10th EUROPEAN CONFERENCE on INFECTIONS in LEUKAEMIA

Final slide set
Post meeting

- **CONFERENCE**
  From September 19th to 21st, 2024
- **Golden Tulip Sophia Antipolis**
  Nice, France

Working Group COVID 19

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Definitions

SARS-COV-2 and COVID 19 acronyms

- SARS-CoV-2 infection = asymptomatic infection = positive test indicating viral replication

- COVID 19 = disease/symptomatic infection

Prevention

1	Hand hygiene and face mask (surgical mask or high-filtering capacity mask*), are recommended measures for HM patients to prevent SARS-CoV-2 and other respiratory virus infection, while distancing, and ventilation of rooms are recommended in case of high circulation of SARS-CoV-2 virus	AII
2	Caring for a SARS-CoV-2 positive HM patient requires the use of personal protective equipment (high-filtering capacity mask*, mask, gloves, gown, glasses) by health personnel and isolation in single room.	AII
3	Placing a SARS-CoV-2 positive HM patient into positive pressure rooms is not recommended.	DIII
5	In HM patient with SARS-CoV-2 infection, ensure the best possible treatment of underlying HM disease weighing individual patient related risks and benefits.	AIIu
10	Depending on severity of COVID-19 and vaccination status, after assessment of the clinical risk/benefit ratio, deferral until clinical and virological recovery is appropriate before proceeding with hematological treatment	No grading
11	Therapy with JAK2-inhibitors and TKI/BTKi should be continued in HM patients with SARS-CoV-2 infection.	AIIu
12	In case of high circulation of SARS-CoV-2 virus, aim to reduce the risk of SARS-CoV-2 exposure by avoiding hospital visits, where feasible, and promoting use of telemedicine and of home care, when clinically appropriate	BIIu

- Certified mask with high filtering capacity of 94-95% are FFP2, N95, KN95

HM = hematological malignant ….

Diagnosis (I)

13	Molecular assays are recommended for the diagnosis of SARS-CoV-2 infection.	AII
14	SARS-CoV-2 molecular assays should target at least two distinct viral gene sequences.	AIIt
15	The performance of SARS-CoV-2 molecular assays should be evaluated for newly emerging variants.	AIIt
16	Rapid antigen testing should be used for rapid point-of-care diagnosis.	AII
17	Testing for SARS-CoV-2 RNA in saliva or oropharyngeal gargle may be considered for symptomatic HM and HCT patients.	BIIt
18	Testing for SARS-CoV-2 RNA in saliva or oropharyngeal gargle may have a lower sensitivity in asymptomatic HM and HCT patients, but may be considered for serial (repeated) screening.	BIII
19	Clinical virology laboratories need to document proficiency in external SARS-CoV-2 quality accredited programs.	AII
20	A negative rapid antigen testing should be confirmed by molecular assays to rule out infection.	AII
21	Clinical virology laboratories need to document proficiency in external SARS-CoV-2 quality accredited programs.	AII
22	Nasopharyngeal or combined naso-oropharyngeal swab (with nostrils and throat with one swab) are recommended to diagnose SARS-CoV-2 upper respiratory tract infections.	AII
23	Bronchoalveolar lavage (BAL) should be performed if COVID-19 LRTI is suspected and nasopharyngeal molecular swab is negative for SARS-CoV-2.	AII
24	Testing lower respiratory tract fluid (tracheal aspirate, bronchoalveolar lavage) is recommended if a lung co-infection is suspected despite a positive SARS-CoV-2 nasopharyngeal swab	AII

LTRI = low respiratory tract infection

Diagnosis (II)

25	Screening the patient before hospitalization for chemotherapy, HCT, CAR T is recommended to inform decisions regarding infection control or deferral of therapy, HCT, or CAR T.	BIII
26	The detection of SARS-CoV-2-RNA or N-protein in blood correlates with a more severe course of COVID-19, but harnessing this information for clinical management requires further study.	No grading
27	Patients having consecutive SARS-CoV-2 PCR Ct-values of 30-35 and negative Ag test are unlikely to transmit infection, provided adequate sampling.	No grading
28	SARS-CoV-2 antibody assays are not recommended to diagnose a new-onset acute SARS-CoV-2 infection.	AII
29	Immunocompromised persons such as HM and HCT patients have a mitigated antibody responses.	No grading
30	The role of quantitative antibody assays calibrated to the 1st WHO-approved SARS-CoV-2 antibody standard is not defined for routine clinical-decision making regarding administration of booster vaccine doses or monoclonal antibody therapies.	CIII
31	Antibodies assay targeting N-protein can be considered to ascertain previous SARS-CoV-2 exposure.	AII
32	Antibodies assay targeting S-protein can be considered to ascertain vaccine response or previous exposure to SARS-CoV-2.	AII
33	Antibody assay targeting to N-protein can be considered in patients with suspected multi-inflammatory syndrome in children (MIS-C).	AII
34	The use of “in house” or commercially-available T-cell assays for the diagnosis or the management of SARS-CoV-2 infection requires further study.	No grading

