Supplementary Materials

Supplementary Methods

Univariable and multivariable survival analyses

Cox-proportional hazards were used for OS estimates in univariable (UVA) and multivariable (MVA) analyses with hazard ratios (HR) and 95% confidence intervals (95%CI) reported. Patient-reported items with a frequency of ≥20% on PRO-CTCAE and matched clinician-reported items were included in UVA. A threshold of 20% was chosen as low frequency AE reporting would preclude robust statistical analyses. PRO-CTCAE and CTCAE items with a p-value of ≤0.05 in addition to RMI were included in MVA. Two-sided p-values of ≤0.05 were evaluated for all tests.

Supplementary Tables

Supplementary Table 1: Survey attempts by number of respondents with adjustment for phase 1 study attrition.

Survey Attempts	# Survey responses	Survey Responses/ # Enrolled (N=243)	# of patients left on Phase 1 study	Survey Responses/ # patients left on study
1	243	100.0%	243	*100%
2	192	78.6%	215	*89.3%
3	117	48.6%	186	*62.9%

Abbreviations: #, number
*adjusted for phase 1 study attrition

Supplementary Table 2: Number of cycles received for phase 1 study treatment.

Number of study drug cycles received	N	%
Total Number Evaluable	243	100
Screen Fail	24	9.9%
<1 cycle	12	5.5%
1 or more cycles	207	94.5%
<2 cycles	48	21.9%
2 or more cycles	171	78.1%
< 3 cycles	99	45.2%
3 or more cycles	120	54.8%

Supplementary Table 3: Grouped phase 1 study treatments by mono- or combination therapy.

Monotherapy	**N (%)**
Targeted	16.5%
ICI	7.0%
Miscellaneous	4.1%
Co-Stimulatory	2.9%
Virus	2.9%
Vaccine	2.1%
Epigenetic	1.6%
Chemotherapy	0.4%
Combination therapy	
ICI+ Co-Stimulatory	27.2%
ICI + Immune Miscellaneous	12.8%
ICI + Targeted	5.8%
ICI + ICI	4.1%
Targeted + Targeted	4.1%
ICI + Epigenetic	2.5%
ICI + ICI + Co-Stimulatory	1.2%
Target + Co-Stimulatory	1.2%
Chemotherapy + Chemotherapy	1.2%
ICI + Vaccine	1.2%
Targeted + Chemotherapy	0.8%
Virus + Virus	0.4%

Abbreviations: ICI, Immune checkpoint inhibition

Supplementary Table 4: Number of prior clinical trials for patients enrolling in study.

Number of Prior Clinical Trials	**N (%)**
0	156 (64.2)
1	70 (28.8)
2	14 (5.8)
3	3 (1.2)

Supplementary Table 5: Univariable survival analysis of patient characteristics

Demographic	HR (95% CI)	p-value
Age		
<65	[REF]	0.12
≥65	1.33(0.93-1.90)	
Gender		
Male	[REF]	0.65
Female	1.08(0.77-1.51)	
ECOG		
0	[REF]	0.24
≥1	1.29(0.84-1.98)	
Treatment		
Monotherapy	[REF]	0.17
Combination Therapy	0.78 (0.55-1.11)	
Tumor Type		
Gastrointestinal	[REF]	0.33
Head and Neck	0.61(0.34-1.10)	
Breast	0.93(0.52-1.69)	
Genitourinary	0.73(0.39-1.36)	
Gynecologic	0.69(0.36-1.31)	
Other	1.09(0.71-1.67)	
Education		
Elementary	[REF]	0.51
High School	0.87(0.27-2.81)	
Post-Graduate	0.95(0.29-3.11)	
University	1.16(0.36-3.71)	
Prior Treatment Lines		
0-1	[REF]	0.24
2	1.34(0.89-2.04)	
≥3	1.41(0.92-2.16)	
Treatment Type		
Immune	[REF]	0.21
Targeted	1.40(0.96-2.06)	
Immune-Targeted Combo	1.19(0.68-2.09)	
RMI Score		
0-1	[REF]	
2-3	1.86 (1.31-2.64)	<0.001

