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Dual biologic therapy for recalcitrant psoriasis and psoriatic arthritis

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Key words: combined biologic therapy; dual biologic therapy; psoriasis; psoriatic arthritis.

INTRODUCTION

Numerous biologic medications are available to treat psoriasis and psoriatic arthritis; however, many patients experience differential responses of their skin and joints to the same agent. In patients who do not respond to biologic monotherapy or combination of a biologic with an oral systemic agent, dual biologic therapy is a possible treatment option. Dual biologic therapy is rarely reported in the psoriatic literature (Table I).[1-6] We present a patient with severe psoriatic skin and joint disease who has been treated with multiple combinations of dual biologic therapy, including ustekinumab plus etanercept for 12 months, secukinumab plus etanercept for 6 months, and guselkumab plus etanercept for 15 months. Throughout the patient's treatment, adverse events only occurred with the ustekinumab plus etanercept combination and consisted of an increased incidence of urinary tract and upper respiratory infections, including a hospitalization for H2N1 flu.

Abbreviation used:

TNF: tumor necrosis factor

CASE REPORT

Our patient is a 38-year-old Asian woman with a longstanding history of severe, generalized psoriasis since age 12 and debilitating psoriatic arthritis since age 19. Her history includes numerous joint deformities of the hands and feet and both pustular and erythrodermic psoriasis flares. Her psoriasis was refractory to numerous topical therapies, phototherapy, and Goeckerman therapy.

Early in her treatment course, monotherapy was attempted with adalimumab followed by infliximab, but each was ineffective. She then began combination therapy with etanercept and methotrexate, which controlled her diseases for multiple years but eventually lost efficacy for the skin. She was then put on numerous medication combinations including etanercept plus cyclosporine, golimumab plus cyclosporine, and ustekinumab plus methotrexate. Cyclosporine and methotrexate were discontinued because of hypertension/elevated creatinine and intolerable gastrointestinal side effects, respectively. During this trial-and-error phase, the patient's joint disease improved on etanercept, whereas her skin cleared only with ustekinumab. After a particularly severe flare, the patient requested treatment with 2 biologics simultaneously, and after discussing the potential risks, dual biologic therapy was initiated with ustekinumab, 45 mg every 3 months, and etanercept, 50 mg weekly. Adequate control of her skin and joints was maintained for more than a year, but ustekinumab was eventually discontinued because of mild but frequent urinary tract and upper respiratory infections. She was also hospitalized once for H2N1 flu while on this regimen. Monotherapy with etanercept was again unable to control her psoriasis, so she was transitioned to secukinumab monotherapy and noted 90% improvement in her skin. Despite increasing the maintenance dose of secukinumab from 300 mg

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Table I. Reported cases of dual biologic therapy for psoriasis and psoriatic arthritis

	Patient age/sex	Diagnosis	Prior therapies	Combination biologic therapy	Dose	Follow-up (mo)	Adverse events
Cuchacovich et al[1]	38/Male	PsO + PsA	Infliximab, adalimumab, etanercept, abatacept, ustekinumab	Ustekinumab + etanercept	90 mg Q4W + 50 mg QW	>12	None
Heinecke et al[2]	23/Female	PsO + PsA	Ustekinumab	Ustekinumab + etanercept	90 mg Q8W + 25 mg BiW	8	None
				Ustekinumab + adalimumab	90 mg Q8W + 40 mg QW	Not reported	Furuncles and autoimmune hemolytic anemia
Babalola et al[3]	62/Male	PsO + PsA	Infliximab, adalimumab, etanercept, ustekinumab	Ustekinumab + etanercept	90 mg Q4W + 50 mg QW	6	Unstable angina requiring PCI with DES
Gniadecki et al[4]	67/Male	PsO + PsA	Infliximab, etanercept, adalimumab, ustekinumab	Ustekinumab + etanercept	90 mg Q12W + 50 mg QW	62	Herpes zoster flares
	39/Male	PsO + PsA	Etanercept, adalimumab	Ustekinumab + etanercept	90 mg Q12W + 25 mg QW	50	Retrotonsillar abscess
	49/Female	PsO + PsA	Etanercept, efalizumab, infliximab, adalimumab, ustekinumab	Ustekinumab + adalimumab	90 mg Q12W + 40 mg QoW	25	Erysipelas, bacterial pneumonia
				Ustekinumab + golimumab	90 mg Q12W + 100 mg Q4W	7	Skin infection of lower leg
	44/Female	PsO + PsA	Etanercept, infliximab, adalimumab	Ustekinumab + adalimumab	90 mg Q12W + 40 mg QoW	18	None
				Ustekinumab + certolizumab	90 mg Q12W + 200 mg QoW	36	None
Torre and Payette[5]	33/Male	Palmoplantar pustulosis	Mycophenolate, adalimumab	Ustekinumab + adalimumab	90 mg Q12W + 40 mg QW	8	None
Rathod et al[6]	46/Female	PsO + PsA	Adalimumab, guselkumab	Guselkumab + adalimumab	100 mg Q8W + 40 mg Q2W	6	None
Current study	38/Female	PsO + PsA	Adalimumab, infliximab, etanercept, golimumab, ustekinumab, secukinumab, guselkumab	Ustekinumab + etanercept	45 mg Q12W + 50 mg QW	12	Increased UTI/URI; hospitalized for H2N1 Flu
				Secukinumab + etanercept	300 mg Q2W + 50 mg Q4W	6	None
				Guselkumab + etanercept	100 mg Q4W + 50 mg QW	15	None

