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ADVANCES IN Cancer IMMUNOTHERAPY™

Immunotherapy and COVID-19

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ACCC Association of Community Cancer Centers

HOPA Hematology/Oncology Pharmacy Association

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Disclosures

- I have the following financial relationships to disclose:
  - Consulting fees: Rakuten, Exicure, Shattuck Labs
  - Contracted Research: Merck, BMS, AstraZeneca, Tesaro/GSK
  - Ownership Interest Less Than 5%: High Enroll
- I will not be discussing non-FDA approved indications during my presentation.

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COVID-19 Pandemic

- Caused by SARS-CoV-2 virus which started in Wuhan China in 12/2019
- Common symptoms
  - Cough
  - Fever
  - Loss of smell/taste
  - Lymphocytopenia
- Severe complications
  - Cytokine storm and sepsis
  - Respiratory failure and ARDS
  - Hypercoagulability

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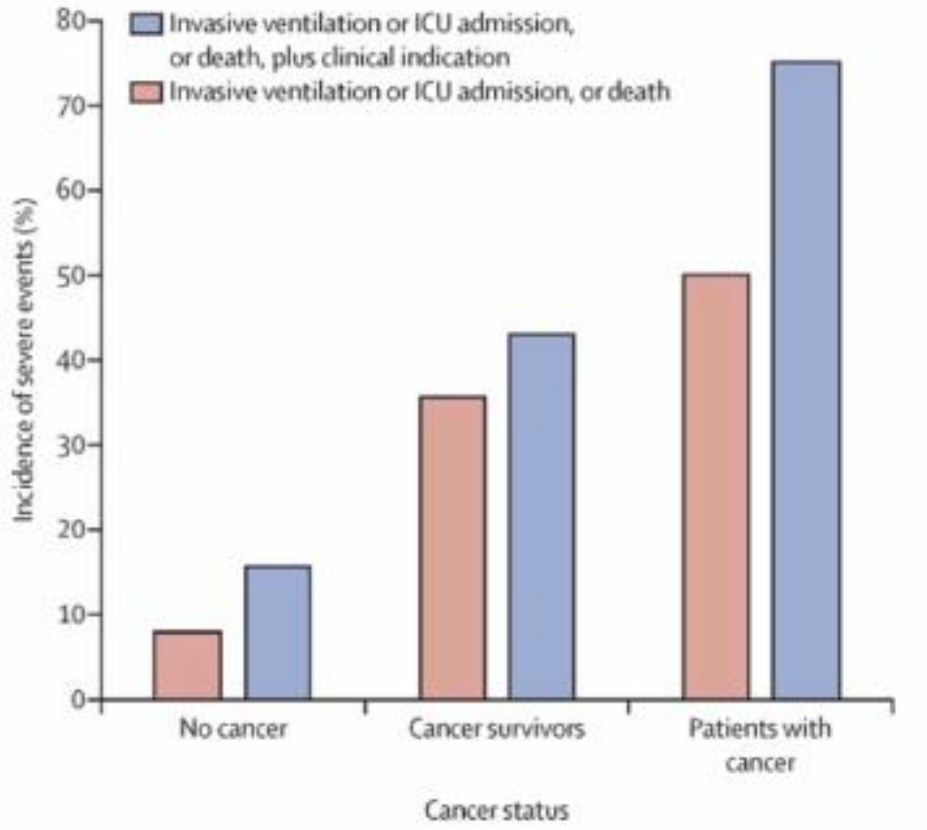
Cancer and COVID-19 Severity

- Patients with cancer are uniquely susceptible to SARS-CoV-2 infection and subsequent complications
- Higher rates of hospitalization, Severe respiratory illness, and mortality



Liang *et al.* Lancet Oncology March 2020

Robilotti et al. 2020, Liang et al. 2020, Xia et al. 2020, Zhang et al., Dai et al. 2020, Lee et al., 2020, Kuderer et al. 2020

