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New study provides rationale for use of a multi-target anticancer drug in patients with malignant pleural mesothelioma

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The multi-target small molecule anticancer drug nintedanib shows promising effectiveness in stopping the growth of human malignant pleural mesothelioma, a fatal thoracic tumor, in preclinical models, according to a new study published jointly by researchers in Austria, Germany and Hungary.

Malignant pleural mesothelioma is a particularly aggressive tumor that occurs in the lining that covers the lungs. It typically results from exposure to asbestos. Standard anti-mesothelioma treatment includes surgery, chemotherapy, irradiation or multimodal therapy, which is the combination of these approaches. Because these conventional therapies have reached their efficacy plateau, new targeted approaches are needed to improve survival.

However, despite proven efficacy of molecularly targeted drugs across a wide spectrum of other cancer types, most mesothelioma patients could not yet benefit from this novel treatment paradigm. The new research suggests that by preventing the growth of new mesothelioma blood vessels and thus starving tumors of nutrients and oxygen, the novel targeted medication called nintedanib is a promising candidate for helping patients with mesothelioma.

Study first author Viktoria Laszlo from the Division of Thoracic Surgery at the Medical University of Vienna, Austria, said: "Nintedanib, an

inhibitor of molecules responsible for promoting mesothelioma growth and new tumor blood capillary development, is already approved for other fatal thoracic diseases such as idiopathic pulmonary fibrosis and lung adenocarcinoma. Now we demonstrated, for the first time, that human mesothelioma cells express the target molecules of nintedanib and, furthermore, that this drug inhibits the growth and migration of mesothelioma cells. Moreover, we showed that nintedanib potently reduces the growth and vascularization of human mesothelioma tumors implanted into the thoracic cavity of mice."

Study leaders Balazs Döme, Head of the Translational Thoracic Oncology Program at the Medical University of Vienna, Austria and Balazs Hegedus, Department of Thoracic Surgery, University Medicine Essen—Ruhrlandklinik, Germany, added: "Importantly, this antitumor effect of nintedanib in experimental animals was stronger than that of bevacizumab—the reference blood vessel growth (angiogenesis) inhibitor in clinical oncology—in the treatment of less vascularized mesotheliomas. A key message of these animal experiments is thus that nintedanib might be considered superior to bevacizumab as part of systemic anti-tumor therapy for patients with less 'angiogenic' mesotheliomas."

The study, which was recently published in the journal *Clinical Cancer Research*, is of clinical relevance as—together with the promising results of the LUME-Meso clinical trials evaluating nintedanib in combination with cisplatin-pemetrexed chemotherapy in mesothelioma patients—it might help nintedanib to become an integral part of the standard-of-care for patients with mesothelioma.

More information: Viktoria Laszlo et al. Nintedanib is active in malignant pleural mesothelioma cell models and inhibits angiogenesis and tumor growth in vivo, *Clinical Cancer Research* (2018). DOI: 10.1158/1078-0432.ccr-17-1507

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