

Supplementary Tables and Figures

Early palliative care and overall survival in patients with metastatic upper gastrointestinal cancers (EPIC): a multicentre, open-label, randomised controlled phase 3 trial

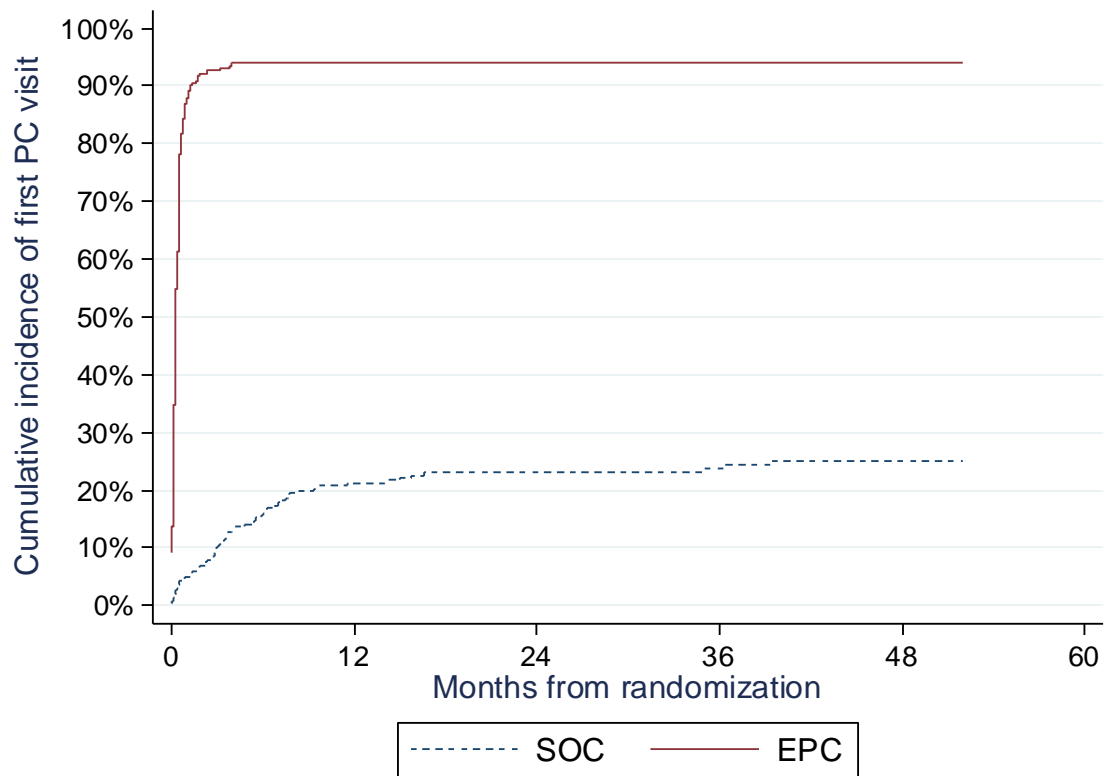
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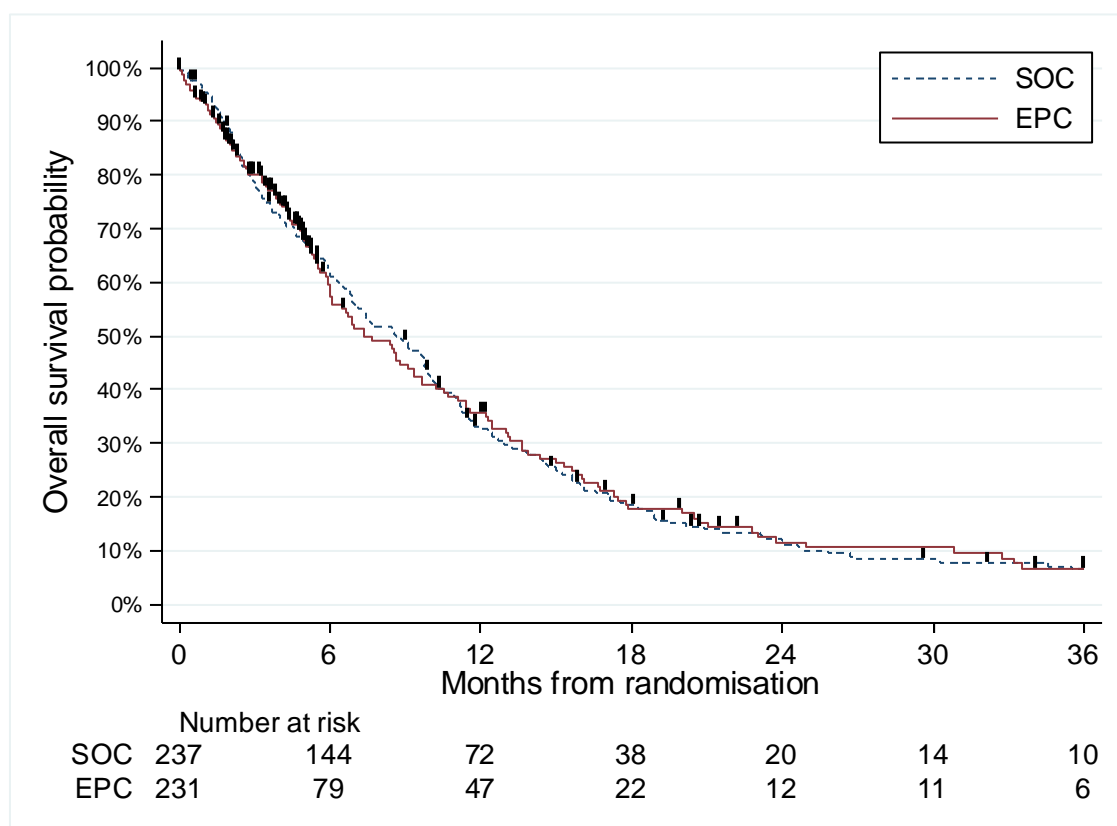
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Supplementary Figure 1 - Cumulative incidence of first palliative care visit



