**Long-Term Tolerability of Ticagrelor in the PEGASUS-TIMI 54 Trial**

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**Objective:** Ticagrelor initiated in patients with prior MI reduced the incidence of CV death, MI, or stroke by 15-16% in PEGASUS-TIMI 54. Premature discontinuation was higher with ticagrelor than placebo. We investigated the rates and reasons for drug discontinuation and the long-term efficacy of ticagrelor in patients who stayed on therapy.

**Methods:** Rates and causes of treatment discontinuation were evaluated overall and by timing relative to randomization. Efficacy analyses were performed examining events occurring while pts were on study drug and up to 7 days after the last dose.

**Results:** Over the duration of the trial (median 33 mos), 32%, 29%, and 21% of patients stopped study drug in the ticagrelor 90 mg, 60 mg and placebo arms, respectively (P<0.001). 10-11% of patients in each arm stopped study drug because of patient decision or administrative reason. Conversely, rates of study drug discontinuation due to an adverse event (AE) were 8.9% in the placebo arm, but 19% and 16.4% in the ticagrelor 90 mg and 60 mg arms (P<0.01). The most frequent AEs leading to discontinuation were bleeding (6.5%, 5.1%, 1.2%, p<0.001) and dyspnea (6.2%, 4.3%, 0.7%, p<0.001). In the ticagrelor arms, only 14% of bleeds were major and only 12% of cases of dyspnea were severe. The rates of AEs leading to drug discontinuation and the differences between arms were greater in the first year and then greatly attenuated thereafter (Fig Left). Overall, in terms of events while on study drug, ticagrelor substantially reduced the risk of CV death, MI or stroke (HR 0.79, 95% CI 0.70-0.88, P<0.0001) as well as each of the individual components and was associated with lower all-cause mortality (Fig Right).

**Conclusion:** When initiated in stable patients with prior MI, discontinuation of ticagrelor was driven primarily by non-severe AEs occurring early after randomization. In patients who remained on study drug, there was a substantial benefit to ticagrelor, suggesting counseling on adherence could improve outcomes.
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