SUPPLEMENTAL MATERIAL

PATIENTS and METHODS

Population and Interventions

Demographic and clinical data

The following demographic and clinical data were extracted: age, sex, MM stage according to the International Staging System (ISS), geriatric vulnerability according to the Multiple Myeloma Frailty Score (MMFS)[1] for patients older than 65 years, type of first line treatment, and number of lines of therapy.

EPC intervention

Consistent with existing literature and with our previous experiences either in solid cancer or AML patients, the EPC visits comprised all palliative care-specific tasks such as assessment and management of symptoms, providing support in decision making and future planning, facilitation of coping, providing physical and emotional support as well as cultivation of the prognostic awareness [2–4]. The palliative care team also provided liaison with specific home-care services and regular phone calls to patients who could not attend scheduled visits. In line with previously reported studies, the frequency of EPC encounters was weekly for the first two months, and then monthly for every two months, according to the phase of treatment, until death[4]. More frequent follow-up EPC consultations were scheduled according to the patients' needs/wishes. The scheduled duration of the first EPC visit was approximately one hour, and follow-up appointments were around 30 minutes[2,4]. For the same reasons, we considered patients who received three or more visits in the EPC clinic to have undergone a full EPC intervention[2,4].

Quality Indicators for Palliative and EOL Care

Quality Indicators for Palliative Care

Consistent with existing literature and with our previous experience in AML patients, the following indicators of quality for PC were considered: providing psychological support, assessing and managing pain, discussing goals of care (GOC), promoting an advance care plan (ACP), and accessing home-care services[5]. *Psychological support* was defined as any of the following: (1) a psychiatric or neurogeriatric consultation; (2) a psychological interview; or (3) a prescription for psychotropic drugs by a specialist[6]. Pain assessment was determined as the number of times the pain intensity, measured using the Numerical Rating Scale (NRS), where evaluated and reported during the visits either EPC or UHC. Pain control was measured as decline of pain intensity at week 1 (time 1) and at week 4 (time 2) from baseline assessment.

The number of patients receiving strong opioids treatment and the duration of opioid therapy, were also recorded.

GOC discussions were considered to be present when the following elements were recorded in the hospital chart: goals and values, prognosis, treatment choices, life-sustaining treatment preferences, and discussion of either hospice or comfort care[5]. The promotion of ACP was abstracted from the chart when all the following elements were documented: (1) presence of a written advance directive; (2) documentation of a GOC discussion; and (3) identification of a surrogate decision maker[5].

Quality indicators for EOL care

In the subset of the cohort that died during the study period, we assessed four EOL care quality indicators deemed acceptable by more than 75% of 349 hematologic oncologists: no anti-MM treatment within 14 days before death; no cardiopulmonary resuscitation (CPR) and no intubation within 30 days before death; hospice length of stay >7days before death[7]. In addition, we assessed three indicators that were reported in the early work endorsing and developing these measures for patients with solid tumours and in our previous work showing the efficacy of EPC in improving EOL care in patients with AML[8]: no anti-MM treatment within 30 days before death; fewer than two hospitalizations and fewer than 2 emergency department accesses within 30 days before death[8,9].

Anti-MM Treatments

For the purpose of this analysis, the anti-MM treatments considered were all classes of drugs used in the treatment of patients with MM, including proteasome inhibitors, immunomodulatory drugs, standard chemotherapeutic agents, monoclonal antibodies, histone deacetylase inhibitors[10,11].

Statistical Analysis

Descriptive characteristics were reported as the mean ± standard deviation (SD) or as the median and range for numerical variables and as the absolute and percentage frequencies for categorical variables. Comparisons between the two groups (EPC and UHC patients) were performed using unadjusted and confounder-adjusted regression models. Variables that we adjusted for in our regression models included: age (years), sex (male, female), stage (I, II, III), MMFS (fit, unfit, frail), intensity of first line therapy (transplant, no transplant).

