19-21 GIUGNO ROMA
UNIVERSITA' CATTOLICA DEL SACRO CUORE CENTRO CONGRESSI EUROPA
RESEARCH and CARE: FROM BENCH, TO BEDSIDE, TO COMMUNITY
Promosso da SIMIT
16° CONGRESSO NAZIONALE ICAR
Italian Conference on AIDS and Antiviral Research
P 205
POSTER 4 YOU ICAR 2024

Specific T-cell responses to Varicella Zoster Virus glycoprotein E one year after vaccination with a recombinant adjuvanted subunit vaccine in people with multiple sclerosis on disease modifying treatments

M. Iannetta[1,2], L. Benedetti[1], L. Coppola[1,3], G. F. Angelone[1], I. Fato1, G. Montagnari[1], D. Landi[4], F. Napoli[4], G. Alessio[1], A. Di Lorenzo[1], A. Imeneo[1], V. Barchi1, G. Mataluni[4], C.G. Nicoletti[4], E. Teti[2], G.A. Marfia[4,5], L. Sarmati[1,2].

1) Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy. 2) Infectious Diseases Unit, Policlinico Tor Vergata, Rome, Italy. 3) PhD Program in Microbiology, Immunology, Infectious Diseases and Transplants (MIMIT), Tor Vergata University, Rome, Italy. 4) University of Rome Tor Vergata, Multiple Sclerosis Clinical and Research Unit, Department of Systems Medicine, Rome, Italy. 5) IRCCS Neuromed, Unit of Neurology, Pozzilli (IS), Italy.

Introduction/Summary

- Varicella-zoster virus (VZV)-specific T-cell–mediated immunity (CMI) is considered fundamental to prevent Herpes Zoster (HZ).
- Age and immunomodulating drugs can impair VZV-specific CMI and contribute to HZ occurrence.
- A new adjuvanted recombinant subunit vaccine (HZ/su) has been recently approved for the prevention of HZ in the elders or in young adults with immune system impairments.
- Here we investigate VZV-specific immunity in patients with multiple sclerosis (PWMS) patients on disease modifying treatments (DMTs) 1 year after HZ/su vaccination.

Study Design

- Patients on active follow-up in the MS Unit of Policlinico Tor Vergata were enrolled in the study.
- Two doses of HZ/su were administered 2 months apart (T0 and T1), with follow-up visits 1 month and 1 year after the second dose (T2 and T3, respectively).

Methods

- CMI was assessed at T0, T1, T2 and T3 with an in-house Interferon Gamma Release Assay (IGRA), consisting of heparin whole blood stimulation with VZV gE and Immediate Early (IE)-63 peptide libraries. Interferon (IFN)-γ production was measured with the automated ELLA platform (Figure 1).
- At T3 CMI was also assessed with an in-house Elispot system, using the same stimuli of the IGRA to stimulate freshly isolated peripheral blood mononuclear cells (PBMCs) (Figure 2).
- Wilcoxon and Friedman tests were used to compare matched data. Correlations were assessed with the Spearman's rank test.

Figure 1 **In-house IGRA for the assessment of VZV gE specific CMI**

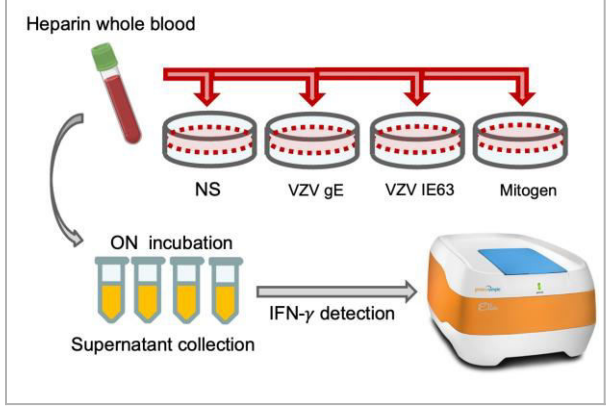

Figure 2 **In-house Elispot for the assessment of VZV gE specific CMI**

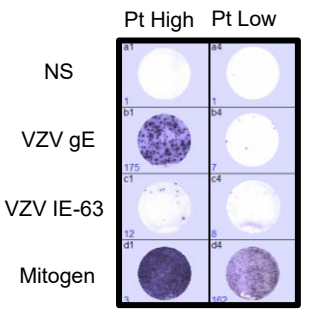

Figure 1: 500µl of fresh heparinized blood were incubated overnight at 37° C and 5% CO2, after stimulation with glycoprotein (g)E and immediate Early (IE)63 peptide libraries of VZV, at a final concentration of 1µg/ml. For each patient a negative (NS) and positive (phytohemagglutinin (Mitogen) 5µg/ml) control was also included. After 18 hours, supernatants were collected and stored at -80° C. IFN-γ production was assessed with the automated ELLA platform. FN-γ response was defined as peptide or PHA stimulated condition minus unstimulated condition.

