UNC LINEBERGER COMPREHENSIVE CANCER CENTER

UNC CANCER CARE

COVID-19 and Oncology Practice

Stephen Kimani, MD, MSc
Clinical Fellow, University of North Carolina
March 24, 2021

1

Disclosures

- **I do not have any financial conflict of interests**
- **I will discuss off-label or investigational use(s) of a product or device**
- **I attest that I am not receiving direct payments from a commercial entity with respect to this activity**

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

2

Disclaimer

- Data about COVID-19 is evolving quickly
- This talk will highlight data supported by peer-reviewed publications
- Any material that is not yet peer reviewed will be flagged as such, if discussed during this talk
- Issues specific to bone marrow transplant or CAR-T population will not be covered

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

3

What are some of the key questions in oncology practice

- Which cancer patients are at greatest risk?
- What are the complications and outcomes?
- What are the best treatment(s) and management situations?
- How do the available COVID-19 vaccines compare?
- Are the available vaccines safe for cancer patients?
- What post-vaccination issues should we watch out for among cancer patients?
- What should we do about patients' anti-cancer treatment(s)?
- How should our oncology practice respond to adopt?

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

4

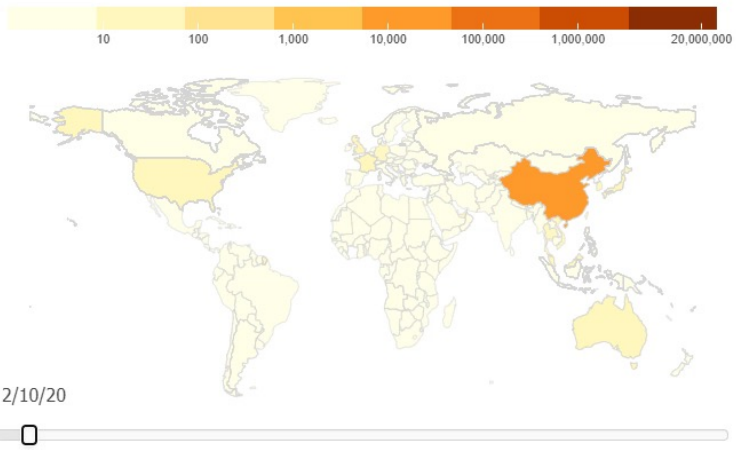
Objectives

- Describe prevalence, incidence, and outcomes of COVID-19 among select populations of cancer patients in the US
- Compare safety and efficacy of available COVID-19 vaccines
- Discuss the impact of COVID-19 on cancer care delivery with emphasis on unique challenges and opportunities in oncology

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

5

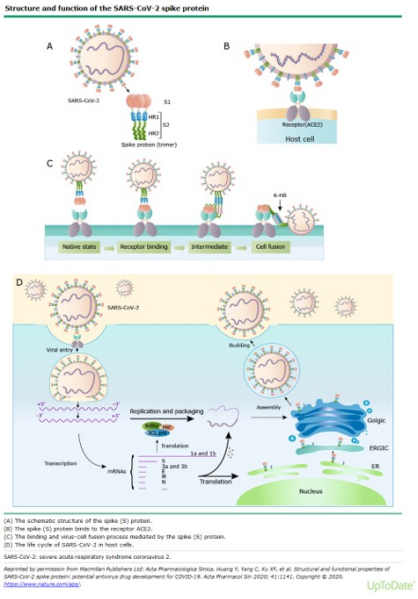
COVID-19 is a rapidly evolving global health issue



UNC LINEBERGER COMPREHENSIVE CANCER CENTER

6

A quick overview of SARS-CoV-2



- Two main processes are thought to drive the pathogenesis of COVID-19(Wiersinga, Rhodes et al. 2020)
  - Viral replication
  - Hyper inflammatory response to the virus leads to tissue damage
- SARS-CoV-2-specific antibodies and cell-mediated responses are induced following infection
  - Duration of protective effects remain unknown
- **Risk of transmission depends on exposure type**
- Notable variants
  - **B.1.1.7 ("UK")**
  - **B.1.351 ("South Africa")**
  - **P.1 ("Brazil")**

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

7

Cancer patients are historically considered at high risk for infections

- **Different mechanisms of immunosuppression**
  - **The cancer itself e.g., bone marrow invasion**
  - **Cancer treatment effects e.g., chemotherapy-induced bone marrow suppression, radiation mucositis**
- **Poor nutrition**
  - **Decreased performance status**
  - **Fragility**
- **High burden of co-morbidities unrelated to cancer**
  - **Advanced age**
  - **Non-communicable diseases**
  - **Frequent exposure to healthcare**(Yu, Ouyang et al. 2020)

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

8

Cancer patients are at higher risk of COVID-19

- Variable incidence but relative higher incidence vs. general population
  - Risk factors: recent cancer diagnosis, older age, comorbidities
- Risk highest for lung cancer and hematologic malignancies
- Incidence rates variable depending on phase of pandemic
  - IR during active treatment ~1-4% (Spring 2020) and ~10 % (Fall 2020)
- Cancer patients have a higher COVID-19 mortality rate
  - Morbidity and mortality in patients with cancer range from 5% to 61% (vs. 2-3% in general population)(Yap, Siu et al. 2021)*

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

9

Cancer is associated with worse clinical outcomes among patients with COVID-19

- **Some COVID-19 clinical studies indicate poorer outcomes for cancer patients, especially those with hematological cancers**(Vijenthira, Gong et al. 2020)(Williamson, Walker et al. 2020)
- **Cancer patients are likely to have more severe illness and death** (Giannakoulis, Papoutsi et al. 2020)
- Factors associated with poor outcomes
  - Cancer disease status (active v. progressive v. stable)
  - Recent anti-cancer therapy
  - Performance status
  - Others: comorbidities, age, socioeconomic status
- Mortality highest for lung cancer (and other thoracic malignancies)

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

10

Cancer is associated with increased need for ICU and mortality among patients with COVID-19

