# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Single Technology Appraisal (STA)

## Idelalisib for previously treated chronic lymphocytic leukaemia

Thank you for agreeing to give us a statement on your view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

**About you**

**Your name:v Francesco Forconi**

**Name of your organisation**
Southampton University Hospital Trust

**Are you (tick all that apply):**

- a specialist in the treatment of people with the condition for which NICE is considering this technology? yes
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)? yes
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)? yes
- other? (please specify)

I have had a consultancy for Gilead on May 8th 2015 at Gilead Sciences Ltd Offices, 280 High Holborn, London, WC1V 7EE, where I asked as clinical expert for the Mock AC meeting for idelalisib in the treatment of chronic lymphocytic leukaemia (CLL) (Mock NICE interview)

## NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Single Technology Appraisal (STA)

**What is the expected place of the technology in current practice?**

CLL is a currently incurable disease and the great majority of treatments aim to control disease and/or delay progression. In patients fit for immunochemotherapy the current standard is FCR immunochemotherapy, while for patients with comorbidities and/or elderly individuals treatments can range from chemotherapy+/-anti-CD20 monoclonal antibody therapy (eg Bendamustine or Chlorambucil +/- rituximab or ofatumomab in the 'slow go' patients), to antibody alone (eg rituximab or ofatumomab) or steroids or best standard of care (in the 'no go' patients). However treatment algorythms are now dramatically changing with the introduction of BCR-associated kinase inhibitors (eg Ibrutinib and idelalisib) or bcl2 inhibitors (eg ABT-199) or type II anti-CD20 monoclonal antibodies (eg obinutuzumab/GA101), which are offered into trials or through CDF in the UK.

While any of these treatments are expected to be largely beneficial (at different degrees) when therapy is indicated in the majority of patients, one unmet need include patients with CLL harbouring TP53 disfunction by 17p deletion and/or TP53 mutation. In this patients current treatments are completely unsatisfactory, while BCR-associated kinase inhibitors seem to be extremely effective and offer the chance to cover clinically unmet needs.

Idelalisib is PI3K delta inhibitor which proves extremely effective either alone and in combination with Rituximab. In a phase 3 trial in R/R CLL patients unfit for immunochemotherapy who required new treatment were randomised to receive rituximab single agent or idelalisib + rituximab (Furman, NEJM, 2014). Over 50% of the population had 17p deletion documented. Although rituximab single agent is known to be suboptimal treatment, idelalisib+rituximab showed superior efficacy and reduced toxicity than rituximab single agent. Median progression free survival was 19.6 months in the ibrutinib+rituximab arm and 6.5 months in the rituximab arm. Overall survival was not reached in the IR arm while it was 20 months in the R arm.

Another study in 17 patients (Hillmen, 2007, study 101-08) 64 patients, who had not received prior treatments, were given IR for 48 weeks. Nine of 64 had TP53 disfunction. These 9 patients had 100% overall response rate.

This technology offers to use IR combination in the setting of i) slow-go or no-go patients who had previously received treatments and where immunochemotherapy is expected to be unlikely beneficial and ii) in the setting of previously untreated patients with CLL carrying deletion of 17p.

The technology is not already available and idelalisib in combination with rituximab can currently be offered to R/R CLL patients requiring a new treatment through CDF.

**The advantages and disadvantages of the technology**

This technology offers to use IR combination in the setting of

## NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

### Single Technology Appraisal (STA)

i) slow-go or no-go patients who had previously received treatments and where immunochemotherapy is expected to be unlikely beneficial.

New BCR-associated inhibitors appear to be highly effective and safe. Major toxicities include skin rashed, liver and gastrointestinal toxicity. Otherwise idelalisib has relatively safe profile and is expected to be 'easier' to use than immunochemotherapy. Treatments with idelalisib are also expected to be more effective than immunochemotherapy although there is no randomised phase III study comparing chemo+antiCD20 antibody with idelalisib based treatments. The current technology takes this in cosifderation sicne it is proposed to offer idelalisib+rituximab in those patients who are not expected to benefit from chemo+antiCD20 therapy or who are expected to suffer too much toxicity from other treatments.

ii) in the setting of previously untreated patients with CLL carrying deletion of 17p.

this group of patients have no currently satisfactory treatments available and the data from Furman and Hilmen should be sufficient to support the benefit of idelalisib to cover unmet clinical needs.

Limitations to its use are the excessive costs.

**Equality and Diversity**

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that this appraisal:

- Could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/will be licensed;

I do not think that treatment can exclude any of these people

- Could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

I do not think that treatment can exclude any of these people

- Could lead to recommendations that have any adverse impact on people with a particular disability or disabilities

I do not think that treatment can exclude any of these people

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts

## NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

### Single Technology Appraisal (STA)

**N/A**

**Any additional sources of evidence**

N/A

**Implementation issues**

The NHS is required by the Department of Health and the Welsh Assembly Government to provide funding and resources for medicines and treatments that have been recommended by NICE technology appraisal guidance. This provision has to be made within 3 months from the date of publication of the guidance.

If the technology is unlikely to be available in sufficient quantity, or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within 3 months, NICE may advise the Department of Health and the Welsh Assembly Government to vary this direction.

Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition? Would NHS staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?

The proposed treatment is tablets plus I.V infusion of rituximab and this should not impact on need of extra education to all known results on toxicity and efficacy for idelalisib.