Figure 2: 0,5 million of freshly isolated PBMCs were incubated overnight at 37° C and 5% CO2, after stimulation with glycoprotein (g)E and immediate Early (IE)63 peptide libraries of VZV, at a final concentration of 1µg/ml. For each subject, a negative (NS) and positive (phytohemagglutinin (Mitogen) 5µg/ml) control was also included. After 18 hours, colored spots were counted by an automated elispot reader. The picture represents two patients (Pt) with high and low responses to VZV gE stimulation.

References

1. Heineman TC, et al. doi: 10.1016/j.coi.2019.02.009.
2. Lasagna A, et al. doi: 10.1080/21645515.2023.2288282.
3. Harbecke R, et al. doi: 10.1093/infdis/jiab387.

Results

- 10 PWMS (6 females) have been sampled at T3, so far.
- Median age was 46 years (IQR 44-59), median Expanded Disability Status Scale (EDSS) was 1,5 (IQR 1-5).
- All patients were on DMTs. Treatments were distributed as follows: dimethyl fumarate (4/10), glatiramer acetate (1/10), natalizumab (2/10), fingolimod (2/10), ocrelizumab (1/10).
- Median IFN-γ production after gE stimulation was 6.6 pg/ml, 12.2 pg/ml, 129.1 pg/ml and 16.58 at T0, T1, T2 and T3, respectively (Friedman p<0,001). According to the Dunn's multiple comparison test, VZV-gE specific CMI significantly increased at T2 compared to T0 (p<0.001), while at T3 IFN-γ production after gE stimulation significantly decreased (Wilcoxon p = 0.01) (Figure 3).
- The results of the IGRA test were confirmed with an in-house Elispot, with a good correlation between the two assays (Spearman's Rho 0.7, p=0.02) (Figure 4).
- PWMS with an impaired VZV-gE specific CMI at T3 were on treatment with fingolimod and dimethyl fumarate.

Figure 3 **Cell mediated immunity elicited in PWMS by the HZ/su vaccine**

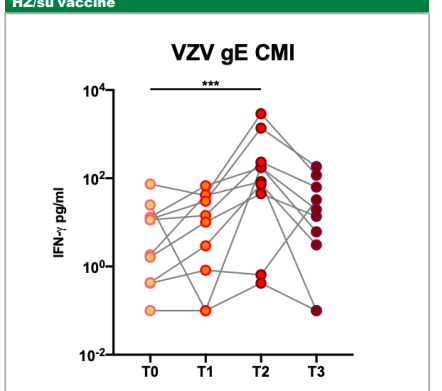

Figure 4 **comparison between the IGRA and Elispot assays to assess VZV-gE specific T-cell responses**

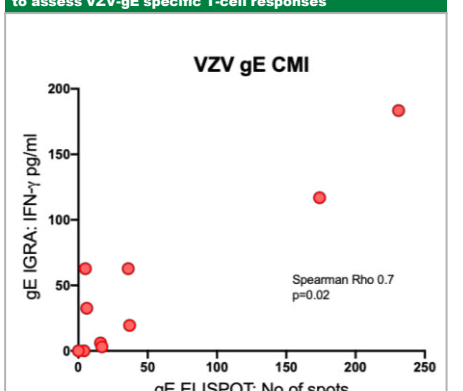

Figure 3: IFN-γ production after VZV gE peptide libraries stimulation of heparin whole blood. Friedman test p<0.001. Post test analysis with the Dunn's statistic showed a statistically significant difference after comparing T0 with T2 (p<0.001), while no statistically significant differences were found after comparing T0 vs T1, and T0 vs T3.

Figure 4: Correlation between the results of the in-house IGRA and in-house Elispot, after stimulation of whole blood and PBMCs, respectively, with gE peptide libraries at T3. Spearman Rho = 0.7, p = 0.02.

T0: baseline (HZ/su 1st dose); T1: +2 months after T0 (HZ/su 2nd dose); T2: +1 month after T2; T3: +12 months after T2.

Conclusions

- Our in-house IGRA is a sensitive and rapid method to assess VZV-gE specific CMI after HZ/su vaccination, as demonstrated by the comparison with the Elispot assay.
- HZ/su significantly increased VZV-specific CMI in PWMS on DMTs one month after the completion of the vaccination schedule.
- However, CMI tends to decrease after 1 year, specifically in PWMS on fingolimod and dimethyl fumarate.
- This evidence needs to be further investigated and correlated with HZ reactivation events in PWMS on DMTs to understand its clinical relevance.

TOR VERGATA UNIVERSITÀ DEGLI STUDI DI ROMA
marco.iannetta@uniroma2.it