

Does **Cyclosporine** *ImpRove* **Clinical oUtcome** in **ST**-elevation myocardial infarction patients ? (the CIRCUS study)

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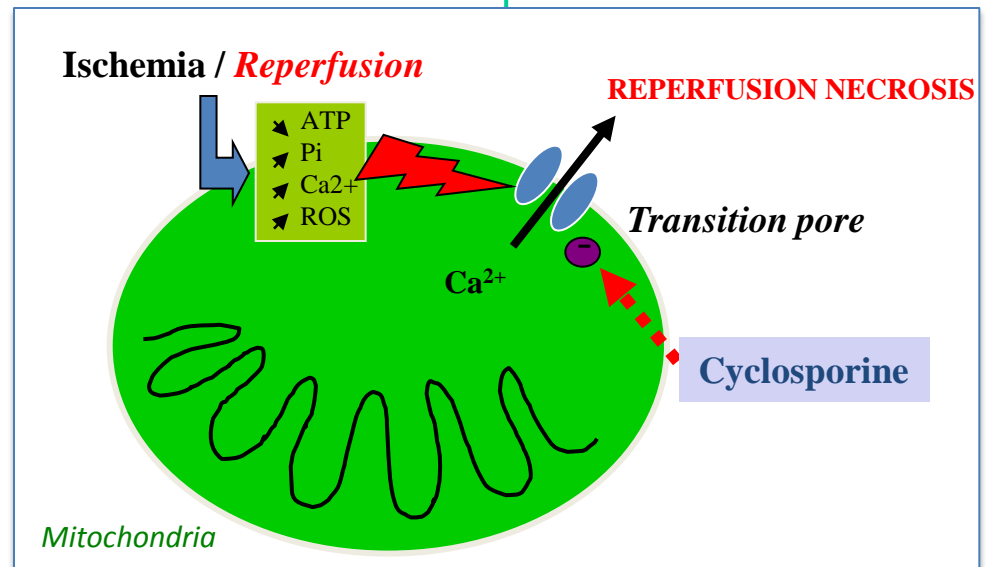
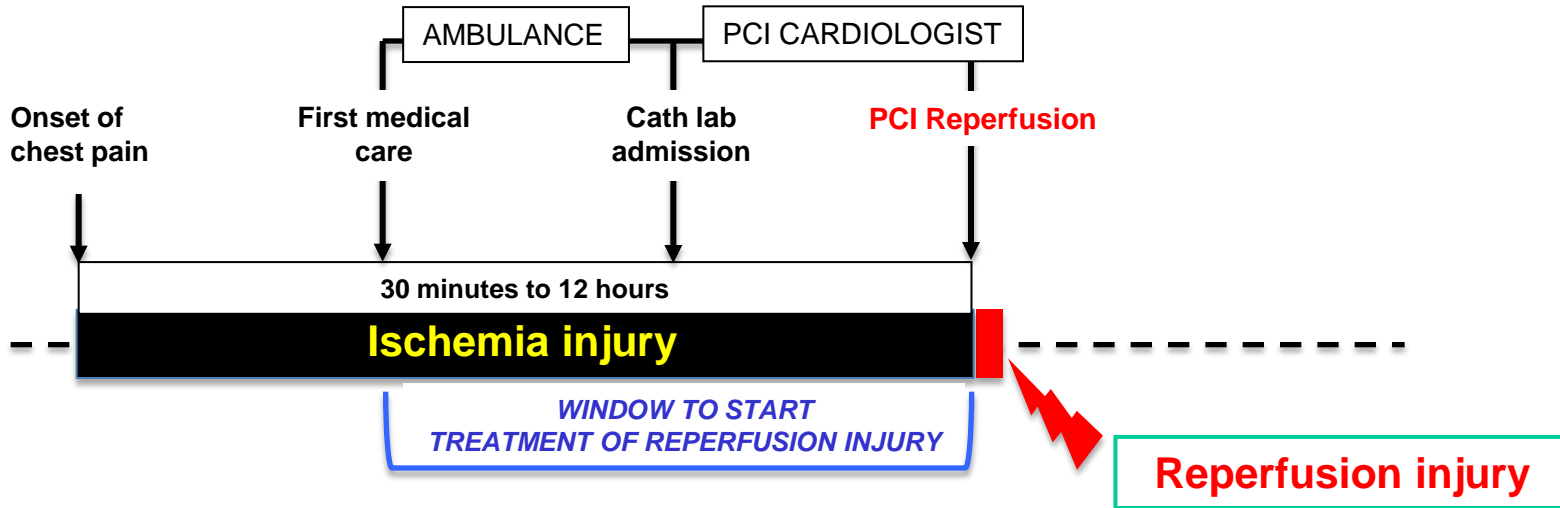
DECLARATION OF INTEREST

