P10. Concomitant gemcitabine therapy negatively affects DC vaccine-induced CD8+ T cell and B cell responses but improves clinical efficacy in a murine pancreatic carcinoma model

Citation

Published Version
doi:10.1186/2051-1426-2-S2-P1

Permanent link
http://nrs.harvard.edu/urn-3:HUL.InstRepos:12406752

Terms of Use
This article was downloaded from Harvard University’s DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA

Share Your Story
The Harvard community has made this article openly available. Please share how this access benefits you. Submit a story.

Accessibility
P10. Concomitant gemcitabine therapy negatively affects DC vaccine-induced CD8+ T cell and B cell responses but improves clinical efficacy in a murine pancreatic carcinoma model

C Bauer1*, A Sterzik1, F Bauernfeind1, P Duewell2, C Conrad3, R Kiefl1, S Endres2, A Eigler4, M Schnurr1, M Dauer5

From 1st Immunotherapy of Cancer Conference (ITOC1)
Munich, Germany. 12-14 March 2014

Background
Multiple studies have shown that dendritic cell (DC)-based vaccines can induce antitumor immunity. Previously, we reported that gemcitabine enhances the efficacy of DC vaccination in a mouse model of pancreatic carcinoma. The present study aimed at investigating the influence of gemcitabine on vaccine-induced anti-tumoral immune responses in a syngeneic pancreatic cancer model.

Material and methods
Subcutaneous or orthotopic pancreatic tumours were induced in C57BL/6 mice using Panc02 cells expressing the model antigen OVA (PancOVA). Bone marrow-derived DC were loaded with soluble OVA protein (OVA-DC). Animals received gemcitabine twice weekly. OVA-specific CD8+ T cells and antibody titers were monitored by FACS analysis and ELISA, respectively.

Results
Gemcitabine enhanced clinical efficacy of the OVA-DC vaccine. Interestingly, gemcitabine significantly suppressed the vaccine-induced frequency of antigen-specific CD8+ T cells and antibody titers. DC migration to draining lymph nodes and antigen cross-presentation were unaffected. Despite reduced numbers of tumour-reactive T cells in peripheral blood, in vivo cytotoxicity assays revealed that CTL-mediated killing was preserved. In vitro assays revealed sensitization of tumour cells to CTL-mediated lysis by gemcitabine. In addition, gemcitabine facilitated recruitment of CD8+ T cells into tumors in DC-vaccinated mice. T and B cell suppression by gemcitabine could be avoided by starting chemotherapy after two cycles of DC vaccination.

Conclusions
Gemcitabine enhances therapeutic efficacy of DC vaccination despite its negative influence on vaccine-induced T cell proliferation. Quantitative analysis of tumour-reactive T cells in peripheral blood may thus not predict vaccination success in the setting of concomitant chemotherapy.

Authors’ details
1Medizinische Klinik und Poliklinik IV LMU Munich, Section of Gastroenterology, Munich, Germany. 2Division of Clinical Pharmacology LMU Munich, Munich, Germany. 3Massachusetts General Hospital Harvard University, Department of Surgery, Boston, MA, USA. 4Klinikum Dritter Orden, Department of Clinical Medicine I, Munich, Germany. 5Kliniken St. Elisabeth, Department of Medicine II, Neuburg/Donau, Germany.

Published: 12 March 2014

doi:10.1186/2051-1426-2-S2-P1