

➔ KIDNEY CANCER

NOVEL DRUG FOR RENAL CELL CARCINOMA

AGS16F—a novel antibody–drug conjugate (ADC)—shows promise for the treatment of renal cell carcinoma (RCC), according to new research.

ADCs are designed to deliver a cytotoxic agent directly to the tumour, while sparing normal tissue. “The specificity of an ADC arises from the antibody component, which binds an antigen that ideally, is highly expressed in tumour cells and minimally or not expressed elsewhere,” explain Doñate and co-workers. The ADC AGS16F is made up of a monoclonal antibody against human ENPP3 conjugated to the microtubule-disrupting agent MMAF. ENPP3 is a basophil activation marker, expression of which has been reported in neoplastic mast cells, acute basophilic leukaemia, some colon cancers, and neoplastic bile duct cells.

Using immunohistochemical techniques, Doñate *et al.* showed that ENPP3 mRNA was highly expressed in clear cell RCC samples: 93.7% of these tumour samples were positive for ENPP3 and 83.9% showed high expression. ENPP3 was also expressed in papillary RCC and hepatocellular carcinoma, but high expression was less frequent in these tumour samples. ENPP3 mRNA expression was minimally expressed in normal tissues, with the exception of the kidney.

Doñate *et al.* demonstrated that AGS16F inhibited tumour growth in three different xenograft models of clear cell RCC. In their paper, they also describe the mechanism of action, whereby AGS16F localizes to tumours, forms the active metabolite Cys-mcMMAF, and induces cell cycle arrest and apoptosis.

“The data ... identify ENPP3 as a novel target against RCC and AGS16F as a potential ADC for the treatment of patients with RCC,” say the authors. They note that four other ADCs, all against CD70, are at different stages of development for RCC therapy.

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ORIGINAL ARTICLE Doñate, F. *et al.* AGS16F is a novel antibody drug conjugate directed against ENPP3 for the treatment of renal cell carcinoma. *Clin. Cancer Res.* <http://dx.doi.org/10.1158/1078-0432.CCR-15-1542>