Lymphoma management during the COVID-19 pandemic: New evidence-based insights and recommendations

Thursday, July 29, 2021 | 17:00–18:30 (CEST)

0721-BGB-3111-MRC-032

Welcome and introductions

Chair: Professor Christian Buske

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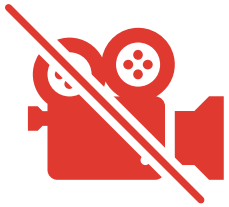
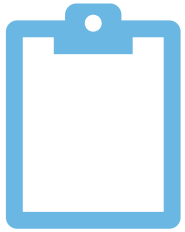
- Zanubrutinib is not approved for the treatment of Waldenström’s macroglobulinemia outside Canada.

Housekeeping



Please note that personal recording of this meeting is not permitted
(a recording will be available to watch soon after the meeting)

Exit full-screen view at any time to submit a question for the panel to answer during the Q&A session



A post-meeting survey will be shared at the end of the webinar;
we would greatly appreciate your feedback

Introducing the speakers

Christian Buske
University Hospital of Ulm, Germany

Meletios A. Dimopoulos
National and Kapodistrian University of Athens School of Medicine, Greece

Wojciech Jurczak
Maria Skłodowska-Curie National Research Institute of Oncology, Poland

Disclosures

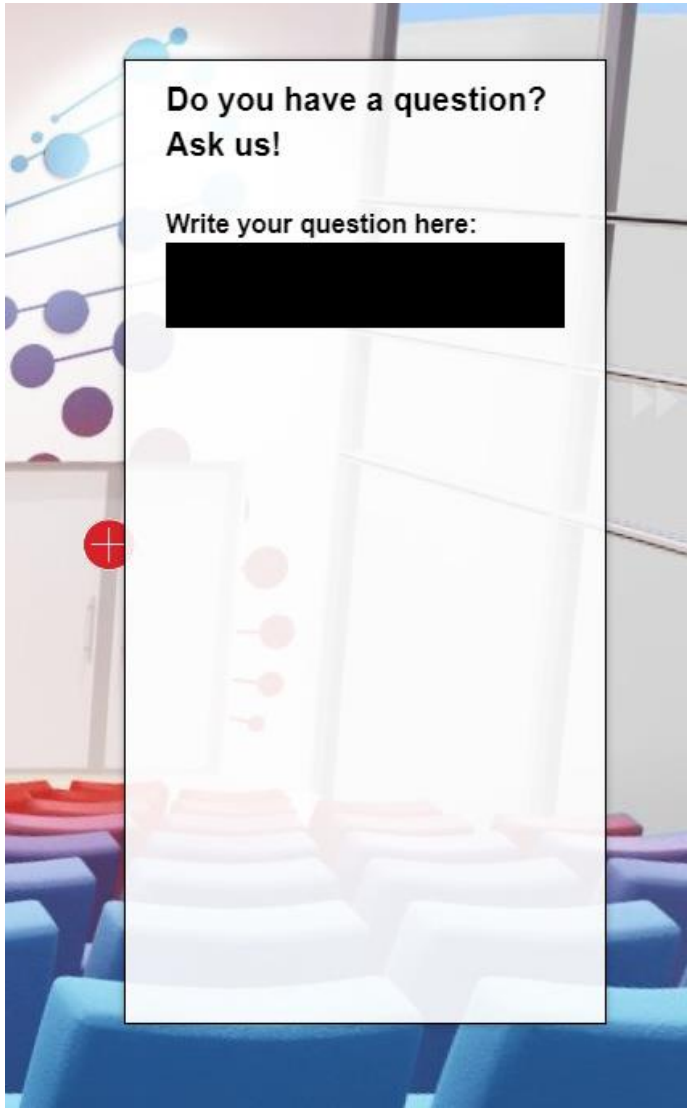
- **Honoraria:** Roche, Janssen, BeiGene, Celltrion, Pfizer, AbbVie
- **Research funding:** Roche, Janssen, Celltrion, AbbVie, Bayer, MSD

Agenda

17:00	**Welcome and introductions**	Christian Buske
17:05	**Plenary presentation** Hematologic malignancies and COVID-19: The key challenges	Meletios A. Dimopoulos
17:20	**Recommendations:** General principles and indolent lymphomas	Christian Buske
17:35	**Recommendations:** Aggressive lymphomas	Wojciech Jurczak
17:50	**Panel discussion**	**Panel:** All
18:10	**Audience Q&A**	
18:25	**Summary and meeting close**	Christian Buske

A guide to the meeting platform: Audience questions

- Please exit full-screen and enter your question in the submission box for the panel to answer during the Q&A session
  - You can vote for the questions you would most like the panel to answer during the Q&A session
- Please note that it may not be possible for the panel to answer all of the questions that are submitted



Hematologic malignancies and COVID-19: The key challenges

Meletios Athanasios Dimopoulos, MD, PhD
Professor of Hematology-Oncology
Plasma Cell Dyscrasias Unit,
National and Kapodistrian University of Athens,
School of Medicine, Athens, Greece

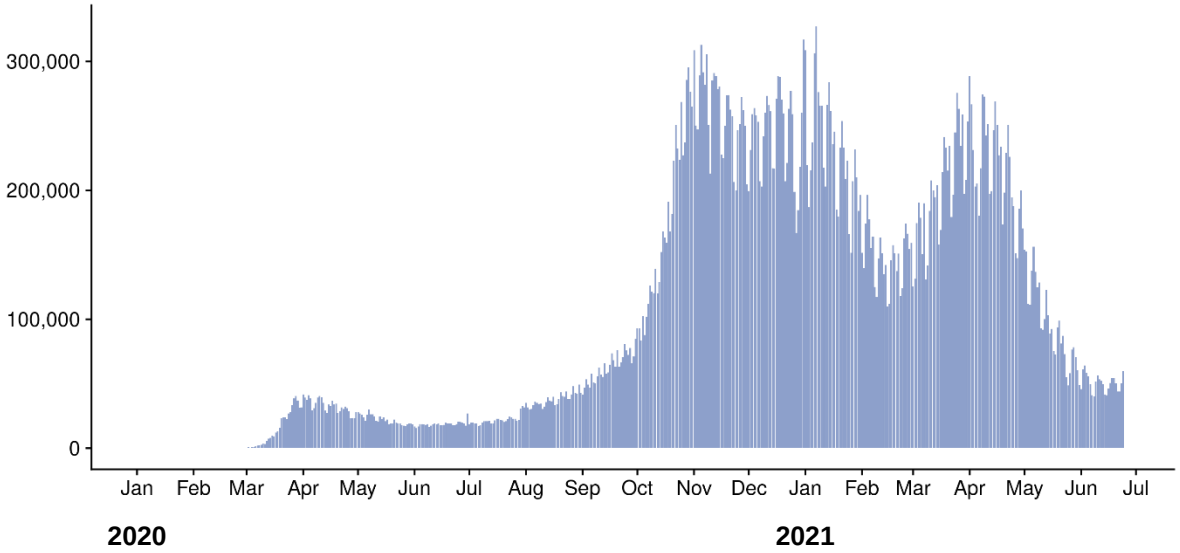
Disclosures

- Over the past 2 years:

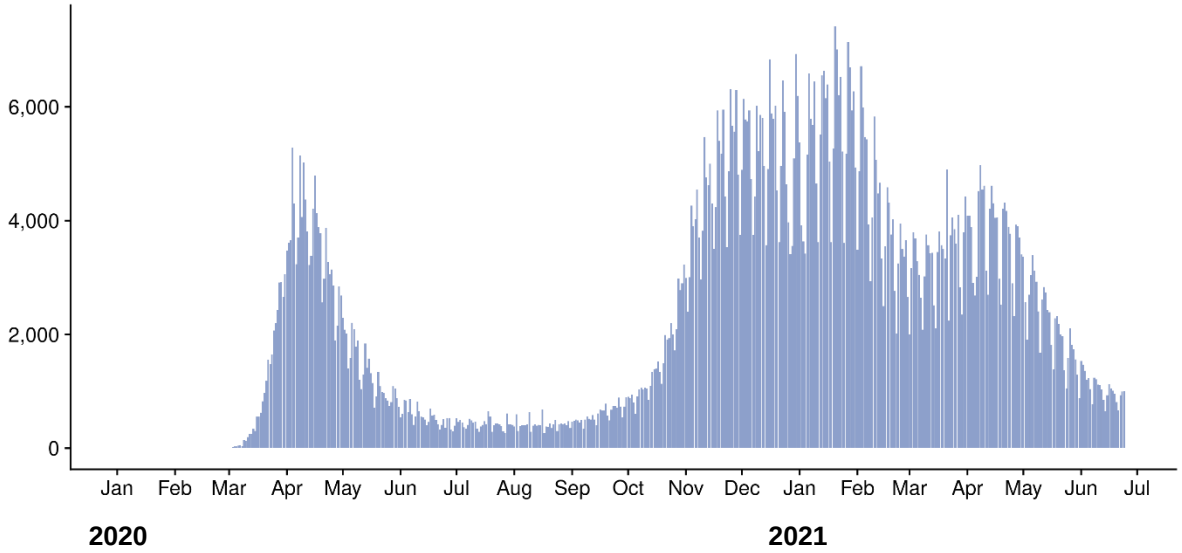
	Advisory board	Honoraria
Amgen	X	X
BeiGene		X
Janssen	X	X
Celgene/Genesis	X	X
Sanofi		X
Takeda	X	X
Karyopharm	X	X
GSK		X

The COVID-19 pandemic in Europe

New cases (N=55,595,648)



New deaths (N=1,178,896)



COVID-19 Explorer. Available at: https://worldhealthorg.shinyapps.io/covid/. Accessed July 2021.

Epidemiology of COVID-19 in cancer patients

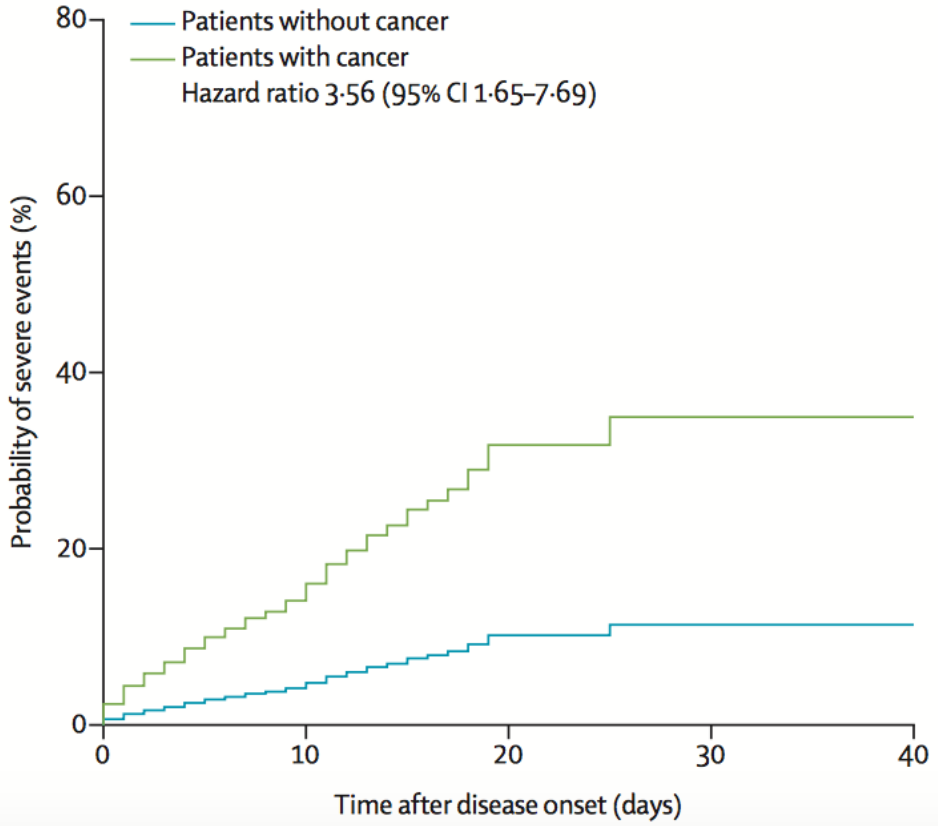
- Incidence of COVID-19 in patients with cancer is higher in patients with a recent diagnosis (even after adjusting for older age and other comorbidities)[1]
  - The risk appears to be highest for those with hematologic and lung cancers[1]
- Most available evidence suggests that incidence rates of COVID-19 among cancer patients receiving active treatment are still fairly low (1%–4%)[2–4]

1. Wang Q *et al*. *JAMA Oncol* 2021; 7 (2): 220–227. 2. Yu J *et al*. *JAMA Oncol* 2020; 6 (7): 1108–1110. 3. Bertuzzi AF *et al*. *Cancers (Basel)* 2020; 12 (9): 2352. 4. Rogado J *et al*. *Clin Transl Oncol* 2020; 22 (12): 2364–2368.

Cancer patients are at a greater risk from COVID-19

- Case fatality rate* higher in patients with cancer[1]
  - 2.3% in all patients
  - 5.6% in patients with cancer
- Significantly higher rate of intubations in cancer patients aged 66–80 years[2]
- Higher risk of severe events if surgery or chemotherapy are performed within the month preceding SARS-CoV-2 diagnosis[3]

Rate of severe events† in 2,007 COVID-19 cases from 575 hospitals in China, including 18 cases with a history of cancer[3]

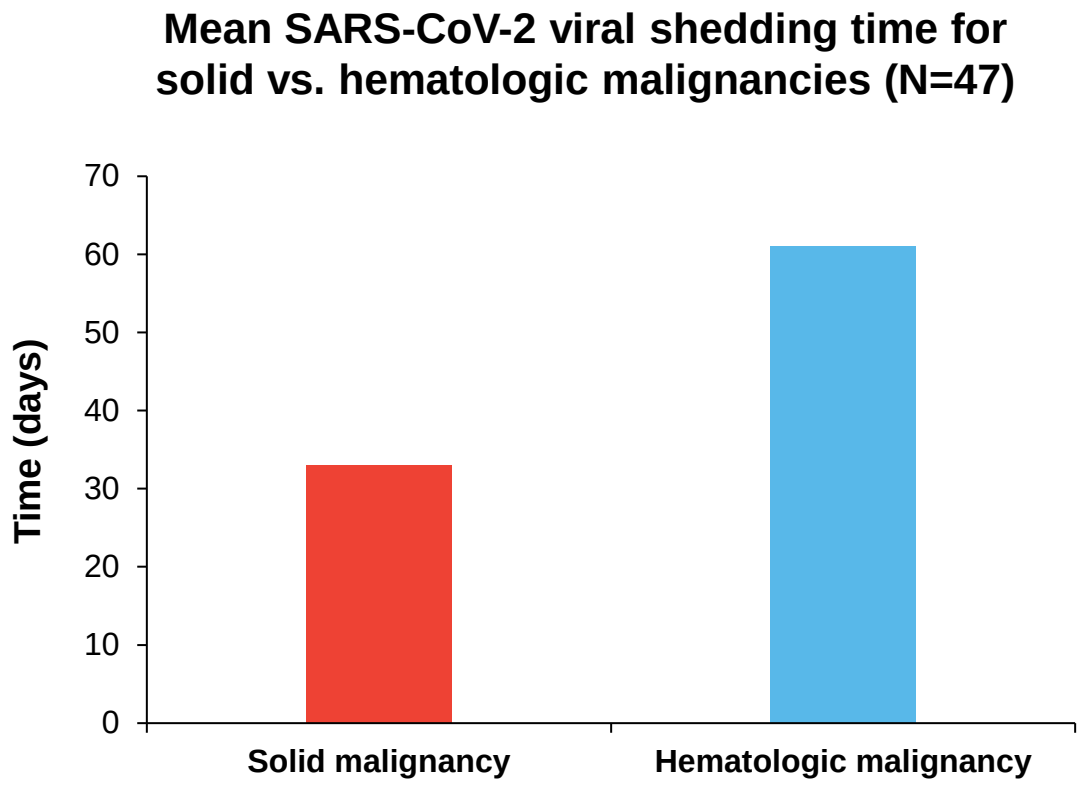


*Number of deaths / SARS-CoV-2-positive patients. †Severe event defined as admission to an intensive care unit requiring invasive ventilation, or death.
CI, confidence interval.

1. Wu Z *et al*. *JAMA* 2020; 323 (13): 1239–1242. 2. Miyashita H *et al*. *Ann Oncol* 2020; 31 (8): 1088–1089. 3. Liang W *et al*. *Lancet Oncol* 2020; 21(3): 335–337.

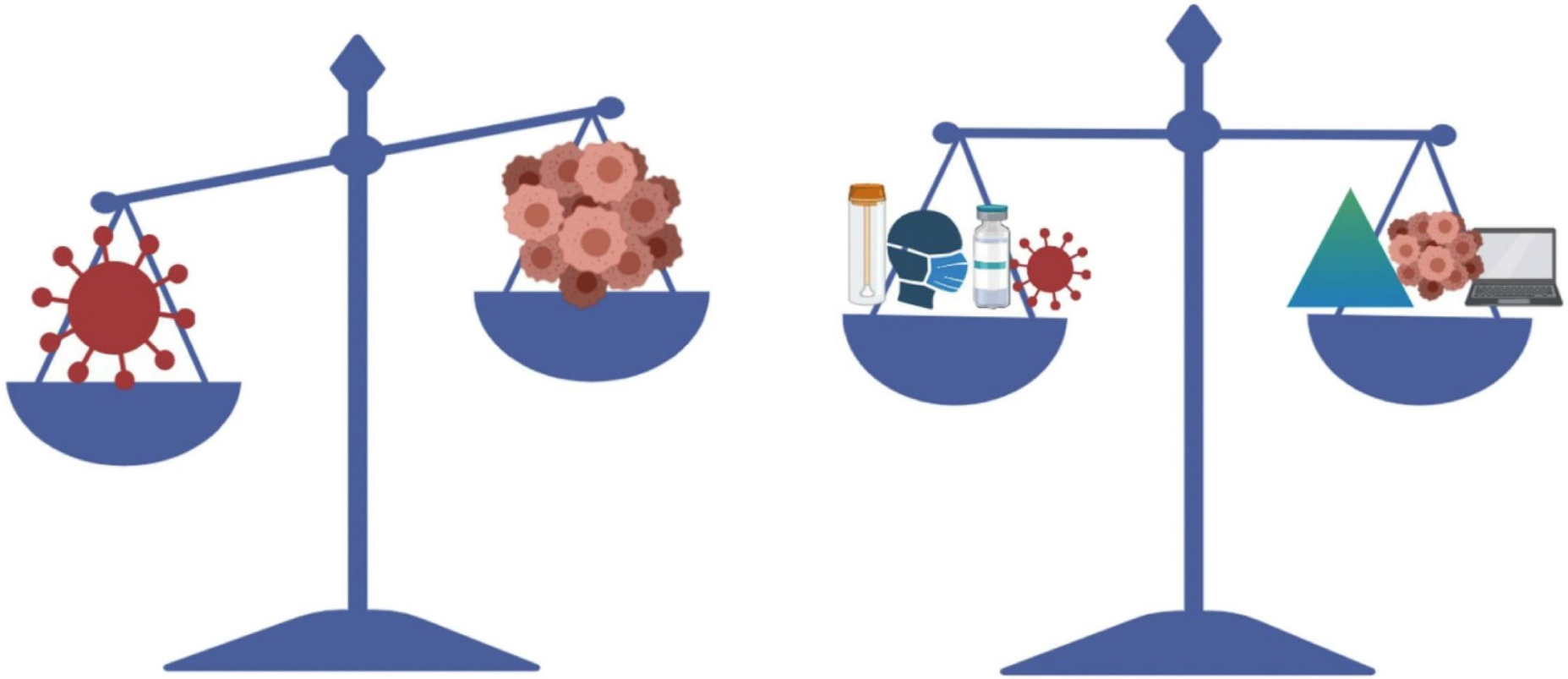
Hematologic cancer is associated with persistent COVID-19

- Patients with lymphoma and COVID-19 infection are more likely than patients without lymphoma to have persistent COVID-19



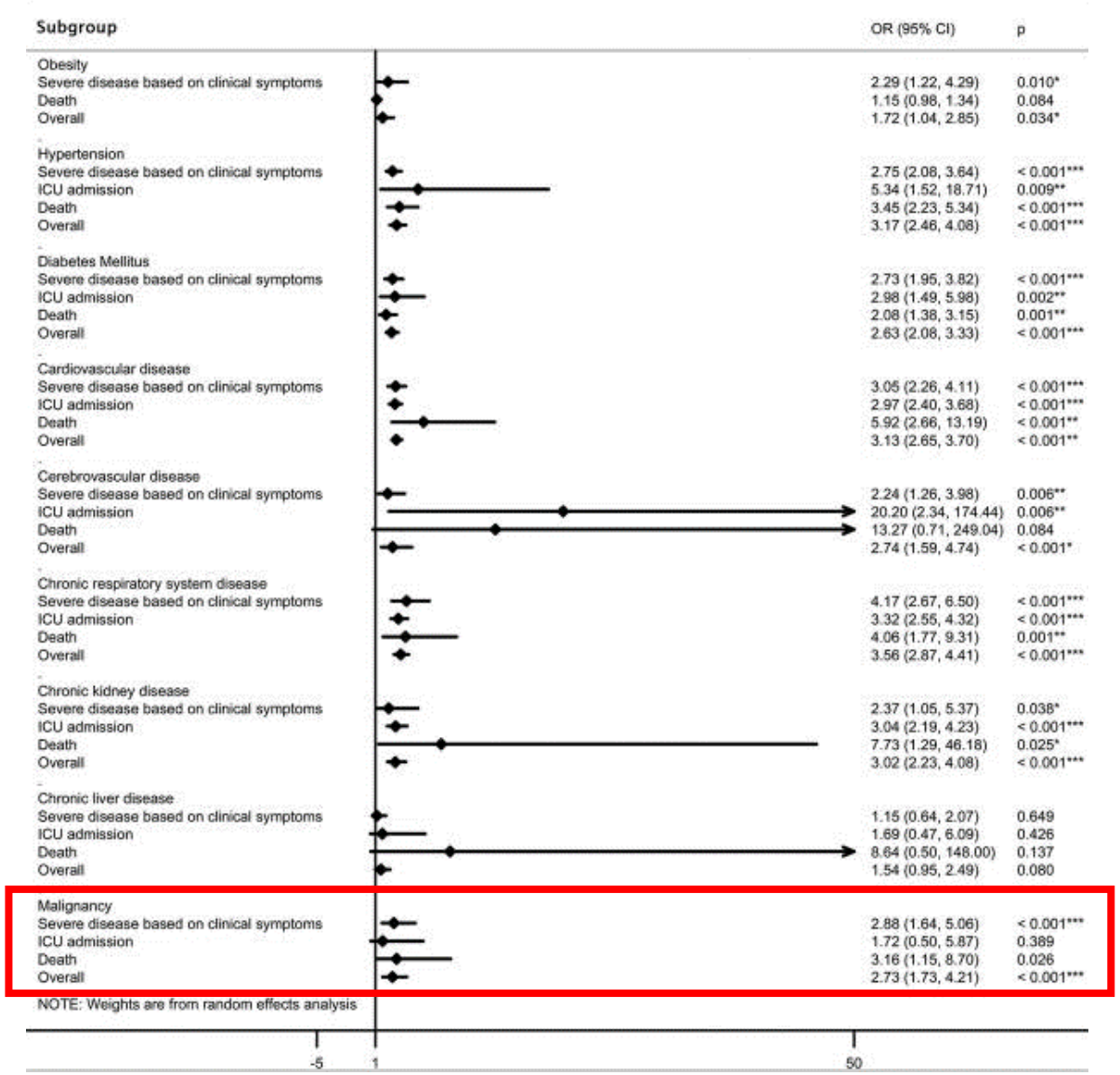
Thakkar A *et al*. *Nat Cancer* 2021; 2: 392–399.

