An analysis of Relative Telomere Length (RTL) during chemotherapy in patients with advanced gastro-oesophageal adenocarcinoma

Nicol Jeff Evans¹, Keith¹, James Paul¹

¹School of Cancer Sciences, University of Glasgow, Glasgow, UK

CAROLINE KELLY

ABSTRACT

OBJECTIVES

The primary objective of this study is:
(a) To analyse Relative Telomere Length (RTL) in blood samples taken from patients during chemotherapy for advanced gastro-oesophageal adenocarcinoma. This will allow us to determine if the baseline (pre-treatment) RTL correlates with tumour response i.e. to determine if the baseline RTL predicts tumours that are sensitive or resistant to chemotherapy.

The secondary objective of this study is:
(a) To analyse changes in markers associated with cellular senescence in blood samples taken from patients during chemotherapy for advanced gastro-oesophageal adenocarcinoma. These may include, but are not limited to, cathelicidin-related antimicrobial protein (CRAMP), EF-1a, stathmin, and chitinase 3-like protein 3.

The tertiary (exploratory) objectives of this study are:
(a) To analyse biomarkers of drug-induced changes in cellular function (e.g. apoptosis markers) in blood samples taken from patients during chemotherapy for advanced gastro-oesophageal adenocarcinoma.
(b) To analyse changes in senescence-associated biomarkers (e.g. micro-RNAs, immuno-profiling) in blood samples taken from patients during chemotherapy for advanced gastro-oesophageal adenocarcinoma.
(c) to analyse if any changes in RTL, or in genes involved in regulation of RTL, in blood samples taken from patients during chemotherapy for advanced gastro-oesophageal adenocarcinoma give an early indication of outcome (objective response, overall survival).

STUDY DESIGN

This will be a multi-centre, open, non-randomised study. Eligible patients will be those with advanced gastric or oesophageal adenocarcinoma who are about to undergo chemotherapy with either the ECX/ECF (epirubicin, cisplatin and capecitabine/5-FU) or EOX/EOF (epirubicin, oxaliplatin and capecitabine/5-FU).
regimens. Additionally, patients randomised in the NCRN REAL-3 study to receive EOX + panitumumab will also be eligible.

Prior to starting therapy, 20 mL of venous blood will be taken, on one occasion, for laboratory analysis. Further samples of 20 mL of venous blood will be taken on day 1 of each subsequent chemotherapy cycle and at the time of any subsequent documented disease progression. Where possible (depending on patient follow-up arrangements at participating Cancer Centres and Cancer Units), 20 mL of venous blood will also be collected at each subsequent follow-up visit after completion of chemotherapy until there is documented disease progression. Patient treatment, supportive care, and disease assessment will be unaffected by participation in this study. Buffy coats will be prepared and plasma will be frozen, and then samples will be transferred to the Translational Pharmacology Laboratory at the Wolfson Wohl Cancer Research Centre, University of Glasgow. Buffy coat samples will then be transferred for analysis of RTL to the Department of Medical Biosciences, Umeå University, Sweden. Analysis of the other biomarkers of telomere-associated genes, cellular senescence, and of biomarkers of drug-induced changes in cellular function, will be performed by the Translational Pharmacology Laboratory at the Wolfson Wohl Cancer Research Centre, University of Glasgow.

ATTACHMENTS

GI159_RTL_Advanced_Version6_05Sep2018.pdf