



octo Newsletter

Oncology Clinical Trials Office

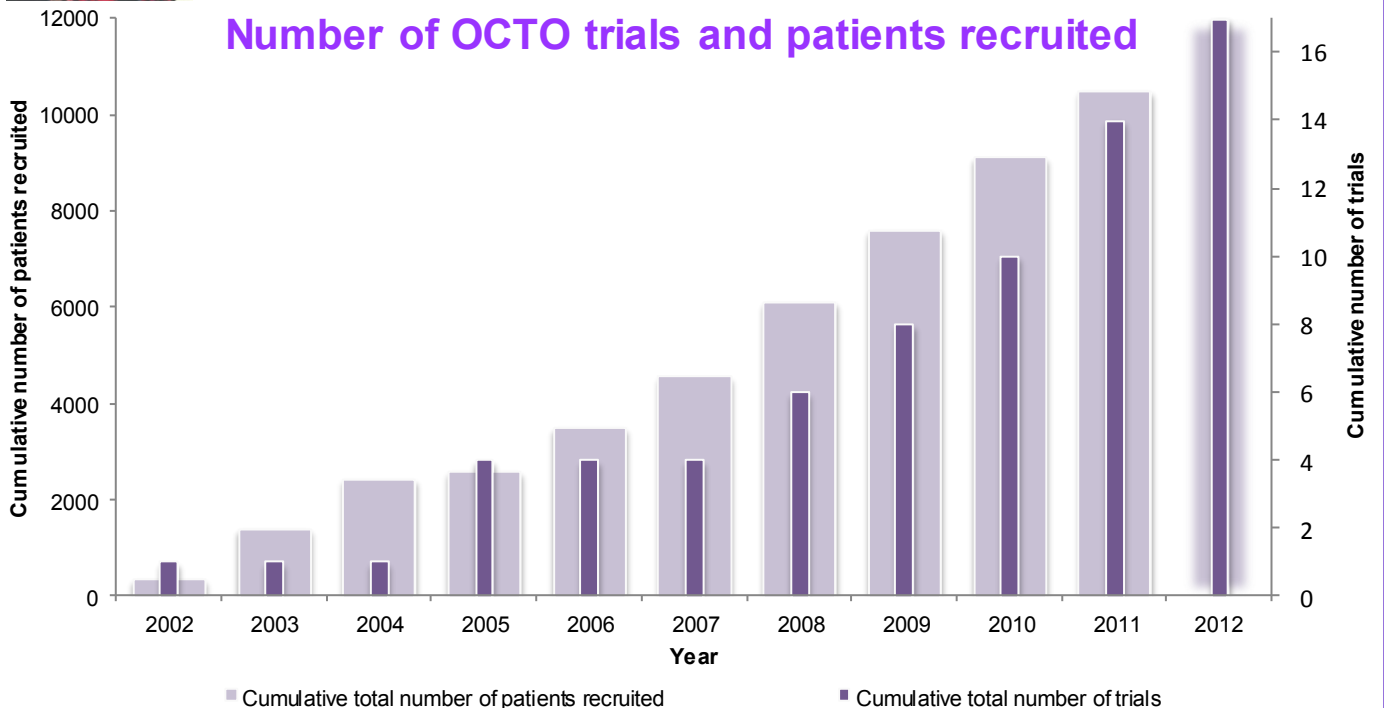
OCTO IS CELEBRATING ITS 10TH ANNIVERSARY!

When Emperor Nero's tutor and advisor, Lucius Annaeus Seneca, wrote: "A gem cannot be polished without friction, nor a man perfected without trials", he may not have been explicitly talking about cancer clinical trials! However his sentiment rings true with us in that, without the proper design and execution of well-thought through studies, we will never make the progress required to beat cancer. This was the impetus and vision behind the birth of OCTO just ten short years ago when Professor David Kerr brought just two members of staff with him to Oxford to build a cancer trials unit.

For two years OCTO was a one-trial unit running the VICTOR study. Over the next three years two further trials, QUASAR2 and AspECT were added. The last five years have seen an explosion in the breadth and depth of our portfolio, and we now run, or have in development, 17 trials ranging from Phase I to Phase III, across the spectrum of tumour types (colorectal, oesophageal, ovarian, breast, and melanoma) and a diverse array of interventions (chemotherapy, biological therapy, radiotherapy, radio-embolisation and surgery). A staggering 10,000 patients have been recruited to OCTO trials in the last decade.



