

New approach to leukemia chemotherapy -- is a cure in sight?

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Speaking at the UK National Stem Cell Network conference in York later today (31 March), Professor Tessa Holyoake from the University of Glasgow will discuss a brand new approach to treating chronic myeloid leukaemia (CML) in which a small number of cancer cells persist despite effective therapy thus preventing cure.

CML is a type of [blood cancer](#) caused by the infamous "Philadelphia Chromosome" genetic abnormality. It is usually treated using a class of drugs called [Tyrosine Kinase Inhibitors](#) and in the majority of cases this treatment is successful, with around 90% of patients recovering from the disease. However in the majority of patients a subset of cancer cells – CML stem cells – are resistant to Tyrosine Kinase Inhibitors.

"At the moment we are working with 9 patients who still have low level evidence of CML despite Tyrosine Kinase Inhibitor treatment. They are helping us to test the use, in principle, of a new type of drug that specifically deals with the resistant CML stem cells," said Professor Holyoake.

"The drug we are using in the trial is hydroxychloroquine – a well established antimalarial drug that has been used commonly since the 1950s and is also used in rheumatoid arthritis. This will allow us to test the principle of using similar drugs to treat CML patients.

"Unfortunately hydroxychloroquine may not be suitable for very long term treatment because of side effects. In particular there is a very low

risk of temporary or permanent eye problems. In our trial the patients will take the drug for up to 12 months with very close monitoring of their eye health, which will allow us to intervene at the very earliest sign of an adverse effect," Professor Holyoake continued.

The patients in the trial have already taken a Tyrosine Kinase Inhibitor drug for at least a year, which has reduced the number of [cancer cells](#) in their blood to a very low level.

Professor Holyoake's team discovered that CML stem cells avoid the impact of Tyrosine Kinase Inhibitor treatments by going into a state called autophagy in response to the drug. This means that they begin to shut down and use nutrients from within the cell to survive in what is effectively suspended animation. In this state the drug cannot kill them and so later they can initiate a resurgence of the disease.

Hydroxychloroquine has been shown to kill cells that are undergoing autophagy and the trial is designed to test whether this is a potential route for treatment in patients.

Professor Holyoake concluded "Although hydroxychloroquine probably isn't the final answer for treating resistant CML stem cells, we are aware that there is interest from the pharmaceuticals industry in developing new drugs that target cells undergoing autophagy. We are therefore very hopeful that once we can prove that in principle this approach works, it could lead relatively quickly to a new treatment for patients for whom Tyrosine Kinase Inhibitors don't provide a full cure."

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