Breaking the Pain Barrier

Suzetrigine in the Treatment of Acute Pain

Maria Hajiharis, PharmD, PGY-1 Pharmacy Resident
Advocate Lutheran General Hospital
December 17, 2025

Disclosures

The planner(s) and speaker(s) have indicated that there are no relevant financial relationships with any ineligible companies to disclose.

Learning Objectives

At the end of this session, learners should be able to:

- Identify risks associated with opioid use and gaps in acute pain management
- Explain the pathophysiology of acute pain and suzetrigine's novel mechanism of action
- Recall the pivotal clinical trials that led to FDA approval of suzetrigine, including their limitations
- Apply clinical evidence to evaluate suzetrigine's current place in therapy

Outline

- Background
- Practical Considerations
- Literature Review
- Future directions
- Conclusion

ADVOCATE HEALTH

Abbreviation Key

- AE: adverse effects
- CDC: Center for Disease Control
- CNS: central nervous system
- ED: emergency department
- EOT: end of treatment
- HB/APAP: hydrocodone bitartrate-acetaminophen
- IR: immediate release, ER: extended release
- MOA: mechanism of action
- Na: sodium
- NPRS: numerical pain rating scale
- NSAIDs: non-steroidal anti-inflammatory drug
- OUD: opioid use disorder
- Vd: volume of distribution
- VRS: verbal categorical rating scale
- PDMP: prescription drug monitoring program
- PGA: patient global assessment
- PK/PD: pharmacokinetics/pharmacodynamics
- PMH: past medical history
- PNS: peripheral nervous system
- PO: by mouth
- SPID: sum of pain intensity difference
- US: United States

ADVOCATE HEALTH

Background

Pain Burden in the US

- In the US alone, nearly 100 million surgeries take place annually
  - More than 80% of surgical patients report postoperative pain
- Over 70% of ED visits are due to pain, with 2.1 million accounting for acute headache alone
- The economic impact of pain has been estimated to cost the US close to $1 trillion

International Association for the Study of Pain (IASP), 2021, Robinson CL, Schatman ME, Hasoon J doi:10.2147/JPR.S527710

ADVOCATE HEALTH

Pain is a perception. Everyone's perception of pain is different.

ADVOCATE HEALTH

Pain by Duration

1. **Acute Pain**
   - Lasts less than one month
2. **Subacute Pain**
   - Lasts one to three months
3. **Chronic Pain**
   - Lasts greater than 3 months

Karcz M, doi:10.2147/JPR.S475351

Types of Pain

Acute pain: "*nociceptive*" - the body's sensory nervous system responds to actual or potentially harmful stimuli

- Myelinated alpha delta fibers
  - Smallest myelinated nerves, fast conduction
  - Short-lasting pricking pain sensation
- Unmyelinated C fibers
  - Slower conduction velocity
  - Poor localization, dull pain sensation

Yam MF, doi:10.3390/ijms19082164

Types of Pain

Chronic pain: "*neuropathic*" - results from abnormal function of the nervous system, due to nerve injury or impairment

- Can occur in the absence of noxious stimuli or have an exaggerated response to minor stimuli
- Major causes could be due to inflammation or metabolic diseases
  - Diabetes, trauma, toxins, tumors, primary neurological diseases, herpes zoster infection

Yam MF, doi:10.3390/ijms19082164

Pathophysiology

- Nociception - the process in which the nervous system detects and responds to potentially harmful or painful stimuli, involving three distinct processes

Transduction

Transmission

Modulation

Yam MF, doi:10.3390/ijms19082164

Pathophysiology

Transduction: nociceptors convert noxious stimuli into electrical signals

- Inflammatory mediators are released at the site of injury
- Neurogenic inflammation
- Activation of nociceptors

Garland EL, doi:10.1016/j.pop.2012.06.013

Pathophysiology

Transmission: impulses travel through fibers transmitting signals to dorsal horn of the spinal cord

- Activation of alpha delta and C fibers
- **Na channels NaV1.7/1.8/1.9**
  - Suzetrigine mechanism of action

