Commentary on TiCAB study

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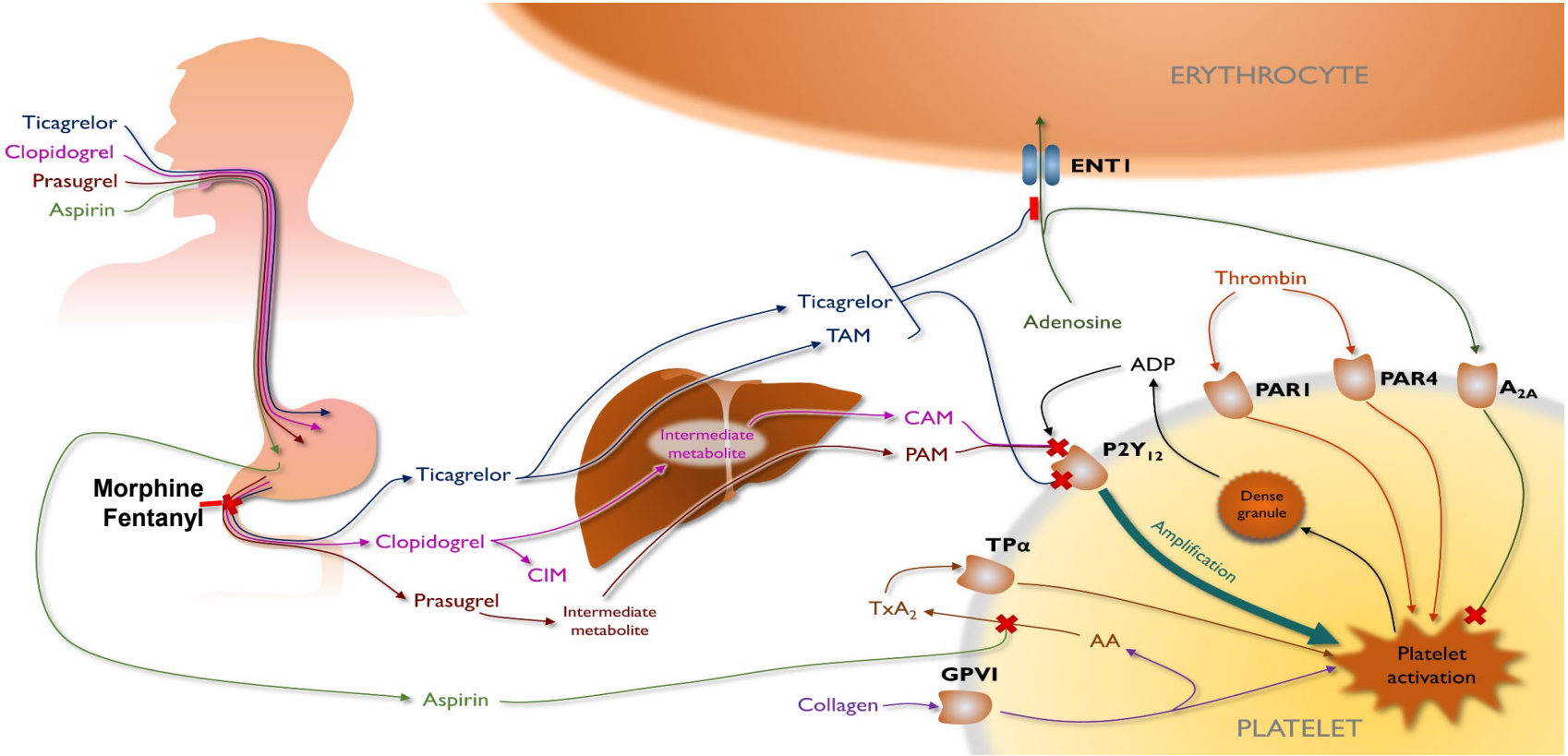
Key findings of the TiCAB study

- 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?

