

Correlation between immune response and adverse events in MS patients after Shingrix vaccine administration

Fato I, Benedetti L, Landi D, Napoli F, Barchi V, Di Lorenzo A, Imeneo A, Alessio G, Angelone F, Massa B, Zingaropoli M.A, Pasculli P, Mastroianni C.M, Ciardi M.R, Andreoni M, Marfia G.A, Sarmati L, Iannetta M

Introduction/Summary

Reactivation of Varicella Zoster Virus (VZV) causes Herpes Zoster (HZ), which is more frequent in patients with an immune system compromise. In 2018 a recombinant vaccine for HZ and postherpetic neuralgia prevention (Shingrix) has been approved for the elders and immunocompromised young adults. We aimed to investigate the association between cell mediated (CMI) and humoral (Hu) immune responses and adverse events (AE) after vaccination, in a cohort of people with multiple sclerosis (PwMS) on disease modifying therapies (DMT).

Methods

- Vaccination schedule consisted of two doses of Shingrix administered two months apart.
- AE were investigated with a structured questionnaire, submitted to patients a week after each dose.
- CMI was assessed through an INF-gamma release assay (IGRA) specific for VZV glycoprotein-E (gE). Hu response was assessed through a commercial ELISA, detecting total anti-gE immune globulin (Ig)-G.
- All the tests and questionnaires were performed after the first (T0) and the second dose (T1).
- One month after the second dose (T2) a supplementary assessment of CMI and Hu responses was performed.
- Categorical variables are presented as absolute frequency and percentages (%) and quantitative variables as medians and interquartile ranges (IQR). Categorical data were analyzed using the Chi2 test. Differences between groups were assessed by the non-parametric Mann-Whitney test. The level of statistical significance was <0.05.

Results

- We enrolled 32 PwMS, mostly women (24/32, 75%), with a median age of 56 years (43-59). All of them were receiving DMTs during the vaccination.
- Severity and duration of the adverse events are reported in Table 1. The symptoms analyzed were pain, redness and swelling at the site of the injection, fever, chills, asthenia, headache, myalgia and arthralgia (frequencies at T0 and T1 reported in Table 2).

	T0 (%)	T1 (%)
Severity	Absent	0.00
	Mild	28.125
	Moderate	28.125
	Severe	43.750
	0 days	0.00
Duration	1-3 days	84.375
	3-5 days	0.00
	>5 days	15.625

- CMI was considered valid (2-fold increase of IFN-gamma production from baseline) in 23 patients (71.87%), while the Hu response was considered valid (50% increase of OD from baseline) in 28 patients (87.5%). 20 patients (62.5%) showed valid both CMI and Hu responses.
- Our data suggest an association between higher levels of CMI or Hu responses and the presence of specific adverse events (Table 3). Higher specific CMI responses at T2 were associated with headache and arthralgia after the first dose and fever, arthralgia and chills after the second dose. Higher Hu responses at T2 were associated with redness and swelling at the site of injection after the first dose and with headache after the second dose.

Conclusion

- Our data suggest an association between systemic symptoms, particularly arthralgia, and higher CMI.
- These data are consistent with other findings showing an association between higher humoral responses and adverse events, while very few studies investigate the same association with CMI.

Adverse events	T0 (%)	T1 (%)
Pain	90.625	93.75
Redness	12.5	21.875
Swelling	25.0	21.875
Fever	28.125	28.125
Chills	18.75	34.375
Asthenia	50.0	56.25
Headache	50.0	50.0
Myalgia	31.25	46.875
Arthralgia	31.25	46.875



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infettivologism@gmail.com
llenia.fato@ptvonline.it

