Blood pressure drug may boost effectiveness of lung cancer treatment

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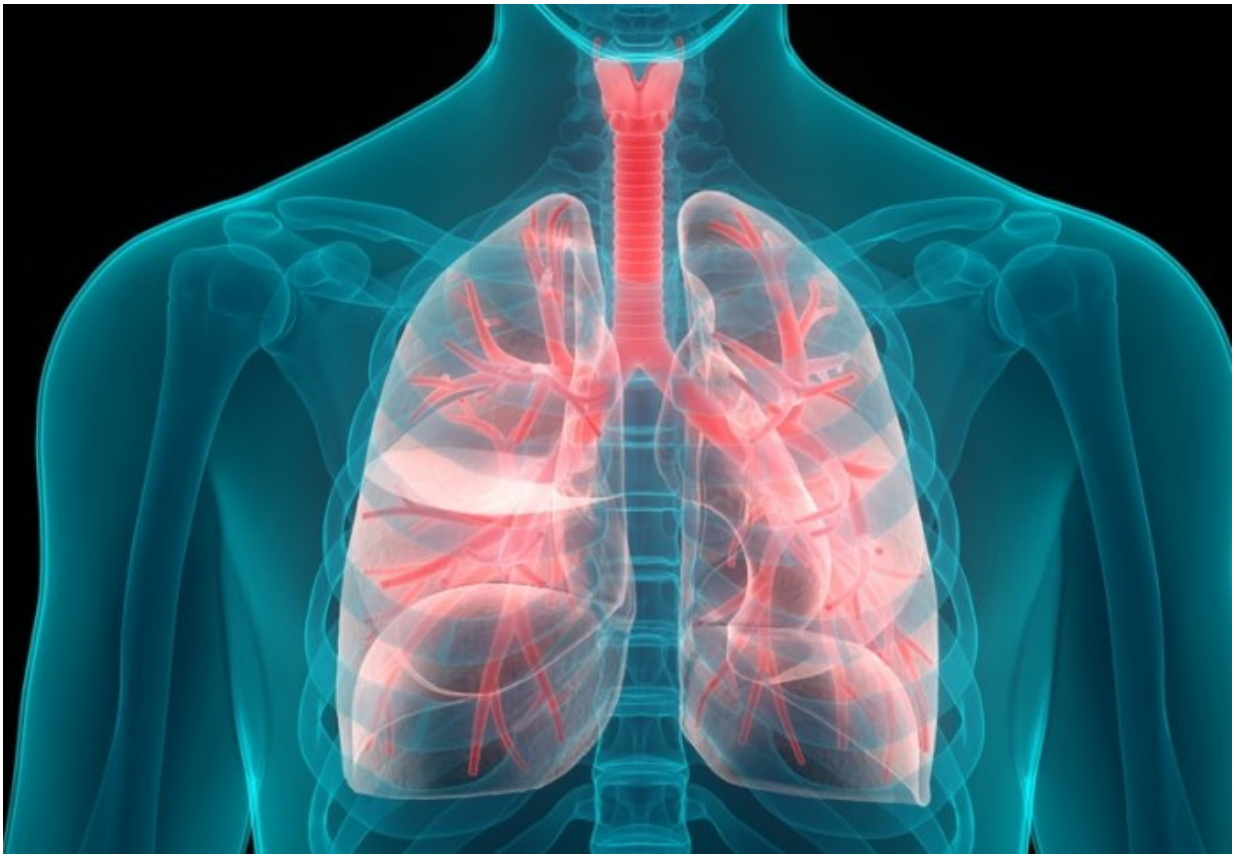

A blood pressure drug may make a type of lung cancer treatment more effective, suggests a new study.

The early-stage research, conducted on human cells in the lab and on mice, was led by scientists from Imperial College London and Fudan University in China, and is published in the journal *Cell Discovery*.

The team studied a lung cancer drug called erlotinib which can be used to treat between 10 and 30 per cent of lung cancer patients.

Unfortunately, the drug usually stops working within a few months, due to cancer cells developing resistance to the treatment.

In the current study the team showed that the resistance could be reversed using a simple and cheap diuretic, or 'water pill', called ethacrynic acid.

Professor Michael Seckl, lead author from the Department of Surgery and Cancer at Imperial said: "Although these are very early-stage results, and are yet to be applied to patients in trials, they suggest the addition of a very cheap diuretic may extend the amount of time we can use the cancer drug erlotinib. This could potentially provide patients with more treatment options and save money in financially challenged health services. "

Almost 2 million people are diagnosed with lung cancer every year worldwide and it is the top international cancer killer. The drug erlotinib is prescribed to between 10 - 30 per cent of patients with non-small cell lung cancer, which accounts for 85 per cent of all lung cancer cases.

Among patients who have this type of lung cancer, nearly one in three will carry a particular genetic mutation on their cancer cells. This mutation is on a particular receptor, or docking site, on the cancer cells that is crucial to the cell's growth and survival. Patients found to have this mutation are prescribed erlotinib, which blocks this mutated receptor and halts cell growth.

However, the cancer cells quickly evolve resistance to the drug's deadly effects.

Although alternative drugs are available once erlotinib stops working, these are much more expensive – and they can also stop working due to cancer cells developing resistance.

Previous studies have found that, in at least half of cases, the cancer cells become resistant to erlotinib by developing a second mutation. But until now scientists only partially understood how this second mutation allowed the cancer cells to protect themselves against erlotinib.

In the latest study, the international team revealed new insights into how this additional mutation leads to resistance, opening avenues for new treatments.

The scientists found this second mutation lowers levels of a naturally-occurring antioxidant called glutathione.

The team found that if they raised glutathione levels in cancer cells in the lab, they reversed resistance to the drug erlotinib, and the treatment was once again able to kill cancer cells.

Spurred on by their finding, the team then looked for any other medicines that have been shown to raise glutathione levels.

They found the 'water pill' ethacrynic acid, a diuretic used for 30 years to treat swelling, fluid retention and high blood pressure, raised glutathione levels. Ethacrynic acid works by triggering the kidneys to remove more water from the body but also blocks the breakdown of glutathione.

Mouse studies then confirmed that using the diuretic alongside the

cancer drug erlotinib reversed resistance to the drug, and enabled it to kill lung cancer cells.

The team are now considering the possibility of translating their findings to human trials, explained Professor Seckl.

"We urgently need new treatments for lung cancer patients, and this research suggests we can boost the effectiveness of an existing drug, rather than switch to another new expensive treatment. We are now seeking funding to enable patient trials within the next three years."

More information: "Decreased glutathione biosynthesis contributes to EGFR T790M-driven 2 erlotinib resistance in non-small cell lung cancer" by H. Li et al is published in *Cell Discovery*

Provided by Imperial College London