Olaparib and Celarasertib (AZD6738) in patients with triple negative advanced breast cancer: results from Cohort E of the plasmaMATCH trial (CRUK/15/010)

Supplementary material

Figure S1. CONSORT diagram

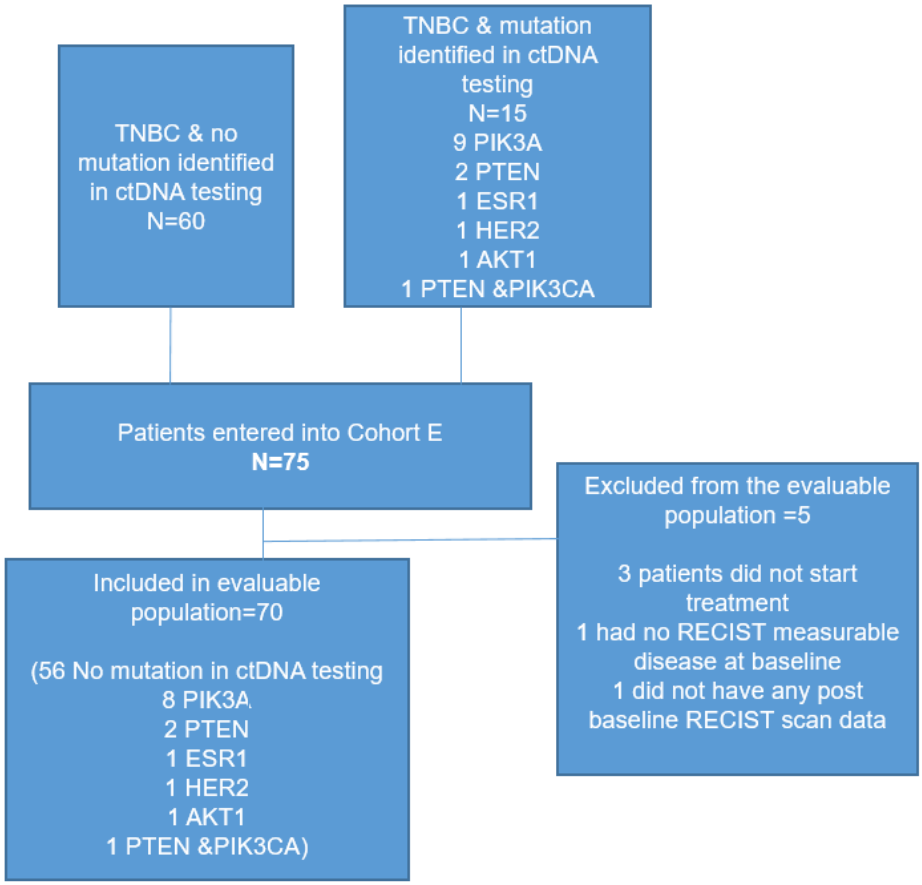

Table S1. Additional baseline characteristics

	N=75	
	n	**%**
Sex		
Female	75	100
Age group (years) at registration		
<50	26	34.7
≥50 & <60	21	28
≥60 & <70	20	26.7
≥70	8	10.7
Ethnicity		
White: British	67	89.3
White: Any other White background	3	4
Asian or Asian British: Indian	1	1.3
Black or Black British: Caribbean	2	2.7
Black or Black British: Any other Black background	1	1.3
Chinese or other ethnic group: Chinese	1	1.3

