Background

- Chemotherapy regimens for patients with MBC that offer robust efficacy while preserving patient quality of life are needed.
- Tesetaxel is a novel taxane that is taken orally Q3W with a low pill burden, no history of hypersensitivity reactions and improved activity against chemotherapy-resistant tumors.12
- Tesetaxel's improved pharmacologic properties include:
  1. High oral bioavailability (2018 ASCO Annual Clinical Trials Symposium, Berlin, Germany; Texas Oncology-Baylor Charles A. Sammons Cancer Center, US Oncology, Dallas, TX; 496 monotherapy; 63 in combination with capecitabine)
  2. Low pill burden (10.9 mg)
  3. Oral administration
  4. No history of hypersensitivity reactions

Preclinical and clinical studies support the effectiveness of a reduced dose of capecitabine when combined with a taxane; taxanes potentiate capecitabine's antitumor activity by up-regulating tumor levels of thymidylate phosphorylase, the enzyme essential for the activation of capecitabine.11,13 (Figure 3)

CONTessa

- CONTESSA is a multinational, multicenter, randomized, Phase 3 registration study of tesetaxel plus a reduced dose of capecitabine as a single agent against capecitabine alone in patients with HER2 negative, HR positive MBC (NCT03236674) (Figure 5)
- Key eligibility criteria are outlined in Table 2
- Eligible patients are stratified according to:
  1. Disease status (progression vs. absence of visceral disease)
  2. Geographic region (North America/Western Europe vs. Rest of World)
- Number of prior chemotherapy regimens for advanced disease (0 vs. 1)
- Tesetaxel and capecitabine dose reductions will be made in consideration of the known toxicity profile of each drug
- Cabapetaxin monotherapy arm dose reductions
- Capecitabine monotherapy arm to start at the FDA-approved dose

CONTESSA Study Design

- Tesetaxel 27 mg/m²
- Capecitabine 1,650 mg/m²

Target Enrollment

- Patients with HER2 negative, HR positive MBC who have received no more than one chemotherapy regimen for advanced disease and have received a taxane in the neoadjuvant or adjuvant setting
- Where indicated, patients must have had no disease progression, no evidence of unacceptable toxicity or disease control with or without a CDK 4/6 inhibitor
- N=600

BID = twice per day

Primary Endpoint: PFS assessed by an Independent Radiologic Review Committee (IRC)

- Designed (with 80% statistical power) to detect a 42% improvement in PFS (hazard ratio=0.57)

Secondary Endpoints:

- Overall survival, objective response rate assessed by IRC and disease control rate assessed by IRC

References

1. Stroyou et al., Cancer 2003;98(8):1459-66
2. Chan et al., 2006 EORTC-NCl-AACR Molecular Targets and Cancer Therapeutics Symposium
4. McEntee et al., Veterinary and Comparative Oncology 2003;12:105-112
5. Montasser, Toxicity, Stability and Bioavailability 1997
8. Taxotere (docetaxel) prescribing label
10. Trock et al., Journal of the NCI 1997;89(13):917-31
12. Fujimoto-Ouchi et al., Abstract TPS1106

Study Highlights

- Chemotherapy regimens for patients with MBC that offer robust efficacy while preserving patient quality of life are needed
- Tesetaxel is a novel taxane that is taken orally Q3W with a low pill burden, no history of hypersensitivity reactions and improved activity against chemotherapy-resistant tumors
- In a multinational, Phase 2 study, HER2 negative, HR positive MBC patients receiving tesetaxel as a single agent achieved a confirmed response rate of 45% with a low incidence of Grade ≥3 neuropathy and Grade 2 alopecia
- CONTESSA is a multinational, multicenter, randomized, Phase 3 registration study of tesetaxel plus a reduced dose of capecitabine vs. the approved dose of capecitabine alone in patients with HER2 negative, HR positive MBC
- Study enrollment initiated in December 2017, with planned enrollment of approximately 600 patients across 20 countries
- The primary efficacy endpoint is PFS assessed by IRC

Table 1: Tesetaxel's Unique Pharmacologic Properties

<table>
<thead>
<tr>
<th>Property</th>
<th>Tesetaxel</th>
<th>Paclitaxel</th>
<th>Docetaxel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral availability</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Pill burden</td>
<td>Low</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>No history of hypersensitivity reactions</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Table 2: Key Eligibility Criteria

<table>
<thead>
<tr>
<th>Key Inclusion Criteria</th>
<th>Key Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Have HER2 positive or triple-negative breast cancer</td>
<td>1. Have HER2 positive or triple-negative breast cancer</td>
</tr>
<tr>
<td>2. Did not receive a taxane in the neoadjuvant or adjuvant setting</td>
<td>2. Did not receive a taxane in the neoadjuvant or adjuvant setting</td>
</tr>
<tr>
<td>3. Received no number of endocrine therapies (e.g., palbociclib, exemestane)</td>
<td>3. Received any number of endocrine therapies (e.g., palbociclib, exemestane)</td>
</tr>
<tr>
<td>4. Received no targeted therapies (e.g., bevacizumab, erlotinib)</td>
<td>4. Received no targeted therapies (e.g., bevacizumab, erlotinib)</td>
</tr>
<tr>
<td>5. For locally advanced or metastatic breast cancer</td>
<td>5. Previously received capecitabine</td>
</tr>
</tbody>
</table>

FREE CONSULTATION

*All patients must meet full eligibility criteria as stipulated in the Study OD0-TE-06301 Protocol

* Nadir change based on sum of the diameters

Figure 1: PK Profiles of Paclitaxel and Tesetaxel

- Mean Plasma Concentration (ng/mL) vs. Time (hours) for Paclitaxel and Tesetaxel

Figure 2: Study TOB203 Tumor Change from Baseline in Target Lesions for HR Positive Patients Receiving Tesetaxel Q3W

- Tumor Change from Baseline (%) for Confirmed response, Stable disease, and Disease progression

Figure 3: Preclinical Evidence of Synergy when Combining a Taxane with Capecitabine

- Capcitabine at 2/3 MTD + Docetaxel at 1/15 MTD

Figure 4: Study Hypothesis and Objective

- The all-or-none effect of tesetaxel plus a reduced dose of capecitabine was generally well tolerated with minimal overlapping toxicity (Grade ≥3 neuropathy was 6%, Grade ≥3 hand-foot syndrome was 6%, Grade ≥3 diarrhea was 6%, Grade ≥3 alopecia, and no hypersensitivity reactions)

Figure 5: Study Design

- Multinational, Multicenter, Randomized
- Treated until progressive disease or unacceptable toxicity
- Capecitabine 2,500 mg/m² (1,250 mg/m² BID)
- Days 1-14 of a 21-day cycle

Table 1: Tesetaxel's Unique Pharmacologic Properties

- Oral availability: Yes
- Pill burden: Low
- No history of hypersensitivity reactions: Yes