

New cancer inhibitor effective where others fail

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A novel agent called Selinexor has opened up new options for the treatment of patients with refractory myeloma. This was the conclusion of a major international clinical trial in which also the Karl Landsteiner University of Health Sciences in Krems, Austria (KL Krems) participated. The results have now been published in the *New England*

Journal of Medicine. Thanks to a new mode of action, the compound brings hope to the growing number of patients whose tumor cells have become resistant to the three backbone drug classes.

Multiple [myeloma](#) is the second most common form of hematologic malignancies. Besides autologous stem cell transplantation for fit patients and conventional chemotherapy drugs, three classes of agents, which are optimally combined, form the backbone of myeloma therapy: immunomodulatory drugs (IMiDs), proteasome inhibitors, and monoclonal antibodies. If patients develop resistance against one of these types of medication, they often switch to another. At present, no further [drug](#) treatment is available for the increasing number of myeloma patients resistant against all three drug classes thereby precluding further improvement of patient survival. However, an international team including KL Krems' Dr. Klaus Podar (from the Department of Internal Medicine 2, Krems University Hospital) has now uncovered a medication that opens the door to a new treatment option.

Clear result

"More than a quarter of myeloma patients in our trial responded positively to the treatment with the new agent, Selinexor, in combination with dexamethasone, an immunosuppressant," said Klaus Podar, commenting on the study's key finding. The primary endpoint was overall response defined as a confirmed partial response ($\geq 50\%$ reduction in serum protein of myeloma protein). Due to these exciting results, Selinexor was recently authorized in the U.S. following an accelerated approval procedure.

A total of 122 patients from Europe and the U.S. took part in the phase 2b clinical trial. On average, they were 65 years old and had suffered from myeloma for over six years. All patients had undergone between three and 18 treatment regimens and progressed. All of the subjects

received the new drug in combination with dexamethasone.

New opportunities

Selinexor is an attractive alternative primarily because its mode of action is completely new. It is based on inhibition of exportin-1 (XPO-1), a protein responsible for transporting molecules associated with tumor cell proliferation from the cell's nucleus (its "power plant") to its cytoplasm. In addition, Selinexor activates tumor suppressor proteins in the cell nucleus. As a result Selinexor kills cancer cells. The drug, which is available in tablet form, will bring new hope, especially to patients who have undergone various treatments in the past, and for whom there are practically no other options available; as Klaus Podar points out: "The medication has the potential to be a new treatment option for those patients who have failed other therapies."

In Podar's view, accelerated approval of the drug in the US shows just how effective targeted therapies can be under certain circumstances, as well as highlighting the importance of related research for the benefit of patients. Selinexor is only one of many new therapeutic approaches against myeloma that KL Krems oncology researchers are investigating. Others include combined therapies as part of autologous stem cell transplantation and targeted regulation of transcription factors. The ninth Oncology Day held recently at KL Krems gave experts an excellent overview of related activities currently under way, as well as underlining the university's growing reputation as Lower Austria's leading oncology center.

More information: Ajai Chari et al. Oral Selinexor–Dexamethasone for Triple-Class Refractory Multiple Myeloma, *New England Journal of Medicine* (2019). [DOI: 10.1056/NEJMoa1903455](https://doi.org/10.1056/NEJMoa1903455)

Provided by Karl Landsteiner University of Health Sciences

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