9th EUROPEAN CONFERENCE on INFECTIONS in LEUKAEMIA

COVID Group

Clinical symptoms and Infection control

VIRTUAL CONFERENCE
From September 16th to 17th 2021

Final revised slide set post-ECIL meeting

COVID-19: clinical symptoms and course of the disease

Typical symptoms in HM patients

- The most common symptoms of COVID-19 in HM patients are similar to the overall population
- Fever is the most common symptom, ranging between 58.6% and 77% in the most relevant published studies
- Cough ranges between 41% and 67%
- Other common symptoms are breathless (37-49.3%) and fatigue (20.3-50%)
- Immunosuppressed patients may present atypical symptoms such as diarrhea, vomiting, loss of appetite and confusion
- A severe clinical presentation occurs in about 15.5-52.4% of cases
- Critical cases range between 6.9-14% in the most relevant published studies
- So far, there are no clear published data about the real prevalence of COVID-19 in HM patients (i.e. screening in asymptomatic patients)

Patients with HM, especially NHL, have a higher risk of prolonged hospitalisation for COVID-19 and higher mortality (Dulery et al., Am J Hem 2021)

Mention risk of invasive fungal disease because of additional immunosuppression from COVID-therapy. Therefore beware risk for patient if placed in negative pressure room

References. Passamonti, et al. Lancet Haematol 2020; Cattaneo, et al. Cancer 2020; Borah, et al. Blood Cell Molec Dis 2021; Glenthøj, et al. Eur J Haematol 2020; Wood, et al. Blood Adv 2020 Kurderer, et al. Lancet 2020; Lee, et al. Lancet Oncol 2020; Yigenogin, et al. J Med Virol 2021; Regalado-Artamendi, et al. Hemasphere 2021; García Suárez, et al. J Hematol Oncol 2020; Pinana, et al. Exp Hematol Oncol 2020; Sharma, et al. Lancet Haematol 2021; Giesen, et al. Eur J Cancer 2020; Giesen, et al. Eur J Cancer 2021; ElGohary, et al. Hematol Oncol Stem Cell Ther 2020 Ali, et al. Hematol Oncol Stem Cell Ther 2020; Coronavirus disease COVID-19: EBMT recommendations version 15 – February 17, 2021; Ljungman, et al. Leukemia 2021.

COVID-19: clinical symptoms and course of the disease

COVID-19 pneumonia

- COVID-19 pneumonia causing oxygen needing occurs in 57-67.7% of patients
- Imaging studies show focal unilateral or diffuse bilateral ground-glass opacities with or without additional consolidations
- **Low-dose chest CT should is recommended in all pts. with symptoms consistent with LRTID or high-risk adult and pediatric patients (AII)**
- Needing for mechanic ventilation ranges between 6.9-17% in the mot relevant published studies
- Routine bronchoalveolar lavage (BAL) is not recommended if a patient tested positive for SARS-CoV2 (AIII)
- Few data on specific imaging in HM patients have been so far published

References. Passamonti, et al. Lancet Haematol 2020; Cattaneo, et al. Cancer 2020; Borah, et al. Blood Cell Molec Dis 2021; Glenthøj, et al. Eur J Haematol 2020; Wood, et al. Blood Adv 2020 Kurderer, et al. Lancet 2020; Lee, et al. Lancet Oncol 2020; Yigenogin, et al. J Med Virol 2021; Regalado-Artamendi, et al. Hemasphere 2021; García Suárez, et al. J Hematol Oncol 2020; Pinana, et al. Exp Hematol Oncol 2020; Sharma, et al. Lancet Haematol 2021; Giesen, et al. Eur J Cancer 2020; Giesen, et al. Eur J Cancer 2021; ElGohary, et al. Hematol Oncol Stem Cell Ther 2020 Ali, et al. Hematol Oncol Stem Cell Ther 2020; Coronavirus disease COVID-19: EBMT recommendations version 15 – February 17, 2021; Fang, et al. Radiology 2020; Ai, et al. Radiology 2020; Shi, et al. Lancet Infect Dis 2020; Ljungman, et al. Leukemia 2021.

