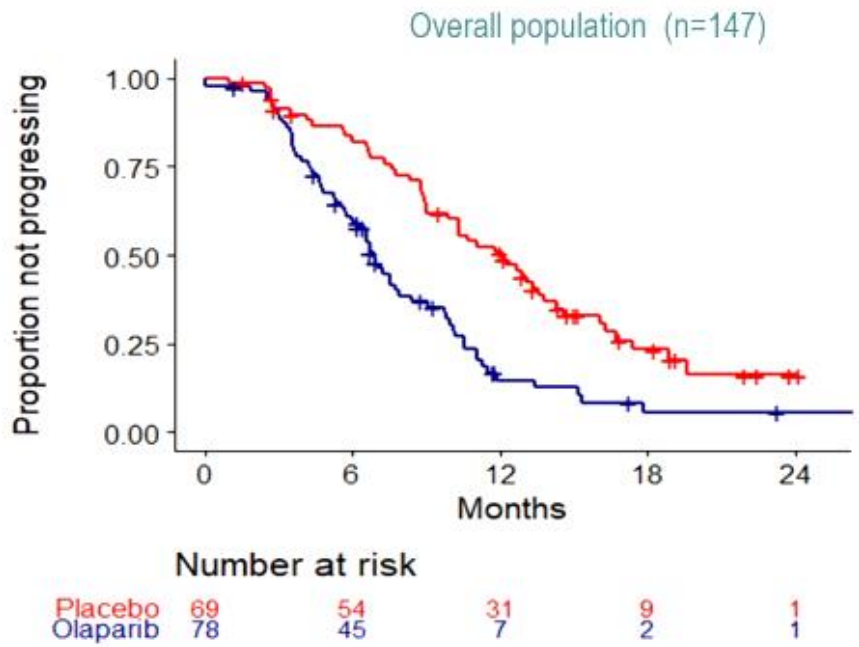
Time to second progression in patients treated with chemotherapy

Olaparib vs Placebo
Median: 6.9 vs 12.6m
HR=2.17; 95%CI [1.47, 3.19]



Time to second progression defined as the time between RECIST first progression to second progression or death

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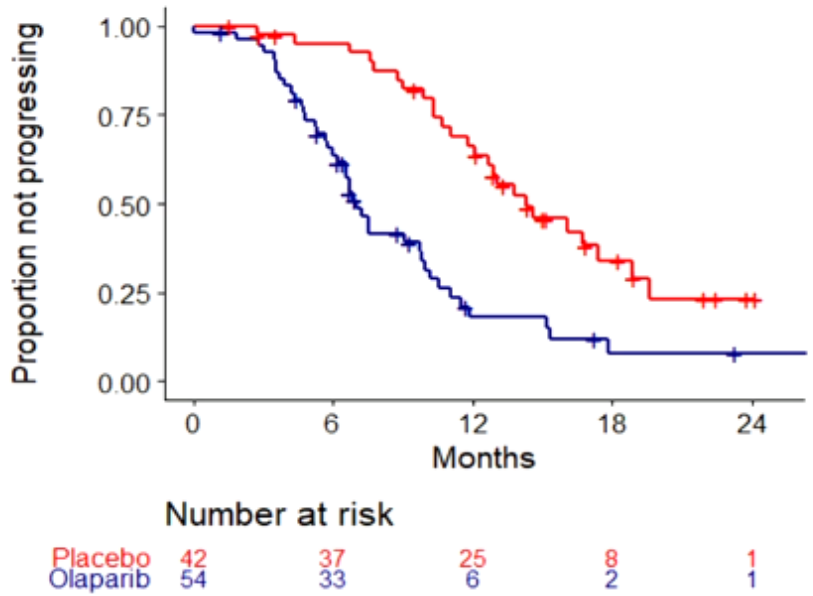
Time to second progression in patients treated with platinum-based chemotherapy (n=96)

18/42 pts received PARPi maintenance after platinum in the placebo arm

Olaparib vs Placebo
median 7.0 vs 14.3 months
HR=2.89; 95%CI [1.73, 4.82]



Time to second progression defined as the time between RECIST first progression to second progression or death

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Conclusions

- In this post-hoc non-randomised analysis of the SOLO2/ENGOT Ov-21 trial, efficacy of subsequent chemotherapy (particularly platinum-based chemotherapy) assessed by time to second progression, appears to be less in patients having received maintenance olaparib compared to placebo
- The exact reason remains to be explored in detail: induction of chemoresistance, selection of poorly chemosensitive relapsing patients by olaparib maintenance or both?
- The best management of patients relapsing after olaparib maintenance should be studied in a prospective manner
- Olaparib maintenance versus placebo increased overall survival in the SOLO2/ENGOT Ov-21 population and remains the best option for these patients.

828P Expected versus observed response to platinum-based chemotherapy after poly (ADP-ribose) polymerase inhibitor treatment for relapsed ovarian cancer

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Background: Poly(ADP-ribose) polymerase inhibitors (PARPi) have become standard of care after response to platinum-based chemotherapy (CTX) for relapsed ovarian cancer (OC). Recently, PARPi have been approved as maintenance after first-line treatment as well. Response to platinum is the key predictor for response to PARPi treatment. Sensitivity and resistance to platinum and PARPi treatment partially overlaps. It remains unclear how prior progression on PARPi treatment might influence response to subsequent platinum-based CTX.

Methods: Patients undergoing platinum-based CTX for 2nd relapse of epithelial OC treated between 2011 and 2020 at the department of gynecologic oncology at Kliniken Essen-Mitte were included in this retrospective study. All patients provided written consent for retrospective analyses. Stratification parameter were defined as follows: Response to 2nd line CTX, PARPi maintenance, cytoreductive surgery for relapsed OC, BRCA status, PFS and treatment-free interval for platinum (TFIp) after 2nd line CTX. Primary outcome parameter was response to 3rd-line platinum-based CTX in patient with and without prior PARPi treatment.

Results: After response to 2nd-line CTX, 57 patients received no PARPi (control) and 35 patients received a PARPi (n=16 olaparib, n=19 niraparib) as maintenance therapy. Baseline characteristics were well balanced between treatment groups. After PARPi maintenance 40% (14/35) of patients progressed on subsequent platinum-based CTX *vs* 9% (5/57) in the control group. Response to 3rd line platinum-based CTX, evaluated as complete response, partial response, stable disease and progressive disease, was significantly altered by prior PARPi maintenance therapy (χ^2 14.19 — df 3 — p=0.003).

Conclusions: Response to platinum-based 3rd line chemotherapy is lower than expected in patients treated with PARPi maintenance after response to 2nd line platinum-based chemotherapy, compared to patients who achieved a similar PFS and TFIp who did not receive a PARPi. Our data provide clinical evidence for altered sensitivity towards platinum-based CTX after prior PARPi treatment.

Poster number: 821P

Timing of Adverse Events During Maintenance Treatment With Rucaparib for Recurrent Ovarian Cancer in the Phase 3 ARIEL3 Study

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HIGHLIGHTS

- **The overall safety profile of rucaparib maintenance treatment in patients with recurrent ovarian cancer from ARIEL3 remains consistent with previous reports,[1,2] with no new safety signals identified**
- **Prevalence of any-grade nausea declined progressively over the 24-month evaluation period**
- **Prevalence of any-grade anaemia/decreased haemoglobin peaked at month 4, decreasing to a plateau after month 8**
- **The first onset of frequently reported TEAEs generally occurred early in treatment (≤45 days). The median duration of the first event of frequently reported TEAEs was generally <60 days (Figure 3)**

Poster Download

Also available at: [illegible]

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1. Coleman et al. Lancet. 2017;390:1949-61.
2. Ledermann et al. Lancet Oncol. 2020;21:710-22.

ACKNOWLEDGEMENTS

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PRESENTING AUTHOR DISCLOSURE

[illegible]

INTRODUCTION

- In the randomised, placebo-controlled, double-blind, phase 3 study ARIEL3 (NCT01968213), the poly(ADP-ribose) polymerase inhibitor rucaparib significantly improved progression-free survival vs placebo as maintenance treatment for patients with platinum-sensitive, recurrent ovarian cancer who were in complete or partial response to platinum-based chemotherapy[1]
- Here we present an analysis of treatment-emergent adverse events (TEAEs) with 2 years of additional follow-up for patients continuing treatment in ARIEL3 compared with the previous safety report[2]
  - We also include new analyses of the prevalence of key TEAEs over time as well as an analysis of the median time to and median duration of first occurrence of TEAEs

METHODS

- Safety data were summarised for all patients who were randomised into ARIEL3 and who received at least one dose of study treatment
  - After treatment discontinuation, patients were followed for TEAEs for up to 28 days
- TEAEs were classified per MedDRA version 19.1 and graded by investigator assessment as per the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03
- Additional safety analyses include:
  - Prevalence of nausea and anaemia/decreased haemoglobin over time
  - Median time to onset of first TEAE
  - Median duration of first TEAE, defined as the duration of first TEAE, regardless of grade; TEAEs overlapping by ≤2 days were considered as the same continuous event; TEAEs occurring after the first event were not included in the duration calculation
    - AE duration was calculated using Kaplan-Meier methodology, in which ongoing events without a known end date were censored at the date of the last dose plus 28 days
- The visit cutoff date for these safety analyses was 31 December 2019

RESULTS

Safety Overview

- The current analysis of TEAEs in ARIEL3 remains consistent with previous reports,[1,2] with no new safety signals identified
  - As of the previous safety data cutoff (31 Dec 2017),[2] 60/372 patients in the safety population were still receiving rucaparib and 5/189 patients were receiving placebo
  - As of the current analysis (31 Dec 2019), 33/372 and 1/189 patients were still receiving rucaparib or placebo, respectively
  - Median treatment duration was 8.3 months in the rucaparib arm and 5.5 months in the placebo arm at both the previous and current safety data cutoff dates
- All patients in the rucaparib arm and 182/189 (96.3%) patients in the placebo arm experienced ≥1 TEAE
  - Grade ≥3 TEAEs were reported by 231/372 (62.1%) patients in the rucaparib arm and 31/189 (16.4%) patients in the placebo arm (**Table 1**)
  - Grade 4 TEAEs were reported by 28/372 (7.5%) and 2/189 patients (1.1%) in the rucaparib and placebo arms, respectively. The most frequent grade 4 TEAEs in the rucaparib arm were neutropenia/decreased neutrophils and thrombocytopenia/decreased platelets (7/372 patients [1.9%] each)

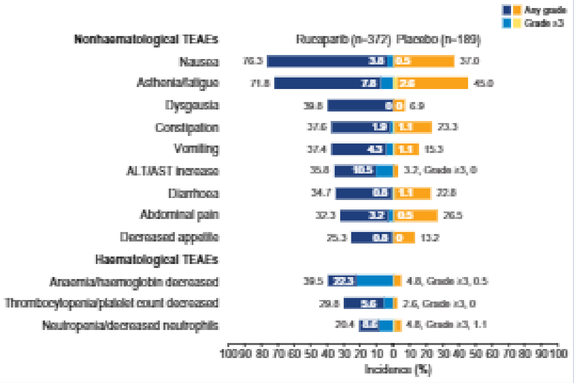
Table 1. Summary of TEAEs

	Rucaparib (n=372)*	Placebo (n=189)
Treatment duration, median (range), mo	8.3 (0–67)	5.5 (0–68)
Patients with at least one TEAE	372 (100)	182 (96.3)
Patients with at least one grade ≥3 TEAE	231 (62.1)	31 (16.4)
Treatment interruption and/or dose reduction due to TEAE	271 (72.8)	20 (10.6)
Treatment interruption due to TEAE	248 (66.7)	19 (10.1)
Dose reduction due to TEAE	209 (56.2)	8 (4.2)
Discontinued due to TEAE†	64 (17.2)	3 (1.6)
Deaths due to TEAE†	6 (1.6)‡	1 (0.5)§
Deaths due to disease progression	2 (0.5)¶	1 (0.5)#

Data are n (%), except where indicated.
[illegible]

- In the rucaparib arm, the most frequently reported TEAEs of any grade were nausea (284/372 [76.3%]) and asthenia/fatigue (267/372 [71.8%]); the most frequently reported grade ≥3 TEAEs were anaemia/decreased haemoglobin (83/372 [22.3%]) and alanine aminotransferase (ALT)/aspartate aminotransferase (AST) increase (39/372 [10.5%]) (**Figure 1**)
- In the rucaparib arm, treatment-emergent myelodysplastic syndrome (MDS) occurred in 4 (1.1%) patients and treatment-emergent acute myeloid leukaemia (AML) occurred in 1 (0.3%) patient, representing 2 additional cases of treatment-emergent MDS than reported previously[2]
  - Of the patients who experienced MDS or AML, 3 had a germline BRCA-mutant carcinoma, 1 had a somatic BRCA-mutant carcinoma and 1 had a BRCA wild-type/low loss of heterozygosity carcinoma
- No patients in the placebo arm reported treatment-emergent MDS or AML

Figure 1. Most Frequent (≥20%) TEAEs of Any Grade in Either Treatment Arm


Any grade
Grade ≥3
Nonhaematological TEAEs
Rucaparib (n=372)
Placebo (n=189)
Nausea
Asthenia/fatigue
Dysgeusia
Constipation
Vomiting
ALT/AST increase
Diarrhoea
Abdominal pain
Decreased appetite
Haematological TEAEs
Anaemia/haemoglobin decreased
Thrombocytopenia/platelet count decreased
Neutropenia/decreased neutrophils
Incidence (%)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; TEAE, treatment-emergent adverse event.