So what are the secrets of our success? We believe these are threefold: a pragmatic approach to designing trials that are simple to run and recruit into, a willingness to listen to staff at our sites and respond quickly and appropriately to problems, and lastly and most importantly, YOU, YOU, YOU!! So thank you to everyone we have worked with over the last 10 years for your dedication and making this venture a success. To finish with another quote: "No one can whistle a symphony; it takes an orchestra to play it". May the next 10 years give us an interesting score to play across our orchestrated trials network!
With best wishes, Dr. Rachel Midgley (Director, OCTO)



MELANOMA PORTFOLIO CHIEF INVESTIGATOR PROF. MARK MIDDLETON SAYS...

Working with OCTO has been a fantastic experience. From a standing start they set up an early phase cancer trials team that has supported a diverse portfolio and realised nearly £2M in grant and industry funding. This has allowed us to bring trials for rarer conditions and/or genetically distinct groups to the UK, enhancing our reputation as a place to bring trials. In 2010 they set a new record for setting up and NCRN-AZ alliance study, going from funding approval to first patient in 6 months, despite this being OCTO's first early phase melanoma trial.

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University of Oxford, Old Road Campus, off Roosevelt Drive, Oxford, OX3 7DQ

QUASAR2 QUASAR 2 is an international study of capecitabine +/- bevacizumab in the adjuvant treatment of colorectal cancer. Recruitment to the study finished in October 2010; at that point 1,952 patients had been recruited to the study which fulfilled our primary endpoint requirements. 123 UK sites and 61 international sites took part in the study which is an incredible integrated academic global effort.

It is the only study that has looked at bevacizumab in combination with single agent capecitabine in the adjuvant setting. Given the problems with long-term neurotoxicity with oxaliplatin in this setting, this is an extremely important question and the results are awaited with interest.

Patients are now in follow-up and we are working towards a safety datalock at the end of 2011. We would like to say a massive thank you to all of our sites who put in an immense effort to send us their outstanding CRFs by October 2011. We are now working through all the data queries relating to these forms and hope that with your continued help we can be equally successful in resolving these.



AspECT AspECT is a chemoprevention trial, researching the effects of aspirin and esomeprazole (a PPI) on the progression of Barrett's oesophagus to oesophageal adenocarcinoma.

Recruitment of 2,500 patients closed in February 2009 and the patients will be treated and followed up for up to ten years. AspECT has some fantastic statistics:

- More than 35,000 individual CRFs received!
- 95.5% overall percentage of data returned!
- 17 sites with 100% data return!

The Trial Management Group will be showing their appreciation to sites with certificates for good data return and special commendation for sites who have returned >99% of CRFs.

Chief Investigator Prof. Jankowski presented AspECT at the AACR International Conference on Frontiers in Cancer Prevention Research in October 2011 and will present at the ASCO Gastrointestinal Cancers Symposium in January 2012.

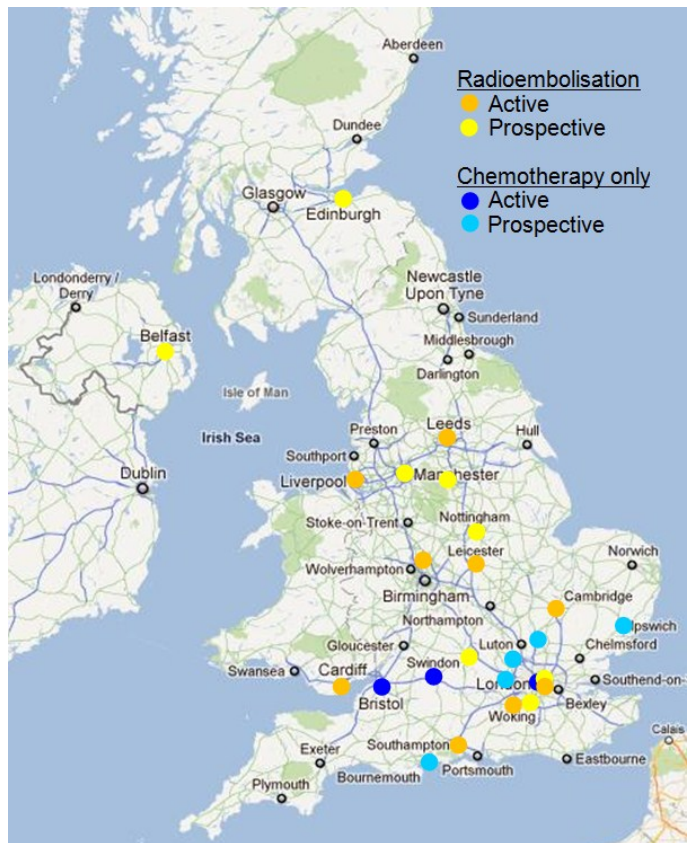
FOXFIRE The FOXFIRE trial is using radioactive SIR-spheres to treat liver metastases from colorectal cancer. 15 sites are now open with 6 to follow by the end of the year. 69 patients have been recruited.