COVID-19: clinical symptoms and course of the disease

Criteria for clinical stages according to WHO

- No specific criteria for clinical stages of COVID-19 in HM patient have been so far reported
- Clinical stages and disease severity are defined according to the World Health Organization criteria

Non-severe	Severe	Critical
Absence of signs of severe or critical disease	$Sp0_2$ < 90% on room air	Requires life sustaining treatment
	Respiratory rate > 30 in adults	ARDS
	Raised respiratory rate in children	Sepsis
	Signs of severe respiratory distress	Septic shock

WHO: 0-3 4-6 >=7

References. COVID-19 clinical management. Living guidance World Health Organization. January 15, 2021. WHO/2019-nCoV/clinical/2021.1; Wu, et al. JAMA 2020.

COVID-19: clinical symptoms and course of the disease

Outcome in HM patients

Reference	Country	No. patients	Severity of disease	Mortality rate
Passamonti, Lancet Haematol 2020	Italy	536	Severe: 36% Critical: 14%	37%
Yigenoglu, J Med Virol 2020	Turkey	740	Severe: 15.5% Critical: 13.2%	13.8%
García Suárez, J Hematol Oncol 2020	Spain	697	Severe: 42% Critical 20%	33%
Glenthøj, Eur J Haematol 2020	Denmark	66	Severe: 36% Critical: 14%	24%
Lee, Lancet Oncol 2020	UK	224	Severe-critical: 52.4%	36%
Pinana, Exp Hematol Oncol 2020	Spain	338	Severe-critical: 45%	31%
Kuderer, Lancet 2020	Global	204	Admitted in ICU: 22%	14%
Wood, Blood Adv 2020	Global	254	Severe: 29%	28%
Cattaneo, Cancer 2020	Italy	102	Oxygen need: 62%	39%
Borah, Blood Cell Mol Dis 2021	India	130	Severe: 26.2%	20%
Sharma, Lancet Haematol 2021	Global	318 (transplant recipients)	Critical: 14%	32.5%
ASH collaborative registry 2021 (July, 18)	Global	1076	Severe: 19%	16.3%
Ljungman, Leukemia 2021	Europe	382 (tranplant recipients)	Admitted in ICU: 22%	28%

COVID-19: clinical symptoms and course of the disease

Long-COVID: definition

- Long-COVID (or post-acute COVID-19 syndrome) is defined as persistent symptoms and/or delayed or long-term complication beyond 4 weeks from the onset of symptoms

- The most common signs and symptoms of long-COVID are:

  - Fatigue and decline in quality of life
  - Muscular weakness, joint pain
  - Dyspnea
  - Cough
  - Permanent oxygen requiring
  - Anxiety, sleep disturbances and cognitive disturbances
  - Headache
  - Palpitations and chest pain
  - Thromboembolism
  - Chronic kidney disease
  - Hair loss

References. Nalbandian, et al. Nat Med 2021; Carfi, et al. JAMA 2020; Halpin, et al. J Med Virol 2021; Carvalho-Schneider, et al. Clin Microbiol Infect 2021; Chopra, et al. Ann Intern Med 2020 Arnold, et al. Thorax 2020; Moreno-Péerez, et al. J Infect 2021; Garrigues, et al. J Infect 2020; Huang, et al. Lancet 2021.

