ILC 2017: Selective internal radiation therapy is better tolerated compared to sorafenib, but does not increase overall survival in patients with HCC

Selective internal radiation therapy (SIRT) also resulted in tumour response rates of 19% versus 11.6% in the sorafenib group

April 22, 2017, Amsterdam, The Netherlands: Results of the SARAH trial presented today demonstrate that SIRT resulted in median overall survival (OS) of 8.0 months compared to 9.9 months with sorafenib (p=0.179), in patients with locally advanced and inoperable hepatocellular carcinoma (HCC). The trial, presented at The International Liver Congress™ 2017 in Amsterdam, The Netherlands, further demonstrated that the cumulative incidence of radiologic progression in the liver as the first event was significantly lower in the SIRT group compared to the sorafenib group (p=0.014), and the response rate was significantly higher in the SIRT group compared to the sorafenib group (19.0% vs 11.6%, p=0.042). Both the side-effect profile and quality of life scores were significantly better over time in the SIRT group compared to the sorafenib group (p=0.005).

Liver cancer, or HCC, is the second most common cause of cancer-related deaths worldwide.¹² HCC represents more than 90% of primary liver cancers and is a major global health problem.³ The prognosis for patients with advanced liver cancer is poor,² and the multikinase inhibitor, sorafenib, is the only approved first-line systemic treatment.³ If patients are not tolerant or have contraindications for sorafenib therapy, there is currently no standard of care and patients lack effective treatment options.³ SIRT with yttrium-90 (Y-90) resin microspheres has shown promising anti-tumour results with a safe profile; further trials are needed to establish this treatment as a viable option for patients.³

“Patients with advanced or inoperable hepatocellular carcinoma have a poor prognosis, often with underlying cirrhosis, and the treatment option currently available, sorafenib, has a high level of toxicity. As cohort studies have demonstrated the efficacy of SIRT with Y-90 resin microspheres, we set out to compare the efficacy of this treatment versus the current standard of care,” said Prof Valérie Vilgrain, Hôpital Beaujon Service de Radiologie, Paris, France, and lead author of the study. “While SIRT demonstrated significantly reduced side effects, better quality of life, higher response rates and more effectively controlled tumour progression in the liver, the overall survival of patients was not higher than in the sorafenib group. Nonetheless, this study provides evidence that SIRT may be a better-tolerated alternative for managing this complex and difficult-to-treat disease, deserving further evaluation.”

The SARAH trial was a randomised, controlled, open-label, multicentre investigator initiated Phase 3 trial. Patients with locally advanced or inoperable HCC, who did not respond to other treatments or had two failed rounds of transarterial chemoembolisation, were randomised to SIRT with Y-90 resin microspheres, or oral sorafenib 400 mg twice daily. The
primary endpoint of the study was OS and secondary endpoints included progression-free survival (PFS), time to radiological progression at any site and in the liver as the first event, tumour response, quality of life, and safety and toxicity.

There were 459 patients from 25 French clinical centres included in the study, 237 of whom received SIRT. Median PFS was 4.1 months and 3.7 months in the SIRT and sorafenib groups, respectively (p=0.765). Cumulative incidence of radiological progression at any site did not differ in either group (p=0.256). Overall, there were 1,297 and 2,837 treatment-related adverse events (AEs) including 230 and 411 grade ≥3, in the SIRT and sorafenib groups, respectively. The number of patients with at least one treatment-related adverse event was 173 (76.5%) and 203 (94.0%), (p<0.001), including 92 (40.7%) and 136 (63.0%) grade ≥3 adverse events, (p<0.001), in the SIRT and sorafenib groups, respectively. Quality of life, assessed using the Global Health Status scale of the EORTC QLQ-C30 questionnaire, was significantly better in patients who received SIRT compared to the sorafenib group (p=0.005), an advantage that tended to increase with time (p=0.045).

“The SARAH trial is the first reported randomised controlled trial evaluating the survival benefit of SIRT in locally advanced HCC compared to sorafenib. SIRT was found to be safe, but regrettably the study failed to meet the primary endpoint and SIRT did not show an overall survival superior to sorafenib. Further trials are needed to establish this treatment as a viable option for patients,” said Prof Alejandro Forner, BCLC group, Liver Unit, Hospital Clinic Barcelona, Spain and EASL Governing Board Member.

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Yttrium-90 resin microspheres
Y-90 resin microspheres are miniscule radioactive ‘beads’ that are used in SIRT. They contain the radioactive component yttrium-90. These microspheres are injected in huge quantities into the liver tumours, where they become stuck in the small blood vessels that are in and around the tumours. The microspheres then emit high doses of radiation, which enable doctors to deliver up to 40 times more radiation to the liver tumours than would be possible using standard radiation therapy, all while sparing surrounding healthy tissue.4

About The International Liver Congress™
This annual congress is the biggest event in the EASL calendar, attracting scientific and medical experts from around the world to learn about the latest in liver research. Attending specialists present, share, debate and conclude on the latest science and research in hepatology, working to enhance the treatment and management of liver disease in clinical practice. This year, the congress is expected to attract approximately 10,000 delegates from all corners of the globe. The International Liver Congress™ 2017 will take place from April 19 – 23, at the RAI Amsterdam, Amsterdam, The Netherlands.

About The European Association for the Study of the Liver (EASL) (www.easl.eu)
Since its foundation in 1966, this not-for-profit organisation has grown to over 4,000 members from all over the world, including many of the leading hepatologists in Europe and beyond. EASL is the leading liver association in Europe, having evolved into a major European Association with international influence, with an impressive track record in
promoting research in liver disease, supporting wider education and promoting changes in European liver policy.

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Onsite location reference
Session title: General session III and award ceremony II
Time, date and location of session: 10:00 – 12:00, Saturday 22 April, Hall 5
Presenter: Valérie Vilgrain, France
Abstract: SARAH: a randomised controlled trial comparing efficacy and safety of selective internal radiation therapy (with yttrium-90 microspheres) and sorafenib in patients with locally advanced hepatocellular carcinoma (GS012), 10:00 – 10:15

Author disclosures
Speaker fees: Guerbet, SIRTEX, Supersonic, Toshiba. SIRTEX: Funding of SARAH trial. Guerbet: Study Investigator.

References