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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Ledermann JA, Oza AM, Lorusso D, et al. Rucaparib for patients with platinum-sensitive, recurrent ovarian carcinoma (ARIEL3): post-progression outcomes and updated safety results from a randomised, placebo-controlled, phase 3 trial. *Lancet Oncol* 2020; **21:** 710–22.

Online Supplementary Appendix

Rucaparib for patients with platinum-sensitive, recurrent ovarian carcinoma (ARIEL3): postprogression outcomes and updated safety from a randomised, placebo-controlled, phase 3 trial

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Table of contents

ARIEL3 Centres 1

Supplemental results 4

Table S1: Summary of TEAEs in the safety population: comparison of previously reported and updated data 4

Table S2: Grade 3 or higher TEAEs occurring in at least one patient in the safety population (31 Dec 2017 visit cutoff date) 5

Figure S1: Plots of the log of the cumulative hazard 8

Figure S2: Kaplan-Meier estimates of CFI (A), TFST (B), PFS2 (C), and TSST (D) in the *BRCA*-mutant cohort 9

Figure S3: Kaplan-Meier estimates of CFI (A), TFST (B), PFS2 (C), and TSST (D) in the HRD cohort 11

Figure S4. Kaplan-Meier estimates of PFS2–PFS1 in the *BRCA*-mutant cohort (A), HRD cohort (B), and ITT population (C) 13

Figure S5: Postprogression outcomes in predefined cohorts and subgroups of patients with *BRCA* wild-type carcinomas based on LOH status 14

ARIEL3 CENTRES

Principal Investigator	Site	Patients enrolled
Oza, Amit	Princess Margaret Cancer Centre, University Health Network, Toronto, Canada	28
Lorusso, Domenica	Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy	25
Aghajanian, Carol	Memorial Sloan Kettering Cancer Center, New York, USA	13
	Memorial Sloan Kettering Cancer Center, Rockville Centre, USA	3
	Memorial Sloan Kettering at Phelps Memorial Hospital Center, Sleepy Hollow, USA	3
	Memorial Sloan Kettering Cancer Center, Basking Ridge, USA	2
Coleman, Robert	The University of Texas MD Anderson Cancer Center, Houston, USA	20
Oaknin, Ana	Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain	19
Ledermann, Jonathan	UCL Cancer Institute, University College London and UCL Hospitals, London, UK	18
Colombo, Nicoletta	University of Milan-Bicocca and European Institute of Oncology (IEO), Milan, Italy	16
Weberpals, Johanne	Ottawa Hospital Research Institute, Ottawa, Canada	16
Dean, Andrew	Saint John of God Subiaco Hospital, Subiaco, Australia	16
Clamp, Andrew	The Christie NHS Foundation Trust and University of Manchester, Manchester, UK	15
Scambia, Giovanni	Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy	14
Leary, Alexandra	Gustave Roussy Cancer Center, INSERM U981, and Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens (GINECO), Villejuif, France	13

Principal Investigator	Site	Patients enrolled
Holloway, Robert	Florida Hospital Cancer Care, Orlando, USA	12
Fong, Peter	Auckland City Hospital, Auckland, New Zealand	11
Goh, Jeffrey	Royal Brisbane and Women's Hospital, Herston, Australia	11
Amenedo Gancedo, Margarita	Oncology Center of Galicia, La Coruña, Spain	11
O'Malley, David	The Ohio State University, James Cancer Center, Columbus, USA	11
Armstrong, Deborah	Johns Hopkins University School of Medicine, Baltimore, USA	10
Swisher, Elizabeth	University of Washington, Seattle, USA	10
García-Donas, Jesus	HM Hospitales—Centro Integral Oncológico Hospital de Madrid Clara Campal, Madrid, Spain	10
Banerjee, Susana	Royal Marsden Hospital, Sutton, UK	5
	The Royal Marsden NHS Foundation Trust, London, UK	5
Floquet, Anne	Institut Bergonié, Bordeaux, France	9
Scott, Clare	Peter MacCallum Cancer Centre, Melbourne, Australia	9
McNeish, Iain	Beatson West of Scotland Cancer Centre, Glasgow, UK	9
Lortholary, Alain	Centre Catherine de Sienne, Nantes, France	8
Chen, Lee-may	University of California San Francisco, San Francisco, USA	8
Tredan, Olivier	Centre Léon Bérard, Lyon, France	8
You, Benoit	Centre Hospitalier Lyon Sud, Pierre-Benite, France	8
Morris, Robert	Karmanos Cancer Institute, Detroit, USA	8
Provencher, Diane	Centre Hospitalier de L'Université de Montréal, Montréal, Canada	7
Harnett, Paul	Westmead Hospital, Westmead, Australia	7
Medioni, Jacques	Hôpital Européen Georges Pompidou, Paris, France	7
Parkinson, Christine	Addenbrooke's Hospital, Cambridge, UK	7
Pignata, Sandro	Istituto Nazionale Tumori IRCCS Fondazione Pascale, Naples, Italy	6
Welch, Stephen	London Regional Cancer Centre, London, Canada	6
Vergote, Ignace	Universitair Ziekenhuis Leuven, Leuven, Belgium	6
Konecny, Gottfried	University of California Los Angeles, Los Angeles, USA	6
Ghatage, Prafull	Tom Baker Cancer Center, Calgary, Canada	6
Elit, Laurie	Juravinski Cancer Centre, Hamilton, Canada	6
Denys, Hannelore	Universitair Ziekenhuis Gent, Gent, Belgium	5
Plante, Marie	Centre Hospitalier Universitaire de Quebec, Quebec, Canada	5
Leviov, Michelle	The Lady Davis Carmel Medical Center, Haifa, Israel	5
Shapira-Frommer, Ronnie	Chaim Sheba Medical Center, Tel HaShomer, Israel	4
Birrer, Michael	Massachusetts General Hospital, Boston, USA	4
Chambers, Setsuko	University of Arizona Cancer Center, Tucson, USA	4
Friedlander, Michael	Prince of Wales Hospital, Randwick, Australia	4
Sabbatini, Roberto	Azienda Ospedaliero-Universitaria Policlinico di Modena, Modena, Italy	4
Morgan, Mark	University of Pennsylvania, Philadelphia, USA	4
Tamberi, Stefano	Ospedale Civile degli Infermi, Faenza, Italy	4
Guerra, Eva María	Hospital Ramón y Cajal, Madrid, Spain	4
Wimberger, Pauline	Technische Universität Dresden, Dresden, Germany	4
Amit, Amnon	Rambam Medical Center, Haifa, Israel	4
Casado Herraez, Antonio	Hospital San Carlos Madrid, Madrid, Spain	4
Gladieff, Laurence	Institut Claudius Régaud, Toulouse, France	3
Kichenadasse, Ganessan	Flinders Medical Centre, Bedford Park, Australia	3
Ma, Ling	Rocky Mountain Cancer Centers, Lakewood, USA	3
Buck, Martin	Sir Charles Gairdner Hospital, Nedlands, USA	3

