

## PF0713 Produced Rapid Induction of General Anesthesia without Injection Pain in a Phase 1 Study

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**Introduction:** PF0713 is an investigational GABA<sub>A</sub> agonist[1] in clinical development for the IV induction and maintenance of general anesthesia and sedation. This Phase 1 study evaluated this agent for the IV induction of anesthesia including safety, pharmacodynamics, pharmacokinetics, and tolerability, specifically injection pain.

**Methods:** PF0713 (1% in a lipid emulsion) was administered to 24 ASA 1 males at doses of 0.0156 mg/kg (N=3), 0.0625 mg/kg (N=3), 0.25 mg/kg (N=3), 1 mg/kg (N=6) and 2 mg/kg (N=9) at 0.4 mL/sec via a 20 gauge dorsal hand IV. Injection pain was assessed by both query and observation at 15 sec intervals. Bispectral index (BIS), Richmond-Agitation Sedation Scale (RASS)[2], HR, BP (radial arterial line), RR, ventilation mode, and any adverse events were recorded. Arterial blood samples were collected, and plasma concentrations of PF0713 were measured.

**Results:** Doses of 0.25 mg/kg or less did not induce general anesthesia, and there were no serious adverse events. Induction of anesthesia was produced by doses of 1 mg/kg and 2 mg/kg, and results from these 15 subjects are described herein. Subjects weighed 82±12 kg (mean±SD) with BMI 26±3 kg/m<sup>2</sup> and age 25±4 years. General anesthesia was induced in all 15 subjects with RASS decreasing to -5 (no response to voice or physical stimulus) and BIS decreasing below 60 in all subjects.[Figure1][Figure2] There was no agitation, and RASS did not exceed 0 (alert and calm) in any subject. None of the 15 subjects reported injection pain in response to the queries. Similarly, no injection pain was noted by the observer in any of these subjects. Ventilation was assisted or controlled by bag and mask for 4.6±4.5 min. Blood pressure and heart rate were adequately maintained. There were no serious adverse events. Plasma levels decreased rapidly after administration and clearance was high.

**Conclusions:** At 1 mg/kg and 2 mg/kg, PF0713 produced rapid induction of general anesthesia without injection pain or agitation. The depth and duration of anesthetic effect were dose-related. Blood pressure and heart rate were adequately maintained, and there were no serious adverse events. Further development of PF0713 is warranted.

### References:

1. Siegel LC, et al, Anesthesiology 2008;109:A642
2. Sessler CN, et al, Am J Respir Crit Care Med 2002;166:1338.

Figure 1:

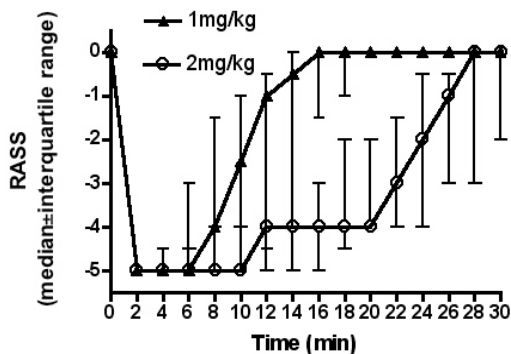


Figure 2:

