Olaparib vs placebo as maintenance therapy after platinum-based chemotherapy in advanced/metastatic endometrial cancer patients: The GINECO randomized phase IIb UTOLA trial


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Background

The TGCA data suggest opportunities to target DNA repair in patients (pts) with endometrial cancer (EC). UTOLA assessed the efficacy of Parp-inhibitor maintenance for advanced/M+ EC pts who achieved disease control after 1st line platinum CT and to analyse efficacy in some molecular subgroups.

Methods

UTOLA is a randomized, double-blind, placebo controlled, phase IIb trial. Adjuvant CT ≥12 mos before inclusion was allowed. Pts were randomized (2:1) to olaparib maintenance arm (ola, 300 mg po BID) or placebo arm (pl) until progression or intolerance with stratification on P53, MMR status, and the response to the previous CT. Molecular profile was assessed by IHC and NGS. Primary endpoint was PFS in ITT. Main secondary endpoints were PFS according to P53 status, CT response, OS, safety. A pre-specified PFS analysis was performed according to HRD status defined by the number of large genomic events. One sided unstratified analyses are presented.

Results

147 pts were randomized (98 to Ola, 49 to pl). 82% of the pts received at least 6 cycles of CT with 46 CR, 64 PR, 34 stable and 3 NED; tumor classification was 53% P53mut, 35% NSMP, 12% MMRd, and 1 tumor POLEmut. In total, 52% (73) were HRD positive, 79% in P53mut & 23% in P53WT. Median PFS in the ITT population was 5.6 mos (90%CI 3.8-7.4) and 4.0 (3.6-7.4) in ola and pl arms respectively (HR:0.94, p=0.29). Median PFS in P53mut were 5.6 mos (3.6-8.8) vs 3.6 ms (1.8-4.9) in ola and pl arms (HR:0.75, p=0.12) whereas 6.1 mos (3.6-11) vs 7.7 mos (2.9-14.5) (HR=1.13, p=0.3) respectively in the P53WT. In the HRD tumors (n=73), median PFS was statistically higher with ola: 5.4 mos (90%CI 3.6-9.6) vs 3.6 mos (1.8-4.9) with pl (HR:0.59, p=0.02) regardless of P53 status. For the 46 pts with CR to previous CT, median PFS in ola arm reached 8.8 mos versus 3.8 mos. No difference for OS was observed in all subgroups. Safety profile was similar and acceptable as seen in other cancers (36% vs 10% of G3/4 toxicities without myelodysplasia with ola).

Conclusions

UTOLA suggests maintenance ola could prolong PFS in HRD-positive advanced/M+ EC. These data should be confirmed and warrants further PARP inhibitor studies in this population.

Clinical trial identification

Clinical trial identification
Legal entity responsible for the study

ARCAGY-GINECO.

Funding

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Disclosure