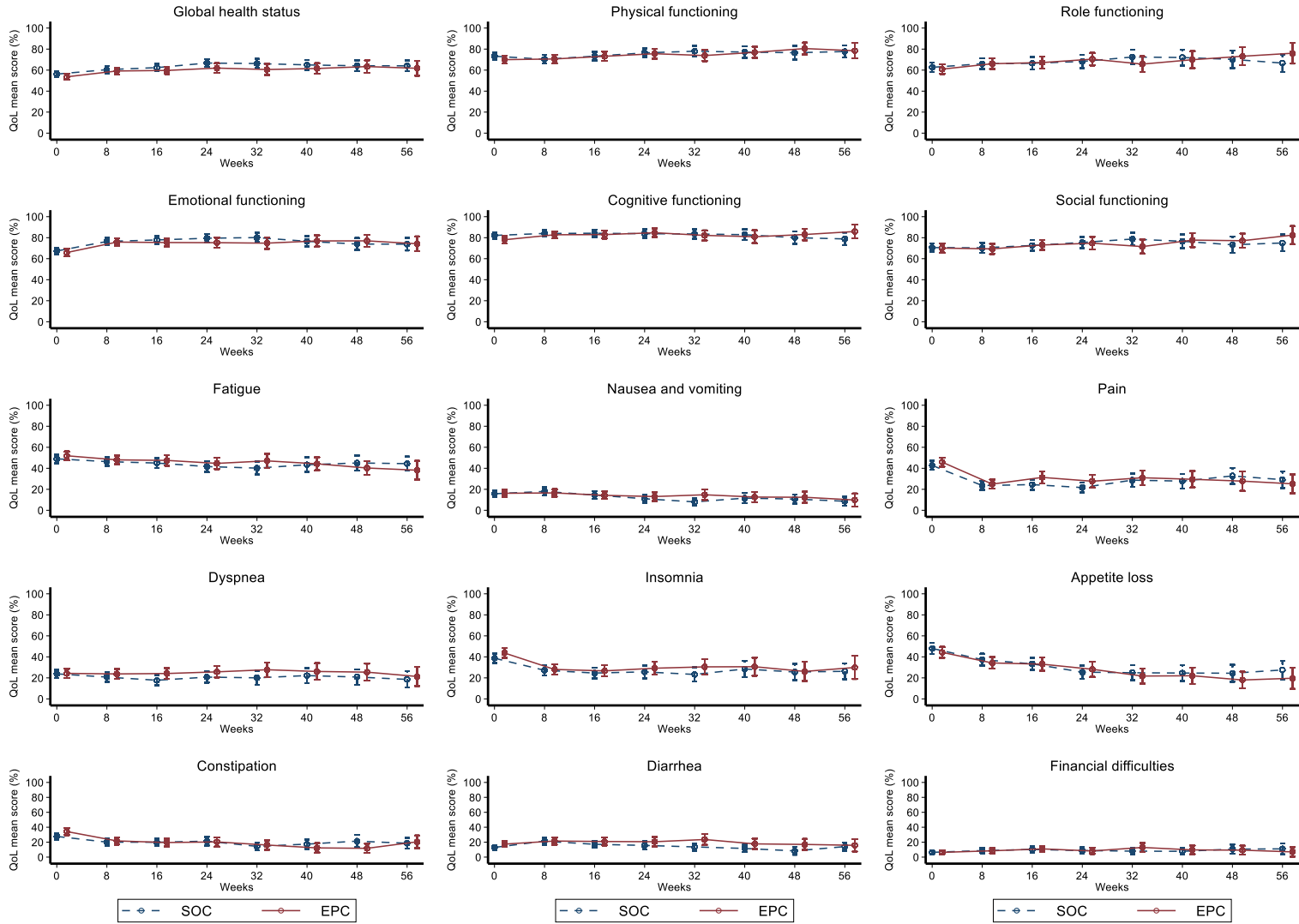
The cumulative incidence of palliative care visits was estimated from the time of randomisation to the first palliative care visit using the Kalbfleish and Prentice method ((Kalbfleisch JD. and Prentice RL. (1980). The statistical analysis of failure time data. John Wiley and Sons, New York), considering death without prior palliative care visits as a competing event.

