Patients’ perceptions of treatment with anti-TNF therapy for rheumatoid arthritis: a qualitative study

N. J. Marshall, G. Wilson, K. Lapworth1 and L. J. Kay

Objectives. Anti-tumour necrosis factor (anti-TNF) therapy is a highly effective treatment for rheumatoid arthritis (RA), as documented using standard outcome measures in clinical trials. Anecdotal experience suggests health benefits for patients other than those measured in this way. We wished to explore patients’ experience of and views about this treatment and the British Society for Rheumatology Biologics Registry (BSR BR) process.

Methods. Separate focus groups for patients treated with infliximab (n = 7) and etanercept (n = 12) were undertaken. They were taped and transcribed verbatim, analysed and subjected to peer review and themes were identified.

Results. Five main themes were identified: expectations of treatment, experience of treatment and its effects, concerns about taking a new class of drug, views about the BSR Biologics Registry process and costs.

Conclusions. Patients’ experience of anti-TNF therapy was good, particularly in terms of physical function and well-being, although it did not live up to the very high expectations of some patients. The BSR BR process caused initial apprehension but patients had personal and altruistic reasons for being happy to comply with monitoring requirements. Qualitative methods add to our understanding of the effects of anti-TNF therapy for people with RA.

Key words: Anti-TNF therapy, Rheumatoid arthritis, Patients’ experience, Focus groups, Registry, Qualitative research.

Anti-tumour necrosis factor (anti-TNF) therapy has been shown to be highly effective in the treatment of rheumatoid arthritis (RA), in randomized controlled trials [1–4] and in clinical practice [5]. The impact of RA on patients can be measured in a variety of ways. Conventional process and outcome measures of the disease include the development of erosions on plain radiographs, raised inflammatory markers, tender and swollen joint counts and validated health status measures such as the Health Assessment Questionnaire [6]. Work with patients, however, has shown that these routinely used outcome measures do not capture the full range of patients’ response to treatment and that there are other factors to consider which are important to patients [7]. Our impression of managing the first few patients treated with anti-TNF therapy in our centre was that not only did they experience improvements in joint pain and swelling, normalization of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) and improvements in function, but that they felt well in themselves, often for the first time in many years.

Access to anti-TNF therapy in UK rheumatology departments is according to guidelines proposed by the British Society for Rheumatology and endorsed by the National Institute for Clinical Excellence [8]. These specify a level of disease activity, a threshold of previous treatment and an absence of exclusion criteria such as chronic infection or recent malignancy. All patients are required to be systematically documented, have treatment withdrawn if they do not respond adequately to it and to be entered into a national registry supervised by the British Society for Rheumatology. Accordingly, any patient meeting these requirements will have severe and established disease, and will have considerable experience of RA and of its management by departments of rheumatology. The necessity of passing a threshold for treatment, and the registry process, are new both to patients and staff outside of clinical trials.

We sought to understand the patients’ experience of this new drug therapy, their impressions of its benefits, or otherwise, and their views on the registry process.

Methods

Qualitative methodology is the most appropriate technique to use for investigation of personal experiences, perceptions, beliefs and meanings related to individuals [9]. We chose a focus group methodology to allow interaction between patients, generation of new ideas and reflection, and brainstorming. Focus groups [10] facilitate exploration and set out to discover the perceptions of specific individuals. The advantages of focus groups are that they are relatively inexpensive [11], they stimulate individual respondents and they allow observation of interaction [12]. The dynamics of a focus group allow participants to question each other and can provide ‘reality checks’ on participants’ responses [13].

We invited all patients who had received treatment in our unit with anti-TNF therapy, whether treatment had stopped or not, to participate. Separate focus groups were held for patients treated with infliximab and those treated with etanercept as we wished to explore whether issues and experiences might differ. It was important that no one present during the focus group was perceived by the patients as influencing their access to therapy as this may have influenced the expression of their views, and direct reassurance on this point was given. A newly appointed Rheumatology Nurse Specialist (GW) and members of the Clinical Effectiveness and Audit Department facilitated participation in these groups.

