

Poster
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Opioid-free Management of Moderate-to-Severe Acute Pain With Suzetrigine

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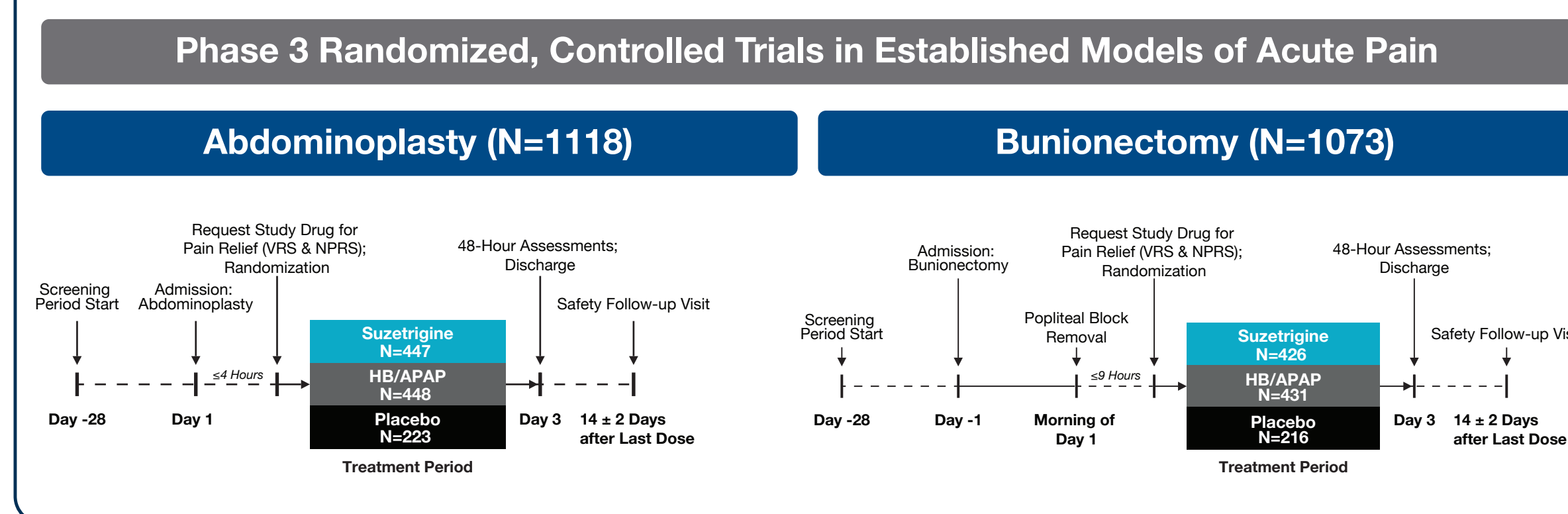
INTRODUCTION

- Moderate-to-severe acute pain presents a significant management challenge due to the need to balance therapeutic efficacy and safety concerns within constraints of available treatments
- While opioids are effective for pain relief, their use is limited by safety, tolerability, and addiction risks¹
- Suzetrigine (SUZ) is a highly selective voltage-gated sodium channel 1.8 (Na_v1.8) inhibitor with no addiction potential based on its mechanism of action²
- In two Phase 3 randomized, double-blind, placebo-controlled trials (RCTs)³:
 - SUZ demonstrated a statistically significant reduction in pain compared to placebo (primary endpoint)
 - Neither trial showed SUZ superiority over hydrocodone bitartrate/acetaminophen (HB/APAP), the most frequently prescribed opioid combination and dose (5/325 mg) in the conditions studied
 - The majority of adverse events (AEs) were mild to moderate in severity and there was a lower incidence of AEs observed in participants receiving SUZ than those receiving HB/APAP or placebo
 - There were fewer AEs of vomiting and/or nausea (common side effects of opioids) in participants receiving SUZ than those receiving HB/APAP
- In a supportive Phase 3 single-arm safety and effectiveness (SASE) trial, most participants (83.2%) rated SUZ effectiveness for treating pain on a patient global assessment (PGA; secondary endpoint) as good, very good, or excellent⁴
- In all three trials, SUZ was generally safe and well tolerated with no serious AEs related to SUZ^{3, 4}
- SUZ is approved in the US to treat moderate-to-severe acute pain in adults
- Here we report on opioid-free pain management with SUZ across these trials in moderate-to-severe acute pain conditions

