

IGCS 2023

Annual Global Meeting

SEOUL

IGCS 2023 Abstracts: Seminal Presentations

Seminal abstracts are included as five-minute oral presentations in the below sessions. The sessions will be recorded for on-demand viewing via the IGCS 360 Educational Portal.

Plenary 01: Oral Abstract Presentations
Sunday, November 5, 2023, 9:00 – 10:30 AM
Auditorium

Plenary 02: Changing the Landscape of Endometrial Cancer
Sunday, November 5, 2023, 4:30 – 5:30 PM
Auditorium

Focused Plenary 01: Quality of Life
Monday, November 6, 2023, 4:15 – 5:45 PM
Grand Ballroom 101+102

Closing Session: The Development of Prognosis and Predictive Markers
Tuesday, November 7, 2023, 3:55 – 5:00 PM
Auditorium

SE001 / #1612 – Seminal Abstract

AN INTERNATIONAL RANDOMIZED PHASE III TRIAL COMPARING RADICAL HYSTERECTOMY VS SIMPLE HYSTERECTOMY IN PATIENTS WITH LOW-RISK EARLY-STAGE CERVICAL CANCER

PLENARY 01: ORAL ABSTRACT PRESENTATIONS

Sarah Ferguson¹, Marie Plante², Janice Kwon³, Vanessa Samouelian⁴, Gwenael Ferron⁵, Amandine Maulard⁶, Cor Dekroon⁷, Willemien Van Driel⁸, John Tidy⁹, Karin Williamson¹⁰, Sven Mahner¹¹, Stefan Kommos¹², Frédéric Goffin¹³, Karl Tamussino¹⁴, Brynhildur Eyjolfssdottir¹⁵, Jae-Weon Kim¹⁶, Noreen Gleeson¹⁷, Lori Brotto¹⁸, Dongsheng Tu¹⁹, Lois Shepherd¹⁹

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Background: In the last 2 decades, there has been a trend towards less radical surgery in patients with low-risk cervical cancer. Retrospective data suggested that less radical surgery may be safe and associated with less morbidity. The objective of this non-inferiority phase III prospective randomized trial was to compare RH to SH in women with low-risk early-stage cervical cancer (LRESCC).

Methods: Women with LRESCC defined as FIGO 2018 1A2 or 1B1 disease were randomized to receive RH or SH after stratification by cooperative group, intended use of sentinel node mapping, stage, histological type, and tumour grade. The primary endpoint was pelvic recurrence rate at 3 years (PRR3). Non-inferiority of SH to RH is claimed when the 95% upper one-sided confidence limit (95% UCL) for the difference in PRR3 of SH to RH (DPRR3), calculated by the Kaplan-Meier method, is lower than or equal to 4%. Primary intention to treat (ITT) analysis included all patients randomized. Per-protocol (PP) analysis included eligible patients at baseline and without evidence of more advanced disease found at the time of surgery or final pathology, based on treatment actually received. Secondary endpoints included extrapelvic relapse-free survival (ERFS), overall survival (OS), and relapse free survival.

Results: 700 women were enrolled from December 2012 to November 2019. Patient characteristics were well balanced: median age was 44 (24-80); 91.7% had FIGO stage 1B1 disease and 61.7% had squamous histology. 50% of the hysterectomies were done laparoscopically (56% SH vs. 44% RH), 25% robotically (24% vs. 25%) and 23% abdominally (17% vs. 29%). On final pathology, lymph node metastasis occurred in 3.7% (3.3% SH and 4.4% RH), positive margins in 2.5% (2.1% SH and 2.9% RH), and lesions >2cm in 4.2% (4.4% SH and 4.1% RH). A total of 8.8% of women received post-surgical adjuvant therapy (9.2% in SH and 8.4% in RH). With a median follow-up of 4.5 years, 21 pelvic recurrences were identified (11 in SH and 10 in RH group). The PRR3 was 2.52% with SH and 2.17% with RH (DPRR3 0.35% with 95% UCL 2.32%) in ITT analysis; 2.8% with SH and 2.3% with RH (DPRR3 0.42% with 95% UCL 2.56%) in PP analysis. The 3-year ERFS and OS were respectively 98.1% and 99.1% with SH; 99.7% and 99.4% with RH. RH had significantly higher surgery related incidence of urinary incontinence (11.0% vs. 4.7% with SH; p=0.003) and urinary retention (9.9% vs. 0.6% with SH; p<0.0001) during follow-up.

Conclusion: The pelvic recurrence rate at 3 years in women with low risk early-stage cervical cancer who underwent a simple hysterectomy was not inferior to a radical hysterectomy and was associated with fewer surgical adverse events.