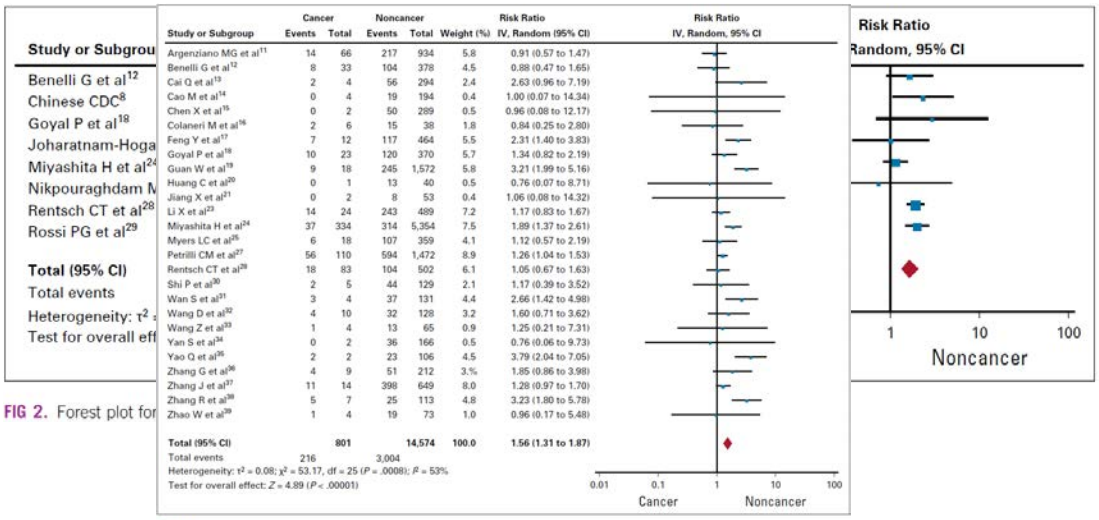


FIG 2. Forest plot for

Study or Subgroup	Cancer Events	Cancer Total	Noncancer Events	Noncancer Total	Weight (%)	Risk Ratio IV, Random (95% CI)
Argenziano MG et al[11]	14	66	217	934	5.8	0.91 (0.57 to 1.47)
Benelli G et al[12]	8	33	104	378	4.5	0.88 (0.47 to 1.65)
Cai Q et al[13]	2	4	56	294	2.4	2.63 (0.96 to 7.19)
Cao M et al[14]	0	4	19	194	0.4	1.00 (0.07 to 14.34)
Chen X et al[15]	0	2	50	289	0.5	0.96 (0.08 to 12.17)
Colaneri M et al[16]	2	6	15	38	1.8	0.84 (0.25 to 2.80)
Feng Y et al[17]	7	12	117	464	5.5	2.31 (1.40 to 3.83)
Goyal P et al[18]	10	23	120	370	5.7	1.34 (0.82 to 2.19)
Guan W et al[19]	9	18	245	1,572	5.8	3.21 (1.99 to 5.16)
Huang C et al[20]	0	1	13	40	0.5	0.76 (0.07 to 8.71)
Jiang X et al[21]	0	2	8	53	0.4	1.06 (0.08 to 14.32)
Li X et al[23]	14	24	243	489	7.2	1.17 (0.83 to 1.67)
Miyashita H et al[24]	37	334	314	5,354	7.5	1.89 (1.37 to 2.61)
Myers LC et al[25]	6	18	107	359	4.1	1.12 (0.57 to 2.19)
Petrilli CM et al[27]	56	110	594	1,472	8.9	1.26 (1.04 to 1.53)
Rentsch CT et al[28]	18	83	104	502	6.1	1.05 (0.67 to 1.63)
Shi P et al[30]	2	5	44	129	2.1	1.17 (0.39 to 3.52)
Wan S et al[31]	3	4	37	131	4.4	2.66 (1.42 to 4.98)
Wang D et al[32]	4	10	32	128	3.2	1.60 (0.71 to 3.62)
Wang Z et al[33]	1	4	13	65	0.9	1.25 (0.21 to 7.31)
Yan S et al[34]	0	2	36	166	0.5	0.76 (0.06 to 9.73)
Yao Q et al[35]	2	2	23	106	4.5	3.79 (2.04 to 7.05)
Zhang G et al[36]	4	9	51	212	3.%	1.85 (0.86 to 3.98)
Zhang J et al[37]	11	14	398	649	8.0	1.28 (0.97 to 1.70)
Zhang R et al[38]	5	7	25	113	4.8	3.23 (1.80 to 5.78)
Zhao W et al[39]	1	4	19	73	1.0	0.96 (0.17 to 5.48)
Total (95% CI)		**801**		**14,574**	**100.0**	**1.56 (1.31 to 1.87)**
Total events	216		3,004			

Heterogeneity: $\tau^2 = 0.09$; $\chi^2 = 53.17$, df = 25 ($P = .0008$); $I^2 = 53\%$
Test for overall effect: $Z = 4.89$ ($P < .00001$)

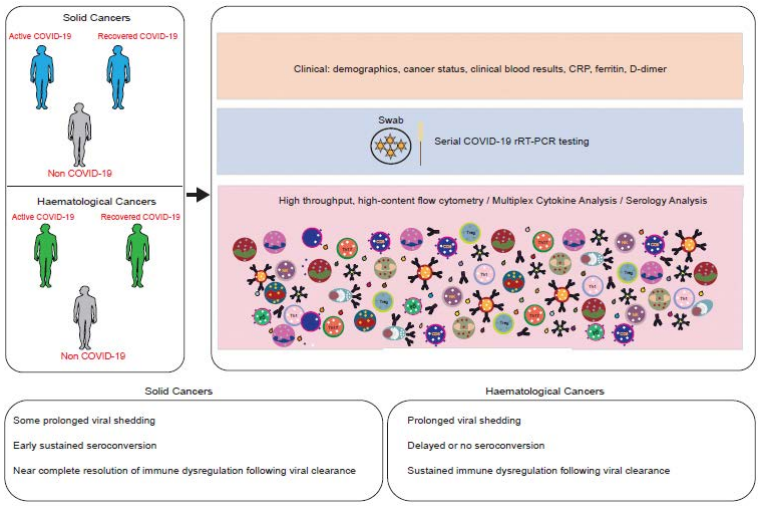
0.01 0.1 1 10 100
Cancer Noncancer

FIG 3. Forest plot for need for intensive care unit admission. IV, inverse-variance.

(Giannakoulis, Papoutsi et al. 2020)

11

Impact of SARS-CoV-2 on cancer patients' immune status



- (Abdul-Jawad, Baù et al. 2021)

12

Duration of cancer history matters

		Fully adjusted HR and 95% CI				
Characteristic	Category	Primary analysis	Early censoring at 6/4/2020	Restricted to those with complete BMI /smoking	Adjusted for ethnicity in those where recorded	Adjusted for ethnicity using multiple imputation
Cancer (non-haematological, vs none)	Diagnosed < 1 year ago	1.72 (1.50-1.96)	1.66 (1.27-2.16)	1.68 (1.46-1.94)	1.67 (1.43-1.96)	1.74 (1.52-1.99)
	Diagnosed 1-4.9 years ago	1.15 (1.05-1.27)	1.34 (1.13-1.60)	1.16 (1.05-1.28)	1.21 (1.09-1.35)	1.17 (1.06-1.28)
	Diagnosed ≥5 years ago	0.96 (0.91-1.03)	0.92 (0.81-1.04)	0.97 (0.91-1.03)	0.98 (0.92-1.06)	0.97 (0.92-1.04)
Haematological malignancy (vs none)	Diagnosed < 1 year ago	2.80 (2.08-3.78)	2.20 (1.14-4.24)	2.86 (2.10-3.88)	2.33 (1.60-3.41)	2.81 (2.08-3.79)
	Diagnosed 1-4.9 years ago	2.46 (2.06-2.95)	3.49 (2.61-4.68)	2.40 (1.99-2.90)	2.53 (2.05-3.11)	2.48 (2.07-2.97)
	Diagnosed ≥5 years ago	1.61 (1.39-1.87)	1.45 (1.06-1.97)	1.61 (1.38-1.89)	1.55 (1.30-1.85)	1.63 (1.40-1.89)

- (Williamson, Walker et al. 2020)

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

13

Are outcomes worse in patients with hematologic malignancies?

