

Supplementary Appendix 1. Search strategies, Characteristics of the included study, Results of risk bias assessment

Pubmed

- #1. "Multiple Myeloma"[Mesh] OR Multiple Myeloma*[tw] OR Plasma-Cell Myeloma*[tw] OR Myelomatos*[tw] OR Kahler Diseas*[tw] OR Myeloma-Multiple*[tw] OR "morbus kahler"[tw]
- #2. "newly diagnos*" [tw] OR untreated[tw] OR "first line"[tw] OR "1ST line"[tw] OR "1 line"[tw] OR "treatment naive"[tw] OR frontline[tw] OR "front line"[tw]
- #3. #1 AND #2 5601
- #4. "carfilzomib" [Supplementary Concept] OR carfilzomib OR "PR-171" OR Kyprolis OR "fp 101" OR ono 7057 OR "ixazomib" [Supplementary Concept] OR ixazomib OR "mln 2238" OR mln2238 OR Ninlaro OR "pomalidomide" [Supplementary Concept] OR pomalidomide OR Imnovid OR Pomalyst OR actimid OR "cdc 394" OR "daratumumab" [Supplementary Concept] OR daratumumab OR Darzalex OR "humax CD38" OR dalinvi OR "isatuximab" [Supplementary Concept] OR isatuximab OR Sarclisa OR "sar 650984" OR "elotuzumab" [Supplementary Concept] OR elotuzumab OR Empliciti OR huluc63 OR "pdl 063" 4509
- #5. #3 AND #4 613
- #6. ("controlled clinical trial"[pt] OR "Controlled Clinical Trials as Topic"[MeSH] OR "Random Allocation"[MeSH] OR "Double-Blind Method"[MeSH] OR "single-blind method"[MeSH] OR "Control Groups"[MeSH] OR random*[tiab]) NOT ("Animals"[Mesh] NOT ("Humans"[Mesh] AND "Animals"[Mesh]))
- #7. #5 AND #6 122

Embase

- #1. 'multiple myeloma'/exp OR ((Multiple NEAR/3 Myeloma*) OR ("Plasma Cell" NEAR/4 (Myeloma* OR tumor OR tumour OR neoplasm*)) OR Myelomatos* OR "Kahler Diseas*" OR "morbus kahler"):ab,ti,kw
- #2. ("newly diagnos*" OR untreated OR "first line" OR "1ST line" OR "1 line" OR "treatment naive" OR frontline OR "front line"):ab,ti,kw
- #3. #1 and #2 14250
- #4. 'carfilzomib'/exp OR 'ixazomib'/exp OR 'pomalidomide'/exp OR 'daratumumab'/exp OR 'isatuximab'/exp OR 'elotuzumab'/exp OR (carfilzomib OR "PR-171" OR Kyprolis OR "fp 101" OR ono 7057 OR ixazomib OR "mln 2238" OR mln2238 OR Ninlaro OR pomalidomide OR Imnovid OR Pomalyst OR actimid OR "cdc 394" OR daratumumab OR Darzalex OR "humax CD38" OR dalinvi OR isatuximab OR Sarclisa OR "sar 650984" OR elotuzumab OR Empliciti OR huluc63 OR "pdl 063"):ab,ti,kw
- #5. #3 AND #4 2695
- #6. ('controlled clinical trial'/exp OR 'Controlled Clinical Trial (Topic)'/exp OR 'double blind procedure'/de OR 'control group'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR 'randomization'/exp OR random*:ab,ti,kw) NOT (('nonhuman'/exp OR 'animal'/exp) NOT 'human'/exp)
- #7. #5 AND #6 783
- #8. #7 AND 'conference abstract'/it 526
- #9. #7 NOT #8 257

Cochrane

- #1 MeSH descriptor: [Multiple Myeloma] explode all trees2782
- #2 ((Multiple NEAR/3 Myeloma*) OR ("Plasma Cell" NEAR/4 (Myeloma* OR tumor OR tumour OR neoplasm*)) OR Myelomatos* OR "Kahler Diseas*" OR "morbus