MATERIAL AND METHODS

- Two Phase 3 RCTs evaluating SUZ for 48 hours in participants with moderate-to-severe acute pain after abdominoplasty or bunionectomy were conducted (**Figure 1**)³
 - Participants were randomized 2:2:1 to SUZ, HB/APAP, or placebo
- A Phase 3 SASE trial enrolled participants with moderate-to-severe acute pain following a scheduled surgical procedure (most common were orthopedic, plastic, and otorhinolaryngologic) or after presenting with moderate-to-severe acute pain of non-surgical origin (most common were sprains and strains of upper and lower extremities) (**Figure 2**)⁴
- Opioid use was not allowed during treatment except for RCT participants who were randomized to receive HB/APAP
- Opioid use was permitted if participants discontinued treatment prematurely
- We analyzed opioid use in participants after early discontinuation of treatment in these three trials

Figure 1. RCT Designs



HB/APAP: hydrocodone bitartrate/acetaminophen; N: number of participants in the analysis set; NPRS: numeric pain rating scale; RCT: randomized controlled trial; VRS: verbal categorical rating scale

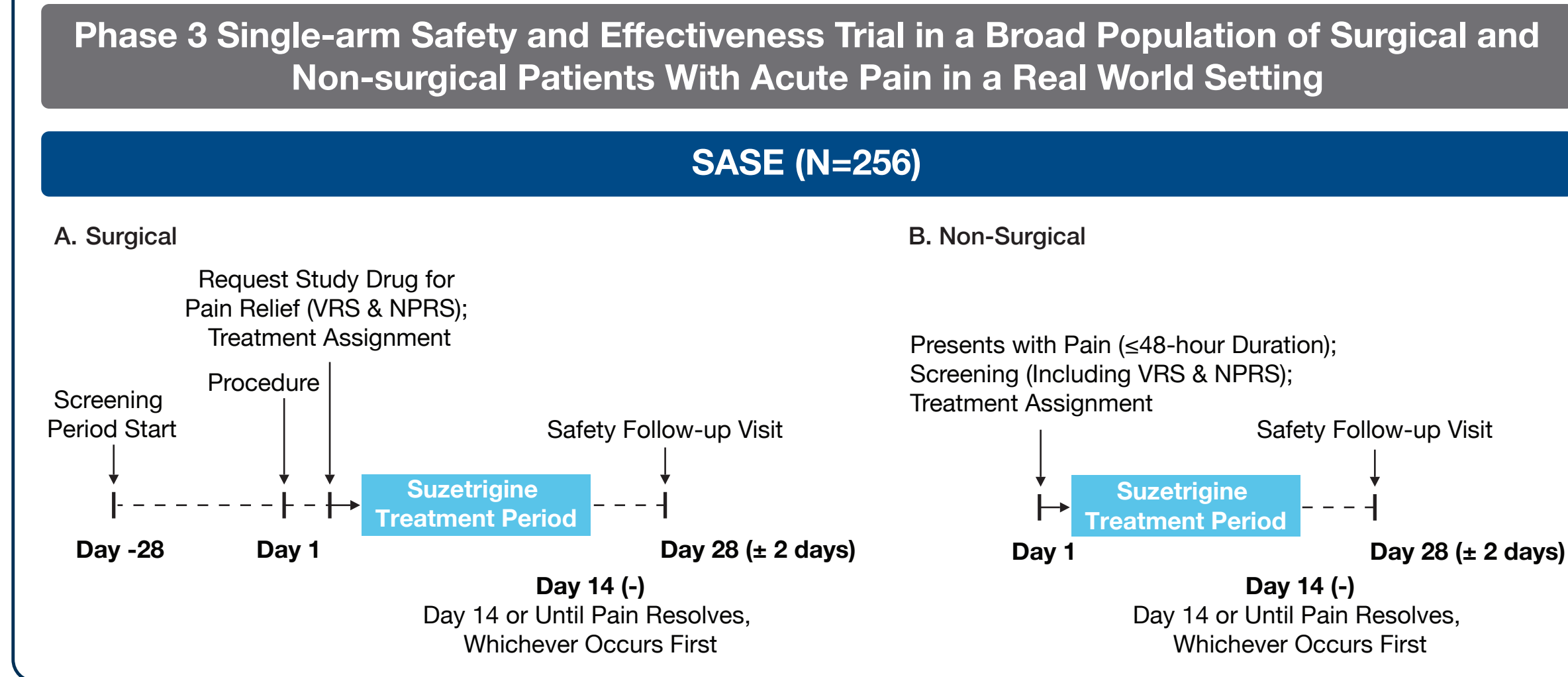
Study Design

- Suzetrigine tablets:** 100-mg then 50-mg every 12 hours administered orally
- HB/APAP capsules:** 5-mg/325-mg every 6 hours administered orally
- Rescue medication:** ibuprofen was permitted, if needed, for pain relief. Opioids and other pain medicines were not allowed during treatment

Key Eligibility Criteria

- Age:** 18 to 80 years
- Reported pain:** moderate or severe on the VRS and ≥ 4 on the NPRS within 4 hours after abdominoplasty or 9 hours after removal of the popliteal sciatic nerve block (with ropivacaine) after a bunionectomy

Figure 2. SASE Trial Design



N: number of participants in the analysis set; NPRS: numeric pain rating scale; SASE: single-arm safety and effectiveness; VRS: verbal categorical rating scale. Note: A total of 256 participants (surgical: n=222; non-surgical: n=34) received suzetrigine.

