ASCO Overview from Saad Z. Usmani, MD, FACP

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Welcome to *Managing Myeloma,* I am Dr. Saad Usmani. We are pleased to present highlights in multiple myeloma from the 2018 ASCO annual meeting in Chicago that took place in June of 2018. There were several important abstracts that were presented, from the smoldering myeloma setting clinical trials, to treatment of newly diagnosed patients in the transplant-eligible as well as in the ineligible setting, as well as data in relapsed/refractory myeloma with single agents as well as with combination chemotherapies and immunotherapies. You will be seeing several faculty from the myeloma research community discussing different abstracts. What I am going to do is try to highlight some salient features on each of these abstract categories.

Within the smoldering myeloma category, you are going to be hearing about some data with daratumumab, as well as some elotuzumab experience. In the newly diagnosed setting, you are going to be hearing about some provocative data that actually led to the discontinuation of the pembrolizumab-lenalidomide-dexamethasone combination, as well as pembrolizumab-pomalidomide-dexamethasone trials that were halted by the FDA last year. You are also going to hear about some of the ongoing clinical trials that are combining the new anti-CD38 monoclonal antibody isatuximab for newly diagnosed patients. Most of the data that was presented on ASCO focused on that relapsed/refractory myeloma patient population. Perhaps the most significant abstracts in the early relapse setting were from the pomalidomide-bortezomib-dexamethasone vs. bortezomib-dexamethasone phase 3 study presented by Dr. Richardson, which will likely impact the clinical practice in the United States once these data lead to the approval of that combination in the early relapse setting. There was also an abstract that was presented about the early experience with daratumumab-carfilzomib-dexamethasone informing a phase 3 trial that is ongoing in the early relapse setting. There is another ongoing clinical trial looking at the other anti-CD38 monoclonal antibody isatuximab with carfilzomib. Each of these studies will not only inform clinical practice, but will also help us plan future trials within that space. Safety data generation is important and you will hear from the faculty about some of the safety data with those combinations.

Among the most exciting immunotherapy data that were presented at ASCO is perhaps the update of the BCMA CAR T study of the compound bb2121. These data were updated by Dr. Noopur Raje demonstrating, in a highly relapsed/refractory patient population, a median progression-free survival of almost a year, which is better than any other single agent that we have seen in the last five years. Those data are quite encouraging, but at the same time, we have to take them with a grain of salt because we are not really curing myeloma with CAR T cell strategies even though we are seeing wonderful results compared to some of the other single agents. Dr. Raje will discuss some of those nuances as she discusses that particular abstract.

With checkpoint inhibition there has been a lot of controversy after the FDA halted the two pembrolizumab phase 3 studies, and you will hear about some of the data that has been released at ASCO with the frontline transplant-ineligible clinical trial as well as in the relapsed/refractory setting. You will get to see the reasons why the FDA rightly halted those studies, but there are caveats to their experience as well, so stay tuned and learn about some of those data.

There were important updates from two phase 3 trials in the relapsed/refractory setting within the 1-3 prior lines of treatment setting. One was an update on the long-term follow up of the combination of elotuzumab-lenalidomide-dexamethasone from the ELOQUENT-2 trial experience showing that beyond three years, the three-drug combination continues to have sustained progression-free survival benefit. The other important update was from the ENDEAVOR trial which had compared carfilzomib-dexamethasone (Kd) with bortezomib-dexamethasone in the 1-3 prior lines of treatment setting. This update was relevant to the overall survival benefit of almost nine months being observed on Kd arm versus the bortezomib-dexamethasone arm. These data will be discussed in more detail as part of this particular activity.

Last, but not least, one of the key issues from a clinician's standpoint with administration of daratumumab is the long time it takes for the intravenous formulation to be administered to the patients. Keeping that in mind, a subcutaneous formulation was developed and has been in early phase clinical trials since 2015. The early data were presented in December 2016 and more recently have been updated at ASCO 2018, demonstrating that the subcutaneous formulation of daratumumab – which can be administered in under 5 minutes – is safe, tolerable, and appears to be at least as active as the IV formulation. Based on this early phase clinical experience, there is a large randomized phase 3 trial that is ongoing comparing IV versus the subcutaneous daratumumab formulation and details about that specific ongoing study were presented as a trial-in-progress at ASCO. Please enjoy the highlights presented in this activity.