Propensity score matching analysis to evaluate Bortezomib/Cyclophosphamide /Dexamethasone and Bortezomib/Thalidomide/Dexamethasone from Real-World Data in Patients with Newly Diagnosed Multiple Myeloma

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On Behalf of Colombian Multiple Myeloma Registry

Abstract

We performed a 1:1 propensity score matching (PSM) analysis in data of patients belonging to Registro Epidemiológico de Neoplasias Hematológicas en Colombia (RENEHOC) to compare the effectiveness of both in terms of response and overall survival (OS). Regarding the overall response rate (ORR) in the unpaired model, the VTD tends to be favored 73.47% vs 63.68% p=0.061, however, when the analysis was made after the PSM the differences dissipate and became non-significant 68.75% vs 73.66% p=0.565. There were not statistically differences per regimen in terms of OS either. The median OS in the transplanted VTD group was 34 months IQR (20-54) and in not transplanted patients it was only 8 months IQR (5-17) p <0.0001. The same occurred in VCD group, 29 months IQR (17-46) versus 12 months IQR (5-25) p <0.0001. VTD or VCD were equally effective in terms of response and survival in real world practice. Overall survival was adversely affected when patients did not undergo ASCT regardless of the regimen used in induction.

Background

Nowadays the triple-drug combination of bortezomib and dexamethasone plus one third agent followed by autologous stem-cell transplantation (ASCT) is a standard of care for most patients with newly diagnosed multiple myeloma (MM) who are transplant-eligible.

In Colombia different protocols are used among which we have VTD with thalidomide, VCD with cyclophosphamide, VRD with lenalidomide and PAD with doxorubicin. To date, there have been no randomized clinical trials (RCTs) that directly compare the efficacy and safety of all of them.

It is difficult to delineate valid conclusions from indirect comparisons between published clinical trials data because unadjusted comparisons of outcomes are prone to confounding factors, due to variation in patient characteristics among all treatment populations. Moreover, randomized controlled trials, that are the gold standard in clinical research are difficult to conduct because of many practical considerations, particularly for low- and middle-income countries (LMIC).

Propensity score (PS) analysis of observational studies is an alternative method of estimating causal treatment effects for clinically important questions in observational studies, and well-designed observational studies can also help enhance and complement the findings of randomized studies.

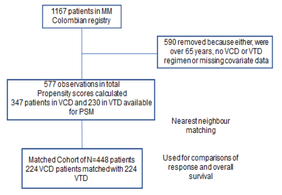
The RENEHOC (Registro Epidemiológico de Neoplasias Hematológicas en Colombia) MM registry encompasses currently over 1.200 of patients of which almost half are under 65 years of age. In this work we decided to investigate the difference in terms of responses and survival considering the two most frequently prescribed regimens for transplant eligible patients VCD or VTD also called CyBorD using PSM analysis methodology.

Objective

The efficacy endpoints included in the PSM analysis were overall response rate (ORR) and overall survival (OS). The following covariates were identified for matching (based on expert opinion): age, sex, myeloma type, international staging system stage at diagnosis, kidney injury, dialysis, extramedullary involvement, and autologous hematopoietic stem cell transplantation. At baseline, the proportion of patients for whom cytogenetic testing was not done was very high as well as exact data regarding maintenance therapy, so these two covariates were not taken in account for the model.

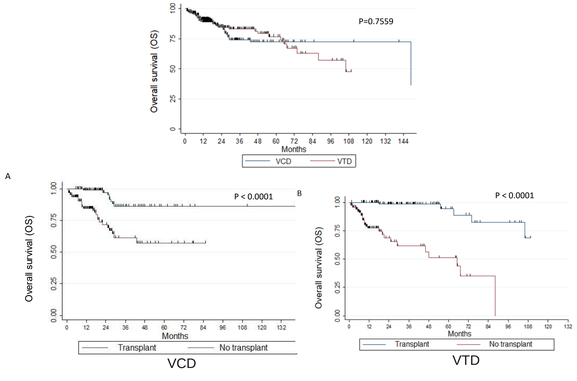
Materials & Methods

A total of 577 patients were identified in unpaired model. After pairing using propensity score matching by nearest neighbor, a total of 448 patients, 224 in each group, were identified.



	Unmatched patient population					Matched Population				
	VCD (n=347)		VTD (n=230)		p value	VCD (n=224)		VTD (n=224)		p value
Age	61.84	(SD 9.22)	64.62	SD(9.72)	**0.001** Mann-Whitney	63.9	(SD 8.86)	64.48	(SD 9.79)	0.678 Mann-Whitney
Sex					0.946					0.705
Men	171	(49.28)	114	(49.57)		109	(48.66)	113	(50.45)	
Women	176	(50.72)	116	(50.43)		115	(51.34)	111	(49.55)	
Renal Failure	97	(27.95)	67	(29.13)	0.759	64	(28.57)	65	(29.02)	0.917
Dyalisis	35	(35.71)	30	(44.12)	0.275	29	(45.31)	30	(46.15)	0.924
Immunofixation					0.464					0.819
IgG	138	(63.59)	85	(58.22)		87	(61.70)	84	(58.74)	
IgA	52	(23.96)	44	(30.14)		35	(24.82)	42	(29.37)	
Negative	15	(6.91)	7	(4.79)		9	(6.38)	7	(4.90)	
Free light chain	12	(5.53)	10	(6.85)		10	(7.09)	10	(6.99)	
ISS					0.312					0.817
1	55	(16.18)	27	(12.05)		26	(11.61)	27	(12.05)	
2	75	(22.06)	44	(19.64)		48	(21.43)	44	(19.64)	
3	124	(36.47)	97	(43.30)		88	(39.29)	97	(43.30)	
Unknown	86	(25.29)	56	(25.00)		62	(27.68)	56	(25.00)	
Extramedular Disease	233	(67.15)	145	(63.04)	0.31	142	(63.39)	142	(63.39)	1
ASCT	124	(35.73)	97	(42.17)	0.119	92	(41.07)	96	(42.86)	0.702

Regarding the global response in the unpaired model, the VTD tends to be favored 73.47% vs 63.68% p = 0.061, however, when the analysis is made after the PSM the differences dissipate and become non-significant 68.75% vs 73.66% p = 0.565.



There was not difference in OS between VTD and VCD group. In addition, we ran an overall survival analysis for each regimen whether they had undergone transplantation.

The median overall survival in the transplanted VTD group was 34 months IQR (20-54) and in VTD not taken to transplantation it was 8 months IQR (5-17) p <0.0001, in the VCD group the same occurs, 29 months IQR (17-46) in the transplanted group versus 12 months in the non-transplant group IQR (5-25) p <0.0001.

Summary

This PSM analysis demonstrated that VTD or CyBorD were equally effective in terms of response and survival in real world practice. Overall survival was adversely affected when patients did not undergo autologous bone marrow transplantation regardless of the regimen used in induction.

Discussion

For Colombian clinical practice, the VTD or the VCD are equally effective. It is necessary to increase the possibility of ASCT in candidate patients. Failure to proceed with ASCT, regardless of the given regimen, negatively impacts survival.

References

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Corresponding author: humbertomartinez48@hotmail.com This is a study from the Colombian Registry of Multiple Myeloma RENEHOC