NICE Appraisal ID764 - Idelalisib in combination with Rituximab

Comments on Appraisal Consultation Document

Response from the CLL Support Association

We are grateful for being invited to the Appraisal Committee Meeting on 21 May and for this opportunity to provide our feedback and to request further responses regarding the Appraisal Consultation Document.

At the Appraisal Committee Meeting we were pleased to hear that it was conclude that more treatment options for the clinical management of CLL were needed (ACD para 4.1) and that Idelalisib in combination with Rituximab was seen as effective.

The CLLSA was therefore very disappointed that the committee has decided not to recommend Idelalisib in combination with Rituximab for:

- untreated chronic lymphocytic leukaemia in adults with a 17p deletion or TP53 mutation or
- chronic lymphocytic leukaemia in adults when the disease has been treated but has relapsed

And that the Committee is minded not to recommend Idelalisib in combination with Rituximab

- in adults whose disease is refractory and retreatment with previous regimens is not considered appropriate

CLL patients have waited many years for the availability of more effective therapies in high risk and relapsed disease and will find it difficult to understand why they should be denied access to Idelalisib in combination with Rituximab which has gained approval in Europe, the US and Scotland. Many patients with high risk CLL have no approved options when they require treatment and consequently have a short OS, similarly for relapsed patients who have run out of treatment options. The recent high take-up of novel therapies made available by the pharmaceutical companies and through the CDF highlights the scale of the unmet need.

We would like to respond to specific paragraphs:

1 - p3 para 1.1 This Committee decision is the opposite of the decision taken by the Scottish Medicines Consortium (SMC) on 9 March 2015 and based on the same evidence and we need to understand the key reasons for this.

"Idelalisib is approved for use within NHS Scotland in combination with Rituximab for the treatment of adult patients with relapsed CLL who are unsuitable for chemotherapy and treatment naïve patients with 17p deletion or TP53 mutation who are unsuitable for chemo-immunotherapy."

Dr. Angus Broom, Consultant Haematologist, Western General Hospital, NHS Lothian said: *"The SMC's decision on Idelalisib marks a significant advance for patients with CLL in Scotland, as it is a life-extending treatment with the potential to help alleviate both the emotional and physical impact*

for patients and families living with CLL. Idelalisib provides physicians with a new treatment option for previously untreated patients with markers of aggressive CLL disease or relapsed CLL."

We would like to further highlight that a Scientific Advisory Group convened during the SMC review of this medicine by the European Medicines Agency (EMA) noted that the size of the treatment effect is unprecedented in this pre-treated and frail patient group and the activity in subgroups with 17p deletion or TP53 mutation is important in view of their poor responsiveness to conventional therapy.

2 - p3. para 1.2 The committee is not minded to approve this combination for refractory patients. This is the hardest decision to understand as the drug combination is clearly uniquely effective for this group and there is no current alternative for these patients. Patients who do not respond are unconcerned by apparently arbitrary definitions of refractory and relapsed, their sole concern is to receive an effective alternative.

3 - p11. para 3.20 We reject the assertion by the ERG that the baseline characteristics of patients in the trial represented a much higher risk patient cohort than what is normally seen in UK clinical practice. Patients experience shorter and shorter remission times with each chemotherapy treatment so inevitably patients require many treatments within a short timeframe. In addition the TP53 deleted/mutated clone will increase over time and with each aggressive treatment.

4 - p11. para 3.21 The ERG noted that the results should be interpreted with caution because the trial was stopped early leading to possible overestimation of treatment effect. What is the evidence for this assertion in trials using novel therapies?

5 - p25. para 4.5. The committee has noted that the trial was conducted in patients who were generally older with more co-morbidities (average age 71) and who had on average at least three prior therapies. We reject this premise because according to SEER data, between 2003 and 2007, the median age at diagnosis for CLL was 72 years. (Source: Neoplastic Diseases of the Blood, Borthakur & O'Brien.). As stated earlier, once patients relapse, subsequent treatments occur more frequently, so an average of 3 prior therapies is not untypical.

6 - p26. para 4.6. The committee noted the lack of comparative evidence for the 17p/TP53 population but acknowledged the drugs' effectiveness in this population. As there is no comparative therapy for this group of patients there is no ethical trial that can be devised to provide further evidence to the committee - we hope that the Committee can reconsider its decision in this regard.

In conclusion, we appeal to the Committee to consider this appraisal holistically, rather than solely through financial modelling which will be sensitive to pricing - a decision between NICE and Gilead, and independent of patient need. There are many hundreds of patients now and in the future whose lives can be immensely improved by the availability of less toxic and more effective treatments. The CLLSA is very concerned about the potential lack of equity in patient access to these drugs. Patients are anxiously awaiting early approval of this novel combination and we trust that the lifeline that it offers them will not be denied.

[redacted], [redacted]

[redacted], On behalf of the CLLSA

6 July 2015