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Can or should stem cell mobilization and collection be delayed until so-called salvage transplant?

Hello, my name is Ray Comenzo. I am a hematologist and professor of medicine and pathology at Tufts University School of Medicine. In my practice, I am frequently asked by patients and physicians, “Can or should stem cell mobilization and collection be delayed until so-called salvage transplant?” This is a difficult question for patients to understand in the era of so many new therapies. At the same time, the most important thing for patients and doctors to put clearly at the top of the list is what the patient wants. And often, it is the case that the patient has a year or two more years left in their job as a teacher or policeman or fireman before they can draw down their pension. And often, it is the case that a mother of two teenagers who have to get to college will not want to take the three to six months out of her time in order to undergo a stem cell transplant. Fortunately, for those patients, we know that delayed stem cell transplant is no less effective than early stem cell transplant. We have trials that have shown this over the years. However, that is not the question that I am asked that frequently. What I am asked is whether or not the patients can delay stem cell mobilization and collection.

Let me tell you a little bit about stem cell mobilization and collection. Stem cell mobilization refers to the administration of medicines that stimulate the stem cells in the bone marrow to leave the bone marrow and come out to the blood. When they come out to the blood, we can actually count them. Collection involves the use of either catheter or of the veins in the arms to remove the blood from a patient, put it through what looks like a washing machine at a high rate of speed and then return the blood to the patient having removed many of the white cells, the lymphocytes and monocytes, that contain the stem cell population. Patients may need to have this procedure done once, twice, perhaps three times in order to collect enough cells for two or three transplants, which is standard practice at most myeloma centers. The dose of cells that we need, the minimum dose about two million stem cells per kilogram, although most of us like to use five to eight million stem cells per kilogram in order to assure prompt recovery of the bone marrow of white blood cells, red blood cells, and platelets after transplant. Once the cells are collected, they are cryopreserved in liquid nitrogen, and they can remain in that state for decades and be used effectively at a much later time if need be. Because the novel agents that we have today worked so quickly in some instances and because some of them can slow down the bone marrow a bit and make it difficult to collect stem cells, and also because we want to collect stem cells at a point in time in the myelomas at a

minimum. We like to collect stem cells after roughly four to six cycles of initial therapy early in the course of disease. Those stem cells represent cells that are collected at a time when a myeloma is at the minimum and when the bone marrow stem cell compartment has not been exposed to a lot of medications. The more medicines that a patient may receive to treat myeloma, the more difficult it may become for the bone marrow to function properly over time. We call those kinds of events low blood counts or cytopenias. Therefore, my bias is to collect stem cells early in the course of disease when we can collect the lot of them, freeze them for decades, and have them available to patients when they are needed. At the same time, it is important to keep in mind that myeloma causes organ damage; and if patients do not have their stem cells available to them at a time when a catastrophic relapse occurs, which fortunately occurs rarely, they will have some difficulty getting through the mobilization and collection process. This also is relevant to patients who are diagnosed in their 60s, better off having their stem cells collected at 67 than trying to have them collected at 74 after you have had multiple therapies. The stem cell compartment does decrease with age. Naturally, we use them up. So, those are my views. My bias is to collect early. It can be more difficult to collect later, and I think the majority of our centers allow us to bank cells, we will bank cells for two or three transplants for each patient. Thank you very much.