Scientific & Clinical

2010 ASCO key myeloma presentations

Myeloma Today in conversation with Dr. Brian G.M. Durie

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Please share with our readers a brief recap of the general themes in myeloma and the key presentations at the 2010 ASCO meeting.

The 2010 annual meeting of the American Society of Clinical Oncologists (ASCO) was held June 4–8 in Chicago, IL. ASCO is one of two major annual meetings that take place in the US and involve key topics in myeloma. The second such meeting is held by the American Society of Hematology (ASH) in December of each year. The format of these two meetings is fairly similar. There are educational sessions, overviews from leading experts in the field, oral sessions, and a large number of poster sessions. In addition, there are many abstracts available only in publication form. In recent years, the general discussions in myeloma have followed a pattern:

1. New data on the three approved novel anti-myeloma agents (thalidomide, bortezomib, and lenalidomide) that have made a significant difference in the field in the last 5–10 years.
2. New data on the two most promising drugs in development (carfilzomib and pomalidomide).
3. Drugs in early development (elotuzumab, vorinostat, and others).
4. Advances in combination therapies.

What were some of the studies presented this year at ASCO that involved lenalidomide and/or bortezomib?

The role of lenalidomide as maintenance is of much interest for discussion, and two significant randomized trials presented at ASCO garnered a lot of attention. One study is from the IFM, which is the French myeloma study group, and the other study is from the Cancer And Leukemia Group B (CALGB) in the US. Both of these studies looked at the role of lenalidomide (REVLIMID®) in the post-transplant setting. Large numbers of myeloma patients who had gone through induction therapy followed by a single autologous stem cell transplant (ASCT), were randomized 6 to 12 months after transplant into two groups. One group took 10 to 15 mg of lenalidomide as maintenance; the other received a placebo.

The IFM study looked at 614 patients. At three years, 68% of the patients who received lenalidomide were still in remission compared to 35% in the placebo arm. With almost double the number of patients in the placebo arm, the statistical difference is highly significant. Obviously, although it is too early to draw a conclusion, we are hopeful that the patients who achieve prolonged remissions will also have increased overall survival (OS).

The patients in the CALGB study had received a broad variety of induction therapies but were standardized by

entering the study after their ASCT. Of the 210 patients randomized to receive lenalidomide maintenance, only 29 patients relapsed. In the placebo arm, 58 of 208 patients relapsed. Both the progression-free survival (PFS) and the time-to-progression (TTP) were better in the lenalidomide arm of the study.

Were there significant studies of bortezomib presented at ASCO?

There were close to 50 abstracts at ASCO that presented data on combination studies with bortezomib (VELCADE®).

One study of particular interest was presented by investigators from Italy. The researchers looked at more than 500 patients on a combination therapy of bortezomib, melphalan, prednisone, and thalidomide followed by maintenance with bortezomib and thalidomide. The four-drug therapy followed by maintenance demonstrated improved responses compared to patients on a three-drug therapy without maintenance. The data had been presented before, but the two significant aspects of the ASCO presentation looked at the possibility of switching to one day a week of bortezomib as induction, with reduced side effects but without reduced efficacy.

Another significant study demonstrating that reduced dosage bortezomib-based regimens may lessen toxicity without compromising efficacy showed the benefit of low-dose bortezomib administered once every two weeks, combined with low-dose daily thalidomide as maintenance.

There were a number of other promising bortezomib trials, including those that combine bortezomib with lenalidomide.

What other trials did you find to be of most interest?

The two multi-center trials of approximately 600 patients, each of which showed a decreased risk of disease progression in more than half of the patients on a lenalidomide-based maintenance therapy following an ASCT, are very significant. In fact, this development was highlighted by ASCO as one of the most important in 2010.

The Italian study directly comparing a lenalidomide-based regimen to ASCT was interesting. The results of drug therapy were shown to be comparable to ASCT but without the risk, recovery time, and debilitating side effects.

Is there a general shift of perspective among myeloma clinicians?

Continuous therapy is becoming the new paradigm of treatment in myeloma. Traditionally, doctors have treated cancer until a desired response is reached and then treatment stops. The novel anti-myeloma therapies can be tolerated long-term and offer physicians and patients the potential to modulate the immune system to maintain remissions. Myeloma doctors have been leaning toward continuing treatment as a way to prevent or at least delay disease relapse. The ASCO data may tip the balance in favor of that approach.

What about the next generation of anti-myeloma agents?

The two new drugs in development that have emerged as being closest to possible approval for myeloma are pomalidomide (a third-generation immunomodulator in the same class as thalidomide and lenalidomide) and carfilzomib (a second-generation proteasome inhibitor in the same class as bortezomib). At ASCO, the “next generation” data of significance to patients include updates on both of these drugs. Also of importance were

presentations on drugs in early development, such as epigenetic drugs that work on the function of genes, as well as drugs that target unique features of myeloma cells.

Any closing comments?

I believe that the clinical and scientific progress being made in myeloma will serve as a roadmap for transforming the treatment of a wide range of cancers. We are seeing myeloma treatments work in lymphomas, leukemias, and even solid tumors. In fact, there is much promise in the early data from studies evaluating lenalidomide in prostate cancer, as well as second-generation proteasome inhibitors (carfilzomib and an oral drug from the makers of VELCADE) in several different malignancies.

As for myeloma patients, the presentations made at the 2010 ASCO conference could change the way they are treated. Overall, the data favor fewer stem cell transplants and increased use of maintenance therapy – continuing therapy even in patients who have achieved a complete response (CR). The progress and positive news presented at ASCO and other medical meetings are truly encouraging. While we must continue to work toward a cure, it is clear that many myeloma patients are already living longer, better lives.