Lori Farrar
Project Manager - Committee C
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1st April, 2015

Dear Lori

Response to DSU Report and Assessment Report relating to the Multiple Technology Appraisal (MTA) Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, abatacept and tocilizumab for the treatment of rheumatoid arthritis (review of TA guidance 130, 186, 224, 234 and part review of TA guidance 225 and 247) [ID537]

Thank you for the opportunity to comment on the above appraisal process in respect of the DSU Report and Addendum to the Assessment Report.

General Comments

NRAS has been alarmed about the findings from the ERG from the last two Appraisal meetings in regard to this MTA review and, as a consequence, we felt there was a need to invest in production and analysis of a survey which we ran for a week between Friday 20th March and Friday 27th March to gather opinion from people with RA about the use of biologics. We also put a call out for short case studies. The results of the survey and the case studies form an important part of our response and are attached hereto as Appendices 1 and 2.

This Committee is well aware of the facts and figures in respect of RA which we don't feel we need to repeat here, but what we believe is often 'glossed over' or inadequately focussed upon at Appraisal meetings, is the devastating ***impacts*** that a lifetime of living with RA can have, not only on the individual, but on their family, and wider society. When I was diagnosed approximately 34 years ago, treatment was so very different, it seems like the dark ages in retrospect. and the approach to treatment and care now, driven by using MTX and other cDMARDs in combination at the point of diagnosis and the introduction of the biologics 15 years ago, has made a sea-change in how we now tackle RA to the huge benefit of patients and their families, but the financial benefits this revolution has brought to the NHS, social care and wider society is immense and, we believe, under-estimated in the cost/benefit health economic analysis .

In many ways, I am a classic example of someone who was treated too little, too late and we have the better treatment and the introduction of biologics to thank for the fact that there will be fewer

patients like me in future (19 operations to date, just failed on 5th biologic, currently on high dose prednisolone to regain disease control before embarking on 6th biologic) . The BSR submission, which we whole-heartedly support, describes very well the savings made through reductions in orthopaedic surgery, in-patient beds, increasing disability etc.

However, whilst we have unquestionably made great strides in the treatment and care of people with RA, there remains clear and urgent **unmet** need for those who do not respond to cDMARDs , and may not be quite eligible (under current criteria) for biologics.

- In total 22% of respondents to our survey described their disease as currently not well controlled by cDMARDS.
    - Of these respondents, 69% said that disease was not well enough controlled to enable them to continue to do valued day to day activities and that it was affecting their confidence and independence.
    - Almost a third (31%) of people whose disease is not well controlled by DMARDs said that it was affecting their ability to remain in their current job and 11% said that they had lost their job as a result.

If you are receiving standard DMARD therapy, but feel that a biologic may be a future option for you, how would you feel if that option were to be taken away?

'*I would be terrified. I am 30 years old, struggle to walk, to cook, have had to downgrade my job and lost a lot of income. I hope I will be put onto biologics as soon as I am eligible, and really really hope they help*.' **– Female RA Patient, aged 25-34 years**

'*I would feel that there wouldn't be any hope for me to be able to work again in the future. I would feel like I was being deprived of probable improvement of my RA.*' **– Female RA Patient, aged 45-54 years**

'*Very worried. At the moment I feel that biologics are future treatment options for when I need them. If that option were taken away it would be like someone telling me that I will be in pain and tired for the rest of my life and will have to try to survive on ever increasing doses of strong, addictive pain relief. I would not want to live like that with no hope of an effective treatment.*' **– Female RA Patient, aged 55-64 years**

In addition, there is a group of RA patients ,including those like me, who do not have lasting benefit from biologics and need to switch. The desperate plight of these groups of individuals is captured in some of our case studies we have included in this letter and further are attached(Appendix 2). Some of the data from our survey (over 1000 people responded, with 850 participants completing all questions) illuminate the significant difficulties they face and the fear they feel at the idea of biologics being taken away.

- A total of 15% of respondents to our survey described their disease as not well controlled by biologics. Of this group of respondents:
    - 73% said that their disease is not well enough controlled to enable them to continue valued day to day activities
    - 60% said it was affecting their confidence and independence,

- 20% said it was affecting their ability to remain in their current job
- 10% said they had lost their job as a result

If you are receiving biologic therapy, how would you feel if you no longer had access to this medication or another biologic therapy in the future? What impact would this have on your life?

