**Major Adverse Cardiac Events (MACE) during aprocitentan treatment: comparison with systematic literature review data**

**Background and objective:** MACE is a key consequence of uncontrolled hypertension and one of the main reasons to reduce high blood pressure.PRECISION evaluated the effect of aprocitentan in patients with resistant hypertension (RHT), using an innovative design to efficiently investigate both short and long-term effects. The study design included 3 parts, an initial double-blind placebo-controlled part, followed by a prolonged single-blind administration of aprocitentan to all patients, and finally a double-blind placebo-controlled part investigating the effect of withdrawing aprocitentan versus continuing therapy.1 The study demonstrated efficacy and safety of aprocitentan in lowering blood pressure2 but poses challenges in evaluating its impact on long term cardiovascular outcomes. The objective of this analysis was to evaluate the incidence of MACE in PRECISION vs external controls.

**Design and method:**  The exposure-corrected incidence of MACE in PRECISION was assessed and a systematic literature review was performed to identify studies similar to the PRECISION study population with respect to baseline characteristics, study duration, sample size and cardiovascular disease exclusion criteria, resulting in the identification of 6 studies appropriate for comparison to PRECISION.

**Results:** In PRECISION, 16/730 (2.2%) randomized participants experienced a MACE. The results for MACE in PRECISION and comparable studies are reported in table 1.

A screenshot of a report

Description automatically generated

The incidence of MI, and stroke reported in PRECISION is consistent with those reported from large outcome studies (table 1) and from a contemporary real-world evidence study of RHT. 3

**Conclusion:** This analysis suggests that the prevalence of MACE events in patients treated with aprocitentan in PRECISION is compatible with beneficial effects of decreasing blood pressure in patients with RHT.

References

1. Danaietash P, Verweij P, Wang JG, et al. Identifying and treating resistant hypertension in PRECISION: A randomized long-term clinical trial with aprocitentan. J Clin Hypertens. 2022;24(7):804-813

2. Schlaich MP, Bellet M, Weber MA, et al. Dual endothelin antagonist aprocitentan for resistant hypertension (PRECISION): a multicentre, blinded, randomised, parallel-group, phase 3 trial. Lancet. 2022;400(10367):1927-1937

3. Bakris G, Chen C, Campbell AK, et al. Association of uncontrolled blood pressure in apparent treatment-resistant hypertension with increased risk of major adverse cardiovascular events plus. J Clin Hypertens. 2023;25(8):737-74