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POSTER ABSTRACTS

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Bortezomib-Cyclophosphamide-Dexamethasone (VCD) Vs Bortezomib-Lenalidomide-Dexamethasone (VRD) in Newly Diagnosed Multiple Myeloma: A Matched Real-World Analysis from the Balkan Myeloma Study Group (BMSG)

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Bortezomib-based triplets have been the mainstay of primary therapy for patients with newly diagnosed symptomatic myeloma (NDMM) for more than a decade. Bortezomib with dexamethasone and cyclophosphamide (VCD or CyBorD) has been a very popular regimen with significant activity and favorable toxicity profile, especially for patients with renal dysfunction and also in a resource poor setting. The combination of bortezomib with lenalidomide and dexamethasone (VRd) is widely used in US and many European countries, especially after the results of phase 3 studies which used this regimen as induction therapy before HDM/ASCT (IFM2009, DETERMINATION) and a prospective comparison to Rd in patients with non-immediate intent to transplant (SWOG S0777). EHA/ESMO guidelines recommend VRd (or VTD-Daratumumab) as preferable options and VCd as alternative if the other two regimens are not available; however, VCd and VRd have not been compared directly in a prospective randomized trial but only in retrospective studies, from referral centers. We aimed to compare the outcomes of patients treated with VCd or VRd in a real-world setting. The analysis included 1911 NDMM patients treated with VCd (N=1326) or VRd (N=585) with available data in the BMSG database.
Initially, we compared the disease and patient characteristics of the two groups: VRd treated patients were more often >65 years (48% vs 36%, p<0.001) and had less often ISS-3 disease while VCd treated patients had more often hypercalcemia (30% vs 18%, p<0.001), eGFR<30 ml/min/1.73 m2 (26% vs 10%, p<0.001), serum LDH>ULN (27% vs 16%, p<0.001), lower platelet counts (<130 K/uL) (12% vs 6%, p=0.001), anemia (Hgb<10 gr/dl) (44% vs 36%, p=0.001), ECOG performance status (PS) 3-4 (16% vs 11%, p=0.011). HDM was used as consolidation in 52% of VCd treated vs 32% of VRd treated patients (p<0.001) while maintenance therapy after induction or consolidation was given in 46% vs 64% respectively (P<0.001). ISS stage distribution

was significantly different (21%, 29% and 50% were ISS-1, -2 & -3 in VCd vs 37%, 33% & 30% for VRd treated pts, p<0.001) and high risk cytogenetics frequency was similar (22% vs 22.5%, p=0.787). Distribution to R-ISS-1, -2 & -3 stages (VCd: 8%, 77% and 15% vs 18%, 71% and 11% for VCd and VRd, respectively, p<0.001) and R2-ISS-I, -II, -III & -IV (VCd: 11.5%, 22%, 48.5%, 18% and VRd: 17.5%, 26%, 39% and 17%, p=0.009) were different. A response (≥PR) after induction with VCd and VRd was recorded in 88% and 97% of evaluable patients (N=1653) (p<0.001) with CR/VGPR in 51.5% and 69% (p<0.001). Median PFS was 31 vs 44 months (p<0.001) and 5-year OS was 63% vs 73% with VCd and VRd respectively(p<0.001). We then performed a multivariate analysis that included major prognostic factors that differed between the two groups (age, ISS-3 disease, eGFR<30, LDH, PS, HDM use, HR cytogenetics, use of maintenance): VRd was independently associated with higher probability of CR/VGPR (OR: 2.3, p<0.001), improved PFS (HR: 0.718, p=0.024) and improved OS (HR:0.61, p=0.023). In ASCT-treated patients that also received lenalidomide maintenance, 3-year PFS was 61% vs 84% (p<0.001) and 5-year OS was 79% vs 93% (p=0.003) for VCd and VRd respectively.

