NHS England

Evidence review: selective internal radiation therapy (SIRT) with ytrrium-90 microspheres for unresectable primary intrahepatic cholangiocarcinoma in patients who are chemotherapy-refractory or chemotherapy-intolerant

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Contents

Abbreviations

BSC	best supportive care
CI	confidence interval
CR	complete response
ECOG	Eastern Cooperative Oncology Group
HR	hazards ratio
ICC	intrahepatic cholangiocarcinoma
IPO	interventional procedure overview
NICE	National Institute for Health and Care Excellence
NR	not reported
OS	overall survival
PD	progressive disease
PFS	progression free survival
PR	partial response
RCT	randomised control trial
RESIST	response evaluation criteria in solid tumours
RILD	radiation induced liver disease
SD	stable disease
SIRT	selective internal radiation therapy
TTP	time to progression

1. Introduction

Intrahepatic cholangiocarcinoma (ICC) is a rare type of primary liver cancer originating in the bile ducts. ICC is the second most frequent primary liver cancer in humans, after hepatocellular carcinoma (HCC). The estimated incidence of ICC in the UK is about 1,800 cases per year and this is rising year on year. The incidence of ICC increases with age, with a majority of patients being diagnosed between 70-80 years. ICC rarely occurs before 40 years and is more frequently observed in males, with a male-to-female ratio of 1.2-1.5 to 1. Incidence also varies with ethnicity and is higher in Asian-Pacific and Hispanic groups.

Several risk factors have been established for ICC, including parasitic infections, primary sclerosing cholangitis, biliary-duct cysts, hepatolithiasis, and toxins; however, more than 50% of patients have no identifiable risk factor. Common signs and symptoms include jaundice, itching, pale coloured stools, fatigue, abdominal pain and weight loss but these often do not appear until late in the course of the disease making early diagnosis difficult.

The prognosis of ICC is very poor, with a 1-year survival rate of less than 30% in men and 25% in women. 5-year survival is around 5% for both sexes. Mortality rates from ICC appear to be rising in most countries worldwide, including England and Wales.

Surgical resection with clear margins (R0) is the only potentially curative approach for patients with ICC and is the treatment of choice. However 60 to 70% of patients are not eligible for surgery because they have advanced disease at diagnosis. These patients are usually managed with palliative treatments and best supportive care. Palliative treatments include chemotherapy, surgical bypass of the bile duct or the insertion of a stent using surgical, endoscopic or percutaneous techniques.

Cisplatin and gemcitabine combination therapy has been demonstrated as an effective first-line systemic treatment for patients needing palliative chemotherapy. This is the only standard first-line therapy used in England to treat ICC. There is no randomised controlled trial evidence supporting the widespread use of second-line chemotherapy for patients who have progressed on first-line chemotherapy. Further treatment options for patients who are resistant or intolerant to first-line chemotherapy are restricted to best supportive care (BSC).

The purpose of this evidence review is to examine the clinical and cost effectiveness of using selective internal radiation therapy (SIRT) with yttrium-90 microspheres compared with BSC for individuals with unresectable ICC who are chemotherapy-resistant or chemotherapy-intolerant.

There are two yttrium-90 products currently available in the UK for this indication that were considered for this review: SIR-Spheres (Sirtex Medical) which are resin yttrium-90 microspheres and TheraSphere (Biocompatibles UK) which are glass yttrium-90 microspheres.

The questions that this review aimed to address were:

1. What is the evidence on clinical effectiveness of using selective internal radiation therapy (SIRT) with yttrium-90 microspheres compared with best supportive care for individuals with unresectable, liver-only or liver-dominant intrahepatic cholangiocarcinoma who are chemotherapy-refractory or chemotherapy-intolerant?
    a) glass yttrium-90 microspheres;
    b) resin yttrium-90 microspheres.

2. What is the evidence relating to the safety of selective internal radiation therapy (SIRT) with yttrium-90 microspheres compared with best supportive care for individuals with

unresectable, liver-only or liver-dominant intrahepatic cholangiocarcinoma who are chemotherapy-refractory or chemotherapy-intolerant?

a) glass yttrium-90 microspheres;
b) resin yttrium-90 microspheres.

