Slingluff et al. Journal for ImmunoTherapy of Cancer 2014, 2(Suppl 3):P60
http://www.immunotherapyofcancer.org/content/2/S3/P60

Journal for ImmunoTherapy of Cancer

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 Petroni[1], Walter C Olson[1], Kimberly A Chianese-bullock[1], Kelly T Smith[1], Mark E Smolkin[1], Nadedja Galeassi[1], William Grosh[1], Geoffrey Weiss[1], Kristy Scott[1], Ana Hornillo[2]

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 (IFNg and TNFα) $CD4^+$ 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 (IFNg and TNFα) 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%	31%	54%	0%	8%	8%
	(11, 58)	(11, 58)	(29, 78)	(0, 21)	(0, 32)	(0, 32)
Arm B	64%	50%	75%	18%	25%	33%
	(35, 86)	(25, 75)	(47, 93)	(3, 47)	(7, 53)	(12, 61)
Total	46%	40%	64%	8%	16%	20%
	(28, 64)	(24, 58)	(46, 80)	(2, 24)	(6, 33)	(8, 38)

[1]University 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 IFNg and TNFα 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
[1]University of Virginia, Charlottesville, USA. [2]Glaxo 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.