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the focus groups. The facilitator used a topic guide (Table 1), open questions and prompting. As there is little published work on patient experience of anti-TNF therapy, the topic guide was constructed using clinical experience and local consensus. Focus groups were tape recorded and then transcribed verbatim. Patients were assured of the confidentiality of the process, and that their statements would have no effect on their future management within the department. After analytical immersion in the data, significant statements were identified and subjected to peer review, to increase their validity. Statements were identified by NJM and GW, and reviewed by LJK and a member of the audit department. They were then subcategorized into themes. Patients gave written consent for participation and Newcastle and North Tyneside local research ethics committee gave ethical approval.

### Results

Seven of 19 patients who had received infliximab therapy responded positively and were allocated to one focus group. Twenty-four of 27 etanercept patients responded to the invitation. Purposive sampling was used to select 12 patients to participate in the second focus group, to ensure a distribution of ages and disease durations (Table 2). One patient in each group had stopped treatment owing to lack of efficacy. The age of patients ranged from 32–69 yr with a median age of 52 yr. Overall disease duration ranged from 2–31 yr with median disease duration of 11 yr. One patient was male. Few distinct differences were voiced between the two groups, apart from specific comments about methods of drug delivery (see below).

The following themes were identified from the transcripts.

#### Expectations of treatment

Many patients expressed hope that the new treatment would help, although not always with high expectations that it would:

- **Patient E**: ‘I just went into it just hoping that something might work…. I just thought well I’ll try you know?…. So I went into it just, not really expecting anything, just hoping and just, you know, em thinking well give it a shot, give it a try, cause that’s all you can do, you know, try anything, basically.’
- **Patient J**: ‘I think I was just glad to try something different, just to see if it was going to work, you know, just the thought of ah, here’s a new drug, at least give it a try and see what happens.’

Not surprisingly, given the degree of severity of their arthritis required for treatment with these drugs, some patients felt desperate to try new agents:

- **Patient F**: ‘I think when you’ve got to a stage where you’ve tried everything, you’ll literally go for anything that’s available. Whatever relief you can get for it.’
- **Patient I**: ‘I desperately wanted to swallow something and be OK.’
- **Patient G**: ‘I’m eating dog dirt at the minute. I would if I thought it would work.’

Others had higher expectations:

- **Patient N**: ‘I expected some improvement because at the time just before I started I was in an awful state, I really was, I didn’t think I could take much more pain.’
- **Patient H**: ‘I thought the minute I went on this drug I’m going to be cured with in a couple of months.’

Higher expectations appeared to be influenced by information from sources such as newspapers and the internet:

- **Patient I**: ‘Well my expectations were perhaps more than yours ‘cos I had read quite a bit about it.’
- **Patient D**: ‘I’d done a lot of research, I had a go on the internet and look, find out about it and there was quite a lot of positive information on people in America who had been on it.’

In contrast there were other members of the group who knew little about the drug and appeared not to want any information about it:

- **Patient E**: ‘I didn’t know anything about it, I didn’t know and I must admit, I didn’t even read the leaflet. I didn’t know anything about it, and hadn’t em, I mean I could have found out it if I’d wanted to.’

#### Experience of treatment and its effects

The majority of patients were very positive about the effects of their treatment:

- **Patient N**: ‘I just couldn’t believe it really, it’s been absolutely marvellous.’
- **Patient E**: ‘So I just think it’s marvellous, long may it continue.’
- **Patient L**: ‘Thrilled to bits, absolutely thrilled to bits.’
- **Patient P**: ‘For me it was wonderful because I had been on every other drug imaginable and it was etanercept which has been very, very good for me.’

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**Table 1. Topic guide used for the focus groups**

<table>
<thead>
<tr>
<th>Question</th>
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<tbody>
<tr>
<td>What were your expectations of [etanercept or infliximab] therapy before starting treatment?</td>
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<tr>
<td>How does that compare with your experiences since commencing treatment?</td>
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<tr>
<td>Can you describe your feeling about starting a newly developed treatment?</td>
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<tr>
<td>In order to start this drug you had to go through an assessment process; how did you feel about this?</td>
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<tr>
<td>What impact has [etanercept or infliximab] had on your life?</td>
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<tr>
<td>What are your feelings about being part of a national registry?</td>
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<tr>
<td>Would you be surprised to hear that [etanercept or infliximab] costs £9295 + VAT per year? In your experience is this good value for money?</td>
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</tbody>
</table>

