

Search Syntax

Search strings:

PubMed:

((colorectal [tiab] OR rectal [tiab] OR colon [tiab] OR rectum [tiab] OR sigmoid [tiab] OR sigmoidal [tiab] OR rectosigmoid [tiab] OR rectosigmoidal [tiab] OR "large bowel" [tiab]) AND (liver [tiab] OR hepar [tiab] OR hepatic [tiab]) AND (metastasis [tiab] OR metastases [tiab] OR metastatic [tiab] OR disseminated [tiab] OR advanced [tiab])) AND ((yttrium [tiab] OR yttrium-90 [tiab] OR y90 [tiab] OR y-90 [tiab] OR 90yttrium [tiab] OR 90-yttrium [tiab] OR 90y [tiab] OR 90-y [tiab] OR "(90)yttrium" [tiab] OR "(90)-yttrium" [tiab] OR radioembolisation [tiab] OR radioembolization [tiab] OR "radio embolisation" [tiab] OR "radio embolization" [tiab] OR "radio-embolisation" [tiab] OR "radio-embolization" [tiab] OR "selective internal radiation therapy" [tiab] OR sirt [tiab] OR "internal radiation" [tiab] OR "intraarterial radiation" [tiab] OR "intra arterial radiation" [tiab]))

EMBASE:

((colorectal:ti,ab OR rectal:ti,ab OR colon:ti,ab OR rectum:ti,ab OR sigmoid:ti,ab OR sigmoidal:ti,ab OR rectosigmoid:ti,ab OR rectosigmoidal:ti,ab OR "large bowel":ti,ab) AND (liver:ti,ab OR hepar:ti,ab OR hepatic:ti,ab) AND (metastasis:ti,ab OR metastases:ti,ab OR metastatic:ti,ab OR disseminated:ti,ab OR advanced:ti,ab)) AND ((yttrium:ti,ab OR yttrium-90:ti,ab OR y90:ti,ab OR y-90:ti,ab OR 90yttrium:ti,ab OR 90-yttrium:ti,ab OR 90y:ti,ab OR 90-y:ti,ab OR "(90)yttrium":ti,ab OR "(90)-yttrium":ti,ab OR radioembolisation:ti,ab OR radioembolization:ti,ab OR "radio embolisation":ti,ab OR "radio embolization":ti,ab OR "radio-embolisation":ti,ab OR "radio-embolization":ti,ab OR "selective internal radiation therapy":ti,ab OR sirt:ti,ab OR "internal radiation":ti,ab OR "intraarterial radiation":ti,ab OR "intra arterial radiation":ti,ab))

Cochrane Library:

((colorectal OR rectal OR colon OR rectum OR sigmoid OR sigmoidal OR rectosigmoid OR rectosigmoidal OR "large bowel") AND (liver OR hepar OR hepatic) AND (metastasis OR metastases OR metastatic OR disseminated OR advanced)) AND ((yttrium OR yttrium-90 OR y90 OR y-90 OR 90yttrium OR 90-yttrium OR 90y OR 90-y OR "(90)yttrium" OR "(90)-yttrium" OR radioembolisation OR radioembolization OR "radio embolisation" OR "radio embolization" OR "radio-embolisation" OR "radio-embolization" OR "selective internal radiation therapy" OR sirt OR "internal radiation" OR "intraarterial radiation" OR "intra arterial radiation"))

Supplemental Table 1. Study characteristics for patient cohorts treated with Y90 radioembolization as monotherapy.

