Phase I Study of DKN-01 in combination with gemcitabine (G) and cisplatin (C) in patients (pts) with advanced biliary cancer (ABC)

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Abstract #3930

Introduction

The ABC-02 Phase 3 trial has established gemcitabine/cisplatin as the standard of care for pts with advanced ABC. Further investigation is ongoing. Clinical trial in-study enrollment is complete. D + GC is well tolerated. Preliminary analysis of 27 pts revealed an overall response rate of 28.0% and a median progression-free survival of 6.0 months. Of 24 evaluable pts, 3 (12.5%) had a confirmed partial response (PR), 5 pts had stable disease (SD), and 1 pt had progressive disease (PD). Among 4 pts dosed at 150 mg D, 3 pts had SD, 1 pt had PD. Responses and SD have been durable. Patients with known HR or unknown, active HER2 + or HER2 - are currently being evaluated.

METHODS

• Study Part A: 2 cohorts, N=22; 150 mg and 300 mg D (n=11 each).
• Study Part B: 23 pts dosed at 300 mg D.

RESULTS

- 18 patients are evaluable for response; 3 pts had a partial response (PR), 5 pts had stable disease (SD), and 1 pt had progressive disease (PD). Among 4 pts dosed at 150 mg D, 3 pts had SD, 1 pt had PD.
- Responses and SD have been durable.
- 8 pts (36%) had D-related grade 3/4 TEAEs; 2 patients (9%) had grade 5 TEAEs: hypophosphatemia and acute kidney injury.
- All grade 3/4 TEAEs: asthenia (n=10), leukopenia, thrombocytopenia (n=3 each), anemia and hypophosphatemia (n=2). All grade 3/4 non-Hematologic TEAEs: nausea, vomiting, pneumonia, intracranial hemorrhage, sigmoid colon perforation, and hypophosphatemia.
- 3 patients had prior adjuvant G and/or C.
- 3 pts had prior chemoembolization (TACE) or photodynamic therapy, and lesions available for submission (sample taken ≤ 24 months prior).
- 1 pt had a prior resection of disease.
- 2 of 27 evaluable pts had a prior resection of disease.
- Overall, the combination of DKN-01 and gemcitabine/cisplatin appears promising and warrants further investigation.

Study Design

• Dose-escalating, open label, multi-center study evaluating the safety, MTD, and clinical activity in combination with gemcitabine/cisplatin.
• Eligible ABC pts: aged ≥ 30 years, ECOG PS 0-1, no prior treatment with ABC or chemotherapy for metastatic ABC, measurable disease per RECIST, histologically or cytologically confirmed carcinoma primary to the esophagus, esophagogastric junction, stomach, or a superficially invasive malignant melanoma.
• Cisplatin: 25 mg/m² Day 1 and gemcitabine 1,000 mg/m² on Days 1 and 8, given every 21 days.
• Study Part A consists of a standard 3 + 3 dose escalation design to identify the MTD, safety and efficacy of D in combination with G and C in pts with ABC.

Conclusions

- The ABC-02 Phase 3 trial has established gemcitabine/cisplatin as the standard of care for pts with advanced ABC. Further investigation is ongoing.

Discussion & Conclusions

DKN-01 and gemcitabine/cisplatin combination change was safe and well tolerated in all doses, the most frequently reported Grade 3/4 TEAEs were hematuria in nature. Preliminary analysis suggests robust clinical activity with many patients continuing to receive clinical benefit at the time of analysis; survival analysis is ongoing with the median follow-up time of 10.6 months.