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| Trial name | Methods / location | Participants | Purpose / Interventions | Outcomes / Results | Conclusions / Comments |
| **GLASSY Study (**GLOBAL LEADERS Adjudication Sub-Study**)**1*Ticagrelor Alone Versus Dual Antiplatelet Therapy From 1 Month After Drug-Eluting Coronary Stenting* | Open-label, randomized, superiority trial.International / multicenter.Designed after start of parent trial but before completion of 2-year follow-up. Study population was all consecutively included patients in the 20 highest recruiting sites, which was 47.5% of the overall original trial.2 | **Control:** n = 3791**Intervention:** n = 3794 | To evaluate a shortened course of DAPT followed by ticagrelor monotherapy.**Controls:** (one of two DAPT regimens)a) If stable CAD:Aspirin + clopidogrelb) If recent ACS: Aspirin + ticagrelor for 12 months followed by aspirin monotherapy for 12 months.**Intervention:** Low-dose aspirin (75 – 100 mg) + ticagrelor for one month followed by 23 months of ticagrelor monotherapy.  | **Co-primary composite efficacy endpoint** = all-cause death, MI, stroke, or urgent target vessel revascularization.**Co-primary safety endpoint** = composite of Bleeding Academic Research Consortium 3 or 5 bleeding events.**At 2 years**:a) No difference in co-primary composite efficacy endpoint; rate ratio 0.85; 95% CI 0.72 - 0.99. This fulfilled noninferiority (p < 0.001), but did not achieve superiority (p = 0.0465, alpha of 2.5%).b) For safety endpoint, rates were identical: 2.48% for both; rate ratio 1.00, 95% CI 0.75 – 1.33; p for superiority = 0.99. | One month of DAPT followed by ticagrelor monotherapy for 23 months was noninferior, but not superior, to conventional therapy in the prevention of ischemic events after PCI. Moreover, this strategy did not decrease major bleeding risks as compared withconventional treatment.In contrast to parent trial, was the use of an expanded set of primary endpoints.3 Generalizability limited by the exclusive use of ticagrelor only in patients with stable CAD and use of single DES type (biolimus A9–eluting biodegradable polymer stent). Also limited by open-label design.Follow-up post-hoc study using GLOBAL LEADERS cohort reported no difference in the risk of the primary endpoint between single-vessel and multivessel PCI patients but there was a significant relationship favoring the experimental arm in multivessel PCI subgroup.4 |
| **SMART-CHOICE**5*Effect of P2Y12 Inhibitor Monotherapy vs Dual Antiplatelet**Therapy on Cardiovascular Events in Patients**Undergoing Percutaneous Coronary Intervention* | Open-label,noninferiority, randomized trial design.South Korea – 33 centers. | **Control:** n = 1498**Intervention:** n = 1495 | To compare a shortened DAPT course followed by P2Y12 inhibitor monotherapy versus conventional 12 months of DAPT.**Control:**12 months of DAPT post-PCI.**Intervention:** 3 months of DAPT post-PCI followed by monotherapy of clopidogrel, prasugrel, or ticagrelor  | **Primary outcome** = composite of all-cause death, MI, or stroke at 12 months after index PCI procedure.a) For primary outcome, intervention noninferior to control; 2.9% vs. 2.5%; 1-sided 95% CI -∞% - 1.3%; p = 0.007.b) No intergroup differences in cumulative rates of the primary endpoint components at 12 months (all-cause death, MI, and stroke), the risk of stent thrombosis, or per-protocol analysis versus the intention-to-treat analyses.c) Rate of bleeding significantly lower in intervention group; HR 0.58, 2.0% vs. 3.4%, 95% CI 0.34 - 0.97; p = 0.4. | Findings suggest shortened DAPT followed by P2Y12 inhibitor monotherapy compared with prolonged DAPT resulted in noninferior rates of major adverse CV and cerebrovascular events.In contrast to ‘GLOBAL LEADERS’, varying P2Y12 inhibitors were used in a variety of clinical scenarios.Limitations include possibly underpowered for primary outcome, open-label design, and not all consecutive patients were screened for enrollment. |
