

1001P Effect of response to last platinum-based chemotherapy in patients (pts) with platinum-sensitive, recurrent ovarian carcinoma in the phase III study ARIEL3 of rucaparib maintenance treatment

J.A. Ledermann¹, A.M. Oza², D. Lorusso³, C. Aghajanian⁴, A. Oaknin⁵, A. Dean⁶, N. Colombo⁷, J.J. Weberpals⁸, A.R. Clamp⁹, G. Scambia³, A. Leary¹⁰, R.W. Holloway¹¹, M. Amenado Gancedo¹², P.C. Fong¹³, J.C. Goh¹⁴, D.M. O'Malley¹⁵, T. Cameron¹⁶, L. Maloney¹⁷, S. Goble¹⁸, R.L. Coleman¹⁹

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

Background: In ARIEL3, rucaparib maintenance treatment significantly improved progression-free survival (PFS) vs placebo and was associated with reductions in tumour burden in pts with measurable disease (Coleman et al. Lancet. 2017;390:1949-61). This exploratory analysis evaluated the efficacy of rucaparib in ARIEL3 pts based on their best response to last platinum-based chemotherapy prior to enrolment.

Methods: Pts were randomised 2:1 to oral rucaparib (600 mg BID) or placebo. Subgroup analysis was based on a randomisation stratification factor of best response to last platinum-based chemotherapy: complete response (CR) or partial response (PR). PFS was assessed in 3 predefined nested cohorts: BRCA mutant, BRCA mutant + BRCA wild type/high loss of heterozygosity (LOH), and the intent-to-treat (ITT) population. Response was also assessed for pts with nonmeasurable disease (eg, lesions <10 mm) at baseline. For PFS and response, tumours were assessed per RECIST v1.1.

Results: The visit cutoff dates for efficacy and safety were 15 Apr 2017 and 31 Dec 2017. Rucaparib significantly improved PFS vs placebo in the CR and PR subgroups, with a similar treatment effect in both subgroups across all cohorts (Table). Of pts with nonmeasurable disease at baseline, 23/104 (22.1%) rucaparib pts and 2/56 (3.6%) placebo pts had a CR, including 7 rucaparib pts without a BRCA mutation or high LOH. The most common grade ≥3 treatment-emergent adverse event (rucaparib vs placebo) was anaemia/decreased haemoglobin (CR subgroup, 24.0% vs 0%; PR subgroup, 20.2% vs 0.8%).

Conclusions: Regardless of response to last platinum-based chemotherapy, rucaparib maintenance treatment significantly improved PFS vs placebo across all cohorts. Similar to pts with measurable disease at baseline, CRs were observed in rucaparib-treated pts with nonmeasurable disease. Safety was consistent across the CR and PR subgroups.

Clinical trial identification: NCT01968213.

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

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

Funding: Clovis Oncology, Inc.

Disclosure: J.A. Ledermann: Honoraria (self), Advisory / Consultancy: Clovis Oncology, Inc.; Honoraria (self), Advisory / Consultancy, Research grant / Funding (institution): AstraZeneca; Honoraria (self), Advisory / Consultancy: Pfizer; Advisory / Consultancy: Artios Pharma; Advisory / Consultancy: Cristal Therapeutics; Advisory / Consultancy, Research grant / Funding (institution): Merck/Merck Sharp & Dohme; Advisory / Consultancy: Regeneron; Advisory / Consultancy: Roche; Advisory / Consultancy: Seattle Genetics; Advisory / Consultancy: Tesaro. A.M. Oza: Advisory / Consultancy: Clovis Oncology, Inc.; Advisory / Consultancy: Amgen; Advisory / Consultancy: Immunovaccine; Advisory / Consultancy: Verastem; Travel / Accommodation / Expenses: AstraZeneca; Honoraria (self): WebRx. D. Lorusso: Advisory / Consultancy: Clovis Oncology, Inc.; Advisory / Consultancy: AstraZeneca; Advisory / Consultancy: ImmunoGen; Advisory / Consultancy: Merck; Advisory / Consultancy, Travel / Accommodation / Expenses: PharmaMar; Advisory / Consultancy, Travel / Accommodation / Expenses: Roche; Advisory / Consultancy: Takeda; Advisory / Consultancy: Tesaro. C. Aghajanian: Honoraria (self), Advisory / Consultancy, Non-remunerated activity/ies: Clovis Oncology, Inc.; Honoraria (self), Non-remunerated activity/ies: Mateon