		Fully adjusted HR and 95% CI				
Characteristic	Category	Primary analysis	Early censoring at 6/4/2020	Restricted to those with complete BMI /smoking	Adjusted for ethnicity in those where recorded	Adjusted for ethnicity using multiple imputation
Cancer (non-haematological, vs none)	Diagnosed < 1 year ago	1.72 (1.50-1.96)	1.66 (1.27-2.16)	1.68 (1.46-1.94)	1.67 (1.43-1.96)	1.74 (1.52-1.99)
	Diagnosed 1-4.9 years ago	1.15 (1.05-1.27)	1.34 (1.13-1.60)	1.16 (1.05-1.28)	1.21 (1.09-1.35)	1.17 (1.06-1.28)
	Diagnosed ≥5 years ago	0.96 (0.91-1.03)	0.92 (0.81-1.04)	0.97 (0.91-1.03)	0.98 (0.92-1.06)	0.97 (0.92-1.04)
Haematological malignancy (vs none)	Diagnosed < 1 year ago	2.80 (2.08-3.78)	2.20 (1.14-4.24)	2.86 (2.10-3.88)	2.33 (1.60-3.41)	2.81 (2.08-3.79)
	Diagnosed 1-4.9 years ago	2.46 (2.06-2.95)	3.49 (2.61-4.68)	2.40 (1.99-2.90)	2.53 (2.05-3.11)	2.48 (2.07-2.97)
	Diagnosed ≥5 years ago	1.61 (1.39-1.87)	1.45 (1.06-1.97)	1.61 (1.38-1.89)	1.55 (1.30-1.85)	1.63 (1.40-1.89)

- (Williamson, Walker et al. 2020)

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

14

Are outco cies?

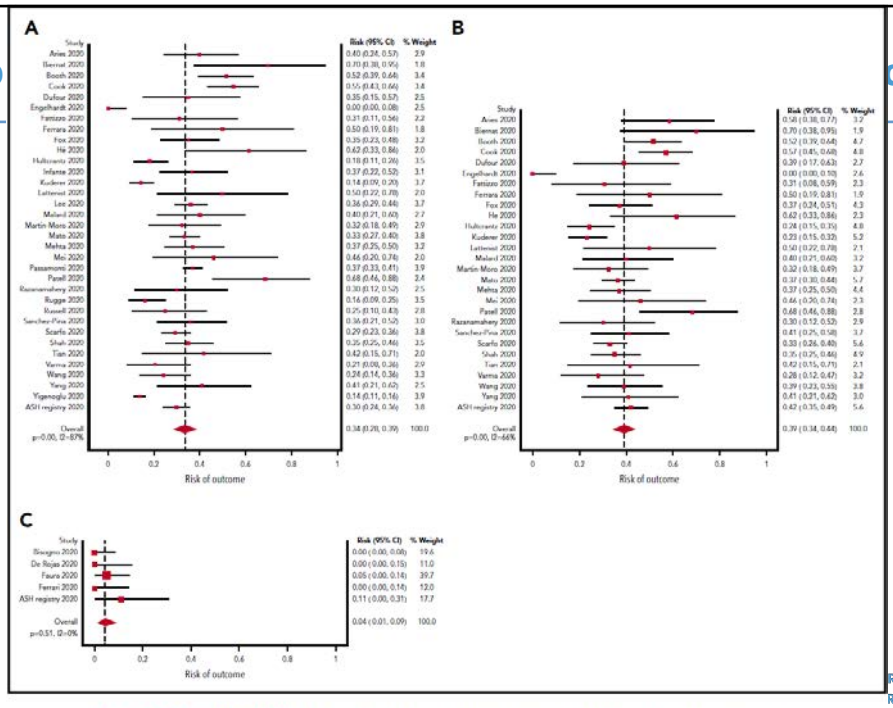


Figure 2. Pooled risk of mortality. (A) In all studies. (B) In hospitalized patients only. (C) Pooled risk of mortality in pediatric patients.

RGER COMPREHENSIVE
R CENTER

15

Impact of cancer-directed treatment on COVID-19 outcomes

- Available data linking recent active therapy to poor outcomes are mixed
  - In earlier studies, receipt of cancer therapy was associated with worse outcomes
  - Recent active oncologic therapy does not necessarily increase the risk of mortality from COVID-19
  - (Kuderer, Choueiri et al. 2020)
- The type of cancer treatment may influence the risk, although again, the data are mixed, particularly with regard to recent immunotherapy

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

16

Impact of cancer-directed chemotherapy treatment on risk of death

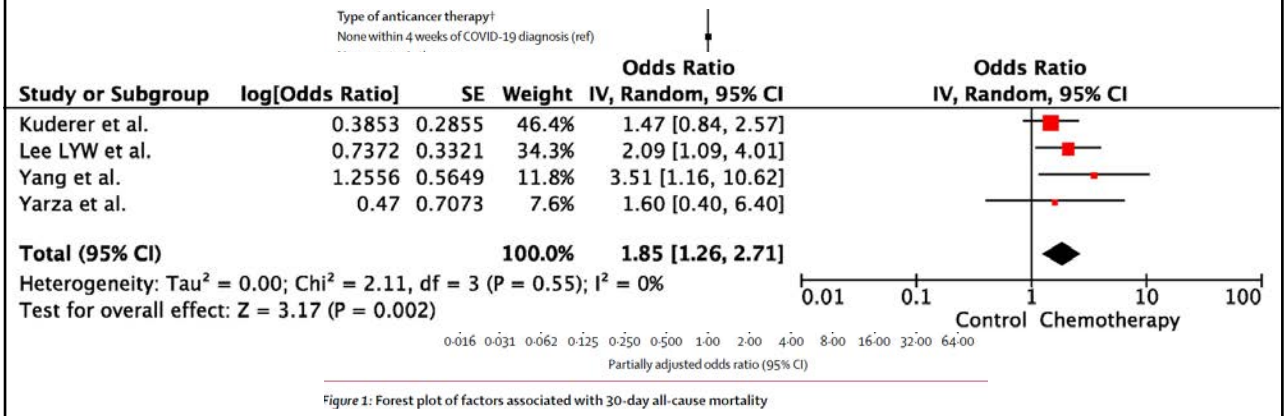
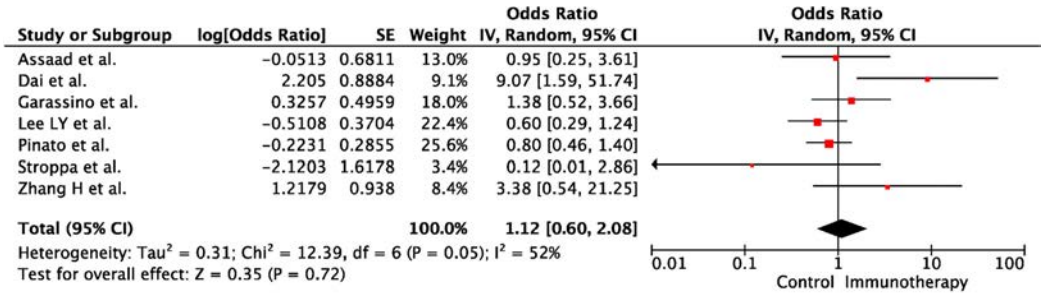


