Update and European consensus on a patient-centered core outcome set for multiple myeloma in clinical practice and research

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Supplementary materials

Supplementary material Table 1. European consensus-based standardized core outcome set (COS) with accompanying definitions or measurement instruments and data source.

	Outcome definition/measure	Data source
Patient conditions		
Age	Date of birth	Clinical data
Gender	Male/Female/Other/prefer not to say	Clinical data
Date of diagnosis	Histological/ cytologic date of diagnosis of Multiple Myeloma	Clinical data
R-ISS disease stage	Based on revised ISS (only ISS if cytogenetics are not available)	Clinical data
Cytogenetic risk aberration	Cytogenetic risk aberration	Clinical data
Comorbidities	Charlson Comorbidity Index (CCI)	Clinical data
Frailty	IMWG Frailty score (>65 year)	Clinical data
Renal failure at baseline	Indicate if eGFR (estimated Glomerular Filtration Rate) < 30	Clinical data
Height	Length in cm	Clinical data
Weight	Weight in kg	Clinical data
Supporting social network	Supporting social network, yes/no	Patient-reported data
Functioning disability and health	ICF-WHO ECOG Performance status	Clinical data
Health care access	Access and barriers to care: Was there any time during the past 12 months when you really needed to consult your healthcare provider but you did not? Does the patient experience any barriers to accessing care? If yes, why?	Patient-reported data and clinical data
Ethnicity	*Optional, not for cross country comparison*	
Socio-economic status	*Optional, to be determined by country*	
Treatment variables		
Number of treatment line	Indicate the therapy line the patient received	Clinical data
Transplant eligible	Indicate if the patient is eligible for stem cell transplantation	Clinical data
Type of treatment	Indicate which treatments patients received (chemotherapy (including type), immune therapy (including type), stem cell transplantation, radiotherapy, CAR T-Cell therapy, bispecifics, other)	Clinical data
Start and stop date per treatment	Per treatment type provide start and stop date	Clinical data
Induction or maintenance therapy	Indicate if the patient received induction or maintenance therapy and what type/combination of maintenance	Clinical data
Reason of treatment discontinuation	Indicate the reason of treatment discontinuation	Clinical data

Clinical outcomes		
Overall survival	Calculated overall survival	Clinical data
Progression free survival	Calculated progression free survival	Clinical data
Minimal residual disease (MRD)	Positive; negative or unknown; Indicate the sensitivity of the method used (e.g. MRD 10^{-5}, MRD 10^{-6}) and the technique used for assessment (e.g. Next Generation Flow Cytometry (NGF), Next Generation Sequencing (NGS))	Clinical data
Response	Per treatment line. Based on International Myeloma Working Group (IMWG) Uniform Response Criteria for Multiple Myeloma	Clinical data
Relapse	Per treatment line. Indicate whether no, a biochemical or clinical relapse occurred, Indicate the date of relapse	Clinical data
Therapy free interval	Calculated variable: stop - start date of treatment (in days)	Clinical data
Treatment adjustment	Date and reason of treatment adjustment	Clinical data
Adverse events:		
-infections	According to CTCAE v 4.0 and indicate whether treatment was adjusted because of this complication	Clinical data
-polyneuropathy	According to CTCAE v 4.0 and indicate whether treatment was adjusted because of this complication	Clinical data
-renal failure	eGFR (estimated Glomerular Filtration Rate) and indicate whether treatment was adjusted because of this complication	Clinical data
-anaemia	Amount of haemoglobin in 100 ml of blood (hgb) and indicate whether treatment was adjusted because of this complication	Clinical data
-venous thromboembolism	What type (e.g. deep vein, pulmonary, arterial). Based on Compression ultrasonography and indicate whether treatment was adjusted because of this complication	Clinical data
-cardiac	According to CTCAE v 4.0 and indicate whether treatment was adjusted because of this complication	Clinical data
-other	According to CTCAE v 4.0 and indicate whether treatment was adjusted because of this complication	Clinical data
Second primary malignancy	Indicate whether or not and what second primary malignancy	Clinical data
Active treatment < 30 days before death	Indicate whether patient received active treatment in 30 days prior to death	Clinical data
Date of death	Date of death	
Cause of death	*Optional: Indicate the cause of death*	
Patient-reported outcomes		
Mobility / ADL	Question 1-5 of EORTC QLQ-C30	Patient-reported data
Social participation and work	Question 6, 7, 26 and 28 of EORTC QLQ-C30	Patient-reported data
Dyspnoea	Question 8 of EORTC QLQ-C30	Patient-reported data
Pain	Question 9 and 19 of EORTC-QLQ-C30 and Question 31, 33-36 of EORTC QLQ-MY20	Patient-reported data

