

ORAL PRESENTATION

Open Access

Targeting KIT on innate immune cells enhances the antitumor activity of checkpoint inhibitors in vivo

Richard Gedrich^{1*}, Scott Seibel¹, Theresa LaVallee¹, Joseph Paul Eder²

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

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

Mast cell infiltrates are associated with tumors, though their role in the tumor microenvironment remains unclear. Mast cells express high levels of KIT throughout differentiation and as mature cells. Mast cells in tumors have been shown to release proinflammatory cytokines and promote angiogenesis, increasing tumor growth and metastasis. KIT signaling and mast cells also appear to modulate myleloid-derived suppressor cell (MDSC) development, recruitment and activity in tumors. Furthermore, treatment of tumor-bearing mice or cancer patients with small molecule KIT inhibitors or an anti-mouse KIT antibody decreased tumoral MDSCs and other immunosuppressive cells including regulatory T cells. KTN0158 is a humanized anti-KIT IgG1 monoclonal antibody that specifically binds KIT and is being developed as a potential therapy for cancer and mast cell-related diseases such as neurofibromatosis type 1 (NF1). It binds canine, feline, non-human primate and human KIT with high affinity, but does not bind mouse or rat KIT. KTN0158 inhibits KIT signaling and function in vitro and in vivo and has shown antitumor activity in dogs with mast cell tumors expressing either wild-type or mutant KIT. Immune checkpoint inhibitors targeting the CTLA-4 and PD-1 pathways have demonstrated single agent efficacy in cancer patients, and the combinations have shown superior efficacy in some preclinical and clinical settings. To test the effects of KIT inhibition on immune tolerance in syngeneic mouse tumor models, the anti-mouse KIT monoclonal antibody ACK2 was used as a surrogate for KTN0158 and tested alone and in combination with CTLA-4 and PD-1 inhibitors. In the Colon26

¹Kolltan Pharmaceuticals, Inc., New Haven, CT, USA Full list of author information is available at the end of the article model, single agent treatment with the anti-KIT antibody had little antitumor activity. However, the combination of anti-KIT and anti-CTLA-4 had substantial antitumor effects, comparable to those observed for anti-CTLA-4 plus anti-PD1. These antitumor effects were dose-dependent. Pharmacodynamic assessments will also be presented. Collectively, these data suggest that the combination of immunotherapies targeting KIT on innate immune cells and checkpoint pathway inhibitors may have clinical benefit.

Authors' details

¹Kolltan Pharmaceuticals, Inc., New Haven, CT, USA. ²Yale Comprehensive Cancer Center, New Haven, CT, USA.

Published: 4 November 2015

doi:10.1186/2051-1426-3-S2-O12

Cite this article as: Gedrich *et al.*: **Targeting KIT on innate immune cells enhances the antitumor activity of checkpoint inhibitors in vivo.** *Journal for ImmunoTherapy of Cancer* 2015 **3**(Suppl 2):O12.

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

) BioMed Central

Submit your manuscript at www.biomedcentral.com/submit



© 2015 Gedrich et al. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http:// creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/ zero/1.0/) applies to the data made available in this article, unless otherwise stated.