Abstract # 101P

Differential expression of PD-L1 and immune biomarkers by age: Decreased expression in pediatric/AYA patients with advanced cancer

CONTRIBUTING RESEARCHERS

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BACKGROUND

- Programmed death-1 (PD-1) and programmed death ligand-1 (PD-L1) inhibitors have been approved across a wide spectrum of cancer types
- Although there is substantial focus on novel biomarkers to predict response to PD-1/PD-L1 inhibitors, it is possible that clinicopathologic factors could be utilized
- It has been observed in settings such as advanced renal cell carcinoma that older patients may have a diminished response to PD-1 inhibitors such as nivolumab
- At the other extreme of age, it has also been speculated that pediatric/AYA patients may have a lesser response to these therapies
- We interrogated a large clinical database comprised of patients with a wide variety of cancer types and interrogated the relationship between age and immune checkpoint expression

METHODS

- Whole transcriptomic sequencing (RNA-Seq; ~200x106 reads/tumor) was performed across 1,467 unselected clinical cases (NantHealth; Culver City, CA), with breast, colon, lung and sarcoma reflecting the most common tumor types assessed
- To reflect the extremes of age, patients age < 25 and ≥ 80 were compared to the remainder of the cohort
- PD-L1 expression was compared across these age-based subsets, along with CTLA4, TIGIT, FOXP3, LAG3, OX40, TIM3 and IDO expression
- Putative markers of ICI resistance (e.g, VEGF-A/B/C) were also explored
- Tumor mutational burden (TMB; defined as total number of somatic-specifc exonic nonsynonymous mutations) was characterized in each subset

PATIENT CHARACTERISTICS

- **Median age of the cohort was 59 (range, 2-97)**
- **Of 1,467 patients, 84 and 65 were age < 25 and ≥ 80, respectively**

RESULTS

Table 1. Distribution of histologies included in the current analysis with accompanying age/gender distribution and PD-L1/TMB data.

	N	% of cases	% Female	TMB avg.	TMB med.	Age med.	% low PDL1	% high PDL1
Breast	270	18.40	99.26	129.54	92	56	10.37	13.70
Colon	140	9.54	55.40	269.81	129	58	17.14	7.14
Lung	112	7.63	53.57	260.13	179	65	8.93	41.07
Sarcoma	111	7.57	45.95	135.41	68	51	27.03	12.61
Pancreatic	93	6.34	44.09	71.39	58	63	8.60	11.83
Ovarian	77	5.25	100.00	91.94	86	58	22.08	9.09
Brain	76	5.18	40.79	96.83	68	47	17.11	13.16
Other Cancer	60	4.09	45.00	114.27	84	63	11.67	23.33
None	48	3.27	41.67	602.50	75	60	18.75	14.58
Prostate	36	2.45	0.00	99.86	61	65	27.78	0.00
Gastric	34	2.32	38.24	124.26	68	61	0.00	20.59
Melanoma	33	2.25	30.30	598.00	231	64	6.06	30.30
Esophageal	33	2.25	27.27	172.21	123	64	18.18	18.18
Head and Neck	32	2.18	21.88	102.63	95	64	9.38	46.88
Kidney	29	1.98	31.03	406.38	74	58	10.34	20.69
Liver	28	1.91	32.14	182.04	103	65	25.00	14.29
Oral	28	1.91	39.29	143.89	88	61	3.57	32.14
Rectal	27	1.84	29.63	251.74	112	57	3.70	18.52
Bladder	22	1.50	45.45	255.55	125	71	4.55	45.45
Unknown Primary	22	1.50	59.09	181.59	86	53	9.09	31.82
Uterine	22	1.50	100.00	188.00	107	67	27.27	4.55
Soft Tissue	20	1.36	30.00	101.55	67	18	40.00	15.00
Overall	1467	100.00	56.99	201.93	91	60	14.38	18.81

Figure 1. Distribution of patients by age.

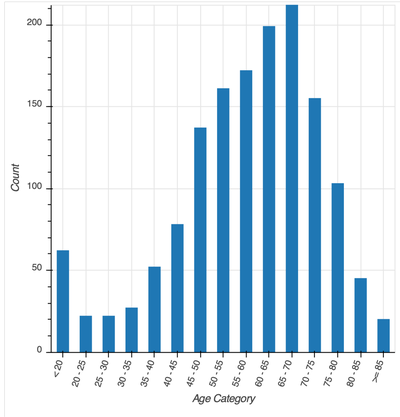


Figure 2. PD-L1 status by age.

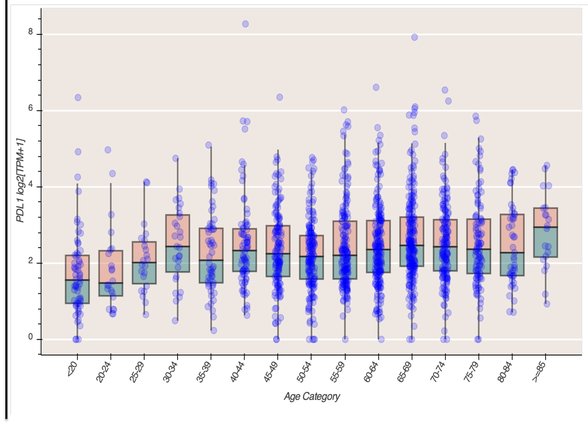
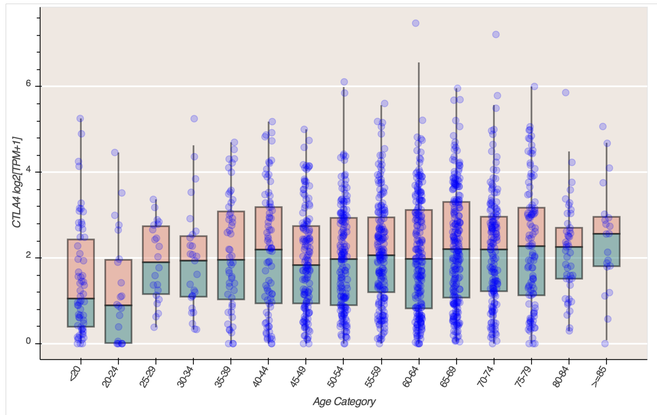


Figure 2. CTLA4 status by age.



KEY FINDINGS

- Younger patients (age < 24) with advanced cancer appear to have lower levels of CTLA4 and PD-L1 expression
- No significant differences were found in expression of LAG3, TIM3, TIGIT and other immune checkpoint markers (data not shown)
- Exploratory analyses of TMB showed no difference across age-based subsets (data not shown)

CONCLUSIONS

In pediatric and adolescent and young adult (AYA) patients, lower expression of multiple immune checkpoint molecules may have implications for drug development. In particular, combination strategies with non-immunotherapeutic approaches may prove optimal. A slight but opposing trend was seen in octagenarians and nonagenarians in our cohort.

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2. Motzer RJ, Escudier B, McDermott DF, et al Nivolumab versus Everolimus in Advanced Renal-Cell Carcinoma. The New England journal of medicine 2015 373 (19):1803-1813.
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