Phase III RCT of SIR-Spheres microspheres + hepatic arterial chemotherapy (HAC) vs. HAC alone in a first-line setting

This randomised phase III study of SIR-Spheres microspheres plus hepatic arterial chemotherapy (HAC) vs. HAC alone in 74 patients with liver-predominant metastases from colorectal cancer demonstrated:

- A significantly higher objective response rate for patients receiving combination SIRT plus HAC compared to HAC alone by both RECIST criteria (44.4% vs. 17.6%; P = 0.002; CT scan 6 months post-SIRT).
- A significantly longer median time to progression of disease (TTP) in the liver for patients receiving combination SIRT plus HAC compared to HAC alone (15.8 months vs. 3.7 months; P = 0.007), and a trend for a survival advantage in those patients surviving more than 15 months who received the combination of SIR-Spheres plus HAC (P = 0.10).
- No major adverse impact on quality of life by the addition of SIR-Spheres microspheres to HAC, with both groups demonstrating an improvement in quality of life.

Phase II RCT of SIR-Spheres microspheres + 5FU/LV first-line chemotherapy vs. 5FU/LV alone

A second randomised study, comparing SIR-Spheres microspheres plus 5FU/LV versus 5FU/LV alone in the first-line treatment of 31 patients with liver metastases from colorectal cancer, was not available for the NICE approval but demonstrates significant benefits in favour of SIR-Spheres microspheres. This pivotal phase II study showed:

- A significantly longer median overall survival for the combination of SIR-Spheres microspheres plus 5FU/LV compared to 5FU/LV alone (MAMS: 18.4 months vs. 12.8 months; P = 0.022).
- A significantly longer median TTP for the combination of SIR-Spheres microspheres plus 5FU/LV (18.6 months vs. 5.6 months; P < 0.0001).
- A significantly greater response rate for patients receiving the combination of SIR-Spheres microspheres plus 5FU/LV (Objective/Response Rate: 72.7% vs. 1%; using Best Confirmed Response by RECIST: P = 0.007).
- There was more Grade 3 or 4 toxicity in patients receiving the combination of SIR-Spheres microspheres plus 5FU/LV, although the investigators concluded that this was largely due to the greater period that these patients received protocol treatment.

The authors concluded the study was not compensated in the short term by the addition of SIR-Spheres microspheres, with no difference over a three-month period between the two treatments when rated by patients or physicians.

Phase I dose-escalation study of SIR-Spheres microspheres + FOLFOX-4 first-line chemotherapy

The recently published results of a Phase I dose-escalation study combining SIR-Spheres microspheres with the first-line FOLFOX-4 (folinic acid, fluorouracil, and oxaliplatin) chemotherapy indicate:

- A response rate by RECIST criteria of 70%, together with a disease control rate of 100%. No patients reported progressive disease.
- 3 patients (15%) died, and 2 (10%) of these were surgically resected.
- Progression-free survival (PFS) was 9.3 months in all patients and 14.2 months in those with liver-only disease at entry. Time to progression in the liver was 12.2 months, rising to more than 13.5 months for those with liver-only disease at entry. "At the time of reporting, 5 patients remained alive and 4 had not progressed in the liver."
- These data compare favourably to phase I/II data on FOLFOX, which report a response rate of 32–65%, and a time to progression or progression-free survival of 7.4–8.2 months.
- The maximum tolerated dose for the first 3 cycles of oxaliplatin was 60 mg/m².

References

5. There were more Grade 3 or 4 toxicities in patients receiving the combination of SIR-Spheres microspheres plus HAC, although the investigators concluded that this was largely due to the greater period that these patients received protocol treatment.
6. The recently published results of a Phase I dose-escalation study combining SIR-Spheres microspheres with first-line FOLFOX-4 (folinic acid, fluorouracil, and oxaliplatin) chemotherapy indicate: a response rate by RECIST criteria of 70%, together with a disease control rate of 100%. No patients reported progressive disease. 3 patients (15%) died, and 2 (10%) of these were surgically resected. Progression-free survival (PFS) was 9.3 months in all patients and 14.2 months in those with liver-only disease at entry. Time to progression in the liver was 12.2 months, rising to more than 13.5 months for those with liver-only disease at entry. At the time of reporting, 5 patients remained alive and 4 had not progressed in the liver. These data compare favourably to phase I/II data on FOLFOX, which report a response rate of 32–65%, and a time to progression or progression-free survival of 7.4–8.2 months. The maximum tolerated dose for the first 3 cycles of oxaliplatin was 60 mg/m².
7. References

