# The following summarises the key data within the broad clinical platform supporting the use of SIR-Spheres microspheres in the treatment of liver metastases arising from colorectal cancer (mCRC) and provides results from various chemotherapy regimens as a comparative reference point.

**First-Line**

| Lead Author | n | Treatment | Cohort | ORR | SD | Median TTP or PFS | Median Survival |
|-------------|---|-----------|--------|-----|----|------------------+----------------|
| Gray        | 74 | SIR-Spheres® + FUDR HAC vs. FUDR HAC | LO     | 44% | 8.3% | 15.9 months\(\text{AL}\) | 9.7 months\(\text{AL}\) |
| van Hazel   | 21 | SIR-Spheres® + 5FU/LV vs. SFU/LV | LO     | 90.1% \(p < 0.001\) | 60.0% | 18.6 months\(\text{AL}\) | 3.6 months\(\text{AL}\) |
| Sharma      | 20 | SIR-Spheres® + FOLFOX4 | LO     | 90% | 10% | 9.3 months\(\text{AL}\) | 14.2 months\(\text{AL}\) |
| Kosmider    | 19 | SIR-Spheres® + FOLFOX4 or 5FU/LV | LO     | 84% | 5% | 10.4 months\(\text{AL}\) | 10.7 months\(\text{AL}\) |
| Tie         | 31 | SIR-Spheres® + FOLFOX4 or 5FU/LV | LO     | 91% | 9% | 13.2 months\(\text{AL}\) | 16.4 months\(\text{AL}\) |

**Consolidation of First-Line**

| Sangro       | 23 | SIR-Spheres® | LO | nr | nr | 6.3\(1/11.2\) months\(\text{AL}\) | 16.8\(1/23.6\) months\(\text{AL}\) |

**Second- or Third-Line**

| Lim         | 30 | SIR-Spheres® (+ 5FU) | LO | 33% | 27% | 5.3 months\(\text{AL}\) | nr |
| van Hazel   | 25 | SIR-Spheres® + irinotecan | LO | 48% | 39% | 6.0 months\(\text{AL}\) | 9.2 months\(\text{AL}\) |

**Salvage Therapy of Treatment-Refractory Disease**

| Hendlitz     | 44 | SIR-Spheres® + SFU vs. SFU (> SIR-Spheres® at PD) | LO | 10% | 76% | 5.5 months\(\text{AL}\) | 2.1 months\(\text{AL}\) |
| Seidensticker | 29 | SIR-Spheres® vs. BSC matched pairs | LO | 41.4% | 17.2% | 5.5 months\(\text{AL}\) | 3.5 months\(\text{AL}\) |
| Bested       | 29 | SIR-Spheres® vs. conventional therapy or BSC | LO | 41.4% | 17.2% | 5.5 months\(\text{AL}\) | 3.5 months\(\text{AL}\) |
| Cosimelli    | 50 | SIR-Spheres® | LO | 24% | 24% | 4 months\(\text{AL}\) | 12.6 months |
| Sofocleous   | 19 | SIR-Spheres® | LO | 70.6% \(\text{CR}\) | 6 months\(\text{AL}\) | 16.0 months |
| Kennedy      | 606 | SIR-Spheres® | LO | nr | nr | 9.6 months |
| Sofocleous   | 18 | SIR-Spheres® | LO | 40.0% \(\text{CR}\) | 5.1 months\(\text{AL}\) | 7.4 months |
| Leoni       | 51 | SIR-Spheres® | LO | 24% \(\text{CR}\) | nr | 8.0 months |
| Nace         | 51 | SIR-Spheres® (+ FUDR HAC) | LO | 12.9% | 64.5% | 10.2 months | 17.0 months |
| Cianni       | 41 | SIR-Spheres® | LO | 46% | 36% | 9.3 months\(\text{AL}\) | 11.8 months |
| Jakobs       | 41 | SIR-Spheres® | LO | 17% | 61% | 5.9 months\(\text{AL}\) | 10.5 months |
| Kennedy      | 208 | SIR-Spheres® responders | LO | 35.5% | 55% | nr | 10.5 months | 4.5 months |

