GPVI inhibition by glenzocimab synergistically inhibits atherosclerotic plaque-induced platelet activation when combined with conventional dual antiplatelet therapy

Introduction

- Platelet GPVI receptors are activated by collagen, which is exposed following atherosclerotic plaque rupture during acute coronary syndromes (ACS). GPVI has also recently been identified as a receptor for fibrin.
- Aspirin and a P2Y12 inhibitor are routine treatments for myocardial infarction (MI). However, these drugs are not always sufficient for heavy coronary thrombus burden during STElevation MI (STEMI).
- More potent antiplatelet drugs (GPⅡb/Ⅲa-inhibitors) may help in this setting, but are limited by excessive bleeding.

AIM

- Since GPVI has major roles in thrombosis but is much less important than GPⅡb/Ⅲa for haemostasis, we aimed to investigate whether a novel platelet GPVI inhibitor, glenzocimab (Acticor Biotech), provides additional antithrombotic effects when combined with aspirin and ticagrelor.

METHODS

- Investigated the antithrombotic effects of adding glenzocimab (previously known as ACT017) to blood from healthy donors and 22 patients with ACS treated with aspirin and ticagrelor.
- Compared the effect of glenzocimab with the GPⅡb/Ⅲa inhibitor epifibatide ex vivo.
- Investigated the effect on platelet aggregation, signalling, adhesion, thrombin generation, thrombus formation and clot stability ex vivo.
- Platelets stimulated with collagen and atherosclerotic plaque material.
- Intravital microscopy in a murine model of ST-elevation myocardial infarction and ischaemia-reperfusion injury to investigate microvascular thrombosis.

RESULTS

- Platelet aggregation
- ATP secretion
- Protein Phosphorylation
- Thrombin generation
- Microvascular thrombosis

CONCLUSIONS

- Glenzocimab provided amplified antithrombotic effects when combined with DAPT.
- Less effect on mechanisms of haemostasis compared to epifibatide.
- Appealing for further development for use in STEMI.