HCT = hematopoietic cell transplantation; CAR T = chimeric antigen receptor T (cell)

Vaccination (I)

General recommendations for all HM patients including HCT or CAR-T cell recipients

35	HM patients, who were never vaccinated or have had a verified COVID-19 infection should receive a primary vaccination program according to recommendations by international and national authorities and authorized age range, preferably starting before initiation of treatment for the underlying disease (2-4 weeks), during maintenance, or when off-therapy.	AIIu
36	HM patients, vaccinated with a full program including those having had SARS-CoV-2 infection should receive at least yearly booster doses with an updated vaccine according to country recommendations	AIItu
37	In preparation of the winter season the co-administration at the same day of COVID-19 vaccine booster dose with influenza, according to the age-appropriate doses for children, adolescents, and adults is recommended	BIIt
38	The data regarding use of protein subunit vaccines in patients with hematological malignancies is limited	No grading
39	In the absence of well-established criteria for protection, it is not recommended to assess anti-SARS-CoV-2 antibody titers nor T-cell response with the aim to determine the need for booster doses.	DIIt
40	For mRNA vaccines, the interval between the first two doses should be at least 3 weeks and the interval between the 2nd and 3rd dose should preferably be 3 months.	AIItu
41	Additional (booster) dose(s) of SARS-CoV-2 vaccine should be given after at least 3 months from the 3rd dose according to the country recommendations.	AIItu
42	For patients having verified SARS-CoV-2 infection, booster dose(s) should be delayed at a minimum of 3 - 4 months after the resolution of the episode.	AIItu
43	HM patients should be informed of the ongoing risk of SARS-Cov-2 infection despite vaccination and follow the hygiene and social distancing recommendations of their community or country.	BIIt

Vaccination (II)

General recommendations for all HM patients including HCT or CAR-T cell recipients

44	Vaccination of health care personnel and of house-hold contacts of HM patients, including children, in accordance with regulatory authority approval and national recommendations for specific age groups, is recommended.	BIIt
45	Primary COVID-19 vaccination and booster administration is recommended in children affected by hematological malignancy, starting from 6 months of age with product and dosage approved for age	AIItu
46	Prophylaxis with MoAbs directed to SARS-CoV-2 should not prevent vaccination against COVID-19 in situations where such are indicated.	BIII

Vaccination in HM non transplanted patients (III)

47	There is until now no specific safety issue of COVID-19 vaccination with either mRNA or protein-subunit vaccines in non-transplanted HM patients.	AIIu
48	COVID-19 vaccination should not delay the treatment of the underlying disease	AII
49	Patients with an expected low or very low antibody response rate to vaccine (eg. anti-CD20 MoAb therapy ongoing or within the 6-12 months from the last dose, CAR T cell or bispecific antibody treatment targeting BCMA or CD19, induction chemotherapy for AL, profound hypogammaglobulinemia, deep lymphopenia), can still benefit from vaccination.	BII

MoAbs = monoclonal antibodies

Vaccination in transplanted patients (IV)

50	HCT recipients should receive a primary schedule of COVID-19 vaccine	AIIu
51	Timing of vaccination should be based on individual consideration taking into account the immune status of the patient and the prevalence of SARS-CoV-2 in the community but no earlier than 3 months after cell infusion	BIIu
52	There might be a risk for worsening/eliciting GVHD in allogeneic HCT recipients receiving primary schedule with mRNA vaccines although data is conflicting. This risk might be considered when deciding about the appropriate timing of vaccination	CII
53	Based on data from other vaccines, it is possible that immunity obtained from either pre-transplant SARS-CoV-2 infection or vaccination will be significantly affected by the transplant procedure. It seems logical from a risk/benefit assessment that allogeneic HCT patients should receive a full primary vaccine schedule after transplantation.	BIII

Vaccination in CAR T patients (V)

