# Unraveling the complexities of myeloma therapy

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For years, debates over the right way to deliver therapies for cancer have included questions on whether to give one drug up front or two (or more), and whether to save your "best" drug for later if your disease returns. For myeloma, the emerging picture is that three drugs are better than two, and two are better than one such that using all your best drugs up front might be best. At this year's American Society of Hematology meeting, a plenary session paper showed that if a proven three-drug regimen is followed with additional therapy, termed maintenance therapy, patients do even better.

The study, conducted by Dr. Maria Mateos and colleagues in Spain, included 260 newly diagnosed patients who were at least 65 years old. The trial compared induction (or initial) therapy with Velcade/melphalan/prednisone (VMP) to Velcade/thalidomide/prednisone (VTP). One aim of the trial was to figure out whether you really need a type of drug called an anthracycline, so the comparator arm replaced the anthracycline melphalan with thalidomide, an immunomodulatory agent. One notable part of the design of this study was the use of Velcade on a weekly rather than twice-weekly schedule. The investigators wanted to know if by reducing the dose, they could reduce the overall adverse event profile without compromising efficacy.

The response rates were very similar between the two regimens in this part of the trial (80 percent versus 81 percent). VMP was associated with more hematologic toxicities, and VTP was associated with more cardiac toxicities. There was less Velcade-related peripheral neuropathy with the weekly schedule than you would expect to see with the twice-weekly schedule.

Once induction therapy was completed, patients in each arm were randomized to receive maintenance with either Velcade/prednisone (VP) or Velcade/thalidomide (VT). Adding maintenance therapy to the induction regimen increased the complete response rate, and the toxicity added by the extended therapy was low. The use of VT following either induction regimen improved progression-free survival by a statistically significant length of time compared to VP (not reached versus 33 months); however, this improvement did not translate into an increase in overall survival. Further, VMP followed by VT was found to be better than VTP followed by VP, which means the anthracycline (melphalan) component of induction therapy is important to keep.

The main take-home messages from this study are that a less intense regimen with follow-up maintenance therapy is safe and effective. These results reinforce the notion that duration of therapy is an important factor in getting the best

results--if you can receive all of your planned therapy without dose reductions or skipping doses, your myeloma is more likely to respond--and that maintenance therapy adds to the benefit.