Table: 1001P

Cohort	Rucaparib, n	Placebo, n	Investigator-assessed PFS (primary endpoint)		BICR-assessed PFS (secondary endpoint)	
			Median PFS, mo; rucaparib vs placebo; P value ^a	HR (95% CI)	Median PFS, mo; rucaparib vs placebo; P value ^a	HR (95% CI)
CR to last platinum-based chemotherapy						
BRCA mutant	43	22	22.9 vs 7.4; P < 0.0001	0.30 (0.15–0.58)	NR vs 7.4; P < 0.0001	0.21 (0.09–0.49)
BRCA mutant or BRCA wild type/high LOH	82	41	13.9 vs 7.3; P < 0.0001	0.37 (0.23–0.60)	24.7 vs 7.4; P < 0.0001	0.36 (0.21–0.64)
ITT	126	64	11.1 vs 5.6; P < 0.0001	0.33 (0.23–0.49)	19.2 vs 5.5; P < 0.0001	0.34 (0.22–0.51)
PR to last platinum-based chemotherapy						
BRCA mutant	87	44	15.7 vs 4.9; P < 0.0001	0.20 (0.13–0.33)	26.8 vs 4.9; P < 0.0001	0.20 (0.11–0.35)
BRCA mutant or BRCA wild type/high LOH	154	77	13.1 vs 4.9; P < 0.0001	0.29 (0.21–0.41)	19.5 vs 4.7; P < 0.0001	0.32 (0.21–0.48)
ITT	249	125	9.0 vs 5.3; P < 0.0001	0.38 (0.30–0.49)	13.6 vs 5.3; P < 0.0001	0.36 (0.27–0.49)

HRs estimated with a Cox proportional hazards model. P values were nonsignificant for the treatment by best response subgroup (CR vs PR) interaction tests for investigator-assessed PFS (BRCA-mutant cohort, P = 0.5680; BRCA-mutant + BRCA wild-type/high LOH cohort, P = 0.4092; ITT population, P = 0.7001) and BICR-assessed PFS (BRCA-mutant cohort, P = 0.9192; BRCA-mutant + BRCA wild-type/high LOH cohort, P = 0.8383; ITT population, P = 0.7976). ^aStratified log-rank P value. BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; NR, not reached.