		Study population									Treatment		Outcome			
Author	Study design	No. of mCRC pts	Total cohort size	Median age (range)	Inclusion criterion for disease status	Patients with EHD	Performance score	Hepatic function ^a	Tumor burden	Previous systemic treatment lines	Microsphere type	Delivered activity (GBq)	Imaging interval - Time of response - Follow-up duration	Response (n) CR - PR - SD - PD - NE	Median progression-free survival (95%-CI)	Median overall survival (95%-CI)
Bester et al. ²⁰¹²	Retrospective cohort	224	339	67 (27-89)	Minor intraabdominal lymphadenopathy, minor bone or lung lesions	85/224 (38%)	85% had ECOG of 0	NR	Most pts had 0-25%	NS for mCRC	Resin	Median 1.8 (range 0.42-2.55)	NA - NA - NA	NR	NR	11.9 months (10.1-14.9)
Fahmueller et al. ²⁰¹²	Prospective cohort	49	49	62.6 (35-77)	Liver dominant (NS)	NR	NR	NR	NR	NR	Resin	NR	At 3 months - At 3 months - 3 months	0 - 9 - 5 - 25 - 10	NR	8.8 months (5.1-18.1)
Martin et al. ²⁰¹²	Retrospective cohort	24	24	63 (35-83)	Liver dominant (NS)	13/24 (54%)	NR	NR	NR	Median number of lines 3 (0-7)	NR	NR	NR - NR - NR	No objective responses	3.9 months (2.4-4.8)	8.9 months (4.2-16.7)
Tochetto et al. ²⁰¹²	Retrospective cohort	20	20	Mean 65.1 (40-86)	NR	NR	NR	NR	NR	NR	Glass	NR	At 1 and 3 months - At 3 months - NR	n=6 CR or PR; n=14 SD or PD	NR	NR
Seidensticker et al. ²⁰¹²	Retrospective cohort	29	229	Mean 61.9 (SD 7.4)	Only nonprogressive extrahepatic deposits	14/29 (48%)	NR	NR	<25%: n=13 26-50%: n=15 >50%: n=0	2 lines: n=8 (28%) 3 lines: n=9 (31%) >3 lines: n=12 (41%)	Resin	Median 1.76 (range 0.93-2.56)	At 6 weeks, then every 3 months - NR - NR	0 - 12 - 5 - 11 - 0	5.5 months (95%-CI NR)	8.3 months (95%-CI NR)
Cosimelli et al. ²⁰¹⁰	Phase 2 trial	50	50	67 (34-85)	≤ 3 nodules in the same organ each < 3 mm	11/50 (22%)	0: n=35 (70%) 1: n=14 (28%) 2: n=0 (0%) 3: n=1 (2%)	Median bilirubin: 0.92 mg/100ml Median ALT: 55 UI-1 Median AST 58 UI-1	<25%: n=20 25-50%: n=30	3 lines: n=12 (24%) 4 lines: n=25 (50%) 5 lines: n=13 (26%)	Resin	Median 1.7 (range 0.9-2.2)	Every 6 weeks - At 6 weeks - 11 months	1 - 11 - 12 - 22 - 4 ^a	3.7 months (2.6-4.9)	12.6 months (7.0-18.3)
Cianni et al. ²⁰⁰⁹	Retrospective cohort	41	41	Mean 61.2 (range NR)	Liver dominant (NS)	4/41 (10%)	Median 0.7	NR	<25%: n=25 25-50%: n=6 >50%: n=10	All pts had undergone >1 line, not further specified	Resin	Mean 1.82	At 2 and 3 months - At 8 weeks - NR	2 - 17 - 14 - 8 - 0	279 days (= 9.2 months) (95%-CI NR)	11.6 months (95%-CI NR)
Hong et al. ²⁰⁰⁹	Retrospective cohort	15	15	62 (51-80)	Liver dominant (NS)	5/15 (33%)	NR	NR	NR	NR	Glass	NR	Every 4 to 6 weeks - NA - 5.7 months	NR	NR	6.9 months (95%-CI NR)
Mulcahy et al. ²⁰⁰⁹	Prospective cohort	72	72	61 (54-86)	EHD not clinical important	29/72 (40%)	0: n=48 (67%) 1: n=16 (22%) 2: n=8 (11%)	Elevated bilirubin: n=7 Elevated AST/ALT: n=27	<25%: n=58 25-50%: n=11 >50%: n=3	0 lines: n=4 (5%) 1 line: n=10 (14%) 2 lines: n=30 (42%) 3 lines: n=28	Glass	Median 2.37 (range 0.67-6.57)	At 1 month, then every 3 months - NR - NR	0 - 29 - 32 - 11 - 0	TTP: 15.4 months (5.4-18)	14.5 months (9.6-21.9)

