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ADJUSTED COMPARISON BETWEEN ELOTUZUMAB AND CARFILZOMIB IN COMBINATION WITH LENALIDOMIDE AND DEXAMETHASONE AS SALVAGE THERAPY FOR MULTIPLE MYELOMA PATIENTS.

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Keywords: Elotuzumab, carfilzomib, lenalidomide, dexamethasone, multiple myeloma, salvage therapy.

Significance statement

- In this current study we weighed the relative usefulness of EloRd over KRd, comparing a multicenter retrospective EloRd cohort with four multicenter retrospective KRd cohorts, all including RRMM cases treated outside of clinical trials.

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- This current clinical practice study's overall results demonstrate that KRd therapy offers a superior outcome than EloRd.

Abstract

The lack of a randomized trial comparing carfilzomib (K) *versus* elotuzumab (Elo) associated with lenalidomide and dexamethasone (Rd) prompted us to assess the relative usefulness of one triplet over the other.

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Five independent retrospective cohorts of 883 relapsed/refractory multiple myeloma (RRMM) patients, including 300 EloRd and 583 KRd cases, outside clinical trials, entered this non-randomized comparison. KRd cohort accounted for a higher incidence of younger patients, cases with >3 lines of therapy, already exposed to lenalidomide, International Staging System (ISS) stage III, and abnormal lactic dehydrogenase (LDH) level compared to EloRd cohort. Moreover, cytogenetic risk categories, detected in roughly one-third of cases, were equally distributed between the two therapy arms.

The probability of CR+VGPR response was significantly higher in KRd (n=314, 53.9%) than in EloRd patients (n=111, 37.0%). Likewise, the cumulative incidence function of CR+VGPR, taking into account the competitive risk of death, was significantly higher in KRd arm patients than those in the EloRd arm (P=0.003). Moreover, KRd treatment significantly reduced the progression or death risk by 46% in an adjusted multivariate analysis (HR: 0.54, 95% CI 0.42-0.69, P<0.0001).

Finally, in an adjusted illness progression/death model, the effect of KRd *versus* EloRd was of higher magnitude among those who achieved CR+VGPR (-39% hazard ratio reduction, P=0.02) than among those who achieved <VGPR (-29% hazard ratio reduction, P=0.007).

With limitations characteristic to any retrospective analysis, this current clinical practice study's overall results demonstrated potential benefits of KRd therapy compared to EloRd. This observation may help the daily clinical practice.

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