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

Rebecca S. Kristeleit, 1 Domenica Lorusso, 2 Ana Oaknin, 3 Tamir Safra, 4 Elizabeth M. Swisher, 5 Igor M. Bondarenko, 6 Tomasz Huzarski, 7 Jaroslav Klat, 8 Vladimir Moiseyenko, 9 Robert Pika, 10 Luciana S. Viola, 11 Chris Tankersley, 12 Lara Maloney, 12 Sandra Goble, 12 Caro Unger, 12 Adam Dowson, 12 Heidi Giordano, 12 Amit M. Oza 13

INTRODUCTION

• In high-grade OC, including fallopian tube and primary peritoneal cancers, ≥10% and ≥7% of patients have cancers associated with a germline BRCA1 or BRCA2 mutation or a somatic BRCA1 or BRCA2 mutation, respectively.

• In cells with homologous recombination deficiency (HRD), poly(ADP-ribose) polymerase (PARP) inhibition leads to cell death. 4–6 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 HRD. 4–6

• Based on pooled efficacy and safety data from 2 single-arm clinical trials, 7–10 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 limited. 11

• Randomised studies are needed to assess the benefit-risk profile of PARP inhibitors vs current SOC as treatment for patients with BRCA1-mutated, relapsed, high-grade OC, particularly in the third-line or later treatment setting.

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).

TRIAL SUMMARY

• Rucaparib has demonstrated efficacy in the treatment setting in patients with OC and a deleterious BRCA1 or BRCA2 mutation. 4–6

• 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 ≥10 sites worldwide (Figure 3).

Figure 1. Rucaparib-Mediated Synthetic Lethality

Figure 2. ARIEL4 Trial Schema

Figure 3. Countries Participating in ARIEL4

REFERENCES


ACKNOWLEDGEMENTS

This study is funded by Clovis Oncology, Inc. Medical writing and editorial support was funded by Clovis Oncology and provided by Shang T. Yan and Sharon Davis of AstraZeneca HealthCare Communications.