Supplementary Data

Supplementary Table S1: Logistic regression model of odds of experiencing at least one CTCAE Grade 3/4 trAE within the first 12 months of trial treatment

Supplementary Figure S1: Treatment related adverse events occurring in at least 2.5% of all participants by severity

Supplementary Figure S2: Extended progression-free survival by treatment allocation amongst (a) mITT population (b) IMDC intermediate/poor risk population

Supplementary Figure S3: Progression-free survival by IMDC risk group in (a) the modified schedule arm, and (b) the standard schedule

Supplementary Figure S4: Progression-free survival by PD-L1 tumor expression status in (a) the modified schedule arm, and (b) the standard schedule

Supplementary Figure S5: Mean scores and 95% confidence intervals, by treatment allocation and time-point, of QLQ domains

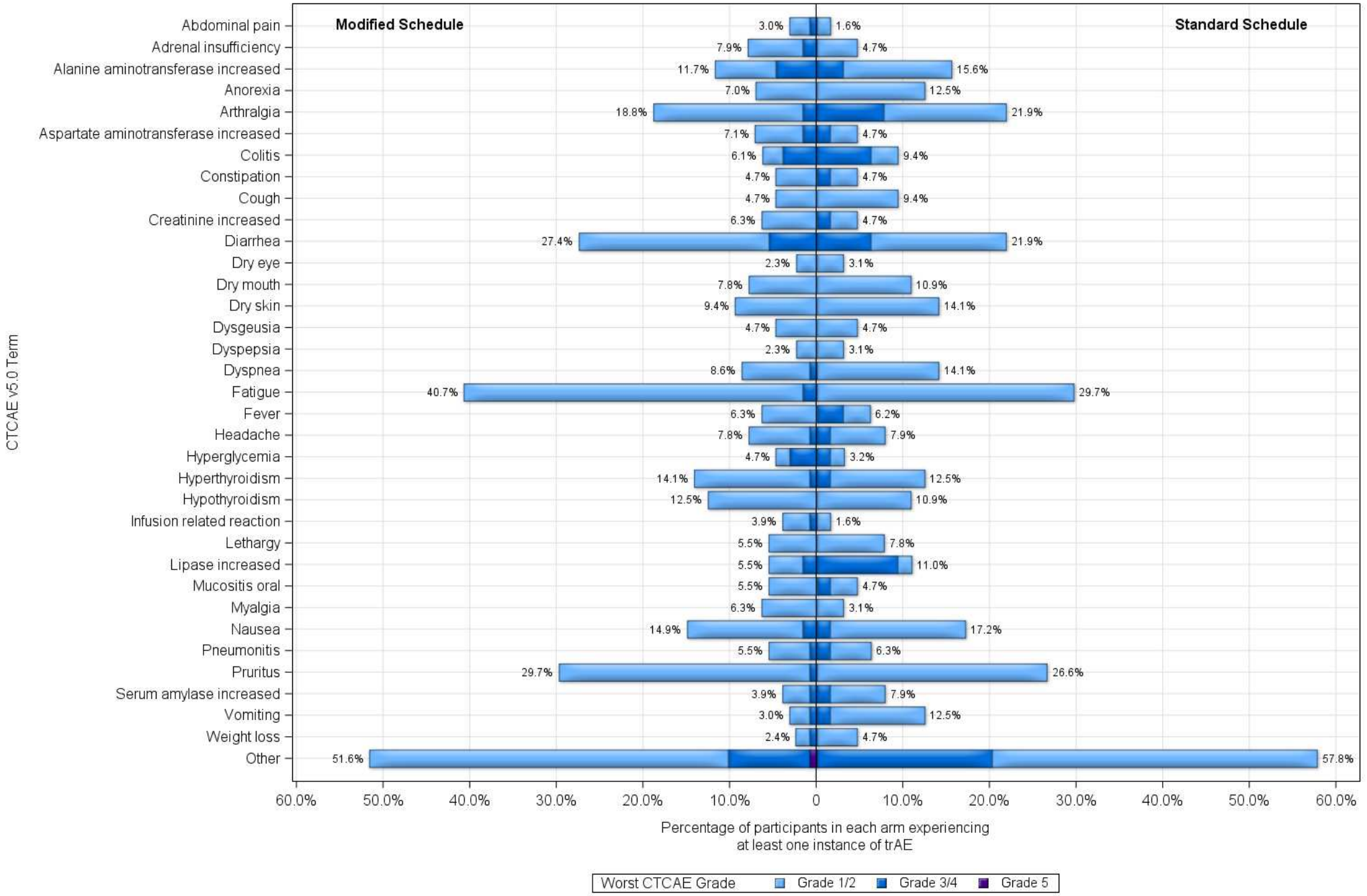
Supplementary Figure S6: Mean scores and 95% confidence intervals by treatment allocation and time-point of (a) FKSI Disease-related symptoms-9 (DRS-9) score and (b) Item GP5 “bothered by side effects”