Neurovive Pharmaceuticals, AB:

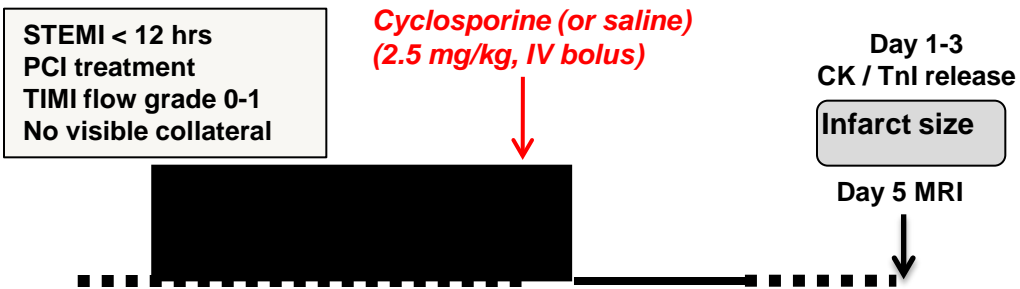
- Research contracts
- Consulting/Royalties/Owner/ Stockholder of a healthcare company



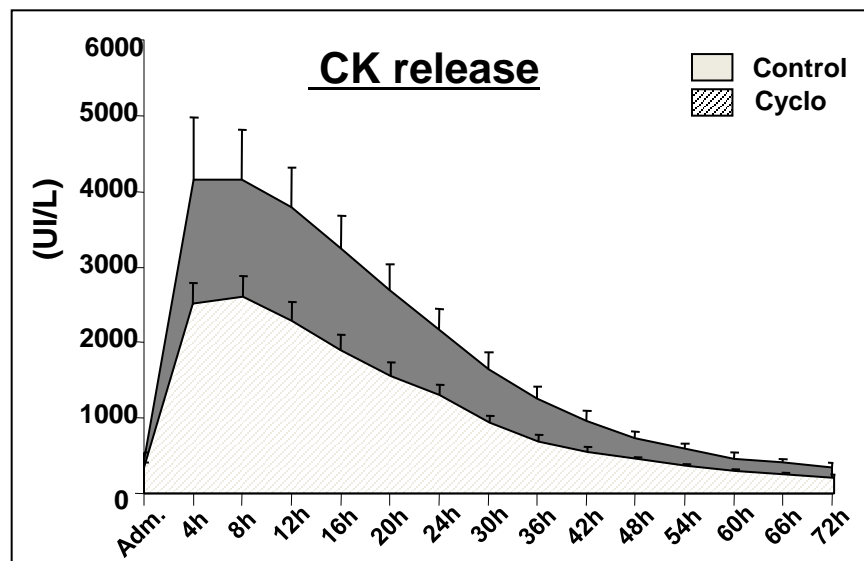
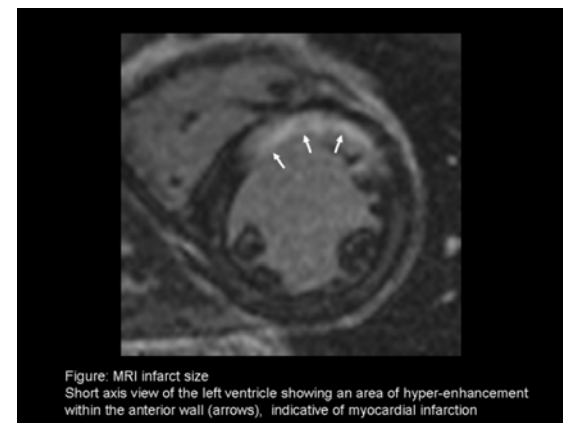
Reperfusion injury contributes to myocardial infarction