3. What is the evidence on the cost effectiveness of selective internal radiation therapy (SIRT) with yttrium-90 microspheres compared with best supportive care for individuals with unresectable, liver-only or liver-dominant intrahepatic cholangiocarcinoma who are chemotherapy-refractory or chemotherapy-intolerant?

    a) glass yttrium-90 microspheres;
    b) resin yttrium-90 microspheres.

4. Does the evidence of clinical and cost-effectiveness identify any subgroups of patients with unresectable, liver-only or liver-dominant intrahepatic cholangiocarcinoma who are chemotherapy-refractory or chemotherapy-intolerant who would gain greater benefit from using selective internal radiation therapy (SIRT) with yttrium-90 microspheres compared with best supportive care?

2. Summary of results

No studies were identified which compared SIRT with yttrium-90 microspheres to best supportive care in patients with unresectable, chemotherapy-refractory intrahepatic cholangiocarcinoma (ICC).

As there were no comparative studies, three non-comparative, retrospective, case series with a total of 113 patients with advanced or unresectable ICC were included to provide some context on the efficacy of SIRT in this population (Hoffman et al. 2012; Beuzit et al. 2016; Paprottka et al. 2017). Patients in Hoffman et al. (2012) and Paprottka et al. (2017) were treated with SIRT using yttrium-90 resin microspheres (SIR-spheres), whereas those in Beuzit et al. (2016) were treated using glass microspheres (TheraSphere). The majority of patients in Hoffman et al. and Beuzit et al. had received prior chemotherapy (79% and 91%, respectively), Paprottka et al. did not report this. Therefore some chemotherapy-naïve patients have been included in this review.

These three studies reported median overall survival for patients with ICC treated with SIRT: 22, 19, and 14 months, respectively. Hoffman et al. (2012) reported a median time to progression (TTP) for patients with ICC treated with SIRT of 9.8 months (neither TTP nor progression-free survival (PFS) were reported by the other 2 studies).

Adverse events (AEs) were poorly reported in all 3 studies. Hoffman et al. (2012) stated that no clinically relevant acute toxicities occurred and there were no cases of radiation induced liver disease (RILD). Beuzit et al. (2016) reported that one patient had a severe toxicity event of hepatic encephalopathy. AEs were not reported in Paprottka et al. (2017).

Quality of life outcomes were not reported in the included studies.

All three studies are of limited quality and at risk of bias. The non-comparative nature of their design means that they do not provide relevant evidence on the clinical-effectiveness or safety of SIRT with yttrium-90 compared to BSC in patients with unresectable, chemotherapy-refractory ICC.

No studies were identified which reported the cost-effectiveness of SIRT with yttrium-90 in this ICC

population.

This review is limited by the absence of high quality comparative evidence. Higher quality comparative studies exploring outcomes of interest are required to address the questions raised in this evidence review.

3. Methodology

Literature search

The search conducted for the NICE IPG459 interventional procedure overview (NICE 2013) of selective internal radiation therapy for primary intrahepatic cholangiocarcinoma was reviewed and updated or adapted where necessary. As the search for the interventional procedure overview (IPO) covered the period from database commencement to November 2011, searches for this review were conducted to cover the period January 2011 to February 2018. In addition, to identify economic evidence that was not included in the IPO, searches were conducted to identify economic evidence relating to SIRT for intrahepatic cholangiocarcinoma (ICC). These searches covered the period from database commencement to February 2018 and used an economic filter where appropriate.

A strategy was developed in Ovid Medline (Section 10) and was adapted to the following databases: Medline In-Process; Embase; Cochrane Library (components: CDSR, DARE, CENTRAL, HTA, NHS EED); Pubmed (epub ahead of press only). The manufacturers' websites were searched for additional studies as well as NHS Evidence. The searches were limited to the English language.

Results of all searches were combined in a Reference Manager 12 database together with the references of studies included in the NICE interventional procedure overview (NICE 2013). The studies included in any relevant systematic reviews were also checked for inclusion in this review.

Study selection

After de-duplication, one reviewer (HM) selected publications that were considered relevant based on titles and/or abstracts using the inclusion and exclusion criteria presented in section 9. In a second selection round, one reviewer (JW) assessed the full text articles for eligibility and selected studies to be included in the review; any uncertainties were discussed and a decision was agreed. Decisions were recorded at each stage.

