The following summarises some of the key data supporting the use of SIR-Spheres microspheres in the treatment of primary liver cancer due to Hepatocellular Carcinoma (HCC).

Prospective study of SIR-Spheres microspheres in HCC, including patients with chronic liver disease

A prospective study of 48 patients with unresectable advanced HCC treated with SIR-Spheres microspheres and including many patients with cirrhosis. Patients were further stratified by the presence of chronic liver disease (71%) that was advanced in 54% and/or who had progressed prior to embolisation procedures (46%), demonstrating:

- a response rate of 24% and disease control rate of 50% in target lesions of 21 patients evaluable by CT using RECIST criteria, with no patients having progressive disease at follow-up, even though most patients had already experienced advanced disease, including bulky tumour or liver portal vein invasion;
- median overall survival of 17 months, 43% progressed, all with new lesions at a median of 3 months;
- the risk of failure in HCC patients could be reduced by avoiding treatment of patients with an intense mismatch between MIA scan and the arterial phase of DSA imaging, and reducing the threshold considered appropriate for individual selection of the activity (dose) administered;
- the authors noted that by using stringent selection criteria and conservative models for calculating the dose to be administered, SIRT can be performed safely even in chronic liver patients requiring whole-liver treatment, and that for patients who can be treated by either liver or segmental fashion, it is likely that less caution will be needed.

Prospective study of SIR-Spheres microspheres in HCC, including relapsed disease post resection

A prospective study of 171 patients with unresectable HCC (median tumour size 13 cm; range 4–20 cm), including some with recurrent disease (28%) and/or undergoing chemotherapy (68%); the authors concluded that SIR-Spheres represents a treatment option for the high percentage of patients (up to 60%) who develop intrahepatic post-operative recurrence after 'curative' resection of HCC, is effective even for large tumours, and that progressive disease should be retreated as far as possible to gain further palliation and prolong survival.

Analysis of factors determining survival following SIR-Spheres microspheres treatment for HCC

A retrospective analysis of the factors affecting long-term survival of 83 patients with unresectable HCC treated at either first-line (85%) or following post-operative recurrence (15%) using SIR-Spheres microspheres revealed:

- 31 patients (38%) lived for one year or more (median 21 months; range 12.9–54.1+ months) following SIR-Spheres treatment, with 4 patients still alive at the time of reporting, compared with 51 patients who lived for less than one year (median 4.5 months; range 1.4–11.4 months);
- comparison between these two cohorts suggested that longer survival was favoured by:
  - lower pre-treatment levels of AFP (P = 0.005); the authors concluded that SIR-Spheres microspheres is safe, with the risk of toxicity in HCC patients could be reduced by avoiding treatment of patients with an intense mismatch between MIA scan and the arterial phase of DSA imaging, and reducing the threshold considered appropriate for individual selection of the activity (dose) administered;
  - the authors also noted that the rapid fall in tumour markers post-SIRT in most patients is not commonly observed with other treatment modalities, and the median survival achieved by the group of patients was encouraging;
  - the results in patients who received multiple treatments indicated that re-treatment is feasible and should be done early, and that the results in patients who had previously been resected indicate that SIRT may be a useful option in re-recurrence.

Phase II/III dose optimisation study of SIR-Spheres microspheres in HCC

A phase II/III study of SIR-Spheres microspheres in the treatment of unresectable HCC in 18 patients (median tumour size 13 cm; range 4–20 cm), including some with recurrent disease (21%) and/or undergoing chemotherapy (68%); the authors concluded that SIR-Spheres is a treatment option for the high percentage of patients (up to 60%) who develop intrahepatic post-operative recurrence after 'curative' resection of HCC, is effective even for large tumours, and that progressive disease should be retreated as far as possible to gain further palliation and prolong survival.