ADVOCATE HEALTH

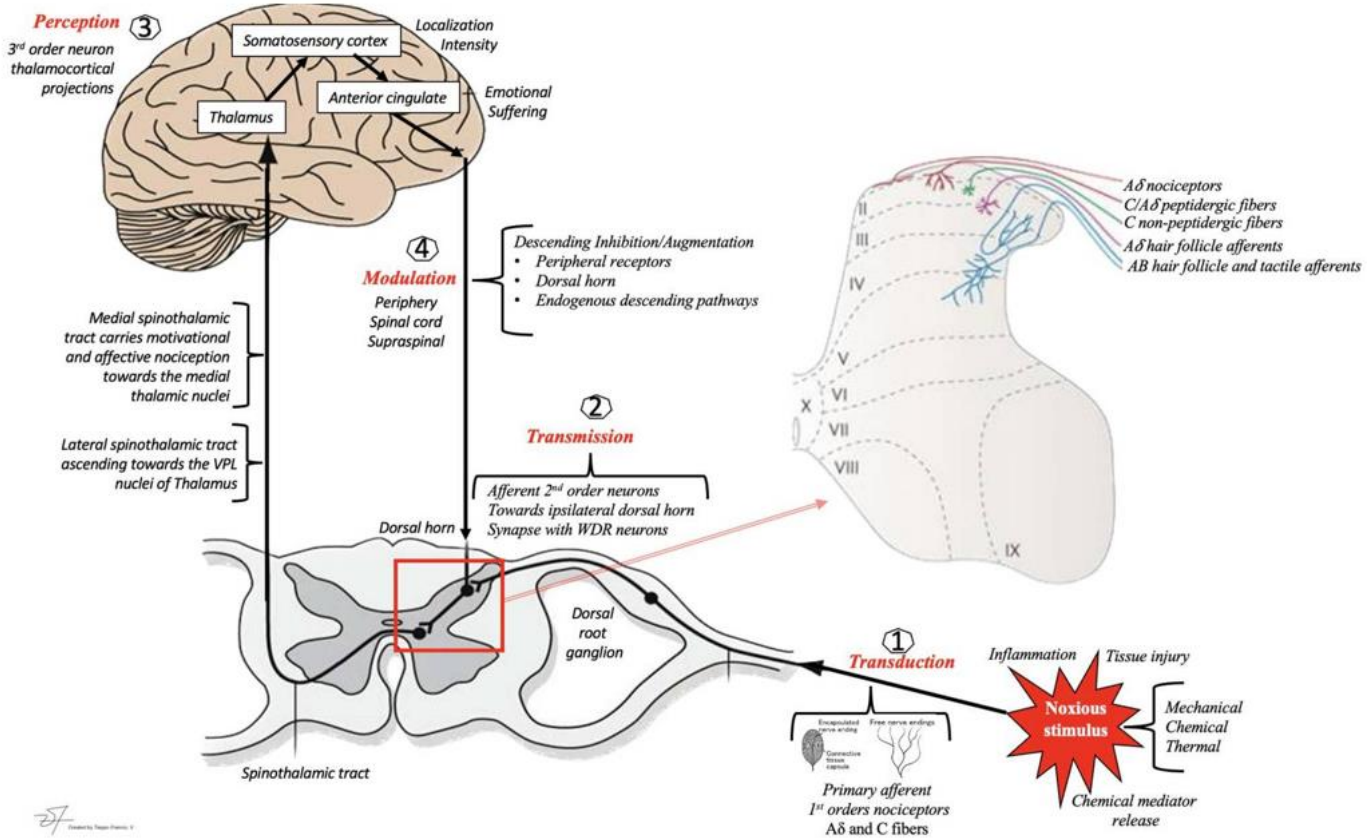
Karcz M, doi:10.2147/JPR.S475351, Garland EL, doi:10.1016/j.pop.2012.06.013, Waxman SG, doi:10.1056/NEJMe2305708

Pathophysiology

Modulation: the brain receives the pain signal and either up or down regulates the response

- Interneurons in the dorsal horn can inhibit and potentiate impulses ascending to higher brain centers
- Site of action for pain relieving drugs

Karcz M, doi:10.2147/JPR.S475351, Garland EL, doi:10.1016/j.pop.2012.06.013



ADVOCATE HEALTH

Karcz M, doi:10.2147/JPR.S475351

Assessment Question #1

The transmission of a pain signal involves several types of fibers. Which of the following will transmit a fast, sharp pricking pain?

a. C nerve fibers
b. Group B fibers
c. Alpha gamma fibers
d. Alpha delta fibers

Multimodal Analgesia

Reducing opioids while providing improved pain control

- Acetaminophen
- Ibuprofen (NSAIDs)
- Gabapentenoids
- Skeletal Muscle Relaxants
- Opioids (Hydrocodone-APAP)

