



**Study Suggests Survival Benefit from Radioactive Microsphere Therapy in Patients with Colorectal Cancer Liver Metastases who have Failed Chemotherapy**

Chicago – June 2, 2008 – Radioactive microspheres appear to be a safe and effective treatment for patients with colorectal cancer that has spread to the liver and who have failed available chemotherapy options, according to the results of a prospective clinical study presented today at the 44<sup>th</sup> American Society of Clinical Oncology (ASCO) conference.<sup>1</sup> The multicentre phase II study was conducted by the Italian Society of Locoregional Therapies in Oncology (SITILO) using SIR-Spheres, which are tiny resin microspheres labelled with radioactive yttrium-90.

The results of the 52-patient study revealed a median overall survival of 13 months. The liver tumors completely disappeared in one patient (2%), and 11 (22%) patients had a partial response involving at least a 30% reduction in tumour size. A further 12 (24%) patients had stable disease. The liver tumors shrank sufficiently in two patients (4%) to enable potentially curative surgery to be planned. The median survival in the 24 (48%) patients that responded to SIR-Spheres was significantly longer compared to non-responders (16 months versus 8 months;  $P = 0.0006$ ), with 40% of the responders remaining alive at two years compared to none of the non-responders. Mild to moderate side effects consisting mostly of fever and pain were reported in 16% of patients in the first 48 hours and 22% after 48 hours.

“These results demonstrate that SIR-Spheres is a promising therapy for patients with colorectal cancer liver metastases who have failed chemotherapy,” said Prof. Maurizio Cosimelli, Professor of Surgery at the Regina Elena National Cancer Institute in Rome, and co-ordinator of the study. “The prolonged 13-month median survival in the SITILO study compares favourably with the clinical trial results of second- or third-line chemotherapy, even though three-quarters of our patients had previously received at least four different combinations of chemotherapy drugs and therefore had a poor prognosis with no other treatment options available.”

“At a minimum, physicians treating colorectal cancer should consider SIR-Spheres for patients who have liver-only or liver-dominant disease and are failing chemotherapy,” said Prof. Cosimelli. “However, previous studies have revealed that the clinical benefits may be even greater from adding SIR-Spheres to chemotherapy.”

Patients recruited into the SITILO study had to have liver metastases from colorectal cancer that could not be removed by surgery and which had progressed despite modern chemotherapy regimens containing oxaliplatin and irinotecan. The presence of metastases outside the liver did not exclude the patients from treatment as long as these were limited in number, size and in the same organ. All patients were heavily pre-treated, having received at least three previous chemotherapy regimens: 24% had received three different lines or courses of chemotherapy, 50% had received four lines and 26% had received five lines.

The SITILO study used a single-arm design since this group of patients had no other treatment options available. Patients were reviewed by a multidisciplinary team of cancer specialists prior to recruitment into the study. The median survival of metastatic colorectal cancer treated in clinical studies using modern chemotherapy regimens such as cetuximab plus irinotecan at second-line and

panitumumab at third-line treatment has been reported to be 8.6 to 10.7 months<sup>2-5</sup> and 6.3 to 9 months<sup>6-9</sup> respectively.

Each year, more than 145,000 Americans and 307,000 Europeans are diagnosed with colorectal cancer. Around half of these patients will develop metastases that have spread from the original site of the disease, predominately to the liver. Up to 90% of these patients ultimately die from liver failure due to the spread of the disease. Selective Internal Radiation Therapy (SIRT) using yttrium-90 microsphere therapy is a novel approach to treating liver metastases. The microspheres are implanted by interventional radiologists to selectively target the tumors with radiation while sparing the much-needed healthy liver tissue.

The SITILO study was conducted by a multidisciplinary team of interventional radiologists, nuclear medicine physicians, medical oncologists, surgeons and other specialists at the Regina Elena National Cancer Institute in Rome, the University of Bologna, the University of Udine and the Cancer Institute of Naples in Italy. SIR-Spheres was developed by and is manufactured by Sirtex Medical, and is the only FDA-approved microsphere therapy for colorectal cancer liver metastases.

SITILO is the only Italian multidisciplinary oncology society. Different specialties work together within SITILO to design prospective clinical trials on loco-regional therapies in the field of liver metastases and primary carcinoma, melanoma, soft tissue sarcoma, and other cancers. Each protocol includes a biological component aimed at identifying predictive factors in serum and tissue.

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## References

1. Cosimelli M, Mancini R, Carpanese L *et al.* Clinical safety and efficacy of <sup>90</sup>yttrium resin microspheres alone in unresectable, heavily pre-treated colorectal liver metastases: results of a phase II trial. ASCO Annual Meeting Proceedings *Journal of Clinical Oncology* 2008; **26** (May 20 Supplement): Abs. 4078.
2. Sobrero AF, Maurel J, Fehrenbacher L *et al.* EPIC: Phase III trial of cetuximab plus irinotecan after fluoropyrimidine and oxaliplatin failure in patients with metastatic colorectal cancer. *J Clin Oncol* 2008; Epub Apr 7; 10.1200/JCO.2007.13.1193.
3. de Cerqueira Mathias, Perazzo F, Simon S C *et al.* Front cetuximab plus irinotecan in patients (pts) with metastatic colorectal cancer (mCRC) progressing on or after prior irinotecan therapy: final results of the LABEL study. *ECCO meeting Euro J Cancer Supplements* 2007; **5**: Abs. P3055.
4. Wilke H, Siena S, Thaler J *et al.* Impact of pre-medication on the frequency of infusion-related reactions (IRRs) and efficacy in patients (pts) treated with cetuximab plus irinotecan for metastatic colorectal cancer (mCRC): the MABEL study. *ECCO meeting European Journal of Cancer Supplements* 2007; **5**: Abs. P3025.
5. Cunningham D, Humblet Y, Siena S *et al.* Cetuximab monotherapy and cetuximab plus irinotecan in irinotecan-refractory metastatic colorectal cancer. *N Engl J Med* 2004; **351**: 337–345.
6. Hecht JR, Patnaik A, Berlin J, *et al.* Panitumumab monotherapy in patients with previously treated metastatic colorectal cancer. *Cancer* 2007; **110**: 980–988.
7. Van Cutsem E, Peeters M, Siena S *et al.* Open-label phase III trial of panitumumab plus best supportive care compared with best supportive care alone in patients with chemotherapy-refractory metastatic colorectal cancer. *J Clin Oncol* 2007; **25**: 1658–1664.
8. Van Cutsem E, Siena S, Humblet Y *et al.* An open-label, single-arm study assessing safety and efficacy of panitumumab in patients with metastatic colorectal cancer refractory to standard chemotherapy. *Ann Oncol* 2008; **19**: 92–98.
9. Yoshino T, Muro K, Doi T *et al.* Phase II study of panitumumab (Pmab) monotherapy in Japanese patients (pts) with metastatic colorectal cancer (mCRC) after the failure of fluoropyrimidine, irinotecan (CPT-11), and oxaliplatin (OHP) chemotherapy. *ASCO GI Symposium* 2008; Abs. 366.