Figure 1: Forest plot of factors associated with 30-day all-cause mortality

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

17

Impact of cancer-directed immunotherapy on risk of death



UNC LINEBERGER COMPREHENSIVE CANCER CENTER

18

A comment on thrombosis and VTE risk

- COVID-19 is associated with an increased risk of both arterial and venous thrombotic events, termed COVID-19-associated hypercoagulable state
- Limited evidence suggests that cancer patients who develop COVID-19 are not necessarily at a higher risk of COVID-19-associated hypercoagulable state(Patell, Bogue et al. 2020)

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

19

COVID-19 treatments and clinical outcomes among patients with cancer

- Baseline COVID-19 severity was strongly associated with receipt of any treatment
  - No statistically significant 30-day all-cause mortality benefit with hydroxychloroquine or high-dose corticosteroids alone or in combination; Remdesivir showed potential benefit.
- Disparities in medication access
  - Black patients were approximately half as likely to receive Remdesivir as white patients.
- No RCT data yet on treatment and outcomes among cancer patients

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

20

Challenges in the care of cancer patients with COVID-19

- Cancer patients with profound immunosuppression may shed viable SARS-CoV-2 for a prolonged period (Aydillo, Gonzalez-Reiche et al. 2020)(Karataş, İnkaya et al. 2020)
  - Post-HSCT or CAR-T, on active therapy (≥2 months)
- Risk of immune-related pneumonitis of immunotherapy (Naidoo, Reuss et al. 2020)

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

21

NIH COVID-19 treatment guidance (updated Feb 11, 2021)

- Off-label use
  - Dexamethasone
- FDA-approved
  - Remdesivir for hospitalized & supplemental oxygen
- FDA EUA for anti-SARS-CoV-2 monoclonal antibodies
  - Outpatient with mild to moderate COVID-19 & at high risk for progressing to severe disease or hospitalization
  - Casirivimab plus Imdevimab
  - Bamlanivimab plus Etesevimab

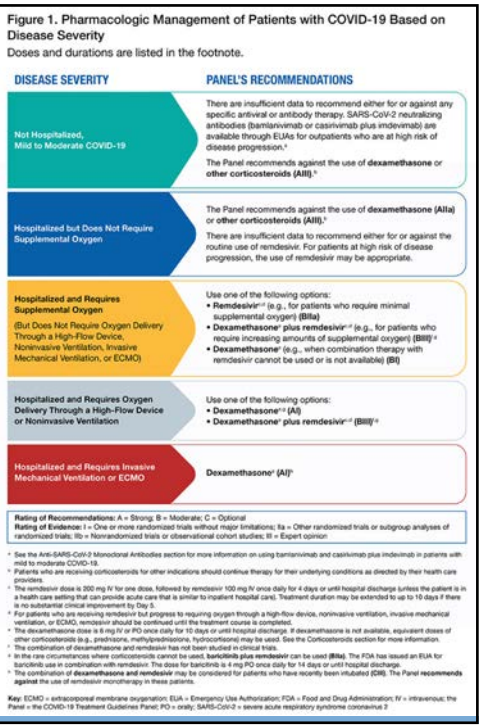


Figure 1. Pharmacologic Management of Patients with COVID-19 Based on Disease Severity

Doses and durations are listed in the footnote.

DISEASE SEVERITY	PANEL'S RECOMMENDATIONS
Not Hospitalized, Mild to Moderate COVID-19	There are insufficient data to recommend either for or against any specific antiviral or antibody therapy. SARS-CoV-2 neutralizing antibodies (bamlanivimab or casirivimab plus imdevimab) are available through EUAs for outpatients who are at high risk of disease progression.[a] The Panel recommends against the use of **dexamethasone** or **other corticosteroids (AIII)**.[b]
Hospitalized but Does Not Require Supplemental Oxygen	The Panel recommends against the use of **dexamethasone (AIIa)** or **other corticosteroids (AIII)**.[b] There are insufficient data to recommend either for or against the routine use of remdesivir. For patients at high risk of disease progression, the use of remdesivir may be appropriate.
Hospitalized and Requires Supplemental Oxygen (But Does Not Require Oxygen Delivery Through a High-Flow Device, Noninvasive Ventilation, Invasive Mechanical Ventilation, or ECMO)	Use one of the following options: • **Remdesivir**[c,d] (e.g., for patients who require minimal supplemental oxygen) **(BIIa)** • **Dexamethasone**[e] **plus remdesivir**[c,d] (e.g., for patients who require increasing amounts of supplemental oxygen) **(BIII)**[f,g] • **Dexamethasone**[e] (e.g., when combination therapy with remdesivir cannot be used or is not available) **(BI)**
Hospitalized and Requires Oxygen Delivery Through a High-Flow Device or Noninvasive Ventilation	Use one of the following options: • **Dexamethasone**[e,h] **(AI)** • **Dexamethasone**[e] **plus remdesivir**[c,d] **(BIII)**[f,g]
Hospitalized and Requires Invasive Mechanical Ventilation or ECMO	**Dexamethasone**[e] **(AI)**[h]

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

[a] See the *Anti-SARS-CoV-2 Monoclonal Antibodies* section for more information on using bamlanivimab and casirivimab plus imdevimab in patients with mild to moderate COVID-19.
[b] Patients who are receiving corticosteroids for other indications should continue therapy for their underlying conditions as directed by their health care providers.
[c] The remdesivir dose is 200 mg IV for one dose, followed by remdesivir 100 mg IV once daily for 4 days or until hospital discharge (unless the patient is in a health care setting that can provide acute care that is similar to inpatient hospital care). Treatment duration may be extended to up to 10 days if there is no substantial clinical improvement by Day 5.
[d] For patients who are receiving remdesivir but progress to requiring oxygen through a high-flow device, noninvasive ventilation, invasive mechanical ventilation, or ECMO, remdesivir should be continued until the treatment course is completed.
[e] The dexamethasone dose is 6 mg IV or PO once daily for 10 days or until hospital discharge. If dexamethasone is not available, equivalent doses of other corticosteroids (e.g., prednisone, methylprednisolone, hydrocortisone) may be used. See the *Corticosteroids* section for more information.
[f] The combination of dexamethasone and remdesivir has not been studied in clinical trials.
[g] In the rare circumstances where corticosteroids cannot be used, **baricitinib plus remdesivir** can be used **(BIIa)**. The FDA has issued an EUA for baricitinib use in combination with remdesivir. The dose for baricitinib is 4 mg PO once daily for 14 days or until hospital discharge.
[h] The combination of **dexamethasone and remdesivir** may be considered for patients who have recently been intubated **(CIII)**. The Panel **recommends against** the use of remdesivir monotherapy in these patients.

