

NCRI Colorectal Cancer Clinical Studies Group

The Colorectal Clinical Studies Group has had another busy and successful year. We have launched four more trials Quasar 2, Xerxes, PICCOLO and COIN-B. We are very excited by the results from CR07, have a number of studies in development, which have been successful at the outline stage of CTAAC and developed our strategy for the next three years. In addition we are now seeing potentially important results from the molecular pathology sub-studies attached to FOCUS and QUASAR.

Three members of our group, Dr Ledermann, Professor Burn and Ms Stone have demitted office this year, and we thank them for their hard work and support over the recent years. We are in the process of appointing their successors. A number of members were reappointed to the Group.

Meetings

Our annual trialists' meeting was held at the Royal College of Physicians in March 2006. This was a new venue for us, which worked well. We had a very successful day with external speakers on the Human Tissue Act and the NHS Bowel Cancer Screening Programme. Over 350 delegates attended and the meeting was very well received. The highlight of the meeting was the first public airing of the results from CR07, which promise to change the management of rectal cancer across Europe and which were subsequently presented at ASCO

In November we held a two- day residential, which included meetings of the subgroups and also a half- day to plan our strategy for the next three years. We invited external facilitators and speakers and the strategy session generated a lot of discussion and ideas for the Group's future direction. Three particularly hot topics emerged: the need to continue to strengthen our links and negotiating status with pharmaceutical companies for access to new agents; the importance of managing and allowing equity of access to the tissue samples generated by trials; and optimising our use of new technologies. A summary of the Group's three-year strategy is given below.

The Group hosted a successful parallel session at the October 2005 NCRI Cancer Conference and will host a session at the 2006 conference.

Portfolio and accrual

Accrual to trials continues to rise each year, being 18.7% of incidence cases in 05/06, 14.2% in 04/05 and 10.3% in 03/04. Notable successes with respect to accrual are the NSCCG genetic epidemiology study, (6990 patients and 1785 controls to date) and the COIN trial in first line metastatic disease (600 patients in year 1).

There were a number of other notable successes amongst our trials this year:

- 1) Quasar 2 finally started recruitment and the number of centres recruiting patients is increasing rapidly
- 2) FACS has been amended to allow a CT scan at 1 year in the low intensity follow up group and this has helped boost recruitment. However there is still a long way to go!
- 3) ACT II, our chemoradiation trial for patients with anal cancer is due to close in early summer
- 4) FOCUS2 our trial of chemotherapy options for fail/elderly patients with advanced colorectal cancer has accrued ahead of target and will close in June 2006.

PICCOLO, a trial testing irinotecan modulation with ciclosporin and the novel targeted drug panitumumab, will open to accrual in the near future. The Group continues to develop new trials. The following have been successful at the outline stage of CTAAC and full submissions are being prepared

- 1) FOXTROT – a study of neoadjuvant chemotherapy and targeted receptor antibody in high risk operable colon cancer
- 2) ARISTOTLE – a phase III trial comparing standard vs novel chemo-radiation as pre-operative treatment for MRI defined locally advanced rectal cancer.
- 3) SCOT –Short Course Oncology Therapy – a study of adjuvant chemotherapy in colorectal cancer
- 4) ENROL - Enhanced Recovery Open Laproscopic Surgery for Colorectal Cancer

A summary of trials in the portfolio is given below.

Three year strategy

The Group's strategy will, in addition to the day to day business of developing and running clinical trials in the treatment and management of colorectal cancer and so become recognised throughout the world as a leader in colorectal clinical research focus on four themes, each with a number of specific actions

