

EUCLID Discussant

Carl J Pepine, MD
University of Florida
Gainesville, FL

EUCLID Discussion



SCIENTIFIC
SESSIONS

What was known before EUCLID

PAD- ~10% of Americans >60 yo and associated with high risk for adverse outcomes (large athero RF burden, more diffuse athero, enhanced platelet activation, inflammation, etc.).

Secondary prevention limited (RF modification, exercise, ASA, clopidogrel).

Ticagrelor (oral, direct acting, reversibly binding P2Y₁₂ receptor antagonist) prevents atherothrombotic events in ACS (>clopidogrel+ASA) but not previously evaluated in PAD.

What EUCLID Adds

In PAD patients, ticagrelor, essentially same as clopidogrel in preventing adverse events.

Additionally, there was a signal for reduction in stroke.

EUCLID Discussion

What could explain these findings?

Essentially same outcomes with ticagrelor (T) v clopidogrel (C) in PAD?

PLATO (ACS+RFs) T v C, both+ASA, T reduced PO (CV death, MI, or stroke (HR 0.84 [0.77, 0.92] p 0.0003).

CYP2C19 polymorphism testing- 27% had LoF of at least one CYP2C19 allele.

These pts, treated with C had a HR=1.37 (CI 1.04, 1.82; P = 0.028) for PO.

EUCLID excluded “*Poor metabolizer status for CYP2C19, possessing a genotype consisting of 2 loss-of-function alleles*”.

Additionally, a signal for reduction in stroke.

DISPERSE-2 significantly more hypotension with T 90 and 180mg/d v C in NSTEMI-ACS.

PEGASUS significantly reduced stroke risk (HR 0.75, 95% CI 0.57, 0.98) with T+ASA) vs ASA alone in prior MI+RFs.

Recall-PAD amplifies central Ao press, so small reductions in brachial SBP translate to large reductions in central Ao press. Actual BPs- at baseline and on-treatment were not reported.

EUCLID Discussion



**SCIENTIFIC
SESSIONS**

Summary

- Clearly, many knowledge gaps remain relative to PAD
- We need more studies like EUCLID to determine:
 - Optimal antiplatelet therapy (drug/drugs, dose) to prevent CV and limb-related events.
 - Additional medical therapies (biologics) for claudication.
 - Role of dietary intervention, in addition to statins and other drugs, to prevent and modify PAD.