Pre-PCI Colchicine

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The Importance of Peri-PCI Inflammation

- Peri-PCI vascular inflammation (either primary or secondary) has been independently associated with atherothrombotic outcomes.

- Activation of both the innate and adaptive immune systems can lead to aberrant vessel repair, re-endothelialization, restenosis and recurrent events.
1-Year Impact of Residual Inflammatory Risk in Patients Undergoing PCI with Baseline LDL-C ≤70 mg/dL

CANTOS: A Critical Proof of Concept in patients with a history of myocardial infarction

C DLCOT – Colchicine for post MI

Hazard ratio, 0.77 (95% CI, 0.61–0.96)  
P=0.02

Cumulative Incidence (%)
Colchicine reduced infarct size in patients with STEMI undergoing primary PCI

Creatine kinase-myocardial brain fraction (CK-MB)

MRI with late gadolinium enhancement (MRI-LGE)
An important question was asked:

Does pre-procedural colchicine reduce inflammation and myocardial injury?
How was the question addressed?

<table>
<thead>
<tr>
<th>Population</th>
<th>Intervention</th>
<th>1º Outcomes</th>
<th>Follow-up</th>
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</table>
| Patients undergoing diagnostic coronary angiography (with or without possible PCI) | Pre-cath 1.8 mg colchicine single dose | • Change in IL-6 (baseline to 1h post PCI)  
• PCI-related myocardial injury (troponin I) | • 1h  
• 6-8h  
• 22-24h  
• 30-day |
What did they find?

**Primary Outcome**

<table>
<thead>
<tr>
<th>Group</th>
<th>PCI-Related Myocardial Injury (%)</th>
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<tbody>
<tr>
<td>Colchicine (n=206)</td>
<td>118 (57.3%)</td>
</tr>
<tr>
<td>Placebo (n=194)</td>
<td>122 (64.2%)</td>
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</tbody>
</table>

p=0.19
What did they find?

**Percent Change in IL-6 Concentration Compared to Baseline (%)**
- Colchicine: p=0.18
- Placebo: p=0.02
- p=0.31

**Percent Change in IL-1β Concentration Compared to Baseline (%)**
- Colchicine: p=0.71
- Placebo: p=0.68
- p=0.65

**Percent Change in hsCRP Concentration Compared to Baseline (%)**
- p=0.001

Time Post-PCI (hours): 1, 6 to 8, 22 to 24
Study Analysis and Implications (1)

- Well conducted and executed study
- Single center experience
- Mixed population of patients undergoing diagnostic angiography or ACS
- Inflammatory biomarkers during ACS are highly variable (acute phase reactant)
- Baseline levels of inflammatory markers not reported

- Do patients with increased baseline inflammation have greater benefit (analogous to CANTOS)?
- Study was powered to detect a 40% RRR in primary outcome and 35% RRR in IL-6
- Single dose
- Excluded patients on high intensity statin within preceding 24 hours
Local changes in inflammatory biomarkers may be missed (coronary sinus effluent)
Lack of changes in circulating IL-6 and IL-1β may be an issue of sensitivity, variability and confounded by the milieu of ACS
Reassuring to see lower hsCRP at 24 hours post-PCI (p<0.001)

- 93.7% were men
- Background medical therapy and lipid levels?
- Excluded patients without CAD what were the results?
- Good safety profile
CLEAR SYNERGY (OASIS 9)

Colchicine and spironolactone in patients with ST elevation myocardial infarction – OASIS 9 Trial/SYNERGY Stent Registry

Sanjit S. Jolly MD, MSc.
PHRI, McMaster University,
Hamilton Health Sciences
CLEAR SYNERGY (OASIS 9) Study Design

4000 patients diagnosed with STEMI referred for PCI

Initial 800 patients
SYNERGY Stent REQUIRED where commercially available

Within 48 hours of successful PCI and during initial hospitalization, RANDOMIZED to (2 x 2 factorial):

- Colchicine Placebo + Spironolactone Placebo
- Colchicine ACTIVE + Spironolactone Placebo
- Colchicine Placebo + Spironolactone ACTIVE
- Colchicine ACTIVE + Spironolactone ACTIVE

Follow-up: Discharge, 3, 6, 12 months; 24, and 36 months, or Common Study End Date

Primary Outcomes

SYNERGY Stent: Major adverse cardiac events (MACE) compared to performance goal within 1 year
Colchicine vs. placebo: Composite of CV death, recurrent MI, or stroke over duration of follow-up
Spironolactone vs. placebo: Composite of CV death or new or worsening HF over duration of follow-up

MACE was defined as the composite of death, recurrent target vessel MI, stroke or ischemia driven target vessel revascularization.
So what’s the bottom line for colchicine?

Recent MI: YES - COLCOT
Acute peri-STEMI: ? CLEAR SYNERGY
Pre-PCI: ? Not yet

More studies targeting patients with RIR with acute + chronic Rx
High risk primary prevention patients (COLCOT-2) (TDM)