Linear models were used for continuous outcomes, logistic models for binary outcomes, Poisson models for count outcomes and Cox models for time-to-event outcomes. Results of regression models were reported as the mean difference (MD), odds ratio (OR), mean ratio (MR) and hazard ratio (HR), respectively. Uncertainty in results was expressed by using 95%

confidence intervals (CI). NRS score values at week1 and 4 were compared to the baseline scores using a Wilcoxon signed-rank test for paired data. For time-to-event outcomes, Kaplan-Meier curves were used to graphically display the incidence of events over time and to calculate median survival times. Statistical analyses were carried out by using R 3.6.3 software (The R Foundation for Statistical Computing, Wien). The significance level was set at $p < 0.05$.

Supplementary Tables

Table S1. Patients' Clinical Characteristics.

	Patients	EPC	UHC
	286	55	231
Age [median (range)]	66.5 (33-93)	67 (33-89)	66 (40-93)
Sex (N/%)			
Male	161 (56)	29 (53)	132 (57)
Female	125 (43)	26 (47)	99 (43)
MM ISS (N/%)			
1	83 (29)	22 (40)	61 (26,4)
2	63 (22)	12 (22)	51 (22,1)
3	67 (23.4)	21 (38)	46 (19,9)
n.a.	73 (25.6)	0 (0)	73 (31,6)
MMFS* (N/Pts >65y/%)			
Fit	47/157 (30)	13/37 (35.2)	34/120 (28,3)
Unfit	54/157 (34.3)	12/37 (32.4)	42/120 (35)
Frail	56/157 (35.7)	12/37 (32.4)	44/120 (36,7)
First Line Treatment (N/%)			
AutoSCT	113 (41.3)	17 (32.2)	96 (43.3)
Alkilating agents + Proteasome inhibitors	98 (34.2)	25 (45.4)	73 (30.3)
Proteasome inhibitors + steroids	14 (4.8)	2 (3.6)	12 (5.2)
Immunomodulatory drugs±Proteasome inhibitors	42 (14.6)	9 (16.3)	33 (14.2)
Alkylating agents	18 (6.2)	1 (1.8)	17 (7.3)
BSC	1 (0.3)	1 (1.8)	0 (0)
N° of AutoSCT (N/%)			
1	67 (23,4)	10 (18,6)	57 (24,7)
2	46 (15,9)	7 (11,9)	39 (16,9)
N° of Treatment Lines (N/%)			
1^-2	228 (79.7)	49 (89.1)	179 (77.5)

3-4	45 (15.8)	6 (10.9)	39 (16.9)
>4	13 (4.5)	0 (0)	13 (5.6)

EPC = Early Palliative Care; UHC = Usual Hematologic Care; M = male; F = female; MM = Multiple Myeloma; ISS = International Staging System; MMFS*[1] = Multiple Myeloma Frailty Score; *only for patients older than 65; ^ = only one extremely frail patient did not receive any treatment.

Table S2A,B. Duration of Treatment with Opiates and Pain Management.

A.	Pain Management over time (mean NRS±SD)				
	T0	W1	p	W4	p
EPC	1.86±2.78	1.03±2.24	0.0184	0.41±1.57	**0.001**
UHC	0.93±2.20	0.71±1.69	0.0678	0.73±1.75	0.0608
B.	Duration of Treatment with Opiates (mean days±SD)		p		
EPC	1061.33±946.45		**0.00007**		
UHC	556±604.02				

SD = standard deviation; EPC = early palliative care patients; UHC = usual hematologic care; NRS = Numerical Rating Scale; T0 = first evaluation; W1 = week 1; W4 = week 4.

Table S3. Quality measures of end-of-life care among Multiple Myeloma decedents who received EPC or UHC.