54	Patients with B-cell aplasia after treatment with CD19+ CAR T cells are unlikely to mount good antibody responses. After vaccination, T cell responses can be elicited in a majority of patients, but the importance for protection is unclear.	No grading
55	Timing of vaccination should be based on individual consideration taking into consideration the immune status of the patient and the prevalence of SARS-CoV-2 in the community but no earlier than 3 months after cell infusion	BII

GVHD = graft versus host disease

Vaccines approved by EMA

Vaccine	Type (date of authorization)	Dose(s)	Indications
Bimervax (Hipra)	Recombinant S protein, adjuvanted	40 µg	➢ Age ≥ 16 years in subject who previously received mRNA vaccine ➢ Interval of 6 months between doses
Comirnaty (Pfizer/BioNtech)	mRNA JN.1 (adapted) (3Jul24) Omicron XBB.1.5 (31Aug23) Original/OmicronBA.4-5 (12Sept22) Original/Omicron BA.1 (1Sept22)	3 µg, 10 µg, 30 µg	➢ Primary immunization and booster
Spikevax (Moderna)	mRNA JN.1 (adapted) (10Sept24) Omicron XBB.1.5 (15Sept23) Original/OmicronBA.4-5 (20Oct22) Original/Omicron BA.1 (1Sept22)	25 µg, 50 µg, 100 µg	➢ Primary immunization and booster
Nuvaxovid (Novavax)	Recombinant S protein, adjuvanted Omicron XBB.1.5 Original	5 µg	➢ Age ≥ 12 years ➢ Primary immunization

https://www.ema.europa.eu/en/human-regulatory-overview/public-health-threats/coronavirus-disease-covid-19/covid-19-medicines

Updated 2023-2024 vaccine formula for COVID 19: indications in immunocompromised patients

Vaccination status	Age 6 mo-4 yrs	5-11 yrs	12 yrs and older
Unvaccinated	Pfizer BNT 3 x 3 µg dose or Moderna 3 x 25 µg doses	Pfizer BNT 3 x 10 µg dose or Moderna 3 x 25 µg dose	Pfizer BNT 3 x 30 µg dose or Moderna 3 x 50 µg dose or Novavax 2 x 5 µg dose
Patient received 1 dose PfizerBNT Moderna Novavax	Pfizer BNT 2 x 3 µg dose Moderna 2 x 25 µg dose Not approved	Pfizer BNT 2 x 10 µg dose Moderna 2 x 25 µg dose Not approved	Pfizer BNT 2 x 30 µg dose Moderna 2 x 50 µg dose Novavax 1 x 5 µg dose (in specific cases)
Patient received 2 doses Pfizer BNT Moderna Novavax	Pfizer BNT 1 x 3 µg dose Moderna 1 x 25 µg dose Not approved	Pfizer BNT 1 x 10 µ g dose Moderna 1 x 25 µg dose Not approved	Pfizer BNT 1 x 30 µg dose Moderna 1 x 50 µg dose /
Patient received ≥ 3 doses Pfizer BNT Moderna	Pfizer BNT 1 x 3 µg dose or Moderna 1 x 25 µg dose	Pfizer BNT 1 x 10 µg dose or Moderna 1 x 25 µg dose	Pfizer BNT 1 x 10 µg dose or Moderna 1 x 25 µg dose or Novavax 1 x 5 µg dose
Interval dose 1-2	Pfizer BNT 3 weeks Moderna 4 weeks	Pfizer BNT 3 weeks Moderna 4 weeks	Pfizer BNT & Novavax 3 weeks Moderna 4 weeks
Interval dose 2-3	Pfizer BNT ≥-8 weeks Moderna ≥ 4 weeks	Pfizer BNT & Moderna ≥ 4 weeks	Pfizer BNT & Moderna ≥ 4 weeks
Interval dose 3 (dose 2 for Novavax) - booster	≥ 8 weeks	≥ 8 weeks	≥ 8 weeks
Interval booster-additional dose	≥ 8 weeks optional a second dose after ≥ 8 weeks	≥ 8 weeks, optional a second dose aft	≥ 8 weeks, optional a 2° dose ≥ 8weeks Recommended a second dose after ≥ 8 weeks for patients aged ≥ 65 yrs

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Therapy (I)

