J Mol Genet Med 2018, Volume 12
DOI: 10.4172/1747-0862-C1-025

Characteristics of the specific humoral response elicited in patients with advanced solid tumors using a VEGF-based vaccine, at different antigen doses and with two distinct adjuvants

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Statement of the Problem: The CENTAURO study was a first-in-human phase 1 trial to evaluate a cancer therapeutic vaccine based on human VEGF (vascular endothelial growth factor). This clinical trial included three antigen levels (50, 100 and 400 μg), all in combination with 200 μg of VSSP as adjuvant. Vaccination with the maximum dose of antigen showed an excellent safety profile, exhibited the highest immunogenicity and was the only one showing a reduction on platelet VEGF bioavailability. However, this antigen dose level did not achieve a complete seroconversion rate in vaccinated patients.

Methodology & Theoretical Orientation: To address this matter, CENTAURO-2 clinical trial was conducted where antigen and VSSP dose scale up were studied and also incorporated the exploration of aluminum phosphate as adjuvant.

Findings: Vaccination with different CIGB-247 formulations exhibited a very positive safety profile. The majority of the documented adverse effects attributable to vaccination were low grade injection site events. Cancer patients developed predominantly IgG, but also IgM and IgA antibodies specific to human VEGF. Elicited polyclonal antibodies had the ability to block the interaction between VEGF and its receptors, VEGFR1 and VEGFR2 and also reduced in vivo platelet VEGF bioavailability. The sVEGFR-2 (soluble version of membrane VEGFR2) levels did not show any significant changes with respect to pre-vaccination levels. All these properties are preserved with monthly immunizations up to one year. As immunizations number increases, anti-VEGF IgG response shifts gradually from IgG1 to IgG4, being the former the predominant subclass. The highest humoral response was detected in patients immunized with 800 μg of antigen +200 μg of VSSP.

Conclusion & Significance: Vaccination with a human VEGF variant molecule as antigen in combination with VSSP or aluminum phosphate is immunogenic. Both adjuvants combined with the highest dose of antigen (800 μg) deserve further evaluations in phase II clinical trials.

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