Managing Myeloma

A Quadruplet Regimen Comprising Carfilzomib, Cyclophosphamide, Lenalidomide, Dexamethasone (KCRD) vs an Immunomodulatory Agent Containing Triplet (CTD/CRD) Induction Therapy Prior to Autologous Stem Cell Transplant: Results of the Myeloma XI Study

Faith Davies, MD, MBBCh, MRCP, FRCPath
Professor of Medicine
University of Arkansas for Medical Sciences
Little Rock, Arkansas

Hi there, I am Faith Davies and I am live at the ASH conference in San Diego. Today, I am going to be reviewing a study which is a UK-based study where we looked at the quadruplet regimen of carfilzomib, cyclophosphamide, lenalidomide, and dexamethasone against a triplet regimen including IMiDs as induction therapy prior to a stem cell transplant.

The main hypothesis behind our study is really, can we improve the response to therapy prior to a transplant and if we do that, what is the overall outcome? Does it affect progression-free survival? Clearly and importantly, when we are thinking about having a four-drug regimen rather than a three-drug regimen, what is the toxicity, is it deliverable and what can happen? As part of the Myeloma XI study, we have a good number, over 500 patients were randomized to receive quadruplet including carfilzomib, cyclophosphamide, lenalidomide, and dexamethasone. Then we have 250 patients who received either cyclophosphamide, thalidomide, and dexamethasone regimen; and then another 250 patients who received the triplet with cyclophosphamide, lenalidomide and dexamethasone. Importantly, the regimens were extremely tolerable and induced great responses. An average of four cycles of the four-drug regimen were delivered compared to five to six cycles of the three-drug regimen. Importantly, the response rates for the four-drug regimen were dramatically improved compared to the three-drug regimen. So, the carfilzomib-containing regimen induced very good and complete responses at over 80% compared to 50% to 60% for the triplet regimen. As I say, the toxicity was very similar and importantly the neutropenia rate was no different for the four-drug regimen compared to the three-drug regimen.

As far as the overall responses, again, responses post-transplant translated with more patients responding in the KCRD arm. Importantly, the MRD rate was three times higher in the KCRD arm compared to the triplet regimen. I guess we did prove our hypothesis for the very simple reason that progression-free survival was very much improved in the four-drug regimen. With a hazard ratio of 0.6 and at the three-year timepoint 50.3% for three-year PFS in the three-drug regimen compared to over 65% in the four-drug regimen. I think the conclusion of our study is that a four-drug regimen can be delivered safely. It can induce very deep responses in a much shorter timeframe than a three-drug regimen. Importantly, this translates to good responses and a longer progression-free survival after transplant.

Now, clearly we use a carfilzomib, lenalidomide, cyclophosphamide, dexamethasone regimen. There is a number of other studies at ASH that are also looking at other four-drug regimens and again is finding very similar things, that the four drugs are tolerable and they induce very deep and good responses. I think that there is a movement now to perhaps use four-drug regimens. As long as we can deliver them safely, then this may be another option for our patients.

Reference

Jackson G, Davies F, Pawlyn C, et al. A Quadruplet Regimen Comprising Carfilzomib, Cyclophosphamide, Lenalidomide, Dexamethasone (KCRD) Vs an Immunomodulatory Agent Containing Triplet (CTD/CRD) Induction Therapy Prior to Autologous Stem Cell Transplant: Results of the Myeloma XI Study. ASH 2018. Abstract 302.