Protocol Title: Efficacy of the liposomal bupivacaine for postoperative pain control in urologic procedures

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PROTOCOL OUTLINE AND GUIDELINES

Investigators must submit well-organized, detailed information about the study, demonstrating sound research design that minimizes risks to the subject. PI should assure that the content outlined below is addressed and may exercise some discretion as to how the information is organized. The quality and content of the protocol should demonstrate that scientific and merit review of the study has occurred at the departmental level prior to submission to the IRB.

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1. PROTOCOL INFORMATION

Title: Efficacy of the liposomal bupivacaine for postoperative pain control in urologic procedures.
Phase of Study: Prospective Study. Phase IV

2. PRINCIPAL INVESTIGATOR'S INFORMATION

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3. STUDY PERSONNEL

Duane Baldwin, Andrea Staack, Mohamed Keheila, Jim Shen, Salim Cheriyan, Patrick Yang, Nazih Khater (see application for contact info)

4. STUDY INFORMATION

Location(s) of Research Activity: Loma Linda University Medical Center
Expected Start/Stop Dates of Research: 5-30-2016/5-30-2018
Special Time Sensitivities: None
Type of Research: Prospective randomized controlled study using patient information from medical records.

5. INCLUSION / EXCLUSION CRITERIA

Inclusion criteria:

- Males or females 18-years-old or older.
- Undergoing urologic surgery.

Exclusion Criteria:

- Pregnant and/or nursing mothers.
- Allergy to bupivacaine.
- History of drug/alcohol abuse
- Severe cardiovascular, hepatic, renal disease or neurological impairment.

6. SUBJECT RECRUITMENT & SCREENING

Fifty subjects will be recruited for the study with an expected attrition rate of 10%. Sample size has been minimized, but is necessary for statistical power and

conclusions. Subjects will be male and female 18 years or older, of all ethnicities, denominations or other social/economical variations. All participants will speak English fluently in order for consent to be performed properly. Baseline pain score will be calculated through a questionnaire in at the urology clinic

Subjects of prospective study will be randomly divided using electronic program into two groups:

- The first group will receive intraoperative local Liposomal Bupivacaine injection at the port placement site.
- The control group will receive will local Marcaine (bupivacaine HCl) injection

Primary Outcome Measures:

- Total opioid consumption measured in intravenous morphine equivalents dose during the postoperative hospital Stay
- Postoperative pain assessment using visual Analog Pain Scores & Brief Pain Inventory form.
- Length of Hospital Stay
- Time to First Opioid Use.
- Postopreative Constipation , paralytic ileus

Time Frame: All data was recorded during the patient's hospital stay. All data will be collected from the electronic medical record, typically within 30 days of discharge from hospital.

7. INFORMED CONSENT PROCESS

Informed consent will be accomplished and signed at the Urology offices in the LLUMC or at the Urology FMO clinic. Consent will be obtained by the research coordinator or other trained investigators. Subjects will be randomly assigned as they are enrolled using a code system.

8. STUDY DESIGN

Background or rationale for this study:

Liposomal bupivacaine was developed to extend the duration of efficacy of bupivacaine from the typical 6 - 8 hours up to 72 hours. The prolonged duration of liposomal bupivacaine was initially demonstrated in mice in 1994. Two randomized controlled trials using liposomal bupivacaine for bunionectomy and hemorrhoidectomy resulted in FDA approval for its use in humans. More recently, liposomal bupivacaine has also been found to improve pain control for patients undergoing total knee arthroplasty. Infiltration of a local anesthetic into laparoscopic port sites is a common practice that has been shown in some studies to improve postoperative pain. Currently, no standard of care exists for postoperative pain and management is based on surgeon and anesthesiologist preferences. Liposomal bupivacaine has been one form of administered local, long-acting analgesia that

surgical centers have turned to. In addition, the analgesia has fewer adverse effects than opioids, with comparable adverse effects to those seen in bupivacaine alone.

Objectives: A prospective, randomized controlled study to determine the efficacy of liposomal bupivacaine given by local injection at all the wound sites in patients undergoing urologic surgeries.

Procedures involved (Research Interventions):

- The first group will receive intraoperative local Liposomal Bupivacaine injection at the surgical site.
- The control group will receive and will receive local Marcaine (bupivacaine HCl) injection.

