MICRO LABS LIMITED

DERMA

Volume2| Issue 23|2021

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:

1. ***Efficacy of Brodalumab and Guselkumab in Patients with Moderate-to-Severe Plaque Psoriasis Who are Inadequate Responders to Ustekinumab: A Matching Adjusted Indirect Compariso***
2. ***Can SARS-CoV-2 vaccine increase the risk of reactivation of Varicella zoster? A systematic review***
3. ***Severe Pancytopenia and Stomatitis Case due to the Treatment with High Dose Methotrexate***

Should you require any article or, medical information, please feel free to contact us medicalservices@microlabs.in

Looking forward to your valuable feedback.

Best Regards,

Medical Team, Micro Labs Limited.

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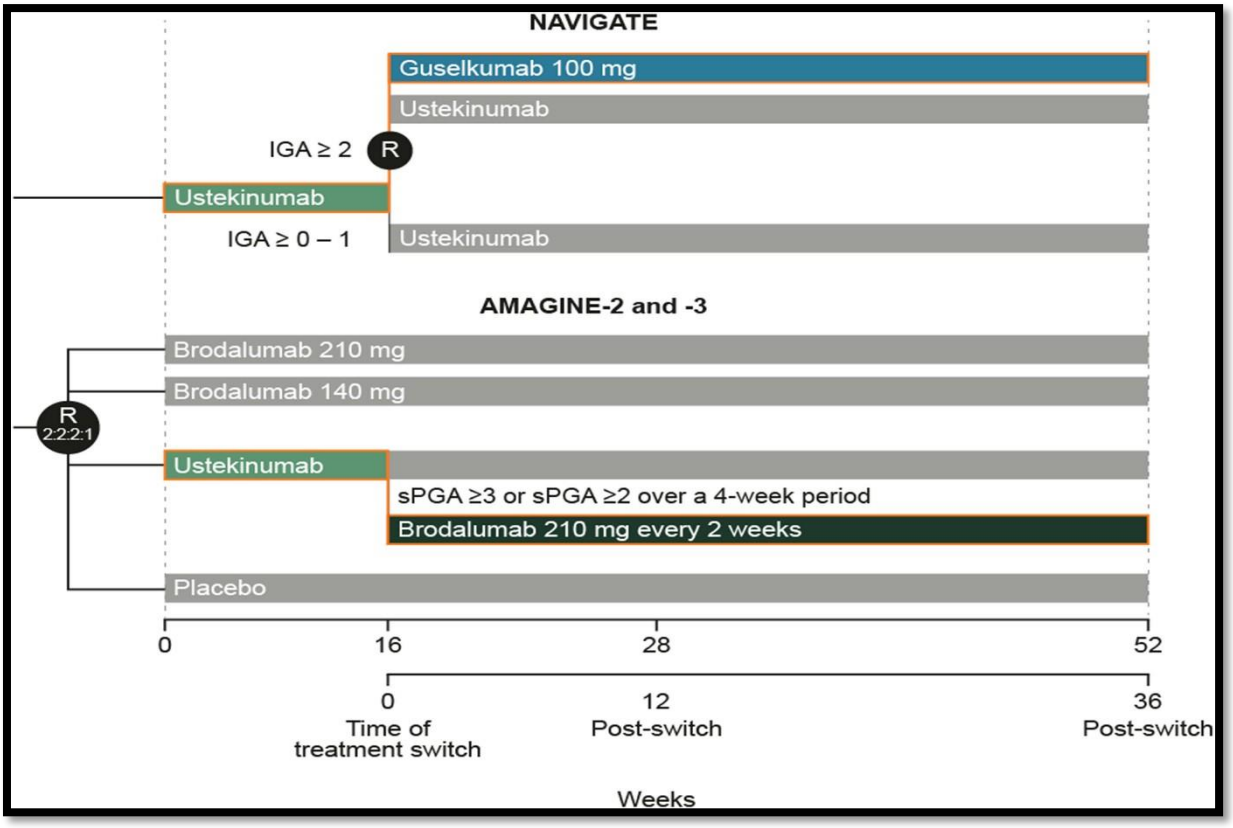
Efficacy of Brodalumab and Guselkumab in Patients with Moderate-to-Severe Plaque Psoriasis Who are Inadequate Responders to Ustekinumab: A Matching Adjusted Indirect Comparison

Introduction: With an increasing number of biological therapies available for the treatment of plaque psoriasis, data on relative efficacy in different patient populations has become important to optimize clinical decision making. Due to loss of response over time or drug relate adverse effects, many patients fail to respond initially or discontinue therapy. In such cases, switching to an alternative biological therapy remains the option. Brodalumab and guselkumab are approved for the treatment of moderate to severe plaque psoriasis in adult patients eligible for systemic therapies. In the absence of comparative randomized controlled trials, matching adjusted indirect comparisons can be used to estimate the relative efficacy of treatments.