Supplementary Table S1: Logistic regression model of odds of experiencing at least one CTCAE Grade 3/4 trAE within the first 12 months of trial treatment

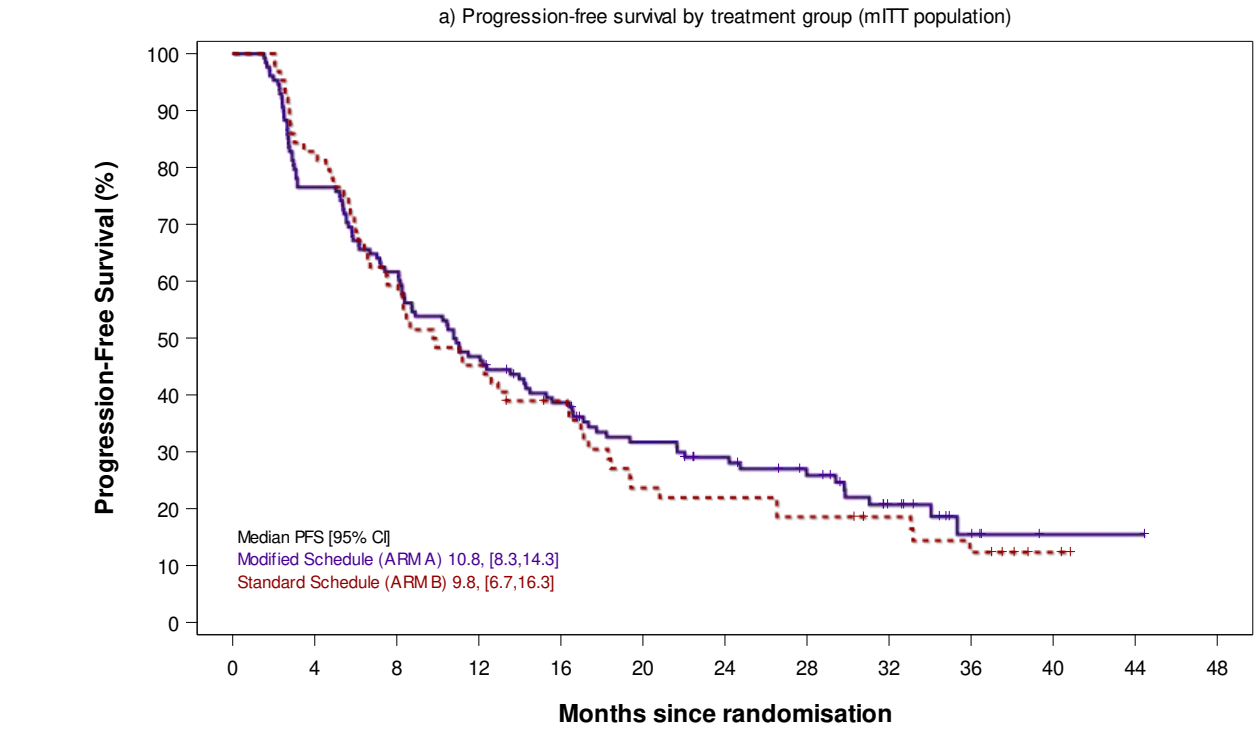
Effect*	Adjusted odds ratio (90% CI)	P-value
Randomized allocation		
Modified schedule	0.43 (0.25, 0.72)	0.0075
Standard schedule	1 [Reference]	
IMDC risk group		
Favorable	1.67 (0.69, 4.05)	0.3415
Intermediate	1.82 (0.86, 3.86)	0.1922
Poor	1 [Reference]	
Nephrectomy status		
Nephrectomy	1.50 (0.81 2.78)	0.2824
No nephrectomy	1 [Reference]	
Disease type		
Locally advanced	1.00 (0.21, 4.85)	0.9995
Metastatic	1 [Reference]	