Is COVID-19 more severe in patients with malignancy?



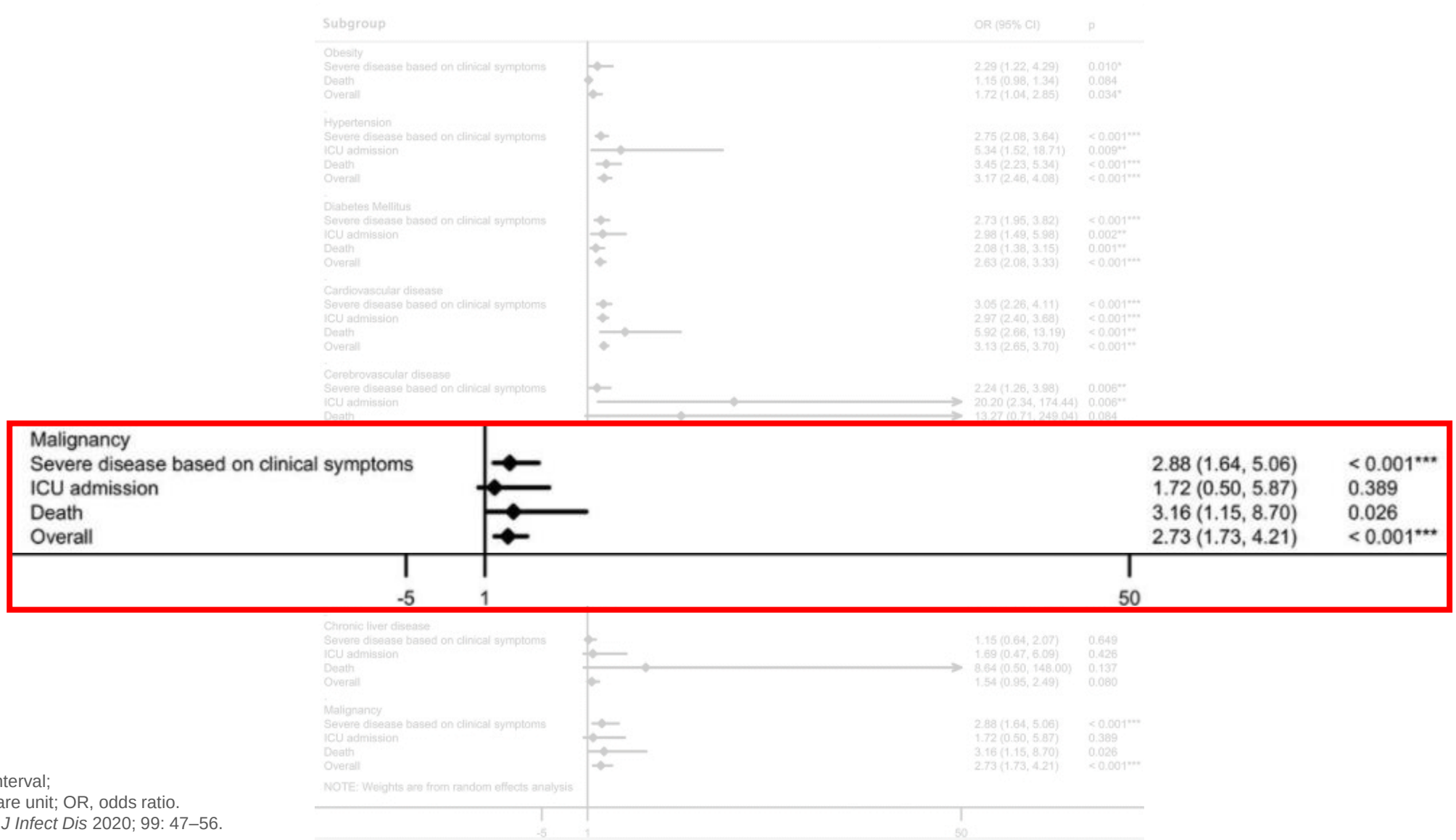
Alhalabi O *et al*. *Trends Cancer* 2020; 6 (7): 533–535.

Comorbidities and risk of severe COVID-19 outcomes



CI, confidence interval;
ICU, intensive care unit; OR, odds ratio.
Zhou Y *et al*. *Int J Infect Dis* 2020; 99: 47–56.

Comorbidities and risk of severe COVID-19 outcomes



CI, confidence interval;
ICU, intensive care unit; OR, odds ratio.
Zhou Y *et al*. *Int J Infect Dis* 2020; 99: 47–56.

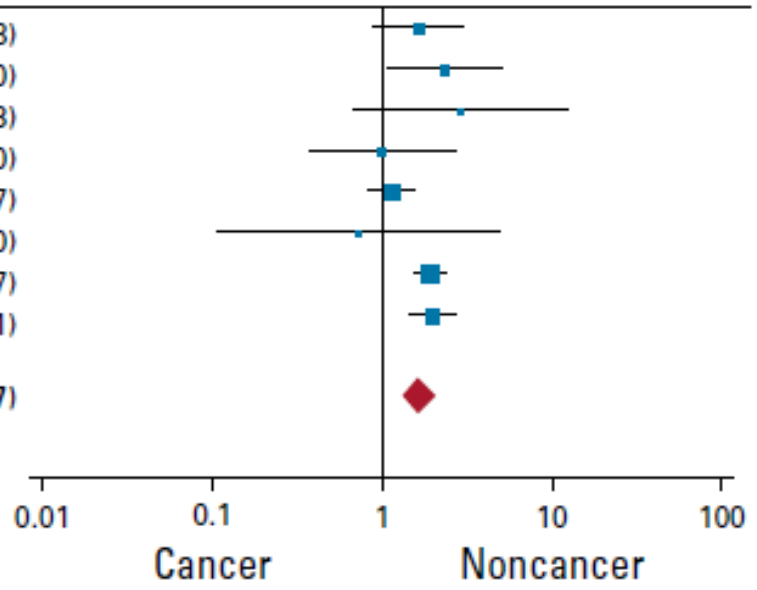
Mortality in patients with cancer and COVID-19

- A meta-analysis of outcomes in patients with COVID-19 included 32 international studies
  - 46,499 patients (1,776 with cancer) with COVID-19 from Asia, Europe, and the USA

	Cancer		Noncancer			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight (%)	IV, Random (95% CI)
Benelli G et al[12]	9	33	63	378	10.3	1.64 (0.90 to 2.98)
Chinese CDC[8]	6	107	498	20,705	6.8	2.33 (1.07 to 5.10)
Goyal P et al[18]	2	23	11	370	2.3	2.92 (0.69 to 12.43)
Joharatnam-Hogan N et al[22]	6	26	6	26	4.5	1.00 (0.37 to 2.70)
Miyashita H et al[24]	37	334	518	5,354	22.5	1.14 (0.84 to 1.57)
Nikpouraghdam M et al[26]	1	17	238	2,947	1.3	0.73 (0.11 to 4.90)
Rentsch CT et al[28]	88	587	334	4,247	29.3	1.91 (1.53 to 2.37)
Rossi PG et al[29]	44	301	173	2,352	22.9	1.99 (1.46 to 2.71)
Total (95% CI)		**1,428**		**36,379**	**100.0**	**1.66 (1.33 to 2.07)**
Total events	193		1,841			

Heterogeneity: $\tau^2 = 0.03$; $\chi^2 = 11.14$, df = 7 ($P = .13$); $I^2 = 37\%$

Test for overall effect: $Z = 4.44$ ($P < .00001$)



CI, confidence interval; IV, inverse variance.

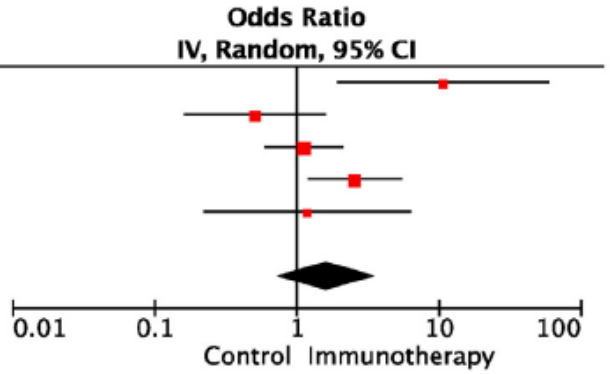
Giannakoulis VG *et al*. *JCO Glob Oncol* 2020; 6: 799–808.

Risk of severe COVID-19 outcomes by cancer treatment

Risk of severe COVID-19 with immunotherapy

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Dai et al.	2.3618	0.8749	13.1%	10.61 [1.91, 58.94]
Garassino et al.	−0.6812	0.5874	19.8%	0.51 [0.16, 1.60]
Pinato et al.	0.1133	0.327	27.8%	1.12 [0.59, 2.13]
Robilotti et al.	0.9282	0.3891	25.9%	2.53 [1.18, 5.42]
Zhang H et al.	0.1655	0.857	13.4%	1.18 [0.22, 6.33]
Total (95% CI)			**100.0%**	**1.60 [0.72, 3.52]**

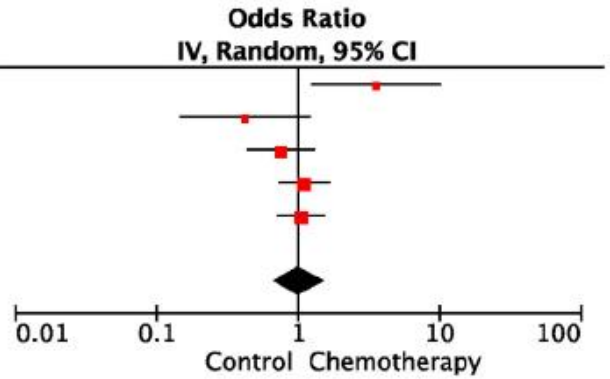
Heterogeneity: $Tau^2 = 0.48$; $Chi^2 = 11.10$, df = 4 (P = 0.03); $I^2 = 64\%$
Test for overall effect: Z = 1.16 (P = 0.25)



Risk of severe COVID-19 with chemotherapy

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Dai et al.	1.2641	0.5394	10.9%	3.54 [1.23, 10.19]
Garassino et al.	−0.8699	0.5449	10.7%	0.42 [0.14, 1.22]
Kuderer et al.	−0.2877	0.2838	22.6%	0.75 [0.43, 1.31]
Pinato et al.	0.0953	0.2161	27.4%	1.10 [0.72, 1.68]
Robilotti et al.	0.0392	0.202	28.4%	1.04 [0.70, 1.55]
Total (95% CI)			**100.0%**	**1.02 [0.67, 1.53]**

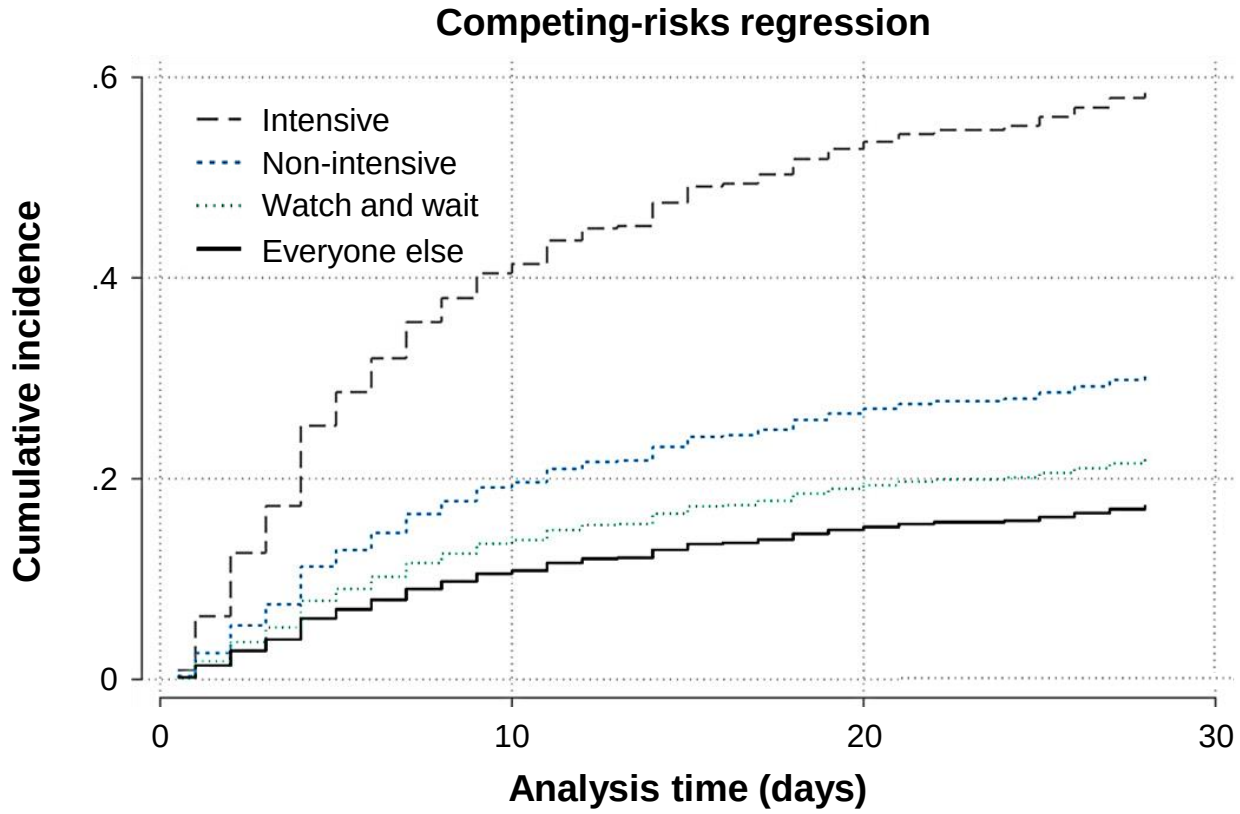
Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 9.29$, df = 4 (P = 0.05); $I^2 = 57\%$
Test for overall effect: Z = 0.08 (P = 0.94)



CI, confidence interval; IV, inverse variance.
Yekedüz E *et al*. *Eur J Cancer* 2020; 141: 92–104.

Cancer treatments may increase mortality

Mortality for patients with hematologic cancers hospitalized with COVID-19 by treatment type

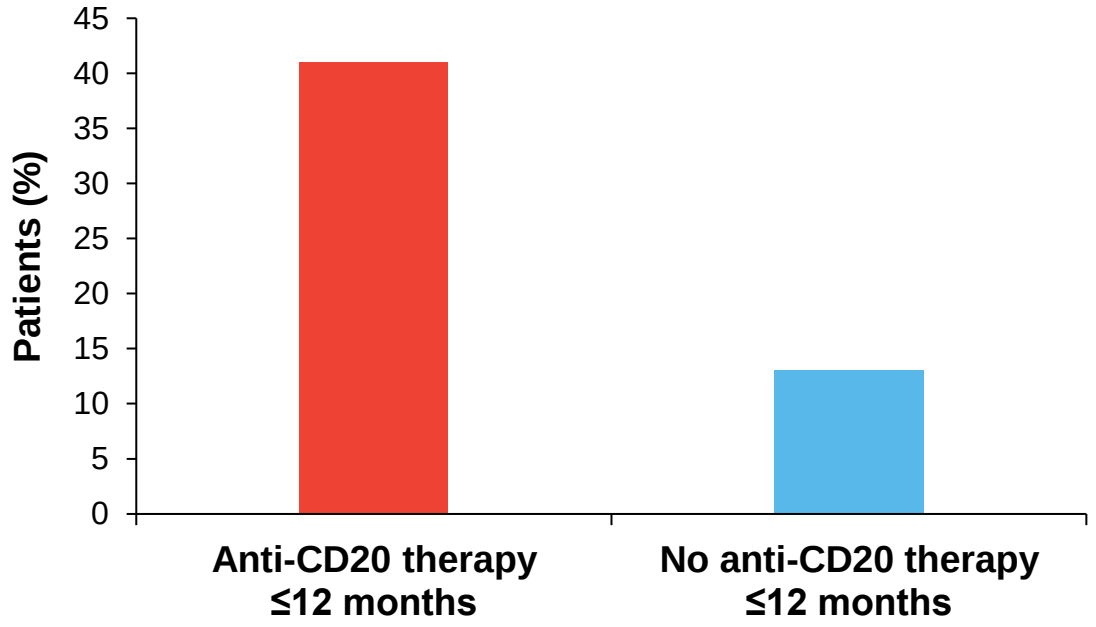


Shah V *et al*. *Br J Haematol* 2020; 190 (5): e279-e282.

