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Commentary
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Rucaparib: A New Lease of Life for Ovarian Cancer Patients

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Keywords

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Background

High grade epithelial ovarian cancer, along with fallopian tube and primary peritoneal cancers are generally responsive (partially or completely) to platinum based chemotherapy [1]. Significant scientific evidence has proven Rucaparib to be of substantial promise as monotherapy for maintenance of ovarian cancer patients regardless of genetic mutation [2]. The ARIEL3 Randomised Controlled trial has shown statistically significant reduction in the time required for third line chemotherapy when maintenance therapy with Rucaparib was instituted promptly in candidate patients [3].

The ARIEL 3 Trial

Study design

Multicentric, randomised, double-blind, parallel, placebo-controlled, phase 3 intervention trial.

Inclusion criteria

Adult females (above 18 years of age) with recurrent high grade epithelial, fallopian tube or primary peritoneal cancer having undergone at least 2 prior platinum based chemotherapies and attained complete or partial response to immediate prior platinum based therapy with CA 125 concentrations less than the upper limit of normal. Also, Rucaparib must have been commenced within 8 weeks of last chemotherapy dose as well in order to qualify for inclusion. Size of (any) residual tumour was not a constraint.

Exclusion criteria

Patients who had received previous treatment with PARPi drug(s) and those with an ECOG performance score surpassing 1.

Randomisation

All comers (ITT population) including BRCA or HRD+ mutations were stratified to enable a step down analysis in three prospectively defined nested cohorts.

A total of 564 patients were enrolled and a parallel double blinded randomization effected with 375 patients receiving Rupacarib and a placebo for 189 recruits. Randomisation was effected in a 2:1 proportion. Stratification was by HRR status, NGS mutation and progression free response to the penultimate regimen to recent platinum-based regimen.

Results and Conclusion

The investigator based results of the AERIAL 3 after 1 year revealed a statistically significant improvement in median PFS with administration of Rupacarib among all the three cohorts. A marked 64% reduction in the risk of disease progression or mortality was noted thereof. In the ITT subgroup, the mPFS was 10.8 months (HR=0.36; 95% CI, 0.30-0.45); $p<0.0001$) whereas in the BRCA and HRD+ patients, the same were 16.6 months and 22.9 months respectively. These figures tantamounted to be 'highly' statistically significant ($p<0.001$) Results from the BICR-assessed PFS corroborated investigators', reinforcing Rucaparib efficacy. Further evidence surfaced when

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enhanced responses in a subset of patients with quantifiable residual disease were demonstrated. Rucaparib is thus a strong contender for auxillary therapy in rather bulkier tumours, again irrespective of genetic imports.

Rupacarib can be given orally (600 mg twice daily) and is generally well tolerated apart from a few manageable side effects, thereby ensuring better patient compliance [4].

Evidence based medicine thus supports the use of maintenance Rupacarib therapy in patients with relapsed ovarian cancer, and among those with partial or complete response to platinum based chemotherapy. Rupacarib is thus a cost effective and resourceful strategy towards potential cure of female pelvic malignancies, despite the inherent genetic heterogeneities.

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