



incorporating Rarer Cancers Forum

**Rarer Cancers Foundation response to the Appraisal Consultation Document:
Trastuzumab for the treatment of HER2-positive metastatic gastric cancer**

27 July 2010

We are extremely disappointed that the recently issued Appraisal Consultation Document (ACD) on trastuzumab for the treatment of HER2-positive metastatic gastric cancer is negative. New treatments for metastatic gastric cancer are desperately needed and this treatment, which NICE is minded to reject, has been shown to be clinically effective and extend the lives of people with this subset of a rare form of cancer.

1. Clinical trials

- 1.1 It is difficult to establish robust clinical trials in England and Wales for rare and very rare conditions, due to small patient populations. This is true in the case of gastric cancer and is perpetuated for this treatment as trastuzumab is only effective in HER2-positive patients.

- 1.2 In point 4.3 of the ACD, the Appraisal Committee noted that the main pivotal trial (the ToGA trial) was an international trial and therefore the regimen and comparator were not standard clinical practice in England and Wales. Due to the small patient population (approximately 500 patients) it would be extremely difficult to recruit enough patients to a clinical trial exclusively in England and Wales in this instance, and end points in collection of trial data would take a long time to reach. Conducting an international trial is the only feasible way of making available a treatment for such a small patient population in a timely manner.

2. Innovation

- 2.1 In section 4.8 of the ACD, the Appraisal Committee considers the innovation provided by the product and the impact on health-related benefits. Given that trastuzumab has been used in breast cancer for a number of years the Committee does not consider this treatment to provide an innovation to the NHS. Despite this, targeting of therapy is innovative in the treatment of metastatic gastric cancer. We would therefore urge the Committee to weight their considerations to appropriately recognise the innovation that this product provides in gastric cancer.
- 2.2 NICE has clarified that the small patient population criterion exists to encourage and reward innovation. However, innovation can occur in different forms. The use of an existing molecule in a rare group of patients can be every bit as significant in terms of the relative health benefits it brings as the development of an entirely new chemical entity.

3. Criteria for appraising life extending, end of life treatments

- 3.1 When the addition to the NICE Technology Appraisal methodology, '*Appraising life-extending, end of life treatments*' was introduced in January 2009, it was seen as a great step forward in the appraisal of treatments for rarer cancers. The supplementary guidance gave patients renewed confidence that NICE recognises the specific problems experienced when appraising treatments at the end of life for small patient populations by allowing greater flexibility in appraising medicines, particularly for treatments for advanced cancers. In this appraisal however, we believe that the Committee has interpreted this guidance in a perverse way in relation to trastuzumab.
- 3.2 In point 4.20 of the ACD the Appraisal Committee has interpreted the 'patient population' to mean not only the appropriate patient population for HER2-positive metastatic gastric cancer, but also the other potential patients for which trastuzumab has licences (HER2-positive early and locally advanced breast cancer, and HER2-positive metastatic breast cancer). The total patient population who could benefit from trastuzumab across all of its licences is noted

to be 7,144 people. This in itself could be considered on the margins of what is considered a small and therefore acceptable patient population for acceptance under the scheme. Of this figure, it is estimated that there are only 500 patients with HER2-positive metastatic gastric cancer.

- 3.3 By counting all of the patients for which trastuzumab has licences this significantly increases the patient population and as such the Appraisal Committee has not allowed trastuzumab to be considered under the supplementary guidance. We consider this to be perverse and not in the spirit in which the guidance was developed.

- 3.4 In the guidance '*Appraising life-extending, end of life treatments*', point 3.2 of the guidance states, '*second and subsequent licences for the same product will be considered on their individual merits.*' We strongly believe that licences for other conditions should not be 'counted' in the size of the patient population because, as in this case, it is patients with rarer diseases that miss out on important new treatment options. We believe that in the case of trastuzumab for metastatic gastric cancer the individual licences should be considered separately.

- 3.5 Furthermore, trastuzumab was licenced for breast cancer approximately ten years ago and, to all extents and purposes, its clinical development for gastric cancer has been entirely separate. We therefore do not believe that the cumulative patient population for breast and gastric indications is relevant.

Conclusions

The Rarer Cancers Foundation urges the NICE Appraisal Committee to reconsider its interim decision, allowing HER2-positive patients with metastatic gastric cancer access to trastuzumab. By recommending this treatment NICE would give clinicians and patients a much needed alternative option in treating this disease.