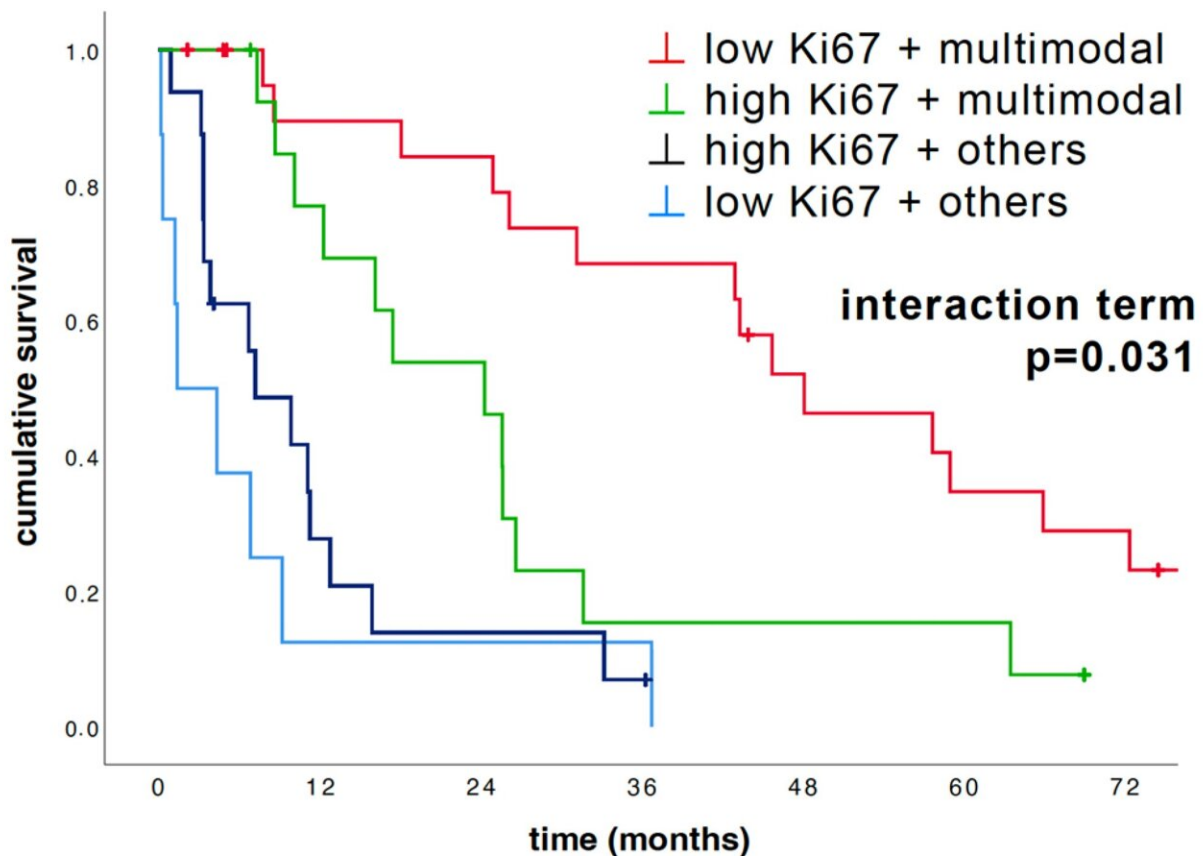# Researchers find biomarker Ki67 useful for personalized treatment of malignant tumors

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Impact of Ki67 expression on outcome after multimodality therapy and other therapy options. Credit: *Cancers* (2024). DOI: 10.3390/cancers16101817

The nuclear protein Ki67 is a meaningful biomarker for tumor

aggressiveness and for the success of surgical therapy in pleural mesothelioma, a malignant disease of the pleura. This is the clear and promising result of an international study now published in *Cancers* by Karl Landsteiner University of Health Sciences (KL Krems) in collaboration with Gazi University, Ankara, Turkey.

The study compared the survival rates and overall survival of patients with high and low expression of Ki67 in tumor tissue. It was found that low expression was associated with significantly better prognosis and a better response to surgery for those affected.

Pleural mesothelioma is an aggressive tumor of the pleura, a tissue that surrounds the lungs. It is often triggered by exposure to asbestos, but other causes are also known. Its diagnosis and treatment remain a major challenge, and the prognosis for those affected is still not good.

Biomarkers that allow the characterization of individual tumors would help. However, even the few candidates that have been considered so far are not yet sufficiently established for everyday clinical use.

Now a study by KL Krems is attracting widespread attention. It shows that the extent of expression of the cell nucleus protein Ki67 makes it possible to draw conclusions about the aggressiveness of the tumor and the prospects of success of certain treatment strategies.

## Aggressiveness

"Ki67 is a protein of the cell nucleus that is specifically expressed, i.e., produced, during cell division," explains study leader Dr. Bahil Ghanim from the Division of General and Thoracic Surgery at Krems University Hospital (a teaching and research site of KL Krems).

In simple terms, tissue with many dividing cells contains more Ki67 than

tissue with fewer such cells. As tumor tissue with a particularly large number of cell divisions is considered to be extremely aggressive, Ki67 can provide information on biological aggressiveness.

"The expression rate of the Ki67 genes is a suitable measurement. This indicates the proportion of cells in a tissue that are currently dividing and therefore producing Ki67," explains Dr. Ghanim. "And indeed, my team and I were already able to show in a previous study that this value has prognostic value, particularly in epithelioid pleural mesothelioma. Now we have taken a closer look at this."

Dr. Sarah Hintermair, co-first author of the study and colleague of Dr. Ghanim explains, "We analyzed tumor samples from 70 patients, about half of whom were treated in Krems, the other half in Turkey, Gazi University, an important scientific partner.

"After measuring the expression rate, the patients were divided into two groups: those with an expression rate above and those with an expression rate below 15%. We then compared five-year survival and average overall survival—and saw differences with clear statistical significance and high clinical importance."

## Clear evidence

The results now published in *Cancers* show that the 5-year survival rate for patients with low Ki67 expression was more than four times higher than for those with higher expression. These results reveal that the expression rate of Ki67 can be used to predict the further course of the disease.

Dr. Ghanim's team then investigated whether Ki67 could also provide information about the likely success of certain forms of therapy. In fact, pleural mesothelioma is currently being treated in a variety of

controversial ways, with multimodal treatments—i.e., treatments that combine several therapeutic approaches including surgery—being quite common.

"We therefore correlated our data on the Ki67 expression rate not only with the survival values, but also with the treatment options that the respective patients received," says Dr. Stephanie Iser, who is the first author of the study together with Dr. Hintermaier.

Here, too, the study shows a clear result: If the disease was treated multimodally, including surgery, the average overall survival of four years in the group with a low Ki67 expression rate was twice as long as in the equally treated group with high Ki67 expression.

Dr. Iser states, "Ki67 is therefore also very well suited as a predictive biomarker that can provide information on the suitability of a specific form of treatment, including thoracic surgery. This means that Ki67 makes it possible for the first time to individualize the treatment of epithelioid pleural mesothelioma."