Ticagrelor and Major Adverse Limb Events: A Systematic Review and Meta-Analysis

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BACKGROUND

- Major adverse limb events including acute limb ischemia (ALI), major amputation of vascular etiology and urgent peripheral revascularization for ischemia are morbid events associated with significant disability, limb loss and death.
- Although thrombosis is a primary driver of these outcomes, prior trials of dual antplatelet therapy (DAPT) with aspirin and clopidogrel or with therapeutic warfarin have not significantly reduced this risk.1,2

METHODS

- A search for randomized, double-blind, clinical trials of ticagrelor added to aspirin versus aspirin alone that had adjudicated limb outcomes, more than a year of follow up and at least 25 MALE events was performed.
- Reported effects on MALE were meta-analyzed using a fixed effects model.

RESULTS – SYSTEMATIC REVIEW

- Two trials were identified meeting criteria for meta-analysis.
- PEGASUS-TIMI 54 (Figure 2) included 21,162 patients with prior MI randomized to ticagrelor 60 mg twice daily, ticagrelor 90 mg twice daily, placebo and reported rates at 3 years.3
- Major adverse limb events were adjudicated as acute limb ischemia or revascularization for ischemia with a total of 108 events.4
- With both doses pooled there was a ~35% reduction in major adverse limb events.4

- THEMIS (Figure 3) randomized 19,220 with diabetes mellitus and coronary disease to ticagrelor twice daily (initially 90 mg twice daily and later 60 mg twice daily) or placebo and reported rates at 3 years.5,6
- Major adverse limb events were adjudicated as acute limb ischemia or major amputation of a vascular cause with a total of 42 events.5,6
- Overall there was a ~55% reduction in major adverse limb events.5,6

RESULTS – META-ANALYSIS

- Across both trials there were a total of 150 first major adverse limb outcomes in a total of 40,392 patients with event rates of 0.7% and 0.3% in the placebo arms respectively.
- When combining the 60 mg and 90 mg doses, ticagrelor reduced the risk of major adverse limb events by 41% (HR 0.59, 95% CI 0.42 – 0.83, p=0.002), Figure 4

CONCLUSIONS

- Ticagrelor added to aspirin reduces major adverse limb events in stable patients with atherosclerosis by ~40%.
- Although event rates in broad atherosclerosis populations and in the stable setting are relatively low, rates and absolute benefits would be expected to be greater in patients with lower extremity peripheral artery disease.

DISCLOSURES


- A search for randomized, double-blind, clinical trials of ticagrelor added to aspirin versus aspirin alone that had adjudicated limb outcomes, more than a year of follow up and at least 25 MALE events was performed. Reported effects on MALE were meta-analyzed using a fixed effects model.

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