In July 2011, NICE issued guidelines on the use of SIRT and specifically referred to the FOXFIRE clinical trial as a "well-designed clinical trial". It was used as an example for others to follow to answer important research questions that may impact the future treatment of patients with cancer.

We recently gained national press coverage from an interview with a FOXFIRE patient who was delighted with the outcome. His story was published in the Daily Mail and the Daily Telegraph and the Chief Clinician for Cancer Research UK gave an interview to ITV on the FOXFIRE trial. This extensive media coverage has led to a lot of interest from patients, doctors and the public. We hope that this increased interest will help to further raise the profile of this clinical trial.

We thank the Bobby Moore Fund at Cancer Research UK, SIRTEX Medical and Windsurfing for Cancer for their continued support of this large clinical trial.

FOXFIRE Trial Sites



AspECT Sites with 100% data return		
Ayr Hospital	New Cross Hospital, Wolverhampton	University Hospital, Coventry
Blackpool Victoria Hospital	Royal Alexandra Hospital, Paisley	Victoria Infirmary, Glasgow
City Hospital Birmingham	Royal Bournemouth Hospital	Weston General Hospital, Weston-Super-Mare
Croydon University Hospital	Southern General, Glasgow	Wycombe Hospital, High Wycombe
Hereford County Hospital	Stepping Hill Hospital, Stockport	York District Hospital
Neath Port Talbot Hospital	Tameside General Hospital, Ashton-under-Lyne	

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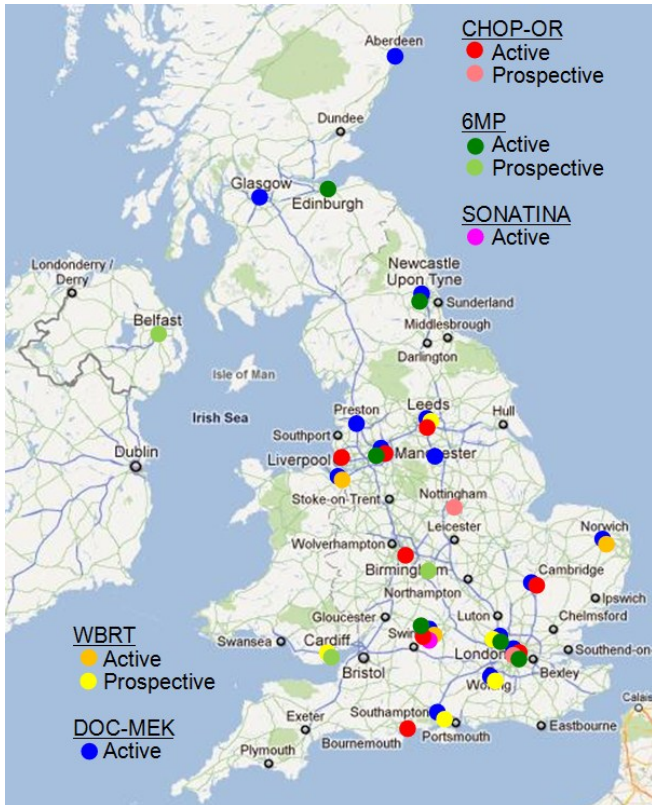
PHASE II TRIALS

The last year has brought an explosion in the number of earlier phase trials that OCTO is managing. We see this as an extremely important part of our expanding portfolio and we are always on the look-out for new investigators with excellent scientifically-driven novel ideas to take in to phase II studies.

