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Gastric cancer: after surgery chemoradiotherapy delivers no additional benefits over chemotherapy

In patients with gastric cancer postoperative treatment intensification with chemoradiotherapy (CRT) delivered no additional overall survival benefits compared to postoperative chemotherapy (CT), reported the phase III CRITICS study.

Perioperative (pre and postoperative) chemotherapy are the current standard treatments for gastric cancer, but studies have suggested postoperative chemoradiotherapy alone might improve outcomes.

Between January 2007 and April 2015 in the CRITICS study, 788 patients with stage Ib-IVa resectable gastric cancer all received preoperative chemotherapy consisting of three courses of epirubicin, a platinum compound (cisplatin or oxaliplatin) and capecitabine. Following surgery, patients were randomised to 'standard' treatment with another three courses of the CT regime (n=393) or to CRT (n=395), involving 45Gy in 25 fractions combined with weekly cisplatin and daily capecitabine.

Results showed five year survival rates of 40.8% in the chemotherapy arm versus 40.9% in the chemoradiotherapy arm (P=.99). The five year progression free survival rates were 38.5% for chemotherapy versus 39.5% for chemoradiotherapy (P=.99). There was a higher incidence of grade 3 or higher haematological

adverse events in the chemotherapy arm (44% versus 34%); but a higher incidence of gastrointestinal adverse events in the chemotherapy arm (42% versus 37%).

It is also noteworthy only 47% and 52% of patients completed postoperative CT and CRT respectively, with reasons for stopping including personal preference, progressive disease and toxicity in the preoperative setting.

"Based on the currently available data, no advice can be given on the preferred adjuvant strategy," said Marcel Verheij, the principal investigator, from The Netherlands Cancer Institute, Amsterdam.

Since less than half of patients could complete full treatment, he said, greater emphasis should be placed on preoperative strategies. Ongoing analyses, he added, may identify treatment benefits for specific subgroups.

Reference

Verheij M. A multicenter randomized phase III trial of neo-adjuvant chemotherapy followed by surgery and chemotherapy or by surgery and chemoradiotherapy in resectable gastric cancer. LBA-02

Janet Fricker, Medical Journalist.

Internal radiation found to be more effective in larger metastatic colorectal liver tumours

Metastatic colorectal cancer (mCRC) patients with baseline liver tumour burdens ($\geq 12\%$) treated with mFOLFOX6 and selective internal radiation therapy (SIRT) SIR-Spheres Y-90 resin treatment achieved greater depth of response (DpR) than those receiving chemotherapy alone, reports a German study. The new analysis of the phase III SIRFLOX study found no differences in DpR rates between the two treatment groups for patients with liver tumour burden ($\leq 12\%$) at study entry.

SIRT, also known as radioembolisation, allows tumours to be selectively irradiated leaving healthy tissue relatively unaffected. For the technique, tens of millions of Yttrium-90 labelled coated resin microspheres (Sirtex) are injected into the hepatic arterial supply of the liver via a catheter inserted into the femoral artery through an incision in the groin. The spheres, which are 32 microns in diameter, deliver high doses of ionising pure beta radiation to tumours.

In the SIRFLOX study, 530 patients with previously untreated metastatic colorectal cancer were randomly assigned 1:1 to FOLFOX (\pm bev) plus SIRT or FOLFOX (\pm bev) alone. Results, published this February in the Journal of Clinical Oncology, showed although SIRT did not influence progression free survival (PFS) at any site, it delivered a 7.9 month prolongation of PFS in the liver.



Volker Heinemann

In the current analysis, Volker Heinemann and colleagues developed the DpR analysis where shrinkage of up to five target liver tumours was tracked until reaching the shortest length or 'nadir'. The investigators identified patients from the SIRTEX study with baseline tumour loads $\geq 12\%$ (n=245 patients) and tumour loads $\leq 12\%$ (n=239 patients).

Results show for patients with $\geq 12\%$ tumour burden, depth of response was 77.5% for FOLFOX (\pm bev) + SIRT compared to 57.2% for FOLFOX (\pm bev) (P=0.003). In contrast, for patients with $\leq 12\%$ tumour burden the depth of response was 72.5% for FOLFOX (\pm bev) +SIRT versus 80.6% for those receiving FOLFOX (\pm bev) (p=0.763).

"The greater depth of response following SIR-Spheres Y-90 resin microspheres, together with the prolonged PFS in the liver, are very encouraging and increase our anticipation for the survival data we hope to see in 2017," said Heinemann, from the Ludwig-Maximillan University, Munich.

Reference

Heinemann V, Hazel GA, Sharma NK et al. Evaluation of depth of response within a volumetric model in patients with metastatic colorectal cancer: Results of the SIRFLOX study. Annals of Oncology 2016; 27 (Suppl 2): Abs. 0-014.

Janet Fricker, Medical Journalist.

Novel endpoints show benefit for new agent in advanced colorectal cancer

Xilonix™, a novel anti-interleukin 1-alpha antibody, demonstrated significantly improved clinical response rates (CRRs) at eight weeks using a novel endpoint compared with placebo in advanced colorectal cancer, reported a phase III study.

Xilonix™ (XBiotech) is the first monoclonal antibody immunotherapy that specifically targets and neutralises interleukin-1 alpha (IL-1), a potent anti-inflammatory signalling molecule known to promote angiogenesis and break down of connective tissue. The same signals, it is believed, may be involved in metastasis and messaging to the brain to cause pain, fatigue, anxiety, appetite suppression and hypermetabolic syndrome that are seen in advanced cancer.