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Mortality is High in Cancer Patients

	Region	Number of Cases	Mortality in Cancer Patients (%)
Miyashita et al.	New York (Mt Sinai)	334	11%
Mehta et al.	New York (Montefiore)	218	28%
Robilitti et al.	New York (MSKCC)	423	12%
Barlesi et al.	Paris (IGR)	137	15%
Lee et al.	United Kingdom (UKCCMP)	1044	30.6%
Garassino et al.	Global (TERAVOLT)	200	33%
Kuderer et al.	USA, Canada & Spain (CCC-19)	928	13%
Zhang et al.	USA, Europe, Asia (Meta-analysis: 15 studies)	3019	22.4%

Adapted from Solomon, ESMO 2020

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COVID-19-induced cytokine storm

- Serious complication leading to ARDS and often fatality
- Clinically, most commonly characterized by:
  - Hypotension, hypoxia, fevers, coagulopathies
  - Increased ferritin, cytokine and chemokine levels
- Cytokine/chemokines commonly associated with COVID-19 cytokine storm:
  - IL-2, IL-6, IL-8, IL-4, IL-1B, IL-12, IL-18, IL-10, INFg, TNF-α, CXCL10, CCL2 (Chen et al. 2020, Coperchini et al, 2020)
- Anti-IL-6 antibody as well as other treatments are under investigation

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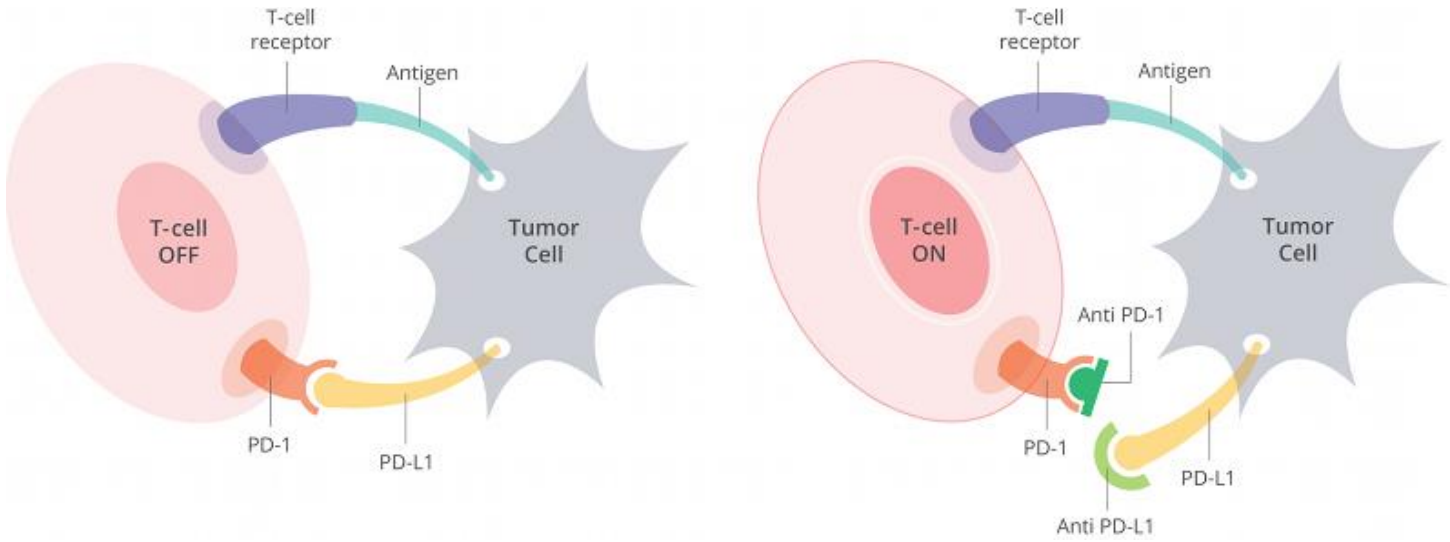
Immune Checkpoint Inhibitors (ICI) in COVID-19 Patients

