Phase IV multicenter study evaluating RWE and the safety of talazoparib in patients with locally advanced or metastatic negative HER2 breast cancer and a BRCA1/2 mutation (ViTAL) - Cohort 2: patients treated according to the EMA

P4-01-04

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BACKGROUND

Talazoparib (TALA) is a highly potent PARP inhibitor that has demonstrated clinical benefit in the phase III EMBRACA trial for patients with germline BRCA1 or BRCA2-mutation and a locally advanced or metastatic HER2 negative (HER2-) breast cancer (BC) (Litton JK, et al. Talazoparib in Patients with Advanced Breast Cancer and a Germline BRCA Mutation. N Engl J Med. 2018; 379:753-763).

OBJECTIVES

ViTAL (EUPAS30803) is an ambispective, multi-center longitudinal, phase IV study that aims to ensure the effectiveness and safety of TALA in the real-world setting among patients with locally advanced or metastatic HER2- BC, with somatic or germline BRCA mutation (sBRCA or gBRCA).

METHODS

INCLUSION CRITERIA

Cohort 1
- Patient has been treated or treated through the French Early Access Program
- Patient's consent before any specific procedures of the study including the assessments requested for inclusion

Cohort 2
- Patient for who a talazoparib treatment must be initiated or has been initiated according to the Summary Product Characteristic
- ECOG PS = 0 to 2
- Patient's consent before any specific procedures of the study including the assessments requested for inclusion
- Patient affiliated to a French social security

Cohort 1
Patients treated through the French Early Access Program from November 2018 to September 2019. Inclusion of patients with sBRCA mutation was allowed
86 patients enrolled

Cohort 2
Patients treated according to the European Marketing Approval granted 09/21/2021
85 patients enrolled

Screen Failure
5 patients

80 patients treated

3 patients with no BRCA mutation
2 patients not treated

Primary endpoint: Time to Treatment Discontinuation (TTD) for TALA defined as time between the date of first dose of TALA and the date of last dose or death.

Secondary endpoints:
- Safety of talazoparib
- TTD of the subsequent treatment
- Overall survival
- Best response
- For patients with Central Nervous System (CNS) metastasis at the inclusion, the duration of CNS metastases control and the time before a local treatment of CNS metastases
- Patient satisfaction of treatment by talazoparib: the satisfaction of the patient for his treatment by talazoparib will measured at M3 and M6 only by the Cancer Therapy Satisfaction Questionnaire (CTSQ).

The results presented in this poster concerns the cohort 2.

The results for the cohort 1 presented at SABCS 2022 (**P4-01-20**)

1.BASELINE CHARACTERISTICS

From December 2019 to October 2021, 80 patients were treated in the cohort 2. The baseline characteristics in all cohort 2 and Hormone Receptor (HR) status are detailed in table 1.

Table 1 – Baseline characteristics

	HR+* N = 52	TNBC** N = 28	Cohort 2 N = 80
Age (years)			
Median	54	48	51
Range	31 – 77	28 – 82	28 – 82
ECOG status, n (%)			
0 or 1	45 (87)	23 (82)	68 (85)
≥ 2	6 (12)	2 (7)	8 (10)
NA	1 (2)	3 (11)	4 (5)
Premenopausal women, n (%)	10 (21)	8 (33)	18 (25)
Ovarian or breast cancer in the 1st degree relative, n (%)	31 (60)	10 (36)	41 (51)
BRCA mutation, n (%)			
BRCA 1	13 (25)	18 (64)	31 (39)
BRCA 2	38 (73)	9 (32)	47 (59)
BRCA 1 & 2	1 (2)	1 (4)	2 (3)
De novo metastatic BC, n (%)	9 (18)	6 (21)	15 (19)
Site of metastases, n (%)			
Visceral	34 (65)	19 (68)	53 (66)
Bones	37 (71)	9 (32)	46 (58)
CNS	4 (8)	5 (18)	9 (11)

* HR: Hormone receptor ; ** TNBC: Triple Negative Breast Cancer

2.PRIOR THERAPIES

The prior treatments received are detailed in the Table 2.

Table 2 – Prior therapies

	HR+ N = 52	TNBC N = 28	Cohort 2 N = 80
Prior cytotoxic regimens, n (%)	33 (64)	17 (61)	50 (63)
Prior cytotoxic regimens for mBC, n (%)			
Median	1	1	1
0	19 (37)	11 (39)	30 (38)
1	18 (35)	11 (39)	29 (36)
≥ 2	15 (29)	6 (21)	21 (26)
Prior platinum therapy, n (%)			
All setting	8 (15)	8 (29)	16 (20)
(Neo)adjuvant setting	1 (2)	1 (4)	2 (3)
Advanced/metastatic setting	7 (14)	7 (25)	14 (18)
Prior endocrine therapy for mBC, n (%)			
Median	1	0	1
0	9 (17)	27 (96)	36 (45)
1	22 (42)	0 (0)	22 (28)
≥ 2	21 (40)	1 (4)	22 (28)
Received CDK4/6 inhibitor, n (%)	33 (64)	0 (0)	33 (41)
Endocrine therapy associated to CDK4/6 inhibitor, n(%)			
Aromatase inhibitor	15 (46)	0 (0)	15 (46)
Fulvestrant	19 (58)	0 (0)	19 (58)
Other or none	4 (12)	0 (0)	4 (0)

3. PRIMARY ENDPOINT : TTD OF TALAZOPARIB

At 10/26/2022, the median of follow-up was 12.0 months.