The review search yielded 335 potentially relevant publications, 6 were retained for assessment of eligibility at full-text. Following this assessment 3 were retained for inclusion in the review.

Data extraction

One reviewer (JW) extracted data from eligible study reports into the evidence summary tables in section 7; these were subsequently checked by another reviewer (HM).

Quality assessment of evidence

The quality of the evidence was assessed in accordance with the NHS England guidance for conducting evidence reviews and critically appraised using the SURE critical appraisal checklists.

4. Results

The literature search identified 335 records. On screening the title and abstracts, 6 were deemed to be relevant and the full text articles of these records were assessed for eligibility using the inclusion and exclusion criteria presented in section 9. Following this assessment, 3 publications were retained as being relevant to the review, these comprised of 3 reports of 3 non-comparative effectiveness studies. No comparative studies or cost-effectiveness studies were identified.

Three non-comparative studies were included in this review (Hoffman et al. 2012; Beuzit et al. 2016; Paprottka et al. 2017). All were retrospective, non-comparative, case series. As there was an absence of high quality comparative studies, the three non-comparative studies have been summarised in the evidence summary tables (section 7).

Hoffman et al. (2012) included 33 consecutive patients with unresectable intrahepatic cholangiocarcinoma (ICC) or chemotherapy-refractory liver metastases from ICC, treated with yttrium-90 SIRT (resin microspheres) in Germany between 2007 and 2010. A total of 27 patients (79%) had received previous systemic chemotherapy, therefore some chemotherapy-naïve patients were included in this study (reasons not reported). Median overall survival (OS) was 22 months (95% CIs 7.9-29.4) and median time to progression (TTP) was 9.8 months (95% CIs 4.0-31.9). Adverse events were poorly reported; the authors reported that no clinically relevant acute or delayed toxicities occurred and there were no cases of radiation induced liver disease. Quality of life was not measured.

Beuzit et al. (2016) included 45 patients with locally advanced ICC treated with yttrium-90 SIRT (glass microspheres) at a single institution in France between 2010 and 2014. A total of 41 patients (91%) had received previous systemic chemotherapy and 13 (29%) had concomitant chemotherapy, therefore some chemotherapy-naïve patients were included in this study (reasons not reported). Median OS was 19.0 months (95% CIs 8.6-29.3) and progression-free survival (PFS) was not reported. Adverse events were poorly reported; the authors stated that one patient had severe toxicity (hepatic encephalopathy). Quality of life was not measured.

Paprottka et al. (2017) included 35 consecutive patients (from a mixed cohort) with refractory ICC treated with yttrium-90 SIRT (resin microspheres) at a single institution in Germany in 2013. The number of patients who had received previous chemotherapy was not reported. Median OS for the ICC group was 14.1 months (95% CIs 8.9-19.3) and PFS was not reported. Adverse events were not reported. Baseline characteristics and several outcome measures are not presented separately for the ICC population. Quality of life was not measured.

Review questions:

1. What is the evidence on clinical effectiveness of using selective internal radiation therapy (SIRT) with yttrium-90 microspheres compared with best supportive care for individuals with unresectable, liver-only or liver-dominant intrahepatic cholangiocarcinoma who are chemotherapy-refractory or chemotherapy-intolerant?

    a) glass yttrium-90 microspheres;

None. No comparative studies were identified in this population. One selected non-comparative study reported OS for patients treated with yttrium-90 SIRT glass microspheres.

    b) resin yttrium-90 microspheres.

None. No comparative studies were identified in this population. Two selected non-comparative studies reported OS for patients treated with yttrium-90 SIRT resin microspheres.

2. What is the evidence relating to the safety of selective internal radiation therapy (SIRT) with yttrium-90 microspheres compared with best supportive care for individuals with

unresectable, liver-only or liver-dominant intrahepatic cholangiocarcinoma who are chemotherapy-refractory or chemotherapy-intolerant?

a) glass yttrium-90 microspheres;

None. No comparative studies were identified in this population. Selected non-comparative studies did not adequately report adverse events.

b) resin yttrium-90 microspheres

None. No comparative studies were identified in this population. Selected non-comparative studies did not adequately report adverse events.