Anti-CD20 therapy is associated with poor outcomes

- In a study of 111 patients with lymphoma hospitalized with COVID-19, anti-CD20 therapy within 12 months was associated with:[1]
  - Decreased overall survival (HR: 2.13; 95% CI: 1.03–4.44)
  - Prolonged hospital stay (HR: 1.97; 95% CI: 1.24–3.13)

Patients with lymphoma hospitalized >30 days after admission with COVID-19 according to anti-CD20 therapy status[2]

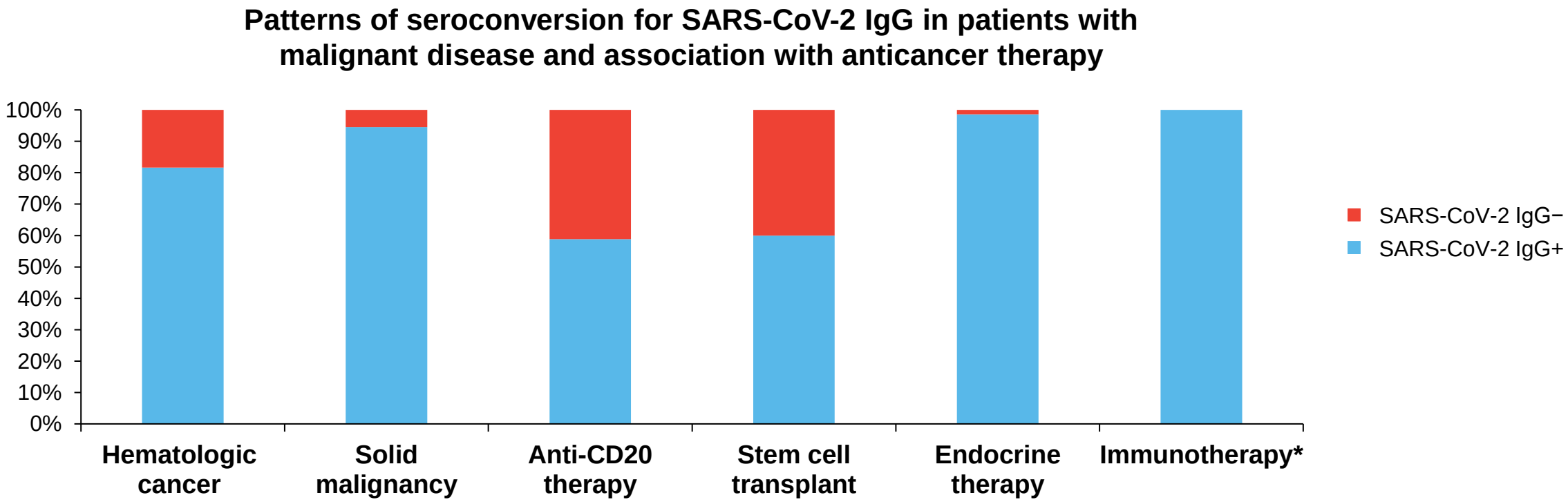


CD, cluster of differentiation; CI, confidence interval; HR, hazard ratio.

1. Lamure S *et al*. *Clin Cancer Res* 2021; 27 (6): Abstract S09-02. 2. Anti-CD20 monoclonal antibodies and risk of severe COVID-19 infection and death in patients with lymphoma. Available at: https://ascopost.com/issues/march-10-2021/anti-cd20-monoclonal-antibodies-and-risk-of-severe-covid-19-infection-and-death-in-patients-with-lymphoma/. Accessed July 2021.

Anti-CD20 therapy reduces SARS-CoV-2 antibody production

- Patients treated with anti-CD20 therapy are less likely to develop specific antibodies against SARS-CoV-2

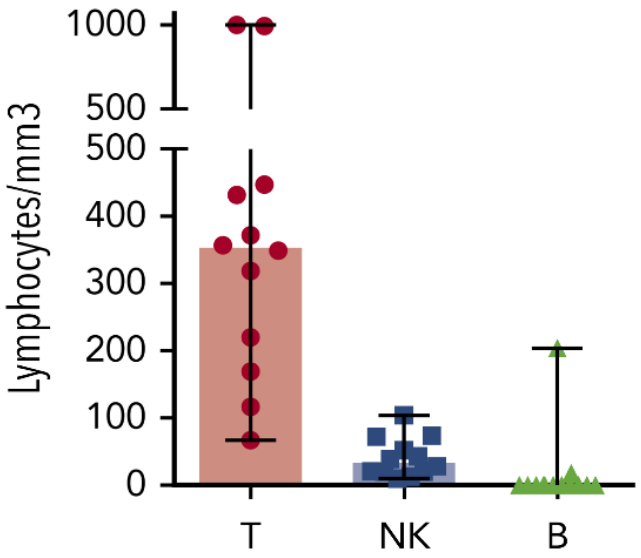


*Agents that stimulate the immune system, including anti-PD-1/PD-L1 monoclonal antibodies.
CD, cluster of differentiation; IgG, immunoglobulin G; PD-1, programmed cell death protein-1; PD-L1, programmed death-ligand 1.
Thakkar A *et al*. *Nat Cancer* 2021; 2: 392–399.

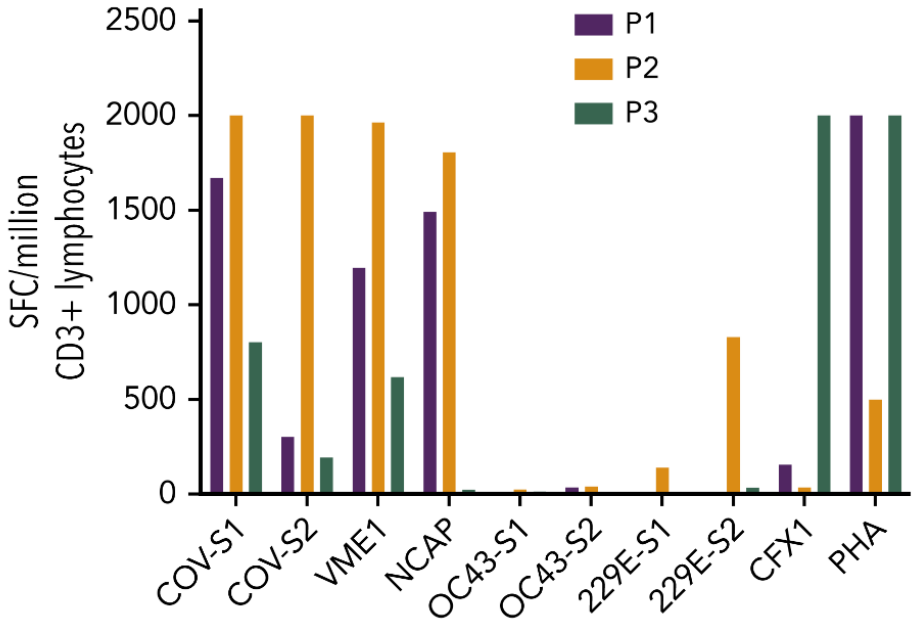
Anti-CD20–treated patients have a cellular immune response

- Immune and vaccine responses may occur through a cellular or T-cell-mediated response, even in patients treated with anti-CD20 therapy

Lymphocyte immunophenotyping in anti-CD20–treated patients with protracted COVID-19 (n=12)



SARS-CoV-2–specific T cells in anti-CD20–treated patients (P) with protracted COVID-19 (n=3)



"… specific T-cell responses to SARS-CoV-2 are not sufficient to control viral infection in the absence of neutralizing antibodies"

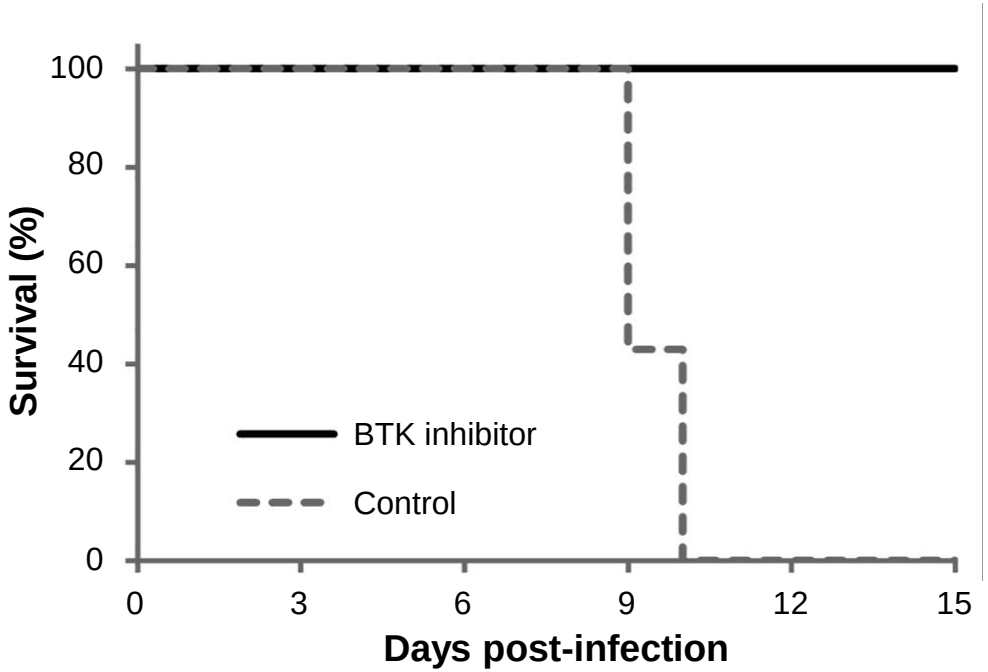
B, B cell; CD, cluster of differentiation; CFX1, positive control peptide pool; COV-S1, spike glycoprotein S1; COV-S2, spike glycoprotein S2; NCAP, nucleoprotein; NK, natural killer cell; PHA, phytohemagglutinin A (positive control mitogen); SFC, spot-forming cells; T, T cell; VME1, membrane protein.

Hueso T *et al*. *Blood* 2020; 136 (20): 2290–2295.

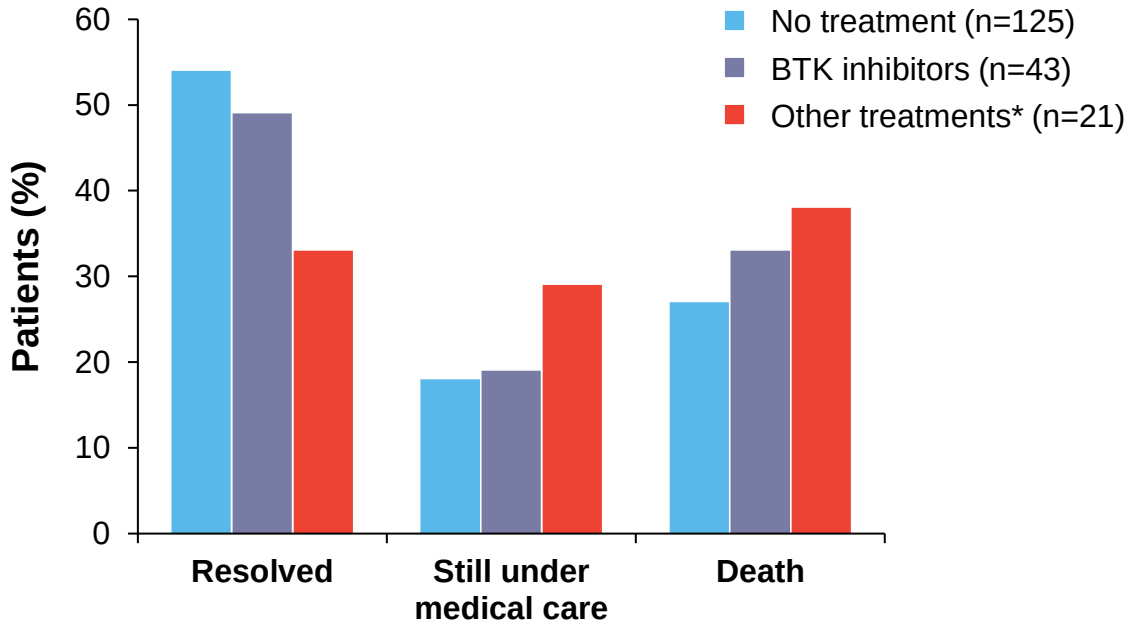
BTK inhibitors have been associated with protective effects

- Laboratory studies and limited real-world data suggest BTK inhibitors may have a protective effect against respiratory viruses and COVID-19

Survival in mice injected with influenza A virus with/without BTK inhibitors (N=17)[1]



Outcomes for patients with chronic lymphocytic leukemia and COVID-19 (N=219)[2]



*Other treatments included venetoclax-based regimen; chlorambucil +/− obinutuzumab; idelalisib; and other chemotherapies and/or steroids.
BTK, Bruton's tyrosine kinase.

1. Florence JM *et al*. *Am J Physiol Lung Cell Mol Physiol* 2018; 315 (1): L52–L58. 2. Scarfò L *et al*. *Leukemia* 2020; 34: 2354–2363 – supplementary information.

BTK inhibitors: Caution necessary

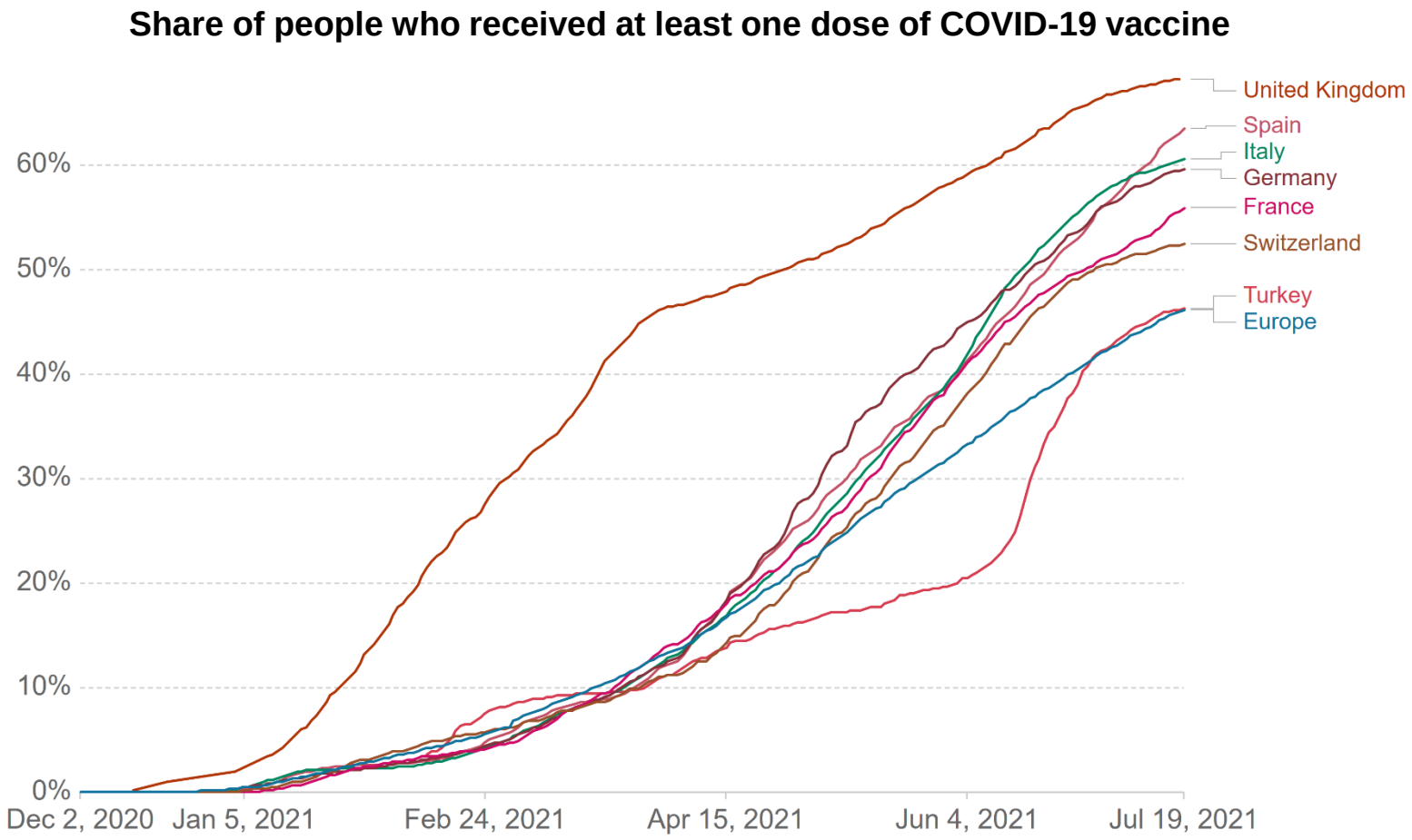
CALAVI did not meet the primary endpoint of increasing the proportion of patients who remained alive and free of respiratory failure

The CALAVI Phase II trials for *Calquence* (acalabrutinib) in patients hospitalised with respiratory symptoms of COVID-19 did not meet the primary efficacy endpoint. The addition of *Calquence* to best supportive care (BSC) did not increase the proportion of patients who remained alive and free of respiratory failure. No new safety signal for *Calquence* was observed in the trials.

BTK, Bruton's tyrosine kinase.

AstraZeneca press release; November 2020. Available at: https://www.astrazeneca.com/media-centre/press-releases/2020/update-on-calavi-phase-ii-trials-for-calquence-in-patients-hospitalised-with-respiratory-symptoms-of-covid-19.html. Accessed July 2021.

The COVID-19 pandemic in Europe: Vaccination programs



Coronavirus (COVID-19) vaccinations. Available at: https://ourworldindata.org/covid-vaccinations. Accessed July 2021.

mRNA vaccines are extremely efficacious against SARS-CoV-2

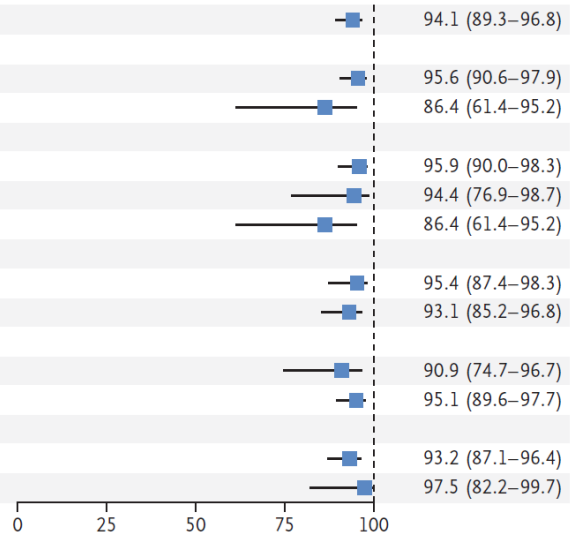
BNT162b2[1]

Table 2. Vaccine Efficacy against Covid-19 at Least 7 days after the Second Dose.*

Efficacy End Point	BNT162b2		Placebo		Vaccine Efficacy, % (95% Credible Interval)‡	Posterior Probability (Vaccine Efficacy >30%)§
	No. of Cases	Surveillance Time (n)†	No. of Cases	Surveillance Time (n)†		
		(N=18,198)		(N=18,325)		
Covid-19 occurrence at least 7 days after the second dose in participants without evidence of infection	8	2.214 (17,411)	162	2.222 (17,511)	95.0 (90.3–97.6)	>0.9999
		(N=19,965)		(N=20,172)		
Covid-19 occurrence at least 7 days after the second dose in participants with and those without evidence of infection	9	2.332 (18,559)	169	2.345 (18,708)	94.6 (89.9–97.3)	>0.9999

mRNA-1273[2]

Subgroup	Placebo (N=14,073)	mRNA-1273 (N=14,134)	Vaccine Efficacy (95% CI)
	no. of events/total no.		
All patients	185/14,073	11/14,134	94.1 (89.3–96.8)
Age			
≥18 to <65 yr	156/10,521	7/10,551	95.6 (90.6–97.9)
≥65 yr	29/3552	4/3583	86.4 (61.4–95.2)
Age, risk for severe Covid-19			
18 to <65 yr, not at risk	121/8403	5/8396	95.9 (90.0–98.3)
18 to <65 yr, at risk	35/2118	2/2155	94.4 (76.9–98.7)
≥65 yr	29/3552	4/3583	86.4 (61.4–95.2)
Sex			
Male	87/7462	4/7366	95.4 (87.4–98.3)
Female	98/6611	7/6768	93.1 (85.2–96.8)
At risk for severe Covid-19			
Yes	43/3167	4/3206	90.9 (74.7–96.7)
No	142/10,906	7/10,928	95.1 (89.6–97.7)
Race and ethnic group			
White	144/8916	10/9023	93.2 (87.1–96.4)
Communities of color	41/5132	1/5088	97.5 (82.2–99.7)



- ChAdOx1 nCoV-19 (AZD1222)[3] and Ad26.COV2.S[4] vaccines are also efficacious

CI, confidence interval.

