NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Obinutuzumab in combination with chlorambucil for previously untreated chronic lymphocytic leukaemia

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

Patients and patient advocates can provide a unique perspective on the technology, which is not typically available from the published literature.

To help you give your views, we have provided a template. The questions are there as prompts to guide you. You do not have to answer every question. Please do not exceed the 8-page limit.

About you

Your name:

Name of your organisation: CLL Support Association

Are you (tick all that apply):

* a patient with the condition for which NICE is considering this technology?

Patient

- a carer of a patient with the condition for which NICE is considering this technology?

- * an employee of a patient organisation that represents patients with the condition for which NICE is considering the technology? If so, give your position in the organisation where appropriate (e.g. policy officer, trustee, member, etc)

Trustee

- other? (please specify)

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What do patients and/or carers consider to be the advantages and disadvantages of the technology for the condition?

1. Advantages

(a) Please list the specific aspect(s) of the condition that you expect the technology to help with. For each aspect you list please describe, if possible, what difference you expect the technology to make.

Co morbidities: This technology may offer benefits over existing treatments for patients with significant co morbidities. The CLL 11 trial recruited older patients, most over 70, and with 'clinically meaningful health problems in addition to CLL'. The results suggest that this technology will be beneficial to this group of patients.

Progression Free Survival (PFS): This technology may offer significantly improved PFS compared with with Rituximab + Chlorambucil (R-Clb). The results from the German CLL trial show that median PFS for Obinutuzumab + Chlorambucil (G-Clb) was 26.7 months compared to 15.2 months for R-Clb.

Minimum Residual Disease (MRD): This technology may increase the likelihood of achieving MRD which has been shown to provide a longer PFS.

(b) Please list any short-term and/or long-term benefits that patients expect to gain from using the technology. These might include the effect of the technology on:

- the course and/or outcome of the condition
- physical symptoms
- pain
- level of disability
- mental health
- quality of life (lifestyle, work, social functioning etc.)
- other quality of life issues not listed above
- other people (for example family, friends, employers)
- other issues not listed above

Longer PFS may result in a better Quality if Life (QoL) particularly as this may reduce the overall use of invasive and/or toxic treatments.

Our caveat is that the long term effects of Obinutuzumab are not yet known.

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2. Disadvantages
Please list any problems with or concerns you have about the technology.
Disadvantages might include:
- aspects of the condition that the technology cannot help with or might make worse
- difficulties in taking or using the technology
- side effects (please describe which side effects patients might be willing to accept or tolerate and which would be difficult to accept or tolerate)
- impact on others (for example family, friends, employers)
- financial impact on the patient and/or thier family (for example cost of travel needed to access the technology, or the cost of paying a carer)

The technology involves IV administration of Obinutuzumab, however, this is common with the other monoclonal antibodies, ie Rituximab and would only be a disadvantage over the use of Chlorambucil alone.

The CLL 11 trial administered Obinutuzumab over two days compared to Rituximab over one day. This may impact negatively on both the patient and carer both on their time and finance.

Adverse Events: Results from the CLL 11 trial showed that patients on the Obinutuzumab arm had more infusion related events during the first infusion of Obinutuzumab which may have resulted in more patients in this arm discontinuing therapy. However, the study reported no deaths from infusion related events in patients having Obinutuzumab.

Apart from Thrombocytopenia, other adverse events appear relatively balanced between the Obinutuzumab and Rituximab arms. Patients may well balance these adverse events against the benefits of the technology and would be willing to accept them.

The long term safety of Obinutuzumab is not yet known

3. Are there differences in opinion between patients about the usefulness or otherwise of this technology? If so, please describe them.

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4. Are there any groups of patients who might benefit **more** from the technology than others?

Older patients and those with co morbidities may benefit from this technology. Additionally the technology would be of interest to patients, although fit for FCR, would prefer a less toxic treatment.

Are there any groups of patients who might benefit **less** from the technology than others?

Younger patients with no or few co morbidities may not benefit from this technology over the current treatment of FCR for this group. To our knowledge no trials comparing FCR with any combination with Obinutuzumab have been done. However, Obinutuzumab + Chlorambucil may offer a less toxic treatment when compared with FCR but again we are not aware of any evidence to support this.

Comparing the technology with alternative available treatments or technologies
NICE is interested in your views on how the technology compares with existing treatments for this condition in the UK.

(i) Please list any current standard practice (alternatives if any) used in the UK.

Patients unfit for first line treatment with FCR currently have single agent Chlorambucil or single agent Bendamustine.

The UK CLL Guidelines also recommend entry of patients into trials. Currently for this group of patients this is: CLL9 RiAltO (Chlorambucil+Ofatumamab vs Bendamustin+Ofatumamab)

The UKCLL 208 trial; Rituximab + Chlorambucil as a first line treatment has been reported in JCO. (Peter Hillman et al; March 17 2014 JCO:2013.49.6547). This may be a competitor to Obinutuzumab + Chlorambucil.

(ii) If you think that the new technology has any **advantages** for patients over other current standard practice, please describe them. Advantages might include:
- improvement of the condition overall
- improvement in certain aspects of the condition
- ease of use (for example tablets rather than injection)
- where the technology has to be used (for example at home rather than in hospital)
- side effects (please describe nature and number of problems, frequency, duration, severity etc)

The CLL 11 Study shows that the new technology has advantages over single agent Chlorambucil with increased median PFS and complete response. A similar improvement over single agent Bendamustine may be expected.

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(iii) If you think that the new technology has any **disadvantages** for patients compared with current standard practice, please describe them. Disadvantages might include:
- worsening of the condition overall
- worsening of specific aspects of the condition
- difficulty in use (for example injection rather than tablets)
- where the technology has to be used (for example in hospital rather than at home)
- side effects (for example nature or number of problems, how often, for how long, how severe).

The new technology involves IV administration of Obinutuzumab which involves additional hospital visits compared to the current oral administration of single agent Chlorambucil or Bendamustine.

There may be an increase in adverse events but patients may well balance these against the benefits of the technology and would be willing to accept them.

Research evidence on patient or carer views of the technology
If you are familiar with the evidence base for the technology, please comment on whether patients' experience of using the technology as part of their routine NHS care reflects that observed under clinical trial conditions.

Are there any adverse effects that were not apparent in the clinical trials but have come to light since, during routine NHS care?

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Are you aware of any research carried out on patient or carer views of the condition or existing treatments that is relevant to an appraisal of this technology? If yes, please provide references to the relevant studies.

Availability of this technology to patients in the NHS
What key differences, if any, would it make to patients and/or carers if this technology was made available on the NHS?

This technology has the potential to improve patient outcomes over the current single agent treatments for patients unfit for FCR. It offers benefits of increased median PFS and Overall Survival with the associated better Quality of Life for both the patient, carer and family.

What implications would it have for patients and/or carers if the technology was **not** made available to patients on the NHS?

Patients not fit for FCR currently have little choice for treatment and rely on old technology drugs. If the new technology is not approved then this group of patients will not benefit from improved treatments and the associated better outcomes. This may well impact not only on the patient but also their carers and family.

Are there groups of patients that have difficulties using the technology?

Elderly patients with little or no carer support, or those living distant from hospital may have difficulties attending for extended treatments.

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Equality
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;
- 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;
- could lead to recommendations that have any adverse impact on people with a particular disability or disabilities.

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

Other Issues
Please consider here any other issues you would like the Appraisal Committee to consider when appraising this technology.

We are currently awaiting availability and review of safety data