Identification of an RNF43 mutant gastric cancer patient population with potential sensitivity to porcine inhibitor RXC004 and development of a complimentary ctDNA liquid biopsy assay for patient screening

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Introduction

RXC004 is a small molecule inhibitor of the overexpressed downstream transforming signaling pathway component RNF43 (Porcupine). RNF43 is required for efficient Wnt signaling, and loss of function mutations in RNF43 cause both Wnt and non-Wnt signaling to become constitutively active in a wide range of tumors, leading to an achievable predicted human efficacious dose following oral administration.

Objectives

- To identify patients with RNF43 mutant gastric cancers who may benefit from RXC004 treatment
- To develop a complementary liquid biopsy assay to detect RNF43 mutations in ctDNA
- To evaluate the safety and tolerability of RXC004 in patients with RNF43 mutant gastric cancers

Methods

- Genomic DNA was isolated from tumor biopsies and ctDNA was isolated from plasma using the TumorMutation ctDNA Test (NewGene, Biocytex, EU). ctDNA was sequenced using the benchtop MALDI-TOF mass spectrometer MALDI Biotyper (Bruker Daltonik, Germany)

Results

- RNF43 mutations were detected in 16/115 (14%) plasma samples
- The ctDNA ctDNA assay had a sensitivity of 54% and a specificity of 95%

Conclusions

- A ctDNA liquid biopsy assay has been developed for the detection of RNF43 mutations in gastric cancer patients
- The assay has a sensitivity of 54% and a specificity of 95%
- Patients with RNF43 mutant gastric cancer may benefit from RXC004 treatment