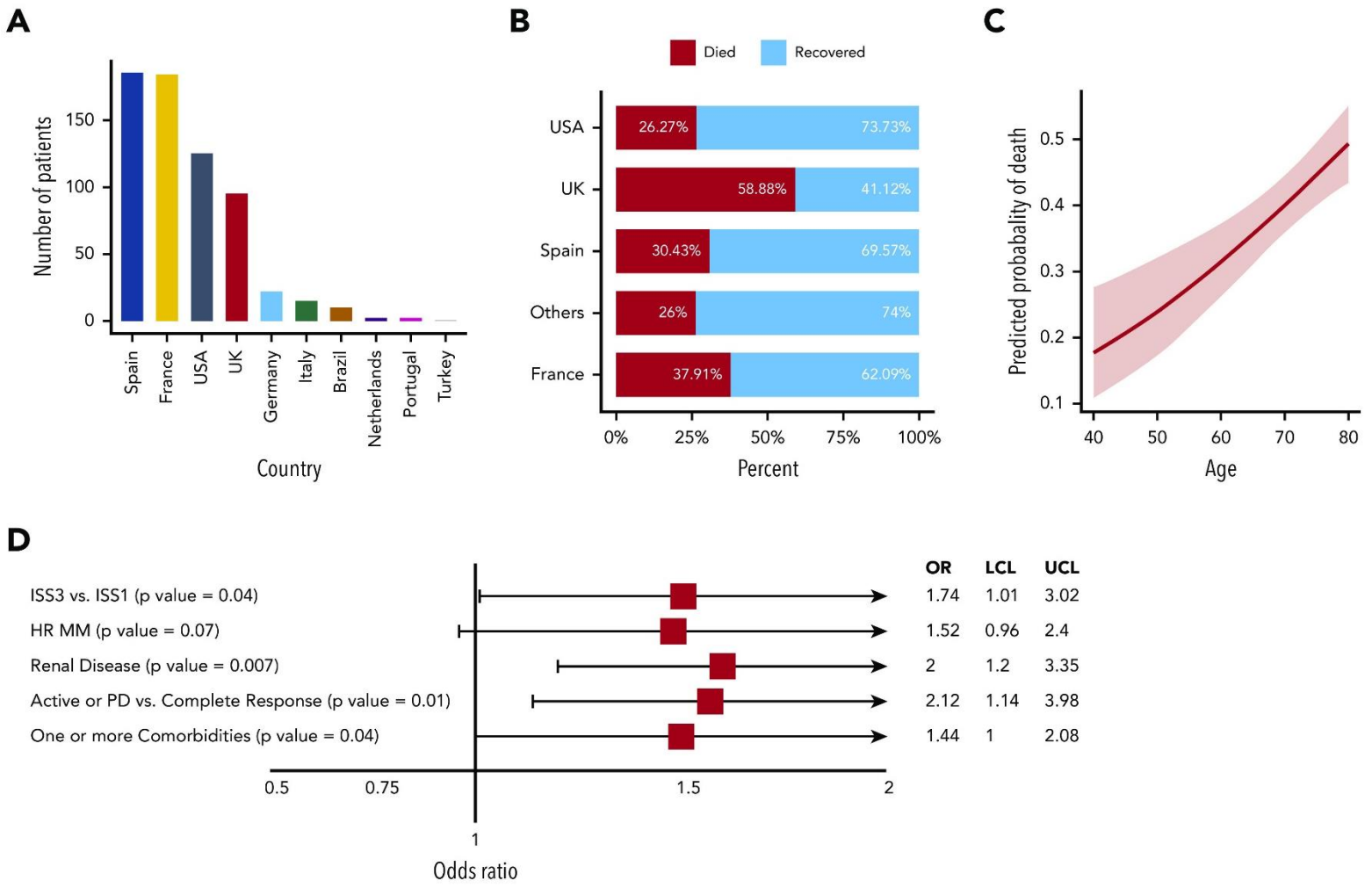
1. Polack FP *et al*. *N Engl J Med* 2020; 383 (27): 2603–2615. 2. Baden LR *et al*. *N Engl J Med* 2021; 384 (5): 403–416.
3. Voysey M *et al*. *Lancet* 2021; 397 (10277): 881–891. 4. Sadoff J *et al*. *N Engl J Med* 2021; 384 (19): 1824–1835.

COVID-19 vaccines in cancer patients

- It seems reasonable to administer COVID-19 vaccination before cytotoxic chemotherapy or chemoradiation
- Delay the second dose post the cytopenia nadir and before the next cycle of chemotherapy, in order to increase immunogenicity of the vaccine
- The same principle should be applied, if feasible, to cancer patients receiving lympholytic agents, such as monoclonal antibodies (e.g. rituximab) or chronic corticosteroids
  - Note the significant intrapatient variability in the kinetics of lymphocyte recovery[1]
- Households have emerged as a significant venue for transmission of SARS-CoV-2[2]
  - COVID-19 vaccination for co-habitees and/or caregivers is also of extreme importance

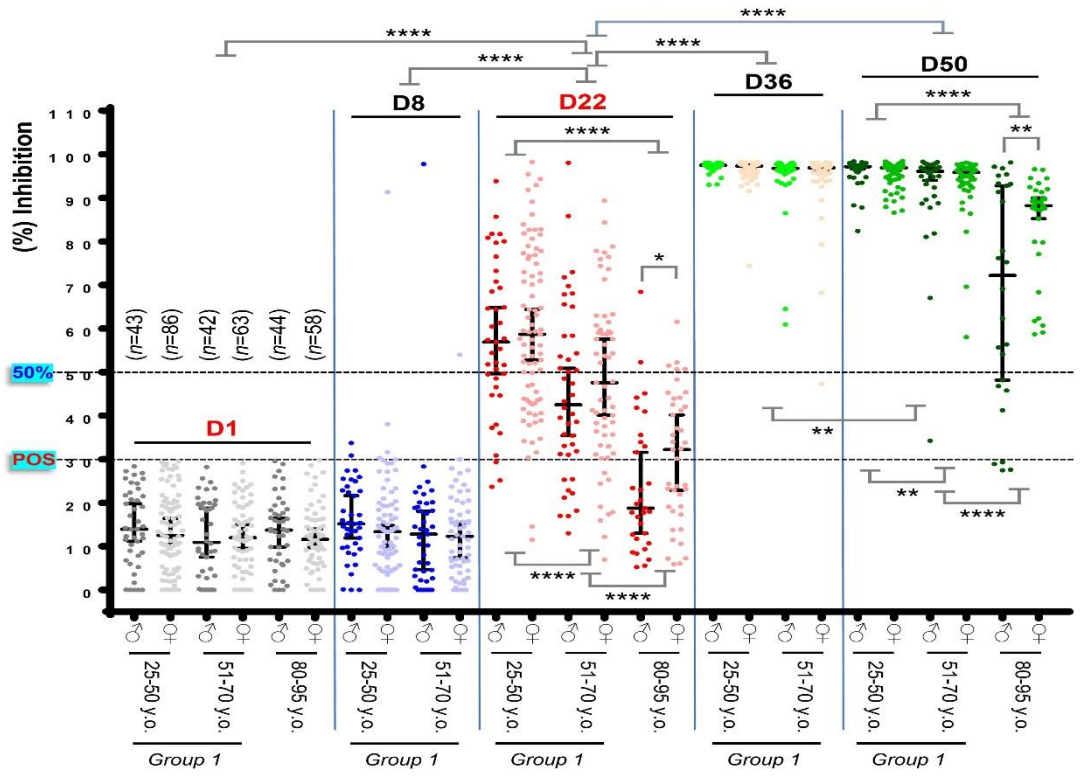
1. Pavletic ZS *et al*. *Bone Marrow Transplant* 1998; 21: 33–41. 2. Bi Q *et al*. *Nat Commun* 2021; 12 (1): 3643.

COVID-19 and myeloma patients: First results of the IMS study



HR, high risk; IMS, International Myeloma Society; ISS, International Staging System; LCL, lower confidence level; MM, multiple myeloma; OR, odds ratio; PD, progressive disease; UCL, upper confidence level.
Chari A *et al*. *Blood* 2020; 136 (26): 3033–3040.

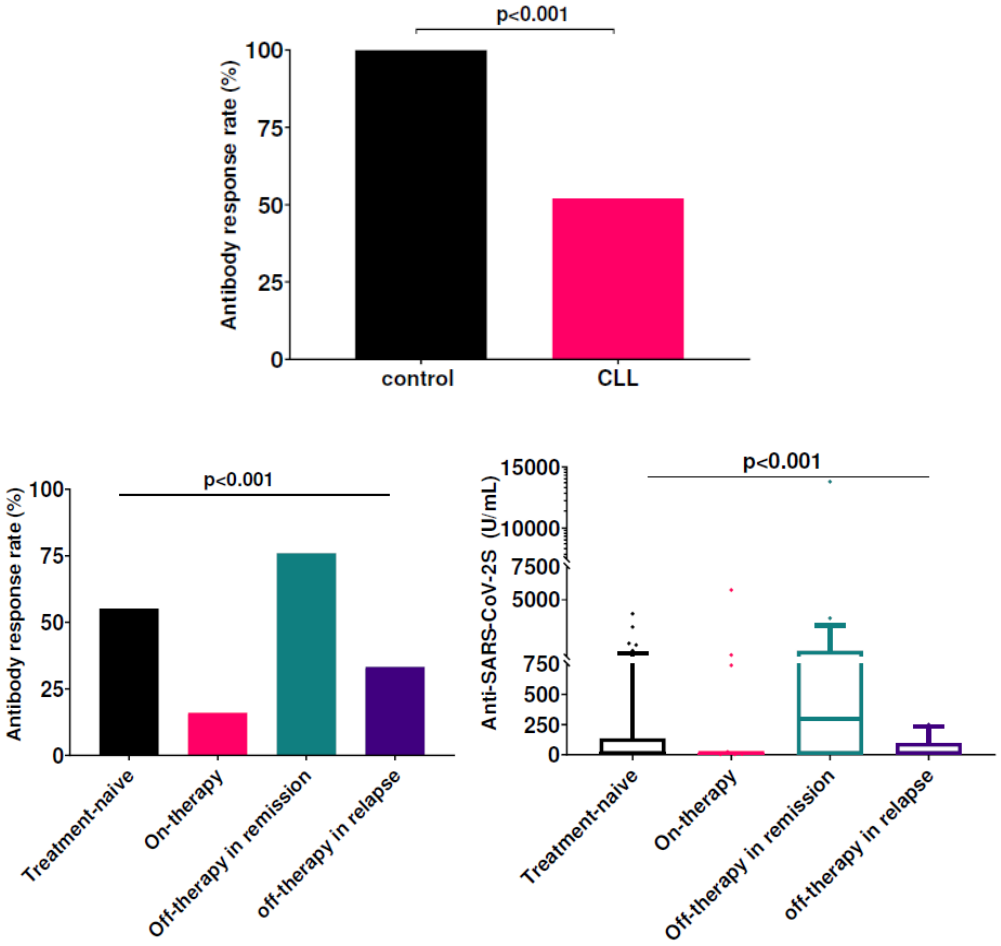
Age- and gender-dependent rates of NAb development

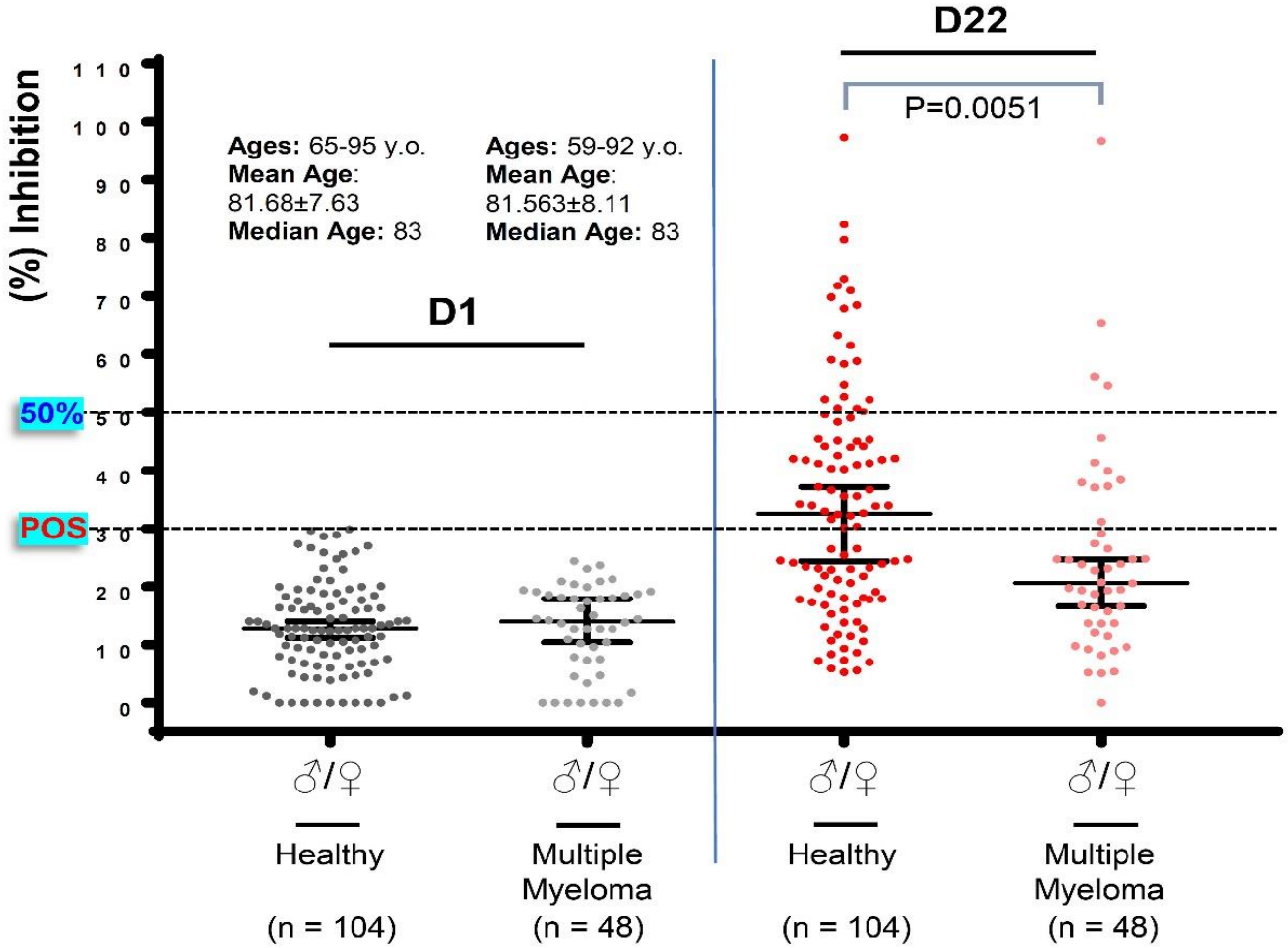


- 255 health workers
  - 92 male, 163 female
  - Median age: 49 years (range: 25–70)
- 112 volunteered octogenarians
  - 51 male, 61 female
  - Median age: 85 years (range: 80–95)

D, Day; NAb, neutralizing antibody; POS, positivity threshold; y.o., years old.
Terpos E *et al*. *Am J Hematol* 2021; 96 (7): E257–E259.

Antibody response is low after vaccination in patients with hematologic malignancies: First results in CLL and MM

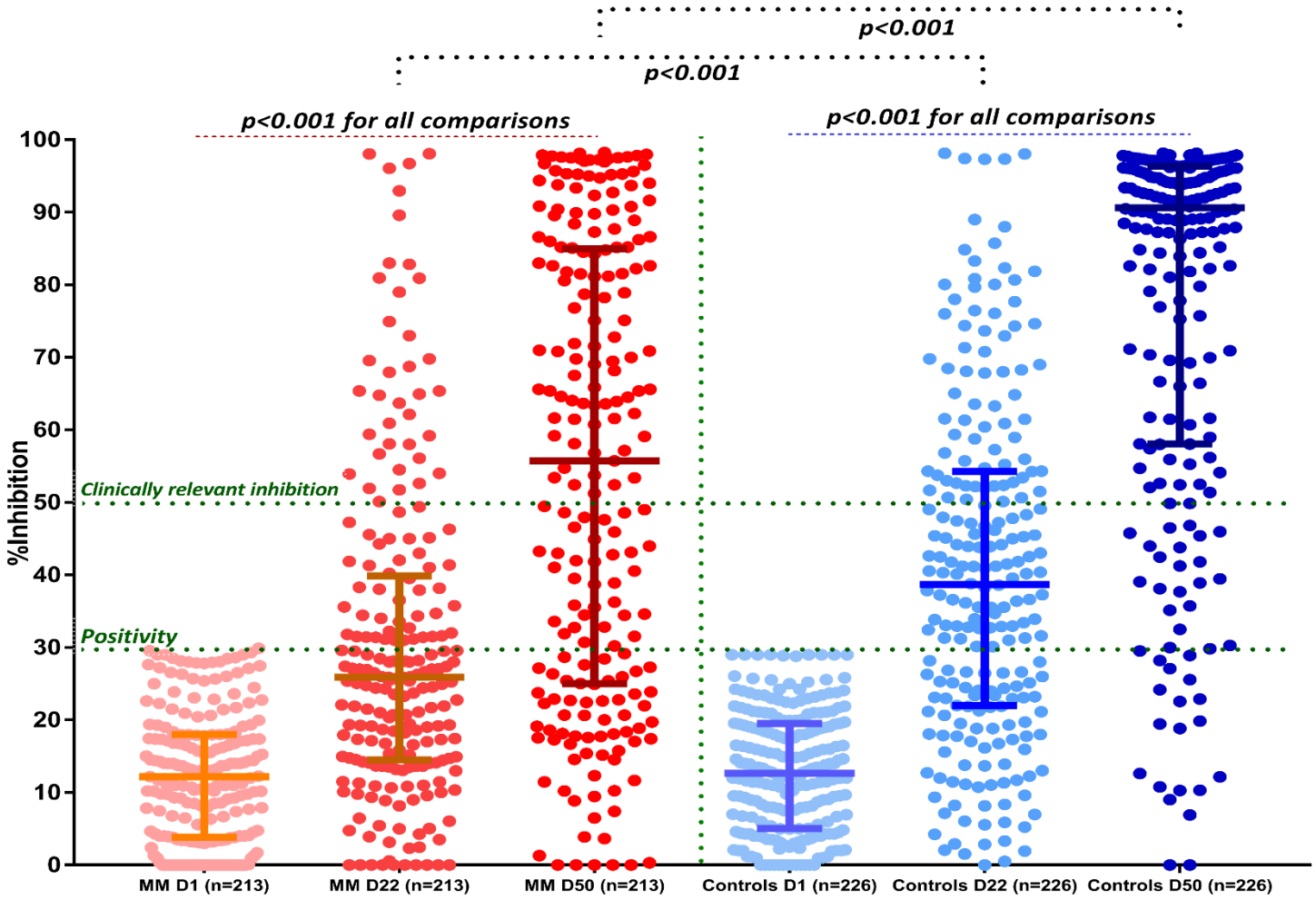




CLL, chronic lymphocytic leukemia; D, Day; MM, multiple myeloma; POS, positivity threshold; U, units; y.o., years old.

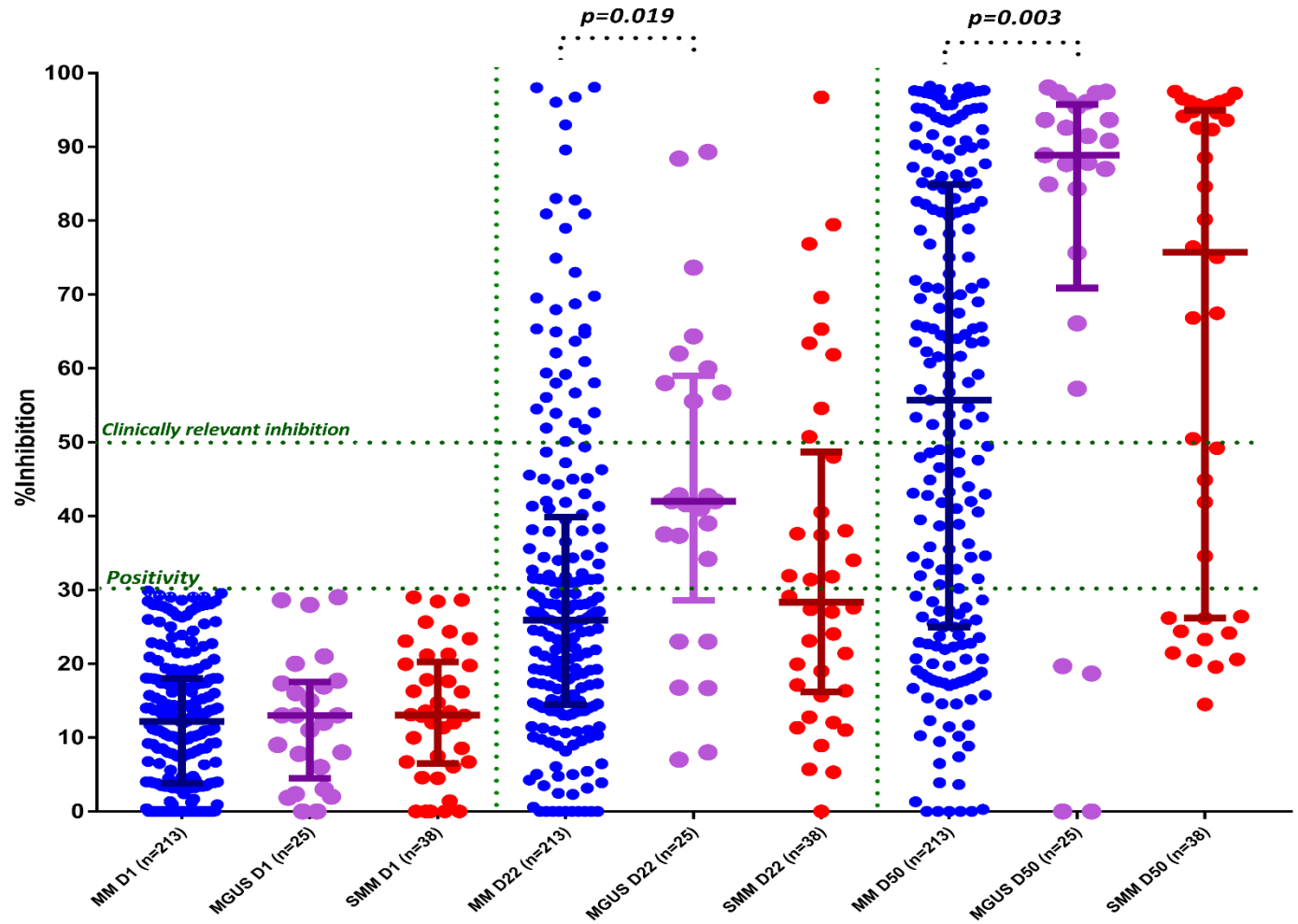
1. Herishanu Y *et al*. *Blood* 2021; 137 (23): 3165–3173. 2. Terpos E *et al*. *Blood* 2021: 137 (26): 3674–3676.

