Proposed Study Design for a Miltuximab® Phase 1 Trial ^{89}Zr/^{177}Lu theranostic trial

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Background: Miltuximab® is a chimeric antibody targeting Glypican-1 which is overexpressed in prostate cancer and other cancers. Miltuximab® has shown promising targeting, safety and efficacy in radioimmunotherapy models of prostate cancer.

Methods: In a first in human trial, metastatic cancer patients (9 prostate, 2 pancreatic and 1 bladder) were dosed with unlabelled Miltuximab® followed by the infusion of 1mg/250MBq ^{67}Ga-Miltuximab®. Patients underwent whole body gamma and SPECT/CT scans up to 144 hours post-infusion. Standard of care imaging was performed at least 14 days before and after participation. Safety was evaluated by an external monitoring committee. Total organ exposure was determined by dosimetry of whole-body gamma scans. Antibody pharmacokinetics were also determined.

Results: 12 patients were enrolled into the trial. Miltuximab® was well tolerated and did not elicit any drug-related adverse reactions. Liver and spleen uptake of ^{67}Ga-Miltuximab® was observed from 30 min to 72 hours post dose. Pre-infusion of unlabelled Miltuximab® resulted in reduced liver accumulation and increased distribution in the rest of the body. Miltuximab® targeting to sites of active progressive disease was observed in certain prostate cancer patients who had failed enzalutamide treatment.

Dosimetry analysis combined with antibody pharmacokinetic data was used to establish safe dose limits for a Phase 1 ^{89}Zr/^{177}Lu Miltuximab® theranostic study.

Conclusions: The first in human for Miltuximab® demonstrated its potential for further clinical evaluation as a theranostic in prostate cancers and formed the basis for a Phase I imaging and therapy study planned for 2020. This study will use ^{89}Zr-labelled Miltuximab® to screen eligible patients and confirm tumour localisation, followed by treatment with ^{177}Lu-labelled Miltuximab®.

Conflict of interest:
None of the authors have any potential conflicts to disclose.

Funding acknowledgments:
Funding for the present work was provided by Glytherix Ltd