SELECTIVE CYTOTOXICITY OF ABERTRANTLY GLYCOSYLATED MUC1 BINDING-PS1 PHOTOIMMUNOCONJUGATES FOR OEOSOPHAGEAL ADENOCARCINOMA TARGETED PHOTODYNAMIC THERAPY IN PRIMARY AND METASTATIC DISEASE

doi:10.1136/gutjnl-2012-302514d.13

1M A Butt, 3,4 J Stamati, 2 H Pye, 3 G Yahioglu, 1,2 R J Haidry, 3 O Oukrif, 2 M R Novelli, 3 M P Deonaran, 2 L B Lovat. 1National Medical Laser Centre, University College London, London, UK; 2University College Hospital, London, UK; 3Recombinant Antibody Therapeutics Laboratory, London, UK; 4PhotoBiotics Ltd, Imperial College London, London, UK, 4University College London, London, UK

Introduction Targeted photodynamic therapy (PDT) has the potential to overcome current limitations of PDT agents by offering specific tumour kill with reduced side effects. We have previously shown expression of AG-MUC1, an epithelial cancer target bound by the antibody HuHMFG1, in patients with Barrett’s with dysplasia, oesophageal adenocarcinoma (OA) and on OE19, an OA cell line. We have recently developed and characterised photoimmunocojugates (PIC) of HuHMFG1 with the photosensitisier PS1 to specifically target PDT to OA. This is the first study to test the cytotoxic efficacy of HuHMFG1:PS1 PIC’s against cancer cells in vitro. Methods Hu-HMFG1 was conjugated with PS1 (PhotoBiotics) using recently optimised methods. Binding of the HuHMFG1:PS1 PIC to the cancer cell lines SKOV-3 (ovarian), MCF-7 (breast), OE19 (oesophageal) and HT-29 (colon) was examined with flow cytometry and analysed with FlowJo software. The efficacy of HMFG1:PS1 PICs on these lines were compared with equivalent free PS1 in the presence or absence of laser activation. Power was set to a clinically relevant light dose. Cell viability was measured with standard MTS assay and the plates read on an ELISA plate reader at 490 nm.

Results Flow cytometry confirmed binding of HMFG1:PS1 PIC to SKOV-3, OE19 and MCF-7 but not HT-29 cells. Cell viability counts in all plates were initially corrected for untreated plate controls and then plotted on a log scale to produce dose response curves. This confirmed significantly superior cytotoxic efficacy of HuHMFG1:PS1 over PS1 in SKOV-3 (F=104.93, p=0.00051) and OE19 (F=11.13, p=0.0125), and a trend towards effect for MCF-7 (F=3.15, p=0.116) cells using linear regression analysis and an F test to compare treatments. HuHMFG1:PS1 did not kill HT-29 effectively over control (p=0.84) or differ significantly from PS1 in its efficacy (F=0.155, p=0.71) confirming cytotoxicity to be limited to HuHMFG1 expressing cells.

Conclusion This pilot study is the first to successfully demonstrate binding and potential cytotoxicity of targeting HuHMFG1:PS1 PICs against OA cells in vitro. Absence of photosensitisier effect in the negative control (HT29 cells) confirmed selective cytotoxicity of HuHMFG1:PS1 to AG-MUC1 expressing cells. We further demonstrated that HuHMFG1:PS1 can effectively kill other AG-MUC1 expressing tumours which have historically been treated with HuHMFG1 related therapies.

Competing interests None declared.

POLO-LIKE KINASE 1 EXPRESSION PREDICTS ANEUPLOIDY IN THE BARRETT’S METAPLASIA-DYSPLASIA-ADENOCARCINOMA SEQUENCE

doi:10.1136/gutjnl-2012-302514d.14

1M A Butt, 1,2 R J Haidry, 3 O Oukrif, 2 H Pye, 2 J Stamati, 3 G Yahioglu, 2 M Rodriguez-Justo, 1,2 R Banks, 2,3 M P Deonaran, 2 L B Lovat. 1National Medical Laser Centre, University College London, London, UK; 2University College Hospital, London, UK; 3Research Department of Pathology, University College London, London, UK, 2University Hospital Lewisham, London, UK

Introduction There is increasing attention on the integration of targeted agents for oesophageal adenocarcinoma (OA) therapy. The most notable example of success of oesophagogastric targeted therapy was the addition of a HER2 targeting agent in the Phase III ToGA study. However, there is limited data on the expression of HER2 in the Barrett’s metaplasia-dysplasia-OA sequence.
PWE-013 Selective cytotoxicity of aberrantly glycosylated MUC1 binding-PS1 photoimmunoconjugates for oesophageal adenocarcinoma targeted photodynamic therapy in primary and metastatic disease

M A Butt, I Stamati, H Pye, G Yahioglu, R J Haidry, D Oukrif, M R Novelli, M P Deonarain and L B Lovat

Gut 2012 61: A302
doi: 10.1136/gutjnl-2012-302514d.13

Updated information and services can be found at:
http://gut.bmj.com/content/61/Suppl_2/A302.1

Email alerting service

These include:

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/