Fatigue	Question 10, 12 and 18 of EORTC QLQ-C30	Patient-reported data
Loss of appetite	Question 13 of EORTC QLQ-C30	Patient-reported data
Nausea and vomiting	Question 14 and 15 of EORTC QLQ-C30	Patient-reported data
Gastrointestinal problems	Question 16 and 17 of EORTC QLQ-C30 and Question 45 of EORTC QLQ-MY20	Patient-reported data
Cognitive function	Question 20 and 25 of EORTC QLQ-C30	Patient-reported data
Anxiety and depression	Question 21-24 of EORTC QLQ-C30 and Question 44, 48-50 of EORTC QLQ-MY20	Patient-reported data
Global health and HRQoL	Question 29 and 30 of EORTC QLQ-C30	Patient-reported data
Sensory neuropathy	Question 43 of EORTC-MY20 and two items EORTC QLG item library: Did you have numbness in your fingers or toes? And Did you have shooting or burning pain in your hands or feet?	Patient-reported data
Motor neuropathy	2 items EORTC QLG item library: Did you have difficulty opening a jar or bottle because of weakness in your hands? And Did you have difficulty climbing stairs or getting up out of a chair because of weakness in your legs?	Patient-reported data
Body image	Question 47 of EORTC QLQ-MY20	Patient-reported data
Skin disorders	1 item EORTC item library: Have you had skin problems (e.g. colour changes, itchy, dry or flaking skin)?	Patient-reported data
Intimacy	1 item EORTC item library: Have you been satisfied with your level of intimacy?	Patient-reported data
Sexual function	1 item EORTC item library: Have you been satisfied with your sex life?	Patient-reported data
Financial problems	Question 28 of EORTC-QLQ-C30	Patient-reported data

Note. Some questions part of the EORTC QLQ-MY20 (items 37-42) were not included as outcome, but the expert team agreed to include the full questionnaire.

Supplementary material Table 2: Similarities and differences between the IMPORTA, VBHC-MM and HARMONY-Alliance Core Outcome Set (COS).

OUTCOME NAME	Included in Spanish IMPORTA set*	Definition/measure IMPORTA set	Included in Dutch VBHC set	Definition/measure Dutch VBHC set*	Included in HARMONY Alliance set	Definition/measure HARMONY Alliance set	H2O consensus meeting result
Patient conditions					**Not determined**		
Age	Yes	Date of birth	Yes	Age at time of diagnosis	-		Include
Gender	Yes	Male/female	Yes	Male/female/other	-		Include
Date of diagnosis	Yes	Not defined	Yes	Date MM/DD/YYYY	-		Include
R-ISS disease stage	Yes	R-ISS	Yes	R-ISS/ISS 1/2/3	-		Include
Comorbidities	Yes	Comorbidities and/or other non-related myeloma diseases	Yes	Charlson Comorbidity Index	-		Include
Educational level/ socio-economic status	No		Yes	Please indicate the highest level of schooling completed: primary, secondary, or tertiary (university or equivalent)	-		Optional (not for cross country comparison)
Living situation / social network	No		Yes	Single or multi-person household	-		Include
Family history	Yes	Family history of MM other type of cancer	No		-		Exclude
Functioning disability and health	Yes	ECOG	Yes	WHO classification	-		Include
Cytogenetic risk	No		Yes	Low/intermediate/high/NA	-		Include
Frailty	No		Yes	IMWG Frailty score	-		Include
Length	No		Yes	In centimetres	-		Include

Weight	No		Yes	In kilograms	-		Include
Ethnicity	Yes	Race	No		-		Optional (not for cross country comparison)
Renal failure at baseline	Yes	Renal failure prior to treatment/creatinine clearance	No		-		Include
Anaemia at baseline	Yes	Anaemia prior to treatment/haemoglobin	No		-		Exclude
Bone lesions	Yes	Number and location/X-ray, PET etc	No		-		Exclude
Neuropathy at baseline	Yes	Neuropathies prior to treatment	No		-		Exclude
Number of treatment line	No		Yes	Number of treatment line	-		Include
Treatment	Yes	Type of treatment initiated (standard or not), after deciding to treat	Yes	Type of treatment initiated (standard or not), after deciding to treat	-		Include
Transplant eligible	No		No		-		Include
Induction or maintenance therapy	No		No		-		Include
Reason of treatment discontinuation	No		No		-		Include
Healthcare access	No		No		-		Include, optional
Clinical outcomes							
Overall survival	Yes	Overall survival/data of diagnosis and death	Yes	Length of time from diagnosis until death	Yes	Not defined	Include
Progression free survival	Yes	Progression-free survival/ from treatment initiation to progression or death.	Yes	The length of time from diagnosis and start of first line or subsequent treatment until disease	Yes	Not defined	Include