However, the significant differences in the baseline disease and clinical characteristics between the two groups do not allow direct comparisons. In order to decrease bias, we performed an analysis in pts matched for age, country, eGFR, ISS stage, cytogenetics, HDM and maintenance use. The matched groups included 182 patients each (N=364): ORR was 90% vs 98% (p<0.001), CR/VGPR rate was 51% vs 71% (p=0.001), 3-year PFS rate was 55% vs 69% (p=0.016) and the 5-year OS was 70% with VCd vs 71% with VRd (p=0.269). In the ASCT-treated subgroup, 5-year PFS and OS were 54% vs 69% (p=0.086) and 87% vs 94% (p=0.335) for VCd vs VRd.

In conclusion, VCd remains an important regimen for the management of NDMM, especially in a resource poor setting and in special circumstances, although VRD is associated with a significant reduction in the risk of primary induction failure and deeper responses. In matched analysis, VCd does not seem to be associated with significantly inferior OS compared to VRd, which is associated with better responses and longer PFS. With the implementation of new drugs, such as monoclonal antibodies, VCd backbone is a reasonable option for patients that do not have access or do not tolerate VRd or in newer combinations in the upfront setting.

Disclosures Kastritis: *GSK:* Honoraria, Research Funding; *Pfizer:* Honoraria, Research Funding; *Janssen:* Honoraria, Research Funding; *Sanofi:* Honoraria. **Beksac:** *Sanofi:* Speakers Bureau; *Menarini:* Membership on an entity's Board of Directors or advisory committees; *BMS:* Speakers Bureau; *Janssen:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Takeda:* Speakers Bureau. **Katodritou:** *Janssen Cilag, Amgen, Abbvie, Pfizer, GSK, Takeda, Sanofi, Karyopharm:* Honoraria, Research Funding. **Dalampira:** *Pfizer:* Research Funding. **Coriu:** *Genesis BioPharma:* Other: TRAVEL, ACCOMMODATIONS, EXPENSES; *Accord Healthcare:* Other: TRAVEL, ACCOMMODATIONS, EXPENSES. **Gavriatopoulou:** *Celgene/Genesis:* Honoraria; *Amgen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Sanofi:* Honoraria; *Janssen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Takeda:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *GSK:* Honoraria; *X4 Pharmaceuticals:* Research Funding; *Karyopharm:* Honoraria, Research Funding. **Terpos:** *BMS:* Honoraria; *Takeda:* Honoraria, Other: Travel expenses, Research Funding; *Menarini/Stemline:* Honoraria; *Janssen:* Honoraria, Research Funding; *GSK:* Honoraria, Research Funding; *EUSA Pharma:* Honoraria, Other: Travel expenses; *ASTRA/Zeneca:* Honoraria, Other: Travel Expenses; *Amgen:* Honoraria, Other: Travel Expenses, Research Funding; *Pfizer:* Honoraria; *Sanofi:* Honoraria, Other: Travel expenses, Research Funding. **Dimopoulos:** *Takeda:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Sanofi:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Regeneron:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Menarini:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Janssen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *GlaxoSmithKline:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *BeiGene Inc:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Bristol Myers Squibb:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Amgen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *AbbVie:* Honoraria, Membership on an entity's Board of Directors or advisory committees.

	unmatched			matched		
	VCd	VRd	p-value	VCd	VRd	p-value
	N=1326	N=585		N=182	N=182	
Age > 65 years	36%	48%	<0.001	29%	29%	1.000
eGFR<30	25%	9.5%	<0.001	13%	13%	1.000
Hypercalcemia	30%	18%	<0.001	16%	16%	1.000
PLT < 130	12%	6%	0.001	10%	6%	0.119
HgB<10	44%	35%	0.001	41%	36%	0.333
PS 3-4	16%	11%	0.011	6%	6%	0.958
ISS	21% / 29% / 50%	37% / 33% / 30%	<0.001	30% / 32% / 38%	38% / 34% / 28%	0.089
R2-ISS	12%/22%/48%/18%	18%/26%/ 39%/17%	0.009	17% / 18% / 42% / 24%	18% / 23% / 38% / 21%	0.674
R2-ISS-High	18%	17%	0.611	24%	21%	0.595
R-ISS	8% / 77% / 15%	18% /71% / 12%	<0.001	21% / 56%v / 23%	23% / 62% / 15%	0.216
HR cytogenetics	22%	23%	0.787	29%	29%	1.000
LDH high	27%	16%	<0.001	23%	22%	0.780
HDM	52%	32%	<0.001	44.5%	44.5%	1.000
Maintenance	46%	64%	<0.001	61%	61%	1.000
ORR	88%	97%	<0.001	90%	98%	<0.001
CR/VGPR	51.5%	69%	<0.001	51%	71%	0.001
3-year PFS	44%	58%	<0.001	55%	69%	0.016
5-year OS	63%	73%	<0.001	70%	71%	0.269