**Table 2. Demographic details of patients involved in the study**

<table>
<thead>
<tr>
<th>Patient code</th>
<th>Age (yr)</th>
<th>Disease duration (yr)</th>
<th>Treatment</th>
<th>Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient A</td>
<td>32</td>
<td>7</td>
<td>Etanercept</td>
<td>Female</td>
</tr>
<tr>
<td>Patient B</td>
<td>36</td>
<td>5</td>
<td>Infliximab</td>
<td>Female</td>
</tr>
<tr>
<td>Patient C</td>
<td>41</td>
<td>22</td>
<td>Infliximab</td>
<td>Male</td>
</tr>
<tr>
<td>Patient D</td>
<td>45</td>
<td>21</td>
<td>Infliximab</td>
<td>Female</td>
</tr>
<tr>
<td>Patient E</td>
<td>46</td>
<td>11</td>
<td>Infliximab</td>
<td>Female</td>
</tr>
<tr>
<td>Patient F</td>
<td>46</td>
<td>13</td>
<td>Etanercept</td>
<td>Female</td>
</tr>
<tr>
<td>Patient G</td>
<td>60</td>
<td>7</td>
<td>Etanercept</td>
<td>Female</td>
</tr>
<tr>
<td>Patient H</td>
<td>55</td>
<td>10</td>
<td>Etanercept</td>
<td>Female</td>
</tr>
<tr>
<td>Patient I</td>
<td>56</td>
<td>5</td>
<td>Infliximab</td>
<td>Female</td>
</tr>
<tr>
<td>Patient J</td>
<td>56</td>
<td>19</td>
<td>Etanercept</td>
<td>Female</td>
</tr>
<tr>
<td>Patient K</td>
<td>57</td>
<td>31</td>
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<td>Female</td>
</tr>
<tr>
<td>Patient L</td>
<td>59</td>
<td>8</td>
<td>Infliximab</td>
<td>Female</td>
</tr>
<tr>
<td>Patient M</td>
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<td>Female</td>
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<tr>
<td>Patient N</td>
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<td>3</td>
<td>Infliximab</td>
<td>Female</td>
</tr>
<tr>
<td>Patient O</td>
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<td>Etanercept</td>
<td>Female</td>
</tr>
<tr>
<td>Patient P</td>
<td>66</td>
<td>21</td>
<td>Etanercept</td>
<td>Female</td>
</tr>
<tr>
<td>Patient Q</td>
<td>69</td>
<td>11</td>
<td>Etanercept</td>
<td>Female</td>
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Many positive statements were to do with their perceived improvements in quality of life, particularly relating to physical ability, that have led to independence in everyday tasks. This appears to have a ‘knock-on’ effect psychologically—feeling like a ‘normal’ person. Also highlighted was the fact that they were socially more dynamic and could perform tasks previously beyond them:

- Patient L: ‘Well I’ve been just delighted with the progress. I got the bus; yesterday would never have been able to deal with that. Couple of years really.’
- Patient P: ‘Here I was up and away and feeling so much more confident in myself.’
- Patient O: ‘Now I can go sometimes 4 or 5 hours shopping like everybody else.’
- Patient K: ‘It’s like being a normal person, I mean its, I’ve even got myself going back to the gym and starting walking.’
- Patient E: ‘I can play with the grandchildren and pick them up.’
- Patient L: ‘You take more of an interest emotionally to everything around you.’
- Patient N: ‘Tremendous, you know when you were saying you’ve taken more interest and that, I think you’re more alert now, you know.’

They talked about improvements in early morning joint stiffness:

- Patient I: ‘I had four and a half to five hours of stiffness every morning till I could do anything and so it’s great you know to be able to get up.’
- Patient N: ‘It’s just lovely to be able to get out of bed quicker and not have the anxiety of not getting to the loo in time.’

Improvements led to feelings of well-being:

- Patient N: ‘Tremendous… I think you’re more alert now.’
- Patient E: ‘My life is 99% better.’
- Patient D: ‘I found that I felt so much better I kind of forgot that I had arthritis and I pushed myself a bit too much.’
- Patient N: ‘You take more of an interest emotionally to everything around you.’

