The First-in-Class Anti-CD47 Antibody Magrolimab (5F9) in Combination with Azacitidine Is Effective in MDS and AML Patients: Ongoing Phase 1b Results

Guillermo Garcia-Manero, MD
Professor
Dr. Kenneth B. McCredie Chair in Clinical Leukemia Research
Chief, Section of Myelodysplastic Syndromes
Department of Leukemia
The University of Texas MD Anderson Cancer Center
Houston, Texas

I'm Dr. Guillermo Garcia-Manero and I'm live at the 61st ASH Conference in Orlando, Florida. Today I will be reviewing Abstract 569, which reported on a first-in-class anti-CD47 antibody known as magrolimab, or 5F9, in combination with azacitidine in patients with MDS and AML. This was an initial report of a phase IB study that was presented by Dr. Sallman from the Moffitt Cancer Center. We have multiple centers in North America. Magrolimab, known previously as 5F9, is the first-in-class antibody that targets CD47. This is a very important immune checkpoint for macrophages and it basically inhibits the so-called, “Don't eat me” signal, basically rendering this macrophages active and with potential clinical activity in patients with leukemia. Prior studies performed mainly at Stanford have indicated that CD47 expression was associated with distinct prognosis, and that in the initial phases of this trial, this combination was highly active when given with azacitidine. In this presentation, Dr. Sallman gave us a further update on the group of patients with both MDS and/or AML that were treated on this trial as frontline type of therapy.

The first question is about the safety of this compound. Basically, the toxicity profile looked to be very similar to what you will expect with azacitidine. These drugs have had typical, meaning the anti-CD47 antibody have a potential on-target toxicity that is anemia. This is related to the expression of the targeting aging red cells. The schedule that was developed on this particular trial actually ameliorated the development of anemia quite significantly in this particular protocol, allowing very safe administration of this combination in patients with MDS and AML. We use a standard dosing of azacitidine and the drug actually had a dose escalation through the first cycle of therapy and is administered later on weekly. The authors have reported on 43 patients, including 18 patients with MDS and 25 with AML. The characteristics are similar to what you will expect in common patients with this disease in a community with a median age of 73 years of age, and some of them actually had very poor or adverse features including high-risk cytogenetics in 63% of the patients, and very importantly, TP53 mutation in close to 50% of the patients. As expected, there were some hematological toxicity, some reactions, but the toxicity profile, again I said earlier, doesn't seem to be dissimilar to what you will see right now with this preliminary data with single-agent azacitidine. The activity of this compound was very

significant in those patients that we evaluated for response, meaning that they had received at least two cycles of therapy because that's when the bone marrow for assessment is performed on this trial. There was almost 100% response rate in patients with MDS including 54% of those achieving complete remission. Another group of patients actually achieved a marrow CR with hematological improvement, and a fraction of these patients have just hematological improvement alone. This is very significant data if you compared to the expectation with single-agent azacitidine.

Of interest, the response rate in patients with AML was also very high. In the group of patients with AML, there was an overall response rate close to 69% and half of these patients achieve a CR and/or CRi with patient achieving partial responses, and as one fraction of them achieving these so-called minimal leukemia-free state. A third of these patients also achieved stable disease. Right now, there is no data in terms of the duration of the responses, because the follow up of this study is very short. But these responses in the frontline is stating both MDS and AML are quite remarkable. The authors also showed evidence of cytogenetic and molecular responses. This data is being evaluated. Again, very nice improvement in transfusion requirements when these patients respond, both in terms of red cells and platelets. So, this now basically suggests a total innovative way to combine a new immune checkpoint inhibitor targeting macrophages with azacitidine data that was presented also by the authors of this presentation indicate that this may have a very deep effect attacking leukemia stem cells. And there was also a very interesting subset analysis in this presentation looking at patients with p53 mutation, where the small cohort of patients that adhere showed a very significant high rate of response for a group of patients that we know very well that they tend to be refractory to all therapies.

In my conclusion, this appears to be a safe combination with a very high rate of response that may even affect the stem cell. The caution is that the follow up is very short. And we need a little bit longer follow up to really evaluate this data. But I think this is very interesting doublet presented at this ASH that would have great future for our patients with both MDS and AML. Again, thank you very much for viewing this activity.

Reference: Sallman DA, et al. The First-in-Class Anti-CD47 Antibody Magrolimab (5F9) in Combination with Azacitidine Is Effective in MDS and AML Patients: Ongoing Phase 1b Results. Abstract 569. ASH 2019.
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