COVID-19: clinical symptoms and course of the disease

Long-COVID: prevalence

Reference	Country	No. pts	Prevalence	Main symptoms	Onset	Cancer pts	HM pts
Carfi, JAMA 2020	Italy	143	87.4%	Fatigue, dyspnea, chest pain, declined QoL	After 2 months	5	No
Halpin, J Med Virol	UK	100	-	Fatigue, dyspnea, PTSD, declined QoL	1-2 months after discharge	21	No
Carvalho-Schneider, CMI 2021	France	150	66%	Fatigue, dyspnea, loss of taste/smell	After 2 months	Not specified	No
Chopra, Ann Intern Med 2020	USA	488	32.6%	Dyspnea, cough, loss of taste/smell	2 months after discharge	89	Yes
Arnold, Thorax 2020	UK	110	74%	Fatigue, dyspnea, sleep disturbance, declined QoL	3 months after first symptoms	No	No
Moreno-Pérez, J Infect 2021	Spain	277	50.9%	Fatigue, dyspnea, loss of taste/smell, declined QoL	2-3 months after first symptoms	Not specified	No
Garrigues, J Infect 2020	France	120	-	Fatigue, dyspnea, sleep disturbance, declined QoL	3-4 months post-admission	Not specified	No
Huang, Lancet 2021	China	1773	76%	Fatigue, dyspnea, sleep disturbance, declined QoL	6 months after first symptoms	44	No
Seeβle, Clin Infect Dis 2021	Germany	96	77.1%	Reduce exercise capacity, fatigue, dyspnea	12 months after first symptoms	4	No
Barbui, Blood Cancer J 2021	Europe	180	32.1%	Fatigue, dyspnea, muscoloskeletal disorders	6 months after acute phase	No	Yes (MPN)

References. Carfi, et al. JAMA 2020; Halpin, et al. J Med Virol 2021; Carvalho-Schneider, et al. Clin Microbiol Infect 2021; Chopra, et al. Ann Intern Med 2020; Arnold, et al. Thorax 2020; Moreno-Péerez, et al. J Infect 2021; Garrigues, et al. J Infect 2020; Huang, et al. Lancet 2021; Seeβle, et al. Clin Infect Dis 2021; Barbui, et al. Blood Cancer Journal 2021.

COVID-19: clinical symptoms and course of the disease

Long-COVID: prevalence

- No specific data have been so far published about risk factors for long-COVID in HM patients. In the overall population, the most common risk factors for long-COVID are:

  - Severity of illness during acute COVID-19

  - Pre-existing respiratory disease

  - High body mass index

  - Older age

  - Race (black, Asian and minority ethnic)

  - Women

  - Other conditions (i.e. cancer) remain to be determined.

References. Nalbandian, et al. Nat Med 2021; Carfi, et al. JAMA 2020; Halpin, et al. J Med Virol 2021; Carvalho-Schneider, et al. Clin Microbiol Infect 2021; Chopra, et al. Ann Intern Med 2020 Arnold, et al. Thorax 2020; Moreno-Péerez, et al. J Infect 2021; Garrigues, et al. J Infect 2020; Huang, et al. Lancet 2021.

Pediatric SARS-COV-2 infection and COVID 19 disease

General pediatric population:

- Clinical symptoms and signs of presentation as in adults, but lower incidence of severe forms (1-8%) and lower mortaliy (0.1-0.4%)
- Most frequent symptoms: headache 60-74%, fever 52-58%, cough 42-49%
- Typical for pediatric age the complication of “Multisystem Inflammatory Syndrome in Children (MIS-C)” 3-6 weeks from SARS-COV-2 infection
- Low incidence of Long-COVID19 (4.4% at week 4, 1.8% at week 8)

Badal et al J Clin Virol 2021; Jiang et al lancet Infect Dis 2020; Molteni et al. Lancet Child Adolesc Health 2021)

Pediatric Hematology Oncology population:

- Incidence of severe COVID 19 variable, comparing countries with low-middle versus high income
- Clinical course: asymptomatic 30-35%, hospitalization 47-68%, PICU/ICU admission 9-10%, mortality 4-4.9%
- Severity, morbidity, and mortality of COVID 19 is higher than that of the general pediatric population
- All over the world, mortality and survival was influenced by the socioeconomic situation of the country

Meena et al. Ped Blood Cancer 2021; Mukkada et al. Lancet Oncol 2021)

Multisystem Inflammatory Syndrome in Children (MIS-C)

Up to 11% of hospitalized pediatric cases

Definition (WHO):