				progression, calculated over a period of three years			
Minimal residual disease (MRD)	Yes	Minimal residual disease/flow cytometry: 4–8 colours panel	No		No		Include
Response	Yes	Time for best response, according to the IMWG	No		No		Include
Therapy free interval	No		Yes	The period that patients do not receive active treatment (i.e. chemo/immune therapy, radiotherapy, stem cell transplantation)	No		Include
Completion of treatment	Yes	Completed treatment (with or without dosage reduction)	No		No		Exclude
Complications: Infection	Yes	Simplified version of the CTCAE	Yes	If CTCAE grade>=2; grade number	Yes	AEs, SAEs	Include
Complications: neuropathy	Yes	Simplified version of the CTCAE	Yes	CTCAE grade	Yes	AEs, SAEs	Include
Complications: renal failure	Yes	Simplified version of the CTCAE	Yes	If EGFR <30; yes, no, unknown	Yes	AEs, SAEs	Include
Complications: anaemia	Yes	Simplified version of the CTCAE	Yes	Yes, no, unknown	Yes	AEs, SAEs	Include
Complications: venous thromboembolism	Yes	Simplified version of the CTCAE	Yes	Yes, no, unknown	Yes	AEs, SAEs	Include
Complication reason for treatment adjustment?	No		No		No		Include

Cardiovascular toxicities	Yes	Simplified version of the CTCAE	No		Yes	Not defined	Include
Date of death	No		Yes	Length of time from diagnosis until death			Include
Place of death hospital?	No		Yes	Yes, no, unknown			Exclude
Active treatment < 30 days before death	No		Yes	Yes, no, unknown			Include
Cause of death	No						Include
Relapse	No						Include
Relapse date	No						Include
Treatment adjustment: Date	No						Include
Treatment adjustment: Reason	Yes						Include
Second primary malignancy	No						Include
PROMs							
HRQoL	Yes	EORTC QLQ-C30	Yes	EORTC QLQ-C30; PROMIS-2		EORTC QLQ-C30	Include
Mobility	Yes	EORTC QLQ-C30	Yes	EORTC QLQ-C30		EORTC QLQ-C30	Include
Overall functioning / ADL	Yes	ECOG; EORTC QLQ-C30	Yes	EORTC QLQ-C30		EORTC QLQ-C30	Include
Anxiety	Yes	EORTC QLQ-C30	Yes	EORTC QLQ-C30		EORTC QLQ-C30	Include
Depressive symptoms	Yes	EORTC QLQ-C30	Yes	EORTC QLQ-C30	Yes	EORTC QLQ-C30	Include
Cognitive problems	Yes	EORTC QLQ-C30	Yes	EORTC QLQ-C30		EORTC QLQ-C30	Include
Social participation and work	Yes	EORTC QLQ-C30	Yes	EORTC QLQ-C30		EORTC QLQ-C30	Include
Fatigue	Yes	EORTC QLQ-C30	Yes	EORTC QLQ-C30	Yes	EORTC QLQ-C30	Include
Nausea	Yes	EORTC QLQ-C30	Yes	EORTC QLQ-C30		EORTC QLQ-C30	Include

Pain/ Back pain	Yes	EORTC QLQ-C30/ VAS	Yes	EORTC QLQ-C30/ VAS/ EORTC QLQ-MY20	Yes	EORTC QLQ-MY20	Include
Dyspnoea	Yes	EORTC QLQ-C30		EORTC QLQ-C30	Yes	EORTC QLQ-C30	Include
Sleep	Yes	EORTC QLQ-C30	Yes	EORTC QLQ-C30		EORTC QLQ-MY20	Include
Loss of appetite	Yes	EORTC QLQ-C30	Yes	EORTC QLQ-C30, EORTC QLQ-MY20		EORTC QLQ-MY20	Include
Gastrointestinal problems	Yes	EORTC QLQ-C30	Yes	EORTC QLQ-C30, EORTC QLQ-MY20		EORTC QLQ-MY20	Include
Financial problems	Yes	EORTC QLQ-C30	Yes	EORTC QLQ-C30		EORTC QLQ-C30	Include
Body image	Yes	EORTC QLQ-MY20	Yes	EORTC QLQ-MY20		EORTC QLQ-MY20	Include
Sensory neuropathy		EORTC QLQ-MY20	Yes	EORTC QLQ-MY20	Yes	EORTC QLQ-MY20	Include
Motor neuropathy							Include
Pathological fractures					Yes	Not defined	Exclude
Fear of physical exercise			Yes	single item			Exclude
Relational and sexual problems	Yes	Self-perception on sexual life/adapted from EORTC-QLQ-BR23 (sexual functioning scale	Yes	single items			Change to intimacy and sexuality
Preferences and satisfaction	Yes	Ad hoc items					Exclude
Treatment adherence	Yes						Exclude

*Measures used may cover more items than defined in core outcome set.