

Active agent from the Caribbean sea cucumber could improve treatment for malignant pleural mesothelioma

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Active agent from the Caribbean sea cucumber could improve treatment for malignant pleural mesothelioma. Credit: Medical University of Vienna

Researchers at the Comprehensive Cancer Center of MedUni Vienna

and Vienna General Hospital have discovered a new option for treating malignant pleural mesothelioma. For the first time in the world, they were able to show in a preclinical study, both in the cell culture and in the animal model, that trabectedin, a chemotherapy drug that is already successfully used for other types of cancer, is also effective against malignant pleural mesothelioma. The active agent originally occurs in the Caribbean sea cucumber, a marine-dwelling tunicate. The study results were recently published in *Molecular Cancer Therapeutics*, the therapy-oriented journal of the American Association for Cancer Research (AACR). The initial interim results of a clinical study from Italy confirm these results and show that they are transferable to clinical practice.

With around 90 new cases per year in Austria, [malignant pleural mesothelioma](#) is one of the rarer forms of cancer. However, it is on the increase. Malignant pleural mesothelioma is a very aggressive form of cancer that is associated with asbestos and is routinely treated with a combination of chemotherapy, surgery and radiotherapy. Since this particular type of tumour often develops resistance to chemotherapy and radiotherapy, the prognosis is very poor.

In order to improve the treatment options for pleural mesothelioma, an interdisciplinary research cooperative was set up at the CCC in 2008 and this has been very successful in the preclinical discovery and development of therapeutics to treat malignant pleural mesothelioma. In its latest [preclinical study](#), the platform scientists investigated the action of trabectedin in malignant pleural mesothelioma. Trabectedin is an active substance that occurs in the Caribbean sea cucumber, can be synthetically manufactured for therapeutic purposes and has already been successfully used clinically for malignant soft tissue tumours and ovarian cancer.

Combination enhances effectiveness

The researchers led by Walter Berger, Deputy Head of MedUni Vienna's Institute for Cancer Research, and Alireza Hoda, Division of Thoracic Surgery at the Department of Surgery of MedUni Vienna/Vienna General Hospital, had already shown in previous works that trabectedin is very effective against cancer cells, while having minimal impact on healthy pleural cells. Furthermore, the researchers were able to demonstrate clear synergies with cisplatin, a standard therapeutic drug. In order to develop further potential combination therapies with trabectedin, the genome signatures of cells that were sensitive to the administration of trabectedin were compared with those of cell lines that were less sensitive.

Berger: "Using bioinformatics, we were able to show that the increased formation of the protein bcl-2, which prevents cell death, reduces the effectiveness of trabectedin." Consequently, the scientists treated the [malignant cells](#) with a combination of trabectedin and the bcl-2 inhibitors obatoclax and venetoclax. Hoda: "When trabectedin is combined with these bcl-2 inhibitors, there is a significant improvement in destruction of malignant pleural mesothelioma cells. Trabectedin therefore seems to be a new, effective and safe treatment option for this disease." These preclinical results have just been confirmed by initial positive interim results from a clinical study conducted in Italy.

Berger: "The study has even been met with great interest from people affected. This is evidenced by the fact that the Comprehensive Cancer Centre publication has already been posted online and discussed in several international fora for asbestos and mesothelioma (e.g. asbestos.com)."

More information: M. A. Hoda et al. Trabectedin Is Active against Malignant Pleural Mesothelioma Cell and Xenograft Models and Synergizes with Chemotherapy and Bcl-2 Inhibition In Vitro, *Molecular Cancer Therapeutics* (2016). [DOI: 10.1158/1535-7163.MCT-15-0846](https://doi.org/10.1158/1535-7163.MCT-15-0846)

Provided by Medical University of Vienna

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