Strategy	Action
1. Develop a prevention and screening portfolio of studies (Overall lead RS)	1. Collect data and if possible DNA from stool based tests in the NBCSP
	2. Develop studies in the de novo population from the first round of screening
	3. Develop a study on the epidemiology of polyps
	4. Study different gene pools in different ethnic groups
	5. Link with other groups such as those working on heart disease and diabetes to develop interventions and lifestyles studies in the selected groups e.g. consider a study of the addition of folate to the diet and to include e.g. the incidence of colorectal cancer as a secondary endpoint in their trials
	6. Link with the Screening/Risk Management and Early Diagnosis Subgroup to ensure cross representation on subgroups, unnecessary competition and prevent duplication of effort
2. Develop a translational studies programme for the CSG (Overall leads MS)	7. Establish a funding source for the collection of tissues
	8. Establish an inter-trial group to determine how to optimise and maximise translational studies
	9. Develop templates for obtaining tissue and serum
	10. Develop a template for molecular/translational research and a facility to adjust a trial when it is up and

	running
	11. Develop and have funded a demonstrator project to look at the efficacy of SNPs deletions, RNA analyses etc
	12. Seek funding from Bioinformatics initiative to use web based technology to integrate pathology
	13. Resolve statistical issues arising from the use of predictive genes
3. Extend current and develop new relationships with pharma (Overall leadsTM)	14. Develop policies for working with Pharma
	15. Establish a team of negotiators to facilitate interactions with pharma
	16. Develop a phase I/II to phase III strategy that pharma companies can look at and decide whether or not to buy into
	17. Encourage more centre to be involved in large phase II studies leading to phase III trials
4. Resolve a number of governance issues (Overall leads JS)	18. Resolve issues to do with intellectual property rights, particularly in the case of collaborative trials with industry
	19. Clarify the need for DMCs and TSCs and establish an appropriate committee structure for trials within the portfolio
	20. Establish closer links between NCRI and NICE to inform funding decisions
	21. Ensure that access to subvention funding is understood and consistently applied
	22. Review the effect of removing subvention funding
	23. Establish a series of templates for "coal face issues" e.g. delays with R&D over imaging, follow up

Colorectal Cancer Group Portfolio

Acronym	Title	PI(s)	Status
ACT II	A Second UK Phase III Anal Cancer Trial: A Trial of Chemoradiation and Maintenance Therapy for Patients with Anal Cancer	Professor Roger James	Open
Big ET	Study Endothelin levels in patients with Colorectal Cancer	Mr David Hemmingway	Open
CAPP2 Study	A randomised controlled trial of colorectal polyp and cancer prevention using aspirin and resistant starch in carriers of HNPCC (Lynch Syndrome)	Professor John Burn	Open
CHRONICLE	Chemotherapy or no chemotherapy in clear margins after neoadjuvant chemoradiation in locally advanced rectal cancer. A randomised phase III trial of control vs. capecitabine plus oxaliplatin	Dr Rob Glynne-Jones	Open

CLASICC	Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer	Professor PJ Guillou	Closed
CLOCC	Randomised phase III study of the local treatment of liver metastases by radiofrequency combined with chemotherapy versus chemotherapy alone in patients with colorectal liver metastases.	Dr Jonathan Ledermann, Mr Graeme Poston, Professor William Lees	Open
COIN	A Phase III trial comparing either COntinuous chemotherapy plus cetuximab or INtermittent chemotherapy with standard continuous palliative combination chemotherapy with oxaliplatin and a fluoropyrimidine in first line treatment of metastatic colorectal cancer.	Professor Tim Maughan	Open
COIN-B	A two- arm randomised phase II trial of ntermittent chemotherapy with continuous cetuximab and of intermittent chemotherapy with intermittent cetuximab in first line treatment of metastatic colorectal cancer.	Dr Harpreet Wasan	In set up
CR07	A Randomised Trial Comparing Pre-Operative Radiotherapy and Selective Post-Operative Chemoradiotherapy in Rectal Cancer	Professor Phil Quirke, Dr David Sebag-Montefiore, Professor RJ Steele	Closed
Enhanced Recovery Trial	The Development of a Multi-Modal Care Pathway for Patients Undergoing Surgical Resection for Colorectal Cancer	Mr Robin Kennedy	Closed
EORTC/GITC CG 40983	Pre and Post operative chemotherapy with Oxaliplatin, 5FU/LV versus surgery alone in resectable liver metastases from colorectal origin	Dr Tim Iveson, Professor John Primrose	Closed
EXTRA	Evaluation of Xeloda Treatment with radiotherapy in Anal Cancer	Dr Rob Glynne-Jones	Open
FAB2	The impact of folate and its interaction with riboflavin on biomarkers in colorectal cancer risk	Professor John Mathers	Closed
FACS	A randomised controlled trial to assess the cost-effectiveness of intensive versus no scheduled follow-up in patients who have undergone resection for colorectal cancer with curative intent	Professor David Mant, Professor John Primrose	Open
FOCUS	A randomised trial to assess the role of irinotecan and oxaliplatin in advanced colorectal cancer	Professor Matt Seymour	Closed
FOCUS2	Drug treatment for bowel cancer: making the best choices when a milder treatment is needed.	Professor Matt Seymour	Open
Genetic Factors in Colorectal Cancer	The role of genetic factors in clinical outcome for colorectal cancer patients	Dr Angela Cox	Open
MERCURY	Magnetic Resonance Imaging and Rectal Cancer European Equivalence Study	Professor RJ Heald	Closed