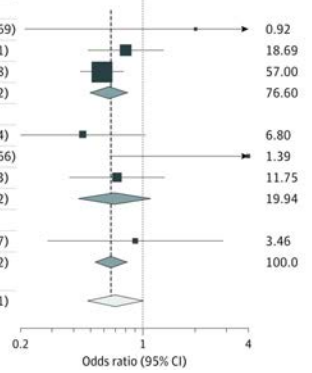
Key: ECMO = extracorporeal membrane oxygenation; EUA = Emergency Use Authorization; FDA = Food and Drug Administration; IV = intravenous; the Panel = the COVID-19 Treatment Guidelines Panel; PO = orally; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

22

From: **Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19: A Meta-analysis**

Sterne, Murthy et al. 2020, JAMA. 2020;324(13):1330-1341. doi:10.1001/jama.2020.17023

Drug and trial	ClinicalTrials.gov identifier	Initial dose and administration	No. of deaths/total No. of patients: Steroids	No steroids	Odds ratio (95% CI)	Weight, %
Dexamethasone						
DEXA-COVID 19	NCT04325061	High: 20 mg/d intravenously	2/7	2/12	2.00 (0.21-18.69)	0.92
CoDEX	NCT04327401	High: 20 mg/d intravenously	69/128	76/128	0.80 (0.49-1.31)	18.69
RECOVERY	NCT04381936	Low: 6 mg/d orally or intravenously	95/324	283/683	0.59 (0.44-0.78)	57.00
Subgroup fixed effect			166/459	361/823	0.64 (0.50-0.82)	76.60
Hydrocortisone						
CAPE COVID	NCT02517489	Low: 200 mg/d intravenously	11/75	20/73	0.46 (0.20-1.04)	6.80
COVID STEROID	NCT04348305	Low: 200 mg/d intravenously	6/15	2/14	4.00 (0.65-24.66)	1.39
REMAP-CAP	NCT02735707	Low: 50 mg every 6 h intravenously	26/105	29/92	0.71 (0.38-1.33)	11.75
Subgroup fixed effect			43/195	51/179	0.69 (0.43-1.12)	19.94
Methylprednisolone						
Steroids-SARI	NCT04244591	High: 40 mg every 12 h intravenously	13/24	13/23	0.91 (0.29-2.87)	3.46
Overall (fixed effect) $P = .31$ for heterogeneity; $I^2 = 15.6\%$			222/678	425/1025	0.66 (0.53-0.82)	100.0
Overall (random effects[a])			222/678	425/1025	0.70 (0.48-1.01)	



[a]The random-effects analysis estimates both the average and variability of effects across studies. The 95% CI for the average effect (shown here) is wide because there is a small number of studies, some of which have very small sample size. The prespecified primary analysis was the fixed-effect analysis, which should be used to guide clinical interpretation of the results.

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

23

Summary

- **Which cancer patients are at greatest risk?** Lung cancer and hematological malignancies
- **What are the complications and outcomes?** Increased risk of death
- **What are the best treatment(s) and management situations?** Dexamethasone +/- Remdesivir depending on severity. Consider anti-SARS-CoV-2 monoclonal antibodies in select cases

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

24

Objectives

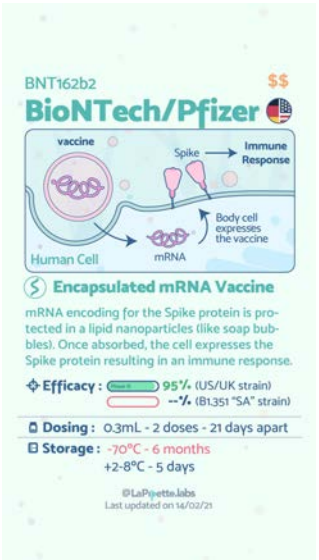
- Describe prevalence, incidence, and outcomes of COVID-19 among select populations of cancer patients in the US
- Compare safety and efficacy of available COVID-19 vaccines
- Discuss the impact of COVID-19 on cancer care delivery with emphasis on unique challenges and opportunities in oncology

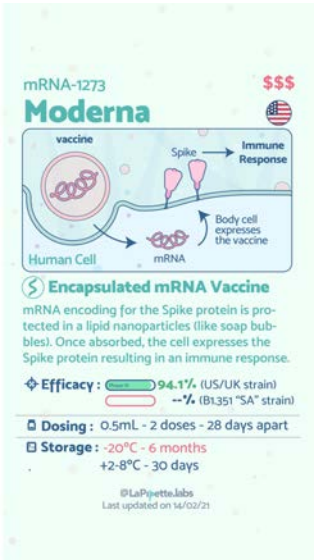
UNC LINEBERGER COMPREHENSIVE CANCER CENTER

25

Overview of COVID-19 vaccines (Moderna & Pfizer)

- mRNA-based vaccines
- Double shot
- Approval studies did not include cancer patients
- Infograms courtesy of lapipette.labs
- (Baden, El Sahly et al. 2021) (Polack, Thomas et al. 2020)



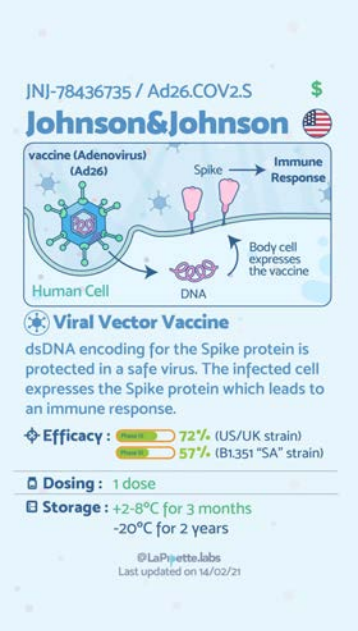


UNC LINEBERGER COMPREHENSIVE CANCER CENTER

26

Overview of COVID-19 vaccines (J&J)

- Adenovirus-vector vaccine
- Single shot
- Approval study included some cancer patients
- (Sadoff, Le Gars et al. 2021)



