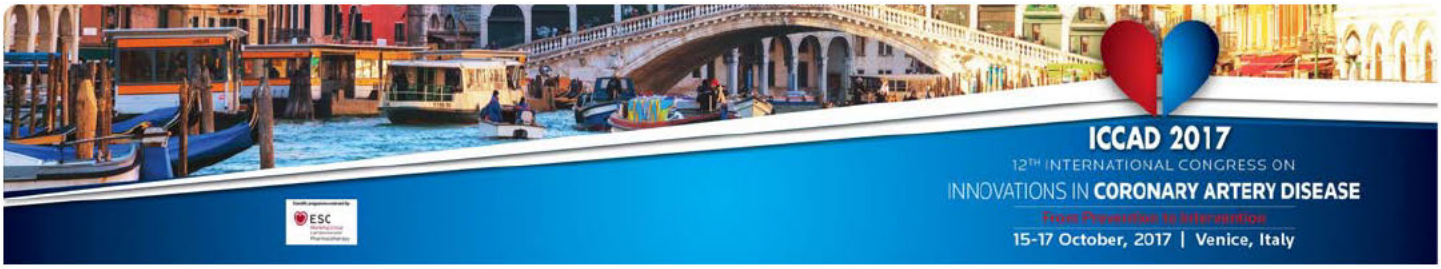


# Safety of Ivabradine Modified Release Formulation Compared to Ivabradine Immediate Release Formulation in Patients with Stable Coronary Artery Disease

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**Background:** Ivabradine immediate release (IR, twice-a-day) has been approved for symptomatic treatment of chronic stable angina pectoris in patients with elevated heart rate (HR). In order to ensure better patient compliance and to minimize fluctuations of ivabradine concentration in plasma, a modified release (MR, once-a-day) formulation has been evaluated.

**Purpose:** This phase III, randomised, double-blind parallel group study, compared safety profiles of both formulations in coronary artery disease (CAD).

**Methods:** Patients had sinus rhythm and HR ≥ 60 bpm. Overall, the ivabradine MR doses of 7.5, 15, 22.5 and 30 mg once-a-day corresponded to the IR doses of 2.5, 5, 7.5 and 10 mg twice-a-day respectively. Ivabradine MR and IR starting doses were 15 mg once-a-day and 5 mg twice-a-day. Doses were titrated according to tolerability and HR. The primary endpoint was the emergent adverse events (EAEs) over the first 6-month follow-up period.

**Results:** 842 patients were randomised (421 in each group). Baseline age was 62.9 ± 9.5 years, CAD was diagnosed for 74.3 ± 70.7 months and documented by previous myocardial infarction (61.3%), coronary revascularisation (81.2%), angiographically proven significant coronary atherosclerosis (70.6%) and non-invasive evidence of myocardial ischemia (12.8%).

At least one EAE was reported in 57.3% of the patients in the MR group versus 62.9% in the IR group, serious EAE in 12.9% in the MR group versus 16.4% in the IR group and EAE leading to withdrawal in 10.0% in the MR group versus 9.0% in the IR group.

**Conclusion:** Ivabradine MR and IR were well tolerated.