- kahler");ti,ab,kw6099
- #3 #1 or #26099
- #4 ("newly diagnos*" OR untreated OR "first line" OR "1ST line" OR "1 line" OR "treatment naive" OR frontline OR "front line");ti,ab,kw53251
- #5 (carfilzomib OR "PR-171" OR Kyprolis OR "fp 101" OR ono 7057 OR ixazomib OR "mln 2238" OR mln2238 OR Ninlaro OR pomalidomide OR Imnovid OR Pomalyst OR actimid OR "cdc 394" OR daratumumab OR Darzalex OR "humax CD38" OR dalinvi OR isatuximab OR Sarclisa OR "sar 650984" OR elotuzumab OR Empliciti OR huluc63 OR "pdl 063");ti,ab,kw 1661
- #6 #3 and #4 and #5

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Dimopoulos 2019: Ixazomib vs. Placebo	+	+	+	+	+	+	+
Dimopoulos 2020: Ixazomib vs. Placebo	+	+	+	+	+	+	+
Dimopoulos 2022: Elotuzumab-Rd vs. Rd	+	+	-	+	+	+	-
Dytfeld 2023: KRd vs. R	+	+	-	+	+	+	+
Facon 2019a: D-Rd vs. Rd	+	?	-	+	+	+	+
Facon 2019b: KMP vs. VMP	+	?	-	+	+	+	-
Facon 2021: Ixazomib-Rd vs. Rd	+	?	+	+	+	+	+
Facon 2024: Isatuximab-VRd vs. VRd	+	?	-	+	+	+	+
Francesca 2023: Isatuximab-KRd vs. KRd	+	?	-	+	+	+	+
Gay 2018: KCd vs. KRd	+	?	?	+	+	+	+
Goldschmidt 2022: Isatuximab-VRd vs. VRd	+	?	-	+	+	+	+
Kumar 2020: KRd vs. VRd	+	?	-	+	+	+	+
Mateos 2018: D-VMP vs. VMP	+	+	-	+	+	+	+
Mina 2023: KRd+ASCT vs. KCd+ASCT; KR vs. R	+	+	-	+	+	+	+
Moreau 2019: D-VTd vs. VTd; D vs. Obs	+	+	-	+	+	+	+
Sonneveld 2023: D-VRd vs. VRd	+	?	-	?	+	+	?
Usmani 2021: Elotuzumab-RVd vs. RVd	+	+	-	+	+	+	+
Voorhees 2020: D-VRd vs. VRd	+	?	-	+	+	+	+
Yong 2023: KCd vs. HSCT	+	+	-	+	+	+	+

Supplementary Appendix 2. Results of different treatment regimens

For Transplant Eligible Patients

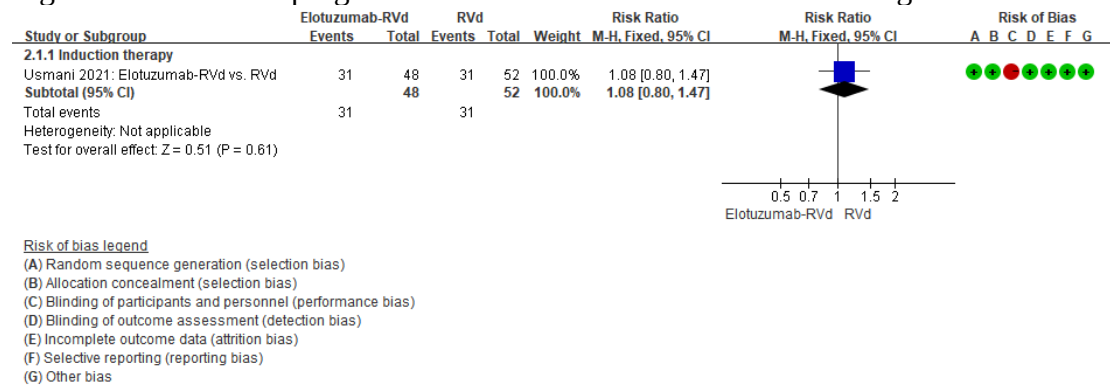
Table S3. Results of minimal residual disease negativity in different patients