Some described feelings of well-being because other people noticed an improvement:

- Patient B: ‘I mean one of the kids at [the dancing school] had asked my little girl, “…has your mammy got new legs, ‘cause she walks alright now”, it’s a bit like you, people saying that you walk properly, you know. ‘Cause they knew I’d been in and out of hospital quite a bit, “has she got new legs” and said “no, she’s got new treatment”, you know, so it keeps her noticing as well. It makes you feel a lot better as well I think.’

Some of the group were quite philosophical about their response:

- Patient E: ‘Take the good days and enjoy them and the bad days you just have to think “well tomorrow might be better”.’
- Patient D: ‘It’s not a cure you know and that’s what it’s still there it’s just bearable, you know.’
- Patient I: ‘I don’t mind if I overdo it and I end up going “oh my God, I can’t move a muscle”, because I know why and I know it will get better and it’s not really the arthritis, it’s not really the arthritis itself.’

Negative experiences were related to lack of effect or side-effects. These were mainly due to infection, for which one patient had had to stop treatment altogether. Those that had developed infection and had to stop treatment temporarily felt it took a while to get back up to pre-infection levels of effectiveness, if at all:

- Patient H: ‘I didn’t get any benefit from it but then I was only on it for the three months and had to come off it once during the three months because I had an infection.’
- Patient G: ‘I was gutted when it didn’t work for me.’

Some mentioned problems with mouth ulcers that resolved or they had suffered from when using other DMARDs, others expressed trouble with dry skin. Another said it was the first time they had not had any side-effects whilst on treatment. Some patients treated with infliximab experienced a loss of effect of the treatment before the next infusion was due:

- Patient N: ‘About the six weeks, you start to remember exactly what that pain’s like, you think, “oh my God”; you know. Let’s hurry up and get the next treatment.’
- Patient C: ‘After six weeks, well after four weeks, it’s starting to wear off. After six weeks I practically can’t move again, unless I increase my steroids.’

One patient had been concerned about her ability to perform the subcutaneous injections of etanercept but had mastered it very quickly. The training and support was appreciated.

There was mention of expectations being too high because of reading about the drug from different sources

- Patient I: ‘I think it’s marvellous but it hasn’t quite lived quite up to the expectations that I was led to believe not by anyone here, but what from what I’d… well I’d had loads of information from Canada.’

Concerns about taking a new class of drug

There appeared to be little concern about the lack of clinical experience with these drugs but there was some anxiety about the fact that they form a new class of drugs for the treatment of RA:

- Patient D: ‘I was really scared in the beginning, I didn’t know what to expect with it being a new drug…I was quite excited at the fact that, scared but quite excited.’

Another patient commented that they felt ‘honoured and privileged’ to be able to try them.

Views about the British Society for Rheumatology Biologics Registry process

In response to questions about the BSR BR process most of the group expressed anxiety about the assessment. Several patients were worried when waiting to see if they would fit the BSR/NICE guidelines following the initial two assessments. Once they fulfilled these criteria some of the patients had to wait for funding to be arranged and this proved to be a very anxious time for these individuals:

- Patient P: ‘Very worrying, not worrying about what the drug was like, worrying if you would have been allowed.’

Even those who had had to discontinue the drug, however, had no concerns or dissatisfaction about attending for assessment. Perceived benefits included measurement of their own progress:

- Patient N: ‘I wanted to come back because obviously I want to know what is going on.’

and possible benefit of the results of the registry to others, particularly younger patients:

- Patient E: ‘I mean if I had to come in for an assessment every week I’d come for an assessment every week, if it helped.’
They felt that the close monitoring and easy access to health care professionals worked well:

- Patient O: ‘I felt that the backup was absolutely super, you knew you were not on your own and that you knew you could phone for anything, which was super.’

Some were apprehensive that they might be taken off the treatment if the assessments showed an inadequate response:

- Patient I: ‘does that mean after 6 months you might say you don’t, we’re not going to give you the drug any more?’
- Patient N: ‘This is a thing that worries me you know, you know that you might reach the stage where you say right, you’ve got to come off it now.’