									(39%)							
Jakobs et al. ²⁰⁰⁸	Retrospective cohort	41	41	Mean 61 (37-77)	Liver dominant (NS)	7/41 (17%)	NR	NR	NR	Mean number of regimes 2.8 (1-5)	Resin	Mean 1.9 (range 0.7-2.8)	NR - NR - 7.9 months	0 - 7 - 25 - 4 - 0	TTLP: 5.9 months (95%-CI NR)	10.5 months (1.3-38.3)
Sato et al. ²⁰⁰⁸	Phase 2 trial	51	137	Mean 63 (range NR)	EHD not clinical important	NR	0: n=34 (67%) 1: n=12 (23%) 2: n=5 (10%)	NR	NR	NS for mCRC	Glass	NS for mCRC	Every 3 months - NA - 5.2 months	NS for mCRC	NR	457 days (= 15.2 months) (95%-CI NR)
Kennedy et al. ²⁰⁰⁶	Retrospective cohort	208	208	61.5 (30-94)	Liver dominant (NS)	NR	NR	NR	NR	1 line: n=12 (6%) 2 lines: n=15 (7%) 3 lines: n=181 (87%)	Resin	Median 1.7 (range 0.4-2.9)	NR - At 3 months - NR	0 - 74 - 114 - 21 - 0 ^c	NR	Resp: 10.5 months Nonresp: 4.5 months (95%-CIs NR)
Lewandowski et al. ²⁰⁰⁵	Phase 2 trial	27	27	68 (54-86)	EHD not clinical important	21/27 (78%)	0: n=19 (70%) 1: n=7 (26%) 2: n=1 (4%)	Elevated bilirubin: n=3 Elevated ALT: n=6 Elevated AST: n=13	<25% n=21 25-50% n=5 >50% n=1	3 pts chemo naive	Glass	Median 2.37 (range 0.67-6.57)	At 3 months - At 3 months - 3 months	0 - 9 - 14 - 2 - 0 ^d	NR	283 days (218-406) (= 9.3 months)

In case of cohorts consisting only of part of patients with colorectal cancer liver metastases, data in this table are from those patients only. All studies included patients with unresectable and chemorefractory tumors.

mCRC colorectal cancer liver metastases; NR not reported; EHD extrahepatic disease; SD standard deviation; NS not specified; CI confidence interval

CR complete response; PR partial response; SD stable disease; PD progressive disease; NE not evaluable; TTLP time to liver progression

AST aspartate transaminase, ALT alanine transaminase.

^a *Two patients were lost to follow-up. Another two patients were excluded from the analysis due to excessive extrahepatic disease.*

^b *Two patients were lost to follow-up. Two patients had not yet completed first follow-up and one patient died before first imaging follow-up.*

^c *Patients numbers in publication do not add to exactly 208.*

^d *Responses are represented per treated lobe, per patient response are not unequivocally extractable and numbers do not add to 26.*

^e *Including bilirubin, AST, ALT, and albumin.*

Supplemental Table 2. Study characteristics for patient cohorts treated with Y90 radioembolization in combination with chemotherapy.

