

ARIEL4: An International, Randomised Phase 3 Study of Rucaparib vs Chemotherapy in *BRCA1*- or *BRCA2*-Mutated, Relapsed Ovarian Cancer (OC)

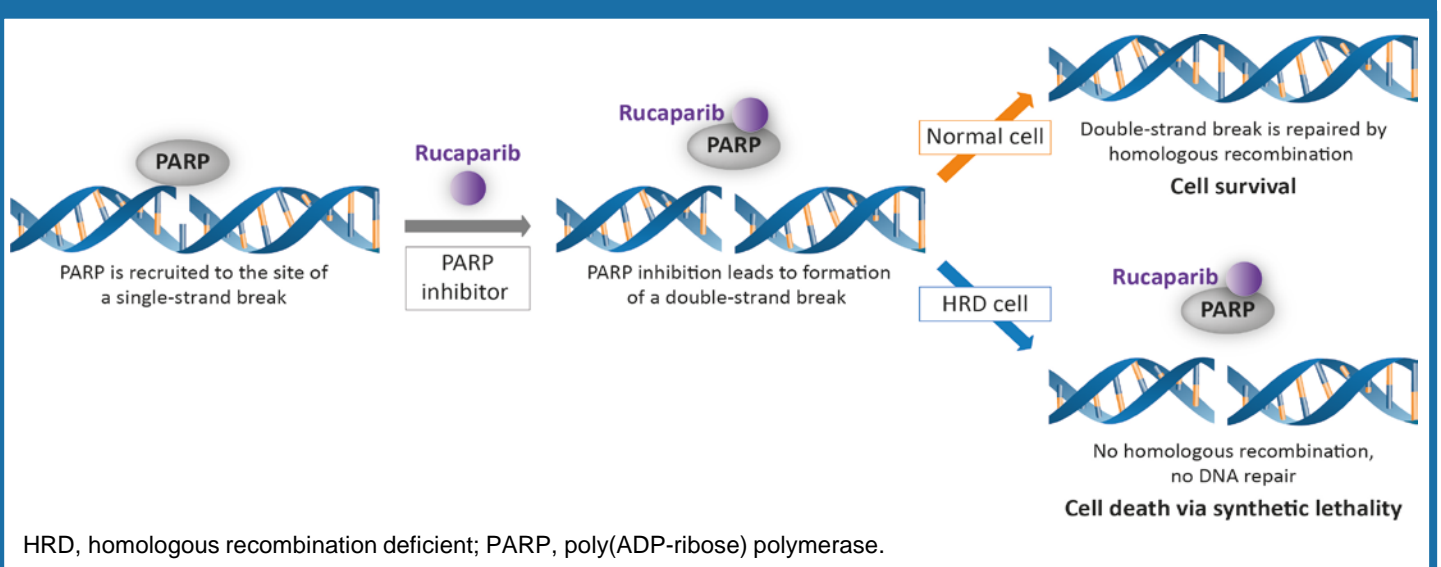
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INTRODUCTION

- In high-grade OC, including fallopian tube and primary peritoneal cancer, ~18% and ~7% of patients have carcinomas associated with a germline *BRCA1* or *BRCA2* mutation or a somatic *BRCA1* or *BRCA2* mutation, respectively¹
- In cells with homologous recombination deficiency (HRD), poly(ADP-ribose) polymerase (PARP) inhibition leads to cell death²⁻⁴ (**Figure 1**)
 - Rucaparib has been shown to inhibit PARP enzymatic activity and increase formation of PARP-DNA complexes ("PARP trapping") in preclinical studies and has demonstrated efficacy in carcinomas with HRD⁵⁻⁹
- Based on pooled efficacy and safety data from 2 single-arm clinical trials,⁸⁻¹⁰ rucaparib received accelerated approval in the United States as monotherapy for the treatment of patients with deleterious *BRCA* mutation (germline and/or somatic) associated advanced OC who have been treated with ≥2 chemotherapies
- Data comparing PARP inhibitors to standard of care (SOC) treatment for relapsed OC are limited¹¹
- Randomised studies are needed to assess the benefit-risk profile of PARP inhibitors vs current SOC as treatment for patients with *BRCA*-mutated, relapsed, high-grade OC, particularly in the third-line or later treatment setting