Adverse events T0	T resp gE T1 (median - IQR)	T resp gE T1 p value	T resp gE T2 (median - IQR)	T resp gE T2 p value	ANTI-gE T2 1/30.00 (median - IQR)	ANTI-gE T2 1/30.00 p value			
Pain	no	0.01 (0.01-122.9)	no	14.4 (7.2-172.2)	no	0.44 (0.41-0.51)			
	yes	6.55 (0.01-24.25)	0.659	yes	42.72 (3.95-161.1)	0.867	yes	0.44 (0.13-0.89)	0.948
Redness	no	0.82 (0.01-21.38)	0.549	no	36.6 (0.53-155.23)	0.165	no	0.41 (0.12-0.82)	0.021
	yes	22.76 (11.46-32.62)	yes	151.87 (96.15-474.9)	yes	1.18 (0.87-1.85)	yes	1.18 (0.87-1.85)	0.058
Swelling	no	2.94 (0.01-21.38)	0.696	no	36.6 (0.53-139.62)	0.249	no	0.36 (0.098-0.82)	0.058
	yes	7.39 (0.32-32.62)	yes	116.8 (7.92-497.6)	yes	0.78 (0.48-1.05)	yes	0.78 (0.48-1.05)	0.883
Fever	no	0.49 (0.01-17.89)	0.207	no	36.6 (0.41-165.52)	0.268	no	0.44 (0.11-0.91)	0.883
	yes	21.05 (7.62-40.96)	yes	64.3 (13.99-438.8)	yes	0.44 (0.19-0.81)	yes	0.44 (0.19-0.81)	0.546
Chills	no	2.94 (0.01-22.26)	0.919	no	36.6 (0.65-125.45)	0.075	no	0.41 (0.11-0.88)	0.546
	yes	7.15 (0.01-35.32)	yes	205.3 (55.38-1028.4)	yes	0.47 (0.44-0.76)	yes	0.47 (0.44-0.76)	0.559
Asthenia	no	10.16 (0.01-20.17)	0.717	no	12.76 (0.3-85.16)	0.276	no	0.39 (0.12-0.87)	0.559
	yes	1.88 (0.01-32.82)	yes	78.66 (6.44-175.35)	yes	0.47 (0.28-0.86)	yes	0.47 (0.28-0.86)	0.346
Headache	no	0.61 (0.01-16.59)	0.220	no	7.08 (0.14-86.53)	0.038	no	0.36 (0.12-0.65)	0.346
	yes	14.3 (0.22-41.42)	yes	83.75 (13.58-205.26)	yes	0.58 (0.18-0.97)	yes	0.58 (0.18-0.97)	0.792
Myalgia	no	0.49 (0.01-20.5)	0.334	no	12.76 (0.42-125.45)	0.228	no	0.41 (0.13-0.91)	0.792
	yes	8.62 (0.53-35.95)	yes	118.78 (29.19-172.9)	yes	0.47 (0.34-0.85)	yes	0.47 (0.34-0.85)	0.339
Arthralgia	no	0.49 (0.01-19.83)	0.138	no	8.26 (0.42-55.3)	0.029	no	0.36 (0.11-0.87)	0.339
	yes	18.28 (1.06-41.87)	yes	155.23 (76.11-218.7)	yes	0.65 (0.44-0.853)	yes	0.65 (0.44-0.853)	

Adverse events T1	T resp gE T1 (median - IQR)	T resp gE T1 p value	T resp gE T2 (median - IQR)	T resp gE T2 p value	ANTI-gE T2 1/30.00 (median - IQR)	ANTI-gE T2 1/30.00 p value			
Pain	no	0.21 (0.11-0.3)	0.252	no	0.095 (0.05-0.14)	0.070	no	0.1 (0.09-0.12)	0.102
	yes	10.16 (0.01-30.25)	yes	44.87 (5.89-174.4)	yes	0.47 (0.19-0.88)	yes	0.47 (0.19-0.88)	0.194
Redness	no	1.88 (0.01-20.94)	0.442	no	38.59 (3.95-158.94)	0.723	no	0.44 (0.13-0.81)	0.194
	yes	15.28 (0.42-34.99)	yes	125.45 (4.22-167.5)	yes	0.89 (0.4-1.18)	yes	0.89 (0.4-1.18)	0.294
Swelling	no	0.66 (0.01-20.94)	0.269	no	38.6 (3.95-191.78)	0.554	no	0.44 (0.13-0.67)	0.294
	yes	15.28 (5.3-40.12)	yes	44.87 (4.14-104.6)	yes	0.89 (0.45-1.08)	yes	0.89 (0.45-1.08)	0.476
Fever	no	0.43 (0.01-14.79)	0.022	no	14.4 (0.42-141.06)	0.074	no	0.44 (0.11-0.87)	0.476
	yes	34.99 (19.24-40.96)	yes	118.8 (35.72-1311.5)	yes	0.67 (0.31-0.84)	yes	0.67 (0.31-0.84)	0.361
Chills	no	0.21 (0.01-11.7)	0.006	no	9.83 (0.14-72.84)	0.016	no	0.38 (0.1-0.89)	0.361
	yes	30.25 (12.23-41.42)	yes	153.8 (59.2-281.12)	yes	0.67 (0.38-0.85)	yes	0.67 (0.38-0.85)	0.970
Asthenia	no	0.4 (0.01-20.5)	0.393	no	36.6 (0.65-178.3)	0.794	no	0.48 (0.11-0.91)	0.970
	yes	12.41 (0.12-28.25)	yes	64.43 (5.51-155.95)	yes	0.44 (0.19-0.85)	yes	0.44 (0.19-0.85)	0.038
Headache	no	10.51 (0.01-30.99)	0.560	no	8.26 (0.42-139.63)	0.172	no	0.26 (0.09-0.53)	0.038
	yes	1.72 (0.01-22.44)	yes	64.43 (10.84-249.2)	yes	0.74 (0.44-0.97)	yes	0.74 (0.44-0.97)	0.385
Myalgia	no	0.59 (0.01-20.0)	0.433	no	9.83 (0.13-72.84)	0.100	no	0.33 (0.1-0.85)	0.385
	yes	10.16 (0.22-34.99)	yes	83.75 (11.33-205.26)	yes	0.49 (0.37-0.87)	yes	0.49 (0.37-0.87)	0.131
Arthralgia	no	0.45 (0.01-16.42)	0.205	no	6.4 (0.14-44.26)	0.011	no	0.2 (0.1-0.58)	0.131
	yes	14.3 (0.22-40.12)	yes	153.8 (29.64-266.2)	yes	0.67 (0.44-0.87)	yes	0.67 (0.44-0.87)	