ImmunoScience Academy

Partnering for Education & Optimizing Treatment in ImmunoScience

Patients with oncological malignancies and COVID-19

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Bristol Myers Squibb™

466-BE-2100025 – 10/21

Disclosures

- **Honoraria**: Novartis, Roche, Lilly, Pfizer, Amgen, Bristol Myers Squibb, Seagen
- **Consulting or Advisory Role**: Novartis, Roche, Amgen, Pfizer, Bristol Myers Squibb, Lilly, AstraZeneca, Daiichi Sankyo, Abbvie
- **Research funding**: Roche, Pfizer
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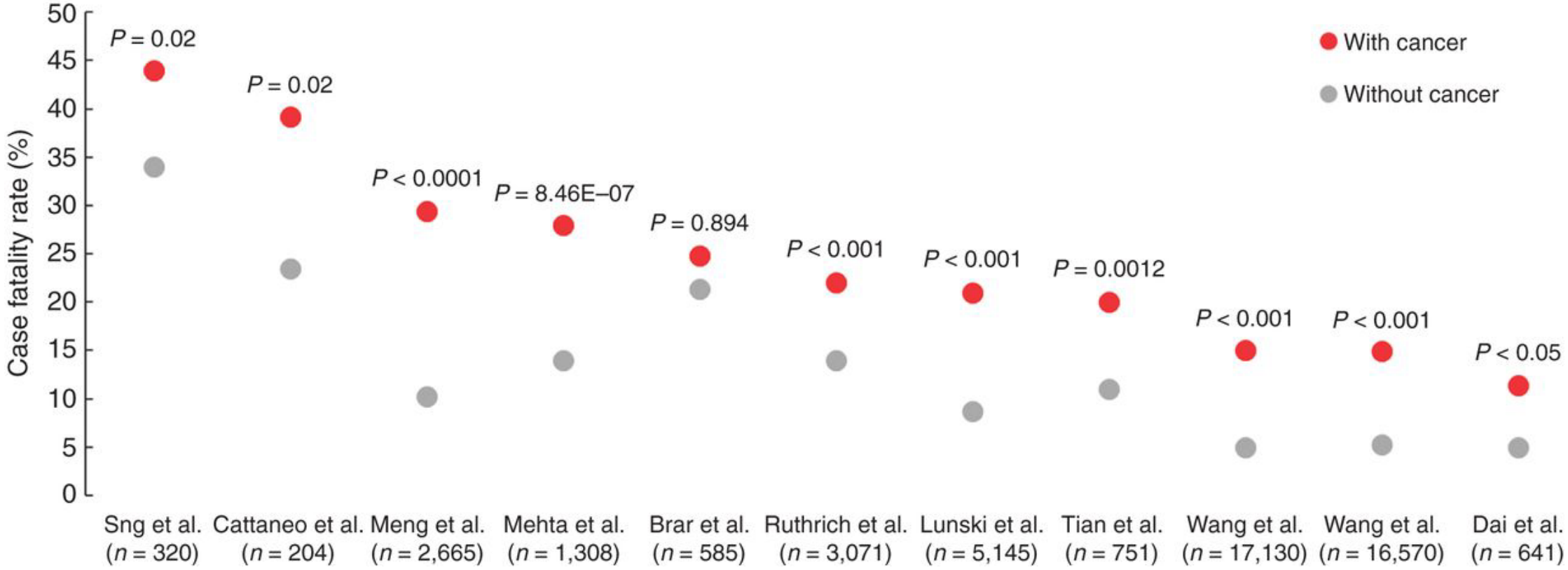
COVID-19 case fatality rate in patients with or without cancer



Ribas A. et al. *Cancer Discov*. 2021;11(2):233-236.

COVID-19: Risk factors for fatal outcome

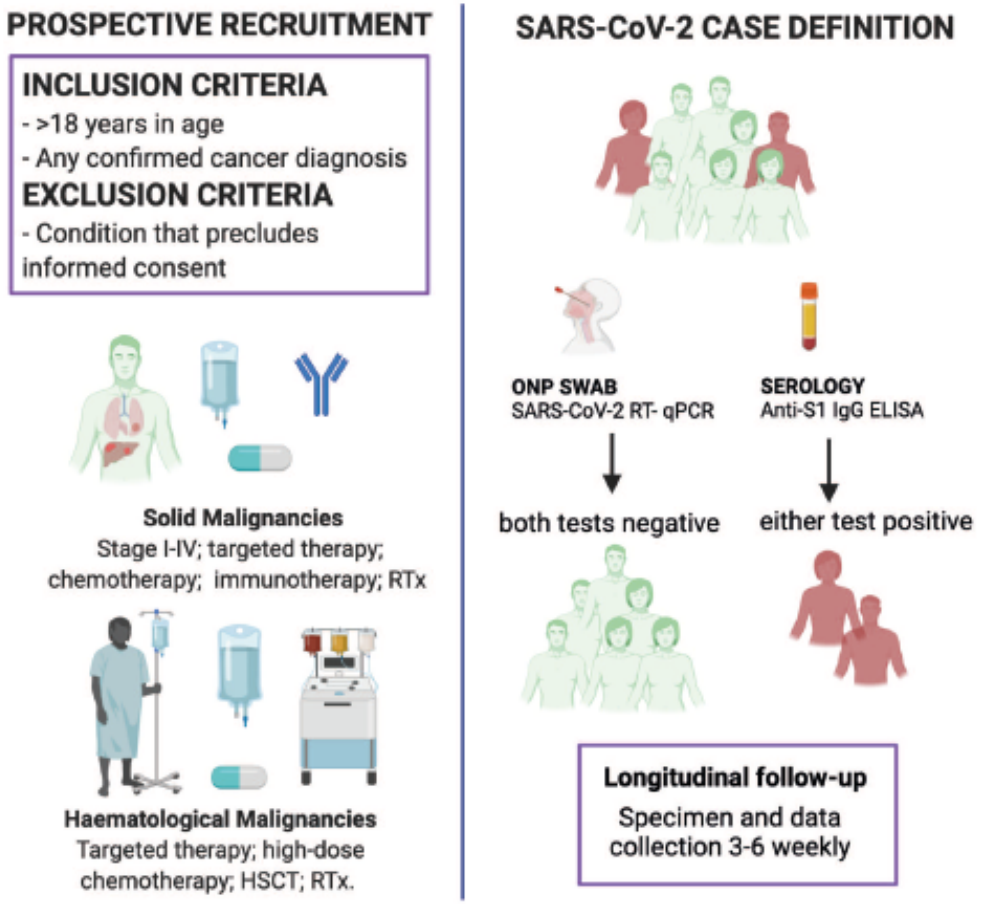
	Univariate logistic regression analysis		Multivariable logistic regression analysis	
Variables	Odds Ratio (95% CI)	P[a]	Odds Ratio (95% CI)	P[a]
Age (>65 y)	3.57 (1.80 to 7.06)	< .001	3.16 (1.45 to 6.88)	.004
Sex (male)	2.10 (1.07 to 4.13)	.03	2.29 (1.07 to 4.87)	.03
Comorbidities (all)	2.00 (1.04 to 3.85)	.04	_	_
Hypertension vs no	3.10 (1.38 to 6.99)	.006	1.37 (0.51 to 3.71)	.53
Diabetes vs no	4.16 (1.31 to 13.20)	.02	2.73 (0.76 to 9.81)	.13
Cardiovascular disease vs no	2.13 (0.74 to 6.14)	.16	_	_
Hematological vs lung	0.68 (0.14 to 3.28)	.63	_	_
Other solid cancer vs lung	0.80 (0.37 to 1.74)	.58	_	_
Treatment vs no	0.98 (0.51 to 1.90)	.95	_	_
Chemotherapy vs no	0.94 (0.40 to 2.20)	.89	_	_
Immunotherapy vs no	4.00 (0.77 to 20.90)	.10	_	_
Target Therapy vs no	0.38 (0.08 to 1.94)	.25	_	_
Radiotherapy vs no	0.56 (0.18 to 1.71)	.31	_	_
Surgery vs no	1.00 (0.32 to 3.12)	1.00	_	_

[a]P values were calculated using the Wald χ^2 2-sided test. CI = confidence interval.