**Key:** ORR: objective response rate (complete response + partial response) by RECIST unless indicated (\(\text{W}\) WHO criteria); SD: stable disease; TTP: time to progression; PFS: progression-free survival; AL: TTP or PFS in the liver; SIR-Spheres microspheres; LO: liver-only disease; LD: liver-dominant disease; \(\text{W}\) 90.1% by First Integrated Response, 72.7% by Best Confirmed Response; HR: hazard ratio; \(\text{AL}\): not reported; \(\text{AL}\): retrospective study; \(\text{AL}\): from date of SIRT; \(\text{AL}\): from first course of chemotherapy; BSC: best supportive care; DCR: disease control rate; \(\text{AL}\): disease control rate; \(\text{AL}\): Choi criteria.
Studies of SIR-Spheres microspheres in Combination with First-line Chemotherapy

The combination of SIR-Spheres microspheres with first-line chemotherapy have reported impressive results in 2 randomised controlled trials (RCTs) and a dose-escalation study, as well as in retrospective analyses including consolidation therapy.

RCT of SIR-Spheres microspheres + hepatic arterial chemotherapy vs. HAC alone at first-line

A RCT by Gray et al of SIR-Spheres microspheres plus hepatic arterial chemotherapy (HAC) using flouxuridine compared to HAC alone in 74 patients with liver metastases with mCRC was halted prematurely after the FDA stated that treatment-related response and time to progression were acceptable criteria for registration. The predominately first-line study (14.3% of patients had received prior chemotherapy for their liver metastases) showed:

- patients (mean age 60 years) had WHO performance status 0–2 and metastases limited to the liver and the lymph nodes of the porta hepatitis;
- a significantly higher objective response rate for patients receiving SIR-Spheres microspheres + HAC compared to HAC alone by both WHO criteria confirmed at 3 months (44.4% vs. 17.6%; \( P = 0.01 \)) and ≥50% reduction in elevated CEA values (72.2% vs. 47.1%; \( P = 0.004 \));
- a significantly longer median time to progression (TTP) of disease in the liver for patients receiving SIR-Spheres microspheres + HAC compared to HAC alone (15.9 vs. 9.7 months; \( P = 0.001 \)) and a trend for a survival advantage in those patients surviving more than 15 months (\( P = 0.06 \));
- the risk of death from progression of liver metastases was 3.1 times higher for patients in the HAC-only arm (95% CI 1.1–8.8; \( P = 0.03 \));
- no difference in the rate of grade 3 or 4 toxicity events, with 23 in each arm;
- no major adverse impact on quality of life by the addition of SIR-Spheres microspheres to HAC, with improved quality of life in both arms;
- the authors concluded that adding a single administration of SIR-Spheres microspheres to hepatic arterial chemotherapy significantly increased treatment effectiveness measured by tumour response and time to disease progression.

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

A second RCT by van Hazel and colleagues, comparing SIR-Spheres microspheres plus 5FU/LV versus 5FU/LV alone in the first-line treatment of 21 patients with liver metastases from CRC demonstrated significant benefits in favour of SIR-Spheres microspheres. This study reported:

- patients (mean age 64.5 years) had WHO performance status 0–2 with 24% having extra-hepatic disease in either the lung or peritoneum;
- all patients had multiple bilobar metastases and were reviewed by a surgical oncology unit to confirm that they were not amenable to either resection or ablation;
- significantly greater ORR for patients receiving the combination of SIR-Spheres microspheres + 5FU/LV (ORR: 90.1% using First Integrated Response, 72.7% using Best Confirmed Response vs. 0% by RECIST; \( P < 0.001 \));
- significantly longer median TTP for the combination of SIR-Spheres microspheres + 5FU/LV (18.6 vs. 3.6 months; \( P < 0.0005 \)), with patients in the combination arm able to receive chemotherapy for a longer period (median 8.1 vs. 3.8 cycles; \( P = 0.03 \));
- significantly longer median overall survival for SIR-Spheres microspheres + 5FU/LV compared to 5FU/LV alone (29.4 vs. 12.8 months; HR 0.33, 95% CI 0.12–0.91; \( P = 0.025 \));
- there were more Grade 3 to 4 toxicities in patients receiving the combination of SIR-Spheres microspheres + 5FU/LV, although the investigators considered that this was largely due to the greater period that these patients received protocol treatment;
- the health-related quality of life (HRQoL) of patients was not compromised by the addition of SIR-Spheres microspheres and that compared to 5FU/LV, patients receiving SIR-Spheres microspheres + 5FU/LV showed a significant improvement in HRQoL at 3 months (\( P = 0.03 \)). This improvement was sustained at 6, 12, 15 and 24 months;
- the investigators concluded that this small RCT demonstrated that the addition of a single administration of SIR-Spheres microspheres to 5FU/LV systemic chemotherapy increased treatment-related response, time to progression, quality of life and survival with acceptable toxicity.

Dose-escalation study of SIR-Spheres microspheres + FOLFOX4 first-line chemotherapy

The results of a dose-escalation study by Sharma et al combining SIR-Spheres microspheres with first-line FOLFOX4 (oxaliplatin + 5FU/LV) chemotherapy in 20 mCRC patients demonstrated:

- patients (median age 59 years) had WHO performance status 0–1, 35% had their primary disease in situ and 65% had extra-hepatic disease to the lung, lymph nodes, peritoneum and/or spleen;
- a 90% response rate by RECIST, together with a disease control rate of 100%; No patients reported progressive disease;
- 3 patients (15%) were down-staged and 2 (10%) were surgically resected;
- decreased serum CEA levels were seen in all patients with a baseline elevation, from a median of 470 ng/mL pre-treatment to 9 ng/mL at 6 months;
SIR-Spheres microspheres combined with first-line systemic chemotherapy

A retrospective analysis by Kosmider et al of SIR-Spheres microspheres in combination with chemotherapy (5FU/LV or FOLFOX4) as first-line treatment in 19 patients with unresectable CRC liver metastases demonstrated:

- patients (median age 62 years) had ECOG performance status 0–1. Most patients (95%) presented with synchronous metastases, good performance status (ECOG 0: 53%) with a median of 40% liver involvement (range 25–65%); 26% had extra-hepatic metastases;
- chemotherapy selection was at clinician discretion and according to local protocols; 12 of the 19 patients (63%) received FOLFOX4 chemotherapy and 7 patients (37%) received 5FU/LV;
- 2 patients (11%) with disease confined to the liver showed a complete response, 14 (74%) had a partial response and 1 (5%) had stable disease;
- median PFS was 10.4 months, with a trend for improved PFS in patients with liver-confined disease (10.7 vs. 3.6 months; \(P = 0.09\));
- median overall survival for all patients was 29.4 months. When patients were stratified by the presence or absence of extra-hepatic disease at diagnosis, overall survival was significantly longer for those with liver-only disease (median 37.8 vs. 13.4 months; \(P = 0.03\)). One patient had been disease-free per RECIST for more than 6 years, and two others remained in partial remission after more than 3 years of follow-up;
- the majority of adverse events that occurred in the first month were abdominal pain (7 patients; 37%) and fatigue (10 patients; 53%). One patient who received FOLFOX chemotherapy with full-dose oxaliplatin (85 mg/m²) experienced an episode of febrile neutropenia within the first 3 cycles. No other patients had grade 3/4 toxicity. The most serious adverse event was a treatment-related death from hepatic failure, presumed to represent radiation hepatitis, 2 months after treatment with SIRT and FOLFOX. One patient with gastroduodenitis at 12 weeks was diagnosed with a perforated duodenal ulcer; this patient had not undergone embolisation of the GDA or RGA before radioembolisation;
- the authors concluded that the present early series provides some valuable insights into the potential of radioembolisation with SIR-Spheres microspheres when used in combination with chemotherapy for the first-line treatment of patients with liver-dominant metastases from colorectal cancer. Patients with liver-only disease derived the greatest benefit.

