HemaSphere

EHA EUROPEAN HEMATOLOGY ASSOCIATION

P895 DARATUMUMAB PLUS POMALIDOMIDE AND DEXAMETHASONE (DPD) IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA AND 17P DELETION: UPDATED ANALYSIS OF THE DEDALO PHASE II TRIAL

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

Vittorio Montefusco*[1], Anna Maria Cafro[2], Gloria Margiotta-Casaluci[3], Francesca Patriarca[4], Roberto Mina[5,6], Mattia D'Agostino[5,6], Anna Benedetta Dalla Palma[7], Rita Rizzi[8,9], Angelo Genua[10], Francesca Fazio[11], Laura Paris[12], Angelo Belotti[13], Ilaria Rizzello[14,15], Concetta Conticello[16], Carmelo Carlo-Stella[17,18], Mario Boccadoro[19]

[1]Onco-Hematology Deapartment, Asst Santi Paolo E Carlo, Milano, Italy; [2]Asst Grande Ospedale Metropolitano Niguarda, Milano, Italy; [3]Division Of Hematology, Department Of Translational Medicine, University Of Eastern Piedmont, Novara, Italy; [4]Hematologic Clinic And Transplant Center, University Hospital Of Central Friuli, Dame, University Of Udine, Udine, Italy; [5]Division Of Hematology, Azienda Ospedaliero-Universitaria Città Della Salute E Della Scienza Di Torino, Torino, Italy; [6]Division Of Hematology, Department Of Molecular Biotechnology And Health Sciences, University Of Torino, Torino, Italy; [7]Hematology Unit, Azienda Ospedaliero-Universitaria Di Parma, Parma, Italy; [8]University School Of Medicine, aldo Moro, Department Of Precision And Regenerative Medicine And Ionian Area, Bari; [9]Hematology And Stem Cell Transplantation Unit, Aou Consorziale Policlinico, Bari, Italy; [10]Oncohematology Unit, Azienda Ospedaliera S. Maria Di Terni, University Of Perugia, Terni, Italy; [11]Haematology, Department Of Translational And Precision Medicine, Azienda Ospedaliera Policlinico Umberto I, Sapienza University Of Rome, Rome, Italy; [12]Division Of Hematology, Asst Papa Giovanni Xxiii, Bergamo, Italy; [13]Department Of Haematology, Asst Spedali Civili Di Brescia, Brescia, Italy; [14]Seràgnoli Institute Of Hematology, Irccs Azienda Ospedaliero-Universitaria Di Bologna, Bologna, Italy; [15]Dipartimento Di Scienze Mediche E Chirurgiche, University Of Bologna, Bologna, Italy; [16]Division Of Hematology, Aou Policlinico Ove, University Of Catania, Catania, Italy; [17]Department Of Oncology And Hematology, Humanitas Cancer Center, Humanitas Clinical And Research Center, Rozzano, Italy; [18]Department Of Biomedical Sciences, Humanitas University, Rozzano, Italy; [19]European Myeloma Network (Emn), Italy

Background:

Deletion of the short arm of chromosome 17 (del(17p)) is a well-established high-risk feature included in the current staging criteria for multiple myeloma (MM). Treatment of del(17p) MM is challenging because it is characterized by rapid development of chemoresistance and short survival. The del(17p) clone size correlates with prognosis, and the threshold value of 55%–60% has the worst prognosis. Approximately a third of patients (pts) have a concomitant TP53 mutation, with a complete abolition of the protein function. TP53 biallelic inactivation is defined as double-hit MM.

Few studies investigated tailored treatments for del(17p) MM. The IFM 2010-02 trial showed that the pomalidomide-dexamethasone doublet is promising in this setting (Leleu et al, Blood 2014), while immunotherapy is an attractive strategy due to its mechanism of killing, which is independent from TP53-mediated DNA repair.

Aims:

In this updated analysis of the phase II DEDALO trial (NCT04124497), we aimed to investigate the efficacy of daratumumab-pomalidomide-dexamethasone (DPd) in relapsed MM pts harboring a del(17p) clone.