Principal Investigator	Site	Patients enrolled
Zamagni, Claudio	Azienda Ospedaliero Universitaria di Bologna, Bologna, Italy	3
Dirix, Luc	AZ Sint Augustinus, Antwerp, Belgium	3
Jackson, David	Saint James's University Hospital, Leeds, UK	3
Buss, Mary	Beth Israel Deaconess Medical Center, Boston, USA	2
Krabisch, Petra	Klinikum Chemnitz gGmbH, Chemnitz, Germany	2
Kovel, Svetlana	Assaf Harofeh Medical Center, Zerifin, Israel	2
Powell, Melanie	Saint Bartholomew's Hospital, London, UK	2
O'Donnell, Anne	Wellington Regional Hospital, Wellington, New Zealand	2
Neunhöffer, Tanja	HELIOS Dr. Horst Schmidt Kliniken Wiesbaden, Klinik für Gynäkologie und Gyn. Onkologie, Wiesbaden, Germany	2
Lotz, Jean-Pierre	Hôpital Tenon, Paris, France	2
Romero, Ignacio	Instituto Valenciano de Oncología, Valencia, Spain	2
Vanderkwaak, Timothy	Hope Women's Cancer Centers, Asheville, USA	2
Safra, Tamar	Tel Aviv Sourasky Medical Center, Tel Aviv, Israel	2
Gabra, Hani	Imperial College Healthcare NHS Trust	2
Sánchez, Alfonso	Hospital Regional Universitario Carlos Haya de Málaga, Málaga, Spain	2
Stemmer, Salomon	Rabin Medical Center, Petah Tikva, Israel	2
Hänle, Claudia	Klinikum Ludwigsburg-Bietigheim gGmbH, Ludwigsburg, Germany	1
Bologna, Alessandra	Arcispedale Santa Maria Nuova IRCCS, Reggio Emilia, Italy	1
Mutch, David	Washington University School of Medicine, Saint Louis, USA	1
Joly, Florence	Cancer François Baclesse, Caen, France	1
Palacio, Isabel	Hospital Universitario Central de Asturias, Asturias, Spain	1
Slomovitz, Brian	Sylvester Comprehensive Cancer Center, Miami, USA	1
Drew, Yvette	Freeman Hospital - Northern Centre for Cancer Care, Newcastle upon Tyne, UK	1
Pölcher, Martin	Rotkreuzklinikum München gGmbH, Munich, Germany	1
Vulfovich, Michel	Memorial Healthcare System, Hollywood, USA	1
El-Balat, Ahmed	Universitätsklinikum Frankfurt, Frankfurt, Germany	1
Total		**564**

SUPPLEMENTAL RESULTS

Table S1: **Summary of TEAEs in the safety population: comparison of previously reported and updated data**

	Previous report*: 15 Apr 2017 visit cutoff date		**Updated data: 31 Dec 2017 visit cutoff date**	
	Rucaparib (n=372)	**Placebo (n=189)**	**Rucaparib (n=372)**	**Placebo (n=189)**
Any grade TEAE	372 (100%)	182 (96%)	372 (100%)	182 (96%)
Grade ≥3 TEAE	209 (56%)	28 (15%)	222 (60%)	30 (16%)
Treatment interruption and/or dose reduction	263 (71%)	20 (11%)	267 (72%)	20 (11%)
Treatment interruption due to a TEAE	237 (64%)	19 (10%)	243 (65%)	19 (10%)
Dose reduction due to a TEAE	203 (55%)	8 (4%)	206 (55%)	8 (4%)
Discontinuation due to a TEAE†	50 (13%)	3 (2%)	57 (15%)	3 (2%)
Deaths relating to a TEAE	6 (2%)	2 (1%)	7 (2%)	2 (1%)

Data are n (%).
*****Coleman RL et al. *Lancet*. 2017; 390(10106): 1949-1961.
†Excluding disease progression.
TEAE=treatment-emergent adverse event.

Table S2: **Grade 3 or higher TEAEs occurring in at least one patient in the safety population (31 Dec 2017 visit cutoff date)**