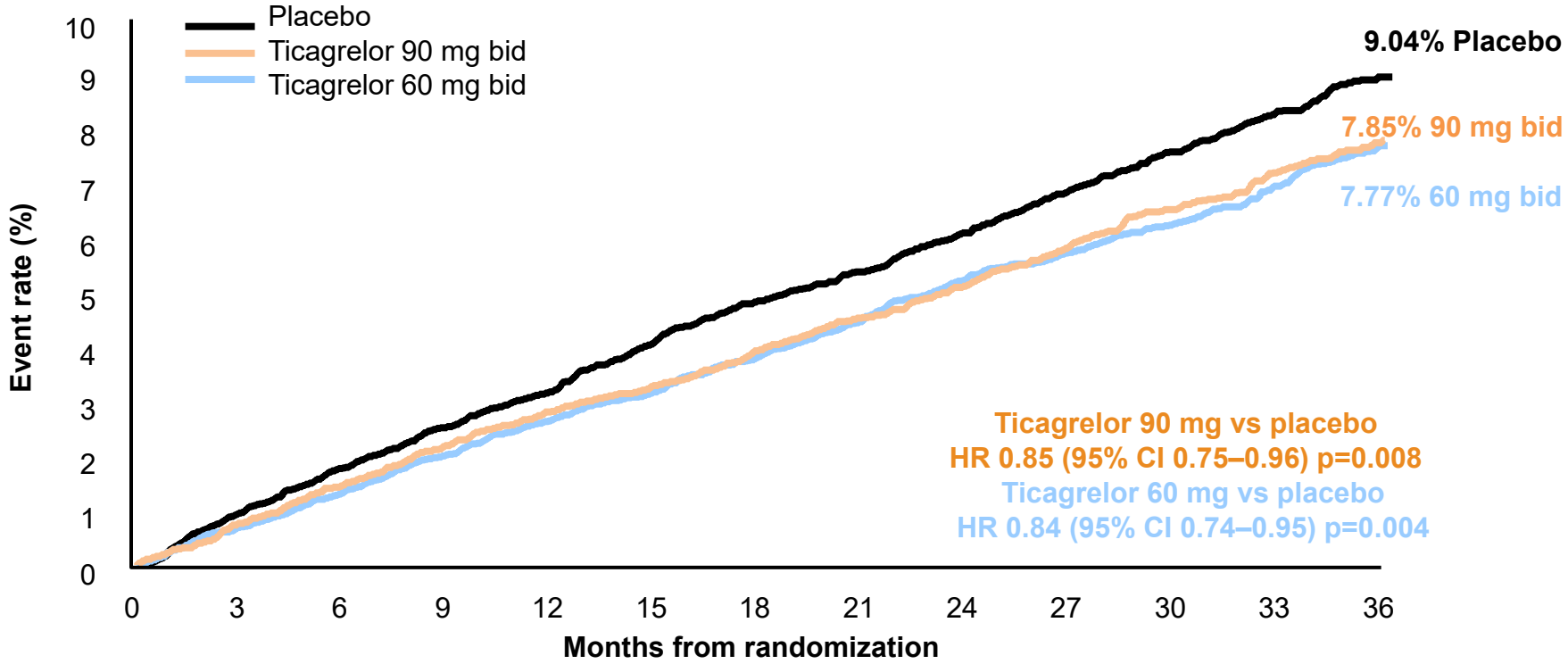
Pharmacology of aspirin and oral $P2Y_{12}$ inhibitors



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

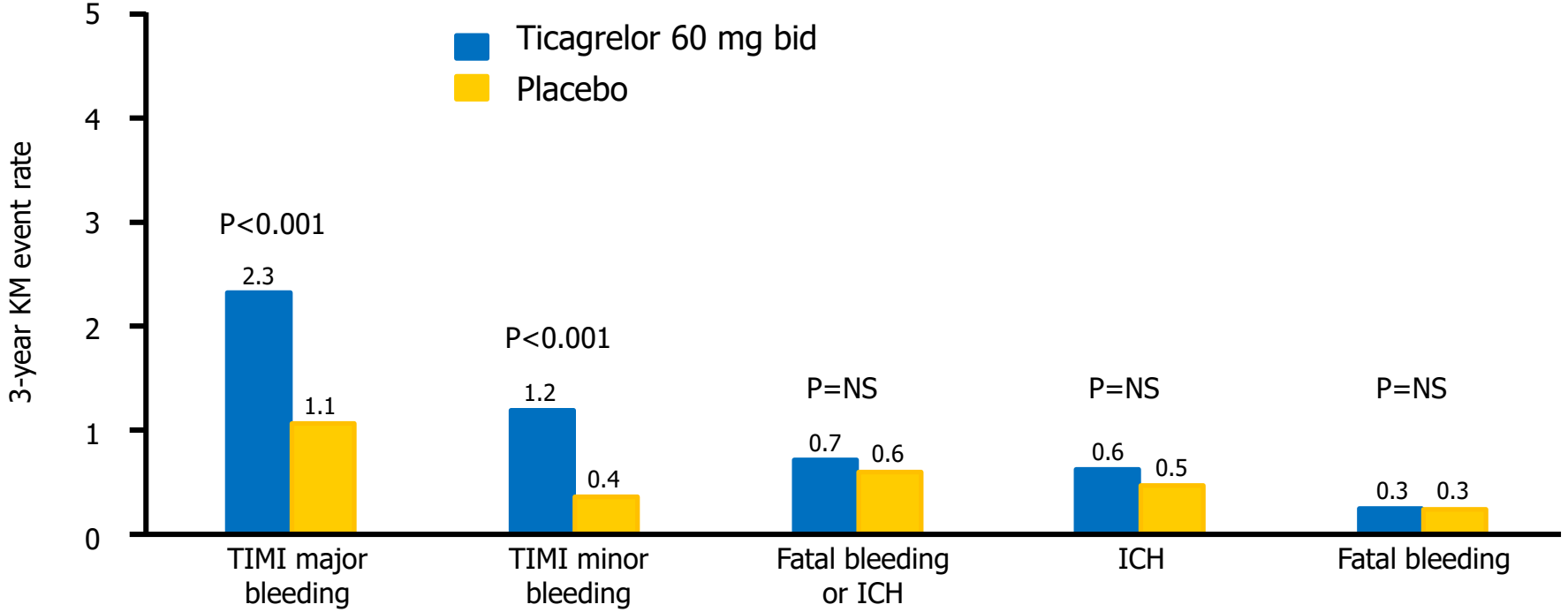


Bonaca MP et al. *N Engl J Med.* 2015;372:1791–1800

DAPT = dual antiplatelet therapy

PEGASUS-TIMI 54: Bleeding Endpoints

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



Bonaca MP *et al*. *N Engl J Med* 2015;372:1791–1800

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 $P2Y_{12}$ inhibitors should be considered in the design of future post-operative studies