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#1084: Safety Interim Analysis of ATRACTIB: A Phase 2 Trial of First-Line Atezolizumab in Combination with Paclitaxel and Bevacizumab in Metastatic Triple-Negative Breast Cancer

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BACKGROUND

- Based on the results from three phase 3 studies [1-3], taxane-based chemotherapy plus bevacizumab is a widely used regimen as first-line (1L) therapy for metastatic triple-negative breast cancer (mTNBC) in Europe.
- The IMpassion130 and KEYNOTE-355 trials confirmed a substantial benefit from adding an immune checkpoint inhibitor to 1L chemotherapy for patients with programmed death-ligand 1 (PD-L1)–positive mTNBC [4,5]. However, despite recent advances, many mTNBC patients still have a poor outcome with paucity of alternative treatment options.
- Synergism between antiangiogenic therapy and immunotherapy-based strategies has been shown preclinically and in different tumor types including breast cancer [6-9]. Therefore, this combination should be evaluated in clinical studies with the aim to improve patient outcomes without adding significant toxicity.
- ATRACTIB is an international, investigator-initiated, open-label, single-arm, phase 2 trial assessing the efficacy and safety of atezolizumab combined with paclitaxel and bevacizumab as 1L regimen for mTNBC patients irrespective of PD-L1 status.

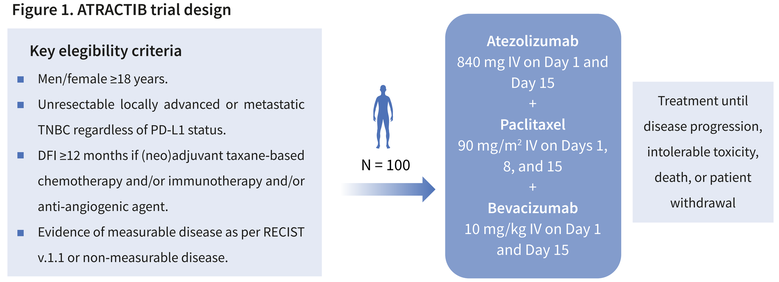
OBJECTIVES

- Primary objective is investigator-assessed progression-free survival (PFS) as per RECIST v.1.1. Secondary objectives include objective response and clinical benefit rates, overall survival, and safety.
- One safety interim analysis was planned for evaluating safety as per the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v.5.0 on the first 20 patients who had completed a 3-month follow-up or reached the end of study.

METHODS

Patients and Study Design

Figure 1. ATRACTIB trial design



Abbreviations: DFI, disease-free interval; IV; intravenously; TNBC, triple-negative breast cancer; RECIST, Response Evaluation Criteria In Solid Tumors.

Safety Assessments

- Safety assessments included blood analysis and collection of vital signs at screening, day 1 and 15 of each cycle, and end of treatment/withdrawal.
- Adverse events (AEs), treatment-emergent adverse events (TEAEs), serious adverse events (SAEs), and events of clinical interest (ECIs) were assessed to determine the safety and tolerability of the different drug combinations as per CTCAE v.5.0.

Trial Registration NCT04408118 on May 29th. First patient included October 6th, 2020.

RESULTS

Patients´ Baseline Characteristics

Table 1. Description of baseline characteristics

Baseline characteristics N (%)	Overall (N=34)
Median age (range), years	57.5 (40.0; 84.0)
ECOG performance status	
0	25 (73.5)
1	9 (26.5)
Menopausal status	
Post-menopausal	28 (82.4)
Pre-menopausal	6 (17.6)
Measurable disease	
No	5 (14.7)
Yes	29 (85.3)
Disease status	
Recurrent	* 23 (67.6)
De novo	11 (32.4)
Number of metastatic sites	
1	7 (20.6)
2	10 (29.4)
≥ 3	17 (50)
Types of metastatic disease	
Visceral	19 (55.9)
Non-visceral	15 (44.1)

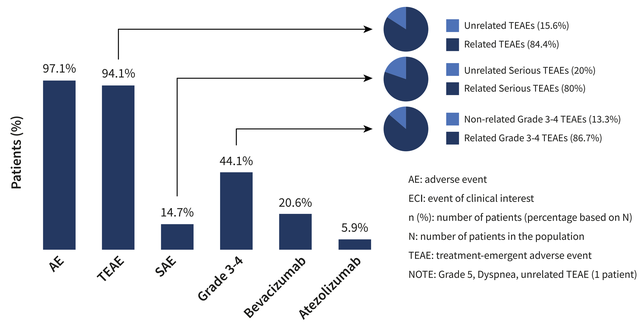
n (%), number of patients (percentage based on N);
N, Number of patients in the population
* These patients also received neo(adjuvant) therapy

