Cancer breakthrough as experts find existing drug can fight aggressive tumors

Ponatinib - already approved in the US for the treatment of a type of bone marrow cancer - was shown to stop certain types of cancer cells from reproducing without limit in cell experiments and mice tests.

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4BOOKMARK

An existing cancer drug could be repurposed to target aggressive forms of cancer (Image: Getty Images)

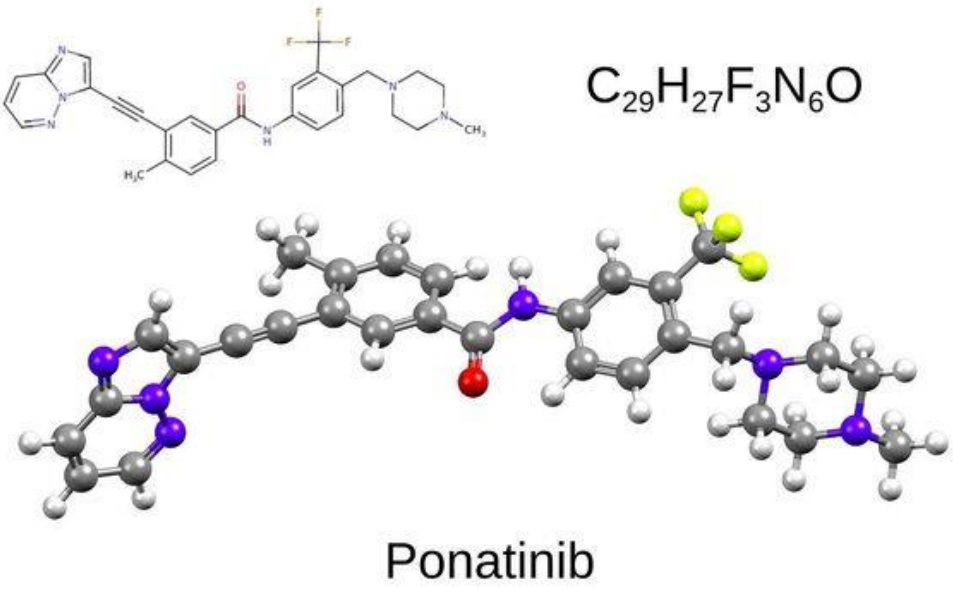
An existing cancer drug could be repurposed to target aggressive forms of cancer that currently lack targeted treatments and are associated with poor outcomes.

This is the conclusion of a study by researchers from Singapore, who found that ponatinib can block the alternative lengthening of telomeres (ALT) mechanism by which these cancers manage to stay “immortal”. This leads to the cancer cells’ deaths.

According to the team, 15 percent of all cancers are ALT positive, with such especially prevalent in aggressive tumors of the bone (osteosarcoma) and brain (glioblastoma).

These — and many other ALT positive cancers — tend to be resistant to chemotherapy, and other treatment methods are keenly sought by researchers.

Ponatinib has already been approved by the US Food and Drug Administration for the treatment of a certain type of bone marrow cancer.



Ponatinib (depicted) is already approved in the US for the treatment of a type of bone marrow cancer (Image: Getty Images)

Our DNA is contained in thread-like structures known as chromosomes — the tips of which end in protective caps dubbed telomeres.

