Supplementary Table S1. Baseline characteristics for overall ITT population and population evaluable for F1CDx.

	Overall ITT population		**ITT population evaluable for F1CDx**	
Characteristic	**Talazoparib (*N* = 287)**	**Chemotherapy (*N* = 144)**	**Talazoparib (*N* = 201)**	**Chemotherapy (*N* = 107)**
Age, y				
Median	45.0	50.0	46.0	51.0
Range	27.0–84.0	24.0–88.0	27.0–84.0	24.0–88.0
Age <50 y, *n* (%)	182 (63.4)	67 (46.5)	123 (61.2)	47 (43.9)
Female sex, *n* (%)	283 (98.6)	141 (97.9)	198 (98.5)	106 (99.1)
ECOG performance status score, *n* (%)				
0	153 (53.3)	84 (58.3)	103 (51.2)	59 (55.1)
1	127 (44.3)	57 (39.6)	93 (46.3)	46 (43.0)
2	6 (2.1)	2 (1.4)	4 (2.0)	2 (1.9)
Breast cancer stage, *n* (%)				
Locally advanced	15 (5.2)	9 (6.3)	11 (5.5)	6 (5.6)
Metastatic	271 (94.4)	135 (93.8)	189 (94.0)	101 (94.4)
Measurable disease assessed by investigator,[a] *n* (%)	219 (76.3)	114 (79.2)	158 (78.6)	87 (81.3)
History of CNS metastases, *n* (%)	43 (15.0)	20 (13.9)	33 (16.4)	17 (15.9)
Visceral disease,[b] *n* (%)	201 (70.0)	103 (71.5)	141 (70.1)	81 (75.7)
Hormone-receptor status, *n* (%)				
Triple-negative	130 (45.3)	60 (41.7)	89 (44.3)	43 (40.2)
Hormone receptor-positive	157 (54.7)	84 (58.3)	112 (55.7)	64 (59.8)
BRCA status,[c] *n* (%)				
BRCA1-positive	133 (46.3)	63 (43.8)	94 (46.8)	48 (44.9)
BRCA2-positive	154 (53.7)	81 (56.3)	107 (53.2)	59 (55.1)
<12-mo disease-free interval from initial diagnosis to advanced breast cancer, *n* (%)	108 (37.6)	42 (29.2)	68 (33.8)	29 (27.1)

Previous adjuvant or neoadjuvant therapy, *n* (%)	238 (82.9)	121 (84.0)	169 (84.1)	92 (86.0)
No. of previous hormone therapy-based regimens for hormone receptor-positive breast cancer[d]				
Median	2.0	2.0	2.0	2.0
Range	0–6	0–6	0–6	0–6
Previous platinum therapy, *n* (%)	46 (16.0)	30 (20.8)	33 (16.4)	22 (20.6)
Previous cytotoxic regimens for advanced cancer, *n* (%)				
0	111 (38.7)	54 (37.5)	80 (39.8)	41 (38.3)
1	107 (37.3)	54 (37.5)	73 (36.3)	35 (32.7)
2	57 (19.9)	28 (19.4)	41 (20.4)	25 (23.4)
3	11 (3.8)	8 (5.6)	6 (3.0)	6 (5.6)

Abbreviations: CNS, central nervous system; ECOG, Eastern Cooperative Oncology Group; y, years.

[a]Measurable disease is defined as the presence of at least one target lesion at baseline.

[b]Visceral disease is defined as non-nodal target or non-target lesions identified at lung, liver, kidney, heart, stomach, small intestine, colon, rectum, ovary, uterus/endometrium, pancreas, thyroid, adrenal, and spleen at baseline.

[c]If both a Myriad and a local laboratory result exist in the database, the Myriad result (if positive) will be used. If both a Myriad and a local laboratory result exist in the database, the local result (if the Myriad result is negative) will be used**.**

[d]n=157 (talazoparib) and n=84 (chemotherapy) for the hormone receptor-positive ITT population and n=112 (talazoparib) and n=64 (chemotherapy) for the hormone receptor-positive ITT population evaluable for F1CDx.

Supplementary Table S2. Listing of *BRCA* variant profiles and selected clinical outcomes in patients lacking t*BRCA*mut – evaluable ITT.

