COVID-19 and Peds ALL FAQs (V1 Posted 4/1x/2020)

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Q1. Are you changing your approach to initial induction and intensive post-remission therapy?

Severe coronavirus disease (COVID-19) is rare in healthy children (link: https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e4.htm). Few COVID-19 positive ALL cases have been reported during the pandemic, and courses have generally been mild.[1-3] Thus, the *major threat* to children with ALL, particularly those in remission when they acquire COVID-19, is the malignancy itself, although anecdotal reports of severe infections and fatal outcomes are emerging. Treatment needs to be individualized based on local conditions, whether the patient is already enrolled in a clinical trial, and whether new trial enrollment is feasible. Thus, it is appropriate to consult local and national regulatory bodies for guidance on management for patients enrolled on trials.

Newly diagnosed ALL is highly curable in children and most adolescents and young adults (AYA). Brief (1-2 weeks) interruptions of therapy may be appropriate for those in remission with asymptomatic/presymptomatic or mild COVID-19 infections. Longer interruptions may be indicated in cases with more severe, symptomatic infection. Patients who have COVID-19 at ALL presentation, during ALL induction or while in overt relapse should have their therapy individualized to balance the risk of leukemia vs COVID-19 complications.

Some of the investigational therapies used to treat COVID-19 are immune modulatory and may increase the risk of opportunistic infection in immunocompromised patients. Other investigational therapies can interact with agents commonly used to treat leukemia. Accordingly, additional supportive care measures and dose modifications may be warranted to address the risk of such complications.

To minimize the risk of infection, efforts to avoid clinic visits unless necessary to deliver chemotherapy or supportive care are warranted. Dose modifications, especially pre-maintenance, should be very cautiously approached and generally avoided, as it is unknown whether the current excellent cure rates can be preserved with modified therapy. Importantly, it is unclear if modifying pre-maintenance therapy will lessen the severity, or risk of, contracting COVID-19. Adherence to self-isolation measures, good handwashing, and the use of face masks is paramount. Extreme vigilance to other causes of infection in this population must be maintained.

Q2. Are you changing your recommendations for Philadelphia chromosome positive ALL?

No, we continue to recommend multi-drug induction and TKI given the rarity of COVID-19 in younger patients and the importance in early achievement of MRD negative response in pediatric Ph+ ALL. While some practitioners suggest TKI treatment with minimal steroid exposure as initial therapy for adults, we recommend no modifications to induction.

Q3. Are you changing your recommendations for infant ALL?

No, national or international protocols for this population should be followed although the risk of serious forms of COVID19 in children under the age of one year has been reported. Testing for COVID-19, possibly repeated, even without symptoms, is strongly recommended.

Q4. Are you changing your recommendations for ALL in children with Down syndrome?

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No, although vigilance is essential in these children who are susceptible to infections in general, even if this susceptibility has been rarely described for viral infections. Maximal supportive care, including potential mandatory hospitalization until signs of count recovery, is practiced by some.

Q5. Are you changing your recommendations for adolescents and young adults?

No, although considerations for leukemia therapy must include the presence of co-morbid risk factors observed in adults with fatal COVID-19, such as asthma, obesity, or diabetes. See

Kommentiert [DC([1]: Add link for Adult ALL

References

1. SARS-CoV-2 Infection in Children. Link https://www.ncbi.nlm.nih.gov/pubmed/32187458

2. Hrusak O, Kalina T, Wolf J, Balduzzi A, Provenzi M, Rizzari C, Rives S, del Pozo Carlavilla M, Alonso MEV, Pinilla ND, Bourquin J-P, Schmiegelow K, Attarbaschi A, Grillner P, Mellgren K, van der Werff JTB, Pieters R, Brozou T, Borkhardt A, Escherich G, Lauten M, Stanulla M, Smith O, Yeoh AEJ, Elitzur S, Vora A, Li C-K, Ariffin H, Kolenova A, Dallapozza L, Farah R, Lazic J, Manabe A, Styczynski J, Kovacs G, Ottoffy G, Felice M, Buldini B, Conter V, Stary J, Schrappe M. Flash Survey on SARS-CoV-2 Infections in Pediatric Patients on anti-Cancer Treatment. Eur J Cancer 2020 (In press).

3. Balduzzi A, Brivio E, Rovelli A, Rizzari C, Gasperini S, Melzi ML, Conter V, Biondi A. Lessons after the early management of the COVID-19 outbreak in a pediatric transplant and hemato-oncology center embedded within a COVID-19 dedicated hospital in Lombardia, Italy. Bone Marrow Transplantation (In press).