Consolidation therapy using SIR-Spheres microspheres following first-line chemotherapy

A retrospective analysis by Sangro et al of SIR-Spheres microspheres in 23 patients with liver-dominant mCRC who were deemed to still be unresectable 12–26 weeks (median 21 weeks) after the start of first-line chemotherapy showed:

- patients (median age 60.2 years) had received oxaliplatin (100%), 5FU (8.7%) or capecitabine (91.3%), plus cetuximab (60.9%), irinotecan (21.7%) or bevacizumab (8.7%), with many (43.5%) having received hepatic arterial chemotherapy. Most patients had bilobar disease (82.6%) and extra-hepatic metastases (56.5%) in the lymph nodes, lung and/or peritoneum;
- the best response to chemotherapy was partial response or stable disease (91.3%), or progressive disease (8.7%);
- following treatment with SIR-Spheres microspheres, 3 patients (13%) had their tumours sufficiently down-sized to enable surgical resection ± RFA. These patients were censored at time of surgery for the PFS and survival analyses;
- patients received further chemotherapy either upon progression or as maintenance therapy, with 14 patients receiving no chemotherapy in the 3-month period following SIR-Spheres microspheres;
- median PFS was 6.3 months post-SIRT and 11.2 months from the first course of chemotherapy;
- median overall survival was 16.8 months post-SIRT and 23.6 months from the first course of chemotherapy;
- no grade 3 or 4 acute adverse events were recorded following treatment. There was a statistically significant but clinically irrelevant increase in bilirubin levels peaking at 2–3 months post-SIRT. 4 patients developed grade 1–2 radiation induced liver disease, defined by peak bilirubin >2 mg/dL and ascites 2–3 months post-SIRT;
- the investigators concluded that consolidation using SIR-Spheres microspheres after first-line treatment is a safe procedure that may reduce the rate of liver progression, further extend the proportion of patients receiving surgical resection and help provide long-term survival.

Studies of SIR-Spheres microspheres in Combination with Second- or Third-line Chemotherapy

In patients who have failed at least first-line chemotherapy, encouraging results have been reported with SIR-Spheres microspheres combined with chemotherapy.

Dose-escalation study of SIR-Spheres microspheres + irinotecan second-line chemotherapy

A multi-centre dose-escalation study by van Hazel et al combining SIR-Spheres microspheres with irinotecan in 25 patients failing prior chemotherapy showed:
• patients (mean age 59 years) had all failed at least first-line chemotherapy, with 32% having also failed second- or third-line regimens, and 60% having failed oxaliplatin-based regimens.13 Half of patients (52%) had liver-only metastases, with the remainder having extra-hepatic disease in the lymph nodes (12%) or lungs (36%).13
• an objective response rate of 48% by RECIST, with a disease control rate of 87%;13
• median serum CEA decreased by 82% at 3 months post-SIRT;13
• the median PFS was 6.0 months (range 1.6–11.4), and the PFS in the liver was 9.2 months (1.6–25.8);13
• median overall survival of 12.2 months (range 2.8–60+ months), with 3 patients still alive at the time of reporting;13
• these data compare favourably to phase II/III studies on irinotecan alone and irinotecan-based regimens;13-22
• the authors noted that the combination of SIR-Spheres microspheres with irinotecan had a safety profile equivalent to single-agent irinotecan in this disease setting, with significantly less myelosuppression than that reported in the dose-escalation study with FOLFOX4,13
• the authors concluded that SIR-Spheres microspheres in combination with weekly irinotecan at 100 mg/m² demonstrated an acceptable toxicity profile and promising efficacy.13

