A Phase 1b Study of Oraxol in Combination with Ramucirumab in Patients with Gastric or Esophageal Cancers Who Failed Previous Chemotherapy

Ming-Huang Chen1, Yee Chao1, Laura Tenner2, Noelyn Anne Hung3, David Cutler4, Douglas Kramer4, Rudolf Kwan4, Cheung-Tak Hung5, Wing Kai Chan4

1Department of Oncology, Taipei Veterans General Hospital, Taipei, Taiwan, 2Cancer Therapy & Research Center, University of Texas Health Science Center at San Antonio, USA, 3University of Otago, Dunedin, New Zealand, 4Athenex Pharmaceuticals, Buffalo, NY, USA, 5Zenith Technology Corporation Limited, Dunedin, New Zealand

BACKGROUND

- Oraxol consists of oral paclitaxel administered with the novel P-glycoprotein inhibitor encequidar (HM30181A) (15mg) which enables the oral absorption of paclitaxel. Ramucirumab (RAM) + intravenous paclitaxel is FDA approved 2nd line treatment of gastric cancer. Oraxol 200mg/m² days 1-3, weekly has similar exposure to weekly paclitaxel 80/m2 intravenously.
- This study was to determine the maximum tolerated dose (MTD) of Oraxol + RAM

METHODS

- 17 patients with gastric or esophageal cancers who failed prior fluoropyrimidine or platinum containing chemotherapies were studied.
- Dose escalation followed the standard 3+3 design:
  - Cohort 1: oral paclitaxel and encequidar 200mg/m² days 1-3, weekly.
  - Cohort 2: oral paclitaxel and encequidar 250mg/m² days 1-3, weekly.
  - Cohort 3: oral paclitaxel and encequidar 300mg/m² days 1-3, weekly.
  - RAM 8 mg/kg IV every 2 weeks.
- Dose limiting toxicity (DLT) were assessed by week 4.
- Adverse events (AEs) were assessed per CTCAE v4.03 and response by RECIST v1.1.

RESULTS

- Table 1 shows patient demographics and cancer diagnosis
- Table 2 summarises the AE, DLT data and reason for discontinuation
- Figure 1 shows waterfall plots of tumour response data
- Cohort 1: One grade-4 febrile neutropenia (DLT) occurred in 6 patients. Partial response (PR)=2/6, stable disease (SD)=1/6 and progressive disease (PD)=3/6.
- Cohort 2: Two DLT (grade-3 neutropenia with treatment delay (DLT) occurred in 7 patients. PR=3/6 and PD=3/6 in 6 evaluable patients.
- Cohort 3: Two DLT (grade-3 febrile neutropenia and grade-3 gastric hemorrhage) occurred in 4 patients.
- MTD of Oraxol & RAM: Oraxol 300mg/m² days 1-3, weekly in combination with RAM 8 mg/kg IV every 2 weeks.
- All patients in this study had complete recovery of their DLT.
- Oral paclitaxel PK did not increase significantly in Cohort-2 and Cohort-3. (See Table 3)

CONCLUSION

Based on the lack of significant increase in exposure to Oraxol at higher doses, with similar efficacy and DLT in Cohorts 1 and 2, the stage 2 of this study using Oraxol 200mg/m² Days 1-3, weekly + Ramucirumab 8 mg/kg every 2 weeks as in Cohort-1 has been initiated.