The following summarises the key data supporting the use of SIR-Spheres microspheres in the treatment of liver metastases from melanoma, predominantly from ocular or uveal primary tumours:

**Retrospective study of patients with ocular melanoma treated with SIR-Spheres microspheres**

An international, multi-centre retrospective study of 11 patients with unresectable liver metastases from ocular (uveal) melanoma treated with SIR-Spheres microspheres revealed:

- patients (mean age 56 years; range 36–66) all had bilateral lesions with >4 lesions and a Karnofsky performance status ≥60. Duration of time from original diagnosis to SIRT was a median of 25.5 months (range 1–118). One patient was lost to follow-up after 2.5 months;
- toxicity was considered minimal by the investigators, with only one grade 3 event, a gastric ulcer that healed uneventfully within 6 weeks with supportive care. There was no radiation-induced liver disease observed;
- in the 9 patients completing PET scans at 3 months post-treatment, all (100%) showed a response with 1 complete response (CR), 6 partial responses and 2 patients with stable disease. The CR was in a patient who had failed 13 prior bland transarterial embolisation procedures;
- by CT or MRI using RECIST, there was an overall response rate of 77% in evaluable patients with a complete response in 1 patient, 6 partial responses (PR), 1 stable disease (SD) and 1 with disease progression;
- 3 patients died from extra-hepatic metastases at 2.5, 3 and 18 months following SIRT. One patient developed new hepatic lesions at 14 months post-SIRT and was re-treated with SIR-Spheres microspheres. Median survival had not been reached at the time of publication, with a one-year survival of 80% excluding the patient lost to follow-up;
- the investigators noted the poor prognosis of patients with ocular melanoma liver metastases, which occurs as the first site of disease spread in 90% of curatively treated patients. Systemic chemotherapy is viewed as largely ineffective, with response rates following chemotherapy or chemo-immunotherapy reported to be <10%. Median survival of patients with metastatic ocular melanoma is just 2–7 months, with 15% one-year survival;
- the authors concluded that SIR-Spheres microspheres resulted in a reasonable response rate by imaging, overall survival and one-year survival rate that is improved over best chemotherapy, chemo-immunotherapy and observation/best supportive care with a low incidence of acute toxicity and without radiation liver damage.

---

**Lead Author**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>ORR</th>
<th>SD</th>
<th>Median PFS</th>
<th>Median Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kennedy¹</td>
<td>11 SIR-Spheres microspheres</td>
<td>77%</td>
<td>11%</td>
<td>nr</td>
</tr>
<tr>
<td>Dhanasekaran²</td>
<td>12 SIR-Spheres microspheres</td>
<td>nr</td>
<td>nr</td>
<td>nr</td>
</tr>
<tr>
<td>6 vs. TACE and/or TAIE</td>
<td>nr</td>
<td>nr</td>
<td>nr</td>
<td>2.1 months</td>
</tr>
<tr>
<td>Gonsalves³</td>
<td>32 SIR-Spheres microspheres</td>
<td>6%</td>
<td>56%</td>
<td>4.7 months</td>
</tr>
<tr>
<td>&lt;25% tumour burden</td>
<td>6.4 months</td>
<td>10.5 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥25% tumour burden</td>
<td>3.0 months</td>
<td>3.9 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>34 first-line TAIE (GM-CSF)</td>
<td>nr</td>
<td>nr</td>
<td>4.8 months</td>
<td>14.4 months</td>
</tr>
<tr>
<td>19 first-line TACE (BCNU)</td>
<td>nr</td>
<td>nr</td>
<td>6.4 months</td>
<td>9.8 months</td>
</tr>
</tbody>
</table>

**Key:** ORR: objective response rate (complete response + partial response) by RECIST; SD: stable disease; PFS: progression free survival; nr: not reported; Tx: treatment; Dx: diagnosis; mM: metastatic melanoma; TACE: trans-arterial chemoembolisation; TAIE: trans-arterial immunoembolisation; GM-CSF: granulocyte-macrophage colony stimulating factor; BCNU: carmustine

---

**SIR-Spheres® microspheres in ocular melanoma: Overall survival**

- 11 patients; 12 treatments
- Median Survival: not reached
- 1-year Survival: 80%
- 95% CI
Preliminary study of patients with chemotherapy-refractory melanoma treated with SIR-Spheres microspheres or other therapies