Lower antibody response in patients with MM vs. controls



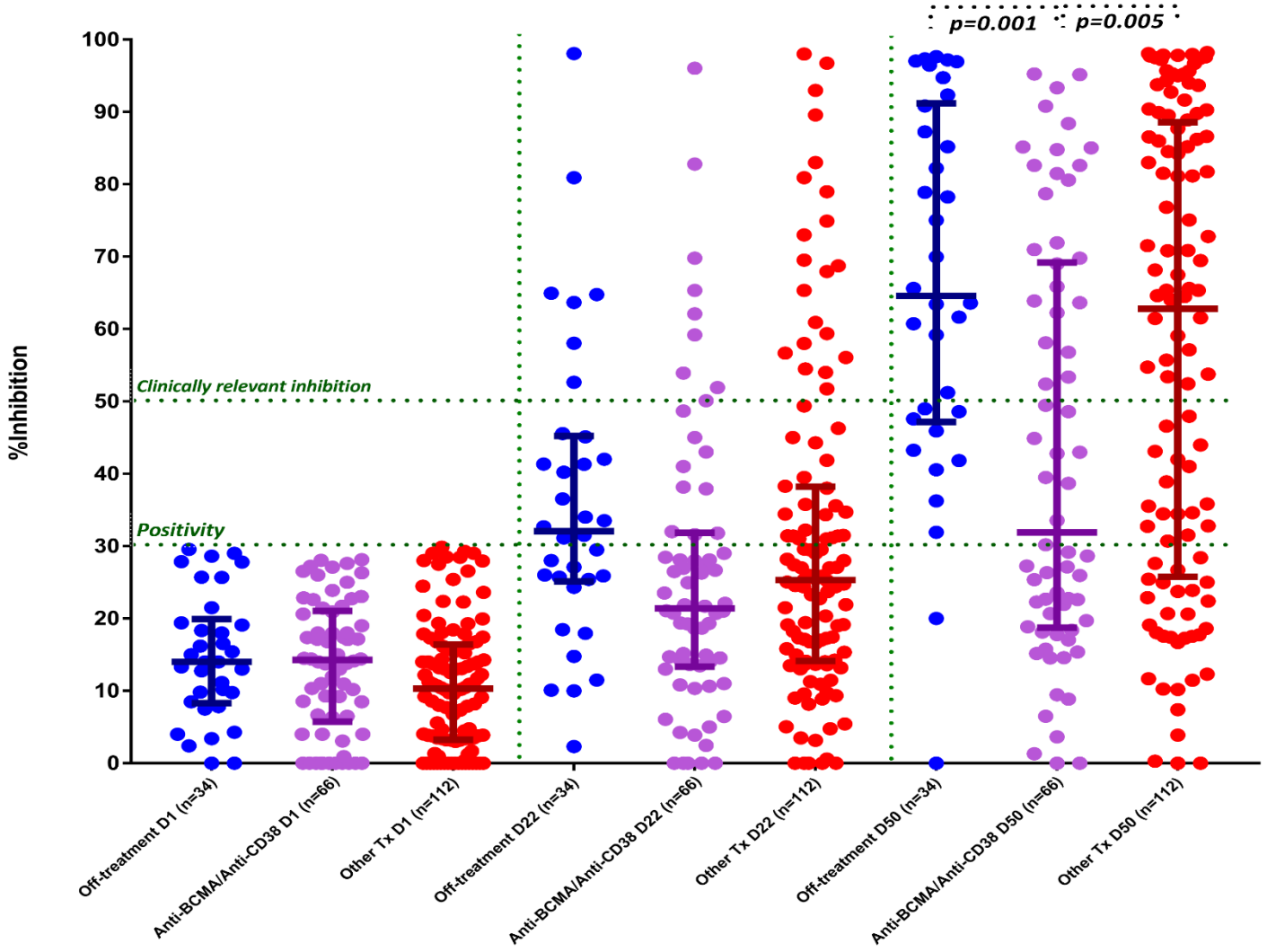
D, Day; MM, multiple myeloma.
Terpos E *et al*. *Blood Cancer J* 2021 (submitted).

NAbs with MM vs. SMM and MGUS



D, Day; MGUS, monoclonal gammopathy of undetermined significance; MM, multiple myeloma; NAb, neutralizing antibody; SMM, smoldering multiple myeloma.
Terpos E *et al*. *Blood Cancer J* 2021 (submitted).

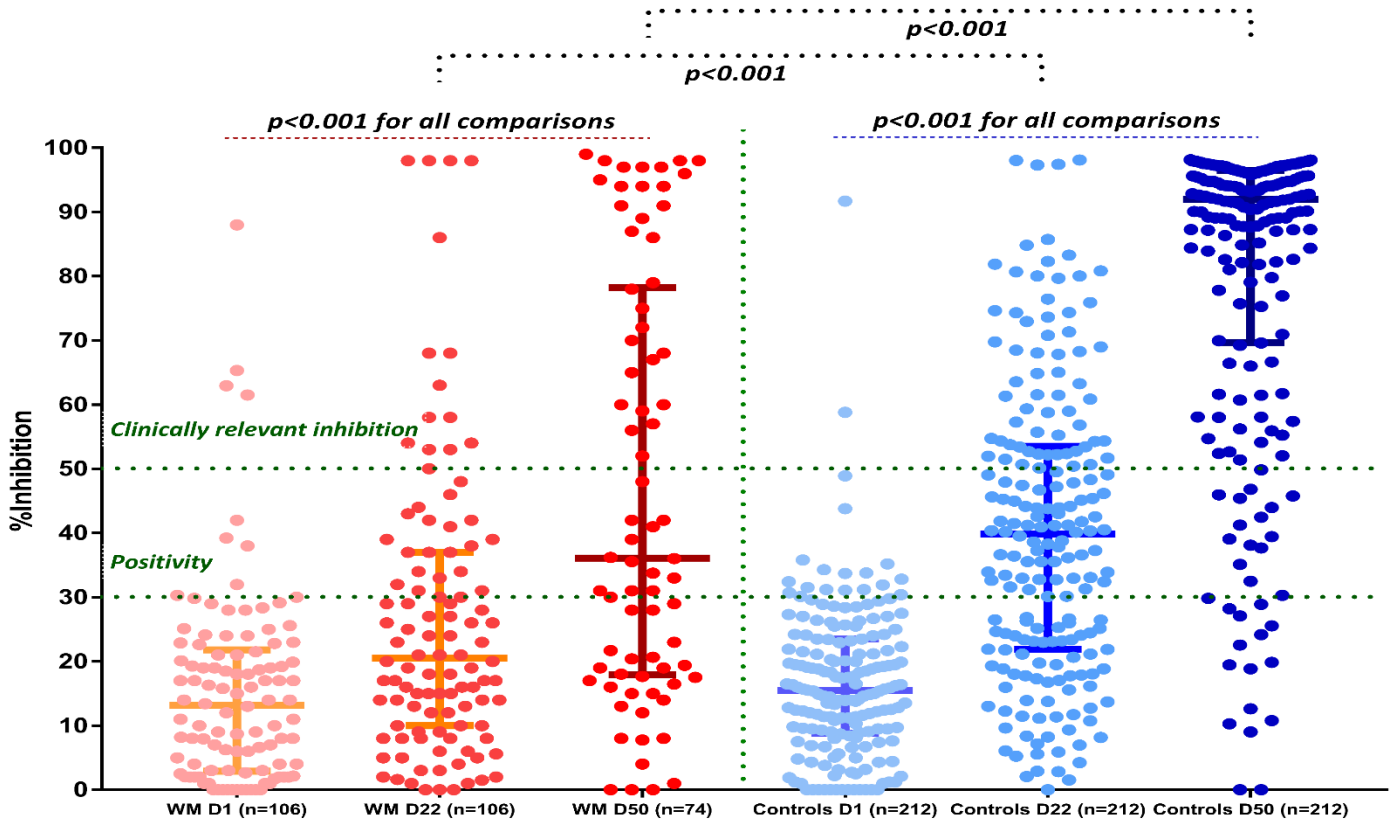
Antibody response in MM patients: Correlation with treatment



BCMA, B-cell maturation antigen; CD, cluster of differentiation; D, Day; MM, multiple myeloma; Tx, treatment.
Terpos E *et al*. *Blood Cancer J* 2021 (submitted).

Lower antibody response in patients with WM vs. controls

- Vaccination with either:
  - 2 doses of BNT162b2, or
  - 1 dose of AZD1222
- Active treatment with rituximab or BTK inhibitors was associated with a suboptimal antibody response
- Patients with WM have a low humoral response following COVID-19 vaccination
  - Underlines the need for timely vaccination, ideally during a treatment-free period, and for continuous vigilance on infection control measures



BTK, Bruton's tyrosine kinase; D, Day; WM, Waldenström's macroglobulinemia.
Gavriatopoulou M *et al*. *Blood Adv* 2021 (accepted for publication).

Summary

- BNT162b2 mRNA and AZD1222 vaccines are effective in producing high neutralizing antibody titers in healthy individuals*,[1]
- The antibody immune response is age- and gender-dependent[2]
  - Peaks 2 weeks post-D22 (second dose) and starts to decline 4 weeks post-D22[2]
- Patients with MM or WM have lower antibody responses to vaccination[3,4]
  - Particularly low in patients receiving targeted therapies (anti-CD38, anti-BCMA, rituximab, or BTK inhibitors) or with lymphopenia at the time of vaccination[3,4]

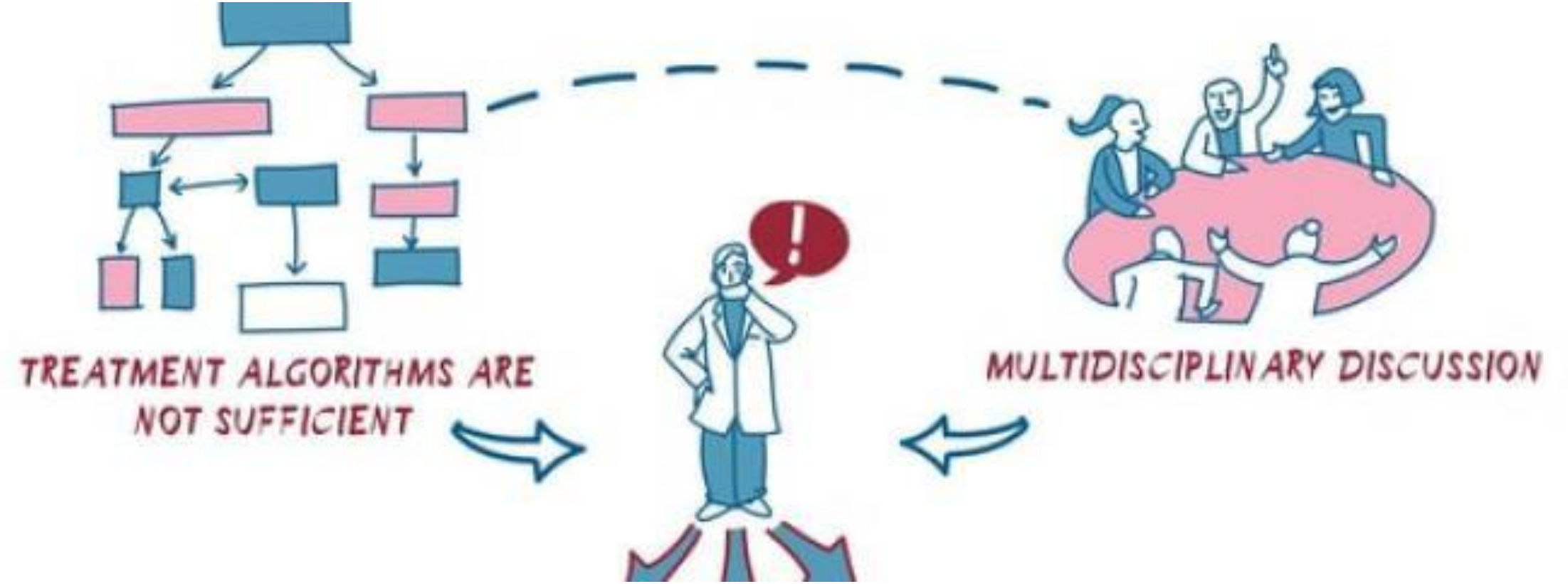
*No active malignancy, autoimmune disease under immunosuppressive therapy, or end-stage renal dysfunction.
BCMA, B-cell maturation antigen; BTK, Bruton's tyrosine kinase; CD, cluster of differentiation; D, Day; MM, multiple myeloma; WM, Waldenström's macroglobulinemia.
1. Terpos E *et al*. *Am J Hematol* 2021; Epub ahead of print (DOI: 10.1002/ajh.26248). 2. Terpos E *et al*. *Am J Hematol* 2021; 96 (7): E257–E259. 2. 3. Terpos E *et al*. *Blood Cancer J* 2021 (submitted).
4. Gavriatopoulou M *et al*. *Blood Adv* 2021 (accepted for publication).

Summary

- What is the optimal time of immunization in these patients?
- What is the solution?
  - A third vaccine shot?
  - Monthly IgGs against the SARS-CoV-2?
  - Is T-cell immunity in these patients enough to produce immunity against the SARS-CoV-2?

IgG, immunoglobulin G.

Conclusion


TREATMENT ALGORITHMS ARE NOT SUFFICIENT
MULTIDISCIPLINARY DISCUSSION

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NCI, National Cancer Institute; NKUA, National and Kapodistrian University of Athens.

Thank you

Recommendations: General principles and indolent lymphomas

Professor Christian Buske
University Hospital of Ulm, Germany

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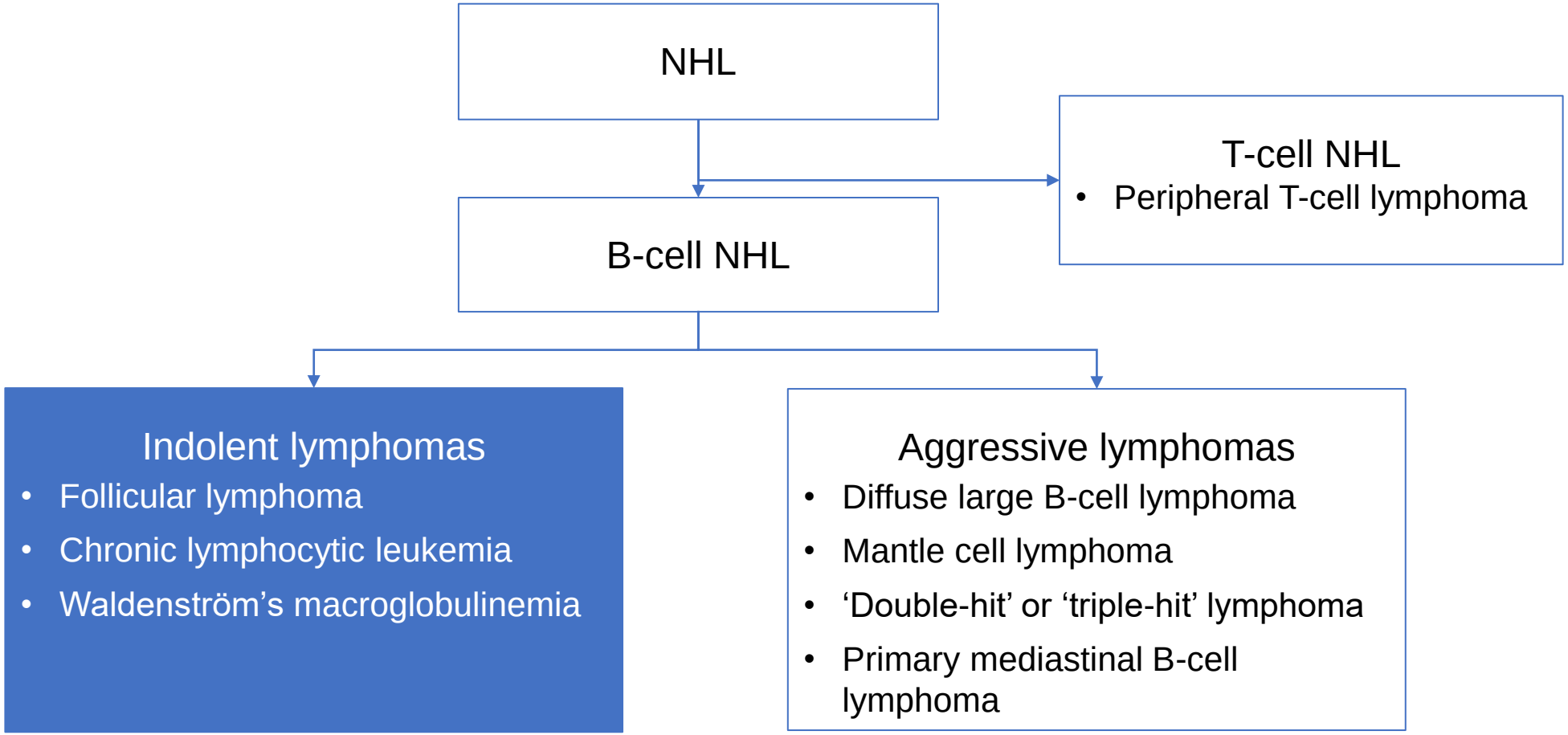
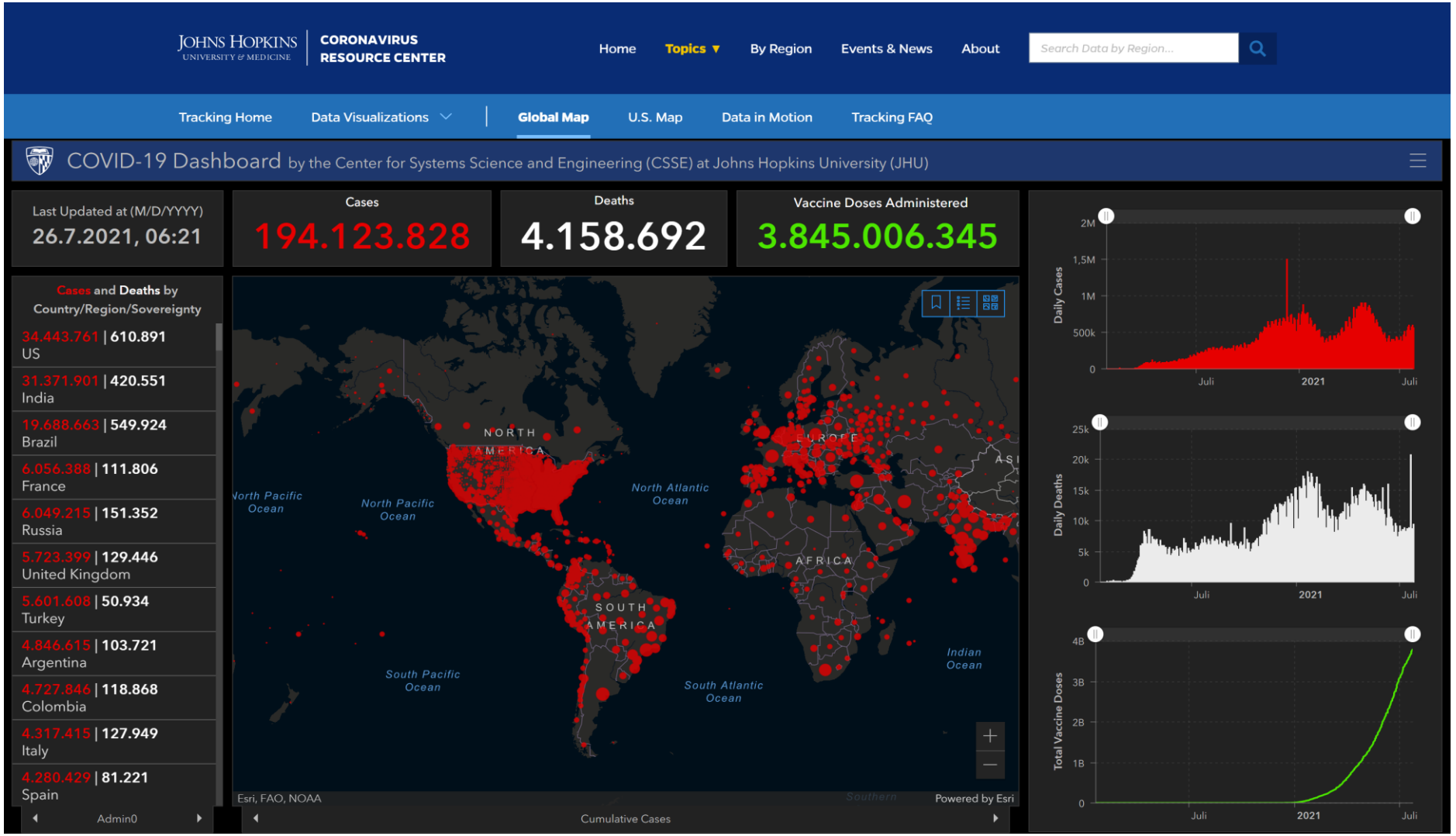
- **Research funding:** Roche, Janssen, Celltrion, AbbVie, Bayer, MSD

Indolent lymphomas



NHL, non-Hodgkin lymphoma.