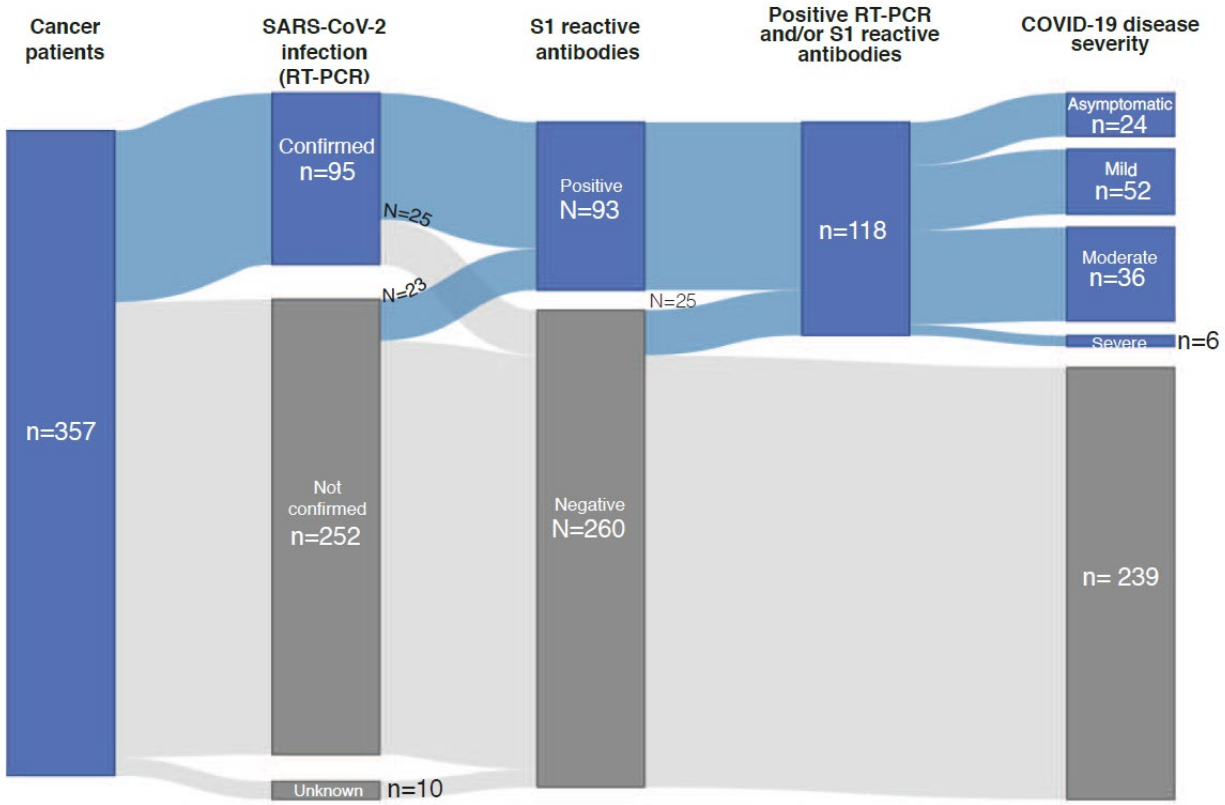
Zhang H. et al. *J Natl Cancer Inst*. 2021;113(4):371-380.

The Capture Study

(Royal Marsden, NCT03226886)



n = 118, solid tumors: 97, hematological malignancies: 21



Shepherd S et al, Oral presentation at Presidential Symposium 3 “Sars-CoV-2 and cancer “ .European Society for Medical Oncology (ESMO) Annual Meeting; September 16-21, 2021; Virtual Meeting.

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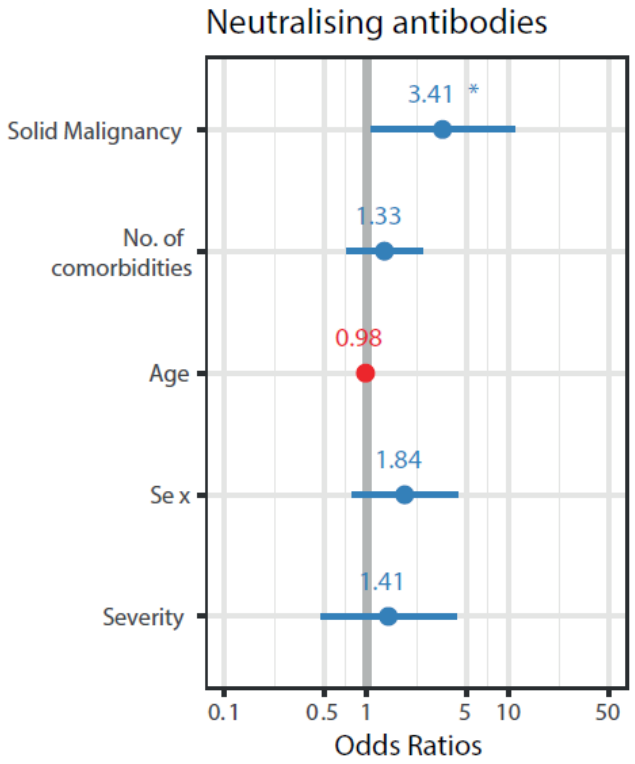
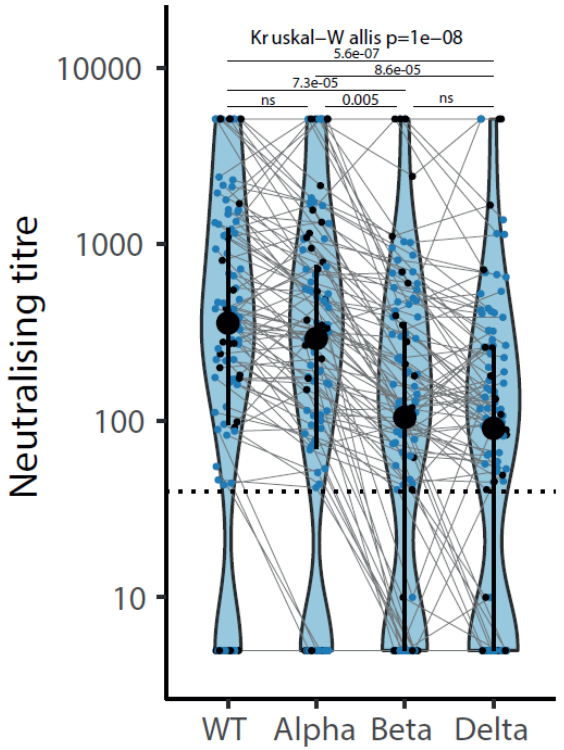
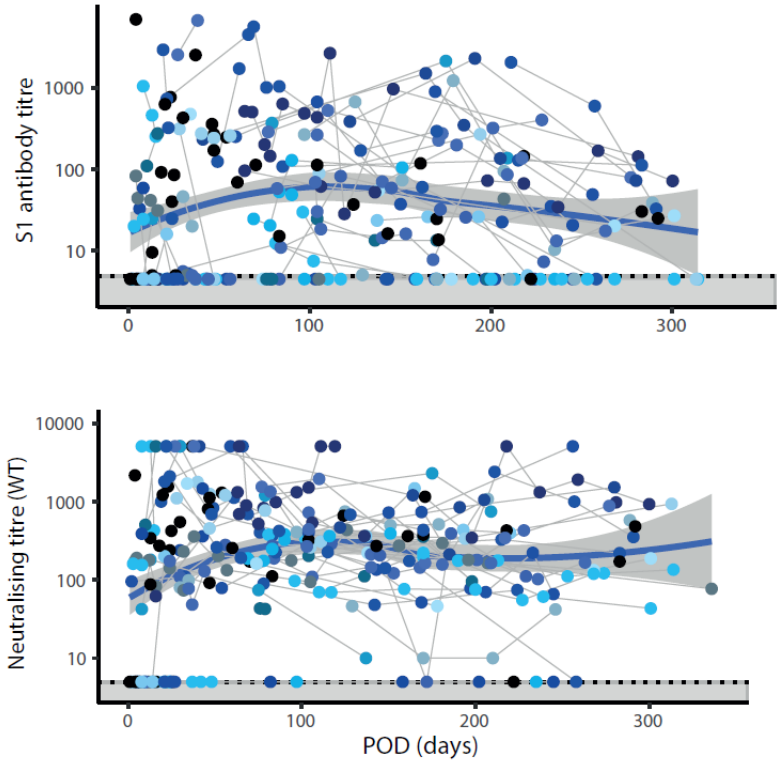
The Capture Study

Infections induce robust and durable neutralising responses in most cancer patients

Reduced in patients with haematological malignancies







Shepherd S et al, Oral presentation at Presidential Symposium 3 “Sars-CoV-2 and cancer “ .European Society for Medical Oncology (ESMO) Annual Meeting; September 16-21, 2021; Virtual Meeting.

