LIPOSOMAL BUPIVACAINE USE IN ERECTOR SPINAE PLANE BLOCKS
REQUEST FOR PROPOSAL

BACKGROUND

Pacira BioSciences, Inc. is committed to supporting independent research initiatives that foster the advancement of scientific and clinical information and improve patient care. To that end, Pacira extends a new grant opportunity by way of a request for proposal (RFP) focused on research trials that seek to result in optimized patient care. These research trials will provide valued information on the efficacy of the company's marketed products.

All proposals are reviewed for scientific merit, innovation, clinical impact on patients, and compliance with Pacira policy and requirements. If you are interested in applying for support of a research proposal, please review the submission process and apply online by clicking here. Pacira will review and consider all relevant research proposals but is not obligated to provide support for any research proposals received.

While the Pacira Grant Review Committee (PGRC) reviews all research proposals, the principal investigator (and ultimately the grantee) is responsible for the design, implementation, and conduct of the independent initiative supported by the grant. Pacira will not be involved in the conduct or monitoring of the proposed trial, including drafting the research study protocol.

PURPOSE AND INTENT

Pacira issues this RFP for a prospective clinical research study evaluating liposomal bupivacaine erector spinae plane (ESP) block in spine, abdominal, hip, thoracic, and pediatric surgical procedures. This RFP is funded through the investigator-initiated trial (IIT) grant program at Pacira. Funding is available for the fiscal year 2022 and may be extended at the company's discretion.

ELIGIBILITY

To be eligible for consideration, the requestor must be an independent third party. Examples of appropriate requestors include, but are not limited to:

- Academic medical centers
- Healthcare institutions, including private practice settings and ambulatory care facilities

Note: If the research involves multiple departments within an institution and/or between different institutions/organizations/associations, please note each institution's role in the grant application.

TARGET AUDIENCE

Health care professionals involved in the care of patients requiring an ESP block.

TIMELINE

The RFP application will remain open until the grant has been awarded.

Note: The PGRC may award multiple awards at its discretion.

ERECTOR SPINAE PLANE BLOCKS

The erector spine plane block

The erector spinae plane (ESP) block is an emerging regional anesthetic technique first described in the literature for the management of thoracic neuropathic pain (1). In this technique, local anesthetic is infiltrated into the fascial plane between the erector spinae muscle and the transverse process of the spinal vertebrae. The erector spinae muscle is a formed by the spinalis, longissimus thoracis, and iliocostalis muscles that run along the spinal column.

Use of liposomal bupivacaine in erector spine plane blocks

The literature contains few reports of liposomal bupivacaine ESP blocks (2-5). However, evidence suggests that use of the ESP block with liposomal bupivacaine is worth further exploration and may be clinically beneficial. Published evidence includes the use of liposomal bupivacaine ESP block for post-mastectomy pain, hepatopancreaticobiliary (HPB) surgery, cardiac surgery, and spine surgery (2, 4-6).

A case report documented the management of a patient with a history of opioid intolerance who presented for mastectomy and prepectoral tissue expander placement. The patient received a liposomal bupivacaine ESP block in addition to a supplemental T1 paravertebral block. Postoperatively, the patient reported minimal pain (i.e., axillary discomfort) and subsequently received a total of 20 mg of oxycodone through 2 weeks postoperatively. Furthermore, the patient did not require any opioids after hospital discharge (2).

A retrospective analysis compared historical controls (n=40) undergoing open HPB surgery (i.e., pancreaticoduodenectomy, distal pancreatectomy, and hepatectomy) with thoracic epidural anesthesia (TEA) to liposomal bupivacaine ESP block (n=27). A greater percentage of subjects who received an ESP block had less postoperative hypotension (22% versus 55%; $P = 0.03$) and no subjects in the ESP block group required patient controlled analgesia ($P < 0.001$) (6).

A retrospective case control study assessed subjects undergoing cardiac surgery via median sternotomy. Subjects either received a liposomal bupivacaine ESP block (n=8) or a control treatment (n=77). The study found that intraoperative opioid consumption in the liposomal bupivacaine group was significantly lower than the control group. It was also determined that the liposomal bupivacaine group consumed less opioids at 4 and 12 hours after surgery. No other outcomes were statistically significant (4).

A case series detailed three pediatric cardiac surgery patients ranging from 10 months to 8 years that received a liposomal bupivacaine ESP block. In all cases, the ESP blocks were well tolerated with no signs of local anesthetic toxicity and no patient required additional opioids following chest tube removal (7).

A case series explored the use of liposomal bupivacaine ESP block in two adolescent idiopathic scoliosis pediatric patients undergoing posterior spinal fusion surgery and compared outcomes to intravenous (IV) methadone (n=13). Both patients in the ESP block group tolerated treatment well and had a shorter length of stay (LOS) and less opioid use when compared to the control group. The authors note that the ESP block patients appeared to have higher average pain scores compared to the control group (5).

