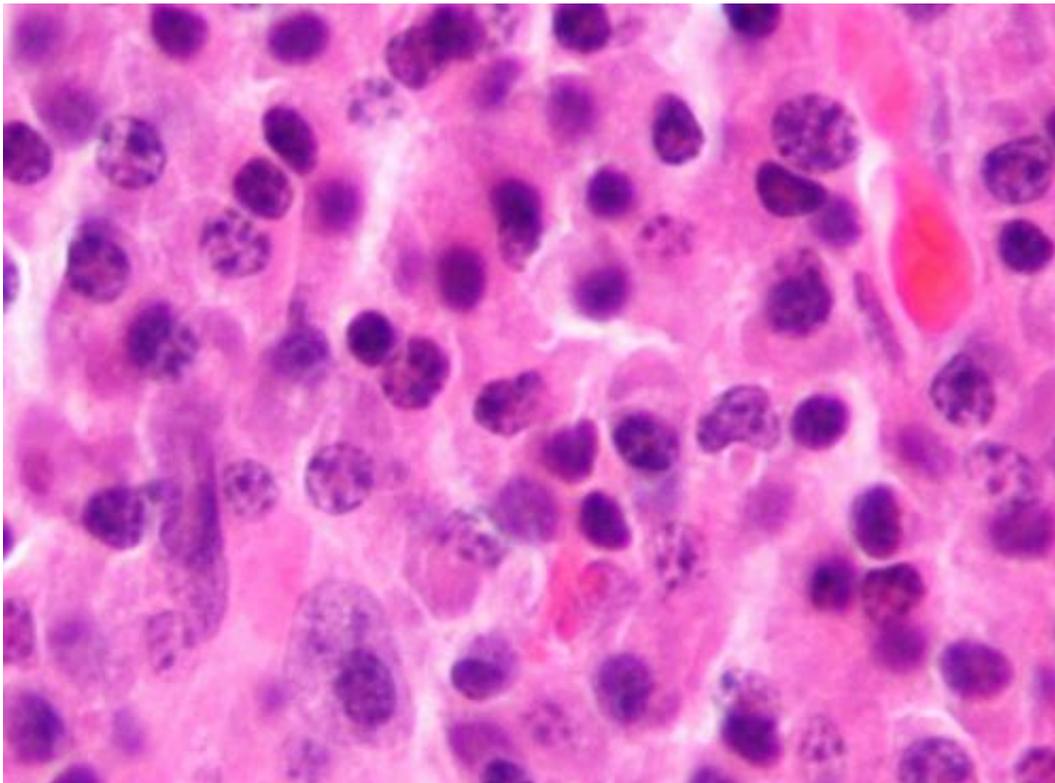


Study: Older multiple myeloma patients can be spared of long-term steroids

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Micrograph of a plasmacytoma, the histologic correlate of multiple myeloma. H&E stain. Credit: Wikipedia/CC BY-SA 3.0

The combination of cancer therapy lenalidomide plus the steroid dexamethasone (together called Rd) is considered standard treatment for elderly patients with multiple myeloma. However, prolonged steroid use can be harmful for some older adults.

A new study published in *Blood* found that switching select [older patients](#) to a lower dose of lenalidomide and discontinuing dexamethasone after nine months was not only safe, but it also yielded similar outcomes as compared with patients who received continuous Rd.

Multiple [myeloma](#), a cancer affecting the blood plasma cells (a type of white blood cell in the bone marrow), most commonly occurs in people over 60. Because of patients' older age, they are generally more susceptible to adverse events due to a higher likelihood of having other health conditions or functional impairments, and some treatments affect the body differently as we age.

This phase III clinical trial involved 33 medical centers in Italy and is the first to evaluate an adapted Rd treatment schedule that spares steroid use in older patients. Participants included people with newly diagnosed multiple myeloma (median age 76) who were deemed intermediate fitness for treatment, either because of their age or deficits in their ability to perform activities of daily living, such as bathing or dressing.

"Myeloma patients are a very diverse population, including fit patients who may tolerate full-dose treatments, and intermediate-fit and frail patients who are more susceptible to adverse events that may negatively affect the duration and outcome of treatment due to the presence of comorbidities and functional impairments, thus requiring an adapted therapy," said lead author Alessandra Larocca, MD, Ph.D. of the University of Turin in Italy. "Our study shows, for the first time, that reducing the dose or intensity of treatment is a feasible option and produces similar outcomes as standard dose treatments for intermediate-fit patients."

Nowadays, multiple myeloma patients usually receive continuous treatment including steroids, which are typically given until a patient's

disease progresses or they are unable to tolerate the therapy, according to Dr. Larocca. But as she explained, "Prolonged steroid use is scarcely tolerated in the long term, even in younger patients, and patients may often require dose reduction or interruption."

In fact, long-term use of dexamethasone-based regimens have been associated with insomnia, anxiety, agitation, weight gain, and swelling (edema) in the legs.

Finding ways to adapt treatments for older patients and those with functional deficits to allow them to remain on treatment longer and maintain disease control is critically important. As such, researchers wanted to evaluate whether stopping dexamethasone early, after initial therapy, and tapering the dose of lenalidomide (to 10 mg/day) would still benefit older intermediate-fit patients with newly diagnosed multiple myeloma who were not eligible for transplantation.

A total of 199 patients were enrolled and randomized to one of two study groups between October 2014 and October 2017. Only individuals deemed intermediate-fit were eligible for the study; patients were excluded if they were considered to be either fit or frail based on the International Myeloma Working Group frailty scale. Of these participants, 98 were randomized to receive continuous Rd and 101 received the adjusted dose and schedule after nine Rd induction cycles (called induction therapy).

After a median follow-up of 37 months, those who were no longer taking dexamethasone experienced a significantly longer period without an adverse event or relapse compared with those who continued on the standard Rd therapy (event-free survival of 10.4 months vs. 6.9 months, respectively). The tailored approach was also better tolerated, resulting in fewer adverse effects. Of the adverse events observed on the tailored approach, most were minor, including low white blood cell counts,

infections, and skin disorders. The groups showed similar response rates, as well as similar chances of staying free of disease progression.

The findings could have important implications for practice. Dr. Larocca estimates that about one-third of myeloma patients not eligible for stem cell transplantation, a risky but common and effective treatment approach, fit the criteria used in this study.

"We expect the results of this study may help to improve and optimize the treatment of [elderly patients](#) who may be at greater risk of treatment toxicity and poor survival due to their age or comorbidities," she said, adding that ongoing trials are now evaluating steroid sparing in combination with monoclonal antibody or the role of frailty-guided treatment.

More information: Alessandra Larocca et al. The Combination of Frailty and ISS Scores Identifies a Simple Prognostic Index for Overall Survival in Elderly Patients Treated with Novel Agents-Based Induction Therapy, *Blood* (2019). [DOI: 10.1182/blood.V124.21.4740.4740](https://doi.org/10.1182/blood.V124.21.4740.4740)

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