Table 1. Sequential use of biologics in PsA.

	First line biologic	Second line biologic	Third line biologic	Fourth line biologic
Patients (n)	548	94	18	1
Reasons for switching (n)	–	Inefficacy: Secondary: 41 Primary: 27 Adverse events: 20 NR: 6	Inefficacy Secondary: 3 Primary: 15	Inefficacy Primary: 1
Biological drug (n)				
Adalimumab	350	46	5	–
Etanercept	186	36	2	–
Infliximab	11	6	7	–
Golimumab	1	3	2	–
Certolizumab pegol	–	1	–	–
Rituximab	–	2	1	–
Tocilizumab	–	–	–	1
Ustekinumab	–	–	1	–
Outcome of switching (%)				
Adequate response to 2nd biologic	–	52	–	–
Adequate response to third/fourth line biologic	–	8	–	–
Awaiting follow up*	–	2	–	–
Adverse events	–	19	–	–
Inadequate response	–	19	–	–

NR = not recorded; PsA = psoriatic arthritis.
*Awaiting assessment of disease activity after switching at time of survey.

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JONATHAN GAMBLE
Foundation year 1 doctor

VEDAMURTHY ADHIYAMAN
Consultant geriatrician

Department of Care of the Elderly, Glan Clwyd Hopsital, Rhyl, UK

Effectiveness of switching between biologics in psoriatic arthritis- results of a large regional survey

The outlook of chronic inflammatory conditions such as rheumatoid arthritis (RA), spondyloarthritis, psoriasis and inflammatory bowel disease has been revolutionised by the use of tumour necrosis factor inhibitors (TNFi). In the management of moderate to severe psoriatic arthritis (PsA), infliximab, etanercept and adalimumab were approved by The National Institute of Health and Care Excellence (NICE) by August 2007, followed by golimumab in April 2011. Although NICE permits the use of sequential biologics in RA, it states that, at present, there is 'insufficient data to make a recommendation on the sequential use of TNF inhibitors in psoriatic arthritis'[1] Increasingly, PsA patients who fail on first line TNFi therapy due to inefficacy or adverse effects are left with no further therapeutic options due to their local care provider strictly adhering to NICE guidance. There have been no randomised controlled trials of switching between TNFis in PsA and until recently there has been limited evidence to support this practice.

We conducted a regional survey in the north-west of England of PsA patients who started biologic therapy between August 2007 and June 2012. The aims were to assess compliance with current NICE guidance with regards to sequential TNFi use and the effectiveness of switching biologics. Every centre in the region participated; most sites included all eligible patients, representing an accurate reflection of current practice.

We collected data on 548 patients with PsA across 18 sites in the region. Median age was 49 years (interquartile range[IQR]

40–57 years) and 51% of patients were female. Median time from diagnosis to starting TNFi was 4.6 years (IQR 2.0–10.0 years). At baseline, 72% were on a concomitant disease modifying anti-rheumatic drug, of which 84% comprised methotrexate. The majority of patients were started on adalimumab first line (64%), followed by etanercept (34%), infliximab (2%) and golimumab (1%). At 12-week assessment, 74% of patients had an adequate response to TNFi. The main reason for cessation of initial biologic and sequential use was secondary inefficacy initial response followed by lack of efficacy over time (Table 1). Of all PsA patients on TNFi, 17% switched between biologics against NICE guidance (n = 94), with a further 3% switching between 3–4 biologics (n = 19) (Table 1). Subsequent lines of biologics included TNFis, but also treatments not currently licensed for PsA such as certolizumab pegol, rituximab, ustekinumab and tocilizumab. Only 24% of switchers obtained permission from their primary care trust (PCT) and four patients across the region had an individual funding request for switching rejected. PCTs varied significantly regarding their policy on switching TNFis in PsA patients – certain trusts therefore resorted to labelling their PsA patients 'RA with psoriasis' to allow eligibility for a second biologic.

The majority of patients (60%) were recorded to have an adequate response to a second or third line biologic, with a further 18% of switched patients awaiting assessment of their disease activity at the time of survey. These results support the effectiveness of switching biologics in PsA and are in line with the latest British Society Of Rheumatology[2] and European guidelines.[3] Recently published European data has shown that, although there may be a reduced response to a second or third TNFi when compared to first line therapy,[4] a significant proportion still have a substantial response. The mechanisms behind secondary inefficacy are not fully elucidated. However, in monoclonal antibodies this may be due to the development of anti-drug antibodies. Detection of these in clinical practice may help predict response to switching biologics, as reported in a recent study,[5] and may be a potential cost-effective strategy to stratify patients in the future. In the interim, with tighter commissioning regulations, local care providers are likely to comply rigorously with NICE appraisals, therefore highlighting a need for updating current guidance to allow more therapeutic alternatives for the most severely affected PsA patients.

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MEGHNA JANI[1]
ELIZABETH MACPHIE[2]
CHANDANI RAO[3]
SARAH MOORE[4]
HODA MIRJAFARI[5]
YOKEMIE MCLOUGHLIN[4]
HECTOR CHINOY[1,6]
PREETI SHAH[4]

[1]*Arthritis Research UK Epidemiology Unit, The University of Manchester, Manchester Academic Health Science Centre, Manchester, UK;*
[2]*Royal Preston Hospital, Lancashire Care Foundation Trust, Preston, UK;*
[3]*Blackpool Teaching Hospitals NHS Foundation Trust, Blackpool, UK;*
[4]*Trafford General Hospital, Central Manchester University Hospitals NHS Foundation Trust, Manchester, UK;*
[5]*University Hospital of South Manchester NHS Foundation Trust, Manchester, UK;*
[6]*The University Of Manchester Rheumatic Diseases Centre, Salford Royal NHS Foundation Trust, Salford, UK*