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Personalised medicine: using infliximab drug trough and anti-drug antibody levels improves clinical treatment decisions and is cost effective in spondyloarthritis and psoriatic arthritis

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Aims

Personalised medicine tailors treatment to the individual's needs. The advent of biosimilars has led to therapy re-appraisals driven by the clinical commissioning group's demand for cost-effective interventions. Yet biologic drug dosing is standardised and little is known about the rationale and efficacy of dose adjustment. As part of a service evaluation exercise within the Leeds Spondyloarthritis (SpA) Service, we measured serum drug trough levels (DLs) and anti-drug antibodies (ADAbs) in our cohort of SpA patients receiving bio-originator infliximab (Remicade) with the aims of a) informing our decision making before a possible switch to biosimilar and b) assessing the possible impact of this approach to our clinical practice.

Methods

Eligible patients were identified, counselled and consented by an experienced specialist nurse on DLs and ADAb testing including the possible associated outcomes such as a change in drug class, dose and infusion time interval. Subjects were also counselled on switching from bio-originator infliximab to the biosimilar infliximab CT-P13 (Infectra). We developed a treatment algorithm to act as a guide for the treating physician. Clinical and outcome data were recorded as per NHS practice including concomitant disease modifying anti-rheumatic drugs (DMARDs), disease status and the DLs and ADAb titre.

Results

A total of 35 subjects were identified. Infliximab was discontinued in two (6%) subjects, dose interval was extended in 6 (17%) and decreased in one (3%; Table 1). The infliximab dose was reduced in two (6%) patients with no change in time interval. Two patients (6%) changed to an alternative biologic either within the same class or to a different mode of action due to persistent high disease activity on infliximab. ADAbs were absent in 14 of 16 (86%) subjects on concomitant methotrexate. Very high titre ADAbs were identified in four (11%) subjects with corresponding very low or undetectable DLs indicating a highly likely drug-neutralising effect. A total of 20 (57%) subjects were switched to a biosimilar. The total cost-savings were an added £25,720 per annum over the estimates for 'blind' switches of £34,000.

Conclusion

These data from a small cohort suggest that measuring ADAbs and DLs to characterise treatment response and inform biosimilar switching is a clinically efficacious and cost-effective strategy in infliximab-treated SpA patients. We anticipate further significant savings with our cohort receiving subcutaneous therapies. This approach unlocks the potential of 'personalised medicine' which supports individualised treatment and brings significant savings to the NHS. ■

Table 1. Patient characteristics

Patient characteristics	Diagnosis	
	axSpA (n=22, 61%)	PsA (n=13, 39%)
Male:female ratio	21:1	3:11
Concomitant csDMARD, n (%), proportion by drug, n (%) drug	10 (45), 10 (100) MTX	8 (62), 7 (86) MTX and 1 (14) HCQ
Previous biologic drug:		
Adalimumab, n (%)	2 (9)	2 (15)
Etanercept, n (%)	1 (5)	2 (15)

axSpA = Axial spondyloarthritis; csDMARD = conventional synthetic disease-modifying antirheumatic drug; HCQ = hydroxychloroquine; MTX = Methotrexate; PsA = psoriatic arthritis.

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Table 2. Results

Results, n (%)	axSpA (n=22, 61%)	PsA (n=13, 39%)
Positive ADAbs	8 (22)	2 (15)
Therapeutic drug levels	14 (39)	6 (43)
High ADAbs and very low or undetectable drug (likely drug-neutralising)[1]	2 (9)	2 (15)
Drug discontinuation (no alternative biologic required)[2]	1 (5)	1 (5)
Change to alternative biologic (either within same class or different mode of action biologic)[3]	0 (0)	2 (6)
Switched to biosimilar	12 (54)	8 (62)

[1]Undetectable DL in 3 subjects.
[2]Subjects in clinical remission and undetectable drug level.
[3]One subject with active skin disease (PsA) and one subject with active joint disease (PsA).
axSpA = Axial spondyloarthritis; PsA = psoriatic arthritis.