The following summarises some of the key data supporting the use of SIR-Spheres microspheres and selective internal radiation therapy (SIRT) in the treatment of liver tumours from Neuroendocrine Tumours (mNET). A retrospective analysis of 24 patients with unresectable bilobar liver metastases from neuroendocrine tumours that had progressed under chemotherapy and/or TACE, and who were subsequently treated with SIRT in seven US centres reported that:

- a partial response rate of 30% by CT using RECIST criteria at 3 months, with stable disease in the remaining 70%4;
- survival was 70% at a follow up of 8–35 months, with three patients having died at 8, 11 and 15 months due to progressive extraparenchymal disease;4
- there was no evidence of hepatic toxicity or acute carcinoid crisis following therapy;4
- symptomatic improvement was reported in 2 of 3 patients with moderate to severe symptoms at baseline.4

The authors concluded that SIRT microspheres were acceptable and feasible in mNET patients with unresectable bilobar liver metastases, with low toxicity or short-term morbidity. The authors also noted that SIRT-Spheres microspheres appeared to be tolerated as well if not better than TACE, and that it compares favourably with other loco-regional therapies.4

Interim results of a phase IV (II) pilot study of SIR-Spheres microspheres in mNET salvage therapy

A prospective pilot study of SIR-Spheres microspheres in 10 patients with unresectable or symptomatic mNET liver metastases treated mainly (90%) in the first-line setting demonstrated:

- a partial response rate of 30% by CT using RECIST criteria at 3 months, with stable disease in the remaining 70%;2
- survival was 70% at a follow up of 8–35 months, with three patients having died at 8, 11 and 15 months due to progressive extraparenchymal disease;2
- there was no evidence of hepatic toxicity or acute carcinoid crisis following therapy;2
- symptomatic improvement was reported in 2 of 3 patients with moderate to severe symptoms at baseline.2

The authors concluded that use of SIR-Spheres microspheres in mNET resulted in stable disease or partial response over 3 to 12 months with little toxicity or short-term morbidity. The authors also noted that SIRT-Spheres microspheres appeared to be tolerated as well if not better than TACE, and that it compares favourably with other loco-regional therapies.2

Interim results of a phase IV (I) pilot study of SIR-Spheres microspheres in mNET salvage therapy

A retrospective review of 18 consecutive patients with mNET, including 13 with carcinoid symptoms, who were treated second-line with a total of 24 fractions of SIR-Spheres microspheres revealed:

- an objective response rate of 85% by imaging and CgA6;
- 16 of the 18 patients (89%) were alive at a median follow-up of 27 months (4–44 months), thus median survival had not yet been reached;6
- there were no treatment-related deaths, radiation-induced liver disease or veno-occlusive disease;6
- the authors concluded that whole liver and multiple fraction SIRT are safe, feasible and produce a high response rate, even with extensive metastatic disease;6
- the authors noted that acute and delayed toxicity was low, without any treatment-related grade 4 events or radiation-induced liver disease.6

Interim results of a phase IV (II) study of SIR-Spheres microspheres in mNET

The interim results of an on-going phase IV (I) study of SIR-Spheres microspheres in combination with SPU used to treat 34 patients with unresectable mNET, including those failing prior liver treatment as well as those with extraparenchymal disease, demonstrated:

- 24% of patients treated having a partial response of large lesions by RECIST criteria at 1 month together with 69% experiencing stable disease and 9% progressive disease, and 80% of evaluable patients having stable disease at 16 months;5
- the disease control rate was 81% at 1 month, 80% at 3 months, 80% at 12 months and 80% at 18 months;5
- response by tumour marker CgA from baseline was seen in 53% of patients at 1 month, 60% at 3 months, 50% at 6 months, 65% at 12 months and 80% at 18 months;5
- 4 patients (12%) died from progressive liver disease at 1, 4, 7 and 15 months, with a median follow-up of 8.9 months;5
- 3 patients developed duodenal ulcers and 1 developed small-resolving pancreatitis due to inappropriate perturbation of SIRT to extra-hepatic arteries; 2 patients developed self-limiting jaundice, and all patients reported abdominal pain, nausea and lethargy from 1 to 6 weeks post-SIRT;5
- the authors concluded that SIRT appears to have efficacy in treating unresectable neuroendocrine tumours liver metastases.5

