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Emerging data with potentially guideline-changing implications in CLL/SLL and MCL

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. Bhat:
This is CME on ReachMD, and I'm Dr. Seema Bhat.

Dr. Abramson:
And I'm Dr. Jeremy Abramson.

Dr. Bhat:
In this brief discussion, we will take you through some emerging data with potentially guideline-changing implications in CLL SLL and mantle cell lymphoma.

Dr. Abramson, can you tell us about the latest data? What trials are you excited about?

Dr. Abramson:
Well, there's a lot of exciting ongoing trials of noncovalent BTK inhibitors in patients with both previously untreated and relapsed refractory CLL. For example, in patients who are treatment naive, we have a couple of trials of pirtobrutinib being randomized against alternate treatments. There's a study called the BRUIN CLL-313 study comparing pirtobrutinib with bendamustine/rituximab, and then there's a BRUIN CLL-314 study comparing pirtobrutinib to the covalent BTK inhibitor, ibrutinib.

In patients with relapsed or refractory CLL, we actually have a couple of randomized trials as well. There's a trial called the BRUIN CLL-321 study comparing pirtobrutinib versus the dealer's choice of either idelalisib/rituximab or BR. And then there's the BRUIN CLL-322 study, which is evaluating the addition of pirtobrutinib to venetoclax/rituximab compared to patients receiving venetoclax/rituximab alone. We did see initial data from the study I mentioned, BRUIN CLL-321, comparing pirtobrutinib to either idelalisib/rituximab or BR. This data, presented just recently at the ASH annual meeting in San Diego, not surprisingly, showed superiority for the pirtobrutinib arm over idelalisib/rituximab or BR. Specifically, the median progression-free survival was 14 months for pirtobrutinib, and only 8.7 months for idelalisib/rituximab or BR. Additionally, the median event-free survival was 14.1 months for pirtobrutinib versus 7.6 months for idelalisib/rituximab or BR.

Additionally, we have data for a different noncovalent BTK inhibitor, called nemtabrutinib. There are several ongoing studies of nemtabrutinib in either treatment naive or patients with relapsed refractory CLL. In treatment naïve CLL, we have the BELLWAVE-011 study comparing nemtabrutinib versus either ibrutinib or acalabrutinib.

In patients who were previously untreated and have no TP53 mutation, there's also a study (BELLWAVE-008) comparing nemtabrutinib with chemoimmunotherapy, and the chemoimmunotherapy is either FCR or BR, based on the choice of the treating investigator. And then, in patients with relapsed disease, we have a study (BELLWAVE-010) comparing nemtabrutinib plus venetoclax versus venetoclax/rituximab.

We do have some initial data from the BELLWAVE-001 study, which is looking at patients receiving nemtabrutinib monotherapy in

patients with relapsed CLL with or without a cysteine 481 BTK mutation. And among all patients, we see an overall response rate of 56% and a median duration of response of 26 months.

If we turn our attention to mantle cell lymphoma, we also have a number of ongoing Phase 2 and Phase 3 trials looking at noncovalent BTK inhibitors. There's a Phase 3 BRUIN MCL-321 study comparing pirtobrutinib with the investigator's choice of covalent BTK inhibitor, which is either ibrutinib, acalabrutinib, or zanubrutinib.

Additionally, for patients with relapsed mantle cell lymphoma, there's a combination study of pirtobrutinib plus venetoclax, a combination study of pirtobrutinib plus brexu-cel, and finally, a combination of pirtobrutinib plus the bispecific antibody glofitamab. In patients with previously untreated low and intermediate risk, there's also an ongoing study looking at pirtobrutinib plus rituximab. So, lots of ongoing, exciting trials with noncovalent BTK inhibitors in both CLL and mantle cell lymphoma.

Dr. Bhat:

These are all very exciting studies. The common theme for CLL is that the field is moving more towards fixed duration therapy. Data from AMPLIFY study was presented at ASH 2024.This is a Phase 3 trial comparing acalabrutinib plus venetoclax with or without obinutuzumab to chemoimmunotherapy in fit patients without deletion 17p or TP53 mutation in the frontline setting. Based on this study, we may see the first all oral fixed duration therapy approved in the United States soon.

Zanubrutinib plus sonrotoclax also looks good, and pirtobrutinib is being evaluated in the frontline space with amazing results from the PVO study. In the relapsed setting, we may see pirtobrutinib move to second-line setting based on the BRUIN CLL-321 study, which you just discussed. So, these are a few practice-implicating studies from ASH 2024 and as far as the future is concerned, just as you said, that too looks exciting. I was very encouraged to see data from EPCORE CLL-1 trial of epcoritamab, which is a bispecific antibody. CR rates are very impressive in the refractory patients and these were seen across all high risk groups. The study's actually planning some exciting combinations with venetoclax and pirtobrutinib.

BTK degraders are an emerging class. Trial results from two BTK degraders show responses of over 75% and notably, there were very low atrial fibrillation rates.

That is all the time we have. I hope we gave you something to think about, and thanks for tuning in.

Announcer:
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