Prevalence of TEAEs by Month and Grade

- Nausea, the most common nonhaematological TEAE, was predominantly grade 1, and the prevalence declined from a peak of 66.9% in month 1 of treatment to 22.2% in month 24 (**Figure 2A**)
- The prevalence of any-grade anaemia/decreased haemoglobin, the most common haematological TEAE, peaked at 31.4% during month 4, thereafter declining to a plateau of ~20% after month 8, with a corresponding decrease in prevalence of grade ≥2 anaemia/decreased haemoglobin over this time period (**Figure 2B**)

Figure 2A. Prevalence of Nausea by Month and Grade in the Treatment Arms

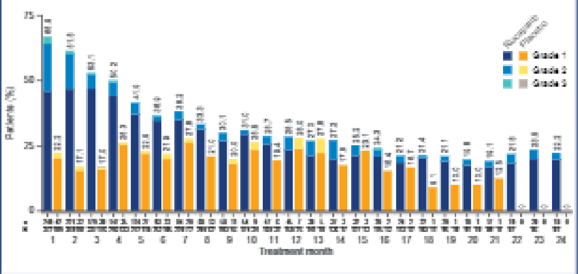


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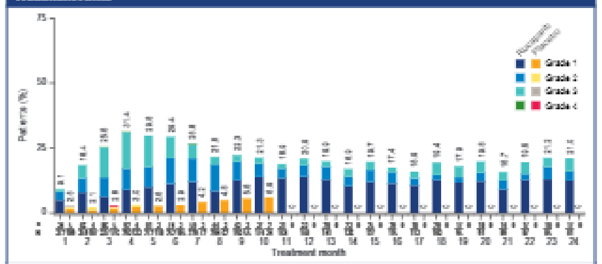
Figure 2B. Prevalence of Anaemia/Decreased Haemoglobin by Month and Grade in the Treatment Arms



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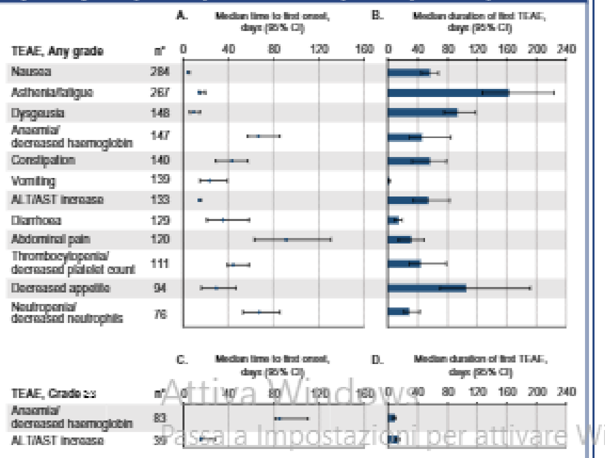
Time to Onset and Duration of First TEAE in the Rucaparib Arm

- For the majority of frequently reported (≥20%) any-grade TEAEs, median time to first onset was ≤45 days, except for anaemia/decreased haemoglobin, abdominal pain and neutropenia/decreased neutrophils which had median first onset times >45 days (**Figure 3A**)
  - Median time to first onset of grade ≥3 anaemia/decreased haemoglobin and ALT/AST increase was 85 and 16 days, respectively (**Figure 3C**)
  - Median time to onset of MDS was 844 days (95% CI, 365–1611); and of AML was 421 days
- For the frequently reported any-grade TEAEs, the median duration of the first event was generally <60 days, with the exception of asthenia/fatigue, decreased appetite and dysgeusia, for which it was ~90–160 days (**Figure 3B**)
  - Median duration of the first event of grade ≥3 anaemia/decreased haemoglobin and ALT/AST increase was <14 days (**Figure 3D**), which was shorter than the duration of the corresponding any-grade TEAEs (**Figure 3B**)

Figure 3. Median Time to First Onset and Median Duration of First TEAE of Most Frequently Reported Any-Grade (≥20%; A, B) and Grade ≥3 TEAEs (≥10%; C, D) in the Rucaparib Arm


A. Median time to first onset, days (95% CI)
B. Median duration of first TEAE, days (95% CI)
TEAE, Any grade
n*
Nausea 284
Asthenia/fatigue 267
Dysgeusia 148
Anaemia/decreased haemoglobin 147
Constipation 140
Vomiting 139
ALT/AST increase 133
Diarrhoea 129
Abdominal pain 120
Thrombocytopenia/decreased platelet count 111
Decreased appetite 94
Neutropenia/decreased neutrophils 76
C. Median time to first onset, days (95% CI)
D. Median duration of first TEAE, days (95% CI)
TEAE, Grade ≥3
Anaemia/decreased haemoglobin 83
ALT/AST increase 39

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ARCAGY - GINECO

Centre François Baclesse

Paclitaxel with or without pazopanib in ovarian cancer patients with relapse during bevacizumab maintenance therapy

The GINECO randomized phase 2 TAPAZ study

E. Joly Lobbedez[1], M. Fabbro[2], D. Berton[3], J. Lequesne[4], A. Anota[5], A. Puszkiel[6], A. Floquet[7], M. Cancel[8], H. Bourgeois[9], L. Bengrine Lefevre[10], B. You[11], F. Pommeret[12], A. Lortholary[13], D. Spaeth[14], J. Martin-Babau[15], C. Abdeddaim[16], M.-C. Kaminsky-Forrett[17], D. Petran[18], M. Provansal Gross[19], P.-E. Brachet[1].

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Florence JOLY LOBBEDEZ

Centre François Baclesse / GINECO Group

2020

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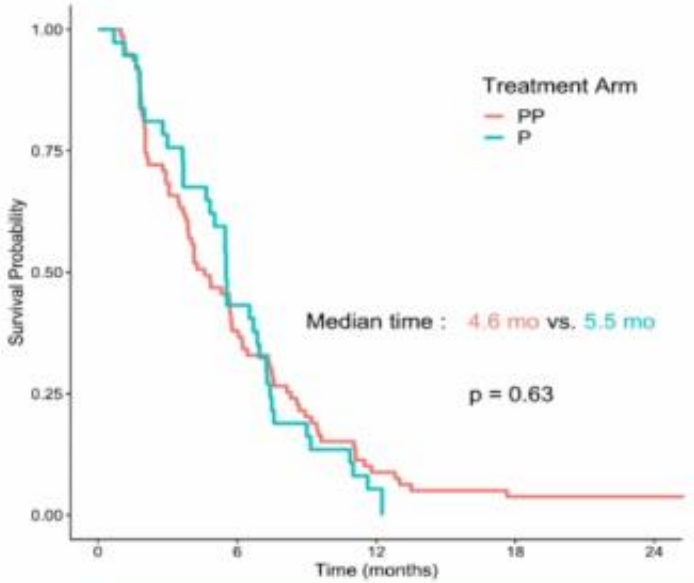
TAPAZ : Efficacy results

Progression-Free Survival

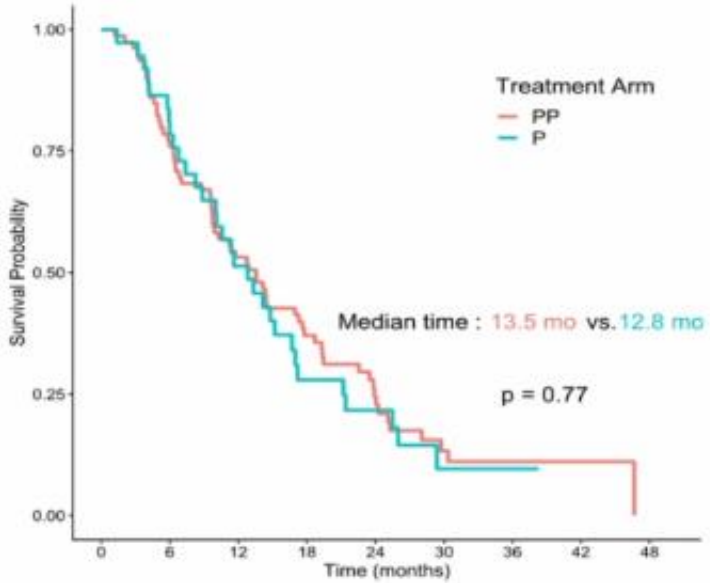


Main endpoint

4-months PFS rate :

- 57 % [95%CI 47-69] in PP arm
- 67.6% [54-84.5] in P arm

Overall Survival



Median follow-up of 12.8 months

Case & Morgan design :
Z-test statistic -10.9<Rejection limit : H0 retained.
Median PFS 4.6 mo [3.9-6.1]

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Phase II study of olaparib plus durvalumab and bevacizumab (MEDIOLA): initial results in patients with non-germline BRCA-mutated platinum sensitive relapsed ovarian cancer

Yvette Drew,[1] Richard Penson,[2] David M O'Malley,[3] Jae-Weon Kim,[4] Stefan Zimmermann,[5] Patricia Roxburgh,[6] Joohyuk Sohn,[7] Salomon M Stemmer,[8] Sara Bastian,[9] Michelle Ferguson,[10] Benoit You,[11] Susan Domchek,[12] Haiyan Gao,[13] Helen K Angell,[13] Kassondra Meyer,[14] Laura Opincar,[14] Lone Ottesen,[13] Susana Banerjee[15]

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ClinicalTrials.gov identifier: NCT02734004
This study was sponsored by AstraZeneca

Plain-language summary

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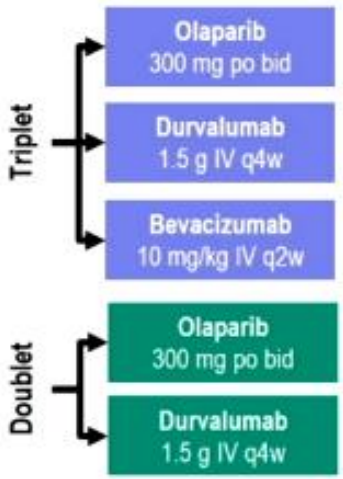
MEDIOLA: gBRCAwt cohorts

Study schema

Patient population

- gBRCAwt
- PSR ovarian cancer
- ≤2 prior lines of chemotherapy
- PARP inhibitor and IO agent naïve



Treatment to disease progression

Primary endpoints

- DCR at 24 weeks (target 80%)
- Safety and tolerability

Secondary endpoints include:

- DCR at 56 weeks, ORR, DOR, PFS, OS, PK

Exploratory endpoints include:

- Tumour genetics and immunology biomarkers

Sequential enrolment

Tumour assessments every 8 weeks

Bid, twice daily; DCR, disease control rate; DOR, duration of response; IO, immuno-oncology; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; po, by mouth; PSR, platinum-sensitive relapsed; q2w, every 2 weeks; q4w, every 4 weeks

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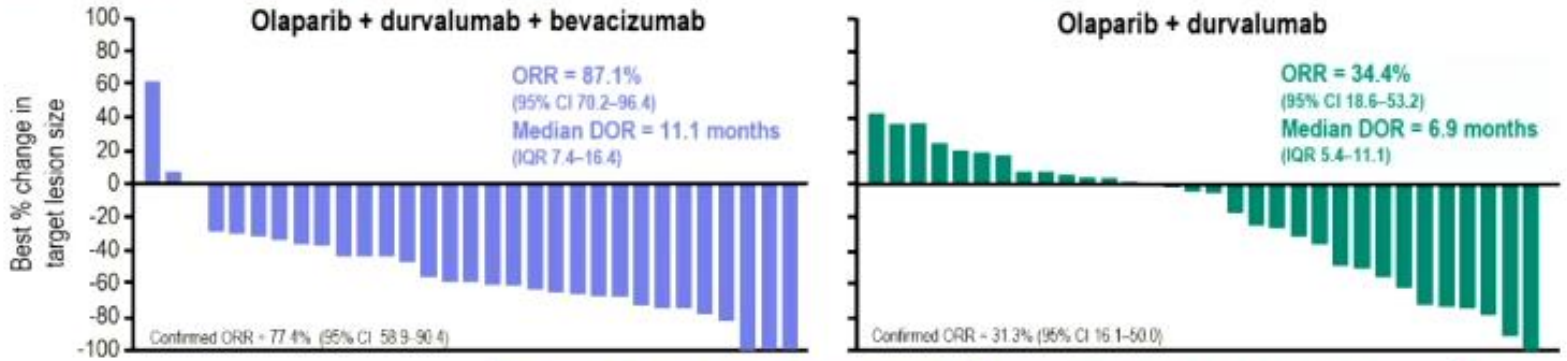
Triplet cohort demonstrates high ORR

Exploratory analysis suggests triplet cohort ORR is not GIS-dependent



Genomic instability status* subgroup	Olaparib + durvalumab + bevacizumab		Olaparib + durvalumab	
	ORR (95% CI), %	n/N patients	ORR (95% CI), %	n/N patients
GIS-positive	100.0 (69.2–100.0)	10/10	50.0 (18.7–81.3)	5/10
GIS-negative	75.0 (34.9–96.8)	6/8	16.7 (0.4–64.1)	1/6
GIS-unknown	84.6 (54.6–98.1)	11/13	31.3 (11.0–58.7)	5/16