SE002 / #1304 – Seminal Abstract

A RANDOMISED PHASE III TRIAL OF INDUCTION CHEMOTHERAPY FOLLOWED BY CHEMORADIATION COMPARED WITH CHEMORADIATION ALONE IN LOCALLY ADVANCED CERVICAL CANCER. THE GCIG INTERLACE TRIAL

PLENARY 01: ORAL ABSTRACT PRESENTATIONS

Mary McCormack

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Background Locally advanced cervical cancer (LACC) is treated with chemoradiation (CRT). However, many patients relapse and die from metastatic disease. A feasibility study demonstrated a good response rate to the short course weekly induction chemotherapy (IC) delivered before standard CRT and the INTERLACE trial investigated whether this approach improves both progression free survival (PFS) and overall survival (OS).

Methods Women with squamous, adeno or adenosquamous carcinoma FIGO (2008) stage IB1 node positive, IB2, II, IIIB, IVA were eligible. Patients were randomised (1:1) to receive either CRT alone (5 cycles weekly cisplatin) or IC (6 weeks carboplatin AUC2 and paclitaxel 80mg/m²) followed by the same CRT in week 7. Mandated minimum total EQD2 dose 78Gy to Point A with 3D brachytherapy recommended. All centres underwent radiation quality assurance. Primary endpoints were PFS (target hazard ratio [HR] 0.65) and OS (target HR 0.65-0.70).

Results 500 Patients were recruited from 32 centres in 5 countries (Nov 2012 – Nov 2022). Median age 46 (range 24-78 years). Stage distribution was: IB1/2;9%, II;77%, IIIB;11% and IVA;3%. 57% were node negative and 82% squamous subtype. Arms were balanced. 92% of IC patients had 5/6 cycles of carboplatin/paclitaxel. Median interval from IC to CRT was 7 days. 84% IC/CRT vs. 89% (CRT alone) had 4/5 cycles cisplatin. In the CRT arm 92% and 89% completed external beam and brachytherapy respectively; corresponding figures in the IC/CRT arm were 97% and 95%. The median overall treatment time for CRT was 45 days in both arms. Grade ≥3 adverse events were seen in 59% (IC/CRT) vs. 48% (CRT alone). Median follow up 64 months. 5-year PFS rate is 73% with IC/CRT and 64% with CRT alone (HR 0.65; 95%CI:0.46-0.91, p=0.013). The corresponding 5 year OS rates are 80% and 72% (HR 0.61;95%CI:0.40-0.91, p=0.04).

Conclusions Induction chemotherapy followed by CRT significantly improves PFS and OS in LACC and should be considered a new standard of care. INTERLACE recruited patients from diverse health care settings demonstrating that IC followed by CRT is feasible in all countries.

Clinical trial identification EUDRACT no: 2011-001300-35

SE003 / #1613 – Seminal Abstract

PHASE 3 MIRASOL (GOG 3045/ENGOT-OV55) TRIAL: MIRVETUXIMAB SORAVTANSINE (MIRV) PROLONGS OVERALL SURVIVAL VS INVESTIGATOR'S CHOICE CHEMOTHERAPY (IC) IN PLATINUM-RESISTANT OVARIAN CANCER (PROC) WITH HIGH FOLATE RECEPTOR-ALPHA (FR α) EXPRESSION

PLENARY 01: ORAL ABSTRACT PRESENTATIONS

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Introduction: Mirvetuximab soravtansine (MIRV), an antibody drug conjugate targeting FR α , demonstrated clinically meaningful antitumor activity in a single arm trial reported previously (Matulonis, JCO 2023). MIRASOL is a randomized phase 3 trial to confirm the efficacy of MIRV vs IC chemotherapy in patients (pts) with FR α high, PROC.

Methods: 453 pts with FR α high (Roche FOLR1 Assay) PROC were randomized 1:1 to MIRV 6 mg/kg, adjusted ideal body weight, Day 1 of a 21-day cycle or IC: paclitaxel, pegylated liposomal doxorubicin, or topotecan. The primary efficacy endpoint was progression-free survival (PFS) by investigator (INV) with key secondary endpoints ORR, and overall survival (OS), in hierarchical order; other endpoints included safety and tolerability.

Results: With a data cutoff of March 6, 2023, 227 pts were randomized to the MIRV arm; 226 to the IC arm. Median follow-up was 13.1 months. Baseline characteristics were well balanced across arms; 14% of pts had one, 39% two, and 47% three prior lines of therapy (LOT); 62% received prior bev; and 55% received prior PARPi therapy. The study met its primary and key secondary endpoints with statistically significant results in PFS (INV), ORR (INV), and OS (Table). In subset analyses, pts with 1 or 2 PLOT, PFS HR was 0.61 (0.45, 0.81) and ORR 46% vs 15%; and 3 PLOT, PFS HR was 0.71 (0.52, 0.98) and ORR 38% vs 18%, favoring MIRV. In pts with prior PARPi, PFS HR was 0.58 (0.43, 0.78) and ORR 45% vs 17%. In PARPi naïve, PFS HR was 0.74 (0.54, 1.03) and ORR 40% vs 14%, favoring MIRV. The adverse event (AE) profile of MIRV was consistent with prior reports: predominantly low-grade ocular (MIRV vs IC all grade 56% vs 9%; grade 3+ 14% vs 0%) and gastrointestinal events (MIRV vs IC all grade 70% vs 66%; grade 3+ 13% vs 15%). Compared with IC, MIRV was associated with lower rates of grade 3+ treatment-emergent AEs (42% vs 54%), serious AEs (24% vs 33%), and discontinuations due to

TEAEs (9% vs 16%).