1) age 0-19 years
2) fever for ≥ 3 days
3) at least 2 clinical signs of multisystem involvement:
   a) rash, bilateral conjuntivitis, or mucocutaneous inflammation signs (oral, hands, feet)
   b) hypotension or shock
   c) cardiac dysfunction, pericarditis, valvulitis or coronary abnormalities (including echocardiografy or troponin/BNP)
   d) coagulopathy (prolonged PT, PTT, high d-dimer)
   e) acute GI symptoms (diarrhea, vomiting, adominal pain)
4) elevated markers of inflammation (CRP, procalcitonin, ESR)
5) exclusion of other causes (bacterial sepsis, staphylococcal -streptococcal toxic shock syndromes, HLH)
6) Evidence of SARS-COV-2 Infection:
   i) positive SARS-COV-2 RT-PCR
   ii) positive serology
   Iii) positive antigen test
   iv) contact with an individual with COVID 19

https://www.who.int/publications/i/item/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19

Infection Control

Population / Clinical situation	Intention	Intervention	SoR	QoE	References
Hygiene measures					
Any population	To prevent SARS-CoV-2 transmission and infection	Physical distancing measures and surgical face masks and hand washing	A	II_u	Cowling BJ et al, Lancet Public Health. 2020;**5**(5):e279-e288; Matrajt L, Leung T. Emerg Infect Dis. 2020;26(8); Lewnard JA et al. BMJ. 2020;369:m1923; Prem K et al. Lancet Public Health. 2020;5(5):e261-e270; Cheng VC et al. . J Infect. 2020;81(1):107-114.
Cancer patients, health care setting, and health care workers	To prevent SARS-CoV-2 infection	Hand disinfection with ethanol or 2-propanol at >30% concentration for 30s and diseinfection of frequently touched surfaces	A	II_u	Kratzel A et al. Emerg Infect Dis. 2020;**26**(7):1592-1595; van Doremalen N et al. N Engl J Med. 2020;**382**(16):1564-1567; Ryu BH et al. Am J Infect Control. 2020; Kampf Get al. J Hosp Infect. 2020;**104**(3):246-251.
Cancer patients	To prevent SARS-CoV-2 infection	Regular ventilation of rooms	B	III	van Doremalen N et al. N Engl J Med. 2020;**382**(16):1564-1567
Cancer patients with SARS-CoV-2 infection	**To prevent SARS-CoV-2 transmission**	**Place in positive pressure rooms**	**D**	**III**	
Cancer patients with SARS-CoV-2 infection	**To avoid superinfection**	**Place in negative pressure rooms**	**D**	**III**	
Health care workers in contact with (confirmed/suspected) SARS-CoV-2-positive patients	To prevent SARS-CoV-2 infection	Personal protective equipment (PPE) incl. FFP2/N95 respirator	A	$II_{r,t}$	MacIntyre CR et al. Influenza Other Respir Viruses. 2011;**5**(3):170-179; Yan Y et al. Dermatol Ther. 2020:e13310; Chu DK et al. Lancet. 2020; Dockery DM et al. J Emerg Med. 2020.
Cancer patients with SARS-CoV-2 infection	To prevent SARS-CoV-2 transmission	Single room isolation, cohort isolation or self-quarantine	A	$II_{t,u}$	Park HC et al. Medicine (Baltimore). 2020;**99**(3):e18782
Cancer patients with SARS-CoV-2 infection	To prevent SARS-CoV-2 transmission	Requirement of negative SARS-CoV-2 test result prior to discontinuation of isolation	A	$II_{t,u}$	He X et al. Nat Med. 2020;**26**(5):672-675; Hao S et al. J Infect Dis. 2020; Zhu et al. Eur Urol. 2020;**77**(6):748-754; Xu K et al. Clin Infect Dis. 2020; Zou Y et al. J Infect Dis. 2020.