Acetaminophen

Exact mechanism is unclear, possible activation of descending serotonergic inhibitory pathways in the CNS

Peak plasma concentrations in 30-60 min, duration 4-6 hours

Dosing range: 325 – 4000 mg/day

ADVOCATE HEALTH

Lexicomp, Joshi GP, doi:10.1007/s11916-023-01137-y

Ibuprofen (NSAIDs)

Reversibly inhibit cyclooxygenase 1/2 enzymes, decreased formation of prostaglandin precursors

Peak plasma concentrations in 30-60 min, duration 6-8 hours

Dosing range: 200 – 3200 mg/day

ADVOCATE HEALTH

Lexicomp, Joshi GP, doi:10.1007/s11916-023-01137-y

Gabapentin

Modulates the release of excitatory neurotransmitters that participate in nociception

Variable absorption, dose dependent

2-4 hours peak plasma concentration in IR, 8 hours for ER

When used chronically should taper when to avoid withdrawal symptoms

Dosing range: 100-3600mg/day

ADVOCATE HEALTH

Lexicomp, Joshi GP, doi:10.1007/s11916-023-01137-y

Hydrocodone-Acetaminophen

- Binds to and activates mu receptors, full opioid agonist
- Peak plasma concentration in 1 hour, duration 3-4 hours
- US Boxed Warning: addiction/abuse/misuse, life-threatening respiratory depression, accidental ingestion, neonatal opioid withdrawal syndrome
- 5-10 mg hydrocodone every 4-6 hours as needed

ADVOCATE HEALTH

Lexicomp, Joshi GP, doi:10.1007/s11916-023-01137-y

Opioid Risks

- Efficacious, inexpensive, widely used analgesics
- Well know tolerability issues, risk of dependence and addiction due to their effects on the CNS
- Need for safe and effective non-opioid medications to treat pain without the risk for addiction

Addiction & Abuse Potential

Tolerance: additional medication is needed to provide the same pain relief

- Decrease in duration of effective analgesia

Physical dependence: withdrawal symptoms occur when a medication is stopped or less is taken

- Anxiety, irritability, chills, hot flashes, salivation, diaphoresis, nausea, abdominal cramps, insomnia
- Severity of withdrawal is a function of the dose/duration of administration of the discontinued opioid

ADVOCATE HEALTH

Inturrisi CE, doi:10.1097/00002508-200207001-00002

Opioid Adverse Effects

- Respiratory Depression
- Nausea and Vomiting
- Sedation
- Constipation
- Urinary Retention

Prevalence of AEs

Adverse Effect	Prevalence
Constipation	30-40%
Nausea/Vomiting	25%
Breathing problems during sleep	25%
Depression/Anxiety	30-40%
Dry Mouth	25%
Sedation	15%

ADVOCATE HEALTH

Baldini A, doi:10.4088/PCC.11m01326

Opioid Use Disorder

Approximately 105,000 people died from drug overdose in 2023 and nearly 80,000 of those deaths involved opioids (about 76%)

- ***Prescription*** opioids have been detected in up to 77% of opioid-related overdose fatalities
- The CDC recommends non-pharmacologic and non-opioid therapies be maximized as appropriate
  - Importance of screening for OUD

ADVOCATEHEALTH

Klimas J, doi:10.1001/jamanetworkopen.2019.3365, CDC

Screening for OUD

High risk patients include:

- History of opioid or nonopioid substance use disorder
- Concomitant prescription of certain psychiatric medications
- Prolonged duration of opioid prescriptions (≥30 days)
- Higher daily opioid doses

Prescribers should screen patients and evaluate the PDMP

Assessment Question #2

Which of the following is not a consequence of short and long-term opioid use?

a. Addiction and abuse potential
b. Constipation, ileus
c. Sedation and drowsiness
d. Tachycardia, arrhythmias

