NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Talimogene laherparepvec for treating metastatic melanoma [ID508]

Thank you for agreeing to give us a statement on your 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:

Name of your organisation
Southampton University Hospitals NHS Foundation trust and University of Southampton

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology?
- yes
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)?
- yes
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)?
- consultant Medical oncologist
- other? (please specify)

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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?

Metastatic malignant melanoma (MMM) is a condition, which remains fatal in the majority of patients. Recent clinical data have led to the approval of antic-CTLA4 (Ipilimumab) and anti-PD1 antibodies (Nivolumab, pembrolizumab) in the treatment of metastatic malignant melanoma. While these drugs have led to a significant improvement in outcome and the possibility of cure in some patients under 50% fall into this group. Chemothearpy plays no role in the management of metastatic malignant melanoma. Targeted therapies with BRAF inhibitors alone (Vemurafenib or dabrafinib) or in combination with MEK inhibitors improve survival in the ~40% of patients with cutaneous melanoma who have a mutation in the BRAF gene. They however do not offer cure but only palliative extension of live.
There is an urgent need to improve treatment options for patients with melanoma.

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?

Patients with MMM who have no visceral involvement, who have no brain involvement and who have normal LDH have per se a better outcome (M1a, M1b disease) compared to patients who have one or more of these high risk features. Nonetheless the overall outcome is that the majority of these patients die of their MMM.

This is the type of melanoma, in which the clinical Phase III trial data support the use of and benefit for patients by using **Talimogene laherparepvec.**
There is little risk from the technology to the patient, the injections are given into the injectable cancer lesions and therefore the risk is mainly from the need to physically deliver the **Talimogene laherparepvec** by injection.

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)?

It should be used in a specialist oncology unit and managed and prescribed by an oncologist experienced in the use of immunotherapies.

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?

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The Technology is not currently available to patients with MMM.

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.

No formal guidance exists with respect to this technology.

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?

The technology will be easy to use but is time consuming (need to repeatedly inject tumour lesions). There is the need to discard of any clinical waste as GMO waste.
There is no alternative treatment – the treatment is first in class. It is expected that data will emerge over time of the use of this technology with anti-PD1 and anti-CTLA4 antibodies and that this combination may offer future potent further benefit for patients.

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.

The injections are stopped if there is lack of clinical benefit. Globally speaking this would be progression in visceral organs or progression of injected sites of disease.

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?

I believe that the clinical trials evidence reflects clinical practice including that in the UK. It is however a small portion of all MMM that would be suitable for this technology.
Local disease control, distant disease control (by stimulating an immune response that can attack non-injected lesions) and prevention of systemic disease progression are most likely benefits and these were measures in the published data.

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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?

The injections are well tolerated. It is unlikely that any new adverse events will emerge in clinical practice.

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

I do not believe that there is any likelihood that this appraisal will affect equality of opportunity, cause unlawful discrimination or impair good relations to or between people with particular protected characteristics and others.

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.

None identified

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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)?

I think that given the relatively small number of patients for whom this technology would be beneficial, it is unlikekly that there will be significant resource implications.

However specific training will have to be provided to the clinical teams for the appropriate management of the release and injection of the technology and the disposal of any waste related to the technology