Conclusion: MIRV is the first treatment to demonstrate a statistically significant PFS, ORR and OS benefit in PROC compared to IC and demonstrates clinical benefit across subgroups. The efficacy data, along with the well-characterized safety profile, position MIRV as a new, standard of care for pts with FRα positive PROC. Trial information: NCT04209855

	MIRV (n=227)	IC (n=226)	Hazard Ratio	P-value
mPFS (INV) (months, 95% CI)	5.62 (4.34, 5.95)	3.98 (2.86, 4.47)	0.65 (0.52, 0.81)	<0.0001
ORR (INV) (95% CI)	42.3 (35.8, 49.0)	15.9 (11.4, 21.4)	NA	<0.0001
Complete response % (n)	5.3 (12)	0	NA	NA
Partial response % (n)	37.0 (84)	15.9 (36)	NA	NA
mOS (months, 95% CI)	16.46 (14.46, 24.57)	12.75 (10.91, 14.36)	0.67 (0.50, 0.88)	0.0046

SE004 / #1614 – Seminal Abstract

ENGOT-CX11/GOG-3047/KEYNOTE-A18: A RANDOMIZED, DOUBLE-BLIND, PHASE 3 STUDY OF PEMBROLIZUMAB PLUS CONCURRENT CHEMORADIOTHERAPY FOR HIGH-RISK LOCALLY ADVANCED CERVICAL CANCER

PLENARY 01: ORAL ABSTRACT PRESENTATIONS

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Introduction: Pembrolizumab has shown efficacy in patients with cervical cancer. The effect of chemoradiotherapy may be enhanced by immunotherapy. ENGOT-cx11/GOG-3047/KEYNOTE-A18 (NCT04221945) assessed pembrolizumab with concurrent chemoradiotherapy (CCRT) for locally advanced cervical cancer (LACC).

Methods: Pts with newly diagnosed, previously untreated, high-risk LACC (FIGO 2014 stage IB2-IIB with node-positive disease or stage III-IVA) were randomized to receive 5 cycles of pembrolizumab 200 mg or placebo Q3W + CCRT, then 15 cycles of pembrolizumab 400 mg or placebo Q6W. CCRT included 5 cycles (with optional 6th dose) of cisplatin 40 mg/m² Q1W + EBRT then brachytherapy. Primary endpoints were PFS per RECIST v1.1 by investigator and OS.

Results: Pts were randomized to pembrolizumab+CCRT (n=529) or placebo+CCRT (n=531). At IA1 (January 9, 2023), median follow-up was 17.9 mo (range, 0.9-31.0). Pembrolizumab+CCRT showed a statistically significant improvement in PFS vs placebo+CCRT. 24-mo PFS was 67.8% with pembrolizumab + CCRT vs 57.3% with placebo+CCRT; median PFS was not reached in either group (HR=0.70 [95% CI, 0.55-0.89; P=0.0020]). With 103 events (42.9% maturity), addition of pembrolizumab to CCRT showed a favorable trend in OS (HR=0.73 [95% CI, 0.49-1.07]); these data have not crossed the boundary of statistical significance. Grade ≥3 TRAE incidence was 67.0% with pembrolizumab+CCRT group versus 60.0% with placebo+CCRT.

Conclusion/Implications: Pembrolizumab+CCRT showed a statistically significant and clinically meaningful improvement in PFS and a favorable trend in OS compared with placebo+CCRT in pts with high-risk LACC and had a manageable safety profile. These data suggest pembrolizumab+CCRT can be considered as a new standard of care for this population.

SE005 / #1615 – Seminal Abstract

PRIMARY RESULTS FROM BEATCC (ENGOT-CX10/GEICO 68-C/JGOG1084/GOG-3030), A RANDOMISED PHASE 3 TRIAL OF FIRST-LINE ATEZOLIZUMAB COMBINED WITH A PLATINUM DOUBLET AND BEVACIZUMAB FOR METASTATIC (STAGE IVB), PERSISTENT OR RECURRENT CERVICAL CANCER

PLENARY 01: ORAL ABSTRACT PRESENTATIONS

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Background: The open-label randomised phase 3 BEATcc academic trial (NCT03556839) evaluated atezolizumab (anti-PD-L1) combined with first-line chemotherapy (CT) + bevacizumab for metastatic (stage IVB), persistent or recurrent cervical cancer (R/M CC), irrespective of PD-L1 status. We report final progression-free survival (PFS) and interim overall survival (OS) results.

