947P Subgroup analysis of rucaparib in platinum-sensitive recurrent ovarian carcinoma: Effect of prior chemotherapy regimens in ARIEL3

D. Lorusso[1], R.L. Coleman[2], A.M. Oza[3], C. Aghajanian[4], A. Oaknin[5], A. Dean[6], N. Colombo[7], J.I. Weberpals[8], A.R. Clamp[9], G. Scambia[10], A. Leary[11], R.W. Holloway[12], M. Amenedo Gancedo[13], P.C. Fong[14], J.C. Goh[15], D.M. O'Malley[16], S. Banerjee[17], S. Goble[18], T. Cameron[19], J.A. Ledermann[20]

[1]Unità di Ginecologia Oncologica, Fondazione IRCCS Istituto Nazionale dei Tumori and MITO, Milan, Italy, [2]Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, [3]Division of Medical Oncology and Hematology, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada, [4]Gynecologic Medical Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, USA, [5]Medical Oncology Department, Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain, [6]Department of Oncology, Saint John of God Subiaco Hospital, Subiaco, Australia, [7]Gynecologic Cancer Program, European Institute of Oncology and University of Milan-Bicocca, Milan, Italy, [8]Division of Gynecologic Oncology, Ottawa Hospital Research Institute, Ottawa, ON, Canada, [9]Department of Medical Oncology, The Christie NHS Foundation Trust and University of Manchester, Manchester, UK, [10]Gynecologic Oncology, Policlinico Universitario A. Gemelli IRCCS Università Cattolica del Sacro Cuore Roma, Rome, Italy, [11]Gynecological Unit, Gustave Roussy Cancer Center, INSERM U981, and Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens (GINECO), Villejuif, France, [12]Department of Gynecologic Oncology, Florida Hospital Cancer Institute, Orlando, FL, USA, [13]Medical Oncology Department, Oncology Center of Galicia, La Coruña, Spain, [14]Medical Oncology Department, Auckland City Hospital, Auckland, New Zealand, [15]Department of Oncology, Cancer Care Services, Royal Brisbane and Women's Hospital and University of Queensland, Herston, Australia, [16]Clinical Research Gynecologic Oncology, The Ohio State University, James Cancer Center, Columbus, OH, USA, [17]Gynaecology Unit, The Royal Marsden NHS Foundation Trust, London, UK, [18]Biostatistics, Clovis Oncology, Inc., Boulder, CO, USA, [19]Clinical Science, Clovis Oncology, Inc., Boulder, CO, USA, [20]Department of Oncology, UCL Cancer Institute and UCL Hospitals, London, UK

Background: In the randomised, placebo-controlled, phase 3 study ARIEL3, patients were randomised 2:1 to oral rucaparib (600 mg BID) or placebo as maintenance treatment following response to platinum-based chemotherapy. Rucaparib significantly improved progression-free survival (PFS) vs placebo in all patient populations regardless of biomarker status (Coleman et al. *Lancet.* 2017;390:1949-61). This post hoc exploratory analysis investigated the effect of the number of prior chemotherapy regimens on the primary and secondary endpoints of investigator-assessed and blinded independent central review (BICR)-assessed PFS in ARIEL3.

Methods: In ARIEL3, all patients received ≥2 prior platinum-based regimens in accordance with the protocol. PFS was explored in subgroups of patients who received 2 or ≥ 3 prior chemotherapy regimens. These subgroup analyses were presented for the following predefined cohorts: *BRCA* mutant; *BRCA* mutant or *BRCA* wild type/high loss of heterozygosity (LOH); and intent-to-treat (ITT) population (ie, all randomised patients).

Results: The visit cutoff dates for efficacy and safety were 15 April 2017 and 15 August 2017, respectively. In each predefined cohort, rucaparib significantly improved PFS compared to placebo irrespective of the number of prior chemotherapy regimens (ie, 2 or ≥ 3) (Table). Rucaparib's safety profile was consistent between patients who received 2 or ≥ 3 prior chemotherapy regimens as assessed by the rate of all grade (100% and 100%) and grade ≥3 (59% and 59%) treatment-emergent adverse events (TEAEs) and dose modifications (ie, treatment interruptions and/or dose reductions due to a TEAE) (70% and 74%) in each respective subgroup.

Table: 947P

Cohort	Rucaparib, n	Placebo, n	PFS (investigator review)		PFS (BICR)	
			HR* (95% CI) Rucaparib vs placebo	Median PFS, mo; *P* value† Rucaparib vs placebo	HR* (95% CI) Rucaparib vs placebo	Median PFS, mo; *P* value† Rucaparib vs placebo
Patients with 2 prior chemotherapy regimens						
BRCA mutant	73	40	0.24 (0.14–0.40)	21.9 vs 5.4; *P*<0.0001	0.24 (0.13–0.45)	26.8 vs 5.5; *P*<0.0001
BRCA mutant or *BRCA* wild type/ high LOH	136	75	0.34 (0.23–0.49)	14.1 vs 5.5; *P*<0.0001	0.33 (0.21–0.52)	26.8 vs 5.5; P < 0.0001
ITT	231	124	0.42 (0.32–0.55)	10.4 vs 5.4; *P*<0.0001	0.37 (0.27–0.50)	17.1 vs 5.4; *P*<0.0001
Patients with ≥3 prior chemotherapy regimens						
BRCA mutant	57	26	0.21 (0.11–0.40)	13.7 vs 5.4; *P*<0.0001	0.17 (0.08–0.35)	18.0 vs 5.4; *P*<0.0001
BRCA mutant or *BRCA* wild type/high LOH	100	43	0.27 (0.16–0.44)	11.1 vs 5.4; *P*<0.0001	0.30 (0.18–0.52)	13.6 vs 5.4; *P*<0.0001
ITT	144	65	0.28 (0.19–0.41)	11.1 vs 5.3; *P*<0.0001	0.36 (0.24–0.53)	13.3 vs 5.3; *P*<0.0001

∗Cox proportional hazards model; *P* values for treatment-by-prior chemotherapy regimen subgroup interaction were nonsignificant for all analyses. †Stratified log-rank *P* value. CI, confidence interval; HR, hazard ratio.