UNC LINEBERGER COMPREHENSIVE CANCER CENTER

27

Summary of vaccines available in the US

	Pfizer/BioNTech	Moderna	Johnson & Johnson
Mechanism	mRNA vaccine	mRNA vaccine	Adenovirus vector vaccine
Schedule	2 doses, 21 days apart	2 doses, 28 days apart	1 dose
Trial participants	43,548 people, ≥16 yo	30,420 people, ≥18 yo	43,783 people, ≥18 yo
Study endpoint	Symptomatic disease	Symptomatic disease	Moderate-to-severe disease
Primary efficacy	95% at least 7 days after dose 2	94.1% at least 14 days after dose 2	72% (≥moderate), 85% severe, at least 28 days after a single dose
Variant efficacy	-	-	57% efficacy in South Africa

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

28

Important considerations on vaccine safety and efficacy in cancer patients

- Vaccine efficacy response cannot be assumed in immunocompromised patients
  - Seroprotection rates following flu vaccination ~30% (vs. immunocompetent) (Landmark Study: Beck, McKenzie et al. 2012)
  - Immunosuppression greater in heme vs. non-heme malignancies
  - Vaccine efficacy likely variable depending on "net immunosuppression"
  - Immunogenicity after anti-B cell antibodies is poor (Landmark Study: Yri, Torfoss et al. 2011)
  - Post-vaccination antibody testing available, but utility unclear
- Eligible individuals with an immunocompromising condition can receive COVID-19 vaccines
- Expert groups recommend holding certain immunosuppressive agents around the time of vaccination or adjusting the timing of vaccination to optimize the vaccine response

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

29

Post-vaccine reactive lymphadenopathy and imaging studies

- Case reports and anecdotes (Lehman, Lamb et al. 2021)
- Affects mammogram, chest CT, FDG-PET
- Moderna:
  - 16% (vs. 4.3% placebo), 2-4 days post-vaccine, median duration 1-2 days
- Pfizer:
  - 64 cases (vs 6 placebo), 2-4 days post-vaccine, mean 10 days
- Not yet reported to date with the Janssen/Johnson & Johnson
- ? Whether a class effect of mRNA vaccines

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

30

How to manage reactive post-vaccine lymphadenopathy

- Limited data, expert guidance
- Management to balance caution and patient safety
- Document vaccination history & site of injection
- Contralateral injection if h/o breast cancer
- Scheduling <u>screening</u> breast imaging 4-6 weeks post-vaccine, when possible

Table 1-Breast Imaging Management of Axillary Adenopathy in Setting of Recent (< 6 weeks) Ipsilateral Deltoid COVID-19 Vaccination

Patient Population	Principles	Imaging Finding
1.Asymptomatic: due for screening (mammogram or MRI, all risk categories)	Encourage screening of all patients regardless of vaccination status. At time of imaging, technologist documents vaccination status (1st or 2nd dose, location (leg or arm), side, date).	1a. In the setting of documented recent (< 6 weeks) COVID-19 vaccination, isolated ipsilateral axillary adenopathy is a benign imaging finding (BI-RADS 2). No further imaging is indicated at this time. If there is clinical concern that persists > 6 weeks after the final vaccine dose, axillary US is recommended. In 1a setting, vaccination status, imaging findings, and recommendations will be documented in imaging report and communicated to patient in lay language.
2. Symptomatic (in breast and/or axilla)	Encourage diagnostic imaging of all patients with breast signs/symptoms regardless of vaccination status. In the setting of documented recent (< 6 weeks) COVID-19 vaccination and post vaccine palpable ipsilateral axillary adenopathy, in absence of breast signs/symptoms, clinical follow-up of axilla is recommended. If clinical concerns persist > 6 weeks after final vaccine dose, axillary US is recommended, with mammography if patient is due, or at discretion of radiologist. At time of imaging, technologist documents vaccination status (1st or 2nd dose, location, side, date).	2a.Palpable isolated unilateral adenopathy > 6 weeks after vaccination is managed following standard protocol for imaging management of unilateral adenopathy (US +/- mammography). 2b.Unilateral adenopathy on side of vaccination, identified incidentally during diagnostic imaging work-up for breast sign/symptom: i.BI-RADS 2 (no suspicious imaging finding in the breast): follow 1a above. ii.BI-RADS 4/5 (suspicious imaging finding in the breast): management at discretion of attending procedural radiologist based on suspicion of lesion, appearance of adenopathy, and/or pathology results.
3. Current breast cancer (pre/peri treatment)	Encourage recommended imaging regardless of vaccination status. Encourage contralateral arm or anterolateral thigh vaccine injection. At time of imaging, technologist documents vaccination status (1st or 2nd dose, location, side, date).	3a. Unilateral adenopathy on side of (arm) vaccine and side of breast cancer: biopsy versus imaging/clinical follow-up at discretion of surgeon and/or medical or radiation oncologist in consultation with radiologist.

31

Summary

- **How do the available COVID-19 vaccines compare?** All three vaccines are quite similar in efficacy for the endpoints we care about (severe illness and hospitalization)
- **Are the available vaccines safe for cancer patients?** There is no evidence to suggest they would not be safe for most cancer patients, although data on safety in patients with cancer is lacking from the published vaccine trials to date
- **What post-vaccination issues should we watch out for among cancer patients?** There are emerging reports of post-vaccine adenopathy that may affect interpretation of cancer imaging studies. Due to lack efficacy data, patients should continue to adhere to public health measures (3 W's)

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

32

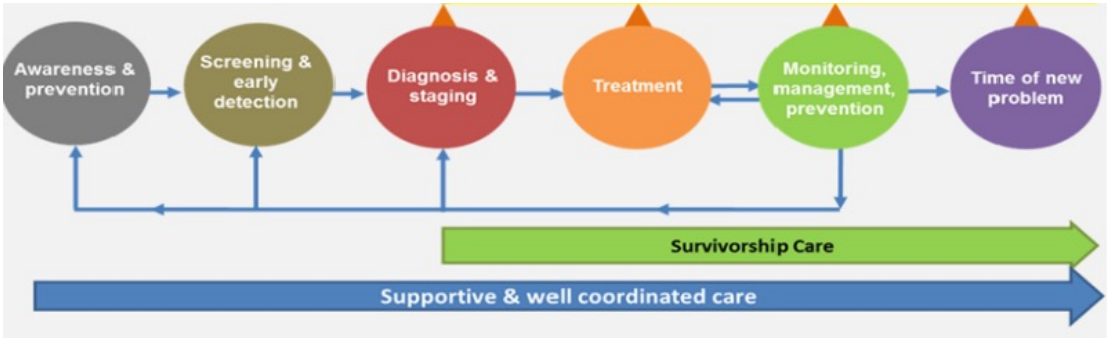
Content

- Describe prevalence, incidence, and outcomes of COVID-19 among select populations of cancer patients in the US
- Compare safety and efficacy of available COVID-19 vaccines
- Discuss the impact of COVID-19 on cancer care delivery with emphasis on unique challenges and opportunities in oncology