Patient ID	Treatment arm	g*BRCA1*mut	g*BRCA2*mut	Tumor				Clinical benefit[a]	Best response[b]	PFS (months)[c]
				t*BRCA1*	Pathogenic?	t*BRCA2*	Pathogenic?			
1	Talazoparib	IVS19-12G>A						N	PD	9.4
2	Talazoparib	del exons 8–24		CNA	Known			N	SD	24.3
3	Talazoparib		del exons 14–16			CNA	Known	Y	PR	8.2
4	Talazoparib	del exons 1–23		CNA	Known			Y	SD	21.5
5	Chemotherapy		8096A>G (H2623R)			7868A>G (H2623R)	Unknown	Y	PR	4.3
6	Talazoparib	del exons 14–20		CNA	Known			Y	PR	17.3
				Rearrangement (*BRCA1-BRCA1*)	Unknown					
7	Chemotherapy		del exon 14			CNA	Known	Y	SD	11.1
8	Talazoparib	del exons 8–13		CNA	Known	9976A>T (K3326*)	Unknown	Y	PR	11.1
9	Chemotherapy	del exons 8–13		CNA	Known			N	PD	1.5
10	Talazoparib		9424C>T (Q3066X)			9196C>T (Q3066*)	Unknown	Y	CR	5.4
11	Chemotherapy							Y	PR	4.4
12	Talazoparib		IVS3+5G>A					N	SD	4.5

[a]Clinical benefit assessment was based on target, non-target, and new lesions per RECIST 1.1, and confirmation of CR, PR, and SD was not required. CBR24 was defined as the proportion of patients with a best overall response of CR, PR, or SD lasting ≥24 weeks from randomization per RECIST v1.1 as determined by investigator.

[b]Best response using RECIST 1.1 by investigator (unconfirmed).

[c]PFS is using RECIST 1.1 by IRF assessment.

*Amino acid is replaced by stop codon.

t*BRCA*mut is defined as known/likely pathologic variant (CNAs excluded). Patient 11 lacked a g*BRCA*mut based on Central testing, and was enrolled on the basis of local g*BRCA* test results. The test results are from central laboratories (Myriad BRACAnalysis® CDx for g*BRCA*, FoundationOne® CDx for t*BRCA*).

Supplementary Table S3. Baseline characteristics for patients without *BRCA* LOH.

Characteristic	Talazoparib (*N* = 27)	Chemotherapy (*N* = 14)
Age, y		
Median	47.0	52.5
Range	28.0–77.0	29.0–64.0
Age <50 y, *n* (%)	15 (55.6)	4 (28.6)
Female sex, *n* (%)	27 (100.0)	14 (100.0)
ECOG performance status score, *n* (%)		
0	14 (51.9)	9 (64.3)
1	12 (44.4)	5 (35.7)
2	–	–
Breast cancer stage, *n* (%)		
Locally advanced	–	–
Metastatic	27 (100.0)	14 (100.0)
Measurable disease assessed by investigator,[a] *n* (%)	19 (70.4)	10 (71.4)
History of CNS metastases, *n* (%)	2 (7.4)	2 (14.3)
Visceral disease,[b] *n* (%)	18 (66.7)	8 (57.1)
Hormone-receptor status, *n* (%)		
Triple-negative	4 (14.8)	5 (35.7)
Hormone receptor-positive	23 (85.2)	9 (64.3)
BRCA status,[c] *n* (%)		
BRCA1-positive	9 (33.3)	2 (14.3)
BRCA2-positive	18 (66.7)	12 (85.7)
<12-mo disease-free interval from initial diagnosis to advanced breast cancer, *n* (%)	7 (25.9)	3 (21.4)
Previous adjuvant or neoadjuvant therapy, *n* (%)	22 (81.5)	13 (92.9)

No. of previous hormone therapy-based regimens for hormone receptor-positive breast cancer[d]		
Median	2.0	3.0
Range	0–4	0–5
Previous platinum therapy, *n* (%)	4 (14.8)	6 (42.9)
Previous cytotoxic regimens for advanced cancer, *n* (%)		
0	8 (29.6)	6 (42.9)
1	16 (59.3)	3 (21.4)
2	3 (11.1)	5 (35.7)
3	–	–

Abbreviations: CNS, central nervous system; ECOG, Eastern Cooperative Oncology Group, y, years.