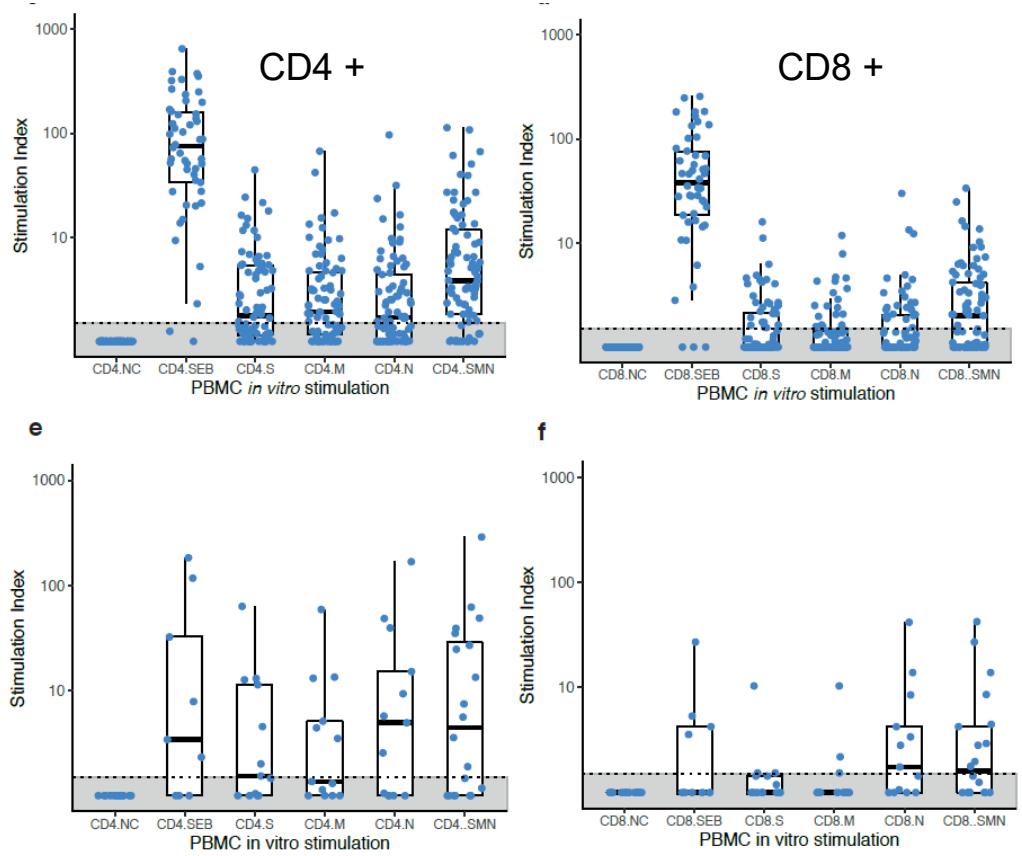
The Capture Study

T cell responses are reduced in patients with haematological malignancies

CD4 + response predominates over CD8 + T cell response

Solid tumours

Haematological malignancies

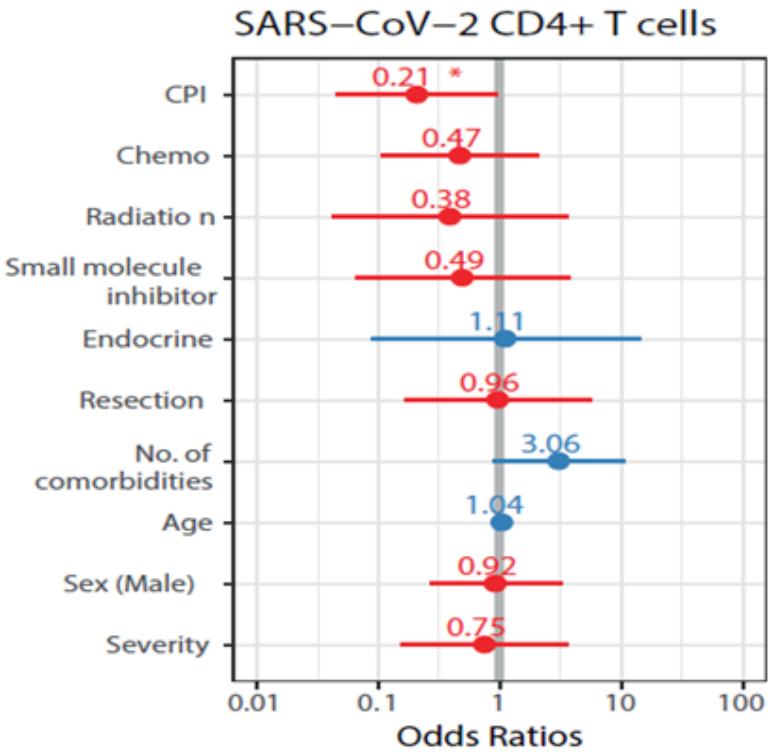


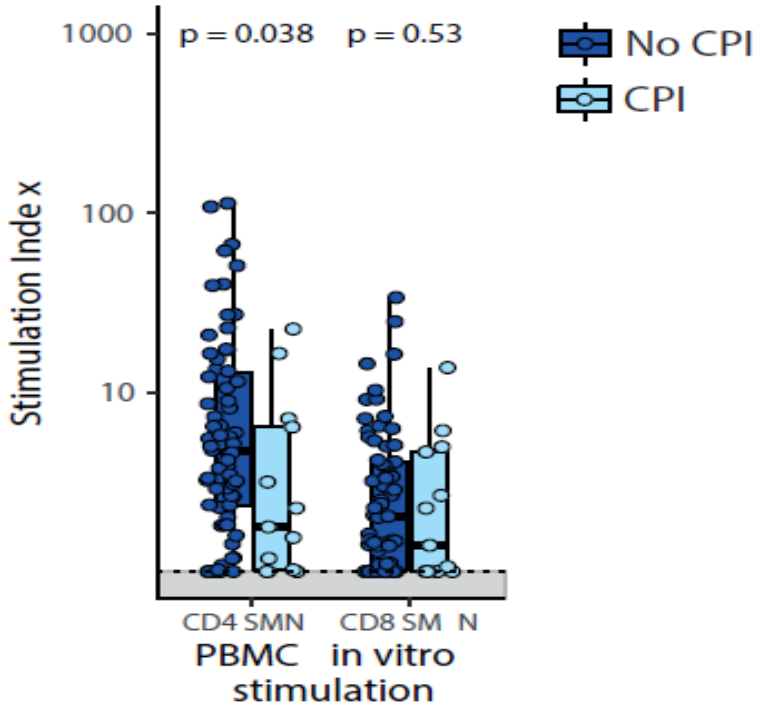
Shepherd S et al, Oral presentation at Presidential Symposium 3 “Sars-CoV-2 and cancer “. European Society for Medical Oncology (ESMO) Annual Meeting; September 16-21, 2021; Virtual Meeting.

The Capture Study

CD4 + T cells suppressed in immune checkpoint treated patients

No effect of other systemic therapies on cellular responses





Shepherd S et al, Oral presentation at Presidential Symposium 3 “Sars-CoV-2 and cancer “ .European Society for Medical Oncology (ESMO) Annual Meeting; September 16-21, 2021; Virtual Meeting.

