These patients can achieve long-lasting remissions after treatment with 6 cycles of chemoimmunotherapy with FCR.

Increasingly, we are now making treatment decisions based on the patient’s genomic subtype. This strategy was not possible a few years ago, before the advent of targeted therapies.

What has been learned about targeted therapies as they progressed from clinical trials to use in the clinic?

The enrollment criteria of clinical trials tend to select a more homogeneous patient population than is seen in clinical practice. There are now substantial data from “real-world” studies of patients treated outside of clinical trials. These patients may be less fit and have comorbidities that would have excluded them from clinical trials. The real-world studies report that more patients are developing adverse events during treatment, leading to discontinuation of therapy.

What are the findings of studies evaluating different doses of these drugs?

This is an area of active research. Phase 1 studies led to the identification of drug doses that were then tested in larger phase 2 and 3 studies. However, we are now learning that it may be possible to lower the doses in some cases. Several retrospective studies of the use of ibrutinib have shown that dose reductions done to alleviate toxicities did not impact outcome. There are no data from...
The treatment landscape in CLL continues to evolve. Several other novel BTK inhibitors are currently in early-phase studies for patients with CLL. There is a novel PI3 kinase inhibitor in phase 3 studies. Depending on the results of ongoing phase 3 studies, there may be new drug approvals for CLL in the next few years.

Novel targeted therapies, such as myeloid cell leukemia 1 (MCL-1) inhibitors, are in early stages of development for patients with CLL. There are emerging data with the use of chimeric antigen receptor (CAR) T-cell therapy for patients with CLL. This therapy appears to be a very exciting approach.

Another clinical paradigm shift is the attempt to design treatment regimens consisting of a combination of targeted therapies that are time-limited, such as given for 1 to 2 years. The goal is to achieve a deep remission, or what is called a minimal residual disease–negative remission, and to eventually stop treatment. In the next 1 to 2 years, there should be data indicating whether these strategies will become valid options for patients with CLL.

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Suggested Readings


The real-world studies are showing that more patients are developing adverse events during treatment, leading to discontinuation of therapy.

Doses, the BTK occupancy of ibrutinib was still very high. Therefore, lower-dose ibrutinib was able to circumvent or overcome the BTK enzyme. Whether this strategy will be effective clinically remains unknown at this time.

H&O Are modified dosing strategies being used in the clinic?

NJ In clinical practice, many patients treated with ibrutinib will require a dose reduction after they develop toxicities with the standard dose of 420 mg once daily. Clinicians should follow the prescribing guidelines for ibrutinib to decrease the dose of the drug in patients experiencing a toxicity.

H&O Should a clinician aim to resume the full prescribing dose after some time?

NJ In most cases, when the dosage is reduced to alleviate a toxicity, the patient should remain on the lower dose. There is a possibility that the toxicity may recur with dose escalation. If there is concern about efficacy, then the full dose can be resumed. However, clinicians must monitor the patient closely to identify any recurrence of adverse events.

H&O Are there novel agents or treatment regimens in development for CLL?