Safety and Tolerability

- Fatigue, diarrhea, neurotoxicity, anemia, and neutropenia were the most frequent AEs.
- At the time of the data cut-off (September 30th, 2021), 25 (71.4%) patients were still receiving the drug regimen, and 9 (28.6%) patients have been discontinued: 4 patients due to progressive disease, 3 patients due to unacceptable toxicity, 1 due to patient's decision, and 1 death due to unrelated AEs.
- Mean relative dose intensity was 90.2% for atezolizumab, 96.5% for paclitaxel, and 95.7% for bevacizumab. Paclitaxel dose reduction was reported in 7 (20.6%) patients.
- Five (14.7%) patients required a dose delay due to AEs (11.8% for atezolizumab, 11.8% for paclitaxel, and 8.8% for bevacizumab).

Incidence Rate of Adverse Events

Figure 2. Total adverse events summary (N=34)



AE: adverse event
ECI: event of clinical interest
n (%): number of patients (percentage based on N)
N: number of patients in the population
TEAE: treatment-emergent adverse event
NOTE: Grade 5, Dyspnea, unrelated TEAE (1 patient)

Table 2. Serious adverse events related to any study

	Related TEAE		
Overall (N=34)	Any grade n (%)	Grade 3 n (%)	Grade 4 n (%)
Related to any IMP	4 (11.8)	2 (5.9)	2 (5.9)
Related to bevacizumab	2 (5.9)	0	1 (2.9)
Hypertensive crisis (hypertension)	1 (2.9)	0	1 (2.9)
Cerebrovascular accident	1 (2.9)	0	0
Related to atezolizumab	3 (8.8)	2 (5.9)	0
Fatigue	1 (2.9)	1 (2.9)	0
Thrombocytopenia *	1 (2.9)	-	-
Autoimmune hepatitis Alanine aminotransferase increased	1 (2.9)	1 (2.9)	0
Related to paclitaxel	1 (2.9)	0	1 (2.9)
Stomatitis	1 (2.9)	0	0
Febrile neutropenia	1 (2.9)	0	1 (2.9)

n (%), number of patients (percentage based on N); N, Number of patients in the population;
* Thrombocytopenia; Grade not reported,

Table 3. Adverse events by grade (>15% of patients)

	TEAE		Related TEAE	
Overall (N=34)	Any grade n (%)	Grade 3-4 n (%)	Any grade n (%)	Grade 3-4 n (%)
TEAE	32 (94.1)	15 (44.1)	27 (79.4)	13 (38.2)
Hematologic	11 (32.4)	4 (11.8)	9 (26.5)	4 (11.8)
Anemia	7 (20.6)	0	5 (14.7)	0
Neutropenia	6 (17.6)	3 (8.8)	6 (17.6)	3 (8.8)
Non-hematologic	31 (91.2)	12 (35.3)	26 (76.5)	9 (26.5)
Fatigue	16 (47.1)	3 (8.8)	15 (44.1)	3 (8.8)
Diarrhea	13 (38.2)	0	9 (26.5)	0
Neurotoxicity	12 (35.3)	3 (8.8)	11 (32.4)	3 (8.8)
Alopecia	9 (26.5)	0	9 (26.5)	0
Headache	8 (23.5)	0	5 (14.7)	0
Dysgeusia	7 (20.6)	0	7 (20.6)	0
Vomiting	7 (20.6)	0	4 (11.8)	0
Hypertension	5 (14.7)	1 (2.9)	6 (17.6)	1 (2.9)
Nausea	6 (17.6)	0	5 (14.7)	0
Arthralgia	6 (17.6)	0	5 (14.7)	0
Myalgia	6 (17.6)	0	5 (14.7)	0

n (%), number of patients (percentage based on N);
N, Number of patients in the population

Table 4. Events of clinical interest

	ECIs		
Overall (N=34)	Any grade n (%)	Grade 3 n (%)	Grade 4 n (%)
For bevacizumab	7 (20.6)	1 (2.9)	0
Hypertension	6 (17.6)	1 (2.9)	0
Pulmonary embolism	1 (2.9)	0	0
For atezolizumab	2 (5.9)	1 (2.9)	0
Pneumonitis	1 (2.9)	0	0
Autoimmune hepatitis Alanine aminotransferase increased	1 (2.9)	1 (2.9)	0

n (%), number of patients (percentage based on N);
N, Number of patients in the population

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CONCLUSIONS

- The addition of atezolizumab to paclitaxel and bevacizumab as 1L therapy for mTNBC shows a tolerable safety profile which is consistent with the known safety profile of each agent without a significant synergistic toxicity.
- Based on the independent data monitoring committee recommendation, patient recruitment is ongoing.