3. What is the evidence on the cost effectiveness of selective internal radiation therapy (SIRT) with yttrium-90 microspheres compared with best supportive care for individuals with unresectable, liver-only or liver-dominant intrahepatic cholangiocarcinoma who are chemotherapy-refractory or chemotherapy-intolerant?

a) glass yttrium-90 microspheres;

None. No cost-effectiveness studies were identified for this population.

b) resin yttrium-90 microspheres.

None. No cost-effectiveness studies were identified for this population.

4. Does the evidence of clinical and cost-effectiveness identify any subgroups of patients with unresectable, liver-only or liver-dominant intrahepatic cholangiocarcinoma who are chemotherapy-refractory or chemotherapy-intolerant who would gain greater benefit from using selective internal radiation therapy (SIRT) with yttrium-90 microspheres compared with best supportive care?

No. No comparative studies were identified in this population. Results of subgroup analysis from selected non-comparative studies are reported in the evidence tables (section 7).

5. Discussion

There is an absence of high quality evidence evaluating the efficacy of yttrium-90 SIRT for treating unresectable ICC; no comparative studies were identified for this review. Three small, non-comparative studies were included, all of which were retrospective in design. The most important outcome, overall survival, ranged from 14 to 22 months across the included studies. The poor study design means that no conclusions can be made about clinical-effectiveness of yttrium-90 SIRT compared to best supportive care.

Adverse events were either not reported or reported inadequately in the three studies; as such no conclusion can be drawn about the safety of Y90 SIRT in this ICC population. Quality of life was not measured in these studies. No cost-effectiveness studies were identified.

Large, prospective, studies of yttrium-90 SIRT compared to best supportive care in patients with unresectable, chemotherapy-refractory ICC are needed to address the question of clinical-effectiveness. These should use OS as the primary outcome, with PFS, quality of life, and adverse events/complications as secondary outcomes. However, because ICC is a rare form of cancer, large randomised trials of a complex intervention such as SIRT are very challenging to carry out. Cost-effectiveness studies in this population, with best supportive care as the comparator group, are also required.

6. Conclusion

This review provides limited evidence on the clinical- and cost-effectiveness of SIRT with yttrium-90 for the treatment of unresectable, chemotherapy-refractory ICC due to a paucity of high quality comparative studies. Furthermore, the available evidence did not provide any relevant evidence on the safety of this technology in this population. Future studies must include a control group using best supportive care, and report data on adverse events.

7. Evidence summary tables

Use of yttrium-90 SIRT to treat unresectable chemotherapy-refractory liver-dominant intrahepatic cholangiocarcinoma NON-COMPARATIVE STUDIES								
Study reference	**Study Design & setting**	**Population characteristics**	**Intervention**	**Outcome measures**	**Results**	**Quality of evidence score**	**Applicability**	**Critical appraisal summary**
Hoffman et al. 2012	P1 - retrospective, non-comparative case series Germany, April 2007 - January 2010	33 consecutive patients with unresectable ICC or chemotherapy-refractory liver metastases from ICC Mean age (yrs): 65.2 (46 – 84.3) ECOG performance status: 0-2. Female: 15 (45.5%); Male: 18 (54.5%) Prior chemotherapy: 78.8% Prior resection: 36.4% Extrahepatic metastases 24.2% Concomitant chemotherapy: NR Exclusions:	Yttrium-90 resin microspheres (SIR-spheres) were delivered using standard SIRT approach following work-up procedures.	Median overall survival (months; 95% CI)	22 (7.9-29.4)	6	Direct	Limitations (review team): small study size and retrospective design means results are at risk of bias. Non-comparative design limits relevance of study to this evidence review. Number of centres not described. TTP reported instead of PFS. Study includes some chemotherapy-naïve patients. Adverse events inadequately reported. Funding and conflicts of interest not reported.
				Median follow-up (months; range)	10 (3.1-44)			
				Median time to progression (months; 95% CI)	9.8 (4.0-31.9)			
				Median liver-specific progression free survival (months; 95% CI)	Not reported			
				% survival	Not reported			
				Tumour response (RECIST criteria; CR	CR 0 (0%) PR 12 (36%)			

		occluded portal vein, tumour burden ≥50%, severe comorbidities		– complete response, PR – partial response, SD – stable disease, PD – progressive disease)	SD 17 (52%) PD 5 (15%)			
				Quality of life	Not reported			
				Sub-group analysis (baseline covariates)	An ECOG score of 0, and liver involvement of ≤25%, was associated with prolonged survival. Tumour burden ≤ 25% was associated with prolonger survival			
				Adverse events	No clinically relevant acute or delayed toxicities. No radiation induced liver disease noted. Other adverse events not described.			

