The following summarises the key data supporting the use of SIR-Spheres Y-90 resin microspheres in the treatment of liver metastases from breast cancer:

### Lead Author n Treatment ORR SD Median TTP Median Survival

#### Treatment Hiatus or Chemorefractory Disease

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<th>Author</th>
<th>n</th>
<th>Treatment</th>
<th>ORR</th>
<th>SD</th>
<th>Median TTP</th>
<th>Median Survival</th>
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<tbody>
<tr>
<td>Coldwell</td>
<td>44</td>
<td>SIR-Spheres®</td>
<td>47%</td>
<td>47%</td>
<td>nr</td>
<td>86% alive at 14 months</td>
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</tbody>
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#### Chemorefractory Disease

<table>
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<tr>
<th>Author</th>
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<tr>
<td>Haug</td>
<td>58</td>
<td>SIR-Spheres®</td>
<td>26%</td>
<td>63%</td>
<td>nr</td>
<td>10.8 months</td>
</tr>
<tr>
<td>Saxena</td>
<td>40</td>
<td>SIR-Spheres®</td>
<td>31%</td>
<td>39%</td>
<td>6.8</td>
<td>13.6 months</td>
</tr>
<tr>
<td>Cianni</td>
<td>71</td>
<td>SIR-Spheres®</td>
<td>62%</td>
<td>27%</td>
<td>nr</td>
<td>13.6 months</td>
</tr>
</tbody>
</table>

Key: ORR: objective response rate (complete response + partial response) by RECIST; SD: stable disease; TTP: time to progression; †: SIR-Spheres Y-90 resin microspheres; nr: not reported; §: CT/MRI data only available for 43 patients.

### Retrospective study of patients with breast cancer liver metastases treated with SIR-Spheres Y-90 resin microspheres

A retrospective study of 44 patients with unresectable liver metastases from breast cancer who were chemotherapy refractory and subsequently treated with SIR-Spheres Y-90 resin microspheres revealed:

- patients (mean age 58 years; range 42–71) all had bilateral lesions and liver-related symptoms prior to SIRT and 66% had bone or nodal metastases. All had received doxorubicin and docetaxel; 31 (70%) were ER-positive and had received endocrine therapy, whilst 12 (27%) were HER2 receptor positive and 10 had received trastuzumab;
- 73% of the patients were considered chemotherapy refractory, having failed three or more regimens, with the remainder (27%) treated for liver progression during a treatment hiatus after first- or second-line chemotherapy;
- all patients reported mild-to-moderate post-embolisation syndrome, but only 8 (18%) needed hospitalisation for one night for pain control (3) or dehydration (5), with the remainder treated as out-patients. Grade 3 toxicities of nausea, vomiting and pain were present in 16% of patients. No patients required surgery;
- there was a complete response in 17% of evaluable patients by PET imaging at 12 weeks, a partial response in 58%, stable disease in 20%, and disease progression in 5%;
- by CT using RECIST criteria, there were partial responses in 47% of evaluable patients, with stable disease or minor response in 47%, and disease progression in 6%;
- 38 of 44 patients were still alive (86%) at a median follow-up of 14 months – 92% surviving in the treatment-hiatus cohort and 84% in the chemotherapy refractory group. The deaths were due to brain metastases (3 patients), recurrent hepatic disease (1 patient) or both (2 patients). Survival was short (median 3.6 months) if patients did not experience a response by PET or CT. No deaths were attributable to the procedure;
- the authors concluded that SIR-Spheres Y-90 resin microspheres demonstrated efficacy in treating hepatic metastases from breast cancer, both in chemotherapy refractory disease and during a treatment hiatus. They also noted that they expected these patients to show an increase in their overall survival since they had not reached their median survival even at 14 months post-SIRT; in comparison, two large cohorts of 350 and 500 breast cancer patients with liver metastases reported a median survival following diagnosis of 14–16.3 months respectively, which included the time spent on standard of care chemotherapy.

