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Lung infections offer clue to unlocking the mystery of life-saving heart drug

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Scientists from the University of Sheffield have discovered ground breaking clues as to how the pioneering heart drug ticagrelor might reduce the risk of dying following a heart attack, in comparison to previous standard treatments.

The new findings, published in *Platelets*, show that ticagrelor may reduce the risk of dying as a result of a lung infection after suffering a heart attack compared to patients treated with the drug clopidogrel.

The analysis, which was led by researchers from the University of Sheffield and Uppsala University Sweden, is the latest to come from the PLATO study which originally included over 18,000 patients worldwide.

In the initial PLATO study, the annual mortality rate for patients treated with clopidogrel was 5.9 per cent and this rate was significantly reduced to 4.5 per cent for patients treated with ticagrelor.

The extent of this reduced risk was unexpected, as previous similar trials had not been so successful in reducing mortality risk - prompting speculation as to the possible mechanisms for this benefit.

Professor Robert Storey said: "We have now shown that there were fewer deaths due to overwhelming bacterial infection (sepsis) in patients treated with ticagrelor, with lung infection accounting for the source of this sepsis in many cases.

"This is a surprising finding but does seem to provide a potential lead in explaining why ticagrelor saved so many lives in comparison to clopidogrel treatment.

"Ticagrelor not only has greater anticlotting activity compared to clopidogrel, which easily explains its greater effectiveness in preventing further heart attacks, but also has another property not possessed by clopidogrel that allows it to prevent adenosine from being cleared from the blood stream.

"Adenosine has many different effects in the body including influencing the activity of white blood cells that are involved in tackling pneumonia and other infections."

Another intriguing finding was subtle but highly significant differences in blood markers of immune cell activity with evidence of slightly greater activity in ticagrelor-treatment patients.

This appeared to be partly accounted for by clopidogrel slightly suppressing the number of circulating white blood cells since levels increased when clopidogrel was stopped. It is less clear whether ticagrelor was marginally increasing the levels of immune cell activity.

"These findings warrant further research in order to understand the reasons for these differences in immune system activity and whether or not there might be a link with the lung infection findings," said Professor Storey.

"We are pursuing several avenues at the moment to increase our understanding of ticagrelor's effects and the reasons for its life-saving properties."

The National Institute for Clinical Health and Excellence (NICE)

approved ticagrelor as a cost-effective treatment for heart attack patients in October 2011. After waiting for this approval, hospitals and GP practices across South Yorkshire were early adopters of ticagrelor and have used this instead of clopidogrel in the majority of heart attack victims since February 2012, in line with recommendations by the European Society of Cardiology.

However, some areas of the UK have faced barriers to the introduction of ticagrelor as a consequence of its higher cost compared to clopidogrel, despite the endorsement by NICE that ticagrelor is cost-effective. This has led to inequity of access to a treatment that has the best evidence for reducing the risk of dying in the year after a heart attack.

Provided by University of Sheffield