# Lay Summary for completed research projects

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<th>CCR No and Study Title:</th>
<th>Molecular analysis of tumour cells in pleural and ascitic fluid from patients with ovarian and other solid cancers CCR 2932</th>
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| CI and Sponsor names:  | Sponsor RMH NHS Trust  
CI: Prof Stan Kaye 5\textsuperscript{th} Dec 2007-22\textsuperscript{nd} Feb 2012  
Prof Kaye retired from the Gynae Unit  
CI: Dr Susana Banerjee 22\textsuperscript{nd} Feb 2012 – 21\textsuperscript{st} Dec 2017 (end of trial) |
| Study opening date:    | 5\textsuperscript{th} December 2007  
Study closing date:     | 21\textsuperscript{st} December 2017 |
| Proposal and Objectives: | The phosphoinositide 3-kinase (PI3K) pathway is one of mechanisms that cancer cells use to grow and divide. This may be an important target for drug treatment. Evidence that this pathway is abnormal in ovarian cancer is largely based on the analysis of surgical specimens sampled at diagnosis and may not reflect the biology of advanced ovarian cancer. Prof Kaye, Prof Udai Banerji and colleagues aimed to investigate PI3K signalling in cancer cells isolated from patients with advanced ovarian cancer. They used samples from fluid in the abdominal cavity called “ascites” as these were easier to collect from patients in routine practice compared to going through a biopsy procedure.  
**Objectives.**  
1. To characterise and isolate cancer stem cells from ascitic fluid obtained from patients with ovarian cancer. Having identified the stem cells, to then determine their potential contribution to drug resistance and aim to identify targets by which this can be overcome.  
2. To examine purified tumour cells and supernatants from malignant ascites or pleural effusions for molecular predictors of response to treatments.  
3. To perform in vitro studies of resistance modulation using freshly cultured ovarian tumour cells.  
4. To compare mutation in primary tumour from prospective or archival surgical specimens.  
5. To study mutation in circulating somatic DNA and compare it with isolated cancer cells.  
6. To evaluate the feasibility of metabolites in blood and ascites which could be used to study pharmacodynamic change.**Add objectives from protocol** |

Samples were collected between 2007-2013
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Main Findings:

Publication:

Ascites samples were analyzed from 88 patients, of whom 61 received further treatment. Cancer cells were separated from ascites, and examined. Levels of a protein: p-p70S6K levels were measured and found to be significantly higher in cells from 37 of 61 patients who did not respond to subsequent chemotherapy (0.7184 vs. 0.3496; P = 0.010), and this difference was greater in patients who had not received previous chemotherapy. PIK3CA and AKT mutations were present in 5% and 0% of samples, respectively. Amplification of PIK3CA and AKT2 and deletion of PTEN was seen in 10%, 10%, and 27% of samples, respectively. Mutations of PIK3CA and amplification of PIK3CA/AKT2 or deletion of PTEN did not correlate with levels of p-AKT, p-p70S6K, and p-GSK3β.

In patients with advanced ovarian cancer, there is an association between levels of p-p70S6K and response to subsequent chemotherapy. There is no clear evidence that this is driven specifically by PIK3CA or AKT mutations or by amplifications or deletion of PTEN.

Implications for practice/future research:

This study contributed to knowledge in the field of translational research in ovarian cancer by showing at the time, that ascites from patients can be used to assess molecular pathways which could be driving the disease. The findings that the level of a molecule called p-p70S6K in the PI3kinase pathway was significantly higher in ascites samples from patients who did not respond to subsequent chemotherapy led to further work in Prof Udai Banerji’s lab targeting the pathway. This led to a phase I clinical trial reported in 2018 in Annals of Oncology (TAX-TORC trial, Prof Udai Banerji) and a phase II muti-centre trial (OCTOPUS) due to report in 2019.

Further research- ascites from patients with gynaecological cancers can be collected in a subsequent study led by Dr Susana Banerjee (CCR3705, Biomarkers in Gynaecological Cancers) and clinical trials in order to help understand resistance to therapies.

Dissemination Plan:

Publication