A preliminary study of 18 patients with unresectable liver metastases from either ocular (uveal) or cutaneous melanoma who had failed systemic therapy showed:

- patients received either SIR-Spheres microspheres (12), or TACE and/or TAIE using GM-CSF (6) in a non-randomised, retrospective analysis; the median overall survival from diagnosis of primary melanoma and from the diagnosis of liver metastases were 101.6 months (66.9–139.2) and 13.9 months (6.2–21.6), respectively.
- median (and mean) survival in patients treated with SIR-Spheres microspheres was 15.5 months (43.8 months) from the diagnosis of metastases, compared to 5.9 months (9.3 months) following TACE and/or TAIE (P = 0.04). Median (and mean) survival from the date of transcatheter therapy was 10.9 months (27.3 months) for SIR-Spheres microspheres vs. 2.1 months (6.1 months) following TACE and/or TAIE (P = 0.10); the duration of stable disease by RECIST in patients treated with SIR-Spheres microspheres was significantly longer compared to other catheter-directed therapies (10.1 vs. 2.3 months; P = 0.04);
- there was a significant positive correlation between progression-free duration and survival (P = 0.03); the investigators concluded that treatment of melanoma hepatic metastases using SIR-Spheres microspheres was feasible and may be associated with prolonged survival and longer progression-free duration compared to other transcatheter therapies.

Study of patients with treatment-refractory ocular melanoma treated with SIR-Spheres microspheres

A retrospective study of 32 patients with unresectable treatment-refractory liver metastases from ocular (uveal) melanoma treated with SIR-Spheres microspheres as salvage therapy reported:

- patients were considered eligible if they had tumour progression following prior trans-arterial catheter-directed therapy, no extensive extra-hepatic disease limiting life expectancy <3 months, adequate performance status (ECOG 0–2), and adequate liver function (bilirubin <1.8 mg/dL; albumin >3 g/dL; no ascites) and normal renal function (creatinine <2 mg/dL); patients (mean age 61; range 29–89) had a median of 9 prior trans-arterial catheter-directed therapies per patient (range 1–23). The majority of patients (78%) had liver tumour burden of <25%, 16% had 25–50% and the remaining 6% had >50%.
- the treatment activity was reduced by 25% due to the numerous prior trans-arterial therapies, with 25% of cases conducted as whole-liver treatments, 13% as single-lobe procedures and 59% as sequential right and left lobes separate by 3–5 weeks. The median SIR-Spheres microspheres activity delivered was 1.08 GBq (range 0.63–1.86); there were no severe adverse events or procedure-related deaths due to SIRT, with 4 grade 3–4 liver toxicities due to tumour progression; best response by RECIST was a CR in 1 patient (3%), 1 PR (3%), and 18 SD (56%), with progressive disease in the remaining 12 patients (38%); median progression-free survival of hepatic metastases was 4.7 months (1.0–26.5) for the whole cohort, with the investigators reporting a significantly prolonged liver PFS of 6.4 months in patients with <25% tumour burden compared to 3.0 months in those with >25% tumour burden (P = 0.03); median overall survival was 10.0 months (1.0–29.0) for the whole cohort, with 10 patients remaining alive after a median follow up of 10.0 months (1.0–29.0). Deaths were due to progression of liver metastases (13), extra-hepatic disease (4) or both (5); median survival was significantly longer in patients with <25% tumour burden compared to those with >25% tumour burden (10.5 vs. 9.3 months; P = 0.0003). Median survival was also significantly longer in patients with an objective response or stable disease following SIR-Spheres microspheres compared to those with progressive disease (14.7 vs. 4.9 months; P = 0.0006); the median overall survival of 10.0 months in patients with <50% tumour involvement treated using SIR-Spheres microspheres as a salvage therapy compared favourably with a median survival for patients treated at first line with either TACE using BCNU or TAIE using GM-CSF, at 9.8 and 14.4 months, respectively; the investigators concluded that SIRT was a safe and effective salvage therapy for patients with limited tumour burden who have failed first-line therapies.

**Kaplan-Meier survival analysis following SIR-Spheres microspheres in patients with unresectable ocular melanoma stratified by:**

**References**