Study reference	Study Design & setting	Population characteristics	Intervention	Outcome measures	Results	Quality of evidence score	Applicability	Critical appraisal summary
Beuzit et al. 2016	P1 - retrospective, non-comparative	45 patients with locally advanced ICC	Yttrium-90 glass microspheres (TheraSphere) were delivered	Median overall survival (months;	19.0 (8.6-29.3)	5	Direct	Limitations (review team): small study size from single centre and retrospective design means results are at risk of bias. Non-comparative

	case series Single centre, France, April 2010 – February 2014	ECOG performance status: 0-2. Male: 24 (53.3%); Female: 21 (46.7%) Prior chemotherapy: 41 (91.1%) Prior ablation: 2 (4.4%); prior chemoembolisation: 1(2.2%) Extrahepatic metastases: 0% Concomitant chemotherapy: 13 (28.9%) Exclusions: extrahepatic spread	using standard SIRT approach following work-up procedures.	95% CI)				design limits relevance of study to this evidence review. Authors do not specifically describe consecutive recruitment. Study includes some chemotherapy-naïve patients. Adverse events inadequately reported. Two authors declared that they are consultants for BTG international inc. (manufacturer of TheraSphere). Authors report that no funding was received.
				Median follow-up (months; range)	Not reported			
				Median progression free survival (months; 95% CI)	Not reported			
				Median liver-specific progression free survival (months; 95% CI)	Not reported			
				% survival	1 year: 54.0% 2 year: 40.7%			
				Tumour response (RECIST criteria; CR – complete response, PR – partial response, SD – stable disease, PD – progressive disease)	Best responses as assessed by RECIST CR 0 (0%) PR 6 (13.3%) SD 32 (71.1%) PD 7 (15.6%)			
				Quality of life	Not reported			

				Sub-group analysis (baseline covariates)	Albumin and bilirubin levels were associated with longer survival. Increasing age was associated with decreased survival.			
				Adverse events	Severe toxicity (hepatic encephalopathy) reported in 1 patient. Adverse events not reported.			

Study reference	Study Design & setting	Population characteristics	Intervention	Outcome measures	Results	Quality of evidence score	Applicability	Critical appraisal summary
Paprottka et al. 2017	P1 - Retrospective, non-comparative case series Single centre, Germany, January 2013 – February 2013	35 consecutive patients (of a total mixed cohort of 389) with refractory liver-dominant cholangiocarcinoma treated with Y90 SIRT Patient characteristics not stratified on primary diagnosis; therefore data for ICC patients cannot be reported. Exclusions: significant extrahepatic spread, limited hepatic	Yttrium-90 resin microspheres (SIR-spheres) were delivered using standard SIRT approach following work-up procedures.	Median overall survival (months; 95% CI)	14.1 (8.9-19.3)	5	Direct	Limitations (review team): small study size, single centre, and retrospective design means results are at risk of bias. Non-comparative design limits relevance of study to this evidence review. This study included a mixed population. Baseline characteristics and outcomes other than OS were not reported separately for ICC group. PFS and adverse not reported. Unclear whether all patients were chemotherapy-refractory. Authors declare no conflicts of interest. Authors report no funding was received.
				Median follow-up (months; range)	Not reported separately for ICC patients			
				Median progression free survival (months; 95% CI)	Not reported			
				Median liver-specific progression	Not reported			

		reserve, ascites, clinical signs of liver failure, severe comorbidities.		free survival (months; 95% CI)				
				% survival	Not reported			
				Tumour response (RECIST criteria; CR – complete response, PR – partial response, SD – stable disease, PD – progressive disease)	Not reported separately for ICC patients			
				Quality of life	Not reported			
				Sub-group analysis (baseline covariates)	Not reported separately for ICC patients			
				Adverse events	Not reported			

8. Grade of evidence table

Use of yttrium-90 SIRT to treat unresectable chemotherapy-refractory liver-dominant intrahepatic cholangiocarcinoma non-comparative studies					
Outcome Measure	**Reference**	**Quality of Evidence**	**Applicability**	**Grade of Evidence**	**Interpretation of Evidence**