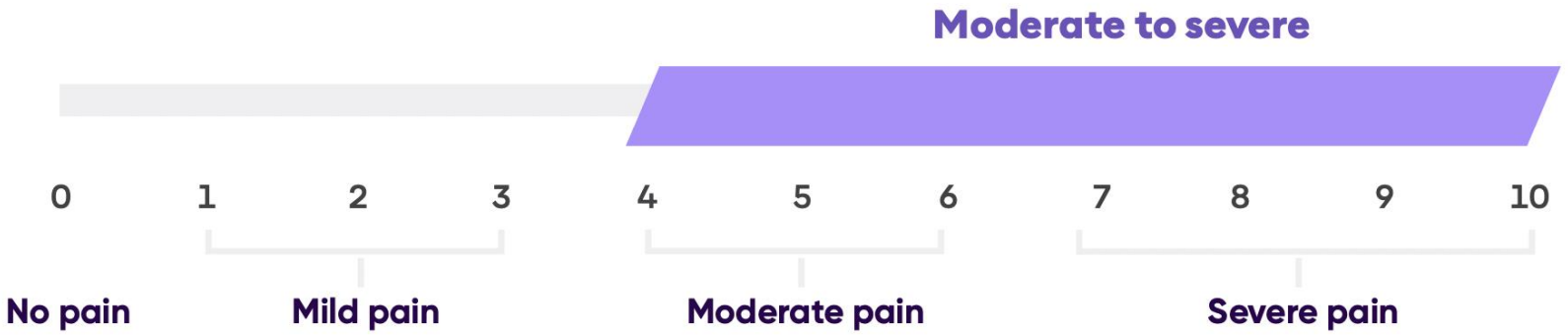
suzetrigine (Journavx®)

ADVOCATE HEALTH

NaV1.8 Inhibitor

FDA approved in January 2025 for the treatment of moderate to severe acute pain

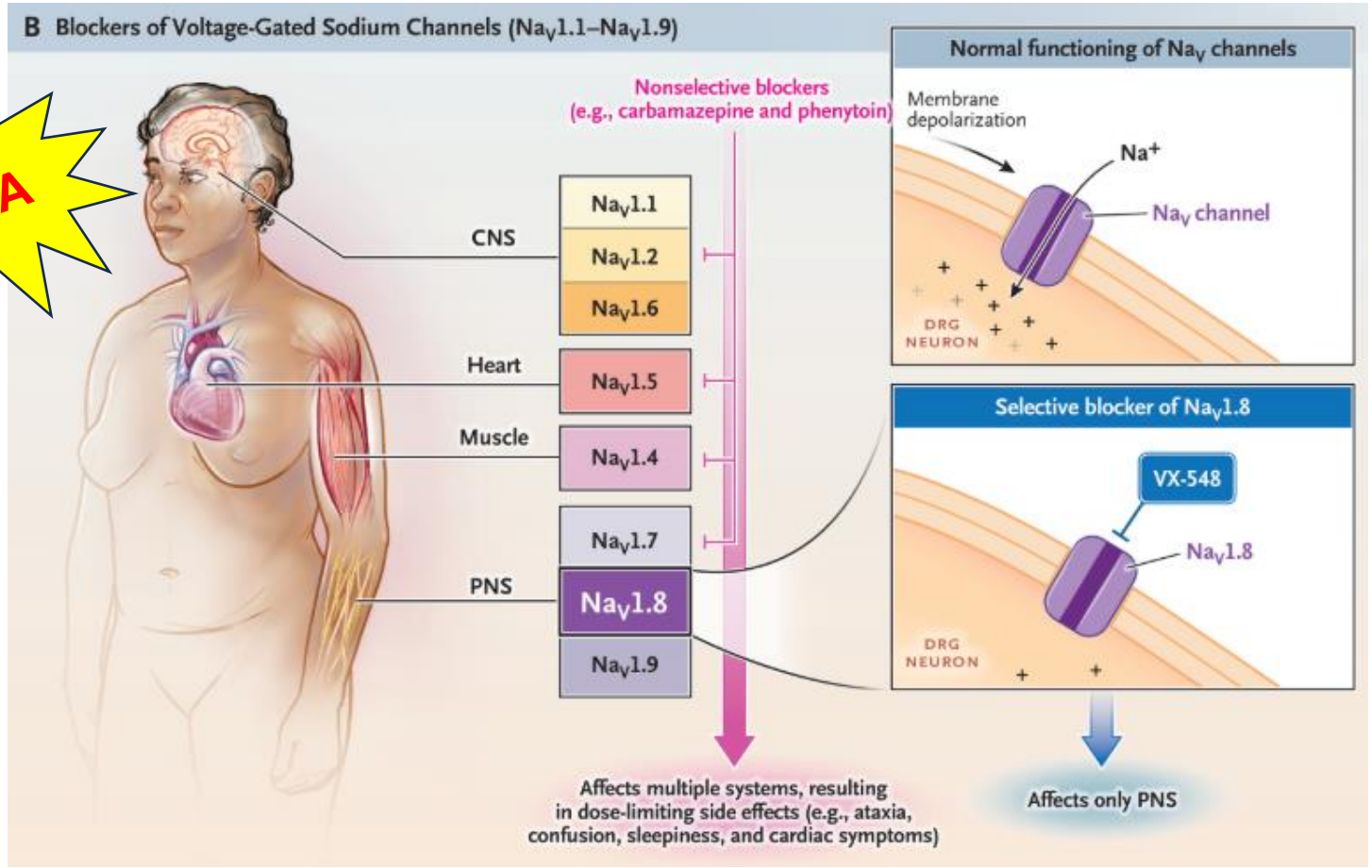
Reduces pain signals before they reach the brain



