Clinical efficacy of Intravenous OT-101 a TGF-β antisense and proposed confirmatory phase 2/3 trial in Pancreatic Cancer (PC)
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ABSTRACT

Objective: The purpose of this secondary endpoint analysis was to assess the various subgroups of the pancreatic cancer patients in the primary endpoint to define the clinical development pathway for OT-101, focusing on maximizing tumor reduction while extending the overall survival of patients in an approvable endpoint. Overall survival (OS) in terms of chemotherapies. Median OS of 1006 days with disease control as best response had extended OS with subsequent chemotherapy.

Secondary Endpoints for PO01

1. Study Objective: To assess OS in approvable endpoint to define the target population for subsequent confirmatory phase 2/3.

2. Primary Objective has been reported previously: to determine the maximum tolerated dose (MTD) and the dose limiting toxicities (DLTs) of two cycles of trabedersen administered every other week.

3. Secondary Endpoints: OS

RESULTS

Target Population

1. OT-101 exhibited promising single agent clinical activity as second line therapy in patients with advanced metastatic pancreatic cancer with a median OS of 6.1 mos for Oxitin-Oxit/GEM versus 4.8 mos for Oxitin/GEM. The OS proportion which would benefit the most from OT-101 was defined as end stage pancreatic cancer pts with poor performance score.

2. A 1-year survival rate (OS at 12 mos) of which is significantly higher than the 7% (8 of 117 pts alive) and 67% (11 of 17 pts alive) among comparable treatment groups with Oxitin/GEM and Oxitin/GEM-101, respectively.

3. The OS proportion which would benefit the most from OT-101 was defined as end stage pancreatic cancer pts with poor performance score.

Safety Analysis

1. About 10% (267 of 2600) of AEs that have been reported during the treatment phase of this study were assessed by the investigator to be either related (227 AEs) or possibly related (40 AEs) to OT-101. The study medication tolerability, while 82% (493 of 600 AEs) were assessed by the investigator to be either unrelated (227 AEs) or not related (366 AEs) to OT-101, or not assessed.

Proposed Phase 2/3 Confirmatory Trial

1. Target POPulation: Eligible stage IV pancreatic cancer pts with 4 or more metastatic sites (multiple disease sites). (primary choice)

2. Target POPulation: Eligible stage IV pancreatic cancer pts with 4 or more metastatic sites (multiple disease sites). (secondary choice)

CONCLUSIONS

1. Endpoints实现了 Clinical Phase III Study AP12009-001 of OT-101 in pancreatic cancer in order to identify the target population and clinical pathway for OT-101 in clinical development.

2. The following endpoints are being reported here:

a. Median OS in end stage pancreatic cancer pts with poor performance score.

b. Tolerability of OT-101 treatment excepted OS when followed with subsequent chemotherapy.

3. Maximum of 4 cycles of OT-101 is needed for the observed effect with subsequent chemotherapy.

4. Minimum toxicity is associated with intravenous delivered OT-101.

5. Safety Analysis: 9. About 10% (267 of 2600) of AEs that have been reported during the treatment phase of this study were assessed by the investigator to be either related (227 AEs) or possibly related (40 AEs) to OT-101. The study medication tolerability, while 82% (493 of 600 AEs) were assessed by the investigator to be either unrelated (227 AEs) or not related (366 AEs) to OT-101, or not assessed.

6. Among the 107 AEs considered as related or possibly related there were 2 SAEs which were considered as possibly related (1 SAE of gastrointestinal hemorrhage, 1 SAE of pancreatitis, both with outcome recovered). The remaining 105 AEs that were assessed as (possibly) related to trabedersen were non-serious.

In conclusion, OT-101 is a promising novel agent against TGF-β with clear clinical efficacy and potential capability in TME. Further testing of OT-101 against pancreatic cancer is needed.