Methods: Patients (pts) with previously untreated measurable R/M CC not amenable to curative surgery/radiation were randomised 1:1 to standard therapy (cisplatin 50 mg/m² or carboplatin AUC5 + paclitaxel 175 mg/m² + bevacizumab 15 mg/kg) ± atezolizumab 1200 mg d1 q3w. Cycles were repeated until disease progression or unacceptable toxicity. Stratification factors were prior concomitant chemoradiation (yes vs no), histology (squamous cell carcinoma vs adenocarcinoma) and platinum agent (cisplatin vs carboplatin). Dual primary endpoints were investigator-assessed PFS per RECIST v1.1 and OS. Secondary endpoints included objective response rate (ORR), duration of response (DoR), time to first subsequent therapy (TFST), PFS2, and safety.

Results: Between Oct 2018 and Aug 2021, 410 pts were randomised. At the data cut-off (median follow-up 32.9 mo), median treatment duration was 8.5 vs 12.7 mo in the control vs atezolizumab arms, respectively; treatment was ongoing in 7% vs 23%, respectively. Both PFS and OS were statistically significantly improved with the addition of atezolizumab to CT + bevacizumab (Table). Secondary endpoints and subgroup analyses showed consistent results. Grade ≥3 adverse events (any cause) occurred in 75% vs 79% of the control and atezolizumab arms, respectively. Safety profiles were as

expected with bevacizumab + platinum-based CT. Grade 1/2 diarrhoea, arthralgia, pyrexia and rash were increased with atezolizumab.

Endpoint		CT + bevacizumab (n=204)	Atezolizumab + CT + bevacizumab (n=206)
PFS	Events, n (%)	166 (81)	138 (67)
	HR	0.62 (0.49–0.78); p<0.0001	
	Median, mo	10.4 (9.7–11.7)	13.7 (12.3–16.6)
	2-year rate, %	19 (14–25)	36 (29–43)
OS	Events, n (%)	129 (63)	105 (51)
	HR	0.68 (0.52–0.88); p=0.0046*	
	Median, mo	22.8 (20.3–28.0)	32.1 (25.3–36.8)
	2-year rate, %	49 (41–56)	61 (53–67)
TFST	Median, mo	13.2 (12.0–14.3)	19.0 (16.4–24.0)
	HR	0.60 (0.47–0.76)	
PFS2	Median, mo	20.3 (17.8–22.3)	25.8 (22.1–32.1)
	HR	0.61 (0.48–0.79)	
ORR per RECIST v1.1, %		72 (66–78)	84 (79–89)
DoR	n	147	173
	Median, mo	8.6 (8.0–10.6)	13.6 (10.6–21.3)
	HR	0.60 (0.46–0.78)	

Brackets denote 95% CIs unless otherwise stated. HR = hazard ratio.
*Statistically significant at interim analysis.

Conclusions: Adding atezolizumab to first-line CT + bevacizumab for R/M CC significantly improved all efficacy outcomes. Median OS with atezolizumab + CT + bevacizumab exceeded 2.5 years.

SE006 / #1616 – Seminal Abstract

INNOVATV 301/ENGOT-CX12/GOG-3057: A GLOBAL, RANDOMIZED, OPEN-LABEL, PHASE 3 STUDY OF TISOTUMAB VEDOTIN VS INVESTIGATOR'S CHOICE OF CHEMOTHERAPY IN 2L OR 3L RECURRENT OR METASTATIC CERVICAL CANCER

PLENARY 01: ORAL ABSTRACT PRESENTATIONS

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Background: Tisotumab vedotin (TV) is an investigational antibody-drug conjugate directed to tissue factor. In the US, TV monotherapy received accelerated approval for the treatment of adult patients with recurrent or metastatic cervical cancer (r/mCC) with disease progression on or after chemotherapy. Here, innovaTV 301 (NCT04697628) study results are presented.

Methods: Eligible patients had r/mCC with disease progression on/after treatment with standard of care chemotherapy doublet ± bevacizumab ± anti-PD-(L)1 therapy, measurable disease per RECIST v1.1, and ECOG PS 0-1. Patients were randomized 1:1 to TV monotherapy or investigator's choice of topotecan, vinorelbine, gemcitabine, irinotecan, or pemetrexed. The primary endpoint was OS. Key secondary endpoints included PFS and confirmed ORR by investigator.

Results: 502 patients were randomized (TV: 253; chemotherapy: 249); median survival follow-up was 10.8 months (95% CI, 10.3-11.6). Arms were balanced for demographics and disease characteristics, with 63.9% and 27.5% of patients receiving prior bevacizumab and prior anti-PD-(L)1 therapy, respectively. The TV arm had a 30% reduction in risk of death versus chemotherapy (HR 0.70; 95% CI 0.54-0.89; P=0.0038), with significantly longer median OS (11.5 months [95% CI 9.8-14.9] versus 9.5 months [95% CI 7.9-10.7]). PFS was superior in the TV versus chemotherapy arm (HR: 0.67 [95% CI, 0.54-0.82]; P<0.0001). The OS and PFS benefits in the prespecified subgroups were generally consistent with the ITT population. Confirmed ORR was 17.8% and 5.2% in the TV and chemotherapy arms, respectively (odds ratio: 4.0; 95% CI, 2.1-7.6; P<0.0001). Most patients experienced ≥1 treatment-related adverse event (TV: 87.6% [grade ≥3: 29.2%] versus chemotherapy: 85.4% [grade ≥3: 45.2%]). AEs were consistent with the known TV safety profile.

