

Practical guidelines for managing CLL in COVID-19 pandemic

The points below are for consideration and do not constitute a guideline or firm recommendations for practice. There will understandably be considerable local geographical and patient-specific factors that will influence how individual patients are managed during the COVID pandemic.

For all patients with CLL, a risk benefit analysis needs to be made between the need to manage the underlying CLL and its complications versus the risks of exposure to COVID-19 through physical attendance at hospital or other units, for example local phlebotomy services at GP practices. The following guidelines are to support physicians and patients in the ideal management of each individual patient.

1. Anti COVID vaccines should be encouraged as per government guidance
<https://www.gov.uk/government/publications/covid-19-the-green-book-chapter-14a>, NB currently published trials have not included immunocompromised patients nor patients on immunosuppressive treatments. People with a history of severe allergic reactions should not have the Pfizer/BioNTech COVID-19 vaccine. Also the response to vaccine in patients with CLL may be suboptimal and those close to them should be vaccinated; the behavioral discipline regarding social distancing, isolating and shielding as currently recommended should continue. Please direct patients for more information and support to our partner charities: <https://www.clisupport.org.uk/cll-support-statement-on-covid-19-vaccines/>
<https://www.leukaemiacare.org.uk/support-and-information/latest-from-leukaemia-care/blog/covid-vaccine-faqs/>

CLL patients need to have inactive flu vaccines at least two weeks before receiving a COVID vaccine and should isolate from children having the nasal flu vaccination for 7 days.
2. Consider telephone or video conference appointments if feasible.
3. Watch and Wait and query progressing- at the next scheduled appointment perform local blood test with “bleed and go” with f/u telephone consult.
4. Consider anti-microbial prophylaxis (e.g. PJP) for all treatment regimens in CLL.
5. Always test for COVID-19 prior starting the therapy, have low threshold for re-testing. Assess local COVID infection rates.
6. Involve patients into decision making, explain options; especially if level of local COVID infections effects your choice
7. For patients who meet criteria for front line treatment the following additional options to chemo-immunotherapy are now available:
 - A. Venetoclax Obinutuzumab is now available as a front line treatment for all patients.
 - B. AstraZeneca have launched an acalabrutinib CLL program for treatment naïve patients (fulfilling eligibility criteria for ELEVATE-TN population), contact haem.eap@astrazeneca.com for more details. We recommend Acalabrutinib monotherapy. The early access programme will be open for new requests until 1st April 2021, or NICE reimbursement, whichever is earlier.
Acalabrutinib available for patients with 17p deletion/TP53 mutation as alternative to Ibrutinib or for those previously treated with ibrutinib who are intolerant to it (CDF criteria apply).
8. Continue to consider clinical trials if appropriate.
9. If on oral BTKi or Venetoclax- consider initial telephone consult , prescribe medication in advance, “bleed, sign consent and go” on day with immediate prescription pick up or preferably home delivery and locally performed blood tests, to ensure home delivery for vulnerable and elderly patients register on <https://www.gov.uk/coronavirus-extremely-vulnerable>; increase intervals for patients being seen, check shielding advice on government website.

10. Adjust re-starting/holding infusion therapy to current local prevalence of COVID infections (<https://www.nice.org.uk/guidance/ng161/chapter/7-Modifications-to-usual-service>)
11. If initiating relapse therapy, patients should be offered the choice between Ibrutinib, Acalabrutinib and Venetoclax-R , made aware of the risk:benefit profile of each option at this time;
 - a. Important BlueTeq update: Patients who have failed Ibrutinib-monotherapy as part of the frontline NCRI FLAIR trial can now receive Ven+R as second-line therapy
 - b. Acalabrutinib is now available for relapsed patients with no prior BTKi exposure (NB. Prior chemotherapy is not mandated) or for those who have received ibrutinib at relapse and are intolerant to it, (CDF criteria apply).
12. If patient develops COVID-19 infection, consider interrupting CLL therapy until resolution of the infection
13. COVID-19 prediction models. QCOVID is a risk prediction model for covid-19 related mortality for use in the general population (doi:[10.1136/bmj.m3731](https://doi.org/10.1136/bmj.m3731)), whereas the 4C mortality score is for use on admission to hospital (doi:[10.1136/bmj.m3339](https://doi.org/10.1136/bmj.m3339)).
14. Shielding advice: CLL patients should be considered on the clinically extremely vulnerable subgroup and should follow guidance <https://www.gov.uk/government/publications/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19>.
15. Please help us with the CLL patients' survey filled out by patients <https://forms.gle/9wdskUgyn7PwSWJq6> (current round of the survey has been closed), for the clinical survey of CLL patients who had Covid test positive or negative please fill this form <https://redcap.swan.ac.uk/surveys/?s=NL3LMLAWXJ> or please contact Fegancd1@cardiff.ac.uk.

If there are any queries regarding management and not covered by this guideline, please send the query through the website and we will try to respond in a timely manner.