**Studies of SIR-Spheres microspheres in Chemorefractory Disease**

In heavily pre-treated, chemorefractory patients who have failed standard of care, SIR-Spheres microspheres demonstrated consistent and clinically meaningful results in a RCT and two comparative studies, as well as in retrospective analyses of routine clinical practice.27-28

**RCT of SIR-Spheres microspheres + 5FU chemotherapy vs. 5FU alone**

In a multi-centre RCT conducted in Belgium by Hendliz et al, 44 patients with CRC liver metastases that were refractory to or could not tolerate multiple prior lines of standard-of-care chemotherapy including oxaliplatin and irinotecan were randomised to either SIR-Spheres microspheres plus infusional 5FU or 5FU alone.27 On disease progression, patients in the control arm were reassessed for cross-over to salvage therapy with SIR-Spheres microspheres. The investigators reported:

• all patients (median age 62; range 45–91) had liver-only metastases and were balanced between the two arms without significant differences;27
• disease control rate (PR + SD) was significantly higher in patients receiving SIR-Spheres microspheres + 5FU compared to 5FU alone (86% vs. 35%, respectively; P = 0.001).27 Despite no previous objective response to both FOLFOX and FOLFIRI chemotherapy, one patient receiving SIR-Spheres microspheres + 5FU had a sufficiently large reduction in tumour size to permit potentially curative surgical resection of the remaining disease;21
• median TTP in the liver – the primary endpoint of the study – was significantly increased in the SIR-Spheres microspheres + 5FU arm compared to the 5FU-only arm (5.5 vs. 2.1 months, respectively; HR 0.38, 95% CI 0.20–0.72; P = 0.003);27
• median TTP anywhere in the body was also significantly longer for patients receiving SIR-Spheres microspheres + 5FU compared to 5FU alone (4.5 vs. 2.1 months, respectively; HR 0.51, 95% CI 0.28–0.94; P = 0.03);27
• following progression of disease, 10 patients (43.5%) in the 5FU-only arm subsequently crossed over to receive SIR-Spheres microspheres alone as salvage therapy and so overall survival was extended in both treatment arms by the targeted treatment of liver tumours.27 Overall, there was 2.5 months’ difference in the median survival (10.0 vs. 7.3 months) between the combination and 5FU-only arms, respectively (HR 0.92; P = 0.80);24
• treatment with SIR-Spheres microspheres + 5FU was well tolerated, with more patients experiencing a serious adverse event in the 5FU-only control arm (6 vs. 1, respectively; P = 0.10).27 The investigators noted that this increase was probably due to the lower efficacy of 5FU alone and more rapidly progressing disease;27
• the authors concluded that SIR-Spheres microspheres combined with systemic 5FU significantly prolongs both liver and overall TTP, compared with 5FU alone in a cohort of patients with liver-only disease at the time of randomisation, and that toxicities with the combination remained very low and easily manageable.27 The investigators recommended that SIRT/radioembolisation using SIR-Spheres microspheres should be considered as a valid therapeutic option in patients with liver-limited chemotherapy refractory mCRC.27

**Comparative study of SIR-Spheres microspheres vs. a matched-pair cohort receiving best supportive care**

A retrospective study was performed by Seidensticker et al to investigate the efficacy and safety of SIR-Spheres microspheres as salvage therapy in 29 heavily pre-treated patients with extensive (≥20% liver involvement) and progressive liver-dominant disease which were followed prospectively, compared to 29 matched-pair control patients who received best supportive care (BSC).28 Control patients were matched by tumour burden, synchronous vs. metachronous metastases, ALP increase and CEA >200 U/mL.28 The results showed:

