

Published Data in metastatic Neuroendocrine Tumors

The following tables summarize the prospective and retrospective studies on the use of SIR-Spheres Y-90 resin microspheres in the treatment of liver metastases from neuroendocrine tumors (NETLM). Tumor response and/or survival results are listed accordingly.

For studies in which multiple tumor types were investigated, outcomes include all tumor types, unless otherwise noted.

Prospective studies

Treatment/Line of Therapy (n)	N (n)	ORR ^a	SD ^a	Median TTP or PFS	Median survival from diagnosis	Reference
CapTem followed by SIR-Spheres ^b 2nd line	19	74% intrahepatic; 55% extrahepatic	26% intrahepatic; 45% extrahepatic	Hepatic PFS: 42.5 mo; TTP (any site): 38.5 mo	40.9 mo (mean, after treatment) 106 mo (mean, after dx)	Soulen, 2018
SIR-Spheres + pasireotide + everolimus ≥1st line (13)	13	46% (PR)	23%	18.6 mo	46.3 mo	Kim, 2018
SIR-Spheres ≥2nd line (6) or HAE ≥2nd line (5)	11	33% (2/6) (PR)	nr	nr	nr	Elf, 2018
SIR-Spheres ≥1st line (44) TACE ≥1st line (28)	72	nr	nr	nr	SIR-Spheres: 66.8 mo TACE: 81.9 mo	Singla, 2016
SIR-Spheres ≥2nd line (30)	30	nr	nr	nr	32.8 mo (mean)	Cramer, 2016
SIR-Spheres ≥10% lung shunt fraction ≥1st line (15); <10% lung shunt fraction ≥1st line (29)	44	nr	nr	nr	80.3 mo (after primary NET dx) 45.3 mo (after mNET dx) 27.4 mo (after first SIRT)	Ludwig, 2016
SIR-Spheres > 1st line (15)	15	nr	nr	PFS: 24.8 mo (mean)	31.0 mo (mean)	Filippi, 2016
SIR-Spheres ≥1st line (1); 2nd line (5); 3rd line (6); 4th line (1)	13	¹¹¹ In-octreotide scintigraphy evaluation: 77% (PR) CT evaluation: 10% (CR) 40% (PR)	¹¹¹ In-octreotide scintigraphy evaluation: 15% CT evaluation: 40%	PFS: 17 mo, for 11 pts	18 mo (mean; entire cohort) ¹¹¹ In-octreotide scintigraphy evaluation: 21.3 mo (CR + PR); 15.3 mo (SD + PD) CT evaluation: 20.4 mo (CR+PR); 18.5 mo (SD + PD)	Lacin, 2011
SIR-Spheres ≥1st line (48)	48	54%	23%	nr	35 mo	Saxena, 2010
SIR-Spheres ≥2nd line (9)	9	67% (PR)	33%	TTP: 11.1 mo (mean)	median OS nr [100%, 1-y rate] [57%, 2- and 3-y rates]	Kalinowski, 2009
≥2nd line (34) SIR-Spheres + 5-FU	34	51% (17/33)	15%, [5/3]	nr	27.6 mo (mean)	King, 2008
SIR-Spheres ≥2nd line (20) TheraSphere ^c ≥2nd line (22)	42	50% (PR) 54% (PR)	44% [7/16] 38% [5/13]	nr	28 mo 22 mo (projected)	Rhee, 2008

Retrospective studies

Treatment/Line of Therapy (n)	N	ORR ^a	SD ^a	Median TTP or PFS	Median survival from diagnosis	Reference
SIR-Spheres ≥2nd line (6) TheraSphere ≥2nd line (3)	HCC (5); CRCLM (3); NETLM (1)	100% (PR)	nr	nr	nr	Mafeld, 2019
SIR-Spheres ≥2nd line (24)	24	At 3 mo: 58% (14/24); DCR: 88% (21/24)	At 3 mo: SD: 29.2% (7/24); MR: 8.3%, (2/24) At 6 months: SD: 33.3% (8/2); MR: 8.3% (2/24)	PFS: 41 mo	OS: 57 mo	Frilling, 2019
SIR-Spheres ≥1st line	All tumor types: 26; HCC (7); NETLM (8) ; CRCLM (4); BCLM (3); melanoma LM (3); sarcoma LM (1)	PR: 25% (for liver mets only)	67% (for liver mets)	nr	nr	Li, 2019
SIR-Spheres ≥2nd line (38) or TheraSphere ≥2nd line (21)	59	mRECIST: 57.7% (30/52) EASL: 59.6% (31/52)	mRECIST: 59.6% (18/52) EASL: 29% (15/52)	PFS from Tx: 13 mo Hepatic PFS from Tx: 18 mo	31 mo from Tx	Zuckerman, 2019
SIR-Spheres ≥2nd line	All tumor types: 38 non-HCC group (15), including NETLM (7)	42.9% (PR only; non-HCC group) qEASL: 28.6% (PR only; non-HCC group)	57.1% (non-HCC group) qEASL: 71.4% (non-HCC group)	nr	19.0 mo (non-HCC group; from Tx)	Schobert, 2019
SIR-Spheres ≥1st line (244)	244 (NENLM)	15.7% at 3 mo; 28.5% at 6 mo mRECIST: 42.8% at 3 mo; 62.9% at 6 mo	75.6% at 3 mo; 62.9% at 6 mo; mRECIST: 48.4% at 3 mo; 28.6% at 6 mo	nr	31.2 mo ^d (entire population) 37.2 mo (G1NET); 28.8 mo (G2NET); 10.8 mo (G3NET/NEC); P <0.001	Braat, 2018
SIR-Spheres ≥1st line (366)	All tumor types: 366 ^e NETLM (51)	nr	nr	nr	11.4 mo	Ingrisch, 2018
SIR-Spheres 1st line (35); ≥2nd line (58)	93	25% (PR)	67%	nr	28 mo	Tomozawa, 2018 ^a
SIR-Spheres ≥1st line (1), TACE ≥1st line (53), or TAE ≥1st line (3)	57	WHO: 17% (PR)	WHO: 78%	14 mo (TACE only)	22 mo	Grozinsky-Glasberg, 2018
SIR-Spheres > 1st line	15	WHO: 46.7%	WHO: 53.3%	nr	nr	Chansanti, 2017
SIR-Spheres ≥2nd line (389)	All tumor types: 389; NETLM (56)	<1% (CR) 22% (PR)	41%	nr	11.7 mo ^f	Paprottka, 2017
SIR-Spheres ≥2nd line (29) or TheraSphere ≥2nd line (7)	36	nr	nr	nr	41 mo	Jia, 2017
≥1st line SIR-Spheres (43) or TheraSphere (21); lipiodol and doxorubicin ± mitomycin C and cisplatin (TACE) ≥1st line (50); Embosphere ^g or PVA (TAE) ≥1st line (41)	155	nr	nr	HPFS: 13.2 mo	48.2 mo	Chen, 2017
SIR-Spheres ≥2nd line (40)	40	Imaging response (PR only): 54% (3 mo); 34% (20 mo) Biochemical response (PR only): 21% (3 mo); 8% (20 mo)	Imaging response: 41% (3 mo); 23% (20 mo) Biochemical response: 71% (3 mo); 60% (20 mo)	9.0 mo	24.7 mo	Barbier, 2016