Objective: This study aimed to find out if brodalumab shows greater improvements than guselkumab in inadequate responders to ustekinumab

Methods: Aggregate data for guselkumab were derived from the published navigate trial and IPD for brodalumab were pooled from the amagine-2 and amagine-3 trials. All three trials enrolled patients aged 18–75 years on biologic therapy for stable moderate-to- severe plaque psoriasis, with a psoriasis area and severity index score of ≥12, an investigator's global assessment score of ≥3, and involvement of ≥10% of body surface area. Navigate trial was a phase 3 trial that evaluated skin clearance in patients treated with guselkumab who previously had an inadequate response to ustekinumab. Patients received ustekinumab 45 or 90 mg at weeks 0 and 4 of a 16-week open label run in period. Patients with an inadequate response at week 16 were randomized to continued ustekinumab or guselkumab 100 mg at weeks 16, 20, 28, 36 and 44. Amagine-2 and −3 were two Phase III trials, identical in design, in which patients were randomized 2:2:1:1 to double-blind treatment with brodalumab 140 mg, brodalumab 210 mg, ustekinumab 45 mg (if body weight ≤100 kg) or 90 mg (if body weight >100 kg), or placebo. Patients receiving ustekinumab and not responding at week 16, were switched to rescue treatment of brodalumab 210 mg every 2 weeks. In the Amagine 2 and 3 trials, inadequate response to ustekinumab at week 16 was defined as a single static PGA (sPGA) ≥3 or sPGA ≥2 over a 4-week period. The sPGA that was used had a 6-point scale (0 to 5). All statistical analyses were performed using SAS version 9.4 or higher.

Trial designs of NAVIGATE and AMAGINE 2/3



Results: In the navigate trial, 6871 patients at weeks 0 and 4 received open-label ustekinumab 45 mg or 90 mg. 268 patients at week 16 had an inadequate response to ustekinumab and were randomized to double-blind treatment with continued ustekinumab (n = 133) or to guselkumab 100 mg (n = 135). In the amagine-2 and −3 trials, 124 of 590 patients (21.0%) had an inadequate response to ustekinumab at week 16 and were switched to brodalumab and three patients were excluded from the analyses as the data were missing. After reweighting, the effective sample size were 90 patients for PASI 90 (psoriasis area and severity index) and PASI 100, 89 for physician's global assessment and 75 for Dermatology Life Quality Index. Continued ustekinumab (n = 133) or to guselkumab 100 mg (n = 135), the 135 patients who switched from ustekinumab to guselkumab were included in this analysis. After inadequate response to ustekinumab, brodalumab resulted in significantly higher psoriasis area and severity index 90 rates vs guselkumab at post-treatment switch week 12 (62.7% vs 48.1%, relative difference 14.6% [95% confidence interval [CI] 5.3–23.9], p = 0.002 [number needed to treat [NNT] = 6.8]) and week 36 (63.7% vs 51.1%; relative difference 12.6% [95% CI 4.1–21.0]; p = 0.004 [NNT = 7.9]) and PASI 100 rate at week 36 (40.3% vs 20.0%; relative difference 20.3% [95% CI 11.8–28.7]; p < 0.001 [NNT = 4.9]).

