MICRO LABS LIMITED

DERMA

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Dear Doctor,

Greetings from Micro Labs. We are happy to bring you "Derma Today" which contains latest and interesting news in the field of Dermatology.

This issue contains:

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Should you require any article or, medical information, please feel free to contact us
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Looking forward to your valuable feedback.

Best Regards,

Medical Team, Micro Labs Limited.

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Effect of Costimulatory Blockade With Abatacept After Ustekinumab Withdrawal in Patients With Moderate to Severe Plaque Psoriasis: The PAUSE Randomized Clinical Trial

Background:

Psoriasis is a systemic immune mediated disease that predominantly involves the skin and joints. Ustekinumab is a US FDA approved biologic agent for psoriasis that targets the IL-12/IL-23 pathways. Discontinuation of Ustekinumab leads to psoriasis relapse. Abatacept is a costimulatory-blocking fusion protein that consists of the extracellular domain of the CTLA4 ligand for CD80/CD86 coupled to a modified Fc portion of human IgG. Psoriasis relapse may involve compensatory T-cell activation pathways in the presence of CD28-CD80/CD86 blockade with abatacept.

Objective:

This study aimed to determine whether costimulatory signalling blockade with abatacept prevents psoriasis relapse after ustekinumab withdrawal.

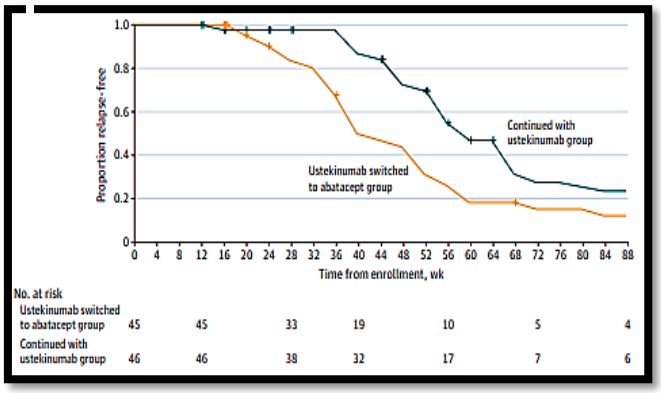
Methods:

This multicentre parallel-design, double-blind, placebo-controlled randomized clinical trial. The trial was divided into 3 phase lead-in phase (weeks 0 to 12), a randomized treatment phase (weeks 12 to 40), and an observation phase. 108 participants were enrolled and treated with open-label ustekinumab, with 91 being randomized for blind treatment. Each participant in the ustekinumab group had moderate to severe psoriasis vulgaris. Participants who weighed 100 kg or less received 45 mg per dose while participants who weighed more than 100 kg received 90 mg per dose. On week 12, participant's response to ustekinumab was assessed using the Psoriasis Area and Severity Index (PASI), and participants were eligible for randomization if they achieved 75% or greater improvement from baseline. The abatacept group received subcutaneous abatacept, 125 mg, which was administered weekly from weeks 12 to 39, and ustekinumab placebo at weeks 16 and 28. The ustekinumab group received ustekinumab at weeks 16 and 28 and abatacept placebo weekly from weeks 12 to 39. Additionally, statistical analyses were performed in the intention-to-treat (ITT) sample.

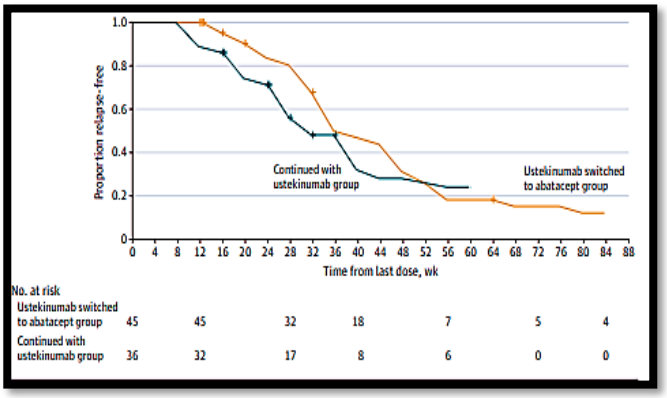
Results:

Investigators reported that more participants experienced psoriasis relapse in the abatacept group before week 88 compared to participants in the ustekinumab group (41 of 45 [91.1%] vs 40 of 46 [87.0%]; *P* = .41).

