A New Endoscopic Device to Treat Oesophageal Cancer.

The majority of patients diagnosed with oesophageal cancer have a poor prognosis due in part to late stage diagnosis and the limited ability for patients to receive standard of care options such as surgery, chemotherapy or radiotherapy. For palliative treatment current methods of relieving oesophageal obstruction are often ineffective and problematic. Most patients remain symptomatic to some degree after stent therapy, worthwhile responses to chemotherapy/radiotherapy occur in only a minority of patients and major palliative operations are too intrusive for those with advanced diseases.

The research funded by the Oesophageal Cancer Fund at the Cork Cancer Research Centre is focused on enabling patients to receive localised endoscopic treatment of their cancer using a technology called electropermeabilisation. This involves short electrical pulses delivered directly to the tumour tissue rendering the local area temporarily porous and allowing for up to a 1000 fold increase in specific large chemotherapy drugs/molecules. The drug toxicity is localised to the tumour while healthy tissue in other organs remains unaffected. Relatively low drug doses are employed and the approach has been successfully applied to several other cancer types (malignant melanoma, glioma/brain, colorectal) to excellent effect in terms of tumour regression but also importantly in terms of the patient's quality of life after treatment.

This potential treatment option for patients will be provided as an endoscopic outpatient procedure conducted in less than 30 minutes. Current research is focussed on developed a device appropriate for the oesophagus and optimising the electrical pulses for application within the specific anatomy of foregut. In addition to this work has been conducted in preclinical models to demonstrate that electropermeabilisation can facilitate local drug delivery (drugs tested – bleomycin and cisplatin) and consequently a measure of the treatment efficacy is seen in murine oesophageal tumour regression (figure 1).

Data collected from preclinical studies using human oesophageal tumour cell lines (OE19 and OE21) has established an excellent response of this approach in resolving these oesophageal tumours when grown in mice. Study groups (8 mice per group) included control/untreated; electroporation alone; drug alone and drug plus EP/electropermeabilisation.

Figure 1: Two examples of oesophageal tumours treated with 'electropermeabilisation', on the left column OE19 and on the right OE21. The tumours were grown in nude immunocompromised mice, which allow human tumours to grow. The treatment procedure was injection of 0.2ml of bleomycin – 200IU directly into the tumour followed immediately by delivery of electrical pulses using a specially developed flexible electrode array – right hand side above.

Future work will complete the preclinical studies and examine if additional chemotherapy drugs have additional benefit when used in combination with electropermeabilisation. Ideal drug candidates ironically are large and poorly porous across the tumour cell membrane under normal circumstances, consequently making their chemotherapeutic efficacy alone relatively poor. Translation of the work to a large animal model is also required in order to validate the safety of electropermeabilisation in for foregut specifically with regard to any effect it may have on the cardiac cycle and to prepare the necessary safety documentation should the research progress through to Irish Medicines Board ethics approval. Patent approval is currently being sought for the novel device developed (not shown here for IP disclosure reasons) and it is anticipated that translation of the work to an oesophageal cancer phase I/II trial should be feasible within an 18-24month timeframe.

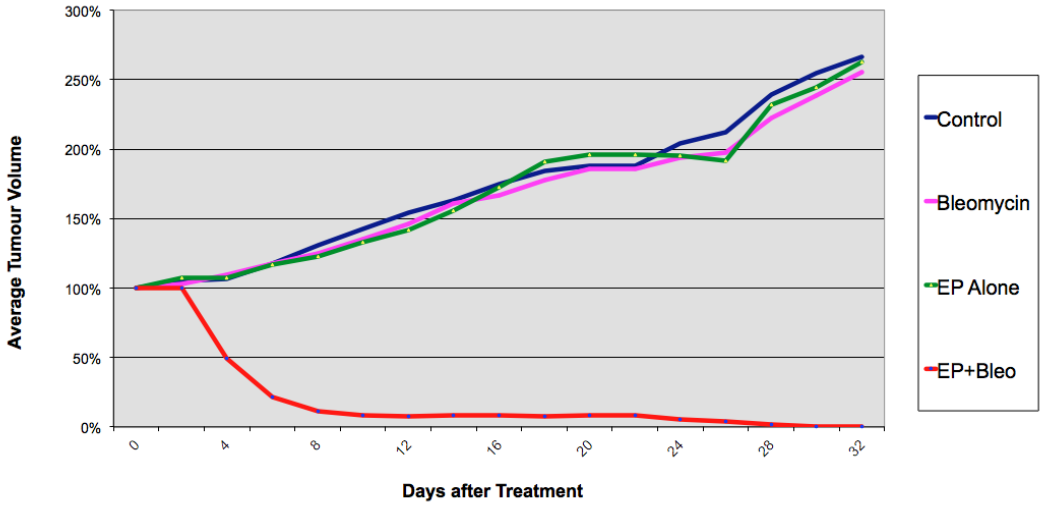

Figure 2: Effect of electropermeabilisation (EP) on OE19 human oesophageal tumour cell line grown in nude mice (as shown in figure 1). EP alone, drug (bleomycin) and the control groups all grew at equivalent rates while the EP plus drug group showed dramatic responses to treatment.