

Liver metastatic disease: Year end review

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Disclosures

Consultant: Abbott Vascular, Baxter Healthcare Corporation, Bard Peripheral Vascular, Boston Scientific, W.L. Gore, Sirtex Medical, Guerbet, Eisai Medical, Trisalus, Astra Zeneca.

Grants: BTG, Medtronic, Bard Peripheral Vascular, Boston Scientific, Sirtex Medical.

Objective

- To present the most important publications on loco-regional therapy for liver metastasis in 2020-2021

Colorectal Cancer Liver Metastasis



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Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial

Aim:

- To investigate the impact of transarterial Yttrium-90 radioembolization in combination with second line systemic chemotherapy for colorectal liver metastases.

Mulcahy et al, J clin Oncol 2021

Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial

Study Design:

- Multicenter, open-label phase III trial
- 428 patients
- 95 centers in North America, Europe, and Asia

Mulcahy et al, J clin Oncol 2021

Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial

Study Design:

- CLM who progressed on oxaliplatin or irinotecan-based first-line therapy were randomly assigned 1:1 to receive:
 - Second-line chemotherapy and TARE (n=215).
 - Second-line chemotherapy (n=213).
- Random assignment was performed by:
 - Unilobar or bilobar disease
 - oxaliplatin- or irinotecan-based first-line chemotherapy
 - KRAS mutation status

Mulcahy et al, J clin Oncol 2021

Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial

Inclusion criteria:

- Age >18 years,
- Unresectable unilobar or bilobar CLM
- Ability to receive second-line irinotecan- or oxaliplatin-based chemotherapy
- Measurable disease by RECIST 1.1
- ECOG Performance status 0 or 1
- Bilirubin < 1.2 upper limit normal
- Albumin > 3.0 g/dL.

Mulcahy et al, J clin Oncol 2021

Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial

Exclusion criteria:

- Prior arterial or radiotherapy to the liver
- Clinically evident ascites
- Unresolved toxicities from first-line therapy
- Confirmed extrahepatic metastases
- Contraindication to angiography.

Mulcahy et al, J clin Oncol 2021

Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial

Treatments and procedures:

- Treatment was planned for 120 Gy +/- 10% using single-compartment dosimetry to either:
 - One lobe
 - Both lobes in a single setting
- Glass-based TARE (Therasphere) was performed.

Mulcahy et al, J clin Oncol 2021

Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial

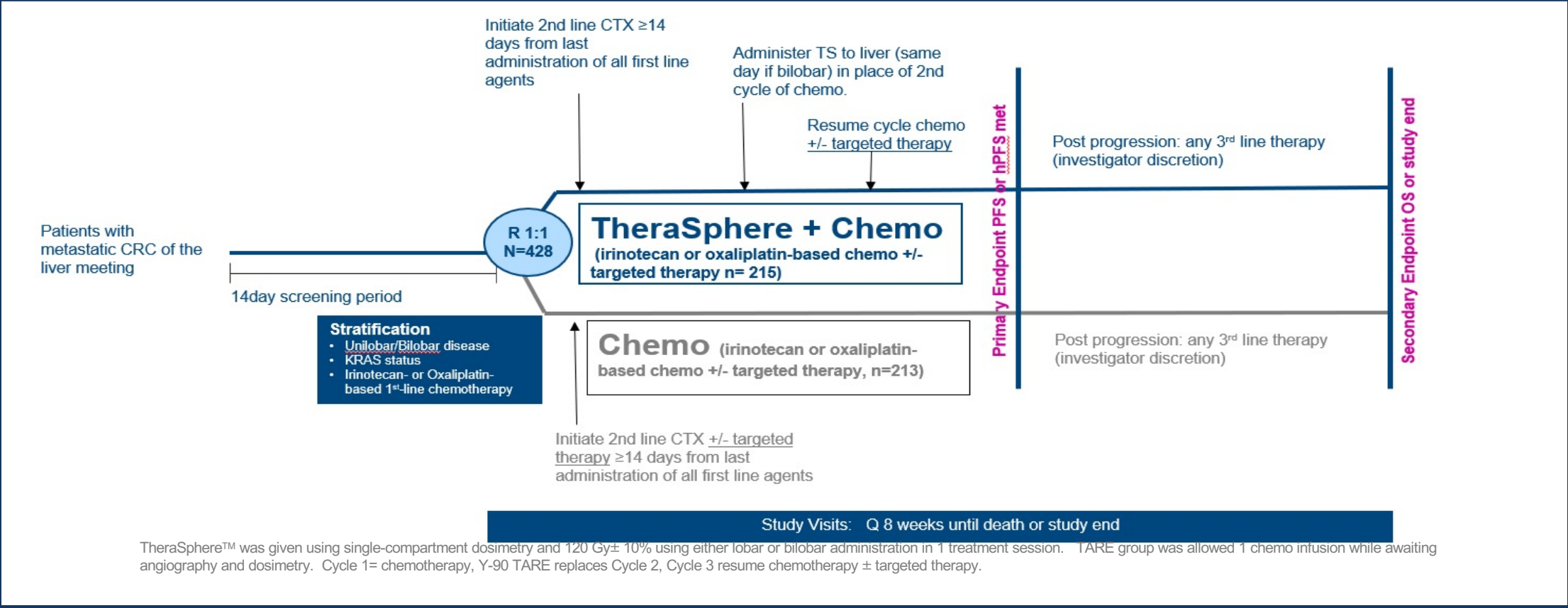
End Points:

- **Primary end points:**
 - Progression-free survival (PFS)
 - Hepatic progression-free survival (hPFS)
- **Secondary endpoints:**
 - Overall survival (OS)
 - Objective response rate (ORR)
 - Disease control rate (DCR)

Study success:
either PFS or
hPFS must
statistically
significant

Mulcahy et al, J clin Oncol 2021

Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial



Mulcahy et al, J clin Oncol 2021

Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial

The groups were well balanced

	Y-90 + Chemo (N=215)	Chemo (N=213)
Median Age	63.0 years	60.0 years
Male	135 (62.8%)	138(64.8%)
Region		
North America	63 (29.3%)	56 (26.3%)
Europe	131 (60.9%)	145 (68.1%)
Asia	21 (9.8%)	12 (5.6%)
ECOG 0	119 (55.3%)	133 (62.4%)
Albumin \geq site LLN	182 (84.7%)	177 (83.1%)
CEA \geq 35 ng/mL	116 (54.0%)	105 (49.3%)
KRAS Status (stratification parameter)		
Mutant	100 (46.5%)	101 (47.4%)
Wild type	115 (53.5%)	112 (52.6%)

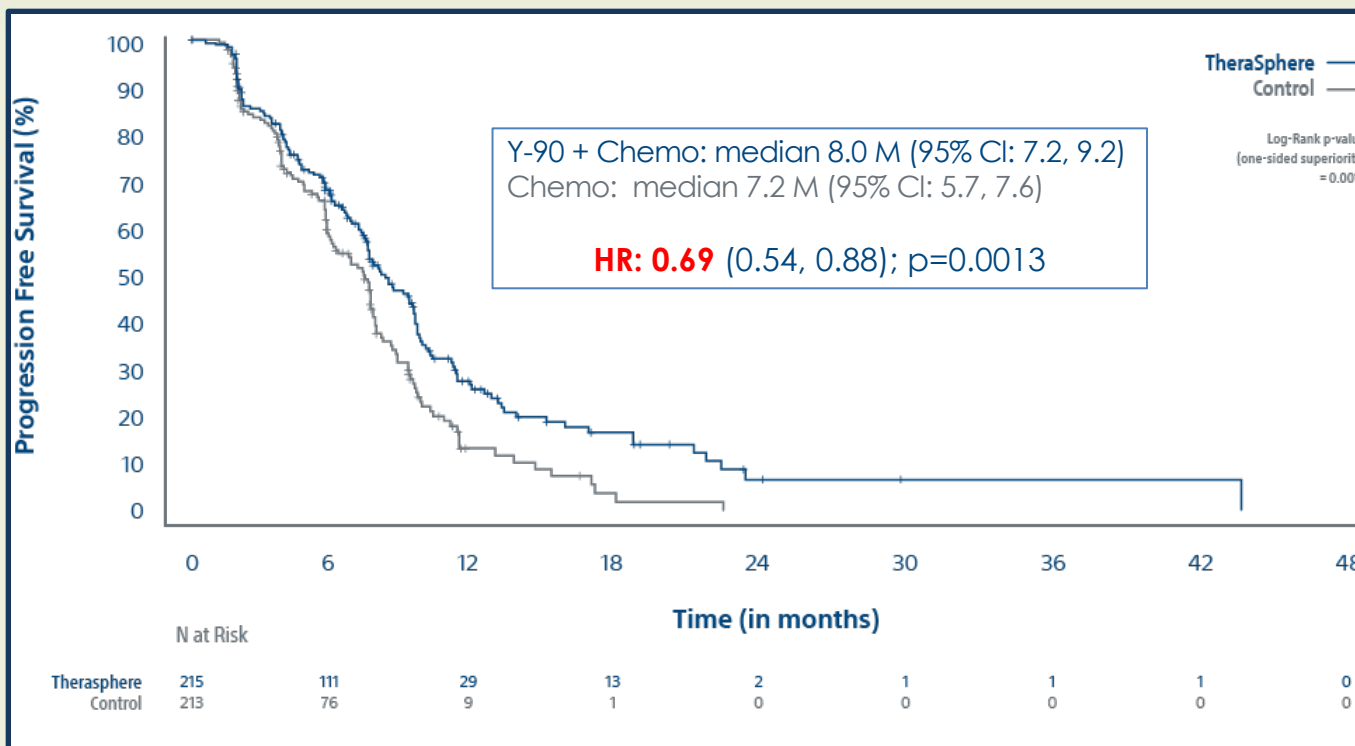
	Y-90 + Chemo (N=215)	Chemo (N=213)
Bilobar disease (stratification parameter)	176 (81.9%)	173 (81.2%)
Liver Tumor Burden ^a		
<10%	124 (57.7%)	121 (56.8%)
\geq 10% to <25%	54 (25.1%)	47 (22.1%)
\geq 25%	29 (13.5%)	28 (13.1%)
Maximum Liver Lesion Size \geq 40 mm ^a	162 (75.3%)	142 (66.7%)
Primary tumor in situ	83 (38.6%)	69 (32.4%)
Left side primary tumor location	150 (69.8%)	136 (63.8%)
Extrahepatic Lesions at Baseline	113 (52.6%)	95 (44.6%)
Number of Lesions		
<3	25 (11.6%)	21 (9.9%)
3-5	40 (18.6%)	38 (17.8%)
6-10	54 (25.1%)	60 (28.2%)
>10	88 (40.9%)	77 (36.2%)
Missing	8 (3.7%)	17 (8.0%)