		Score			
Median overall survival (months; 95% CI)	Hoffman et al. 2012	6	Direct	B	Median overall survival 22 months (95% CI 7.9-29.4) from Hoffman et al. (2012), n=33; funding source not reported. Median overall survival and 95% confidence intervals were estimated by the Kaplan–Meier method. Three studies provided overall survival data. All 3 studies are case series which are at high risk of bias from their retrospective design, small sample size and absence of control group. Therefore 'survival benefit' cannot be determined.
	Beuzit et al. 2016	5	Direct		
	Paprottka et al. 2017	5	Direct		
Median time to progression (months; 95% CI)	Hoffman et al. 2012	6	Direct	C	Median time to progression 9.8 months (95% CI 4.0-31.9), from Hoffman et al. (2012), n=33; funding source not reported. TTP assessed from date of radioembolization. Only one study provided TTP data; this is a case series which, due to the fact that there is no control group, has a high risk of bias and therefore cannot be used to determine the efficacy of a treatment. Furthermore, TTP may be biased by the retrospective design of this study as it relies on accurate recording of date of progression.
Overall response rate *Sum of complete response and partial response*	Hoffman et al. 2012	6	Direct	B	Overall response rate: 12 (36%), from Hoffman et al. (2012), n=33; funding source not reported. Tumour response was assessed by contrast enhanced computed tomography (CT) and magnetic resonance imaging (MRI) using the Response Evaluation Criteria in Solid Tumours. Two studies provided tumour response data. Both studies are case series which, due to the fact that there is no control group, have a high risk of bias and therefore cannot be used to determine the efficacy of a treatment.
	Beuzit et al. 2016	5	Direct		
Disease control rate *Sum of complete response, partial response and stable disease*	Hoffman et al. 2012	6	Direct	B	Disease control rate: 19(58%), from Hoffman et al. (2012), n=33; funding source not reported. Tumour response was assessed by contrast enhanced computed tomography (CT) and magnetic resonance imaging (MRI) using the Response Evaluation Criteria in Solid Tumours. Two studies provided tumour response data. Both studies are case series which, due to the fact that there is no control group, have a high risk of bias and therefore cannot be used to determine the efficacy of a treatment.
	Beuzit et al. 2016	5	Direct		
Toxicity	Hoffman et al. 2012	6	Direct	B	No clinically relevant acute or delayed toxicities. No radiation induced liver disease noted. Other adverse events not described, from Hoffman et al. (2012), n=33; funding source not reported. Most recent history was taken for side effects during follow-up. Severe toxicity (hepatic encephalopathy) reported in 1 patient. Adverse events not reported, from Beuzit et al. (2016), n=45. Two studies provided safety and adverse event data. Both studies are case series which, due to the fact that there is no control group, have a high risk of bias and therefore cannot be used to determine the efficacy of a treatment.
	Beuzit et al. 2016	5	Direct		

9. Literature search terms

Search strategy (terms in bold in the right-hand column were used to construct the search)	
P – Patients / Population Which patients or populations of patients are we interested in? How can they be best described? Are there subgroups that need to be considered?	Individuals with unresectable, liver-only or liver-dominant intrahepatic **cholangiocarcinoma** who are chemotherapy-refractory or chemotherapy-intolerant.
I – Intervention Which intervention, treatment or approach should be used?	**Selective internal radiation therapy** (SIRT) with: a) **glass yttrium-90 microspheres;** b) **resin yttrium-90 microspheres.**
C – Comparison What is/are the main alternative/s to compare with the intervention being considered?	Best supportive care (BSC)
O – Outcomes What is really important for the patient? Which outcomes should be considered? Examples include intermediate or short-term outcomes; mortality; morbidity and quality of life; treatment complications; adverse effects; rates of relapse; late morbidity and re-admission	<u>Critical to decision-making:</u> • Overall survival • Progression free survival • Liver specific progression free survival • Overall response rate • Disease control rate • Adverse events • Quality of life (HRQoL) • Cost effectiveness Any other relevant outcome from included studies.
Assumptions / limits applied to search	
Inclusion Criteria	Patients with liver-only or liver-dominant intrahepatic cholangiocarcinoma English language

