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 progression. The HER2-targeted ADC 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 disease progression occurred in all patients, requiring additional therapeutic options. The use of second-generation anti-HER2 ADCs using alternative molecules is being investigated to overcome drug resistance.

Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients (N = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hormone-receptor status — no. (%)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>2 (28.6%)</td>
</tr>
<tr>
<td>Negative</td>
<td>5 (71.4%)</td>
</tr>
<tr>
<td>HER2 IHC</td>
<td></td>
</tr>
<tr>
<td>IHC 3+</td>
<td>5 (71.4%)</td>
</tr>
<tr>
<td>IHC 2+, IHC-positive</td>
<td>2 (28.6%)</td>
</tr>
<tr>
<td>Median number of targeted lesions on breast (range)</td>
<td>97 (16-253)</td>
</tr>
<tr>
<td>Median no. of previous cancer regimens (range)</td>
<td>5 (2-12)</td>
</tr>
</tbody>
</table>

Efficacy Results

Protocol Number: ACE-Breast-03
Status: Active, not recruiting
Contact: breast03trialinquiry@ambrx.com
Clinicaltrials.gov Identifier: NCT04829604
EudraCT Number: 2021-001246-36

Acknowledgment

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 contributed to patients’ clinical benefit (DCR) was 100%.)

Previous Treatment History

Patient No. Prior therapies
Patient 1 Trastuzumab, Docetaxel, Paclitaxel, T-DM1, Pertuzumab, Cetuximab, Bevacizumab
Patient 2 Trastuzumab, Pertuzumab, Docetaxel, T-DM1, Fulvestrant, Everolimus, Enzalutamide
Patient 3 Docetaxel, Carboplatin, Trastuzumab, Venetoclax, Letrozole, Pertuzumab, T-DM1, Everolimus, Trastuzumab, Exemestane, T-DM1, Pertuzumab
Patient 4 Carboplatin, Docetaxel, Pertuzumab, T-DM1, and Lapatinib
Patient 5 Carboplatin, Docetaxel, Trastuzumab, Venetoclax, Letrozole, Lapatinib, Carboplatin, T-DM1, T-DM1, Fulvestrant, Everolimus, Enzalutamide, Pertuzumab
Patient 6 Cyclophosphamide, Docetaxel, Pertuzumab, T-DM1
Patient 7 Cyclophosphamide, Epirubicin, Fluorouracil, Paclitaxel, Trastuzumab, Pertuzumab, T-DM1, T-DM1, ATRI1: Investigational Drug (HER2 Neo Antibody Drug Conjugate)

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

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%).

Conclusion

- 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
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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%).