*All effects were fitted as fixed effects. All model effects are included in the table.

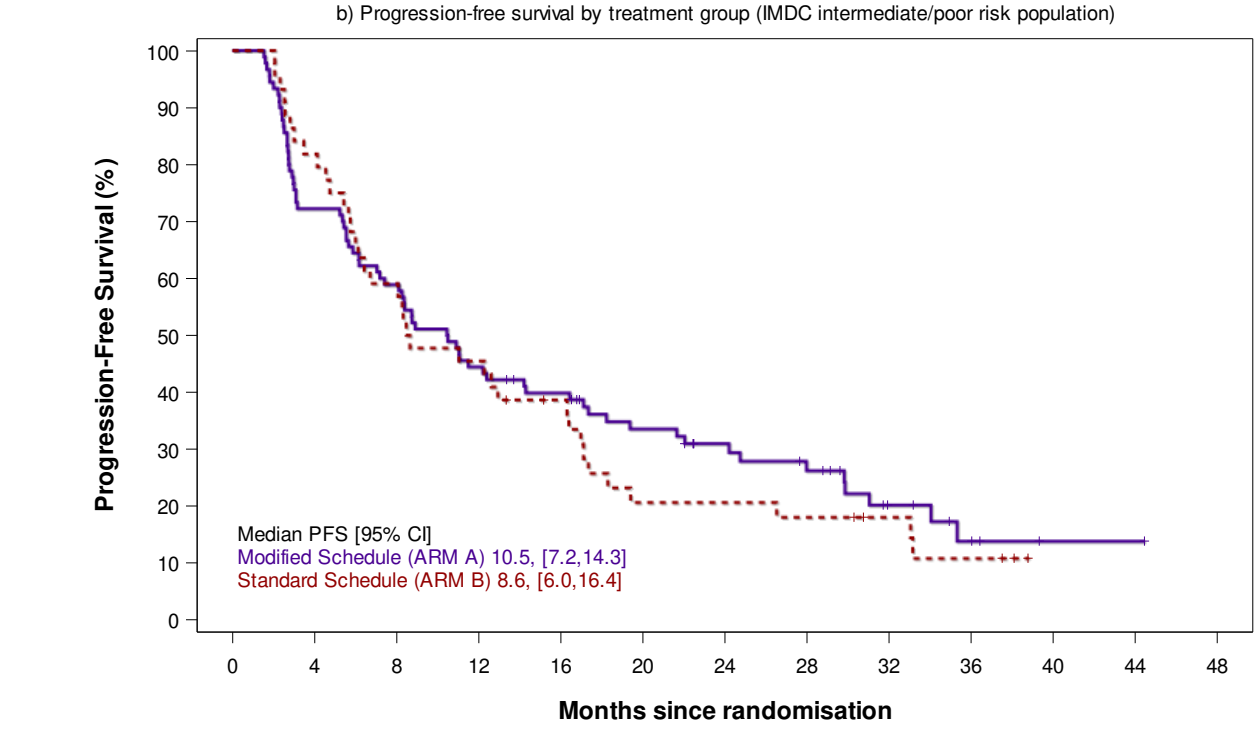
Supplementary figure S1: Treatment related adverse events occurring in at least 2.5% of all participants by severity



Supplementary Figure S2: Extended progression-free survival* by treatment allocation amongst (a) mITT population (b) IMDC intermediate/poor risk population