*GIS, as determined by Foundation Medicine tumour analysis; must have genome-wide LOH ≥14, a somatic *BRCA1* and/or *BRCA2* mutation, or a mutation in *ATM*, *BRIP1*, *PALB2*, *RAD51C*, *BARD1*, *CDK12*, *CHEK1*, *CHEK2*, *FANCL*, *PPP2R2A*, *RAD51B*, *RAD51D* or *RAD54L* to be considered positive. At the time of the DCO, the prespecified cut-off for genome-wide LOH of 14% was used[1]; GIS, genomic instability status; IQR, interquartile range; LOH, loss of heterozygosity. [1]Swisher *et al. Lancet Oncol* 2017;18:75–87

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Conclusions

- The triplet combination of olaparib, durvalumab and bevacizumab showed promising efficacy as treatment in the absence of chemotherapy for women with germline BRCA wild type platinum-sensitive relapsed advanced ovarian cancer, with 77% DCR at 24 weeks and median PFS of 15 months
- Exploratory analysis suggests the high ORR in the triplet cohort was not driven by differences in genomic instability status; ORR was ≥75% in the GIS+, GIS− and GIS unknown subgroups
- The safety profile of the combination of olaparib plus durvalumab with or without bevacizumab was consistent with the known safety profiles expected for the single agents
- The combination of olaparib, durvalumab and bevacizumab is now being tested as part of first-line maintenance treatment in the Phase III study, DUO-O (NCT03737643)

Plain-language summary

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Nivolumab versus gemcitabine or pegylated liposomal doxorubicin for patients with platinum-resistant (advanced or recurrent) ovarian cancer: open-label, randomized trial in Japan (NINJA trial)

Kohei Omatsu[1], Junzo Hamanishi[2], Noriyuki Katsumata[3], Shin Nishio[4], Kenjiro Sawada[5], Satoshi Takeuchi[6*], Daisuke Aoki[7], Keiichi Fujiwara[8], Toru Sugiyama[9*], Ikuo Konishi[10]

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*Affiliation at the time of the study was Iwate Medical University, Iwate, Japan

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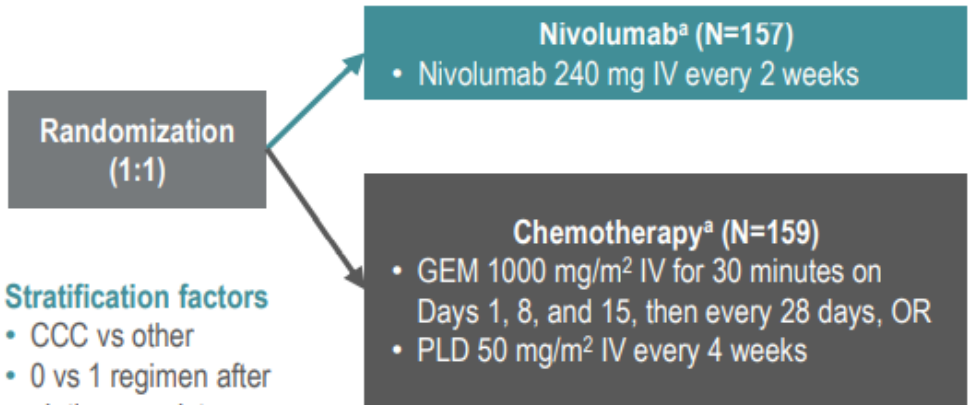
STUDY DESIGN

Key inclusion criteria
- Platinum-resistant advanced or recurrent ovarian cancer
- ≥20 years of age
- Received ≤1 regimen after diagnosis of platinum resistance
- ECOG PS ≤1

Key exclusion criteria
- Current or previous severe hypersensitivity reactions to antibody products
- Current, recurrent, or chronic autoimmune disease
- Multiple primary cancers and/or CNS metastases
- Pregnant or breastfeeding



Stratification factors
- CCC vs other
- 0 vs 1 regimen after platinum resistance diagnosis

Planned sample size
- 316 patients (158 per group)

- Tumor was assessed every 8 weeks through Week 48, then every 12 weeks thereafter
- Patients were followed up for 28 days after end of treatment administration

Primary efficacy endpoint:
- OS

Secondary efficacy endpoints[b]:
- PFS
- ORR
- BOR
- DoR (RECIST v1.1), etc.

Safety
- TEAEs
- Treatment-related AEs, etc.

[a]Treatment continued until disease progression or unacceptable toxicity.
[b]Investigator assessed.
AE, adverse event; BOR, best overall response; CCC, clear cell carcinoma; CNS, central nervous system; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; GEM, gemcitabine; IV, intravenous; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PLD, pegylated liposomal doxorubicin; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; TEAE, treatment-emergent adverse event.

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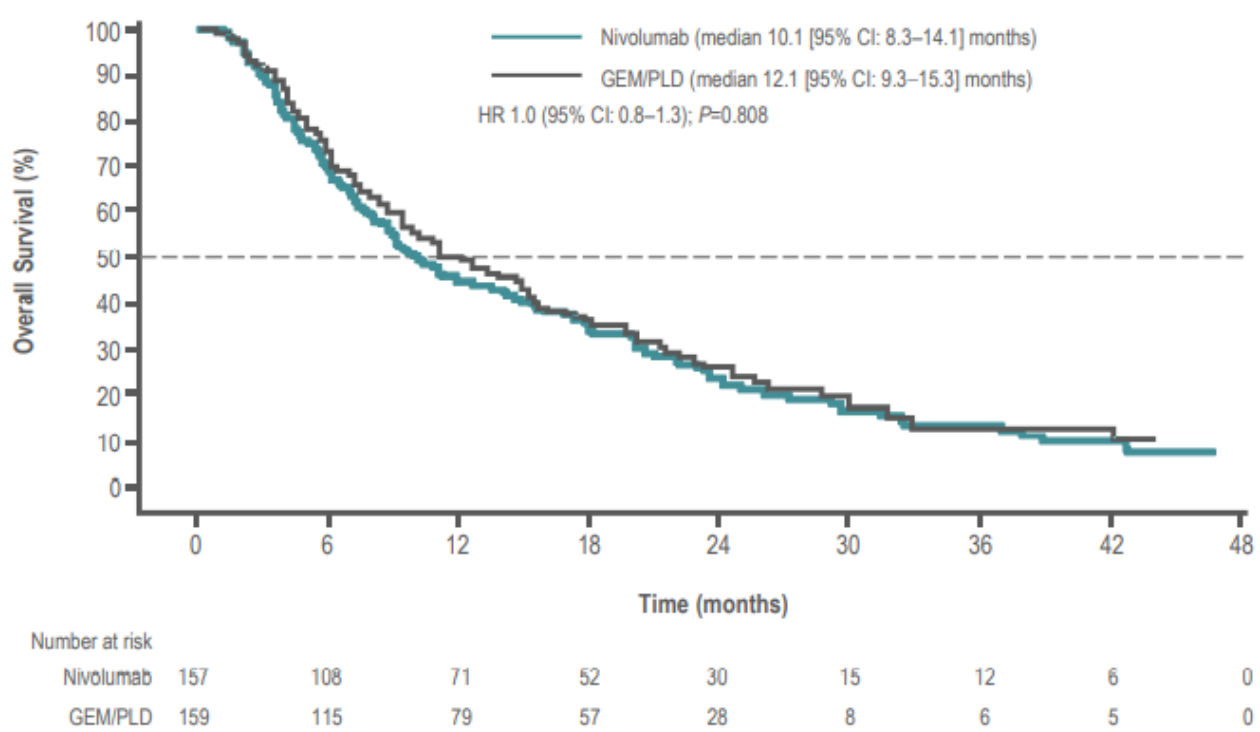
OVERALL SURVIVAL

- Nivolumab showed no superiority over GEM/PLD in OS



CI, confidence interval; GEM, gemcitabine; HR, hazard ratio; OS, overall survival; PLD, pegylated liposomal doxorubicin.

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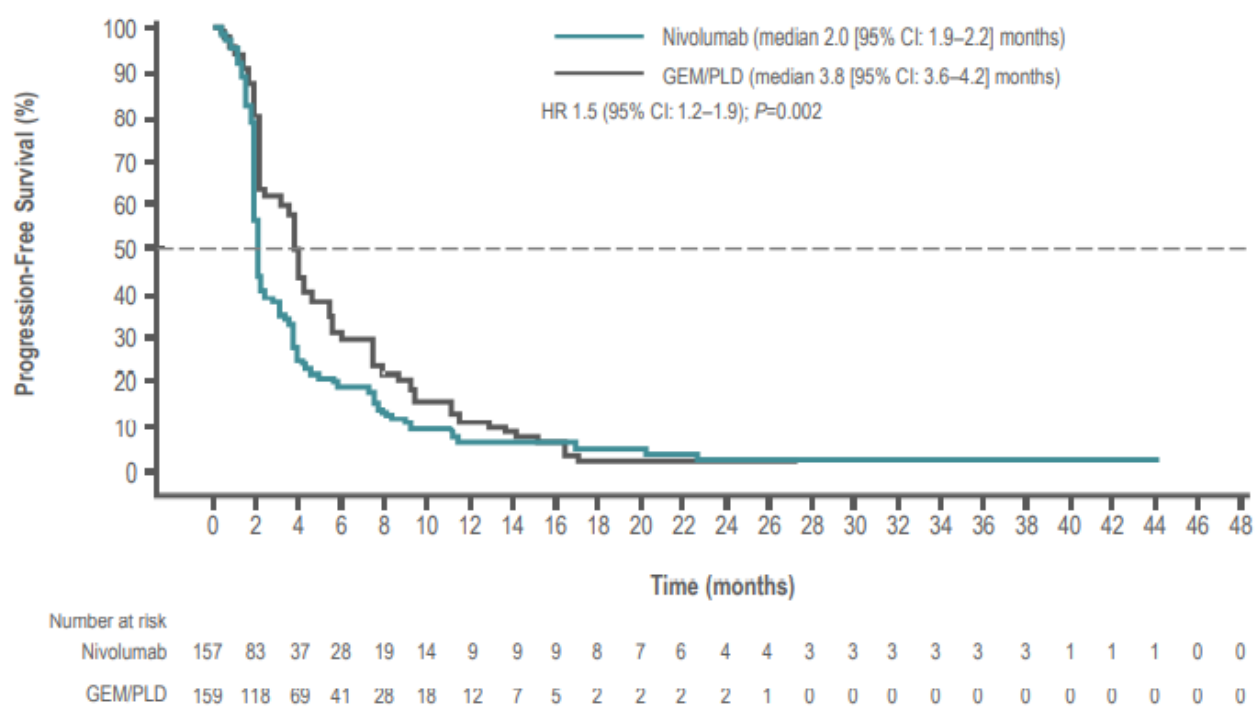
PROGRESSION-FREE SURVIVAL

- Nivolumab showed no superiority over GEM/PLD in PFS



CI, confidence interval; GEM, gemcitabine; HR, hazard ratio; PFS, progression-free survival; PLD, pegylated liposomal doxorubicin.

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CONCLUSIONS

- Nivolumab did not improve OS compared with GEM/PLD in patients with platinum-resistant (advanced or recurrent) ovarian cancer
- Nivolumab may show prolonged response compared with GEM/PLD in those who were responsive
  - Further subgroup analyses are currently being conducted
- In this study, there was a lower incidence of treatment-related AEs and Grade 3-4 treatment-related AEs with nivolumab than with GEM/PLD

AE, adverse event; GEM, gemcitabine; OS, overall survival; PLD, pegylated liposomal doxorubicin.

