Trial synopsis

1. EU trial number and full trial title

EU-CT number: 2025-524320-21-00

Prehospital pulse-dose glucocorticoid in patients with STEMI – the PULSE-MI 2 trial

2. Rationale

Inflammation is induced immediately after the onset of acute myocardial ischemia and is subsequently exacerbated following reperfusion. Hence, inflammation in the setting of STEMI is a pivotal factor in both acute myocardial ischemia and the subsequent healing of the infarcted myocardium. Glucocorticoids are crucial in regulation of the systemic inflammatory response and may therefore be beneficial in limiting myocardial injury after STEMI.

We conducted the phase II randomized, placebo-controlled PULSE-MI trial (Nov 2022–Oct 2023) in 742 prehospital STEMI patients, showing pulse-dose glucocorticoid was safe and improved LVEF, infarct size, and microvascular obstruction, with a trend toward lower 3-month mortality. However, as the trial was not powered for clinical outcomes, it remains unproven whether this treatment reduces post-STEMI mortality. Thus, the aim of this prospective, randomized trial is to evaluate the effect of prehospital pulse-dose glucocorticoid on all-cause mortality in patients with STEMI.

3. Objective

The aim of this nationwide trial is to evaluate the effect of prehospital pulse-dose glucocorticoid on all-cause mortality compared to placebo in patients with STEMI

4. Main trial endpoints

The main trial endpoint is all-cause mortality, which will be assessed during the study period (2026-2031).

5. Secondary trial endpoints

The secondary endpoints are the following:

Cardiovascular mortality, spontaneous myocardial infarction, admission for heart failure, all-cause mortality or admission for heart failure, cardiovascular mortality or admission for heart failure, and recurrent non-fatal cardiovascular events (spontaneous myocardial infarction and admission for heart failure) with death treated as a terminal event.

All secondary endpoints will be assessed during the study period (2026-2031)

6. Trial design

This multicenter trial is an investigator-initiated, 1:1 randomized, blinded, placebo-controlled clinical trial to investigate whether pulse-dose glucocorticoid (250 mg methylprednisolone) in the prehospital setting reduces all-cause mortality in patients with STEMI. The follow-up period will be completed after five years. All patients will be followed for a minimum of one year. Following completion of the trial, the hospital records will be accessed up to 10 years to obtain information on clinical events

7. Trial population

Inclusion criteria for recruitment are listed below and must be fulfilled for the patient to be randomized:

1. Age ≥18 years including fertile women*
2. Acute onset of chest pain with < 24 hours duration
3. STEMI as characterized on electrocardiogram (ECG) by one of the following:

   1) at least two contiguous leads with ST-segment elevation ≥2.5 mm in men < 40 years, ≥2 mm in men ≥40 years, or ≥1.5 mm in women in leads V2-V3 and/or ≥1 mm in the other leads,

   2) presumed new left bundle branch block with ≥1 mm concordant ST-segment elevation in leads with a positive QRS complex, or concordant ST-segment depression ≥1 mm in V1-V3, or discordant ST-segment elevation ≥5 mm in leads with a negative QRS complex

   3) Isolated ST depression ≥0.5 mm in leads V1-V3 indicating posterior acute myocardial infarction (AMI)

   4) ST-segment depression ≥1 mm in eight or more surface leads, coupled with ST-segment elevation in aVR and/or V1 suggesting left main-, or left main equivalent-coronary obstruction

Exclusion criteria for recruitment are listed below and none of the criteria must be fulfilled for a patient to be eligible:

1. Suspected other type I acute myocardial infarction at time of potential randomization
2. Initial presentation with cardiac arrest (out of hospital cardiac arrest)
3. Known allergy to glucocorticoid

8. Interventions

Patients will be randomized to prehospital infusion of glucocorticoid (250 mg methylprednisolone) or placebo (0.9% NaCl), administered over 5 minutes during transport.
All subsequent care including acute CAG/PCI, antithrombotic therapy, possible CABG (~4%), and guideline-based follow-up treatment will be performed according to standard clinical practice.

9. Ethical considerations

The study will be approved by the ethics committee, registered with the Danish Data Protection Agency, and conducted according to the Declaration of Helsinki, ICH-GCP, and applicable legislation, with oversight by an independent DSMB.
Due to the emergency nature of STEMI, treatment will be initiated before consent; informed consent will be obtained as soon as possible after PCI, with representative consent used when required, following established practice in comparable acute trials.
The intervention poses minimal risk, does not delay standard care, and may provide clinical benefit. We refer to the protocol sections 9.1, 9.2, 9.2.1, and 9.3, for a more thorough description of the ethical considerations.