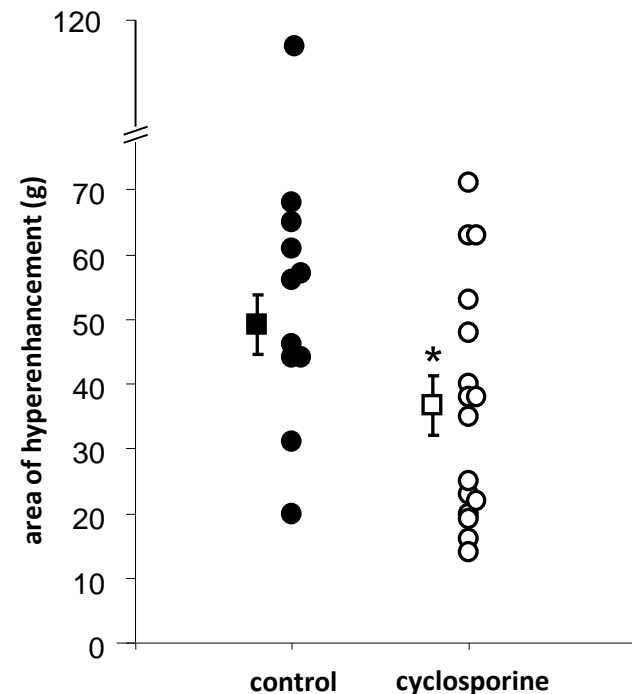
Phase II trial: cyclosporine reduces infarct size in STEMI



CMR infarct size



Piot et al. NEJM 2008



➤ **OBJECTIVE**

To determine whether cyclosporine might improve clinical outcome in STEMI patients

➤ **PRIMARY ENDPOINT**

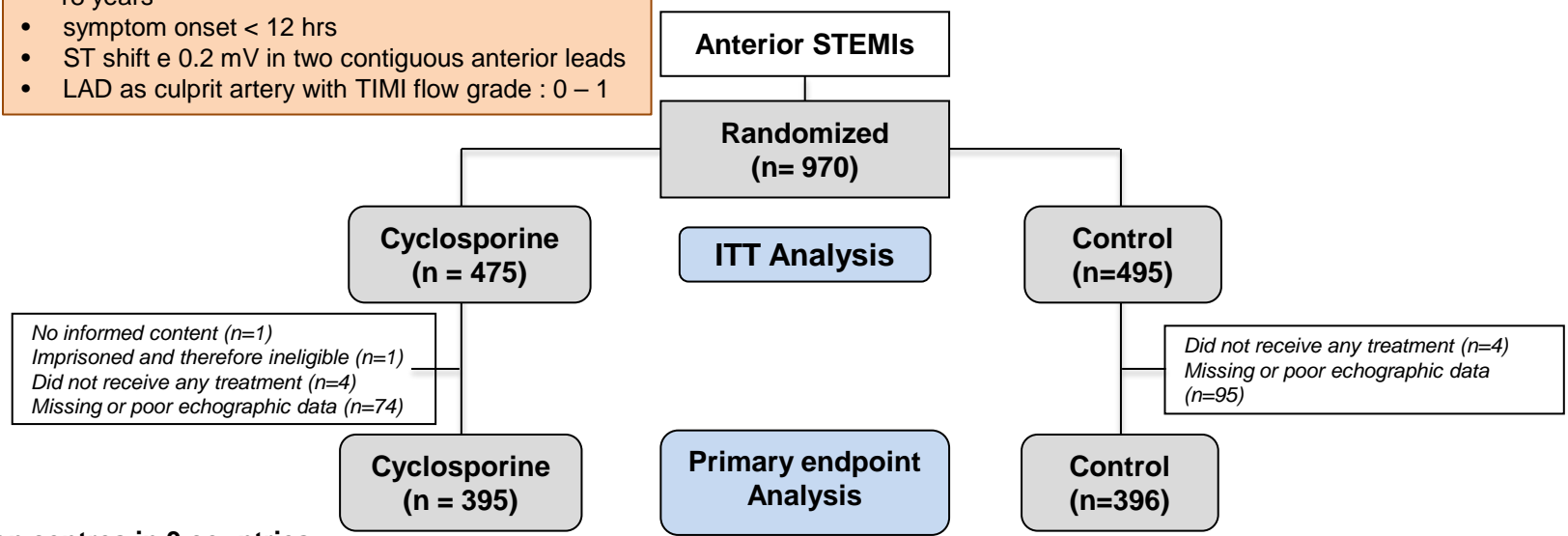
Combined incidence within 1 year after STEMI of :

[all-cause mortality; worsening of heart failure during initial hospitalization or re-hospitalisation for heart failure ; LV remodeling]