MOONSTONE/GOG-3032: A Phase 2, Open-Label, Single-Arm Study to Evaluate the Efficacy and Safety of Niraparib + Dostarlimab in Patients with Platinum-Resistant Ovarian Cancer

Poster number: 883TiP | Presenting author: Leslie M. Randall Leslie.Randall@vcuhealth.org

Leslie M. Randall[1], David M. O'Malley[2], Bradley J. Monk[3], Robert L. Coleman[4], Roisin E. O'Cearbhaill[5], Stephanie Gaillard[6], Sarah Adams[7], Fabio Cappuccini[8], Marilyn Huang[9], Hye Sook Chon[10], Angeles Alvarez Secord[11], Sujata Arora[12], Erika Keeton[12], Divya Gupta[12], Vivek Samnotra[12], Panagiotis Konstantinopoulos[13]

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Background

Therapeutic area

Ovarian cancer has one of the highest mortality rates of all gynaecologic cancers[1]

While initial response to surgery and first-line platinum-based chemotherapy might be favourable, up to 70% of patients relapse and the majority of tumours become platinum resistant[2,3]

The anti-VEGF monoclonal antibody, bevacizumab, is approved for treatment of recurrent platinum-resistant ovarian cancer in combination with single-agent chemotherapy[2]

However, there is still a strong clinical need for new treatment options[2]

Niraparib

Niraparib is a PARPi approved for:

- First-line maintenance treatment of adult patients with platinum-sensitive advanced epithelial ovarian, fallopian tube or primary peritoneal cancer (USA)[4]
- Maintenance treatment of adult patients with platinum-sensitive recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer (USA and EU)[4,5]
- Treatment of adult patients with advanced ovarian, fallopian tube or primary peritoneal cancer who have received ≥3 prior chemotherapy regimens whose cancer is associated with HRD-positive status defined by a deleterious or suspected deleterious *BRCA* mutation or genomic instability and progression >6 months after response to last platinum-based chemotherapy (USA)[4]

Niraparib monotherapy has shown antitumour activity in patients with platinum-refractory ovarian cancer, in a Phase II study of late-line treatment.[4,6] This included efficacy in patients with *BRCA* wild-type tumours who, in advanced ovarian cancer, have worse survival outcomes than those with *BRCA* mutations[6,7]

Niraparib in combination regimens

Dostarlimab is an anti–PD-1 humanised monoclonal antibody that binds with high affinity to the PD-1 receptor, effectively blocks interaction with the PD-1 ligands (PD-L1 and PD-L2), and has shown activity in solid tumours, including in patients who have progressed after a platinum-based regimen[8,9]

PARPi + anti–PD-1 combinations have shown synergistic antitumour effect, regardless of *BRCA* mutation status[10,11]

Trial objective

The objective of this study is to evaluate the safety and efficacy of niraparib + dostarlimab in patients with advanced, relapsed, high-grade, *BRCA* wild-type platinum-resistant ovarian cancer who have progressed and have received prior bevacizumab

Study population

Key inclusion criteria

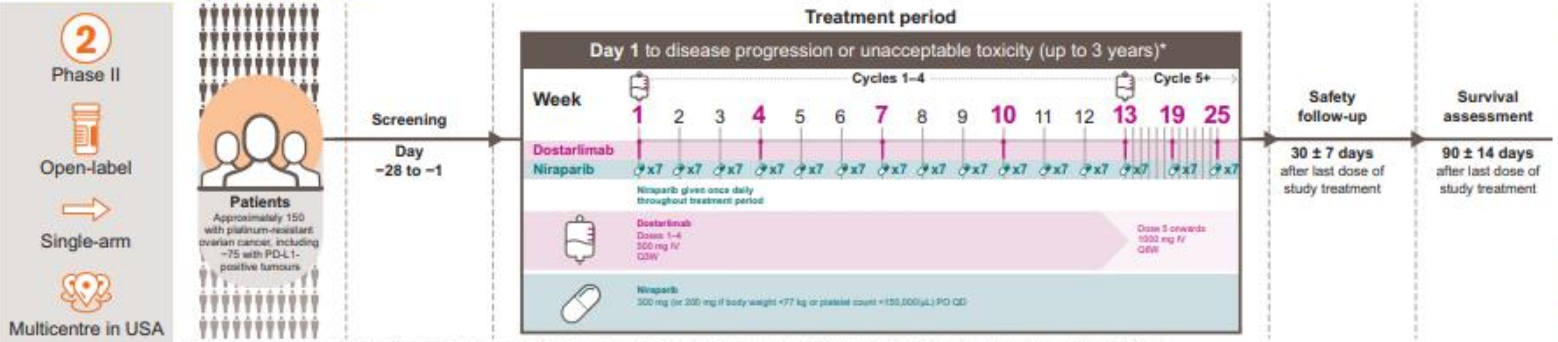
- Female, ≥18 years of age
- Recurrent high-grade serous, endometrioid or clear cell ovarian, fallopian tube or primary peritoneal cancer
- Have received 1–3 lines of prior therapy with platinum, taxane and bevacizumab
- Have had disease progression <6 months from the last administered platinum therapy (as evidenced by radiographic progression per RECIST v.1.1[12])
- Measurable disease (according to RECIST version v.1.1[12])
- ECOG performance status of 0 or 1
- Adequate organ function

Key exclusion criteria

- Prior treatment with a PARPi or anti–PD-(L)1 or anti–PD-L2 agent
- Known or suspected deleterious germline *BRCA* mutations, including *BRCA* mutations within the tumour
- Disease progression within 3 months (as evidenced by radiographic progression per RECIST v.1.1[12]) of first-line platinum therapy

Methods

The MOONSTONE study (NCT03955471) is:



*Other reasons for discontinuation include withdrawal of consent, investigator's decision or death. Patients who discontinue one of the treatments due to adverse events will be able to continue treatment with the second agent until disease progression or unacceptable toxicity.

Study objectives and endpoints

*Primary endpoint**

- ORR assessed by investigator
  - In the overall population
  - In the subset of patients with PD-L1+ tumours

*Key secondary endpoints**

- DoR
- PFS
- OS
- DCR
- ORR assessed by an independent review committee
- Safety and tolerability of combination treatment

Exploratory endpoints

- Efficacy in patients with confirmed *BRCA* wild-type tumours*†
- Duration of disease control in patients with best overall response of SD, PR or CR
- HRQoL as measured by FOSI
- Disease-related and treatment-related biomarkers of response, including:
  - Measures of homologous recombination repair pathway defects
  - Optimal PD-L1 levels for efficacy

*Response evaluated using RECIST v1.1[12] in the overall population and in the subset of patients with PD-L1+ tumours; †definitive germline *BRCA* mutation status per tumour sample obtained during study.

Current status

- **Currently recruiting**
- **Primary completion: September 2021**
- **Study completion: February 2024**

Abbreviations

BRCA, breast cancer gene; CR, complete response; DCR, disease control rate; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; FOSI, Functional Assessment of Cancer Therapy: Ovarian Symptom Index; HRD, homologous recombination deficiency; HRQoL, health-related quality of life; ORR, objective response rate; OS, overall survival; PARPi, poly (ADP-ribose) polymerase inhibitor; PD-1, programmed cell death receptor 1; PD-L, programmed cell death ligand; PFS, progression-free survival; PR, partial response; PO, oral; Q3W, every 3 weeks; Q6W, every 6 weeks; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumours; SD, stable disease; VEGF, vascular endothelial growth factor

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Presented at the European Society for Medical Oncology (ESMO) Virtual Congress 2020, 19–21 September 2020

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Tisotumab Vedotin in Previously Treated Recurrent or Metastatic Cervical Cancer: Results From the Phase 2 innovaTV 204/ GOG-3023/ENGOT-cx6 Study

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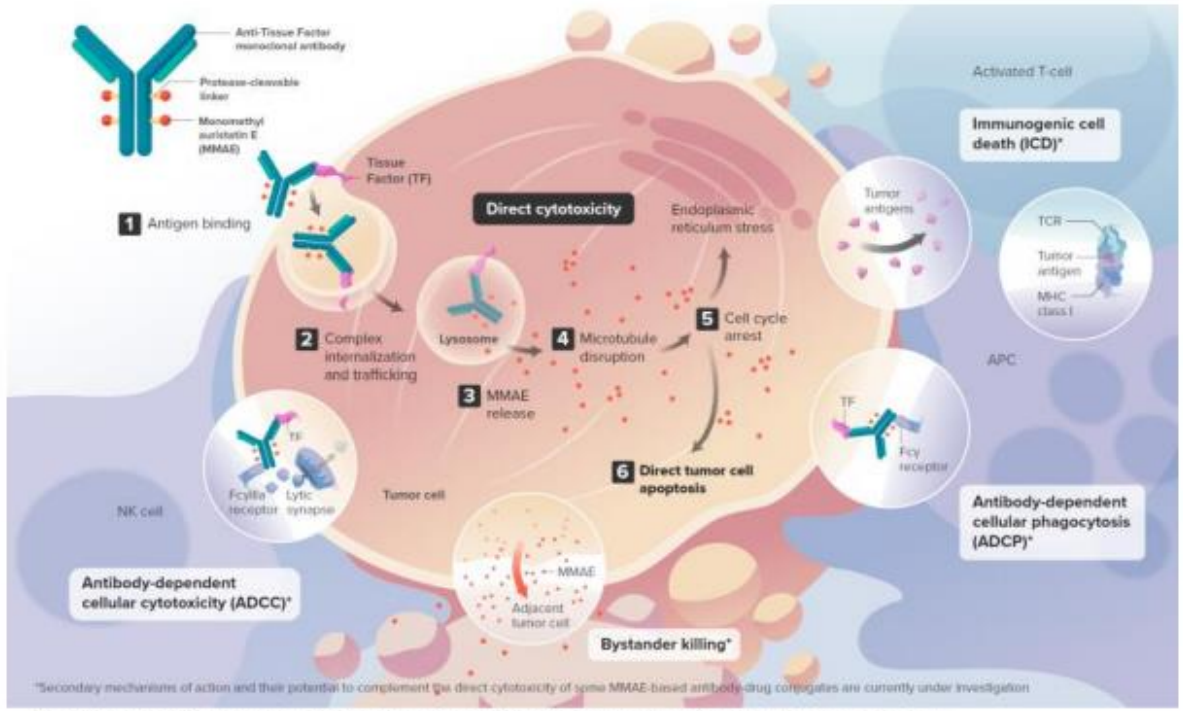
Proposed MOA of Tisotumab Vedotin

- Tisotumab vedotin is an investigational antibody-drug conjugate directed to tissue factor (TF) and covalently linked to the microtubule-disrupting agent MMAE via a protease-cleavable linker[1,2]
- TF is highly prevalent in cervical cancer and other solid tumors and is associated with cancer pathophysiology and poor prognosis[3-5]
  - TF is co-opted by tumor cells to promote tumor growth, angiogenesis, and metastasis[6]
  - In normal physiology, TF's primary role is to initiate the coagulation cascade after vascular injury[6]
- Tisotumab vedotin has multiple anti-tumor effects[1,2,7]



Tisotumab vedotin is an investigational agent, and its safety and efficacy have not been established.

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ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; MMAE, monomethyl auristatin E; MOA, mechanism of action; TF, tissue factor.

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innovaTV 204 Study Design

innovaTV 204 (NCT03438396) is a pivotal phase 2 single-arm, multicenter (United States and Europe) study evaluating tisotumab vedotin in patients with previously treated recurrent and/or metastatic cervical cancer

Key Eligibility Criteria

- Recurrent or extrapelvic metastatic cervical cancer
- Progressed during or after doublet chemotherapy[a] with bevacizumab (if eligible)
- Received ≤2 prior systemic regimens[b]
- ECOG PS 0-1

Enrolled: 102[c]
Treated: 101*

Tisotumab vedotin
2.0 mg/kg IV Q3W

Until PD or unacceptable toxicity

Tumor responses assessed using CT or MRI at baseline, every 6 weeks for the first 30 weeks, and every 12 weeks thereafter

*Study sample size calculated assuming a confirmed ORR of 21% to 25% with tisotumab vedotin and to provide ≥80% power to exclude an ORR of ≤11%[e]

Primary Endpoint
- ORR[d] per RECIST v1.1, by independent imaging review committee (IRC)

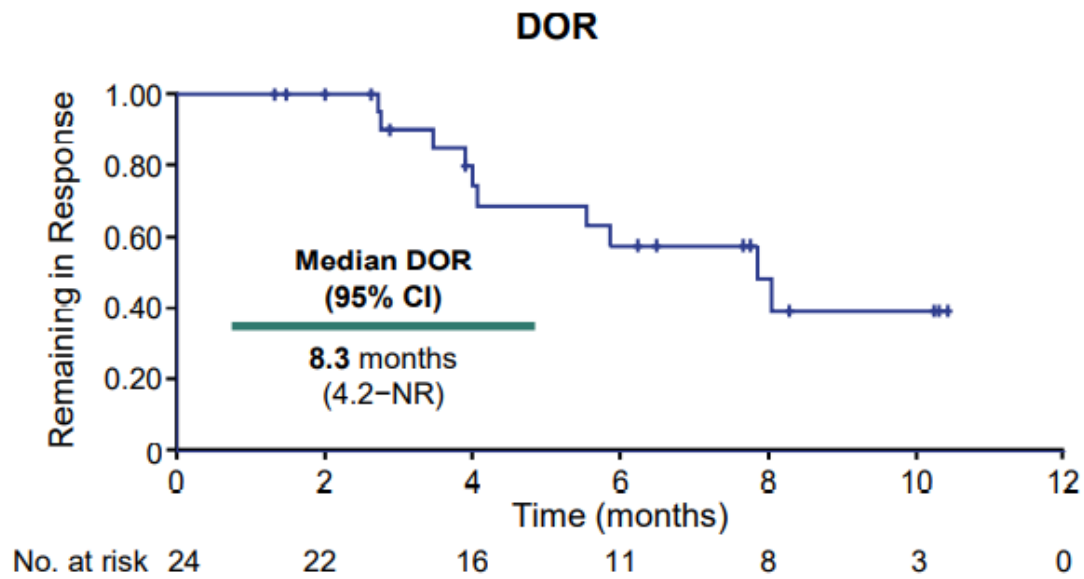
Secondary Endpoints
- ORR[d] per RECIST v1.1, by investigator
- DOR, TTR, and PFS by IRC and investigator
- OS
- Safety

Exploratory Endpoints
- Biomarkers
- HRQoL

[a]Paclitaxel plus platinum (cisplatin or carboplatin) or paclitaxel plus topotecan. [b]Adjuvant or neoadjuvant chemotherapy or if administered with radiation therapy, was not counted as a prior systemic regimen. [c]June 2018 to April 2019. [d]Responses were confirmed by subsequent repeat imaging performed ≥4 weeks after initial response assessment. [e]Using one-sided exact binomial test at 0.025 significance level.
CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQoL, health-related quality of life; IRC, independent review committee; IV, intravenous; MRI, magnetic resonance imaging; OS, overall survival; PD, progressive disease; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria In Solid Tumors version 1.1; TTR, time to response.