COVID-19 pandemic: It will stay a challenge!



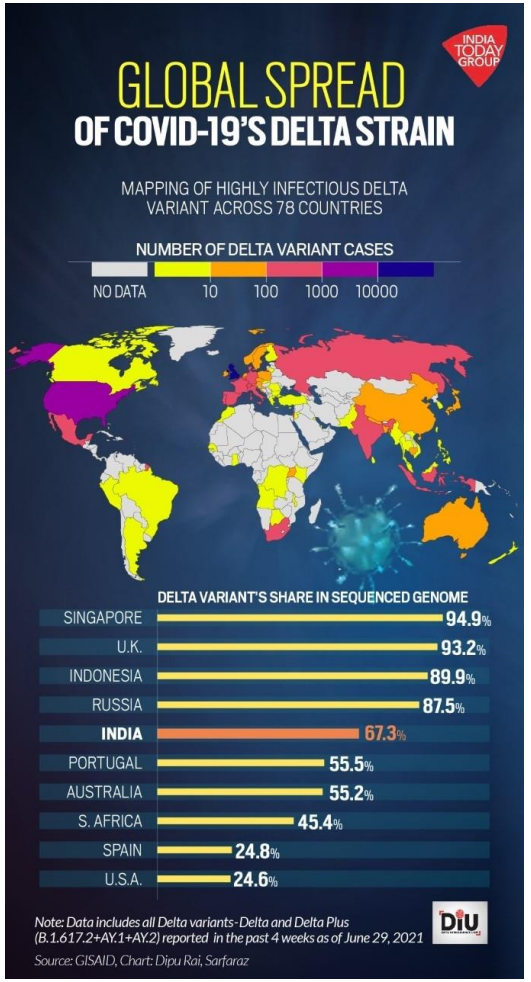
COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). Available at: https://coronavirus.jhu.edu/map.html. Accessed July 2021.

COVID-19 pandemic: It will stay a challenge!

Currently designated Variants of Concern:

WHO label	Pango lineages	GISAID clade	Nextstrain clade	Additional amino acid changes monitored*	Earliest documented samples	Date of designation
Alpha	B.1.1.7	GRY	20I (V1)	+S:484K +S:452R	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351 B.1.351.2 B.1.351.3	GH/501Y.V2	20H (V2)	+S:L18F	South Africa, May-2020	18-Dec-2020
Gamma	P.1 P.1.1 P.1.2	GR/501Y.V3	20J (V3)	+S:681H	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2 AY.1 AY.2 AY.3	G/478K.V1	21A	+S:417N	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021

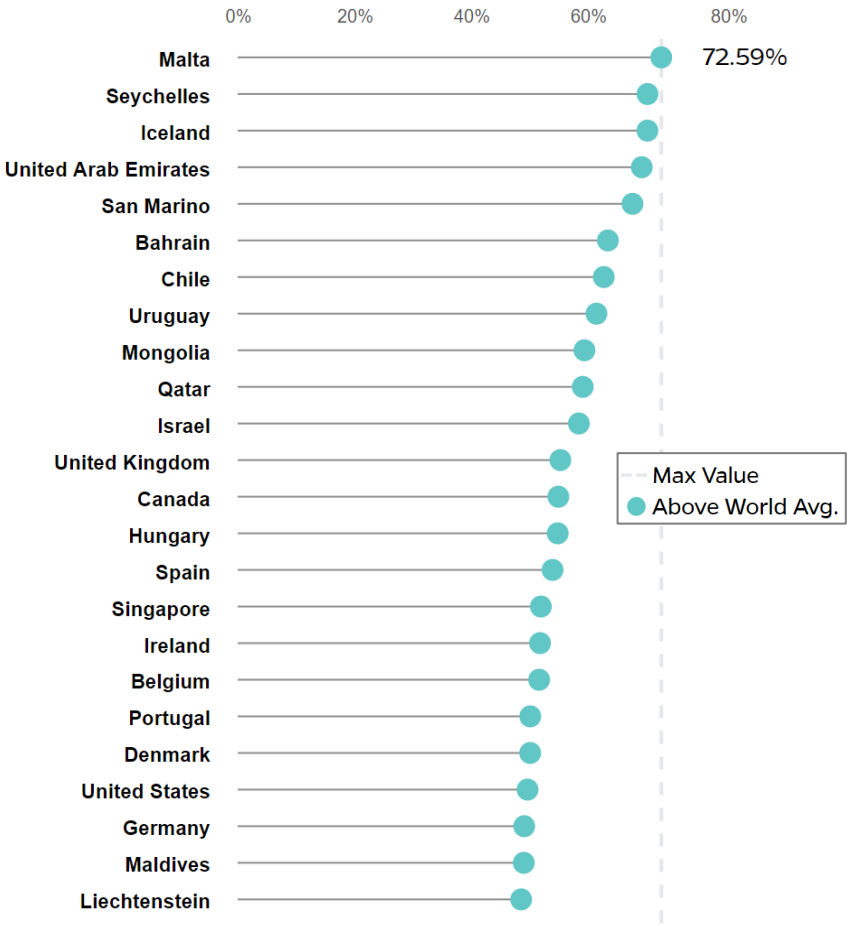
**Notable spike (S) amino acid changes under monitoring, which are currently reported in a minority of sequenced samples.*



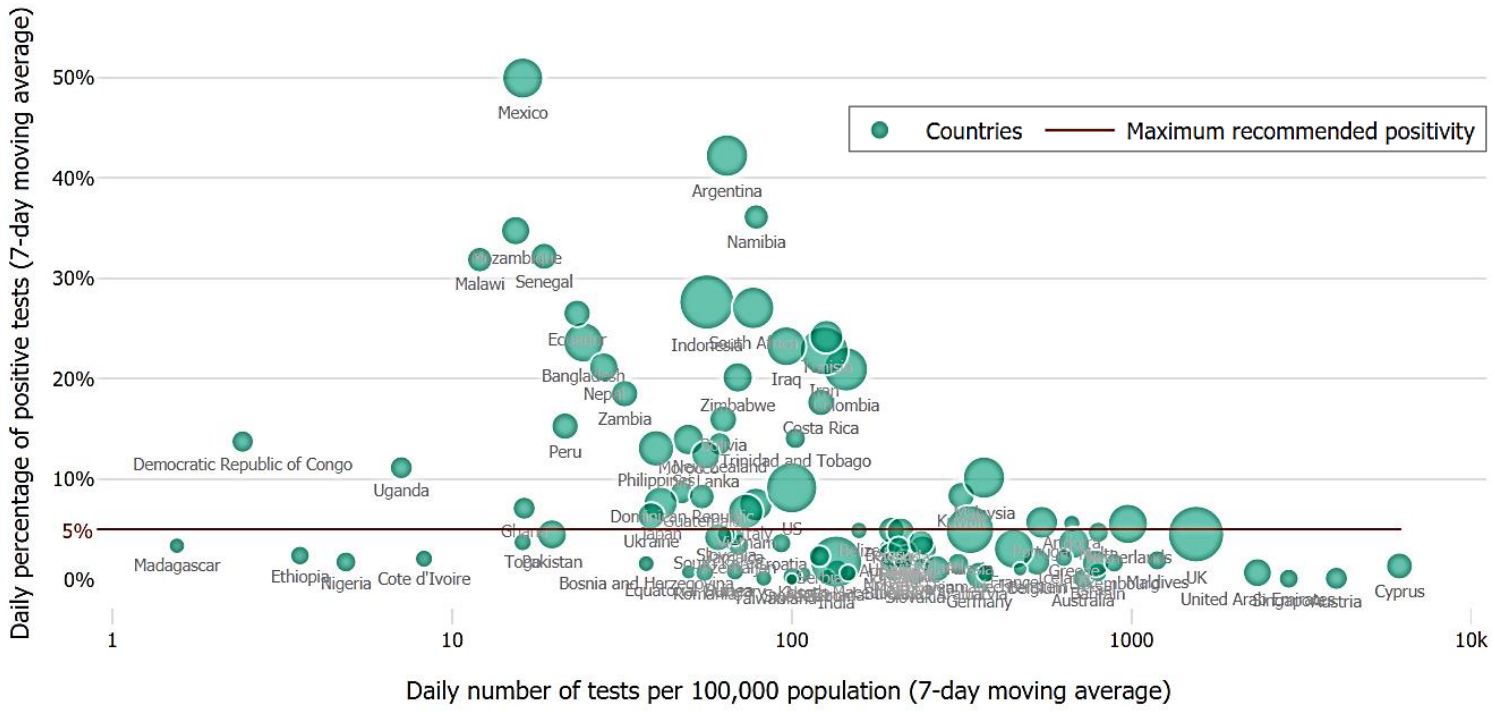
Tracking SARS-CoV-2 variants. Available at: https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/. Accessed July 2021.
Delta variant spreading rapidly, behind most new infections in major countries. Available at: https://www.indiatoday.in/diu/story/corona-s-delta-variant-spreading-rapidly-across-the-globe-behind-most-new-infections-in-major-countries-1821366-2021-06-30. Accessed July 2021.

COVID-19: Multiple factors impact healthcare situation

% of population fully vaccinated[1]



International positivity rates and tests per 100,000 population*,[2]

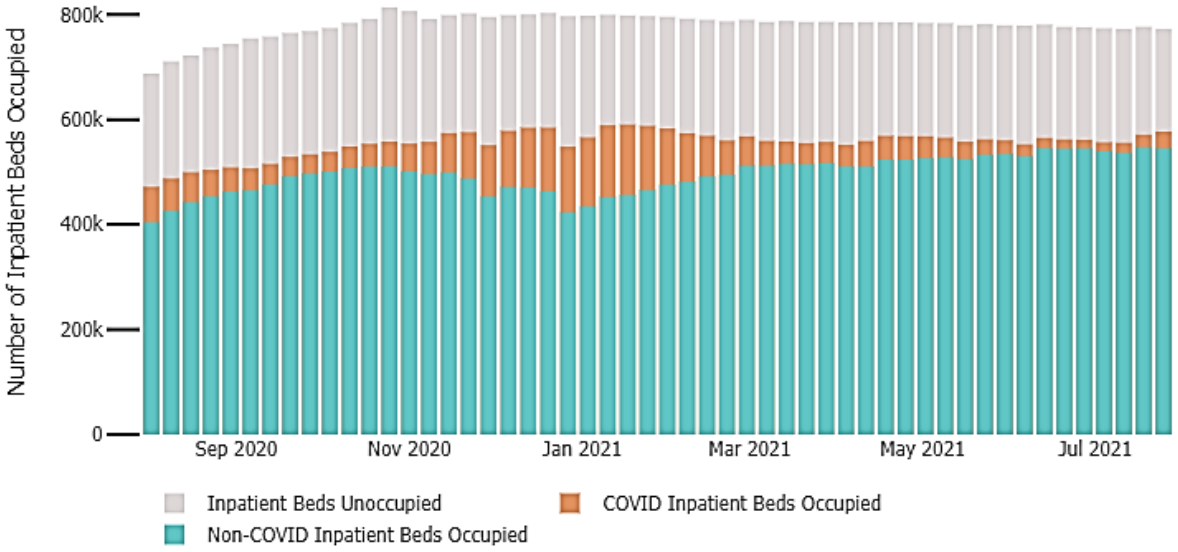


*The size of the circles indicates the size of the epidemic in each location

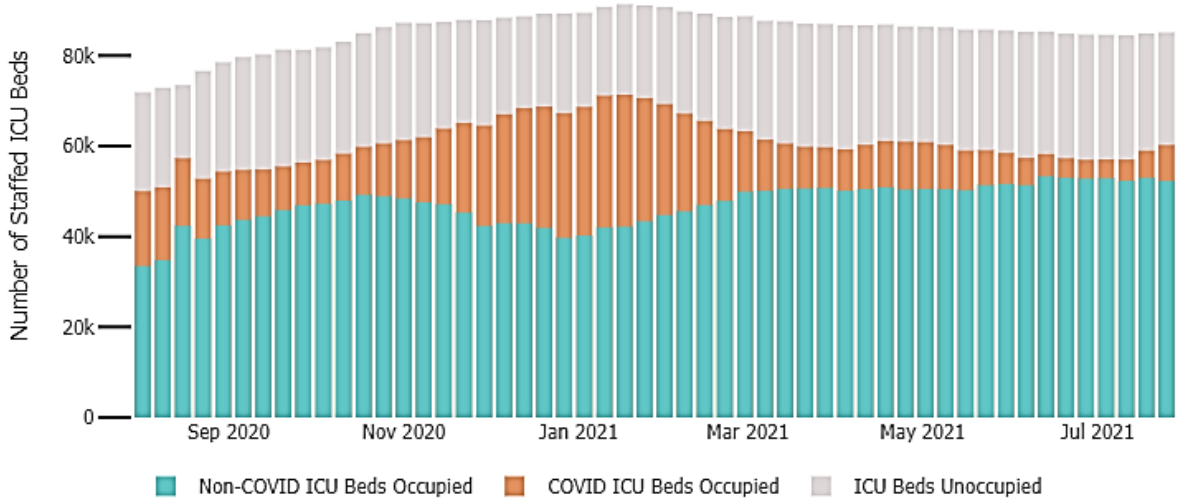
1. Understanding vaccination progress: The race to vaccinate the world. Available at: https://coronavirus.jhu.edu/vaccines/international. Accessed July 2021. 2. How does testing in the U.S. compare to other countries? Available at: https://coronavirus.jhu.edu/testing/international-comparison. Accessed July 2021.

COVID-19 pandemic: A moving field!

Weekly hospitalization trends in the US: Inpatient capacity

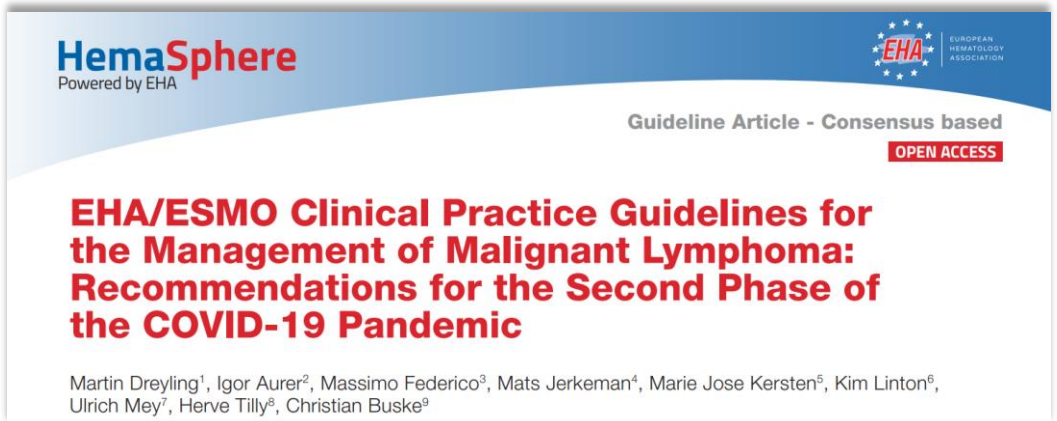


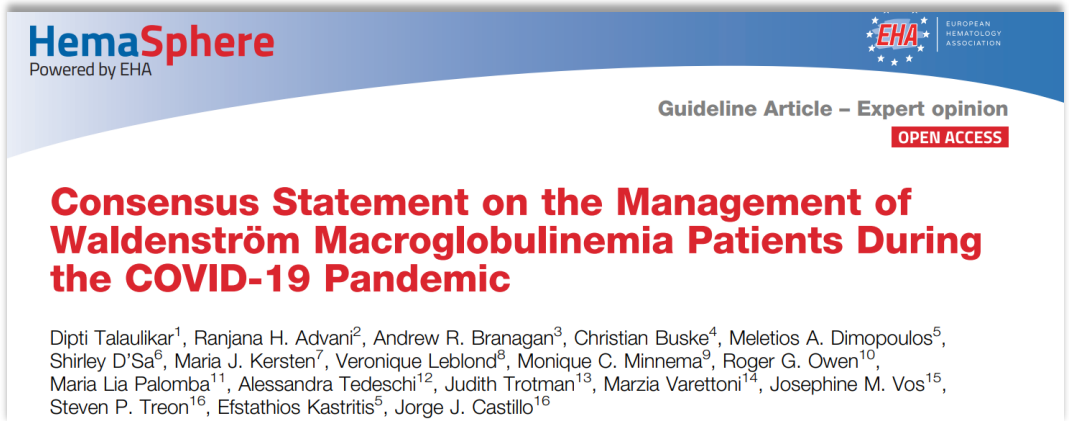
Weekly hospitalization trends in the US: ICU capacity

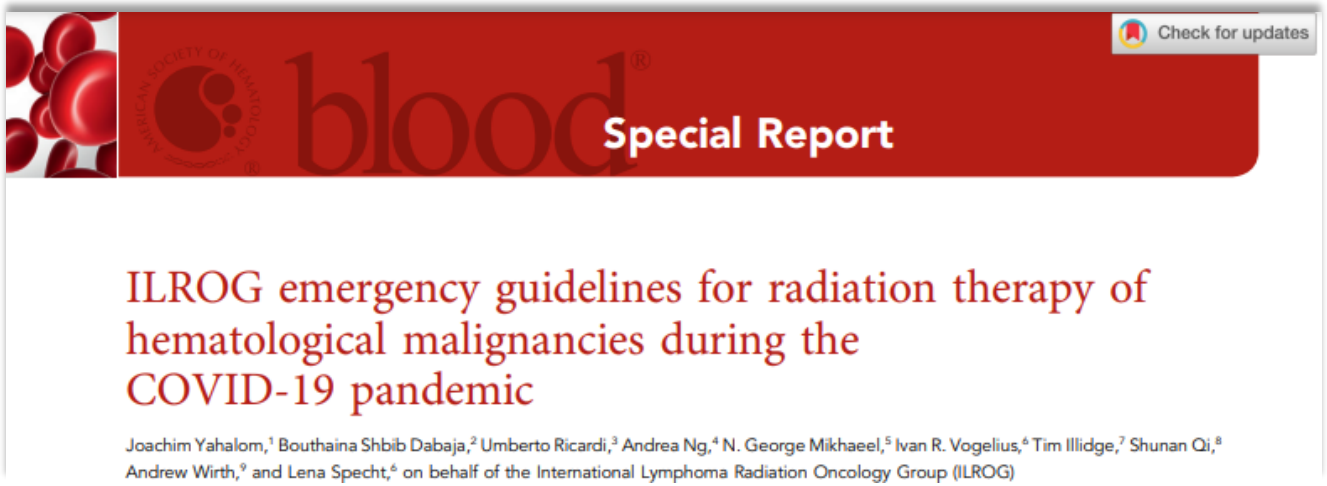


ICU, intensive care unit.
Weekly hospitalization trends: U.S. Available at: https://coronavirus.jhu.edu/data/hospitalization-7-day-trend/inpatient-capacity. Accessed July 2021.

Guidelines for management of patients with lymphoma in the COVID-19 pandemic?







EHA, European Hematology Association; ESMO, European Society for Medical Oncology; ILROG, International Lymphoma Radiation Oncology Group.
Dreyling M *et al*. *Hemasphere* 2021; 5 (2): e529. Talaulikar D *et al*. *Hemasphere* 2020; 4 (4): e433. Yahalom J *et al*. *Blood* 2020; 135 (21): 1829–1832.

Guidelines for management of patients with lymphoma in the COVID-19 pandemic?