• 58 patients’ (mean age 61.6 years) characteristics were well balanced between the SIR-Spheres microspheres and BSC cohorts, with extensive liver tumour involvement: median 30% (range 20–50%) vs. 25% (10–75%), respectively.28 Patients in each cohort received a median of 3 (2–6) prior lines of chemotherapy.28
• the two cohorts were matched on all 4 criteria in 16 pairs (55.2%), with the remainder matching by 3 and 2 criteria (37.9% and 6.9%, respectively);28
• a partial response was observed in 12 patients (41.4%), with stable disease in a further 5 patients (17.2%);28
• median PFS was 5.5 months in patients receiving SIR-Spheres microspheres, compared with 2.1 months in the BSC cohort;28
• median overall survival was significantly longer for the patients receiving SIR-Spheres microspheres compared with BSC (8.3 vs. 3.5 months; HR 0.26, 95% CI 0.15–0.48; \( P < 0.001 \)). This benefit was clearly evident at 3 months (97% vs. 59% survival) and was sustained through 12-months follow up (24% vs. 0% survival);28
• adverse events following SIR-Spheres microspheres included grade 1–2 fatigue (69%), grade 1 abdominal pain/nausea (48.3%) and 3 patients (10.3%) experienced grade 2 GI ulcers. Three cases (10.3%) of radiation-induced liver disease were medically managed and not considered life-threatening (median survival 9.8 months; range 9.0–16.6);28
• a multivariate Cox proportional hazard model analysis revealed that treatment with SIR-Spheres microspheres was the only significant predictor for prolonged survival (HR 0.30; 95% CI 0.16–0.55; \( P < 0.001 \)), whereas the extent of liver involvement was associated with an increased risk of death (HR 1.03; 95% CI 1.0–1.06; \( P = 0.028 \));28
• the investigators concluded that SIR-Spheres microspheres in addition to BSC provides substantial clinical benefit as evidenced by significantly prolonged overall survival compared with BSC alone in a well-matched cohort of patients with extensive liver-dominant treatment-refractory disease for whom there are limited treatment options.28

Comparative study of SIR-Spheres microspheres vs. control patients receiving standard care
A retrospective study by Bester et al analysed the survival outcomes for patients receiving SIR-Spheres microspheres compared to control patients referred back to their treating physician for conventional therapy or best supportive care in 339 patients with unresectable chemotherapy-refractory liver-dominant metastases, including 253 patients with mCRC:29
• the study excluded patients with extensive extrahepatic metastases, ECOG performance status score >2, excessive hepatic tumour burden (>75%), and/or compromised residual liver function. This ensured that the standard-care control group, which comprised patients unsuitable for SIRT due to potential for non-target delivery to the GI tract or lungs, or reasons relating to patient consent (e.g. refusal or other treatment option chosen), was unlikely to represent patients with more advanced disease;29
• patients with mCRC presented with good performance status (ECOG 0, 85%), with bilobar disease (87%) and typically 0–25% tumour burden in the liver, although 38% had limited extrapancreatic disease;29
• the investigators reported that overall survival was significantly prolonged in 224 patients with chemotherapy refractory mCRC receiving SIR-Spheres microspheres compared with 29 control mCRC patients receiving standard care (median 11.9 vs. 6.6 months; HR 0.50; \( P < 0.001 \));29
• in a multivariate analysis, SIRT using SIR-Spheres microspheres was the only significant predictor for prolonged survival (HR 0.57; \( P = 0.002 \));29
• treatment was well tolerated, with minor adverse events at the time of SIRT (grade 1 abdominal pain, nausea/vomiting) in 22% of patients. Grade 1 abdominal pain (18%) and lethargy (12%) was reported in the first month following SIRT, with 1.8% grade 2 gastritis, 0.6% grade 2 gallbladder complications, 0.6% grade 2 ulceration and 0.3% mild (grade 2) radiation-induced liver disease. At the 3-month follow-up, there were 3.2% grade 2/3 GI ulcers, 2.9% radiation-induced liver disease and 1.8% gallbladder complications. These adverse events were all medically managed, with no deaths within the 3-month follow-up;29
• the authors concluded that SIRT using SIR-Spheres microspheres is an effective and safe treatment for patients with chemotherapy-refractory liver metastases and improves overall survival in a select population compared with standard care alone.29

