Abstract:

ARIEL3: PHASE 3, RANDOMISED, DOUBLE-BLIND STUDY OF RUCAPARIB VS PLACEBO FOLLOWING RESPONSE TO PLATINUM-BASED CHEMOTHERAPY FOR RECURRENT OVARIAN CARCINOMA (OC)

Aims

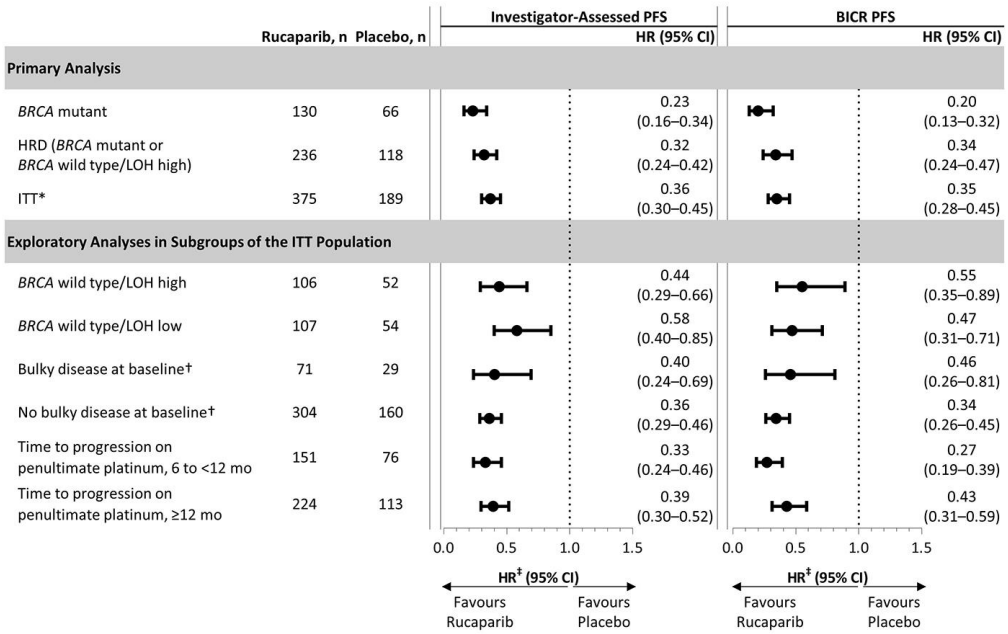
ARIEL3 (NCT01968213) evaluated rucaparib vs placebo as maintenance treatment in patients with recurrent platinum-sensitive OC.

Method

Eligibility: ≥2 prior platinum-based therapies, platinum-sensitive OC (progressive disease [PD] ≥6 months after penultimate platinum), complete (RECIST v1.1) or partial response (RECIST v1.1 or GCIG CA-125 criteria) to most recent platinum, and CA-125 less than the upper limit of normal. Patients were randomised 2:1 to oral rucaparib 600 mg BID or placebo. Investigator-assessed progression-free survival (PFS) (primary endpoint) was assessed in a step-down procedure for 3 nested groups: (1) *BRCA* mutant (germline or somatic *BRCA* mutation); (2) homologous recombination deficient (*BRCA* mutant or *BRCA* wild type/loss of heterozygosity [LOH] high); and (3) intent-to-treat (ITT) population. PFS was also assessed by blinded independent central review (key secondary endpoint) and in subgroups of the ITT population (exploratory endpoint).

Results

ARIEL3 enrolled 564 patients (375, rucaparib; 189, placebo). PFS data are summarised in the Figure. The most common grade ≥3 treatment-emergent adverse events (TEAEs) were anaemia (18.8%, rucaparib; 0.5%, placebo) and alanine/aspartate aminotransferase increase (10.5%; 0%). As of 15 Apr 2017, 13.4% (rucaparib) and 1.6% (placebo) of patients discontinued due to TEAEs (excluding PD); 1.6% and 1.1% of patients died due to AEs including PD).



BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; HRD, homologous recombination deficient. *Includes patients with *BRCA*-mutant (130, rucaparib; 66, placebo), *BRCA* wild-type/genomic LOH high (106, rucaparib; 52, placebo), *BRCA* wild-type/genomic LOH low (107, rucaparib; 54, placebo), or *BRCA* wild-type/genomic LOH indeterminate (32, rucaparib; 17, placebo) OC. †Bulky disease was defined as any lesion >2 cm identified by independent radiological review. ‡Estimated with a Cox proportional hazards model.

Conclusion

Rucaparib significantly improved PFS vs placebo in all primary analysis groups, including the ITT patient population.

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