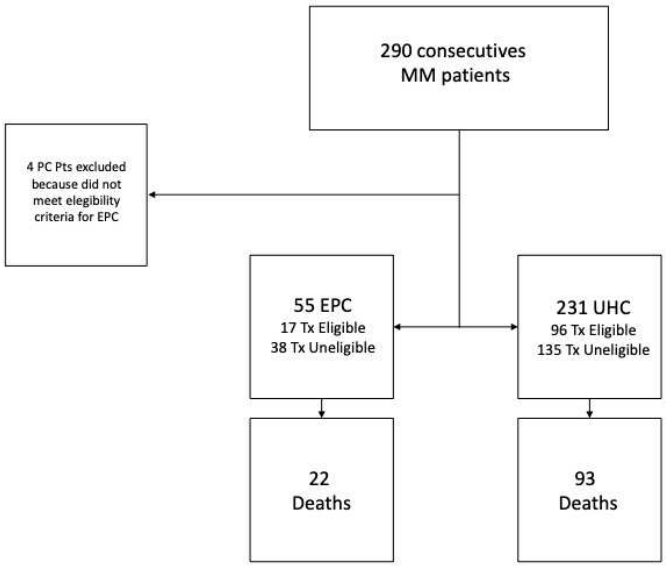
Indicators	EPC N=22 (%)	UHC N=93 (%)	Measure	Adjusted (95%CI)	p
No Anti-Myeloma Treatment					
Within 14 days of death	95.5	76.3	OR	8.33 (0.89-100)	0.06
Within 30 days of death	72.7	58.1	OR	2(0.60-6.66)	0.25
No Intubation					
within 30 days of death	100	96.7	OR	nc	nc
No CPR					
within 30 days of death	100	98.9	OR	nc	nc
Access to ED					
≥2 within 30 days of death	0	2.2	OR	nc	nc
Hospitalisation					
≥2 within 30 days of death	9.1	12.9	OR	1.63 (0.24-11.12)	0.61
Hospice					
length of stay >7days before death	13.6	9.7	OR	0.94 (0.20-4.553)	0.94

EPC = early palliative care patients; UHC = usual hematologic care; n = number; OR = odds ratio; ICU = intensive care unit; CPR = cardio-pulmonary resuscitation; nc= no calculable;

ED = emergency department. The analysis was adjusted for the following variables in the regression models: age (years), sex (male, female), stage (I, II, III), MMFS (fit, unfit, frail), intensity of first line therapy (transplant, no transplant).

Supplementary Figures

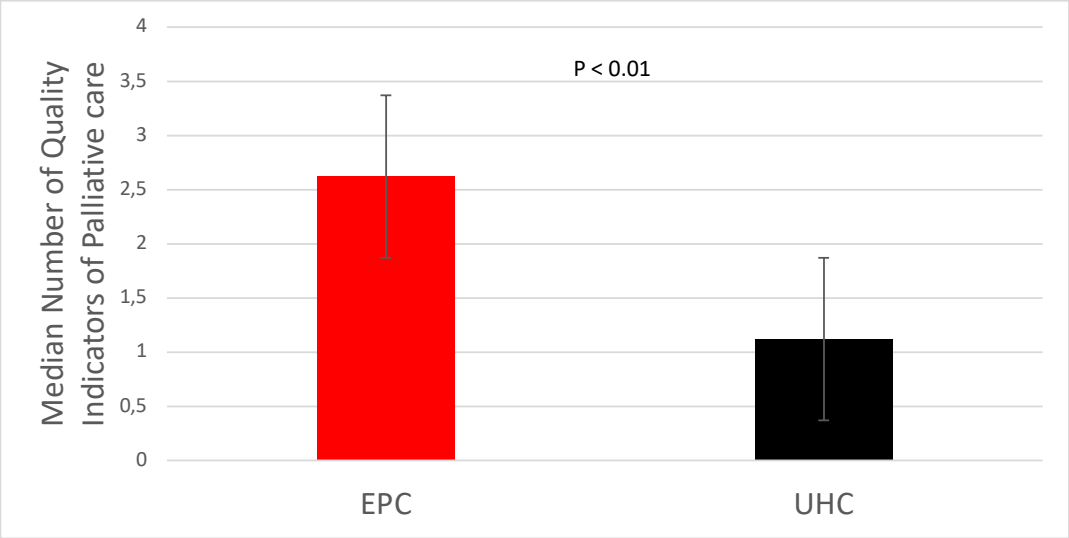
Figure S1. Study Flow Chart.



