# Immune responses to Herpes Zoster Vaccine Responses in Rheumatic Patients on JAK Inhibitors: insights in humoral and cellular response

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## Background

- **Patients with immune-mediated rheumatic diseases treated with JAK inhibitors face an elevated risk of herpes zoster (HZ) infection**.
- Shingrix, a recombinant inactive vaccine, offers protection against HZ. However, limited data exist on Shingrix vaccine responses in patients with immune-mediated rheumatic diseases (IMRD).

## Methods

- We investigated **humoral, CD4, and CD8 immune responses in 43 JAK inhibitor-naïve patients with specific rheumatic diseases following a two-dose regimen of the Shingrix vaccine**. The responses were compared with age, gender, and disease-matched healthy controls.
- Additionally, the **serum cytokine profile (IL-17, IL-4, IL-6, IL-10, IL-2, TNF-α, INF- γ),** including the **expression of granzyme A and B and the level of VZV IgG antibodies post-vaccination**, was assessed.

## Results

- **Patients with IMRDs treated with JAK inhibitors exhibited lower seroconversion rates than healthy controls** (74% vs. 96%, p=0.04). **T-CD4 cellular immune responses displayed a significant difference** (81% vs. 4%, p<0.0001), as did **T-CD8 cellular immune response**s (26% vs. 67%, p=0.009).
- Post-vaccination, IMRD patients revealed reduced levels of IL-17, INF-γ, IL-10, IL-6, and IL-4 compared to healthy counterparts (Table 1 and Figure 1). Notably, no distinct differences in seroconversion, antibody titers, T-CD4 and T-CD8 cellular immune response emerged between distinct treatment subgroups.
- **Negative correlations were observed between VHZ IgG Ab and T-CD4 cellular response with age >60 years, disease duration, MTX cumulative dose, GC cumulative dose, history of treatment with 2 or more b/tsDMARDs,** (Table 2). Additionally, a **positive correlation between T-CD4 and T-CD8 cellular response** was identified (β =0.36, p=0.003).

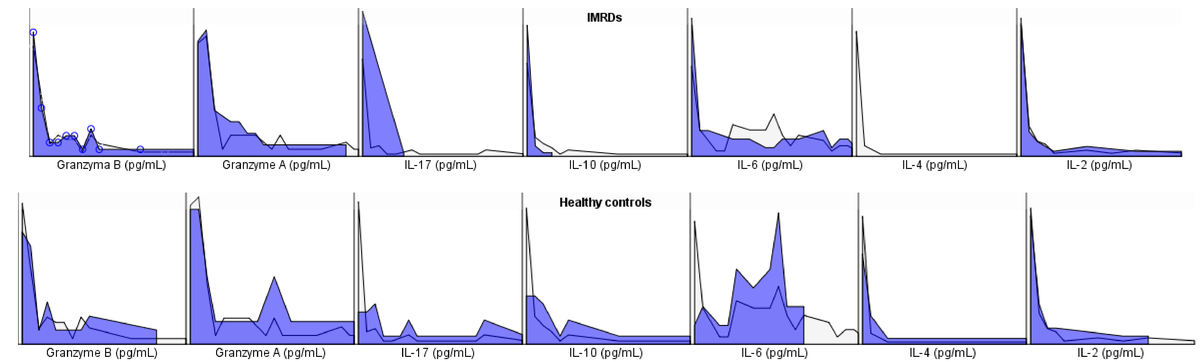
## Results

- Patients with IMRD treated with JAK inhibitors exhibit lower seroconversion rates and distinct T-CD4 and CD8 cell responses compared to healthy controls. The findings contribute valuable information for optimizing vaccine efficacy in this vulnerable patient population.

| | IMRD | Healthy controls | P value |
|---|---|---|---|
| VHZ IgG Ab (Ab Index) | 3.1 (1.2-5) | 4.8 (1-5) | 0.03 |
| Granzyme A (pg/mL) | 439,33+573,31 | 678,61+1061,8 | 0.44 |
| Granzyme B (pg/mL) | 133,98+207 | 138,61+151 | 0.31 |
| IL-17 (pg/mL) | 0 | 6.97+9.28 | **<0.00001** |
| INF-γ (pg/mL) | 2.91 (0-117,38) | 94.9 (0.11-1484) | **<0.00001** |
| TNF (pg/mL) | 501,01 (0-12234) | 98,98 (0-1579) | 0.35 |
| IL-10 (pg/mL) | 3,31 (0-35,48) | 38,98 (0-234) | **<0.0001** |
| IL-6 (pg/mL) | 458,29 (0-6450) | 10039,43 (1-34434) | **<0.0001** |
| IL-4 (pg/mL) | 0 | 0.36 (0-3.02) | **<0.0001** |
| IL-2 (pg/mL) | 26 (0-478) | 44 (1.1-351.80) | 0.51 |

**Table 2: Correlations between humoral and cellular response**

| β coefficient (p value) | Age >60 years | Disease duration | Cumulative glucocorticoid dose | Cumulative methotrexate dose | Treatment with 2 or more b/tsDMARDs |
|---|---|---|---|---|---|
| VHZ IgG Ab | β = -0.29, p=0.02 | β = -0.24, p=0.04 | β =-0.22, p=0.04 | β =- 0.42, p=0.0007 | β =-0.351, p=0.003 |
| CD4 T-cell response | β =-0.46, p 0.0007 | β = - 0.643, p=0.0007 | β = -0.32, p=0.007 | β = -0.46, p=0.001 | β =-0.20, p=0.001 |
| CD8 T-cell response | β =0.155, p=0.2 | β =-0.24, p=0.04 | β =-0.19, p=0.1 | β = -0.18, p=0.13 | β = -0.19, p=0.12 |

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