Study Design

- Suzetrigine tablets:** 100-mg first dose, then 50-mg every 12 hours administered orally for 14 days or until pain resolved
- Rescue medication:** ibuprofen and acetaminophen were permitted, if needed, for pain relief, in line with standard multimodal therapy. Opioids and other pain medications were not allowed during treatment

Key Eligibility Criteria

- Age:** 18 to 80 years
- Reported pain:** moderate or severe on the VRS and ≥ 4 on the NPRS following surgical procedures or after presenting to a medical facility with non-surgical pain of new origin (prior 48 hours; not related to a prior known condition)

RESULTS

Most Participants Receiving Suzetrigine Completed Treatment in the 48-hour RCTs With a Small Percentage Discontinuing Early

Table 1. Disposition of RCT Participants

	Abdominoplasty			Bunionectomy		
	Placebo N = 223 n (%)	HB/APAP N = 448 n (%)	SUZ N = 447 n (%)	Placebo N = 216 n (%)	HB/APAP N = 431 n (%)	SUZ N = 426 n (%)
Completed treatment	168 (75.3)	382 (85.3)	396 (88.6)	177 (81.9)	389 (90.3)	372 (87.3)
Discontinued treatment	55 (24.7)	66 (14.7)	51 (11.4)	39 (18.1)	42 (9.7)	54 (12.7)
Reason for discontinuation of treatment						
Adverse event	1 (0.4)	5 (1.1)	6 (1.3)	0	1 (0.2)	0
Participant refused further dosing (not due to adverse event)	1 (0.4)	0	0	0	3 (0.7)	1 (0.2)
Lack of efficacy	48 (21.5)	59 (13.2)	42 (9.4)	35 (16.2)	34 (7.9)	51 (12.0)
Did not meet eligibility criteria	0	0	1 (0.2)	0	1 (0.2)	0
Other non-compliance	0	0	0	2 (0.9)	1 (0.2)	1 (0.2)
Physician decision	3 (1.3)	1 (0.2)	1 (0.2)	0	0	0
Sponsor decision	1 (0.4)	0	1 (0.2)	0	0	1 (0.2)
Other	1 (0.4)	1 (0.2)	0	2 (0.9)	2 (0.5)	0

HB/APAP: hydrocodone bitartrate/acetaminophen, n: number of participants, N: number of participants in the analysis set, RCT: randomized controlled trial, SUZ: suzetrigine. Note: Percentages were calculated relative to the number of participants in the analysis set (participants who were randomized and received at least one dose of study drug).

