Response by the MDS UK Patient Support Group to the STA appraisal consultation document on Azacitidine for the treatment of myelodyplastic syndrome, chronic myelomonocytic leukaemia, and acute myeloid leukaemia

- ***Has all of the relevant evidence been taken into account?***
  Yes, to the best of our knowledge, all the evidence that currently exists has been considered. Azacitidine is the only effective first-line treatment for MDS, but the diversity of the group of conditions embraced as MDS, and the nature of the patient population available with their co-morbidities, make the accumulation of valid clinical trial data difficult and time-consuming.

  We ask NICE to stand by its recognition of the clinical effectiveness of azacitidine in terms of the significant increase in survival time that it provides for patients with high-risk MDS, and the greatly enhanced quality of that survival time. The evidence also indicates a lower risk of progression to AML and higher rates of complete remission, partial remission, haematological improvement and independence of blood transfusion.

  We request that NICE give a provisional recommendation for use of azacitidine in the NHS for high-risk MDS, subject to the presentation of more evidence on the accumulated experience of use in a larger population of MDS patients over a longer period of time. The data submitted through the physician survey was by definition an estimate of use, since azacitidine has not been easily available throughout the UK. Having the drug available for a period of time would vastly increase the chances of producing more reliable, complete and valid information about its use in MDS.

- ***Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?***
  We believe that the clinical summaries are a reasonable interpretation of the trial evidence.

  We are concerned that the evidence on cost effectiveness is based on a number of assumptions. The most important one, in the absence of additional trial data, is that patients will continue on a full dose of azacitidine for the duration of their treatment, however long that might be. A number of patients will go on to a maintenance dosage, either due to an effective response or because of impaired tolerance, which could reduce the cost by up to 65%, once control of the aberrant cell production is established. Even allowing for issues around vial size and wastage, this could still result in a considerable reduction in the cost of treatment of the order of at least 50% compared with continuing full dose treatment.

  Experience with azacitidine is limited because of the relatively small number of patients available for and suitable for treatment, the logistics of undertaking large

scale trials, and the additional difficulty of defining the criteria for stratification to maintenance treatment as opposed to full dose treatment. Until such trial data becomes available, we recommend that provisional approval be given for azacitidine to be available for use in treatment of patients with MDS with a recommendation that a controlled trial be established to evaluate the benefits and effectiveness of maintenance treatment in suitable patients. A similar situation was addressed in the Netherlands recently, where approval for azacitidine was given for a limited number of years, allowing the accumulation of necessary data, whilst not depriving patients of this life-line of treatment in the process.

Currently there is important on-going research about the efficacy of azacitidine to establish pre-treatment markers of potential response, which would help identify sub-groups of patients who would have a higher rate of response, thereby improving both clinical efficacy and cost-effectiveness. Preliminary research from King's College London seems to indicate a higher response rate to azacitidine in some sub-groups of patients. This data is currently being prepared for publication.

Data on efficacy in the subgroup of patients with the del-7 chromosomal abnormality is also not yet clear. Until such data is published, and it is clearly established that it presents advantages in this patient group, we believe it is wholly unethical to deprive all patients of the benefit of this drug, condemning them to continued poor quality of life, reduced life expectancy or premature death.

In addition partial responders draw some benefit from the treatment as a haematological improvement, as opposed to an increase in overall survival, can make a significant difference to the quality of life of these patients.

- ***Are the provisional recommendations sound and a suitable basis for guidance to the NHS?***
  The negative recommendations do not appear to be sound on the basis of the very clear evidence for the clinical efficacy of azacitidine. The recommendations appear to be driven entirely on the basis of the apparent lack of cost effectiveness based on the current health economic modelling. If the costs could be controlled, then we believe that the STA would result in a positive recommendation for azacitidine on grounds that it is manifestly more clinically effective than many of the other drugs used in the treatment of cancer which have been approved by NICE in recent years. We believe that the only barrier which exists to its availability to MDS patients is its present cost. If that obstruction can be removed, then azacitidine should become a recommended treatment for use in the NHS in England - a development that we would support most strongly.

- ***Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of gender, race, disability, age, sexual orientation, religion or belief?***
  We are not aware of any.
  However, NICE stated that no data was presented on efficacy in sub-groups of patients, such as those patients unable to receive transfusions for religious reasons. We believe it would be inappropriate to positively discriminate such patients. This drug should be made available to all those who need it.

- ***Are there any equality -related issues that need special consideration and are not covered in the appraisal consultation document?***
  Not that we are aware.

Additional comments

- The majority [around 84%] of the population of the United Kingdom live in England, to which NICE's recommendations apply. However the remaining 16% of the British population living in Scotland, Wales and Northern Ireland also have needs for medication for the treatment of MDS. Though NICE has no power there, the corresponding evaluatory bodies in those countries look to NICE for guidance, especially in specialist areas such as this. We are extremely concerned that a negative recommendation for azacitidine in England will be replicated throughout the rest of the United Kingdom, thereby denying even more patients of access to this highly effective treatment on grounds of cost alone. This is of particular importance, given the fact that the Interim Cancer Drug Fund is unavailable in those areas, and neither will the substantive cancer drug funding from next April be available for those British citizens living in Scotland, Wales and Northern Ireland.

- If cost is the sole barrier to a positive recommendation and thus availability of azacitidine, then we would encourage NICE to find a means of having a dialogue with the manufacturer in which the nature of cost barriers might be explored. We realise that this is not part of the remit of NICE but believe that this is an issue for the Department of Health, especially in the light of the recently announced recommendations for reforms in the NHS and the role of NICE in the future.

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