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What is the recommended baseline cytogenetic molecular and immune profiling workup in a patient with newly diagnosed acute myeloid leukemia (AML)?

Welcome to *Managing AML*. I am Dr. Naval Daver. I am frequently asked, "What is the recommended baseline cytogenetic molecular and immune profiling workup in a patient with newly diagnosed acute myeloid leukemia (AML)?" So, when we get a new patient with acute myeloid leukemia who presents to our institution at MD Anderson, the initial workup is usually done very rapidly. Being an acute condition, these patients often have significant organ damage in the form of liver or kidney inflammation. Often they will also present with very high white count and this leukocytosis, if not controlled early on, could result in further organ damage. So, the initial step is usually to get a bone marrow aspirate the same day and send the bone marrow for three particular types of workup. One of them is cytogenic or chromosome analysis, and we will be looking for general chromosome analysis. Additionally we will also do a FISH probe looking for other specific chromosome abnormalities such as inv(16), t(8;21), and t(15;17).

These three are very important because if the patient has either inv(16) or t(8;21), they are considered core-binding factor leukemia. Patients with core-binding factor AML do much better than patients who do not have core-binding factor AML, and also these patients respond very well to FLAG IDA based therapy rather than 7+3.* So, usually they benefit from high-dose AraC-based treatments. The second cytogenic abnormality that one must rule out before embarking on treatment of the AML is t(15;17), which is also known as APL (acute promyelocytic leukemia). It is extremely important to look for this one because if the patient does have acute promyelocytic leukemia the treatment is extremely different from general AML therapy. These patients are treated with two targeted agents, ATRA in combination with arsenic, having remission rates of 97% and 98%, and 5-year plus survival rates of 94%.

Once we rule out these three groups and we know that this patient does not have APL or core-binding factor acute myeloid leukemia, the further workup and treatment decisions are based on molecular profiling. So, we will then look for presence of molecular mutations, at this time specifically FLT3 or IDH1 or IDH2, and if the patient does have one of these mutations, we would try to get them onto a clinical trial that includes standard chemo or standard hypomethylating therapy in combination with either a FLT3 inhibitor or IDH inhibitor. Additionally, there is a new class of treatments that will be available for acute myeloid leukemia; these are currently in clinical trials and are called monoclonal antibodies as

well as checkpoint inhibitors. What we notice is that if the patient expresses a particular antigen, such as CD33 or CD123 which are expressed in a majority of AML cases, then we can target these antigens with antibodies that carry a toxic payload. There are a number of anti-CD33 antibodies as well as anti-CD123 and now anti-CD38 antibodies that are being developed. We will also get a flow cytometry immune workup in addition to the cytogenetic and molecular workup to look for the presence of these antigens such as CD33 and CD123 to see if the patient would be a candidate.

In addition to letting us know if these patients are candidates for these monoclonal antibodies, the immune phenotype is also important, because we will then use this at the time of remission to look for the presence of minimal residual disease (MRD). So, once you have a baseline immunophenotype, we can repeat that after induction and after consolidation to see if the person has any minimal residual disease. This is very important because this gives us an additional layer of detail beyond the morphological remission that is read by the pathologist. Now, a number of studies have shown that if the patient becomes MRD-negative or has a major MRD response, they have significantly better survival than those who achieve their remission but remain MRD-positive.

In summary, chromosome workup followed by molecular workup and immune phenotyping with flow cytometry should be done in all newly diagnosed AML patients. This can not only help us select treatment, but may also help us monitor response to therapy and long-term outcome in these patients. Thank you for viewing this activity.

**7+3, referred to in the video as 3+7, is most often used today as first-line induction therapy in AML, and consists of 7 days of standard dose cytarabine and 3 days of an anthracycline, most often daunorubicin.*