

Comments on the Appraisal Consultation Document (ACD) produced for the NICE single technology appraisal of azacitidine for the treatment of myelodysplastic syndromes, chronic myelomonocytic leukaemia and acute myeloid leukaemia

Thank you for the opportunity to comment on the ACD on behalf of the Royal College of Pathologists (RCPATH) and The British Committee for Standards in Haematology (BCSH)

In keeping with my written and verbal evidence to the NICE Committee meeting of 1st July 2009 robustly supporting the introduction of azacitidine as the treatment of choice for patients suffering with the appropriate categories of MDS, AML and CMML, I am very disappointed at the preliminary recommendation to reject on the basis of cost effectiveness. I am certain that haematology colleagues throughout the UK will be similarly dismayed. As stated in my original written evidence, I would emphasise once again the nihilism that currently exists for the treatment of these elderly people. The denial of the first and only widely applicable effective treatment for this group of patients would re-enforce this nihilism. It would also strongly re-enforce the recently publicised very negative perception that elderly patients with malignant diseases are poorly served in the UK. I believe denying access to azacitidine would indirectly discriminate against elderly people and generate issues of equality with respect to access to effective therapy. I address this important issue in heading 4 along with my comments for each of the other headings below.

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

I agree that the main focus of evidence for the licensed indication is The AZA 001 trial. I also believe that important data supporting a survival benefit and quality of life benefit comes from the randomised trial of Lewis R Silverman et al. I accept that this included patients with lower risk MDS but it highlighted the benefit of azacitidine for MDS across high risk and low risk FAB groups and was the initiator of the AZA 001 trial. I understand that there are extended follow up data available from the AZA 001 study which might inform the cost effectiveness model and these data should be presented by the company.

2) 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?

I am delighted that the ACD acknowledges and accepts the evidence of significant clinical effectiveness for azacitidine use within the licensed indication. It should be emphasized that for the vast majority of elderly patients with disease falling within the licensed indication there is currently no effective therapy and these patients receive supportive care only. That azacitidine has shown a survival benefit of some 10 months compared to conventional care is, to my mind, a major clinical development in the care of these patients.

From the point of view of the cost-effectiveness model I accept that the evidence of the ERG presented on 1st July suggests that there is a lack of face validity with the submitted model, especially in terms of the size of the actual benefit gained and the realistic nature of the predicted survival tail. It is important that these are addressed by the company. There clearly are some deficiencies in the AZA 001 trial in terms of assessing time to AML and the lack of quality of life

data. However, there are plenty of examples within clinical practice to date of remissions and survival being measured in several years with azacitidine. The revised model produced by the ERG generated a high incremental cost but it is clear that aspects of this type of modeling are controversial. I believe that the clinical effectiveness, clearly proven by a randomized and peer reviewed trial, published in a high quality journal, should in this instance over- ride the high cost. This is because firstly there are currently no effective alternative treatments, because secondly the size of the clinical benefit achieved is very significant and because thirdly given the age of the patients and the nature of the underlying disease this is clearly an end –of- life modifying therapy.

3) 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?

I consider that the ACD acknowledgement and acceptance of the clinical effectiveness is a sound interpretation of the clinical data. There are some issues with the various cost effectiveness models which need to be addressed.

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

I think there are issues here which are currently very important. The median age of patients with MDS is well in excess of 70 years of age and only some 6% of MDS patients are diagnosed under the age of 50 years. Whilst I accept that the ACD does not directly discriminate between old and younger patients with MDS in terms of access to azacitidine it does generate issues of equality in terms of access to effective therapy. Younger patients (a minority of cases) can be effectively treated with intensive chemotherapy followed by an allogeneic stem cell transplant. Denying this young minority of patients access to azacitidine does not necessarily, therefore, deny them effective therapy. However, for the elderly majority, intensive chemotherapy and allogeneic stem cell transplantation is not an option because of toxicity. Consequently, to deny them azacitidine will be denying them the single most effective and currently applicable therapy and to my mind, therefore, indirectly discriminates against elderly people.

A recent study by the North West Cancer Intelligence Service (NWCIS) presented at the National Cancer Intelligence Network (NCIN) claimed there had been little progress in cancer death rates in the over 75s over the last decade whereas significant benefit had been seen in the under 75s. The gap in death rates in this older age group between the UK and other countries in Europe and USA is widening. Professor Mike Richards, National Cancer Director, in response to this study is quoted in the press as saying 'This is an important study and urgent action needs to be taken on the findings. We need to ensure that cancer patients of all ages are diagnosed as early as possible and receive appropriate treatment. The findings have already been shared with the National Cancer Equality Initiative and we will be working with the NHS and other interested parties to tackle any age inequalities.' High risk MDS is a malignant disease predominantly of elderly people. Denying these elderly patients the only effective therapy currently available, would, to my mind, be a direct contradiction of the above statement by Professor Richards and would be a blatant example of sub- optimal care of elderly patients suffering with cancer in the UK.

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(Representing the Royal College of Pathologists and the British Committee for Standards in Haematology).