		Study population											Treatment		Outcome			
Author	Study design	No. of mCRC pts	Total cohort size	Median age (range)	Concomitant chemotherapy	Clinical setting	Inclusion criterion disease status	Patients with EHD	Performance score	Hepatic function ^a	Tumor burden	Previous systemic treatment lines	Microsphere type	Delivered activity (GBq)	Imaging interval - Time of response - Follow-up duration	Response (n) CR - PR - SD - PD - NE	Median progression-free survival (95%-CI)	Median overall survival (95%-CI)
Nace et al. ²⁰¹¹	Retrospective cohort	51	51	64 (37-83)	Intra hepatic floxuridine in 17/51 pts	Unresectable, chemorefractory	Tumor burden outside liver <10% of liver burden	28/51 (58%)	NR	Normal bilirubin: n=47	NR	capecitabine: n=14 becav/cetux: n=33	Resin	Median 0.89 (range 0.16-2.20)	Every 3 months - Between 30-180 days - 30-180 days	0 - 4 - 20 - 7 - 0	NR	10.2 months (7.5-13.0)
Zerizer et al. ²⁰¹²	Retrospective cohort	25	25	58.5 (30-78)	FOLFOX in 5/25 pts	Unresectable	Max one lung or one bone metastasis amenable for local treatment	3/25 (12%)	NR	NR	NR	All pts received prior chemotherapy	Resin	Mean 2.2 (0.8-2.3)	At 6 to 8 weeks - 6 to 8 weeks - NR	0 - 2 - 23 - 0 - 0	9 months (95%-CI)	NR
Kosmider et al. ²⁰¹¹	Retrospective cohort	19	19	62 (44-75)	5FU/LV or FOLFOX	Unresectable. Pts on first-line chemotherapy	Limited pulmonary nodules or abdominal lymphadenopathy	NR	0: n=10 (53%) 1: n=9 (47%)	NR	Median 40% (25-65%)	None	Resin	Median 1.96 (range 1.60-2.60)	Every 2 months - 4.4 months (for liver) - 18.6 months	Liver: 2 - 15 - 1 - 1 - 0 Overall: 2 - 14 - 1 - 2 - 0	10.4 months (95%-CI)	29.4 months (95%-CI NR)
Chua et al. ²⁰¹¹	Prospective database	48	48	NS ^b	5FU (concomitant or post-Y90)	Unresectable, chemorefractory	EHD limited to one site	NS ^b	NS ^b	NR	NR	NS ^b	Resin	NS ^b	Every 6 months - NR - NR	n=25 CR or PR, n=23 SD or PD	NR	13 months (95%-CI NR)
Hendlisz et al. ²⁰¹⁰	RCT (phase 3)	21	21	62 (46 - 91)	FU intravenous	Unresectable, chemorefractory	No EHD accepted	0/21 (0%)	0: n=15 (71%) 1: n=5 (24%) 2: n=1 (5%)	NR	NR	Last regime irinotecan based: n=13 oxaliplatin based: n=4 other based: n=4	Resin	Median 1.79 (range 1.32-2.15)	Every 6 weeks - NR - NR	0 - 2 - 16 - 2 - 1	5.5 months (95%-CI)	10.0 months (95%-CI NR)
Inarrairaegui et al. ²⁰¹⁰	Retrospective cohort	71	225	NR	Standard chemotherapy	A rescue or consolidation treatment	EHD under control or not influencing prognosis	NR	NR	NR	NR	NR	Resin	NS for mCRC	Every 2-3 months - NA - NS for mCRC	NR	NR	12 months (8.4-15.5)
Van Hazel et al. ²⁰⁰⁹	Phase 1 trial	25	25	59 (34-78)	Irinotecan	Unresectable, chemorefractory Naive to irinotecan	Liver dominant (NS)	12/25 (48%)	0: n=18 (72%) 1: n=7 (28%)	Median ALT: 49 (22-346)	Median 20% (5-60%)	1 line: n=17 2 lines: n=6 3 lines: n=2	Resin	Median 1.80 (range 0.75-2.44)	Every 3 months - NR - NR	0 - 11 - 9 - 3 - 0	6.0 months (range 1.6-11.4)	12.2 months (range 2.8->60)