Antitumor Activity by IRC Assessment

	N=101
Confirmed ORR (95% CI),[a] %	**24 (15.9–33.3)**
CR, n (%)	7 (7)
PR, n (%)	17 (17)
SD, n (%)	49 (49)
PD, n (%)	24 (24)
Not evaluable, n (%)	4 (4)



Clinically meaningful and durable responses were observed

Data cutoff: February 06, 2020. Median duration of follow-up: 10.0 months.
[a]Based on the Clopper-Pearson method.
CI, confidence interval; CR, complete response; DOR, duration of response; IRC, independent review committee; NR, not reached; ORR, objective response rate; PD, disease progression; PR, partial response; SD, stable disease.

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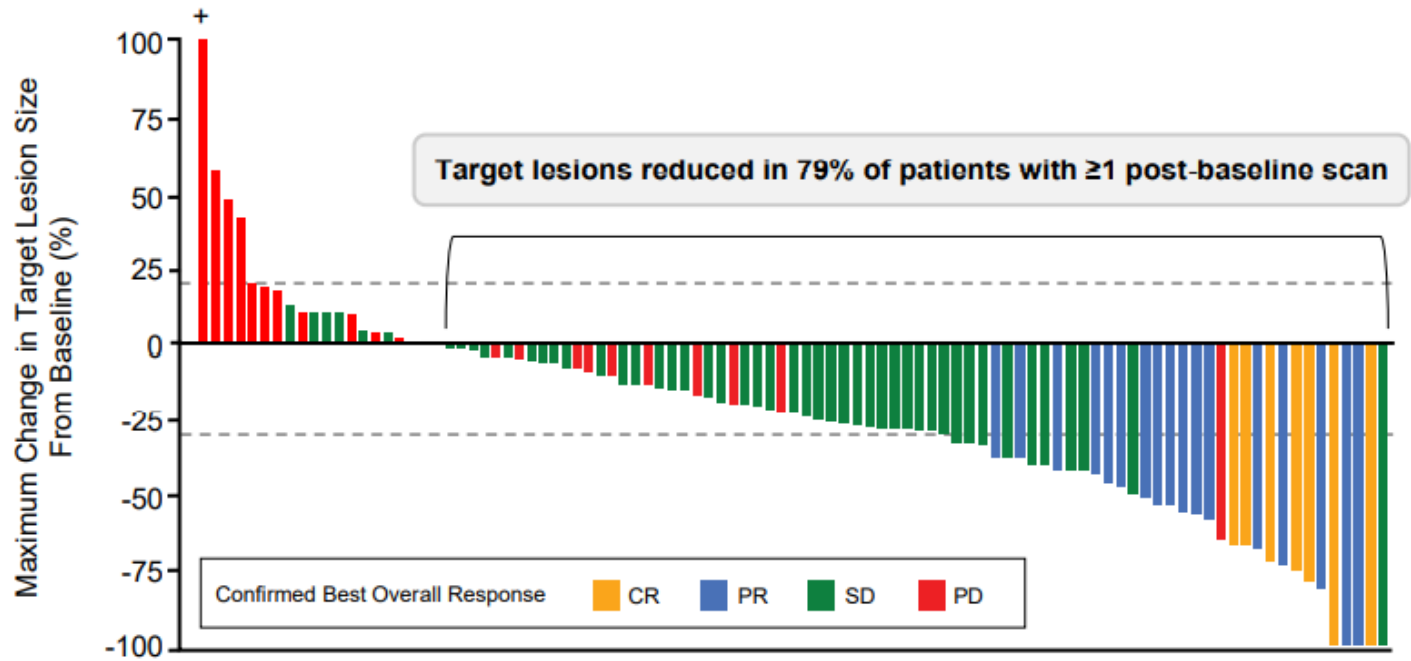
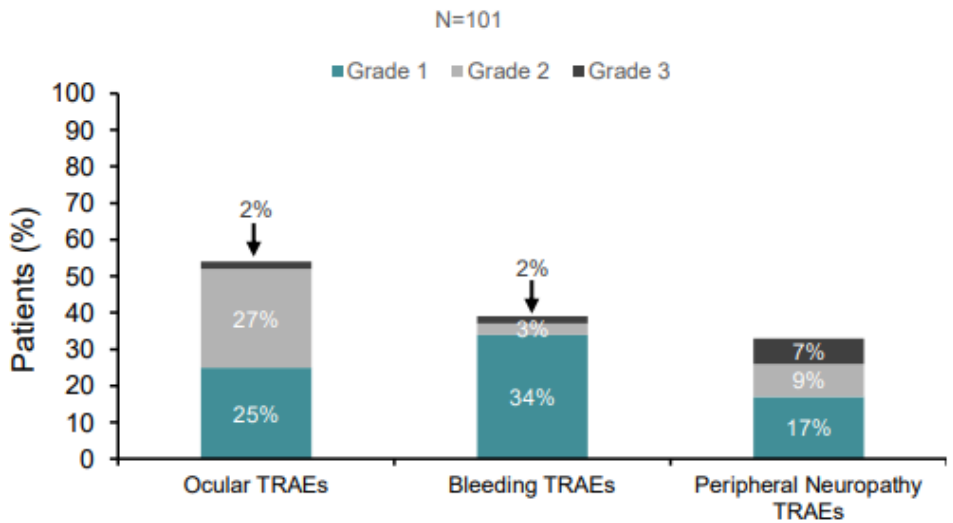
Maximum Change in Target Lesion Size by IRC Assessment



Data cutoff: February 06, 2020. Median duration of follow-up: 10.0 months. + indicates a change greater than 100%. Horizontal dashed lines indicate 20% increase and 30% decrease in target lesion diameters from baseline for RECIST v1.1 assessment. Colored bars represent the best overall confirmed response. CR, PR, SD, and PD were based on RECIST v1.1 as evaluated by IRC.
CR, complete response; IRC, independent review committee; PD, disease progression; PR, partial response; RECIST v1.1, Response Evaluation Criteria In Solid Tumors version 1.1; SD, stable disease.

Prespecified AEs of Interest of Tisotumab Vedotin

Ocular,[a] bleeding,[b] and peripheral neuropathy[c] TRAEs



	Ocular	Bleeding	Peripheral Neuropathy
Time to onset (median, months)	1.4	0.3	3.1
Events resolved, %	86	90	21
Time to resolution[d] (median, months)	0.7	0.5	0.6

- **Ocular AEs were mostly mild to moderate, resolved, and were manageable with an eye care plan**
- **Most bleeding events were grade 1 epistaxis (28%) of which majority resolved**
- **Most peripheral neuropathy events (known MMAE-related toxicity) were grade 1 and manageable with dose modifications; resolution was limited by follow-up period**

Data cutoff: February 06, 2020. Median duration of follow-up: 10.0 months.
[a]Any ocular SMQ (conjunctival disorders SMQ, corneal disorders SMQ, scleral disorders SMQ, retinal disorders SMQ, periorbital and eyelid disorders SMQ, ocular infections SMQ, optic nerve disorders SMQ, glaucoma SMQ, lacrimal disorders SMQ, and eye disorders SMQ). [b]Hemorrhage SMQ. [c]Peripheral neuropathy SMQ. [d]Assessment limited by the protocol-defined follow-up period for AE of only 30 days after the last dose.
AE, adverse event; MMAE, monomethyl auristatin E; SMQ, standardized MedDRA queries; TRAE, treatment-related adverse events.

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Conclusions

- Tisotumab vedotin demonstrated compelling (ORR: 24%; CR: 7%) and durable (median DOR: 8.3 months) antitumor activity in recurrent and/or metastatic cervical cancer previously treated with doublet chemotherapy with bevacizumab (if eligible)
  - Most responses were rapid (median TTR: 1.4 months), with activity observed within the first 2 treatment cycles
  - Median PFS (4.2 months) and OS (12.1 months) are encouraging
  - Clinically meaningful responses were observed regardless of TF expression, histology subtype, or prior therapy
- Tisotumab vedotin had a manageable and tolerable safety profile with no new safety signals
  - Ocular, bleeding, and peripheral neuropathy adverse events were generally mild and effectively managed with an eye care plan and dose modifications
- Tisotumab vedotin is a potential novel treatment for women with previously treated recurrent and/or metastatic cervical cancer

Evaluation is ongoing in 37 (37%) patients.
AE, adverse event; CR, complete response, DOR, duration of response; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; TF, tissue factor; TTR, time to response.

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#5401

Balstilimab (anti-PD-1) Alone and in Combination with Zalifrelimab (anti-CTLA-4)

for Recurrent/Metastatic (R/M) Cervical Cancer (CC)

Preliminary Results of Two Independent Ph2 Trials

(NCT03104699 and NCT03495882)

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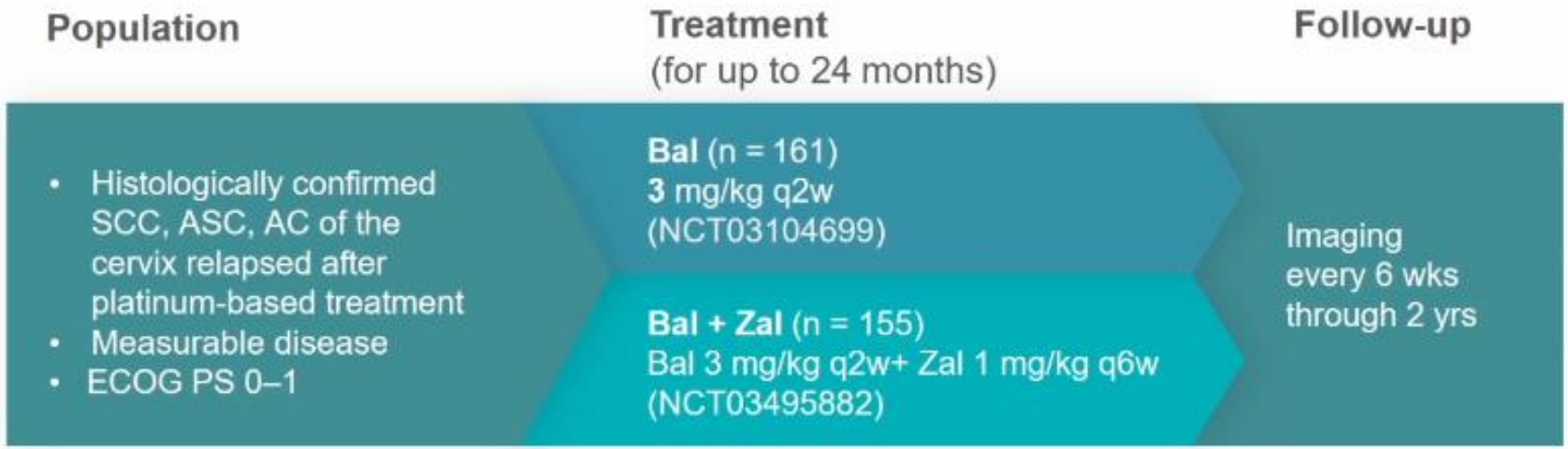
ATION: 16-18 OCTOBER 2020

Study Design

Two Parallel, Single-arm Trials Testing Balstilimab Alone and with Zalifrelimab in Recurrent/Metastatic Cervical Cancer



- **Primary endpoint:** Independent Review Committee (IRC) ORR by RECIST 1.1
- **Secondary endpoints:** DOR,PFS, OS,

SCC – Squamous-cell cancer; ASC – Adenosquamous cancer; AC – Adenocarcinoma

Primary Endpoint: Tumor Response

Responses in all patients	Balstilimab Only		Balstilimab + Zalifrelimab	
	mITT (n=160)	≥1 Prior chemotherapy (n=138)	mITT (N=143)	≥1 Prior chemotherapy (n=119)
Best Overall Response %, (95% CI)	**23 (14%) [10, 21]**	**18 (13%) [8, 20]**	**31 (22%) [16, 29]**	**24 (20%) [14, 28]**
Complete Response	3 (2%)	3 (2%)	8 (6%)	6 (5%)
Partial Response	20 (12%)	15 (11%)	23 (16%)	18 (15%)
Duration (mon) of Response, median [range obs]	15.4 [1.1+,15.4]	15.4 [1.3+,15.4]	NR [1.3+,16.6+]	NR [1.3+,15.4+]
ORR by tumor histology				
SCC # responders/# treated (%)	18/100 (18%)	13/83 (16%)	29/106 (27%)	22/82 (27%)
AdenoCa/AdnoSq # responders/# treated (%)	5/59 (8%)	5/55 (9%)	2/37 (5%)	2/37 (5%)

