

Did liposomal bupivacaine overpromise and underdeliver?

Breaking Down the Recent Data Behind Liposomal Bupivacaine (LB)

A clinical review of the three articles around liposomal bupivacaine in the February 2021 issue of ANESTHESIOLOGY.

'Perineural Liposomal Bupivacaine Is Not Superior to Nonliposomal Bupivacaine for Peripheral Nerve Block Analgesia' **Meta-analysis** by Hussain, et al.

'Clinical Effectiveness of Liposomal Bupivacaine Administered by Infiltration or Peripheral Nerve Block to Treat Postoperative Pain: A Narrative Review' **Narrative Review** by Ilfeld et al.

'Liposomal Bupivacaine Effective, Cost-effective, or (Just) Costly?' **Editorial** by McCann

9 TRIALS
(619 PATIENTS)
ANALYZED

evaluating the difference in 24 hr to 72 hr rest pain severity scores for liposomal and nonliposomal bupivacaine

Outcome difference in area under the curve pain rest scores was **statistically significant** but **not clinically meaningful**

Excluding the industry-sponsored study rendered the difference between the groups **nonsignificant**.

Oral Morphine Consumption (mg)

| Time | Liposomal Bupivacaine | Nonliposomal Bupivacaine |
|-----------|-----------------------|--------------------------|
| 0-24 hrs | 22 +/- 23 | 27 +/- 30 |
| 25-48 hrs | 21 +/- 23 | 29 +/- 30 |
| 49-72 hrs | 15 +/- 20 | 21 +/- 22 |

Rest Pain (cm)

| Time | Liposomal Bupivacaine | Nonliposomal Bupivacaine |
|--------|-----------------------|--------------------------|
| 1 hr | 2.8 +/- 2.8 | 3.2 +/- 2.8 |
| 24 hrs | 3.0 +/- 2.5 | 3.2 +/- 2.4 |
| 48 hrs | 3.4 +/- 2.3 | 4.1 +/- 2.5 |
| 72 hrs | 3.4 +/- 2.1 | 4.0 +/- 2.5 |

76 RANDOMIZED, CONTROLLED TRIALS

involving the clinical administration, by infiltration or peripheral nerve block, of LB to control postoperative pain.

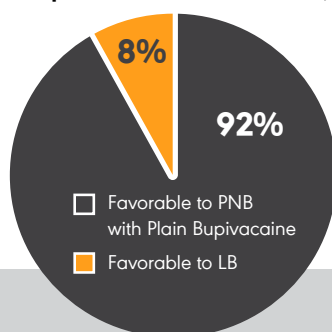
30 were **not registered** or **registered after enrollment** and...



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had a missing or improperly defined primary outcome potentially **leading to a high risk of bias**

12 Studies with **Surgical LB vs. Plain Bupivacaine Nerve Block (PNB)**



DR. MCCANN

out of Harvard Medical School and Boston Children's Hospital was the acting chair for the FDA's Anesthetic and Analgesic Drug Products Advisory Committee February 14 and 15, 2018.

Advised on Pacira's sNDA application for expanded indication for Exparel for nerve blocks.



Calls out lack of clinical superiority of Exparel to generic bupivacaine and their relative costs



CONCLUSION

"Perineural liposomal bupivacaine provided a **statistically significant** but **clinically unimportant** improvement in the AUC of postoperative pain scores compared with plain local anesthetic."

"The preponderance of evidence **fails to support** the routine use of liposomal bupivacaine over standard local anesthetics."

"In this era of medical austerity, when the benefits and costs of expensive drugs are being considered, one would hope that newly approved expensive drugs **would at least be an improvement** over existing, inexpensive drugs."