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/mutational-testing-to-guide-therapy-in-cll-why-and-when/26496/

Released: 08/16/2024
Valid until: 08/16/2025
Time needed to complete: 1h 13m

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

Mutational Testing to Guide Therapy in CLL: Why and When

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. Munir:
Hi, this is CME on ReachMD, and I'm Dr. Talha Munir. Today, I'll review the importance of mutational testing in CLL [chronic lymphocytic leukemia] and when it should be done.

So the mutational testing is important in CLL, and the main objective is to risk stratify the patients before they start any therapy. So the first thing to talk about is the IGHV mutational status, which can be only done once in the lifetime of a CLL patient. And we normally classify the patients into IGHV-mutated or unmutated IGHV status. And the main benefit of using that is that it tells us that the time to first treatment for a patient with IGHV-mutated CLL could be quite long as compared to unmutated patient. And subsequently, the most useful thing is now choosing therapy for mutated and unmutated patients because we know that the mutated IGHV patients can benefit from any targeted drugs that we can give them, as well as chemoimmunotherapy, which we have used in the past, but we are hardly using it now. But for unmutated patients, it is becoming quite important because the outcomes to different treatments are slightly different in the unmutated IGHV status. So as a rule, the fixed-duration therapy outcomes are slightly inferior to when we are using continuous treatments in these patients where both mutated and unmutated IGHV patients are doing very well.

Secondly, it is also important to check for TP53 deletion by FISH [fluorescence in situ hybridization] analysis, but TP53 mutation analysis has become very important as well as we know that even patients who have no TP53 deletion, some of these patients would have a mutated status. And again, it will help to risk stratify in our patients. So all the NCCN Guidelines, as well as the guidelines from the UK group, as well as the ESMO guidelines, will suggest that the patients should have IGHV mutational status checked, as well as TP53 mutation checked, right at the start of the treatment. And the other test that we can do is FISH analysis for our CLL patients, and those tests help us to risk stratify our patients. But the concept of complex karyotyping by stimulated FISH is becoming more and more, prevalent in the clinical trials, but in normal practice, it hasn't resulted in any change in practice as such. In terms of any patient starting therapy, I would definitely recommend doing IGHV mutational status as well as TP53 mutational status and FISH, especially for high-risk markers, such as TP53 deletion.

Lastly, patients who have had multiple lines of therapy and have seen targeted drugs, there is a concept now developing of using drug-specific mutations. So for example, with covalent BTK inhibitors, we know that the binding site mutation of 16 at 481 is quite important. Especially when patients are becoming intolerant to one BTK inhibitor and moving them on to another BTK inhibitor, it is a useful test to check whether these patients have had development of these mutations. And also, when the patients are moving from one line of therapy to another line of therapy, it is important to see whether change in the class of the drugs is important. However, the testing is not universal, and I will say it needs to be recognized that the variant frequency or the allele burden of these mutations is very important, but where patients do need a change in therapy, especially when they are on previous drug which can induce a mutation status, these

© 2024 ReachMD

mutations are important to look at. And this is becoming a more and more important question as we come into the era of non-covalent BTK inhibitors where the mutational profile will look very different.

So in short, please do check for IGHV mutations and TP53 mutational status of a patient, and drug-specific mutations only in very specific scenarios.

And thank you for listening. My time is up. I hope you found my perspective useful for your practice and thank you for listening.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by Prova Education 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.

© 2024 ReachMD