Well-balanced patient and disease characteristics between treatment and control arms in this advanced disease patients

Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial

	Y-90 + Chemo (N=215)	Chemo (N=213)
Received Assigned Therapy	187 (87.0%)*	191 (89.7%)
2 nd Line Chemo Administered (stratification parameter)	203 (94.4%)	191 (89.7%)
Irinotecan-based	130 (60.5%)	123 (57.7%)
Irinotecan Mean Number of Cycles / Median of Average Dose per Cycle (mg/m ²)	9.0 / 180	9.3 / 180
Oxaliplatin-based	73 (34.0%)	68 (31.9%)
Oxaliplatin Mean Number of Cycles / Median of Average Dose per Cycle (mg/m ²)	8.5 / 85	8.8 / 85
Biological Agent	88 (40.9%)	93 (43.7%)
Aflibercept	9 (4.2%)	11 (5.2%)
Bevacizumab	74 (34.4%)	65 (30.5%)
Cetuximab	5 (2.3%)	10 (4.7%)
Panitumumab / Ramucirumab	2 (0.9%) / 0	6 (2.8%) / 1 (0.5%)
Y-90 Treatment		
Median absorbed dose to perfused volume prior to progression by investigator determination, Gy (range)	117 (61.7, 156)	NA
Median time to Y-90, days (range)	25 (12-90)	NA

Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial

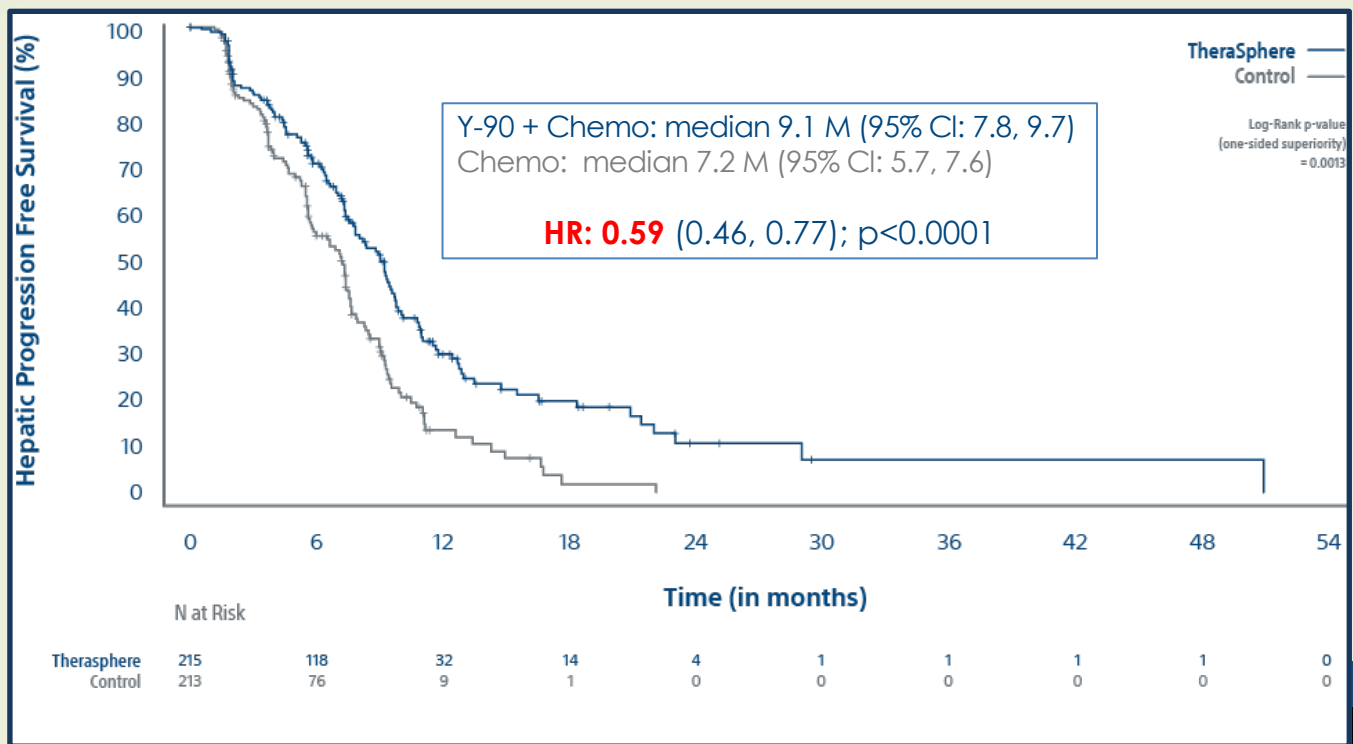


Positive Outcome

	% Progression-Free Survival (95% CI)		
	6 M	12 M	18 M
Y-90 + Chemo (N=215)	65.2 (58.0, 71.5)	25.8 (18.9, 33.1)	16.7 (10.6, 23.9)
Chemo (N=213)	55.4 (47.2, 62.8)	13.2 (7.5, 20.5)	1.8 (0.2, 8.1)

Patients receiving Y90 + chemo were 31% less likely to show disease progression or death vs. chemo alone

Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial



Positive Outcome

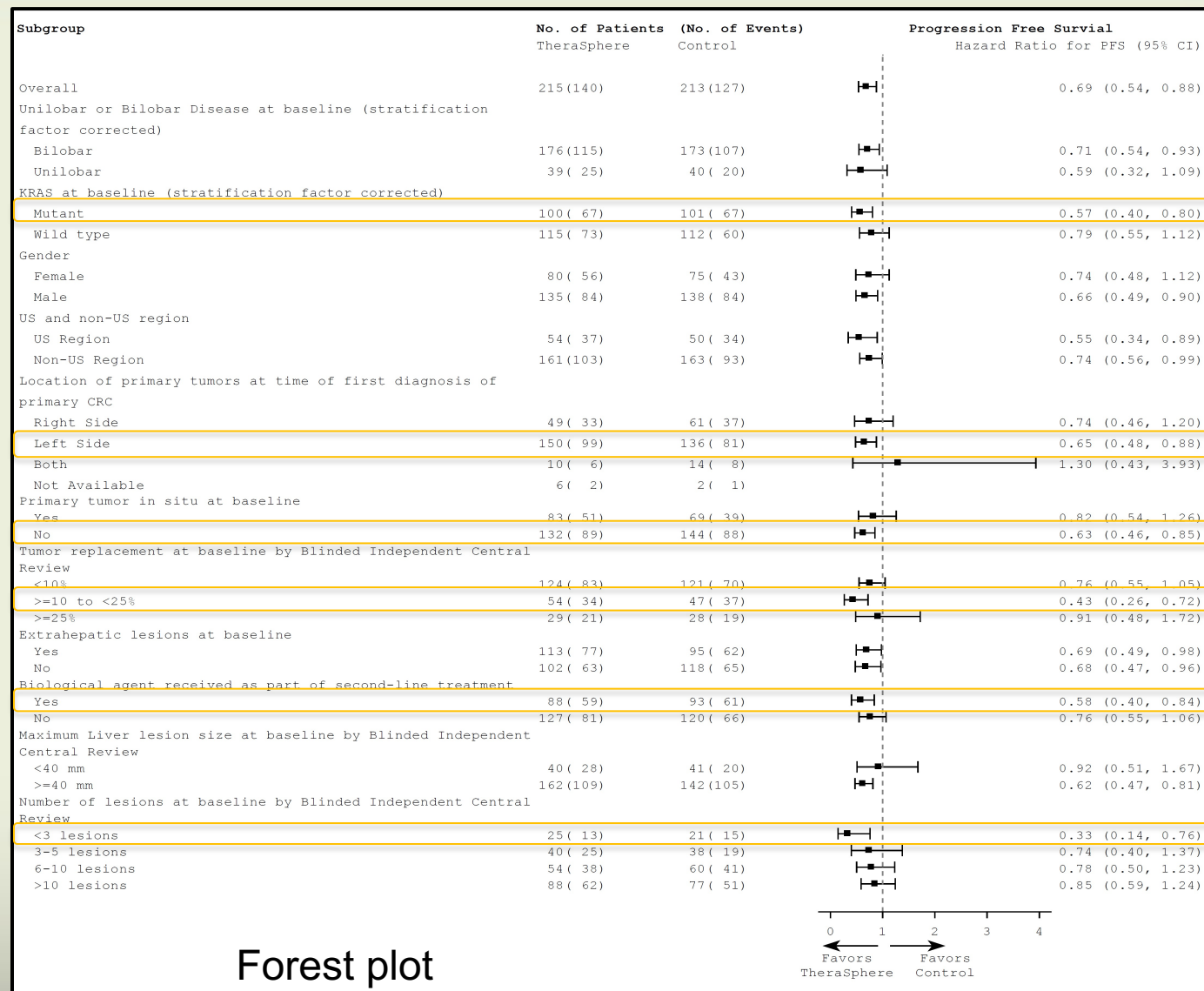
	% Hepatic Progression-Free Survival (95% CI)		
	6 M	12 M	18 M
Y-90 + Chemo (N=215)	70.7 (63.6, 76.6)	29.8 (22.4, 37.6)	19.8 (13.0, 27.6)
Control	55.2 (47.1, 62.7)	13.5 (7.7, 20.9)	1.9 (0.2, 8.3)

Patients receiving Y90 + chemo were 41% less likely to show hepatic disease progression or death vs. chemo alone