Data cut-off: 7/31/2020

SUMMARY

- Largest reported study of checkpoint inhibitors in recurrent/metastatic cervical cancer
- Results demonstrate both single-agent Bal and Bal/Zal combination are effective and well tolerated in second-line treatment for advanced/metastatic cervical cancer.
- Bal and Bal/Zal demonstrated responses in all biological (PDL1+ or PDL1 – patients) and histological (SCC and AdenoCa patients) subgroups
- Response rates are similar regardless of prior therapy
- With a median follow up ~12 months, median DOR was >15mos in Bal and is *not yet reached* in the Bal/Zal combination
- Bal monotherapy and the Combination of Bal + Zal improves clinical benefit with tolerable safety profile
- Given the limited treatments for patients with recurrent/metastatic cervical cancer, both Bal and Bal/Zal represent an important treatment option

Radical hysterectomy in cervical cancer patients with intraoperatively detected positive lymph node: ABRAX multicentric retrospective cohort study (ENGOT-Cx3/CEEGOG CX2)

Cibula D (VFN Prague; CEEGOG, Czech R.), Dostalek L (CEEGOG, Czech R.), Hillemanns P (MHH, Germany), Scambia G (MITO, Italy), Persson J (SUL, Sweden), Raspagliesi F (MITO, Italy), Novak Z (CEEGOG, Hungary), Jaeger A (AGO, Germany), Capilna ME(CEEGOG, Romania), Weinberger V (CEEGOG, Czech R.), Klat J (CEEGOG, Czech R.), Schmidt RL (BCH, Brazil), Lopez A (INEN, Peru), Scibilia G MITO, Italy), Pareja R (IACR, Colombia), Kucukmetin A (QE Gateshead, UK), Kreitner L (AGO, Germany), El-Balat A (AGO, Germany), Laufhutte S (AGO, Germany), Runnenbaum I (AGO, Germany)

NCT04037124

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First Faculty of Medicine, Charles University in Prague; and General University Hospital in Prague, Czech Republic
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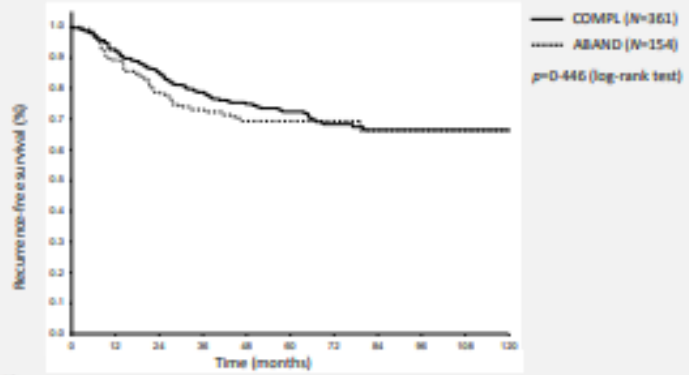
Results: recurrence-free survival



No at risk (No censored)	0	12	24	36	48	60	72	84	96	108	120
COMPL	361 (0)	336 (20)	277 (36)	217 (74)	170 (107)	126 (150)	88 (182)	60 (208)	47 (221)	33 (234)	16 (252)
ABAND	154 (0)	122 (17)	103 (22)	83 (35)	65 (49)	48 (71)	30 (86)	15 (98)	9 (104)	7 (106)	6 (109)

Time 0 was defined as the date of the scheduled operation in each patient.
COMPL=cervical procedure completed as planned;
ABAND=cervical procedure was abandoned

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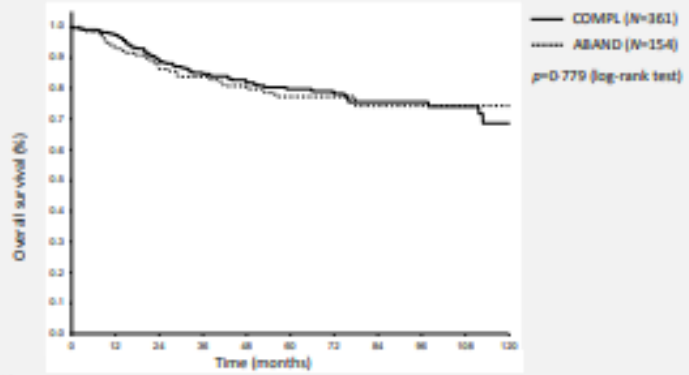
Central and Eastern European Gynecologic Oncology Group (CEEGOG)

Results: overall survival



No at risk (No censored)	0	12	24	36	48	60	72	84	96	108	120
COMPL	361 (0)	332 (20)	286 (36)	226 (80)	179 (126)	127 (171)	95 (203)	65 (230)	51 (244)	36 (258)	17 (275)
ABAND	154 (0)	130 (14)	110 (21)	90 (42)	72 (56)	47 (79)	33 (93)	17 (108)	11 (114)	8 (117)	6 (121)

Time 0 was defined as the date of the scheduled operation in each patient.
COMPL=cervical procedure completed as planned;
ABAND=cervical procedure was abandoned

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CEEGOG

Summary

- Disease free survival of the whole cohort reached 74% (381/515) with a median follow-up of 58 months.
- Radical hysterectomy completion did not improve oncological outcome of lymph-node positive cervical cancer patients.
- No subgroup of patients benefited from completion of radical hysterectomy irrespective of tumour size, tumour type, or other traditional risk factors

<u>If lymph node involvement is found intraoperatively, abandoning further radical surgery should be considered and the patient should be referred for definitive (chemo)radiation.</u>

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A randomised double-blind placebo-controlled phase II trial of palbociclib combined with letrozole in patients with oestrogen receptor-positive advanced/recurrent endometrial cancer

ENGOT-EN3 / NSGO-PALEO

MR Mirza[1], L Bjørge[2], F Marmé[3], R DePont Christensen[4], M Gil-Martin[5], A Auranen[6], B Ataseven[7], MJ Rubio[8], V Salutari[9], B Lund[10], I Runnebaum[11], A Redondo[12], K Lindemann[13], F Trillsch[14], MP Barretina Ginesta[15], H Roed[16], J Loehndorf[17], G-B Nyvang[18], J Sehouli[19]

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NSGO-CTU ENGOT

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Background

NSGO-CTU

ENGOT

- Targeting cell-cycle checkpoints is an increasingly used treatment modality
  - Cyclin A (a CDK) is involved in the transition from G1 to S and G2 to M
  - Its activity can be inhibited by palbociclib, a selective inhibitor of the CDKs 4 and 6
- In ER+ breast cancer, the combination of palbociclib and letrozole is superior to letrozole alone[a]
- Endometrial endometrioid adenocarcinomas are hormone-dependent; endocrine treatment with an AI is well established
- This is the first global randomised trial to evaluate the efficacy of a CDK4/6 inhibitor in combination with an AI in patients with advanced or recurrent ER+ endometrial cancer.

AI = aromatase inhibitor; CDK = cyclin-dependent kinase; ER+ = oestrogen receptor-positive
[a]Finn RS et al., NEJM 1916; 375:1925-1936

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ENGOT-EN3 / NSGO-PALEO trial design

ENGOT model A, sponsor NSGO-CTU, NCT02730429

- **Measurable/evaluable endometrial cancer**
- **Primary stage 4 or relapsed disease**
- **≥1 prior systemic therapy**
- **ER+ (≥10%) endometrioid adenocarcinoma**
- **ECOG PS 0/1**
- **No prior endocrine therapy except MPA and megestrol acetate**
- **No prior CDK inhibitor**

1:1 randomisation

Placebo 125 mg days 1–21
Letrozole 2.5 mg days 1–28

Repeated every 28 days until progression

Palbociclib 125 mg days 1–21
Letrozole 2.5 mg days 1–28

Stratification:
- No. of prior lines (primary advanced disease vs 1st relapse vs ≥2 relapses)
- Measurable vs evaluable disease per RECIST
- Prior use of MPA/megestrol acetate

Primary endpoint: Investigator-assessed PFS (target HR 0.625, 80% power, 15% 1-sided α)

Secondary endpoints:
- PFS in subgroups
- Objective response rate, disease control rate, PFS2, overall survival
- PROs
- Safety and tolerability

HR = hazard ratio; MPA = medroxyprogesterone acetate; PROs = patient-reported outcomes

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Efficacy (ITT population)

NSGO-CTL

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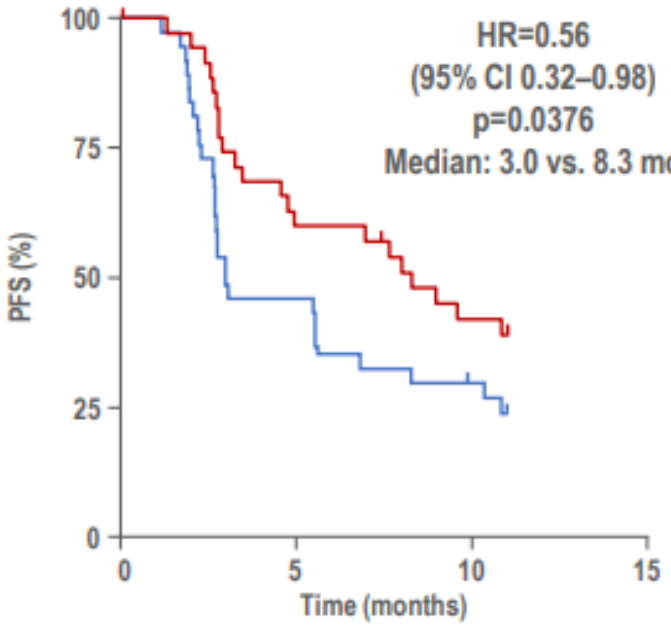
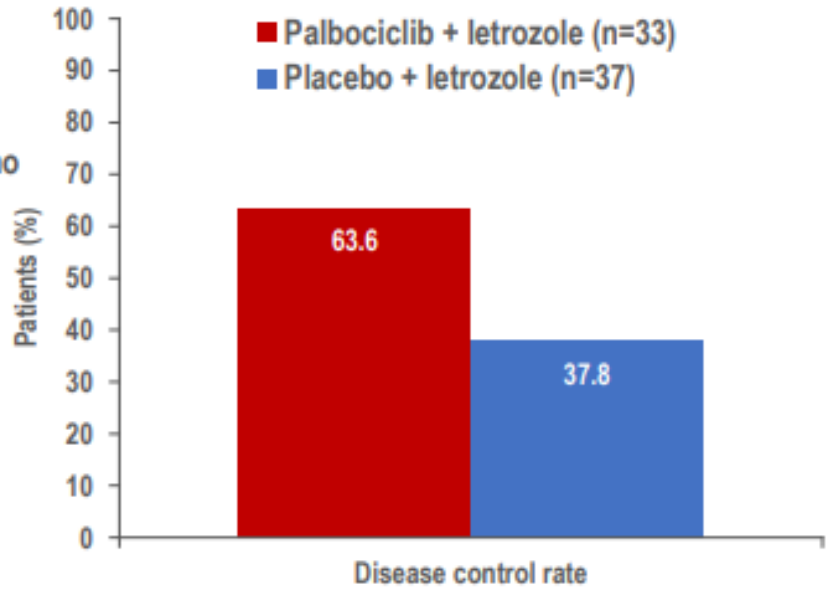
Primary endpoint: PFS



Number at risk			
Palbociclib + letrozole	36	21	14
Placebo + letrozole	37	17	10

CI = confidence interval; HR = hazard ratio

Secondary endpoint: Disease control rate*



* = at 24 weeks

ENGOT-EN3 / NSGO-PALEO

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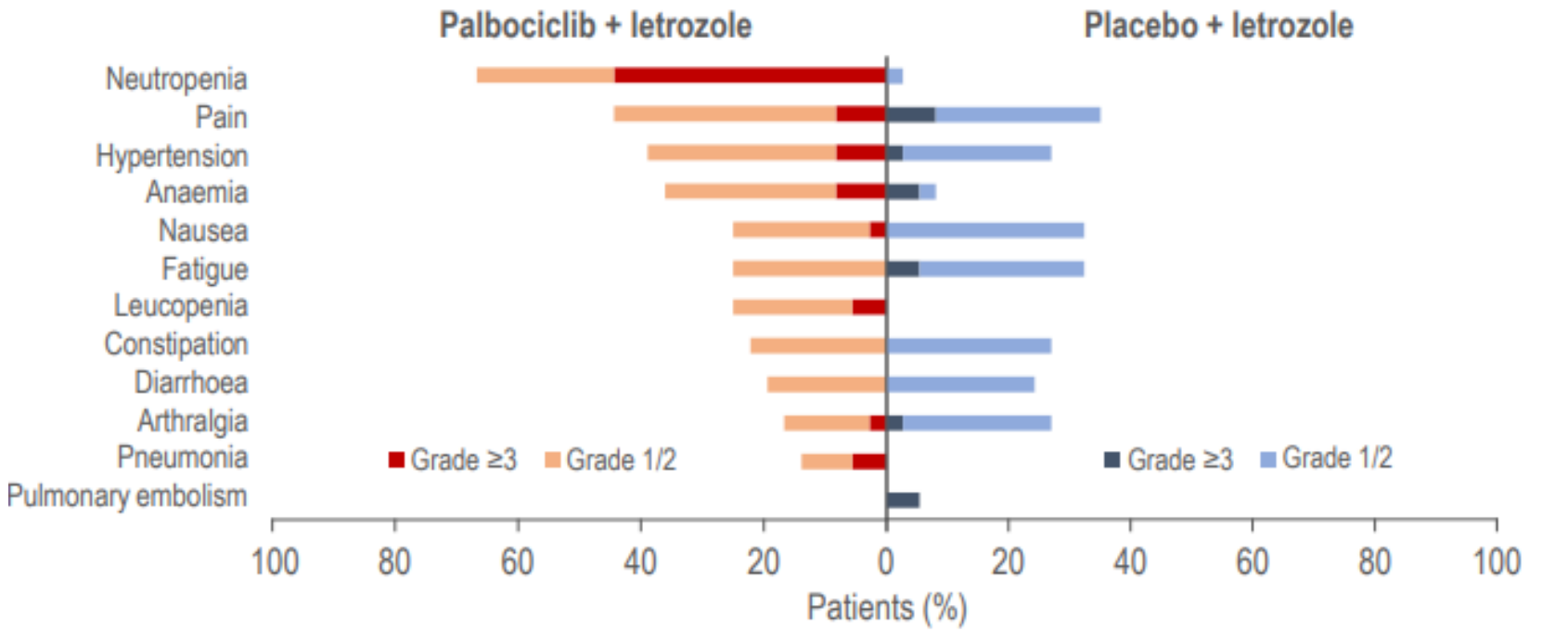
Summary of adverse events