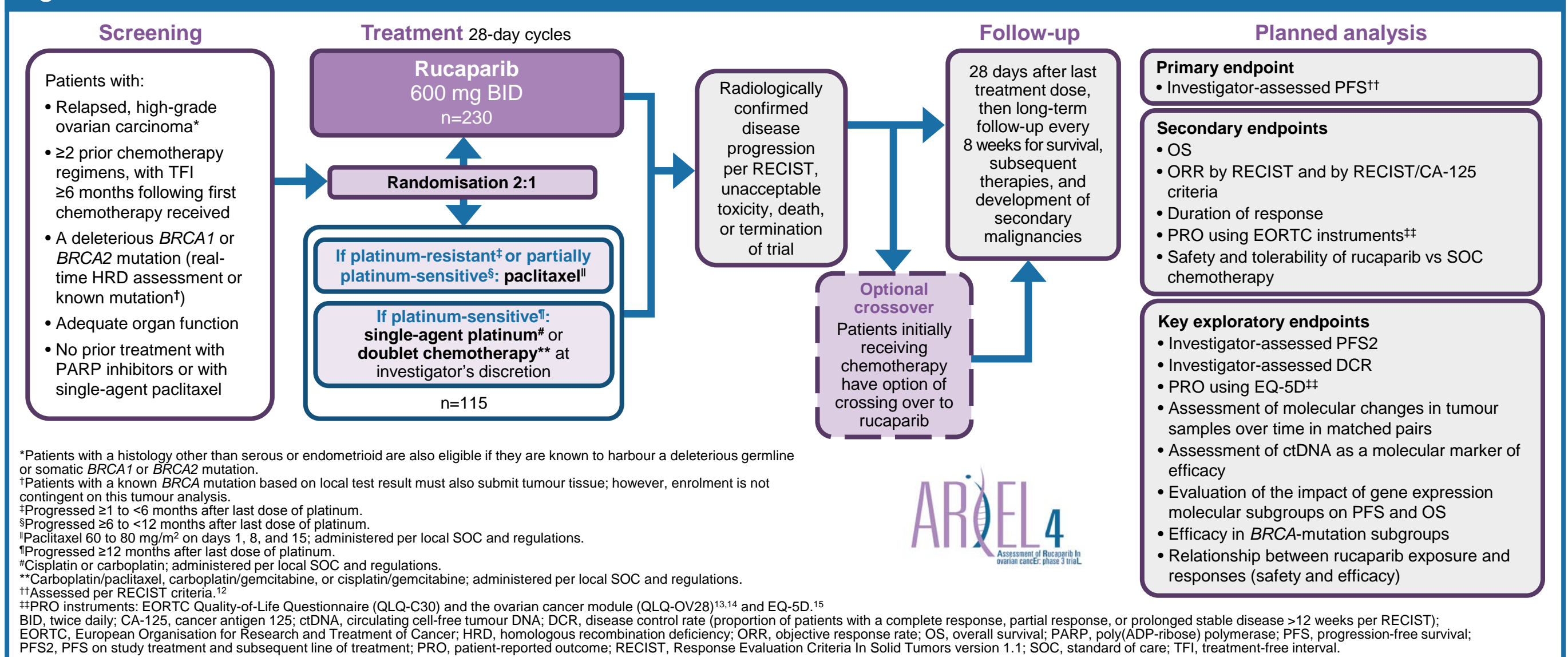
Figure 1. Rucaparib-Mediated Synthetic Lethality



ARIEL4 TRIAL OVERVIEW

- ARIEL4 (CO-338-043; EudraCT 2016-000816-14; NCT02855944) is an international, multicentre, randomised, phase 3 study evaluating rucaparib 600 mg twice daily vs SOC chemotherapy as treatment for patients with germline or somatic *BRCA1*- or *BRCA2*-mutated, relapsed, high-grade OC who have received ≥2 prior chemotherapy regimens (**Figure 2**)

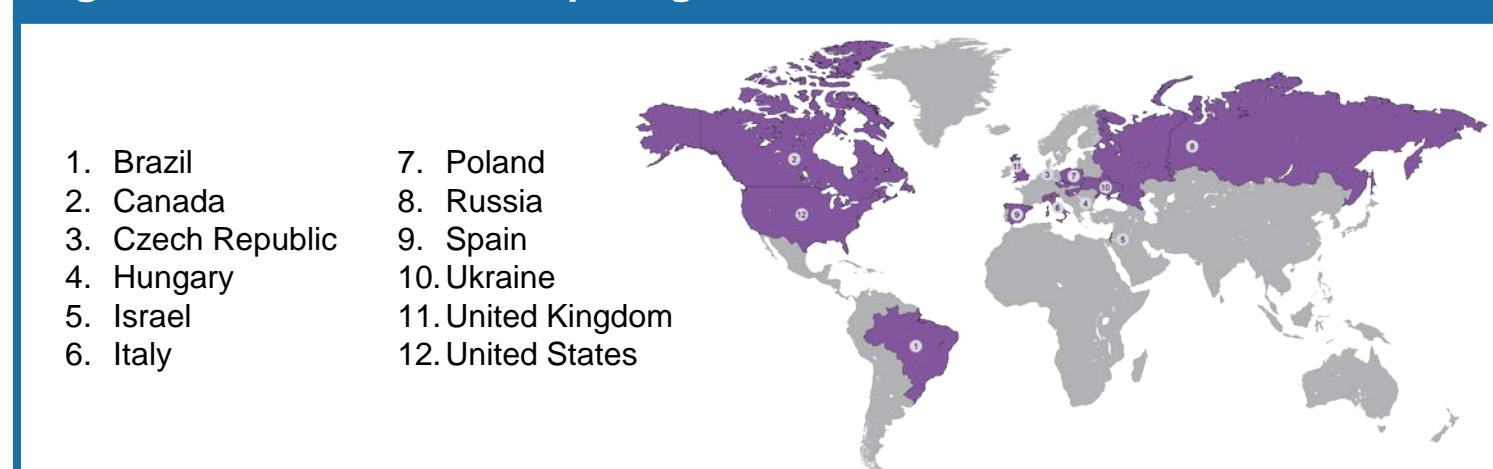
Figure 2. ARIEL4 Trial Schema



TRIAL SUMMARY

- Rucaparib has demonstrated efficacy in the treatment setting in patients with OC and a deleterious *BRCA1* or *BRCA2* mutation⁷⁻⁹
- The ARIEL4 phase 3 study aims to assess the benefit-risk profile of rucaparib vs current SOC chemotherapy as treatment for patients with *BRCA1*- or *BRCA2*-mutated, relapsed, high-grade OC
- ARIEL4 is actively recruiting patients, with a goal of enrolling 345 patients from ~100 sites worldwide (**Figure 3**)

Figure 3. Countries Participating in ARIEL4



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ACKNOWLEDGEMENTS

This study is funded by Clovis Oncology, Inc. Medical writing and editorial support was funded by Clovis Oncology and provided by Nathan Yardley and Shannon Davis of Ashfield Healthcare Communications.