Time to psoriasis relapse since enrollment (week 0) for all participants in the ITT population



Time to psoriasis relapse since the last dose of ustekinumab for all participants in the ITT population who received the last scheduled



Additionally, the psoriasis relapse had not decreased in the abatacept group compared with the ustekinumab group, and the primary end point of psoriasis relapse between weeks 12 and 88 was not met. The median time to relapse from enrollment for the abatacept group was 40 weeks (95% CI, 40-52 weeks) and 60 weeks (95% CI, 56-68 weeks) in the ustekinumab group.

Conclusion:

This study concluded that psoriasis relapse that occurred after ustekinumab withdrawal was not prevented by abatacept treatment because it did not completely block the pathogenic psoriasis molecular pathways that led to relapse**.**

Reference:

Harris KM, et al. Effect of Costimulatory Blockade With Abatacept After Ustekinumab Withdrawal in Patients With Moderate to Severe Plaque Psoriasis: The PAUSE Randomized Clinical Trial. JAMA dermatology. 2021 Oct 13.

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Clinical Aspects in Stevens-Johnson syndrome and toxic epidermal necrolysis associated with acute severe ocular complications

Background:
Stevens Johnson syndrome and toxic epidermal necrolysis are severe, inflammatory cutaneous adverse reactions of the skin and mucous membranes.SJS is a less severe form, with skin sloughing of less than 10% of body surface area, whereas TEN is more severe, with sloughing of more than 30% of body surface area. When the involvement is greater than 10% but less than 30% of the body surface, it is referred to as the SJS/TEN overlap syndrome. Ocular complications are the major, severe, long-term sequelae of SJS/TEN overlap syndrome. Acute ocular complications develop in 43–81% of patients hospitalized for SJS/TEN while chronic ocular sequelae occur in 35%–63% of patient

Method:
In this retrospective cross-sectional study 47 patients with SJS/TEN were enrolled and were divided into two groups according to ocular severity at acute onset: non-severe ocular complications group (n= 27) with 0–2 ocular severity grades and severe ocular complications group (n= 20) with ocular severity grade 3. The mean initial visual acuity at the onset of SJS/TEN was compared in both groups. Multivariate logistic regression analysis was performed to find out the association between clinical parameters and biological markers and acute severe ocular complications in SJS/TEN.

Acute ocular severity grading of Stevens–Johnson syndrome and toxic epidermal necrolysis

