Ανοικτά θέματα στο STEMI.
Αντίσταση στην κλοπιδογρέλη. Ποιά η κλινική της αξία σήμερα?

Ξανθοπούλου Ιωάννα
Καρδιολόγος Επιμ Β ΠΓΝΠατρών
No conflict of interest
CURE

12,562 pts with NSTE-ACS were treated with aspirin and randomized to clopidogrel vs. placebo and followed for up to 12 months

Primary endpoint = CV Death, MI, or Stroke

CLARITY-TIMI 28: Clopidogrel 300 mg/75 mg qd vs Placebo With Thrombolysis for STEMI (n = 3491)

Primary End Point: Occluded Artery (or Death/MI through Angio/HD)

- Clopidogrel: 15.0
- Placebo: 25.0

Odds Reduction:
- 36% for Clopidogrel
- 21.7% for Placebo

CV Death, MI, RI → Urg Revasc

Odds Ratio: 0.80 (95% CI, 0.65-0.97)

P = .03

Variability in Clopidogrel Response

Maximal aggregation to 5 µmol/L ADP (%) after 600 mg loading dose

N=1001

Change in 5 µmol/L ADP-induced platelet aggregation with 75 mg chronic dosing

N=544

Hochholzer W et al. Circ 2005;11:2560-4
Serebruany V et al. JACC 2005;45:246-51
Platelet reactivity and clinical outcomes after coronary artery implantation of drug-eluting stents (ADAPT-DES): a prospective multicentre registry study

Gregg W Stone, Bernhard Witzenbichler, Giora Weisz, Michael J Rinaldi, Franz-Josef Neumann, D Christopher Metzger, Timothy D Henry, David A Cox, Peter L Duffy, Ernest Mazzaferri, Paul A Gurbel, Ke Xu, Helen Parise, Ajay J Kirtane, Bruce R Brodie, Roxana Mehran, Thomas D Stuckey, for the ADAPT-DES Investigators*

---

**Graph A**

- Unadjusted HR 2.54 (95% CI 1.55–4.16)
- \( p = 0.0002 \)

**Graph B**

- Unadjusted HR 1.47 (95% CI 1.15–1.87)
- \( p = 0.002 \)
Primary EP (CV death, MI and stroke at 15 months)

HR = 0.79 (0.65 - 0.97) NNT = 42
Age-adjusted HR = 0.81 (0.66 - 0.99)

Montalescot et al. Lancet 2009
Primary endpoint: CV death, MI or stroke

No. at risk

<table>
<thead>
<tr>
<th>Drug</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ticagrelor</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>4,201</td>
</tr>
<tr>
<td>1</td>
<td>3,887</td>
</tr>
<tr>
<td>2</td>
<td>3,834</td>
</tr>
<tr>
<td>3</td>
<td>3,732</td>
</tr>
<tr>
<td>4</td>
<td>3,011</td>
</tr>
<tr>
<td>5</td>
<td>2,297</td>
</tr>
<tr>
<td>6</td>
<td>1,891</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>4,229</td>
</tr>
<tr>
<td>1</td>
<td>3,892</td>
</tr>
<tr>
<td>2</td>
<td>3,823</td>
</tr>
<tr>
<td>3</td>
<td>3,730</td>
</tr>
<tr>
<td>4</td>
<td>3,022</td>
</tr>
<tr>
<td>5</td>
<td>2,333</td>
</tr>
<tr>
<td>6</td>
<td>1,868</td>
</tr>
</tbody>
</table>

HR: 0.85 (95% CI = 0.74–0.97), p=0.02

PLATO STEMI cohort *
*final diagnosis of STEMI
Clopidogrel is the P2Y12 inhibitor of choice as co-adjuvant and after fibrinolysis, but 48 h after fibrinolysis, switch to prasugrel/ticagrelor may be considered in patients who underwent PCI.
The use of ticagrelor or prasugrel is not recommended as part of triple antithrombotic therapy with aspirin and oral anticoagulation.

