Comparing the clinical trial efficacy *versus* real-world effectiveness of treatments for multiple myeloma: a population-based study

Authors

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Table S1. Comparison of clinical trial inclusion criteria and Cancer Care Ontario (CCO) drug regimen funding. The CCO criteria that differ from RCT trial inclusion/exclusion criteria are bolded.

Regimen	CCO criteria				RCT inclusion criteria			
	Funding date	Patient population	Prior lines	Prior drug exposure/ refractory requirements	Date of first publication	Prior lines	Inclusion criteria (based on prior treatment)	Exclusion criteria (based on prior treatment)
Pd	February 6, 2015	RRMM	-	Bortezomib and lenalidomide refractory. **No requirement for prior alkylator exposure**	September 3, 2013 (12)	-	bortezomib refractory or intolerance AND lenalidomide refractory AND alkylator exposure	Prior pomalidomide exposure
Rd	March 14, 2017	TIE-NDMM	None	Same as trial	September 4, 2014 (5)	None	No prior treatment	-
KRd	May 1, 2018	RRMM	**≥1**	Same as trial	January 8, 2015 (8)	1-3	Prior bortezomib and lenalidomide exposure allowed	Lenalidomide refractory
Kd	May 1, 2018	RRMM	1-3	If prior PI exposure, **no requirement to be PI unexposed within 6 months pre-treatment. Otherwise, same as trial**.	December 5, 2015 (9)	1-3	Prior bortezomib and carfilzomib exposure allowed (6-month PI treatment free interval before enrollment required)	Bortezomib or carfilzomib refractory
DVd	March 15, 2019	RRMM	≥1	Same as trial	August 25, 2016 (11)	≥1	-	Bortezomib refractory (or intolerant) OR Proteosome inhibitor refractory
DRd	March 15, 2019	RRMM	≥1	Same as trial	October 6, 2016 (10)	≥1	-	Lenalidomide refractory (or intolerant)
VRd	December 16, 2020	TIE-NDMM	None	Same as trial	February 4, 2017 (6)	None	No prior treatment	-

Abbreviations: lenalidomide & dex (Rd); bortezomib & Rd (VRd); carfilzomib & dex (Kd); carfilzomib & Rd (KRd); daratumumab & bortezomib & dex (DVd); daratumumab & Rd (DRd); Pomalidomide & dex (Pd); transplant ineligible newly diagnosed multiple myeloma (TIE-NDMM); relapsed refractory multiple myeloma (RRMM); proteosome inhibitor (PI)
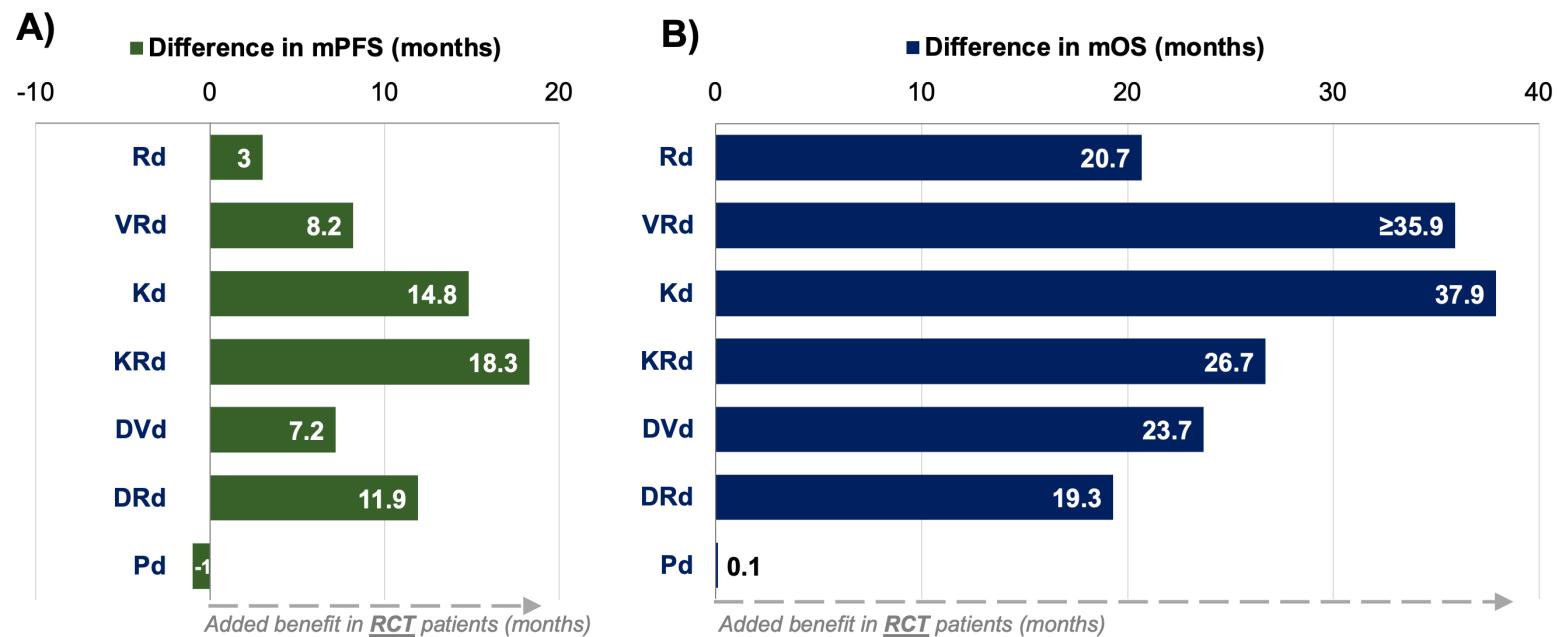
A)

