

## **Thalidomide-based induction regimens are as effective as bortezomib-based regimens in elderly patients with multiple myeloma with cereblon expression**

**Seoyeon Ahn<sup>1</sup>**, Sung-Hoon Jung<sup>1</sup>, Hyung-Jung Choi<sup>2</sup>, Myung-Geun Shin<sup>2</sup>, Seung-Shin Lee<sup>1</sup>, Deok-Hwan Yang<sup>1</sup>, Jae-Sook Ahn<sup>1</sup>, Yeo-Kyeong Kim<sup>1</sup>, Hyeoung-Joon Kim<sup>1</sup>, Je-Jung Lee<sup>1</sup>

<sup>1</sup>*Departement of Hematology-Oncology, Chonnam National University Hwasun Hospital, South Korea*

<sup>2</sup>*Department of Laboratory Medicine, Chonnam National University Hwasun Hospital, South Korea*

Cereblon (CRBN) has been identified as a primary target of immunomodulatory drugs and is considered a biomarker for the prediction of outcomes after thalidomide- or lenalidomide-based treatments. In this study, we evaluated CRBN expression in bone marrow (BM) tissue at diagnosis and investigated the relationship between CRBN expression and treatment outcomes after thalidomide- or bortezomib-based front-line therapies in 89 elderly patients with multiple myeloma (MM). CRBN expression at the time of diagnosis was evaluated with immunohistochemical (IHC) staining for myeloma cells in paraffin wax-embedded BM tissue. CRBN-immunostained slides were scored by intensity and diffuseness, and a total score of 6 was defined as CRBN-positive (CRBN<sup>+</sup>). Thirty-eight patients (45.2%) were CRBN<sup>+</sup>. Among patients treated with thalidomide-based regimens, CRBN<sup>+</sup> patients showed a better treatment response than did CRBN-negative patients (35.0% vs. 11.8% complete response rate, respectively; HR = 4.038, P = 0.137). During a median follow-up of 31.8 months, patients treated with bortezomib-based regimens had a longer time to progression (TTP) than did patients treated with thalidomide-based regimens (15.6 vs. 13.2 months, respectively; P = 0.047), but early mortality occurred frequently in patients treated with bortezomib-based regimens. Additionally, there was no significant difference in survival outcomes between thalidomide- and bortezomib-based regimens in CRBN<sup>+</sup> patients (median TTP, 13.8 vs. 15.6 months, respectively; P = 0.842 and median OS, 39.3 vs. 30.1 months, respectively; P = 0.074). These data suggest that thalidomide-based regimens are as effective as bortezomib-based regimens in elderly patients with MM who are CRBN<sup>+</sup>. Thus, CRBN positivity, by IHC staining, may be useful in deciding appropriate treatment options in elderly patients with MM.