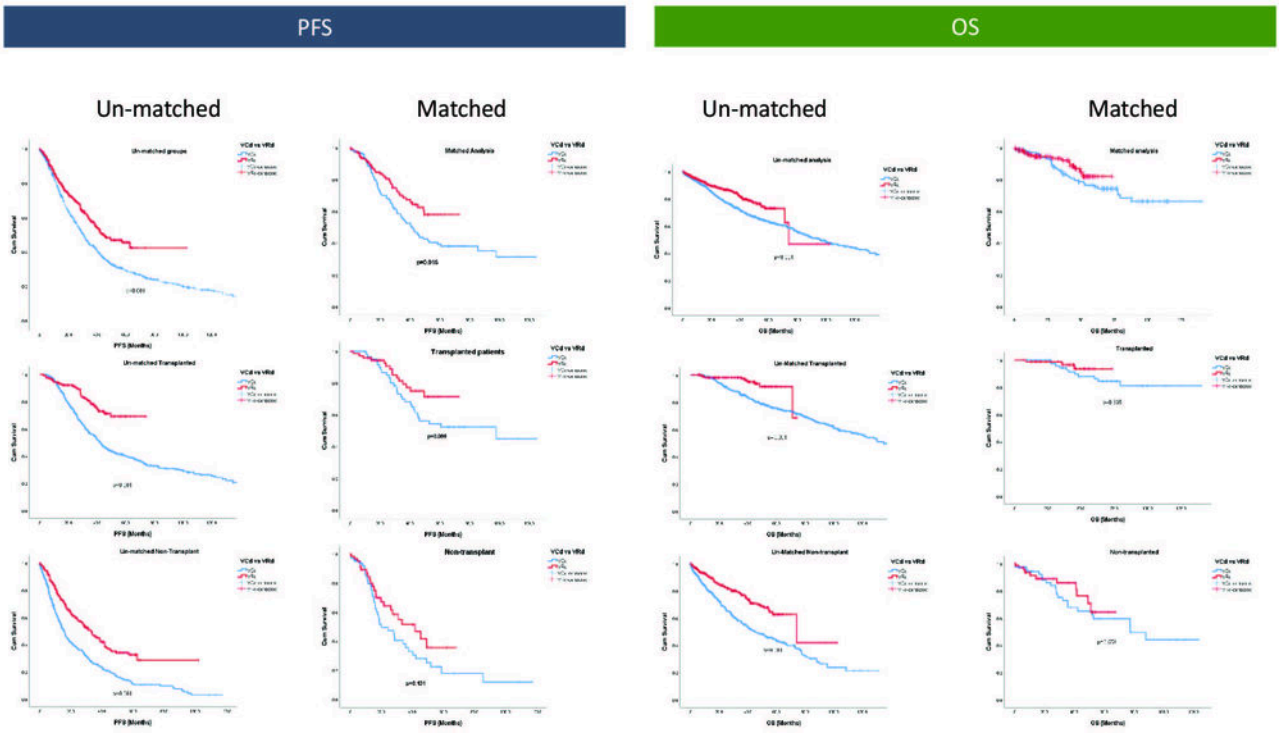

Figure 1

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