Study ID	Treatment	Population	Method	n/N; OR (95%CI)
Francesca 2023	Isa-KRd vs. KRd	1 HRCA	10 ⁻⁵ : NGS.	I: 38/49; C: 32/49 1.86 (0.76-4.57)
Francesca 2023	Isa-KRd vs. KRd	2 HRCA	10 ⁻⁵ : NGS.	I: 10/13; C: 8/15 2.76 (0.52-14.56)
Francesca 2023	Isa-KRd vs. KRd	1 HRCA	10 ⁻⁶ : NGS.	I: 34/49; C: 26/49 2.04 (0.88-4.70)
Francesca 2023	Isa-KRd vs. KRd	2 HRCA	10 ⁻⁶ : NGS.	I: 10/13; C: 4/15 9.05 (1.57-52.14)

CI, confidence interval; Isa, isatuximab; HRCA, high-risk cytogenetic abnormalities; K, carfilzomib; R, lenalidomide; d,

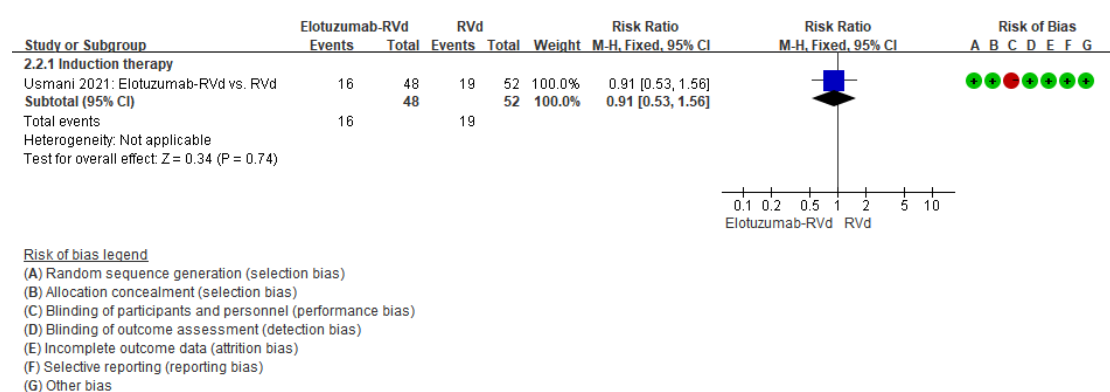
dexamethasone; NGS, next-generation sequencing; OR, odds ratio; MRD, minimal residual disease.

Figure S2. Results of progression or death with Elotuzumab-based regimens



RVd, lenalidomide, bortezomib, dexamethasone;

Figure S3. Results of all-cause mortality with Elotuzumab-based regimens



RVd, lenalidomide, bortezomib, dexamethasone;