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

33

Overview of cancer care delivery continuum



UNC LINEBERGER COMPREHENSIVE CANCER CENTER

34

The impact of COVID-19 pandemic on oncology practice is broad

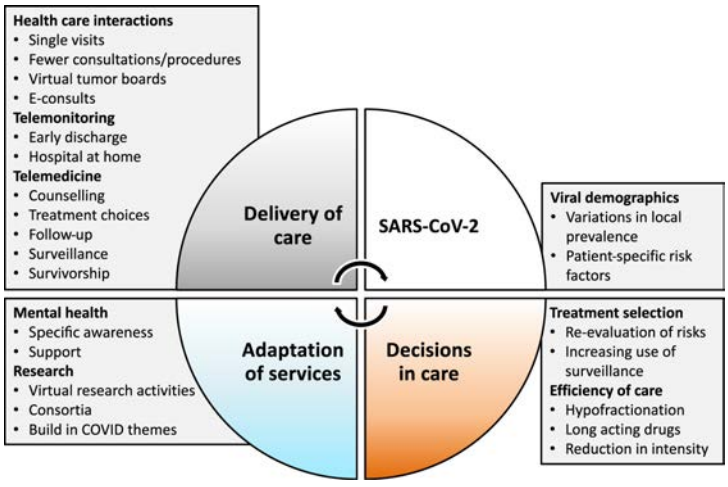
- Managing infection risk
  - Competing risks of death from cancer versus death or serious complications from infection
- Managing systemic anti-cancer therapy
  - Likely higher lethality of COVID-19 in immunocompromised hosts, including those with cancer
- Care interruptions and disruptions
  - Stay-at-home orders
  - Stretched surge capacities
  - Workforce reassignment (and loss)
- Models of care innovations

(Hui, Yuan et al. 2020); (Kaufman, Chen et al. 2020); (Sharpless 2020)

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

35

The impact of COVID-19 pandemic on oncology practice is broad

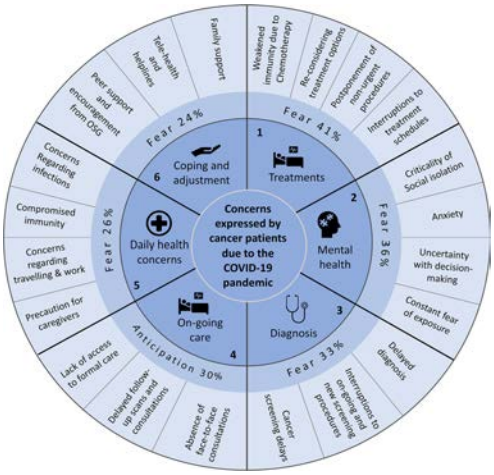


(Wallis, Catto et al. 2020)
European Urology 2020 78731-742DOI: (10.1016/j.eururo.2020.08.030)

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

36

Impact of the COVID-19 Pandemic on Patients with Cancer



- (Moraliyage, De Silva et al. 2021)

Impact on cancer screening, diagnosis and treatment

- Decrease in rates and timeliness of preventative cancer care
  - Colon cancer (Gupta and Lieberman 2020)(Patel, Issaka et al. 2021)
  - Cervical cancer (Miller, Xu et al. 2021)
  - Breast and lung (Patt, Gordan et al. 2020)(Song, Bergman et al. 2021)
- Delay in staging (Freer 2021)
- Prolonged time to treatment initiation (Cone, Marchese et al. 2020)(Ginsburg, Curtis et al. 2021)(Matsuo, Novatt et al. 2020)
- Reasons for changes are multi-level (Ginsburg, Curtis et al. 2021)(London, Fazio-Eynullayeva et al. 2020)
  - Patient factors
  - Health system
- Survival estimates for treatment delay (Hartman, Sun et al. 2020)

Management of anti-cancer therapy in cancer patients who test positive for SARS-CoV-2

- September 2020: ASCO Guidance:
  - "Decisions about interrupting anticancer treatment in patients with active COVID-19 should be based on a clinical benefit: risk assessment that considers the *risk of interrupting cancer treatment* vs. the *still poorly defined risk of adverse COVID-19 outcomes* in patients receiving active cancer treatment.
- Key principles
  - For most patients, immunosuppressive cancer therapy should be withheld in those who test positive
  - BTK inhibitors may be continued
  - Oral non-immunosuppressive therapies such as hormonal therapies or molecular targeted agents may be continued

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

39

Impact on clinical trials – Part II: participation

- **Changes in development and funding of cancer trials** (Karzai, Madan et al. 2020)(Zon, Gomes et al. 2020)
- **A major barrier to enrollment and ongoing participation in clinical trials** (Unger, Blanke et al. 2020) (Waterhouse, Harvey et al. 2020)
  - Enrollment in certain cancer-related clinical trials has dropped ≥50% since the start of the pandemic
  - Ceased research-only visits

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

40

Emerging cancer care delivery innovations and modifications

- ASCO survey initial results
  - New use of telemedicine
  - Use of ancillary lab facilities closer to patients' home
  - Staff changes (reduction or reassignments)
- Virtual care and telemedicine are widely adopted (Loree, Dau et al. 2021)(Lou, Teoh et al. 2020)
- Ambulatory oncology to expand home infusions and supportive care (Yackzan and Shah 2021)
- Telephone triage systems (Elkin, Viele et al. 2021)(Osterman, Triglianos et al. 2021)

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

41

Summary

- **What should we do about patients' anti-cancer treatment(s)?** There is no evidence of interaction for targeted therapy and immunotherapy, but mixed results with respect to chemotherapy. Recommend individualized clinical benefit: risk assessment
- **How should our oncology practice respond to adopt?** Embrace new models of care including telemedicine for remote monitoring

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

42

Active registries for cancer patients

- The COVID-19 and Cancer Consortium (https://ccc19.org/)
  - Includes 114 sites (includes comprehensive cancer centers and community sites) collecting data on cancer patients and their outcomes with COVID-19.