Abbreviations: HR, hazard ratio; ECOG, Eastern Cooperative Oncology Group; RMI, Royal Marsden Index

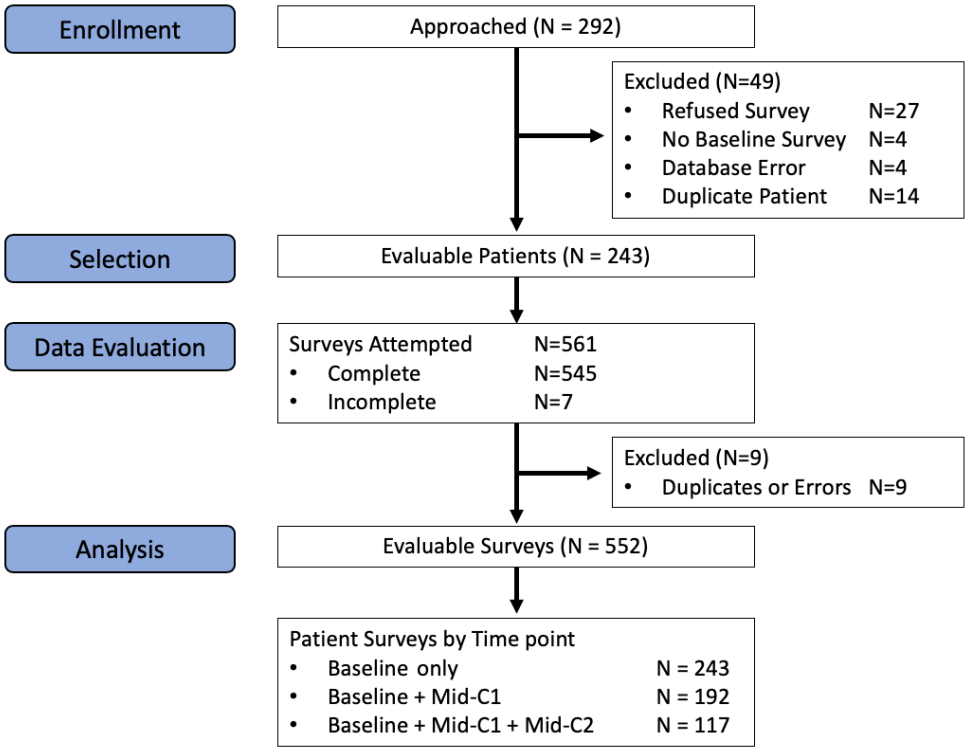
Supplementary Table 6: Univariable survival analysis and select (p<0.05 on univariable) multivariable survival analysis of patient (PRO-CTCAE) and clinician (CTCAE) reported symptomatic-AEs with an overall frequency ≥20% with inclusion of Royal Marsden Index score.