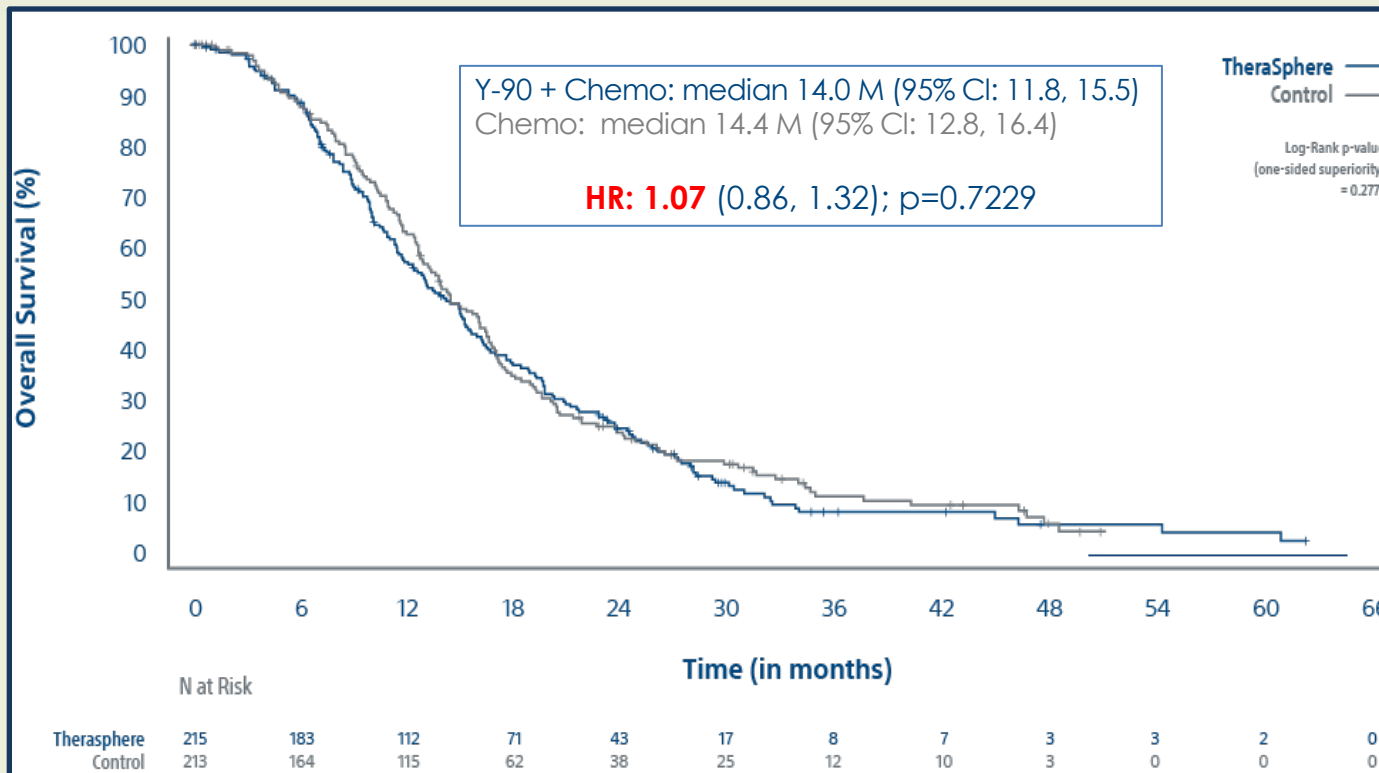
Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial

PFS benefit with Y-90+chemo include:

- Tumors with KRAS mutation
- Hepatic tumor burden 10 - 25%
- < 3 lesions
- Left sided primary tumor
- Addition of a biologic agent
- Resected Primary



Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial



Did not meet secondary endpoint

	% Overall Survival (95% CI)		
	6 M	12 M	18 M
Y-90 + Chemo (N=215)	88.5 (83.3, 92.1)	56.3 (49.2, 62.8)	36.4 (29.7, 43.1)
Control	87.8 (82.3, 91.7)	62.4 (55.0, 68.9)	34.3 (27.5, 41.2)

**PER PROTOCOL OS: TARE+Chemo 15.2 M (95% CI: 12.7-17.7) versus Chemo 14.3 M (95% CI: 12.6, 16.4)
HR: 0.96 (0.74, 1.24); p=0.3841**

Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial

Outcome	TARE (n = 215)	Control (n = 213)
Best overall response, ^a No. (%)		
CR	2 (0.9)	3 (1.4)
PR	71 (33.0)	42 (19.7)
SD	98 (45.6)	110 (51.6)
PD	27 (12.6)	27 (12.7)
Not evaluable or missing	0/17 (7.9)	1 (0.5)/30 (14.1)
ORR		
CR plus PR, No. (%) (95% CI)	73 (34.0) (28.0 to 40.5)	45 (21.1) (16.2 to 27.1)
Difference (95% CI)	12.8% (4.0 to 21.4)	
Superiority 1-sided <i>P</i>	.0019	
DCR		
CR plus PR plus SD, No. (%) (95% CI)	171 (79.5) (73.6 to 84.4)	155 (72.8) (66.4 to 78.3)
Difference (95% CI)	6.8% (-1.6 to 15.1)	
Superiority 1-sided <i>P</i>	.0626	

Mulcahy et al, J clin Oncol 2021

Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial

	Y-90 + Chemo (N=187)	Chemo (N=207)
Any TEAEs (n, %)	181 (96.8%)	194 (93.7%)
Chemotherapy-Related TEAEs	172 (92.0%)	189 (91.3%)
Adverse Device Events (ADEs)	103 (55.1%)	0
Angiographic Procedure-Related TEAEs	55 (29.4%)	2 (1.0%)
TEAEs with CTCAE \geq Grade 3	128 (68.4%)	102 (49.3%)
Serious TEAEs	70 (37.4%)	43 (20.8%)
Serious Treatment Emergent ADEs	20 (4.3%)	0
TEAEs Leading to Fatal Outcome	8 (4.3%)	4 (1.9%)
TEAEs Requiring Discontinuation of Chemotherapy	24 (12.8%)	25 (12.1%)

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TEAEs with CTCAE \geq Grade 3	128 (68.4%)	102 (49.3%)
Serious TEAEs	<ul style="list-style-type: none"> • Exposure to chemotherapy was similar for both groups • No reduction in dose intensity or ability to receive planned chemotherapy 	
Serious Treatment Emergent ADEs		
TEAEs Leading to Fatal Outcome		
TEAEs Requiring Discontinuation of Chemotherapy	24 (12.8%)	25 (12.1%)

Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial

Conclusion:

- The addition of TARE to second line chemotherapy for CLM led to longer PFS and hPFS.

Mulcahy et al, J clin Oncol 2021

Efficacy and Tolerability of Selective Internal Radiotherapy With Yttrium-90 as Consolidation Treatment After Chemotherapy in Metastatic Colorectal Cancer

Aim:

- To analyze the outcomes in patients who had received Y90 radioembolization as consolidation therapy after one or more lines of chemotherapy.

Cortesi et al, clinical colorectal cancer, 2020

Efficacy and Tolerability of Selective Internal Radiotherapy With Yttrium-90 as Consolidation Treatment After Chemotherapy in Metastatic Colorectal Cancer

- Retrospective study
- 68 patients
- Eligibility Criteria:
 - Confirmed colorectal liver metastases.
 - Unsuitable for surgical resection or local ablation with curative intent.
 - Received Resin Y90 as consolidation therapy after one or more lines of chemotherapy.
- The primary endpoint was **progression-free survival**.

Cortesi et al, clinical colorectal cancer, 2020

Efficacy and Tolerability of Selective Internal Radiotherapy With Yttrium-90 as Consolidation Treatment After Chemotherapy in Metastatic Colorectal Cancer

Characteristic	Value
Total no. of patients	68
Median age (years)	67
Age	
≥65 y	40 (59)
<65 y	28 (41)
Gender	
Female	20 (29.4)
Male	48 (70.6)
Site of metastasis	
Liver only	27 (39.7)
Extrahepatic	41 (60.3)

Characteristic	Value
Chemotherapy	
FOLFOX—bevacizumab	21 (30.9)
FOLFOXIRI—bevacizumab	20 (29.4)
FOLFIRI—bevacizumab	16 (23.5)
FOLFIRI—cetuximab	3 (4.4)
Capecitabine—bevacizumab	3 (4.4)
Irinotecan—cetuximab	1 (1.5)
Other	4 (5.9)
Prior lines of chemotherapy	
1	42 (61.8)
2	15 (22.1)
3 or more	11 (16.1)
ECOG PS before SIRT	
0	46 (61.8)
1	20 (29.4)
2	2 (3.2%)
<i>RAS</i> mutation status (64/68 patients tested)	
Wild-type <i>RAS</i>	34 (53.1) ^a
<i>RAS</i> mutated	30 (47.9) ^a

