ARIEL Trial - Plain English Summary of Research

Not all bowel (colon) cancers are the same. It is known that tumours which start in the right side of the bowel (right-sided), behave differently than those on the left side. Patients with advanced cancer (cancer that has spread to other areas) whose tumours are right-sided do not tend to live as long as those with left-sided. Right-sided tumours may not respond as well to drugs used to treat cancer. It is therefore important for researchers to find ways to improve the treatments and cancer outcomes for patients with right-sided tumours.

Anti-EGFR agents (cetuximab and panitumumab) are drugs that switch off the growth signals from the Epidermal Growth Factor Receptor (EGFR), which is a protein on the cancer cell which makes cancer grow and spread. We know that if a protein (RAS) is altered and becomes abnormal on the tumour then a patient will not respond to treatment with anti-EGFR drugs. Doctors now test the tumours of all patients and only treat those patients without these abnormal RAS proteins (RAS-wt) with anti-EGFR drugs.

These drugs are available to patients in the UK with RAS-wt advanced bowel cancer alongside chemotherapy. However in some patients with RAS-wt cancers the drugs do not work, despite the proteins being normal. This means that patients experience unpleasant side effects without any benefits. Cancer researchers have tried to understand why some patients benefit from anti-EGFR drugs, and some do not.

Research has shown that some patients with tumours that start in the right-side of the bowel do not respond to this treatment and in many countries anti-EGFR drugs are not recommended for patients with a right-sided tumour. UK data shows that some patients with right-sided bowel cancers respond well to anti-EGFR drugs, but some patients do worse and their cancer grows more quickly and the side effects are more severe, than when treated with chemotherapy alone. This creates a problem for oncologists and patients. An extra test to help identify patients with right-sided bowel cancer that are most likely to benefit from anti-EGFR drugs would help resolve this.

Further research has found different tumour proteins (EREG and AREG) that identify those patients most likely to respond to anti-EGFR drugs, including patients with right-sided bowel cancers. Further research on the importance of this protein is needed before it can be used in clinics.

This trial will form a part of this research. We will test whether EREG and AREG levels in the tumour can help doctors identify the patients with advanced right-sided bowel cancer for whom treatment with anti-EGFR drugs will be helpful. The patient's tumour sample can be tested for both RAS and EREG/AREG, meaning that there will be no need for an extra hospital visit. Only patients with high EREG/AREG levels measured in their tumour can enter the trial. Half the patients will be randomly selected by a computer to have chemotherapy, and half will be selected to have chemotherapy plus an anti-EGFR drug. At the end of

treatment we will be able to tell whether testing for a tumour's EREG/AREG level was able to predict which patients had a good response to using the anti-EGFR drug.

Results from this trial may lead to a new test to help oncologists and patients make better decisions about their treatment. Further research on tumour samples may help us find new ways to treat patients with right-sided bowel cancers.