- ASH RC COVID-19 Registry for Hematology (https://www.ashresearchcollaborative.org/s/covid-19-registry)

ASH RESEARCH COLLABORATIVE
Accelerating Progress in Hematology

- ASCO COVID-19 Registry Data Dashboard (https://www.asco.org/asco-coronavirus-information/coronavirus-registry/covid-19-registry-data-dashboard)

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

43

UK Recovery trial

RECOVERY
Randomised Evaluation of COVID-19 Therapy

- **World's largest adaptive clinical trial for COVID-19 treatments**
  - Not cancer-specific
  - Regeneron's antibody cocktail
  - Aspirin
  - Baricitinib (an immunomodulatory drug used in rheumatoid arthritis)
  - Dimethyl fumarate (an immunomodulatory drug used in psoriasis and multiple sclerosis)
- **March 11, 2021: 38954 Participants, 180 Active sites**

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

44

Additional Resources

- **ASCO Coronavirus Resources**
  - https://www.asco.org/asco-coronavirus-information
- **NIH Coronavirus Disease 2019 (COVID-19) Treatment Guidelines**
  - https://www.covid19treatmentguidelines.nih.gov/whats-new/
- **NCCN: NCCN COVID-19 Vaccination Advisory Committee guidance**
  - https://www.nccn.org/covid-19/pdf/COVID-19_Vaccination_Guidance_V2.0.pdf (Cancer and COVID-19 Vaccination Version 2.0 03/10/2021)

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

45

Acknowledgements

- Samuel Rubinstein MD (UNC faculty advisor)
- UNC Lineberger Cancer Network
  - Tim Poe, PhD
  - Jon Powell, PhD
  - William Wood, MD
- FellowsACHIEVE collaboration

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

46

Selected cited references

1. Williamson, E. J., et al. (2020). "Factors associated with COVID-19-related death using OpenSAFELY." Nature **584**(7821): 430-436.
2. Vijenthira, A., et al. (2020). "Outcomes of patients with hematologic malignancies and COVID-19: a systematic review and meta-analysis of 3377 patients." Blood **136**(25): 2881-2892.
3. Kuderer, N. M., et al. (2020). "Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study." The Lancet **395**(10241): 1907-1918.
4. Patell, R., et al. (2020). "Incidence of thrombosis and hemorrhage in hospitalized cancer patients with COVID-19." Journal of Thrombosis and Haemostasis **18**(9): 2349-2357.
5. Zon, L., et al. (2020). "Impact of COVID-19 Pandemic on Cancer Research." Cancer Cell **38**(5): 591-593.
6. Abdul-Jawad, S., et al. (2021). "Acute Immune Signatures and Their Legacies in Severe Acute Respiratory Syndrome Coronavirus-2 Infected Cancer Patients." Cancer Cell **39**(2): 257-275.e256.
7. Rivera, D. R., et al. (2020). "Utilization of COVID-19 Treatments and Clinical Outcomes among Patients with Cancer: A COVID-19 and Cancer Consortium (CCC19) Cohort Study." Cancer Discov **10**(10): 1514-1527.
8. Baden, L. R., et al. (2021). "Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine." New England Journal of Medicine **384**(5): 403-416.
9. Brar, G., et al. (2020). "COVID-19 Severity and Outcomes in Patients With Cancer: A Matched Cohort Study." J Clin Oncol **38**(33): 3914-3924.
10. Song, H., et al. (2021). "Disruptions in preventive care: Mammograms during the COVID-19 pandemic." Health Serv Res **56**(1): 95-101.
11. Sterne, J. A. C., et al. (2020). "Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19." JAMA **324**(13): 1330.
12. Wiersinga, W. J., et al. (2020). "Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19)." JAMA **324**(8): 782.
13. Huang, J., et al. (2020). "Considerations for the Management of Oncology Patients During the COVID-19 Pandemic." Oncology (Williston Park) **34**(10): 432-441.

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

47

Selected cited references

16. Hui, J. Y. C., et al. (2020). "Cancer Management During the COVID-19 Pandemic in the United States: Results From a National Physician Cross-sectional Survey." Am J Clin Oncol 43(10): 679-684.
17. Yekedüz, E., et al. (2020). "A systematic review and meta-analysis: the effect of active cancer treatment on severity of COVID-19." European Journal of Cancer 141: 92-104.
18. Yu, J., et al. (2020). "SARS-CoV-2 Transmission in Patients With Cancer at a Tertiary Care Hospital in Wuhan, China." JAMA Oncology **6**(7): 1108.
19. Giannakoulis VG, Papoutsi E, Siempos II. Effect of Cancer on Clinical Outcomes of Patients With COVID-19: A Meta-Analysis of Patient Data. *JCO Global Oncology* 2020; (6): 799-808.
20. Waterhouse DM, Harvey RD, Hurley P, et al. Early Impact of COVID-19 on the Conduct of Oncology Clinical Trials and Long-Term Opportunities for Transformation: Findings From an American Society of Clinical Oncology Survey. *JCO Oncol Pract* 2020; **16**(7): 417-21.
21. Yap TA, Siu LL, Calvo E, et al. SARS-CoV-2 vaccination and phase 1 cancer clinical trials. *The Lancet Oncology* 2021; **22**(3): 298-301.
22. Naidoo J, Reuss JE, Suresh K, et al. Immune-related (IR)-pneumonitis during the COVID-19 pandemic: multidisciplinary recommendations for diagnosis and management. *J Immunother Cancer* 2020; **8**(1).
23. Osterman, C. K., et al. (2021). "Risk stratification and outreach to hematology/oncology patients during the COVID-19 pandemic." Supportive Care in Cancer **29**(3): 1161-1164.
24. Aydillo T, Gonzalez-Reiche AS, Aslam S, et al. Shedding of Viable SARS-CoV-2 after Immunosuppressive Therapy for Cancer. New England Journal of Medicine 2020; 383(26): 2586-8.
25. Karataş A, İnkaya AÇ, Demiroğlu H, et al. Prolonged viral shedding in a lymphoma patient with COVID-19 infection receiving convalescent plasma. Transfusion and Apheresis Science 2020; 59(5): 102871.

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

48

Selected cited references

26. Lehman CD, Lamb LR, D'Alessandro HA. Mitigating the Impact of Coronavirus Disease (COVID-19) Vaccinations on Patients Undergoing Breast Imaging Examinations: A Pragmatic Approach. *American Journal of Roentgenology* 2021.
27. Yri OE, Torfoss D, Hungnes O, et al. Rituximab blocks protective serologic response to influenza A (H1N1) 2009 vaccination in lymphoma patients during or within 6 months after treatment. *Blood* 2011; **118**(26): 6769-71. Landmark Study
28. Beck CR, McKenzie BC, Hashim AB, Harris RC, Nguyen-Van-Tam JS. Influenza Vaccination for Immunocompromised Patients: Systematic Review and Meta-analysis by Etiology. *Journal of Infectious Diseases* 2012; **206**(8): 1250-9. Landmark Study
29. Polack FP, Thomas SJ, Kitchin N, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *New England Journal of Medicine* 2020; **383**(27): 2603-15.
30. Sharpless, N. E. (2020). "COVID-19 and cancer." Science **368**(6497): 1290.
31. Pennell, N. A., et al. (2021). "American Society of Clinical Oncology Road to Recovery Report: Learning From the COVID-19 Experience to Improve Clinical Research and Cancer Care." Journal of Clinical Oncology **39**(2): 155-169.
32. Moraliyage, H., et al. (2021). "Cancer in Lockdown: Impact of the COVID -19 Pandemic on Patients with Cancer." The Oncologist **26**(2).
33. Wallis, C. J. D., et al. (2020). "The Impact of the COVID-19 Pandemic on Genitourinary Cancer Care: Re-envisioning the Future." European Urology **78**(5): 731-742.

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

49

Thank you for listening

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

50