Impact of Immunosuppressive Therapies on Shingrix Vaccine Response in Immune-Mediated Inflammatory Diseases

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Background

- **Shingrix™, a recombinant adjuvanted subunit vaccine, has been shown to be effective in reducing HZ risk, especially in older adults, by inducing strong CD4 and CD8 T-cell responses.** Although Shingrix has demonstrated safety and efficacy in various immunosuppressed populations, its direct use in patients with immune-mediated rheumatic diseases (IMRDs) has not been extensively studied. This study aimed to **evaluate and compare antibody responses to the Shingrix vaccine among patients with immune-mediated inflammatory diseases (IMIDs) receiving JAK inhibitors (JAKi), anti-TNF-alpha therapies, or methotrexate, alongside healthy controls matched for age and sex.**

Methods

- Participants, including patients with selected IMIDs and healthy controls, received two doses of the intramuscular Shingrix vaccine (0.5 mL each), spaced two months apart. Blood samples were collected 4–8 weeks after the second dose to assess post-vaccination antibody responses. These were measured using the **Anti-Varicella Zoster Virus (VZV) IgG Multiplex Flow Immunoassay (MFI).** Immune profiling was also conducted, evaluating **lymphocyte subpopulations (CD3+, CD4+, CD8+, CD19+), natural killer (NK) cells, total serum IgG and IgM levels, and VZV-specific IgG and IgM antibodies**, providing a comprehensive assessment of immune responses post-vaccination.

Results

- A total of **156 participants were enrolled in the study**, comprising **86 females (55%)** with a **mean age of 58.2 ± 10.1 years**. **Mean use of b/tsDMARDs was 23+40 months.**

- Post-vaccination humoral responses were significantly lower in the JAK-i group (86%) compared to anti-TNF/MTX (97%) and controls (100%, P = 0.03). **VZV IgG antibody levels were markedly lower in the JAK-i group (1842.28 ± 1146 U/mL) than in anti-TNF/MTX (3092.91 ± 830.19 U/mL) and controls (3048.70 ± 475.73 U/mL, P < 0.0001).**

- Results from multivariate regression analysis adjusted by age, gender and disease duration, **showed a negative correlation between VHZ-IgG and MTX cumulative dose (β=-0.28, p<0.0001), GC cumulative dose (β=-0.39, p<0.0001), history of treatment with more than 2 DMARDs (β=-0.26, p=0.001) and history of treatment with JAK-I (β=-0.49, p<0.0001) and positive correlations with NK cells (β=0.16, p=0.008) and IgG levels (β=0.35, p=0.0001).**

Conclusions

- This study found that **patients with immune-mediated inflammatory diseases (IMIDs) on JAK inhibitors had significantly lower vaccine responses to Shingrix compared to those on anti-TNF therapies or methotrexate, and healthy controls**. Factors such as higher cumulative doses of methotrexate and glucocorticoids, a history of multiple DMARDs, and JAK inhibitor use were associated with reduced antibody responses. These results suggest that immunosuppressive treatments, particularly JAK inhibitors, may impair vaccine effectiveness, highlighting the need for personalized vaccination strategies in these populations.

	JAK-I (93)	Anti-TNF and/or MTX (36)	Healthy controls (27)	P value
Diagnosis (n, %)				
SLE	3 (3%)	1 (3%)	-	0.89
PsA	34 (37%)	5 (14%)	-	**0.02**
SpA	17 (18%)	6 (17%)	-	0.83
RA	24 (26%)	22 (61%)	-	**0.0003**
Enteropathic arthritis	6 (6%)	1 (3%)	-	0.43
SAPHO	1 (1%)	0		0.92
IBD	7 (8%)	0	-	0.21
Vasculitis	1 (1%)	1 (3%)	-	0.50
History of more than 2 ts/bDMARDs (n, %)	58 (62%)	4 (11%)	0	**<0.0001**
History of herpes zoster before vaccination (n, %)	12 (13%)	3 (8%)	2 (7%)	0.62
Recurrence after vaccination (n, %)	5 (5%)	3 (8%)	0	0.17
Time with ts/bDMRD (months)	18.17+14.84	56.64+69.87	-	**<0.0001**
MTX cumulative dose (mg)	3510.5+3622	3341.5+3470	-	0.76
Glucocorticoid cumulative dose (mg)	2380.5+1982	2011.9+1045.7	-	0.65
Total serum IgG (mg/dL)	1033.84+261.7	1162.47+292.9	1074.9+284.2	0.20
Total serum IgM (mg/dL)	121.20+67.3	136.6+100.1	123.3+73.0	**0.02**
Humoral response (n,%)	80 (86%)	35 (97%)	27 (100%)	**0.03**
VZV IgG antibody concentration(mUI/mL)	1842.28+1146	3092.91+830.19	3048.70+475.73	**<0.0001**
CD3 (cells/mm3)	1241.75+533.9	1269.4+582.7	1285.8+525.5	0.30
CD19 (cells/mm3)	210.57+39.0	362.7+60.5	228.4+181.5	0.74
CD4 (cells/mm3)	860.7+376.2	869.2+362.8	977.9+343.84	0.99
CD8 (cells/mm3)	374.0+183.1	400.9+306.1	471.7+267.1	0.07
NK (cells/mm3)	201.1+132.3	279.3+162.5	373.4+172.8	0.20

Table 1: Varicella Zoster Virus IgG Antibody Levels and Immune Cell Subpopulation Distributions in Peripheral Blood Post-Vaccination, Stratified by Treatment Groups

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