A Phase 1 Study of E7386, a CREB-Binding Protein/β-Catenin Interaction Inhibitor, in Patients With Advanced Solid Tumors Including Colorectal Cancer

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Objectives

- E7386 is a novel small-molecule drug that inhibits the binding of CREB to β-catenin (transcriptional co-activator CREB-binding protein). It thereby modulating Wnt/β-catenin signaling (Figure 1).
- The Wnt/β-catenin signaling pathway is associated with the development of numerous types of cancer.

Design

- This was an open-label phase 1 study of E7386 in Japanese patients with advanced solid tumors including CRC.
- Entry criteria included: age ≥20 years, ECOG performance status (PS) 0 or 1, adequate organ function, and no prior anti-cancer treatment for at least 4 weeks. Patients with hormone-refractory prostate cancer were excluded.

Methods

- Preliminary Pharmacokinetic Parameter Results for E7386
  - E7386 is well tolerated at doses up to 100 mg BID—the dose selected for the expansion phase.

Efficacy

- Tumor responses were assessed using Response Evaluation Criteria in Solid Tumors (RECIST 1.1) by an independent radiology and/or pathologist.
- Grade 3/4 treatment-related adverse events are presented in Table 2.

Results

- Across doses, the overall objective response rate was 3.6% (95% CI 0.1–18.3%)
- One patient with small bowel adenocarcinoma had a partial response to 15 mg BID.

Safety

- Treatment-related adverse events were assessed using the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0.
- The most common grade ≥3 treatment-related adverse events were decreased appetite (3/28), nausea (2/28), vomiting (1/28), and fatigue (1/28).

Molecular Correlates

- Median weight was 67.1 kg (range 43.0–105.5)
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Conclusion

- Preliminary Pharmacokinetic Parameter Results for E7386
  - E7386 was well tolerated at doses up to 100 mg BID—the dose selected as the recommended dose for the expansion phase.

- Further investigations of safety, preliminary efficacy, pharmacokinetics, and biomarker analyses of E7386 are ongoing.

Acknowledgments

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References

- Kawazoe A et al. World J Gastroenterol. 2017
- J Clin Oncol. 2017
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Key Experimental Figure

- Figure 5. Circulating Tumor DNA Analysis in % and Percentages Change in Baseline of the Development of Tumors Over Time (0) of Patient With Small Bowel Adenocarcinoma, All With the Best Overall Response of Partial Response.