SCAF/19/01 - Development and evaluation of novel treatment strategies using immuneoncology agents in combination with radiotherapy in rectal cancer.

Rectal cancer affects 14,000 people in the UK each year. The standard treatment for many patients is radiotherapy to shrink tumours so that surgery has the highest chance of cure. This major surgery unfortunately has a significant risk of complications and is associated with long-term bowel, urinary and sexual dysfunction. Over two thirds of patients require a stoma at the time of surgery which, for one third of patients is permanent.

Recent years have seen a paradigm shift in rectal cancer management with appreciation that, in a small proportion of patients (10-20%), the radiotherapy component of treatment can completely eradicate the cancer. This has allows the concept of 'organ preservation' to develop where patients are managed non-operatively with active surveillance instead of surgery. For 75% of these patients, they achieve long term rectal preservation without the need for surgery.

My previous research has identified that the immune system may play a role in how tumours respond to radiotherapy. The idea is that radiotherapy may charge the immune system making immunotherapies more effective in mounting an anti-tumour response. There is a rationale for assessing this treatment, and I am leading a trial of Durvalumab immunotherapy in combination with radiotherapy in rectal cancer. However other immune cell types and their interaction with tumour cells are likely to be important and may lead to the development of other new treatments.

During this fellowship I will develop new strategies to better target and eradicate rectal cancer in combination with radiotherapy. My ultimate goal is to enable more patients to be managed with organ preservation strategies. I will study biopsy specimens from patients receiving radiotherapy to better define the immune and molecular changes related to treatment response and at the same time I will work with state-of-the-art pre-clinical laboratory based models of rectal cancer in which changes in the immune response to radiotherapy will be defined and harnessed for treatment benefit using immunotherapy treatments. Through these techniques I aim to develop strategies that can be used in clinical trials with patients.