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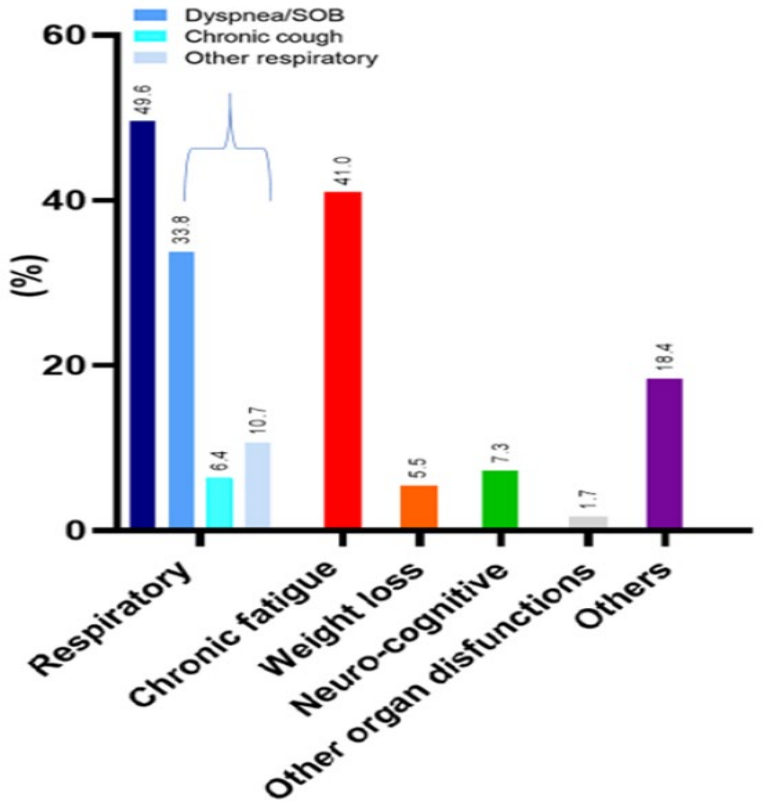
Prevalence and impact of COVID-19 sequelae

234 (**15%**) pts experienced at least one long-term sequela from COVID-19

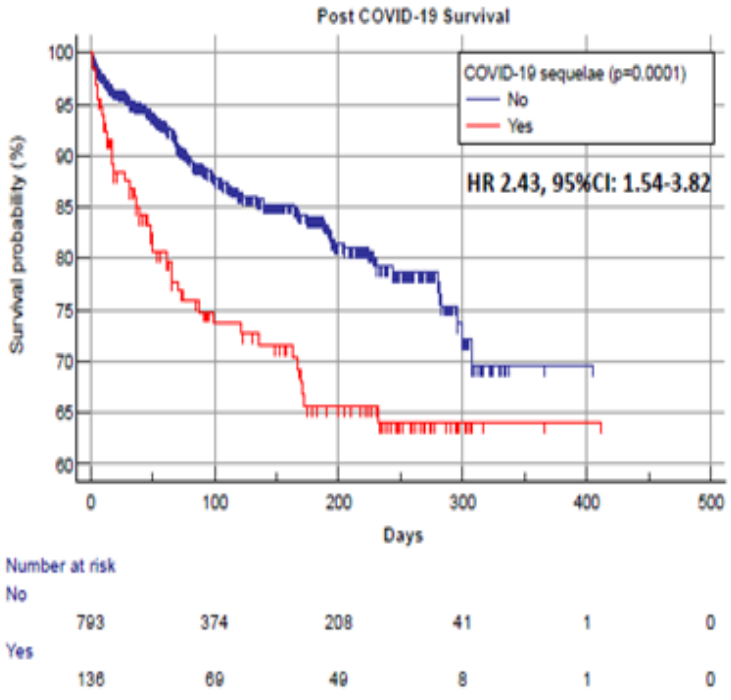
Patients experiencing sequelae were more likely:

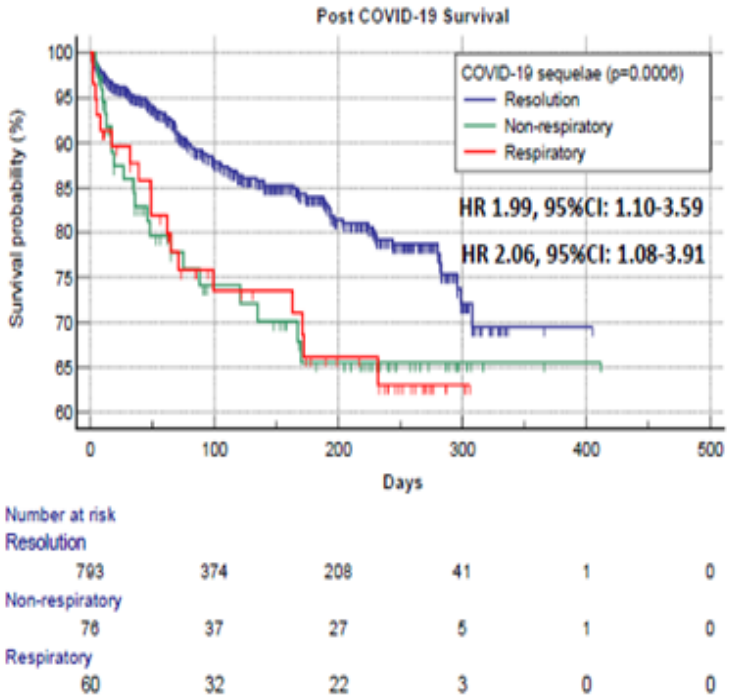
- **Males** (54.5% vs 47.2%, p=0.0407)
- Aged **≥ 65 years** (55.1% vs 48.1%, p=0.0489)
- With **≥ 2 comorbidities** (48.3% vs 36.4%, p=0.0006)
- With positive history of **smoking** (55.9% vs 42.3%, p=0.0004)
- With higher rates of prior **complicated COVID-19** (54.3 vs 20.9%, p<0.0001)
- Requiring **COVID-19 therapy** (65.8% vs 52.6%, p<0.0001)
- Requiring prior **hospitalization** for COVID-19 (72.2% vs 41.2%, p<0.0001).

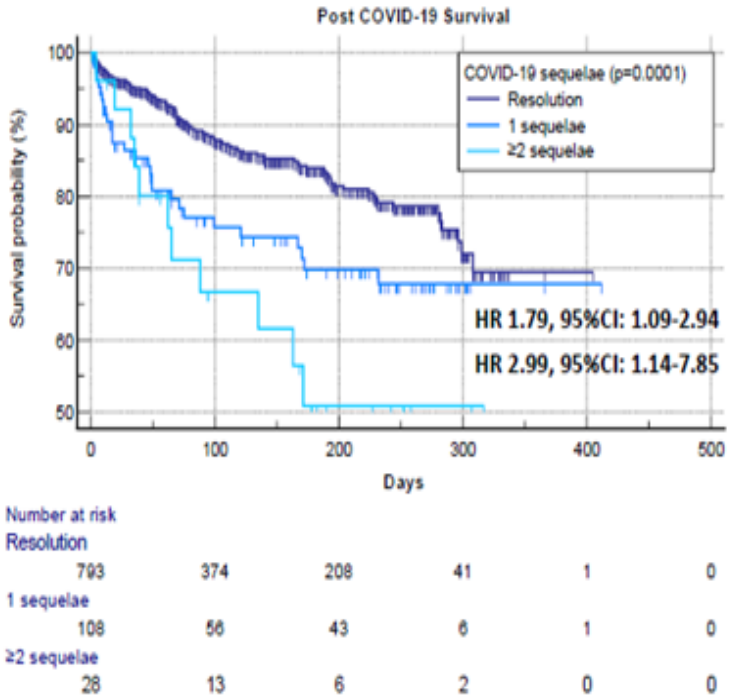


Cortellini A.et al, Oral presentation at European Society for Medical Oncology (ESMO) Annual Meeting; September 16-21, 2021; Virtual Meeting.

