POSTER PRESENTATION

Open Access

A randomized pilot trial evaluating safety and immunogenicity of recMAGE-A3 + AS15 immunotherapeutic administered by intramuscular versus intradermal/subcutaneous routes

Craig L Slingluff^{1*}, Gina R Petroni¹, Walter C Olson¹, Kimberly A Chianese-bullock¹, Kelly T Smith¹, Mark E Smolkin¹, Nadedja Galeassi¹, William Grosh¹, Geoffrey Weiss¹, Kristy Scott¹, Ana Hornillo²

From Society for Immunotherapy of Cancer 29th Annual Meeting
National Harbor, MD, USA. 6-9 November 2014

Introduction

The recMAGE-A3 protein has been administered intramuscularly (IM) with immunostimulant AS15 as an experimental immunotherapeutic. AS15 contains 3-O-desacyl-4'-monophosphoryl lipid A (MPL), QS-21, CpG 7909 and liposome. This MAGE-A3/AS15 immunotherapeutic has not been studied for intradermal (ID) or subcutaneous (SC) use. A clinical trial (NCT01425749) was initiated to test the hypotheses that ID/SQ administration is safe and may induce CD4⁺ and CD8⁺ T cell responses to MAGE-A3.

Patients and methods

Twenty-five eligible patients with resected stage IIB-IV MAGE-A3⁺ melanoma were randomized to 2 arms, treated with MAGE-A3/AS15 Immunotherapeutic IM (Arm A, n = 13) or ID/SC (Arm B, n = 12). Adverse events (CTCAE 4) were recorded. Antibody (Ab) responses to MAGE-A3 protein were assessed by ELISA assay. T cell responses were assessed by flow cytometry after intracellular cytokine staining (ICS) for multifunctional CD4⁺ and CD8⁺ responses to overlapping MAGE-A3 peptides, assaying lymphocytes from peripheral blood (PBMC) and sentinel immunized node (SIN), after one *in vitro* stimulation.

Results

In both arms, the recMAGE-A3/AS15 immunotherapeutic was well-tolerated, with only one grade 3 treatment-related adverse event (hyperglycemia, Arm B), and no grade 4 or

5 events. Grade 2 injection site reactions were observed in 10 patients in Arm A and 7 in Arm B (P > 0.3). Ab responses were detected in all patients, most with high titers persisting at least 6 months, without difference between arms. Preliminary T cell data are that multifunctional (IFN γ and TNF α) CD4⁺ T cell responses to MAGE-A3 were detected in 64% of patients (54% A; 75% B; Table 1). Multifunctional CD8⁺ T cell responses were evident in 20% of patients (8% A, 33% B). CD4⁺ responses were higher magnitude in SIN than in PBMC.

Conclusion

Safety profiles were comparable for ID/SC and IM administration of the MAGE-A3/AS15 immunotherapeutic, which induced high-titer Ab, multifunctional CD4⁺ Th1 responses, and CD8⁺ responses when administered by either route. Immune responses were more readily detected in the SIN than in PBMC. These pilot data

Table 1 Multifunctional (IFN γ and TNF α) T cell responses to MAGE-A3

	% of CD4 ⁺ T cells			% of CD8 ⁺ T cells		
	(90% CI)			(90% CI)		
	SIN	PBMC	Either	SIN	PBMC	Either
Arm A	31% (11, 58)	31% (11, 58)	54% (29, 78)	0% (0, 21)	8% (0, 32)	8% (0, 32)
Arm B	64% (35, 86)	50% (25, 75)	75% (47, 93)	18% (3, 47)	25% (7, 53)	33% (12, 61)
Total	46% (28, 64)	40% (24, 58)	64% (46, 80)	8% (2, 24)	16% (6, 33)	20% (8, 38)

¹University of Virginia, Charlottesville, USA

Full list of author information is available at the end of the article

support further investigation of ID/SC immunization with antigen plus AS15 to support Th1 CD4⁺ responses and CD8⁺ responses. Production of Th1 cytokines IFN γ and TNF α suggests the induced CD4⁺ responses may support CD8⁺ T cells. Other forms of antigen (e.g.: long peptides) may further support induction of CD8⁺ T cell responses in combination with AS15.

Funding source: GlaxoSmithKline Biologicals SA

Authors' details

¹University of Virginia, Charlottesville, USA. ²Glaxo Smith Kline, Belgium.

Published: 6 November 2014

doi:10.1186/2051-1426-2-S3-P60

Cite this article as: Slingluff et al.: A randomized pilot trial evaluating safety and immunogenicity of recMAGE-A3 + AS15 immunotherapeutic administered by intramuscular versus intradermal/subcutaneous routes. *Journal for ImmunoTherapy of Cancer* 2014 **2**(Suppl 3):P60.

**Submit your next manuscript to BioMed Central
and take full advantage of:**

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at
www.biomedcentral.com/submit