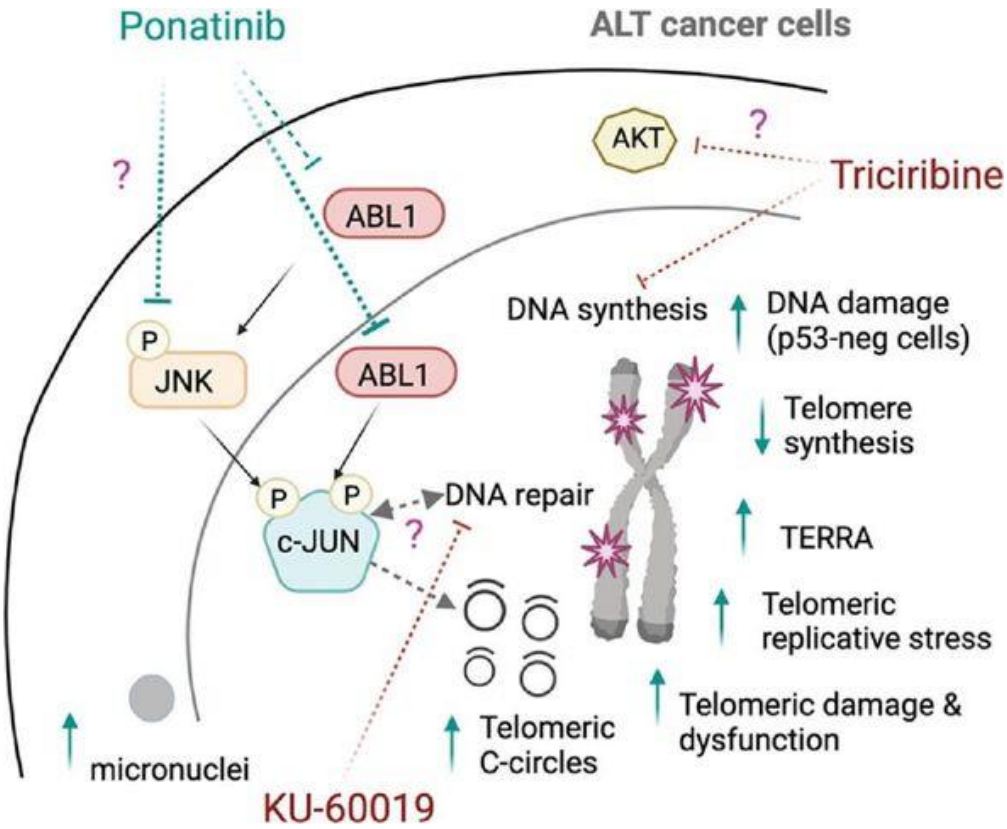
Every time a cell divides, a piece of these telomeres are naturally lost in the process. When telomeres become too short, the cell dies.

In most cancer cells, this end is averted by the activation of an enzyme called telomerase, which lengthens telomeres such that the cells can replicate indefinitely.

However, around 15 percent of cancers lengthen their telomeres by alternate means — hence their designation as “alternative lengthening of telomeres” positive cancers.

https://www.express.co.uk/news/science/1789965/cancer-alt-positive-repurpose-ponatinib

To date, there is no clinically approved treatment that specifically targets ALT positive cancers.



Ponatinib can block the alternative lengthening of telomeres (ALT) mechanism used by 15% of cancers (Image: Kusuma et al. / Nature Communications)

The study was undertaken by molecular biologist Dr Maya Jeitany of the Nanyang Technological University in Singapore and her colleagues.

Dr Jeitany: “A prominent feature of cancer is its ability to evade cell death and acquire indefinite replication — to stay immortal, in other words — which it can do through the alternative lengthening of telomeres (ALT) mechanism.

“While a sizable portion of cancer cells depend on this mechanism, there is no clinically approved targeted therapy available.

“Through our study, we identified a novel signaling pathway in the ALT mechanism and showed that the FDA-approved drug ponatinib inhibits this pathway and holds exceptional promise in stopping the growth of ALT cancer cells.

“Our findings may provide a new direction for the treatment of ALT cancers by repurposing an FDA-approved drug for these types of tumors.”

In mice with transplanted human bone cancer cells, treatment with ponatinib reduced tumor size (Image: Getty Images)

The researchers identified the potential for ponatinib to be used to treat ALT positive cancers first via high-throughput screening — in which they analyzed a large number of biological and pharmacological compounds — followed by actual tests of a shortlist of drugs.

The team found that when they treated cells from osteosarcoma and liposarcoma (a type of tumor that grows in fatty tissues) with ponatinib in the lab, the cells experienced DNA damage, telomere dysfunction, and ultimately stopped dividing.

Furthermore, telomere synthesis was found to decrease within 18–20 hours after the drug was administered to the cells.

In pre-clinical studies on mice with transplanted human bone cancer cells, treatment with ponatinib was similarly found to reduce tumor size without affecting the rodent's body weight — which is a common side effect of cancer treatments.

Dr Jeitany and her colleagues also noted that these mice experience a reduction in a biomarker for ALT positive cancer, in comparison with untreated mice — indicating that the drug is indeed effective at inhibiting the cancer's growth.

With their initial study complete, Dr Jeitany and her colleagues are now studying how ponatinib affects telomeres in greater detail, alongside exploring potential drug combinations involving ponatinib that could be used for the clinical treatment of ALT positive cancers.

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Professor Valeria Yang is a medical oncologist from the National Cancer Center in Singapore who was not involved in the present study.

She commented: “Sarcomas and glioblastomas are both highly complex cancers that are more prevalent in young people and currently have limited treatment options.

“The identification of a drug that is FDA-approved which can be repurposed to target ALT, an Achilles heel in these cancers, is very exciting.”

The full findings of the study were published in the journal Nature Communications.