Table S2.Representativeness of Study Participants

Cancer type/subtype/stage	**Breast cancer/Triple negative/Advanced**
Considerations related to:	
Sex	TNBC, as all other subtypes of breast cancer, is a predominantly female disease and is rare in men. Male breast cancer represents only between 0.5 and 1% of all breast cancers diagnosed each year. TNBC incidence is around 10-15% among all breast cancer subtypes in the overall largely female population (Breast Cancer Res and Treatment 2008;1132(2):357-60).
Age	The median age of presentation of breast cancer in the UK is 62 years in white patients and 50 years in black patients (www.ncin.org.uk). Patients with TNBC present at a younger age, than the overall population of patients with breast cancer. (Cancer 2019;125(19):3412-3417)
Race/Ethnicity	In England, 87% of breast cancer diagnoses are made in women who are white, and 7% in non-white women (6% unknown). (British Journal of Cancer 2022;1765-1773). Incidence rates for breast cancer are lower in the Asian and Black ethnic groups, and in people of mixed or multiple ethnicity compared with the white ethnic group. However, TNBC is known to be more common in non-white women (Cancer 2019;125(19):3412-3417).
Geography	The incidence rate of breast cancer varies in different geographical regions on England (between 162 and 183 per 100,000 people, from lowest to highest). Other social determinants (such as poverty, lack of education, social isolation) also influence breast cancer incidence, treatment and survival.
Overall representativeness of the study:	
The median age of patients in this study was 57 years, similar to the average age distribution in the literature. Eleven percent of patients in this study were non-white, representing the population distribution of breast cancer, although this may be a slight under-representation of the population of women with TNBC. Patients were recruited from 20 sites: representing a broad range of urban and rural and social demographics across England, Scotland and Wales.	

Table S3. List of centres and recruitment

Centre Name	Total
Royal Marsden Hospital, London	8
Royal Marsden Hospital, Sutton	7
Royal Bournemouth Hospital, Bournemouth	4
University College London Hospital, London	3
Addenbrooke's Hospital, Cambridge	2
West of Scotland Beatson Cancer Centre, Glasgow	9
Royal Devon and Exeter, Exeter	4
The Christie Hospital, Manchester	15
Western General Hospital, Edinburgh	1
Barts Health NHS Trust, London	0
Oxford University Hospitals NHS Trust, Oxford	1
Velindre Cancer Centre, Cardiff	1
Royal Cornwall Hospital, Truro	0
Weston Park Hospital, Sheffield	6
University Hospitals Bristol NHS Foundation Trust, Bristol	2
University Hospital Southampton, Southampton	6
Derriford Hospital, Plymouth	1
Nottingham University Hospitals NHS Trust, Nottingham	0
Clatterbridge Cancer Centre, Clatterbridge	1
Kent Oncology Centre, Maidstone	4
	75

Figure S2. Progression free survival Kaplan Meier curve

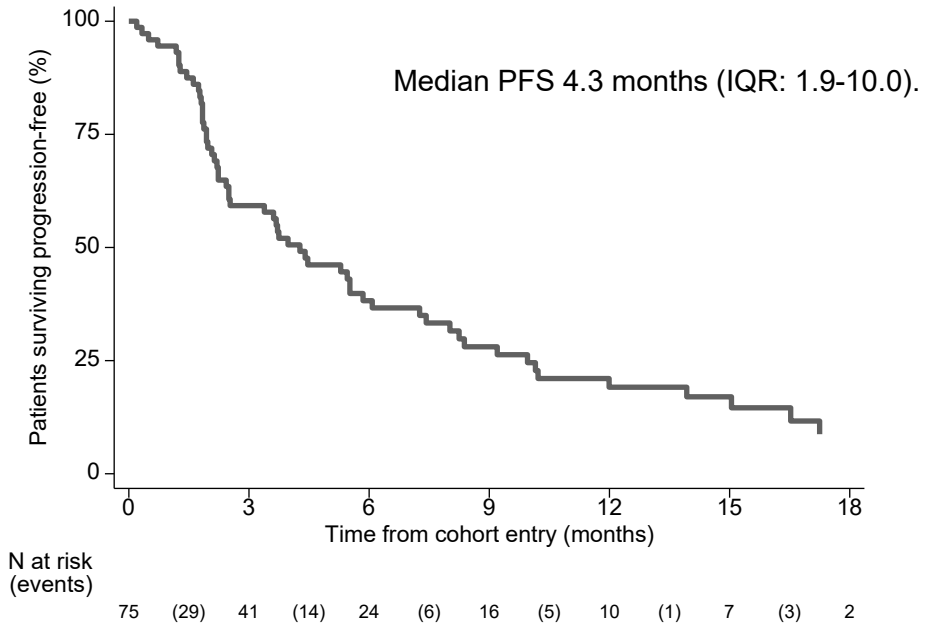

Table S4: Activity according to biomarker subgroups: Progression free survival (median, IQR, months) in patients with *BRCA1/2* mutations (germline or somatic)