### Table 9
Recommended doses of antithrombotic agents in the acute care of patients with chronic kidney disease

<table>
<thead>
<tr>
<th>Agent</th>
<th>Normal renal function and stage 1–3 CKD (eGFR ≥30 mL/min/1.73 m²)</th>
<th>Stage 4 CKD (eGFR 15 to &lt;30 mL/min/1.73 m²)</th>
<th>Stage 5 CKD (eGFR &lt;15 mL/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>Loading dose of 150–300 mg orally followed by a maintenance dose of 75–100 mg/day</td>
<td>No dose adjustment</td>
<td>No dose adjustment</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>Loading dose of 300–600 mg orally followed by 75 mg/day</td>
<td>No dose adjustment</td>
<td>No information available</td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>Loading dose of 180 mg orally followed 90 mg twice a day</td>
<td>No dose adjustment</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>Loading dose of 60 mg orally followed by 10 mg/day</td>
<td>No dose adjustment</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>
Πότε δίνουμε κλοπιδογρέλη σε ασθενή με STEMI?

- Oral anticoagulation (atrial fibrillation, LV thrombus...)
- Non-availability of prasugrel or ticagrelor
- Economic reasons
- ↑ bleeding risk
- Contraindications to prasugrel (prior stroke, age>75, weight<60) AND to ticagrelor (prior intracranial bleeding, severe uncontrolled COPD)
- eGFR<15ml/min/1.73m²
Πότε δίνουμε κλοπιδογρέλη σε ασθενή με STEMI?

- Oral anticoagulation (atrial fibrillation, LV thrombus...)
- Non-availability of prasugrel or ticagrelor
- Economic reasons
- ↑ bleeding risk
- Contraindications to prasugrel (prior stroke, age>75, weight<60) AND to ticagrelor (prior intracranial bleeding, severe uncontrolled COPD)
- eGFR<15ml/min/1.73m²
Πότε δίνουμε κλοπιδογρέλη σε ασθενή με STEMI?

More potent P2Y12 receptor antagonist after risk stratification in patients with....

- Need for long term oral anticoagulation (atrial fibrillation, LV thrombus...)
- eGFR<15ml/min/1.73m²
Absence of ↑ bleeding risk AND Potent P2Y12 receptor antagonist

Table 9  High-risk features for ischaemic events

<table>
<thead>
<tr>
<th>feature</th>
<th>description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior stent thrombosis on adequate antiplatelet therapy</td>
<td></td>
</tr>
<tr>
<td>Stenting of the last remaining patent coronary artery</td>
<td></td>
</tr>
<tr>
<td>Diffuse multivessel disease, especially in diabetic patients</td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease (i.e. creatinine clearance &lt;60 mL/min)</td>
<td></td>
</tr>
<tr>
<td>At least three stents implanted</td>
<td></td>
</tr>
<tr>
<td>At least three lesions treated</td>
<td></td>
</tr>
<tr>
<td>Bifurcation with two stents implanted</td>
<td></td>
</tr>
<tr>
<td>Total stented length &gt;60 mm</td>
<td></td>
</tr>
<tr>
<td>Treatment of a chronic total occlusion</td>
<td></td>
</tr>
<tr>
<td>History of STEMI</td>
<td></td>
</tr>
</tbody>
</table>

STEMI = ST-elevation myocardial infarction.
Absence of ↑ bleeding risk AND Platelet Function Testing While on Clopidogrel

**Table 9** High-risk features for ischaemic events

- Prior stent thrombosis on adequate antiplatelet therapy
- Stenting of the last remaining patent coronary artery
- Diffuse multivessel disease, especially in diabetic patients
- Chronic kidney disease (i.e. creatinine clearance <60 mL/min)
- At least three stents implanted
- At least three lesions treated
- Bifurcation with two stents implanted
- Total stented length >60 mm
- Treatment of a chronic total occlusion
- History of STEMI

**STEMI** = ST-elevation myocardial infarction.

Switch to a potent agent for those with "Clopidogrel resistance" Stay on Clopidogrel for those without "Clopidogrel resistance"
Absence of ↑ bleeding risk AND PLATELET FUNCTION TESTING WHILE ON CLOPIDOGREL

**Table 9** High-risk features for ischaemic events

- Prior stent thrombosis on adequate antiplatelet therapy
- Stenting of the last remaining patent coronary artery
- Diffuse multivessel disease, especially in diabetic patients
- Chronic kidney disease (i.e. creatinine clearance <60 mL/min)
- At least three stents implanted
- At least three lesions treated
- Bifurcation with two stents implanted
- Total stented length >60 mm
- Treatment of a chronic total occlusion
- History of STEMI

STEMI = ST-elevation myocardial infarction.

