**Supplemental Appendix**

**Orally Inhaled Flecainide for Conversion of Atrial Fibrillation to Sinus Rhythm: INSTANT Phase 2 Trial**

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**Supplemental Table 1: Cardiovascular Adverse Events of Special Interest**

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| Patient Number; Age/Sex | Event | Severity SAE (Yes/No) | Duration/Outcome |
| Patient 1; 70/F | Hypotension | Mild  No | Two reported transient episodes of hypotension occurred; one that lasted 1 min and another that lasted 27 min. During the first hypotensive episode, the patient reported dizziness and sweating; no symptoms were reported during the second episode. The lowest BP value measured was 61/48 mmHg. Upon the start of the second hypotensive episode, the patient was given a bolus of 250 mL of IV saline. |
| Patient 2; 60/M | Hypotension | Moderate  No | Approximately 10 min after the end of the second inhalation, the patient became hypotensive (BP 80/57 mmHg). This patient was given 1 L of IV saline, starting 4 minutes after the BP value of 80/57 mmHg was noted. The lowest BP recorded for this patient was 78/54 mmHg at the time of conversion of AF to SR when the HR was 56 bpm. The hypotensive episode lasted approximately 80 minutes. Patient was asymptomatic. |
| Patient 3; 76/F | Bradycardia | Severe  Yes | Based on Holter data, approximately 30 min after the end of the second inhalation there were 11 episodes of RR intervals > 2 sec, with the longest being 3.36 sec. The decreases in HR (long RR intervals) each lasted 10 – 30 sec. The subject reported nausea, felt ‘moist’, mild tiredness, and was described as ’not responsive.’ No treatment was given. The dizziness and tiredness were ongoing at the end of the study. |
| Hypotension | Mild  No | Due to the bradycardic event, the patient also become hypotensive. BP values ranged from 69/54 mmHg to 80/50 mmHg. The reported symptoms were dizziness and headache. No treatment was given. These events started at 26 minutes after completion of inhalation and lasted for approximately 34 minutes. |
| Patient 4; 53/M | Bradycardia | Mild  No | Approximately 31 min after the end of the first inhalation of flecainide and approximately 33 min after conversion of AF to SR, the HR dropped to 49 bpm and BP was 130/89 mmHg. The lowest HR observed on the Holter was 43 bpm, which lasted approximately 15 minutes. Patient was asymptomatic and no treatment was given. |
| Patient 5; 42/M | Atrial flutter (with 1:1 AV conduction) | Severe  Yes | Approximately 1 min after the start of the first inhalation, the patient developed atrial flutter with variable AV conduction (1:1, 2:1), lasting a total of 12 minutes, prior to conversion to SR. The fastest ventricular rate (VR > 200) occurred during 1:1 AV conduction and lasted 6 minutes. Approximately 40 min after resolution of flutter, the patient was given verapamil to prevent recurrences of fast AV conduction. The oral verapamil treatment was ongoing at the end of the study. |