Exclusion Criteria	Abstracts Conference papers Papers published greater than 10 years ago Studies in which results from patients with ICC are not analysed separately Studies with at least 30 patients with a primary diagnosis of ICC Studies with only chemotherapy-naïve patients

10. Search strategy

Database: Ovid MEDLINE(R) ALL <1946 to February 07, 2018>
1 Yttrium/ (2737)
2 exp Yttrium Radioisotopes/ (2697)
3 yttrium*.tw. (5518)
4 (90Y or Y-90).tw. (2105)
5 SIR-Sphere*.tw. (95)
6 TheraSphere*.tw. (64)
7 (sirtex or nordion).tw. (58)
8 SIRT.tw. (961)
9 (selective* adj3 internal* adj3 radiotherap*).tw. (72)
10 (selective* adj3 internal* adj3 radiation* adj3 therap*).tw. (290)
11 (internal* adj3 radiation* adj3 therap*).tw. (410)
12 radioemboli*.tw. (1181)
13 or/1-12 (11091)
14 (bile duct adj (cancer or neoplasm)).tw. (1112)
15 Bile Duct Neoplasms/ (12840)
16 Cholangiocarcinoma/ (7204)
17 Cholangiocarcinoma*.tw. (10146)
18 or/14-17 (18382)
19 13 and 18 (106)
20 limit 19 to (english language and yr="2011 -Current") (90)
21 Economics/ (26861)
22 exp "costs and cost analysis"/ (211788)
23 Economics, Dental/ (1891)
24 exp economics, hospital/ (22633)
25 Economics, Medical/ (8934)
26 Economics, Nursing/ (3978)
27 Economics, Pharmaceutical/ (2735)
28 (economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab. (647245)
29 (expenditure$ not energy).ti,ab. (24823)
30 value for money.ti,ab. (1376)
31 budget$.ti,ab. (25059)
32 or/21-31 (788278)
33 ((energy or oxygen) adj cost).ti,ab. (3600)
34 (metabolic adj cost).ti,ab. (1187)

35	((energy or oxygen) adj expenditure).ti,ab. (21772)
36	or/33-35 (25668)
37	32 not 36 (782388)
38	letter.pt. (975328)
39	editorial.pt. (449387)
40	historical article.pt. (343202)
41	or/38-40 (1750533)
42	37 not 41 (749612)
43	exp animals/ not humans/ (4422724)
44	42 not 43 (703609)
45	bmj.jn. (73094)
46	"cochrane database of systematic reviews".jn. (13420)
47	health technology assessment winchester england.jn. (1150)
48	or/45-47 (87664)
49	44 not 48 (697920)
50	19 and 49 (0)
51	20 or 50 (90)

11. Evidence selection

- Total number of publications reviewed: 335
- Total number of publications considered relevant: 6
- Total number of publications selected for inclusion in this briefing: 3

12. References

Beuzit, L., Edeline, J., Brun, V., Ronot, M., Guillygomarc'h, A., Boudjema, K., Gandon, Y., Garin, E. and Rolland, Y., 2016. Comparison of Choi criteria and Response Evaluation Criteria in Solid Tumors (RECIST) for intrahepatic cholangiocarcinoma treated with glass-microspheres Yttrium-90 selective internal radiation therapy (SIRT). *European journal of radiology*, *85*(8), pp.1445-1452.

Hoffmann, R.T., Paprottka, P.M., Schön, A., Bamberg, F., Haug, A., Dürr, E.M., Rauch, B., Trumm, C.T., Jakobs, T.F., Helmberger, T.K. and Reiser, M.F., 2012. Transarterial hepatic yttrium-90 radioembolization in patients with unresectable intrahepatic cholangiocarcinoma: factors associated with prolonged survival. *Cardiovascular and interventional radiology*, *35*(1), pp.105-116.

Paprottka, K.J., Schoeppe, F., Ingrisch, M., Rübenthaler, J., Sommer, N.N., De Toni, E., Ilhan, H., Zacherl, M., Todica, A. and Paprottka, P.M., 2017. Pre-therapeutic factors for predicting survival after radioembolization: a single-center experience in 389 patients. *European journal of nuclear medicine and molecular imaging*, *44*(7), pp.1185-1193.