Prevalence and impact of COVID-19 sequelae



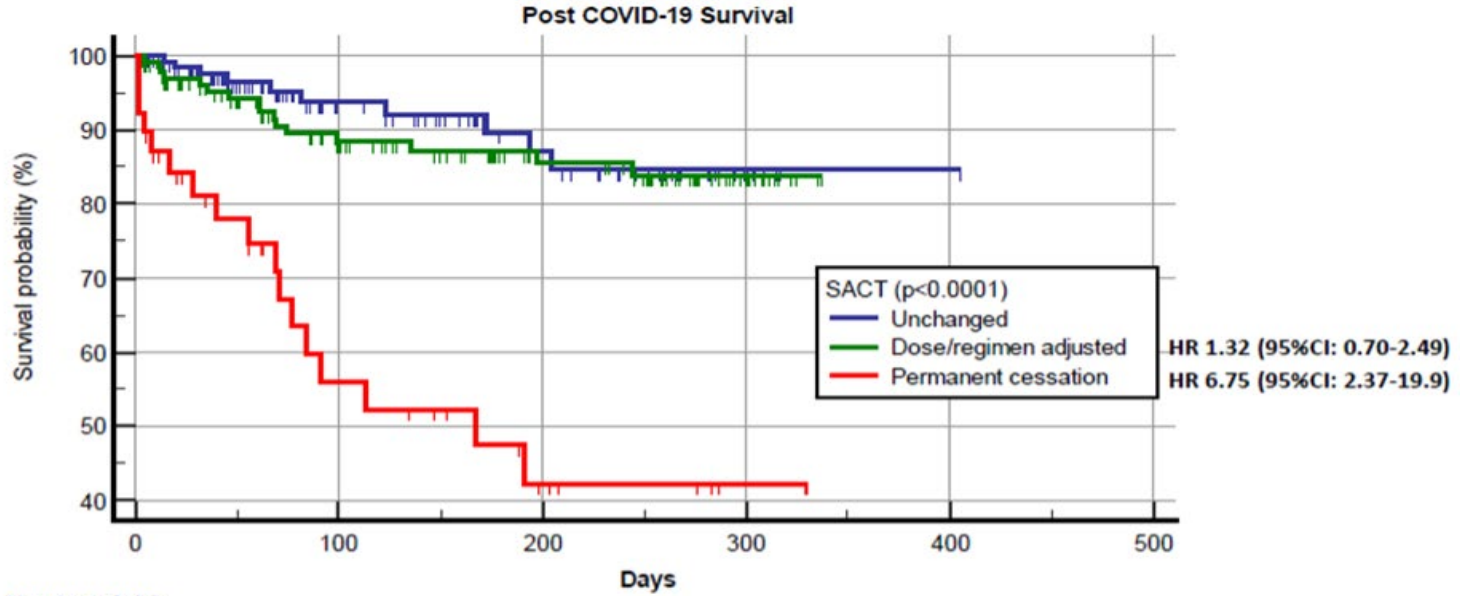




After adjusting for gender, age, comorbidities burden, primary tumour, stage and status, receipt of anticancer and COVID-19 therapy, COVID-19 complications and hospitalization, **COVID-19 sequelae was confirmed to be independently associated with an increased risk of death HR 1.76; 95%CI: 1.16 – 2.66**

Cortellini A.et al, Oral presentation at European Society for Medical Oncology (ESMO) Annual Meeting; September 16-21, 2021; Virtual Meeting.

Systemic anticancer therapy resumption and outcome in COVID-19 survivors



Number at risk					
Unchanged					
145	56	35	7	1	0
Dose/regimen adjusted					
138	81	54	16	0	0
Permanent cessation					
39	15	7	2	0	0

After adjusting for gender, age, comorbidities burden, primary tumour, tumour stage and status, receipt of COVID-19 therapy, COVID-19 complications, hospitalization and sequelae, **permanent SACT cessation was confirmed to be independently associated with an increased risk of death HR 3.53; 95%CI: 1.45 – 8.59**

Cortellini A.et al, Oral presentation at European Society for Medical Oncology (ESMO) Annual Meeting; September 16-21, 2021; Virtual Meeting.

Conclusions:
Patients with oncological malignancies and COVID-19

- Increased risk of fatal outcome
- Durable neutralising antibody responses in solid tumors
- Neutralising responses to Beta and Delta VOC are reduced
- Majority of patients with cancer have detectable cellular responses
- COVID-19 sequelae are associated with increased risk of death

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COVID-19 vaccination in patients with oncological malignancies

Marc Peeters MD, PhD - UZA

Peter van Dam MD, PhD, Timon Vandamme MD, PhD, Yana Debie PhD student
MOCA-team in collaboration UAntwerpen, Sciensano, KCE, KotK

Bristol Myers Squibb™

466-BE-2100026 - 10/21

Disclosures

▪ Advisory Board	Amgen, Bayer, Bimini, BMS, Ipsen, Merck, MSD, Qurin, Remedus, Sanofi, Sirtex, Terumo
▪ Speakers Fee	Amgen, Bayer, BMS, Merck, MSD, Roche, Sanofi, Servier, Sirtex
▪ Scientific Grants	Amgen (Inst.), Bayer (Inst.), BMS (Inst.), Ipsen (Inst.), Novartis (Inst.), Roche (Inst.)

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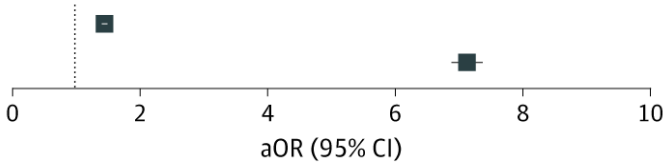
Odds of COVID-19 infection

- Cancer patients have an increased risk for COVID-19
- Strongest association for recently diagnosed leukemia, non–Hodgkin lymphoma and lung cancer
- Worse outcomes for patients with cancer and COVID-19 (hospitalization, 47.46%; death, 14.93%)

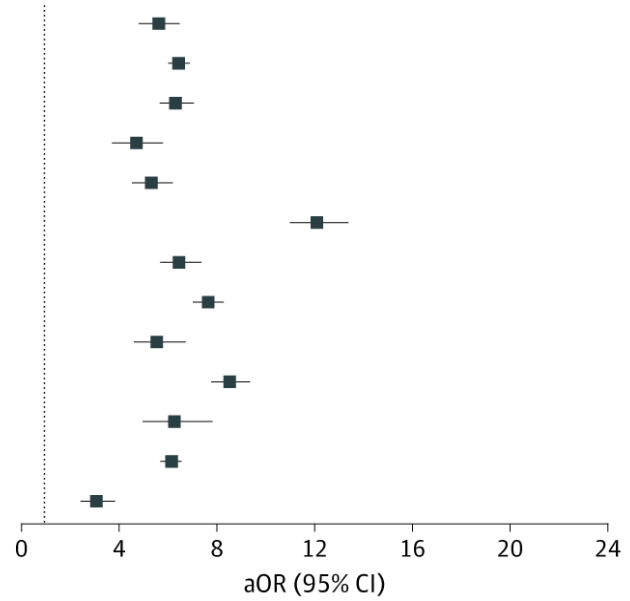
A Comparison of COVID-19 risk associations with all vs recent cancer diagnosis

Exposure	Outcome	aOR (95% CI)	*P* value
All cancer	COVID-19	1.46 (1.42-1.50)	<.001
Recent cancer	COVID-19	7.14 (6.91-7.39)	<.001



B Associations between recent diagnosis of cancer and COVID-19 infection

Exposure	Outcome	aOR (95% CI)	*P* value
Bladder cancer	COVID-19	5.63 (4.86-6.52)	<.001
Breast cancer	COVID-19	6.47 (6.06-6.91)	<.001
Colorectal cancer	COVID-19	6.36 (5.71-7.08)	<.001
Endometrial cancer	COVID-19	4.70 (3.79-5.82)	<.001
Kidney cancer	COVID-19	5.33 (4.58-6.21)	<.001
Leukemia	COVID-19	12.16 (11.03-13.40)	<.001
Liver cancer	COVID-19	6.49 (5.71-7.38)	<.001
Lung cancer	COVID-19	7.66 (7.07-8.29)	<.001
Melanoma	COVID-19	5.58 (4.62-6.73)	<.001
Non-Hodgkin lymphoma	COVID-19	8.54 (7.80-9.36)	<.001
Pancreatic cancer	COVID-19	6.26 (4.98-7.87)	<.001
Prostate cancer	COVID-19	6.14 (5.72-6.60)	<.001
Thyroid cancer	COVID-19	3.10 (2.47-3.87)	<.001