Supplementary Figure 2 – Kaplan-Meier survival curves for overall survival (per protocol dataset)

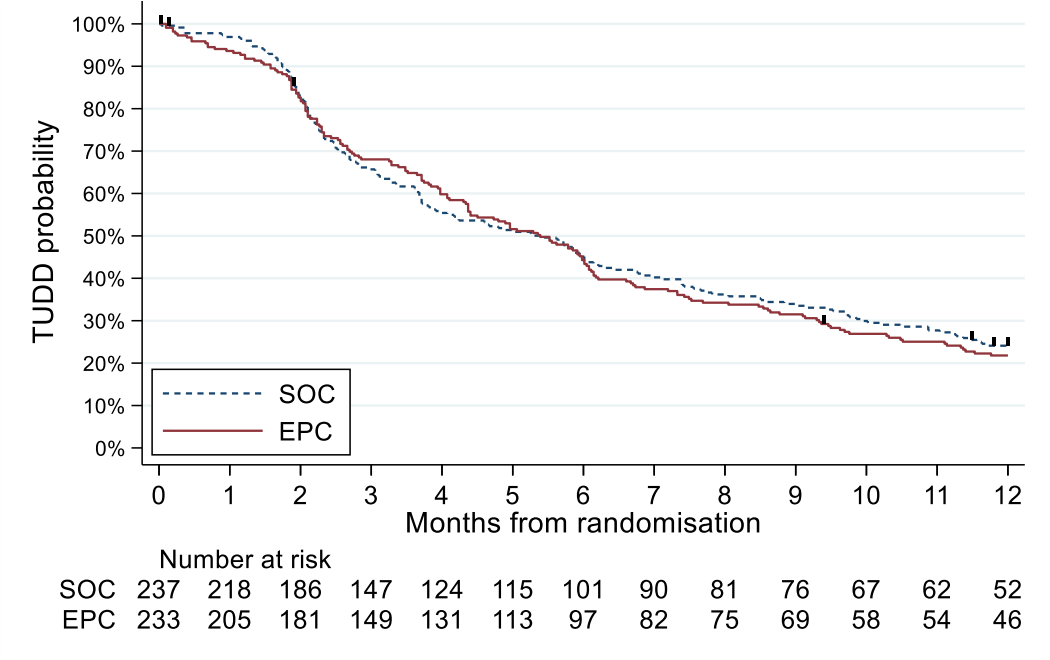


In the per protocol analysis, the median overall survival was 7.4 (6.0-9.6) the EPC group and 8.6 (6.9-9.9) in the SOC group. The 1-year overall survival was 35.8% (28.1-43.4) in the EPC group and 32.8% (26.8-38.9) in the SOC group. The hazard ratio of EPC/SOC was 1.04 (0.84-1.29) (p-value=0.71) in the Cox model stratified on the primary tumour site (with the four strata previously defined), and the ECOG performance status was 0-1 versus 2.

Supplementary Figure 3 - Quality of life scores over time for the 15 QLQ-C30 dimensions



Supplementary Figure 4 - Kaplan–Meier curve of the time until definitive deterioration (TUDD) for the global health status.



Supplementary Table 1 - Treatments

Primary tumour location	Chemotherapy	SOC (n=236 ⁽¹⁾)	EPC (n=231 ⁽¹⁾)
Oesophageal	Folfox [#]	12	14
	Folfiri [#]	0	1
	others	8	4
Gastric or Oesogastric junctional	Folfox [#]	18	11
	Folfiri [#]	0	2
	others	6	11
Pancreatic	Gemcitabine-based	37	41
	Folfox [#]	5	9
	Folfirinox [#]	96	85
	Others (including 1 MD in EPC)	10	11
Biliary tract	gemcitabine	8	6
	Gemox [#]	11	13
	Gemcis [#]	20	22
	Others (including 1 MD in SOC)	5	2
Median 1st-line chemotherapy duration (interquartile range)		2.8m (1.4-5.1)	2.6m (1.0-5.1)

MD, missing data

[#] Chemotherapy regimen: Folfox, fluorouracil+leucovorin+oxaliplatin; Folfiri, fluorouracil+leucovorin+irinotecan; Folfirinox, fluorouracil+leucovorin+oxaliplatin+irinotecan; Gemox, gemcitabine+oxaliplatin; Gemcis, gemcitabine+cisplatin.