'*This is my second biologic therapy. It has been amazing and my quality of life is 100% improved. I would be very concerned if it was taken away as I have had many of the other drugs (DMARDS and one other biologic) and had problems or no help from all of them. If biologicals were taken away I wouldn't have anything else left to try and would go back to all the pain etc I had before. I wouldn't fancy a life on steroids either. Life would be extremely difficult and I doubt I would be able to continue the work I have now which is quite manual. I play in an orchestra and enjoy world travel - both of which would suffer greatly without my current medication. Quality of life is SO important and with my biological my quality of life is amazing! Long may it last!*' **– Female RA Patient, aged 45-54 years**

'*I would feel that I would then be condemned to a life of eternal pain and would be unable to continue the active sports I am now capable of doing. It would also limit my ability to go abroad on holiday since, before the generic therapy, I was struggling to walk any great distance and could not be lift my l luggage*.' **– Male RA Patient, aged 65 years or over**

'My life would be ruined. I've tried 3 biologic drugs, this is the first one to work' **– Female RA Patient, aged 35-44 years**

Costs and Benefits

It is inconceivable to NRAS that not only are NICE not addressing the earlier introduction of biologics for those for whom costly palliative care is currently the only option, but are suggesting that these drugs are suddenly, after 15 years' demonstrably successful use in the UK, no longer cost effective at all.

We do not believe that ***all*** of the cost saving impact of the use of biologics has been adequately captured in the various health economic analyses conducted by NICE. The benefits of the current treat-to-target strategies which have remission as an early goal include the use of Anti-TNF therapy when cDMARDs fail, and to remove the option of moving to a biologic at this point in a patient's pathway would be such a retrograde step by comparison to the way in which the rest of the world treats RA that we struggle to contemplate such a situation. The UK RA population is already disadvantaged when it comes to use of biologics by comparison with most of the rest of Europe. I have just come back from a visit to Norway, where patients are able to access biologic therapies at a much earlier stage in their pathway after failure on Methotrexate alone.

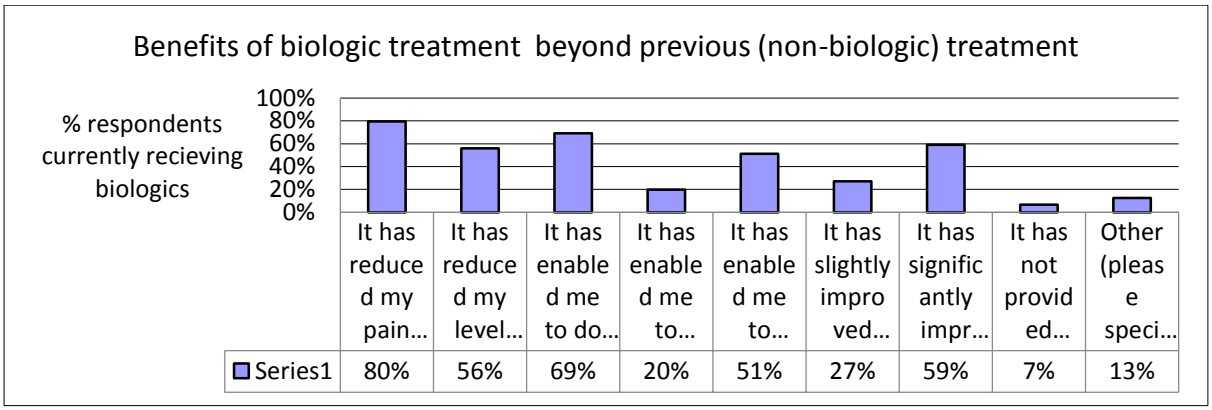
The BSR in their submission point to a number of inaccuracies in regard to estimation of costs based on previous TAs and quote an example of 10% of sub-cut injections of bDMARDs being administered by District Nurses. In our experience, as a national organisation interacting daily with people with RA all over the UK, we are not aware of any patients receiving such a service. We also agree with their point in regard to over-estimation of the costs of MTX monitoring. By the time patients are established on bDMARD therapy, it is much more likely that their MTX monitoring will happen on a

three monthly, not monthly, basis and be done at their GP surgery, not the hospital. We absolutely concur with the BSR in regard to the under-estimation of palliative care costs which do not adequately reflect the increased healthcare utilisation incurred by the NHS, social care and employers (through lost productivity, presenteeism, absenteeism) and I have experienced this personally in the last 12 months. Just as an exercise I went back through my diary for 2014. Normally, under good control, I would see my consultant maybe 3 or 4 times a year maximum. In 2014, with my disease uncontrolled, I had **21 consultant visits**, CT scans, MRI scans and x-rays as well as many more blood tests than usual. All of that additional healthcare usage alone is extremely costly and not untypical for someone in my situation.