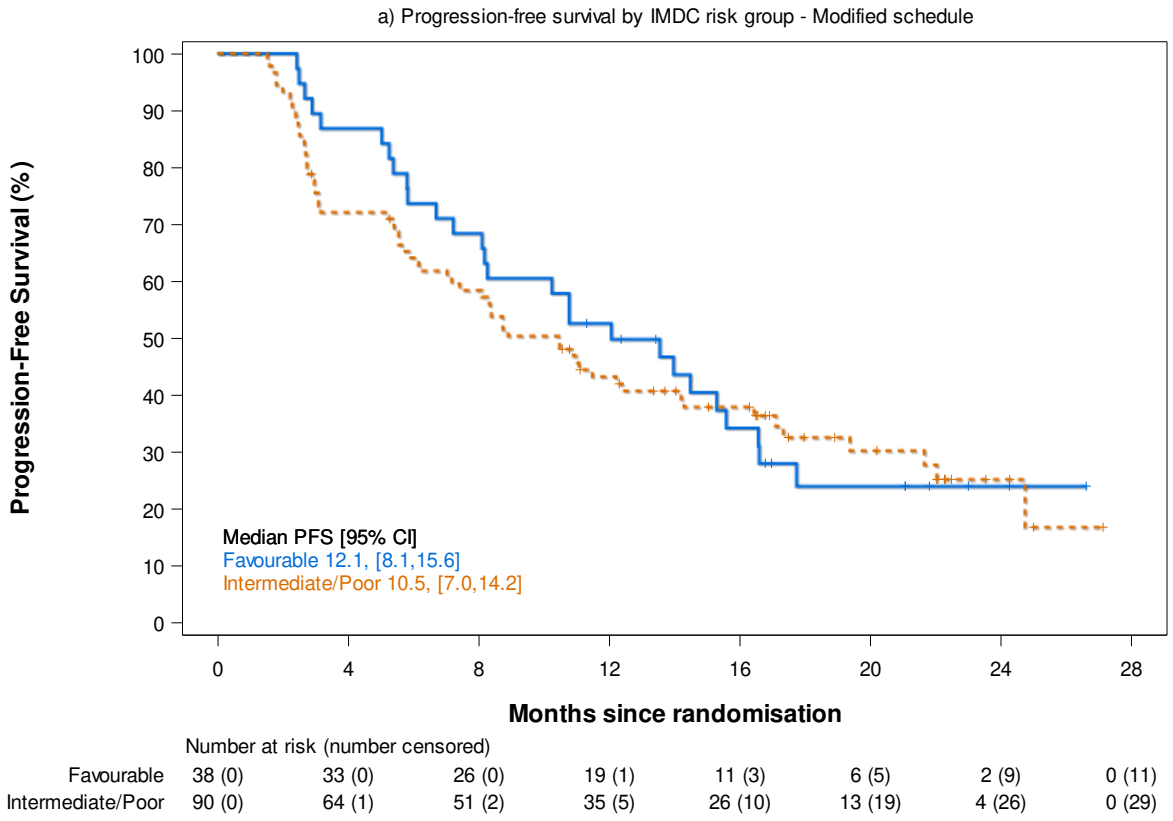
Number at risk (number censored)													
Modified schedule	128 (0)	98 (0)	79 (0)	60 (0)	47 (3)	36 (6)	29 (10)	23 (13)	13 (19)	5 (25)	1 (29)	1 (29)	0 (30)
Standard schedule	64 (0)	53 (0)	38 (0)	29 (0)	23 (2)	14 (2)	13 (2)	11 (2)	9 (4)	6 (4)	2 (8)	0 (10)	