(1) Chemotherapy was not administered to one patient in the SOC group and to two patients in the EPC group.

Supplementary Table 2 - Quality of life analysis of time until definitive deterioration for each dimension of the quality of life questionnaires (QLQ-C30)

QLQ-C30 dimension	SOC group			EPC group			HR (95% CI)	p-value
	Total number of events	Number of QoL deteriorations	Median (months) (95% CI)	Total number of events	Number of QoL deteriorations	Median (months) (95% CI)		
Global health status	216	62	5.4 (3.8-6.1)	210	50	5.4 (4.4-6)	1.02 (0.84-1.24)	0.83
Physical functioning	215	27	6.8 (5.3-8.5)	210	35	5.8 (4.9-6.6)	1.06 (0.88-1.29)	0.52
Role functioning	219	38	6.3 (5-7.7)	211	54	5 (4.1-5.9)	1.10 (0.91-1.33)	0.31
Emotional functioning	219	73	4.2 (3.6-5.6)	212	73	4.4 (3.6-5.3)	1.02 (0.84-1.23)	0.86
Cognitive functioning	213	40	6.1 (5-7.5)	210	50	5 (4.1-6)	1.09 (0.90-1.31)	0.40
Social functioning	217	38	6.6 (5.3-8.4)	209	48	5.4 (4.4-6.1)	1.08 (0.89-1.30)	0.44
Fatigue	216	53	5.8 (4.2-7)	215	60	4.9 (4-5.9)	1.09 (0.91-1.32)	0.35
Nausea and vomiting	220	41	6.3 (5.1-7.5)	210	38	5.8 (4.5-6.2)	1.02 (0.85-1.24)	0.82
Pain	222	77	4.2 (3.2-5.7)	214	76	4 (3.3-5.1)	0.99 (0.82-1.19)	0.88
Dyspnoea	216	38	6.8 (5.3-7.6)	207	44	5.4 (4.4-6)	1.06 (0.87-1.28)	0.57
Insomnia	220	72	4.4 (3.5-5.7)	216	91	3.6 (2.8-4.3)	1.19 (0.99-1.44)	0.068
Appetite loss	217	63	5.3 (4-6.2)	213	54	5 (4.1-5.9)	1.03 (0.85-1.24)	0.79
Constipation	217	60	6 (4.2-6.8)	210	64	3.9 (3.3-5)	1.05 (0.87-1.27)	0.62
Diarrhoea	212	31	6.8 (5.8-8)	206	35	6 (5-6.8)	1.08 (0.89-1.31)	0.41
Financial difficulties	211	16	7.5 (6.2-9.1)	202	11	6.4 (5.8-8.5)	1.00 (0.82-1.22)	0.98
Pain alone	217	73	4 (3.1-5.6)	217	67	4.3 (3.6-5.1)	1.01 (0.84-1.22)	0.90

