
1. Front-line treatment

section and text: treatment of advanced disease stage -Front-line treatment

The Btk inhibitor ibrutinib was superior to chlorambucil alone regarding PFS and overall survival in a phase III study including mostly elderly patients [1]. If access is available, ibrutinib can be considered as an alternative treatment option to chlorambucil-based chemoimmunotherapy. However, lack of long-term experience with front-line therapy with ibrutinib must be taken into consideration [I, C].

Patients with TP53 deletion/mutation have a poor prognosis even after FCR therapy [2]. Therefore, it is recommended that patients with TP53 deletion/mutation are treated with ibrutinib in front-line [V, A]. Because of severe infectious complications, the PI3K inhibitor idelalisib combined with rituximab is only recommended for frontline therapy in patients not suitable for Btk inhibitors, if anti-infective prophylaxis is taken and

confirmed diagnosis of CL/LCLL

SLL or early stage CLL (Binet A/B) without active disease

Watch and wait until symptomatic

SLL or early stage CLL (Binet A/B) with active disease or advanced stage (Binet C)

No del (17p) or TP 53 mutation

Fit: FCR (OR may be considered in fit elderly with previous history of infections)

Less fit: Cb + CD20 antibody ibrutinib

del (17p) or TP 53 mutation

Fit: Btk inhibitor, P13K inhibitor + CD20 antibody only if not suitable for alternative treatment

Less fit: Btk inhibitor, P13K inhibitor + CD20 antibody only if not suitable for alternative treatment

Figure 1. Algorithm for frontline treatment.

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measures to prevent infection are followed. In the relapse setting, ibrutinib and idelalisib plus rituximab are treatment options.

**recommendations.**

- Frontline therapy with ibrutinib can be considered as an alternative to chlorambucil-based chemoimmunotherapy, if access is available [I, C].
- It is recommended that patients with TP53 deletion/mutation are treated with ibrutinib or idelalisib plus rituximab in frontline and relapse settings [V, A]. In front-line, idelalisib plus rituximab should only be considered if patients are not suitable for ibrutinib.

**references**


2. Treatment of complications

**section and text: treatment of advanced disease stage - Treatment of CLL complications**

Infections are a common complication in CLL patients, therefore use of immunosuppressive agents, as for example corticosteroids, should be restricted to a possible minimum. The use of prophylactic systemic immunoglobulin does not have an impact on OS [1, 2], and is only recommended in patients with severe hypogammaglobulinaemia and repeated infections [I, A]. Antibiotic and antiviral prophylaxis should be used in patients with recurrent infections and/or very high risk of developing infections (for example, pneumocystis prophylaxis with cotrimoxazole during treatment with chemoimmunotherapies based on purine analogues or bendamustine or during treatment with idelalisib plus rituximab) [IV, B]. Pneumococcal vaccination as well as seasonal flu vaccination is recommended in early stage CLL [IV, B]. Cytomegaly virus surveillance is recommended during treatment with idelalisib plus rituximab.

**recommendations.**

- The use of prophylactic systemic immunoglobulin is only recommended in patients with severe hypogammaglobulinaemia and repeated infections [I, A].
- Antibiotic and antiviral prophylaxis should be used in patients with recurrent infections and/or very high risk of developing infections [IV, B].
- Pneumococcal vaccination as well as seasonal flu vaccination is recommended in early stage CLL [IV, B].

**references**