	Rucaparib (n=372)			Placebo (n=189)		
	Grade 3	**Grade 4**	**Grade 5**	**Grade 3**	**Grade 4**	**Grade 5**
TEAE						
Anaemia or haemoglobin decreased	77 (21%)	3 (1%)	0	0	1 (1%)	0
ALT or AST increased	38 (10%)	0	0	0	0	0
Neutropenia or neutrophil count decreased	22 (6%)	7 (2%)	0	1 (1%)	1 (1%)	0
Asthenia or fatigue	26 (7%)	0	0	5 (3%)	0	0
Thrombocytopenia or platelet count decreased	13 (3%)	7 (2%)	0	0	0	0
Vomiting	15 (4%)	0	0	2 (1%)	0	0
Nausea	14 (4%)	0	0	1 (1%)	0	0
Abdominal pain	11 (3%)	0	0	1 (1%)	0	0
Hypertension	9 (2%)	0	0	4 (2%)	0	0
Constipation	7 (2%)	0	0	2 (1%)	0	0
Febrile neutropenia	0	5 (1%)	0	0	0	0
Malignant neoplasm progression	3 (1%)	0	2 (1%)	2 (1%)	0	0
Transaminases increased	5 (1%)	0	0	0	0	0
White blood cell count decreased	4 (1%)	1 (<1%)	0	0	0	0
Dehydration	4 (1%)	0	0	0	0	0
Intestinal obstruction	4 (1%)	0	0	1 (1%)	1 (1%)	0
Small intestinal obstruction	3 (1%)	1 (<1%)	0	4 (2%)	0	0
Weight decreased	4 (1%)	0	0	0	0	0
Decreased appetite	3 (1%)	0	0	0	0	0
Gamma-glutamyltransferase increased	3 (1%)	0	0	0	0	0
Pancytopenia	2 (1%)	1 (<1%)	0	0	0	0
Pulmonary embolism	2 (1%)	1 (<1%)	0	0	0	1 (1%)
Urinary tract obstruction	3 (1%)	0	0	0	0	0
Abdominal pain upper	2 (1%)	0	0	0	0	0
Acute kidney injury	1 (<1%)	1 (<1%)	0	0	0	0
Arthralgia	2 (1%)	0	0	0	0	0
Ascites	2 (1%)	0	0	1 (1%)	0	0
Cell death	2 (1%)	0	0	0	0	0
Diarrhoea	2 (1%)	0	0	2 (1%)	0	0
Gastroenteritis	2 (1%)	0	0	0	0	0
Hepatic enzyme increased	2 (1%)	0	0	0	0	0
Incarcerated hernia	1 (<1%)	1 (<1%)	0	0	0	0
Lethargy	2 (1%)	0	0	0	0	0
Leukopenia	2 (1%)	0	0	0	0	0
Lymphocyte count decreased	2 (1%)	0	0	0	0	0
Lymphoedema	2 (1%)	0	0	0	0	0
Mucosal inflammation	2 (1%)	0	0	1 (1%)	0	0
Myelodysplastic syndrome	0	1 (<1%)	1 (<1%)	0	0	0
Photosensitivity reaction	2 (1%)	0	0	0	0	0
Sepsis	0	2 (1%)	0	0	0	0
Syncope	2 (1%)	0	0	0	0	0
Urinary tract infection	2 (1%)	0	0	1 (1%)	0	0
Abdominal hernia	1 (<1%)	0	0	0	0	0
Acute myeloid leukaemia	0	0	1 (<1%)	0	0	0
Acute pulmonary oedema	1 (<1%)	0	0	0	0	0
Acute respiratory distress syndrome	0	1 (<1%)	0	0	0	0
Anxiety	1 (<1%)	0	0	0	0	0
Arthritis infective	1 (<1%)	0	0	0	0	0
Atrial fibrillation	1 (<1%)	0	0	0	0	0
Atypical pneumonia	1 (<1%)	0	0	0	0	0

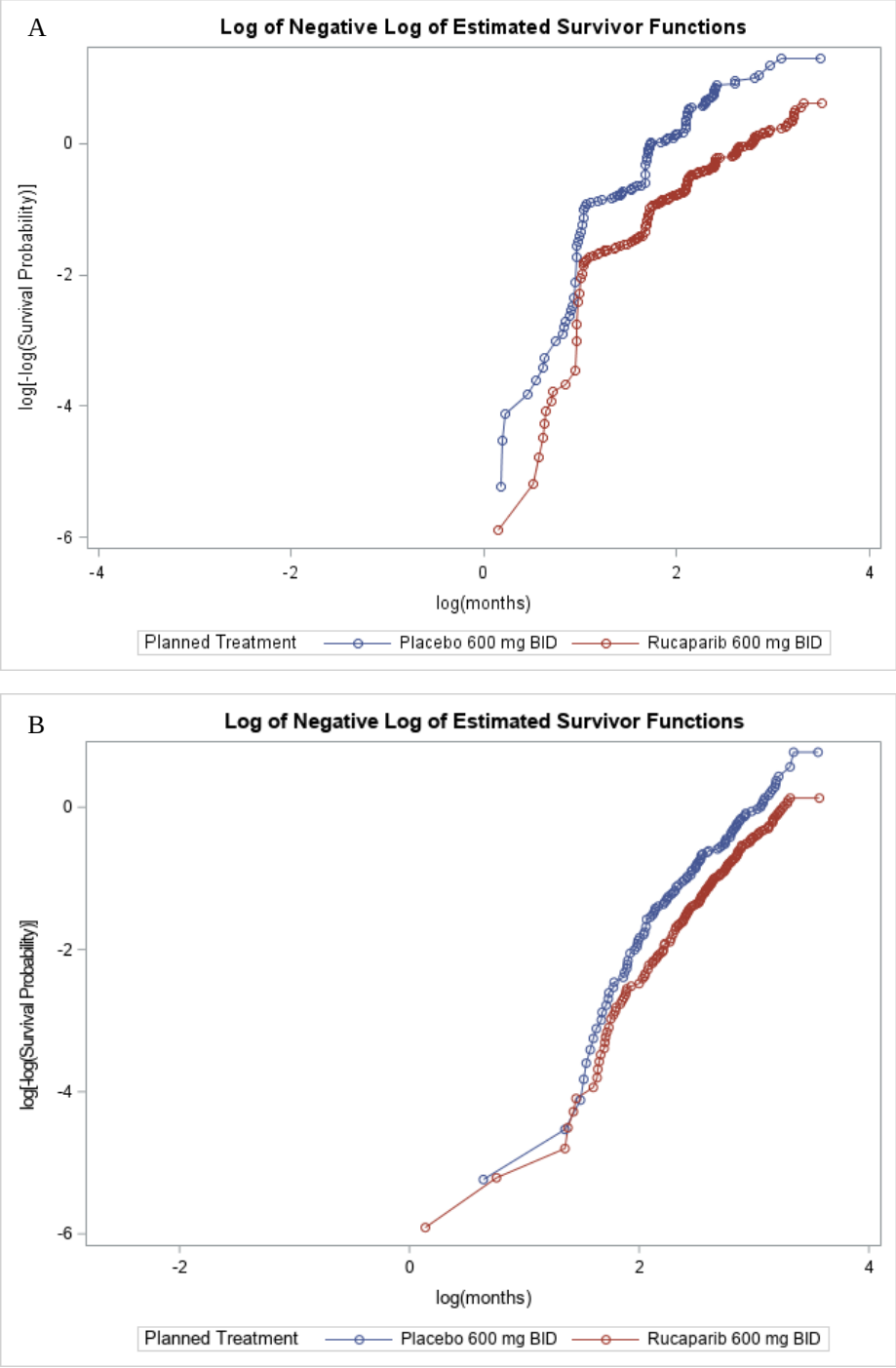
	Rucaparib (n=372)			Placebo (n=189)		
	Grade 3	**Grade 4**	**Grade 5**	**Grade 3**	**Grade 4**	**Grade 5**
B-cell unclassifiable lymphoma high grade	0	0	1 (<1%)	0	0	0
Bile duct obstruction	1 (<1%)	0	0	0	0	0
Blood cholesterol increased	1 (<1%)	0	0	0	0	0
Blood creatinine increased	1 (<1%)	0	0	0	0	0
Bowen's disease	1 (<1%)	0	0	0	0	0
Cardiac arrest	0	0	1 (<1%)	0	0	0
Cellulitis	1 (<1%)	0	0	0	0	0
Cholecystisis	1 (<1%)	0	0	0	0	0
Cholelithiasis	1 (<1%)	0	0	0	0	0
Cholestasis	0	1 (<1%)	0	0	0	0
Cognitive disorder	1 (<1%)	0	0	0	0	0
Colonic pseudo-obstruction	1 (<1%)	0	0	0	0	0
Creatinine renal clearance increased	1 (<1%)	0	0	0	0	0
Device related infection	1 (<1%)	0	0	0	0	0
Drug-induced liver injury	0	1 (<1%)	0	0	0	0
Duodenal obstruction	1 (<1%)	0	0	0	0	0
Dyslipidaemia	1 (<1%)	0	0	0	0	0
Dyspepsia	1 (<1%)	0	0	0	0	0
Exostosis	1 (<1%)	0	0	0	0	0
Faecaloma	1 (<1%)	0	0	0	0	0
Female genital tract fistula	0	1 (<1%)	0	0	0	0
Femoral neck fracture	1 (<1%)	0	0	1 (1%)	0	0
Femur fracture	1 (<1%)	0	0	0	0	0
Fibula fracture	1 (<1%)	0	0	0	0	0
Gastrointestinal pain	1 (<1%)	0	0	0	0	0
Gastrointestinal stoma output increased	1 (<1%)	0	0	0	0	0
General physical health deterioration	1 (<1%)	0	0	0	0	0
Glomerular filtration rate decreased	1 (<1%)	0	0	0	0	0
Haematocrit decreased	1 (<1%)	0	0	0	0	0
Headache	1 (<1%)	0	0	1 (1%)	0	0
Hepatic failure	1 (<1%)	0	0	0	0	0
Histiocytosis haematophagic	0	0	1 (<1%)	0	0	0
Hypercholesterolaemia	0	1 (<1%)	0	0	0	0
Hypernatraemia	1 (<1%)	0	0	0	0	0
Hypertransaminasaemia	1 (<1%)	0	0	0	0	0
Hypertriglyceridaemia	1 (<1%)	0	0	0	0	0
Hyperuricaemia	1 (<1%)	0	0	0	0	0
Hypoacusis	1 (<1%)	0	0	0	0	0
Hypoalbuminaemia	1 (<1%)	0	0	0	0	0
Hypocalcaemia	1 (<1%)	0	0	0	0	0
Hypokalaemia	1 (<1%)	0	0	0	0	0
Hypomagnesaemia	1 (<1%)	0	0	0	0	0
Hypophosphataemia	1 (<1%)	0	0	0	0	0
Hypotension	1 (<1%)	0	0	0	0	0
Infusion related reaction	1 (<1%)	0	0	0	0	0
Jaundice	1 (<1%)	0	0	0	0	0
Leukocytosis	1 (<1%)	0	0	1 (1%)	0	0
Lower respiratory tract infection	1 (<1%)	0	0	0	0	0
Malignant bowel obstruction	1 (<1%)	0	0	0	0	0
Muscular weakness	1 (<1%)	0	0	0	0	0
Neutropenic colitis	1 (<1%)	0	0	0	0	0
Oedema peripheral	1 (<1%)	0	0	0	0	0
Oral herpes	1 (<1%)	0	0	0	0	0
Osteoarthritis	1 (<1%)	0	0	0	0	0