In Both RCTs, a Numerically Lower Proportion of Participants Receiving Suzetrigine Discontinued Treatment Early and Received Opioids Compared to Placebo; A Total of 9.6% (Abdominoplasty) and 11.7% (Bunionectomy) of RCT Participants Receiving Suzetrigine Discontinued Treatment Early and Received Opioids

Table 2. Opioid Medication use Among all Participants who Discontinued Treatment Early in Suzetrigine Phase 3 RCTs

Statistic	Abdominoplasty			Bunionectomy		
	Placebo N = 223	HB/APAP N = 448	SUZ N = 447	Placebo N = 216	HB/APAP N = 431	SUZ N = 426
All participants who discontinued treatment and used concomitant opioid medication, n (%)^a	49 (22.0)	61 (13.6)	43 (9.6)	31 (14.4)	30 (7.0)	50 (11.7)

HB/APAP: hydrocodone bitartrate/acetaminophen, n: number of participants, N: number of participants in the analysis set, RCT: randomized controlled trial, SUZ: suzetrigine. Note: Analysis was ad hoc and included opioid medications started after first dose of study drug. The reasons participants discontinued treatment are provided in Table 1. ^aAmong participants in any treatment group who were randomized and received at least one dose of study drug.

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Most Participants Completed Treatment With Suzetrigine in the SASE Trial With Only a Small Percentage Discontinuing Treatment Early;

Only 1 (0.4%) SASE Participant Discontinued Treatment Early and Received Opioids

Table 3. Disposition of SASE Participants

	SUZ N = 256 n (%)
Completed treatment	242 (94.5)
Reason for completion of treatment	
Pain resolution	137 (53.5)
Completed dosing until Day 14 ^a	105 (41.0)
Discontinued treatment	14 (5.5)
Reason for discontinuation of treatment	
Adverse event	5 (2.0)
Lack of efficacy	4 (1.6)
Sponsor decision	1 (0.4)
Other	4 (1.6)
All participants who discontinued treatment and used concomitant opioid medication	1 (0.4) ^b

n: number of participants, N: number of participants in the analysis set, SASE: single-arm safety and effectiveness, SUZ: suzetrigine. Notes: Percentages were calculated relative to the number of participants in the analysis set (participants who received at least one dose of SUZ). ^aParticipants received SUZ for a maximum of 14 days; dosing until Day 14 does not necessarily reflect participant pain at Day 14. ^bThe surgical type/region for this participant was otorhinolaryngologic/nasal cavity and tonsils.

DISCUSSION

- Current pain management practices strive for effective pain relief while minimizing side effects
- The benefit/risk profile of SUZ in various moderate-to-severe acute pain conditions suggests opioid-free pain relief is possible with SUZ after surgical procedures and non-surgical conditions, which is beneficial even in the acute setting

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Author Disclosures

TB, JM, DS, LT, JU, JO, MWS, SGW have reported personal fees from Vertex Pharmaceuticals as members of the Acute Pain Steering Committee. JU is a consultant and has received payment or honoraria from Pacira BioSciences. SGW has received grants or contracts from NIH, Foundation for Opioid Response Efforts, Yale University, and Elevance Foundation and is a consultant for Cessation Therapeutics. MWS's institution has received funding and/or product from the following companies for other research studies of this author: Epimed International (Farmers Branch, Texas, USA), SPR Therapeutics (Cleveland, Ohio, USA), Infutrix (Natick, Massachusetts, USA), and Avaros Medical (Irvine, California, USA). DD has nothing to disclose. IJ, TH, WK, and DJC are employees of Vertex Pharmaceuticals and hold stock and/or stock options in the company

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