- Anti-PD1-related cytokine storm: increased IL-6, IL-8, IL-10, IFN-gamma in a case study (Rotz et al. 2017)



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Predictors of severe respiratory illness

Variable	Univariate		Multivariate	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age (>65 years)	2.02 (1.33 – 3.08)	0.001	1.67 (1.07 – 2.60)	0.024
Sex (female)	1.04 (0.68 – 1.58)	0.859		
Race (non-white)	1.20 (0.79 – 1.84)	0.394		
BMI (≥30)	1.01 (0.64 – 1.59)	0.965		
Smoking (Current/Former)	1.78 (1.17 – 2.72)	0.007	1.39 (0.89 – 2.17)	0.148
Asthma/COPD	1.63 (0.98 – 2.71)	0.059	1.24 (0.72 – 2.13)	0.436
Cancer (non-met solid)	1.00 (*Ref*)	-	1.00 (*Ref*)	-
Cancer (met solid)	0.87 (0.48 – 1.59)	0.658	0.75 (0.40 – 1.41)	0.371
Cancer (hematologic)	1.69 (0.92 – 3.10)	0.092	1.79 (0.97 – 3.32)	0.063
Major Surgery (within 30d)	1.31 (0.63 – 2.71)	0.464		
Diabetes	1.09 (0.65 – 1.83)	0.745		
Cardiac Disorder	2.02 (1.28 – 3.19)	0.002	1.44 (0.88 – 2.37)	0.147
HTN/chronic kidney disease	1.68 (1.09 – 2.58)	0.020	1.18 (0.73 – 1.89)	0.505
Systemic chemotherapy (within 30d)	1.19 (0.78 – 1.82)	0.407		
Chronic lymphopenia or corticosteroids	1.59 (0.97 – 2.59)	0.066	1.42 (0.86 – 2.34)	0.165
Immune checkpoint inhibitor	2.38 (1.29 – 4.38)	0.005	2.74 (1.37 – 5.46)	0.004

Cox proportional hazard (N=423)