■ Difference in mPFS (months)

Rd	3
VRd	8.2
Kd	14.8
KRd	18.3
DVd	7.2
DRd	11.9
Pd	-1

Added benefit in RCT patients (months)

B)

■ Difference in mOS (months)

Rd	20.7
VRd	≥35.9
Kd	37.9
KRd	26.7
DVd	23.7
DRd	19.3
Pd	0.1

Added benefit in RCT patients (months)

Figure S1. Difference in absolute the median A) PFS and B) OS between clinical trial (RCT) and real-world (RW) patient cohorts. A positive number represents an improved PFS or OS, respectively, in the CT cohort compared to the RW cohort. In the SWOG0777 VRd study, the median OS was not reached in the VRD CT cohort at 84 months of follow up, and therefore the absolute improvement in OS noted is at least 35.9 months compared to the RW cohort. Abbreviations: lenalidomide & dex (Rd); bortezomib & Rd (VRd); carfilzomib & dex (Kd); carfilzomib & Rd (KRd); daratumumab & bortezomib & dex (DVd); daratumumab & Rd (DRd); Pomalidomide & dex (Pd)

Table S2. Summary of mPFS and mOS in the RW cohort, stratified by baseline age

	Number of patients		mPFS		mOS	
	Age <70	Age ≥70	Age <70	Age ≥70	Age <70	Age ≥70
RD	49	775	25.5 (20-39.5)	22.9 (20.7-26.9)	37.5 (29.7-64.2)	38.4 (34.3-40.4)
VRD	26	256	14.1 (5.2-NR)	32.6 (25.1-44.2)	28.4 (5.5-NR)	52.7 (43.5-NR)
KD	287	211	3.8 (2.8-4.6)	4.3 (2.9-5.7)	9.9 (8.4-13.5)	9.9 (7.3-13)
KRD	169	118	6.3 (4.7-8.6)	9.6 (7.3-11.7)	21.6 (17.2-30.1)	21.9 (13.9-32.3)
DVD	304	323	8.7 (7-9.9)	10.9 (8.7-14.5)	29.8 (22.4-40.3)	23.2 (18.5-30.2)
DRD	310	475	27.8 (21.2-NR)	NR (28.6-NR)	NR (45.2-NR)	43.4 (38.6-NR)
PD	318	330	3.9 (3.3-5.1)	6.1 (5-7.6)	13.6 (11.6-17.3)	10.5 (9.3-14)
	CCI <2	CCI ≥2	CCI <2	CCI ≥2	CCI <2	CCI ≥2
RD	489	335	26 (22.5-31.3)	20 (16.1-23.5)	45.3 (38.7-49.5)	29 (23.5-35)
VRD	166	116	35.8 (25.6-44.2)	24.3 (16.1-NR)	48.1 (43.5-NR)	52.7 (26.8-NR)
KD	73	425	7.6 (5.4-10.2)	3.3 (2.8-4.1)	20.5 (12.3-38.6)	8.6 (7.1-10.5)
KRD	41	246	9.7 (5.7-14)	8 (5.6-9.4)	35 (20.2-59.5)	21.2 (16.7-27.9)
DVD	120	507	12.6 (8.5-17.8)	9 (7.7-10.5)	33.2 (22.8-NR)	24.2 (20-30.2)
DRD	221	564	NR (34.8-NR)	27.5 (22.6-34)	NR (NR-NR)	43.4 (35.8-NR)
PD	127	521	6.4 (5-8.3)	4.6 (3.9-5.6)	16.6 (12.3-21.8)	11.6 (9.9-13.5)

Abbreviations: charlson comorbidity index (**CCI**); median progression free survival (**mPFS**); median overall survival (**mOS**); real world (**RW**); randomized clinical trial (**RCT**); confidence interval (**CI**); lenalidomide & dex (**Rd**); bortezomib & Rd (**VRd**); carfilzomib & dex (**Kd**); carfilzomib & Rd (**KRd**); daratumumab & bortezomib & dex (**DVd**); daratumumab & Rd (**DRd**); Pomalidomide & dex (**Pd**); transplant ineligible newly diagnosed multiple myeloma (**TIE-NDMM**); relapsed refractory multiple myeloma (**RRMM**); proteosome inhibitor (**PI**)