Wang Q et al. *JAMA Oncol*. 2021;7(2):220–227

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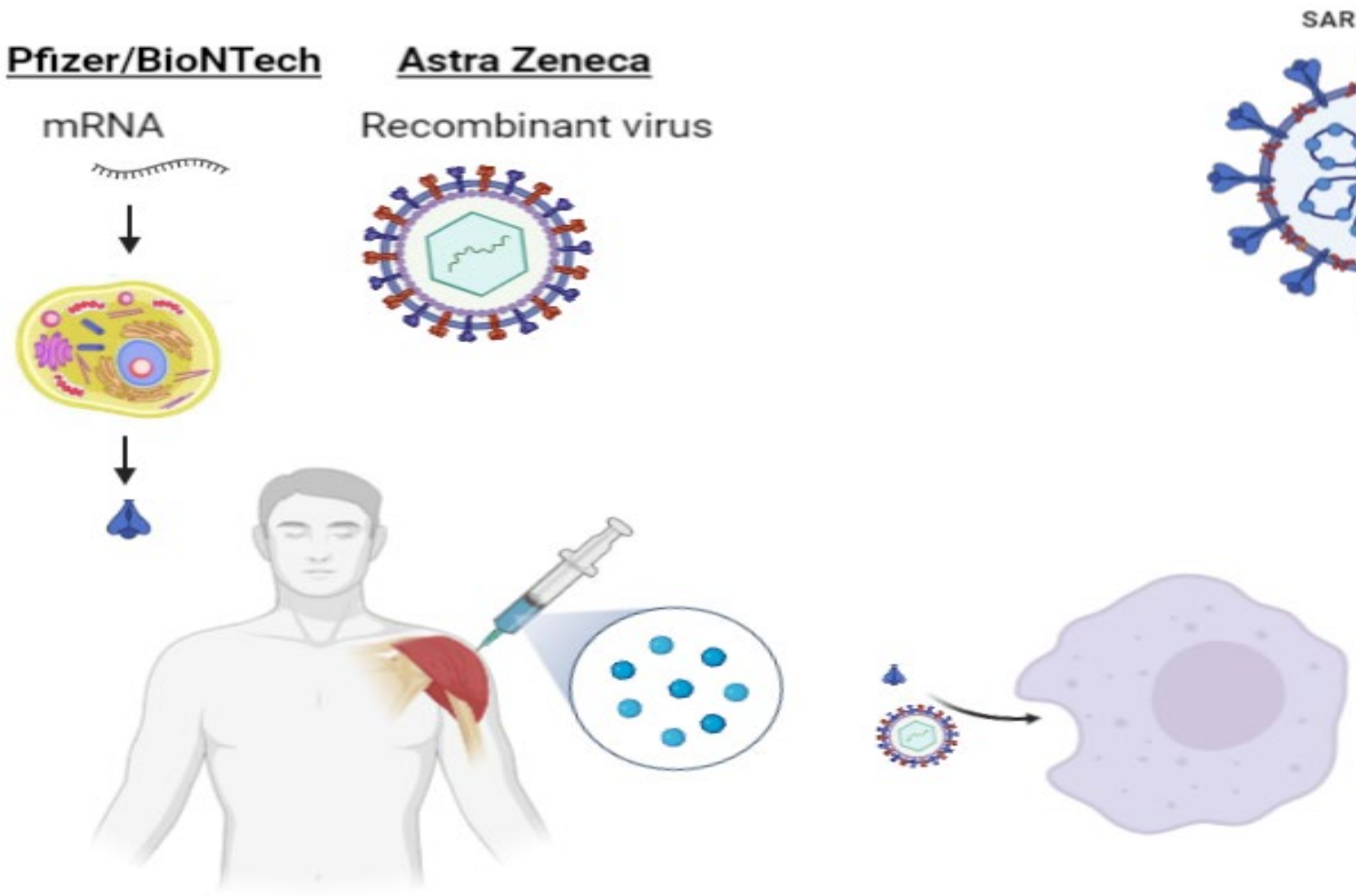
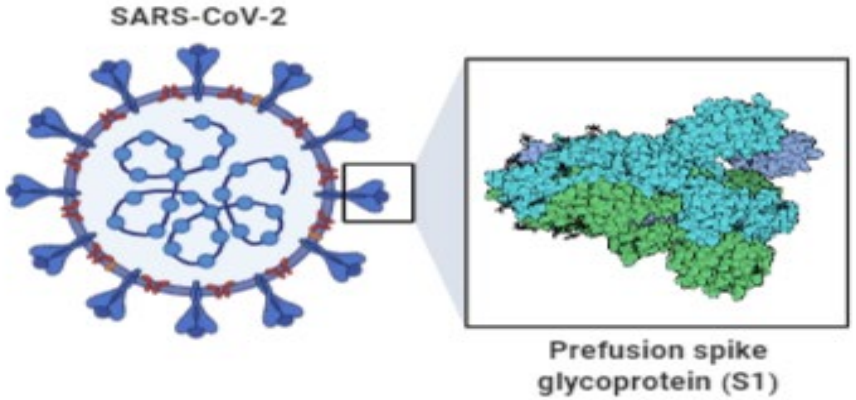
COVID-19 vaccines – background

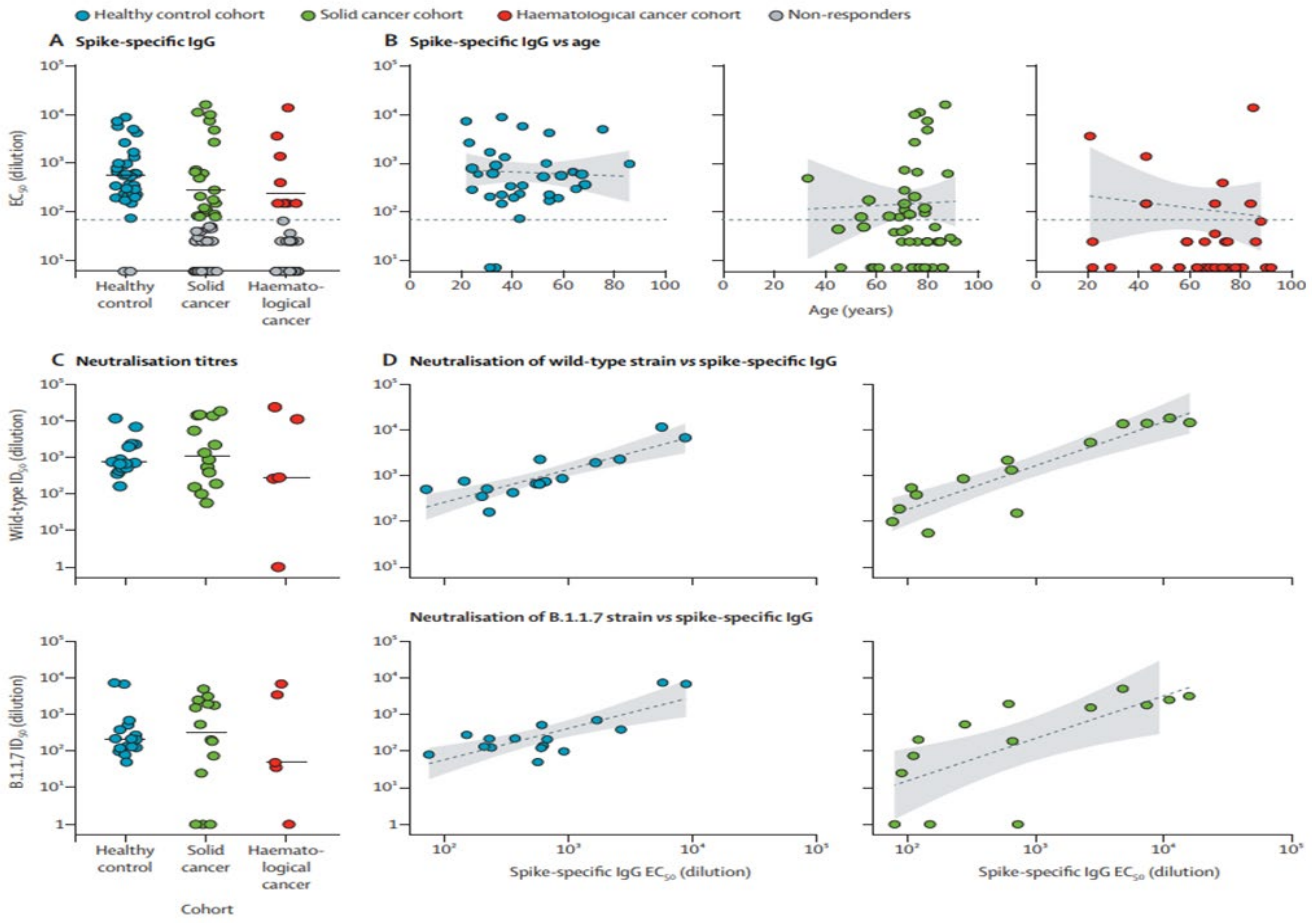




Serological response to BNT162b2 COVID-19 vaccine

- Median titers largely similar in each cohort
- Failure to produce response

Cohort	% Responders
Healthy controls	94%
Solid cancer	38%
Haematological malignancy	18%



