9th EUROPEAN CONFERENCE on INFECTIONS in LEUKAEMIA

▶ IN-PERSON CONFERENCE
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Final
slide set

2022 – COVID-19 treatment update

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Recommendations summary update 17/09/2022

Treatment of SARS-CoV-2 infection and COVID-19 in immunocompromised patients with haematological malignancies and in HSCT recipients

Phase	Pre-exposure prophylaxis	Post-exposure prophylaxis	Mild/moderate COVID-19, no O2 for COVID required	Moderate with O2 for COVID required /Severe COVID-19	Critical COVID-19
Treatment	Mabs, if active against the circulating variants ^, currently tixagevimab + cilgavimab B II t	Mabs, if active against the circulating variants ^ A II t	**Give early treatment A I** Mabs, if active against the circulating variants A II t or nirmatrelvir/r A II t or remdesivir B II t or molnupiravir B II t Dexamethasone D II t	Dexamethasone A II t Remdesivir B II t Mabs, if active against the circulating variants B II t or high titre° CVP if Mabs not available C III	Dexamethasone A II t Remdesivir C II t Mabs, if active against the circulating variants C II t in NIV (no data in MIV)
				If severe COVID-19- related inflammation**, including worsening despite dexamethasone, add the 2nd immunosuppressant A II t: Anti-IL-6 (tocilizumab, sarilumab) B II t or JAK –inhibitor JAK – inhibitor - baricitinib (tofacitinib***) C II t or anti-IL1 (anakinra) C II t	If present COVID-19- related inflammation**, add the 2nd immunosuppressant A II t: Anti-IL-6 (tocilizumab, sarilumab) B II t

^ in moderately or severely immunocompromised patients, irrespective of the vaccination status

° as defined by FDA

** e.g. CRP > 75 mg/dl in the absence of bacterial coinfection (based on RECOVERY trial, Lancet 2021) or other available inflammation parameters or scores (if not altered due to the underlying haematological disease).

*** Baricitinib to be preferred, tofacitinib only if other options not available

The effects of immunomodulatory therapies targeting COVID-19 on the course of disease in already immunosuppressed patients are poorly understood and deserve special consideration

CVP, convalescent plasma; Mabs, anti-spike monoclonal antibodies; MV, mechanical ventilation: MIV, invasive, NIV, non-invasive.

Comments

- There is reduced or abolished activity of most anti-S MAbs against various VOCs of SARS-CoV-2 virus
- For establishing the activity of Mabs against circulating VOCs, follow indications for the general population at given time and geographical location
- Pre-exposure prophylaxis with Mabs, if active against the circulating variants, currently tixagevimab + cilgavimab, in moderately or severely immunocompromised patients, irrespective of the vaccination status, is recommended (B IIt), but:
  - It is not a substitute to vaccination - complete vaccination schedule should be pursued
  - If possible, higher doses and repeated dosing seem reasonable, considering the potentially diminished actvity against some VOCs
- CVP has no role in monotherapy of mild/moderate COVID-19
  - High titre (FDA definition) CVP might be useful in addition to antivirals in selected very immunocompromised/high risk patients if active Mabs are not available C III

CVP, convalescent plasma; Mabs, anti-spike monoclonal antibodies; VOC, variant of concern.

Pediatrics

- Data very limited. No studies dedicated to children

- No data suggesting the need for different treatment in children and adults, although children have much lower risk of severe COVID-19 as age is one of the most important risk factors.

    - The need for treatment of mild/moderate infection is probably much lower then in adults, and the main reason for providing it would be hastening the cure from SARS-CoV-2 infection to allow continuing HM treatment program

- **Practical information**

Antivirals

- 1) Nirmatrelvir/ritonavir: approved for 12 years old or above and 40kg
- 2) Remdesivir: approved for 12 years old or above and 40 kg (EMA) and for children ≥28 days of age who weigh ≥3 kg (FDA)
- ≥3 to <40 kg – 5 mg/kg intravenous (IV) loading dose on day 1, followed by 2.5 mg/kg IV every 24 hours
- ≥40 kg – 200 mg IV loading dose on day 1, followed by 100 mg IV every 24 hours
- The usual duration of therapy is up to 5 days for children with severe disease; for children with critical disease who are not improving after 5 days, the duration may be extended to up to 10 days.
- 3) Molnupiravir: not approved for age < 18 years

Monoclonals

- Most Mabs (sotrovimab, bebtelovimab, tixagevimab and cilgavimab) approved for 12 years old or above and 40kg

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B III for all

In **the most severely** immunocompromised haematological malignancy patients, the proposed treatment strategies for the challenging situations are:

1. Management of **new asymptomatic infection:** consider to manage the patient as in case of mild COVID-19, with the rationale to reduce the risk of progression, the length of shedding and the risk of delaying chemotherapy/transplant
2. Management of **clinical/virological rebound** (defined as reappearance of symptoms and/or SARS-CoV-2 positivity shortly after clinical improvement): consider new course of treatment since all the treatment schedules with antivirals are short
3. **Prolonged COVID-19**
   - **Consider** treatment with a combination of antiviral(s), particularly those with high antiviral potency, and Mabs (or high titre CVP) in order to obtain clinical improvement and prevent disease progression
   - Potential development of resistance to Mabs, and, less frequently, to antivirals should be considered
4. **Prolonged asymptomatic SARS-COV-2 positivity/infection**
   - **Consider** treatment with a combination of antiviral(s) and Mabs (or high titre CVP) in order to prevent disease progression and allow to resume haematological treatment
   - Potential development of resistance to Mabs, and, less frequently, to antivirals should be considered

*FDA definition

Unmet needs specific for patients with haematological malignancies and in HSCT recipients

- The role of combination of antiviral(s) and Mabs
- The need for prolonged course of antivirals in mild and in moderate/severe COVID-19
- Management of the underlying disease/deferral of transplant in case of positivity
- Use of T cell therapies against SARS-CoV-2
- The role of recent high titre CVP, as it might be less affected by the changes depending on VOC
- Risk of complications during HSCT in patients with previous COVID-19