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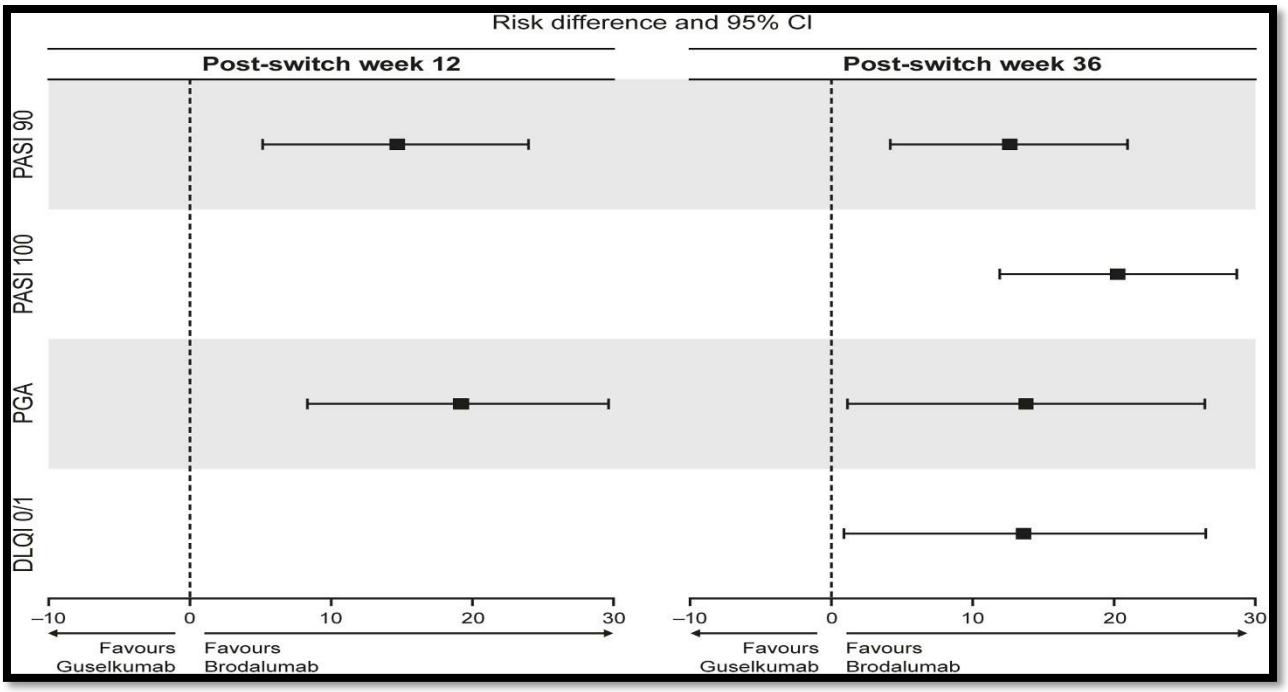
PASI 90, PASI 100, PGA and DLQI Rates with Brodalumab and Guselkumab After Switching from Ustekinumab

End points	Week after switch	Brodalumab, After Reweighting	Brodalumab, After Reweighting	Guselkumab	Unanchored risk difference	p-value	Effective sample size	NNT
PASI 90	12	57.9%(48.1-67.6%)	62.7%(48.1-67.6%)	48.1% (39.7–56.6%)	14.6% (5.3–23.9%)	0.002	90.2	6.8
	36	58.7%(57.1-60.2%)	63.7%(48.1-67.6%)	51.1% (42.7–59.5%)	12.6% (4.1–21.0%)	0.004	90.2	7.9
PASI 100	36	37.2%(37.0-37.4%)	40.3% (35.2–45.3%)	20.0% (13.3–26.7%)	20.3% (11.8–28.7%)	<0.001	90.2	4.9
PGA success	12	50.0%(48.8-51.2%)	50.2% (42.8–57.6%)	31.1% (23.3–38.9%)	19.1% (8.3–29.9%)	<0.001	89.2	5.2
	36	50.0%(46.5-53.5%)	50.0% (40.3–59.7%)	36.3% (28.2–44.4%)	13.7% (1.1–26.4%)	0.033	89.2	7.3
DLQI 0/1	36	45.1%40.4-49.8%)	52.5% (43.8–61.2%)	38.8% (29.4–48.2%)	13.7% (0.8–26.5%)	0.037	74.8	7.3

Forest plot of PASI 90, PASI 100, PGA success and DLQI 0/1 rates at 12 and 36 weeks after switching from ustekinumab.



Conclusion: In this Matching Adjusted Indirect Comparison, brodalumab showed greater improvements than guselkumab in inadequate responders to ustekinumab. Switching to brodalumab in patient with inadequate respond to ustekinumab may be a more effective strategy than switching to guselkumab.

Reference: Hampton P, Borg E, Hansen JB, Augustin M. Efficacy of Brodalumab and Guselkumab in Patients with Moderate-to-Severe Plaque Psoriasis Who are Inadequate Responders to Ustekinumab: A Matching Adjusted Indirect Comparison. Psoriasis: Targets and Therapy. 2021 Nov 3;11:123-31.

