Transcript Details

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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Selection of BTK inhibitor following frontline chemoimmunotherapy in older patients with comorbidities

Announcer:
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Dr. Shadman:
Hi, this is CME on ReachMD and I'm doctor Mazyar Shadman. Today I'm going to review and discuss selection of BTK inhibitor therapy in a CLL patient progressing after frontline chemoimmunotherapy. So, we'll start with the case. We have a 68-year-old man with history of CLL for 6 years. And patient presents for assessment of bilateral lymphadenopathy in the axillary and cervical areas, which started 2 months ago.

Six years ago, at the time of diagnosis, patient was checked and the FISH analysis showed 13q deletion, and patient had a mutated IGHV. So, first-line therapy, he received bendamustine and rituximab. This was 4 years ago. And patient has had 3 years of remission, and then had progression and he was monitored at a separate period but recently since 2 months ago, he's becoming symptomatic and noted progressive lymphadenopathy. The white blood cell count is 35,000 with 93% being lymphocytes. But patient is not anemic or thrombocytopenic. You repeat the FISH panel and now patient has evidence of del 17p, in addition to the previously known 13q deletion. This is a known phenomena that happens when you give chemotherapy to patients with CLL, and you have development of clones that were not available at the time of diagnosis. So, this patient is a businessman, and he travels a lot and it's important to note these subtle kind of pieces of information, because some of the treatment options that we have may have to do with the schedule of treatment. So, basically, we decide to go with the BTK inhibitor and not venetoclax, because of the patient's inability to be present for the ramp-up and the CD20 antibody therapy, and now the discussion is around which BTK inhibitors should we be using for a patient like this.

If you look at the data from the head-to-head randomized trials, we have two studies that have specifically looked at patients in this situation. ELEVATE-RR was a randomized trial comparing acalabrutinib to ibrutinib in an open-label randomized study and the study is focused on patients with 11q or 17p deletion, so high-risk population. The study had the primary endpoint of non-inferiority of PFS, and in fact, the study reached that endpoint, meaning that acalabrutinib was not inferior to ibrutinib, with the hazard ratio of 1. But the study also showed that acalabrutinib was superior to ibrutinib with lower rates and lower incidence of cardiac events of interest, like atrial fibrillation, atrial flutter, hypertension, bleeding, diarrhea, arthralgia, some of the adverse events of interest when we use the BTK inhibitor. So, basically, ELEVATE-RR in summary showed that acalabrutinib, from the efficiency standpoint, is not inferior to ibrutinib and it's better tolerated with a better safety profile.

Now, ALPINE was another study, a randomized study in relapse CLL, was not limited to high-risk features, it randomized previously treated CLL patients to receive either zanubrutinib versus ibrutinib. And this study showed the superiority of zanubrutinib over ibrutinib with the same duration of follow up similar to ELEVATE-RR and the study was recently updated and presented at the ASH meeting in

‘23 after 30 months of follow – 39 months of follow-up, the 36-month PFS was 64.9% with zanubrutinib, 54.8% with the ibrutinib. On a pre-planned analysis on del 17p/tp53 abnormal patients, zanubrutinib continued to show the superior efficacy with a PFS of 58.6% versus 41.3% in ibrutinib.

So, in a high-risk patient, like our patient here that we present, zanubrutinib has shown a superior efficacy compared to ibrutinib. And basically in terms of safety profile, one difference was that hypertension rate was not different between zanubrutinib and ibrutinib. This is, again, in contrast with the ELEVATE-RR study. But other cardiac events, including atrial fibrillation, AFlutter, was much less common with zanubrutinib, and there were no cardiac deaths in the zanubrutinib arm in the ALPINE trial, even with the longer follow up. So, the two great options, both zanubrutinib and acalabrutinib, to summarize, zanubrutinib has shown clinical efficacy over ibrutinib, acalabrutinib showed non-inferiority and they had both a favorable safety profile.

Our time is up, and I hope you found this information helpful and thank you for listening.

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