	Rucaparib (n=372)			Placebo (n=189)		
	Grade 3	**Grade 4**	**Grade 5**	**Grade 3**	**Grade 4**	**Grade 5**
Palmar-plantar erythrodysaesthesia syndrome	1 (<1%)	0	0	0	0	0
Pelvic pain	1 (<1%)	0	0	0	0	0
Pericardial effusion	0	1 (<1%)	0	0	0	0
Pleural effusion	1 (<1%)	0	0	0	0	0
Pyelonephritis	0	1 (<1%)	0	0	0	0
Rash	1 (<1%)	0	0	0	0	0
Renal failure	1 (<1%)	0	0	0	0	0
Renal impairment	1 (<1%)	0	0	0	0	0
Sciatica	1 (<1%)	0	0	0	0	0
Seizure	1 (<1%)	0	0	0	0	0
Squamous cell carcinoma of lung	1 (<1%)	0	0	0	0	0
Tibia fracture	1 (<1%)	0	0	0	0	0
Tonsilitis	1 (<1%)	0	0	0	0	0
Tooth abscess	1 (<1%)	0	0	0	0	0
Toothache	1 (<1%)	0	0	0	0	0
Traumatic fracture	1 (<1%)	0	0	0	0	0
Type 2 diabetes mellitus	1 (<1%)	0	0	0	0	0
Viral infection	1 (<1%)	0	0	0	0	0
Viral upper respiratory tract infection	1 (<1%)	0	0	0	0	0
Wound complication	1 (<1%)	0	0	0	0	0
Upper respiratory tract infection	0	0	0	2 (1%)	0	0
Abnormal behaviour	0	0	0	1 (1%)	0	0
Blepharitis	0	0	0	1 (1%)	0	0
Bone pain	0	0	0	1 (1%)	0	0
Cataract	0	0	0	1 (1%)	0	0
Dizziness	0	0	0	1 (1%)	0	0
Forearm fracture	0	0	0	1 (1%)	0	0
Hyponatraemia	0	0	0	1 (1%)	0	0
Incisional hernia	0	0	0	1 (1%)	0	0
Lung infection	0	0	0	1 (1%)	0	0
Metastases to meninges	0	0	0	0	0	1 (1%)
Sinus bradycardia	0	0	0	1 (1%)	0	0
Stoma site infection	0	0	0	1 (1%)	0	0

Data are n (%).
Sorted by decreasing incidence of grade ≥3 TEAEs in the rucaparib arm of the updated safety analysis.
ALT=alanine aminotransferase. AST=aspartate aminotransferase. TEAE=treatment-emergent adverse event.