Prospective study of SIR-Spheres microspheres in salvage therapy of chemorefractory patients
A prospective multi-centre study by Cosimelli and colleagues of patients who had all failed oxaliplatin- and irinotecan-based regimens revealed:30
• 50 patients (median age 67 years) had a median WHO performance status of 0 (range 0–3), with most having extensive liver involvement (25–50%).30 All patients had failed ≥3 lines of chemotherapy and 76% had failed 4 or 5 lines; 22% had received prior bevacizumab;30
• the objective response rate of 24% (2% CR + 22% PR) met the pre-defined criteria for significance (\( P = 0.05 \)), with 2 patients becoming sufficiently down-staged to plan radical surgical resection of ≥3 segments;30
• the median overall survival was 12.6 months, with a significant difference between responders (CR + PR + SD = 48%) and non-responders (PD) or unconfirmed response (16 vs. 8 months; \( P = 0.0006 \));30
the investigators concluded that SIRT-Spheres microspheres “represents a promising salvage therapy for patients with unresectable, highly pre-treated colorectal liver metastases.”

• the authors noted that the results compared favourably with phase II/III studies of chemotherapy regimens at 2nd or subsequent lines of therapy, and also reflected previous experience with SIRT-Spheres microspheres in retrospective studies.

Dose-escalation study of SIRT-Spheres microspheres in patients refractory to systemic and hepatic arterial chemotherapy

A prospective dose-escalation study by Sofocleous and colleagues in 19 patients with colon cancer liver metastases who had failed hepatic arterial (pump) and systemic chemotherapy demonstrated:

• treatment with SIRT-Spheres microspheres was administered in 3 escalating activity levels: the first cohort received 70%, the second 85%, and the third 100% of the calculated activity. All 19 patients received post-SIRT chemotherapy as determined by the patients’ medical oncologist.

• 12 patients (70.6%) responded (defined as stable disease or better) while 5 (29.4%) had progressive disease.

• median PFS was 6 months (95% CI 3.2–9.7); median overall survival was 16 months (95% CI 5.8–17.6).

• common post-treatment side effects were grade 1–2 fatigue and grade 1 fever. No dose-limiting toxicities were observed. Grade 3 nausea and pain was recorded for 2 patients and was attributed to progressive disease; one patient in the third cohort suffered grade 3 nausea and pain.

• the authors concluded that it is safe to administer the full calculated activity of SIRT-Spheres microspheres in patients with colorectal liver metastases who progressed despite prior pump and systemic chemotherapy. The authors noted that oncologic outcomes were promising.

Largest US multi-centre evaluation of safety and survival of SIRT-Spheres microspheres in unresectable colorectal liver metastases

An investigator-initiated retrospective multi-centre study by Kennedy and colleagues of heavily pre-treated patients analysed the outcomes following SIRT-Spheres microspheres in U.S. patients treated since 2002. The study’s endpoints included safety and tolerability, tumour response and survival.

• 606 patients (233 women; 373 men) at 10 institutions received a total of 966 SIRT procedures. Their mean age was 61.5 years (range, 20.8 to 91.9 years). Active extra-hepatic disease was present prior to the first SIRT procedure in 35.1% of patients. The vast majority (at least 92.6%) of patients had received prior chemotherapy, with over 30% having also received prior liver surgery or ablation.

• median overall survival for these heavily pre-treated patients was 9.6 months (95% CI 9.0–11.1) from their first SIRT treatment, with a median follow-up of 8.6 months (0.1–77.7 months).

• reported adverse events were typically transient in duration and mild or moderate in severity. In total, 45% of patients had fatigue, 28% experienced nausea and 1% had liver failure. Only 2.1% of all treatments required an overnight stay following the procedure.

• the authors concluded that the modern USA experience of SIRT for unresectable, heavily pretreated mCRC liver metastases is encouraging with a median survival of 9.6 months from the first procedure. Toxicity was mild and of short duration in most patients.

References

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