Vedolizumab ACD response

Many thanks for forwarding the ACD document for comment.

As a patient expert I am delighted that the committee has taken on board what was said as to how debilitating ulcerative colitis can be, and how desperate we are, as a patient group, for new treatment options. It is fantastic news that vedolizumab is being recommended as a treatment option for moderate to severe UC and this will make a difference for many patients.

It is however very disappointing that the committee proposes to restrict access to patients who have not received anti TNF treatment which I do not feel is correct or fair.

Although as patient experts we feel that we have been listened to, it is striking that neither myself nor [redacted] would be eligible to receive the treatment under these draft guidelines. For [redacted] this would have meant missing out on the treatment that has given him six years of remission after all other treatments had failed.

The guidelines leave me with no treatment option other than surgery if I lose the exceptional case funding for my infliximab treatment, or if I lose response to this treatment, which could happen within the next year. Yet the committee have accepted that surgery is not an acceptable alternative treatment option. I never had the option to choose vedolizumab before anti TNF because this was not available at the time that I needed it. A number of patients with moderate to severe UC will have received anti TNF at some point, yet they are being prevented from accessing vedolizumab and in my view the evidence does not justify this. The guidelines are also cutting out some of the patients who are most at need. Although we are still awaiting the final outcome of the infliximab/andalimumab/golimumab appraisal, it is looking like these treatments will not be recommended for UC which leaves many patients with no remaining treatment options other than surgery.

Uncertainty of the exception for those who are intolerant to anti-TNF

There is some uncertainty as to the significance of the exception in relation to patients who have had anti TNF but could not tolerate this treatment. It is known that anti-TNFs can lead to the development of antibodies against the drug which can either lead to allergic reaction or to loss of response in patients. It appears that some patients have an allergic reaction when the anti TNF treatment is stopped ands re-started again. Does the exception in the guidelines cover patients who have had an adverse reaction at any time in their treatment or only at the start? Does this mean that if I have an allergic reaction to my infliximab tomorrow, after 18 months of treatment, then I am eligible to receive vedolizumab, but not if I lose response? What medical evidence is there that I am less likely to respond to vedolizumab in the first, rather than the second scenario? I would consider that in both cases my disease is still classified as amenable to treatment.

Distinction between patients who have had no response to anti TNF, and those who responded to anti-TNF but lost response over time

I note in paragraph 3.8 that '*the company commented that people in whom* **prior treatment with a TNF-alpha inhibitor had failed** *may be less likely to have a successful response to subsequent treatment than people* **whose disease had lost response to, or who could not tolerate a TNF-alpha inhibitor'.** A distinction is drawn between those who have failed, and therefore not responded to anti TNF, and this who had lost response or were intolerant. The draft guidelines however place those who have lost response in the same group as those who did not respond to anti TNF at all. This cannot be correct and contradicts what the company suggested.

There is very little evidence to suggest that a distinction should be made between these subgroups. GEMINI I suggested only a 11% difference in response to vedolizumab between those who had anti TNFs before, and those who had not (paragraph 3.5 36% vs 47%). The committee itself accepted in paragraph 4.8 that GEMINI I was not empowered to test for a statistically significant difference between subgroups yet this is what has been done in these draft guidelines.

Distinction between patients who were intolerant to anti-TNF, and those who were tolerant and have responded but lost response over time

In paragraph 4.3 the committee accepted that the cost effectiveness of vedolizumab for patients who have had anti TNF but were intolerant, and the cost effectiveness for those who have not had anti TNF were comparable, because we must assume that some patients who were intolerant may have responded to anti TNF if they had been able to continue treatment. However those who have had anti TNFs and have responded well to these, but eventually lost response (which is common due to antibody development) are shut out. This is an incorrect and unfair distinction.

Conventional therapy is not a relevant comparator

In paragraph 4.9 I note that the committee is referring to conventional therapy as an appropriate comparator. This is a flawed analysis again (as in the other biologics appraisal). Patients who have failed conventional therapy cannot go back to conventional therapy, they have no option other than surgery. Of course patients who lose their other treatment options go back to treatment with high doses of steroids. This is because without them they could die while waiting for surgery, this is not because long term high dose steroid treatment is an option.

Innovative treatment

I further note that paragraph 4.21 concludes that vedolizumab is an innovative treatment. I completely agree with this, which is why it should be accessible to as many patients as possible. I note that when a treatment is particularly innovative then NICE can recommend this as cost effective even when ICERs are higher than usual. Why was this not done here?

Equality and diversity

I also welcome NICE's conclusion that there are equality and diversity issues at play for young people who have not yet started a family. It is disappointing that as a 28 year old female, based on these draft guidelines I am still left with surgery as my only alternative treatment option if I lose my infliximab treatment.

The reason that vedolizumab is such an exciting treatment option is that it has been proven to work for patients who have failed all other treatment, including anti TNF. It is an additional line of treatment for patients, but under these draft guidelines it is not. It also has less side effects and may enable patients to achieve remission for longer, without the need for concurrent immunosuppressive treatments, but many patients who could gain substantial benefit could miss out under these draft guidelines.

Suggested amendments to the recommendations in paragraph 1

I would propose that the draft guidelines be amended to recommend treatment for those who have had anti-TNF treatment and responded to this, but then lost response to treatment.

I would also suggest an amendment that enables patients who did not respond to anti TNF, to still access this treatment, but with an earlier review as to whether clinical response has been achieved. This will manage cost effectiveness by only allowing patients who are responding to continue treatment, but without cutting out large groups of patients who could still gain substantial benefit from vedolizumab treatment. The guidelines could provide for a review at week 14, as suggested by the clinical experts, with discontinuation of treatment just before the fourth dose if no clinical response has been achieved.