Of 80 treated patients, 65 patients (81%) experienced permanent discontinuation of TALA due to progressive disease (89%), toxicity (6%), cancer-related death (2%), or other reasons (3%).

For TTD, the data is available for 79 patients.

Regarding of some interesting subgroups, the median TTD are detailed in the Table 3.

Table 3 – mTTD for subgroups of interest

	N (%)	Months [95% C.I]
All population	79 (100)	9.1 [6,9 ; 10,5]
De novo metastatic BC, n (%)		
Yes	15 (19)	10.8 [6.0 ; 16.6]
No	63 (81)	9.0 [6.4 ; 10.3]
CNS metastasis		
Yes	9 (11)	12.0 [0.3 ; 26.1]
No	70 (89)	9.0 [6.4 ; 10.5]

The TTD, for all population, by HR+ status, by type of BRCA, by treatment by platinum, by number of previous lines of chemotherapy are detailed in Figure 1, 2, 3, 4 and 5, respectively.

Figure 1 – TTD of TALA in cohort 2

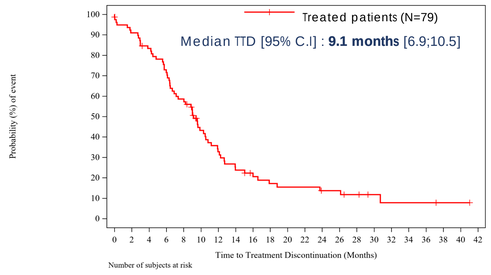


Figure 2 – TTD of TALA according to the HR status

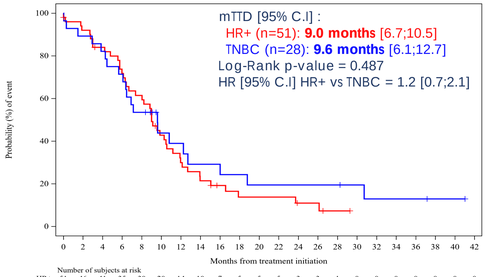


Figure 3 – TTD of TALA by type of BRCA

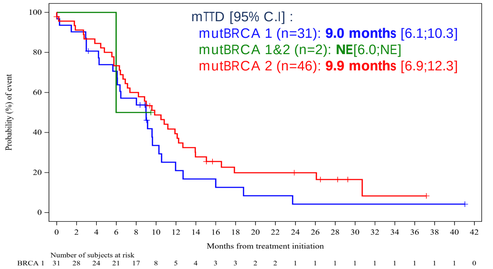
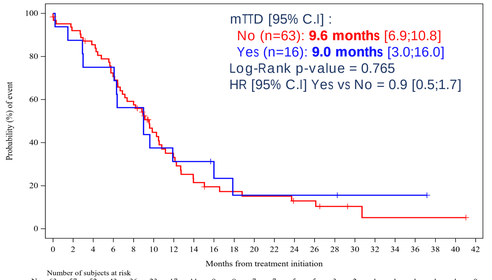
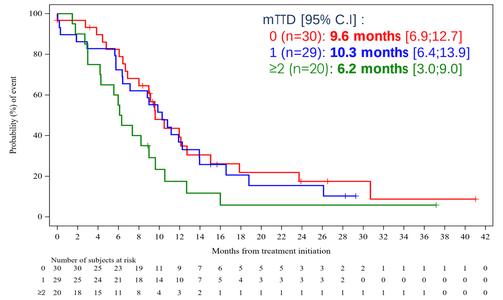


Figure 4 – TTD of TALA by treatment by platinum*



* As neoadjuvant/adjuvant or advanced/metastatic treatment

Figure 5 – TTD of TALA by number of previous lines of chemotherapy



4. SECONDARY ENDPOINTS

After discontinuation of TALA, 55 (69%) of patients received a subsequent treatment, with a TTD of 3.9 months [95% CI 2.1-4.7].

The most common subsequent treatments were non-platinum chemotherapy (67%), platinum therapy (6%) and other (27%).

The overall survival data were immature.

At least one adverse event (AEs) was recorded in 74% of patients: 41% anemia, 19% neutropenia, 15% thrombocytopenia, 25% asthenia, 19% nausea, 11% diarrhea, 10% headache and 10% fatigue.

Related serious AEs occurred in 7 (9%) patients including 3% anemia and 4% thrombocytopenia.

Dose modification, temporary interruption or permanent discontinuation due to intolerance, associated with talazoparib occurred in 26 (33%), 30 (38%) and 4 (6%) respectively.

TAKE HOME MESSAGE

- These results are consistent with the outcomes and safety results of the cohort 1 (P4-01-20) and EMBRACA study (Litton et.al. NEJM 2018).
- As for Cohort 1 :
  - The earlier talazoparib is given, the better the activity of talazoparib.
  - BRCA2 mutated patients benefit more than BRCA1 mutated patients.
  - The potential existence of long responder for TNBC patients.

CONCLUSION

In order to obtain more significant results, data from cohorts 1 and 2 will be analyzed together in a future publication.

REFERENCE

Litton JK, et al. Talazoparib in Patients with Advanced Breast Cancer and a Germline BRCA Mutation. N Engl J Med. 2018; 379:753-763.

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