Any grade in ≥20% of patients and/or >1 patient with grade ≥3 in either arm



ENGOT-EN3 / NSGO-PALEO

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Conclusions

- ENGOT-EN3 / NSGO-PALEO is the first randomized trial to evaluate the efficacy of a CDK4/6 inhibitor in combination with an aromatase inhibitor in patients with advanced or recurrent ER+ endometrial cancer
- Compared with placebo + letrozole, the combination of palbociclib + letrozole demonstrated clinically meaningful improvement in PFS
- The toxicity of palbociclib + letrozole combination therapy was manageable; most patients remained on treatment until disease progression
- No detrimental effect on quality of life was observed with combination therapy
- These results merit phase 3 validation trial

A Phase I Study of Mirvetuximab Soravtansine (MIRV) and Gemcitabine (G) in Patients (Pts) with selected FRα -positive solid tumors: Results in the Endometrial Cancer (EC) Cohort

Mihaela C. Cristea[1], Paul Frankel[1], Christopher Ruel[1], Timothy Synold[1], Daphne Stewart[1], Edward Wang[1], Alexander Jung[1], Sharon Wilczynski[1], Michael Tran, Gottfried E. Konecny[2], Melissa Eng[1], Lindsay Kilpatrick[1], Yi-Jen Chen[1], Scott Glaser[1], Ernest Han[1], Thanh Dellinger[1], Amy Hakim[1], Stephen Lee[1], Robert J. Morgan[1], Lorna Rodriguez[1], Mark Wakabayashi[1]

[1]City of Hope National Medical Center, Duarte, CA

[2]David Geffen School of Medicine, University of California, Los Angeles, Los Angeles

INTRODUCTION

- Mirvetuximab soravtansine (MIRV) is an ADC comprising a FRα-binding antibody linked to the tubulin-disrupting maytansinoid DM4
- MIRV has promising single agent activity in FRα-positive epithelial ovarian cancer (EOC) in both platinum sensitive1 and resistant settings2. The recommended phase 2 dose (RP2D) was established at 6 mg/kg, based on adjusted ideal body weight (AIBW) IV every (q) 21 days
- FRα positivity is determined by immunohistochemistry (IHC) and is classified in 3 categories:
  - low (25% to 49% of tumor cells with PS2+ staining intensity)
  - medium (50% to 74% of cells with PS2+ staining intensity) or
  - high (≥ 75% of cells with PS2+ staining intensity)
- We conducted a study evaluating MIRV and G in recurrent FRα positive EOC, EC and triple negative breast cancer (TNBC)
- FRα eligibility was revised for EOC and EC patients after results of FORWARD I study were reported3
- At ASCO 2019 we reported the results from the phase I study[4]. The MTD and RP2D for this regimen was reached at MIRV 6 mg/kg AIBW IV, day 1 and G 800 mg/m2 IV, d1, 8 every 21 days
- The regimen was well tolerated with expected hematologic toxicities that related primarily to gemcitabine
- Promising results were seen in FRα-positive EOC patients
- Here we report the preliminary results in the FRα-positive EC cohort treated at the recommended phase 2 dose (RP2D)

Patient Population, Methods and Objectives

- Primary Objective of the EC expansion cohort: Evaluate the safety and activity of MIRV and G
- Treatment schedule: MIRV 6 mg/kg AIBW IV, day 1 and G 800 mg/m2 IV, d1, 8 every 21 days.
- Eligibility for EC expansion cohort:
  - Recurrent FRα-positive EC patients with ≤2 lines of chemotherapy (CT)
  - FRα positivity by IHC was initially defined as ≥25% of cells with PS2+ staining intensity (low to high FRα levels) and was subsequently revised to ≥ 50% of cells with PS2+ (medium/high FRα levels, with high defined as ≥ 75% of cells with PS2+).
  - Measurable disease (per RECIST 1.1)
  - Patients with brain metastases, >grade 1 peripheral neuropathy, corneal disorders, history of interstitial pneumonitis or cirrhotic liver disease were excluded. Previous treatment with gemcitabine was not allowed

Subset Analysis

- The expansion cohort of 12 pts with FRα-positive EC treated at the RP2D, pre-specified that ≥ 2 responders are required to declare the combination promising
- Total population: all pooled EC patients from the escalation and expansion cohort who received the combination at full dosing
- Here we report the results in the first 6 pts with FRα-positive EC

Baseline Demographics

Median Age (range)	66 (51-68) years
FRα positivity (N=6)	
Low	3 (50%)
Medium	3 (50%)
High	0 (0%)
Perf Status (ECOG) (N=6)	
0	4 (67%)
1	2 (33%)
Histology (N=6)	
Endometrioid carcinoma	2 (33%)
High Grade Serous carcinoma	3 (50%)
Adenocarcinoma, NOS	1 (17%)
Tumor Stage (N=6)	
III	1 (17%)
IV	5 (83%)
Prior Lines of Therapy (N=6)	
0	2 (33%)
1*	4 (67%)
Prior Surgery (N=6)	
Yes	6 (100%)
No	0 (0%)
Prior Radiation (N=6)	
Yes	3 (50%)
No	3 (50%)

*Adjuvant chemotherapy and targeted agents not included. One patient continued maintenance Bevacizumab.

Treatment Related AEs

Treatment Related Adverse Events Grade 2 and Above (& All Grade Peripheral Neuropathy)

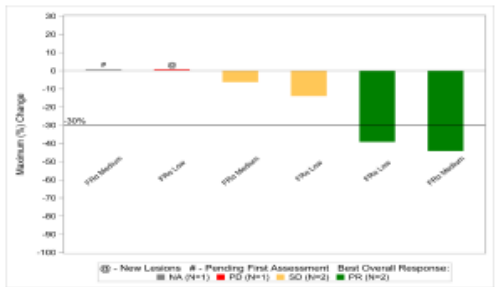
n=6

Adverse Event	Course 1 Grades 1	Course 1 Grade 2	Course 1 Grade 3	Course 1 Grade 4	Course all Grades 1	Course all Grade 2	Course all Grade 3	Course all Grade 4
Lymphocyte count decreased		2 (33%)	1 (17%)	1 (17%)		3 (50%)	1 (17%)	1 (17%)
Platelet count decreased	2 (33%)	2 (33%)	1 (17%)		2 (33%)	1 (17%)	2 (33%)	
Neutrophil count decreased		2 (33%)				2 (33%)	2 (33%)	
White blood cell decreased	1 (17%)	2 (33%)			2 (33%)	3 (50%)	1 (17%)	
Elevated LFTs	3 (50%)	2 (33%)			3 (50%)	2 (33%)		
Hypertension		1 (17%)				1 (17%)		
Diarrhea	2 (33%)	1 (17%)			2 (33%)	1 (17%)		
Electrocardiogram QT corrected interval		1 (17%)				1 (17%)		
Anemia		1 (17%)				1 (17%)	2 (33%)	
Headache	1 (17%)					1 (17%)		
Blurred vision	2 (33%)				2 (33%)	2 (33%)		
Abdominal pain	1 (17%)				1 (17%)	2 (17%)		
Nausea/Vomiting	2 (33%)				2 (33%)	1 (17%)		
Pruritus	1 (17%)				1 (17%)	1 (17%)		
Peripheral sensory neuropathy					1 (17%)			

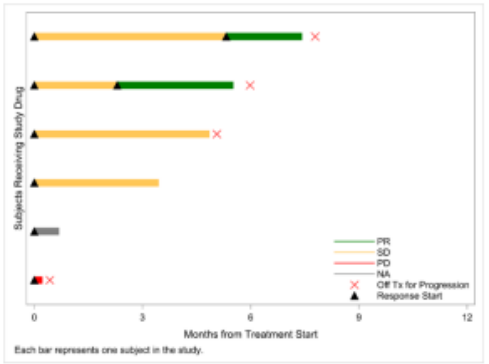
ORR and PFS

Endpoint	Total (n=6)
PFS (months) Median (95% CI)	5.5 (0.2, 7.4)
ORR (95% CI)	33% (4, 78)

Maximum Tumor Change (%) in Target Lesions from Baseline



Time to Response



CONCLUSION

- The combination of MIRV with G has promising clinical activity in FRα-positive EC.
- In this pre-treated EC population, MIRV with G is an active regimen with an ORR of 33% and a median time on treatment for the responders ~ 6.5 months
- The regimen is tolerable with the expected treatment related AEs of these agents.
- Further development of MIRV is warranted in EC

References: 1. K Moore *et al*, Gynecol Oncol 2018 Oct; 151: 46-52; 2. K Moore *et al*, J Clin Oncol. 2017 Apr 1; 35(10): 1112–1118; 3. K Moore *et al* ESMO 2019, abstract 4093; 4. M Cristea *et al* ASCO 2009 abstract 3009.

NCT02996825. This study was approved and funded in part by the National Comprehensive Cancer Network (NCCN) Oncology Research Program from general research support provided by ImmunoGen, Inc and the Cancer Center Support Grant P30CA033572.

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Phase 2 study of PARP inhibitor Talazoparib and PD-L1 inhibitor Avelumab in patients (pts) with Recurrent Microsatellite Stable (MSS) Endometrial Cancer

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Gynecologic Oncology Program
Dana-Farber Cancer Institute
Associate Professor of Medicine
Harvard Medical School

ATION: 16-18 OCTOBER 2020

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Background

- PD-1/PD-L1 inhibitors (PD-1/PD-L1i) **exhibit only modest activity as monotherapy against microsatellite stable (MSS) and non *POLE*-mutated endometrial cancers**
  (ORR: Pembrolizumab = 5.6%[1], Avelumab = 6.3%[2], Durvalumab = 2.8%[3])
- Preclinical studies have demonstrated **synergistic antitumor activity for combinations of PARP inhibitors (PARPi) with PD-1/PD-L1i** which is at least partly mediated by activation of the Stimulator of Interferon Genes (STING) pathway[4-7]
- Specifically, **synergism has been observed**:
  - **Regardless of homologous recombination repair (HRR) deficiency status**
    i.e. in both HRR deficient[4] and HRR proficient models[5]
  - **In a disease-agnostic manner**
    i.e. in ovarian[4,5], breast[6] and small cell lung cancer[7] models

[1]Ott et al. JCO 2017, [2]Konstantinopoulos et al. JCO 2019, [3]Antill et al. ESMO 2019,
[4]Ding et al. Cell Reports 2018, [5]Shen et al. Cancer Res 2018, [6]Pantelidou et al. Cancer Discov 2019, [7]Sen et al. Cancer Discov 2019

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Conclusions

- Avelumab and talazoparib **met the predetermined PFS6 response criterion** (8 patients) **to be considered worthy of further evaluation** in this population of recurrent MSS EC (median 3 prior lines, 43% had ≥4 prior lines)
- Seven (20%) pts had dose reductions of talazoparib (avelumab was not dose reduced); **No pt discontinued protocol therapy due to toxicity**
- Immunogenomic profiling to identify candidate predictors of OR and PFS6 response including known biomarkers of response to PARPi and PD-1/PD-L1i is ongoing

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Safety and antitumor activity of dostarlimab in patients with advanced or recurrent DNA mismatch repair deficient (dMMR) or proficient (MMRp) endometrial cancer: Results from GARNET

Ana Oaknin,[1] Lucy Gilbert,[2] Anna V. Tinker,[3] Renaud Sabatier,[4] Valentina Boni,[5] David M. O'Malley,[6] Sharad Ghamande,[7] Linda Duska,[8] Prafull Ghatage,[9] Wei Guo,[10] Ellie Im,[10] Bhavana Pothuri[11]