Review of sequential, fractionated whole-liver treatment of mNET using SIR-Spheres microspheres

A retrospective review of 18 consecutive patients with mNET, including 13 with carcinoid symptoms, who were treated second-line with a total of 24 fractions of SIR-Spheres microspheres revealed:

- an objective response rate of 85% by imaging and CgA6;
- 16 of the 18 patients (89%) were alive at a median follow-up of 27 months (4–44 months), thus median survival had not yet been reached;6
- there were no treatment-related deaths, radiation-induced liver disease or veno-occlusive disease;6
- the authors concluded that whole liver and multiple fraction SIRT are safe, feasible and produce a high response rate, even with extensive metastatic disease;6
- the authors noted that acute and delayed toxicity was low, without any treatment-related grade 4 events or radiation-induced liver disease.6

References

2. Coldwell D. Personal communication.
SIR-Spheres® Microspheres in Neuroendocrine Tumour Liver Metastases

The following summarises some of the key data supporting the use of SIR-Spheres microspheres and selective internal radiation therapy (SIRT) in the treatment of liver metastases from Neuroendocrine Tumours (mNET):

Retrospective review of SIRT in mNET across US centres

- A retrospective analysis of 94 patients with unresectable bilobar liver metastases from neuroendocrine tumours that had progressed under chemotherapy and/or TACE, and were subsequently treated with SIRT in seven US centres reported that:
  - A response by PET scans in 67% of patients with disease stabilisation in the remaining 33% – PET-positive tumours became normal (or complete response) in 24% of patients, with a partial response in 43%;
  - 80% of patients who had symptomatic disease received relief – a subsequent analysis of 35 patients whose full health records were available revealed that 20 (57%) responded on the basis of symptoms, PET or CtHisto2D scans, and of these, 18 (52%) reduced their somatostatin usage by at least 50%, and 4 (15%) were left off somatostatin completely for in excess of 6 months;
  - there were no significant complications but there were 14 cases of grade 3 GI toxicity which all resolved with medical therapy;
  - the authors concluded that SIRT is a safe and effective treatment for unresectable metastatic neuroendocrine tumours.

Interim results of a phase IV (II) study of SIR-Spheres microspheres in mNET

The interim results of an on-going phase IV (II) study of SIR-Spheres microspheres in combination with SPU used to treat 34 patients with unresectable mNET, including those failing prior liver treatment as well as those with metastatic disease, demonstrated:

- 25% of patients treated having a partial response of large targets by RECIST criteria at 1 month together with 69% experiencing stable disease and 40% of evaluable patients having stable disease at 16 months;
- the disease control rate was 91% at 1 month, 83% at 3 months, 80% at 12 months and 80% at 18 months;
- the authors concluded that SIRT appears to have efficacy in treating unresectable neuroendocrine tumours liver metastases.

Review of sequential, fractionated whole-liver treatment of mNET using SIR-Spheres microspheres

A retrospective review of 18 consecutive patients with mNET, including 13 with carcinoid symptoms, who were treated second-line with a total of 6 fractions of SIR-Spheres microspheres revealed:

- an objective response rate of 85% by imaging and CgA;
- 16 of the 18 patients (89%) were alive at a median follow-up of 27 months (4–44 months), thus median survival had not yet been reached;
- there were no treatment-related deaths, radiation-induced liver disease or veno-occlusive disease;
- 24% of patients treated having a partial response of target lesions by RECIST criteria at 1 month together with 68% experiencing stable disease and 9% progressive disease, and 83% of evaluable patients having stable disease at 18 months;
- the authors concluded that whole liver and multiple fraction SIRT are safe, feasible and produce a high response rate, even with extensive tumour replacement of the liver – nearly all patients experienced a significant objective response.

Please, check this proof carefully. We make every endeavour to ensure complete accuracy, but the final approval rests with you.