Others questioned why the drug was not available for those in the early stages of their disease:

- Patient I: ‘I think of all the people in the very early stage and I think to myself, surely they’ll benefit more before it gets to the point where you knockles and joints, you know and I feel guilty that I’m on it and yet there’s other people who perhaps could end up with a much more severe disease not getting it.’

Costs

Patients were aware of the high cost of treatment. Overall thoughts were that if the treatment prevented the need for joint replacements and patients gained independence by increased mobility then it was good value for money:

- Patient F: ‘To be honest I don’t think you can put a price on quality of life and I don’t think any one of us could put a price on it.’
- Patient B: ‘If it stops you needing joint replacement as well that’s saved the national health a lot of money as well, won’t it?’
- Patient I: ‘It keeps you out of hospital and out of the beds.’
- Patient E: ‘The only thing is if we had to pay for it well then we wouldn’t be able to afford it.’

Conclusions

The use of qualitative methodology in this study has enabled us to gain a fuller picture of the patients’ perspective of being treated with this new class of drugs for RA. The majority had found the agents to be effective and safe, and were pleased with the results. This is in accord with previous quantitative studies [3, 14, 15]. To our knowledge, this is the first qualitative study in this area. Interestingly, the improvements commented on by the patients concerned predominantly physical function, social role, morning stiffness, pain and well-being. Of these, only physical function (as measured by the HAQ) and pain (measured by the patient visual analogue rating scale) are included in the core set of measurements routinely recorded in clinical trials in RA. Inclusion of quality of life measures is recommended in research and in audit [16]. It is conventionally measured using standard questionnaires [6, 17], and improvement has been shown with anti-TNF therapy [18, 19], but there is evidence that outcomes that matter to patients are not always measured [20] or measurable [7] using currently available instruments. Social role and domestic function have previously been shown to be of high importance to patients with RA [21]. The impact of RA on patients is multidimensional [22, 23] and is not fully understood or measurable.

Concerns related to lack of efficacy in a small number of cases, sometimes temporarily between infusions, and the length of time taken to regain therapeutic effect after discontinuation and restarting of therapy. Very few patients in our unit had discontinued therapy, and continuation rates elsewhere have been reported to be high [24] suggesting that rates of serious adverse events are low, and that patients find the drugs worthwhile. There were concerns about the process of the British Society for Rheumatology Biologics Registry, in terms of having to pass a threshold of assessment to be considered, and then having to wait for approval for funding. Once started on treatment, patients were keen to participate in the Registry process, for personal and altruistic reasons, and were appreciative of the benefits for others. One concern held by many clinicians and patients is that the conditions for response meriting continuation of the drug required by the Registry may mean that patients who have experienced improvements in well-being on these therapies, which are hard to measure, may not meet other criteria for continuation for therapy, despite apparent benefit.

Patients showed diversity in their wish for information about the new drugs before they were started. Some deliberately avoided it whilst others had sought information beyond that given routinely by the department. Some of this information was perceived by the patients, in hindsight, as over-optimistic and had led to some disappointments with the drugs’ effects. This should be considered in the provision of education for patients considering treatment with anti-TNF agents and it may be worth specifically cautioning them about such external sources of information. Patients’ expectations of the effects of therapy are important factors in their adherence to treatment plans and their opinions on drug efficacy [25]. The patients’ view that these agents should be used earlier in disease is of interest. They have been shown to be effective in early disease, more so than methotrexate [1] but the difference in effect is not always prolonged [26]. Previous work has shown a diversity of views amongst patients about prioritization decisions for therapy for RA [27] and the need for different approaches at different stages of disease [28].

Anti-TNF agents appear to be rapidly and highly effective for the majority of patients with RA, with relatively low rates of adverse effects [2]. Our patients report a greater range of benefits than those routinely measured in clinical trials. Qualitative research can give additional information beyond and complementary to that derived from randomized controlled trials.

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<thead>
<tr>
<th>Rheumatology</th>
<th>Key messages</th>
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<tr>
<td>Anti-TNF therapy has effects in many health dimensions.</td>
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<tr>
<td>Patients have personal and altruistic reasons for registry participation.</td>
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<td>Qualitative research adds to understanding of information from clinical trials.</td>
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References