Numerous reports exist of dual biologic therapy including a TNF-α inhibitor and either alefacept or efalizumab. Because these agents are no longer available, they have not been included in this table.

BiW, Twice weekly; *DES*, drug-eluting stent; *PCI*, percutaneous coronary intervention; *PsO*, psoriasis; *PsA*, psoriatic arthritis; *QoW*, every other week; *QW*, once a week.

monthly to 300 mg every 2 weeks, her joint symptoms began to worsen. Etanercept, 50 mg weekly, was eventually added to her secukinumab therapy with marked improvement in joint disease activity. The patient continued on this dual biologic regimen for 6 months with good results, but unfortunately, her skin began to worsen. She was transitioned to guselkumab monotherapy and noted excellent skin clearance but continued to experience joint pain despite increasing the maintenance dose from 100 mg every 8 weeks to 100 mg every 4 weeks. Etanercept, 50 mg weekly, was eventually added to the guselkumab to address the joint symptoms.

The patient has now been on dual biologic therapy with 50 mg etanercept weekly and 100 mg guselkumab monthly for 15 months with no adverse events. Her psoriasis and psoriatic arthritis activity have remained minimal, and she is now able to complete her activities of daily living and is no longer forced to comply with an intensive daily topical regimen. She continues to follow closely with the dermatology and rheumatology departments for coordination of her care.

DISCUSSION

Physicians are often reluctant to prescribe dual biologic therapy because of safety concerns. Very little data exist regarding the safety of dual biologic medications for concomitant psoriasis and psoriatic arthritis. This finding is likely because most patients achieve disease control with biologic monotherapy or through combination with an oral systemic agent. Previous reports suggest a higher rate of infectious complications in patients receiving dual biologic therapy, but no large cohorts have been studied.[4] Additionally, the possibility of a major adverse cardiovascular event related to combined biologic therapy has been reported.[3] After careful discussion with our patient, she felt the benefit of potentially improving her severe skin and joint symptoms outweighed the potential safety concerns. Although she did note an increased incidence of upper respiratory and urinary tract infections while on the combination of etanercept and ustekinumab, it is difficult to assign causation; however, she has yet to experience any adverse events on her other dual biologic regimens.

The current literature on dual biologic therapy has only reported combining agents that target different inflammatory pathways (ie, anti–tumor necrosis factor [TNF] plus anti–interleukin 12/23, see Table I). For patients with comorbid psoriatic arthritis, close coordination with rheumatology may be helpful. In addition to concomitant psoriasis and psoriatic arthritis, dual biologic therapy has also been used successfully for recalcitrant palmoplantar pustulosis.[5]

Further study is needed to better characterize the efficacy and safety profile of dual biologic therapy. Future research should also examine the potential role of bispecific monoclonal antibodies in the treatment of psoriasis and psoriatic arthritis. A biologic inhibiting both TNF-α and interleukin-17A improved psoriatic skin and joint disease during a phase 2 trial.[7] For patients with severe, debilitating psoriatic disease who do not respond to biologic monotherapy and combination with oral systemic agents, dual biologic therapy could be considered.

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