Kovacsovics-Bankowski et al. Journal for ImmunoTherapy of Cancer 2013, 1(Suppl 1):P255
http://www.immunotherapyofcancer.org/content/1/S1/P255

Journal for ImmunoTherapy of Cancer

POSTER PRESENTATION Open Access

Phase I/II clinical trial of anti-OX40, radiation and cyclophosphamide in patients with prostate cancer: immunological analysis

Magdalena Kovacsovics-Bankowski*, Lana Chisholm, Jonna Vercellini, Marka Crittenden, Scot Lary, Brendan Curti, Andrew Weinberg

From Society for Immunotherapy of Cancer 28th Annual Meeting
National Harbor, MD, USA. 8-10 November 2013

Introduction

OX40, a member of the Tumor Necrosis Factor Receptor superfamily is a potent co-stimulatory molecule. OX40 engagement increases T cell proliferation, effector function and survival. Pre-clinical studies have shown that OX40 agonist synergizes with radiation and cyclophosphamide to increase survival. A phase I clinical trial has shown that anti-OX40 mAb was well tolerated and induced proliferation of CD8 and CD4 non-Treg cells in the peripheral blood (PB).

Methods

This trial was design to evaluate the toxicity and the effect on peripheral blood lymphocytes of cyclophosphamide and radiation in combination with anti-OX40 agonist in patients with metastatic castrate- and chemotherapy-resistant prostate cancer. The immunological analysis was performed on peripheral blood lymphocytes (PBL) using a multi-color flow analysis panel containing CD3, CD4, CD8, CD95, CD25, CD38, HLA-DR and the intracellular markers, FoxP3 and Ki-67.

Results

Anti-OX40, Cyclophosphamide and radiation had manageable safety and tolerability profile. Transient decreases in PSA were observed in 4/9 patients. Four patients had an increase in PSA DT. In 5/9 patients, bone and lymph node metastases were radiographically stable during the study observation. The immunological response measured in the PB shows a 2-3.5-fold increase in the proliferating CD4+ CD95+ T cells, mostly in the FoxP3- population. In the 3rd cohort, there was also a 3 fold increase, in CD4 + FoxP3+ T cells proliferation (Treg). The proportion of cycling CD8+ CD95+ T cells peaked with a 5-6-fold increase of cycling cells. NK cell proliferation was also observed, with a 2-4.5 fold proliferation increase. In the first anti-OX40 clinical trial, we have observed that the administration of anti-OX40 antibody increased the activation status of the CD8+ T cells as measured by the co-expression of CD38 and HLA-DR on the cycling cells. A similar trend was observed in this study. In some patients, the administration of anti-OX40 modified the cytokine profile of PBMC. We have observed an increase in IFNγ and IL-2, with stable TNFα secretion and a decrease in IL-6, IL-10 and IL-17.

Summary

Administration of anti-OX40 with radiation and cyclophosphamide has not affected the degree of proliferation of PBL. We have observed a similar fold increase in the proliferation of CD4+ FoxP3-, CD8+ and NK cells as in the first clinical trial. With the exception of cohort #3 (highest dose of cyclophosphamide), there was no change in the proliferation of CD4+ FoxP3+ T cells (Treg). There was a trend towards a higher percentage of cycling CD8+ T cells expressing the activation markers CD38 and HLA-DR.

Published: 7 November 2013

doi:10.1186/2051-1426-1-S1-P255
Cite this article as: Kovacsovics-Bankowski *et al.*: Phase I/II clinical trial of anti-OX40, radiation and cyclophosphamide in patients with prostate cancer: immunological analysis. *Journal for ImmunoTherapy of Cancer* 2013 **1**(Suppl 1):P255.

Earle A. Chiles Research Institute, Providence Cancer Center, Portland Providence Medical Center, Portland, OR, USA