The environment of phase II trials is very different compared to our large phase III studies, run as they are in only a handful of centres with a very defined patient cohort. However phase II trials are an extremely important incubator for the multicentre phase III practice-changing studies of the future. If you feel that your site would like to take part in any of our phase II trials and you have the patient population to fit, please do not hesitate to contact us.

6MP The 6MP trial aims to determine the response rate and toxicity of 6MP (mercaptopurine) with low dose methotrexate in patients with breast or ovarian cancer who have a BRCA mutation. 8 patients have currently been recruited at 10 open sites; we aim to open a further 2 sites in England and Northern Ireland by the end of 2011.

CHOP-OR In April 2011 OCTO opened its first haematology trial: the CHOP-OR trial is testing CHOP chemotherapy and monoclonal antibody Ofatumumab in patients with newly diagnosed Richter's syndrome, a rare but very serious transformation of chronic lymphocytic leukaemia. We are on target to reach the first recruitment target of 10 patients in 12 months, with 6 already recruited. GlaxoSmithKline is funding the trial with an educational grant and also providing the Ofatumumab.



SONATINA SONATINA is trialling nelfinavir as neo-adjuvant therapy for rectal carcinoma, aiming to establish safety and activity when administered before and during radiotherapy. 6 patients have been recruited to the initial safety cohort from a single site; in 2012 up to 10 sites will be activated to recruit 80 patients to the randomised trial.

DOC-MEK RADVAN PACMEL WBRT MELANOMA TRIALS

NOW WITH FOUR TRIALS, OCTO'S MELANOMA PORTFOLIO IS GOING FROM STRENGTH TO STRENGTH

DOC-MEK is a phase II trial of docetaxel with or without MEK-inhibitor AZD6244 in patients with wild-type BRAF metastatic melanoma. It is the OCTO's first trial to be opened under the AstraZeneca-NCRN collaboration. All sites (18) are now open, 44 patients out of the target 80 have been recruited and 120 patients have gone through BRAF mutation screening. We are confident that recruitment will be completed in March 2012.

The **WBRT in melanoma** trial is a non-CTIMP phase III trial of WBRT following local treatment of brain metastases from melanoma. OCTO are coordinating the UK sites on behalf of the Australia and New Zealand Melanoma Trials Group and 3 sites in the UK have been opened so far.

WE NEED YOU!
 Please consider your patients for this trial

WBRT Active Sites

- Churchill Hospital, Oxford
- Clatterbridge Centre for Oncology, Wirral
- Norfolk & Norwich University Hospital

WBRT Prospective Sites

- Mount Vernon Cancer Centre, Northwood
- Royal Surrey County Hospital, Guildford
- Southampton General Hospital
- St James's University Hospital, Leeds
- Velindre Cancer Centre, Cardiff

RADVAN is a phase II trial of whole brain radiotherapy +/- the radiosensitiser vandetanib in patients with brain metastases from melanoma. The trial was approved in August and we aim to open the first site in November 2011. A total of 10 sites across the UK will recruit 6 patients to the safety cohort and 80 patients to the randomised trial.

PACMEL is the newest addition to the melanoma trials portfolio. It is a randomised phase II trial of paclitaxel with or without a new selective allosteric inhibitor of MEK from GlaxoSmithKline in patients with advanced wild type BRAF melanoma. PACMEL has already been approved by CTAAC for endorsement by Cancer Research UK.

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SCOT SCOT is an international Phase III study designed to determine the optimal duration of chemotherapy for patients with colorectal cancer in terms of disease free and overall survival, by comparing 24 versus 12 weeks of chemotherapy of XELOX or OxMdG treatment.

OCTO works closely with Glasgow CTU to support sites in the UK, Australia and Spain and OCTO opened the last of its 80 UK sites in June 2011. The study aims to recruit 9,500 patients by March 2013; SCOT is currently recruiting over 100 patients per month and total recruitment is nearing 3,000. OCTO sites contribute about 50% of these patients.