Robilotti et al. Nature Medicine, 2020

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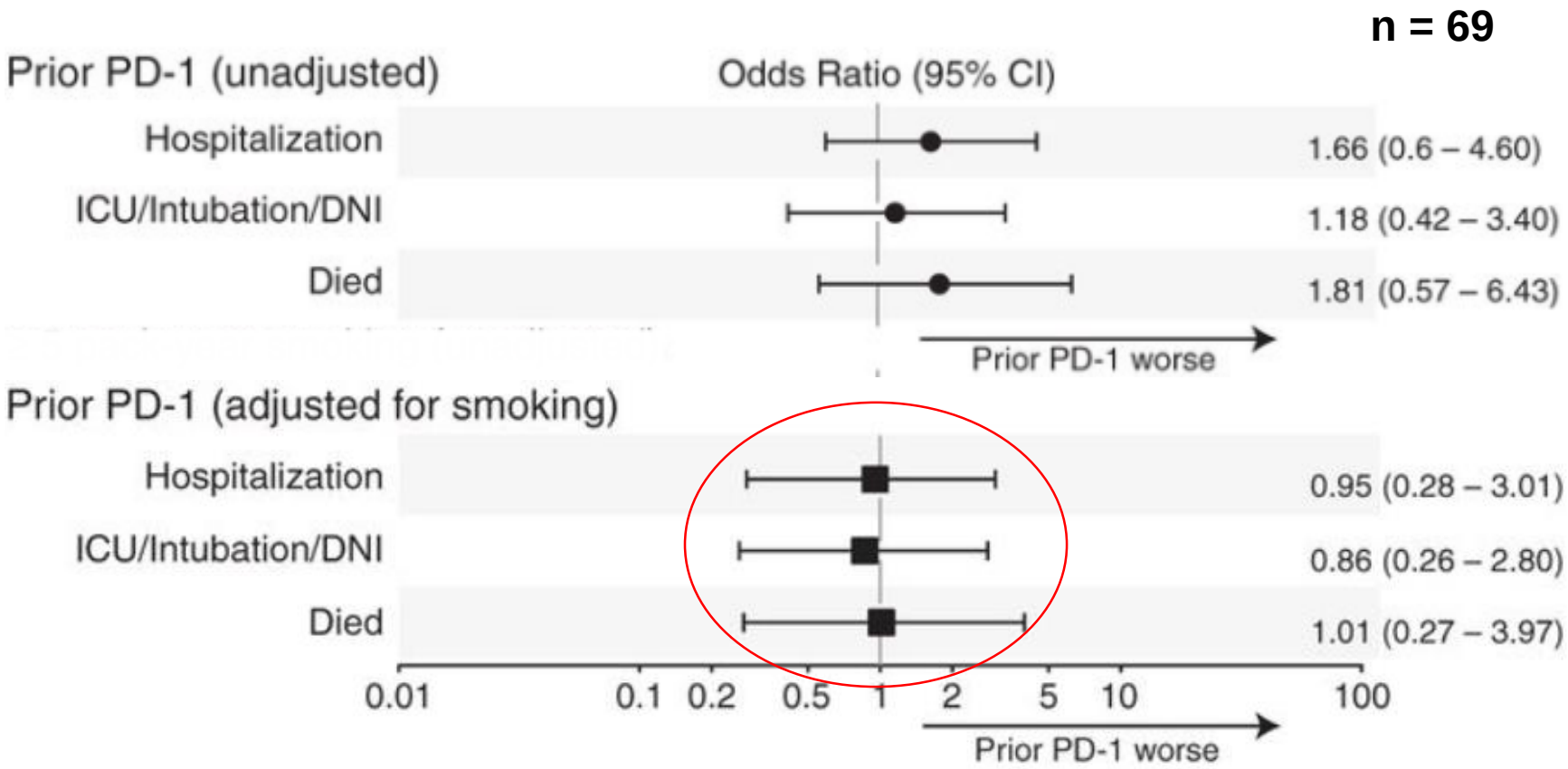
No increased COVID-19 severity with IO in Lung Cancer



Luo et al. Cancer Discovery, 2020

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CCC19 Registry: IO and Cancer

Therapy Type	<2 wk	2-4 wk	1-3 mo	3-12 mo
Total patients	919	300	230	144
Immunotherapy	62	55	19	15
SMR (95%CI)	0.93 (0.44-1.70)	1.15 (0.57-2.06)	NR	NR

1,610 patients with cancer

No increased risk of death with recent therapy

ESMO 2020

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Cohorts of COVID-19 patients with cancer:
Immune Checkpoint Inhibitors

	CCC19[1]	CACOVID-19[2]	UKCCMP[3]	OnCovid[4]	TERAVOLT[5]	LEOSS[6]	IGR cohort [7]	Robilotti[8]	Yang[9]	Tian[10]	ITA-HEMA-COV[11]
Region	Int.	France	UK	Europe	Int.	Europe	France/IGR	US/MSK	China	China	Italy
Number of patients	1610	1289	1044	890	200	435	178	423	205	232	536
Types of cancer	All	All	All	All	Lung	All	All	All	All	All	Heme
Risk Factors for Adverse Outcomes											
Immune Checkpoint Inhibitors	**-**	**-**	**NS**	**NS**	**NS**	**-**	**NS**	**X** (increased risk of severe disease)	**NS**	**-**	**-**