ADVOCATE HEALTH

Waxman SG, doi:10.1056/NEJMe2305708, Vertex Pharmaceuticals

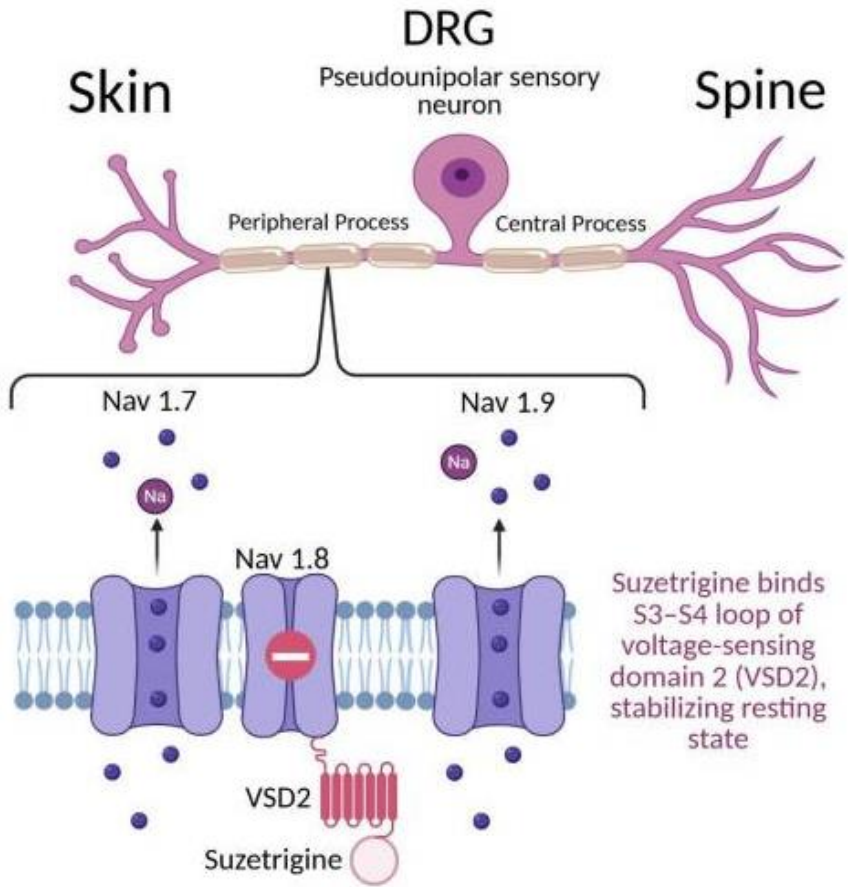
MOA



ADVOCATE HEALTH

Waxman SG, doi:10.1056/NEJMe2305708

Afferent pain signal
initiated by noxious stimulus



Binds NaV1.8 in the "closed" resting state

ADVOCATE HEALTH

Pham A, doi:10.3390/ijms26209865

Dosing

100 mg PO once on an empty stomach	• 1 hour before or 2 hours after food
Then 50 mg PO every 12 hours(with or without food)	• If ≥ 2 doses missed, take 100 mg once then next dose 12 hours later

Renal/Hepatic Adjustment

No renal dose adjustment: Do not use in CrCl ≤ 15ml/min

Child Pugh Class B: 12 hours after dose 4, start taking 50 mg every 24 hours

Child Pugh Class C: Avoid

ADVOCATE HEALTH

Lexicomp, FDA package insert, Osteen JD, doi:10.1007/s40122-024-00697-0

Adverse Effects

Pooled adverse effects that occurred in greater than 1% of patients in trials include:	Pruritus
	Muscle spasms
	Increased blood creatine phosphokinase
	Rash