### Retrospective study of SIR-Spheres Y-90 resin microspheres in patients with treatment-refractory breast cancer liver metastases

The results of a retrospective study of 58 patients with breast cancer liver tumours who had failed prior chemotherapy and were treated using SIR-Spheres Y-90 resin microspheres, which or expanded upon earlier work from the same centre, showed:

- patients (mean age 58 ± 10.9 years) had a mean of 3.1 ±1.8 prior chemotherapies; 85% underwent prior anti-hormonal therapies and 17% received prior local hepatic therapies;
- mean hepatic tumour burden was 17.5%, and 20 patients presented with a hepatic tumour burden of more than 25%. Thirty-eight patients (66%) exhibited extrahepatic metastases;
- grade 4 toxicities appeared in two patients and two deaths were observed within three months after the procedure. The authors stated that death was most probably attributed to treatment-related hepatic toxicity. The first patient had been treated with 2 different chemotherapies (including taxanes and anthracyclines), anti-hormonal therapy, and radiofrequency ablation of hepatic metastases. The second patient had undergone four different chemotherapies (including taxanes, anthracyclines, capectabine, vinorelbine), bevacizumab, and trastuzumab;
- six patients experienced SIRT-induced gastric or duodenal ulcerations; five of these patients were treated before the study site started to do frequent monitoring of hepatic arterial flow during the procedure;
- CT/MRI findings were available for 43 patients, of which 11 (25.6%) showed a partial response, 27 (62.8%) showed stable disease, and five (11.6%) showed progressive disease;
- median overall survival was 47 weeks (10.8 months), with a significant correlation to SUV max assessed by 18F-FDG PET/CT, with responders having significantly longer survival (65 weeks) than non-responders (43 weeks; P < 0.05). A pre-therapeutic SUV max > 20 for the most intense hepatic metastasis per patient was associated with significantly shorter survival than was an SUV max of 20 or less (median survival: 52 weeks vs. 21 weeks; P < 0.005). The presence of extrahepatic metastases was not associated with a shorter survival (median survival in both groups was 47 weeks; P = 0.92);
the authors conclude that 18F-FDG PET using SUVmax is able to predict survival of breast cancer patients with hepatic metastases independently of their hormone or Her2/neu receptor status, hepatic tumour burden, response as assessed with CT or MRI, and the presence of extrahepatic disease;³
three of the first 16 patients treated by the authors were sufficiently downsized for potentially curative radiofrequency ablation (RFA) to be performed successfully. The authors concluded that SIR-Spheres Y-90 resin microspheres are able to downsize liver metastases making RFA suitable and the combination of SIRT + RFA could increase the number of patients with a complete response after minimally invasive therapy and should be taken into account for the best tailored approach;⁴
in a retrospective analysis of baseline biomarkers prior to SIRT, bivariate Cox regression models (using the Wald test) revealed a significant correlation of CEA (P = 0.022), CA 15-3 (P = 0.006) and LDH (P = 0.012) with overall survival;⁵
in a separate analysis, the investigators noted that treatment was associated with a significant mean decrease in the whole liver volume of 10.2% (median 16.7%; P = 0.0024), mainly caused by a reduction in the right lobe volume (median 16.0%; P = 0.0001). These changes were accompanied by a significant increase in the diameter of the main portal vein (mean 6.8%; P < 0.0001) as well as splenic volume (mean 50.4%; P < 0.0001).

Liver-tumour volume and diameter decreased by a median of 24% and 39.7%, respectively. The authors concluded that radioembolisation is associated with changes of hepatic parenchymal volume, splenic volume and portal vein size that appear not to represent clinically important sequelae in this patient cohort.⁶

Retrospective study of SIR-Spheres Y-90 resin microspheres in patients with chemoresistant breast cancer liver metastases

A single-centre study of 40 patients with unresectable, chemoresistant breast cancer liver metastases treated using SIR-Spheres Y-90 resin microspheres showed:

• the mean age of patients was 54.4 years (range 28–77);³
• 17 patients (43%) had ≥ 26% replacement of the liver by tumour. 24 patients (60%) had evidence of limited extrahepatic disease. All patients (100%) had been previously treated with at least one line of systemic chemotherapy. One patient (3%) underwent concomitant treatment with systemic chemotherapy and 15 patients (38%) were treated with systemic chemotherapy post SIRT;⁷
• a complete response was observed in two of 38 patients (5%), a partial response was observed in 10 patients (26%), stable disease in 15 patients (39%), and progressive disease in 11 patients (29%). One patient (3%) who had a partial response to treatment was downsized to resection after treatment;³
• the median survival after SIR-Spheres Y-90 resin microspheres was 13.6 months. The median time to progression was 6.8 months;³
• two factors were associated with an improved survival on multivariate analysis: CR/PR to treatment (vs. SD vs. PD; P < 0.001) and chemotherapy after radioembolisation (vs. no chemotherapy; P = 0.004);³
• 16 patients (40%) developed clinical toxicity after treatment; all complications were minor grade I/II and resolved without active intervention;³
• the authors concluded that treatment with SIR-Spheres Y-90 resin microspheres is a safe and effective treatment for patients with liver-dominant, chemoresistant breast cancer liver metastases and that the survival outcomes in this study are significantly superior to historical controls.⁷

References