Commentary on TiCAB study

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Key findings of the TiCAB study

• Out of 1893 patients randomized, 896 patients received aspirin monotherapy and 898 patients received ticagrelor monotherapy for up to 1 year post-CABG
• No significant difference between the groups for the 1-year primary endpoint (CV death, stroke, MI, repeat revasc) – in fact, a small numerical excess of major CV events occurred within the first month in the ticagrelor group
• No significant interaction was seen for any of the analyzed subgroups
• Major bleeding rates were similar and not significantly different between the groups
Power of the study

• Event rate in aspirin group 8.2%
• My post hoc estimate: Based on sample size of 928 patients per group, the study had 33% power to show a relative risk of 0.775 in the ticagrelor group for alpha 0.0492 (adjusted for interim analysis), reducing to 17% power to show relative risk of 0.85
• Confidence intervals on primary endpoint HR were wide: HR 1.19; 95% CI 0.87-1.62
• Is a larger oral-monotherapy CABG study warranted?
Pharmacology of aspirin and oral P2Y$_{12}$ inhibitors

TAM: ticagrelor active metabolite; CIM: clopidogrel inactive metabolite; CAM: clopidogrel active metabolite; PAM: prasugrel active metabolite

Adapted from Storey RF & Parker WAE. Circulation 2016; 134:793-6
PEGASUS-TIMI 54: CV death/MI/stroke in aspirin-treated patients with prior MI

Clinical efficacy of ticagrelor-based DAPT vs aspirin monotherapy


DAPT = dual antiplatelet therapy

**Event rate (%)**

<table>
<thead>
<tr>
<th>Months from randomization</th>
<th>Placebo</th>
<th>Ticagrelor 90 mg bid</th>
<th>Ticagrelor 60 mg bid</th>
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<tbody>
<tr>
<td>0</td>
<td>9.04%</td>
<td>7.85%</td>
<td>7.77%</td>
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**Ticagrelor 90 mg vs placebo**

HR 0.85 (95% CI 0.75–0.96) p=0.008

**Ticagrelor 60 mg vs placebo**

HR 0.84 (95% CI 0.74–0.95) p=0.004
PEGASUS-TIMI 54: Bleeding Endpoints

Ticagrelor-based DAPT increased non-fatal but not fatal bleeding vs aspirin monotherapy

Ticagrelor-based DAPT RCTs after CABG

Evidence of improved graft patency with DAPT

- Saw J et al: ticagrelor + aspirin appeared more effective than aspirin in preventing graft occlusion in 56 patients at 1 month
  Heart 2016; 102:763-9
- Zhao Q et al: ticagrelor + aspirin more effective than aspirin alone at preventing saphenous vein graft occlusion in 461 patients at 1 year
  JAMA 2018;319:1677-1686
Ticagrelor monotherapy vs aspirin monotherapy
Large RCTs

Lack of superiority of ticagrelor vs aspirin

- GLOBAL LEADERS study: 15,991 PCI patients randomized to standard therapy (DAPT for 1 year then aspirin monotherapy for second year) vs DAPT for 1 month then ticagrelor monotherapy from 1 month to 2 years, no benefit of ticagrelor monotherapy vs aspirin monotherapy in year 2, similar bleeding rates
  Lancet 2018; 392:940-949

- SOCRATES study: 13,199 patients with ischemic stroke/TIA, ticagrelor monotherapy not superior to aspirin monotherapy, possible benefit of early DAPT effect
  NEJM 2016; 375:35-43
Conclusions

• Ticagrelor monotherapy appears to offer no advantage compared with aspirin monotherapy post CABG surgery but has similar safety.

• The TiCAB results add to a larger body of evidence indicating non-inferiority and lack of superiority of ticagrelor monotherapy compared with aspirin monotherapy in patients with CAD or ischemic stroke/TIA.

• Current evidence favors a strategy of dual antiplatelet therapy for achieving greater reduction of CV events at the expense of higher bleeding rates.

• Large clinical outcomes trials of dual antiplatelet therapy following CABG surgery are warranted whereas larger monotherapy studies do not appear to be well justified.

• The effects of opiates on absorption of oral P2Y12 inhibitors should be considered in the design of future post-operative studies.