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SIR-Spheres® Microspheres in Hepatocellular Carcinoma

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Prospective study of SIR-Spheres microspheres in HCC, including patients with chronic liver disease

A prospective study of 91 patients with unresectable HCC (median tumour size 8.5 cm; range 1–22.6 cm), including 28% who had relapsed disease post resection, showed:

- partial resection in 19 patients (27%) by CT imaging, minor resection or stable disease in 45 patients (60%), and progressive disease in only 4 patients (6%), either due to new intra-hepatic lesions (3) or distant metastases (2).
- down-staging to resection in 4 patients (6%), with 2 of the resected tumours showing complete histological remission and confirmed complete response, and only occasional stable tumour cells found in the resected centre of the other 2 resected tumours.
- the tumour marker AFP dropped after the first treatment by median of 34% (20–99+%) in 46 patients (100%) who had an elevated AFP pre-SIRT, with a complete response in 10 patients (21%) by normalization of AFP levels, and a partial response in 31 patients (67%) by >50% decrease of AFP.
- median overall survival of 3.4 months (1.6–6.4 months), with no significant difference in survival between the 20 patients with post-operative recurrences and 51 patients receiving SIRT (median 3.4 months; P = 0.34).
- 21% of patients were able to receive follow-up SIRT treatment, which further supported the significant median interval between re-treatments was 5.2 months (range 2.8–24.5 months).
- 63% of patients had no side effects from treatment, with 17% experiencing post-embolisation symptoms and 14% having low-grade fever. These adverse effects were transient and subsided in a few days.
- the majority of patients enjoyed a normal quality of life with Karnofsky performance scores of 100% until very near to the terminal stage of their disease.
- the authors concluded that SIR-Spheres is a valuable alternative for patients with portal vein invasion and preserved liver function, a subset for whom no effective therapy can be currently offered.

A prospective study in 71 patients with unresectable HCC (median tumour size 8.5 cm; range 1–22.6 cm), including 28% who had relapsed after resection, showed:

- a valuable alternative for patients with portal vein invasion and preserved liver function, a subset for whom no effective therapy can be currently offered.
- an adjunct to liver transplantation, through prolonged disease control and potential to down-stage into transplant criteria.

A retrospective analysis of the factors affecting long-term survival of 82 patients with unresectable HCC treated at either first–line (68%) or following disease in 46 patients (65%), and progressive disease in only 6 patients (8%), compared between these two cohorts suggested that longer survival was favoured by:

- longer pre-treatment survival (P = 0.006) – the AFP level is a known prognostic predictor of survival.
- lower tumour marker AFP levels (P = 0.006), reflecting higher radiation levels to the tumour.

The authors concluded that SIR-Spheres is a treatment option for the high percentage of patients (up to 60%) who develop intrahepatic recurrence after ‘curative’ resection of HCC, is effective even for large tumours, and that progressive disease should be retreated as far as possible to gain further palliation and prolong survival.

SIR-Spheres microspheres treatment ends down-staging to resection and long-term disease control

Analysis of 49 patients with initially unresectable HCC who were down-staged by either systemic chemotherapy (65%) or sequential systemic chemotherapy/SIRT (10%) to permit salvage surgery, showed:

- 21 patients (42.9%) had recurrence after surgery, and the median overall survival of the cohort was 33.9 months, with 1-year, 3-year and 5-year survival rates of 86%, 56% and 53% respectively.
- the authors concluded that salvage surgery after successful down-staging can provide long-term disease control.

Phase I/II dose optimisation study of SIR-Spheres microspheres in HCC

A phase I/II study of SIR-Spheres microspheres in the treatment of unresectable HCC in 18 patients, (median tumour size 13 cm; range 4–20 cm), including some with recurrent disease (2; 11%) and/or underlying cirrhosis (Child’s Grade B: 2; 11%), within a dose range of 120–192 Gy to 1 or 2 lesions (8% or cumulative tumour dose; 3

- the median overall survival of 55.9 weeks was significantly longer in those receiving an adequate tumour dose (>120 Gy), compared to 26.2 weeks in those receiving a lower dose (≤120 Gy) to one or more tumours (P = 0.005).
- the partial and complete response rate to CT for patients receiving a tumour dose ≥120 Gy was 87.5% with a further 12.5% of patients achieving stable disease, equating to a disease control rate of 100%.
- AFP levels dropped by >50% in all 10 patients (100%) who had an elevated AFP (>300 mcg/ml), and dropped by >80% in 8 patients (80%).
- the tumour marker serum ferritin dropped by >50% in all 8 patients (100%) of those achieving a partial or complete response.

The authors concluded that SIR-Spheres microspheres is safe, with the treatment being well-tolerated without major complications.

The authors also noted that tumour response is dose related, and that a tumour dose of >120 Gy is recommended.

References