9. DATA COLLECTION

We will be using electronic medical records to retrieve data from subjects who will undergo urologic surgery and save it in s secured excel file.

10. LABELING & STORAGE OF DATA & SPECIMENS

Code linking to subject identifiers will be stored securely on the LLU/LLUMC secured server. If research data is to be stored in hard copy format it will be in a locked office. Research data will also be primarily stored electronically on the LLU/LLUMC secured server. Electronic information will be kept on a secure server (department shared drive) and only shared through LLUMC secured email

11. DATA ANALYSIS

We will compare the outcomes by comparing similar surgeries and in patients with similar epidemiology characteristics between who will receive liposomal bupivacaine injection to those who will receive (bupivacaine HCl) injection. It with focus on the pain related outcomes using SPSS.

12. RISK AND INJURY

The safety of EXPAREL was evaluated in 10 randomized, double-blind, local administration into the surgical site clinical studies involving 823 patients undergoing various surgical procedures. Patients were administered a dose ranging from 66 to 532 mg of EXPAREL. In these studies, the most common adverse reactions (incidence greater than or equal to 10%) following EXPAREL administration were nausea, constipation, and vomiting. The common adverse reactions (incidence greater than or equal to 2% to less than 10%) following EXPAREL administration were pyrexia, dizziness, edema peripheral, anemia, hypotension, pruritus, tachycardia, headache, insomnia, anemia postoperative, muscle spasms, hemorrhagic anemia, back pain, somnolence, and procedural pain. The less common/rare adverse reactions (incidence less than 2%) following EXPAREL administration were chills, erythema, bradycardia, anxiety, urinary retention, pain, edema, tremor, dizziness postural, paresthesia, syncope, incision site edema, procedural hypertension, procedural hypotension, procedural nausea, muscular weakness, neck pain, pruritus generalized, rash pruritic, hyperhidrosis, cold sweat, urticaria, bradycardia, palpitations, sinus bradycardia, supraventricular extrasystoles, ventricular extrasystoles, ventricular tachycardia, hypertension, pallor, anxiety, confusional state, depression, agitation, restlessness, hypoxia, laryngospasm, apnea, respiratory depression, respiratory failure, body temperature increased, blood pressure increased, blood pressure decreased, oxygen saturation decreased, urinary incontinence, vision blurred, tinnitus, drug

hypersensitivity, and hypersensitivity. Subject privacy will be protected as subject identifiers will be removed after data collection and before data analysis.

13. BENEFIT(S)

Patient may benefit if you are not in the control group and find less postoperative pain and/or shorter hospital stay. In addition, the information learned from this study will determine if the drug has favorable outcomes on urologic surgeries. Future benefits may be present in improving the pain control after urologic surgeries and improve the overall patients' satisfaction.

14. COMPENSATION

Subjects will receive no compensation.

15. CONFIDENTIALITY

Medical records will only be used for data collection and will be removed after data analysis.

16. LITERATURE REVIEW

1-Comparative Study of Liposomal Bupivacaine Versus Paravertebral Block for Pain Control Following Mastectomy with Immediate Tissue Expander Reconstruction.

Abdelsattar JM[1], Boughey JC, Fahy AS, Jakub JW, Farley DR, Hieken TJ, Degnim AC, Goede W, Mohan AT, Harmsen WS, Niesen AD, Tran NV, Bakri K,Jacobson SR, Lemaine V, Saint-Cyr M.

2-Pilot study of a novel pain management strategy: evaluating the impact on patient outcomes.

Keller DS[1], Tahilramani RN, Flores-Gonzalez JR, Ibarra S, Haas EM

3-Ultrasound guided subcostal transversus abdominis plane (TAP) infiltration with liposomal bupivacaine for patients undergoing robotic assisted hysterectomy: A prospective randomized controlled study.

Hutchins J[1], Delaney D[1], Vogel RI[2], Ghebre RG[3], Downs LS Jr[3], Carson L[3], Mullany S[3], Teoh D[3], Geller MA[4].

4- Impact of liposomal bupivacaine administration on postoperative pain in patients undergoing total knee replacement.

White S[1], Vaughan C[2], Raiff D[2], Eward W[3], Bolognesi M[2].