PHASE 1 STUDY OF ODM-203, A SELECTIVE DUAL FGFR/VEGFR INHIBITOR, IN PATIENTS WITH ADVANCED SOLID TUMOURS

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Introduction

ODM-203 is a small molecule with balanced inhibitory effects on both FGFR 1-4 and VEGFR 1-3 subtypes and also RET.1,2 The agent has an impact on patient survival in different tumour types such as bladder, breast, lung and gastric.3,4,5,6,7,8,9 While both VEGFR and FGFR are drivers for angiogenesis and consequently hallmarks of tumorigenesis. We present here the updated results of the ongoing phase I KIDES trial.

Study design

Figure 1. Dose escalation design of KIDES

Figure 2. ODM-203 Day 1 mean concentrations

Figure 3. Biomarkers of FGFR and VEGF pathways

Table 2. Common adverse events in >10% of patients on ODM-203

Table 3. Common adverse events in >10% of patients on ODM-203

Results

As of 1st Sept 2016 a total of 43 patients had been treated with ODM-203 with 8 weeks or disease progression. Ongoing cohorts are confirming the dose and dosing schedule and implementing a new formulation.

Table 1. Baseline characteristics

Table 4. Changes in bilirubin

Figure 4. Changes in bilirubin

Figure 5. ODM-203 best tumour response (RECIST)

Antimutual activity

Patients were generally not selected by molecular screening and tumour genetic profiling data is incomplete.

3 confirmed partial responses (per investigator) were seen with durable stable disease in a number of other patients. 2 patients have received ODM-203 treatment for >1 year.

In this cohort, the only dose reduction was for diarrhoea in 2 patients, and this was not related to PK or laboratory data.

Figure 6. Duration of treatment with ODM-203

Conclusions

• ODM-203 is a balanced FGFR1-4 and VEGFR1-3 inhibitor.
• Adequate exposure was achieved but was somewhat variable using the capsule formulation. A new formulation is being tested in the study.
• Adverse events reported were mostly typical for FGFR or VEGFR inhibitors. Anticipated phosphate and blood pressure increases were less pronounced than with selective inhibitors although may have been somewhat affected by dose interruptions due to bilirubin increase. Diarrhoea and mucocutaneous events occurred uncommonly after several weeks treatment, and responded to temporary discontinuation or dose reduction of ODM-203.
• Bilirubin increases due to UGT1A1 inhibition by ODM-203 were very common but not associated with other signs of liver injury and responded rapidly to dose reductions.
• Durational tumour responses have been seen in both FGFR aberrant and VEGF sensitive (FGFR negative) tumours, confirming clinically important activity on both FGFR and VEGF pathways.

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