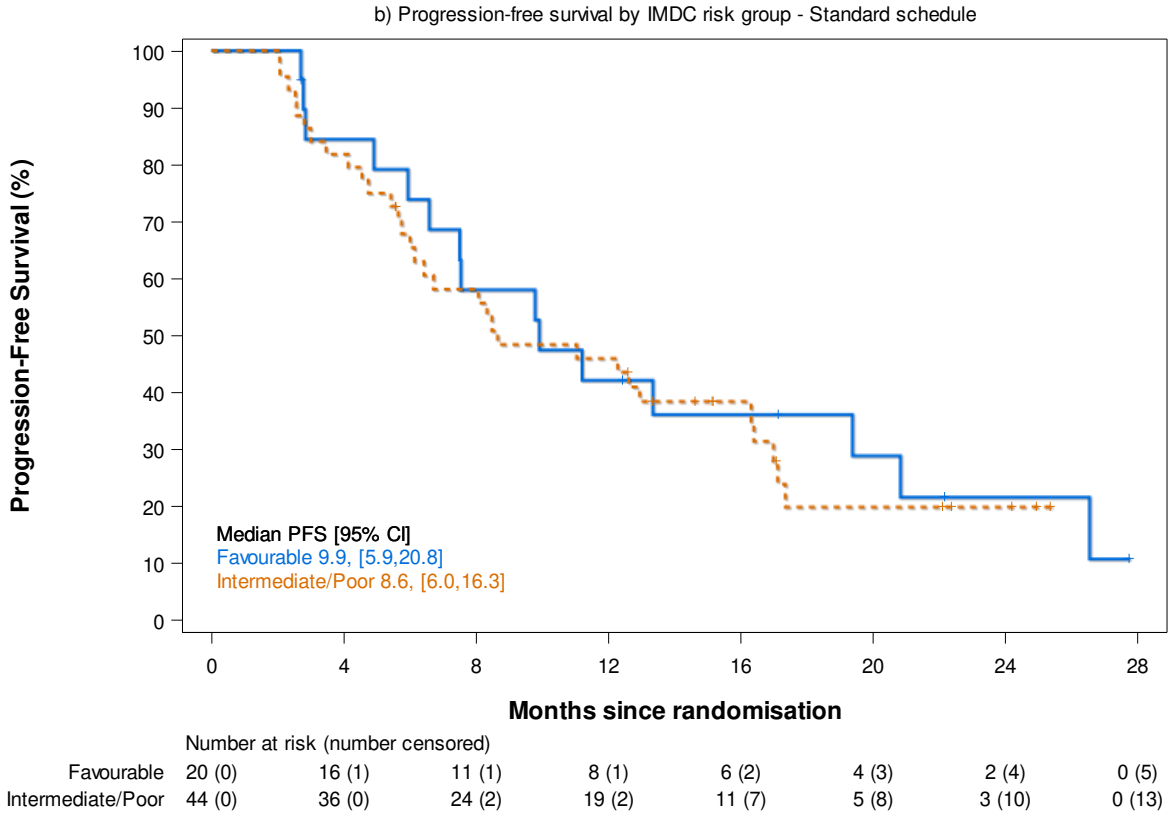


Number at risk (number censored)													
Modified schedule	90 (0)	65 (0)	53 (0)	40 (0)	34 (2)	26 (5)	20 (9)	16 (10)	8 (15)	4 (17)	1 (20)	1 (20)	0 (21)
Standard schedule	44 (0)	36 (0)	26 (0)	20 (0)	15 (2)	8 (2)	8 (2)	7 (2)	5 (4)	3 (4)	0 (7)		

