Transcript Details

This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/project-oncology/managing-high-risk-myeloma-from-cytogenetic-abnormalities-to-therapeutic-approaches/26583/

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Managing High-Risk Myeloma: From Cytogenetic Abnormalities to Therapeutic Approaches

Announcer:
You're listening to *Project Oncology* on ReachMD. On this episode, we'll discuss high-risk multiple myeloma with Dr. Gareth Morgan, who's the Director of Multiple Myeloma Research at NYU Langone's Perlmutter Cancer Center. Here's Dr. Morgan now.

Dr. Morgan:
So the definitions of high-risk myeloma are a complex area that has been evolving maybe over the last 15 to 20 years, but I'm very hopeful now that there's a standardized definition, both clinically and genetically, that we can take forward to structure the space going forward so we can do well-designed clinical trials that take account of a standardized entry criteria.

It's a group of patients that is difficult to treat, they respond poorly to treatment, they have a tendency to relapse within a year to a year and a half of initiating treatment, and the majority of patients with high risk, despite the fact of modern treatment, are passed by three years. And so this is an outstanding group of patients that requires us to work very intently on trying to define optimized treatment strategies and definitions so we can do clinical trials and novel therapies designed especially for this group.

So it's important to consider what it is about the biology of a cancer that drive aggressive behavior, and I think we do know that it's the genetics that drive aggressive behavior, so we need to consider the factors that make myeloma behave more aggressively. So we know there's an excess of high-risk patients in a group defined by a translocation between chromosome 4 and chromosome 14, which deregulates a gene called NSD2. And so NSD2 might be a target that you should somehow try and target with your therapy because the 4;14 is only present in 10 percent of all myelomas, and maybe only 5 percent of those 4;14s or 50 percent of the patients with a 4;14 do have adverse biology.

There are other factors, of course. So gain and amplification of chromosome 1 is also an adverse prognostic factor. It's important that we try to understand more about chromosome 1, which are the genes involved, how it brings about deregulation, and how the copy numbers expand to increase adverse outcomes. So then there's a third abnormality, which is called 17p-, and this is really all focused on the p53 tumor suppressor gene and mutations and loss of copy number of that p53. And really, the cases with the worst outcome are those that have loss of both copies of the p53 gene, so both mutation and loss of a copy. And the interesting question around cytogenetics is if you have 5 percent 17p- on cytogenetics, does that mean you're high risk? Well, I think we're coming to realize that you need at least 20 percent loss in cytogenetics and maybe even 60 percent with cutoff values of 60 percent of the cells with the abnormality being really important.

So despite the significant improvements in outcome, we still have an issue with the treatment of high-risk myeloma. So there's a small percentage up front, maybe 20 percent, that have high-risk disease, but at each relapse, the percentage of patients with high-risk disease gets small. I think quadruplet therapies are the current standard induction regimens, and for me, I think a regimen that includes an anti-CD38, a highly effective proteosome inhibitor like carfilzomib, and an IMiD drug with dexamethasone is the way to go.

Currently, we're offering autologous stem cell transplantation to try and consolidate responses, and then a highly effective maintenance, again with more than one drug, trying to maximize exposure to effective proteosome inhibitors with drugs like carfilzomib and the use of an IMiD and an anti-CD38 longer term, so that's about the optimum therapy.

Announcer:
That was Dr. Gareth Morgan discussing high-risk multiple myeloma. To access this and other episodes in our series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!