Conclusions: Maintenance treatment with rucaparib improved PFS vs placebo in all 3 predefined cohorts regardless of the number of prior chemotherapy regimens received.

Clinical trial identification: NCT01968213.

Editorial acknowledgement: Writing and editorial support, funded by Clovis Oncology, Inc. (Boulder, CO, USA) was provided by Nathan Yardley, PhD, and Shannon Davis of Ashfield Healthcare Communications (Middletown, CT, USA).

Legal entity responsible for the study: Clovis Oncology, Inc.

Funding: Clovis Oncology, Inc.

Disclosure: D. Lorusso: Consulting or advisory role: AstraZeneca, Clovis Oncology, Roche, Tesaro, PharmaMar; Support for travel or accommodation: Roche, PharmaMar. R.L. Coleman: Grants: AstraZeneca, Roche/Genentech, Janssen, OncoMed, Millennium, Merck, Clovis Oncology, Esperance, AbbVie; Advisor: AstraZeneca, Roche/Genentech, Janssen, OncoMed, Millennium, Merck, Clovis Oncology, Esperance, Tesaro, GamaMabs, Pfizer, Genmab, Gradalis, Bayer, AbbVie. A.M. Oza: Steering committees: AstraZeneca, Clovis Oncology, Tesaro. C. Aghajanian: Steering committee: Mateon Therapeutics, Clovis Oncology; Advisory boards: Clovis Oncology, Cerulean Pharma, Bayer, VentiRx, Tesaro; Honorarium: Mateon Therapeutics, Clovis Oncology, Cerulean Pharma, Bayer, VentiRx, Tesaro. A. Oaknin: Advisory boards: Roche, AstraZeneca, PharmaMar, Clovis Oncology, Tesaro; Travel or accommodation: Roche, AstraZeneca, PharmaMar. A. Dean: Consulting or advisory role: Specialised Therapeutics Australia, Shire Pharmaceuticals, Precision Oncology Australia. N. Colombo: Consulting or advisory role: Roche, AstraZeneca, Tesaro, PharmaMar, Clovis Oncology, Pfizer, Advaxis. J.I. Weberpals: Research support: AbbVie and AstraZeneca; Advisory boards: AstraZeneca. A.R. Clamp: Advisory boards: AstraZeneca, Roche; Research funding: AstraZeneca; Travel and accommodation for congress attendance: AstraZeneca. G. Scambia: Consulting or advisory role: Roche, AstraZeneca, PharmaMar, Clovis Oncology, Tesaro. A. Leary: Advisory board: Clovis Oncology, Pfizer, PharmaMar; Institutional research grant support: GamaMabs, Merus; Boarding and travel expenses for congress activities: AstraZeneca. R.W. Holloway: Speakers bureau: AstraZeneca, Clovis Oncology, Tesaro; Advisory board: Clovis Oncology. P.C. Fong: Advisory boards: Clovis Oncology, AstraZeneca; Honoraria: AstraZeneca. J.C. Goh: Honoraria: Bristol-Myers Squibb, AstraZeneca; Consulting or advisory role: Bristol-Myers, Squibb, AstraZeneca, Janssen; Speakers bureau: AstraZeneca, Novartis; Support for travel or accommodation: Roche, Bristol-Myers Squibb, Astellas. D.M. O'Malley: Advisory board: Clovis Oncology, AstraZeneca, Janssen, Gynecologic Oncology Group, Myriad, Tesaro; Steering committees: Clovis Oncology, Amgen, Immunogen; Consultant to AbbVie, AstraZeneca, Tesaro, Health Analytics, Ambry; Institution received research support from Agenus, Ajinomoto, Array BioPharma, AstraZeneca, Bristol-Myers Squibb, Clovis Oncology, Ergomed Clinical Research, Exelixis, Genentech, GlaxoSmithKline, Gynecologic Oncology Group, ImmunoGen, INC Research, inVentiv Health Clinical, Janssen Research and Development, Ludwig Institute for Cancer Research, Novartis Pharmaceuticals, PRA International, Regeneron Pharmaceuticals, Serono, Stemcentrx, Tesaro, Tracon Pharmaceuticals. S. Banerjee: Institutional research support: AstraZeneca, Janssen-Cilag; Consulting or advisory role: AstraZeneca, Roche, GamaMabs Pharma, PharmaMar, AstraZeneca/MedImmune, Tesaro, Clovis Oncology; Support for travel or accommodation: AstraZeneca, Clovis Oncology, Tesaro. S. Goble, T. Cameron: Employee of Clovis Oncology and may own stock or have stock options in that company. J.A. Ledermann: Advisory role: Clovis Oncology, AstraZeneca, Pfizer; Speakers bureau for and research grants from: AstraZeneca, Merck/MSD. All other authors have declared no conflicts of interest.