New hope of a treatment for aggressive T-PLL leukaemia

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New hope of a treatment for aggressive T-PLL leukaemia. Credit: Medical University of Vienna

Until now, there has been no adequate treatment available for the rare and highly aggressive malignant blood disease T-PLL leukaemia. By

screening blood samples from patients with haematological diseases, a team of doctors and researchers from MedUni Vienna and CeMM, led by haemato-oncologist Philipp Staber, has now shown that the drug venetoclax is a successful treatment for T-PLL leukaemia. The study has recently been published in leading haematology journal *Blood*.

T-prolymphocytic leukaemia (T-PLL) is the most aggressive of all known forms of leukaemia. However, it is extremely rare and is the result of degenerated mature T-cells. Every year, there are around 40 new cases in Austria, predominantly involving people over 60 years-of-age. Up until now, T-PLL has been treated with antibodies but sadly not very successfully. Since the disease is so rare, it is difficult to conduct studies that might lead to improved treatments.

A research group led by haemato-oncologist Philipp Staber from MedUni Vienna's Division of Hematology and Hemastaseology and biochemist Stefan Kubicek from the Research Center for Molecular Medicine CeMM has now conducted a "High Throughput Screening" using 86 blood and tissue samples from patients. This involved mixing the samples with around 100 active substances and analysing them after 72 hours. This relatively new technique operates using robotic systems and is extremely efficient due to the rapid throughput.

The scientists found that T-PLL responds particularly well to the drug venetoclax, which was licensed 10 months ago for the treatment of chronic lymphatic leukaemia (CLL). This substance accumulates on the protein BCL-2, which is present in large quantities in CLL cancer cells. The cancer cells need BCL-2 to survive. They develop a resistance to anti-cancer drugs. Ventoclax inhibits the action of the protein and causes the cancer cells to die off.

The protein BCL-2 is also necessary for survival of T-PLL cells, which is why venetoclax also specifically eliminates cancer cells in this form of

leukaemia. Another advantage is that, in contrast to chemotherapy, treatment with this drug only causes minimal side-effects in patients. Moreover, two T-PLL patients, who did not respond to other standard treatments, have already been successfully treated with venetoclax.

This positive result is to be scientifically confirmed in an international clinical trial commencing in 2018.

More information: Bernd Boidol et al. First in human response of BCL-2 inhibitor venetoclax in T-cell prolymphocytic leukemia, *Blood* (2017). DOI: 10.1182/blood-2017-05-785683

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