Appendix G - professional organisation statement template

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Trastuzumab emtansine for treating HER2-positive, locally advanced or metastatic breast cancer after treatment with trastuzumab and a taxane

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: [redacted] **registrar submitting comments on behalf of:**

Name of your organisation: NCRI Breast Cancer CSG/RCP/RCR/ACP/JCCO

Comments coordinated by: [redacted]

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology?
- 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)?
- 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 Her2+ Breast Cancer is currently treated with a combination of chemotherapy (usually a taxane ie 3 weekly docetaxol or weekly paclitaxel) and trastuzumab, the monoclonal antibody to Her2. Patients generally receive a 4-6 month course of chemotherapy and then continue on trastuzumab until disease progression. On progression further chemotherapy is indicated to try to gain further disease control. There is evidence that giving chemotherapy with ongoing Her2-targeted treatment is superior to second line chemotherapy alone[1] and many clinicians would prescribe ongoing trastuzumab with a second chemotherapy agent (eg capecitabine or vinorelbine) or access the combination of lapatinib and capecitabine via the Cancer Drug Fund. The vast majority of patients will remain fit enough for third line chemotherapy (and beyond) and here there will be more variations in practice due to the lack of evidence base to guide treatment decisions for late lines of treatment. Many patients will receive chemotherapy alone, some will access capecitabine and lapatinib via the Cancer Drug Fund, some will have local access to ongoing trastuzumab and 3rd line chemotherapy.

T-DM1 is a novel anti-body drug conjugate in which the chemotherapy drug DM1 is attached by a stable linker protein to trastuzumab, allowing the delivery of a chemotherapy drug, DM1 direct to the Her2+ cancer cells. The toxicity profile of DM1 precludes its use as a single agent. The recently published EMILIA trial compared the use of T-DM1 in patients who had previously been treated with a taxane and trastuzumab to treatment with lapatinib and capecitabine in patients. Patients who received T-DM1had a statistically significant and clinically relevant improvement in both progression free (9.6 versus 6.4 months) and overall survival (30.9 versus 25.1 months) compared to those who received the standard arm. T-DM1 is also well tolerated with a lower rate of grade 3 or 4 toxicities compared to lapatinib and capecitabine (41% versus 57%). Although quality of life differences were not reported in the publication TDM1 achieves good efficacy without the toxicities generally associated with chemotherapy (including risk of febrile neutropaenia, alopecia, nausea and vomiting as well as significant lethargy).

The alternatives to TDM-1 are then the comparator arm within EMILIA ie lapatanib and capecitabine, trastuzumab and chemotherapy or chemotherapy alone. Lapatinib and capecitabine, both oral agents, is easier for units to administer due to reduced need for chemotherapy chairs and nursing time. Some patients prefer oral chemotherapy regimens but lapatinib and capecitabine require patients to take a large number of large tablets twice a day with each drug having different restrictions around timings with food which some patients find difficult. T-DM1 is given as an iv treatment every 3 weeks and is easier to administer therefore than chemotherapy and trastuzumab prescribed separately, though the availability of subcutaneous

trastuzumab will reduce some of the convenience of T-DM1 over separate chemotherapy and trastuzumab administration.

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?

T-DM1 has proven efficacy in patients with Her2+ metastatic breast cancer whose cancer has progressed on a taxane and trastuzumab. Within this group no particular subgroups derived more or less benefit from the intervention. Patients with stable brain metastases were included in the EMILIA trial.

n 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)?

T-DM1 would be administered via specialist oncology clinics and would require administration via specialist nurses as for other systemic anti-cancer agents.

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?

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.

T-DM1 is currently going through the licensing process. It is not as yet available outside clinical trial use in the UK. T-DM1 is not currently on national guidelines. The 2013 update to the NCCN (National Comprehensive Cancer Network) guidelines included T-DM1 as the preferred treatment for the management patients with metastatic Her2+ breast cancer whose cancer has progressed on trastuzumab and a taxane. T-DM1, where available is likely to become the international standard of care in this setting and likely to be the standard arm of multinational clinical trials investigating new treatments for Her2+ breast cancer.

Reference

1. von Minckwitz et al., J Clin Onc 2009 (27) 12 1999-2006

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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?

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.

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?

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?

T-DM1 is easier to administer than intravenous trastuzumab and intravenous chemotherapy, comparable to subcutaneous trastuzumab and intravenous chemotherapy and somewhat more complex than lapatinib and capecitabine. All of these treatments require supervision by specialist chemotherapy units, regular blood tests, cardiac scans and radiological imaging to assess response. Some patients prefer oral chemotherapy treatments to intravenous treatments but the disadvantages of visits to the chemotherapy unit for intravenous treatments may not be outweighed by the disadvantages of a relatively complex oral treatment regimen.

Patients receiving T-DM1 would continue on the drug until disease progression. The patients would require regular imaging to monitor their response which is standard of care when patients receive and anti-cancer treatment.

The technology was compared against an internationally accepted standard of care for beyond 1st line treatment for metastatic Her2+ breast cancer ie lapatinib and capecitabine. As already stated in the UK patients receive various treatments in the beyond 1st line setting but lapatinib and capecitabine would be an accepted standard of care in the UK. It is important to also state that centres in the UK were involved in the EMILIA trial. T-DM1 demonstrated a 6 month overall survival advantage compared to treatment with lapatinib and capecitabine. This is impressive with few

drugs demonstrate clear improvements in survival in metastatic breast cancer. In fact the last drug to demonstrate a 6 month survival advantage compared to standard of care was trastuzumab itself.

The published data suggests T-DM1 is better tolerated than lapatinib and capecitabine which is an important consideration for patients with an incurable disease for whom quality of life is an important issue. There is a small risk of transaminitis, for which 3 patients stopped T-DM1 and thrombocytopaenia, for which 10 patients (2%) stopped T-DM1.

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.

Implementation issues

T-DM1 would be administered by cancer centres and units. We cannot see any significant issues with implementation.

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.

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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)?

Equality

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.