ACE-Breast-03:

Efficacy and safety of ARX788 in patients with HER2+ metastatic breast cancer previously treated with T-DM1

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SAN ANTONIO BREAST CANCER SYMPOSIUM®

Background

Amplification of the human epidermal growth factor receptor 2 (HER2) gene with consequent HER2 protein overexpression occurs in approximately ***20%*** of ***breast cancers (BC)*** and is a major driver of tumor development and progression. The HER2-targeted ADC trastuzumab emtansine (T-DM1) has been ***approved*** for the ***treatment*** of HER2-positive metastatic BC (mBC) after prior trastuzumab and taxane therapy. However, disease progression occurs in all patients, requiring additional therapeutic options. The use of second-generation anti-HER20 ADCs using alternative molecules is being investigated to overcome drug resistance.

Methods

ACE-Breast-03 (NCT04829604) is an ***ongoing global***, phase 2, single-arm study evaluating ARX788 in patients with HER2+ mBC whose disease has progressed following T-DM1, T-DXd, and/or tucatinib-containing regimens. ARX788 was administered with an initial dose of 1.5 mg/kg Q4W and subsequent doses of 1.3 mg/kg Q4W. ***Eligibility criteria*** included central laboratory confirmed HER2+ mBC per ASCO/CAP guidelines, measurable disease, and adequate organ function. Stable treated brain metastases are allowed. Patients with interstitial lung disease (ILD) or pneumonitis in prior 12 months; active ocular infections or any chronic corneal disorder; are excluded. The ***primary endpoint*** is overall response rate (ORR). Data cutoff was 11-Jul-2022.

Demographics

Characteristic	Patients (N = 7)
Age	
Median (range) — year	59
≥65 year — no. (%)	1 (14.3%)
Female sex — no. (%)	7 (100%)
Race — no. (%)†	
Asian	4 (57.1%)
White	2 (28.6%)
Black or African American	1 (14.3%)
Missing data	0 (0%)
Region — no. (%)	
Asian Pacific	5 (71.4%)
North America	2 (28.6%)
ECOG performance-status score — no. (%)‡	
0	5 (71.4%)
1	2 (28.6%)

Clinical Characteristics

Characteristic	Patients (N = 7)
Hormone-receptor status — no. (%)	
Positive	2 (28.6%)
Negative	5 (71.4%)
HER2 expression	**No. (%)**
IHC 3+	5 (71.4%)
IHC 2+, ISH-positive	2 (28.6%)
Median sum of diameters of target lesions at baseline (range) -mm	**97 (16-251)**
Median no. of previous cancer regimens (range)	**5 (2-8)**
Previous systemic cancer therapy	**No. (%)**
Trastuzumab	7 (100%)
Pertuzumab	5 (71.4%)
HER2 TKI	4 (57.1%)
Other anti-HER2 therapy	7 (100%)
Hormone therapy	2 (28.6%)
Other systemic therapy	7 (100%)
Best response to trastuzumab emtansine therapy	**No. (%)**
Complete or partial response or stable disease	4 (57.1%)
Progressive disease	1 (14.3%)
Could not be evaluated	2 (28.6%)

Safety Results

Safety profile	
All AEs (regardless of causality)	7 (100%)
Drug-related AEs (any grade)	6 (85.7%)
All AEs ≥ Grade 3	2 (28.6%)
Drug-related AEs ≥ Grade 3	1 (14.3%)
All SAEs	1 (14.3%)
Drug-related SAEs	0
AEs leading to dose delays	3 (42.9%)
AEs leading to dose reductions	1 (14.3%)
AEs leading to dose interruptions	1 (14.3%)
AEs leading to discontinuation	0
Drug-related Deaths	0

Adverse Events of Special Interest	All Grades	Grade 3 or 4
Pneumonitis/ILD	0	0
AST increased	0	0
ALT increased	0	0
All ocular AEs	4 (57.1%)	1 (14.3%)