NSCCG	Nationwide Study of Colorectal Cancer Genetics	Professor Richard Gray, Dr Richard Houlston, Professor Julian Peto	Open
OxaliCap-RT	Integrating intravenous oxaliplatin plus oral capecitabine with pelvic radiation for rectal cancer.	Dr David Sebag-Montefiore, Professor Matt Seymour	Open
PACT	Patient Preferences in Adjuvant Colorectal Cancer Therapy: a randomised crossover clinical trial comparing Bolus Fluorouracil/Leucovorin to Capecitabine as treatment for moderate to high risk resected colorectal cancer	Professor Matt Seymour	In set-up
PICCOLO (Panitumumab, Irinotecan & Cyclosporin in Colorectal cancer therapy)	A randomised clinical trial of treatment for fluorouracil-resistant advanced colorectal cancer comparing standard single-agent irinotecan versus irinotecan plus panitumumab and versus irinotecan plus cyclosporin	Professor Matt Seymour	in Set-up
	Biological sample from patients entering into the PICCOLO clinical trial	Professor Matt Seymour	In set up
QUASAR	Quick and Simple and Reliable A Study of Colorectal Cancer Treatment	Professor David Kerr, Professor Richard Grey	Closed
QUASAR 2	Multicentre International study of 5-Fluorouracil and Folinic Acid, vs. capecitabine plus irinotecan as adjuvant treatment of colorectal cancer	Professor David Kerr	Open
RICE	A phase I/II study of Radiotherapy, Irinotecan, Capecitabine then Excision for locally advanced rectal cancer	Dr Simon Gollins	Open
SIGGAR1	CT colonography, colonoscopy, or barium enema for diagnosis of colorectal cancer in older symptomatic patients.	Dr Steve Halligan	Open
ukCAP	A multi-centre double blind randomised controlled trial of Aspirin and / or Folate supplementation for the prevention of recurrent colorectal adenomas	Professor Richard Logan	Closed
VICTOR	Phase III randomised double-blind placebo controlled study of rofecoxib (VIOXX) in colorectal cancer patients following potentially curable therapy	Professor David Kerr, Professor MJ Langman	Closed
W.O.R.M.S	Does intraoperative fluid volume optimisation using oesophageal Doppler cardiac output measurement improve patient outcome and reduce length of stay after major bowel surgery?	Dr Howard Wakeling	Closed

Wales Polyp Study	A prospective case controlled study investigating the frequency of specific APC gene sequence variants and their relative contribution to the AFAP phenotype as compared to the previously known AFAP associated APC alleles in patients with multiple colorectal adenomas and their spouses or partners	Dr Sunil Dolwani	Open
XERXES	A phase I/II dose escalation study of intravenous cetuximab in combination with 5 day weekly oral Xeloda (capecitabine) and preoperative radiotherapy in rectal cancer.	Dr Rob Glynne-Jones	Open
	The efficacy of curcumin in patients with familial adenomatous polyposis – a pilot study	Professor Will Steward	In set up

Professor John H Scholefield, Chair