In the double blind study, 309 patients with metastatic colorectal cancer refractory to standard chemotherapy were randomly assigned 2:1 to receive Xilonix™ plus best supportive care or placebo plus best supportive care.

The primary endpoint used in the study was clinical response rate (CRR) at eight weeks, developed in collaboration with European Medicines Agency (EMA), to assess the anti-tumour benefit of therapy based on control of symptoms known to be inversely correlated with overall survival, including pain, fatigue, appetite loss and muscle loss.

In the study Xilonix™-treated patients with advanced disease and multiple symptoms known to inversely correlate with overall survival experienced a 76% relative increase in clinical response rate compared to placebo (33% versus 19%, respectively; $p=0.0045$). Among subjects in both groups (treatment and placebo), clinical response was associated with a 2.7 fold increase in overall survival 11.5 months in responders versus 4.2 months in non-responders. In addition, responders gained more lean body mass compared to non-responders ($p<0.0007$), had reduced fatigue and pain ($P<0.001$) and improved appetite ($p<0.001$). Furthermore, control of thrombocytosis and systemic inflammation, both known to be prognosticators of overall survival, were significantly improved in responders. There were one-quarter fewer serious adverse events in the treatment arm of the study compared to placebo.

“In this first-of-its-kind study, not only did treatment with Xilonix™ demonstrate clinical benefit but it was also very well-tolerated, suggesting Xilonix™ has the potential to meet the real and urgent need for more effective, less toxic therapies for patients with advanced colorectal cancer,” said study presenter Tamas Hickish, from the Royal Bournemouth Hospital NHS Foundation Trust, UK. The study, he added, provides evidence novel endpoints based on symptom recovery can serve as a predictor of overall survival benefits.

Reference

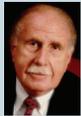
Hickish T. A pivotal phase 3 Trial of MABp1 in advanced colorectal cancer. Abstract O-027

Janet Fricker, Medical Journalist.

Meet the Editorial Team



Professor Denys Wheatley is Editor, and is Director of BioMedES. He has strong research ties in Albany, Davis, Auckland, Valencia, Detroit, Budapest, St Petersburg, Heidelberg, Zürich and Hong Kong. He is eager to establish strong interaction with cancer and cell biology teams worldwide, and initiate programmes in the areas in which his expertise lies. His work in cancer research, other scientific fields, with IFCB, and in publishing and scientific communication has led to his receiving awards in recent years.



Dr Richard J Ablin (Associate Editor), is Professor, Pathology, University of Arizona College of Medicine and a Member of the Arizona Cancer Center, Tucson, Arizona. He received the First Award for scientific excellence from The Haakon Ragde Foundation for Advanced Cancer Studies. Dr Ablin discovered prostate-specific antigen (PSA) in 1970. A pioneer of cryosurgery and cryoimmunotherapy, he has extensive experience in cancer research.



Alan Cooper is Assistant Co-Editor – Urology, and is Lead Scientist with the urology research group in Southampton University Hospitals and senior lecturer (albeit with virtually no lecturing burden) in the Department of Biomedical Sciences at Portsmouth University.



Mr Richard Novell is Assistant Co-Editor – Gastrointestinal Section, and is a Consultant Colorectal Surgeon at the Royal Free Hospital. He was a member of the Court of Examiners of the Royal College of Surgeons for eight years and has been an advisor to NICE, NCEPOD and CORESS, the Confidential Reporting System in Surgery.



Dr Miriam Dwek is Assistant Co-Editor – Breast Cancer, she is a Senior Lecturer in Biochemistry at the Department of Molecular and Applied Biosciences, School of Life Sciences, University of Westminster in London.



Prof Mohammed RS Keshtgar BSc, FRCSI, FRCS (Gen), PhD is Assistant Co-Editor – Breast Cancer, and is a Professor of Cancer Surgery and Surgical Oncology, Royal Free London Foundation Trust. His main area of interest is minimally invasive approaches in diagnosis and treatment of breast cancer. His research interest is in sentinel node biopsy, intra-operative radiotherapy, quantum dot nanotechnology in breast cancer.



Professor Geoffrey J Pilkington is Assistant Editor Neuro-Oncology, is a Professor of Cellular and Molecular Neuro-oncology at the Institute of Biomedical and Biomolecular Sciences, Portsmouth. His research focuses on the development of models for the study of intrinsic brain tumours, elucidation of their metabolism and mechanisms underlying diffuse local invasive behaviour.



Farrokh Pakzad is Assistant Editor – Skin Cancer, and is currently Consultant Oncoplastic Breast and Melanoma Surgeon at Royal Surrey County Hospital. His main areas of specialist interest are in the management of breast disease, oncoplastic and reconstructive breast surgery and the management of skin cancers, in particular, melanoma. Farrokh completed his higher surgical training in London, during which he was selected onto the highly competitive National Oncoplastic Fellowship program.



Dr Constantino Carlos Reyes-Aldasoro is Assistant Editor – Image Analysis. He is a Lecturer in Biomedical Image Analysis at the School of Engineering and Mathematical Sciences, City University London. He has developed a unique portfolio of interdisciplinary skills that span from the acquisition of microscopical images to the analysis of biomedical datasets such as magnetic resonance, computed tomography and microscopy to advanced computer programming and website development.



Mriganka De is Assistant Editor – Head & Neck Oncology. Mr De is a Consultant ENT/Head and Neck surgeon at Royal Derby Hospital, Derby. His interest is head and neck cancer with particular focus on management of early laryngeal cancers.



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