

## Comments on NICE ACD for 5-azacitidine for the treatment of MDS, CMML and AML

- i) Do you consider that all of the relevant evidence has been taken into account?

Yes. I found the ERG analysis of the Celgene submission to be inciteful and informative. The NICE process has been robust but can only be as good as the data presented. It is unfortunate that a detailed academic health economic analysis was presumably beyond the resources and scope of the ERG as the costs of BSC could have been more comprehensive.

- ii) Do you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence, and that the preliminary views on the resource impact and implications for the NHS are appropriate?

Having re-examined the healthcare resource use documentation from the Celgene submission I conclude that this could have been much more accurate if an academic health economist and expert Haematologists had been commissioned. For example the cost of blood products is not simply as quoted in table 7.12; this is merely the collection, processing and delivery cost of a unit of blood. Excluded are a number of significant costs such as hospital blood bank costs (cross matching particularly with a relatively high frequency of alloantibodies and their associated additional costs), premedication for patients with transfusion reactions (common in MDS), management of the complications of transfusion including transfusion reactions, fluid overload and iron overload. These costs are all lower in the azacitidine arm as 40% patients become red cell transfusion independent. In addition some of the HRG costs in Table 7.9 are presumably extrapolated and are wildly different from the real costs, not that this would affect the ICER significantly.

Given the data presented to the ERG and having heard and understood the critique of the Markov modelling in Celgene's submission, the preliminary views on resource impact are as expected.

- iii) Do you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS?

Given the data presented to the ERG and having heard and understood the critique of the Markov modelling in Celgene's submission, the provisional recommendations of the Appraisal Committee are the only conclusion that could be reached. I now feel that there are more flaws in the Celgene health economic data than I had previously realised which could lead to a higher cost for Best Supportive Care, although the impact that this would have on the ICER is unknown.

I believe that a negative recommendation by NICE will have serious ramifications for MDS patients, and for physicians and researchers with an interest in MDS which will extend beyond the health economic sphere as follows:

- This will perpetuate the nihilism amongst the UK Haematology community towards the management of patients with MDS, whose median age is 75 years. This will certainly be contributing to the poor outcome for such cancer patients compared with other developed countries recently highlighted in the media and which the government has pledged to redress.
- The UK will be perhaps the only developed country in which MDS, CMML and AML patients will be deprived of access to 5-azacitidine which NICE accepts as a treatment capable of prolonging survival compared with alternative therapies. 5-azacitidine is the worldwide standard of care within its' licensed indication. UK MDS patients have access to no licensed drugs, compared with other European countries who have access to two drugs (azacitidine and deferasirox) and the US which has access to 4 drugs (azacitidine, decitabine, deferasirox and lenalidomide).
- This decision will take the wind out of the sails for the development of internationally competitive clinical trials in high-risk MDS by the NCRI Haematological Oncology MDS subgroup. A randomised phase 2/3 trials programme is under development to explore combinations of new agents with 5-azacitidine as the standard of care. This was to be highly internationally competitive and may now have to be abandoned or postponed to a future timepoint when it will no longer be competitive. This is clearly not an issue directly concerning NICE but the wider implications of NICE decisions must be acknowledged.

iv) Are there any equality related issues that need special consideration that are not covered in the ACD?

No.

21<sup>st</sup> August 2009