Royal College
of Physicians
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Dear Dr Longson

Re: Lapatinib and trastuzumab in combination with an aromatase inhibitor for the first-line treatment of metastatic hormone receptor positive breast cancer which over-expresses HER2: Assessment Report

The Royal College of Physicians is grateful for the opportunity to respond to the above. We would like to make the following comments which have been coordinated by our clinical expert nominee Dr Rob Stein.

We have no major comments to make on the assessment report methodologies or assumptions. There a few comparatively minor points:

The estimate of the incidence of HR+ HER2+ metastatic breast cancer in section 1.1.5 seems wrong as it takes as its base the 5% of women with metastatic disease at diagnosis rather than the 25-30% of women who relapse following treatment for primary disease. The estimate of 350 women developing HR+ HER2+ MBC per annum seems to be rather low. Assuming the frequency of HER2+ HR+ breast cancer is about 8% (e.g. Lal, Am J Clin Pathol 2005 123:541) rather than the 15% based on historical population studies and that this frequency applies to the metastatic population in the era of adjuvant trastuzumab, then about 1000 women a year in the UK develop HR+ HER2+ MBC.

In section 1.1.17 and subsequently, the authors discuss the lack of effect of anti-HER2 treatment on overall survival in the TaNDEM and EGF30008 trials. Historically a small proportion of trials in advanced breast cancer have demonstrated an overall survival benefit. Breast cancer is a disease where multiple treatment options are available and in both of these trials, median OS in the experimental arms was approximately 4-fold longer than the PFS suggesting that patients were extensively treated post-progression. The use of trastuzumab following progression is documented in TaNDEM and it is inconceivable that HER2+ patients in both arms of EGF30008 were not also offered trastuzumab-based treatment after completing the trial. Neither trial was therefore likely to demonstrate an OS benefit for HER2-targeted therapy.

Yours sincerely

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