How do cytogenetics and molecular risk guide your treatment decisions?

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Hello, I am Dr. Pinkal Desai, Leukemia Physician at Weill Cornell Medicine and New York-Presbyterian Hospital. I really, really believe that AML is not a one disease state. It is so heterogeneous. There is so much variation within one patient versus another on cytogenetics and molecular risks. It is very, very important that these risks are defined ahead of time, and it's important for a variety of reasons. Everybody who has newly diagnosed leukemia should have a karyotype or cytogenetic risk identified and the tests done. In addition, there has to be a molecular profile that should also be done at diagnosis. This is important for several reasons. The first one is selecting the treatment itself. There are certain mutations that are targetable and there are approved drugs for those mutations in the newly diagnosed upfront setting, for example midostaurin. It's absolutely important that we know whether somebody has a FLT3 mutation or not. There are several other targeted treatments that are coming up in clinical trial so it's important to identify that at baseline. Patients should obviously be encouraged to join any of these trials because those are the key things to improve survival in patients.

The second reason why molecular risk and identification of the individual molecular profiling is important is to figure out what to do after a patient goes into remission. It's not just the upfront induction treatment that would matter but also what we do after the patient is already in remission. Depending on this molecular profiling and cytogenetic risk, one should make individualized decisions on whether somebody should be consolidated with allogeneic stem cell transplantation, or whether there should be more consolidation in the form of chemotherapy; and that distinction is completely based on these molecular and cytogenetic risks.

I would argue that getting into remission is just part of the work in AML. In fact, most patients who have AML and are in remission still have some amount of residual disease. It's just not identifiable on regular morphologic testing, so it's important that the right consolidation follow the remission in order to increase the chances of cure. These molecular classifications help us identify what patients are more likely to relapse.

The third reason why these mutations may be helpful – and this is not currently the standard in AML, but I believe will be at some point – is for some of these mutations, for example NPM1 and also some other proteins that we could identify like the core binding factor leukemia, there is a push towards monitoring them over time, even in remission, and what we call MRD testing

(measurable residual disease testing). If you know that a patient has a particular mutation and we determine that that mutation is one of those founder mutations and could be prospectively monitored, that helps us understand whether somebody is going to relapse. If we see that these mutations could be followed over time and that their transcripts are rising, that will help us understand, okay, this patient is more likely to relapse; should we do something at this point to prevent the oncoming relapse? I think that the molecular mutation profiling and personalization of care is extremely important for not just upfront treatment but also consolidation, and also eventually monitoring these people after all of the treatments are done. I would strongly, strongly feel that this should be always done.