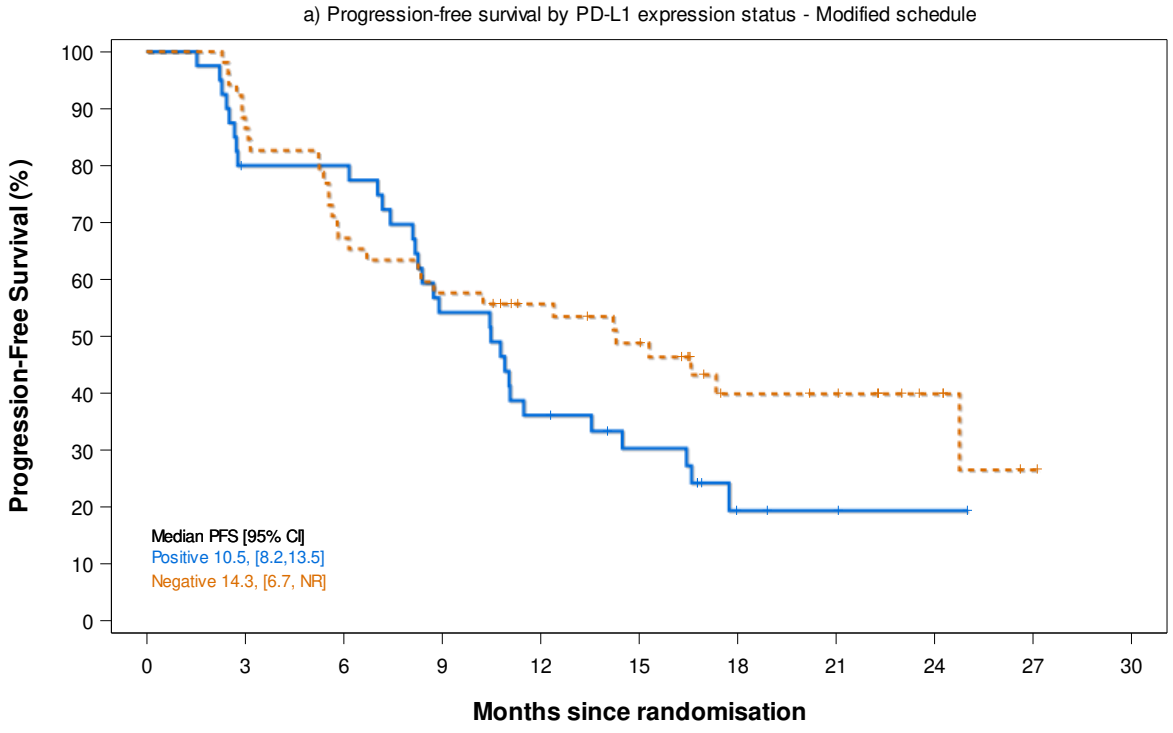
*Unlike the main trial data, extended progression-free survival is according to locally assessed progression. Where RECIST and locally assessed progression information was available for a participant, the RECIST assessment is used. Median follow-up for the extended progression-free survival was 32 months (95% CI: 29, 35) using the modified schedule and 38 months (95% CI: 31, 40) using the standard schedule.

Supplementary Figure S3: Progression-free survival by IMDC risk group in (a) the modified schedule arm and (b) the standard schedule arm