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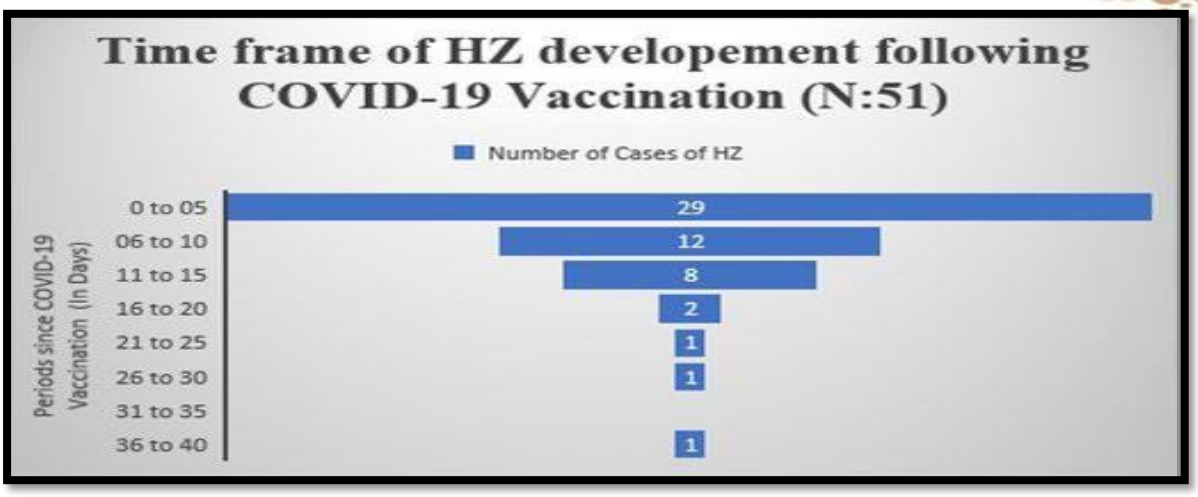
Can SARS-CoV-2 vaccine increase the risk of reactivation of Varicella zoster? A systematic review

Introduction: To prevent SARS-CoV-2 transmission, non-replicating viral vector vaccines, DNA-based or RNA-based vaccines, and inactivated vaccines, protein subunit recombinant vaccines have been developed recently. Adverse drug reactions after vaccination can be a coincidence or a direct result of the vaccine. unknown. Clinical studies have reported that the most common cutaneous adverse effects are injection site reaction, pruritus and allergic reactions such as urticaria and erythematous rashes. Study revealed various cutaneous conditions including anecdotal cases of erythema multiforme with morbilliform rash, delayed-type hypersensitivity reaction, bullous drug eruption, pernio/chilblains, erythromelalgia, and pityriasis rosea-like exanthems, and herpes zoster. Development of herpes zoster due to SARS-CoV-2 infection have been reported either at the time of disease progression or following recovery from the disease. In order to answer this question, a temporal relationship between vaccination and Adverse drug reactions is required, as well as a biological mechanism is necessary to explain the link.

Objective: To identify temporal relationship between COVID-19 vaccine and development of herpes zoster virus.

Method: Systemic review of articles was done from PubMed and Embase using MeSH and keywords like “Shingles,” “Herpes zoster,” “Varicella zoster,” “COVID-19,” “Vaccine,” “SARS-CoV-2.” No filters including country of publication, language, type of articles were applied. Individual case report references were filtered for any pertinent cases.

Results: 54 cases consisting of 27 male and 27 female patients were included in this study. Of 54 cases, 36 cases (> 50 years) had the past history of herpes zoster, 10 cases had immunological disorders, 25 cases were having chronic disease, 13 cases were known case of metabolic disorder,4 cases had malignancy, and 2 were having psychiatric disorder. The mean period between development of herpes zoster and COVID-19 vaccination was 7.64 days. Most of the cases were from the high-income and middle-income countries. 86.27% of the cases of Herper zoster were reported due to mRNA vaccine. 36 patients out of 45 (80%) developed herpes zoster following the priming dose of COVID-19 vaccine among those who received mRNA vaccine. 52 (96.07%)cases developed herper zoster within 1–3 weeks following COVID-19 vaccine. Among, 29 (50.98%) of the cases it developed within 1st week of vaccination irrespective of the number of vaccine dose. Only 1 case reported after the 1st month of COVID-19 vaccine.



Period of herpes zoster development following COVID-19 vaccination (n = 51)

Conclusion: This study could not establish definite link but there may be possible association between SARS cov2 vaccine and Herper zoster. Large-scale studies may help to understand the cause-effect relationship. Vaccinating older and immunocompromised patients requires strict monitoring.

Reference: Desai HD, et al. Can SARS-CoV-2 vaccine increase the risk of reactivation of Varicella zoster? A systematic review. Journal of Cosmetic Dermatology. 2021 Nov;20(11):3350-61.