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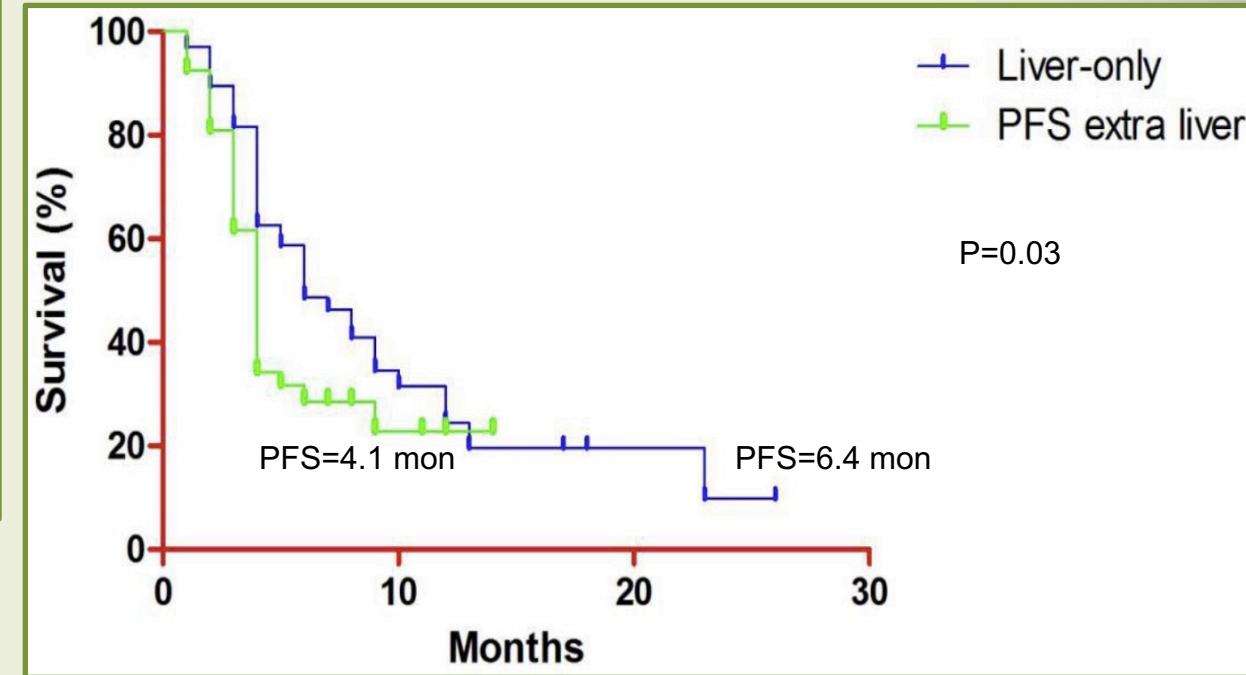
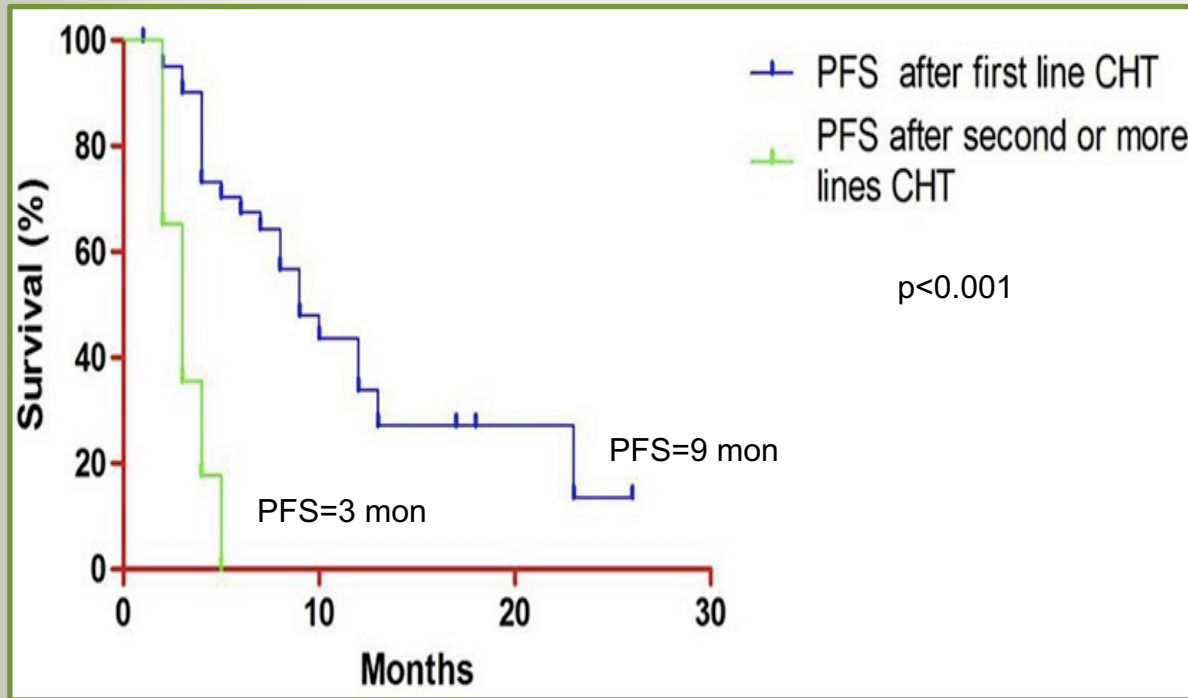
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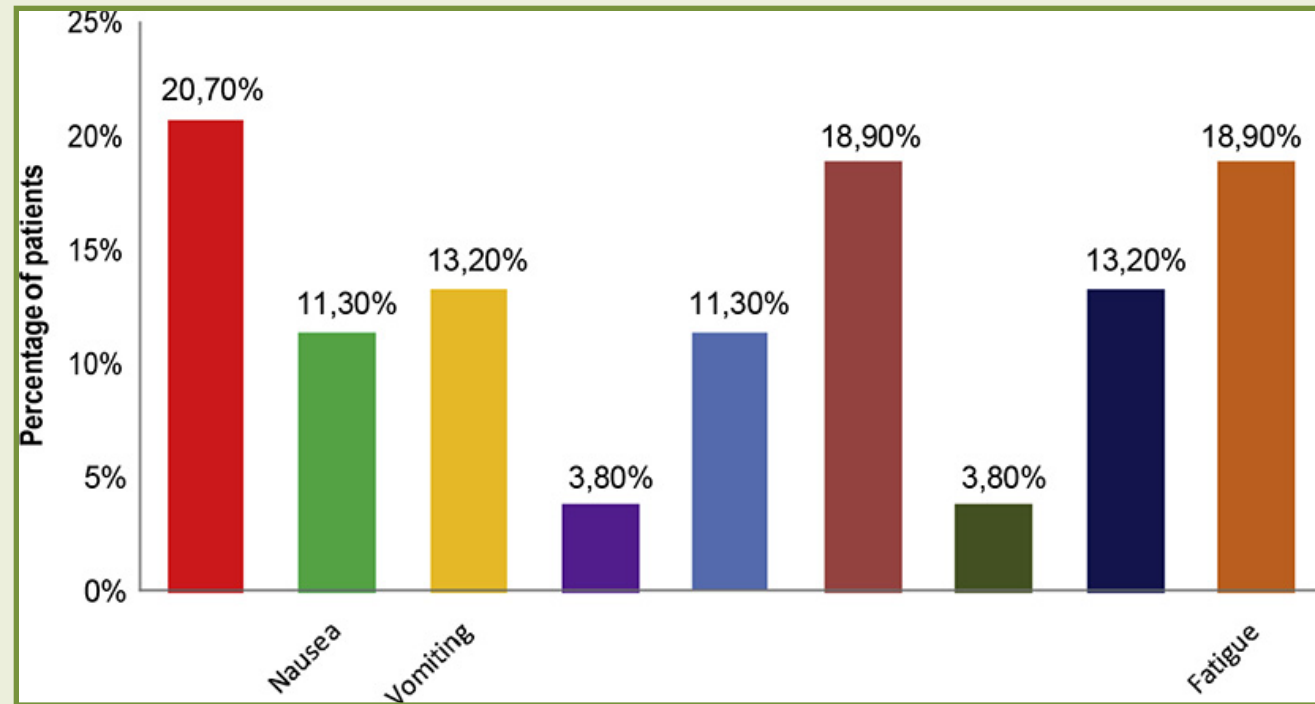
Cortesi et al, clinical colorectal cancer, 2020

Efficacy and Tolerability of Selective Internal Radiotherapy With Yttrium-90 as Consolidation Treatment After Chemotherapy in Metastatic Colorectal Cancer



Cortesi et al, clinical colorectal cancer, 2020

Efficacy and Tolerability of Selective Internal Radiotherapy With Yttrium-90 as Consolidation Treatment After Chemotherapy in Metastatic Colorectal Cancer



There was no grade 3 or higher Adverse events

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Efficacy and Tolerability of Selective Internal Radiotherapy With Yttrium-90 as Consolidation Treatment After Chemotherapy in Metastatic Colorectal Cancer

Conclusion:

- Earlier use of Y90 Radioembolization may provide a greater survival benefit compared to that in salvage settings.

Cortesi et al, clinical colorectal cancer, 2020



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Breast Cancer Liver Metastasis



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Yttrium-90 dosimetry and implications on tumour response and survival after radioembolisation of chemo-refractory hepatic metastases from breast cancer

Aim:

- To evaluate the effects of tumor dose on tumor response and overall survival (OS) in patients with chemo-refractory metastatic breast cancer (MBC) to the liver undergoing yttrium-90 radioembolization (Y90 RE).

Yttrium-90 dosimetry and implications on tumour response and survival after radioembolisation of chemo-refractory hepatic metastases from breast cancer

Study design:

- Retrospective study
- 20 patients with chemo-refractory MBC to the liver
- 33 total Resin Y90 RE treatments
- Volumes of interest were drawn around the five largest tumors of the targeted liver lobe on SPECT/CT
- MIM software used to calculate dose-volume histograms were calculated.

Yttrium-90 dosimetry and implications on tumour response and survival after radioembolisation of chemo-refractory hepatic metastases from breast cancer

Age	
Median	62 years old
Range	43–77 years old
Gender	
Female	100%
Metastases	
Bone	15 patients (75%)
Brain	6 patients (30%)
Lymph nodes	6 patients (30%)
Lungs	3 patients (15%)
Skin	2 patients (10%)
Peritoneum	1 patient (5%)
Soft tissue	1 patient (5%)
Brachial plexus	1 patient (5%)
Receptor sensitivities ^a	
ER+, PR+, HER2–	9 patients (45%)
ER+, PR–, HER2–	5 patients (25%)
ER–, PR–, HER2–	2 patients (10%)
ER–, PR–, HER2+	1 patient (5%)
ER+, PR–, HER2+	1 patient (5%)

ECOG status ^b	
ECOG 0	17 patients (85%)
ECOG 1	0 patients
ECOG 2	2 patients (10%)
Child-Pugh Grade	
A	18 patients (90%)
B	2 patients (10%)
LFTs ^c preoperative ^d	
Albumin	3.81
Alanine aminotransferase	49.7
Aspartate aminotransferase	59.5
Total bilirubin	0.61
LFTs postoperative ^e	
Albumin	3.64
Alanine aminotransferase	44.82
Aspartate aminotransferase	60.04
Total bilirubin	0.63
Number of metastases	
Median	10
Range	1–30

Cheng et al, Nuclear Medicine Communications, 2021

Yttrium-90 dosimetry and implications on tumour response and survival after radioembolisation of chemo-refractory hepatic metastases from breast cancer