ADVOCATE HEALTH

Lexicomp, FDA package insert, Osteen JD, doi:10.1007/s40122-024-00697-0, Bertoch T, doi:10.1097/ALN.0000000000005460

PK/PD

- Major CYP3A substrate
- Time to peak: 3 hours
- Half life elimination: 23.6 hours
- M6-SUZ is the major active metabolite

ADVOCATE HEALTH

Lexicomp, Osteen JD, doi:10.1007/s40122-024-00697-0

Drug Interactions

CYP3A inhibitors

- Azole antifungals, protease inhibitors, clarithromycin, grapefruit juice

Hormonal contraceptives containing progestins other than levonorgestrel or norethindrone

- Use additional contraceptive during treatment and for 28 days following discontinuation

ADVOCATEHEALTH

Lexicomp, FDA package insert, Osteen JD, doi:10.1007/s40122-024-00697-0

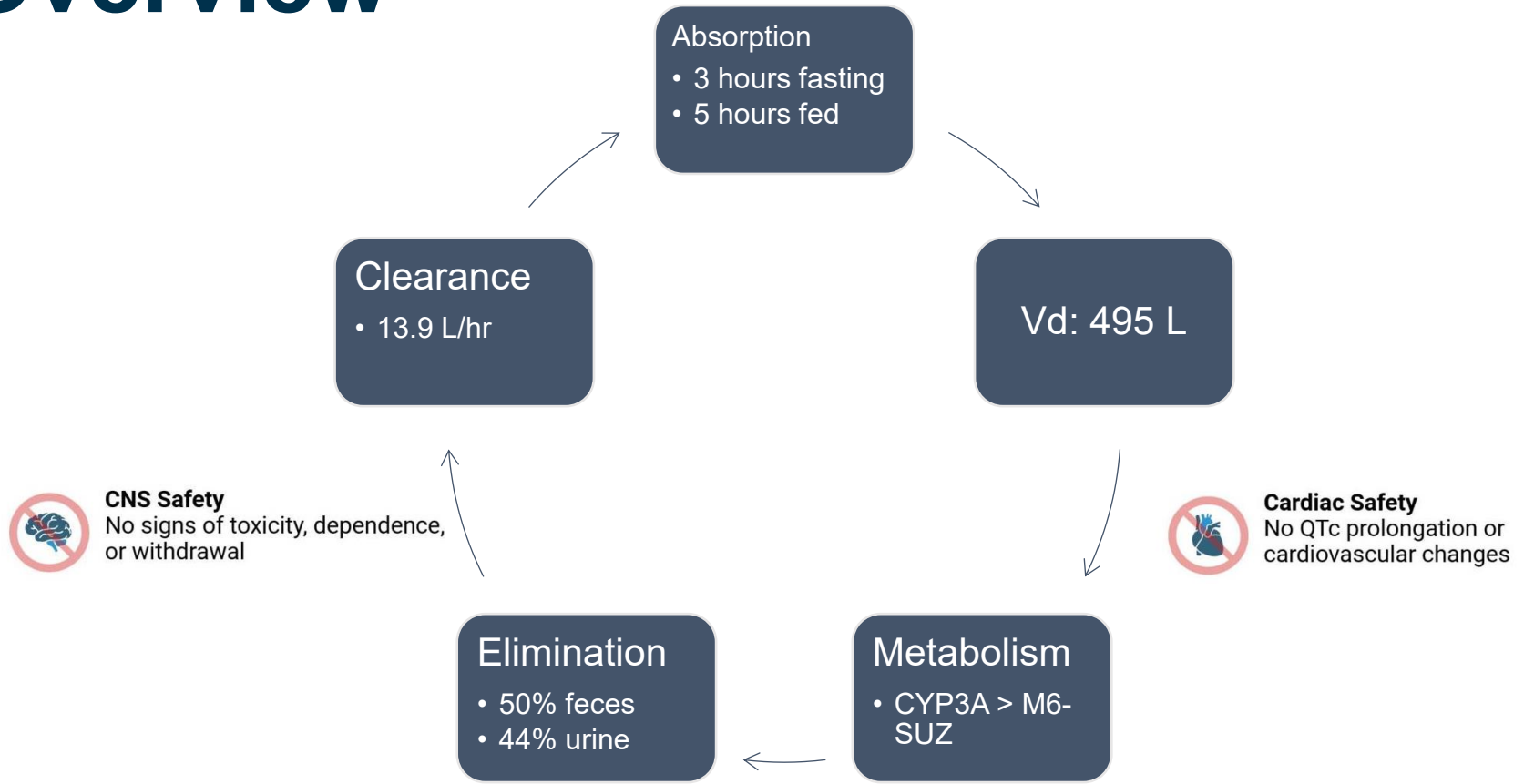
Pricing

MCK ITEM #	IMAGE	PREF	HIST	DESCRIPTION	NDC	STRENGTH	PURCHASE PRICE	FORM	UNIT PRICE ▲ 2	DC QTY	ORD QTY	AVAIL QTY	VENDOR SUPPLY
3036142				JOURNAVX 50MG TB 100	51167054834	50 MG	$1403.10	TABLET	$14.0310	2		2	
3014602				JOURNAVX TB 50 MG 30	51167054830	50 MG	$420.93	TABLET	$14.0310	>100		>100	

- US pricing is about $18.60 per 50 mg tablet
- Our pricing $14.03 per 50 mg tablet
  - Comes in 30 and 100 count packaging
- Currently **not** on Advocate formulary

ADVOCATE HEALTH

Overview



ADVOCATE HEALTH

Literature Review

ADVOCATE HEALTH

suzetrigine (Journavx®)

A selective inhibitor of NaV1.8 channels for moderate-severe acute pain, FDA approved January 2025

- Two Phase 3 Randomized Clinical Trials
  - NAVIGATE1 and NAVIGATE2
- A Phase 3 Single-Arm Study for Surgical or Non-Surgical Acute Pain

NAVIGATE1/2

Suzetrigine, a Nonopioid Na V 1.8 Inhibitor for Treatment of Moderate-to-severe Acute Pain: Two Phase 3 Randomized Clinical Trials

- NAVIGATE1: bunionectomy (N=1073)
- NAVIGATE2: abdominoplasty (N=1118)