SOC, standard oncological care alone; EPC, early palliative care; HR, hazard ratio; 95% CI, 95% confidence interval; QoL, quality of life.

Total number of events: For each dimension and each treatment group, the total number of events was considered in the estimate of the time until definitive deterioration curve, including definitive deterioration of the QLQ-C30 score and deaths.

Number of QoL deteriorations: Number of patients with a decrease in the QoL score by more than 10 points compared with the score at baseline, without later improvement superior to 10 points compared with baseline, or with no further evaluation available.

Supplementary Table 3 - HADS analysis

HADS Questionnaire	SOC						EPIC					
	Baseline		Week 8		Week 16		Baseline		Week 8		Week 16	
	N	%	N	%	N	%	N	%	N	%	N	%
Questionnaire completion												
Missing	15	6.3%	41	17.3%	47	19.8%	13	5.6%	52	22.3%	48	20.6%
Completed	222	93.7%	161	67.9%	124	52.3%	220	94.4%	145	62.2%	121	51.9%
Patient deceased	0	0.0%	35	14.8%	66	27.8%	0	0.0%	36	15.5%	64	27.5%
HADS Anxiety score	N=221		N=161		N=124		N=220		N=145		N=121	
Median - (Range)	7	(4-10)	5	(3-8)	5	(3-8)	8	(5-11)	6	(3-9)	6	(4-9)
Mean - SD	7.3	4.2	6	4	5.4	3.7	8.6	4.4	6.4	3.7	6.6	3.7
No anxiety (score ≤7)	129	58.4%	112	69.6%	90	72.6%	95	43.2%	89	61.4%	73	60.3%
Doubtful anxiety (score between 8 and 10)	46	20.8%	30	18.6%	24	19.4%	54	24.5%	39	26.9%	34	28.1%
Definite anxiety (score ≥11)	46	20.8%	19	11.8%	10	8.1%	71	32.3%	17	11.7%	14	11.6%
HADS Depression score	N=222		N=161		N=124		N=220		N=145		N=121	
Median - (Range)	6	(3-10)	6	(3-9)	6	(2.5-8)	7	(4-11)	6	(3-10)	6	(3-9)
Mean - SD	6.6	4.8	6.3	4.1	5.9	4.3	7.5	5.1	6.8	4.5	6.3	4.3
No depression (score ≤7)	133	59.9%	100	62.1%	84	67.7%	125	56.8%	86	59.3%	80	66.1%
Doubtful depression (score between 8 and 10)	48	21.6%	34	21.1%	20	16.1%	37	16.8%	30	20.7%	21	17.4%
Definite depression (score ≥11)	41	18.5%	27	16.8%	20	16.1%	58	26.4%	29	20.0%	20	16.5%

SOC, standard oncological care alone; EPC, early palliative care; HADS, hospital anxiety and depression scale; SD, standard deviation