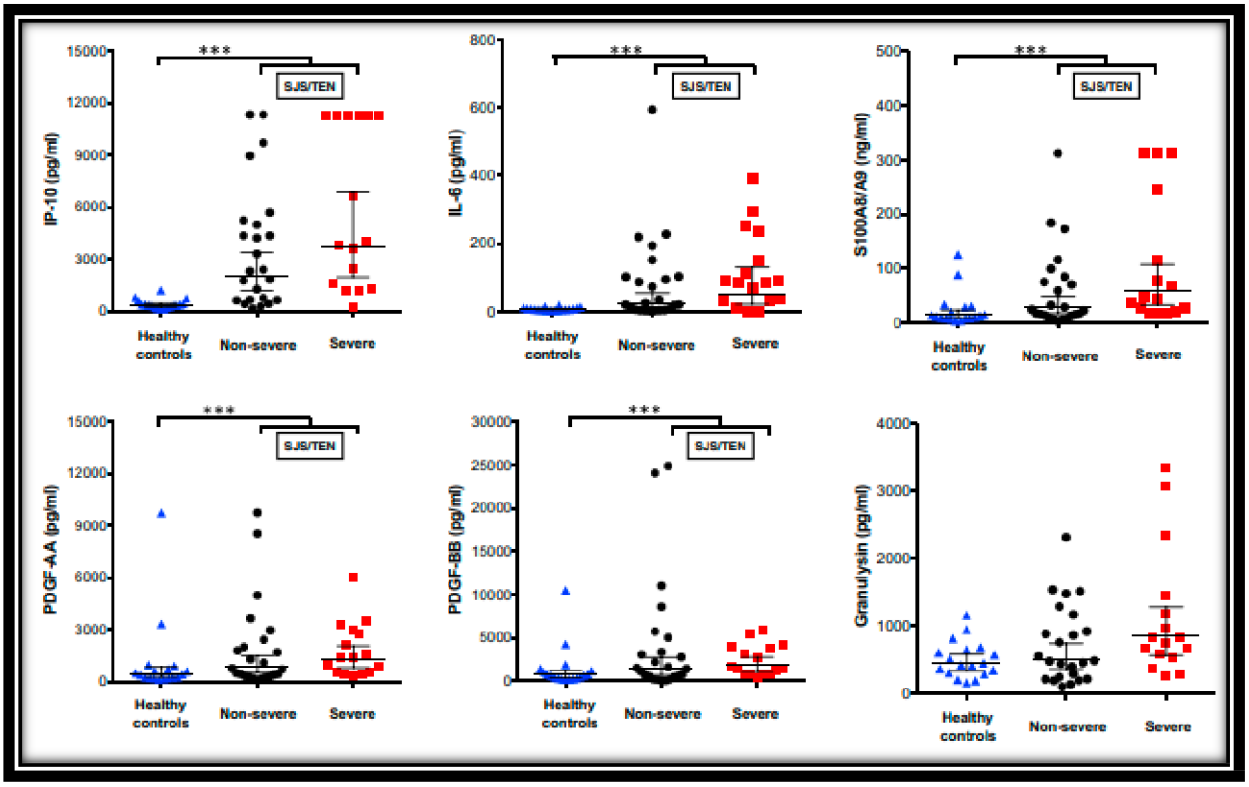
Acute ocular manifestations	Grade	Number of patients (%)
No ocular involvement	0	4 (8.51)
Conjunctival hyperaemia	1	11 (23.40)
Either ocular surface epithelial defect or pseudo membrane formation	2	12 (25.53)
Both ocular surface epithelial defect and pseudo membrane formation	3	20 (42.55

Causative drugs of Stevens–Johnson syndrome or toxic epidermal necrolysis

Causative drugs	Number of culprit drugs*	Percentage (%)
Antibiotics	19	35.84
Trimethoprim-Sulfamethoxazole	6	
Beta lactam	4	
Quinolones	2	
Isoniazid	3	
Rifampicin	3	
Dapsone	1	
Anticonvulsants	12	22.64
Phenytoin	6	
Carbamazepine	3	
Lamotrigine	3	
Allopurinol	9	17.00
Antifungal	4	7.55
Antiviral	2	3.77
NSAIDs	2	3.77
Cold remedies	1	1.89
Others	4	7.54
DMARDs	1	
Antiasthma (Doxofylline)	1	
Oral whitening pill containing gluthathione	1	
Cancer Immunotherapy (Atezolizumab)	1	

Results: Among the enrolled 47 patients, the mean SCORTEN score (mean±SD) was 1.80±1.27. The Severe ocular complications group showed higher scores than the non-severe ocular complications group (2.25±1.37 vs. 1.44±1.08). The mean initial visual acuity at the onset of SJS/TEN (log MAR_±SD) was comparable in both groups (0.37±0.53 and 0.46±0.57 in the non-severe group and severe group, respectively). Among all causative drugs, antibiotics were the most common cause (35.84%), followed by anticonvulsants (22.64%) and allopurinol (17.00%). Thirty-five patients (74.46%) had underlying diseases, including human immunodeficiency virus (HIV) infection (14 cases; 22.79%), autoimmune disease (6 cases; 12.76%), and malignancy (8 cases; 17.02%). 13 out of 14 patients with HIV infection (92.85%) had a CD4 count of less than 200 cells/µl (mean, 116.79±87.096; range 12–688).