- Included: ages 18-80 with mod-severe acute pain on the VRS and ≥ 4 on the NPRS following the procedure

ADVOCATE HEALTH

Bertoch T, doi:10.1097/ALN.0000000000005460

NAVIGATE1/2

Randomized to one of three groups for 48 hours:

- **Suzetrigine**:100 mg PO then 50 mg PO every 12 hours scheduled
- **HB/APAP**: 5-325 mg PO every 6 hours scheduled
- **Placebo**

NAVIGATE1	NAVIGATE2
Suzetrigine N = 426	Suzetrigine N = 447
HB/APAP N = 431	HB/APAP N = 448
Placebo N = 216	Placebo N = 223

ADVOCATE HEALTH

Bertoch T, doi:10.1097/ALN.0000000000005460

Patient Demographics

- **Abdominoplasty**: Mean ± SD age for participants was 42 ± 9 yr; most participants were women (98%) and White (70%)
  - Greater baseline pain: 7.4 ± 1.7

- **Bunionectomy**: Mean ± SD age was 48 ± 13 yr; most participants were women (85%) and White (71%)
  - Baseline pain reported: 6.8 ± 1.8

ADVOCATE HEALTH

Bertoch T, doi:10.1097/ALN.0000000000005460

NAVIGATE1/2

Primary endpoint: time-weighted sum of the pain intensity difference(SPID48) in the numeric pain rating scale from 0 to 48 hours vs placebo

Secondary endpoints: SPID48 vs HB/APAP, time to ≥ 2 point reduction in numeric pain rating scale from baseline vs placebo, safety assessment

ADVOCATE HEALTH

Bertoch T, doi:10.1097/ALN.0000000000005460

SPID48

- Calculated by first determining the pain intensity difference between the numeric pain rating scale at 19 scheduled timepoints and the baseline
  - 0.5, 1.0, 1.5, 2, 3, 4, 5, 6, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48 h after the first dose of study drug
- Then multiplying each pain intensity difference by the time interval since the last measurement
- A **positive SPID48** value indicates a **reduction in pain** from baseline, with a higher value indicating a greater reduction