Protocol Number: ACE-Breast-03

Status: Active, not recruiting

Contact: breast03trialinquiry@ambrx.com

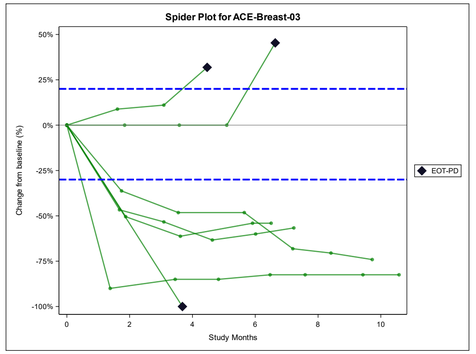
Clinicaltrials.gov Identifier: NCT04829604

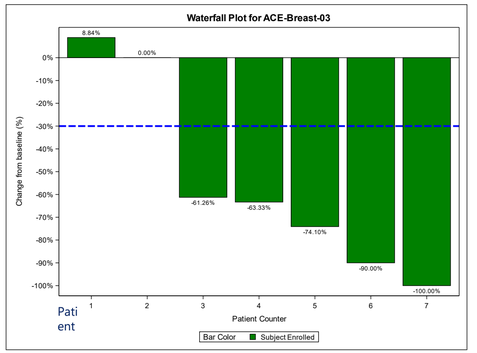
EudraCT Number: 2021-001246-36

Appreciation:

We thank all of the patients who have enrolled in the ACE-Breast-03 trial. We appreciate all of the hard work of our Investigators and site staff who have contributed their knowledge and expertise in the design and conduct of this trial.

Efficacy Results





Key Takeaways

- ARX788 provided ***clinical benefit*** to patients previously treated with T-DM1 who had disease progression
- 4/7 patients also previously received HER2 TKI treatment
- The confirmed objective ***response rate*** (ORR) was 57.1% (4/7 pts) and an unconfirmed ORR of 71.4% (5/7 pts)
- The disease ***control rate*** (DCR) was 100% (7/7 pts)
- Treatment with ARX788 remains ongoing with the median time of ARX788 therapy of 7.2 months
- No drug-related SAEs. ARX788 was ***well-tolerated***, and AEs were manageable

Conclusion

In this small cohort of patients previously treated with T-DM1 who had disease progression, ARX788 had a ***manageable*** AE profile and ***demonstrated*** promising clinical activity (confirmed ORR 57%; DCR 100%).

Previous Treatment History

Patient No.	Prior therapies
Patient 1	Trastuzumab, Docetaxel, Paclitaxel, T-DM1, Capecitabine, Lapatinib, Trastuzuma0b , Eribulin, Vinorelbine
Patient 2	Trastuzumab, Pertuzumab, Docetaxel, T-DM1, Lapatinib, Capecitabine, Trastuzumab, Paclitaxel, Eribulin
Patient 3	Docetaxel, Carboplatin, Trastuzumab, Tamoxifen, Letrozole, Pertuzumab, Trastuzumab, Paclitaxel, Exemestane, T-DM1, Capecitabine, Trastuzumab, Neratinib
Patient 4	Carboplatin, Docetaxel, Pertuzumab, Trastuzumab, T-DM1, and Trastuzumab
Patient 5	Carboplatin, Docetaxel, Trastuzumab, Tamoxifen, Letrozole, Lapatinib, Capecitabine, T-DM1, Trastuzumab, Fulvestrant, Everolimus, Exemestane, Bevacizumab
Patient 6	Cyclophosphamide, Docetaxel, Pertuzumab, Trastuzumab, T-DM1
Patient 7	Cyclophosphamide, Epirubicin, Fluorouracil, Paclitaxel, Trastuzumab, Paclitaxel, Trastuzumab, Pertuzumab, T-DM1, SHR-A1811 Investigational Drug (HER2 New Antibody Drug Conjugate)

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