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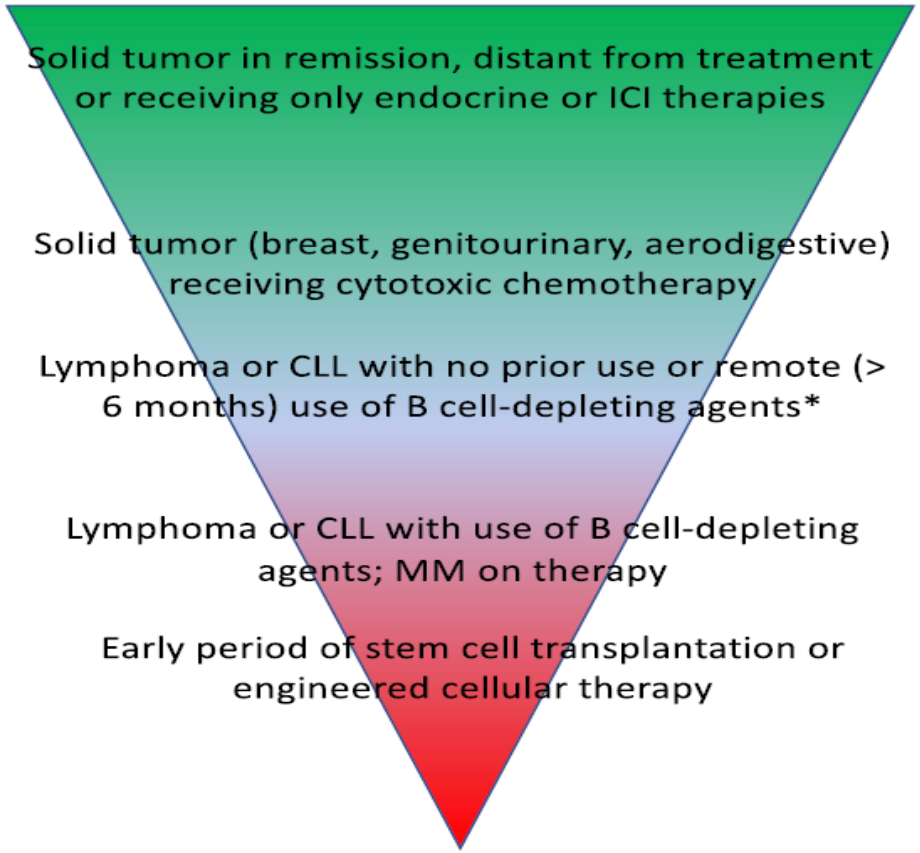
Monin L. et al. *Lancet Oncol*. 2021;22(6):765-778

Prediction of COVID-19 vaccine efficacy in cancer



Protection likely equivalent to general population

Protection Status Unknown

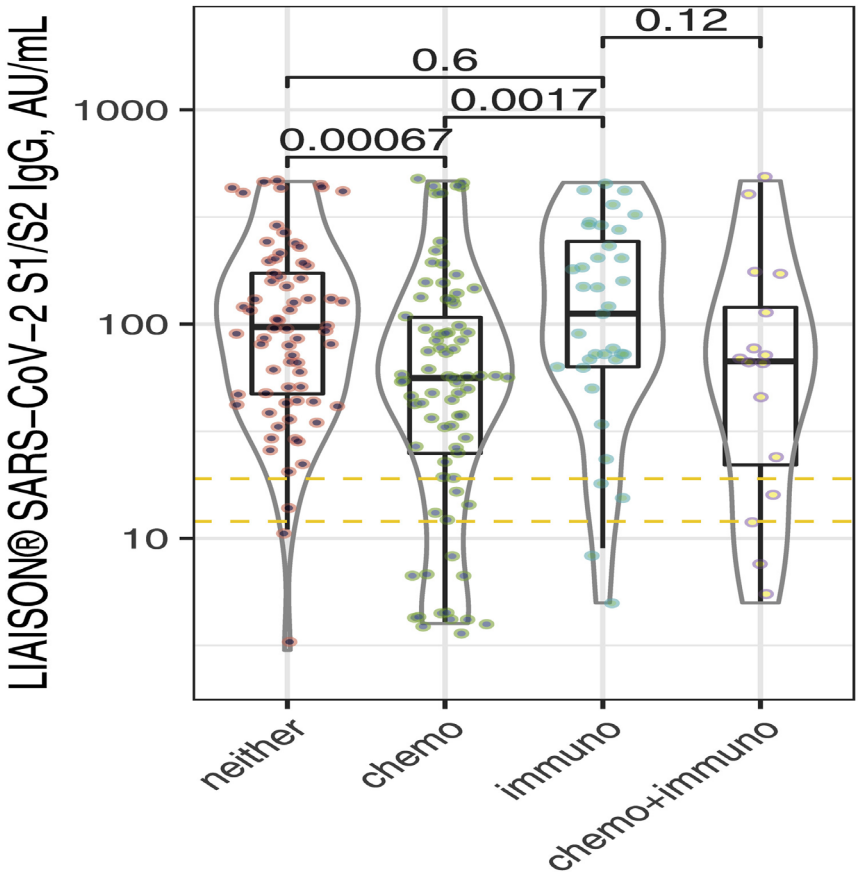
- Targeted pathway inhibitors
- Intensive cytotoxic regimens (e.g. for sarcoma or germ cell tumors)
- Relapsed/refractory cancer with exposure to multiple lines of chemotherapy
- Myeloproliferative neoplasms with and without JAK and tyrosine kinase inhibitors
- Myelodysplastic syndrome with and without therapy
- Acute leukemia
- Investigational cancer therapies

No protection

Griffiths EA, Segal BH. *Cancer Cell*. 2021;39(8):1045-1047

COVID-19 vaccine and natural infection in cancer patients

- Highly immunogenic
- Patients receiving chemotherapy are less responsive
- Lower efficacy among patients with comorbidities



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Grinshpun, A. et al. ESMO Open 2021 Sep 27;6(6):100283. doi: 10.1016/j.esmoop.2021.100283. Epub ahead of print.

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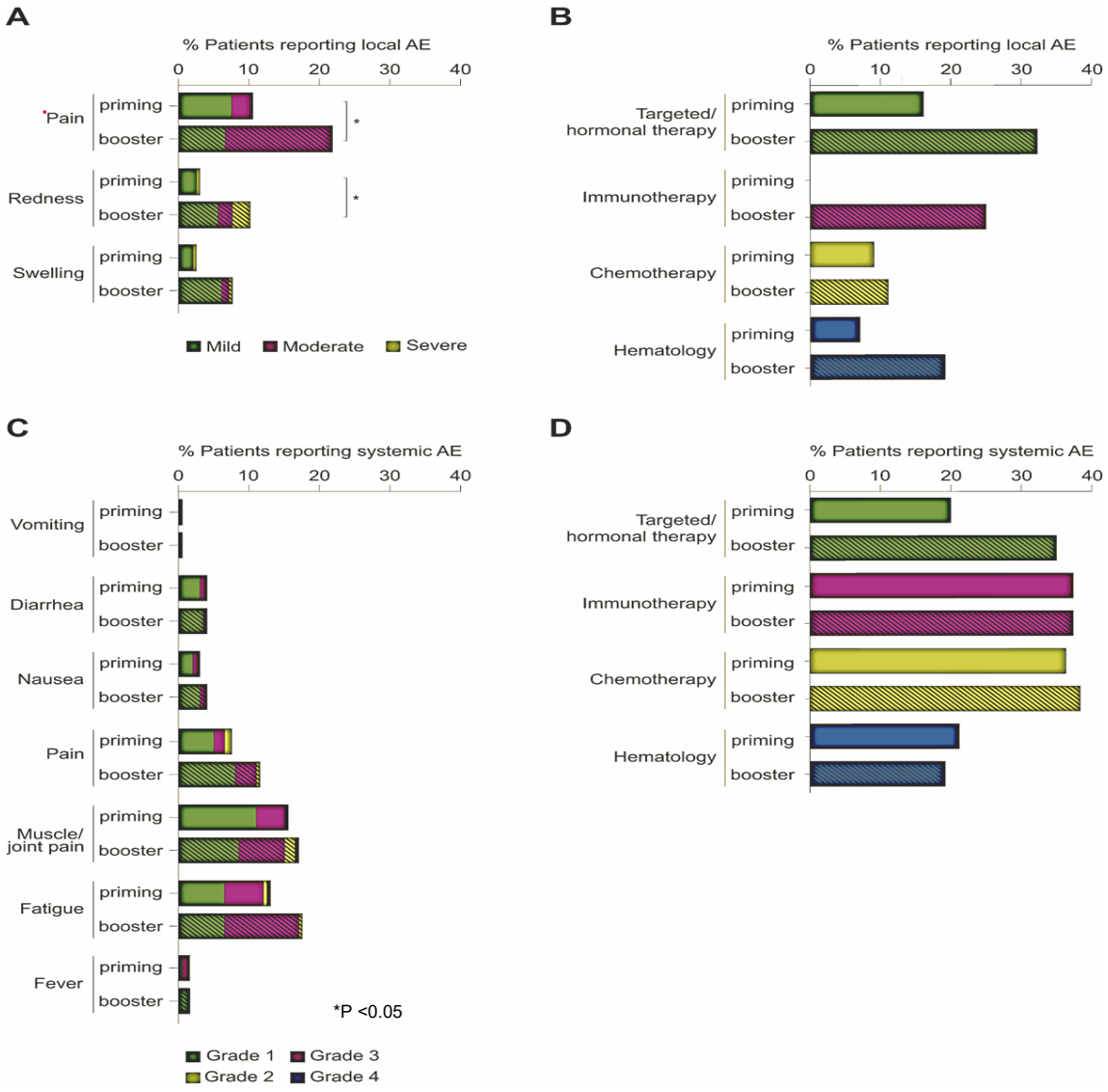
Research questions

- Do the different types of **anti-cancer treatment** affect the efficacy of COVID-19 vaccines?
  - Antibodies
  - T-cell immunity
- Are COVID-19 vaccines **safe** for patients receiving anti-cancer treatment?
- Do the approved vaccines elicit **equally effective antibody** responses in patients under anti-neoplastic treatment?

