Selective internal radiation therapy for primary intrahepatic cholangiocarcinoma

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NICE interventional procedure guidance 459
guidance.nice.org.uk/ipg459
1 Guidance

1.1 Current evidence on the safety and efficacy of selective internal radiation therapy (SIRT) for primary intrahepatic cholangiocarcinoma is limited in both quantity and quality. Therefore this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

1.2 Clinicians wishing to undertake SIRT for primary intrahepatic cholangiocarcinoma should take the following actions.

- Inform the clinical governance leads in their Trusts.
- Ensure that patients understand the uncertainty about the procedure's safety and efficacy, and provide them with clear written information. In addition, the use of NICE's information for the public is recommended.

1.3 Patients with primary intrahepatic cholangiocarcinoma should be selected for treatment by SIRT or for entry into trials by a multidisciplinary hepatobiliary cancer team.

1.4 SIRT should only be carried out by clinicians with specific training in its use and in techniques to minimise the risk of side effects from the procedure.

1.5 Clinicians should enter details about all patients undergoing SIRT for primary intrahepatic cholangiocarcinoma onto the UK SIRT register. They should audit and review clinical outcomes locally and should document them and consider their relationship to patient characteristics.

1.6 NICE encourages research to guide future use of SIRT for primary intrahepatic cholangiocarcinoma. This should document patient characteristics, tumour response, survival and quality of life measures, and details of other treatments used adjunctively or sequentially. NICE may review the procedure on publication of further evidence.
2 The procedure

2.1 Indications and current treatments

2.1.1 Intrahepatic cholangiocarcinoma is a rare type of primary liver cancer originating in the bile ducts.

2.1.2 The choice of treatment depends on a number of factors, including the exact location and stage of the cancer, and the patient's liver function. Cholangiocarcinoma is not usually diagnosed before the symptoms of biliary obstruction occur, by which time the cancer may be too advanced for curative surgical resection. Occasionally, surgical removal with curative intent may be possible: this may sometimes be achieved by downstaging the tumour using other treatment modalities first. The standard options for palliative treatment include chemotherapy, surgical bypass of the bile duct or the insertion of a stent using surgical, endoscopic or percutaneous techniques.

2.2 Outline of the procedure

2.2.1 Selective internal radiation therapy (SIRT) for primary intrahepatic cholangiocarcinoma involves infusion of microspheres loaded with yttrium-90, which aims to deliver radiation directly into the tumour, minimising the risk of radiation damage to healthy surrounding tissues.

2.2.2 Before undertaking the treatment, a nuclear medicine liver-to-lung shunt study is carried out to assess the risk of radioactive microspheres causing lung damage. Radiographic imaging and selective coil embolisation of arteries to the stomach and duodenum are also commonly carried out.

2.2.3 Using local anaesthesia, radioactive microspheres that are designed to lodge in the small arteries are injected into branches of the hepatic artery, usually by a percutaneous femoral approach.

2.2.4 The procedure may be repeated depending on the response.
Sections 2.3 and 2.4 describe efficacy and safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the overview.

### 2.3 Efficacy

2.3.1 A case series of 24 patients reported a median survival of 4 months in patients with previous exposure to systemic chemotherapy (n=7), and a median survival of 32 months in patients who were chemotherapy-naive (n=17) (p=0.03). A case series of 19 patients reported a median survival of 12 months from first treatment.

2.3.2 The case series of 24 patients reported stable disease (using World Health Organization [WHO] criteria) in 68% (15/22) of patients, partial response in 27% (6/22) of patients, and disease progression in 5% (1/22) of patients at a median follow-up of 18 months.

2.3.3 Downstaging to resection was reported in 1 patient in the case series of 24 patients (timing of resection unclear; median follow-up of study was 18 months). Downstaging to resection was reported in 1 patient who had a partial response to treatment in a case series of 25 patients (timing of resection unclear; median follow-up of study was 8 months).

2.3.4 Bridging to liver transplantation was reported in 1 patient in the case series of 24 patients at a median follow-up of 18 months.

2.3.5 The Specialist Advisers listed efficacy outcomes as overall survival, tumour response, quality of life, increase in time to progression, downsizing or downstaging to potentially curative treatments, and bridging to liver transplantation.

### 2.4 Safety

2.4.1 Death within 30 days was reported in 2 patients (1 patient had pulmonary embolus and the other patient had a tumour burden greater than 50%; no further details available) in the case series of 24 patients.
2.4.2 Gastroduodenal ulcer was reported after SIRT in 1 patient in the case series of 24 patients. No details were given about when the ulcer occurred; it was treated by gastrojejunostomy.

2.4.3 Fatigue (64%), nausea (16%) and vomiting (8%) (numbers of patients not reported) were reported in the case series of 25 patients at a median follow-up of 8 months.

2.4.4 Severe thrombocytopenia (within 30 days of first treatment) was reported in 1 patient in the case series of 19 patients.

2.4.5 Pleural effusion (no further details given) was reported in 9% (2/22) of patients in the case series of 24 patients at a median follow-up of 18 months.

2.4.6 The Specialist Advisers listed additional anecdotal adverse events as fibrosis and skin ulceration; and additional theoretical adverse events as liver failure, portal hypertension, and radiation-induced liver disease.

### 2.5 Other comments

2.5.1 The Committee noted that primary intrahepatic cholangiocarcinoma is a rare condition with a variable natural history, so that the accumulation of useful evidence is difficult. This underpinned the recommendation to encourage research.

### 3 Further information

3.1 For related NICE guidance see the NICE website.

**Information for patients**

NICE has produced information on this procedure for patients and carers (Information for the public). It explains the nature of the procedure and the guidance issued by NICE, and has been written with patient consent in mind.
About this guidance

NICE interventional procedure guidance makes recommendations on the safety and efficacy of the procedure. It does not cover whether or not the NHS should fund a procedure. Funding decisions are taken by local NHS bodies after considering the clinical effectiveness of the procedure and whether it represents value for money for the NHS. It is for healthcare professionals and people using the NHS in England, Wales, Scotland and Northern Ireland, and is endorsed by Healthcare Improvement Scotland for implementation by NHSScotland.

This guidance was developed using the NICE interventional procedures guidance process.

We have produced a summary of this guidance for patients and carers.

Your responsibility

This guidance represents the views of NICE and was arrived at after careful consideration of the available evidence. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

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