[a]Measurable disease is defined as the presence of at least one target lesion at baseline.

[b]Visceral disease is defined as non-nodal target or non-target lesions identified at lung, liver, kidney, heart, stomach, small intestine, colon, rectum, ovary, uterus/endometrium, pancreas, thyroid, adrenal, and spleen at baseline.

[c]If both a Myriad and a local laboratory result exist in the database, the Myriad result (if positive) will be used. If both a Myriad and a local laboratory result exist in the database, the local result (if the Myriad result is negative) will be used.

[d]n=23 (talazoparib) and n=9 (chemotherapy) for the hormone receptor-positive ITT population evaluable for F1CDx and *BRCA* zygosity without *BRCA* LOH.

Supplementary Table S4. PFS according to alteration status of selected tumor tissue non-*BRCA* genes – t*BRCA*mut ITT population.

Evaluable ITT population with tumors bearing *BRCA1/2*mut	**Talazoparib (*n* = 193)**		**Chemotherapy (*n* = 103)**	
	Mutations	**CNAs**	**Mutations**	**CNAs**
TP53				
HR (95% CI)	1.693 (1.186–2.418)	NE	1.439 (0.859–2.411)	NE
n, altered/unaltered	99/94		55/48	
n, events altered/unaltered	73/53		34/28	
P Value	0.0033	NE	0.1614	NE
RAD21				
HR (95% CI)	NE	0.634 (0.369–1.088)	NE	1.174 (0.672–2.049)
n, altered/unaltered		33/160		30/73
n, events altered/unaltered		16/110		18/44
P Value	NE	0.0940	NE	0.5699
MYC				
HR (95% CI)	NE	1.323 (0.852–2.057)	NE	1.052 (0.586–1.892)
n, altered/unaltered		37/156		25/78
n, events altered/unaltered		25/101		16/46
P Value	NE	0.2103	NE	0.8634
PTEN				
HR (95% CI)	1.813 (0.973–3.378)	0.963 (0.530–1.750)	1.762 (0.834–3.725)	NE
n, altered/unaltered	13/180	18/175	11/92	
n, events altered/unaltered	11/115	12/114	8/54	
P Value	0.0564	0.8992	0.1302	NE
PIK3CA				
HR (95% CI)	1.198 (0.697–2.058)	NE	0.639 (0.272–1.499)	NE
n, altered/unaltered	22/171		10/93	

n, events altered/unaltered	15/111		7/55	
P Value	0.5119	NE	0.2962	NE

Abbreviation: NE, not evaluable.

Cox proportional hazards model with wildtype as the reference group was used to calculate HR and 95% CI. HR <1 indicates better survival in the alteration group, while HR >1 indicates better survival in the no alteration group. Log-rank 2-sided test was performed to compare between no alteration/alteration groups. The t*BRCA*mut ITT population includes all patients with tumor samples suitable for the genomic evaluation and analyzed using FoundationOne® CDx who have known or likely pathogenic *BRCA* variants (*BRCA* CNAs excluded). For *TP53*, *RAD21*, *MYC*, *PTEN*, and *PIK3CA*, known/likely pathogenic variants are included, segregated as mutations (CNAs excluded) or CNAs only. PFS is using RECIST 1.1 by IRF assessment. For the analyses shown, both mutant/copy number altered (i.e., alteration) and non-mutant/non-copy number altered (i.e., no alteration) subgroups had ≥10 patients, otherwise analyses were deemed NE.

Supplementary Table S5. PFS based on IRF by gLOH – ITT population with gLOH results.

PFS	**Talazoparib (*N* = 140)**	**Chemotherapy (*N* = 81)**
Duration of PFS,[a] mo		
n	140	81
Censored, *n* (%)	47 (33.6)	32 (39.5)
Treatment comparison (talazoparib vs. chemotherapy)		
Hazard ratio (95% CI)[b]	0.993 (0.975–1.012)	
P Value[b]	0.9668	

[a]Based on Kaplan–Meier estimates.

[b]Hazard ratio is based on stratified Cox regression model with treatment and gLOH as the covariates (stratification factors are number of prior cytotoxic chemotherapy regimens, triple negative status, history of central nervous system metastases) and indicates the change in the duration of PFS if the value of gLOH rises by one unit. *P* Value is based on a stratified log-rank test.