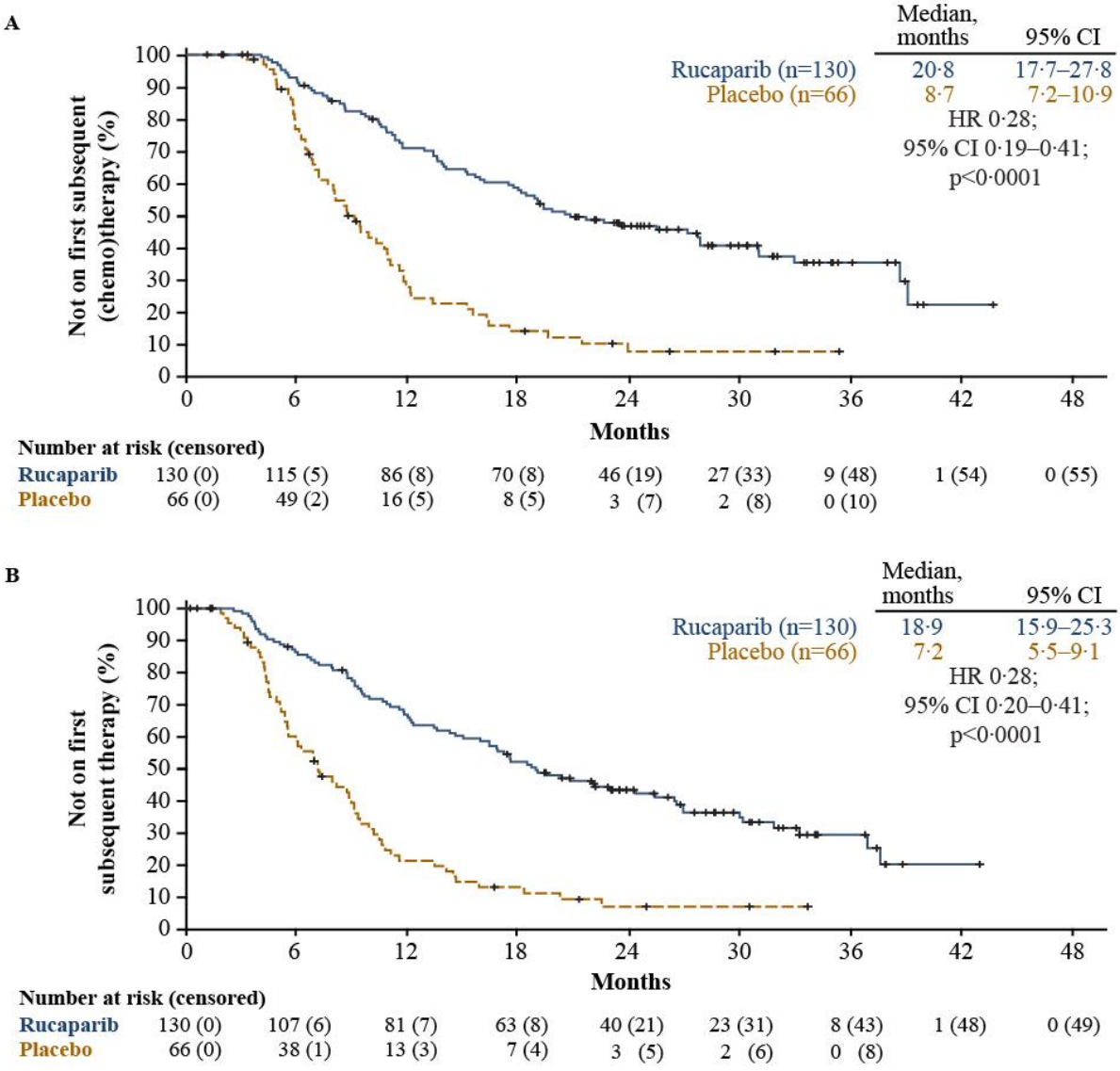
Figure S1: **Plots of the log of the cumulative hazard**

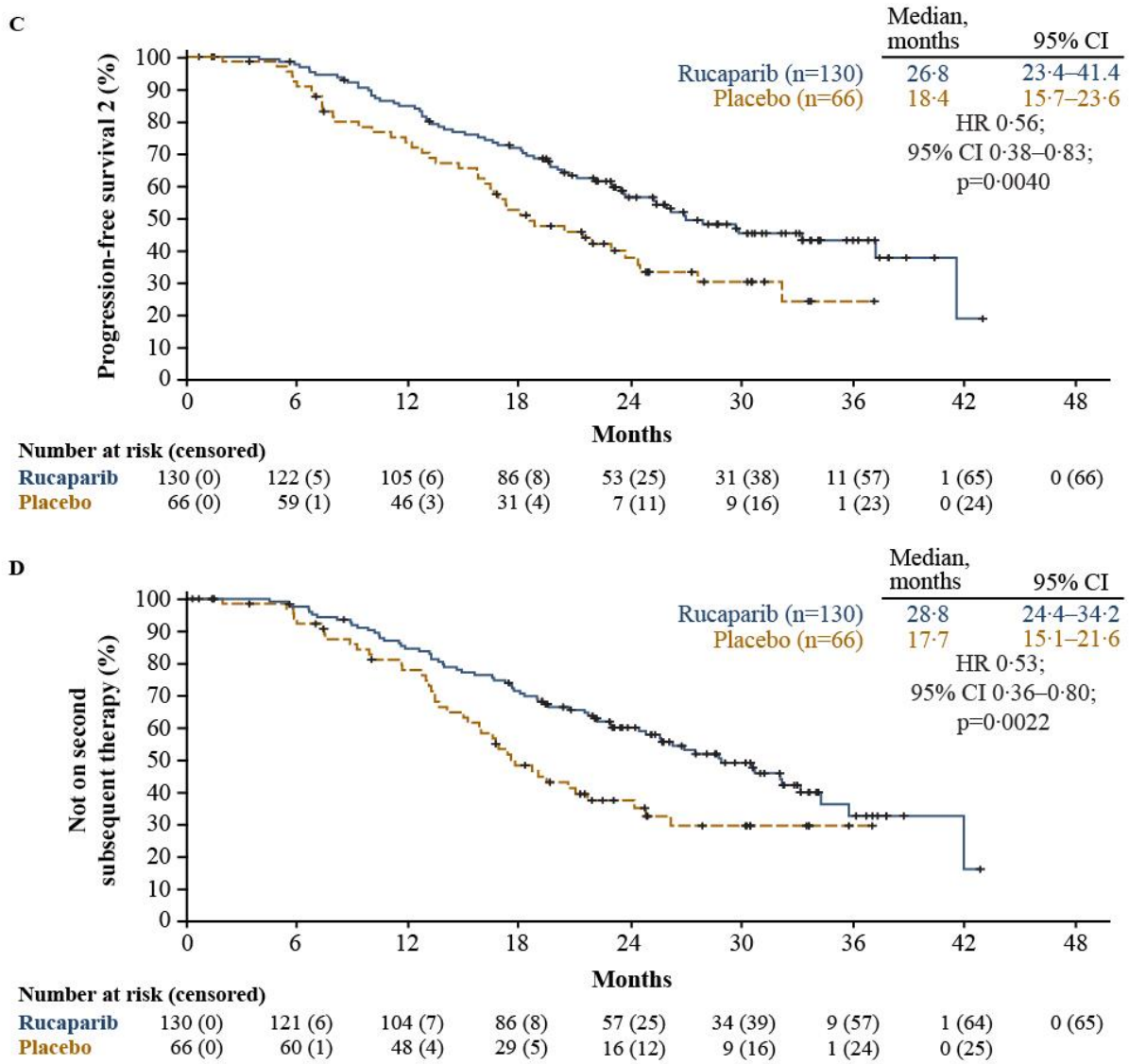
Log-log plots of the time to investigator-assessed disease progression or death during ARIEL3 (PFS1; A) and the time to investigator-assessed disease progression on subsequent therapy or death (PFS2; B) in the rucaparib (red) and placebo (blue) groups for patients in the intention-to-treat population.