Thank you to all the OCTO sites for their continued support and special thanks to Addenbrooke's, Royal United Bath & Southampton General who are currently the top 3 OCTO SCOT recruiters. CRF return is excellent with over 90% forms returned and entered. Thank you to everyone who is working hard on this progress.



The COG trial is testing gefitinib in patients with oesophageal cancer and progressive disease following chemotherapy. The primary aim is to assess overall survival with gefitinib (Iressa®) compared to placebo.

We are delighted to say that COG has now reached the recruitment target of 450 patients! Recruitment closed on 18 November 2011; patients will be followed up until at least March 2012 and the primary publication should be submitted later next year. We send our sincere gratitude to all site staff for their contribution; without them the trial would not have been possible.



EnROL

The EnROL trial compares conventional and laparoscopic surgery for CRC within the multimodal Enhanced Recovery Programme. EnROL opened in 2008 and has since randomised over 160 patients.

We are delighted that in October 2011 we achieved our monthly recruitment target but we still need 40 patients to hit our target by March 2012.

EnROL is OCTO's first surgical trial and it is one of the first multicentre surgical trials to be supported by Cancer Research UK. We anticipate that the results will be published in early 2013; we would like to thank all centres that have entered patients so far for their support.



DATACAP is a pilot study of optimal dose scheduling of capecitabine using mobile phone-based toxicity monitoring for patients with metastatic colorectal or breast cancer.

26 patients were recruited in 09/10; patients completed a symptom, temperature and dose diary twice a day via an application on a mobile phone. This information was transmitted in real-time, with high levels of chemotherapy toxicity prompting a self-care symptom management message on the phone or in severe cases a call from a nurse to give advice.

The trial concluded that it is possible to monitor chemotherapy toxicity in real-time using a mobile phone. We are pleased to say that the final study report is almost ready to be submitted to the Annals of Oncology.

RECENT PUBLICATIONS

- Goldberg, R.M. & Bertagnolli, M.M. *VICTOR spoiled?* J Clin Oncol. 2010; 28:4546-8
- Midgley, R.S., McConkey, C.C., Kerr, D.J. et al. *Phase III randomized trial assessing rofecoxib in the adjuvant setting of colorectal cancer: final results of the VICTOR trial.* J Clin Oncol. 2010; 28:4575-80
- Kerr, D.J. & Midgley, R. *Can we treat cancer for a dollar a day? Guidelines for low-income countries.* N Engl J Med. 2010; 363:801-3
- Kerr, D.J. & Midgley, R. *Defective mismatch repair in colon cancer: a prognostic or predictive biomarker?* J Clin Oncol. 2010; 28:3210-2
- Walther, A., Johnstone, E., Kerr, D. et al. *Genetic prognostic and predictive markers in colorectal cancer.* Nat Rev Cancer. 2009; 9:489-99
- Kerr, D.J., Dunn, J.A., VICTOR Trial Group et al. *Rofecoxib and cardiovascular adverse events in adjuvant treatment of colorectal cancer.* N Engl J Med. 2007; 357:360-9
- Quasar Collaborative Group, Gray, R., Kerr, D.J. et al. *Adjuvant chemotherapy versus observation in patients with colorectal cancer: a randomised study.* Lancet. 2007; 370:2020-9.

QUALITY ASSURANCE

Over the last 10 years the quality of OCTO's work has not gone unnoticed. We have conducted over 800 site visits, ensuring effective communication and excellent links with all our trial sites and ensuring adequate monitoring of the data we collect.

The QA team has expanded the number of SOPs: we started with 40 to cover core activities and we now have over 80, excluding trial specific SOPs and forms. We have also implemented recommendations from the Data Infrastructure Management Systems (DIMS) Project. Our recent Quality Manual emphasises our commitment to quality and our stakeholders and we look forward to continuing our quality work in the future.

AND FINALLY... thank you the Department of Oncology Finance and Personnel teams, and also those in Research Services for their sponsorship and contracts support, without whom we couldn't run our trials.

GENERAL ENQUIRIES

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OCTRU
Oxford Clinical
Trials Research
Unit



OCTRU is a UKCRC Registered Clinical Trials Unit
OCTRU is a joint venture between the Centre for Statistics in
Medicine (CSM) and the Oncology Clinical Trials Office
(OCTO) both based at the University of Oxford