Infection Control

Population / Clinical situation	Intention	Intervention	SoR	QoE	References
Health care providers	To prevent nosocomial SARS-CoV-2 transmission	Implement organisational strategies including surveillance screening, dedicated teams and re-organization of outpatient clinics	A	III	Kung CT et al. J Microbiol Immunol Infect. 2020.; Cho SY et al. Br J Haematol. 2020; van de Haar et al. Nat Med. 2020;26(5):665-671.; Weisel KC et al. Oncol Res Treat. 2020;43(6):307-313; Arons MM et al. N Engl J Med. 2020;382(22):2081-2090.
Health care providers	To prevent SARS-CoV-2 transmission and infection	Consider treatments with fewest and shortest visits to hospital/outpatient clinic	A	III	Wang D et al. JAMA. 2020; Yahalom J et al. Blood. 2020;135(21):1829-1832
Health care providers	To prevent SARS-CoV-2 transmission and infection	Consider erythropoietin as an alternative to red cell transfusion	B	III	Weinkove R et al. Med J Aust. 2020;212(10):481-489; Shander A et al. Anesth Analg. 2020;131(1):74-85; Spicer J et al., Nat Rev Clin Oncol. 2020;17(6):329-331
Health care providers and spouses	To protect cancer patients from COVID-19	Vaccinate against COVID-19	A	IIt	Lemaitre M, et al. *J Am Geriatr Soc* 2009
Cancer patients	To prevent severe COVID-19	Vaccinate against COVID-19	A	IIt	Clinical trials for vaccination (Polack etc.)

Anti-cancer management

Population / Clinical situation	Intention	Intervention	SoR	QoE	References
General recommendations					
Cancer patients during COVID-19 pandemic	To reduce risk of severe COVID-19	Perform cancer therapy to reach best possible remission	A	II_u	Williamson EJ et al. Nature. 2020; Oh et al. Ann Oncol. 2020;31(7):838-839; He W et al. Leukemia. 2020;34(6):1637-1645; Kuderer NM et al. Lancet. 2020;**395**(10241):1907-1918 21,22
Cancer patients during COVID-19 pandemic	To reduce risk of SARS-CoV-2 infection and severe COVID-19	Routinely delay/discontinue anti-cancer therapy	D	II_u	Glenthoj et al., Eur J Haem 2021; Kuderer NM et al. Lancet. 2020;395(10241):1907-1918
Cancer patients with suspected or proven SARS-CoV-2 infection	To reduce risk of severe COVID-19	Quarantine and delay/ discontinue anti-cancer therapy for up to 14 days, if not detrimental for cancer prognosis	A	III	No reference.
Cancer patients with suspected or proven SARS-CoV-2 infection scheduled for allo- or auto- SCT	To reduce risk of severe COVID-19	Defer conditioning	A	IIt	Ljungman et al., Leukemia, 2021; Sharma et al., Lancet Haematol, 2021; Wood et al., Blood Adv, 2020; Hirsch et al., ECIL-8, 2019
Cancer patients with SARS-CoV-2 infection	To reduce mortality	Routinely discontinue TKI/BTKI or ruxolitinib	D	III	Thibaud S et al. Br J Haematol. 2020; Treon SP et al. Blood. 2020;135(21):1912-1915; Barbui et al., Leukemia. 2021 Jan 7 : 1–9; Glenthoj et al., Eur J Haem 2021; Li W et al. Leukemia. 2020

Infection Prevention

Population	Intention	Intervention	SoR	QoE	References
Antiviral or immunomodulatory treatment					
Any patient	To improve outcome	Treatment in clinical trials	A	III	No reference.
Uninfected cancer patients (WHO 0)	To prevent infection	PEP with hydroxychloroquine	D	I	Barnabas et al., Ann Intern Med 2021 Mar;174(3):344-352; Mitja et al., New Engl J Med. 2021 Feb 4;384(5):417-427
		PEP with any other antiviral agent	D	III	No reference.

No G-CSF

Population / Clinical situation	Intention	Intervention	SoR	QoE	References
Patients with neutropenia	To improve outcome	Apply G-CSF	D	II	Zhang et al., CID 2021
Patients with impending neutropenia	To improve outcome	Broaden indication for G-CSF to risk of FN <20%	D	II	Zhang et al., CID 2021

Rationale

- 11 studies on COVID and cancer investigated influence of neutropenia (n= 6273 cancer pts.)
- Neutropenia not a risk factor in 8/11 studies
- Neutropenia risk factor in 3/11 in univariate analysis
- In most studies, raised ANC was associated with worse outcome; in contrast, lymphopenia more consistently risk factor
- In some risk scores, NLR included as adverse prognostic marker

