

# Next generation BRAF inhibitor cancer drug shows promise in early patient trial

October 26 2020

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A new drug designed to work on cancers with an altered BRAF gene has shown promise in an early patient trial presented at the 32nd EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, which is taking place online.

The BRAF gene is involved in telling [healthy cells](#) when to grow and form new cells, but it is also known to go wrong, or mutate, in several types of [cancer](#), including types of bowel, brain and skin cancer. A few BRAF inhibitor drugs have already proved effective in treating patients. However, these 'first generation' BRAF inhibitors do not work on all BRAF mutated cancers and in other cases cancers become resistant to the treatment.

The new [drug](#), PLX8394, is a 'next generation' BRAF inhibitor, designed to avoid this resistance and work against cancers with a wider range of BRAF mutations.

Results of the phase I/II trial were presented to the Symposium by Dr. Filip Janku, Associate Professor for Investigational Cancer Therapeutics (Phase I Clinical Trials Program) and Center Medical Director for Clinical and Translational Research Center at The University of Texas MD Anderson Cancer Center in Houston, Texas, U.S..

In the trial so far, 75 patients have been treated with the next generation BRAF inhibitor PLX8394, taken twice a day by mouth, with or without another drug called cobicistat. Data on 45 of these patients with BRAF

alterations, who received PLX8394 and cobicicistat, were available for researchers to evaluate. These patients had advanced cancers and most had already received three different types of treatments before joining the trial.

The researchers reported that the addition of cobicicistat resulted in doubling to tripling the level of PLX8394 in the blood.

Ten of the 45 patients (22%) had a partial response to the new drug, meaning their tumours shrank by at least 30%. This included three people with glioma (a type of brain tumour), two with ovarian cancer and others with bowel cancer, thyroid cancer or melanoma (a type of [skin cancer](#)). Ten of the 45 patients had remained on the treatment for at least two years when the data were analysed.

Serious side effects of the treatment experienced by some patients were high levels of a liver enzyme and bilirubin in the blood, indicating a risk of liver damage; these levels lowered when PLX-8394 was interrupted and the dose reduced. Some patients also experienced diarrhoea.

Dr. Janku said: "Although we already have some BRAF inhibitor drugs, unfortunately they do not work for all patients with BRAF mutated cancers. In some cases, even when these drugs do work at first, cancers develop resistance. First generation BRAF inhibitors can also cause unpleasant skin lesions and skin cancers in some patients.

"The next generation BRAF inhibitor that we gave to patients in this trial was designed to avoid those problems. These results suggest that the combination of drugs we tested is relatively safe and may be effective for some patients."

Dr. Janku and his colleagues continue to study the combination of PLX8394 and cobicicistat for treating patients, particularly to discover the

optimum dose of the drugs.

William R. Sellers, Professor of Medicine at the Dana-Farber Cancer Institute, Harvard Medical School, U.S., is co-chair of the EORTC-NCI-AACR Symposium on behalf of the NCI and was not involved with the research. He commented: "Understanding which genes go wrong in cancer and how they are mutated is a crucial step towards finding treatments that are targeted to work effectively in individual patients. BRAF is a gene mutated in approximately half of melanoma patients as well as in smaller fractions of colorectal and lung cancer. It is, therefore, an important therapeutic target and, indeed, BRAF inhibitors have significant clinical benefit in such patients.

"This trial shows positive signs for using a [next generation](#) BRAF inhibitor to treat patients with a variety of different cancer types and we look forward to hearing further results from the next stage of this research."

**More information:** Abstract no: 5LBA, "Interim results from a phase 1/2 precision medicine study of PLX8394 - a next generation BRAF inhibitor", by Filip Janu et al, presented in New Drugs on the Horizon, channel 1, 21:00-22:45 CET, Sunday (Dr Janku's presentation is at 21.40): [cm.eortc.org/cmPortal/Searchab ... ctdetails/0000902400](https://cm.eortc.org/cmPortal/Searchab...ctdetails/0000902400)

Provided by European Organisation for Research and Treatment of Cancer

Citation: Next generation BRAF inhibitor cancer drug shows promise in early patient trial (2020, October 26) retrieved 6 May 2024 from <https://medicalxpress.com/news/2020-10-braf-inhibitor-cancer-drug-early.html>

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