LBA40 Phase III double-blind randomized placebo controlled trial of atezolizumab in combination with carboplatin and paclitaxel in women with advanced/recurrent endometrial carcinoma

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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/carcinosarcoma 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.

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LBA41 Durvalumab (durva) plus carboplatin/paclitaxel (CP) followed by maintenance (mtx) durva ± olaparib (ola) as a first-line (1L) treatment for newly diagnosed advanced or recurrent endometrial cancer (EC): Results from the phase III DUO-E/GOG-3041/ENGOT-EN10 trial

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Background: Combination of immunotherapy with CP led to improved progression-free survival (PFS) in patients (pts) with advanced EC. DUO-E (NCT04269200) evaluated addition of durva to standard 1L CP, followed by mtx durva ± ola, in pts with EC.

Methods: Pts with newly diagnosed FIGO Stage III/IV or recurrent EC and naïve to systemic treatment were randomised 1:1:1 to CP (CP + durva placebo [pbo] for 6 cycles followed by mtx durva pbo + ola pbo), CP + durva (CP + durva [1120 mg IV q3w] for 6 cycles followed by mtx durva [1500 mg IV q4w] + ola pbo), or CP + durva + ola (CP + durva for 6 cycles followed by mtx durva + ola [300 mg tablets bid]). Dual primary endpoints were PFS (investigator-assessed RECIST v1.1) in the intent-to-treat (ITT) population for CP + durva vs CP and CP + durva + ola vs 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 was a prespecified subgroup analysis.

Results: In the ITT population (N=718), CP + durva and CP + durva + ola showed statistically significant and clinically meaningful PFS benefit vs CP (Table). Interim OS data were immature (27.7%) yet with a trend towards benefit (CP + durva vs CP: HR [95% CI] 0.77 [0.56–1.07]; P=0.120; CP + durva + ola vs CP: 0.59 [0.42–0.83]; P=0.003). PFS subgroup analysis showed benefit for both arms vs CP in MMR-deficient (dMMR; n=143) and -proficient (pMMR) pts (n=545). In pMMR pts, mtx ola further enhanced PFS benefit (Table). Safety profiles of the treatment arms were generally consistent with individual components.

Table: LBA41

Population	Arm	Median follow-up duration,† months	PFS events, n/N (%)	Median PFS, months	HR* (95% CI)	12-/18-month PFS rate, %
ITT	CP	12.6	173/241 (71.8)	9.6		41.1/21.7
	CP + durva	15.4	139/238 (58.4)	10.2	0.71 (0.57–0.89); P=0.003	48.5/37.8
	CP + durva + ola	15.4	126/239 (52.7)	15.1	0.55 (0.43–0.69); P<0.0001	61.5/46.3
dMMR	CP	10.2	25/49 (51.0)	7.0		43.3/31.7
	CP + durva	15.5	15/46 (32.6)	Not reached	0.42 (0.22–0.80)	67.9/67.9
	CP + durva + ola	19.2	18/48 (37.5)	31.8	0.41 (0.21–0.75)	70.0/62.7
pMMR	CP	12.8	148/192 (77.1)	9.7		40.8/20.0
	CP + durva	15.3	124/192 (64.6)	9.9	0.77 (0.60–0.97)	44.4/31.3
	CP + durva + ola	15.2	108/191 (56.5)	15.0	0.57 (0.44–0.73)	59.4/42.0

*Vs CP; †In censored patients.