Methods:

Key eligibility criteria included relapsed or relapsed/refractory MM; ≤3 prior therapy lines; del(17p) detected by fluorescence *in situ* hybridization (FISH) in ≥10% of plasma cells at any time of MM history; absence of refractoriness or intolerance to pomalidomide and to an anti-CD38 monoclonal antibody; previous exposure to

lenalidomide (Len). All pts provided informed consent. Off label use of drugs was involved. Pts received continuous treatment with daratumumab (1800 mg sc or 16 mg/kg iv) weekly during cycles 1–2, every 2 weeks during cycles 3–6, and every 4 weeks thereafter; oral pomalidomide (4 mg, once daily on days 1–21); and oral or iv dexamethasone (40 mg once daily on days 1,8,15,22; 20 mg for those aged ≥75 years [yr]) at each 28-day cycle. The primary endpoint was minimal residual disease (MRD, 10^{-5}) negativity within the first 12 treatment months (mo), detected by next-generation flow (NGF) and next-generation sequencing (NGS). The key secondary endpoints were progression-free survival (PFS), overall response rate (ORR), and overall survival (OS).

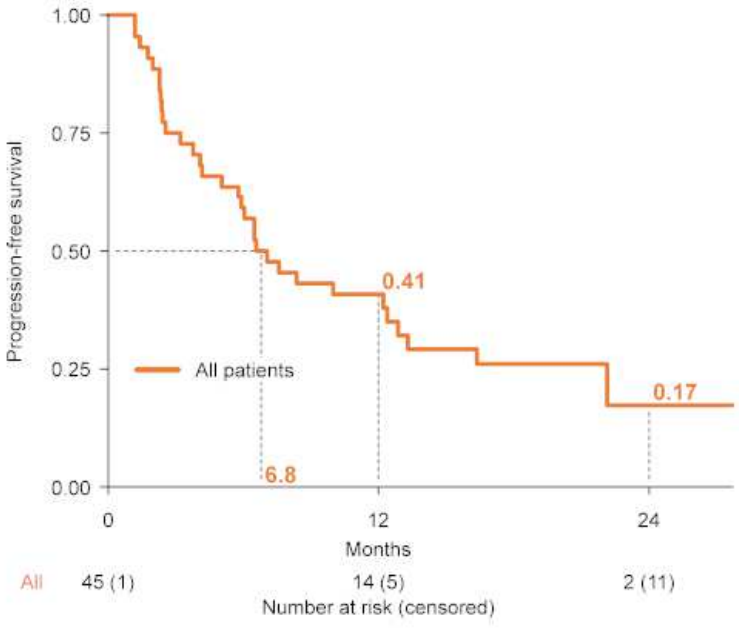
Results:

Forty-five pts were enrolled. Median age was 63 yr (range 43–83), and 60%/29%/11% of pts had International Staging System (ISS) stage I/II/III. At diagnosis, del(17p) clone size was >10% in all pts, and ≥55% in 15 pts; t(4;14) was observed in 7, t(14;16) in 7, del(1p) in 10, and 1q+ in 17 pts. Median number of prior therapy lines was 1 (range 1–3); all pts had been previously exposed to Len and 87% to a proteasome inhibitor (PI). Four pts achieved MRD negativity by NGF, while NGS analysis is ongoing. ORR was 62%, with partial response in 13, very good partial response in 13, and ≥complete response in 2 pts. Median time-to-response was 2.5 mo. With a median follow-up of 14 mo (range 6–29), median PFS was 6.8 mo (95% CI 5.8–13.3; *Figure*). By subgroup analysis, PFS was: 6.5 mo in pts with del(17p) clone size <60% and 7.7 mo with del(17p) clone size ≥60% (HR 1.07, 95% CI 0.53–2.15, *P*=0.85); 12.9 mo in pts with ISS I vs 4.2 mo with ISS II-III (HR 2.50, 95% CI 1.24–5.07, *P*=0.011); 9.2 mo in pts at first relapse vs 6.3 mo beyond first relapse (HR 0.73, 95% CI 0.36–1.47, *P*=0.37); 6.5 mo in pts aged ≤65 yr vs 8.8 mo >65 yr (HR 0.78, 95% CI 0.38–1.63, *P*=0.52). Median OS was not reached. No new safety concerns were observed. TP53 mutational analysis is ongoing.

Summary/Conclusion:

DPd is an option for pts of all ages, showing a promising response in this difficult-to-treat population.

Figure. Progression-free survival



Abstract Book Citations: Authors, Title, HemaSphere, 2023;7(S3):pages. The individual abstract DOIs can be found at https://journals.lww.com/hemasphere/pages/default.aspx.