| **STOPDAPT-2**6*Effect of 1-Month Dual Antiplatelet Therapy Followed by Clopidogrel vs 12-Month Dual Antiplatelet Therapy on Cardiovascular and Bleeding Events in Patients Receiving PCI.* | Multicenter, open-label, adjudicator-blinded randomized.Japan – 90 centers. | **Control:** n = 1522**Intervention:** n = 1523 | To compare a shortened DAPT course followed by clopidogrel monotherapy versus conventional 12 months of DAPT after DES implantation with newer generation stent (cobalt-chromium everolimus-eluting stent).**Control:** 12 months of DAPT (aspirin and clopidogrel) after PCI.**Intervention:** One month DAPT followed by clopidogrel monotherapy after PCI. | **Primary endpoint** = CV death, MI, stroke, stent thrombosis, major or minor bleeding at 12 months.**Major secondary bleeding endpoint** = major or minor bleeding.**At 1 year**:a) Intervention noninferior and superior as compared to control for primary endpoint. Hazard ratio 0.64, 95% CI 0.42 - 0.98; noninferiority (p < 0.001) and superiority (p = 0.04). b) Major secondary endpoint was superior in one-month DAPT group. Hazard ratio 0.26, 95% CI 0.11 - 0.64; p = 0.004 for superiority. | Findings suggest a shortened duration of DAPT may be beneficial and is noninferior to conventional 12 months durations. However, multiple study limitations (i.e. composite endpoints, underpowered for secondary CV endpoints, low actual event rates for primary endpoint, possible exclusion of highest risk patients, and use of specific-type of DES) necessitate additional research on topic. |
| **TWILIGHT**7*Ticagrelor with or without Aspirin in High-Risk Patients after PCI* | Randomized,placebo-controlled double-blind trialInternational – 187 centers. | Enrolled those high-risk for bleeding or ischemic events with one of the following: > 65 years, female, troponin+ ACS, PVD, DM, CKD, multivessel CAD, stent length > 30 mm, thrombotic target lesion, bifurcated lesion with 2 stents, obstructive LM or proximal LAD, calcified target.**Control:** n = 3554**Intervention:** n = 3546 | Starting after 3 months of DAPT post-PCI, purpose was to examine the effect of ticagrelor monotherapy versus DAPT (ticagrelor + aspirin).**Control:** Post-PCI: DAPT for 12 months.**Intervention:**Post-PCI: DAPT for 3 months followed by ticagrelor + placebo for 9 months. | **Primary endpoint** = Bleeding Academic Research Consortium type 2, 3, or 5 bleeding.**Secondary endpoint** = composite of mortality, nonfatal MI, nonfatal stroke.**At 1 year**:a) Intervention associated with lower rate of primary endpoint; 4.0% vs 7.1%; hazard ratio 0.56; 95% CI 0.45 - 0.68; p < 0.001.b) Secondary endpoint incidence was 3.9% for both groups; difference −0.06 % points; 95% CI −0.97 - 0.84; hazard ratio 0.99; 95% CI, 0.78 - 1.25; p < 0.001 for noninferiority. | Following three months of DAPT post-PCI, 9 months of ticagrelor monotherapy was associated with a lower rate of clinically relevant bleeding as compared to DAPT in high-risk patients. There was no evidence of higher risks of death, MI, or stroke with ticagrelor monotherapy.Strengths include use of varying DESs, double blinding, and inclusion of high-risk patients only.Limitations include under-powering for detecting infrequent clinical events (i.e. stent thrombosis) and lack of generalizability to low or medium risk patients. |

*Abbreviations*: ACS, acute coronary syndrome; CAD, coronary artery disease; CKD, chronic kidney disease; CV, cardiovascular; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; DM, diabetes mellitus; MI, myocardial infarction; LAD, left anterior descending; LM, left main; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease.

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