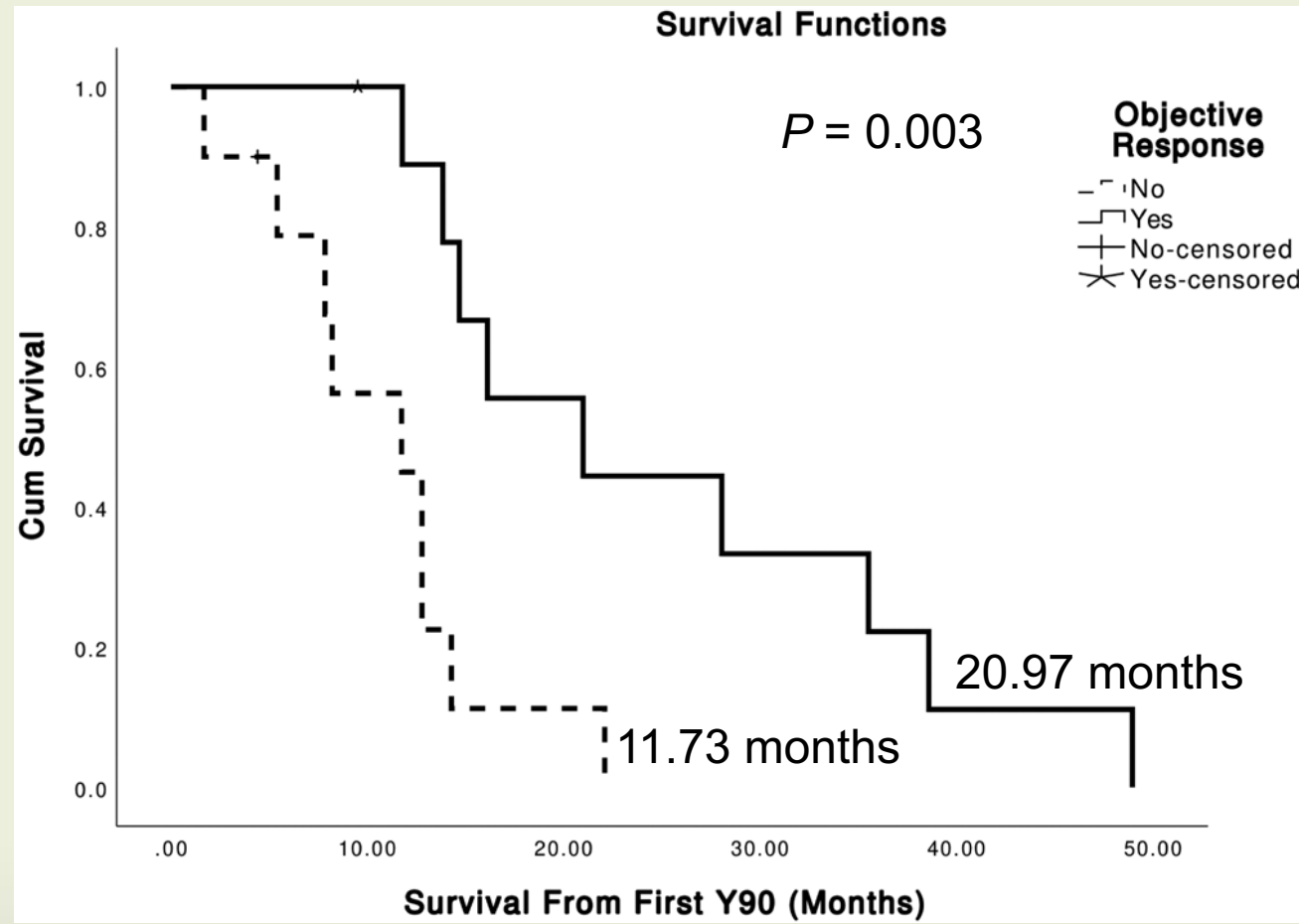
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Alanine aminotransferase	49.7
Aspartate aminotransferase	59.5
Total bilirubin	0.61
LFTs postoperative ^e	
Albumin	3.64
Alanine aminotransferase	44.82
Aspartate aminotransferase	60.04
Total bilirubin	0.63
Number of metastases	
Median	10
Range	1–30

Cheng et al, Nuclear Medicine Communications, 2021

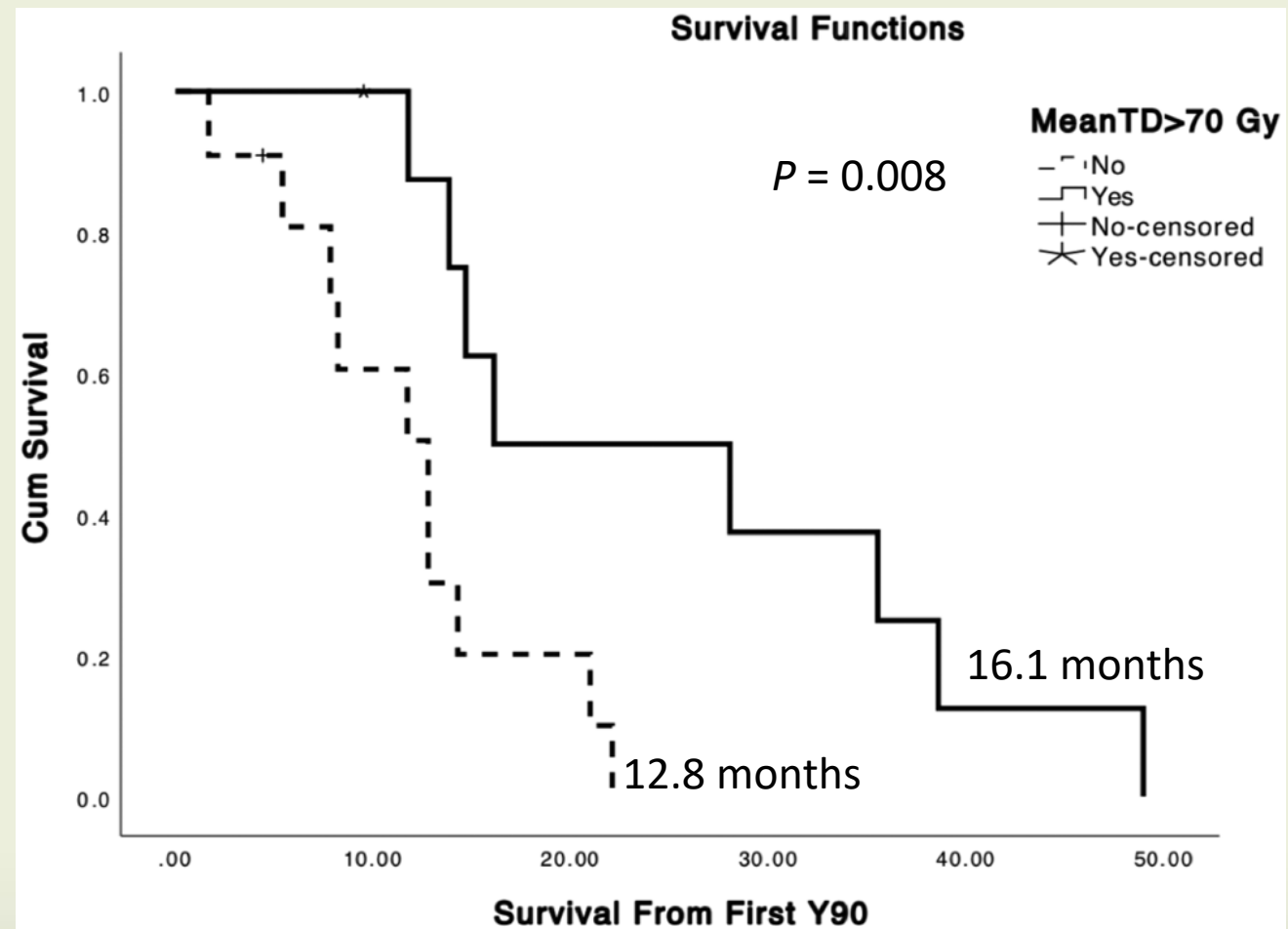
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ORR = 33%
by RECIST
criteria



Cheng et al, Nuclear Medicine Communications, 2021

Yttrium-90 dosimetry and implications on tumour response and survival after radioembolisation of chemo-refractory hepatic metastases from breast cancer



Cheng et al, Nuclear Medicine Communications, 2021

Yttrium-90 dosimetry and implications on tumour response and survival after radioembolisation of chemo-refractory hepatic metastases from breast cancer

Conclusion:

- For patients with chemo-refractory breast cancer with liver metastases, achieving a mean tumor dose >70 Gy is a significant predictor of tumor response and prolonged OS.

Non-resectable Liver Metastasis



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Incidence and risk factors for sustained hepatic function toxicity 6 months after radioembolization: analysis of the radiation-emitting sir-spheres in non-resectable liver tumor (RESIN) registry

Aim:

- To quantify rates and risk factors for toxicity after hepatic radioembolization

Incidence and risk factors for sustained hepatic function toxicity 6 months after radioembolization: analysis of the radiation-emitting sir-spheres in non-resectable liver tumor (RESIN) registry

- 614 patients
- SIR-Spheres in Non-resectable liver tumor (RESIN) registry
- Mean patient age was 63.1±12.5 years.
- The majority of patients were male (n=375, 61%) and white (n=490, 80%).

- Common tumor types were:
 - Hepatocellular (32%)
 - Colorectal (30%)
 - Neuroendocrine (9%)

Incidence and risk factors for sustained hepatic function toxicity 6 months after radioembolization: analysis of the radiation-emitting sir-spheres in non-resectable liver tumor (RESIN) registry

Treatments Prior to Radioembolization

Pathology	Total (N patients)	Surgery	Chemo 1 line	Chemo 2 lines	Chemo 3+ lines	Ablation	SBRT	Arterial
Hepatocellular	197	8, 4.1%	28, 14.2%	20, 10.2%	8, 4.1%	24, 12.2%	2, 1.0%	50, 25.4%
Colorectal	187	29, 15.5%	35, 18.7%	43, 23.0%	61, 32.6%	26, 13.9%	12, 6.4%	14, 7.5%
Neuroendocrine	56	8, 14.3%	20, 35.7%	9, 16.1%	14, 25%	4, 7.1%	3, 5.4%	9, 16.1%
Cholangiocarcinoma	35	3, 8.6%	11, 31.4%	6, 17.1%	5, 14.3%	2, 5.7%	4, 11.4%	4, 11.4%
Breast	27	1, 3.7%	1, 3.7%	3, 11.1%	15, 55.6%	2, 7.4%	1, 3.7%	3, 11.1%
Melanoma	16	0, 0%	6, 37.5%	4, 25%	2, 12.5%	1, 6.3%	1, 6.3%	1, 6.3%
Pancreatic	16	2, 12.5%	4, 25%	4, 25%	4, 25%	0, 0%	2, 12.5%	1, 6.3%
Esophageal	7	0, 0%	1, 14.3%	2, 28.6%	4, 57.1%	0, 0%	1, 14.3%	0, 0%
Other	73	8, 11.0%	20, 27.4%	17, 23.3%	27, 37%	5, 6.8%	7, 9.6%	4, 5.5%
Total	614, 100.0%	59, 9.6%	126, 20.5%	108, 17.6%	140, 22.8%	64, 10.4%	27, 5.1%	86, 14.0%

Chemo, systemic therapy; SBRT, stereotactic body radiation to hepatic malignancy; Arterial, previous embolization or chemoembolization.

