Less intensive drug schedule as effective as standard treatment for blood cancer

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A less intensive bortezomib-based regimen (given once instead of twice per week) followed by maintenance therapy, is as effective as the standard treatment for elderly patients with multiple myeloma, but with fewer serious side effects, and will be a valuable treatment option in these patients, according to an Article published Online First in The *Lancet Oncology*.

For more than 30 years, melphalan plus prednisone has been the mainstay of treatment for elderly patients with multiple myeloma. However, the addition of new agents such as thalidomide, bortezomib, and lenalidomide have improved response rates and extended life expectancies, but often with increased adverse effects. In 2008, the VISTA trial showed that the combination of bortezomib, melphalan, and prednisone was significantly better than the standard treatment of melphalan and prednisone alone, but toxic effects were high.

In this study, a team of researchers from Spain led by Maria-Victoria Mateos from the University Hospital of Salamanca investigated whether a less intensive bortezomib-based regimen of induction therapy supplemented with maintenance treatments could reduce toxic effects while maintaining efficacy.

The researchers designed a two-stage randomised trial to establish whether an alkylating agent (melphalan) or an immunomodulatory drug (thalidomide) would work better with bortezomib. 260 patients aged 65 years or older with untreated myeloma were randomly assigned to initial

treatment with six cycles of reduced dosage bortezomib plus melphalan and prednisone (VMP; 130), or reduced dosage bortezomib plus thalidomide and prednisone (VTP; 130). Patients who completed induction therapy were subsequently randomly assigned to maintenance therapy with bortezomib and prednisone (VP; 87) or bortezomib and thalidomide (VT; 91) for up to three years.

Findings showed that the less intensive VMP and VTP induction regimens were effective and well tolerated with similar response rates —81% patients in the VTP group and 80% in the VMP group, including 36 (28%) VTP patients and 26 (20%) VMP patients had complete remission.

Treatment with VTP resulted in more serious adverse events (40 vs 20) and discontinuations (22 vs 15) than with VMP. Of the most common side effects (grade 3 or worse), infections (1% vs 7%) were more frequent with VMP while cardiac events (8% vs 0) and peripheral neuropathy (nerve pain [9% vs 7%]) were more common in the VTP group.

Importantly, this less intensive schedule was associated with a reduction in the incidence of grade 3 or higher peripheral neuropathy from 13% (in the previous VISTA trial) to 8%, and in gastrointestinal symptoms from 19% to 4%, while maintaining efficacy.

Additionally, maintenance therapy resulted in a substantial improvement in patient responses with good tolerability, increasing complete response from 23% to 42%, with no significant differences in response rates between the two regimens.

The authors conclude: "The therapeutic approach of reduced-intensity induction, followed by maintenance, with bortezomib-based therapy…is a safe and effective treatment for elderly patients with multiple

myeloma."

In a Comment, S Vincent Rajkumar from the Mayo Clinic, Rochester, USA, says that this is an important study that immediately affects clinical practice by providing a safer dosing for bortezomib. However, he points out that there are now five regimens for treatment of elderly patients with newly diagnosed multiple myeloma shown to be effective in randomised trials, but no data on how these regimens compare: "We are faced with the challenge of selecting from treatments with significantly different side-effect profiles and route of administration without the benefit of randomised trials."

More information: www.thelancet.com/journals/lan … (10)70187-X/abstract

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