Switching to biosimilar infliximab: real world data in patients with severe inflammatory arthritis

Sir,

The monoclonal antibody Remicade (infliximab), was licenced in Europe in 1999 for treatment of rheumatoid arthritis (RA). Its use is now widespread and has expanded to treatment of ankylosing spondylitis (AS) and psoriatic arthritis (PsA) (1). The patent for originator Remicade (infliximab) has expired in Europe, allowing pharmaceutical companies to develop biosimilar versions (2). A biosimilar form of originator Remicade (infliximab), initially called CT-P13, was approved for use in Europe in 2013 (3). The guidelines for evaluation of a biosimilar product are stringent (2, 3). A randomised, international, phase III study has compared CT-P13 biosimilar infliximab with the originator product Remicade (infliximab), and demonstrated no difference in clinical efficacy or safety in patients with RA (4). However, adoption of biosimilar infliximab in UK clinical practice remains limited.

The aim of this study was to provide real-world UK follow-up data comparing treatment of inflammatory arthritis (IA) with Remicade (infliximab) versus the biosimilar agent Inflectra (infliximab). Due to current UK rules governing the use of biological therapies all patients had severe, longstanding IA.

All patients receiving Inflectra (infliximab) via the Southampton Biological Therapies Review Service were identified, and patients who commenced treatment without prior use of Remicade (infliximab) were excluded (n=6). All remaining patients receiving Remicade (infliximab) were switched to biosimilar Inflectra (infliximab) from May 2015 onwards. A consultant rheumatologist discussed the potential switch with all patients in clinic in advance and a letter giving details of the switch, an Inflectra (infliximab) information sheet and a helpline number were collated for all patients who stopped treatment. The patient demographics are listed in Table I. Since switching most individuals have received ≥3 infusions of the originator product Remicade (infliximab), prior to commencing the switching process, to allow direct comparison during the follow-up period.

59 patients receiving Remicade (infliximab) were switched to Inflectra (infliximab) at the same dose. The patient demographics are listed in Table I. Since switching most individuals have received ≥3 infusions of the originator product Remicade (infliximab), prior to commencing the switching process, to allow direct comparison during the follow-up period.

59 patients receiving Remicade (infliximab) were switched to Inflectra (infliximab) at the same dose. The patient demographics are listed in Table I. Since switching most individuals have received ≥3 infusions of the originator product Remicade (infliximab), prior to commencing the switching process, to allow direct comparison during the follow-up period.

59 patients receiving Remicade (infliximab) were switched to Inflectra (infliximab) at the same dose. The patient demographics are listed in Table I. Since switching most individuals have received ≥3 infusions of the originator product Remicade (infliximab), prior to commencing the switching process, to allow direct comparison during the follow-up period.

59 patients receiving Remicade (infliximab) were switched to Inflectra (infliximab) at the same dose. The patient demographics are listed in Table I. Since switching most individuals have received ≥3 infusions of the originator product Remicade (infliximab), prior to commencing the switching process, to allow direct comparison during the follow-up period.

59 patients receiving Remicade (infliximab) were switched to Inflectra (infliximab) at the same dose. The patient demographics are listed in Table I. Since switching most individuals have received ≥3 infusions of the originator product Remicade (infliximab), prior to commencing the switching process, to allow direct comparison during the follow-up period.

59 patients receiving Remicade (infliximab) were switched to Inflectra (infliximab) at the same dose. The patient demographics are listed in Table I. Since switching most individuals have received ≥3 infusions of the originator product Remicade (infliximab), prior to commencing the switching process, to allow direct comparison during the follow-up period.

59 patients receiving Remicade (infliximab) were switched to Inflectra (infliximab) at the same dose. The patient demographics are listed in Table I. Since switching most individuals have received ≥3 infusions of the originator product Remicade (infliximab), prior to commencing the switching process, to allow direct comparison during the follow-up period.

59 patients receiving Remicade (infliximab) were switched to Inflectra (infliximab) at the same dose. The patient demographics are listed in Table I. Since switching most individuals have received ≥3 infusions of the originator product Remicade (infliximab), prior to commencing the switching process, to allow direct comparison during the follow-up period.

59 patients receiving Remicade (infliximab) were switched to Inflectra (infliximab) at the same dose. The patient demographics are listed in Table I. Since switching most individuals have received ≥3 infusions of the originator product Remicade (infliximab), prior to commencing the switching process, to allow direct comparison during the follow-up period.

59 patients receiving Remicade (infliximab) were switched to Inflectra (infliximab) at the same dose. The patient demographics are listed in Table I. Since switching most individuals have received ≥3 infusions of the originator product Remicade (infliximab), prior to commencing the switching process, to allow direct comparison during the follow-up period.

