



### **Response to the Appraisal Consultation Document:**

Azacitidine for the treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukaemia (CMML) and acute myeloid leukaemia (AML)

24<sup>th</sup> August 2009

This is a joint submission by:

MDS UK Patient Support Group  
Rarer Cancers Forum  
Leukaemia CARE  
Leukaemia Research Fund  
Leukaemia Society  
Macmillan Cancer Support

We address the four general questions on which comments are requested.

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

- We believe that not enough evidence has been taken into account regarding the decline in health over time for patients receiving only best supportive care (BSC), in comparison with patients receiving active treatment with azacitidine (Vidaza).

Best Supportive Care (BSC) compares very unfavourably with this new technology. BSC does not represent a treatment as such for high-risk MDS. BSC merely deals with chronic symptoms of the condition. Transfusions have to be administered in increased frequency and rapidly lead to a much worse quality of life, and decline in health. Each transfusion at the hospital is increasingly taxing for these patients. BSC does not stop the progression of the condition.

Azacitidine is the only drug that will enable these patients to live longer with an improved quality of life.

*4.7....." It (the Committee) - understood that, given the patient distribution in the UK, best supportive care was the most appropriate comparator. The Committee considered that chemotherapy was not an appropriate comparator since there was limited evidence of statistically significant clinical effectiveness."*

- Quality Of Life issues  
We strongly feel that health related Quality of Life issues – in particular fatigue, was understated: (as acknowledged by the Committee in sections 4.5 & 4.9.)

The patient expert statements as well as many other patient testimonies we have come across are all consistent with the fact that quality of life is immensely improved for patients receiving azacitidine. Many patients who respond to azacitidine become transfusion **independent** and their haemoglobin levels remain at a high and healthy level.

Quality of life for patients with this incurable sub-type of the condition is the most important factor for them. A treatment that relieves daily fatigue and breathlessness is of immeasurable benefit to patients.

Patients do not need any or as many hospital visits as with BSC, hence reducing the cost burden to the NHS.

Patients are able to regain a much higher degree of independence and are able to participate in social activities again – improving the patients' experience (as aimed for in the Cancer Reform Strategy).

Patient testimony gathered from more than 100 Patient and Family Forums worldwide through both written questionnaires administered to MDS patients and through verbal, taped and transcribed quality of life conversations at these Forums provide strong evidence that fatigue is the major reason that MDS patients experience an extremely diminished quality of life. Blood transfusions rank second only to fatigue in their effect on patients' quality of life. The time involved in travel to the transfusion centre, to receive the transfusions, and the necessity to have an accompanying caregiver imposes a hardship on patients' lives and those of their caregivers. With repeated transfusions the burden becomes higher as the disease progresses as does the risk for end organ complications arising from iron overload. Patients treated with azacitidine report that their quality of life both from the standpoint of relief from debilitating fatigue and freedom from transfusions has a huge impact on their quality of life and their ability to function in normal activities of daily living. The MDS Foundation will be happy to share this information with NICE.

4.5..... *"The Committee noted that no quality of life data were collected in the AZA-001 trial, although such data collected in CALGB 9221 suggested improvements in overall health with azacitidine."*

4.9 *"The Committee considered the ERG's concerns that the manufacturer's estimate of patients' quality of life included in the model lacked face validity. The patient experts and clinical specialists stated that treatment with azacitidine reduces symptoms (such as fatigue) and the need for blood transfusions, both of which are probably associated with a degree of disutility. The Committee noted that the manufacturer's model produced **small gains** in health-related quality of life as a result of treatment with azacitidine, and that **greater independence** from blood transfusions was not included in the utility estimate. It noted that the manufacturer had estimated utility by mapping to the EQ-5D, and that the EQ-5D does not include fatigue as a dimension, although some effects of this symptom on ability to undertake normal activities would be captured. The Committee considered that reduced fatigue resulting from treatment with azacitidine may not have been completely captured in the modelled utility values.....The Committee concluded that the manufacturer's model may have underestimated the gains in health-related quality of life resulting from treatment with azacitidine, but noted that the degree of underestimation was not known".*

- Important outcomes:

Overall survival may not be the most important outcome for all of the patients – good quality of life in the last 1-2 years of survival is equally important and the ability to participate actively in life.