Scatter plot graphs of serum biomarker levels (geometric means) in healthy controls, and those from patients with SJS/TEN with non-severe and severe ocular complications



Conclusion:

From the clinical factor analysis, disease severity (body surface area detachment≥10%) and older age were predictive factors for acute severe ocular complications in SJS/TEN. From the serum biomarker analysis, the levels of S100A8/A9, IP-10, IL-6, PDGFAA, and PDGF-BB were increased in the SJS/TEN group The S100A8/A9 and granulysin, levels tended to increase in the severe ocular involvement group, suggesting that S100A8/A9 and granulysin, are involved in the pathogenesis of SOCs and serve as helpful biomarkers to predict acute severe ocular complications in SJS/TEN. Two clinical factors BSA and older age, and increased levels of serum biomarkers, namely S100A8/A9 and granulysin, may guide clinicians in identifying high-risk groups that could develop acute severe ocular complications. Immediate treatment in these patients will minimize the chance of developing chronic ocular sequelae, leading to vision loss.

Source: Panpruk R, et al. Clinical parameters and biological markers associated with acute severe ocular complications in Stevens-Johnson syndrome and toxic epidermal necrolysis. Scientific Reports. 2021 Oct 12;11(1):1-0.

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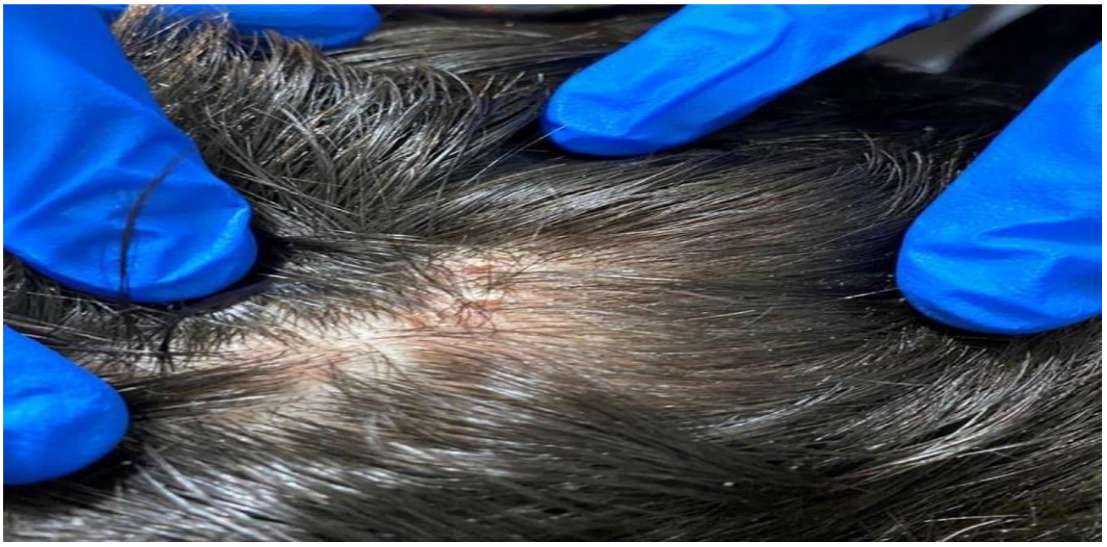
A case report of Rituximab induced psoriasis in a patient with multiple sclerosis

Background:
Rituximab is an anti-CD20 monoclonal antibody that is used as an off-labelled medication in multiple sclerosis. Rituximab, a biological agent has a chances of inducing new immune-mediated diseases such as psoriasis, ulcerative colitis and leukocytoclastic vasculitis. There are studies reporting the development of psoriasis following Rituximab therapy in patients with rheumatoid arthritis(RA), and glomerulonephritis. Hence, it becomes important to properly manage immune-related complications such as psoriasis in patients with Multiple Sclerosis.