Literature for neutropenia as risk factor

paper	n	n solid cancer pts.	n HM pts.	risk factors identified	neutropenia investigated?	supports neutropenia as risk factor?
Tian J,. Lancet Oncol 2020;21(7): 893e903	232			cancer treatment, pneumonia, pro-inflammatory cytokines, lymphopenia, normal ANC	yes	no
Kuderer NM,. Lancet 2020;395(10241): 1907e18.					no	
Mehta V, Cancer Discov 2020; 10(7):935e41	218	164	54	higher ANC; also anemia and inflammatory markers	yes	no
Aries JA. Br J Haematol 2020;190(2):e64e7	35		35	pts. who died had higher ANC; lymphopenia as risk factor identified	yes	no
Yang K,. Lancet Oncol 2020; 21(7):904e13	205	183	22	pts. who died had higher ANC; lymphopenia as risk factor identified	yes	no
FattizzoB. Leukemia 2020:1e4	16		16	pts. who died had higher ANC	yes	no
Williamson EJ,. Nature 2020;584(7821):430e6					no	
Lee LYW. Lancet 2020;395(10241):1919e26.	1044			haematol. malignancy associated with mort.	no	
Yang F. https://doi.org/10.1002/jmv.25972.						could not get paper
Assaad S,. Eur J Cancer 2020;135:251e9	302			lymphopenia identified as risk factor, neutropenia not reported	no	
Yarza R,. Eur J Cancer 2020;135:242e50	63	63		Mortality higher in severely neutropenic pts., lymphopenia risk factor	yes	yes
Rüthrich et al., Annals of Hematology 2020	435	351	124 (some with 2 cancers)	male sex, age and active disease	no	
EPICOVIDEHA	4117		4117	lymphopenia as risk factor identified; neutropenia reported but no risk factor	yes	no
Cattaneo et al., Cancer 2020	102		102	neither neutropenia nor lymphopenia as risk factor identified	yes	no
Borah et al., Blood cells Molecules and Disease 2021	130		130	neutropenia not mentioned as risk factor in abstract; age and active disease associated with worse outcome		could not get paper
Wood et al., Blood Advances 2020 first 250 cases from ASH hub	250		250	lab values not reported	no	
Ljungmann et al., Leukemia 2021	382 SCT recipients only		382 (236 allo-SCT)	neutropenia in univariate analysis, not in multivariate analysis	yes	possibly
Pinana et al. Exp Hematol Oncol 2020	367		367, including SCT and pediatric pts.	neutropenia associated with mortality in multivariate analysis	yes	yes
Palantes-Pastor et al., Leuk Lymphoma 2021 PETHEMA Experience	108		108	?		
Passamonti et al., Lancet Haematol 2020	536			anemia, thrombopenia and raised LDH reported as risk factors but not neutropenia	yes	no
Glenthoj et al, Eur J Haematol. 2021	66		66	no obvious difference in incidence of neutropenia depending on severity of COVID, but low numbers	not really	
Zhang et al., CID 2021	379			neutropenia not associated with advers outcome, G-CSF use associated with adverse outcome		

