Selinexor–dexamethasone for refractory multiple myeloma

Patients with triple-class-refractory multiple myeloma achieve objective responses when treated with selinexor–dexamethasone, according to new research.

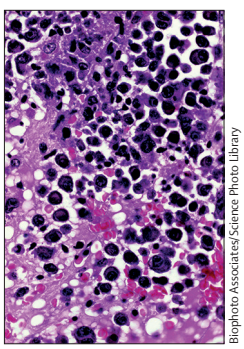
In a multicentre, phase 1b, open-label study by Ajai Chari (Icahn School of Medicine at Mount Sinai, New York, NY, USA) and colleagues, 122 patients with myeloma who had previous exposure to bortezomib, carfilzomib, lenalidomide, pomalidomide, daratumumab, and an alkylating agent, and whose disease was triple-class refractory (ie, resistant to at least one proteasome inhibitor, one immunomodulatory agent, and daratumumab) received 80 mg oral selinexor (a selective inhibitor of XPO1) and 20 mg dexamethasone twice weekly. The primary endpoint was overall response, defined as a confirmed partial response (≥50% reduction in the serum level of myeloma protein) or better. Clinical benefit, defined as a confirmed minimal response (≥25–50% reduction in the serum level of myeloma protein) or better was a secondary endpoint.

32 of 122 patients (26%; 95% CI 19–35) had a partial response or better, which included two (2%) stringent complete responses, six (5%) very good partial responses, and 24 (20%) partial responses. 48 of 122 patients (39%; 95% CI 31–49) achieved clinical benefit. Fatigue, nausea, and decreased appetite, typically of grade 1 or 2 severity, were common side-effects. Thrombocytopenia occurred in 90 (73%) of 123 patients, although it only led to clinically significant bleeding (grade ≥3) in six patients.

Study author Paul Richardson (Dana-Farber Cancer Institute, Boston, MA, USA) said "Despite recent advances in the treatment of multiple myeloma, almost all our patients will develop disease that is resistant to the three main classes of anti-myeloma drugs we currently have available… Together with its unique mechanism of action, this next-generation novel agent marks a significant advance in the treatment paradigm for relapsed and refractory multiple myeloma… which will hopefully prove to be a valuable addition to our therapeutic armamentarium."

Nizar Bahlis (Arnie Charbonneau Cancer Institute, University of Calgary, AB, Canada) added "This study provides myeloma patients that have exhausted approved options with another non-cross-resistant therapy. It also demonstrates that blocking nuclear export is indeed a viable therapeutic target and opens the door for the development of future molecules targeting the exportin family of nuclear transport proteins."

Robert Stirrups



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For the **study by Chari and colleagues** see *N Engl J Med* 2019; **381:** 727–38