Leukemia

Bedewy and El-Maghraby, J Leuk 2014, 2:3
http://dx.doi.org/10.4172/2329-6917.1000143

Short Communication Open Access

What Determines the Response to Immunomodulatory Therapy in Multiple Myeloma?

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Rec date: May 22, 2014, **Acc date:** Jul 18, 2014; **Pub date:** Jul 24, 2014

Introduction

Several mechanisms have been proposed to explain the activity of Immunomodulatory Drugs (IMiDs) in Multiple Myeloma (MM). These included demonstrable anti-angiogenic, antiproliferative and immune modulation effects. The precise cellular targets and molecular mechanisms have only recently become clear [1].

Zhu et al. demonstrated that cereblon (CRBN) is essential for IMiDs activity, and low levels of CRBN correlate with poor drug response, and CRBN expression in MM cells may help to distinguish MM patients that will or will not benefit from thalidomide [2]. In the present study we evaluated CRBN and IL-6R expressions and their impact on clinical efficacy of dexamethasone–thalidomide therapy in Multiple Myeloma (MM) patients, in addition to their association with other clinical and prognostic parameters. Forty-six newly diagnosed MM patients were enrolled in the study. We measured CRBN expression prior to therapy initiation by real-time polymerase chain reaction in 46 Bone Marrow (BM) aspiration samples of patients and 15 controls. In addition, IL-6R expression was evaluated on BM biopsies of patients and controls by Immunohistochemistry (IHC). Median CRBN expression in 46 BM samples of MM patients was significantly higher than in controls ($P < 0.001$).Among established prognostic parameters, International Staging System (ISS), serum Beta-2-Microglobulin (B2M), and serum albumin correlated reversely with CRBN expression. Strong IL-6R expression was significantly higher in patients than in controls.IL-6R expression was significantly associated with poor response to treatment ($P < 0.001$), B2M($P = 0.032$),and ISS($P = 0.028$).Strong intensity expression was associated with low CRBN expression($P = 0.001$).In conclusion, CRBN expression may provide a biomarker to predict response to IMiDs in patients with MM and its high expression can serve as a marker of good prognosis. Strong IL-6R expression is associated with poor response to therapy in multiple myeloma patients and can be used as a prognostic marker [3].

References

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