	Confirmed response rate % (95%CI); n/N	N	Median PFS (IQR), months
ATM loss	33.3 (0.8, 90.6); 1/3	3	6.1 (6.1, 8.4)
No ATM loss	22.2 (2.8, 60.0); 2/9	9	7.3 (4.5, 25.4)
Cyclin E1 high	25.0 (0.6, 80.6); 1/4	4	7.3 (4.3, 25.4)
Cyclin E1 low	33.0 (0.8, 90.6); 1/3	3	6.1 (6.1, 8.4)
RAD51 high	16.7 (0.4, 64.1); 1/6	6	8.4 (5.8-25.4)
RAD51 low	20.0 (0.5, 71.6); 1/5	5	6.1 (4.5-undetermined)

Figure S3. Best percentage change from baseline for sum of the target lesions (n=70) by BRCA mutation status

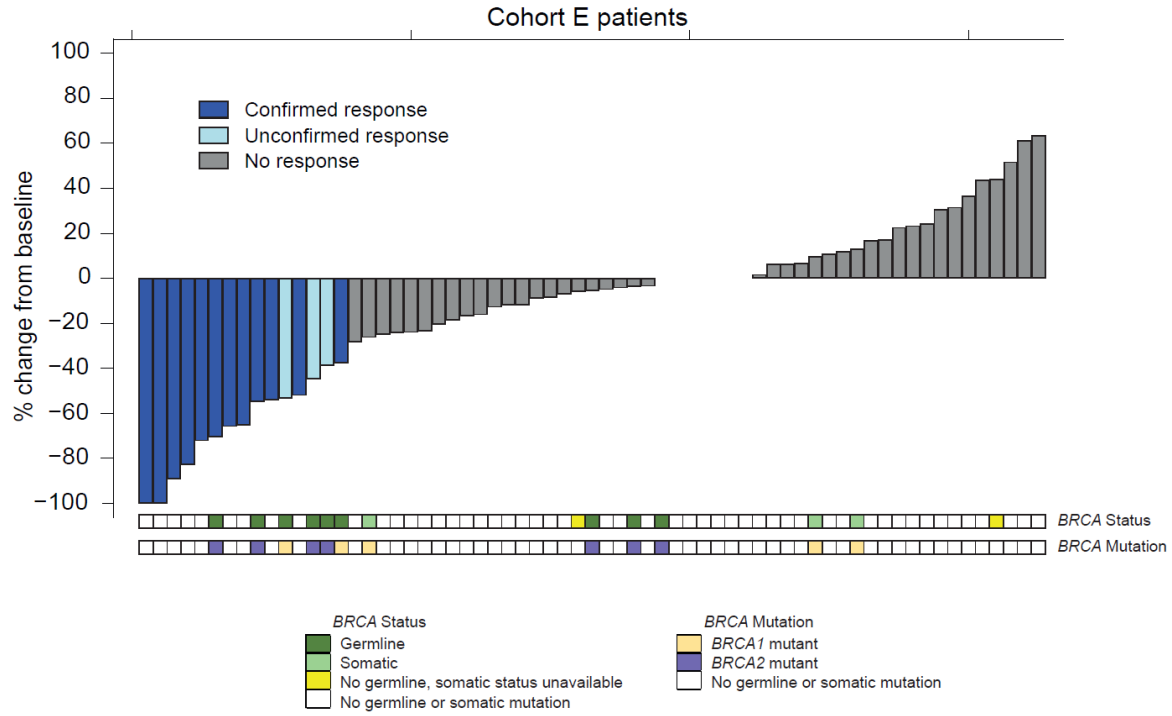

Table S5. Worst grade CTCAE reported during treatment

Note: AEs reported in the table below are where the AE was reported for ≥10% patients at any grade or where at least one patient has a grade 3+ AE. For a full list of AEs see appendix.

