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Generic MUC1 Epitope for Targeted Alpha Therapy of Metastatic Cancer

The limitations of many systemic cancer therapies are that they are not potentially curable and recurrence is common. In particular, radio-immunotherapy with beta emitting radioisotopes is not curative and most vectors are cancer type specific. To overcome these limitations, new therapies are needed that are potentially curative, have minimal adverse events in humans and preferably have generic application to many cancers. These objectives could be met by targeted alpha therapy (TAT) using the C595 MAb against the cancer expression epitope (CE) of the MUC1 receptor, labelled with an alpha emitting radioisotope to form the alpha immunoconjugate (AIC).

In this paper, preclinical testing of the 213Bi-C595 AIC is reviewed for prostate, ovarian and pancreatic cancers, all of which are found to express the targeted MUC1-CE epitope. We have investigated the role of this unique AIC for control of these cancers by preclinical in vitro and in vivo studies of labelling yields, stability, in vitro cytotoxicity, efficacy and toxicity response in preclinical TAT.

Results show conclusively that normal tissues have minimal expression of the MUC1-CE epitope and that the alpha-immunoconjugate can selectively kill cancer cells in vitro and inhibit the development and growth of tumours in vivo in a dose dependant way. As such, generic targeted alpha therapy against the MUC1-CE epitope has potential for the clinical management of epithelial cancers that express this epitope.

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