NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Multiple Technology Appraisal

Selective internal radiation therapies (SIRT) for treating hepatocellular carcinoma

Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of selective internal radiation therapies (SIRT) within their approved indications for treating hepatocellular carcinoma.

Background

Hepatocellular carcinoma (HCC) is the most common form of liver cancer in England, accounting for 55% of primary liver cancer diagnoses in men and 28% of diagnoses in women[1]. It is commonly associated with cirrhosis (scarring of the liver), which can be caused by viral infections such as hepatitis B or C, excessive alcohol intake, or other diseases that result in chronic inflammation of the liver[2].

The risk of developing HCC is higher in men than in women and increases with age, with the average age of diagnosis of HCC at 66 years[2]. There were 4,925 people (3,235 men and 1,690 women) diagnosed with HCC in England in 2016[3].

Treatment for HCC is dependent on liver function, the distribution and volume of tumours within the liver, portal vein involvement and extra-hepatic metastases. As a result of these factors people with HCC are a heterogeneous group and a range of treatments may be used in the NHS.

Several staging systems are used to grade HCC including the Barcelona Clinic Liver Cancer (BCLC) staging and treatment schedule, which incorporates the Child–Pugh assessment of liver impairment. Early and intermediate HCC are categorised as BCLC stages A and stage B (Child-Pugh liver performance status A-B) respectively. Advanced and end-stage HCC are categorised as BCLC stages C (Child-Pugh liver performance status A-B) and D (Child-Pugh liver performance status B-C). People with Child-Pugh grade A liver impairment have the best liver function or the least impairment.The stage at which HCC is detected has a significant impact on survival; people with advanced HCC have a poorer prognosis than people with early stage HCC.

Treatment for HCC depends on the location and stage of the cancer, and how well the liver's functions is preserved. Early stage HCC may be treated with surgery (hepatic resection or liver transplantation), or percutaneous thermal ablation to cure the disease. However, treatment is not curative for many people. The current standard of care for advanced HCC is targeted chemotherapy with sorafenib. NICE's technology appraisal guidance on sorafenib for the treatment of advanced hepatocellular carcinoma (TA 474) recommends sorafenib as an option for treating advanced HCC only for people with Child-Pugh grade A liver impairment. NICE's technology appraisal guidance on regorafenib for treating advanced unresectable hepatocellular carcinoma (TA 514) does not recommend regorafenib for treating advanced unresectable hepatocellular carcinoma in adults who have had sorafenib. Regorafenib is subject to an ongoing NICE rapid review (ID1519).

Other treatment options include interventional procedures such as conventional trans-arterial chemoembolisation (TACE), trans-arterial chemoembolisation using drug-eluting beads ([DEB-TACE],using doxorubicin or cisplatin) for small, single tumours, and selective internal radiation therapy (SIRT) for large or multiple tumours. NICE interventional procedures guidance 460 states that current evidence on the efficacy and safety of SIRT for primary HCC is adequate for use with normal arrangements. However uncertainties remain and the guidance also recommends that clinicians should enter all patient details onto the UK SIRT register (launched in 2013)[a]. Best supportive care is offered if sorafenib, TACE or SIRT is not available or appropriate.

The technologies

Selective internal radiation therapies (SIRT) deliver radiation to the liver tissue via microspheres that are injected into the hepatic artery via a catheter from the femoral artery.

The SIRT technologies to be appraised are TheraSphere, SIR-Sphere and QuiremSphere.

- TheraSphere (BTG) is a CE marked class III active medical device which is indicated for the treatment of hepatic neoplasia. It comprises glass microspheres containing yttrium-90.

[a] NHS England's Interim Clinical Commissioning Policy Statement (2013) for selective internal radiation therapy (SIRT) states that SIRT is not routinely commissioned in the treatment of HCC.

- SIR-Sphere (Sirtex) is a CE marked class III active medical device which is indicated for the treatment of inoperable liver tumours. It comprises resin microspheres containing yttrium-90.

- QuiremSphere (Terumo) is a CE marked class III active medical device which is indicated for the treatment of advanced unresectable liver tumours. It comprises polyester microspheres containing holmium-166.

Intervention(s)	Selective internal radiation therapies (SIRT) Resectable HCC • TheraSphere Unresectable HCC • TheraSphere • SIR-Sphere • QuiremSphere
Population(s)	People with potentially resectable HCC (confined to the liver only) or unresectable HCC (with or without portal vein thrombosis/involvement)
Comparators	People with potentially resectable HCC: • Conventional Trans-arterial chemoembolization (TACE). • Transarterial chemoembolisation using drug-eluting beads (DEB-TACE)(doxorubicin and cisplatin do not currently have a marketing authorisation in the UK for HCC) People with unresectable HCC: • The interventions will be compared with each other. • Sorafenib (only for people with advanced HCC with Child-Pugh grade A liver impairment) • Lenvatinib (subject to NICE ongoing appraisal) • Regorafenib (subject to NICE ongoing appraisal) • Best supportive care.
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • time-to-progression • response rates • rates of liver transplant or surgical resection • adverse effects of treatment • health-related quality of life
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies

	being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial access arrangementsfor the comparator technologies will be taken into account.
Other considerations	Guidance will only be issued in accordance with the CE marking. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the CE marking. If evidence allows, subgroup analysis for people with unresectable HCC with portal vein thrombosis/involvement.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals**: Sorafenib for treating advanced hepatocellular carcinoma (2017). NICE technology appraisal guidance 474. Regorafenib for previously treated unresectable hepatocellular carcinoma (2018). NICE technology appraisals guidance 514. **Appraisals in development:** Regorafenib for previously treated unresectable hepatocellular carcinoma. NICE technology appraisals guidance [ID1519]. Rapid review of TA514. Publication date to be confirmed. Lenvatinib for untreated advanced unresectable hepatocellular carcinoma. NICE technology appraisal guidance [ID1089]. Publication expected December 2018. **Related Interventional Procedures**: Selective internal radiation therapy in primary hepatocellular carcinoma (2013) NICE interventional procedures guidance 460. **Related NICE Pathways:** Liver cancers (2016) NICE pathway **Other NICE advice:** TheraSphere for treating operable and inoperable hepatocellular carcinoma (2016) NICE advice MB062. SIR-Spheres for treating inoperable hepatocellular carcinoma (2016) NICE advice MB063.
Related National Policy	Interim Clinical Commissioning Policy Statement: Selective Internal Radiotherapy (SIRT) June 2013 B01/PS/a

	National Service Framework Cancer Department of Health (2016) NHS outcomes framework 2016 to 2017

References

1. National Cancer Registration and Analysis Service (2010) Trends in incidences in primary liver cancer subtypes. Accessed May 2017.

2. Patient (2015) Hepatocellular carcinoma. Accessed May 2017.

3. Office for National Statistics (2016) Cancer registration statistics. Accessed March 2018.

4. Verslype, C., Rosmorduc, O. and Rougier, P., 2012. Hepatocellular carcinoma: ESMO–ESDO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology*, *23* (suppl_7), pp.vii41-vii48.

Questions for consultation

Is the population defined appropriately?

Have all relevant comparators for SIRT been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for hepatocellular carcinoma?

How should best supportive care be defined?'

Are the outcomes listed appropriate?

Is the subgroup in 'other considerations appropriate? Are there any other subgroups of people in whom SIRT is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider SIRT will fit into the existing NICE pathway Liver cancers?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider SIRT to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of SIRT can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.