POSTER PRESENTATION

Open Access

Level of PD-1 expression on CD8⁺ T cells influence prognosis and respond to PD-1 therapy in a murine model

Benjamin A Kansy^{1*}, Raghvendra M Srivastava², Hyun-Bae Jie², Gulidanna Shayan², Yu Lei², Jing Li², William Gooding³, Sven Brandau⁴, Stephan Lang⁴, Nicole Schmitt⁵, Gordon J Freeman⁶, David A Clump⁷, Robert L Ferris²

From 30th Annual Meeting and Associated Programs of the Society for Immunotherapy of Cancer (SITC 2015)

National Harbor, MD, USA. 4-8 November 2015

Introduction

Prognosis varies dramatically in head and neck squamous cell carcinoma (HNSCC) based on HPV status. In HPV⁺ patients, programmed death (PD)-1 expression has been linked to a better clinical outcome. We hypothesized that extent of PD-1 expression may differentially impact T cell phenotype, patient prognosis and response to anti-PD-1 immunotherapy in a murine HPV⁺ cancer model.

Material and methods

Freshly isolated tumor infiltrating lymphocytes (TIL) from HNSCC patients were stained by flow cytometry for expression level of PD-1 expression (PD-1^{high} vs. PD-1^{low}), granzyme B, or IFN- γ secretion by ELISPOT. The prognostic impact of PD-1^{high} vs. PD-1^{low} T cells was determined in a cohort of HNSCC patients (n=56, median follow up=19 mo). In a murine HNSCC model, PD-1^{high} and PD-1^{low} fractions were compared from CD3⁺ CD8⁺ PD-1⁺ cells and analyzed according to different treatment groups (untreated, anti-PD-1 mAb, radiotherapy and 3 different anti-PD-1/radiotherapy combinations).

Results

CTLA-4 and PD-1 were significantly upregulated on both HPV⁺ and HPV⁻ HNSCC patients' TIL, whereas PD-1⁺ CD8⁺ cells were significantly enriched in TIL from HPV⁺ patients (p=0.006). Interestingly, PD-1^{high} cells represented a more dysfunctional phenotype, with severely

compromised IFN- γ secretion (phigh CD8⁺ TIL were more likely to be HPV⁻ and had a worse disease free survival (HR = 2.25; 95% CI = 1.46 – 3.15; p < .0001), while high fractions of PD-1^{low} T cells were associated with better clinical outcome (HR= 0.19, 95% CI = .07 - .49, p = .0006), and were seen preferentially in HPV⁺ HNSCC patients. In the murine HNSCC model, anti-PD-1 mAb plus radiotherapy resulted in optimal tumor elimination, which was associated with an elimination of PD-1^{high} CD8⁺ T cells and – most importantly – increase in PD-1^{low/intermed} T cell frequencies (p < 0.5).

Discussion

Consideration of different PD-1 expression levels on TIL segregates PD-1 expression as a marker of activated, competent tumor reactive T cells on the one hand (low/intermed expression), and as a marker of exhausted, dysfunctional cells in the tumor microenvironment on the other hand (high expression). These results emphasize the crucial role of differential PD-1 expression levels on HNSCC patients' effector T cells for prognosis and as a potential novel biomarker for anti-PD-1/PD-L1 based immunotherapy.

Authors' details

¹Department of Otorhinolaryngology, University Hospital Essen, Germany; University of Pittsburgh Cancer Institute, Pittsburgh, PA, USA. ²University of Pittsburgh Cancer Institute, Pittsburgh, PA, USA. ³Biostatistics Facility, University of Pittsburgh Cancer Institute, Pittsburgh, PA, Pittsburgh, PA, USA. ⁴Department of Otorhinolaryngology, University Hospital Essen, Germany, Essen, Germany. ⁵Department of Otolaryngology, University of Pittsburgh, Pittsburgh, PA, Pittsburgh, PA, USA. ⁶Dana-Farber/Harvard Cancer Center,

¹Department of Otorhinolaryngology, University Hospital Essen, Germany; University of Pittsburgh Cancer Institute, Pittsburgh, PA, USA
Full list of author information is available at the end of the article

Boston, MA, USA. ⁷Department of Radiation Oncology, University of Pittsburgh Cancer Institute, Pittsburgh, PA, USA.

Published: 4 November 2015

doi:10.1186/2051-1426-3-S2-P228

Cite this article as: Kansy *et al.*: Level of PD-1 expression on CD8+ T cells influence prognosis and respond to PD-1 therapy in a murine model. *Journal for ImmunoTherapy of Cancer* 2015 **3**(Suppl 2):P228.

**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