The additional benefits of bDMARDS can be seen clearly in our survey results:

Of respondents who are currently receiving biological treatments:

- 80% said it had reduced their pain levels
- 56% said it had reduced their level of fatigue
- 69% said it had enabled them to do day to day activities
- 20% said it had enabled them to get back to work
- 51% said it had enabled them to regain more independence
- 59% said it had improved my overall quality of life
- Only 7% said it had not provided any further benefits over previous treatment



We are therefore extremely concerned that the ERG/DSU are indicating that biologic treatment is no longer cost effective. As far as we are aware, there has been no data published to suggest that Anti-TNF treatments are less effective than have been shown to be the case in all previous TAs. As stated by the BSR in their submission, the previous NICE Guidelines on economic evaluation were the first national guidelines to prescribe differential discounting (6% for costs and 1.5% for effects). We do not understand why NICE, after more than a decade, has now suddenly changed the discount rates for both cost and benefits at 3.5%, implying a lower weight for future effects.

Impact on patients' lives

Access to appropriate treatment is also vital for reducing work disability and ensuring patient's can have full and independent lives. Removal of biologics would negatively impact on this and produce knock on economic costs.

In 2014, NICE consulted on proposals to introduce a new method of Valued Based Asessment which would look at the wider impacts of a drug. However since the consultation closed there has been no further progress or developments. NRAS continues to believe that NICE needs to take into account the very clear and demonstrable wider benefits of therapies such as biologic drugs.

Work

- 33% of respondents whose disease is not well controlled by DMARDs and are currently unemployed 33% said they were currently unable to work due to their RA. By comparison only 24% of those who disease is well controlled by biologics said they were currently unable to work because of their RA.
- Of working age respondents, currently in employment and receiving a biologic treatment, 40% said it had enabled them to get back to work.

CASE STUDIES:

'***If [my biologic] was removed I believe that I would not remain in employment***. *Even with this therapy I struggle to remain at work because,of the fatigue and recent deformity of my dominant hand.'* – **Female RA Patient, aged 55-64 years**

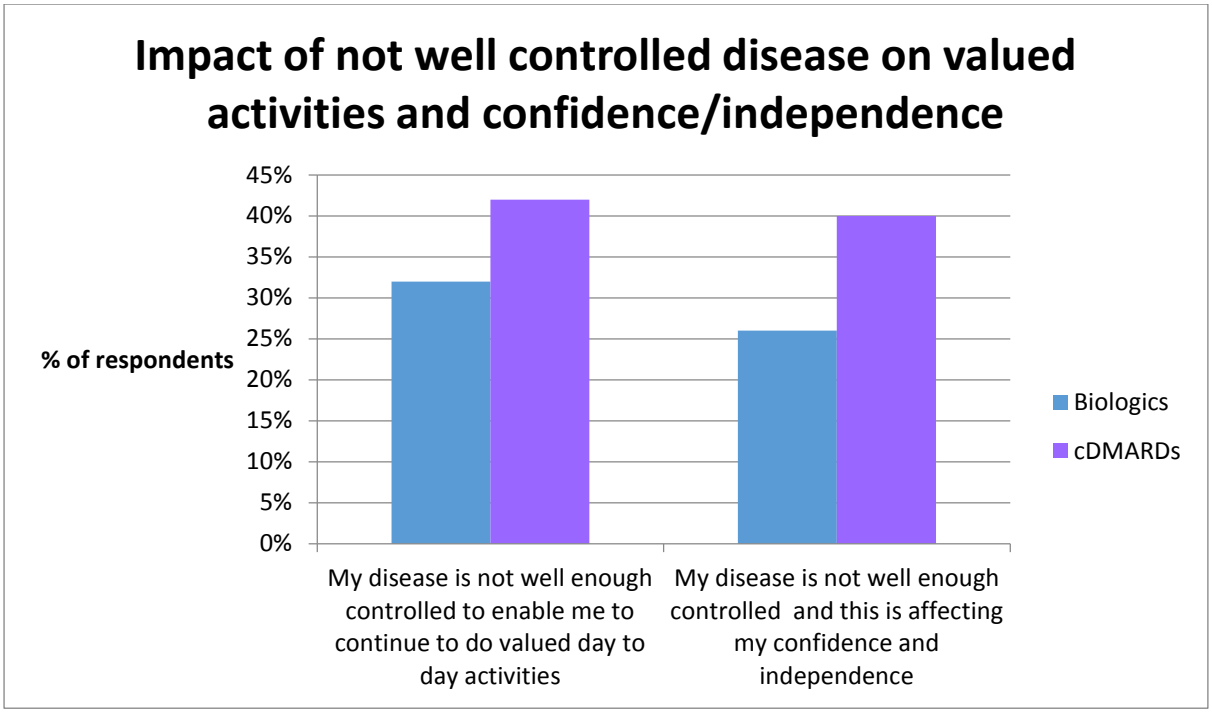
'I would feel suicidal, ***if my arthritis returned to pre-enbrel levels it would ruin my life, leave me unable to work or maintain any quality of life***. *Suicide would genuinely be the first option I would consider.'* **– Male RA Patient, aged 25-34 years**