Treatment/Line of Therapy (n)	N (n)	ORR ^a	SD ^a	Median TTP or PFS	Median survival from diagnosis	Reference
≥1st line (366) SIR-Spheres or TheraSphere	All tumor types: 366; NETLM (73)	nr	nr	nr	14.7 mo (entire cohort) 33.0 mo (mNET, LSF <10%); 9.1 mo (mNET, LSF ≥10%)	Xing, 2016
SIR-Spheres ≥2nd line (30)	30	46%	37%	nr	39 mo	Peker, 2015
SIR-Spheres ≥2nd line (12) HAE ≥2nd line (13) HACE ≥2nd line (17)	42	nr	nr	19.2 mo (from first SIRT) SIR-Spheres: 15.1 mo HAE: 12.1 mo HACE: 33.4 mo (ns) 5-year PFS: 15%	41.9 mo (from first LDT) SIRT: 26.8 mo HAE: 21.3 mo HACE: 68.7 mo (ns)	Engelman, 2014
≥2nd line SIR-Spheres (21) or TheraSphere (2)	23	Imaging response 30.4% (PR only) Biochemical response 7.7% (CR) 46.2% (PR)	Imaging response 60.9% Biochemical response 38.5%	nr	29 mo	Ezziddin, 2012
SIR-Spheres ≥2nd line (42)	42	22.5% (PR only)	75%	12.7 mo	nr	Paprottka, 2012
SIR-Spheres SIRT ≥1st line (58); glass (22); resin (20)	58	39% (20/51)	27% (14/51)	nr	36 mo	Cao, 2010
SIR-Spheres ≥2nd line (148)	148	63.2% (117/185)	22.7%	nr	70 mo	Kennedy, 2008
SIR-Spheres ≥2nd line (8)	8	12.5%	50% (4/8)	nr	14 mo (from SIRT) 36.5 mo (from mNET dx)	Murthy, 2008

In an effort to facilitate the review of data in this table, data originally reported as days/weeks were converted to months.

5-FU: 5-fluorouracil; BCLM: breast cancer liver metastases; CapTem: capecitabine + temozolomide; CRCLM: colorectal cancer liver metastases; DCR: disease control rate; dx: diagnosis; EASL: European Association for the Study of the Liver criteria; G1NET: grade 1 neuroendocrine tumor; G2NET: grade 2 neuroendocrine tumor; G3NET/NEC: grade 3 neuroendocrine tumor/neuroendocrine carcinoma; HACE: hepatic artery chemoembolization; HAE: hepatic arterial embolization; HCC: hepatocellular carcinoma; HPFS: hepatic progression-free survival; LDT: liver-directed therapy; LSF: lung shunt fraction; mNET: metastatic neuroendocrine tumor; MR: mixed result; mRECIST: modified RECIST; mo: months; NENLM: neuroendocrine neoplasms liver metastases; NETLM: neuroendocrine tumor liver metastases; nr: not reported; ns: not significant; ORR: objective response rate [complete response [CR] + partial response [PR]]; OS: overall survival; PFS: progression-free survival; pts: patients; PVA: polyvinyl alcohol; qEASL: Quantitative EASL criteria; SD: stable disease; SIRT: selective internal radiation therapy; TACE: transarterial chemoembolization; TAE: transarterial embolization; TTP: time to progression; Tx: treatment; WHO: World Health Organization criteria; y: year(s).

- a. By RECIST (Response Evaluation Criteria In Solid Tumors) unless otherwise indicated.
- b. SIR-Spheres Y-90 resin microspheres.
- c. TheraSphere Yttrium-90 Glass Microspheres.
- d. Months calculated from years using Google calculator: 1 year = 12 months.
- e. Data represent a subset of data from Paprottka 2017.
- f. Months calculated from days using Google calculator: 1 day = 0.0328767 months.
- g. Embosphere Microspheres

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