Stuart et al. ²⁰⁰⁸	Retrospective cohort	13	30	NS for mCRC	Systemic therapy in 3 pts	Chemorefractory	Liver dominant (NS)	5/13 (38%)	NR	NR	NR	NR	Resin	NS for mCRC	Every 3 months - NR - NR	NS for mCRC	112 days (=3.7 months) (95%-CI NR)	357 days (=11.7 months) (95%-CI NR)
Sharma et al. ²⁰⁰⁷	Phase 1 trial	20	20	59 (47-76)	Modified FOLFOX4	Unresectable. Chemo-naïve for metastatic disease	Liver dominant (NS)	13/20 (65%)	0: n=18 (90%) 1: n=2 (10%)	Elevated ALT: n=6 Elevated AST: n=14	<25%: n=9 26-50%: n=9 >50%: n=2	Only adjuvant chemo, chemo-naïve for metastatic disease	Resin	Median 1.7 (range 0.9-3.1)	Every 3 months - At 12 weeks - NR	0 - 18 - 2 - 0 - 0	9.3 months (range 3.9-30.7)	NR
Stubbs et al. ²⁰⁰⁶	NR	100	100	61 (28-77)	Intra hepatic 5-FU in 87/100 patients	Unresectable	Liver dominant (NS)	25/100 (25%)	0: n=50 (50%) 1: n=38 (38%) 2: n=8 (8%) 3: n=4 (4%)	NR	<25% n=60 25-50% n=21 >50% n=19	NR	Resin	NR	Every 3 months - At 3 and 6 months - 11 months	3mo: 1 - 58 - 16 - 5 - 0 6mo: 2 - 39 - 10 - 14 - 0	NR	11 months (range 0.1-76.6)
Lim et al. ²⁰⁰⁵	Prospective cohort	32	46	NS for mCRC	5FU (in n pts ^a)	n=4 chemo-naïve, n=28 had prior chemotherapy	Liver dominant (NS)	5/32 (16%)	NR for mCRC	NR	NR	0 lines: n=4 >0 lines: n=28	Resin	NR	Every 2 months - At 2 months - NS for mCRC	0 - 10 - 9 - 13 - 0	NR for entire group of mCRC ^c	NR
Van Hazel et al. ²⁰⁰⁴	RCT (phase 2)	11	11	Mean 64 (range NR)	FU/LV	Unresectable. Chemo-naïve for metastatic disease	Liver dominant (NS)	2/11 (18%)	NR	NR	<25%: n=8 >25%: n=3	NR	Resin	Median 2.1 (range 1.5-2.5)	Every 3 months - NR - NR	0 - 8 - 3 - 0 - 0	18.6 months (95%-CI)	29.4 months (95%-CI NR)
Gray et al. ²⁰⁰¹	RCT (phase 3)	36	36	Mean 59 (range NR)	Intrahepatic floxuridine	Unresectable	Only lymph nodes in porta hepatis	NR	NR	NR	<25%: n=24 25-50%: n=9 >50%: n=3	Prior chemo for metastatic disease: n=5	Resin	Mean 2.2 (SD 0.3)	Every 3 months - NR - NR	By area: 2 - 14 - 13 - 3 - 4 By volume: 2 - 16 - 10 - 5 - 3	15.9 months (95%-CI)	17 months (95%-CI NR)

mCRC colorectal cancer liver metastases; RCT randomized controlled trial; NR not reported; FU/LV fluorouracil/leucovorin; EHD extrahepatic disease; NS not specified; bevac/cetux bevacizumab or cetuximab; CI confidence interval; AST aspartate transaminase, ALT alanine transaminase

^a Patients who had not received prior systemic 5FU were given this together with the spheres; for other patients a concurrent bolus 5FU was given as a radiosensitizer at the investigator's discretion.

^b Not specified for the group of patients treated with Y90 and chemotherapy.

^c Progression-free survival in group of mCRC patients previously treated with 5FU was 8.4 months.

^d Including bilirubin, AST, ALT, and albumin.

Supplemental Table 3. Critical appraisal of studies on Y90-RE for colorectal cancer liver metastases.