Incidence and risk factors for sustained hepatic function toxicity 6 months after radioembolization: analysis of the radiation-emitting sir-spheres in non-resectable liver tumor (RESIN) registry

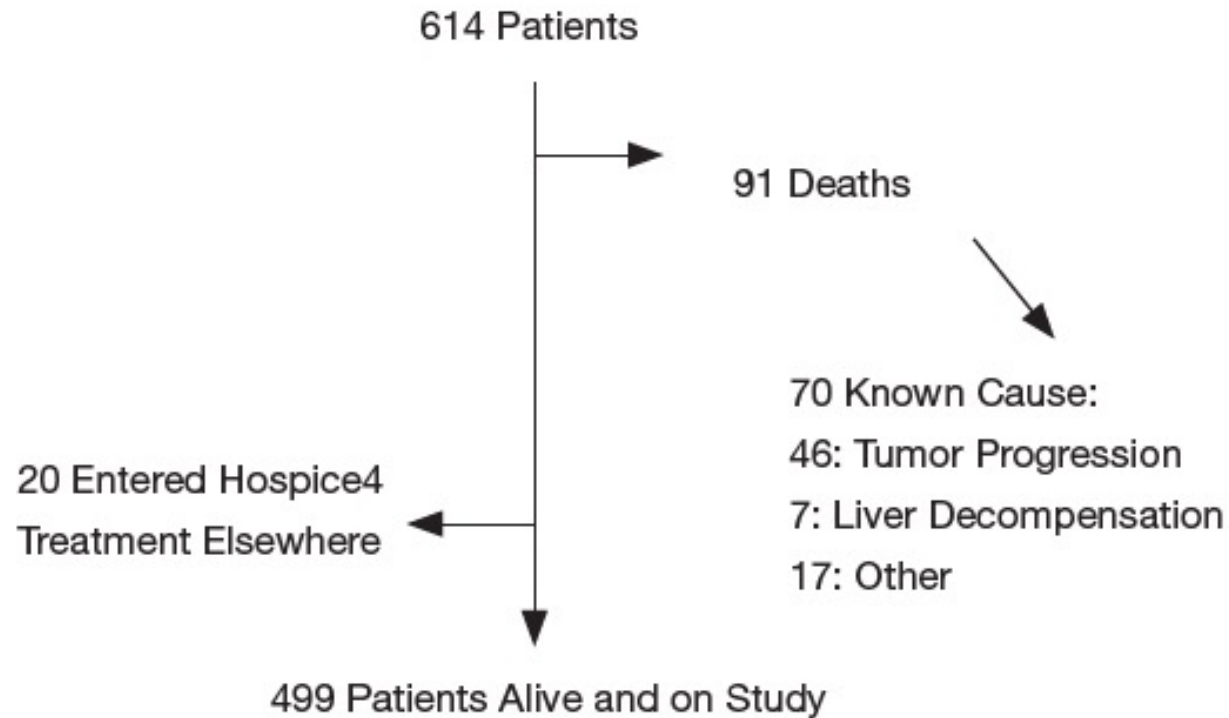
Treatments in the 6 months after Radioembolization

Pathology	Total (N patients)	Surgery	Chemo	Ablation	SBRT	Arterial
Hepatocellular	86/197 (44%)	7 (3.6%)	36 (21.8%)	9 (4.6%)	4 (2%)	30 (15.2%)
Colorectal	58/187 (31.0%)	3 (1.6%)	45 (24%)	7 (3.7%)	2 (1%)	1 (0.5%)
Neuroendocrine	9/56 (16.1%)	0 (0%)	7 (12.5%)	0 (0%)	0 (0%)	2 (3.6%)
Cholangiocarcinoma	11/35 (31.4%)	1 (2.9%)	7 (20%)	0 (0%)	2 (5.7%)	1 (2.9%)
Breast	6/27 (22.2%)	0 (0%)	4 (14.8%)	1 (3.7%)	1 (3.7%)	0 (0%)
Melanoma	4/16 (25%)	0 (0%)	3 (18.8%)	0 (0%)	0 (0%)	1 (6.3%)
Pancreatic	5/16 (31.2%)	0 (0%)	3 (6.3%)	0 (0%)	0 (0%)	2 (12.5%)
Esophageal	2/7 (28.6%)	0 (0%)	2 (28.6%)	0 (0%)	0 (0%)	0 (0%)
Other	24/73 (32.9%)	0 (0%)	22 (30.1%)	0 (0%)	0 (0%)	2 (2.7%)
Total	205/614 (33.4%)	11 (1.8%)	129 (21%)	17 (2.8%)	9 (1.5%)	39 (6.4%)

Chemo, systemic therapy; SBRT, stereotactic body radiation to hepatic malignancy; Arterial, embolization or chemoembolization.

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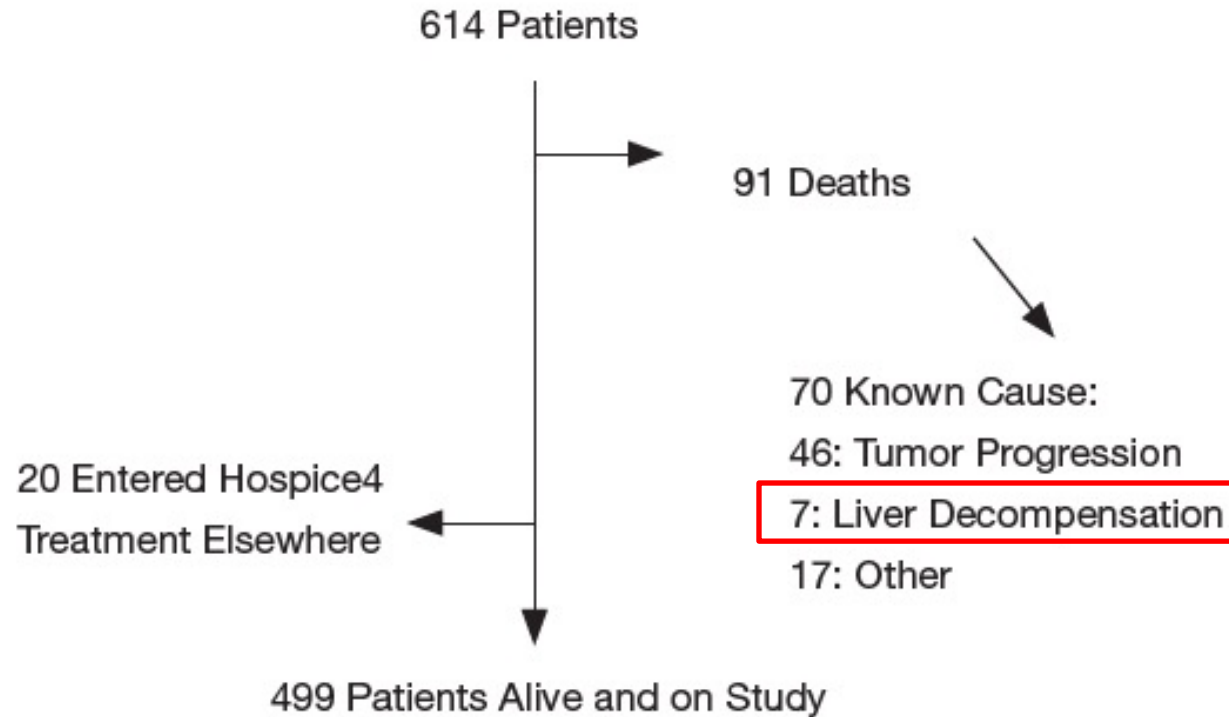
At 6 months after Radioembolization



Brown et al, J Gastrointest Oncol, 2021

Incidence and risk factors for sustained hepatic function toxicity 6 months after radioembolization: analysis of the radiation-emitting sir-spheres in non-resectable liver tumor (RESIN) registry

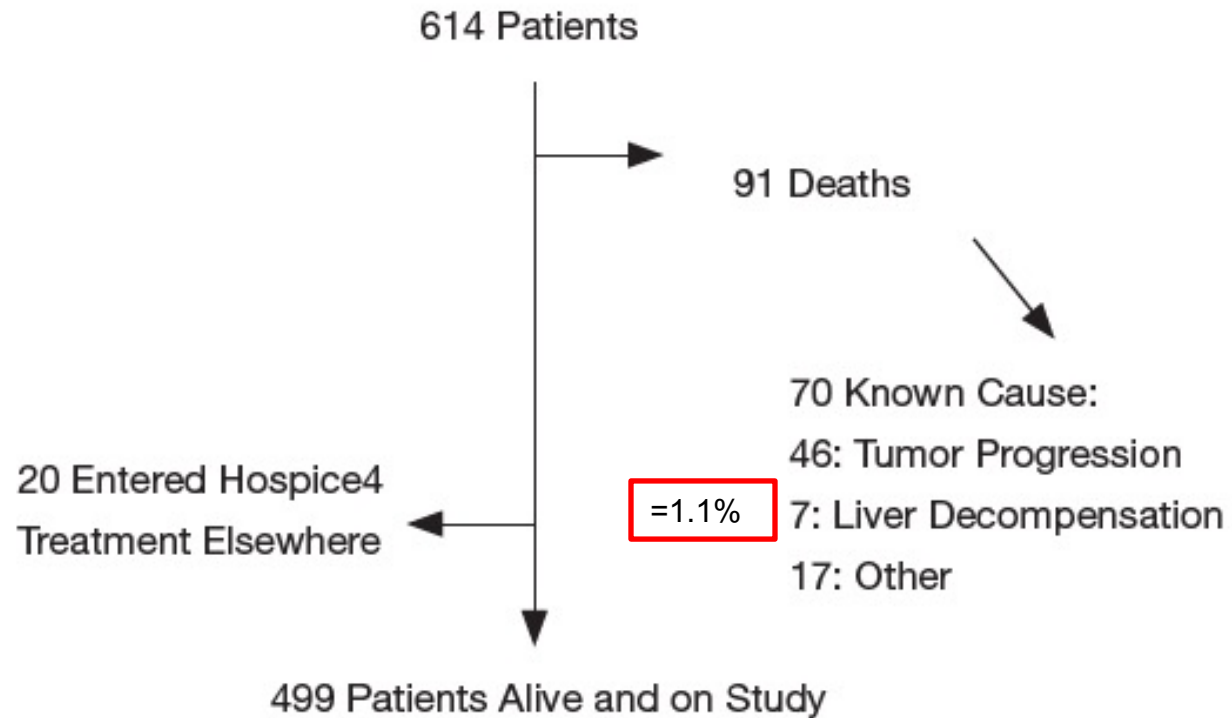
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Brown et al, J Gastrointest Oncol, 2021

Incidence and risk factors for sustained hepatic function toxicity 6 months after radioembolization: analysis of the radiation-emitting sir-spheres in non-resectable liver tumor (RESIN) registry

Liver Function Toxicity:

Tumor	n	Bilirubin		Albumin		INR	
		Gr 1-2	Gr 3+	Gr 1-2	Gr 3	Gr 1-2	Gr 3
Colorectal	187	44 (23.5%)	28 (15%)	80 (42.8%)	10 (5.3%)	20 (10.7%)	5 (2.7%)
Hepatocellular	197	89 (45.2%)	34 (17.3%)	103 (52.3%)	10 (5.1%)	39 (19.8%)	0 (0%)
Neuroendocrine	56	5 (8.9%)	2 (3.6%)	12 (21.4%)	2 (3.6%)	1 (1.8%)	0 (0%)
Cholangiocarcinoma	35	4 (11.4%)	3 (8.6%)	12 (34.3%)	1 (2.9%)	0 (0%)	0 (0%)
Breast	27	6 (22.2%)	2 (7.4%)	11 (40.1%)	1 (3.7%)	2 (7.4%)	0 (0%)
Melanoma	16	1 (6.2%)	3 (18.8%)	6 (37.5%)	0 (0%)	2 (12.5%)	0 (0%)
Pancreatic	16	3 (18.8%)	2 (12.5%)	7 (43.8%)	0 (0%)	3 (18.8%)	0 (0%)
Esophageal	7	3 (42.9%)	2 (28.6%)	5 (71.4%)	1 (14.3%)	1 (14.3%)	1 (14.3%)
Other	73	16 (21.9%)	9 (12.3%)	29 (39.7%)	3 (4.1%)	7 (9.6%)	1 (1.4%)
Total	614	171 (27.9%)	85 (13.8%)	265 (43.2%)	28 (4.6%)	75 (12.2%)	7 (1.1%)