Figure S4. Results of progression or death with Ixazomib-based regimens

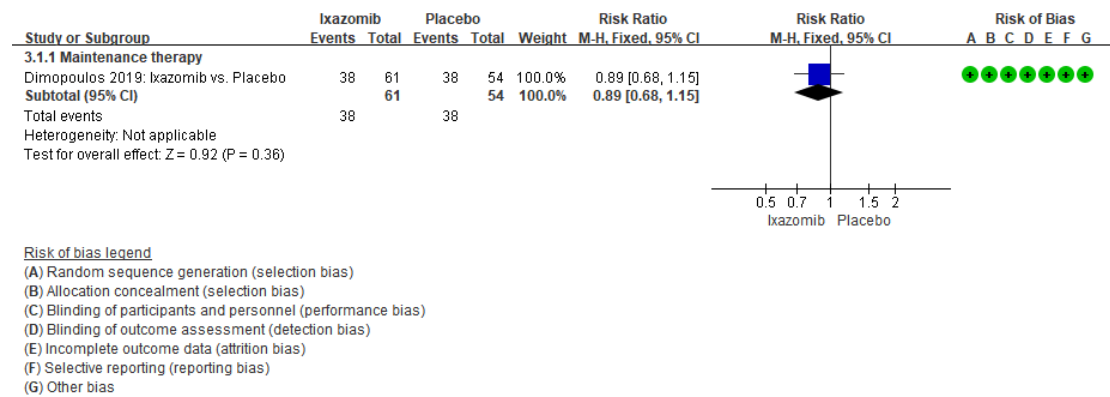


Figure S5. Results of progression or death with Carfilzomib-based regimens

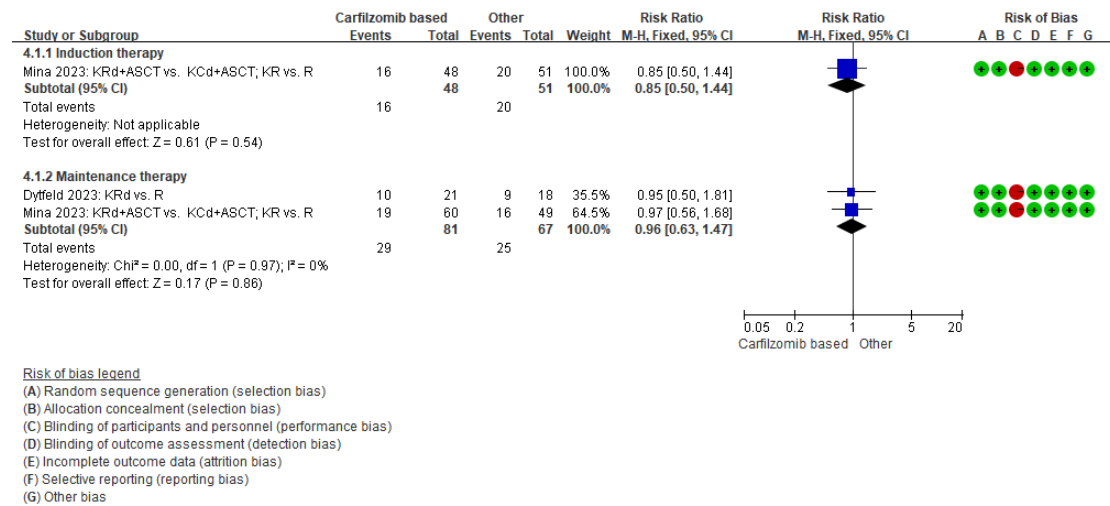


Figure S6. Results of the number of minimal residual disease negative patients with Carfilzomib-based regimens

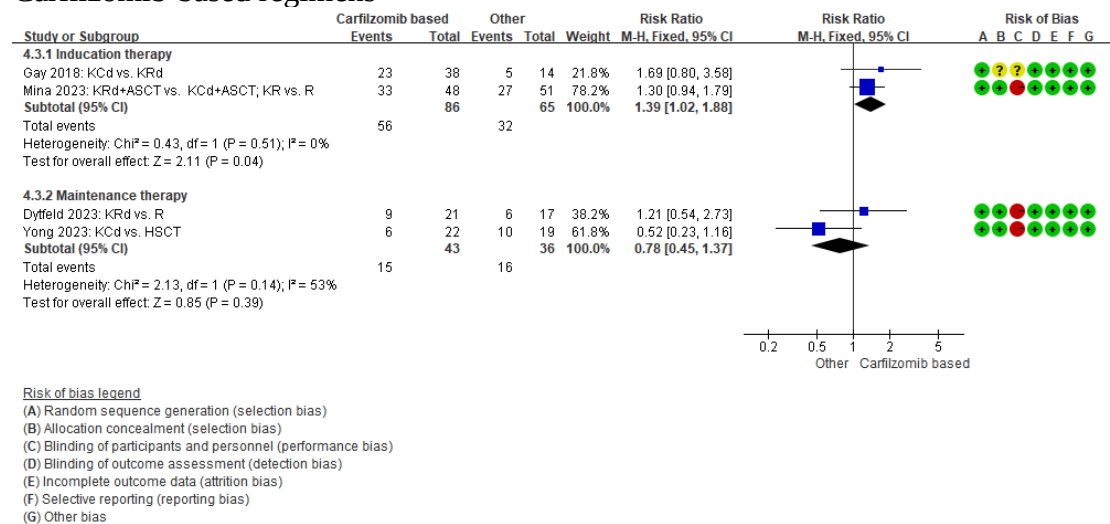
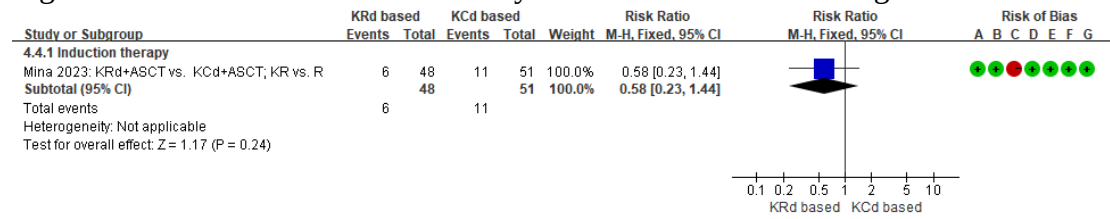