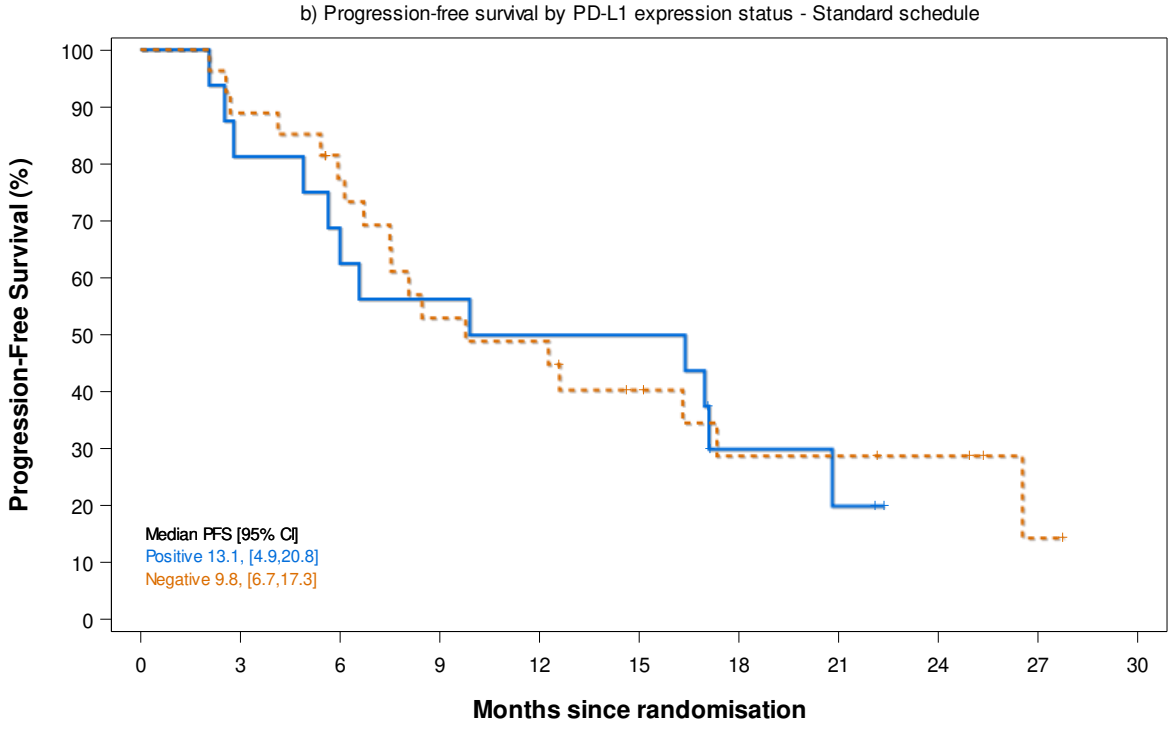


Supplementary Figure S4: Progression-free survival* by PD-L1 tumor expression status in (a) the modified schedule arm and (b) the standard schedule arm



Number at risk (number censored)

Positive	40 (0)	31 (1)	31 (1)	21 (1)	14 (1)	10 (3)	3 (7)	2 (8)	1 (9)	0 (10)	
Negative	52 (0)	46 (0)	35 (0)	30 (0)	25 (4)	21 (5)	11 (12)	10 (13)	5 (18)	1 (21)	0 (22)

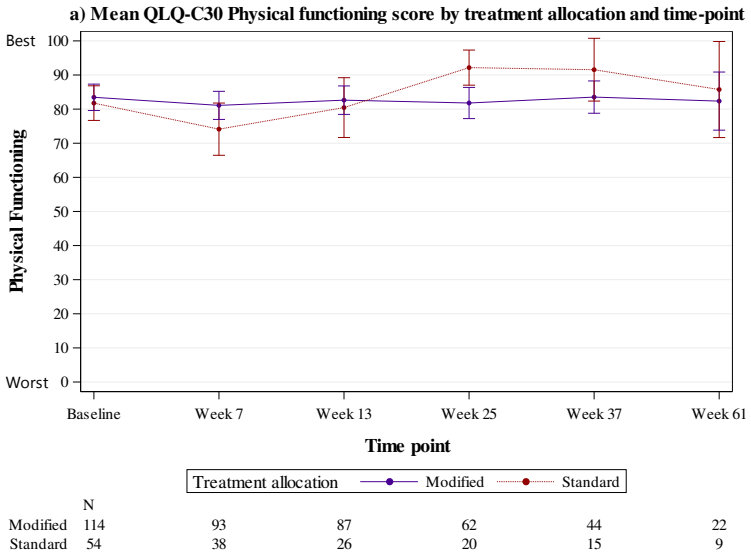


Number at risk (number censored)

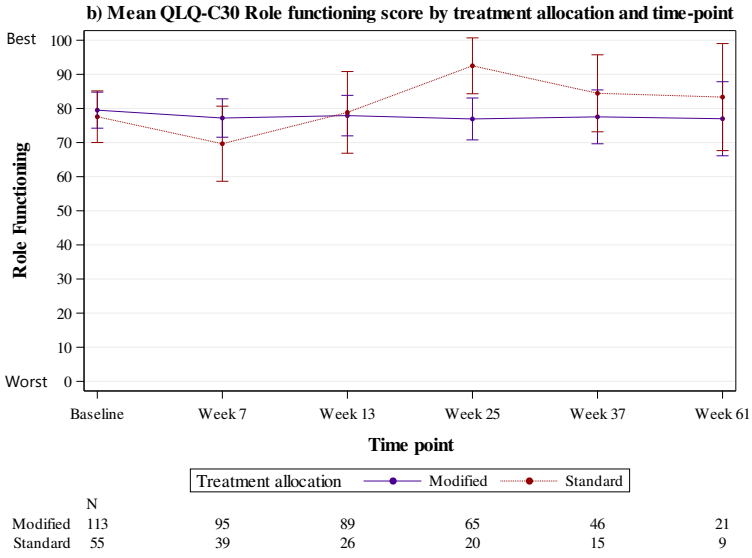
Positive	16 (0)	13 (0)	11 (0)	9 (0)	8 (0)	8 (0)	3 (2)	2 (2)	0 (4)		
Negative	27 (0)	24 (0)	19 (2)	13 (2)	12 (2)	8 (4)	5 (5)	5 (5)	4 (6)	1 (8)	0 (9)

*Assessment of progression in the initial trial follow-up is according to RECIST v1.1 criteria. Additionally, there were some participants for whom PD-L1 tumor expression status was not available. PD-L1 expression defined as <1% vs ≥ 1%.