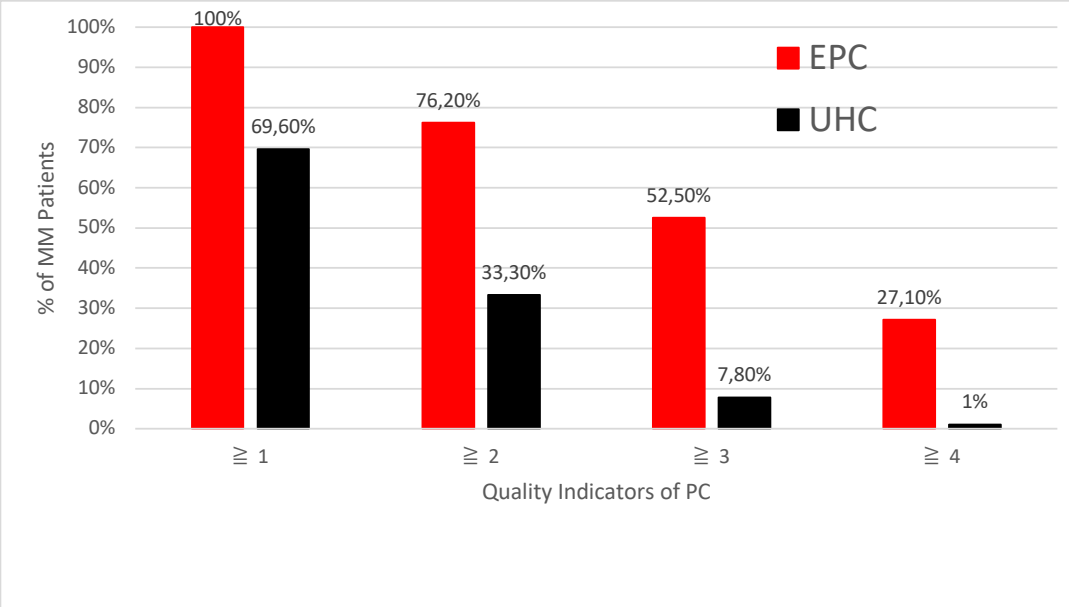
MM = multiple myeloma; PC = Palliative Care; EPC = early Palliative Care; Tx = Transplant; UHC = usual Hematological Care.

Figure S2A, B. Median number (A) and Frequency (B) of Quality Indicators of Palliative Care in MM patients.

A.

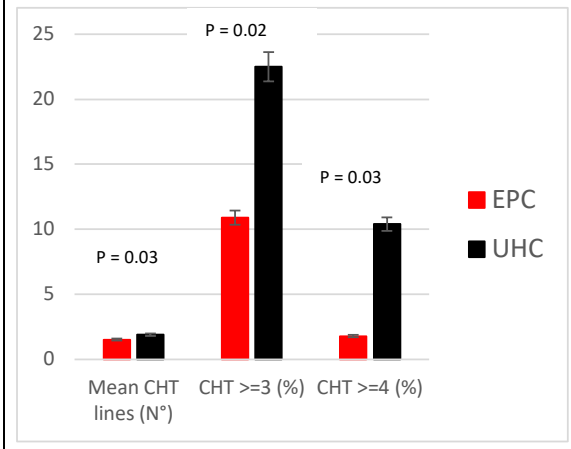


B.



MM = multiple myeloma; PC = palliative care; red columns = early palliative care; black columns = usual hematologic care; EPC = early palliative care patients; UHC = usual hematologic care.

Figure S3 A, B. Number of lines of therapy in Patients with Multiple Myeloma (C) and Overall Survival (B).



Red columns = early palliative care; black columns = usual hematologic care; EPC = early palliative care patients; UHC = usual hematologic care; CHT = anti-Myeloma treatments; red line = early palliative care patients; black line = usual hematologic care. The p values were adjusted for the following variables in the regression models: age (years), sex (male, female), stage (I, II, III), MMFS (fit, unfit, frail), intensity of first line therapy (transplant, no transplant).

Supplemental References

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