	No. of pts	Consecutive patients	Reported on							EHD included in response assessment	Loss to follow-up	Subsequent treatment
			Baseline EHD	Baseline tumor burden	Baseline PS	Previous systemic therapy	Imaging interval	Time of response	Follow-up duration			
Y90-RE as monotherapy												
Beste et al. ²⁰¹²	224	+	+	+/-	+/-	- ^a	- ^b	- ^b	- ^b	- ^b	NR	NR
Fahmueller et al. ²⁰¹²	49	+	-	-	-	-	+	+	+	+	1/49 (2%)	NR
Martin et al. ²⁰¹²	24	+	+	-	-	+/-	-	-	-	+	NR	NR
Tochetto et al. ²⁰¹²	20	-	-	-	-	-	+	+	-	NR	0/20 (0%)	NR
Seidensticker et al. ²⁰¹¹	29	+	+	+	-	+	+	-	-	NR	1/29 (3%)	n=9 further chemo
Cosimelli et al. ²⁰¹⁰	50	NR	+	+	+	+	+	+	+	+	2/50 (4%)	n=14 further chemo
Cianni et al. ²⁰⁰⁹	41	NR	+	+	+/-	+/-	+	+	-	NR	NR	n = 31 re-Y90-RE
Hong et al. ²⁰⁰⁹	15	NR	+	-	-	-	+	-	+	- ^b	NR	NR
Mulcahy et al. ²⁰⁰⁹	72	NR	+	+	+	+	+	-	-	NR	NR	NR
Jakobs et al. ²⁰⁰⁸	41	+	+	-	-	+/-	+	-	+	+	2/41 (5%)	NR
Sato et al. ²⁰⁰⁸	51	NR	-	-	+	- ^a	+	- ^b	+	-	NR	NR
Kennedy et al. ²⁰⁰⁶	208	NR	-	-	-	+	-	+	-	NR	NR	NR
Lewandowski et al. ²⁰⁰⁵	27	NR	+	+	+	+/-	+	+	+	-	1/27 (4%)	NR
Y90-RE with chemotherapy												
Nace et al. ²⁰¹¹	51	+	-	-	-	+	+	+	+	-	20/51 (39%)	n = 27 re-Y90-RE
Zerizer et al. ²⁰¹²	25	NR	+	-	-	+/-	+	+	-	-	1/25 (4%)	n = 2 surgery
Kosmider et al. ²⁰¹¹	19	+	-	+/-	+	+	+	+	+	+	NR	NR
Chua et al. ²⁰¹¹	48	+	- ^a	-	- ^a	- ^a	+	-	-	+	NR	NR
Hendlisz et al. ²⁰¹⁰	21	NR	+	-	+	+/-	+	-	-	-	1/21 (5%)	n = 7 systemic n = 2 locoregional
Inarrairaegui et al. ²⁰¹⁰	71	+	-	-	-	-	+	-	- ^a	- ^b	NR ^a	NR
Van Hazel et al. ²⁰⁰⁹	25	-	+	+/-	+	+	+	-	-	NR	2/25 (8%)	n = 1 RFA

Stuart et al. ²⁰⁰⁸	13	+	+	-	-	-	+	-	-	+	0/13 (0%)	NR ^a
Sharma et al. ²⁰⁰⁷	20	NR	+	+	+	+	+	+	-	NR	NR	n = 2 surgery
Stubbs et al. ²⁰⁰⁶	100	+	+	+	+	-	+	+	+	-	20/100 (20%)	NR
Lim et al. ²⁰⁰⁵	32	NR	+	-	- ^a	+/-	+	+	- ^a	-	1/32 (3%)	n = 1 surgery
Van Hazel et al. ²⁰⁰⁴	11	NR	+	+	-	-	+	-	-	NR	0/11 (0%)	NR
Gray et al. ²⁰⁰¹	36	NR	+	+	-	+/-	+	-	-	-	4/36 (11%)	NR

+ Yes, +/- Incomplete, - No, NR not reported; EHD extrahepatic disease, PS performance score, NA not applicable, RFA radio frequency ablation

a Not specified for patients with colorectal cancer liver metastases.

b Tumor response not a study endpoint.