*'[****If biologics were taken away]I would be unable to function on a day to day level doing everyday things. There would be no possibility of me returning to employment, ever****. I would need assistance again with my personal care and be unable to maintain my independence. Pain levels would be an 8 on a daily basis and pain management would become an issue. Basically life wouldn't be worth living and I would again be house bound.'*

Wider impacts

As previously demonstrated by the results of our survey, and our wider experience with patients, RA can have a significant detrimental impact on wider activities and patients' quality of life. Obtaining control of disease via the necessary treatment, including biologics, is crucial to minimising this impact. From our survey, fewer of those on biological seemed as impacted by uncontrolled disease:

- Of all respondents receiving biological treatment 32% said their disease was not well enough controlled to continue to do valued day to day activity compared to 42% of all those receiving cDMARD treatment.
- Of all respondents receiving biological treatment, 26% said their disease was not well enough controlled and this was affecting their confidence and independence compared to 40% of all those receiving cDMARD treatment.



Our survey respondents spoke about the impact on families of not having access to effective treatment and the consequences for their independence:

CASE STUDIES

'[I was] recently taken off Etanercept which appeared to be fantastic compared to Rituximab which I have just been started on. During the changeover time I was virtually unable to walk, with severe pain and swelling in my knees hips and shoulders...[this] impacted severely with caring for my children and also affected my marriage due to my husband having to take alot of the home responsibilities on.' RA Patient, aged 45-54

'If I didn't have access to biologic therapy I would not be able to function. I would not be able to dress myself, or walk or look after my five year old son. I would probably keep ending up in hospital in severe pain and unable to move properly. It would not be an option for me.'

'Unfortunately I had side effects to biologic therapy, ***the time I took them I was out of pain requiring less input from GP, more independent. It requires negotiation with drug companies. I feel that the cost of disability both personal and to NHS is far more costly than the cost of biologic drugs. Remember quality of life measures****. '*

Fairness

Given that the 2014 PPRS agreement ensures that the NHS budget is capped so that increasing the use of biologic drugs would not increase direct NHS costs, we agree with the BSR position that it is inappropriate to change the discount rate for health benefits from TA130. As a consequence we would robustly challenge that this scenario does not meet the NICE standard of operating 'fairly'. With the introduction of the first biosimilars to the UK market, the whole biologics landscape is going to change significantly over the next few years as more originator products come off patent

and so it will be appropriate to think about an increased discount rate for costs. However, we are just at the start of the biosimilar journey and we need to address the here and now.

Clinical judgement and patient choice

, NRAS is clear that biosimilars should not be used to straightforwardly replace originators for reasons of cost. Any judgement to place a patient on a biosimilar, once available, must be made for clinical reasons and with the full involvement of the patient.

Our survey responses bore out the importance of ability to exercise proper clinical judgement and patient choice.

- 46% said that it was really important that all effective treatments remain available on the NHS.
- Whilst 34% of respondents said that as long as they are effective I would be happy to see lower cost biosimilar drugs replace the current biologics, NRAS stresses that this has not yet been established for biosimilars and further monitoring of their effectiveness is needed. NICE should not therefore feel that biosimilars will straightforwardly be able to replace to biologics.

In addition, a number of respondents provided free-text responses outlining their concerns about the reduction in the options available to a patient and the caveats on their enthusiasm for biologics:

FREE TEXT RESPONSES:

'*As long as they are effective it is fine to have them but it is important that patients are able to get a therapy that works for them regardless of cost and faster than currently able to on NHS.'* **– Female RA patient, aged 35-44**

'Biosimilars may be highly effective for many service users. However, where they are not effective, existing treatments should continue to be available.' **—Female RA patient, aged 65 years or older**

'*I have found that even some brands of well established drugs like methotrexate seem to vary in their effect on me. Consequently I am extremely worried by the thought of biosimilar drugs - 'not identical' can sometimes mean extremely unpleasant and painful effects on patients even though blood results may indicate that inflammation is being controlled.'* **– Female RA Patient, aged 65 years and over**

In conclusion therefore on the point of fairness, we find it astonishing that NICE can overturn all previous appraisals which demonstrated that bDMARDS are cost effective, by summary changes in the discount rates which do not seem to be evidence-based. We believe that to conclude that all the previous NICE Appraisals were incorrect, would in fact reflect badly on NICE's reputation.

The BSR has provided excellent technical evidence to show that there have been incorrect assumptions in the current analysis that over-estimate the cost of bDMARDs and under-estimate the health benefits. We hope that the patient level data which we have been able to provide supports this position clearly and substantially.

There is no question that bDMARDs have had huge positive benefit to the lives of patients, their families and carers and the NHS and we hope the message is clear from the hundreds of patients who have contributed to our survey and case studies attached hereto.

Yours sincerely

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