	G0		G1		G2		G3		G4		G5		Any grade		G3+	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Abdominal pain	63	88	5	7	1	1	3	4	0	0	0	0	9	13	3	4
Anaemia	44	61	10	14	9	13	9	13	0	0	0	0	28	39	9	13
Arthralgia	62	86	8	11	2	3	0	0	0	0	0	0	10	14	0	0
Back pain	60	83	5	7	6	8	1	1	0	0	0	0	12	17	1	1
Chest pain	66	92	4	6	1	1	1	1	0	0	0	0	6	8	1	1
Constipation	60	83	10	14	2	3	0	0	0	0	0	0	12	17	0	0
Corona virus infection	71	99	0	0	0	0	0	0	0	0	1	1	1	1	1	1
Cough	56	78	12	17	4	6	0	0	0	0	0	0	16	22	0	0
Decreased appetite	55	76	13	18	4	6	0	0	0	0	0	0	17	24	0	0
Diarrhoea	49	68	19	26	2	3	1	1	1	1	0	0	23	32	2	3
Dizziness	62	86	6	8	4	6	0	0	0	0	0	0	10	14	0	0
Dyspepsia	63	88	5	7	4	6	0	0	0	0	0	0	9	13	0	0
Dyspnoea	56	78	8	11	6	8	1	1	1	1	0	0	16	22	2	3
Fatigue	21	29	31	43	15	21	5	7	0	0	0	0	51	71	5	7
Febrile neutropenia	71	99	0	0	0	0	1	1	0	0	0	0	1	1	1	1
Gamma-glutamyltransferase increased	62	86	4	6	2	3	4	6	0	0	0	0	10	14	4	6
Haemoglobin decreased	71	99	0	0	0	0	1	1	0	0	0	0	1	1	1	1
Headache	57	79	13	18	1	1	1	1	0	0	0	0	15	21	1	1
Hot flush	65	90	5	7	2	3	0	0	0	0	0	0	7	10	0	0
Hypertension	51	71	4	6	5	7	12	17	0	0	0	0	21	29	12	17
Hypokalaemia	71	99	0	0	0	0	0	0	1	1	0	0	1	1	1	1
Hyponatraemia	71	99	0	0	0	0	1	1	0	0	0	0	1	1	1	1
Intestinal perforation	71	99	0	0	0	0	1	1	0	0	0	0	1	1	1	1

	G0		G1		G2		G3		G4		G5		Any grade		G3+	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Leukopenia	63	88	6	8	3	4	0	0	0	0	0	0	9	13	0	0
Lymphopenia	53	74	8	11	9	13	2	3	0	0	0	0	19	26	2	3
Mucosal inflammation	71	99	0	0	0	0	1	1	0	0	0	0	1	1	1	1
Nausea	29	40	32	44	11	15	0	0	0	0	0	0	43	60	0	0
Neutropenia	65	90	5	7	1	1	0	0	1	1	0	0	7	10	1	1
Neutropenic sepsis	71	99	0	0	0	0	1	1	0	0	0	0	1	1	1	1
Oedema peripheral	68	94	2	3	1	1	1	1	0	0	0	0	4	6	1	1
Pain	61	85	4	6	4	6	3	4	0	0	0	0	11	15	3	4
Pulmonary embolism	71	99	0	0	0	0	1	1	0	0	0	0	1	1	1	1
Thrombocytopenia	66	92	4	6	1	1	1	1	0	0	0	0	6	8	1	1
Transaminases increased	59	82	10	14	2	3	1	1	0	0	0	0	13	18	1	1
Urinary tract infection	65	90	2	3	4	6	1	1	0	0	0	0	7	10	1	1
Vomiting	58	81	11	15	3	4	0	0	0	0	0	0	14	19	0	0