Conclusions: In the phase 3 innovaTV 301 study, TV showed a statistically significant and clinically meaningful improvement in OS, PFS, and ORR versus chemotherapy, with a manageable and tolerable safety profile in patients with 2L/3L r/mCC. *Previously presented in part at ESMO 2023, "LBA9: innovaTV*

301/ENGOT-cx12/GOG-3057: A Global, Randomized, Open-Label, Phase 3 Study of Tisotumab Vedotin vs Investigator's Choice of Chemotherapy in 2L or 3L Recurrent or Metastatic Cervical Cancer ", Ignace Vergote et al. - Reused with permission

SE007 / #1308 – Seminal Abstract

PEMBROLIZUMAB VERSUS PLACEBO IN ADDITION TO CARBOPLATIN AND PACLITAXEL FOR MEASURABLE STAGE III OR IVA, STAGE IVB, OR RECURRENT ENDOMETRIAL CANCER: THE PHASE 3, NRG GY018 STUDY

PLENARY 02: CHANGING THE LANDSCAPE OF ENDOMETRIAL CANCER

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Background: Standard first-line chemotherapy for endometrial cancer is paclitaxel and carboplatin (PC). The benefit of adding pembrolizumab to chemotherapy remains unclear.

Methods: In this blinded, placebo-controlled, randomized phase 3 trial, 816 patients with measurable stage III/IVA, IVB, or recurrent EC (225 dMMR and 591 pMMR) were randomized 1:1 to pembrolizumab or placebo plus PC (planned six 3-weekly cycles), followed by up to 14 q6-week maintenance cycles of pembrolizumab or placebo. Prior adjuvant chemotherapy was permitted if completed ≥ 12 months prior. The primary endpoint was progression-free survival among two cohorts, patients with dMMR and with pMMR endometrial cancer based on central MMR immunohistochemistry. Interim analyses were triggered at ≥ 84 (dMMR cohort) and ≥ 196 (pMMR cohort) progression-free survival events.

Results: At time of analysis of the dMMR cohort (12/16/2022), and with median follow-up of 12 months, the risk of disease progression or death was 70% lower with pembrolizumab than with placebo (Kaplan–Meier estimate of the rate of freedom from disease progression and from death at 12 months, 74% vs. 38%, respectively; HR 0.30; 95% CI: 0.19–0.48. $P < 0.00001$). In the pMMR cohort (analyzed 12/6/2022), with median follow up of 7.9 months, median progression-free survival was 13.1 months with

pembrolizumab versus 8.7 months with placebo (HR, 0.54; 95% CI: 0.41-0.71 $P<0.00001$). Adverse events were as expected for PC and pembrolizumab.

Conclusions: In patients with advanced or recurrent endometrial cancer, addition of pembrolizumab to standard chemotherapy resulted in significantly longer progression-free survival than with chemotherapy alone (NRG Oncology NRG-GY018, ClinicalTrials.gov number: NCT03914612).

SE008 / #1309 – Seminal Abstract

DOSTARLIMAB IN COMBINATION WITH CHEMOTHERAPY FOR THE TREATMENT OF PRIMARY ADVANCED OR RECURRENT ENDOMETRIAL CANCER: A PLACEBO-CONTROLLED RANDOMIZED PHASE 3 TRIAL (ENGOT-EN6-NSGO/GOG-3031/RUBY)

PLENARY 02: CHANGING THE LANDSCAPE OF ENDOMETRIAL CANCER

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Background: The RUBY trial (NCT03981796) evaluated the efficacy and safety of dostarlimab (D)+carboplatin-paclitaxel (CP) vs CP alone in pA/rEC. D+CP significantly improved progression-free survival (PFS) in the mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) (HR 0.28) and overall population (HR 0.64) with a favorable OS trend (HR 0.64).

Methods: Pts were randomised 1:1 to receive D+CP or PBO+CP Q3W for 6 cycles, followed by D or PBO monotherapy Q6W for up to 3 years. PFS2 was a secondary endpoint for the dMMR/MSI-H and overall populations. Post hoc treatment switching adjustment (for subsequent use of dostarlimab, pembrolizumab, durvalumab, nivolumab, lenvatinib, or pembrolizumab with lenvatinib) was implemented using two methods: inverse probability of censoring weights (IPCW) and rank-preserving structural failure time (RPSFT).

Results: Overall, 494 pts were randomised (D+CP, n=245; PBO+CP, n=249); 118 were dMMR/MSI-H (D+CP, n=53; PBO+CP, n=65). PFS2 benefit was observed with D+CP for all populations (Table). When adjusted for subsequent therapy (with dostarlimab, pembrolizumab, durvalumab, nivolumab, lenvatinib, or pembrolizumab with lenvatinib) the HRs for OS for D+CP vs PBO+CP for both IPCW and RPSFT were similar to the unadjusted HR for OS in all populations, with increased survival with D+CP.

