NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Imatinib for the adjuvant treatment of gastrointestinal stromal tumours (review of TA196)

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name:

Dr Newton ACS Wong

Name of your organisation

Royal College of Pathologists and Association of Clinical Pathologists

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology

Yes, in that my role in diagnosis and mutation analysis guides treatment.

- other? (please specify)

I am a histopathologist who is involved in diagnosing GIST, and am also a molecular pathologist who performs mutation analysis of GISTs.

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What is the expected place of the technology in current practice?

How is the condition currently treated in the NHS? Is there significant geographical variation in current practice? Are there differences of opinion between professionals as to what current practice should be? What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

At the time of writing this, I am aware of only six NHS laboratories (four in England) that routinely perform GIST mutation analysis. The English laboratories receive no official PCT renumeration for such analysis. Mutation analysis tends to be commonly performed on GIST cases from hospitals which also host one of these six laboratories, though these laboratories do receive mutation analysis requests for cases from other hospitals. It is not clear what proportion of GIST patients have mutation analysis performed on their tumours to guide imatinib therapy. However, I suspect that this proportion is lower for patients treated in hospitals which do not host a laboratory offering GIST mutation analysis.

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient? Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology?

GIST patients may be sub-grouped according to the genotype (mutation type) of their GISTs. Certain GIST genotypes (e.g. KIT exon 11 mutant) predict for sensitivity to imatinib whereas others (e.g. 'wild type' genotype and PDGFRA D842V mutant) associate with resistance to imatinib. In keeping with this, the ACOSOG Z9001 trial has shown that patients with KIT exon 11 mutant GISTs show a statistically significant improvement in outcome on adjuvant imatinib therapy compared with placebo treatment, whereas D842V mutant GIST patients show no difference in outcome between the two treatments.

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)?

Professional input will be required from laboratories performing GIST mutation testing.

If the technology is already available, is there variation in how it is being used in the NHS? Is it always used within its licensed indications? If not, under what circumstances does this occur?

No comments

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Please tell us about any relevant **clinical guidelines** and comment on the appropriateness of the methodology used in developing the guideline and the specific evidence that underpinned the various recommendations.

Gastrointestinal stromal tumors: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. The ESMO / European Sarcoma Network Working Group. Annals of Oncology 2012; 23 (Supplement 7): vii49–vii55
"Mutational analysis is critical to making a clinical decision about adjuvant therapy. In fact, there is consensus that PDGFRA D842V-mutated GISTs should not be treated with any adjuvant therapy, given the lack of sensitivity of this genotype both in vitro and in vivo [IV, A]."

NCCN Task Force Report: Update on the Management of Patients with Gastrointestinal Stromal Tumors. Demetri GD, et al. J Natl Compr Canc Netw 2010;8:S-1-S-41
"Mutational analysis may be useful in selecting patients for postoperative therapy after complete resection of primary GIST."

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The advantages and disadvantages of the technology

NICE is particularly interested in your views on how the technology, when it becomes available, will compare with current alternatives used in the UK. Will the technology be easier or more difficult to use, and are there any practical implications (for example, concomitant treatments, other additional clinical requirements, patient acceptability/ease of use or the need for additional tests) surrounding its future use?

It is a widely held opinion that adjuvant imatinib therapy should be guided by the genotype of the patient's GIST (see guidelines above). Therefore, a potential consequence of adjuvant imatinib therapy becoming standard practice will be increased requests for mutation testing of GISTs.

If appropriate, please give your view on the nature of any rules, informal or formal, for starting and stopping the use of the technology; this might include any requirements for additional testing to identify appropriate subgroups for treatment or to assess response and the potential for discontinuation.

It is a widely held opinion that adjuvant imatinib therapy should be guided by the genotype of the patient's GIST (see guidelines above).

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology under clinical trial conditions reflects that observed in clinical practice. Do the circumstances in which the trials were conducted reflect current UK practice, and if not, how could the results be extrapolated to a UK setting? What, in your view, are the most important outcomes, and were they measured in the trials? If surrogate measures of outcome were used, do they adequately predict long-term outcomes?

No comments

What is the relative significance of any side effects or adverse reactions? In what ways do these affect the management of the condition and the patient's quality of life? Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?

If adjuvant imatinib therapy is given to a patient with an imatinib-resistant genotype (e.g. D842V mutant) GIST, current data suggest that the patient is unlikely to benefit from the therapy. The cost and potential patient morbidity of such 'inappropriate' therapy should be considered.

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Equality and Diversity

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 this appraisal:

- 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 lead to recommendations that 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

No comments

Any additional sources of evidence

Can you provide information about any relevant evidence that might not be found by a technology-focused systematic review of the available trial evidence? This could be information on recent and informal unpublished evidence, or information from registries and other nationally coordinated clinical audits. Any such information must include sufficient detail to allow a judgement to be made as to the quality of the evidence and to allow potential sources of bias to be determined.

No comments

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Implementation issues

The NHS is required by the Department of Health and the Welsh Assembly Government to provide funding and resources for medicines and treatments that have been recommended by NICE technology appraisal guidance. This provision has to be made within 3 months from the date of publication of the guidance.

If the technology is unlikely to be available in sufficient quantity, or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within 3 months, NICE may advise the Department of Health and the Welsh Assembly Government to vary this direction.

Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition? Would NHS staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?

There should be national funding for GIST mutation testing. This is particularly essential if NICE guidance recommends that mutation testing is performed for all GIST patients who receive adjuvant imatinib therapy.