BID=twice daily.

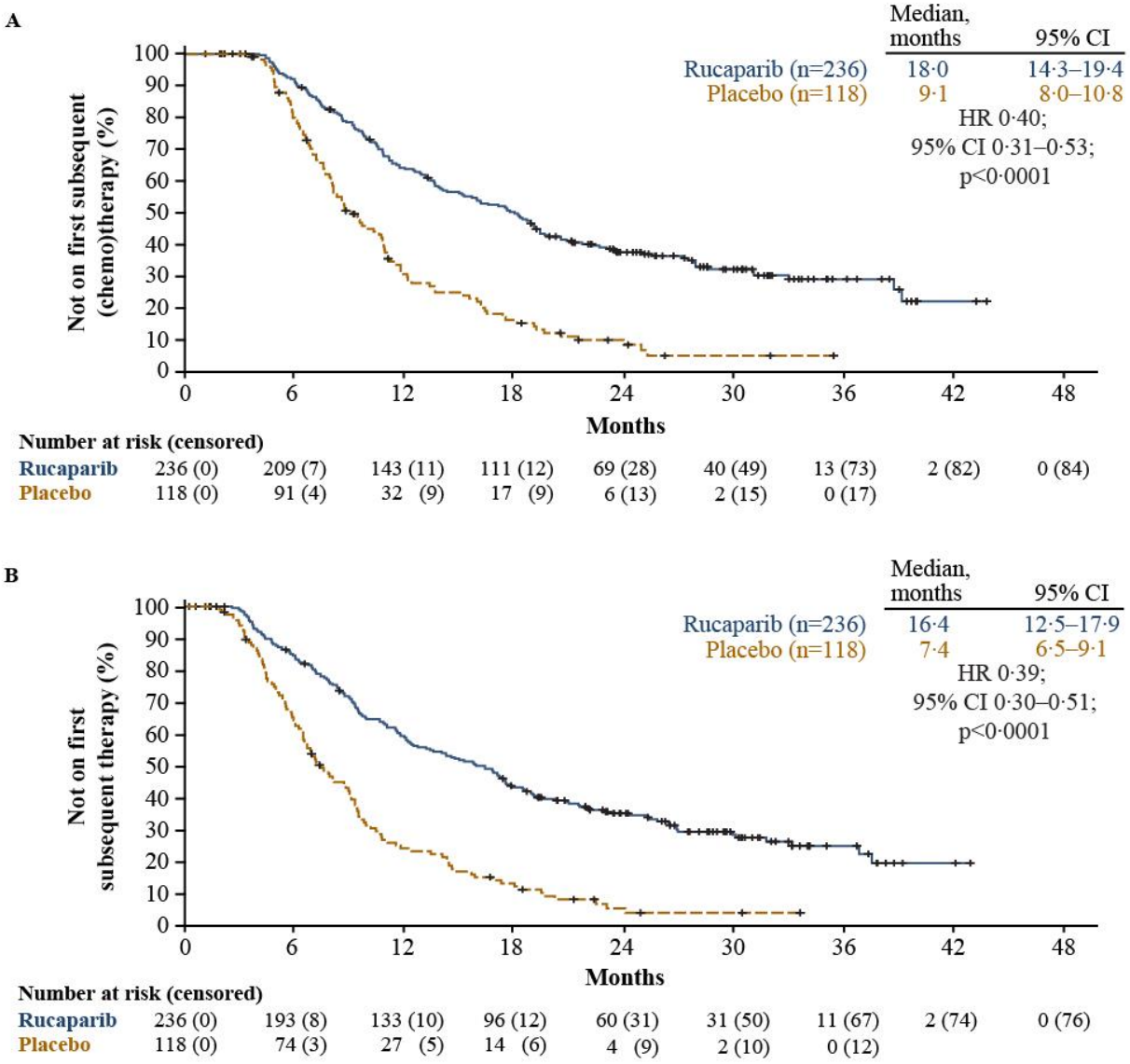
Figure S2: **Kaplan-Meier estimates of CFI (A), TFST (B), PFS2 (C), and TSST (D) in the *BRCA*-mutant cohort**

