PWE-097

PHASE 2 AND PHASE 3 MULTICENTRE STUDIES DEMONSTRATE THE POTENTIAL FOR GLYCANS AS PREDICTIVE BIOMARKERS IN BARRETT'S OESOPHAGUS

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Introduction The prognosis of oesophageal adenocarcinoma (AC) is dramatically improved if detected early. Endoscopic surveillance currently relies on detection of dysplasia which lacks sufficient accuracy and alternative biomarkers are required.
Hypothesis Alterations in complex glycan structures on the oesophageal epithelium alter in the pathway to AC and can be used as biomarkers which can be detected using either antibody or lectin probes.
Aims (1) Identify and validate (EDRN phase 2) potential glycan biomarkers in BE. (2) Apply promising biomarkers to a case control cohort (EDRN phase 3).
Methods Gene set enrichment analysis for glycan pathways was applied to gene expression data from AC samples (n=55) and samples representative of the stages of progression to AC (n=21). External protein validation of candidate glycan genes was performed using immunohistochemistry on paraffin-embedded sections (n=80) from patients known to have a diagnosis of HGD or early AC within BE.
A retrospective longitudinal repository study using a nested case control approach was under taken on patients (n=9332) within the Northern Ireland Barrett's Registry of patients diagnosed with BE between 1993 and 2005. Cases (n=69) were defined as those who progressed to either AC or HGD (with independent histopathological confirmation by 2 experts) at least 6 months after their initial diagnosis; matched (by age, sex and initial year of diagnosis) in up to 5 controls (n=320). Characteristics between cases and controls were compared using independent t tests for continuous variables and χ^2 tests for categorical variables. Conditional logistic regression was conducted to estimate odds ratios.
Results Gene expression analysis shortlisted genes with the greatest altered expression in dysplasia and AC. 5 of the 6 top genes contribute to the synthesis of Lewis (Le) glycan groups. External immunohistochemistry validation confirmed sialyl Le^a and Le^x expression to increase significantly in the progression to AC on the apical epithelial membrane ($p<0.00001$) and in the epithelial cytoplasm ($p<0.001$). Increased sLe^a expression was partially at the expense of a decreased expression within the epithelial mucous globules ($p<0.01$).
Multivariate analysis of the nested case control cohort revealed the staining of sLe^a to be predictive of progression to HGD or AC ($p<0.001$).
Conclusion Glycan biomarkers can predict progression in biopsies taken at BE diagnosis in a phase 3 study. A phase 4 prospective screening study is warranted to confirm the sensitivity and specificity of these biomarkers.
Competing interests None.
Keywords Barrett's oesophagus, biomarker, CA19-9, EDRN, Glycans, Lewis, oesophageal adenocarcinoma, Phase III.