Conclusions: Dostarlimab+CP demonstrates PFS and OS benefits compared with PBO+CP in pts with pA/rEC despite the use of subsequent therapies. These results provide support for the use of dostarlimab+CP as standard of care in patients with pA/rEC.

SE009 / #1499 – Seminal Abstract

A PHASE III DOUBLE-BLIND RANDOMIZED PLACEBO-CONTROLLED TRIAL OF ATEZOLIZUMAB IN COMBINATION WITH PACLITAXEL AND CARBOPLATIN IN WOMEN WITH ADVANCED/RECURRENT ENDOMETRIAL CANCER: THE ATTEND STUDY

PLENARY 02: CHANGING THE LANDSCAPE OF ENDOMETRIAL CANCER

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Background

The standard therapy for advanced/recurrent endometrial cancer includes carboplatin and paclitaxel (CP). Robust biological rationale suggested a synergy between immunotherapy and chemotherapy in this setting.

Methods

AtTEND is an international academic study in endometrial carcinoma/carcinoma patients (pts) with advanced newly diagnosed or recurrent disease with no prior systemic chemotherapy for recurrence. Pts were randomized (2:1 ratio) to receive either CP chemotherapy and atezolizumab (atezo) or placebo, followed by atezo or placebo until disease progression. The mismatch repair (MMR) status was evaluated centrally. Coprimary endpoints with a hierarchical approach were: progression free survival (PFS) in the deficient MMR (dMMR) population, PFS and overall survival (OS) in all comers.

Results

Five hundred and fifty-one pts were enrolled from Oct 2018 to Jan 2022 in 89 sites across 10 countries (median follow-up 28.3 months). Of the 549 pts included in the intention to treat population, 125 (22.8%) had dMMR tumours and 352 (64.1%) had endometrioid carcinoma; 369 (67.2%) had recurrent disease and 148 (82.2%) of newly diagnosed cases had primary stage IV. In the dMMR population, the addition of atezo showed a significant improved PFS (HR 0.36 95% CI: 0.23-0.57; p=0.0005; median PFS: not reached vs. 6.9 months for atezo vs placebo). The superiority in PFS was confirmed in all comers (HR 0.74 95% CI: 0.61-0.91; p=0.0219; median PFS: 10.1 months vs 8.9 months for atezo vs placebo). Interim analysis of OS in all comers indicated a trend in favor for atezo, despite 45 (24.3%) placebo patients received immunotherapy as subsequent therapy. Second PFS and duration of response in the dMMR population confirmed the efficacy of atezo. Grade ≥3 adverse events occurred in 66.9% and 63.8% of pts in atezo vs placebo arm. Safety profile for CP + atezo was manageable and consistent with expected

toxicities.

Conclusions

The addition of atezo to standard CP chemotherapy demonstrated a statistically significant improvement in PFS for pts with advanced/recurrent endometrial carcinomas with a substantial benefit in pts with dMMR carcinomas.

Clinical trial identification

EudraCT 2018-001072-37; NCT03603184;

SE010 / #1556 – Seminal Abstract

DUO-E/GOG-3041/ENGOT-EN10 TRIAL: CARBOPLATIN/PACLITAXEL+DURVALUMAB FOLLOWED BY MAINTENANCE DURVALUMAB±OLAPARIB AS A FIRST-LINE TREATMENT FOR NEWLY DIAGNOSED ADVANCED OR RECURRENT ENDOMETRIAL CANCER

PLENARY 02: CHANGING THE LANDSCAPE OF ENDOMETRIAL CANCER

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DUO-E (NCT04269200) evaluated the addition of durvalumab to standard first-line chemotherapy followed by maintenance durvalumab±olaparib in endometrial cancer (EC). Patients with newly diagnosed FIGO Stage III/IV or recurrent EC and naïve to first-line systemic treatment were randomised 1:1:1 to CP (carboplatin/paclitaxel+durvalumab placebo [six cycles] followed by maintenance durvalumab placebo+olaparib placebo), CP+durvalumab (carboplatin/paclitaxel+durvalumab [1120 mg IV q3w] [six cycles] followed by maintenance durvalumab [1500 mg IV q4w]+olaparib placebo), or CP+durvalumab+olaparib (carboplatin/paclitaxel+durvalumab [six cycles] followed by maintenance durvalumab+olaparib [300 mg tablets bid]). Dual primary endpoints were investigator-assessed progression-free survival (PFS; RECIST v1.1) in the intent-to-treat population for CP+durvalumab versus CP and CP+durvalumab+olaparib versus CP. Overall survival (OS) was a secondary endpoint. A multiple testing procedure with gatekeeping strategy was applied to PFS and OS. PFS by mismatch repair (MMR) status (deficient [dMMR] or proficient [pMMR]) was a prespecified subgroup analysis. CP+durvalumab and CP+durvalumab+olaparib demonstrated clinically meaningful and statistically significant PFS improvements versus CP in the intent-to-treat population (Table). Interim OS data were immature (27.7%; CP+durvalumab vs CP: HR [95% CI] 0.77 [0.56–1.07]; P=0.120; CP+durvalumab+olaparib vs CP: 0.59 [0.42–0.83]; P=0.003). PFS subgroup analysis showed benefit for both arms versus CP in dMMR/pMMR patients. In pMMR patients, maintenance olaparib further enhanced PFS benefit (Table). Safety profiles of the treatment arms were generally consistent with the individual components. DUO-E met both primary endpoints, showing statistically significant and clinically meaningful PFS improvement with the addition of durvalumab to CP followed by maintenance durvalumab±olaparib versus CP.