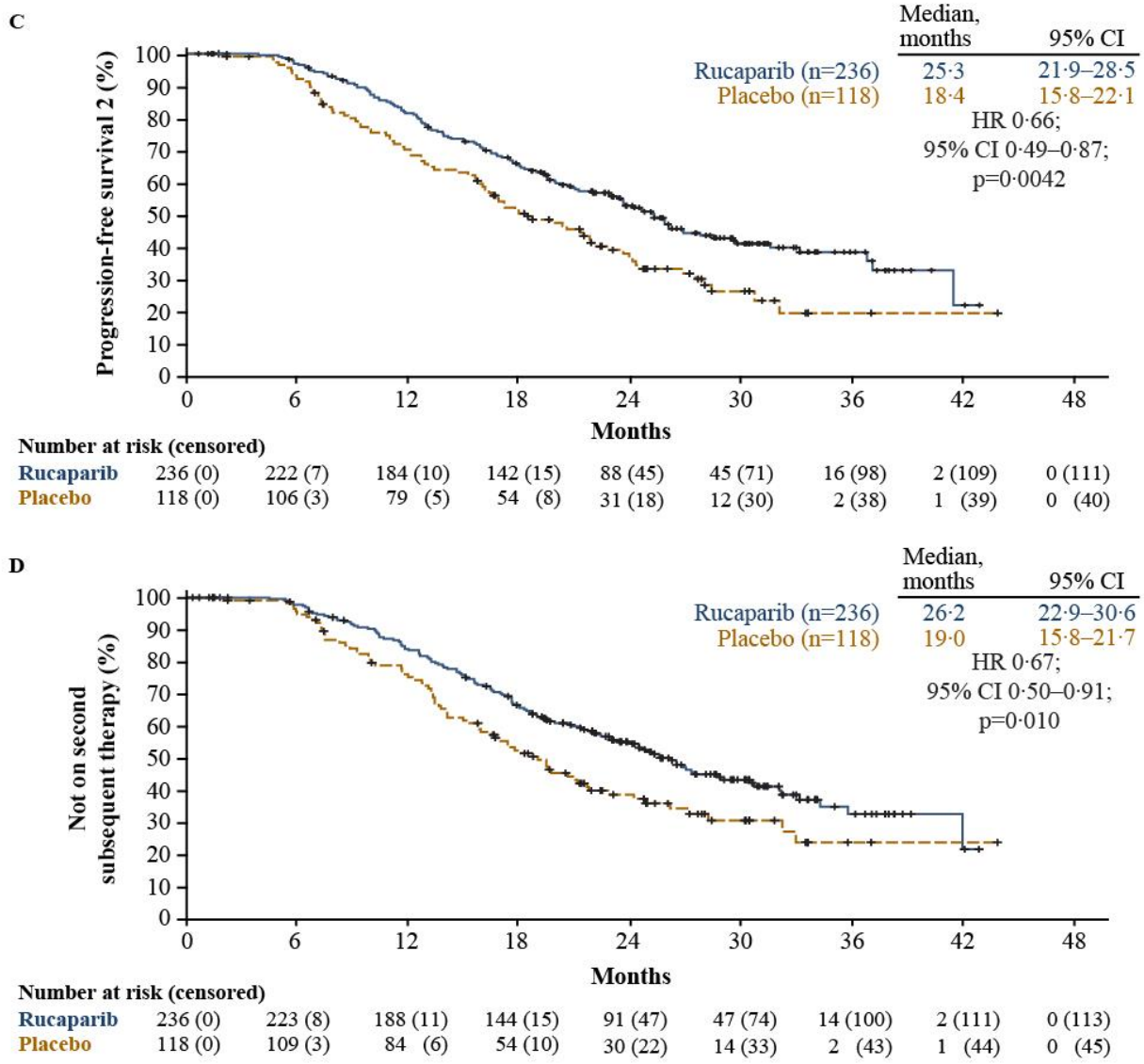




CFI=chemotherapy-free interval. HR=hazard ratio. PFS2=time to disease progression on subsequent therapy or death. TFST=time to start of first subsequent therapy. TSST=time to start of second subsequent therapy.

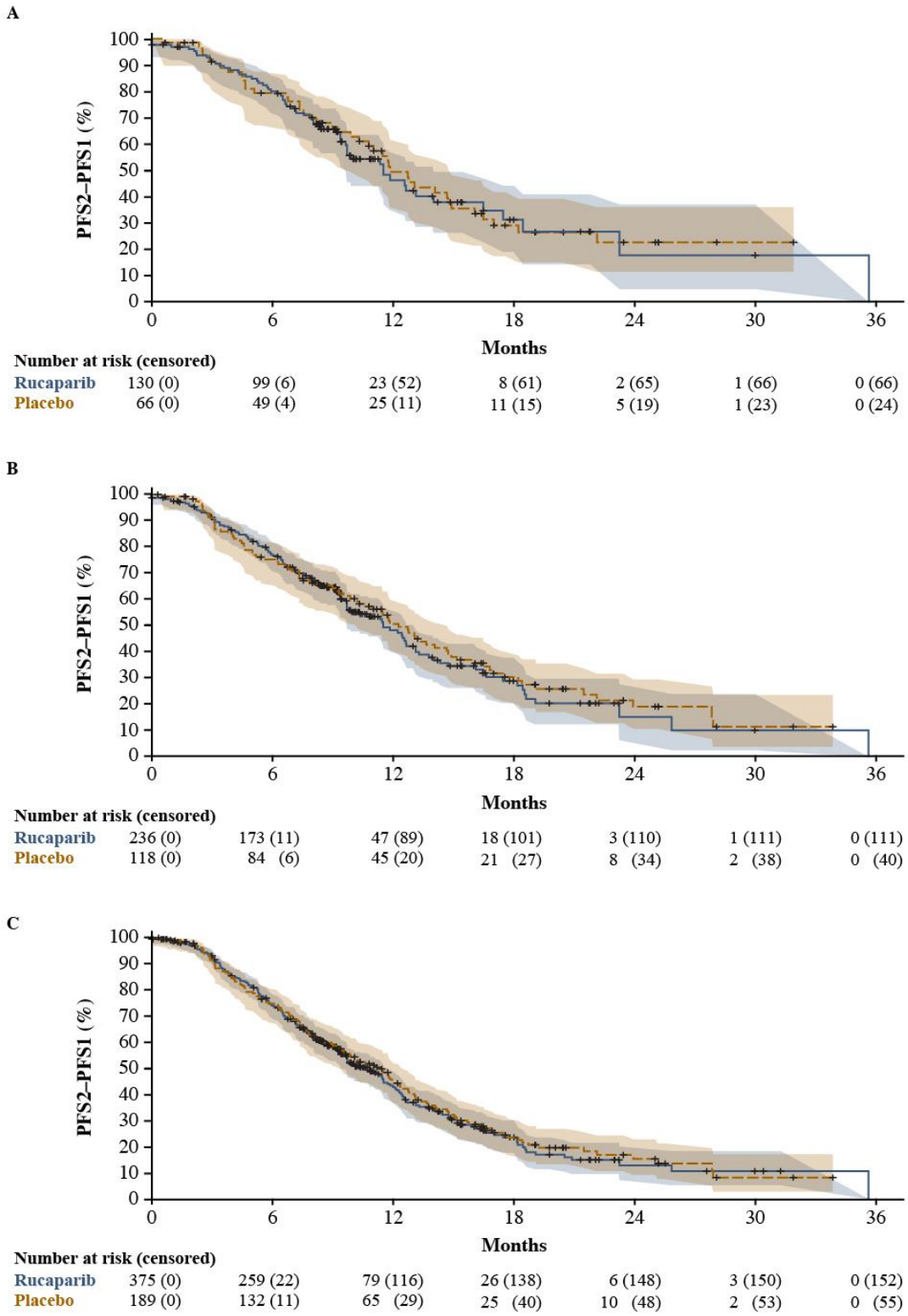
Figure S3: **Kaplan-Meier estimates of CFI (A), TFST (B), PFS2 (C), and TSST (D) in the HRD cohort**