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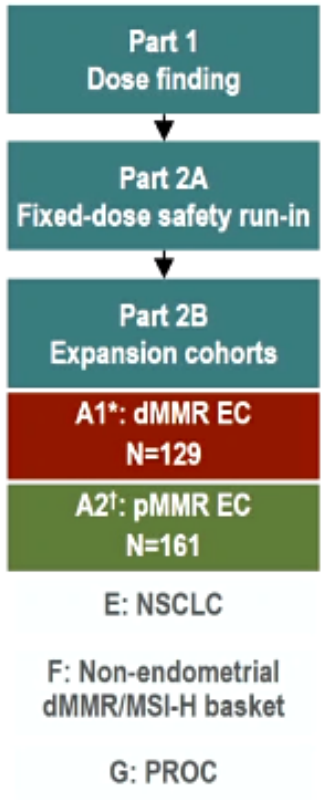
The GARNET Study

GARNET (NCT02715284) is a phase 1, single-arm study of dostarlimab (TSR-042) monotherapy in multiple tumor types

- In part 2B, dostarlimab was dosed at the RTD determined from Part 1 and 2A
  - 500 mg IV Q3W for 4 cycles, then 1000 mg IV Q6W until disease progression
- MMR status was determined by local immunohistochemistry
- Primary endpoint: ORR and DOR



Key inclusion/exclusion criteria for cohorts A1 and A2:

- Patients must have progressed on or after platinum doublet therapy
- Patients must have received ≤2 prior lines of treatment for recurrent or advanced disease
- Patients must have measurable disease at baseline
- Patients must be anti–PD-(L)1 naïve
- Patients could be screened based on local MMR/MSI testing results using IHC, PCR, or NGS performed in a certified local laboratory, but patient eligibility needs to be confirmed by MMR IHC results

DOR, duration of response; IHC, immunohistochemistry; MMR, mismatch mutation repair; MSI, microsatellite instability; NGS, next generation sequencing; NSCLC, non-small cell lung cancer; ORR, objective response rate; PCR, polymerase chain reaction; PD-(L)1, programmed cell death (ligand) 1; PROC, platinum-resistant ovarian cancer; Q3W, every 3 weeks; Q6W, every 6 weeks; RTD, recommended therapeutic dose.

*Cohort enrollment includes 3 patients with MMRunk/MSI-H disease; †Cohort enrollment includes 16 patients with MMRunk/MSS disease

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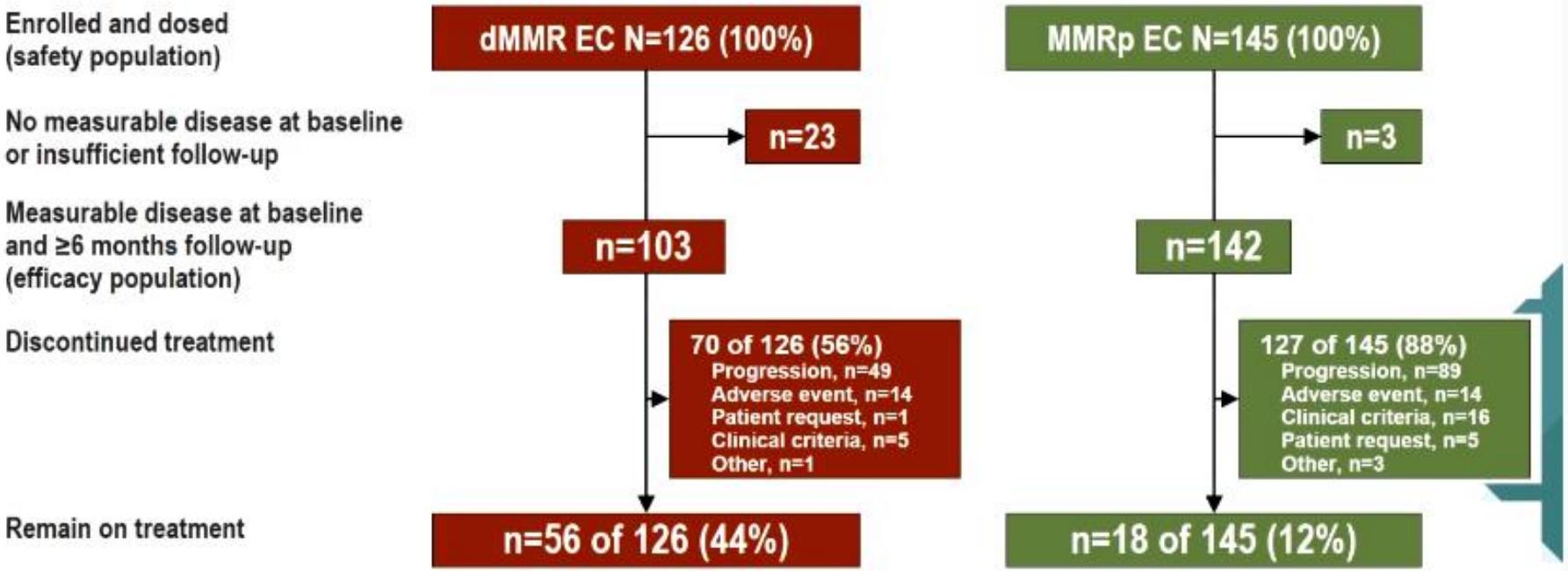
Enrollment and Outcomes



Data cut-off date March 1, 2020. dMMR, mismatch mutation repair deficient; EC, endometrial cancer; MMRp, mismatch mutation repair proficient.

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Demographics and Baseline Characteristics

Characteristic, n (%)	dMMR EC, n=103	MMRp EC, n=142
Age, median (range)	**65 (39–80)**	**66 (30–86)**
Disease stage*		
Stage III or IV at primary diagnosis	56 (54.4)	88 (62.0)
Stage I or II at primary diagnosis	47 (45.6)	53 (37.3)
Histology		
Endometrioid carcinoma Type I (grade 1 and 2)	**70 (68.0)**	**33 (23.2)**
Endometrial carcinoma Type II	**32 (31.1)**	**109 (76.8)**
Serous	4 (3.9)	54 (38.0)
Clear Cell	1 (<1)	9 (6.3)
Squamous	1 (<1)	3 (2.1)
Undifferentiated	4 (3.9)	3 (2.1)
Carcinosarcoma	0	2 (1.4)
Mixed Carcinoma	4 (3.9)	9 (6.3)
Unspecified	14 (13.6)	22 (15.5)
Adenocarcinoma†	4 (3.9)	7 (4.9)
Prior lines of therapy		
1	65 (63.1)	65 (45.8)
2	27 (26.2)	62 (43.7)
≥3	11 (10.7)	15 (10.6)
Prior Radiation	**73 (70.9)**	**88 (62.0)**

*One patient with MMRp EC had disease status/stage unknown; †Includes adenocarcinoma, and adenocarcinoma with ambiguous differentiation.

dMMR, mismatch mutation repair deficient; EC, endometrial cancer; MMRp, mismatch mutation repair proficient.

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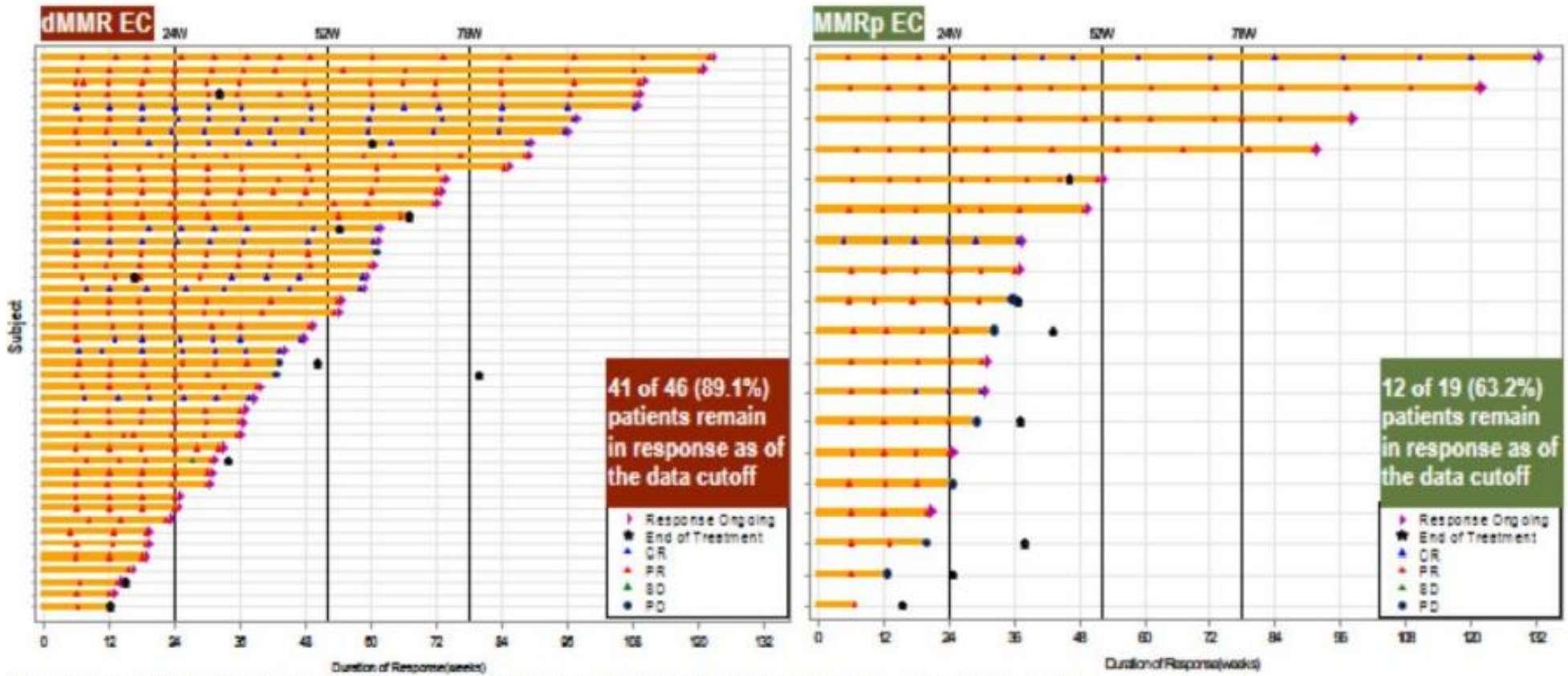
Duration of Response

Measured from first observed response (PR or CR), this response is not shown on the figure



CR, complete response; dMMR, mismatch mutation repair deficient; EC, endometrial cancer; MMRp, mismatch mutation repair proficient; PD, progressive disease; PR, partial response; SD, stable disease.

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Primary Endpoint Analysis

ORR was 44.7% in patients with dMMR EC, and 13.4% in patients with MMRp EC

Variable	dMMR EC, n=103	MMRp EC, n=142
Median follow-up time, mo	**16.3**	**11.5**
Objective response rate*, n (%, 95% CI)	**46 (44.7%, 34.9–54.8)**	**19 (13.4%, 8.3–20.1)**
Complete response, n (%)	11 (10.7)	3 (2.1)
Partial response, n (%)	35 (34.0)	16 (11.3)
Stable disease, n (%)	13 (12.6)	31 (21.8)
Progressive disease, n (%)	39 (37.9)	77 (54.2)
Not evaluable, n (%)	3 (2.9)	0
Not done, n (%)	2 (1.9)	15 (10.6)
Disease control rate†, n (%, 95% CI)	**59 (57.3%, 47.2–67.0)**	**50 (35.2%, 27.4–43.7)**
Response ongoing, n (%)	**41 (89.1)**	**12 (63.2)**
Median duration of response, (range) mo	**Not reached (2.63–28.09+)**	**Not reached (1.54+–30.36+)**
Kaplan–Meier estimated probability of remaining in response		
at 6 mo, %	97.8	83.0
at 12 mo, %	90.6	61.3
at 18 mo, %	79.2	61.3

*Responses required confirmation at a subsequent scan; SD had to be observed at ≥12 weeks on study to qualify as SD; †Includes confirmed CR, PR or SD at ≥12 weeks.

CR, complete response; dMMR, mismatch mutation repair deficient; EC, endometrial cancer; MMRp, mismatch mutation repair proficient; ORR, objective response rate; PR, partial response; SD, stable disease.

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Conclusions

- Dostarlimab demonstrated durable antitumor activity in both dMMR and MMRp advanced/recurrent EC
- dMMR status by IHC was associated with a higher response rate
  - These data support the use of MMR testing as predictive of response to dostarlimab
- Dostarlimab demonstrated a notable disease control rate (35.2%; 2.1% CR, 11.3% PR, 21.8% SD) in patients with MMRp EC, was comprised of a higher percentage of patients with Type II EC which is historically associated with a worse prognosis
- No new safety signals were detected, and only 5.5% of patients discontinued dostarlimab due to a TRAE
  - Most adverse events were grade 1 or 2
  - Safety was consistent between dMMR and MMRp cohorts
- These cohorts are the largest prospective evaluation of a PD-(L)1 therapy in EC to date

CR, complete response; dMMR, mismatch mutation repair deficient; EC, endometrial cancer; IHC, immunohistochemistry MMRp, mismatch mutation repair proficient; PD-(L)1, programmed cell death (ligand) 1; PR, partial response; SD, stable disease.


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16 OTTOBRE 2020
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Grazie!!!