CARFILZOMIB LENALIDOMIDE DEXAMETHASONE (KRD) WITH OR WITHOUT TRANSPLANTATION IN NEWLY DIAGNOSED MYELOMA (FORTE TRIAL): EFFICACY ACCORDING TO RISK STATUS

Author(s): Francesca Gay , Chiara Cerrato , Delia Rota Scalabrini , Angelo Belotti , Monica Galli , Elena Zamagni , Massimo Offidani , Paola Omedé , Federico Monaco , Patrizia Tosi , Ombretta Annibali , Francesco Pisani , Rossella Troia , Anna Pascarella , Felicetto Ferrara , Michele Cea , Benedetta Dalla Palma , Francesca Patriarca , Sara Aquino , Angelo Palmas , Agostina Siniscalchi , Mariella Grasso , Antonio Palumbo , Antonio Ledda , Pellegrino Musto , Michele Cavo , Mario Boccadoro EHA Library. Gay F.

Jun 15, 2019; 267455

Abstract: S872

Type: Oral Presentation

Presentation during EHA24: On Saturday, June 15, 2019 from 16:15 - 16:30

Background
High and comparable rates of response and minimal residual disease (MRD) negativity were reported with four 28-day induction cycles of KRd followed by autologous stem-cell transplantation (ASCT) and 4 KRd consolidation (KRd_ASCT_KRd), and with 12 KRd cycles (KRd12) in newly diagnosed myeloma (NDMM) patients. Of note, both regimens were superior to carfilzomib-cyclophosphamide-dexamethasone (KCd) induction followed by ASCT and KCd consolidation (KCd-ASCT-KCd) (Gay F ASH 2018).

Aims
We evaluated the benefit of KRd_ASCT_KRd vs KRd12 in specific subgroups of patients according to their risk status.

Methods
474 NDMM patients ≤65 years were randomized to KRd_ASCT_KRd or KRd12 or KCd_ASCT_KCd. We compared rate of ≥VGPR, ≥CR, sCR, MRD negativity (centralized, second generation flow cytometry, sensitivity 10^{-5}) after consolidation with KRd_ASCT_KRd vs KRd12 in patients with available Revised International Staging System (R-ISS) 1 and R-ISS 2/3. High-risk patients may sometimes respond rapidly, but subsequently relapse early. Therefore, we also analyzed the rate of early relapse (<18 months from randomization) in the two arms. We performed a multivariate logistic regression analysis to evaluate factors predictive of early relapse.

Results
Median follow-up was 25 months. On intention-to-treat analysis, KRd_ASCT_KRd and KRd12 showed similar rates of ≥VGPR, ≥CR, sCR, MRD negativity in the overall population (Table 1A). Similarly, MRD negativity and response rates in the two treatment arms were comparable in the subgroups of patients with R-ISS Stage 1 and with R-ISS Stage 2/3 (Table 1B). Of note, rate of MRD negativity in high-risk patients was around 50% (Table 1B). In the overall population, early relapses were significantly lower with KRd_ASCT_KRd vs KRd12 (12 patients [8%] vs 26 patients [17%]; P=0.015), mainly related to a significantly lower rate of early relapse in patients with high risk status (R-ISS Stage 2/3) (11 patients [12%] vs 22 patients [23%]; P=0.05, respectively). Very few patients with R-ISS Stage 1 relapsed, with no difference between KRd_ASCT_KRd and KRd12 (0 vs 2 patients). In multivariate regression analysis, patients receiving KRd_ASCT_KRd had a reduced risk of early relapse compared with those treated with KRd12 (OR 0.42; P=0.021); R-ISS Stage 2 (OR 3.6; P=0.001) and R-ISS Stage 3 (OR 4.85; P=0.003) increased the risk of early relapse compared with R-ISS 1.

Table 1A: Overall population			Table 1B: Subgroup analysis			
	KRd_ASCT_KRd N=158	KRd12 N=157	R-ISS 1		R-ISS 2/3	
			KRd_ASCT_KRd N=48	KRd12 N=39	KRd_ASCT_KRd N=92	KRd12

						N=94
sCR	44%	43%	46%	49%	39%	38%
≥CR	60%	61%	60%	64%	56%	57%
≥VGPR	89%	87%	92%	79%	86%	86%
MRD negative	58%	54%	69%	62%	51%	47%

Conclusion

KRd-ASCT-KRd and KRd12 were equally effective in inducing high-quality responses, and approximately 50% of high-risk patients achieved MRD negativity. In addition, ASCT proved to be beneficial in high-risk patients, reducing the risk of early relapse.