P2Y$_{12}$ Inhibitor Switching in Response to Routine Notification of CYP2C19 Clopidogrel Metabolizer Status Following Acute Coronary Syndromes

Discussant

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What Are The Facts About Genotyping?

- **Rationale for switching to potent P2Y$_{12}$ inhibitors in LoF carrier:**
  
  LoF carriage in clopidogrel-treated PCI patients associated with:
  

- **Major rationale for genotyping in GEMINI ACS$^2$:**
  
  Potential lack of low dose rivaroxaban efficacy as “sole antithrombotic” in high risk clopidogrel non-responders$^3$.

- ~2% White; ~4% Black, ~14% Asians are poor metabolizers - HIGHLY RESISTANT TO CLOPIDOGREL$^1$.

- Blanket therapy with potent P2Y$_{12}$ inhibitors – more bleeding$^1$.

- No large scale prospective data yet to support genotype-based personalization.

GEMINI-ACS-1 Genetic Study
Summary and Analysis

GEMINI ACS 1(n=3,037): safety of low dose riva vs. asa on top of clp or tig
- 99% genotyped - results in ~1 wk.
- Genotype consistent with ~ 90% Caucasian population.
- Only 6.5% switched P2Y$_{12}$ inhibitors - timing varied with reason.
- <1% switched for CYP2C19 metabolizer status

Tig $\rightarrow$ Clp (8.5%)
: ~ continued throughout
Non-bleeding/other (8.3%), Recurrent ischemia (0.06%)
CYP2C19 metabolizer status (0.06%).

Clp$\rightarrow$Tig (4.0%)
: ~ plateaued at 3 months
Non-bleeding/other (1.50%), Recurrent ischemia (0.75%)
CYP2C19 metabolizer status (1.73%).

Only 50% of clp-treated pts were planned to switch for RM
- of which 30% of RM didn’t switch.

Only 5.6% of ticagrelor-treated pts were planned to switch for EM/UM
- of which 91% of EM/UM didn’t switch.
One of the largest genetic analyses in an ACS trial: 
~ complete collection of data.

First reported regulatory guidance-required genotype data in large RCT deleting ASA with clopidogrel active-control arms.

Provides insight into cardiologists’ perception of genotyping utility.

Most switching unrelated to genotype.

No evaluation of clinical outcomes in relation to genotype/specific therapy.

Efficacy of treating high risk clopidogrel non-responders with low dose rivaroxaban in place of aspirin remains unresolved.

Bedside genotyping and positive prospective trial data re: personalization would facilitate interest in switching.