Phase 1c trial comparing the anesthetic properties of Phaxan™ and propofol

**Introduction:** Alphaxalone is a neuroactive steroid anesthetic. It is an analogue of natural hormones progesterone and allopregnanolone but it has no hormonal activity.

This water-insoluble drug is given as a Cremophor-based emulsion. Cremophor may cause hypersensitivity reactions. Interactions with other drugs may result in serious adverse effects. Therefore phax can be expected to be an alternative to propofol for anesthesia.

**Methods:** A double-blind, randomized, placebo-controlled, Phase 1c trial was conducted. This trial aimed to determine the anesthetic properties of phax and propofol using a randomized crossover design. The study population consisted of 12 healthy volunteers ASA grade 1 given written informed consent. Parameters assessed included blood pressure, heart rate, blood gases, and respiratory effects. Recovery of sedation was assessed using the Richmond Agitation and Sedation Scale (RASS) and the Oxford Dichotomous Scale (ODS).

**Results:** Eleven subjects given propofol 2.43 (3.00) mg/kg and 11 subjects given phax 0.5 (0.55) mg/kg reached a RASS value of 0 at 30 ± 1 minute. Both propofol and phax-treated subjects showed similar significant differences between treatments in terms of time to return of consciousness and recovery (Figure 1). A cohort of those subjects received doses between the 75/25 IQ range of each agent (n = 8 per group) in a single bolus dose 30 seconds after the first dose. They caused the same profile for BIS depression and recovery (Figure 2). The results of other assessments were: recovery of score for all tests to the next indicates "Cognitive Reserve" in test subjects. A literature search revealed that DSST performance increases stepwise with repeat testing paradigms like that used in the phax study, and this step increase from one time to the next indicated "Cognitive Reserve" in test subjects. From repeat DSST measurements, 31 and 32 minutes before and after propofol and phax, respectively, there was a significant stepwise increase from one test time to the next (Figure 3). This step increase from one test time to the next indicated "Cognitive Reserve" in test subjects (Table 1).

**Conclusions:** Alphaxalone 10mg/ml in an aqueous solution with 13% 70% Cremophor ether beta cyclodextrin (phax) causes fast onset and short duration of anesthesia equivalent to propofol but with less cardiovascular and respiratory depression and no pain on injection. The induction dose and duration of anesthesia with phax is the same as that reported previously for alphaxalone as published. Therefore phax can be an alternative to propofol, sedation, and neuroprotection.

**References:**
3. Alaphaxalone is an analogue of natural neuroactive steroid anesthetic that has lost its hormonal activity. e.g., the alphaxalone, anesthetic properties, and neuroprotection.

**Figure 1.** The dose of drugs given to subjects consists of a single bolus dose, for propofol subjects (A) and phaxan-treated subjects (B). All subjects received 45 (±5) mg/kg except subjects 13 (phax) and 21 (propofol) shown by the gray circle to demonstrate the DSST result.

**Figure 2.** The graphs show the effects of DSST performed in the five subjects who received phaxan™ (10mg/ml in 13% 70% Cremophor EL solution; 7.75 mg/kg) and propofol (2.43 mg/kg) on the DSST. The DSST performance was measured after baseline (0), 15 (±5) minutes after injection of phaxan™ and propofol. The DSST was repeated 15 minutes after the first dose. The DSST was repeated 15 minutes after the first dose. The DSST was repeated 15 minutes after the first dose.

**Figure 3.** The graphs show the effects of DSST performed in the five subjects who received phaxan™ (10mg/ml in 13% 70% Cremophor EL solution; 7.75 mg/kg) and propofol (2.43 mg/kg) on the DSST. The DSST performance was measured after baseline (0), 15 (±5) minutes after injection of phaxan™ and propofol. The DSST was repeated 15 minutes after the first dose. The DSST was repeated 15 minutes after the first dose. The DSST was repeated 15 minutes after the first dose.

**Table 1.** Table 1 shows the effects of DSST performed in the five subjects who received phaxan™ (10mg/ml in 13% 70% Cremophor EL solution; 7.75 mg/kg) and propofol (2.43 mg/kg) on the DSST. The DSST performance was measured after baseline (0), 15 (±5) minutes after injection of phaxan™ and propofol. The DSST was repeated 15 minutes after the first dose.

**Table 2.** Table 2 shows the effects of DSST performed in the five subjects who received phaxan™ (10mg/ml in 13% 70% Cremophor EL solution; 7.75 mg/kg) and propofol (2.43 mg/kg) on the DSST. The DSST performance was measured after baseline (0), 15 (±5) minutes after injection of phaxan™ and propofol. The DSST was repeated 15 minutes after the first dose.

**Table 3.** Table 3 shows the effects of DSST performed in the five subjects who received phaxan™ (10mg/ml in 13% 70% Cremophor EL solution; 7.75 mg/kg) and propofol (2.43 mg/kg) on the DSST. The DSST performance was measured after baseline (0), 15 (±5) minutes after injection of phaxan™ and propofol. The DSST was repeated 15 minutes after the first dose.