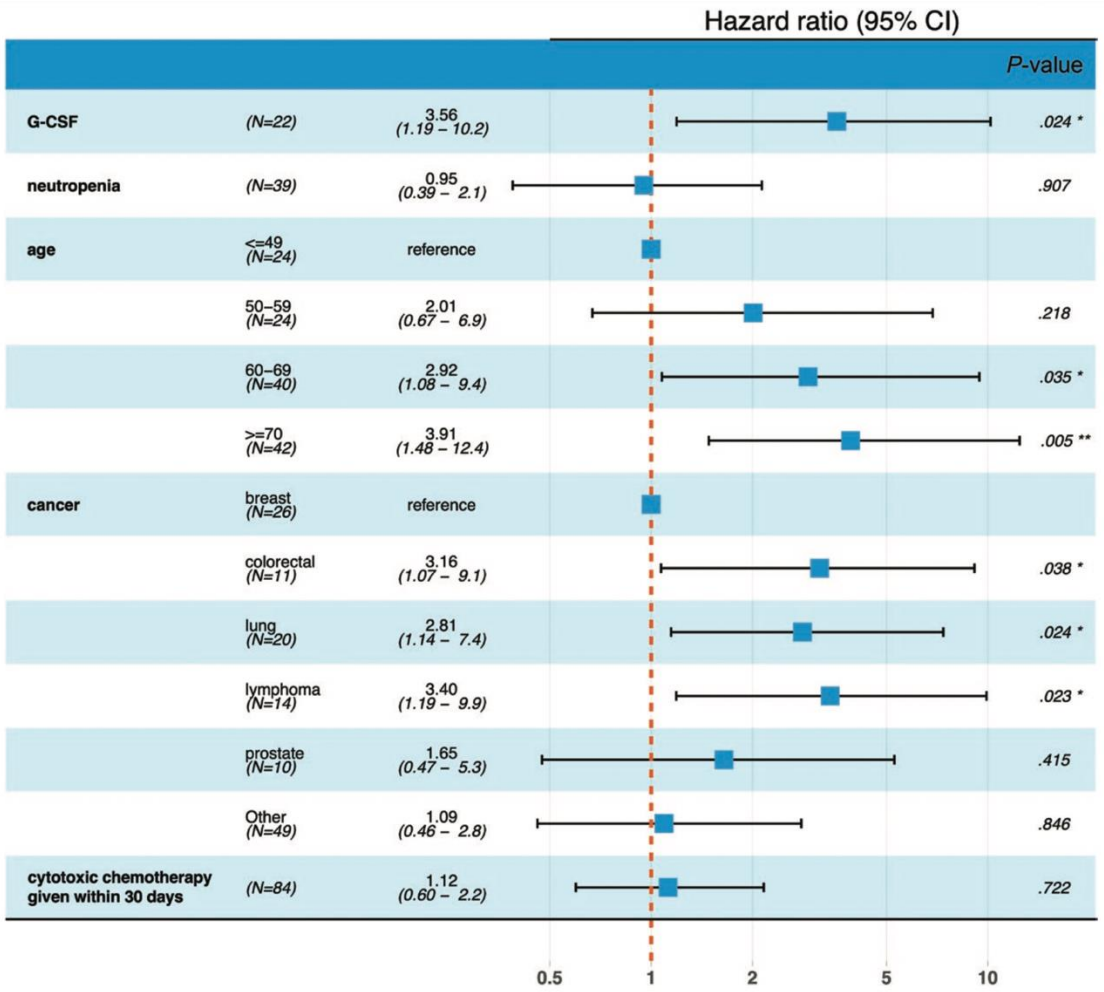

Figure 1. Forest plot showing the effect (HR) of (G-CSF) on the composite endpoint of the first occurrence of "respiratory failure" (defined in Methods) or death. HRs were computed with an extended Cox model, using binned ages and cancer type as time-independent covariates and neutropenia and G-CSF as time-dependent covariates. Abbreviations: CI, confidence interval; G-CSF, granulocyte colony-stimulating factor; HR, hazard ratio.

Zhang et al., CID 2021

DONOR DEFERRALS and cryopreservation

- **Social isolation before donation (AIII):** donors within 14 days of donation should practice good hygiene and be as socially isolated as feasible during this period. Unnecessary travel should be avoided.

- **Donors with close contact or diagnosed with COVID-19:**

Diagnosis of COVID-19	For at least 14 days after recovery **(AIII)**
Contact with a person diagnosed with COVID-19	For at least 14 days after last contact **(AIII)**
Practice good hygiene and socially isolated	Within 14 days of donation **(AIII)**

  - **If the patient's need for transplant is urgent,** the donor is completely well, a test is negative for SARS-CoV-2 and there are no suitable alternative donors, earlier collection may be considered subject to careful risk assessment
  - **Cryopreservation of the graft is an option for PBSC from RD and URD. BIII**
  - **However, graft cryopreservation is not recommended for severe aplastic anemia patients because of high rate of graft failure (Eapen et al., BBMT 2020). DII**

RECOMMENDATIONS FOR DONOR TESTING FOR SARS-CoV-2

WMDA: Any delay in transplant that results from cancellation or rejection of the donation will therefore disadvantage the patient with no known or likely risk of COVID-19 transmission.