SCOPE OF WORK

The successful applicant will prepare a research proposal for a feasibility study that adequately addresses the use of ESP blocks in spine, abdominal, hip, thoracic, or pediatric surgical procedures.

The study proposal should focus on patients who have undergone spinal, abdominal, hip, thoracic, or pediatric surgical procedures. The study will be a case series evaluating patients before and after ESP blocks for up to six months with a 3-month enrollment period. Outcomes may include pain (eg, NRS, VAS), length of stay, opioid use, physical function, and quality of life.

Grant recipients will agree to provide data to Pacira at the time of study completion.

The Pacira Grant Review Committee will consider funding awards inclusive of indirect costs for the conduct of the study based on a budget within fair market value.

PROPOSAL SUBMISSION REQUIREMENTS

All requestors must submit a written proposal that addresses the following topics and includes required supporting documentation including:

- Organization's contact information
- Primary contact name, title, address, phone, and email
- Describe the organization's current activities relevant to the proposal including current standard of care and patient volume
- Project description and specific proposal objectives
- Available data/information relevant to proposal submission (eg, pilot data)
- Describe how the proposal will improve patient care in alignment with grant objectives
- Proposed timeline for completion with associated deliverables. If possible, attach a flow chart outlining the operational steps of the proposed program
- Proposed budget that is within fair market value and reflects the scope of responsibilities to accomplish the goals of this project. No funding match is required; however, requestors

will need to identify any other sources of funding, both in-kind and monetary, that will be used

To apply for a grant, please click here.

A letter of intent on organizational letterhead should be included. The letter of intent should be single-spaced and not exceed four pages (not including the reference page).

The RFP process

Pacira maintains a stepwise process for review of RFPs. In brief, after registering on the online grant portal, the principal investigator submits a brief concept proposal and if accepted after a review by the PGRC, will be invited to submit a full proposal. Details on brief and full proposal contents are below.

Brief concept proposal:

A brief concept proposal must contain an adequate amount of information for the PGRC to determine interest in requesting a full study proposal. When submitting a brief concept proposal, the following information will be requested (if applicable):

- Principal investigator contact information
- Brief background for the study
- Method of administration of the marketed product
- Primary study objectives/endpoints
- Estimated study timelines
- Estimated total study budget
- Estimated study drug or device(s)
- Preliminary grant request: funding, drug, device, or a combination thereof
- Experience as sponsor-investigator
- Letter of intent on the requesting institution's letterhead
- Curriculum vitae from the principal investigator dated within the last calendar year

The PGRC will review all concept proposals for scientific merit, innovation, clinical importance/potential impact on patients, and compliance with company policy and requirements. The PGRC will extend contingent approval to individual applicants to proceed to the second step of the process, which is the submission of a full study proposal. Applicants will be notified of the PGRC's decision via email, and the status will also be available on the portal. Please note that an invitation to submit a full study proposal does not guarantee the approval of funding.

Full study proposal:

A full study proposal submission must contain enough detail about the research study to enable the PGRC to make an evaluation on support. When submitting a full study proposal, the following information will be requested (if applicable):

- Principal investigator contact information
- Study type: non-clinical or clinical
- Objectives: primary and secondary
- Key inclusion and exclusion criteria

- Study design
- Efficacy variables/measures
- Safety variables/measures
- Adverse event/Serious adverse event reporting
- Decision points/statistical methods/interim analysis
- Study product regimens
- Ethical rationale for the study
- Study deliverables
- Value of the study
- Applicable scientific references
- Publication plan
- Research Setting: single-site or multi-site
- Detailed budget
- Grant request: funding, product, or a combination thereof

Pacira reserves the right to reconsider its support if the research objectives outlined in the final protocol are materially different from the approved full study proposal. Pacira will not compensate for any work performed before the execution of a final contract or for impermissible costs, which include:

- Construction funds to build new facilities
- General education and training activities
- Hiring of staff that are not dedicated to the proposed research study
- Study to involve new investigational products or devices
- Studies that are designed to generate business for Pacira
- Purchase of capital equipment unrelated to the study or that would generate revenue
- Requests for support for ongoing or new research without an associated research study protocol
- Start-up funds to establish new clinical or research programs or to expand existing programs
- Support for ongoing clinical programs that are part of an organization's routine operations

PACIRA CONTACT INFORMATION

If you have questions regarding this RFP, please email grants@pacira.com and include in the subject line *ESP block RFP*.

CONFIDENTIALITY

This Request for Proposal constitutes the confidential and proprietary information of Pacira BioSciences, Inc., and its respective subsidiaries and may not, in whole or in part, be copied, reproduced, or otherwise used in any manner whatsoever without the prior express written permission of Pacira. All information provided herein is proprietary to Pacira and is to be used only by your company in its response hereto. Any other use or communication of this information is prohibited.

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