How to proceed with a patient who presents with idiopathic cytopenias of undetermined significance (ICUS)

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Welcome to *Managing MDS*. I am Dr. Stuart Goldberg, and today I am going to briefly discuss how to proceed with a patient who presents with idiopathic cytopenias of undetermined significance, also known as ICUS.

We have all seen patients in our office who come in with vague cytopenias, and we do the workup, but we still do not have an answer. Many of these patients now fall into a category known as ICUS or idiopathic cytopenias of undetermined/uncertain significance; the related diagnosis of CHIP which stands for clonal hematopoiesis of indeterminate potential; and even the more aggressive, but still vague, clonal cytopenias of undetermined significance, or CCUS. What are these three? We know that especially in elderly patients, about 10% of patients will present with anemia; but a third of these patients, we cannot figure out. We have done the vitamin studies, we have looked for autoimmune diseases, we have done clonal studies, and we have even done a bone marrow, and still do not have an answer. Idiopathic cytopenias of uncertain significance is what we call those patients.

Fortunately, most of these patients will end up recovering on their own and over time will just drift away from the hematologists. So, for those patients for whom we have done a full workup and we do not find an answer – and that includes a full bone marrow evaluation – we can follow these patients every three to six months in the office. If they have more significant cytopenias, we may want to follow them a little bit more; but that usually is just an observation.

We also have a group of patients called CHIP where we have done cytogenetics or we have done molecular studies (next-generation sequencing). We may have found an abnormality that suggests that they might have a clonal problem, a TET2 mutation or something like that; but we still do not have an answer and the cytopenias are not that bad in CHIP. So once again, we can follow those patients every three to six months; maybe a little bit more frequently because this group has a higher incidence of moving ahead to a true hematologic malignancy. Once again, observation.

The real group that we need to follow a little more closely is the clonal cytopenias of uncertain significance. These are patients who have meaningful cytopenias. They have

low hemoglobin, low white counts or low platelet counts, and yet the bone marrow does not yet show the dysplasia needed for MDS or some other hematologic malignancy. But we have also found a molecular signal (a TET2, an ASXL); something that really says, wow, this looks like a malignancy. We still do not have enough to make a diagnosis, so once again, we do not treat these patients with chemotherapy. We may want to follow these patients every one to two months in our office with blood counts because unfortunately many of these patients, will end up having a diagnosis of MDS or some other hematologic malignancy over the next year.

That is how I approach my patients with vague cytopenias. I do the bone marrow. I do next-generation sequencing because we are going to find a lot of clonal molecular changes. Then depending on how bad the cytopenia is determines how fast or how many times I see them. However, if they have vague cytopenias and clonal abnormalities on next-generation, I want to really keep my eye on these patients because unfortunately they are the patients who are most likely to progress to a real disease.

Thank you for listening, and this is Dr. Stuart Goldberg for *Managing MDS*. Thank you.