	PRO-CTCAE				CTCAE			
	Univariable		Multivariable		Univariable		Multivariable	
Characteristic	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
RMI*								
2-3	1.86 (1.31-2.64)	<0.001	2.04 (1.42-2.92)	<0.001	1.86 (1.31-2.64)	<0.001	1.83 (1.29-2.54)	<0.001
symptomatic-AE**								
abdominal pain	1.60 (1.13-2.23)	0.01	NS	NS	1.49 (1.03-2.17)	0.03	NS	NS
anorexia	1.80 (1.28-2.52)	< 0.01	1.77 (1.26-2.51)	0.001	1.41 (0.96-2.08)	0.08		
anxiety	1.41 (0.99-2.01)	0.06	---	---	1.08 (0.68-1.72)	0.75		
arthralgia	0.99 (0.70-1.42)	> 0.97	---	---	1.19 (0.70-2.00)	0.52		
bloating	1.16 (0.83-1.63)	0.38	---	---	0.84 (0.41-1.72)	0.64		
chills	1.21 (0.83-1.79)	0.33	---	---	4.07 (0.99-16.73)	0.05	NS	NS
concentration impairment	1.29 (0.89-1.85)	0.18	---	---	0.93 (0.23-3.75)	0.91		
constipation	1.51 (1.07-2.13)	0.02	NS	NS	1.79 (1.26-2.55)	0.00	1.70 (1.19-2.43)	0.003
cough	0.80 (0.56-1.13)	0.21	---	---	1.04 (0.69-1.56)	0.85		
depression	1.63 (1.16-2.29)	0.01	1.64 (1.15-2.32)	0.006	1.18 (0.71-1.97)	0.52		
diarrhea	0.83 (0.58-1.20)	0.32	---	---	0.74 (0.38-1.46)	0.39		
xerostomia	0.92 (0.65-1.30)	0.64	---	---	0.80 (0.42-1.52)	0.49		
dry skin	1.22 (0.87-1.70)	0.25	---	---	0.92 (0.38-2.24)	0.85		
dysgeusia	1.41 (0.97-2.06)	0.07	---	---	1.18 (0.58-2.41)	0.65		
dyspepsia	1.28 (0.89-1.84)	0.19	---	---	0.94 (0.57-1.57)	0.82		
fatigue	1.00 (0.68-1.46)	> 0.95	---	---	1.28 (0.92-1.82)	0.15		
headache	1.05 (0.73-1.51)	0.81	---	---	0.68 (0.41-1.12)	0.13		
dysphonia	1.01 (0.68-1.50)	> 0.95	---	---	1.11 (0.35-3.49)	0.86		
hyperhidrosis	1.31 (0.90-1.91)	0.16	---	---	2.85 (0.70-11.59)	0.14		
insomnia	1.18 (1.84-1.66)	0.35	---	---	1.44 (1.02-2.03)	0.04	NS	NS
memory impairment	1.26 (0.89-1.78)	0.20	---	---	1.00	> 0.95		
myalgia	1.33 (0.95-1.87)	0.10	---	---	0.96 (0.24-3.87)	> 0.95		
nausea	1.44 (1.00-2.08)	0.05	NS	NS	1.57 (1.03-2.40)	0.04	1.61 (1.05-2.44)	0.03
pruritus	0.96 (0.64-1.43)	0.83	---	---	0.57 (0.21-1.55)	0.27		
pain (general)	1.23 (0.85-1.78)	0.28	---	---	1.10 (0.79-1.54)	0.58		
tinnitus	0.91 (0.60-1.38)	0.66	---	---	0.76 (0.31-1.85)	0.54		
urinary frequency	1.35 (0.95-1.93)	0.10	---	---	0.92 (0.29-2.90)	0.88		
peripheral neuropathy	1.16 (0.83-1.62)	0.49	---	---	1.29 (0.90-1.86)	0.16		
dyspnea	1.35 (0.97-1.89)	0.08	---	---	1.27 (0.89-1.83)	0.19		

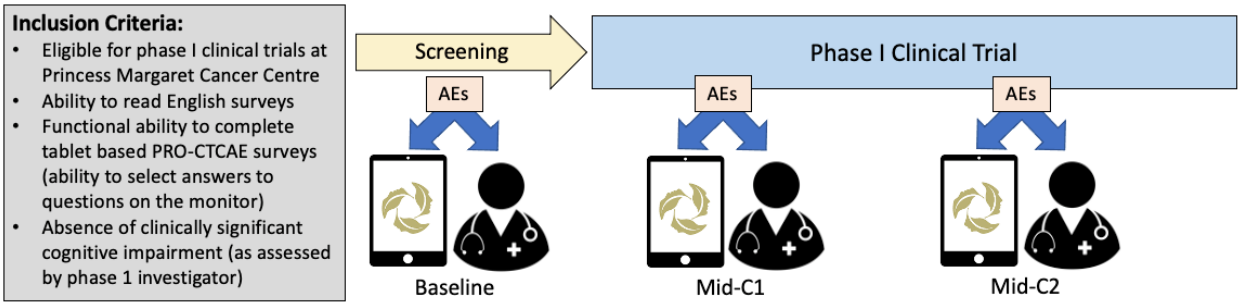
Abbreviations: HR, Hazard Ratio; CI, confidence intervals; AE, adverse event; RMI, Royal Marsden Index; NS, not significant
*RMI reference = 0-1.
**symptomatic-AE reference = absence
***decreased libido excluded due to omitted data including not applicable (N/A) and prefer not to answer (PNTA).

