1733TiP - A Pilot Study of Oral Paclitaxel (ORAXOL) in Subjects With Cutaneous Angiosarcomas (KX-ORAX-010)

Herbert H Loong1, Robert Mennel2, Michael Wagner3, Teresa Tse1, Yat-ming Lau1, Candy Yuen1, Roxanne Moore4, Tom Wei-Wu Chen6, Chueh-Chuan Yen7, Robin L Jones8, Min-Fun Rudolf Kwan4, David Cutler4, Doug Kramer4, Wing Kai Chan4, Vinod Ravi5

Department of Clinical Oncology, The Chinese University of Hong Kong, Hong Kong SAR; 2Texas Oncology, Dallas, TX, USA; 3University of Washington Seattle Cancer Alliance, Seattle, WA, USA; 4Athenex Inc. Buffalo, NY, USA; 5The University of Texas MD Anderson Cancer Center, Houston, TX, USA; 6National Taiwan University Hospital, Taipei, Taiwan; 7Taipei Veterans General Hospital, Taipei, Taiwan; 8Royal Marsden and Institute of Cancer Research, UK

BACKGROUND

- Angiosarcomas are rare, aggressive and heterogeneous tumours accounting for approximately 2% of all soft tissue sarcomas. Only limited treatment options for advanced disease exist with poor outcomes (5-year survival rates 30 – 50%). Phase II trial and retrospective studies have shown that intravenous (IV) paclitaxel has efficacy in angiosarcomas.

- IV paclitaxel is associated with treatment-limited toxicities including peripheral neuropathy and hypersensitivity-type reactions due to the presence of Cremophor EL in the formulation.

- Paclitaxel has poor oral absorption due to active excretion by P-glycoprotein (P-gp) pump in intestinal cells. Encequidar (HM30181A) is a novel oral inhibitor of intestinal P-gp, which when administered with oral paclitaxel, enables the oral administration and systemic exposure of of paclitaxel.

- A clinical pharmacokinetic (PK) study showed that oral paclitaxel (205mg/m²) plus encequidar (15 mg) administered for 3 consecutive days per week can produce a paclitaxel exposure (AUC) similar to that of 80 mg/m² IV paclitaxel per week in cancer patients.

- Oral paclitaxel with encequidar was granted Orphan Drug Designation by the U.S. FDA for the treatment of angiosarcomas in 2018.

- We are currently recruiting patients on a multi-centre pilot study to investigate the efficacy, safety, and tolerability of oral paclitaxel with encequidar in patients with cutaneous angiosarcoma who have not been previously treated with taxanes.

- The first patient started dosing in December 2018

METHODS

- This is a single-arm, multi-centre, pilot study (up to 25 evaluable patients)

- Major inclusion criteria: eligible subject must have (i) cutaneous angiosarcoma that is not amenable to curative intent surgery; (ii) have not received taxanes for treatment of angiosarcoma; (iii) without metastases outside of local lymph node involvement; (iv) have not received wide-field radiotherapy to the pelvis ≤3 or limited-field radiation for palliation ≤3 months prior to oral paclitaxel with encequidar administration; (v) no active bleeding or bleeding diathesis requiring transfusions; (vi) known active viral or nonviral hepatitis or cirrhosis.

- Treatment period: Oral paclitaxel (205mg/m²) with encequidar (15 mg) to be administered once daily for 3 consecutive days every week from Weeks 1 through 25

- Extension period: From week 26, patients without disease progression are eligible to receive further treatment until study withdrawal criteria are met

- Tumour response measured by RECIST v1.1 at specified timepoints and safety assessments

- Primary objective is to determine the response rate (RR) within 6 months of initiation of treatment.

- Secondary objectives include: (i) safety and tolerability; (ii) PFS; (iii) OS; (iv) duration of- and (v) time to-best response.

STUDY SCHEMA