

SUPPLEMENTARY MATERIAL

Table S1A. Chemotherapy-induced toxicity stratified by SMM status

Table S1B. Chemotherapy-induced toxicity stratified by SMD status

Figure S1. Chemotherapy-induced haematological toxicity stratified by SMM and SMD status

Figure S2. Chemotherapy-induced non-haematological toxicity stratified by SMM and SMD status

Table S1A. Chemotherapy-induced toxicity stratified by SMM status

Chemotherapy-induced toxicity	N	All patients	N	Low SMM	N	Intermediate SMM	N	High SMM	p-value*
Haematological toxicities									
Nadir Hb (mmol/L), median (IQR)	295	6.0 (5.5-6.9)	99	5.7 (5.2-6.5)	98	6.0 (5.4-6.8)	98	6.5 (5.8-7.3)	<0.001*
Anaemia, any grade, n (%)	295	225 (76.3)	99	86 (86.9)	98	75 (75.8)	98	64 (64.6)	0.002*
Anaemia, grade 3/4, n (%)	295	27 (9.2)	99	17 (17.2)	98	7 (7.1)	98	3 (3.1)	0.002*
Nadir leukocytes ($\cdot 10^9/L$), median (IQR)	295	3.3 (2.4-4.5)	99	3.1 (2.1-4.3)	98	3.6 (2.4-4.7)	98	3.4 (2.4-4.6)	0.30
Leukocytopenia, any grade, n (%)	295	195 (66.1)	99	67 (67.7)	98	61 (62.2)	98	67 (68.4)	0.61
Leukocytopenia, grade 3/4, n (%)	295	48 (16.3)	99	20 (20.2)	99	13 (13.1)	99	15 (15.2)	0.38
Nadir neutrophils ($\cdot 10^9/L$), median (IQR)	205	1.5 (0.8-2.4)	71	1.2 (0.6-2.4)	63	1.7 (0.7-2.6)	71	1.3 (0.9-2.0)	0.30
Neutropenia, any grade, n (%)	205	110 (53.7)	71	42 (59.2)	63	25 (39.7)	71	43 (60.6)	0.03*
Neutropenia, grade 3/4, n (%)	205	65 (31.7)	71	25 (35.2)	63	17 (27.0)	71	23 (32.4)	0.59
Nadir thrombocytes ($\cdot 10^9/L$), median (IQR)	295	134 (75-203)	99	127 (70-192)	98	149 (92-227)	98	129 (73-195)	0.08
Thrombocytopenia, any grade, n (%)	295	166 (55.9)	99	60 (60.6)	98	48 (49.0)	98	58 (59.2)	0.22
Thrombocytopenia, grade 3/4, n (%)	295	42 (14.2)	99	19 (19.2)	98	13 (13.3)	98	10 (10.2)	0.19
Overall haematological toxicity [^] , any grade, n (%)	295	266 (90.2)	99	92 (92.9)	98	87 (88.8)	98	87 (88.8)	0.41
Overall haematological toxicity [^] , grade 3/4, n (%)	295	108 (36.6)	99	48 (48.5)	98	28 (28.6)	98	32 (32.7)	0.007*
Non-haematological toxicities									
Nephrotoxicity, any grade, n (%)	297	84 (28.3)	99	27 (27.3)	99	30 (30.3)	99	27 (27.3)	0.86
Nephrotoxicity, grade ≥ 2 , n (%)	297	15 (5.1)	99	5 (5.1)	99	4 (4.0)	99	6 (6.1)	0.81
Neurotoxicity, any grade, n (%)	297	84 (28.3)	99	29 (29.3)	99	30 (30.3)	99	25 (25.3)	0.71
Neurotoxicity, grade ≥ 2 , n (%)	297	27 (9.1)	99	11 (11.1)	99	9 (9.1)	99	7 (7.1)	0.61
Esophagitis, any grade, n (%)	297	91 (30.6)	99	30 (30.3)	99	28 (28.3)	99	33 (33.3)	0.74
Esophagitis, grade ≥ 2 , n (%)	297	36 (12.1)	99	10 (10.1)	99	10 (10.1)	99	16 (16.2)	0.32
Overall non-haem. toxicity [^] , any grade, n (%)	297	188 (63.3)	99	68 (68.7)	99	60 (60.6)	99	60 (60.6)	0.40
Overall non-haem. toxicity [^] , grade ≥ 2 , n (%)	297	73 (24.6)	99	22 (22.2)	99	23 (23.2)	99	28 (28.3)	0.57
Dose-limiting toxicities, n (%)									
Switching treatment (cisplatin to carboplatin)	133	30 (22.6)	45	11 (24.4)	44	11 (25.0)	44	8 (18.2)	0.70
Treatment delay (≥ 7 days)	297	49 (16.5)	99	20 (20.2)	99	13 (13.1)	99	16 (16.2)	0.41
Treatment de-escalation ($\geq 25\%$)	297	37 (12.5)	99	17 (17.2)	99	8 (8.1)	99	12 (12.1)	0.15
Treatment termination	297	28 (9.4)	99	6 (6.1)	99	11 (11.1)	99	11 (11.1)	0.37
Treatment-related hospitalization	297	97 (32.7)	99	41 (41.4)	99	30 (30.3)	99	26 (26.3)	0.063
Overall dose-limiting toxicity [^]	297	165 (55.6)	99	64 (64.6)	99	48 (48.5)	99	53 (53.5)	0.065

* p-value < 0.05 based on Kruskal Wallis Test (for continuous independent variable) and Pierson Chi-square test or Fisher's Exact Test (in case the cell count in any of the tables was <5) (for categorical independent variable).

^ Composite endpoints: overall non-haematological toxicity: nephrotoxicity OR neurotoxicity OR esophagitis; overall haematological toxicity: anaemia OR leukocytopenia OR neutropenia OR thrombocytopenia; overall dose-limiting toxicity: switching treatment (cisplatin to carboplatin) OR treatment delay (≥ 7 days) OR treatment de-escalation ($\geq 25\%$) OR treatment termination OR treatment-related hospitalization.

Abbreviations: Hb: haemoglobin; IQR, interquartile range; SMM, skeletal muscle mass.

Table S1B. Chemotherapy-induced toxicity stratified by SMD status

Chemotherapy-induced toxicity	N	All patients	N	Low SMD	N	Intermediate SMD	N	High SMD	p-value*
Haematological toxicities									
Nadir Hb (mmol/L), median (IQR)	282	6.1 (5.5-6.9)	95	5.8 (5.2-6.8)	94	6.2 (5.7-7.0)	93	6.1 (5.5-7.3)	0.012*
Anaemia, any grade, n (%)	282	215 (76.2)	95	79 (83.2)	94	71 (75.5)	93	65 (69.9)	0.10
Anaemia, grade 3/4, n (%)	282	26 (9.2)	95	12 (12.6)	94	8 (8.5)	93	6 (6.5)	0.33
Nadir leukocytes ($\cdot 10^9/L$), median (IQR)	282	3.4 (2.4-4.5)	95	3.0 (2.0-4.1)	94	3.5 (2.5-4.7)	93	3.5 (2.6-4.7)	0.041*
Leukocytopenia, any grade, n (%)	282	185 (65.6)	95	69 (72.6)	94	58 (61.7)	93	58 (62.4)	0.21
Leukocytopenia, grade 3/4, n (%)	282	48 (17.0)	95	22 (23.2)	94	11 (11.6)	93	15 (16.0)	0.10
Nadir neutrophils ($\cdot 10^9/L$), median (IQR)	193	1.5 (0.7-2.4)	60	1.3 (0.6-2.6)	69	1.5 (0.9-2.4)	64	1.6 (0.8-2.4)	0.69
Neutropenia, any grade, n (%)	193	102 (52.8)	60	39 (65.0)	69	35 (50.7)	64	28 (43.8)	0.05
Neutropenia, grade 3/4, n (%)	193	61 (31.6)	60	22 (36.7)	69	19 (27.5)	64	20 (31.3)	0.54
Nadir thrombocytes ($\cdot 10^9/L$), median (IQR)	282	134 (75-203)	95	100 (53-174)	94	150 (96-227)	93	144 (82-225)	<0.001*
Thrombocytopenia, any grade, n (%)	282	157 (55.7)	95	67 (70.5)	94	44 (46.8)	93	46 (49.5)	0.001*
Thrombocytopenia, grade 3/4, n (%)	282	42 (14.9)	95	23 (24.2)	94	8 (8.5)	93	11 (11.8)	0.006*
Overall haematological toxicity [^] , any grade, n (%)	282	253 (89.7)	95	89 (93.7)	94	85 (90.4)	93	79 (84.9)	0.15
Overall haematological toxicity [^] , grade 3/4, n (%)	282	103 (36.5)	95	40 (42.1)	94	32 (34.0)	93	31 (33.3)	0.38
Non-haematological toxicities									
Nephrotoxicity, any grade, n (%)	284	78 (27.5)	95	29 (30.5)	95	25 (26.3)	94	24 (25.5)	0.71
Nephrotoxicity, grade ≥ 2 , n (%)	284	13 (4.6)	95	7 (7.4)	95	4 (4.2)	94	2 (2.1)	0.22
Neurotoxicity, any grade, n (%)	284	83 (29.2)	95	26 (27.4)	95	30 (31.6)	94	27 (28.7)	0.81
Neurotoxicity, grade ≥ 2 , n (%)	284	27 (9.5)	95	11 (11.6)	95	8 (8.4)	94	8 (8.4)	0.70
Esophagitis, any grade, n (%)	284	88 (31.0)	95	33 (34.7)	95	26 (27.4)	94	29 (30.9)	0.55
Esophagitis, grade ≥ 2 , n (%)	284	36 (12.7)	95	14 (14.7)	95	12 (12.6)	94	10 (10.6)	0.70
Overall non-haem. toxicity [^] , any grade, n (%)	284	178 (62.7)	95	59 (62.1)	95	63 (66.3)	94	56 (59.6)	0.63
Overall non-haem. toxicity [^] , grade ≥ 2 , n (%)	284	71 (25.0)	95	27 (28.4)	95	24 (25.3)	94	20 (21.3)	0.52
Dose-limiting toxicities, n (%)									
Switching treatment (cisplatin to carboplatin)	127	29 (22.8)	43	10 (27.8)	43	12 (30.0)	41	7 (13.7)	0.13
Treatment delay (≥ 7 days)	284	47 (16.5)	95	15 (15.8)	95	17 (17.9)	95	15 (16.0)	0.91
Treatment de-escalation ($\geq 25\%$)	284	35 (12.3)	95	16 (16.8)	95	10 (10.5)	95	9 (9.6)	0.26
Treatment termination	284	24 (8.5)	95	9 (9.5)	95	11 (11.6)	95	4 (4.3)	0.18
Treatment-related hospitalization	284	94 (33.1)	95	42 (44.2)	95	32 (33.7)	95	20 (21.3)	0.004*
Overall dose-limiting toxicity [^]	284	157 (55.3)	95	61 (64.2)	95	59 (62.1)	95	37 (39.4)	0.001*

* p-value < 0.05 based on Kruskal Wallis Test (for continuous independent variable) and Pierson Chi-square test or Fisher's Exact Test (in case the cell count in any of the tables was <5) (for categorical independent variable).

^ Composite endpoints: overall non-haematological toxicity: nephrotoxicity OR neurotoxicity OR esophagitis; overall haematological toxicity: anaemia OR leukocytopenia OR neutropenia OR thrombocytopenia; overall dose-limiting toxicity: switching treatment (cisplatin to carboplatin) OR treatment delay (≥ 7 days) OR treatment de-escalation ($\geq 25\%$) OR treatment termination OR treatment-related hospitalization.

Abbreviations: Hb: haemoglobin; IQR, interquartile range; SMD, skeletal muscle density.

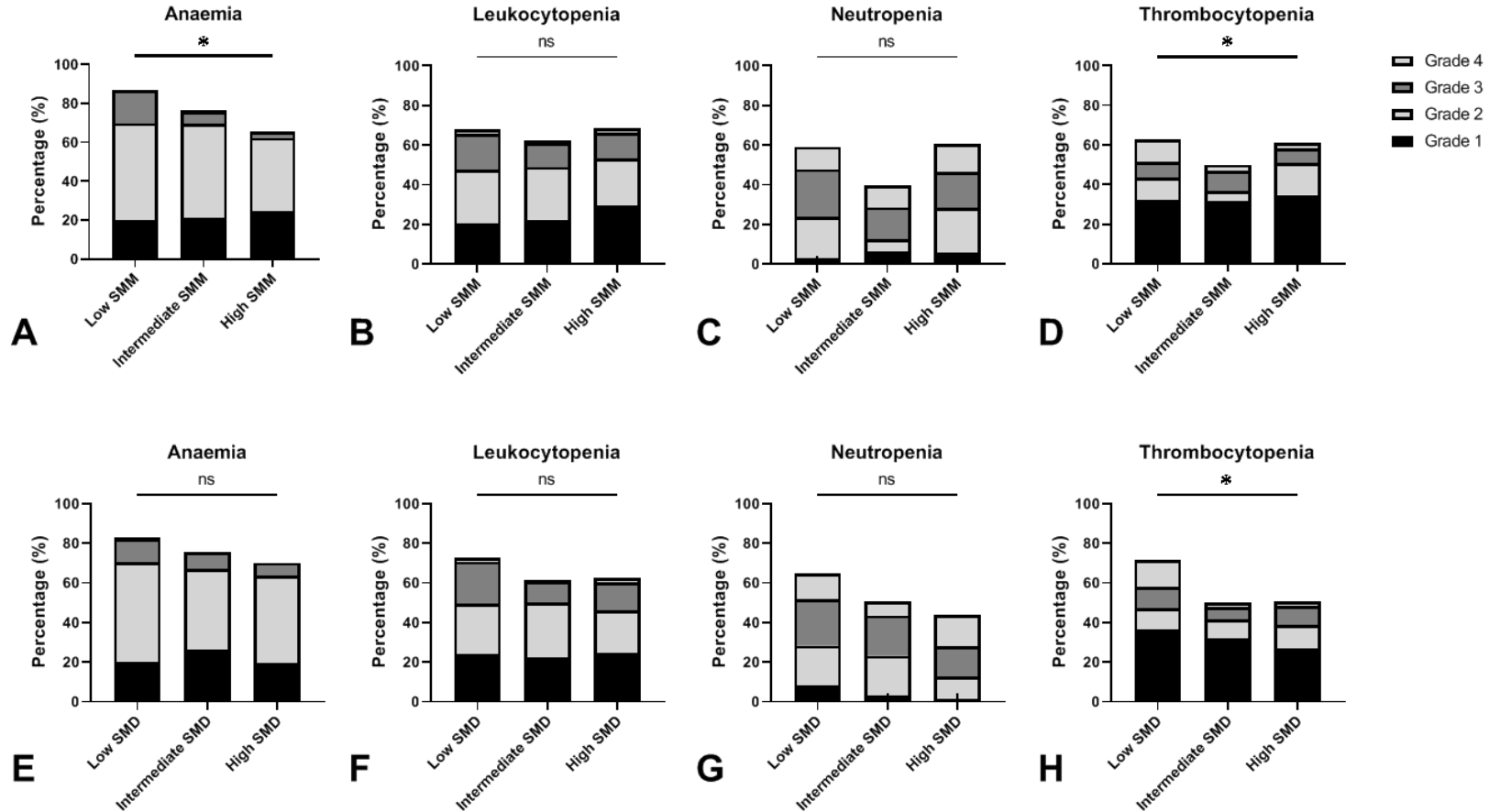


Figure S1. Chemotherapy-induced haematological toxicity stratified by SMM and SMD status.

Percentage of chemotherapy-induced haematological toxicity scored using CTCAE, stratified by low, intermediate and high SMM and SMD status using the Pierson Chi-square test or Fisher's Exact Test (in case the cell count in any of the tables was <5). * $p < 0.05$. **A.** Anaemia stratified by SMM status. **B.** Leukocytopenia stratified by SMM status. **C.** Neutropenia stratified by SMM status. **D.** Thrombocytopenia stratified by SMM status. **E.** Anaemia stratified by SMD status. **F.** Leukocytopenia stratified by SMD status. **G.** Neutropenia stratified by SMD status. **H.** Thrombocytopenia stratified by SMD status. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ns: not statistically significant; SMD: skeletal muscle density; SMM: skeletal muscle mass.

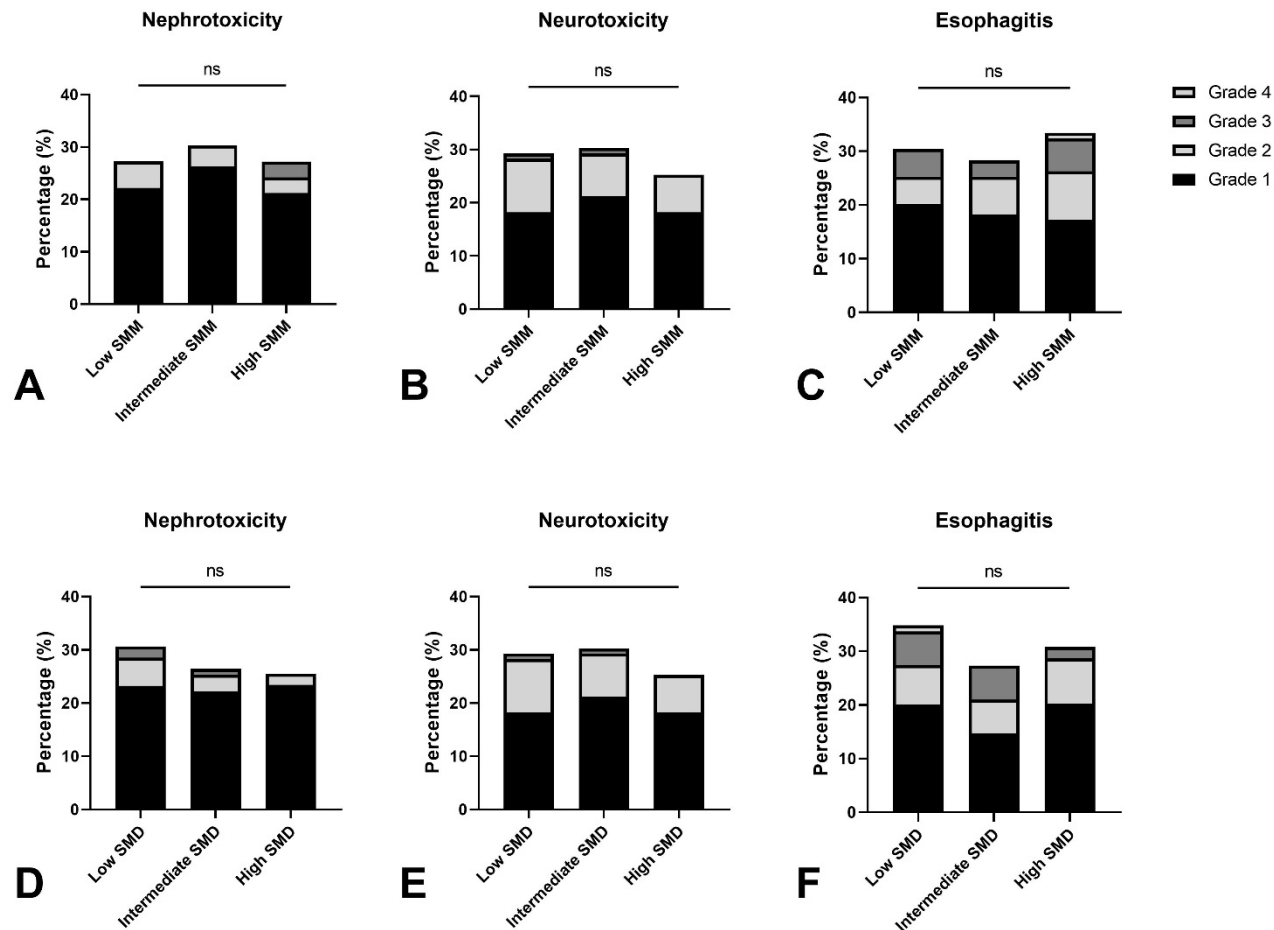


Figure S2. Chemotherapy-induced non-haematological toxicity stratified by SMM and SMD status.

Percentage of chemotherapy-induced non-haematological toxicity scored using CTCAE, stratified by low, intermediate and high SMM and SMD status using the Pearson Chi-square test or Fisher's Exact Test (in case the cell count in any of the tables was <5). * $p < 0.05$. **A.** Nephrotoxicity stratified by SMM status. **B.** Neurotoxicity stratified by SMM status. **C.** Esophagitis stratified by SMM status. **D.** Nephrotoxicity stratified by SMD status. **E.** Neurotoxicity stratified by SMD status. **F.** Esophagitis stratified by SMD status. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ns: not statistically significant; SMD: skeletal muscle density; SMM: skeletal muscle mass.