Table I. Characteristics of the 59 patients switched from Remicade (infliximab) to Inflectra (infliximab).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients switched to biosimilar (n=59)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (S.D.)</td>
<td>58.9 (13.1)</td>
</tr>
<tr>
<td>Gender: female, n (%)</td>
<td>30 (51)</td>
</tr>
<tr>
<td>On methotrexate (%)</td>
<td>33 (56)</td>
</tr>
<tr>
<td>On other DMARD (%)</td>
<td>10 (17)</td>
</tr>
</tbody>
</table>

Table II. Comparison of rates of inefficacy and adverse events in Remicade (infliximab) vs. Inflectra (infliximab).

<table>
<thead>
<tr>
<th>Reason for stopping</th>
<th>12 months prior to switching whilst using Remicade n=67</th>
<th>12 months after switching whilst using Inflectra n=59</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inefficacy</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Adverse events</td>
<td>7</td>
<td>4</td>
</tr>
</tbody>
</table>

* Included 2 deaths: 1 out of hospital cardiac arrest (probable ischaemic event causing VF); 1 death due to malignancy, non-healing foot ulcers, low grade lymphoplasmacytic lymphoma, influenza requiring admission to ICU, infusion reaction, neutropathy.

Inflectra (infliximab) with 51 (86%) continuing at mean follow-up 362 days (12.1 months). During the 12.1 months of follow-up, 8 patients have discontinued treatment with Inflectra (infliximab); 4 patients due to clinical inefficacy and 4 following an adverse event (AE). Of these, 4 patients have switched back to Remicade (infliximab), 2 have switched to ustekinumab, 1 to rituximab, and 1 patient remains off all biological therapy.

The follow-up period on Inflectra (infliximab) of mean 12.1 months has been directly compared with the preceding 12 months of treatment with Remicade (infliximab). Table II shows the rates of both inefficacy and AEs on Inflectra (infliximab) compared to the preceding 12 months of Remicade (infliximab) which are comparable.

Four patients have discontinued Inflectra (infliximab) due to inefficacy (1 RA: DAS-28 prior 1.89, post 5.31; 1 RA: DAS-28 prior 4.72, post 3.31; 1 AS: BASDAI prior 5.2; post 8.0, 1 PsA with grade 3 synovitis on ultrasound of the wrist). All 4 of these patients were switched back onto Remicade (infliximab) in the first instance, but one (RA) developed secondary failure after switching back to Remicade (infliximab) with a flare of disease requiring treatment with corticosteroids, and is now on rituximab therapy.

Four AEs have occurred during the period of follow-up, 3 in patients with PsA and 1 in a patient with RA. One patient developed widespread skin following 2 infusions, which resolved on switching back to Remicade (infliximab). One patient developed myalgia following 2 infusions, and was switched to ustekinumab. One patient reported multiple side-effects also present prior to switching to Inflectra (infliximab); diz-

Clinical and Experimental Rheumatology 2018
In conclusion, from the data provided in this study, there does not appear to be any significant difference in the safety profile or efficacy of Inflectra (infliximab) versus Remicade (infliximab) in real world use. In addition, patients appear accepting of this change.

C.R. Holroyd1,2
L. Parker1
S. Bennett1
J. Zarroug1
C. Underhill1
B. Davidson1
R. Armstrong1
N.C. Harvey2
E. Dennison2
C. Cooper1
C.J. Edwards1,3

1Musculoskeletal Research Unit, University Hospital Southampton NHS Foundation Trust;
2MRC Lifecourse Epidemiology Unit, University of Southampton; 3NIHR Welcome Trust Clinical Research Facility, University Hospital Southampton NHS Foundation Trust, UK.

Please address correspondence to: Dr Christopher Holroyd, Rheumatology Department, University Hospital Southampton, Tremona Road, Southampton SO16 6YD, United Kingdom. E-mail: christopher.holroyd@uhs.nhs.uk

Competing interests: C. Holroyd has delivered educational talks and taken part in advisory boards for Abbvie, UCB, BMS, Janssen, Roche and Novartis; C. Underhill has received honoraria from Pfizer; C. Cooper has received consultancy fees and honoraria from Amgen, Eli Lilly, GSK, Medtronic, Merck, Novartis, Pfizer, Roche, Servier, Shire, Takeda and UCB; C.J. Edwards has received research support, delivered educational talks and taken part in advisory boards for Abbvie, Pfizer, MSD, Biogen, Celltrion, Napp, Roche, Celgene, UCB, and Samsung Bioepis; the other co-authors have declared no competing interests.

Received on April 8, 2017; accepted in revised form on June 12, 2017.

© Copyright CLINICAL AND EXPERIMENTAL RHEUMATOLOGY 2018.

References