Supplementary Figures

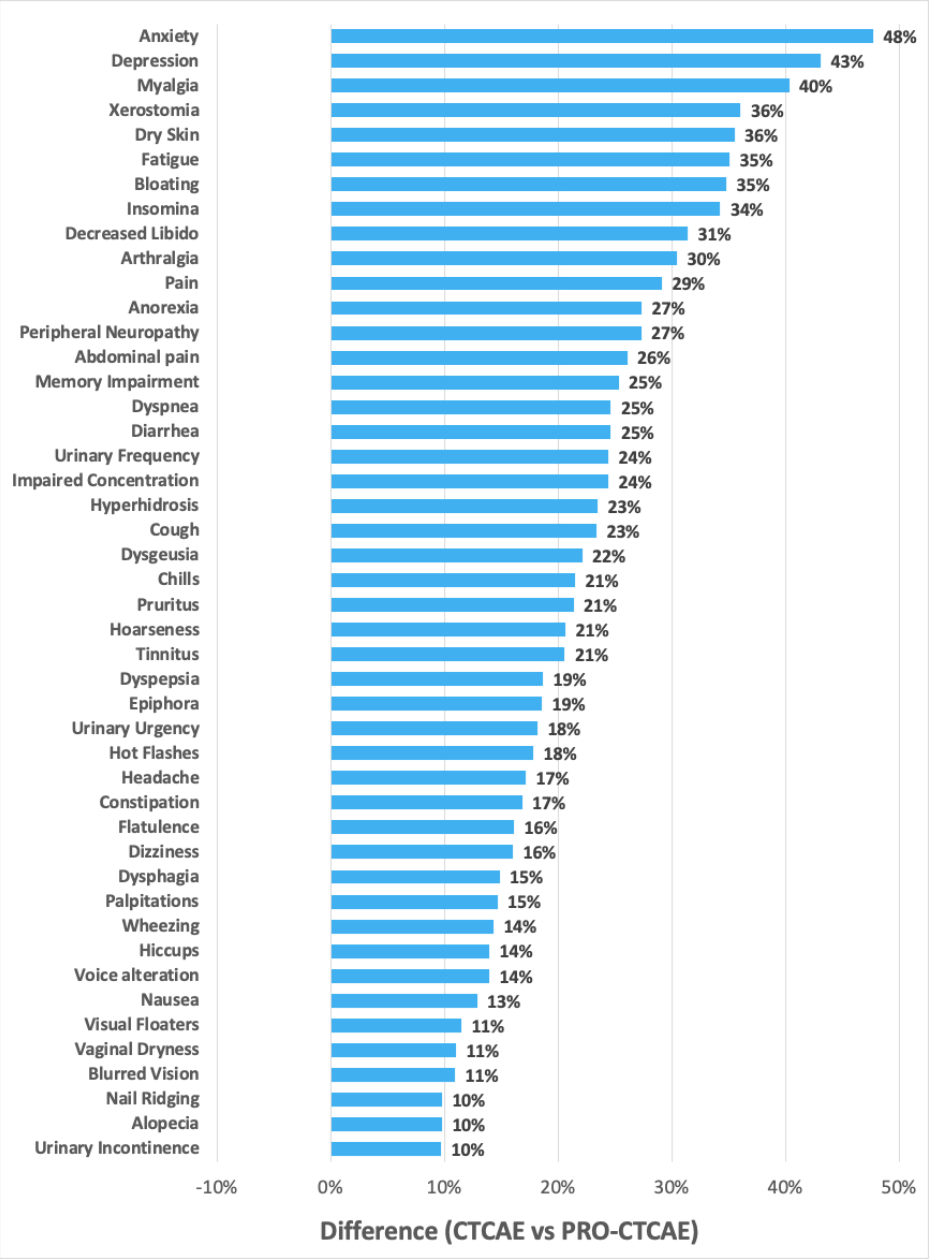
Supplementary Figure 1: Consort Diagram



Supplementary Figure 2: Study design



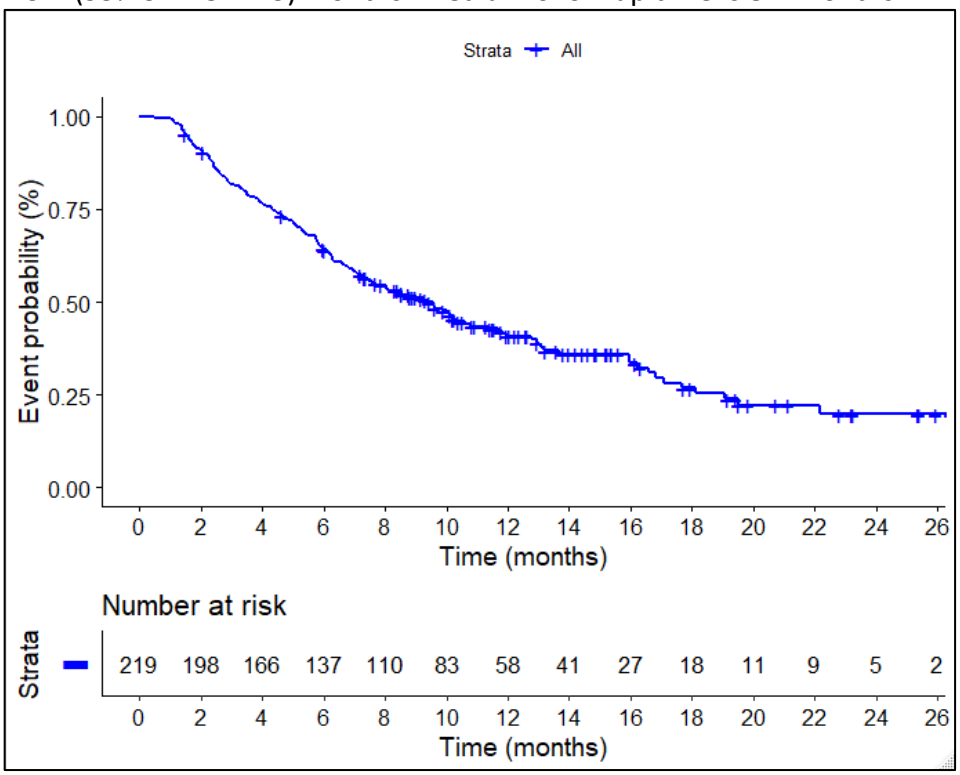
Supplementary Figure 3: Difference* between patient (PRO-CTCAE; blue) and clinician (CTCAE; yellow**) overall symptomatic adverse event reporting (≥10%).



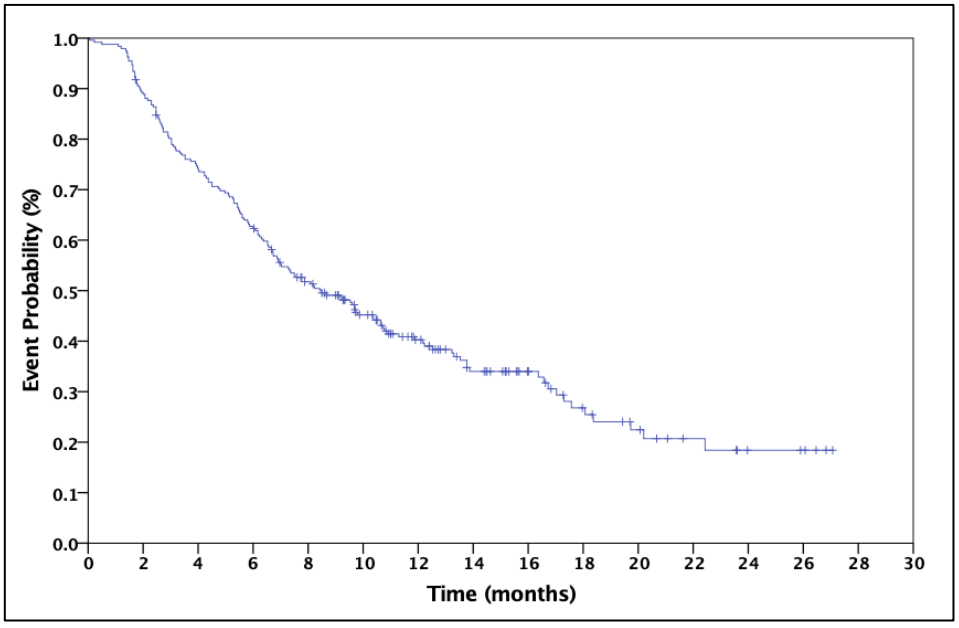
*Calculation for individual AE percentage difference
[ex: fatigue = PRO-CTCAE sy-AE% - CTCAE sy-AE% = % Difference].
**No clinician-reported symptomatic-AEs were reported at a higher frequency than patient-reported symptomatic AEs.

Supplementary Figure 4: Kaplan-Meier survival curves

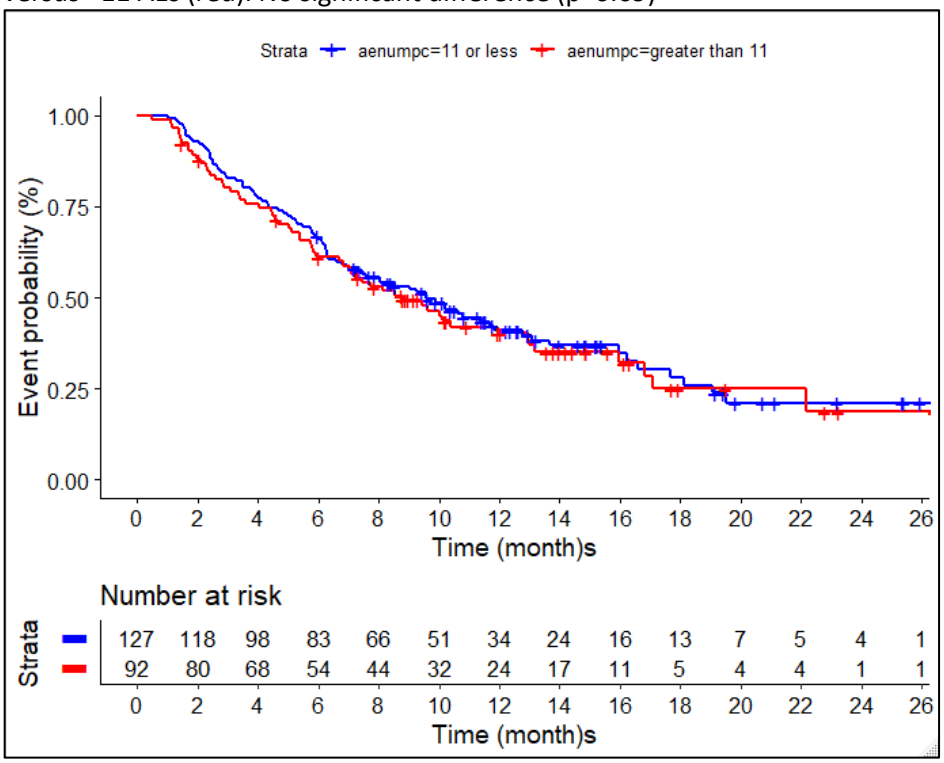
A: Overall survival for patients receiving at least 1 dose of phase 1 study medication. Median OS = 9.4 (95%CI: 7.3-11.3) months. Median follow up time is 8.1 months.



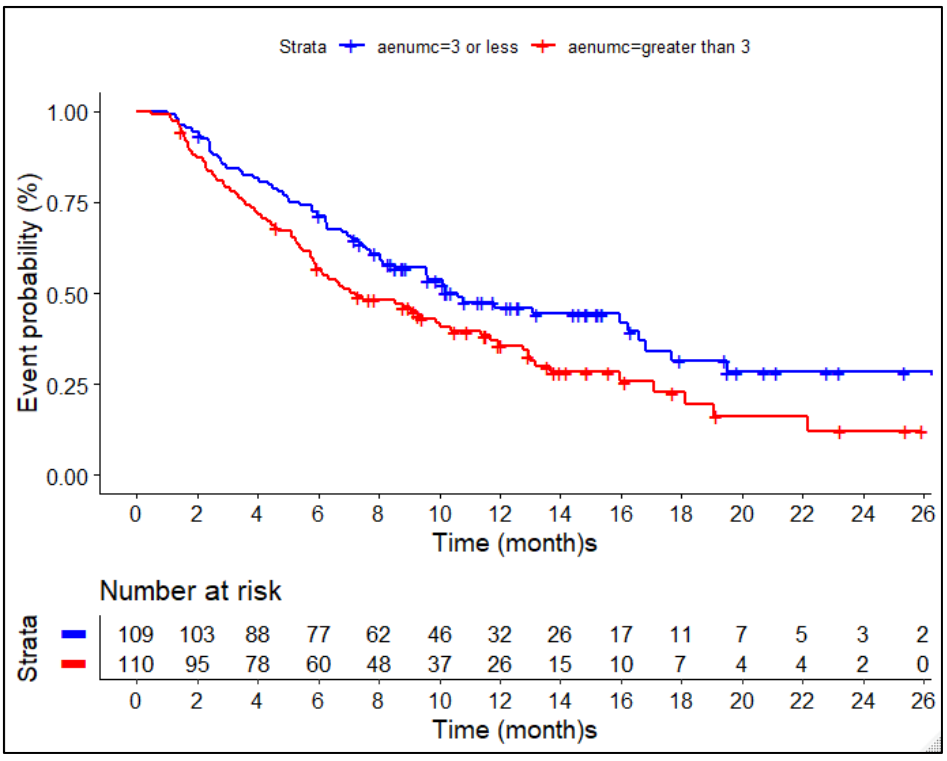
B: Overall survival for all patients enrolled on study. Median OS = 8.4 (95%CI: 6.5-10.8) months. Median follow up time is 7.7 months.



C: Subgroup analysis of patient (PRO-CTCAE) evaluation of median number of toxicities for ≤11 AEs (blue) versus >11 AEs (red). No significant difference (p=0.69)



D: Subgroup analysis of physician (CTCAE) evaluation of toxicity for patients having ≤3 symptomatic-AEs (blue) versus >3 (red) symptomatic-AEs. Median OS was 10.6 (95%CI: 8.1-16.6) months and 7.2b(95% CI: 5.8-10.0) months respectively. Significant difference HR 1.48 (95% CI: 1.06-2.06), p=0.03



E: Subgroup analysis of patient survival by Royal Marsden Index (RMI) score. Median OS for RMI (0-1)[blue] is 10.4 (95% CI: 8.5-13.7) months and median OS for RMI (2-3) [red] is 5.8 (95%CI: 4.1-8.6) months (p<0.001).