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Predictors of toxicity:	P-value
Age	P=0.046
Male gender	P<0.001
Primary liver cancer (HCC)	P<0.001
Metastatic tumor type (CRC)	P<0.001
Increased lung shunt percentage	P=0.004
Increased delivered activity	P=0.04
Bilobar compared with unilobar tumor	P=0.04
Baseline laboratory elevation compared with normal labs	P<0.001
Undergoing previous liver tumor intervention compared to treatment naïve patients	P=0.05
Previous surgery	P=0.01

Incidence and risk factors for sustained hepatic function toxicity 6 months after radioembolization: analysis of the radiation-emitting sir-spheres in non-resectable liver tumor (RESIN) registry

Conclusion:

- Radioembolization was well-tolerated clinically in a heavily pretreated group of patients.
- Baseline liver function abnormalities is the strongest predictor of post-treatment Grade 3 or more toxicity

Incidence and risk factors for sustained hepatic function toxicity 6 months after radioembolization: analysis of the radiation-emitting sir-spheres in non-resectable liver tumor (RESIN) registry

Conclusion:

- For primary hepatic malignancy, future clinical trials would ideally include treatment naïve patients.
- Future trials for metastatic disease should focus primarily on baseline liver function to optimize recruitment and minimize toxicity, particularly if bilobar treatment is planned in the setting of limited tumor volume.

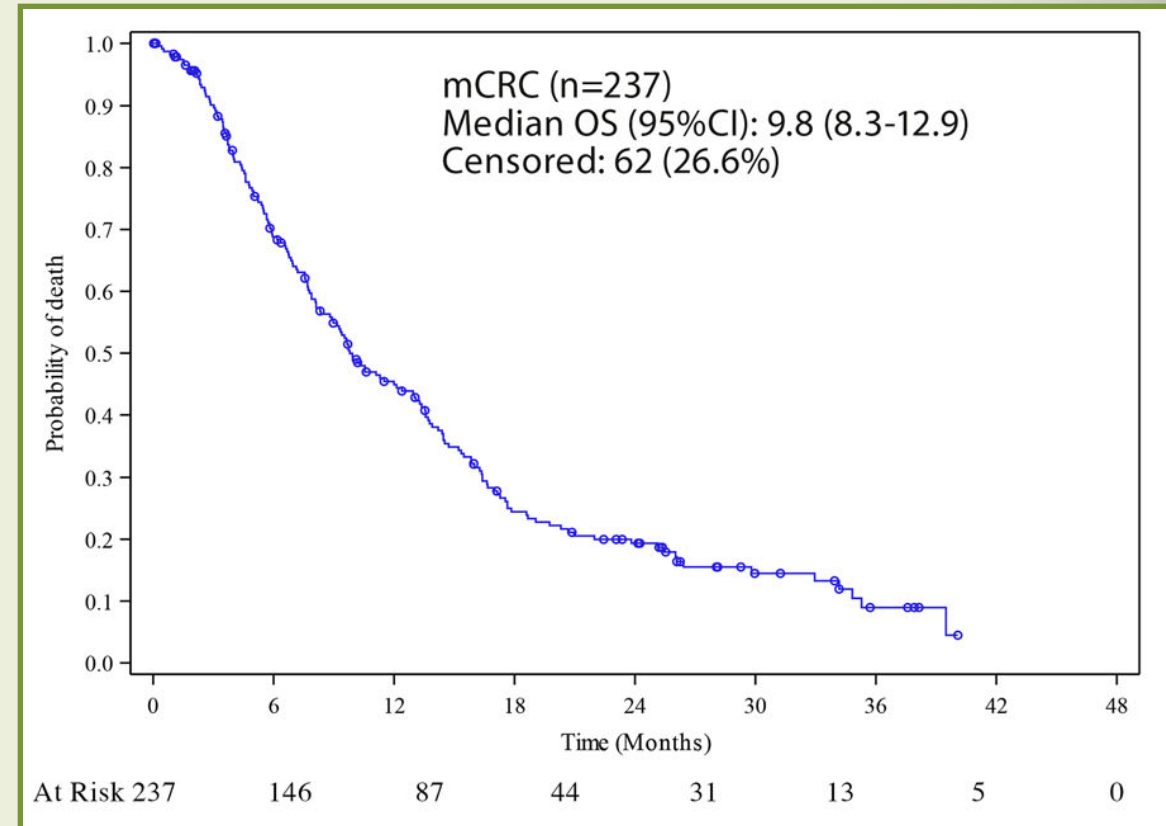
Clinical Application of Trans-Arterial Radioembolization in Hepatic Malignancies in Europe: First Results from the Prospective Multicentre Observational Study CIRSE Registry for SIR-Spheres Therapy (CIRT)

Study Design:

- Prospective observational study initiated by the Cardiovascular and Interventional Radiological Society of Europe (CIRSE)
- CIRSE Registry for SIR-Spheres Therapy (**CIRT**).

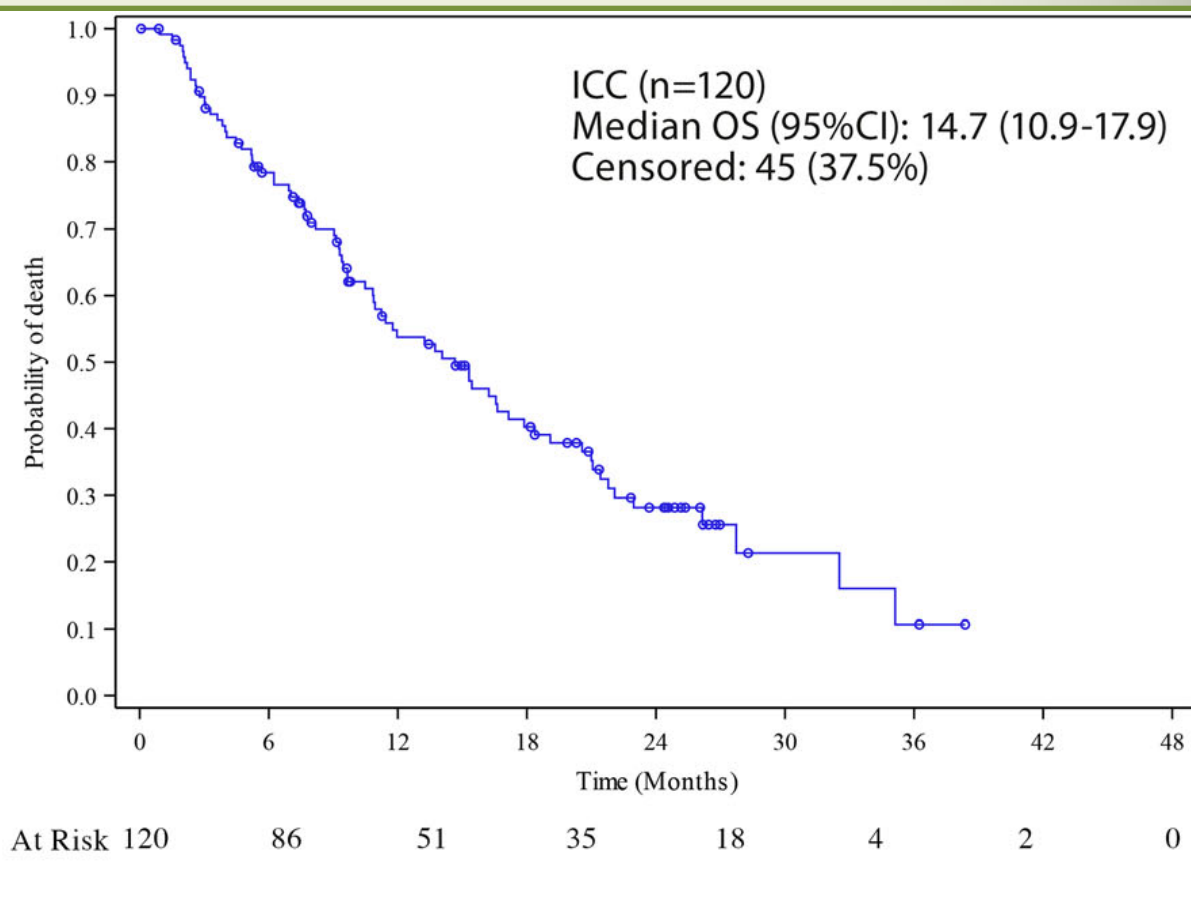
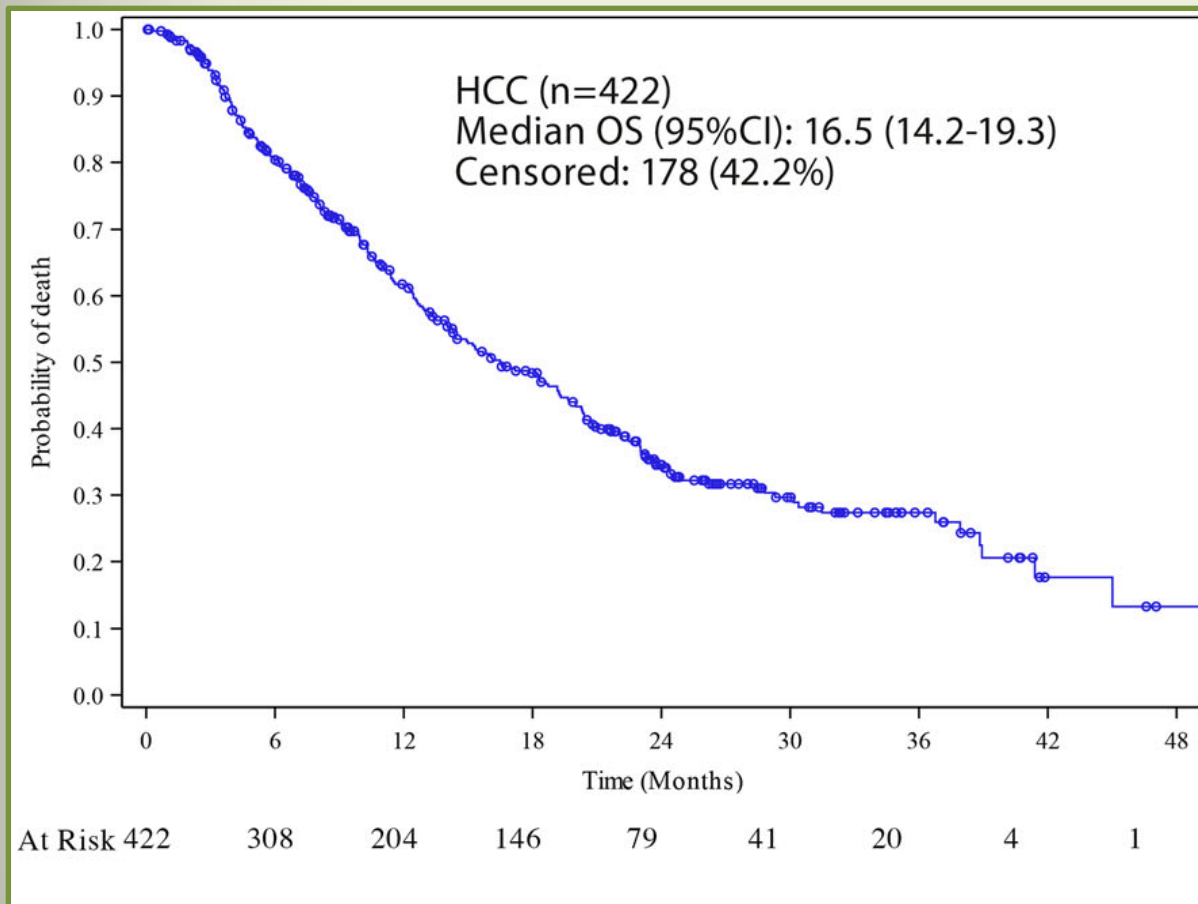
Clinical Application of Trans-Arterial Radioembolization in Hepatic Malignancies in Europe: First Results from the Prospective Multicentre Observational Study CIRSE Registry for SIR-Spheres Therapy (CIRT)