Does it make sense?

Yes, but take the individual patient characteristics and the individual situation of the pandemic in your country and your site into account!

Guidelines can only guide…

Guidelines for management of lymphoma patients in the COVID-19 pandemic
General principles

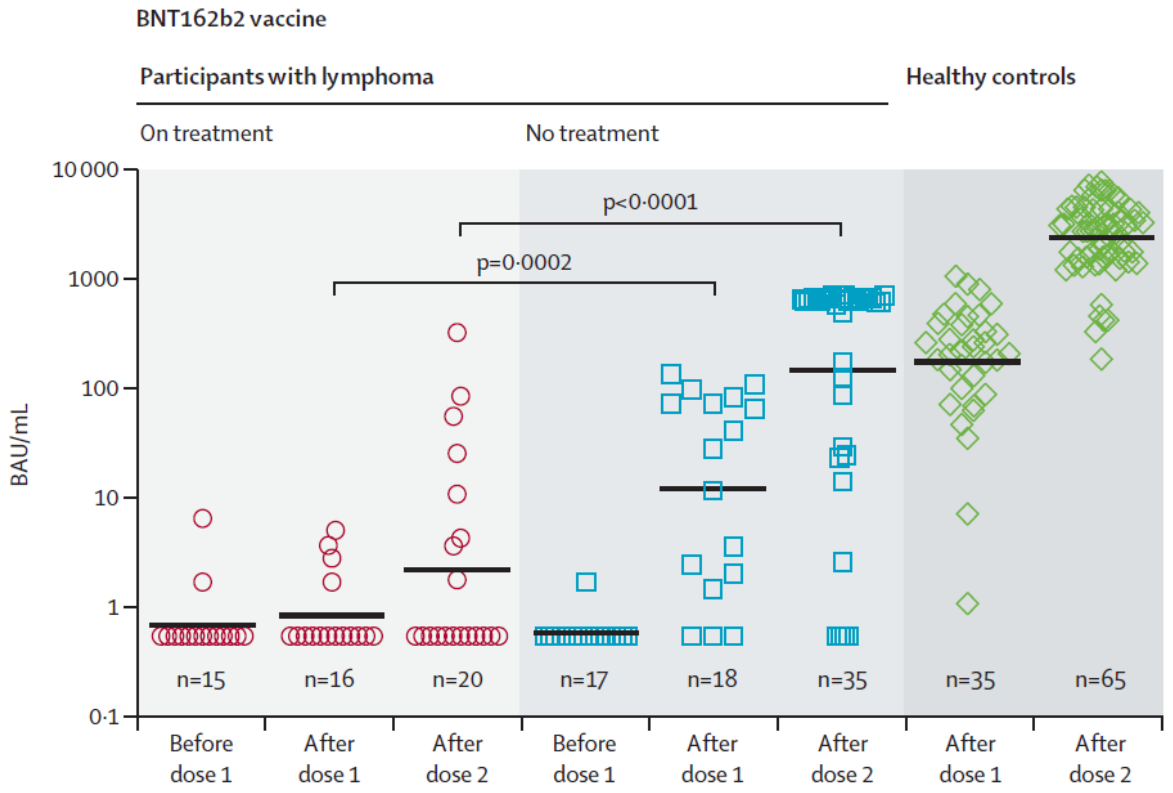
- Initiate anti-lymphoma treatment when indicated by national guidelines
- Treat in specialized hematology centers
- Limit patients' exposure to SARS-CoV-2 infection:
  - Minimize clinic visits
  - Follow up with telemedicine whenever possible
  - Omit non-essential lab sampling or arrange local/home collection
- Question patients on COVID-19 symptoms at each clinic/remote visit
- Test asymptomatic patients for SARS-CoV-2 infection
  - Nasopharyngeal swab RT-PCR
  - Prior to each new treatment course

RT-PCR, reverse transcription polymerase chain reaction.

Vaccinating patients with lymphoma against SARS-CoV-2

- **Vaccinate before initiation of treatment if possible (at least 4 weeks before anti-CD20 treatment)**
- On-treatment serological responses may be poor
- Robust serological responses seen ≥6 months after treatment
- Individuals vaccinated during anti-lymphoma therapy may require revaccination after treatment completion
  - Revaccinate ≥6 months after completion of anti-CD20–containing therapy

Anti-spike IgG response to first and second doses of SARS-CoV-2 vaccination*



*Each datapoint represents an individual's response. Bold horizontal lines show the geometric mean titres. BAU, binding antibody units.
Lim SH *et al. Lancet Haematol* 2021; Epub ahead of print (DOI: 10.1016/S2352-3026(21)00199-X).

When to start treatment in indolent lymphoma

Also before the COVID-19 pandemic:

- Do not forget: Patients with advanced-stage indolent lymphoma are in a non-curative situation
- Many patients undergo a ‘watch and wait’ strategy
- The ‘watch and wait’ period is ill-defined and depends on many factors

When to start treatment in indolent lymphoma

- Indolent lymphomas, including chronic lymphocytic leukemia and Waldenström's macroglobulinemia: 'Watch and wait' is the recommended strategy for asymptomatic patients with low tumor burden

- When treatment is indicated according to consensus guidelines, treatment should be administered
  - However, in unvaccinated patients, treatment deferral after anti-SARS-CoV-2 vaccination should be considered in the absence of urgent treatment indication

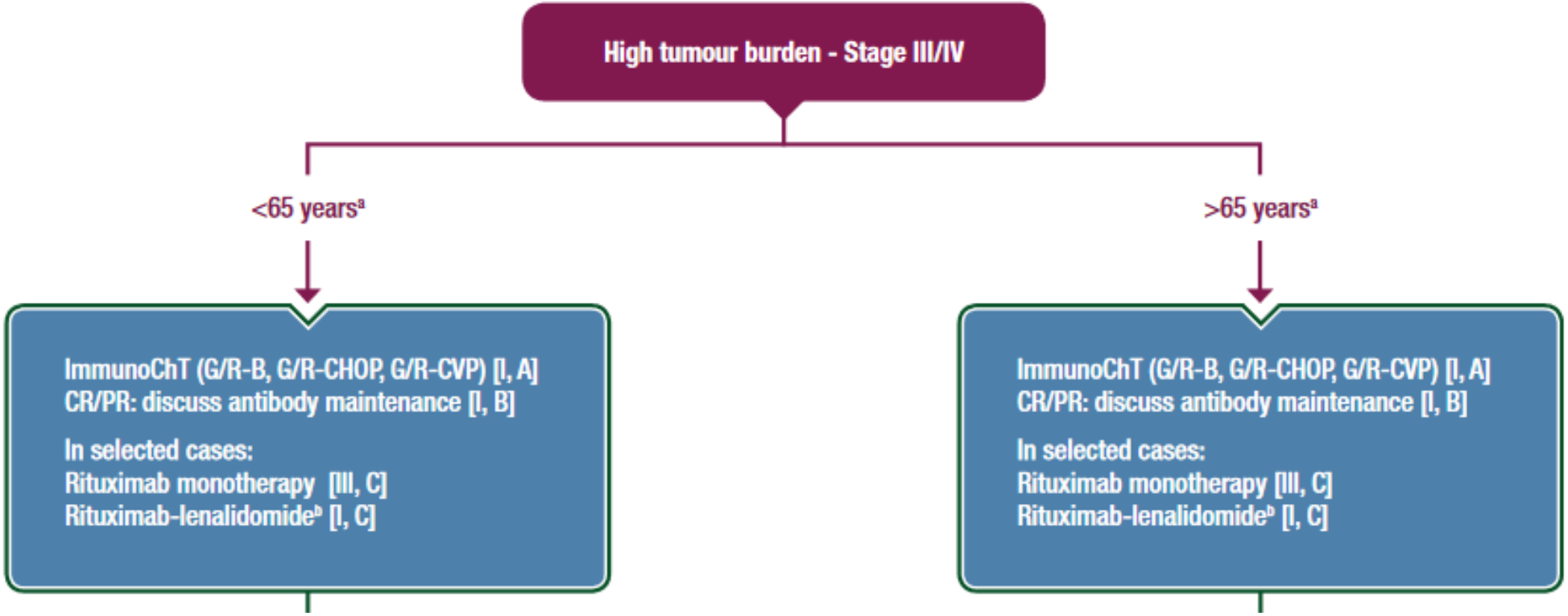
When we have to start treatment…

- Treatment should be administered when indicated by national guidelines
- The primary parameters for treatment choice should be efficacy and availability
- When choosing between options with comparable efficacy:
  - Choose the less immunosuppressive option
  - Consider treatment regimens that can be administered in an outpatient setting
  - Use of anti-CD20 therapy should be carefully evaluated

If treatment is necessary in indolent lymphoma, less immunosuppressive therapies (e.g., therapies avoiding anti-CD20 antibodies) are recommended and treatments with less need for hospital stays without compromising efficacy

Assi T *et al. Front Oncol* 2020; 10: 1267.

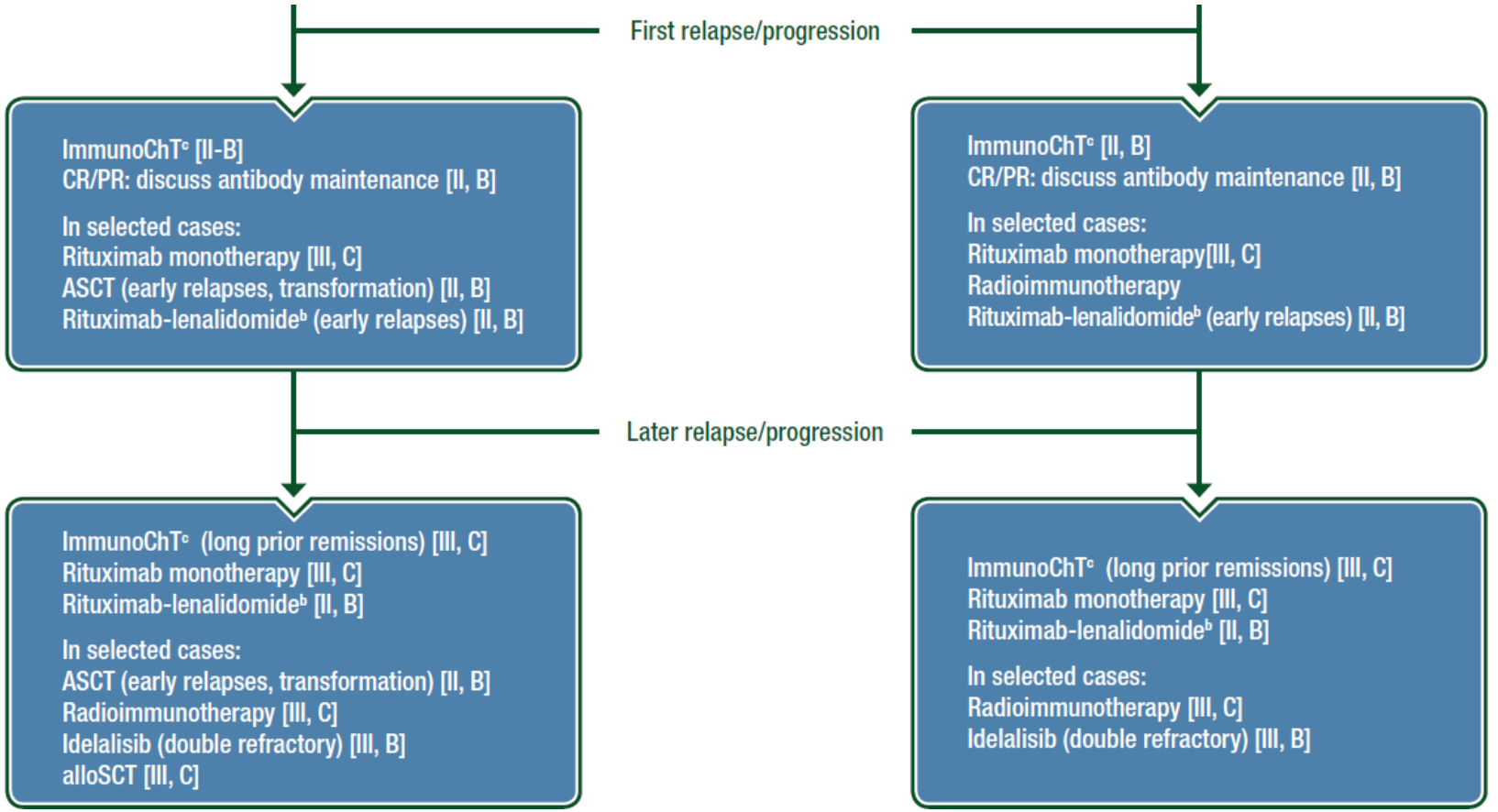
Follicular lymphoma
First-line treatment approach



[a]Biological age (years). [b]Off-label.
B, bendamustine; CHOP, cyclophosphamide, doxorubicin, vincristine, prednisolone; ChT, chemotherapy; CR, complete response; CVP, cyclophosphamide, vincristine, prednisolone; G, obinutuzumab; PR, partial response; R, rituximab.
Dreyling M *et al. Ann Oncol* 2021; 32 (3): 298–308.

Follicular lymphoma

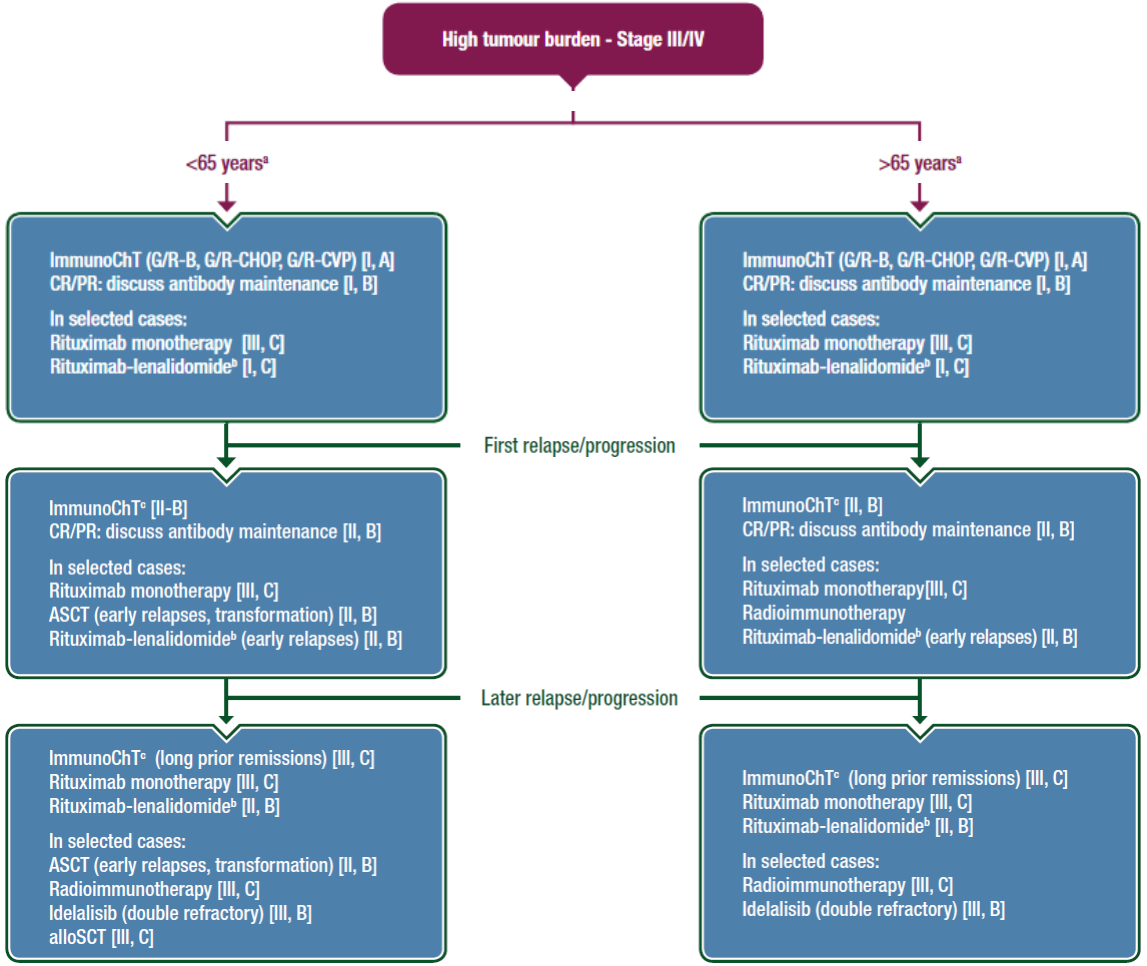
Relapsed/refractory treatment approach



[b]Off-label. [c]Preferred in rituximab-refractory cases.
alloSCT, allogeneic stem cell transplantation; ASCT, autologous stem cell transplantation; ChT, chemotherapy; CR, complete response; PR, partial response.
Dreyling M *et al. Ann Oncol* 2021; 32 (3): 298–308.

Follicular lymphoma

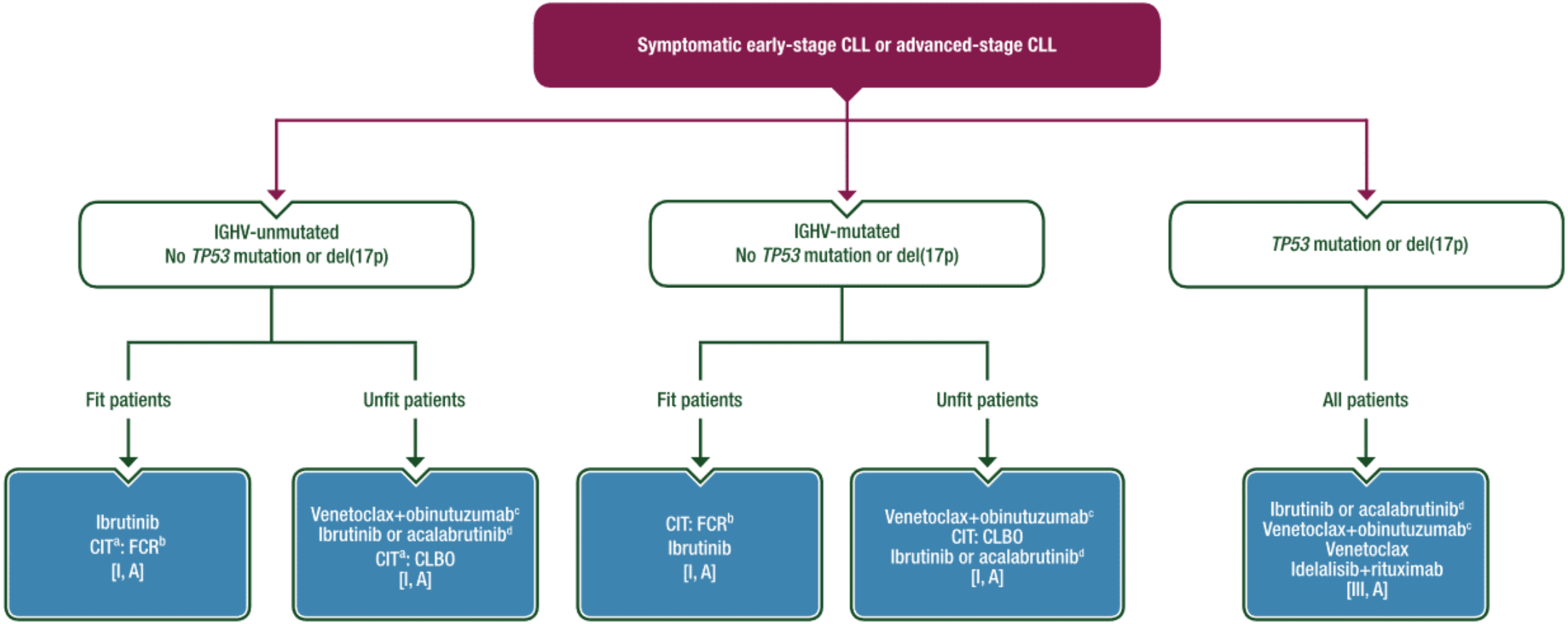
- **Anti-CD20 antibody/chemotherapy treatment? → Yes**
- **Bendamustine? → Consider alternatives**
- **R/lenalidomide → Omit R? → No**
- **Anti-CD20 antibody maintenance? → Avoid**



Dreyling M *et al. Ann Oncol* 2021; 32 (3): 298–308.

