

## Phase 3 Randomized Study of D-Rd Versus Rd in Patients with NDMM Ineligible for Transplant

### Saad Z. Usmani, MD, FACP

Chief, Plasma Cell Disorders Program  
Director, Clinical Research in Hematologic Malignancies  
Levine Cancer Institute/Atrium Health  
Charlotte, North Carolina  
Clinical Professor of Medicine  
UNC-Chapel Hill School of Medicine  
Chapel Hill, North Carolina

Welcome to *Managing Myeloma*. I am Dr. Saad Usmani. Today, I would like to discuss an abstract presented this year at the 60th ASH Annual Meeting in San Diego, California. I would like to spend a few minutes presenting some of the key points of the phase 3 data that were presented from the MAIA trial that was reported as a late-breaking abstract Tuesday morning at ASH. As a reminder, the MAIA trial was a randomized phase 3 study that compared daratumumab along with lenalidomide-dexamethasone versus lenalidomide-dexamethasone for patients with newly diagnosed transplant ineligible multiple myeloma.

It is very important to put things in context of where we are coming from. The older transplant ineligible patients historically have had MP given to them, then we had the pivotal trial, actually three different phase 3 trials, that lead to the approval of MPT with inclusion of thalidomide into the mix as the first novel agent. Then the FIRST trial was the one that compared Rd, or lenalidomide-dexamethasone, either continuously or for a fixed duration of 18 months with MPT and led to the declaration of Rd as a standard of care for transplant ineligible newly diagnosed patients with a median PFS benefit of about 26 months on the Rd arm. With that context, the dara-len/dex versus len/dex MAIA trial was planned a little over three years ago to see if additional anti-CD38 monoclonal antibody daratumumab adds anything to Rd in terms of depth of response as well as survival outcomes. The trial had a median age of 73 years. The randomization was on roughly 737 patients, randomized 1:1 ratio. There were patients up to the age of 90 on this study. The proportion of patients who were 75 years or above was 44%, so that is the largest such population that has been examined in a transplant eligible clinical trial and myeloma. The primary endpoint was progression-free survival and with a median follow-up of roughly 28 hard months, the primary endpoint was reached with the Rd arm achieving almost 32 months of PFS benefit, which is actually better than what was seen with Rd in the FIRST trial, and the median PFS has not been reached in the D-Rd arm, the hazard ratio was 0.56 with a fairly tight confidence interval. In terms of study discontinuations, there were about 30% patients who discontinued treatment in the experimental 3-drug arm compared to 57% I believe in the Rd arm. There were more of dose reductions to lenalidomide in the D-Rd arm

which kind of correlates within the higher rates of neutropenia and pneumonia that were seen in the D-Rd arm. Roughly the median duration of treatment on the D-Rd arm was about 25 months compared to 21 months on the Rd arm, that speaks to probably both tolerability and efficacy with dose reductions to the Rd regimen specifically and the time period is too short for overall survival benefit differences. At this point in time, the overall response rate was about 93% in the D-Rd arm with 79% of patients achieving VGPR (very good partial response) or better, compared to the overall response rate of about 81% with Rd on its own. MRD negativity measured by sequencing at  $10^{-5}$  was about 24% in the experimental arm versus 7% in the Rd arms, so again better depth of response, better PFS benefit that were seen with D-Rd.

Looking at the different subgroup analyses, the 3-drug regimen improved outcomes in almost all subsets, the only place where we did not see a big difference was the high-risk patient population which made up about 14% of the whole study population, a little lower than what we would expect from other clinical trials that have enrolled other nontransplant myeloma trials in the frontline setting. Taking all of these things together, older patient population with around 44% patients 75 or older, the 3-drug combination appeared to be well tolerated despite the higher neutropenias requiring dose reductions to lenalidomide, patients stayed on therapy for longer on the 3-drug combination. There were no untoward new side effects that we saw that we had not seen with this combination in the relapsed trial either. I think this trial will be practice changing, especially in the United States where Rd is used very commonly for older transplant ineligible patients and this will likely become one of the new standards of care for older transplant ineligible myeloma patients. Thank you for viewing this activity.

**Reference:**

Facon T, Kumar S, Plesner T, et al. Phase 3 Randomized Study of Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) Versus Lenalidomide and Dexamethasone (Rd) in Patients with Newly Diagnosed Multiple Myeloma (NDMM) Ineligible for Transplant (MAIA). ASH 2018. Abstract LBA-2