Long-Term Tolerability of Ticagrelor for Secondary Prevention

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

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Main Findings

• Discontinuation in first year:
  – 16% ticagrelor 90 mg
  – 13% ticagrelor 60 mg
  – 6% placebo

• Discontinuation years 2 and 3 low (2.3-3.3%/year)

• Dyspnea (mild-moderate) and bleeding (minimal and med attention) drivers of discontinuation.

• High (>1/3) non-event related discontinuation
Intention-to-treat vs. On-treatment

• Primary endpoint (CV death, MI, stroke) ITT
  – Ticagrelor 60: HR 0.84 (95% CI 0.74-0.95), P=0.004
  – Ticagrelor 90: HR 0.85 (95% CI 0.75-0.96), P=0.008

• Primary endpoint On Treatment
  – Ticagrelor 60: HR 0.79 (95% CI 0.68-0.91), P<0.001
  – Ticagrelor 90: HR 0.78 (95% CI 0.68-0.90), P<0.001

• Relative risk reduction: ITT vs OT
  – Ticagrelor 60: 16% vs. 21% (NNT 83 vs. 62)
  – Ticagrelor 90: 15% vs. 22% (NNT 83 vs. 56)
Implications and Clinical Significance

• Prolonged DAPT non-compliance is real (19%, 22.5% in 3 years).

• Discontinuation likely to be higher outside of clinical trial setting.

• “Personalized” DAPT makes sense, but we need a simple, practical DAPT score (i.e., CHA₂DS₂-VASc and HAS-BLED) that balances ischemic and bleeding risks

• Needs better understanding of human behavior.
Additional Questions

• What is the corresponding intention-to-treat vs. on-treatment analysis for bleeding?
• What are “other” non-biological, non-event related factors that led to discontinuation?
• How much impact non-serious bleeding and dyspnea had on quality of life?
• Could nuisance bleeding that leads to discontinuation be reduced by eliminating aspirin (i.e., ticagrelor monotherapy)?
• Do we know the optimal ticagrelor dose in this post-MI setting? Should we go lower than 60 mg? Would it improve dyspnea?