Maintenance olaparib further improved PFS in pMMR patients.

Table. PFS in the intent-to-treat, dMMR, and pMMR populations from the Phase III DUO-E trial

Population	Intent-to-treat (n=718)			dMMR (n=143)			pMMR (n=575)		
	CP (n=241)	CP+durva (n=238)	CP+durva+ola (n=239)	CP (n=49)	CP+durva (n=46)	CP+durva+ola (n=48)	CP (n=192)	CP+durva (n=192)	CP+durva+ola (n=191)
Median duration of follow-up,* months	12.6	15.4	15.4	10.2	15.5	19.2	12.8	15.3	15.2
Events, n (%)	173 (71.8)	139 (58.4)	126 (52.7)	25 (51.0)	15 (32.6)	18 (37.5)	148 (77.1)	124 (64.6)	108 (56.5)
Median PFS, months	9.6	10.2	15.1	7.0	NR	31.8	9.7	9.9	15.0
HR (95% CI) vs CP		0.71 (0.57–0.89); P=0.003	0.55 (0.43–0.69); P<0.0001		0.42 (0.22–0.80)	0.41 (0.21–0.75)		0.77 (0.60–0.97)	0.57 (0.44–0.73)

Survival rates were estimated by the Kaplan–Meier method. The HR and CI for PFS in the intent-to-treat population are estimated from a Cox proportional hazard model stratified by MMR and disease status. The HR and CI for PFS in the MMR subgroups are estimated from an unstratified Cox proportional hazard model. *In censored patients. At primary data cutoff (12 April 2023).
durva, durvalumab; NR, not reached; ola, olaparib.

SE011 / #1323 – Seminal Abstract

A RANDOMIZED TRIAL COMPARING RADICAL HYSTERECTOMY VERSUS SIMPLE HYSTERECTOMY ON SEXUAL HEALTH, MENOPAUSAL SYMPTOMS, AND QUALITY OF LIFE IN PATIENTS WITH LOW-RISK EARLY-STAGE CERVICAL CANCER

FOCUSED PLENARY 01: QUALITY OF LIFE

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Background: Retrospective data suggested that less radical surgery may be safe, less morbid and associated with improved quality of life (QOL) and sexual health. Secondary objective of this non-inferiority phase III prospective randomized trial was to compare sexual health outcomes and quality of life (QOL) in women with low-risk, early-stage cervical cancer (LRESCC) undergoing radical hysterectomy (RH) and simple hysterectomy (SH).

Methods: Women with LRESCC defined as FIGO 2009 1A2 or 1B1 disease were randomized to receive RH or SH. Sexual health assessment (SHA) was done using the Female Sexual Function Index (FSFI) and Female Sexual Distress Scale – Revised (FSDS-R) and QOL was assessed using EORTC QLQ-C30 with a cervical cancer module QLQ-CX24. These were completed before randomization (baseline) and at 3, 6, 12, 24 and 36 months after surgery. Mean scores were calculated at each time point of assessment and compared by Wilcoxon test between two groups. by linear mixed models. Cohen's D was calculated to determine effect size. Proportion of women who met clinical cut off was compared between two groups by Fisher's exact test.

Results: Among 700 women randomized, 405 (86% of expected) and 508 (73% of expected) completed baseline SHA and QOL, respectively. Clinical and pathologic characteristics were well balanced between surgical groups (median age 42 for SHA and 44 for QOL cohort; < 50 years 81% for SHA and 73% for QOL cohort). Compliance post-baseline was 63% to 79% for SHA and 56% to 69% for QOL with a completion rate of 63% for SHA and 58% for QoL at 36 months. There were no differences in mean baseline scores for QOL or SHA between SH and RH ($p > 0.05$). Mean baseline scores were high for all EORTC QLQ-C30 functional scales except for emotional subscale and all improved over time. The Global Health Status was high at baseline (> 75) however was significantly higher at 36 months for SH group ($P = 0.025$, Cohen's $d = 0.31$). For QLQ-CX24, Symptom Experience was significantly worse up to 24 months ($p = 0.031$ Cohen's $d = 0.21$) and Body Image worse at 3, 24, and 36 months ($p = 0.01-0.002$, Cohen's $d = 0.25$ to 0.33) in the RH group. At 3 months, sexual worry and sexual enjoyment were worse in RH ($P < 0.0001$, Cohen's $d = 0.34$; 0.028 , Cohen's $d = 0.29$). Sexual-Vaginal Functioning was significantly worse with moderate effect size up to 24 months ($p < 0.001-0.022$, Cohen's $d = 0.28$ to 0.53) and less