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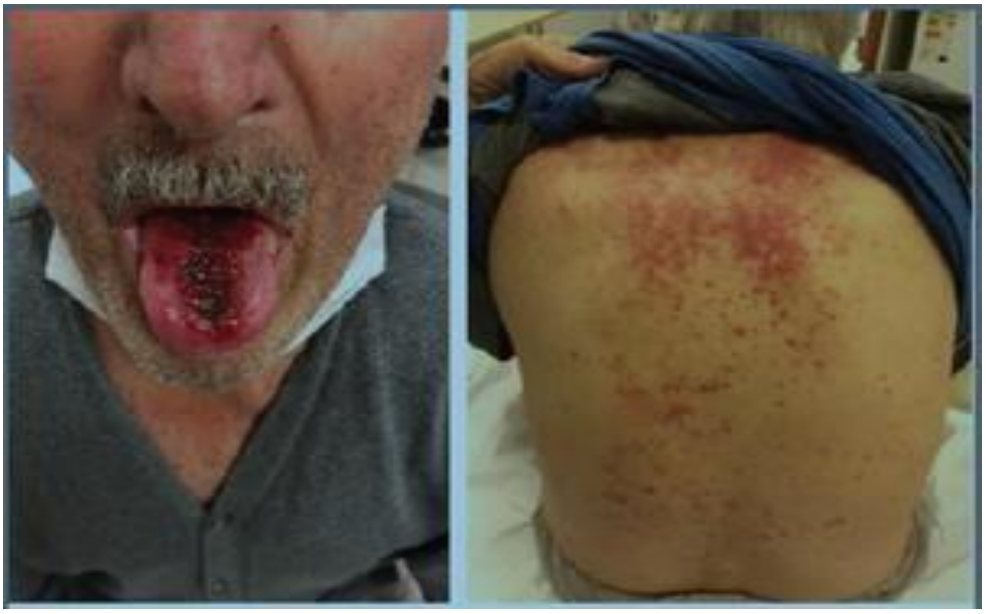
Severe Pancytopenia and Stomatitis Case due to the Treatment with High Dose

Introduction: Methotrexate is used to control severe psoriasis or rheumatoid arthritis, that has not responded to other treatments. It binds to dihydrofolate reductase and decreases thymidylate, purine synthesis and cell proliferation. It shows an anti-inflammatory effect by suppressing adhesion and chemotaxis of the neutrophils. It suppresses keratinocyte proliferation and dermal inflammatory infiltration by decreasing interleukin-22 levels.

Case Presentation: A 78-year-old patient diagnosed with psoriatic arthritis and benign prostatic hyperplasia. Patient had been using 5 mg of methotrexate as 2 tablets BD for 10 days, after diagnosed with psoriatic arthritis 15 days ago. Afterwards, patient showed up with the chief complaint of oral mucosal bleeding, rashes, decrease in oral nutrition and weakness to the emergency clinic. The physical examination revealed fever-36.8 Celsius degree, blood pressures- 120/60 mmHg, saturation-96%, and heart rate-90 beats per minute. Oral examination showed diffuse oral haemorrhagic lesions and palpable purpura overall the skin. Biochemical tests were within the normal range. Serum of vitamin B12, folate and ferritin were 1254 mg/dL, 10 mg/dL and 2000 mg/dL, respectively. Laboratory analyses revealed white blood cell count-1.5k/mm3, neutrophil count-0.01k/mm3, haemoglobin -7.3g/dL and platelet count-4000/mm3.According to the findings, patient was diagnosed with methotrexate intoxication with pancytopenia. Ceftriaxone and clarithromycin treatment were initiated along with dextrose infusion. Folinic acid 10mg/m2 for 6 days and 30 million units of filgastrim for 3 days were administered to reduce the effect of methotrexate. Oral antifungal and antiseptic solutions were given to treat oral lesions. 2 units of pooled platelets and 2 units of erythrocyte suspension were infused during clinical follow up. On the 6th day of the treatment, pancytopenia improved and oral lesions diminished and treatment was stopped. General condition of the patient improved and was discharged with full recovery.

Oral Haemorrhagic Lesions and Purpuric Skin Rash on the Back of the Patient.



Conclusion: Treatment with Methotrexate is a big challenge that all clinicians must be aware of. Methotrexate intoxication can cause serious clinical consequences. To prevent morbidity and mortality, it is essential to diagnose and initiate appropriate treatment without delay.

Reference: Tel BM, et al. Severe Pancytopenia and Stomatitis Case due to the Treatment with High Dose Methotrexate. National Journal. 2021;6(1):33.