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Efficacy and safety of first-line atezolizumab + bevacizumab + paclitaxel in patients with advanced triple-negative breast cancer: the ATRACTIB phase 2 trial

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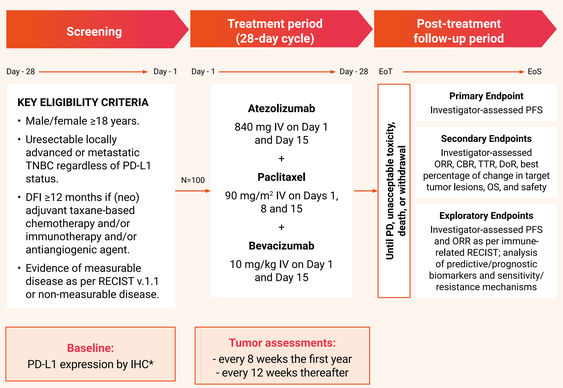
Background

- Triple-negative breast cancer (TNBC) is an aggressive breast cancer subtype that requires new treatment strategies to improve its poor prognosis[1,2].
- Atezolizumab (ATZ), an anti-programmed cell death-ligand 1 (PD-L1) agent, combined with first-line (1L) nab-paclitaxel (nab-PTX) is approved for the treatment of PD-L1-positive patients with advanced TNBC (aTNBC), based on a significant improvement in progression-free survival (PFS) and a numerically higher and clinically meaningful median overall survival (OS)[3].
- A synergism between antiangiogenic therapy and immunotherapy (IO)-based strategies has been observed preclinically and in different tumor types but warrants additional evaluation in aTNBC.
- ATRACTIB evaluated the efficacy and safety of 1L ATZ + bevacizumab (BVZ) + PTX for patients with aTNBC, regardless of their tumors' PD-L1 status.

Study design and Methods

Figure 1. ATRACTIB study design



*Centrally assessed using SP142 (ICs) and 22C3 (CPS) antibodies.

Results

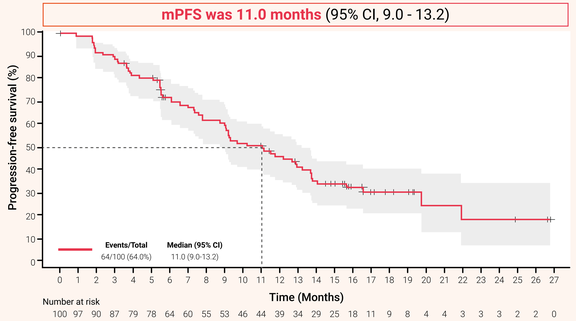
- Patients' baseline characteristics are shown in **Table 1**.
- At data cut-off (15th Sept 2023), 23 patients were still on therapy. Median follow-up was 16.7 months (range 1.1 - 34.1).
- Median PFS (mPFS) was 11.0 months **(Fig. 2)**. Although OS data was immature at data cut-off (30 events), estimated 18-month OS was 69.4% **(Fig. 3)**.

Table 1. Patient Demographic Characteristics at Baseline

Characteristics, n (%)	Overall (N=100)
Age, median (range), years	55.0 (32.0 - 84.0)
ECOG 0 / 1, n (%)	75 (75.0%) / 25 (25.0%)
Disease-free interval (DFI)	
De novo metastatic disease, n (%)	29 (29.0%)
DFI ≥12 months, n (%)	68 (68.0%)
DFI < 12 months*, n (%)	3 (3.0%)
Visceral metastatic disease, n (%)	57 (57.0%)
Number of metastatic sites, n (%)	
1-2	54 (54.0%)
≥ 3	46 (46.0%)
Prior treatment for early disease**, n (%)	70 (70.0%)
Taxane-based chemotherapy	61 (61.0%)
Anthracyclines	55 (55.0%)
PD-L1 expression (SP142 [ICs]; N=85)	
Negative (< 1%)	83 (97.6%)
Positive (≥ 1%)	2 (2.4%)

*N=3 patients with DFI < 12 months were included because they had not received any prior (neo)adjuvant treatment.
**One patient was initially diagnosed at baseline with early disease but had not received any prior treatment for early disease.

Figure 2. Progression-free survival



- Unconfirmed ORR was 63.0% and CBR was 79.0% **(Fig. 4)**.
- Most common treatment emergent adverse events (TEAEs) and immune-related adverse events (irAEs) are shown in **Table 2**.