Therapeutics; Honoraria (self), Advisory / Consultancy: Bayer; Honoraria (self), Advisory / Consultancy: Cerulean Pharma; Honoraria (self), Advisory / Consultancy: Tesaro; Honoraria (self), Advisory / Consultancy: VentiRx. A. Oaknin: Advisory / Consultancy; Clovis Oncology, Inc.; Advisory / Consultancy, Travel / Accommodation / Expenses: AstraZeneca; Advisory / Consultancy: ImmunoGen; Advisory / Consultancy: Genmab/Seattle Genetics; Advisory / Consultancy, Travel / Accommodation / Expenses: PharmaMar; Advisory / Consultancy, Travel / Accommodation / Expenses: Roche; Advisory / Consultancy, Travel / Accommodation / Expenses: Tesaro. A. Dean: Advisory / Consultancy; Precision Oncology Australia; Advisory / Consultancy; Shire Pharmaceuticals; Advisory / Consultancy: Specialised Therapeutics Australia. N. Colombo: Advisory / Consultancy; Clovis Oncology, Inc.; Advisory / Consultancy: Advaxis; Advisory / Consultancy: AstraZeneca; Advisory / Consultancy: BIOCAD; Advisory / Consultancy: Pfizer; Advisory / Consultancy: PharmaMar; Advisory / Consultancy: Roche; Advisory / Consultancy: Tesaro. J.I. Weberpals: Research grant / Funding (institution): AbbVie; Advisory / Consultancy, Research grant / Funding (institution): AstraZeneca. A.R. Clamp: Travel / Accommodation / Expenses: Clovis Oncology, Inc.; Advisory / Consultancy, Research grant / Funding (institution), Travel / Accommodation / Expenses: AstraZeneca; Advisory / Consultancy: Roche. G. Scambia: Advisory / Consultancy: Clovis Oncology, Inc.; Advisory / Consultancy: AstraZeneca; Advisory / Consultancy: PharmaMar; Advisory / Consultancy: Roche; Advisory / Consultancy: Tesaro. A. Leary: Advisory / Consultancy: Clovis Oncology, Inc.; Travel / Accommodation / Expenses: AstraZeneca; Advisory / Consultancy: Pfizer; Advisory / Consultancy: PharmaMar; Research grant / Funding (institution): GamaMabs; Research grant / Funding (institution): Merus. R.W. Holloway: Advisory / Consultancy, Speaker Bureau / Expert testimony: Clovis Oncology, Inc.; Advisory / Consultancy, Speaker Bureau / Expert testimony: AstraZeneca; Speaker Bureau / Expert testimony: Tesaro. M. Amenedo Gancedo: Speaker Bureau / Expert testimony: Clovis Oncology, Inc.; Speaker Bureau / Expert testimony: AstraZeneca; Speaker Bureau / Expert testimony: PharmaMar; Speaker Bureau / Expert testimony: Roche. P.C. Fong: Advisory / Consultancy: Clovis Oncology, Inc.; Honoraria (self), Advisory / Consultancy: AstraZeneca. J.C. Goh: Honoraria (self), Advisory / Consultancy, Speaker Bureau / Expert testimony: AstraZeneca; Honoraria (self), Advisory / Consultancy, Travel / Accommodation / Expenses: Bristol-Myers Squibb; Advisory / Consultancy: Janssen; Speaker Bureau / Expert testimony: Ipsen; Speaker Bureau / Expert testimony: Merck Sharp & Dohme; Travel / Accommodation / Expenses: Astellas Pharma, Inc. D.M. O'Malley: Advisory / Consultancy, Research grant / Funding (institution), Non-remunerated activity/ies: Clovis Oncology, Inc.; Advisory / Consultancy, Research grant / Funding (institution): AstraZeneca; Advisory / Consultancy, Research grant / Funding (institution): Gynecologic Oncology Group; Advisory / Consultancy, Research grant / Funding (institution): Janssen; Advisory / Consultancy: Myriad; Advisory / Consultancy, Research grant / Funding (institution): Tesaro; Non-remunerated activity/ies: Amgen; Research grant / Funding (institution), Non-remunerated activity/ies: ImmunoGen; Advisory / Consultancy: AbbVie; Advisory / Consultancy: Ambray; Advisory / Consultancy: Health Analytics; Research grant / Funding (institution): Agenus; Research grant / Funding (institution): Ajinomoto; Research grant / Funding (institution): Array BioPharma; Research grant / Funding (institution): Bristol-Myers Squibb; Research grant / Funding (institution): ERGOMED Clinical Research; Research grant / Funding (institution): Exelixis; Research grant / Funding (institution): Genentech; Research grant / Funding (institution): GlaxoSmithKline; Research grant / Funding (institution): INC Research. T. Cameron: Shareholder / Stockholder / Stock options, Employee: Clovis Oncology, Inc. L. Maloney: Shareholder / Stockholder / Stock options, Employee: Clovis Oncology, Inc. S. Goble: Shareholder / Stockholder / Stock options, Employee: Clovis Oncology, Inc. R.L. Coleman: Advisory / Consultancy, Research grant / Funding (institution): Clovis Oncology, Inc.; Advisory / Consultancy, Research grant / Funding (institution): AstraZeneca; Advisory / Consultancy: Tesaro; Advisory / Consultancy: Bayer; Advisory / Consultancy, Research grant / Funding (institution): Roche/Genentech; Advisory / Consultancy, Research grant / Funding (institution): AbbVie; Advisory / Consultancy, Research grant / Funding (institution): Esperance; Advisory / Consultancy, Research grant / Funding (institution): Janssen; Advisory / Consultancy, Research grant / Funding (institution): Merck; Advisory / Consultancy, Research grant / Funding (institution): Millennium; Advisory / Consultancy, Research grant / Funding (institution): OncoMed; Research grant / Funding (institution): Pfizer; Research grant / Funding (institution): GamaMabs; Research grant / Funding (institution): Genmab; Research grant / Funding (institution): Gradalis.