Chronic lymphocytic leukemia

First-line treatment approach

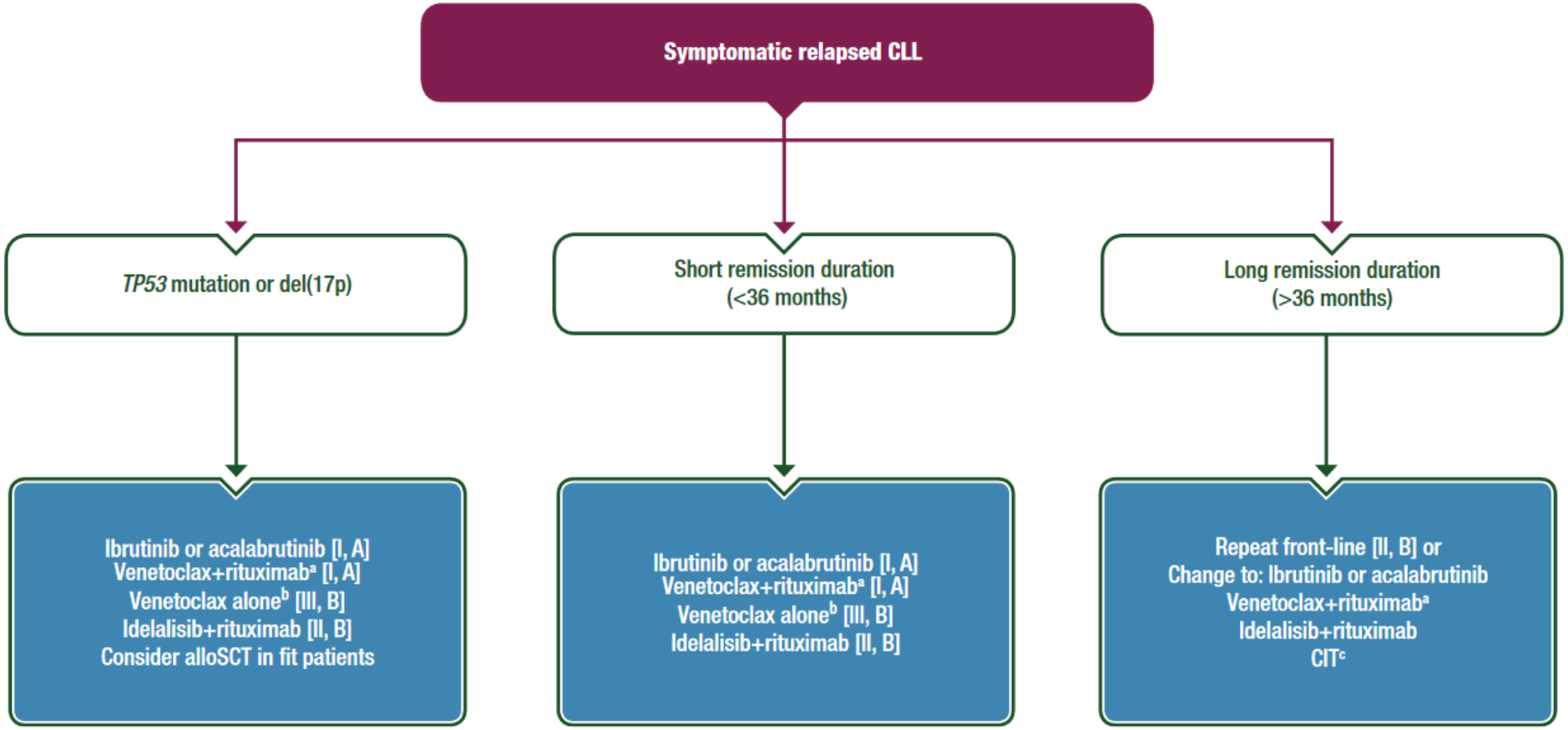


[a]CIT as alternative treatment, only if reasons against treatment with targeted therapies or non-availability. [b]BR might be considered alternatively in patients above the age of 65 years. [c]If available. [d]If approved and available.
BR, bendamustine plus rituximab; CIT, chemoimmunotherapy; CLBO, chlorambucil plus obinutuzumab; CLL, chronic lymphocytic leukemia; FCR, fludarabine, cyclophosphamide, rituximab; IGHV, immunoglobulin heavy chain variable.

Eichhorst B *et al. Ann Oncol* 2020; 32 (1): 23–33.

Chronic lymphocytic leukemia

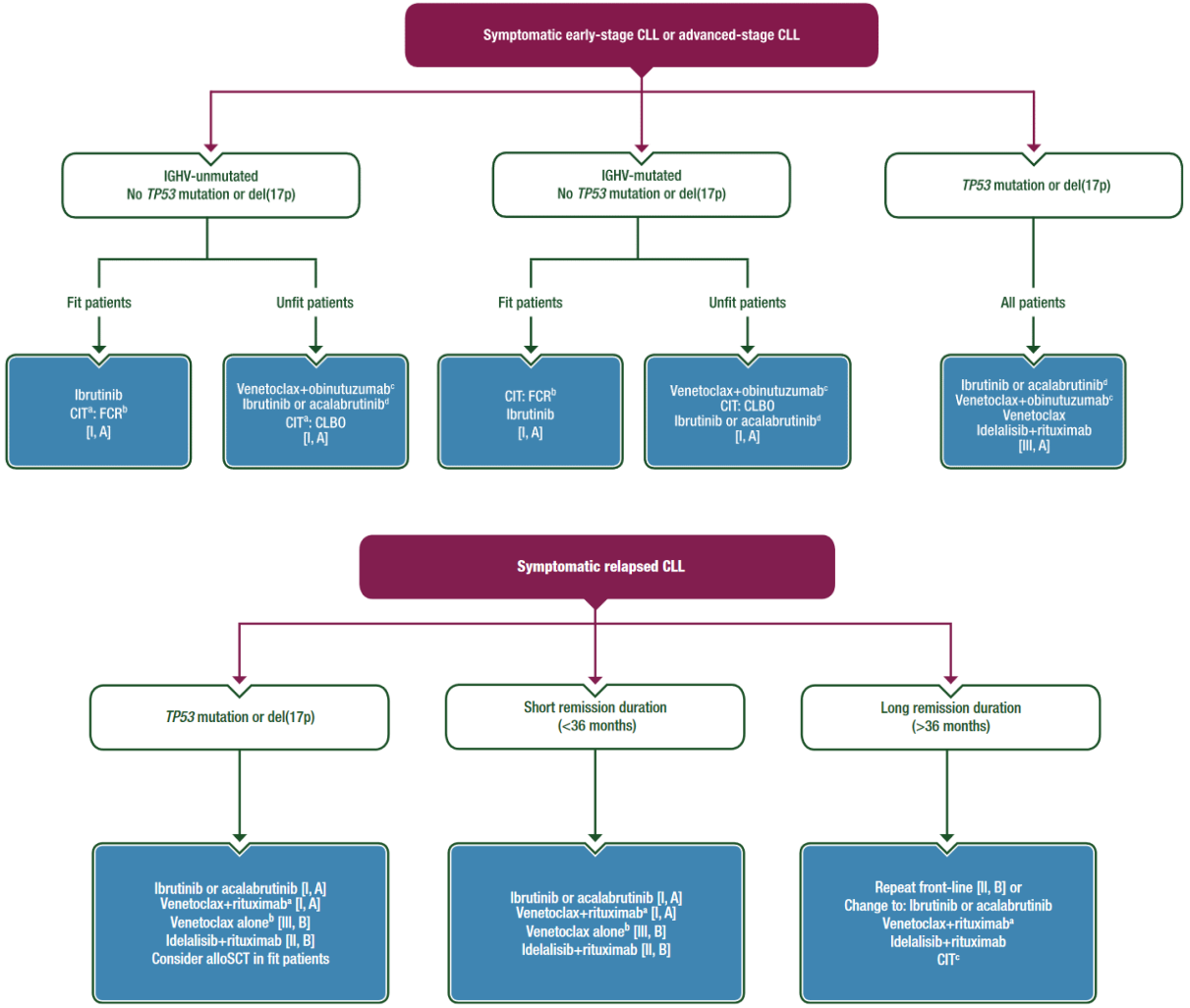
Relapsed/refractory treatment approach



[a]After prior ibrutinib, preferred therapy. [b]After prior CIT and BCRi. [c]Repetition of FCR not recommended.
alloSCT, allogeneic stem cell transplantation; BCRi, B-cell receptor inhibitor; CIT, chemoimmunotherapy; CLL, chronic lymphocytic leukemia; FCR, fludarabine, cyclophosphamide, rituximab.
Eichhorst B *et al. Ann Oncol* 2020; 32 (1): 23–33.

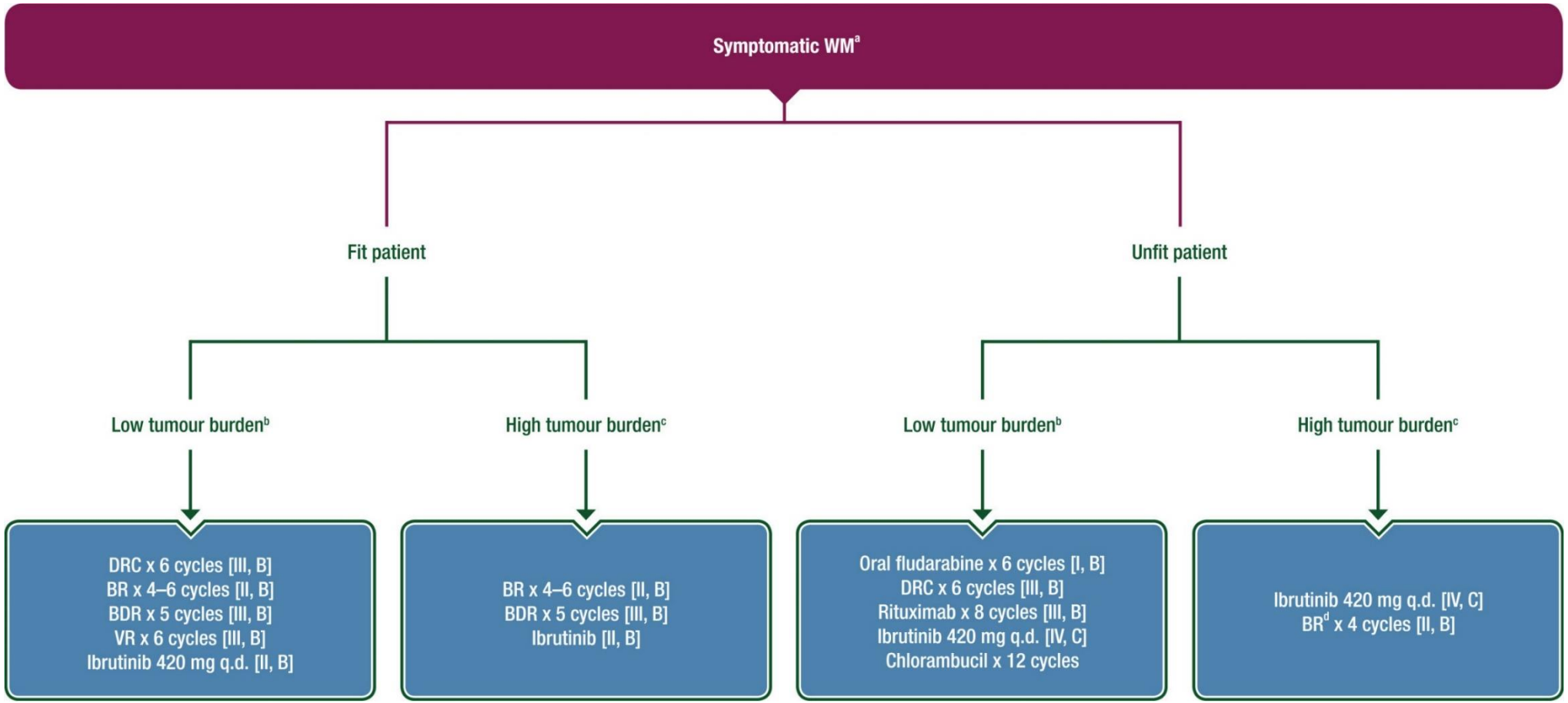
Chronic lymphocytic leukemia

- **Fludarabine? → Avoid**
- **Bendamustine? → Avoid**
- **Timely fixed-duration treatment vs. permanent treatment? → Prefer fixed-duration treatment**
- **Omit anti-CD20 antibodies in combination with venetoclax? → No**



Eichhorst B *et al. Ann Oncol* 2020; 32 (1): 23–33.

Waldenström’s macroglobulinemia

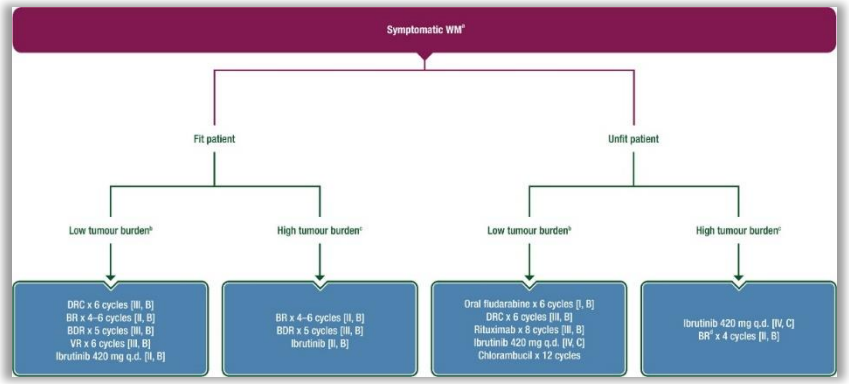


[a]In case of hyperviscosity, plasmapheresis should be used concomitantly with systemic therapy [IV, A]. In case of high IgM levels and at risk for IgM-related complications, plasmapheresis may be used pre-emptively [IV, A]. [b]No major cytopaenias, hyperviscosity or organomegaly. [c]Presence of any of the following: severe cytopaenias, hyperviscosity, organomegaly. [d]BR for unfit patients may require dose reductions for bendamustine and use of G-CSF and/or antibacterial/antiviral prophylaxis.

BDR, bortezomib, dexamethasone, rituximab; BR, bendamustine plus rituximab; DRC, dexamethasone, rituximab, cyclophosphamide; q.d., every day; VR, bortezomib plus rituximab; WM, Waldenström’s macroglobulinemia.

Kastritis E *et al*. *Ann Oncol* 2018; 29 (Suppl 4): iv41–iv50.

Waldenström's macroglobulinemia



- Chemoimmunotherapy and BTK inhibitors remain reasonable options – oral therapy may be a better option for patients who cannot travel
- Many experts have concerns about the immunosuppressive properties of bendamustine and are recommending better tolerated regimens such as dexamethasone, rituximab, and cyclophosphamide over bendamustine plus rituximab
- The use of proteasome inhibitors (i.e., bortezomib and carfilzomib) in combination with steroids and rituximab should be minimized, as it typically implies more frequent (weekly) visits to infusion centers in addition to the immunosuppressive effect of these agents
- Rituximab maintenance is to be avoided given the lack of survival benefit, the added burden of traveling to healthcare centers, and the risk of associated immunosuppression

Kastritis E *et al*. *Ann Oncol* 2018; 29 (Suppl 4): iv41–iv50. Talaulikar D *et al*. *Hemasphere* 2020; 4 (4): e433.

Treating patients with lymphoma who are SARS-CoV-2 positive

Characterize SARS-CoV-2 infection by:
- Lung CT scan
- SARS-CoV-2 viral load and serology

Indolent lymphoma
- Defer treatment initiation if possible
- For patients already receiving treatment, a pause until SARS-CoV-2 infection recovery may be appropriate

Aggressive lymphoma
- Many patients will require immediate therapy, but defer treatment initiation if possible
- Avoid compromising treatment efficacy in the curative setting

Initiate/resume therapy if:
- Patient is asymptomatic for ≥48 hours **AND**
- Duration since SARS-CoV-2 symptom onset is ≥14 days, **AND**
- ≥2 consecutive negative RT-PCR tests are collected ~1 week apart

CT, computed tomography; RT-PCR, reverse transcription polymerase chain reaction.

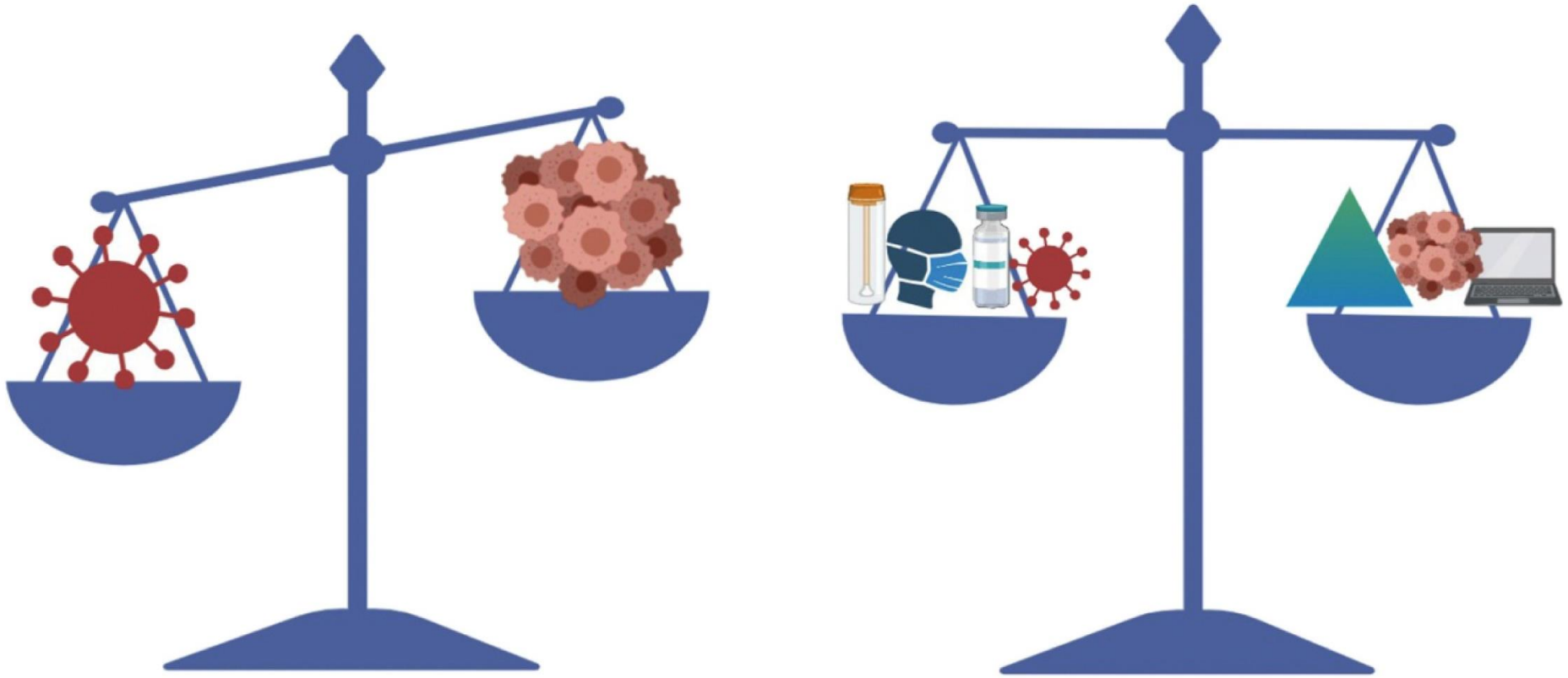
Rossi D *et al*. *Hemasphere* 2020; 4 (4): e432. Perini GF *et al. Hematol Transfus Cell Ther* 2020; 42 (2): 103–110.

After treatment: Follow-up

- Minimize stays in the hospital environment
- Use telemedicine tools
- Perform vigorous COVID-19 testing according to local guidelines for outpatient visits
- Limit diagnostics (e.g., imaging) if no progression of disease is suspected

To the end…

Rebalancing cancer care and COVID-19 protection



Alhalabi O *et al*. *Trends Cancer* 2020; 6 (7): 533–535.

Recommendations: Aggressive lymphomas

Professor Wojciech Jurczak
National Research Institute of Oncology, Poland

Recommendations: Aggressive lymphomas

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Panel discussion

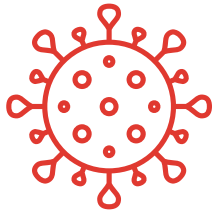
Moderator: Professor Christian Buske

MEETING
PULSE

Summary

Chair: Professor Christian Buske

Summary



Compared with healthy individuals, patients with lymphomas are at greater risk of poorer COVID-19 outcomes and are less likely to have an effective humoral response to vaccination

Effective management of patients with indolent and aggressive lymphomas demands continual balancing of the risks associated with their cancer and treatment versus the risks of COVID-19

It is recommended to treat according to local and national guidelines, preferring less immunosuppressive treatments and treatments that do not require hospital visits where they can be used without compromising efficacy

Save the date!

Next-generation BTK inhibitors for relapsed/refractory B-cell malignancies: What are the options and how do they compare?

Join us in **September 2021** when we explore the benefits and challenges of next-generation BTK inhibitors compared with ibrutinib

We would appreciate your feedback!

Please complete the post-meeting survey.

Thank you for your attention

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