ONT-380 in the Treatment of HER2+ Breast Cancer Central Nervous System (CNS) Metastases (Mets)

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Case Series Description

ONT-380 is currently being evaluated in two ongoing phase II clinical studies (T + P) and a compassionate (T + P + doc) (Figure 1).

Here we present data from patients with asymptomatic CNS metastases treated with ONT-380 + 100 mg PO BD.

Case Study 1: Untreated/Asymptomatic CNS Metastases

Untreated, asymptomatic, lesions in patients without prior treatment histories of surgery to the CNS.

Study Treatments and Assessments

1. Patients treated with ONT-380 380 mg PO bid + T + P (10 mg/week x 1x4 EGFIC, 1390 mg/week FO PO BD x 1x2 EGFIC)

2. MRI screening at Cycle 2 and Cycle 6, then every 1.5 months

Response Assessment and Treatment Decisions per RECIST 1.1

1. CNS response defined as a 30% decrease in sum of the largest diameter (SLD) of CNS target lesions

2. CNS progression defined as a 25% increase from nadir and 5 mm absolute increase in the SLD of all target lesions, or uncontrolled progression in non-target lesions

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Safety Overview

- Majority of AEs Grade 1 or 2 in severity, with no Grade 3 diarrhea

- No significant changes in LVEF

- No treatment-related deaths

- No grade 3 or 4 CNS toxicity

- Overall survival of median and greater than 1 year

- Data from patients 1 to 16; 8 patients treated with T + P + doc; 10 patients treated with T + P

Case Study 2: Progressive CNS Lesions after Prior SRT

Progressive CNS lesions from prior stereotactic radiosurgery (SRS) treated with ONT-380 + T + P.

Study Treatments and Assessments

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2. MRI screening at Cycle 2 and Cycle 6, then every 1.5 months

Response Assessment and Treatment Decisions per RECIST 1.1

1. CNS response defined as a 30% decrease in sum of the largest diameter (SLD) of CNS target lesions

2. CNS progression defined as a 25% increase from nadir and 5 mm absolute increase in the SLD of all target lesions, or uncontrolled progression in non-target lesions

Summary and Conclusions

- Majority of AEs Grade 1 or 2 in severity, with no Grade 3 diarrhea

- Encouraging signs of activity in both systemic and CNS arms in a heavily pretreated population for all evaluated metastases

- Increase in size of target lesions (up to 10%); even in patients with and without prior history of CNS local therapy, with CNS tumor control of 6+ months in some patients

- Further study of ONT-380 alone or in combination with other agents is warranted.