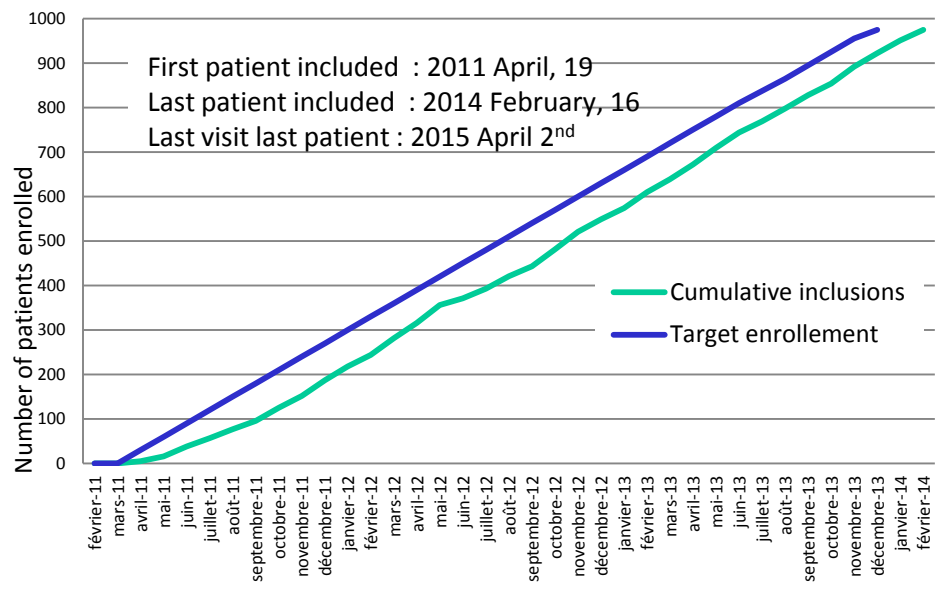
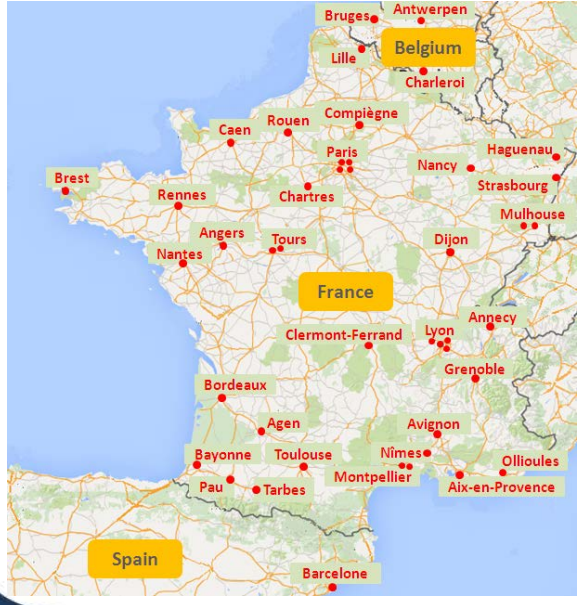
(LV remodeling (echo): increase > 15% of LVEDV at 1 year versus initial discharge)

Study population and recruitment

- 18 years
- symptom onset < 12 hrs
- ST shift e 0.2 mV in two contiguous anterior leads
- LAD as culprit artery with TIMI flow grade : 0 – 1



42 investigation centres in 3 countries



Primary and secondary outcomes at 1 year

	Cyclosporine (n=395)	Control (n=396)	Odds Ratio (95% CI)	P value
(Death / HF / LV remodeling)	233 (59.0 %)	230 (58.1%)	1.04 [0.78; 1.39]	0.77

Death: all-cause	7.1 %	6.6 %	1.09 [0.63 ; 1.90]	0.76
Death: cardiovascular	6.1 %	6.1 %	1.01 [0.56 ; 1.81]	0.98
HF worsening or re-hospitalization for HF	22.8 %	22.7 %	1.01 [0.72 ; 1.41]	0.97
HF worsening	15.7 %	16.9 %	0.92 [0.63 ; 1.34]	0.65
Re-hospitalization for HF	10.6 %	10.4 %	1.03 [0.65 ; 1.63]	0.89
LV remodeling	42.8 %	40.7 %	1.09 [0.82 ; 1.46]	0.53
Cardiogenic shock	6.6 %	6.1 %	1.09 [0.61 ; 1.94]	0.77
Recurrent Myocardial infarction	2.3 %	3.8 %	0.59 [0.26 ; 1.37]	0.22
Stroke	1.8 %	3.0 %	0.58 [0.22 ; 1.48]	0.25
Major bleeding	1.8 %	2.3 %	0.73 [0.27 ; 2.00]	0.54

In anterior STEMI, cyclosporine did not reduce the risk of the composite outcome

- One out of four patients died or was hospitalized for heart failure despite receiving state-of-the-art medical care.
- Despite the results of CIRCUS, the concept that reperfusion injury is clinically important. The impact on clinical outcome of recent encouraging phase II trials remains however to be determined.