A Phase II study of ANG1005, a novel, brain-penetrant taxane derivative, in breast cancer patients with brain metastases

Nancy Lin1, Lee Schwartzberg2, Santosh Kesari3, Anthony Elias4, Carey Anders5, Jeffrey Raizer6, Mark Kozloff7, Lalit Amri-Kordesani8

1 Dana-Farber Cancer Institute, Boston, MA; 2 The West Clinic, Memphis, TN; 3 University of California in San Diego Moores Cancer Center, La Jolla, CA; 4 University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC; 5 Northwestern University, Chicago, IL; 6 Triagels Memorial Hospital, Harvey, IL; 7 National Cancer Institute, Bethesda, MD.

Abstract

Background
- Brain metastases occur in 10-15% of independent breast cancer patients, but in 30-50% with HER2+ phenotype in hormone-resistant breast cancer.
- Currently, no targeted systemic therapies for brain metastases have shown significant survival benefits.

Objectives
- To assess the safety, tolerability, and antitumor activity of ANG1005 in subjects with HER2+ brain metastases.
- To determine the optimal dose and schedule of ANG1005.
- To evaluate the impact of ANG1005 on brain and systemic disease.

Methods
- Multicenter, open-label, single-arm study with 3 cohorts: ANG1005 550 mg/m², 650 mg/m², or 850 mg/m².
- Eligibility criteria: metastatic breast cancer with brain metastases, prior surgical resection, WBRT, or SRS, and KPS ≥ 70.
- Primary endpoint: Best intracranial response by RECIST 1.1.
- Secondary endpoints: Duration of response, OS, PFS, PFS-6, and PFS-12.

Results
- 80 patients enrolled: 28 patients in each arm.
- 69 patients evaluable for efficacy.
- Median PFS: 84 days in HER2+ patients (n=23).
- 9 (75%) patients in HER2+ arm had measurable brain lesions.
- 8 (100%) patients in HER2+ arm had measurable systemic lesions.
- Median OS: Not reached.

Conclusions
- ANG1005 had a measurable anti-cancer effect against brain metastases.
- ANG1005 demonstrated efficacy on extracranial tumors.
- Additional studies with ANG1005 as a therapy for metastatic brain tumors arising from breast and other cancers are warranted.

Study Design

Safety
- • Toxicities were assessed in 78 patients with prior surgical resection, WBRT, or SRS and KPS ≥ 70.
- • All patients with post-surgical resection, WBRT, or SRS were treated with ANG1005 550 mg/m².
- • All patients with prior surgical resection, WBRT, or SRS were treated with ANG1005 650 mg/m².
- • Toxicities were assessed in 10 patients with prior surgical resection, WBRT, or SRS and KPS ≥ 70.
- • All patients with prior surgical resection, WBRT, or SRS were treated with ANG1005 850 mg/m².

Key AEs Associated to ANG1005

- • No grade 5 toxicities were observed.
- • Grade ≥3 toxicities are shown in the Table 1.
- • Myalgia was the most frequent hematological event observed.
- • Grade ≥3 neuropathy was observed in 1 (2.6%) patient.
- • Grade ≥3 peripheral sensory neuropathy was observed in 8 (100%) patients.

Table 1: Summary of Grade ≥3 AEs in 3 ANG1005 arms

<table>
<thead>
<tr>
<th>Arm</th>
<th>N (%)</th>
<th>Grade ≥3 AEs</th>
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<tbody>
<tr>
<td>550 HER2- (n=28)</td>
<td>69 (2.6%)</td>
<td>0</td>
</tr>
<tr>
<td>650 HER2- (n=3)</td>
<td>100%</td>
<td>0</td>
</tr>
<tr>
<td>550 HER2+ (n=23)</td>
<td>100%</td>
<td>8 (100%)</td>
</tr>
<tr>
<td>650 HER2+ (n=7)</td>
<td>9 (23.1%)</td>
<td>9 (23.1%)</td>
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Efficacy
- • ANG1005 had a measurable antitumoral activity against brain metastases.
- • ANG1005 demonstrated efficacy on extracranial tumors.
- • Further studies on the potential of ANG1005 as a therapy for metastatic brain tumors arising from breast and other cancers are warranted.

Acknowledgements

For information about the currently ongoing ANG1005 development program please contact: BLawrence@Angiochem.com

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References
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