sexual activity up to 36 months ($P = 0.024$, Cohen's $d = 0.24$) in the RH arm. Mean FSFI total score met clinical range for sexual dysfunction (<26.55) in the RH up to 6 months ($P = 0.02$, Cohen's $d = 0.16$). There were significant differences in favour of SH for FSFI subscales; desire and arousal at 3 months ($p=0.001$, Cohen's $d=0.28$; $p<0.0001$, Cohen's $d= 0.2$), pain and lubrication up to 12 months ($p<0.0001-0.01$, Cohen's $d=0.17$ to 0.37 ; $p=0.003-0.018$, Cohen's $d = 0.19-0.3$). However, there were no differences in orgasm and satisfaction subscales between surgical groups. Mean sexual distress met clinical cut off (FSDS-R >11) at almost all time points in both groups but was greater in RH at 3 months ($P= 0.018$, Cohen's $d = 0.21$). Proportion of patients meeting clinical range of for sexual dysfunction (46% RH vs 39% SH at 6 months, $P = 0.031$) and sexual distress (52% RH vs 44% SH at 3 months, $p=0.043$) increased significantly in the RH group from baseline and remained elevated up to 6 months.

Conclusion: In this young LRESCC population, QOL is high and symptoms burden is relatively low. However, there is significant toxicity associated with RH on sexual health with high proportion of people having sustained sexual-vaginal dysfunction and sexual distress.

SE012 / #1638 – Seminal Abstract

ICON8B: GCIG PHASE III RANDOMISED TRIAL COMPARING WEEKLY DOSE-DENSE CHEMOTHERAPY + BEVACIZUMAB TO THREE-WEEKLY CHEMOTHERAPY+ BEVACIZUMAB IN FIRST-LINE HIGH-RISK STAGE III-IV EPITHELIAL OVARIAN CANCER TREATMENT: PRIMARY PROGRESSION-FREE SURVIVAL ANALYSIS

CLOSING SESSION: THE DEVELOPMENT OF PROGNOSIS AND PREDICTIVE MARKERS

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Background First-line phase III trials in stage III/IV Epithelial Ovarian Cancer (EOC) have shown improved survival both with addition of bevacizumab (BEV) to three-weekly (q3w) carboplatin (C)-paclitaxel (T) and integration of weekly dose-dense paclitaxel (ddwT) with carboplatin compared to q3wCT alone. ICON8B, a 3-arm trial, compared BEV+q3wCT versus (vs) BEV+q3wCddwT vs q3wCddwT in high-risk stage III (residual disease >1cm diameter after primary surgery or requirement for primary chemotherapy) and stage IV EOC.

Methods Eligible patients were randomised 1:1:1 to Arm B1 (standard- q3w C AUC5/6+q3w T 175mg/m²+ q3w BEV 7.5mg/kg); Arm B2- q3w C AUC5/6+ddwT 80mg/m²; Arm B3- q3w C AUC5/6+ddwT 80mg/m²+ q3w BEV 7.5mg/kg. Up to six cycles chemotherapy and 18 BEV cycles were administered. Arm B2 recruitment discontinued after ICON8 saw no evidence of progression-free survival (PFS) improvement with q3wCddwT vs q3wCT. The consolidated Arm B1 vs B3 trial targeted 509 PFS events to detect B3vB1 HR=0.75 with 90% power.

Results 707 patients randomised from 07/2015 – 03/2020 (B1=292, B2=129, B3=286), median age 64 years, 94% ECOG Performance Status 0-1, 53% stage IIIC, 40% stage IV, 91% High Grade Serous histology. 14% upfront surgery, 84% planned Delayed Primary Surgery, 2% no surgery planned. 88%:83%:82% completed 6 cycles carboplatin-based chemotherapy, 52%:51%:60% experienced ≥grade 3 toxicities in B1:B2:B3. 37%:46% completed 18 cycles bevacizumab in B1:B3. Median 59.0 months follow-up (07/2023-B1 and B3). Given slow additional event rate, the study committee concluded 465 progression events were sufficient for primary analysis, giving 87% power for targeted effect size of 0.75. PFS was better in B3 compared to B1. Median PFS 16.7 months B1 vs 22.2 months B3 (HR=0.75, 95% CI=0.62-0.90, p=0.002). Median OS; B1 40.9 months vs 51.1 months B3 (HR=0.77, 95% CI=0.62-0.96, p=0.020).

Conclusions In primary treatment of high-risk stage IIIC/IV EOC, BEV+q3wCddwT improves median PFS by 5.5 months compared to BEV+q3wCT.