Introduction

Patients with Barrett’s (BE) associated oesophageal adenocarcinoma (OA), show strong expression of the mucin MUC1, but binding is not specific to dysplasia or cancer. Aberrant glycosylation of MUC1 (AG-MUC1) accompanies the development of cancer in most epithelial tumours, exposing peptides hidden on normal cells. Humanised anti-human milk-fat globule-1 (Hu-HMFG1) antibody binds one of these regions. This study assesses expression of AG-MUC1 in the squamous-metaplasia-dysplasia-OA sequence, in OA specimens with infiltrated lymph nodes and in cancer cell lines.

Methods

54 paraffin-embedded oesophageal tissue specimens were selected from patients with squamous (n=5), non-dysplastic BE (NDBE; n=3), low grade dysplasia (LGD; n=6), high grade dysplasia (HGD; n=9) and OA (n=11). 11 OA resection specimens with clear margins containing tumour and infiltrated lymph nodes were also stained. Slides were immunostained with Hu-HMFG1 antibody and scored by an expert pathologist. Binding of HuHMFG1 to the cancer cell lines SKOV-3 (ovarian), MCF-7 (breast), OE-19, OE33 (oesophageal) and HT-29 (colon) was examined with flow cytometry using a secondary FITC-conjugated antibody and analysed with FlowJo.

Results

AG-MUC1 was significantly expressed (>33% positively stained cells) in 22% of HGD and 36% of OA specimens. Non-significant mild staining was seen in NDBE (100%), LGD (53%), HGD (44%) and OA (64%). In 27% of OA and 43% of HGD, adjacent squamous epithelium also stained. In surgically resected OAs, 45% stained significantly for AG-MUC1 in primary tumour. Of these, 80% stained significantly in related lymph nodes. All OA resection margins were clear of significant staining. On flow cytometry, binding was noted on SKOV-3, MCF-7, OE-19 but not HT-29 or OE-33.

Conclusion

This pilot study demonstrates AG-MUC1 to be upregulated in the BE metaplasia-dysplasia-OA sequence with significant staining limited to HGD and cancer. Although some squamous staining was noted, this was likely a field effect as no significant staining was noted in OA resection margins. In patients with significantly stained primary tumour, most had significant staining in infiltrated lymph nodes. Finally, with flow cytometry we identified the OA cell line, OE-19 expressed AG-MUC1 in preparation for in vitro studies. AG-MUC1 targeting with the antibody Hu-HMFG1 offers a novel strategy to target HGD and OA, including those patients presenting with metastatic disease.

Competing interests None declared.

Conclusion

This pilot study is the first to successfully conjugate HuHMFG1 with the photosensitisers PPa and PS1. These PICs could potentially selectively target photosensitisers to tissues of interest preserving the surrounding architecture during PDT. HuHMFG1:PS1 PICs have shown enhanced absorption in the red spectral region which will translate clinically into deeper tissue penetration than currently licensed photosensitisers. Further experiments are needed to both optimise the conjugation protocol and purify the product to GLP standards prior to clinical studies.

Competing interests None declared.
PWE-011 Aberrantly glycosylated muc1 as a potential therapeutic target for Barrett's with high grade dysplasia and primary and metastatic oesophageal adenocarcinoma

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