ARTICLE NAVIGATION

POSTER PRESENTATIONS - PROFFERED ABSTRACTS | APRIL 15 2012

Abstract 2522: The anti-kappa monoclonal antibody MDX-1097 cooperates with Lenalidomide to enhance antibody-dependent cell cytotoxicity of multiple myeloma cells FREE

Andrew R. Cuddihy; Tiffany Khong; Rosanne Dunn; Parisa Asvadi; Andrew Spencer

+ Author & Article Information

Cancer Res (2012) 72 (8_Supplement): 2522.

https://doi.org/10.1158/1538-7445.AM2012-2522

Abstract

Multiple Myeloma (MM) is a malignancy of clonal plasma cells in the bone marrow with median overall survival duration of 3-5 years. Recent advances in the treatment and management of MM have improved progression free survival (PFS) and overall survival (OS) and include the use of high-dose chemotherapy, conditioned autologous stem cell transplantation, immunomodulatory drugs (IMiDs) and proteasome inhibitors. Unfortunately, despite these advances, the majority of patients will ultimately relapse and die from their disease. In thIs context novel therapeutic approaches, including the use of antibody-based therapies, are being investigated to further improve the treatment of MM. Currently the anti-kappa monoclonal antibody, MDX-1097, is being assessed as a single agent in a Phase 2 clinical trial for the treatment of kappa light-chain restricted (α-type) MM. MDX-1097 binds to kappa myeloma antigen (KMA) a tumor-specific membrane-associated protein expressed on malignant plasma cells in patients with α-type MM. Previously we have demonstrated that MDX-1097 exerts its anti-tumour effects predominantly via antibody-dependent cell cytotoxicity (ADCC) in the presence of either normal human peripheral blood mononuclear cells (PBMC) or purified natural killer (NK cells). Lenalidomide is an IMiD currently in use for the treatment of MM and has been shown to exert its anti-tumor effects both directly, via apoptotic mechanisms, and indirectly via a number of different mechanisms including the augmentation of NK-dependent cellular cytotoxicity. In this study we report that lenalidomide and MDX-1097 co-operate to promote enhanced ADCC of MM cells via 2 different mechanisms. First, in vitro pre-incubation of normal PBMC with lenalidomide (PBMC/Len) prior to co-culture with MDX-1097 treated α-type MM JJN3 cells resulted in increased ADCC compared to co-culture with control PBMC from the same donor. Second, pre-incubation of JJN3 cells with lenalidomide (JJN3/Len) resulted in increased JJN3 cell surface expression of KMA resulting in enhanced ADCC with PBMC when compared to control JJN3, with a further increment in cell killing seen when utilising the PBMC/Len and JJN3/Len combination. Finally, use of in vivo lenalidomide exposed PBMC isolated from a MM patient treated with lenalidomide demonstrated that these PBMC/Len were more effective in killing MDX-1097 treated JJN3 cells compared to PBMC obtained from the same patient prior to lenalidomide treatment. This study demonstrates that lenalidomide co-operates with MDX-1097 to enhance ADCC-induced MM cell killing and provides a rationale for the clinical evaluation of MDX-1097 and lenalidomide in the treatment of α-type MM.

Citation Format: {Authors}. {Abstract title} [abstract]. In: Proceedings of the 103rd Annual Meeting of the American Association for Cancer Research; 2012 Mar 31-Apr 4; Chicago, IL. Philadelphia (PA): AACR; Cancer Res 2012;72(8 Suppl):Abstract nr 2522. doi:1538-7445.AM2012-2522

View Metrics

Online ISSN 1538-7445 **Print ISSN** 0008-5472