Case Presentation:
A 39-year-old female patient, diagnosed with Multiple Sclerosis in 2005, based on McDonald criteria with initial presentation of left side optic neuritis, and typical demyelinating lesions in the brain MRI. Medical history revealed bipolar mood disorder, seizure and migraine as a consequence of Multiple Sclerosis for which patient was prescribed levetiracetam 500 mg BID and lithium 300 mg TDS for 4.5 years. Initially patient was prescribed with interferon beta-1a once weekly for 7 years (2005-2012), followed by interferon beta-1b every other day for 4 years (2012-2016) but in 2017 patient started developing severe depression and psychotic disturbances for which her medication was changed to natalizumab. One year later patient was diagnosed with John Cunningham virus and her medication was switched to Rituximab 1g every 6-months. After the 4th cycle of Rituximab, patient started developing scaly skin lesions on scalp, followed by an unbearable itching sensation. On initial evaluation, patient reports no previous history of skin lesions, eczema, allergy, uveitis, or arthritis nor had any vision problems or symptoms of pain or swelling in joints. Clinical evaluations revealed salivary plaques with erythematous base and scaling on the 2 distinct areas of crown and occipital region and there were no pathologic findings on extensor surfaces. Ophthalmologic and rheumatologic examinations showed no evidence of uveitis, synovitis, or arthritis. Later in November 2020, patient was diagnosed with psoriasis and was treated with topical corticosteroids for 4 months and was found to be effective.

Psoriatic plaques on the patient's scalp



Characteristics of the reported cases of new-onset psoriasis following rituximab treatment

First author, Date (Reference)	Age, Gender	Underlying disease	Skin manifestations	Confirmation by biopsy	RTX cycles	Time from the last cycle (months)	Outcome
Our case	39 y, female	Multiple sclerosis	Scalp	No	4	2	Resolved by topical corticosteroids
Alahmari, 2019 [Alahmari et al., 2019]	38 y, female	Granulomatosis with polyangiitis	Extremities, abdomen	Yes	3	3	Improved after switching to adalimumab and topical corticosteroids
Russo, 2018 [Russo et al., 2018]*	-	Inflammatory demyelinating polyneuropathy	-	-	-	-	-
Kim, 2016 [Kim et al., 2016]	6 y, male	Non-Hodgkin lymphoma	Trunk, face, scalp	Yes	3	1	Improved by topical corticosteroids, resolved after RTX D.C.
Aussy, 2015 [Aussy et al., 2015]	66 y, female	Granulomatosis with polyangiitis	No skin manifestation (presented with arthritis)	Yes	5	2	Arthritis resolved by MTX
Venables, 2015 [Venables et al., 2015]	53 y, female	Non-Hodgkin lymphoma	Palmoplantar pustulosis	No	9	1	Resolved after RTX D.C., and topical steroids
Fiorillo, 2014 [Fiorillo et al., 2014]	1.5 y, male	Immune thrombocytopenic purpura	Legs, arms, back, scalp	Yes	6	2	No response to topical hydrocortisone, resolved by MTX
Jayasekera,2014 [Jayasekera et al., 2014]	80 y, female	Rheumatoid arthritis	Plantar pustular psoriasis	No	6	12	Resolved by tocilizumab
Mok, 2014 [Mok et al., 2014]	51 y, male	Idiopathic membranous nephropathy	Trunk, limbs	No	4	3	Treated with topical steroid
Ozen, 2013 [Ozen et al., 2013]	50 y, female	Rheumatoid arthritis	Extremities	Yes	3	5	Stable with topical agents, deteriorated with next RTX cycle
Toussirot, 2013 [Toussirot, 2013]	44 y, female	Rheumatoid arthritis	Scalp	No	1	5	Without progression
Brunasso, 2012 [Brunasso and Massone, 2012]	45 y, female	Rheumatoid arthritis	Plantar pustulosis	Yes	1	4	Slightly improved by topical clobetasol, resolved by MTX
Guidelli, 2013 [Guidelli et al., 2013]	69 y, female	Rheumatoid arthritis	Arm, trunk	Yes	1	3	Resolved by topical fluticasone

Conclusion

Occurrence of psoriasis following treatment with rituximab could be explained by the removal of B- cells regulatory effect on T-cells following depletion with rituximab, a concomitant autoimmune disease with multiple sclerosis, and the development of a new autoimmune entity following long-term immunomodulation in a patient with multiple sclerosis. Psoriasis should be considered as a differential diagnosis in patients with typical skin lesions who are receiving rituximab and it can be continued if the psoriatic plaques are limited and respond properly to corticosteroids.

Source: Molazadeh N, Ala S, Karaminia M, Sahraian MA. Rituximab induced psoriasis in a patient with multiple sclerosis: a case report and literature review. Neuroimmunology Reports. 2021 Oct 1:100027.