**ABSTRACT**

Objective: Liposomal drug-containing formulations are designed to provide slow release of drug over an extended period of time, thus extending duration while minimizing plasma peaks. In this study, we analyzed the pharmacokinetic properties of an investigational extended-release multivesicular liposomal formulation of bupivacaine (DepoFoam bupivacaine, DB, prepared proprietary name, EXPRESS™) in a single injection.

Methods: Plasma data in 46 individuals (age 18–83, 63% males) from phases I, II, and 3 studies were analyzed for DB, bupivacaine HCl, and other pharmacokinetic parameters for conventional or extended-release bupivacaine. Routes of administration included wound infiltration, subcutaneous, epidural, and nerve block. Surgical models included herniorrhaphy, herniorrhaphy, bunionectomy, and total knee arthroplasty. Doses ranged from 75 to 100 mg.

Results: DB formulation had an early peak concentration from 0.25–2 hours likely due to the small amount of extravasiphalgic bupivacaine present in the formulations. This was followed by a slow and prolonged release of bupivacaine from DB, resulting in a peak that occurred at a mean time from 15–22 hours after injection. Major wound infiltration, 15%, up to 34 hours for DB formulations. Higher mean Cmax obtained after local administration of 600 mg bupivacaine, 2059 ng/mL (2.4- to 4-fold below DB formulations' maximum toxicity thresholds).

Conclusions: DB formulation exhibited pharmacokinetic properties consistent with a sustained-release formulation after a single injection. Plasma concentration remained well below bupivacaine's reported toxic levels, even with 600 mg DepoFoam bupivacaine dosing up to 930 mg.

**INTRODUCTION**

Local anesthetic-liposomes are commonly used as part of a multimodal therapy for pain management.

Bupivacaine, which has been shown to reduce postoperative pain when used as an infiltration, is the leading active local anesthetic-liposome, but is limited to a duration of 7 hours or less.

A medical need exists for a local anesthetic-liposome that can extend the duration of pain relief following surgery.

DepoFoam® is a proven product delivery technology that encapsulates drugs without altering their molecular structure and then releasing their contents over a desired time period (Figure 1). It is used in two commercially available products in the US and EU.

DepoFoam® bupivacaine is a multivesicular formulation of bupivacaine over several days, providing up to 72 hours of pain relief.

**POURPOSE OF ANALYSIS**

To examine the PK parameters, including Tmax, t1/2, and Cmax, of traditional bupivacaine compared with DB in order to determine whether DB exhibits similar PK parameters consistent with sustained-release formulations, including this broader distribution.

**METHODS**

**CONCLUSIONS**

**REFERENCES**