Effect of pre-hospital crushed prasugrel tablets in patients with STEMI planned for primary percutaneous coronary intervention

The COMPARE CRUSH trial

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on behalf of the COMPARE CRUSH Investigators
Background

• Dual antiplatelet therapy consisting of aspirin and potent oral P2Y$_{12}$ receptor inhibitor prasugrel or ticagrelor constitute the cornerstone of medical treatment of ST-segment elevation myocardial infarction and are critical in reducing intra- and post-procedural ischemic complications in patients undergoing pPCI $^1$

• **High platelet reactivity** during the acute phase of myocardial infarction correlates with the extent of myocardial damage, suboptimal flow in the infarct-related artery after pPCI, and extent of microvascular obstruction $^{2-4}$

• However, onset of platelet inhibition by oral P2Y$_{12}$ antagonist in patients presenting with STEMI is delayed for several hours due to slow gastrointestinal absorption $^{5,6}$

• **Crushing tablets** of the loading dose of P2Y$_{12}$ inhibitors has been shown to increase bioavailability and to induce faster onset of platelet inhibition in STEMI patients $^{7,8}$

References:

4. Zalewski J. et al, Kardiol Pol 2012;70:677-84
COMPARE CRUSH Study design

Prospective, multicenter, randomized-controlled trial

STEVI patients with symptom onset ≤6 hours planned for primary PCI

In the ambulance
Aspirin, heparin

Prasugrel 60mg Crushed tablets

1:1 randomization
2 interventional centers of Rotterdam / NL
Enrollment Nov 2017 – Feb 2020

Transfer to PCI center

Prasugrel 60mg Integral tablets

Primary PCI
Study Endpoints

Independent Primary Endpoints:
• TIMI 3 flow in the infarct-related artery at first angiography
• ≥70% ST-segment resolution 1 hour after primary PCI

Key Secondary Endpoints:
• Platelet Reactivity Assessment (VerifyNow™)
• Clinical outcomes death, MI, urgent revascularization, stent thrombosis
• Safety endpoint - Bleeding events TIMI major or BARC ≥3
Primary endpoint

TIMI 3 flow in the infarct-related artery (IRA) at first angiography

OR (95%CI): 0.92 [0.65 - 1.30]
Primary endpoint

Complete ST-segment resolution (STR) 1 hour post-pPCI

![Bar chart showing Complete STR (%) with crushed and integral groups.]

- Crushed: 59.9%
- Integral: 57.3%

Statistical significance: $p=0.55$

Odds Ratio (95% CI): 1.11 [0.78 - 1.58]
Key secondary endpoints

Proportion of patients with **high platelet reactivity** at the beginning of pPCI

High platelet reactivity is defined as P2Y\textsubscript{12} reactivity units >208

Median time LD administration – beginning of pPCI 45 [34 – 57] minutes
Conclusion

• Pre-hospital administration of crushed tablets of prasugrel loading dose in STEMI patients planned for pPCI does not improve TIMI 3 flow in the IRA at first angiography, or ST-segment resolution at 1 hour post-PCI

• These findings hold in spite of the fact that crushed tablets of prasugrel lead to more potent platelet inhibition compared with integral tablets

• Whether faster and more potent antiplatelet therapy can improve coronary reperfusion in contemporary STEMI treatment regimen warrants further investigation
EFFECT OF PRE-HOSPITAL CRUSHED PRASUGREL TABLETS IN PATIENTS WITH STEMI PLANNED FOR PRIMARY PERCUTANEOUS CORONARY INTERVENTION: THE RANDOMIZED COMPARE CRUSH TRIAL

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