Adjusted comparison between elotuzumab and carfilzomib in combination with lenalidomide and dexamethasone as salvage therapy for multiple myeloma patients

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

Fortunato Morabito[1,2], Elena Zamagni[3,4], Concetta Conticello[5], Vincenzo Pavone[6], Salvatore Palmieri[7], Sara Bringhen[8], Monica Galli[9], Silvia Mangiacavalli[10], Daniele Derudas[11], Elena Rossi[12], Roberto Ria[13], Lucio Catalano[14], Paola Tacchetti[3], Giuseppe Mele[15], Iolanda Donatella Vincelli[16], Enrica Antonia Martino[17], Ernesto Vigna[17], Cirino Botta[17], Antonella Bruzzese[17], Anna Mele[6], Lucia Pantani[3], Serena Rocchi[3,4], Bruno Garibaldi[5], Nicola Cascavilla[18], Stelvio Ballanti[19], Giovanni Tripepi[20], Ferdinando Frigeri[21], Antonetta Pia Falcone[18], Clotilde Cangialosi[22], Giovanni Reddiconto[23], Giuliana Farina[21], Marialucia Barone[24], Ilaria Rizzello[3,4], Pellegrino Musto[25], Valerio De Stefano[12], Maurizio Musso[26], Maria Teresa Petrucci[27], Massimo Offidani[28], Antonino Neri[29], Nicola Di Renzo[23], Francesco Di Raimondo[5], Mario Boccadoro[8], Michele Cavo[3,4] and Massimo Gentile[17].

[1]Biothecnology Research Unit, AO of Cosenza, Cosenza, Italy; [2]Hematology and Bone Marrow Transplant Unit, Hemato-Oncology Department, Augusta Victoria Hospital, East Jerusalem, Israel;

[3]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Istituto di Ematologia "Seràgnoli", Bologna, Italy; [4]Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale, Università di Bologna, Bologna, Italy; [5]Division of Hematology, Azienda Policlinico-OVE, University of Catania, Catania, Italy; [6]Department of Hematology and Bone Marrow Transplant, Hospital Card. G. Panico, Tricase (LE), Italy; [7]Hematology Unit, Ospedale Cardarelli, Napoli, Italy; [8]Division of Hematology, University of Torino, AOU Città della Salute e della Scienza di Torino, Italy; [9]Hematology and Bone Marrow Transplant Unit, Azienda Socio-Sanitaria Territoriale-Papa Giovanni XXIII, Bergamo, Italy; [10]Hematology Division, Department of Hematology-Oncology, IRCCS Fondazione Policlinico San Matteo, Pavia, Italy; [11]Department of Hematology, Businco Hospital, Cagliari, Italy; [12]Istituto di Ematologia, Università Cattolica, Fondazione Policlinico Gemelli IRCCS, Roma, Italy; [13]Department of Biomedical Science, University of Bari "Aldo Moro" Medical School, Internal Medicine "G. Baccelli", Policlinico, Bari, Italy; [14]Hematology, AUOP "Federico II", Naples, Italy; [15]Department of Hematology, Hospital Perrino, Brindisi, Italy; [16]Hematology Unit, Department of Hemato-Oncology and Radiotherapy, Great Metropolitan

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Hospital "Bianchi-Melacrino-Morelli", Reggio Calabria, Italy; [17]Hematology Unit AO of Cosenza, Cosenza, Italy; [18]Department of Hematology and Bone Marrow Transplant, IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy; [19]Institute of Haematology and Stem Cell transplantation, Ospedale Santa Maria della Misericordia, University of Perugia, Perugia, Italy; [20]Nephrology Center of National Research Institute of Biomedicine and Molecular Immunology, Reggio Calabria, Italy; [21]UOC Ematologia a Indirizzo Oncologico, AORN "Sant'Anna e San Sebastiano", Caserta, Italy; [22]U.O.C. Ematologia A. O. Ospedali Riuniti Villa Sofia-Cervello, Palermo, Italy; [23]Department of Hematology, Hospital Vito Fazzi, Lecce, Italy; [24]Onco-Hematology, "Tortora" Hospital, Pagani, SA, Italy; [25]Hematology Section, University of Bari, Italy; [26]U.O.C. OncoEmatologia e TMO, Dipartimento Oncologico, La Maddalena, Palermo, Italy; [27]Department of Cellular Biotechnologies and Hematology, Sapienza University of Rome, Italy; [28]Hematology Unit, AOU Ospedali Riuniti di Ancona, Italy; [29]Hematology Unit, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy.

Correspondence: Fortunato Morabito, MD, Biotechnology Research Unit, AO of Cosenza, Contrada San Nicola, Cosenza, Italy; 87100 Cosenza, Italy; e-mail: f.morabito53@gmail.com; ph: +39-0984-015863; fax: +39-0984-681329.

Massimo Gentile, MD, Hematology Unit, AO of Cosenza, Italy; 87100 Cosenza, Italy; viale della Repubblica snc, e-mail:massim.gentile@tiscali.it; ph: +39-0984-681329;fax: +39-0984-681329.

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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.

- 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.

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.