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STUDY DEMONSTRATES RADIOEMBOLIZATION USING SIR-SPHERES SIGNIFICANTLY IMPROVES OVERALL SURVIVAL FOR PATIENTS WITH INOPERABLE COLORECTAL CANCER

SURVIVAL OF PATIENTS TREATED WITH SIR-SPHERES MORE THAN DOUBLE THAT OF PATIENTS WHO RECEIVED BEST SUPPORTIVE CARE, BENEFIT RIVALS THAT FOUND WITH NEW BIOLOGICAL AGENTS, AUTHORS NOTE

Magdeburg, 19 October 2012 – The results of a matched-pair comparison of patients with metastatic colorectal cancer predominately affecting the liver, for whom all chemotherapy options had been exhausted, showed that the addition of radioembolization using SIR-Spheres significantly prolonged survival compared with best supportive care (BSC) alone.¹

The study, published in October's edition of *Cardiovascular and Interventional Radiology*, showed that median overall survival was more than doubled in patients receiving radioembolization plus BSC versus BSC alone: 8.3 months vs. 3.5 months (hazard ratio [HR] 0.26; 95% confidence interval 0.15–0.48; $P < 0.001$). A multivariate analysis confirmed that radioembolization was the only significant predictor for prolonged survival among all the baseline parameters investigated (HR 0.30; 95% CI 0.16–0.55; $P < 0.001$).

“Radioembolization significantly prolonged overall survival compared with supportive care alone in a well-matched cohort of patients with extensive, liver-dominant chemotherapy refractory disease for whom there are limited treatment options”, said Prof. Jens Ricke, Director of Radiology and Nuclear Medicine at the University Hospital of Magdeburg, Germany, and senior author of the study. “The evidence suggests that radioembolization should be considered as a treatment option for patients with liver-only or liver-dominant colorectal metastases who have failed or are intolerant of chemotherapy.”

About the Study

The study compared the overall survival of 58 patients with colorectal cancer metastases that were either limited to or predominately affected the liver, who were refractory to all recommended chemotherapy or had refused further chemotherapy, and were unsuitable for other treatment options such as surgical resection, local ablation or other forms of radiotherapy. Twenty-nine patients received radioembolization using SIR-Spheres (⁹⁰Y-labeled resin microspheres; Sirtex Medical Limited, Sydney, Australia) and were followed prospectively. These patients were matched retrospectively for prior treatments and tumour burden with a contemporary cohort of >500 patients who received BSC from 3 centres in Germany to identify 29 consecutive patients with at least 2 of 4 specific matching criteria (the presence of synchronous or metachronous metastases, tumour burden, increased alkaline phosphatase, and/or carcinoembryonic antigen [CEA] >200 U/mL). The primary endpoint of the study was overall survival.

Following radioembolization, 12 patients (41.4%) had a partial response and a further 5 (17.2%) had stable disease, giving a disease control rate of 58.6%. The progression-free survival was 5.5 months in the radioembolization cohort compared to 2.1 months in those

receiving BSC. The adverse events following radioembolization were generally mild-to-moderate in nature, predominately transient, self-limiting and manageable.

“The results of this study are consistent with those from similar cohorts of chemotherapy-refractory patients with colorectal liver metastases treated using radioembolization”, said Dr Ricarda Seidensticker, consultant interventional radiologist and lead author of the study. “This was the first comparative study of radioembolization to use overall survival as the primary endpoint, in an ethical design that avoided the crossover of patients to active therapy, which usually blunts the ability of trials to show a difference in survival. These results also compare favourably with recent studies using new biological agents to treat metastatic colorectal cancer. In one randomized controlled trial of cetuximab, for example, the median overall survival was 6.1 months versus 4.6 months with best supportive care. In a similar trial with panitumumab, median overall survival was 6.4 months versus similar survival with best supportive care followed by crossover to panitumumab at progression.”

Large international randomised controlled trials are currently evaluating the effectiveness of radioembolization using SIR-Spheres combined with first-line chemotherapy in the treatment of patients with colorectal cancer liver metastases compared to chemotherapy alone in order to assess whether this treatment should be used as an early intervention.

About Colorectal Cancer

In 2008, 153,000 people in the United States of Americans and 333,000 in the European Union were diagnosed with colorectal cancer.² 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. Radioembolization (also called Selective Internal Radiation Therapy or SIRT) is a novel approach to treating liver tumours using microspheres labelled with radioactive yttrium-90 (⁹⁰Y). The microspheres are implanted by interventional radiologists to selectively target the tumours with radiation while sparing the remaining healthy liver tissue.

For Further Information:

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The 3 centres involved in the study (and the numbers of control patients screened) were:

- University Hospital of Magdeburg, Germany / Universitätsklinikum Magdeburg (n = 348);
- Charité Campus, University Hospital of Berlin, Germany / Universitätsmedizin Berlin (n = 120);
- Magdeburg Hospital, Germany / Klinikum Magdeburg (n = 86).

SIR-Spheres are approved for use in Australia, the European Union (CE Mark), New Zealand, Switzerland, Turkey and several other countries for the treatment of unresectable liver tumours.

SIR-Spheres are also fully FDA-approved and are indicated in the U.S. for the treatment of non-resectable metastatic liver tumours from primary colorectal cancer in combination with intra-hepatic artery chemotherapy using floxuridine.

References:

1. Seidensticker R, Denecke T, Kraus P *et al.* Matched-pair comparison of radioembolization plus best supportive care versus best supportive care alone for chemotherapy refractory liver-dominant colorectal metastases. *Cardiovascular and Interventional Radiology* 2012; **35**(5): 1066–1073.
2. International Agency for Research on Cancer. GLOBOCAN 2008: Colorectal Cancer Incidence and Mortality Worldwide in 2008. <http://globocan.iarc.fr/factsheets/cancers/colorectal.asp> accessed 12/8/2011.