56	In severely immunocompromised HM patients, particularly with B-cell depletion or inadequately vaccinated, pre-exposure prophylaxis is recommended with long-acting anti-SARS-CoV-2 MoAbs if active against circulating variants, irrespective of previous vaccination	BIIt
57	In HM patients at high risk for COVID-19 progression*, post-exposure prophylaxis can be recommended with anti-SARS-CoV-2 MoAbs, if active against the circulating variants.	CIIt
58	In moderately or severely immunocompromised HM patient with mild-moderate COVID-19, early treatment is recommended, with:	AI
	1) nirmatrelvir/ritonavir	AIIu
	2) remdesivir	BIIu
	3) molnupiravir **	CIIu
	In selected very severely immunocompromised patients or in patients with imminent necessary chemotherapy or cellular therapy, a combination of two antivirals or combination of antiviral + MoAbs/convalescent plasma or prolonged antiviral treatment can be used.	CIIu
	Steroids should not be used in early treatment of mild-moderate COVID-19	DIIt

*not vaccinated, vaccine non-responders or not expected to respond to vaccine, recent B-cell depleting treatments

** lower efficacy and EMA not authorized

Therapy (II)

59	In HM patients with COVID-19 requiring oxygen support, the following treatments are recommended: 1) Antiviral therapy with - Remdesivir	AIIu
	or - Combination of two antivirals or an antiviral and MoAbs/ convalescent plasma	BIIu
	2) Anti-inflammatory treatment with short–term steroid course, is recommended only if COVID-19 related inflammation is present (e.g. clinically significant increase in inflammatory markers compared to pre-COVID19, compatible CT pattern), and no presence of co-infections likely to progress with steroid treatment (e.g. invasive mould infection, other viral pneumonia than COVID-19)	BIIt

Therapy (III)

60	In patients with critical COVID-19 (invasive/non-invasive ventilation and/or vasopressor therapy) the following treatments are recommended*:	
	1) Remdesivir	AIIt
	2) Combination of two antivirals or an antiviral + MoAbs	BIItu
	3) Anti-inflammatory treatment with short–term steroid course, is recommended only if COVID-19 related inflammation is present (e.g. clinically significant increase in inflammatory markers compared to pre-COVID19, compatible CT pattern), and no presence of co-infections likely to progress with steroid treatment (e.g. invasive mould infection, other viral pneumonia than COVID-19)	BIIu
	4) Add 2nd immunosuppressant, if COVID-19-related inflammation is present and worsening despite steroids: anti-IL-6 (tocilizumab, sarilumab) or baricitinib	BIIt
	5) High-titre convalescent plasma can be useful in critical ventilated patients (preferably within the first 48h after ventilation initiation) in addition to standard of care	BIItu

*Vilobelimab, a monoclonal antibody anti-C5a, is authorized in USA in COVID 19 patients on mechanical ventilation (within the first 48 hours after intubation) or ECMO, not approved by EMA and not licensed in Europe.

Drugs approved or in the authorization phase for COVID-19 (Europe and USA)

Class	Type	indication	note
Antivirals	Remdesivir (Veklury), vial. iv.	Treatment hospitalized/not hospitalized with mild-moderate COVID 19	Age 28 days (> 3 kg) and older
	Nirmatrelvir/ritonavir (Paxlovid), oral, tablets,	Treatment mild-moderate COVID 19	Adult
	Molnupirvir (Lagevrio), oral, tablets	Treatment mild-moderate COVID 19, (not authorized by EMA)	Adult
Monoclonals	Pemivibart (Pemgarda), iv. vials , 4500 mg every 3 mos	Pre-exposure prophylaxis (only USA) (CANOPY trial)	Age > 12 yrs (> 40 kg)
	Sipavibart, 300 mg, im, vial	Pre-exposure prophylaxis, (SUPERNOVA trial), active early access program in France	
Immunomodulators	Baricitinb (Olumiant), oral, tablets	Treatment of hospitalized patients with oxygen support, NMV, MV, ECMO	Adult
	Tocilizumab (RoActemera), vial, iv.	Treatment of hospitalized patients on steroids, with oxygen support, NMV, MV, ECMO	$\geq$ 2 years, adult
	Anakinra (Kineret), sc, vial	Treatment of hospitalized patients requiring oxygen, with pneumonia and elevated soluble urokinase plasminogen activator receptor (suPAR)	$\geq$ 8 months (or $\geq$ 10 kg), adult
	Vilobelimab (Gohibic), vials, iv.	Treatment of patients on mechanical ventilation or ECMO, anti-C5a, (available only in USA)	Adult
Blood products	Convalescent plasma, high titre	Treatment of COVID 19 in immuncompromised patients (FDA USA)	