About the TROPICAL-ACS trial

Blood platelets get highly activated in the acute phase of acute coronary syndrome (ACS) when they come into contact with pro-thrombotic mediators of the sub endothelial matrix after atherosclerotic plaque rupture or mechanical injury during percutaneous coronary intervention (PCI) and upon exposure to the thrombogenic metallic coronary stent surface. Therefore, dual antiplatelet therapy with aspirin and an ADP P2Y₁₂ platelet receptor blocker is routinely administered in ACS patients.

Over the past decade the ADP antagonist clopidogrel, a second generation thienopyridine pro-drug has been the standard of treatment in clinical practice for these patients, along with aspirin. However, up to 25% of patients respond inadequately to clopidogrel, i.e. not achieving the desired pharmacological effect of ADP receptor inhibition. This is mainly due to clopidogrel's pharmacological characteristics including delayed onset of action, large response variability, due to reduced absorption or impaired biotransformation to its active metabolite leading to an insufficient antiplatelet action. This phenomenon is termed high on-treatment platelet reactivity (HPR) or clopidogrel non-response.

For this reason, there was an increasing need for alternative drugs to be developed. Today, prasugrel, a third generation thienopyridine is one such drug which has shown its superiority compared to clopidogrel in terms of thrombotic risk reduction, especially in the early and acute period of treatment. However, a higher risk of bleeding, including enhanced life threatening bleeding, was observed with prasugrel, predominantly during the long-term maintenance phase of treatment.

Based on the individual characteristics and similarities of both agents, a combined treatment might help healthcare professionals to maximize clinical benefits while preventing severe side effects: Patients may benefit from consecutive application of the more potent prasugrel in the acute phase, where recurrent thrombotic risk is high and of the less aggressive clopidogrel across the maintenance phase to reduce bleeding risk. However, it is essential to identify patients with HPR on clopidogrel, those requiring the potent prasugrel also in the maintenance phase in order to reduce the risk of recurrent ischemic events.
The tailored approach may carry significant cost saving potential, since clopidogrel is a generic drug which is up to 20 times less costly vs prasugrel, translating to cost savings of up to 1500 US$ per patient for an annual drug therapy, based on US drug pricing.\textsuperscript{12-13}

The objective of the TROPICAL-ACS study is to determine whether a platelet function testing guided approach that employs the Roche Multiplate ADPtest with a controlled switch from prasugrel to clopidogrel antiplatelet maintenance treatment is non-inferior to standard 12 month treatment with prasugrel with regards to a combined ischemic and bleeding event.

\textbf{Fig. 1: TROPICAL-ACS flow-chart}

The figure illustrates the control group and the monitoring group of the study. 1:1 randomization is done after PCI and before discharge of patients. The response to antiplatelet treatment is measured for all study participants in both arms of the study. Based on the derived on clopidogrel treatment aggregation values at day 14 of the study in the monitoring group, the further course of treatment is defined, which is clopidogrel in non-HPR patients and a switch back to prasugrel in HPR patients.

The TROPICAL-ACS study will be conducted in about 15 investigational centers in Europe and recruit 2600 ACS patients undergoing successful PCI over a planned recruitment period of 18 months. The primary study goal is to evaluate the 12-months combined ischemic and bleeding adverse events in either therapy arm, which is a composite primary endpoint consisting of death from cardiovascular cause, myocardial infarction, stroke and bleeding. Secondary end-points are the individual incidence of bleeding, stent thrombosis, all-cause mortality at 12 months and a pre-
specified cost-effectiveness analysis on the economic impact of a platelet function testing guided treatment approach.

The TROPICAL-ACS Steering Committee comprises a group of internationally recognized physicians in the field of cardiology and includes Prof. Steffen Massberg, MD, Prof. Julinda Mehilli, MD, Prof. Jörg Hausleiter, MD, Dr. Dirk Sibbing, MD, all from the Department of Cardiology at the Ludwig-Maximilians University in Munich, Germany; Prof. Franz-Josef Neumann, MD, University Heart Center in Bad Krozingen, Germany; Prof. Kurt Huber, MD, Wilhelminen Hospital in Vienna, Austria; Dr. Daniel Arádi, MD, State Heart Center in Balatonfüred, Hungary.

References

