What are the updates from ASH regarding new treatments or new data for patients with myelofibrosis?

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I think the things that stood out to me that were memorable from ASH and we will definitely hear more about, updated data, for example, on momelotinib, the JAK1/2 ACVR1 inhibitor for myelofibrosis.

They presented data on the 24-week open-label extension phase. This was from the MOMENTUM study comparing momelotinib to danazol in patients who have previously seen a JAK inhibitor and have spleen symptom and anemia burden. In this study, it was quite clear that there was a benefit in terms of symptom improvement compared to danazol, as well as spleen volume reduction and importantly transfusion independence that was durable with a safety profile that was also durable and without any new signal of toxicity concern.

Momelotinib is likely a fourth JAK inhibitor to be approved come summertime of 2023 with the prospect of adding an option to patients with myelofibrosis that need spleen and symptom benefit and have ongoing anemia or transfusion requirements. I think what was also important from the meeting along the same line is there's a lot of attempts to try to address anemia in myelofibrosis which is both a prevalent issue, a progressive issue, and has adverse prognostic influence and clearly leads to poor quality of life.

Data was also presented about pacritinib, the JAK2, FLT3-IRAK1 now known to be ACVR1 inhibitor. So, a similar mechanism to momelotinib in terms of modulating hepcidin in which a quarter of patients from the PERSIST-2 study achieved clinical improvement either by 2 g/dL increase in hemoglobin or transfusion independence with pacritinib. A drug that is now approved for myelofibrosis with thrombocytopenia, so less than 50,000, or irrespective of platelet count as a second or third line agent, which also holds the potential to improve anemia in patients, where that's also an unmet need.

Outside of the JAK inhibitor space, there was a lot of data on ongoing combination studies. Data was presented, as it relates to ruxolitinib and parsaclisib, the PI3-kinase inhibitor, ruxolitinib plus pelabresib, the BET inhibitor in the upfront setting but also as an add-on strategy. And ruxolitinib plus navitoclax, the BCL-2 inhibitor with some data in the upfront setting.

Collectively, I look at this data and it tells me that there are a number of drugs in late-stage testing based on positive phase two data supporting additive benefit of adding these targeted therapies to ruxolitinib, either in the upfront setting in getting deeper spleen responses, symptom improvement, or in the salvage setting to try to improve upon a suboptimal response. What I think we need to look for are the results of the ongoing phase three studies with parsaclisib, with pelabresib, and with navitoclax.

Interestingly and importantly, particularly with navitoclax and pelabresib, there was nice data from those studies that's been presented demonstrating a reduction in bone marrow fibrosis in about a third of the patients, anemia responses in some patients, and deep reductions in cytokine profiles of patients that are treated with these combinations. This is an area of interest in combination therapies upfront or in salvage. We look forward to hearing more of those studies.

I think, lastly, I'll just point out that one very interesting plenary session abstract was on the pre-clinical data supporting the use of a novel mutant CALR-directed antibody that's being developed and will translate into the clinic in 2023. This will be for patients with myelofibrosis, for example, that are CALR-mutated, whether it's type one or type two, and has a mechanism that would appear to induce death in these mutant CALR-expressing tumor cells in these patients. I'm very excited to see how that clinical data pans out, but that's yet to come.

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