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New class of drug shows promise for treating asthma and COPD

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Scientists have developed a new drug (RPL554) that could treat obstructive airway diseases such as asthma and chronic obstructive pulmonary disease (COPD) in two ways at once, according to new research published in The *Lancet Respiratory Medicine*. RPL554 has the potential to both reverse the narrowing of the airways (bronchodilation) and reduce inflammation quicker and with fewer side effects than current therapies.

"Further longer term studies of RPL554 are now eagerly awaited because this could be one of the most substantial advances for some time in the management of patients with chronic airway obstruction", writes Professor Jadwiga A Wedzicha from University College London, UK, in a linked Comment.

The unique inhaled dual inhibitor—two actions in a single molecule—works by impeding the ability of two enzymes from the phosphodiesterase family (PDE3 and PDE4) to inhibit processes that help relax airway smooth muscle and reduce inflammation.

For the past 40 years, the mainstay of treatment for asthma and COPD (eg, chronic bronchitis and emphysema) has been inhaled anti-inflammatory drugs (corticosteroids) plus bronchodilators (usually long-acting ß2 agonists). But corticosteroids can have substantial side effects, while long-acting ß2 agonists have come under scrutiny for their risk of worsening asthma symptoms. What is more, most people with severe disease and frequent flare-ups fail to achieve good control of symptoms

and new treatments are needed.

Between February, 2009 and January 3013, four small proof-of-concept clinical trials were done in the Netherlands, Italy, and the UK to assess the safety and efficacy of inhaled RPL554 in healthy participants (39 people) and people with mild-to-moderate asthma (28) and COPD (12).

In COPD patients, a single dose of nebulised RPL554 improved respiratory function, producing a 17% increase in FEV1 (forced expiratory volume at 1 second; which measures the volume of air that can be forcibly exhaled in one second after taking a deep breath)—a bronchodilator response at least as effective as the widely use ß2 agonist Salbutamol.

Additionally, in patients with asthma and COPD, there was rapid bronchodilation with peak effects similar to those produced with inhaled ß2 agonists. Repeat dosing in asthmatics for 6 days showed that the bronchodilator effects were maintained.

Findings also showed that RPL554 can inhibit the bacterial component lipopolysaccharide (LPS) in healthy subjects suggesting that RPL554 also possesses significant anti-inflammatory activity.

Overall, RPL554 was well tolerated and patients in the treatment and placebo groups experienced similar rates of adverse events, which were generally mild. "Although other PDE4 inhibitors can cause gastrointestinal side effects when given orally, none were reported at any dose of RPL554 tested in these trials", explains study leader Professor Clive Page from King's College London, UK.

According to Professor Page, "These studies give us a glimpse into the potential bronchodilator, bronchoprotective, and anti-inflammatory effects of this drug. So far trials have run for 7 days or less and there is a

need to look at longer-lasting effects. Further studies are needed to better understand the full potential of this new therapy for COPD and asthma."**

More information: www.thelancet.com/journals/lan … (13)70187-5/abstract

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