Figure S7. Results of all-cause mortality with Carfilzomib-based regimens



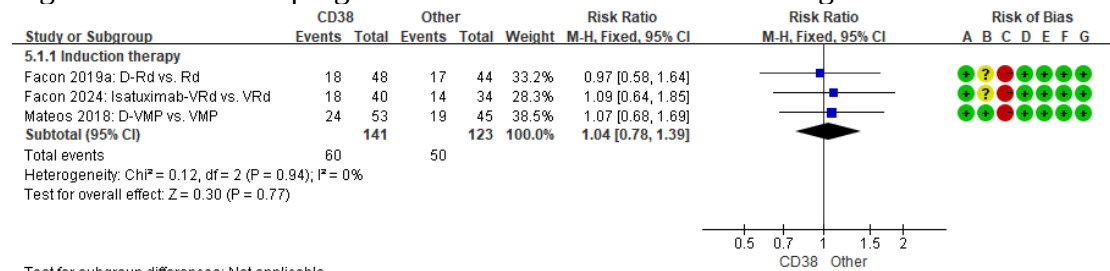
Risk of bias legend

- (A) Random sequence generation (selection bias)
 (B) Allocation concealment (selection bias)
 (C) Blinding of participants and personnel (performance bias)
 (D) Blinding of outcome assessment (detection bias)
 (E) Incomplete outcome data (attrition bias)
 (F) Selective reporting (reporting bias)
 (G) Other bias

KRd, carfilzomib, lenalidomide, dexamethasone; KCd, carfilzomib, cyclophosphamide, dexamethasone

For Non-transplant Eligible Patients

Figure S8. Results of progression or death with CD38-based regimens

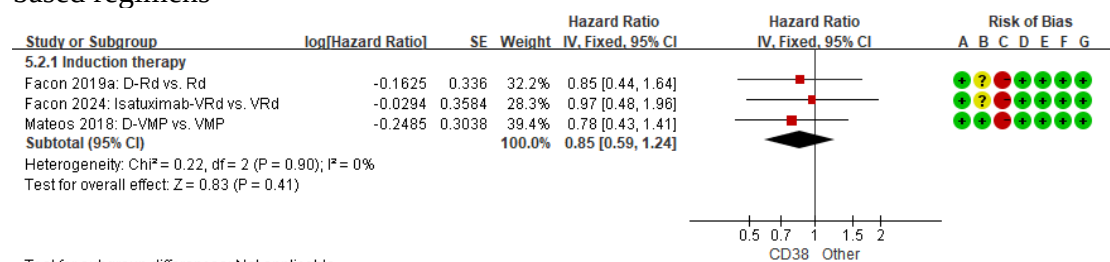


Test for subgroup differences: Not applicable

Risk of bias legend

- (A) Random sequence generation (selection bias)
 (B) Allocation concealment (selection bias)
 (C) Blinding of participants and personnel (performance bias)
 (D) Blinding of outcome assessment (detection bias)
 (E) Incomplete outcome data (attrition bias)
 (F) Selective reporting (reporting bias)
 (G) Other bias

Figure S9. Results of median progression-free survival on hazard ratios with CD38-based regimens