CFI=chemotherapy-free interval. HR=hazard ratio. HRD=homologous recombination deficient. PFS2=time to disease progression on subsequent therapy or death. TFST=time to start of first subsequent therapy. TSST=time to start of second subsequent therapy.

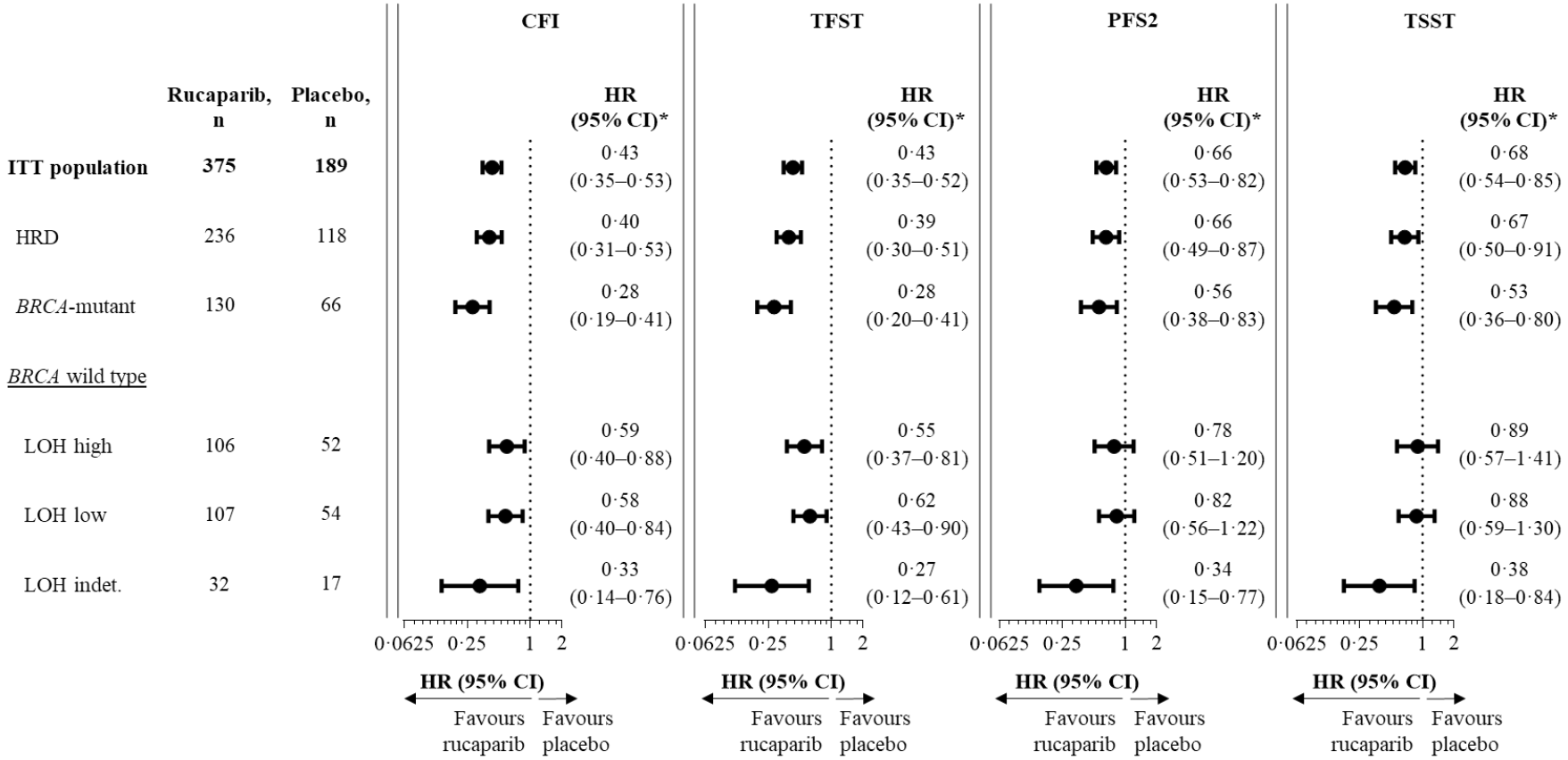
Figure S4. **Kaplan-Meier estimates of PFS2–PFS1 in the *BRCA*-mutant cohort (A), HRD cohort (B), and ITT population (C)**



Shaded areas indicate 95% confidence intervals.

HRD=homologous recombination deficient. ITT=intention to treat. PFS1=time to first disease progression event or death. PFS2=time to disease progression on subsequent therapy or death.

Figure S5: **Postprogression outcomes in predefined cohorts and subgroups of patients with *BRCA* wild-type carcinomas based on LOH status**



*Cox proportional hazard model.
CFI=chemotherapy-free interval. HR=hazard ratio. HRD=homologous recombination deficient. indet.=indeterminate. ITT=intention to treat. LOH=loss of heterozygosity. PFS2=time to disease progression on subsequent therapy or death. TFST=time to start of first subsequent therapy. TSST=time to start of second subsequent therapy.