Risk stratification

- SWITCH TO A POTENT AGENT FOR THOSE WITH "CLOPIDOGREL RESISTANCE"
- STAY ON CLOPIDOGREL FOR THOSE WITHOUT "CLOPIDOGREL RESISTANCE"

DAPT DE-ESCALATION GROUP in TROPICAL ACS STUDY
Guided de-escalation of antiplatelet treatment in patients with acute coronary syndrome undergoing percutaneous coronary intervention (TROPICAL-ACS): a randomised, open-label, multicentre trial
Guided de-escalation of antiplatelet treatment in patients with acute coronary syndrome undergoing percutaneous coronary intervention (TROPICAL-ACS): a randomised, open-label, multicentre trial

- Control group
- Guided de-escalation group

Proportion of patients who achieved combined ischaemic events or BARC ≥2 bleeding (primary endpoint, %)

Number at risk
- Control group: 1306, 1238, 1220, 1190, 1132, 1124, 924
- De-escalation group: 1304, 1234, 1213, 1189, 1129, 1124, 942

HR 0.81 (95% CI 0.62–1.06)

$p_{\text{non-inferiority}}=0.0004$

$p_{\text{superiority}}=0.12$
**Figure 4: Subgroup analyses**

Subgroup analyses of the primary composite endpoint (net clinical benefit) in relevant subgroups of the study cohort (clinical presentation: STEMI/NSTEMI, sex, age, and diabetes). $p_{\text{interaction}}$ represents the likelihood of interaction between the variable and the treatment strategy (platelet function testing-guided de-escalation vs uniform prasugrel treatment). ACS=acute coronary syndrome. HR=hazard ratio. STEMI=ST-segment elevation myocardial infarction. NSTEMI=non-ST-segment elevation myocardial infarction.
# Antithrombotic Therapy in Patients With Atrial Fibrillation Treated With Oral Anticoagulation Undergoing Percutaneous Coronary Intervention

**A North American Perspective—2018 Update**

<table>
<thead>
<tr>
<th>Choice of anticoagulant</th>
<th>2018 Expert Consensus Update</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>An NOAC (rather than a VKA) should generally be preferred in most patients unless contraindicated</td>
</tr>
<tr>
<td>Choice of P2Y$_{12}$ inhibitor</td>
<td>Clopidogrel is the P2Y$_{12}$ inhibitor of choice; ticagrelor may represent a reasonable treatment option in patients at high ischemic/thrombotic and low bleeding risks; avoid prasugrel</td>
</tr>
<tr>
<td>Strategy (double vs triple therapy)</td>
<td>A double-therapy regimen (OAC plus P2Y$_{12}$ inhibitor) immediately after hospital discharge should be considered for most patients, whereas extending the use of aspirin beyond hospital discharge (ie, triple therapy) should be considered only for patients at high ischemic/thrombotic and low bleeding risks and for a limited period of time (eg, 1 mo)</td>
</tr>
</tbody>
</table>
Conclusions

- Η κλοπιδογρέλη δεν αποτελεί αντιαιμοπεταλιακό πρώτης επιλογής σε ασθενείς με STEMI
- Έως 30% των ασθενών παρουσιάζει φαρμακοδυναμική αντίσταση στην δράση της
- Μετά από STEMI, η συχνότερη ένδειξη μακροχρόνιας λήψης κλοπιδογρέλης είναι η ανάγκη για αντιπηκτική αγωγή
- Σε ασθενείς ↑ θρομβωτικού και ↓ αιμορραγικού κινδύνου η ανεύρεση φαρμακοδυναμικής αντίστασης στην κλοπιδογρέλη → αλλαγή σε νεότερο παράγοντα
Σας ευχαριστώ για την προσοχή σας!