4.8.... *"The ERG stated that the most important influence on the model's outputs was overall survival,.."*

**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?**

- Yes. As stated in section 4.6, the Committee concluded on the basis of evidence from clinical specialists and patient experts that azacitidine is a clinically effective treatment for MDS, CMML and AML, and that in section 4.2 from clinical specialists that current treatment for 90 % of this group of patients is best supportive care (BSC).

However we disagree with the committee's conclusion on cost-effectiveness. The Committee should take into consideration that the incremental cost effectiveness ratio per quality adjusted life year gained (ICER per QALY) is of necessity going to be high, because the base comparator (BSC) is going to be low.

This is an unfortunate test of cost-effectiveness, when the condition (MDS) being treated has not seen any real advance in medical treatment for some time, and any new treatment being introduced would suffer from the same fate.

- BSC and risk of increased infections:  
Under BSC, patients may suffer from a lower immunity and may be prone to increased infections, requiring a higher number of hospital stays, antibiotics – hence increasing overall costs for the care of this group of patients.
- Shortage of blood supply AND related costs:  
We realise that this point may not be considered within the remit of NICE, but there is an issue on availability of blood for transfusion and the impact on the NHS. Currently, the National Blood Service is emphasising the additional pressures being created by people who have, or may have, flu being excluded from donation. It seems that one of the major specifically attributable costs of best supportive care is transfusion.

In the first month of azacitidine treatment, patients may require more frequent transfusions (study by Kornblith et al), but transfusion independence reached by many patients subsequently, provides savings on a financial as well as a social level (reducing the pressure for additional blood donors; scarce blood supplies can be directed elsewhere in the NHS).

The sub-group of patients requiring frequent blood transfusions (i.e. weekly or bi-monthly) or also requiring platelets would represent an additional cost-saving to the NHS services.

Similarly, when patients develop an immunity to transfusions, the cost of cross-matching on-going transfusions further increases the cost to the NHS.

*4.14 ... "The Committee considered whether there were any subgroups of patients for whom azacitidine would be considered a cost-effective use of NHS resources, and whether NICE's duties under the equalities legislation required it to alter or to add to its recommendations in any way. The Committee noted that azacitidine may be of specific benefit to those who are unable to receive blood transfusions for clinical or religious reasons. The Committee noted that patients treated with azacitidine required fewer blood transfusions than those treated with best supportive care."*

**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?**

- No – the recommendation for further research (Point 6.1 – Study on health related Q-O-L values) will mean increased delay translating into continued severely impaired quality of life for many patients and/or earlier than necessary death for many. The

MDS Foundation (an international patient advocacy organization) will be happy to share quality of life data gathered worldwide with NICE. In addition, the Foundation has developed a quality of life tool that is currently undergoing validation. The Foundation will be happy to provide NICE with all data gathered from MDS patients on an ongoing basis for future support of azacitidine use.

- Equally, (Point 8.1) the proposed review by the Guidance Executive in November 2012, will also definitely mean depriving hundreds of patients of a better quality of life, and will mean earlier than necessary death for many. Furthermore it will provide a further burden on blood supplies, especially at critical times of diminished number of blood donors.

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

- Equality on a European level – the UK should strive to be leaders in innovative medicine. The major European countries have already adopted the use of azacitidine. By not adopting innovative treatments early on, the UK cannot establish itself as a world leader in promoting innovation in MDS.
- A negative decision by NICE will make it less likely that patients going through the Individual Funding Request process with their Primary Care Trusts (PCTs) will have azacitidine funded. Moreover, the chances of a successful outcome for patients will vary depending on the individual PCT, thereby denying patients equal access to this technology. The only other alternative is to apply to use private insurance, an option not open to most patients.
- The NHS Confederation states: “Every NHS patient deserves to be treated with fairness, dignity and respect and that should be no different for elderly people using the service”. The vast majority of these patients are on average 70 years old – hence it is important they should receive the same level of effective care as a younger working population.