- To protect the staff of the apheresis unit and other donors and patients: **Recommended (AIII)** (with result available prior to starting the collection procedure)

WMDA guidelines, EBMT guidelines

SURVEY ON DEFERRAL (1)

2-25 August 2021: Survey was performed among EBMT centers „Deferral survey”

OBJECTIVE: to assess the current clinical practice in HCT/hematology centers with respect to **attitude to deferral** of HCT/chemotherapy in patients with hematological malignancies or undergoing HCT in case of **asymptomatic** patients with **positive PCR assay**.

PART 1. In case of asymptomatic SARS-CoV-2 infection (no previous COVID19 disease).

PART 2. In case of patient who became asymptomatic after a previous COVID19 disease but is persistently shedding the virus.

RESPONSE: 107 centers (29 countries); Adult (68.2%), Pediatric (24.3%), Both (7.5%)

PCR testing for SARS-CoV-2	YES
• patients before admission for HCT	99.1%
• patients before admission for chemotherapy	84.1%
• vaccinated patients before admission for HCT	91.6%
• vaccinated patients before admission for chemotherapy	73.8%

SURVEY ON DEFERRAL: asymptomatic patients with SARS-CoV-2 infection (no previous COVID19 disease)

PATIENTS	DEFERRAL: % valid YES
Cellular therapy patients	
Allo-HCT high risk (ALL/AML)	90.2%
Allo-HCT low risk (malignant diseases)	88.2%
Allo-HCT non-malignant diseases	91.0%
Auto-HCT	88.0%
CAR-T therapy	83.1%
Non-cellular therapy patients	
Intensive therapy for AML/MDS	71.1%
Non-intensive therapy for AML/MDS	64.9%
Intensive therapy for ALL	70.4%
Non-intensive therapy for ALL	66.0%
Therapy for HD	74.5%
Therapy for NHL with rituximab	82.8%
Therapy for NHL without rituximab	71.0%
Therapy for multiple myeloma with daratumumab	84.6%
Therapy for multiple myeloma without daratumumab	71.4%
Therapy with anti-PD1	81.3%
TKI for CML	33.0%
Therapy with BTKi	51.8%
Therapy with ruxolitinib	50.0%

RECOMMENDATION: In case of asymptomatic SARS-CoV-2 infection (no previous COVID19 disease), it is recommended to defer: HCT/CAR-T therapy (~~AII-u~~), non-cellular therapy with MoAbs (~~AII-u~~), and other non-cellular therapies (~~B/CII-u~~).

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SURVEY ON DEFERRAL: asymptomatic patients after a previous COVID19 disease but is persistently shedding the virus

PATIENTS	DEFERRAL: % valid YES
Cellular therapy patients	
Allo-HCT high risk (ALL/AML)	76.9%
Allo-HCT low risk (malignant diseases)	83.7%
Allo-HCT non-malignant diseases	91.0%
Auto-HCT	79.8%
CAR-T therapy	81.4%
Non-cellular therapy patients	
Intensive therapy for AML/MDS	59.2%
Non-intensive therapy for AML/MDS	55.1%
Intensive therapy for ALL	60.8%
Non-intensive therapy for ALL	58.9%
Therapy for HD	59.6%
Therapy for NHL with rituximab	69.9%
Therapy for NHL without rituximab	57.0%
Therapy for multiple myeloma with daratumumab	64.5%
Therapy for multiple myeloma without daratumumab	57.1%
Therapy with anti-PD1	62.7%
TKI for CML	26.9%
Therapy with BTKi	48.2%
Therapy with ruxolitinib	40.7%

RECOMMENDATION: In case of patient who became asymptomatic after a previous COVID19 disease but is persistently shedding the virus, it is recommended to defer: HCT/CAR-T therapy (~~All-u~~), non-cellular therapy with MoAbs (~~Bll-u~~), and other non-cellular therapies (~~B/Cll-u~~).

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