- Patients treated with TARE with Y90 resin microspheres for primary or metastatic liver tumors.
- 1027 patients were analyzed.
- 53.1% had prior systemic therapy
- 38.3% had prior loco-regional therapy



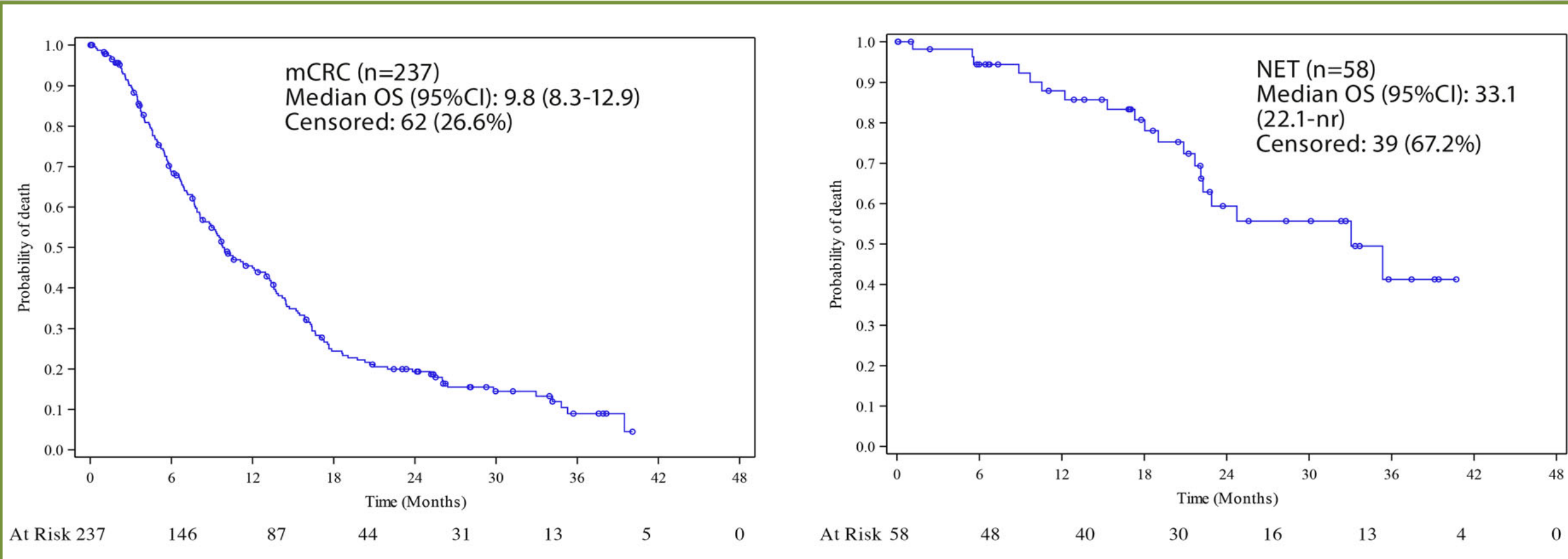
Helmberger et al. Cardiovasc Intervent Radiol (2021) 44:21-35

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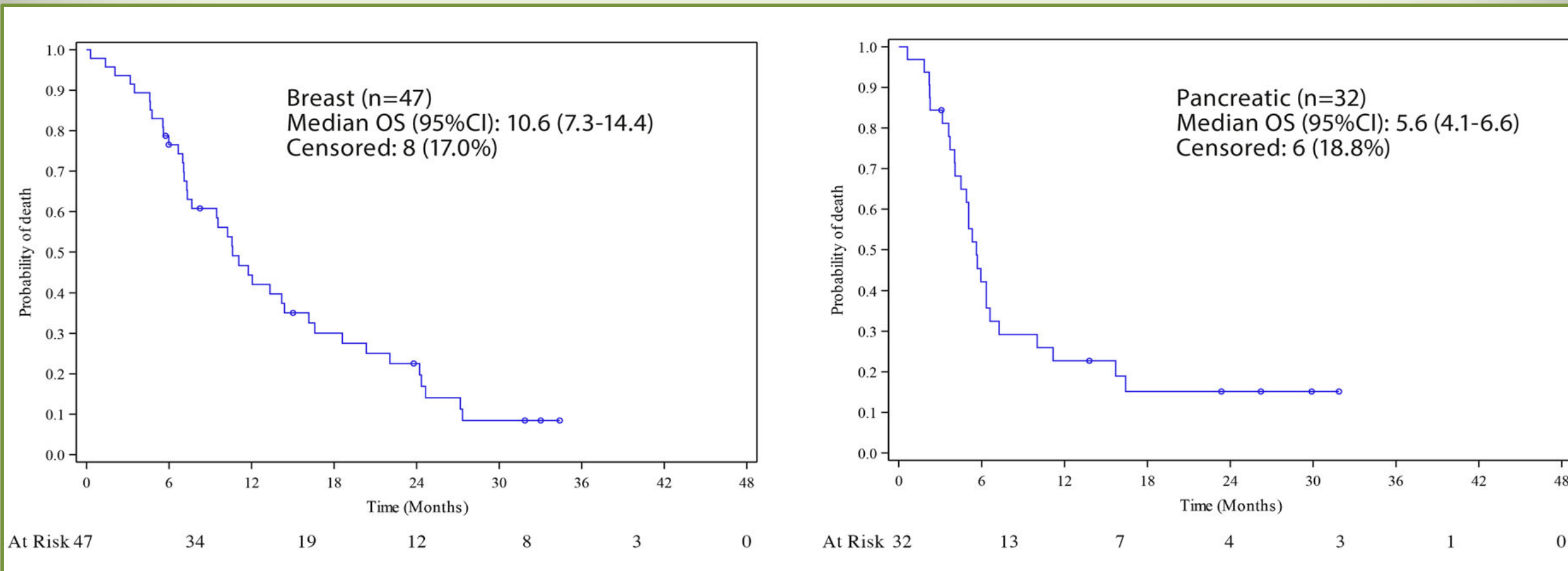
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Significant predictors of OS:

- Presence of ascites
- Cirrhosis
- Extrahepatic disease
- Patient performance status (ECOG)
- Number of chemotherapy lines prior to TARE
- Bilobar disease
- Tumor burden.

Covariate	Level	Events (%)	HR estimate ^a	95% CI	p value ^b
ECOG	0-Fully active	58.7% (352/600)	1.000		
	1-Restricted	73.2% (246/336)	1.513	[1.280, 1.789]	< 0.0001
	2 or higher	70.0% (56/80)	1.624	[1.217, 2.168]	
Extra-hepatic disease prior to treatment	No	59.0% (426/722)	1.000		
	Yes	76.7% (234/305)	1.372	[1.149, 1.638]	< 0.0001
Cirrhosis	No	65.6% (463/706)	1.000		
	Yes	61.4% (197/321)	1.304	[1.063, 1.599]	0.0128
Ascites	No	63.6% (588/925)	1.000		
	Yes	70.6% (72/102)	1.344	[1.035, 1.746]	0.0039
Tumour to liver percentage	Less than 10%	59.0% (242/410)	1.000		
	10%–20%	62.0% (127/205)	1.137	[0.914, 1.413]	0.0195
	Greater than 20%	66.8% (147/220)	1.414	[1.143, 1.750]	
	Unknown	75.0% (144/192)	1.098	[0.879, 1.373]	
Location of liver tumours	Bilobar	71.4% (419/587)	1.000		
	Left only	57.0% (57/100)	0.790	[0.589, 1.059]	0.0024
	Right only	54.3% (184/339)	0.694	[0.572, 0.843]	
Prior chemotherapy: number of lines	0	57.4% (296/516)	1.000		
	1	64.4% (123/191)	1.176	[0.931, 1.485]	< 0.0001
	2–5	76.8% (172/224)	1.855	[1.493, 2.303]	
	6 or more	72.5% (66/91)	1.355	[1.010, 1.818]	

Clinical Application of Trans-Arterial Radioembolization in Hepatic Malignancies in Europe: First Results from the Prospective Multicentre Observational Study CIRSE Registry for SIR-Spheres Therapy (CIRT)

Conclusion:

- TARE is safe and effective in the real-life clinical setting across various indications.
- Careful patient selection has been shown to be essential in the treatment of liver malignancies with TARE.

Helmberger et al. Cardiovasc Intervent Radiol (2021) 44:21-35



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Conclusion

- Y90 Radioembolization is a well tolerated intra-arterial therapy for metastatic disease including pretreated patients.
- There is survival advantage of using Y90 Radioembolization early in the course of disease progression in CRC liver metastasis, particularly with second line chemotherapy.
- Normal baseline liver functions is the most important predictor of toxicity following Y90 Radioembolization treatments.





Thank you

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