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Feasibility of establishing renal cancer patient-specific 'tumouroids' as personalised treatment screening tools

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Introduction & Objectives: Personalised medicine aims to tailor clinical management to the individual patient. We developed an in vitro 3D tumour model – tumouroid – which closely mimics the in vivo tumour microenvironment. Our aim was to test the feasibility of generating patient-specific renal cancer tumouroids to be used as personalised platforms to test drug response.

Materials & Methods: Adult subjects with suspected or confirmed renal cell carcinoma (RCC) were prospectively enrolled at a UK tertiary centre. Multiregional tissue samples were collected after surgery, cells were extracted and grown in 2D culture. Tumouroids were manufactured by seeding cells into collagen type I hydrogels with added collagen IV, laminin and fibronectin and then subjected to plastic compression using the RAFT^{TM} method to create dense tissue mimics (Lonza, UK). Tumouroids were cultured and treated with Pazopanib (10-40μM). A gene panel was used to confirm the presence of RCC related mutations. Response to treatment was assessed using metabolic assays (CellTiter Glo) and immunofluorescent staining for morphological characterisation in 3D, using microscopy. Treatment responses were calibrated against previously determined cell line tumouroid parameters, as strong (~50%), partial (~25%) and non-responders (~10%). Ethics: UK REC 17/LO/1744; Trial registration: NCT03300102; Funding: NIHR i4i.

Results: Fifteen participants provided informed consent for tissue donation, sampling was conducted in 12. One participant with a postoperative diagnosis of epitheloid angiomyolipoma was withdrawn. Out of 11 included participants (5 stage I, 1 stage II, 3 stage III, 2 stage IV), 7 were diagnosed with clear cell RCC, 3 with papillary RCC and 1 with unclassified RCC. Tumouroids from 9 participants (>80% success) were grown and treated, in one case tumouroids from both the primary and the metastatic site were successfully established. Three patient-derived tumouroids, including two established from samples from the same participant, displayed strong response, 1 was a partial responder, and 6 were non responders.

Conclusions: This preliminary study demonstrates the feasibility of generating renal cancer patient-specific tumouroids in a timely fashion, with a high rate of success. Importantly, the parameters used were able to differentiate between responders and non-responders. The tumouroid technique has the potential to be developed as personalised tool to direct systemic therapy for renal cancer patients.