NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Bevacizumab in combination with gemcitabine and carboplatin for treating the first recurrence of platinum-sensitive advanced ovarian cancer

Response to consultee, commentator and public comments on the Appraisal Consultation Document (ACD)

Definitions:

Consultees – Organisations that accept an invitation to participate in the appraisal including the manufacturer or sponsor of the technology, national professional organisations, national patient organisations, the Department of Health and the Welsh Assembly Government and relevant NHS organisations in England. Consultee organisations are invited to submit evidence and/or statements and respond to consultations. They are also have right to appeal against the Final Appraisal Determination (FAD). Consultee organisations representing patients/carers and professionals can nominate clinical specialists and patient experts to present their personal views to the Appraisal Committee.

Clinical specialists and patient experts – Nominated specialists/experts have the opportunity to make comments on the ACD separately from the organisations that nominated them. They do not have the right of appeal against the FAD other than through the nominating organisation.

Commentators – Organisations that engage in the appraisal process but that are not asked to prepare an evidence submission or statement. They are invited to respond to consultations but, unlike consultees, they do not have the right of appeal against the FAD. These organisations include manufacturers of comparator technologies, NHS Quality Improvement Scotland, the relevant National Collaborating Centre (a group commissioned by the Institute to develop clinical guidelines), other related research groups where appropriate (for example, the Medical Research Council and National Cancer Research Institute); other groups (for example, the NHS Confederation, NHS Information Authority and NHS Purchasing and Supplies Agency, and the *British National Formulary*).

Public – Members of the public have the opportunity to comment on the ACD when it is posted on the Institute's web site 5 days after it is sent to consultees and commentators. These comments are usually presented to the appraisal committee in full, but may be summarised by the Institute secretariat – for example when many letters, emails and web site comments are received and recurring themes can be identified.

Comments received from consultees

Consultee	Comment	Response
Roche Products	We are disappointed that the Committee has decided not to recommend bevacizumab for the treatment of women with platinum sensitive recurrent ovarian cancer. We are pleased that the Committee has recognised the difficulty associated with calculating the overall survival benefit of adding bevacizumab to gemcitabine and carboplatin in these patients, due to increasing use of anti-angiogenesis therapies after progression in the key clinical study (OCEANS). We remind the Committee that the effect of this crossover in the placebo controlled arm of OCEANS is likely to confound estimates of any survival benefit and result in inflated estimates of cost-effectiveness. Furthermore, the absence of an external dataset for survival of these patients precludes attempts to explore what would have happened in the control arm in the absence of bevacizumab. However, we do not believe any such adjustment would materially affect the decision reached by the Committee.	Comment noted. The Committee noted that the overall survival results could have been affected by confounding effects because of the use of post-progression treatments. However, the Committee agreed that the high degree of censoring on PFS estimates and the potential biological action of bevacizumab could also be explanations for the difference in the results. See FAD section 4.8
Roche Products	**Factual inaccuracies:** - Section 3.5 (p8): The hazard ratio for the third interim OS analysis is incorrectly stated as “relative to bevacizumab” – this should be changed to “relative to placebo” - Section 3.8 (p9): The wording of the first paragraph suggests that our search identified 4 RCTs which directly compare bevacizumab + carboplatin + gemcitabine with the other comparators listed in the scope – this is incorrect, no other RCTs were identified.	The relevant section has been amended in the FAD (section 3.5) accordingly The relevant paragraph has been amended in the FAD (section 3.8) accordingly

Consultee	Comment	Response
Target Ovarian Cancer	Target Ovarian Cancer is very disappointed that NICE were unable to approve bevacizumab in combination with gemcitabine and carboplatin for treating women with recurrent advanced ovarian cancer. Recurrent ovarian cancer poses a particular challenge for those living with the disease. Women live under the shadow of subsequent recurrence and further treatment. Bevacizumab represents a step wise change in the treatment of ovarian cancer offering women the chance to extend their progression free survival (PFS) period, and therefore the length of time during which they are not receiving debilitating chemotherapy treatment. The PFS period is extremely valuable in helping women adjust emotionally to their recurrent cancer diagnosis and also recover physically from the impact of treatment. Women living with ovarian cancer are justifiably upset and disappointed by the lack of availability of bevacizumab; and feel that the quality of their life is perceived as holding little value. This sense of frustration is only set to increase with the uncertainty surrounding the future of the Cancer Drugs Fund, which up until now has been valuable in helping clinician's access bevacizumab on behalf of their patients. The use of bevacizumab represents the most significant advance in treatment for ovarian cancer in twenty years. If routine NHS access to this drug cannot be given, what hope is there for any future new treatments of which there are almost none on the horizon?	Comment noted. The Committee noted the importance of increasing progression-free survival to patients. See FAD sections 4.3 and 4.11.

Comments received from clinical specialists and patient experts

Nominating organisation	Comment	Response

Nominating organisation	Comment	Response

Comments received from commentators

Commentator	Comment	Response

Comments received from members of the public

Role*	Section	Comment	Response

Summary of comments received from members of the public

Theme	Response

* When comments are submitted via the Institute's web site, individuals are asked to identify their role by choosing from a list as follows: 'patent', 'carer', 'general public', 'health professional (within NHS)', 'health professional (private sector)', 'healthcare industry (pharmaceutical)', 'healthcare industry'(other)', 'local government professional' or, if none of these categories apply, 'other' with a separate box to enter a description.