Please check this proof carefully. We make every endeavour to ensure complete accuracy, but the final approval rests with you.
SIR-Spheres® Microspheres in Colorectal Cancer Liver Metastases

Phase III RCT of SIR-Spheres microspheres + hepatic arterial chemotherapy (HAC) vs. HAC alone in a first-line setting

The randomised Phase III study of SIR-Spheres microspheres plus hepatic arterial chemotherapy (HAC) using floxuridine compared to HAC alone in 74 patients with liver metastases from colorectal cancer (CRC) was the only randomised study considered in the NICE appraisal. The study was halted prematurely after the FDA stated that treatment-related responses and time to progression disease were acceptable criteria for registration, as well as increased toxicity by patients/physicians for randomisation to a control arm and the absence of ongoing funding. The study demonstrated:

- A significantly higher response rate for patients receiving combination SIRT plus HAC compared to HAC alone by both RECIST criteria (44% vs. 17.6%; P = 0.0021) and in terms of patients alive with no evidence of disease (72.7% vs. 47.1%; P = 0.004).

- A significantly longer median time to progression of disease (TTP) in the liver for patients receiving combination SIRT plus HAC compared to HAC alone (15.9 months vs. 3.7 months; P = 0.007), and a trend for a survival advantage in those patients surviving more than 15 months who received the combination of SIR-Spheres plus HAC (P = 0.05).

- No major adverse impact on quality of life by the addition of SIR-Spheres microspheres to HAC, with both groups demonstrating an improvement in quality of life.

Phase II RCT of SIR-Spheres microspheres + 5FU/LV first-line chemotherapy vs. 5FU/LV alone

A second randomised study, comparing SIR-Spheres microspheres plus 5FU/LV versus 5FU/LV alone in the first-line treatment of 31 patients with liver metastases from CRC, was not available for the NICE appraisal but demonstrates significant benefits in favour of SIR-Spheres microspheres. This pivotal Phase II study showed:

- A significantly longer median overall survival for the combination of SIR-Spheres microspheres plus 5FU/LV compared to 5FU/LV alone (24.9 months vs. 12.8 months; P = 0.027).

- A significantly shorter median TTP for the combination of SIR-Spheres microspheres plus 5FU/LV (15.6 months vs. 5.6 months; P < 0.0001).

- A significantly greater response rate for patients receiving the combination of SIR-Spheres microspheres plus 5FU/LV (Objective Response Rate: 72.7% vs. 0% using Best Confirmed Response by RECIST, P < 0.0001).

- There were more Grade 3 or 4 toxicities in patients receiving the combination of SIR-Spheres microspheres plus 5FU/LV, although the investigators concluded that this was owing to the greater period that these patients received protocol treatment.

- The quality of life of patients was not compromised in the short term by the addition of SIR-Spheres microspheres, with no difference over a three-month period between the two treatments when rated by patients or physicians.

Phase I dose-escalation study of SIR-Spheres microspheres + FOLFIRI-4 first-line chemotherapy

The recently published results of a Phase I dose-escalation study combining SIR-Spheres microspheres with first-line FOLFIRI-4 (5FU/LV + irinotecan) chemotherapy in 20 mCRC patients, 65% of whom had extra-hepatic disease, reported:

- A response rate by RECIST criteria of 88%, together with a disease control rate of 100%. No patients reported progressive disease.

- 3 patients (15%) were dose-escalated and 2 (10%) of these were successfully escalated.

- Progression-free survival (PFS) was 3.6 months in all patients and 14.2 months in those with liver-only disease at entry. Time to progression in the liver was 12.3 months, rising to more than 13.6 months for those with liver-only disease at entry.

- At the time of reporting, 5 patients remained alive and 4 had not progressed in the liver.

- These data compare favourably to phase II/III data on FOLFOX4, which report a response rate of 32–59%, and a time to progression or progression-free survival of 7.4–8.0 months.

- The maximum tolerated dose for the first 3 cycles of oxaliplatin was 60 mg/m².

References