Journal of Hematology and Thromboembolic Diseases

Gouri et al., J Hematol Thrombo Dis 2014, 2:4
http://dx.doi.org/10.4172/2329-8790.1000e114

Editorial Open Access

Proteasome Activity as New Approach to the Management of Multiple Myeloma

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Received date: Jun 26, 2014, **Accepted date:** Jun 30, 2014, **Published date:** July 8, 2014

Editorial

The ubiquitin-proteasome pathway plays an essential role in the degradation of cellular proteins involved in a variety of cellular processes, including transcriptional regulation, cell cycle progression, proliferation, and apoptosis [1].

This pathway was also implicated in the pathogenesis of many haematologic malignancies, including multiple myeloma. Under conditions of rapid cell turnover and growth rate, proteasomes are returned into circulation. In this context, the proteasomal system could offer a new approach to diagnosis, prognosis and monitoring of anticancer treatment [2,3].

Inhibition of the proteasome results in perturbation of intracellular protein homeostasis by accumulation of the poly-ubiquitinated proteins, subsequently inducing cellular stress and apoptosis. Numerous proteasome inhibitors have been developed and described [2]. Bortezomib (PS-341, Velcade) was the first proteasome inhibitor (PI) approved by the US Food and Drug Administration (FDA) [4]. Clinical studies have demonstrated the safety and promising efficacy of bortezomib as the single-agent or combined with other drugs against multiple myeloma (MM) [5,6], as well as in several non-Hodgkin's lymphoma subtypes [7]. Other PIs with diverse mechanisms of action have been developed, in an effort to overcome resistance to Bortezomib and develop proteasome inhibitors with different toxicity profiles. These emerging drugs with different mechanisms of action have demonstrated promising antitumor activity in subjects with relapsed/refractory MM, and logically designed combinations with established agents are being investigated in the clinic. These new agents are creating chances to target multiple pathways, overcome resistance, and enhance clinical outcomes, mainly for those subjects who are refractory to approved novel agents [8].

Furthermore, several recent studies have indicated that the measurement of proteasome concentration in the serum or plasma using an enzyme-linked immunosorbent assay (ELISA) can be a new approach to diagnosis, prognosis and monitoring of anticancer treatment of patients with haematological malignancies and certain solid tumours [9–12]. The latest research has established that plasma proteasome concentration correlates with advanced disease in MM and that it may be an independent prognostic factor for survival [12]. More recently, A Oldziej et al. have demonstrated that plasma proteasome concentration and Proteasome chymotrypsin-Like (ChT-L) activity could be useful markers of MM disease activity. Pre-treatment values of proteasome ChT-L activity but not proteasome concentration could also serve as diagnostic and prognostic factors of progression free survival [3]. Further studies are necessary to understand the role of plasma proteasome ChT-L activity in the prognosis of multiple myeloma and the prediction of therapeutic response, especially in patients treated with bortezomib, as it can identify patients likely to benefit most from the use of proteasome inhibition.

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