BNT162b2 vaccine – safety

- AEs in cancer patients after vaccination
- Well-tolerated
- Pain at injection site most frequently reported
- All local AEs resolved within 3-5 days



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Peeters, M. et al. *ESMO Open*. 2021 Sep 8;6(5):100274. doi: 10.1016/j.esmoop.2021.100274. Epub ahead of print.

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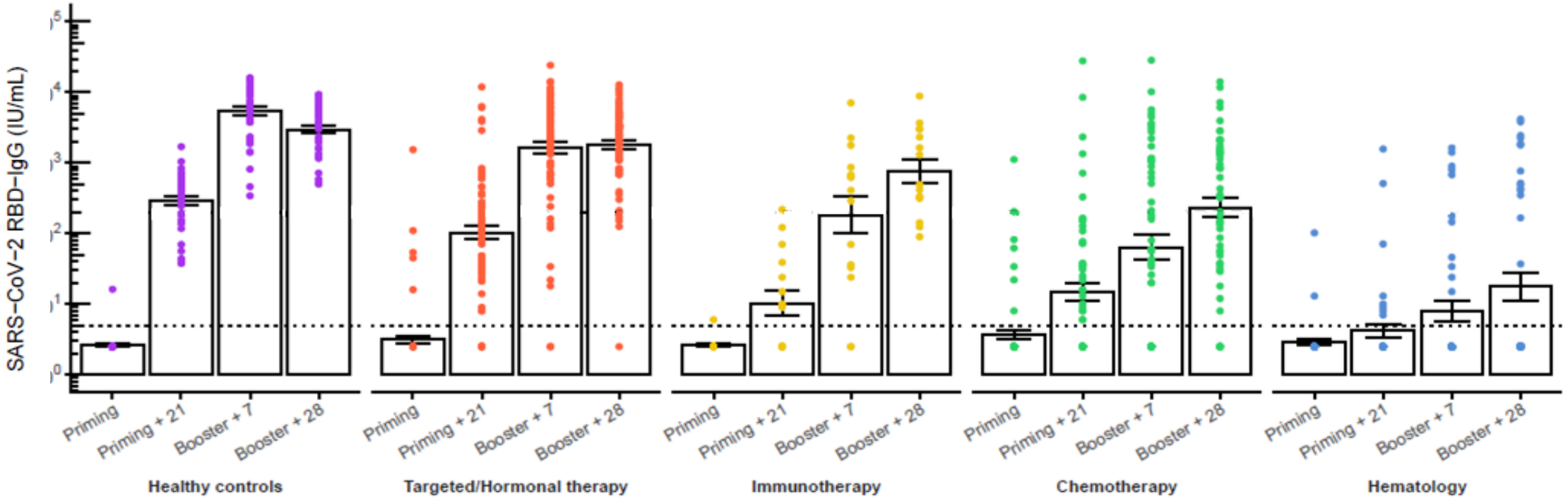
BNT162b2 vaccine – efficacy

- Antibodies: strongly depend on treatment type



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Peeters, M. et al. *ESMO Open*. 2021 Sep 8;6(5):100274. doi: 10.1016/j.esmoop.2021.100274. Epub ahead of print.

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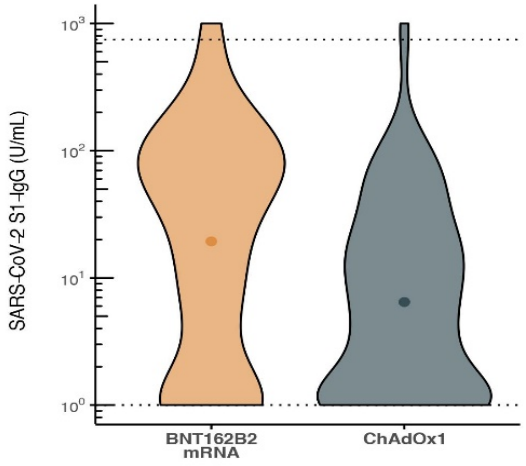
BNT162b2 vs. ChAdOx1vaccine – efficacy

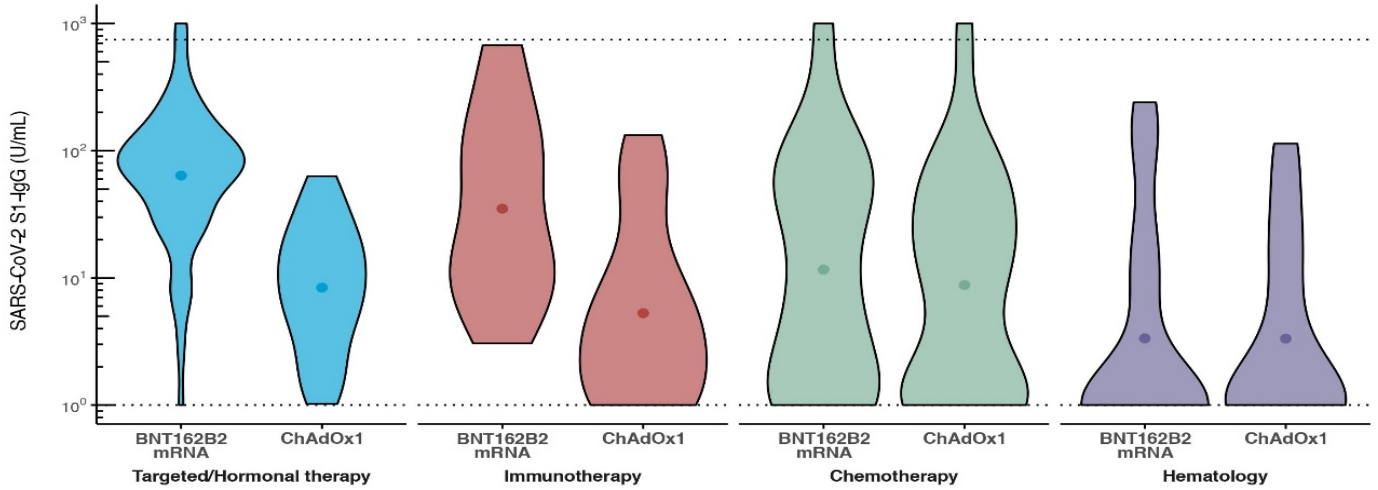
- BNT 162b2 vaccine elicits higher antibody levels than AstraZeneca vaccine in our cancer population
- Significant difference in patients receiving target/hormone therapy and immunotherapy

A



At risk	186	159
GMT	19	6
% IgG seroconversion	78	75

B



At risk	76	40	15	21	54	61	41	34
GMT	64	8	35	5	12	9	3	3
% IgG seroconversion	99	100	100	76	78	75	34	47

(van Dam, Peter A. et al. 2021, unpublished data)

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Take Home Message
Vaccination in patients with oncological malignancies

1. Covid-19 Vaccination in oncological patients – **safe**
2. Vaccination in oncological patients, 2 x – **questionable efficacy**
3. Vaccination in oncological patients, 3 x – **unknown efficacy**

→ Vaccination in patients with oncological malignancies - **work in progress!**

Work in progress = Ongoing research

- **Is there an effect on cellular immunity?**
  - Blood samples are currently analysed
- **How develop antibody levels over time?**
  - Blood collection 6-7 months after first dose
    - BNT162b2 : September/October
    - ChAdOx1 : October/November
- **Is the administration of a third dose useful?**
  - Patients receive a third dose of BNT162b2 vaccine 6-7 months after their first dose
  - Safety is monitored via Remecare App
  - Immune response (antibodies and T-cell immunity) short and long term

Based on the data presented, what would you propose to your patients **under chemotherapy**?

1. No vaccination
2. Standard of 2 vaccine doses
3. Three vaccine doses
4. Vaccination depending on the timing of the chemotherapy
5. I don’t know