Figure 3. Overall survival

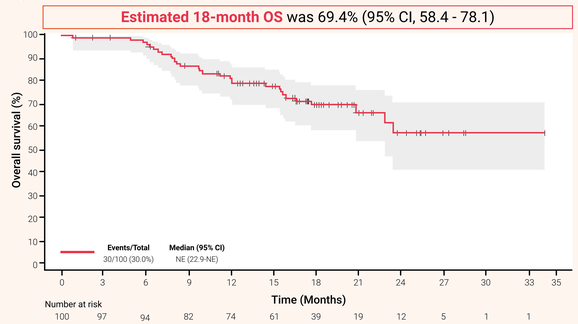
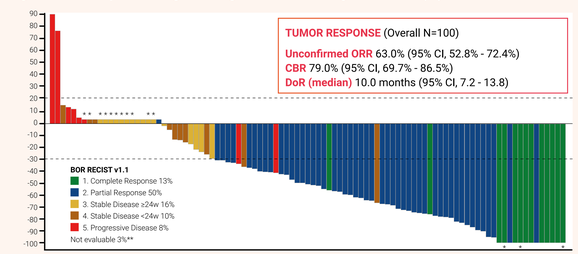


Figure 4. Best percentage change in sum of target lesions (%)



*Patients with only non-target lesions. **Three patients discontinued before post-baseline assessment due to Progressive Disease in one patient and to withdrawal of consent in two patients. BOR, best overall response; CBR, clinical benefit rate; CI, confidence interval; DoR, duration of response; ORR, overall response rate.

Table 2. Summary of TEAEs, most frequent TEAEs (>25%) and irAEs, n(%)

TEAEs, n (%)	Overall (N=100)	Treatment-related
Any TEAEs	100 (100.0%)	97 (97.0%)
Grade 3/4 TEAEs	61 (61.0%)	47 (47.0%)
Any serious TEAEs	34 (34.0%)	18 (18.0%)
ECIs	42 (42.0%)	42 (42.0%)
TEAEs leading to treatment discontinuation of:		
Atezolizumab	14 (14%)	-
Bevacizumab	15 (15%)	-
Paclitaxel	40 (40%)	-
TEAEs leading to death	0 (0.0%)	0 (0.0%)
Dose adjustments		
Reduction of Paclitaxel	22 (22.0%)	22 (22.0%)
Most frequent TEAEs, n (%)	**Any grade**	**Grade 3/4**
Non-hematologic		
Peripheral neuropathy‡	68 (68.0%)	13 (13.0%)
Fatigue	62 (62.0%)	7 (7.0%)
Diarrhea	42 (42.0%)	3 (3.0%)
Alopecia	41 (41.0%)	0 (0.0%)
Stomatitis	37 (37.0%)	3 (3.0%)
Nausea	31 (31.0%)	0 (0.0%)
Hypertension	30 (30.0%)	9 (9.0%)
Hematologic		
Neutropenia	27 (27.0%)	12 (12.0%)
irAEs, n (%)	**Any grade**	**Grade 3/4**
Any irAEs	12 (12.0%)	5 (5.0%)
Thyroid disorders	6 (6.0%)	0 (0.0%)
Immune-mediated hepatitis	3 (3.0%)	3 (3.0%)
Nephritis	2 (2.0%)	2 (2.0%)
Addison's disease	1 (1.0%)	0 (0.0%)

‡Peripheral neuropathy (SMQ), includes Neuropathy peripheral, Neurotoxicity, Polyneuropathy, and Toxic neuropathy (MedDRA v.25.1).
ECI, events of clinical interest.

Conclusions

ATZ + BVZ + PTX demonstrated robust antitumor activity in first-line therapy for aTNBC patients and a manageable safety profile, with no new safety signals.

mPFS with this combination seems to be very promising, specially considering that most of tumors were PD-L1 negative.

These results merit further research on IO + bevacizumab combinations for patients with PD-L1-negative aTNBC.

References

1. **den Brok WD, et al.** Breast Cancer Res Treat 2017; 161:549-56.
2. **Cardoso F, et al.** Ann Oncol 2018;29:1634-57
3. **Schmid P, et al.** N Engl J Med. 2018 Nov 29;379(22):2108-2121.

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Scan here to view a plain language summary of this trial.

CBR, clinical benefit rate; **CPS,** combined positive score; **DFI,** disease-free interval; **DoR,** duration of response; **EoS,** end of study; **EoT,** end of treatment; **ICs,** tumor-infiltrating immune cells; **IHC,** immunohistochemistry; **irAEs,** immune-related adverse events; **ORR,** overall response rate; **OS,** overall survival; **PD,** progressive disease; **PD-L1,** programmed cell death-ligand 1; **PFS,** progression-free survival; **RECIST,** Response Evaluation Criteria in Solid Tumors; **TEAEs,** treatment-emergent adverse events; **TNBC,** triple-negative breast cancer; **TTR,** time to response.