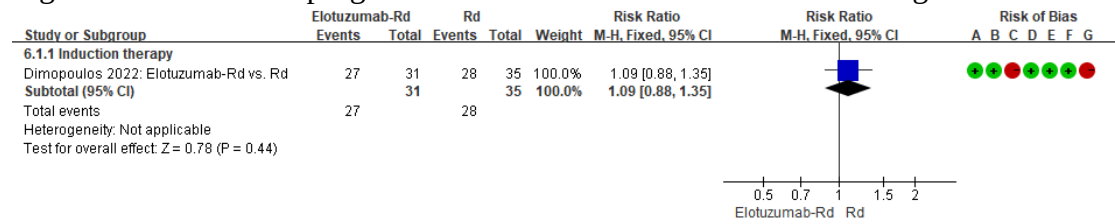


Test for subgroup differences: Not applicable

Risk of bias legend

- (A) Random sequence generation (selection bias)
 (B) Allocation concealment (selection bias)
 (C) Blinding of participants and personnel (performance bias)
 (D) Blinding of outcome assessment (detection bias)
 (E) Incomplete outcome data (attrition bias)
 (F) Selective reporting (reporting bias)
 (G) Other bias

Figure S10. Results of progression or death with Elotuzumab-based regimens

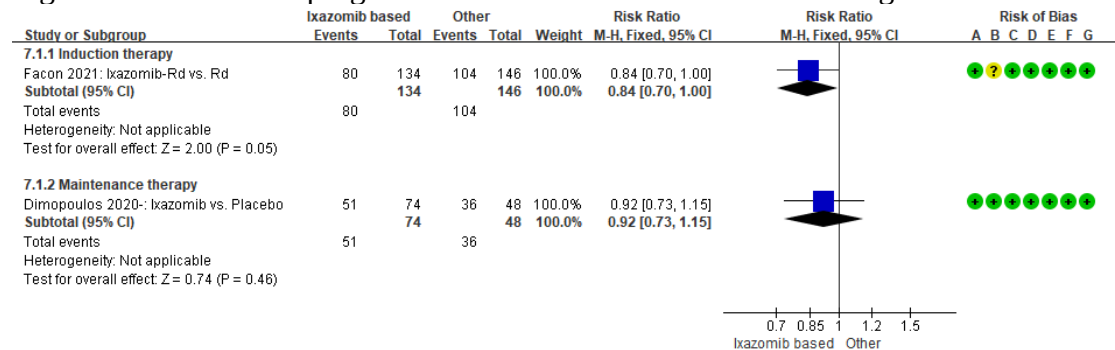


Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Rd, lenalidomide, dexamethasone

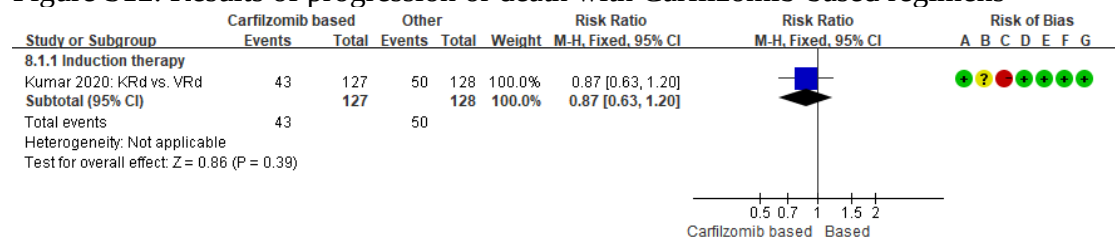
Figure S11. Results of progression or death with Ixazomib-based regimens



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

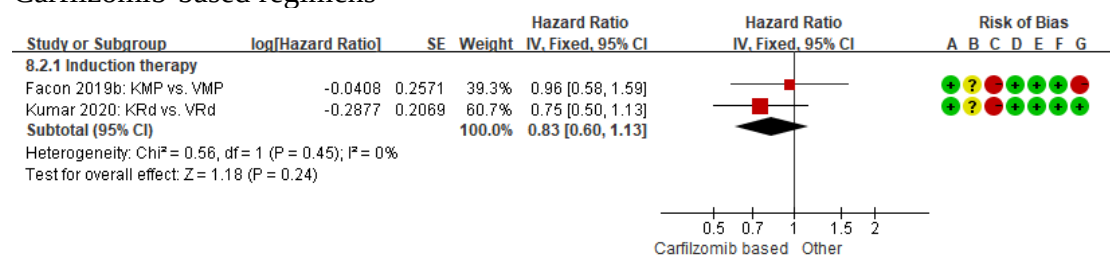
Figure S12. Results of progression or death with Carfilzomib-based regimens



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Figure S13. Results of median progression-free survival on hazard ratios with Carfilzomib-based regimens



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias