

Background

- Early cross-over of Kaplan-Meier survival curves seen in clinical trials of immunotherapy (IO) suggests that a subpopulation of patients with cancer treated with IO is at higher risk for early mortality (EM).
- An accurate estimate of EM post IO start, and a better understanding of factors associated with EM in a real- world setting are crucial to identify patients at risk and avoid potential harm.

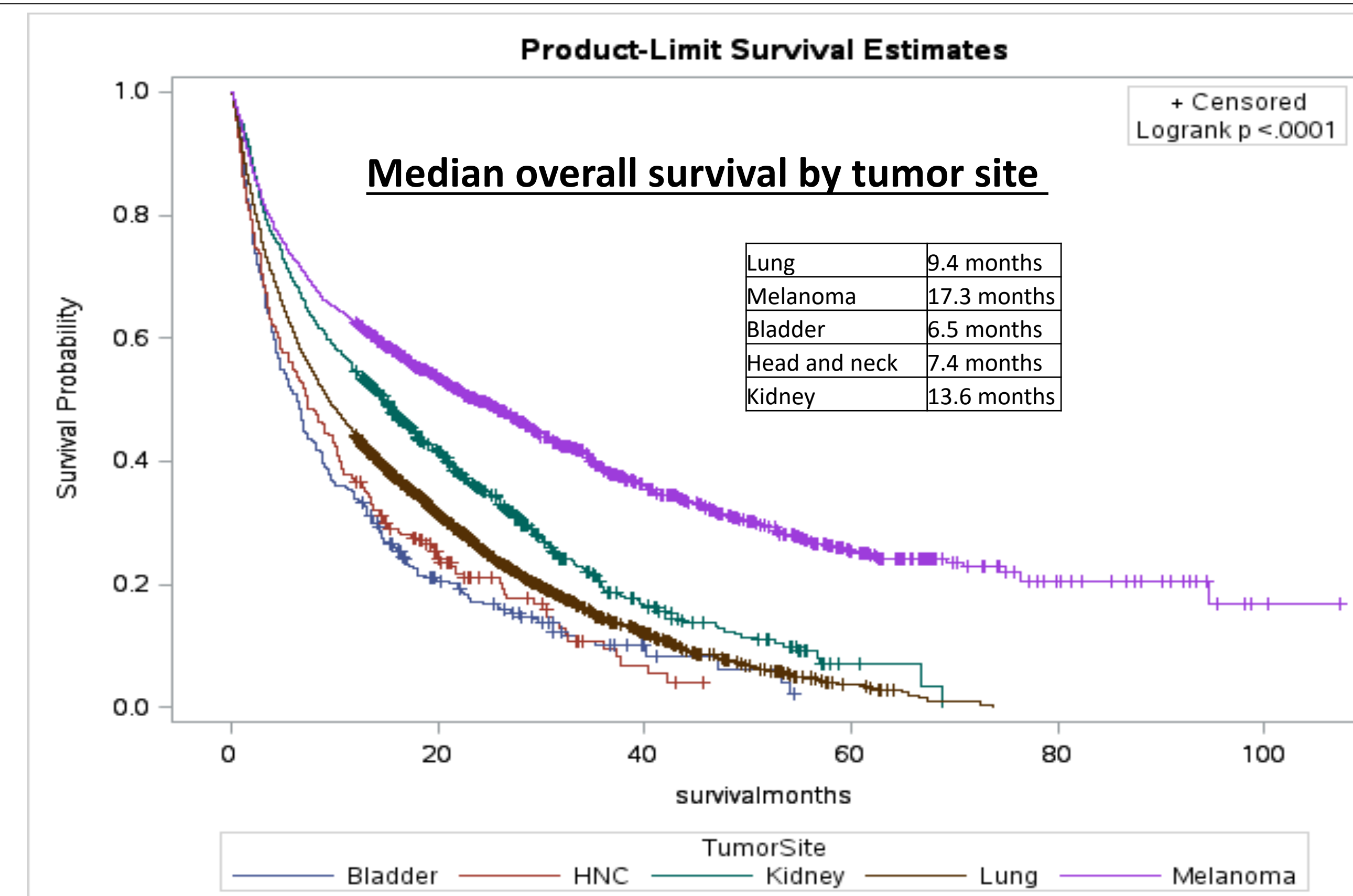
Methods

- Study design:** Retrospective cohort study using health administrative data in Ontario, Canada (ICES)
- Population:** Patients diagnosed with bladder, head and neck, kidney, lung or melanoma cancer and treated with at least one dose of IO between 2012 and 2020
- Primary objective:** EM within 60 days after IO start
- Other objectives:** 1) factors associated with EM, 2) EM within 30 and 90 days, 3) 1-year and median overall survival, 4) median time and number of IO treatment
- Primary analysis:** Proportion of patients with EM
- Assessment of factors associated with EM:** Multivariable regression model with odds ratios (ORs) & 95% confidence intervals (CIs)

Results

Baseline characteristics	Total (N=7,126)		Total (N=7,126)
Median Age (IQR)	67 (60-74)	WBC	
		>11,000/mm3	1,071 (15.0%)
		<=11,000/mm3	4,783 (67.1%)
Female, N (%)	2,971 (41.7%)	Hb	
		<10g/dl	917 (12.9%)
		>=10g/dl	5,311 (74.5%)
Tumor site, N (%)		IO drug type, N (%)	
Head and Neck	233 (3.3%)	Nivolumab	2,643 (37.1%)
Melanoma	1,705 (23.9%)	Pembrolizumab	2,874 (40.3%)
Kidney	757 (10.6%)	Ipilimumab	438 (6.1%)
Bladder	289 (4.1%)	Durvalumab	422 (5.9%)
Lung	4,142 (58.1%)	Other	749 (10.6%)
ESAS		Charlson score	
0	746 (10.5%)	0	2,961 (41.6%)
1	1,152 (16.2%)	1	1,090 (15.3%)
2	913 (12.8%)	2	476 (6.7%)
>2	2116 (29.6%)	3+	377 (5.3%)
		No hospitalization	2,222 (31.2%)
NLR		BMI	
Median (IQR)	5 (3-8)	>=25	2,565 (36.0%)
		<25	2,035 (28.6%)
Use of steroids (age >=65), yes, N (%)	1,263 (32.0%)		

ESAS: Edmonton Symptom Assessment System, NLR: neutrophil/lymphocyte ratio, WBC: white blood cells, Hb: hemoglobin, IO: immunotherapy, BMI: body mass index



Factors associated with EM within 60 days	Unit	Adjusted OR	95%CI	p value
Age	Every additional 10 years	0.96	0.89-1.03	0.31
Gender	Reference: Male	0.94	0.81-1.09	0.46
Tumor site	Lung	0.63	0.49-0.82	<.001
Reference: Melanoma	Kidney	0.47	0.33-0.66	<.001
	Head and neck	0.90	0.58-1.40	0.63
	Bladder	0.78	0.49-1.23	0.28
Hemoglobin	<10 vs. >=10g/dl	1.62	1.34-1.97	<.001
WBC	>11,000 vs. <=11,000/mm3	2.38	1.98-2.86	<.001
NLR	< vs. > median (4.64)	0.36	0.29-0.44	<.001
BMI	Reference: <25	0.75	0.63-0.90	0.002
ESAS	1	1.26	0.67-1.56	0.91
Reference: 0	2	2.21	1.49-3.28	<.001
	3	2.25	1.51-3.36	<.001
	>3			<.001
Charlson score	No hosp	0.87	0.62-1.23	0.44
Reference: 0	1	0.78	0.45-1.36	0.38
	2	0.78	0.52-1.16	0.22
	3+	1.16	0.83-1.61	0.39
Combination therapy	IO + IO	0.68	0.47-0.99	0.04
Reference: single IO	IO + chemotherapy	1.09	0.90-1.31	0.37

Other variables adjusted for: income quartile, rurality, cancer centre level, hospital admission & emergency department visit, previous chemotherapy or radiation therapy, platelets, calcium, creatinine

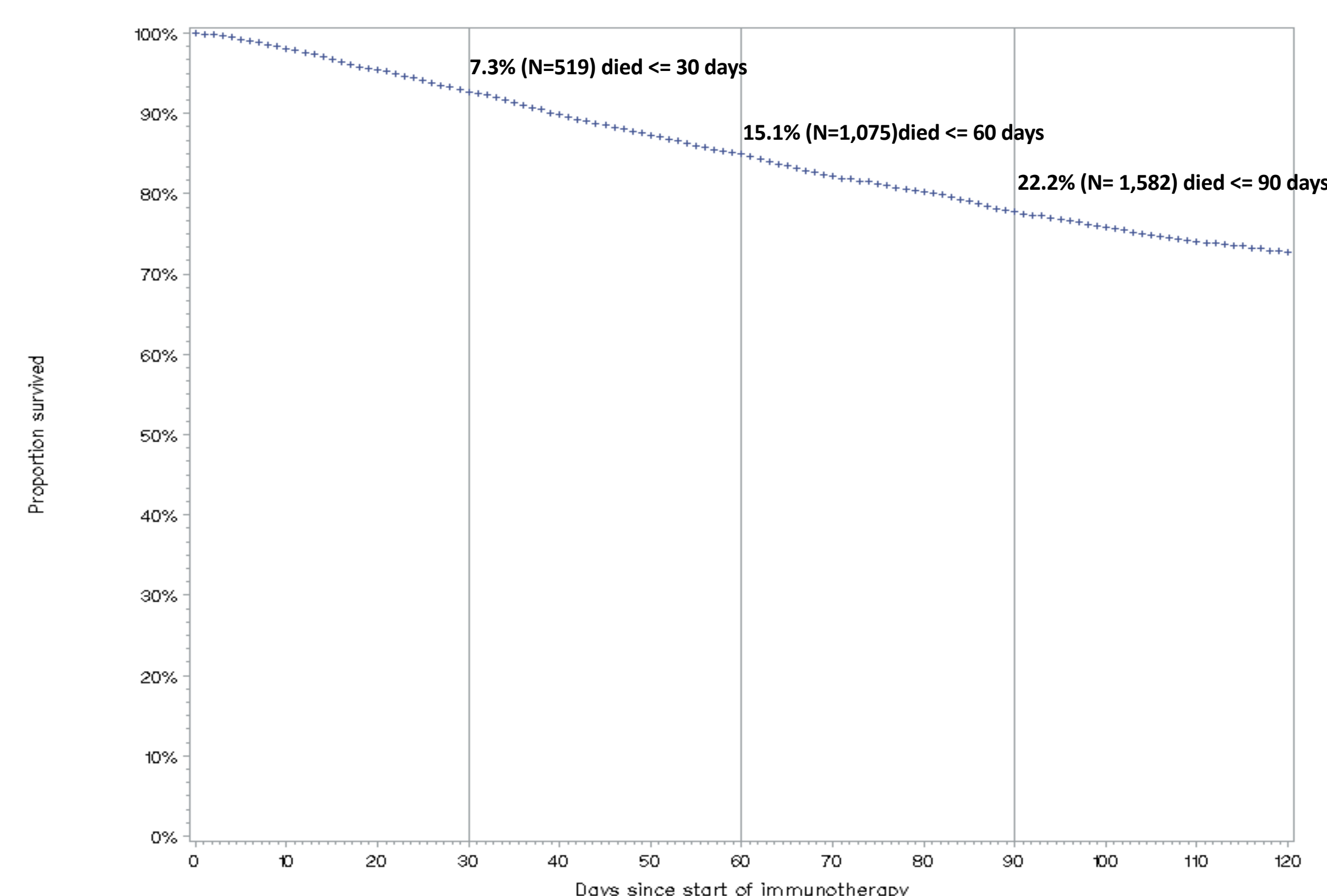
Conclusions

EM is common among patients treated with IO in the real-world setting and is associated with several patient and tumor characteristics. Development of a validated tool to predict EM in this setting may facilitate better patient selection for treatment with IO in routine clinical practice.

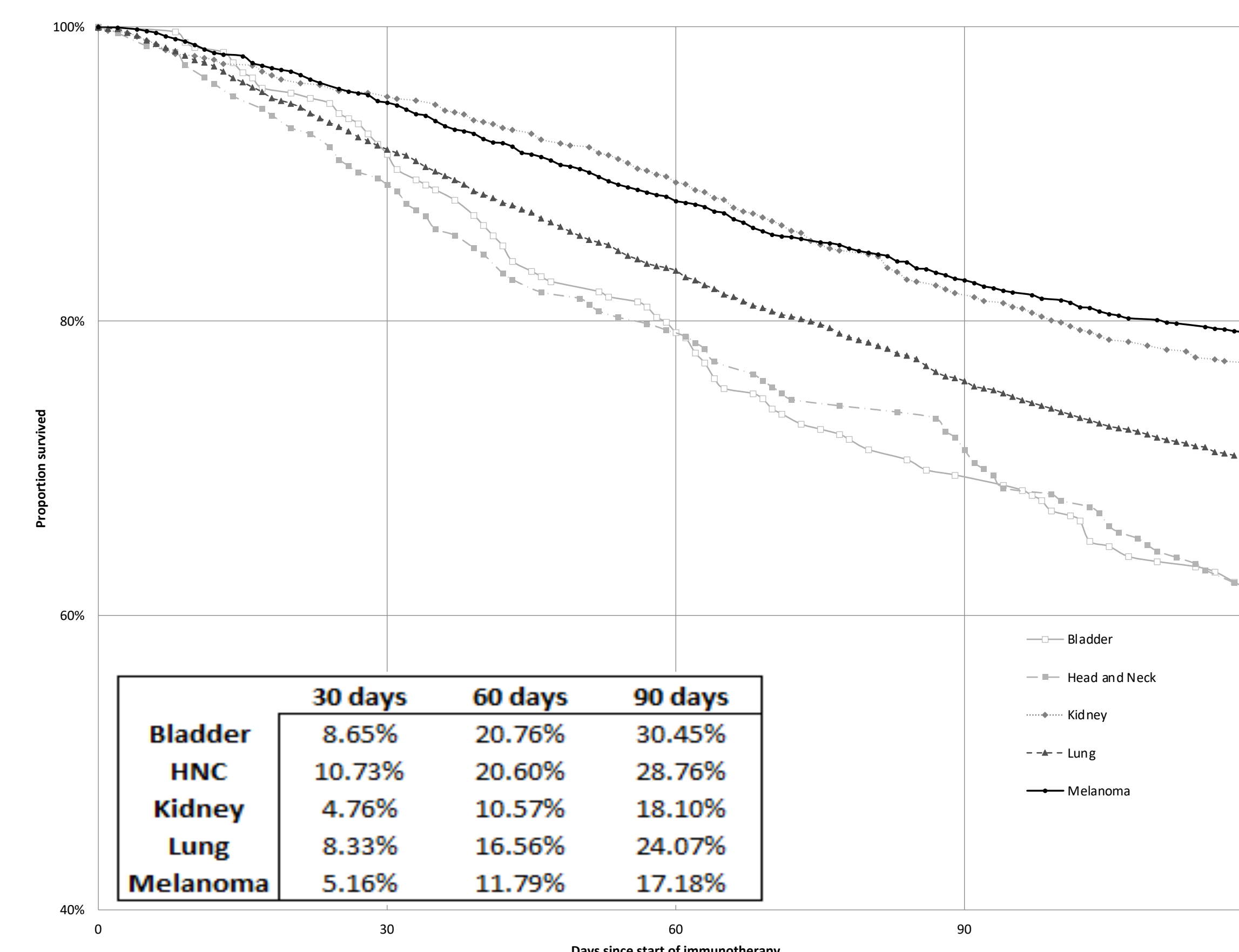
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Results

Early mortality post IO start



Early mortality by tumor site post IO start



Tumor site	Median # treatments	Median duration of treatment (days)
Lung	5	70
Melanoma	4	65
Bladder	4	57
Head & Neck	4	56
Kidney	5	77