Review of TA474; Sorafenib for treating advanced hepatocellular carcinoma

TA474 was published in September 2017 and scheduled to be considered for review in 2020.

Decision

TA474 remains relevant and an update is not needed.

Rationale

No new evidence is available that would require an update of this guidance. The original guidance was an optimised recommendation, no new evidence suggests that the recommendation should be broadened to other subgroups.

Summary of new evidence and implications for review

Has there been any change to the price of the technology(ies) since the guidance was published?

1. No change to the list price.

Are there any existing or proposed changes to the marketing authorisation that would affect the existing guidance?

2. No.

Were any uncertainties identified in the original guidance? Is there any new evidence that might address this?

3. SHARP study was the key source of evidence, but the study was stopped early (cut off-date approximately 19 months). This potentially underestimated the survival benefit of sorafenib. Observational study GIDEON data was adjusted by the company to match baseline characteristics of SHARP population, to validate the extrapolations of overall survival. Overall survival data from new studies is relatively consistent with the findings from SHARP and GIDEON.

The committee noted that SHARP's inclusion criteria specified people with Child-Pugh grade A liver function, though a very small proportion of people with Child-Pugh grade B liver function were enrolled (approximately 3%). Based on clinical expert opinion and the evidence available, the committee concluded that people with Child-Pugh grade A liver function were the appropriate population for its recommendations for treating advanced hepatocellular carcinoma with sorafenib in England. New evidence supports this recommendation. There remains a need for further data collection in this subgroup, particularly long-term follow-up data. A UK audit of outcomes for hepatocellular carcinoma patients treated with sorafenib found that Child-Pugh grade A patients showed similar overall survival to previous RCTs, while Child-Pugh grade B patients seem to derive limited benefit from sorafenib treatment. Other retrospective studies support this conclusion, Child-Pugh grade B patients show similar outcomes in relation to safety and tolerability, but overall survival is worse compared with Child-Pugh grade A liver function. We identified systematic literature reviews and network meta-analyses which broadly support the conclusion in TA474 and are unlikely to change the recommendations.

Are there any related pieces of NICE guidance relevant to this appraisal? If so, what implications might this have for the existing guidance?

4. See Appendix C for a list of related NICE guidance.

Additional comments

5. The search strategy from the original ERG report was adapted for the Cochrane Library, Medline, Medline In-Process and Embase. References from January 2016 to December 2020 were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section above. See Appendix C for further details of ongoing and unpublished studies.

Equality issues

6. None were identified.

Decision paper sign off

Linda Landells – Associate Director, Technology Appraisals

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Contributors to this paper

Information Specialist: Toni Shaw

Technical Analyst: Farhaan Jamadar

Project Manager: Charlotte Downing

Appendix A – Information from existing guidance

Original remit

To appraise the clinical and cost effectiveness of sorafenib, within its licensed indication, for the first line systemic treatment of advanced hepatocellular carcinoma.

Current guidance

1.1 Sorafenib is recommended as an option for treating advanced hepatocellular carcinoma only for people with Child-Pugh grade A liver impairment, only if the company provides sorafenib within the agreed commercial access arrangement.

1.2 This recommendation is not intended to affect treatment with sorafenib that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Appendix B – Explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	Consequence	Selected – 'Yes/No'
A review of the guidance should be planned into the appraisal work programme. The review will be conducted through the STA process.	A review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred to a specific date or trial.	NICE will reconsider whether a review is necessary at the specified date.	No
The guidance should be Cross referred into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance remains relevant until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No

Options	Consequence	Selected – 'Yes/No'
The guidance should be updated in an on-going clinical guideline[1].	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No
The guidance remains relevant and an update is not needed.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider.	Yes
The guidance should be withdrawn	The guidance is no longer relevant and an update of the existing recommendations would not add value to the NHS. The guidance will be stood down and any funding direction associated with a positive recommendation will not be preserved.	No

[1] Information on the criteria for NICE allowing a technology appraisal in an ongoing clinical guideline can be found in section 6.20 of the guide to the processes of technology appraisal.

Appendix C – Other relevant information

Relevant Institute work

Published

Ramucirumab for treating unresectable hepatocellular carcinoma after sorafenib (terminated appraisal) (2019) NICE technology appraisal 609

Cabozantinib for previously treated advanced hepatocellular carcinoma (terminated appraisal) (2019) NICE technology appraisal 582

Regorafenib for previously treated advanced hepatocellular carcinoma (2019) NICE technology appraisal guidance 555

Lenvatinib for untreated advanced hepatocellular carcinoma (2018) NICE technology appraisal guidance 551

Atezolizumab with bevacizumab for untreated unresectable or advanced hepatocellular carcinoma (2020) NICE technology appraisal guidance 666

In progress

Durvalumab with tremelimumab for untreated unresectable hepatocellular carcinoma. NICE technology appraisal guidance. Publication expected August 2021.

Details of changes to the marketing authorisation for the technology

Marketing authorisation and price considered in original appraisal

Sorafenib has a marketing authorisation in the UK for treating hepatocellular carcinoma.

Price: £3576.56 for a pack of 200-mg tablets (112 tablets per pack)

Proposed marketing authorisation (for this appraisal) and current price

The marketing authorisation and price are the same.

Registered and unpublished trials

Trial name and registration number	Details
Mechanism of Sorafenib Resistance in Patients With Advanced Hepatocellular Carcinoma NCT02733809 Other Study ID Number: KSULDRCSSMH001 Open label, single group assignment. Estimated enrollment: 40 participants.	Primary objectives To evaluate the primary and secondary potential mechanisms by which HCC patients on Sorafenib treatment would be resistant to therapy and also identify the favorable genetic makeup of patients responding to treatment. Phase 4, currently recruiting. Start date: January 2014. Estimated primary completion date: December 2024.

References

Apostolidis L (2018) Survival of hepatocellular carcinoma patients treated with sorafenib beyond progression. Gastrointestinal Tumours. 5: 38-46.

Finn R (2017) Therapies for advanced stage hepatocellular carcinoma with macrovascular invasion or metastatic disease: a systematic review and meta-analysis. Hepatology Reviews. 67(1): 422-435.

Gordan J (2020) Systemic therapy for advanced hepatocellular carcinoma: ASCO guideline. Journal of Clinical Oncology. 38(36): 4317-4345.

Hansel (2020) Sorafenib for the treatment of hepatocellular carcinoma: a single-centre real-world study. Radiology and Oncology. 54(2): 233-236.

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Ye S (2016) Safety and efficacy of sorafenib therapy in patients with hepatocellular carcinoma: final outcome from the Chinese patient subset of the GIDEON study. Oncotarget. 7: 6639-6648.