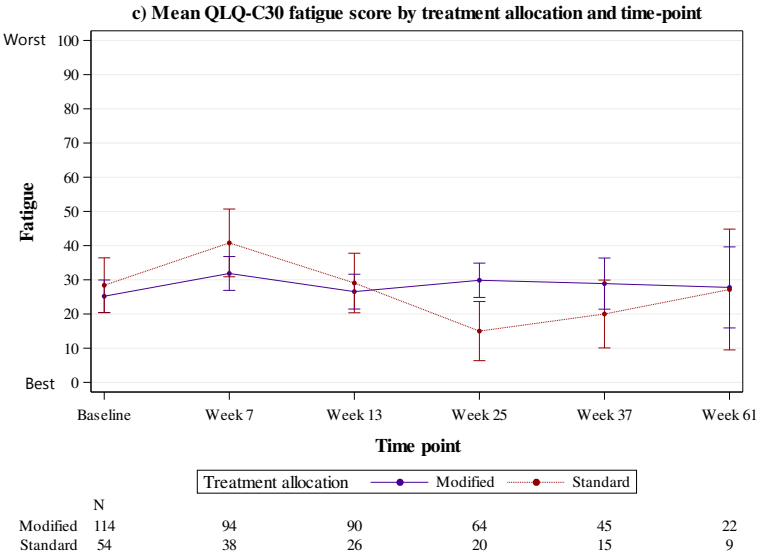
Supplementary Figure S5: Mean scores and 95% confidence intervals, by treatment allocation and time-point, of QLQ domains a) Physical functioning, b) Role functioning, c) Fatigue, and d) Pain



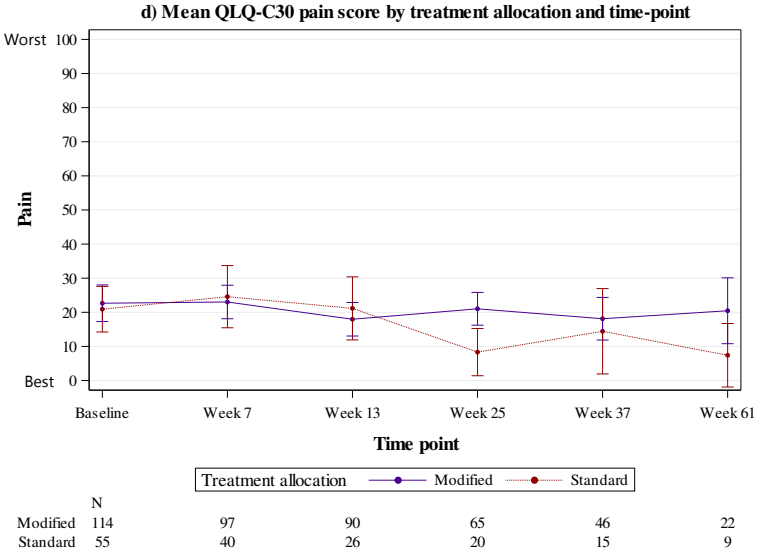
N						
Modified	114	93	87	62	44	22
Standard	54	38	26	20	15	9



N						
Modified	113	95	89	65	46	21
Standard	55	39	26	20	15	9



N						
Modified	114	94	90	64	45	22
Standard	54	38	26	20	15	9



N						
Modified	114	97	90	65	46	22
Standard	55	40	26	20	15	9

Supplementary Figure S6: Mean scores and 95% confidence intervals by treatment allocation and time-point of (a) FKSI Disease-related symptoms-9 (DRS-9) score and (b) Item GP5 "bothered by side effects"