TPS9613 **Poster Session**

A phase II randomised study to evaluate the antitumour activity of roginolisib, a novel non-ATP competitive and allosteric modulator inhibiting PI3Kδ, in patients with metastatic uveal melanoma (OCULE-01).

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Background: Uveal melanoma (UM) is a rare malignancy that develops from melanocytes in the eye. At least half of the patients develop metastases, primarily in the liver, and survival outcome from the time of metastatic disease is poor. Patients with second or third line systemic therapy may have a median Overall Survival (OS) ranging from 7 to 12 months. The small molecule roginolisib (IOA-244) is a novel highly selective, non-ATP competitive, allosteric modulator targeting phosphoinositide 3-kinase delta (PI3Kδ). The clinical development of roginolisib investigates its role in PI3Kδ-dependent malignancies. PI3Kδ in solid tumours, including cutaneous and uveal melanoma. Based on previous non-clinical studies, PI3Kδ appears to be up-regulated in tumour cells through inflammation and cellular transformation. In addition to this tumour-cell intrinsic mechanism, roginolisib is designed to block tumour-cell extrinsic mechanisms, including T regulatory (Treg) cells, B cells, and, to a lesser extent, myeloid-derived immune cells. **Methods:** The study OCULE-01 is a Phase II open-label, randomised, parallel-arm, multi-centre study, which will assess the clinical efficacy of oral roginolisib as monotherapy against a control consisting of Investigator´s treatment in patients with metastatic UM who have progressed on prior first line treatment. Eighty-five patients will be enrolled across 20 sites in the EU, UK, and US. Patients will have progressed following at least 1 prior immunotherapy treatment. Patients will be randomised to one of 3 treatment arms; Arm 1: (n=50) IOA-244 80mg daily, Arm 2: (n=25) Investigator's choice of therapy, Arm 3: (n-10) IOA-244 40 mg daily. The primary objective is to assess the overall survival of roginolisib versus Investigators' choice of therapy. Secondary endpoints include PFS, OR, Safety, and Quality of Life impact. Correlative aims include assessing blood and tissue biomarkers (i.e. Treg, ctDNA, gene expression, proteomics etc.) for association with clinical benefit and radiomic analysis of imaging. A final analysis will be performed to assess efficacy after 72 patients become evaluable. Study Centres are currently being opened for enrolment. Clinical trial information: NCT06717126. Research Sponsor: iOnctura.