Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting: https://reachmd.com/programs/cme/safety-and-tolerability-of-changing-covalent-btk-inhibitor-treatment-in-a-patient-intolerant-to-ibrutinib-or-acalabrutinib/24454/

Released: 05/13/2024
Valid until: 05/13/2025
Time needed to complete: 22m

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

Safety and tolerability of changing covalent BTK inhibitor treatment in a patient intolerant to ibrutinib or acalabrutinib

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Shadman:
Hi, this is CME on ReachMD, and I'm Dr. Mazyar Shadman. Today I'm going to review and discuss managing a patient with CLL who's experiencing intolerance after being treated with acalabrutinib.

We start with a case. A 72-year-old woman with long history of CLL presents with muscle pain and joint pain, arthralgia and myalgia, 9 months after starting a collaborative. This is her third line of therapy. To give some history, patient received fludarabine and rituximab for first-line and was in remission for 3 years. Then, got venetoclax and rituximab. The duration of therapy was 2 years, and patient relapsed pretty quickly after that in 18 months. Now, the current treatment is acalabrutinib started at the standard dose. Patient had great response, great disease control, and initially had no adverse events except for that initial headache that went away after a few days. But now 6 months after the starting therapy, patient has started noting bilateral muscle and joint pain with minimal response to routine over the counter medications.

The dose of acalabrutinib was dropped to once a day with minimal relief, and patient is now presenting to talk about treatment options. She's really frustrated because this treatment finally was working for her, and her disease control was great, but she's not able to continue it despite the dose reduction, and now she's asking opinion regarding the best next treatment option.

So, here I think it's important to look at some data in terms of BTK intolerance. Initially, there were studies that looked at patients who were intolerant to ibrutinib. There were a couple of publications, from different groups looked at use of acalabrutinib in patients who did not tolerate ibrutinib. If you look at the kinome maps here, you see that, compared to ibrutinib, both zanubrutinib and acalabrutinib have a much cleaner kind of map, meaning that they do block BTK as an enzyme, and they have much less impact on the off-target enzymes there, and that translates to a better clinical safety profile. For example, data by Dr. Awan showed that in patients who switched from ibrutinib to acalabrutinib, they had much lower rate of an incidence of adverse events that occurred on ibrutinib, and if they they if the side effects occurred on acalabrutinib, they happened at the lower grade.

We also did a study that looked at zanubrutinib in patients who did not tolerate either ibrutinib or acalabrutinib. The study had 2 cohorts, one cohort was ibrutinib-intolerant patients, the other one was acalabrutinib-intolerant patients. And you see here that the study was published in Lancet Hematology last year, and showed that basically, patients who came off ibrutinib or acalabrutinib and received zanubrutinib, most of their adverse events either didn't happen on zanu, or if they occurred, they occurred at the lower grade. And there was no side effect that occurred at a higher grade, really indicating the fact that zanubrutinib is a very reliable option in patients who did not tolerate other BTK inhibitors for safety reasons.

And at ASH 23, we updated this data, and we focused on patients who came off acalabrutinib and received zanubrutinib, as you see here, to give you some kind of guidance. And the color-coding for this figure, when you see the color blue, first of all, you see the adverse events on the Y axis. Those are adverse events that – for which patients came off acalabrutinib. So, starting from arthralgia on the top, and you go down and you see these are the reasons why people came off acalabrutinib. And then the color under each adverse event tells you what happened on zanubrutinib, so if you see blue or navy, it means that that adverse event did not happen, and you see a lot of blues on this figure. If you see green, it means that the adverse event happened, but at the lower grade. Orange would be an adverse event recurring at the same grade. And there's no red here, but if you saw a red, the red meant that the adverse event happened at the higher grade, which we don't see one.

So, really 63% of patients did not experience any recurrence of their prior acalabrutinib intolerance events, and this is important because acalabrutinib itself is a very well-tolerated drug. So for patients who are considered to be very high risk for having adverse events, because they could not tolerate acalabrutinib, we can keep patients on this important class of drugs, BTK inhibitors, even if they were not tolerant to a drug, like acalabrutinib or ibrutinib. And zanubrutinib remains a viable option for these patients.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by TotalCME, LLC. and is part of our MinuteCE curriculum.

To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.