*Adapted from Dr. Toni Choueiri

1. Wise-Draper T.M. et al., ESMO, 2020.; 2. Lièvre A. et al., *Eur J Cancer*, 2020. PMID: 33129039; 3. Lee L.Y.W. et al., *Lancet Oncol.*, 2020. PMID: 32853557; 4. Pinato D.J. et al., *Cancer Discov.*, 2020. PMID: 32737082; 5. Garassino M.C. et al., *Lancet Oncol.*, 2020. PMID: 32539942; 6. Rüthrich M.M., *Ann. Hematol.*, 2020. PMID: 33159569; 7. Albiges L. et al., *Nat Cancer*, 2020; 8. Robilotti E.V. et al., *Nat Med.*, 2020. PMID: 32581323; 9. Yang K. et al., *Lancet Oncol.*, 2020. PMID: 32479787; 10. Tian J. et al., *Lancet Oncol.*, 2020. PMID: 32479790; 11. Passamonti F. et al., *Lancet Haematol.*, 2020. PMID: 32798473

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NCCN Guidance

- Patients receiving ICIs and who develop SARS-CoV-2 infection may benefit from interruption of ICI therapy.
  - However, at this point in time, consensus recommendations regarding duration of ICI interruptions are ill-defined and should be patient-individualized including considerations for the specific ICI and severity of COVID-19.

- ICIs may enhance viral clearance by upregulating CD8+ T cell response.
  - Cai et al., Viruses, 2020

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Vaccine Administration with IO

Table 1. COVID-19 Vaccination Recommendations for Cancer Patients

Patients Treatment/Cancer Type	Timing†,‡
Hematopoietic Cell Transplantation (HCT)/Cellular Therapy	
Allogeneic transplantation Autologous transplantation Cellular therapy (eg, CAR T cell)	At least 3 months post-HCT/cellular therapy[a,b]
Hematologic Malignancies	
Receiving intensive cytotoxic chemotherapy (eg, cytarabine/anthracycline-based induction regimens for acute myeloid leukemia [AML])	Delay until absolute neutrophil count (ANC) recovery[c]
Marrow failure from disease and/or therapy expected to have limited or no recovery	When vaccine available
Long-term maintenance therapy (eg, targeted agents for chronic lymphocytic leukemia or myeloproliferative neoplasms [MPN])	When vaccine available[c]
Solid Tumor Malignancies	
Receiving cytotoxic chemotherapy	When vaccine available[c,d]
Targeted therapy	When vaccine available
Checkpoint inhibitors and other immunotherapy	When vaccine available[e]
Radiation	When vaccine available
Major surgery	Separate date of surgery from vaccination by at least a few days[f]
Caregivers and Household/Close Contacts (≥16 years of age)	
Any time eligible to receive the vaccine[5]	

†COVID-19 vaccines should be prioritized over other needed vaccines, as data on dual vaccination are not available to date. Fourteen days are recommended between COVID-19 vaccines and other approved vaccines.

‡Discussion with clinical trial leads should be considered in advance to prevent protocol violations or exclusions.

e) Theoretical risk of exacerbated immune-related adverse events in patients receiving immune checkpoint inhibitors; there are no data on timing of vaccine administration, so this may be considered on the same day as immunotherapy for convenience and to reduce added visits to the office whenever possible.

NCCN Guidance

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SOAP Trial- Delaying 2nd Pfizer Vaccine decreases antibody response

- Interim results show antibody response after 1st dose at 3 weeks:
  - 97% for healthy controls
  - 39% for solid tumors
  - 13% for malignant heme
- Antibody response after 2nd dose 3 weeks after the 1st dose:
  - 95% for solid tumors after 2 weeks
- Without a vaccine boost at 3 weeks, antibody response at 5 weeks:
  - 43% of solid tumors
  - 8% of malignant heme
  - 100% of healthy controls

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Conclusions

- ICI therapy does not appear to increase COVID-19 severity
- Caution with ICI therapy in those with lung disease
- Interruption of IO therapy in patients with active SARS-CoV2 infection is controversial
- Vaccination can occur safely during IO therapy and should not be delayed in cancer patients

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