Lay summary for completed research projects

| CCR No and Study Title: | CCR3065  
A study looking at a new treatment plan for locally advanced cancer of the pancreas (PERU) |
|------------------------|------------------------------------------------------|
| CI and Sponsor names:  | Dr Ian Chau  
The Royal Marsden NHS Foundation Trust |
| Study opening date:    | Study closing date:  
03/12/2009  
08/12/2014 |
| Proposal and Objectives: |  
This study looked at giving a  
- GemCap chemotherapy  
- followed by capecitabine oral chemotherapy and radiotherapy  
- with or without cetuximab a monoclonal antibody  

The treatments were given to patients with pancreatic cancer that had spread to surrounding tissue but not to other parts of the body. Patients were randomly selected to receive either gemcitabine, or a combination of gemcitabine and capecitabine called GemCap. If this helped to shrink the tumour, then they also had radiotherapy. This could also be given with capecitabine at the same time. Chemotherapy and radiotherapy together is called chemoradiation [Gloss/Chemoradiation].

In this study everyone had GemCap followed by chemoradiation. But half the people also had the drug cetuximab during radiotherapy. Cetuximab is a type of biological therapy called a monoclonal antibody. Monoclonal antibodies can seek out cancer cells by looking for particular proteins.

The main aim of this study was to see which treatment plan worked best for people with locally advanced pancreatic cancer. |
| Main Findings: | **Summary of results**  
While this study was going on another trial called LAP 07 published its results. LAP 07 showed there was no benefit to having chemotherapy followed by chemoradiation for locally advanced pancreatic cancer. And this had an impact on what the PERU study was looking at. Having considered the LAP 07 results the people who oversaw the study (the Data Monitoring Committee) decided to close the PERU study. Overall 17 patients were enrolled and treated with GemCap with 14... |
13 patients had initial benefit and were thus randomly chosen to enter one of the two arms of the study; i.e. 7 received chemoradiation in combination with cetuximab and the remaining 6 without it. After a median follow-up of more than 5 years, no significant difference in progression free survival (PFS) or overall survival (OS) was found between the two arms of the study, signifying that the two regimens had similar efficacy and tolerability. In this study we collected plasma samples of the patients and looked at the blood levels of a protein called miR-21. We found that patients with high baseline plasma miR-21 had significantly worse outcomes compared to patients with low miR-21. We were also able to validate that the circulating miR-21 levels were a reflection of similar expression of this marker in the tissue.

In summary, in this study it was shown that addition of Cetuximab to chemoradiotherapy following induction chemotherapy did not improve survival.

| Implications for practice/future research: | miR-21 is known to be associated with the development of pancreatic cancer, the aggressiveness of the tumour and poor outcomes for the patient. In this cohort of patients the trial investigators showed that miR-21 may have prognostic role in patients with locally advanced pancreatic cancer. Imaging-defined locally advanced pancreatic cancer may be further classified according to circulating miR-21 levels, as baseline miR-21 expression correlates with clinical outcome. In patients with low miR-21 expression, better clinical outcomes may be achieved with a multimodality approach, while patients with high miR-21 at baseline are likely to gain no benefit from consolidation chemo-radiotherapy. The investigators concluded that free plasma miR-21 reflects the expression of miR-21 in the cancer cells in the tissues and therefore can likely be used as a surrogate tumour biomarker. |