Recapturing adequate control of psoriasis by additional immunosuppressive agents alongside ustekinumab

Prativa S. Jayasekera, BM Medicine, MRCP DERM, Richard A. Parslew, MBCHB, FRCP, and Ali Al-Sharqi, MBCHB, FRCP
Liverpool, United Kingdom

Key words: biological therapy; psoriasis; ustekinumab.

INTRODUCTION

Etanercept, adalimumab, infliximab, and ustekinumab are all biologic therapies licensed for the treatment of chronic plaque psoriasis in the United Kingdom. Although these therapies have advanced the treatment of psoriasis, they can lose effectiveness with time.[1]

Three studies looked at drug survival in particular.[2-4] Warren et al[2] found that in biologic-naïve patients, negative predictors of drug survival were female sex, being a current smoker, having a higher baseline Dermatology Life Quality Index (DLQI), and taking etanercept or infliximab. Positive predictive factors were having psoriatic arthritis and taking ustekinumab. A model for discontinuation because of ineffectiveness found that one of the predictors for discontinuation is a body mass index greater than 35. Warren et al[2] found that survival with biologic therapies decreases over time—77% in the first year, 63% in the second year, and 53% in the third year. Interestingly, ustekinumab had the highest survival rate compared with all the other anti–tumor necrosis factor inhibitors.

Gniadecki et al[4] analyzed data derived from the Danish biologics national registry. Etanercept was found to have the shortest drug survival compared with ustekinumab, which had the longest long-term survival. A total of 81.9% of patients on ustekinumab, as a first biologic, still remained on this therapy 4 years later, and when all patients, biologic naïve and nonnaïve, were included, this percentage decreased to 70% at 4 years.[3]

One possible mechanism in which biologics lose their efficacy is the presence of antidrug antibodies (ADA).[5] Biologic therapies include fusion proteins and monoclonal antibodies. Monoclonal antibodies can either be murine, chimeric, or fully human. Monoclonal antibodies generate variable immunogenic responses and ADA depending on their type with the fully humanized being the least immunogenic.[6,7]

Abbreviations used:

ADA: antidrug antibodies
DLQI: Dermatology Life Quality Index
PASI: Psoriasis Area and Severity Index

METHODS

We undertook a retrospective survey of all patients who took concomitant immunosuppressive agents while taking ustekinumab for psoriasis from October 2009 to April 2015 in an attempt to improve the biologic drug survival at the first indication of loss of efficacy. A total of 76 patients were treated with ustekinumab during this period, and 7 patients were identified who required additional immunosuppression in the form of methotrexate, fumaric acid esters, azathioprine, hydroxyurea, and acitretin. All 7 patients had chronic plaque psoriasis, and 2 had psoriatic arthritis.

RESULTS

Patients 1 through 7 are detailed in Table I. These patients had concomitant immunosuppressive agents with ustekinumab—2 women and 5 men. Two patients took methotrexate, 1 took fumaric acid esters, 3 took hydroxyurea, and 1 took azathioprine. Three patients were biologic naïve and 4 were

From the Royal Liverpool and Broadgreen Hospitals NHS Trust.
Funding sources: None.
Conflicts of interest: None declared.
Correspondence to: Prativa S. Jayasekera, BM Medicine, MRCP DERM, Dermatology Department, Kent Lodge, Royal Liverpool Hospital, Liverpool, Thomas Drive, L14 3LB. E-mail: prativaj@googlemail.com.

JAAD Case Reports 2016;2:310-4.
2352-5126
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http://dx.doi.org/10.1016/j.jdcr.2016.05.004

Table I. Seven patients who required additional immunosuppression while taking ustekinumab

Sex	Age, y	Body mass index	Previous systemic treatment	Previous biologic treatment	PASI/DLQI before ustekinumab	PASI and DLQI at wk 16	Duration between start of ustekinumab and additional immunosuppressive agent added, mo	Immunosuppressive agent	PASI before immuno-suppressive agent	PASI after immuno-suppressive agent	Total survival of ustekinumab in months
Female	47	36.1	Methotrexate, mycophenolate mofetil, hydroxyurea, fumaric acid esters, cyclosporine	None	20/23	0/0	12	Hydroxyurea, 500 mg 3 times a day	6.0	3	49
Male	55	25.6	Hydroxyurea, cyclosporine, acitretin, methotrexate	None	17.2/16	3.6/0	14	Methotrexate, 10 mg weekly	5.2	2.1	37
Male	32	31.5	Methotrexate, cyclosporine	Adalimumab	14.6/11	3/5	15	Fumaric acid esters, 30 mg 3 times a day	5.0	2.4	30
Female	64	47.5	Methotrexate	Adalimumab and infliximab	17.4/10	2.9/0	20	Methotrexate, 7.5 mg weekly	7.6	4.2	65
Male	40	20.4	Methotrexate, hydroxyurea, cyclosporine	None	16.1/13	2.4/1	18	Hydroxyurea, 500 mg twice a day	6.0	5	68
Male	47	32.2	Methotrexate, cyclosporine, acitretin, fumaric acid esters	Raptiva, infliximab, etanercept, adalimumab	20/30	10.8/11	12	Hydroxyurea, 500 mg 3 times a day	9.4	4.7	47
Male	65	30.1	Methotrexate, systemic 5 fluorouracil, cyclosporine, hydroxyurea, fumaric acid esters, acitretin	Etanercept, raptiva, infliximab, adalimumab	22.7/30	17.2/9	8	Azathioprine, 150 mg daily	6.9	4.6	54

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