ADVOCATE HEALTH

Bertoch T, doi:10.1097/ALN.0000000000005460

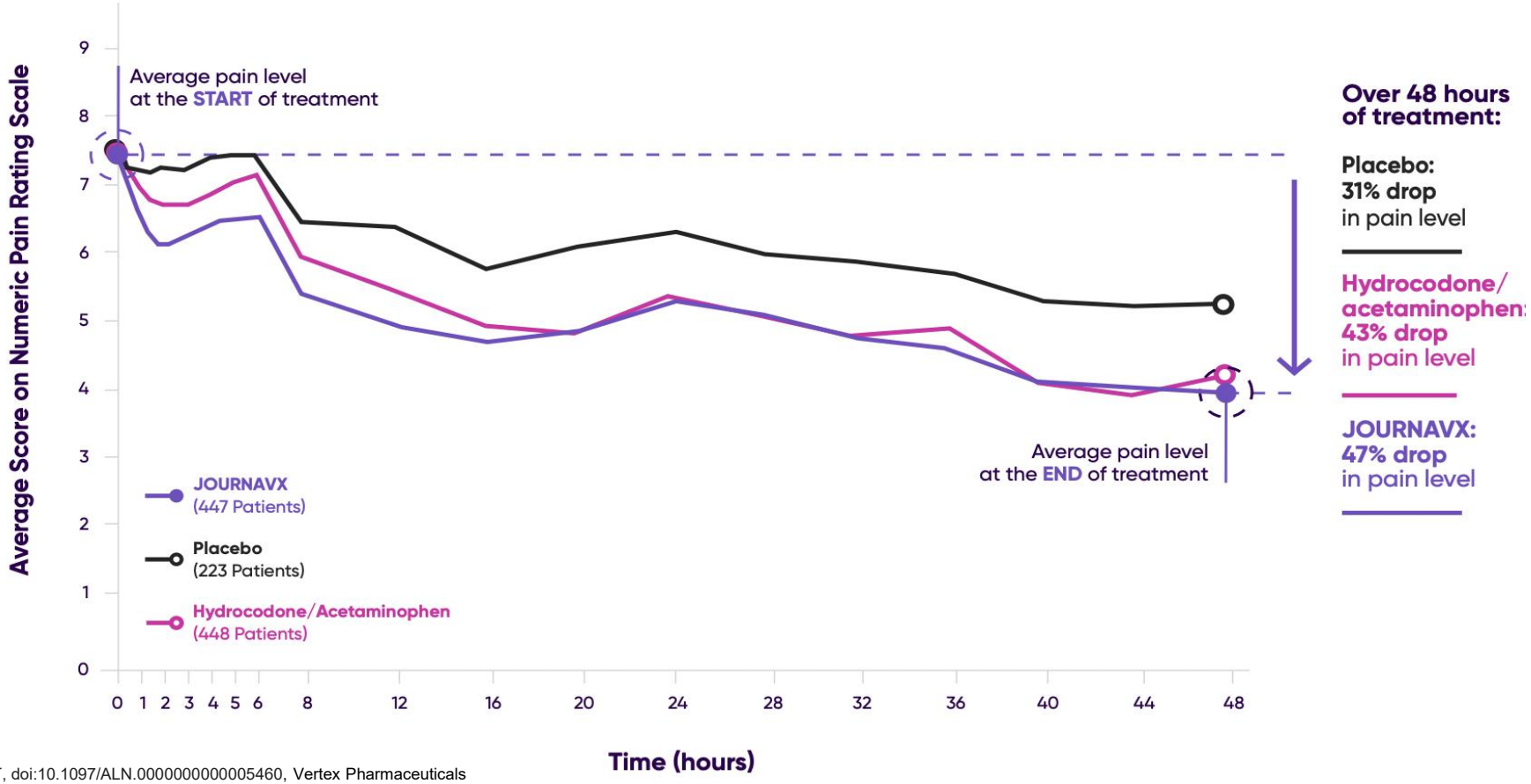
Primary Endpoint

Primary Endpoint: SPID48 Compared to Placebo	Abdominoplasty		Bunionectomy	
	Suzetrigine N=447	Placebo N=223	Suzetrigine N=426	Placebo N=216
With Rescue Imputation (monotherapy)				
LS mean (SE)	118.4 (4.3)	70.1 (6.1)	99.9 (4.5)	70.6 (6.3)
LS mean difference from placebo	48.4	--	29.3	--
95% CI	(33.6, 63.1)	--	(14.0, 44.6)	--
P value versus placebo	<0.0001	--	0.0002	--
Without Rescue Imputation (representative of multimodal therapy in real-world setting)				
LS mean (SE)	153.0 (4.5)	105.4 (6.4)	128.8 (4.7)	100.1 (6.6)
LS mean difference from placebo	47.7	--	28.8	--
95% CI	(32.4, 62.9)	--	(12.9, 44.6)	--
Nominal *P* value versus placebo*	<0.0001	--	0.0004	--

ADVOCATE HEALTH

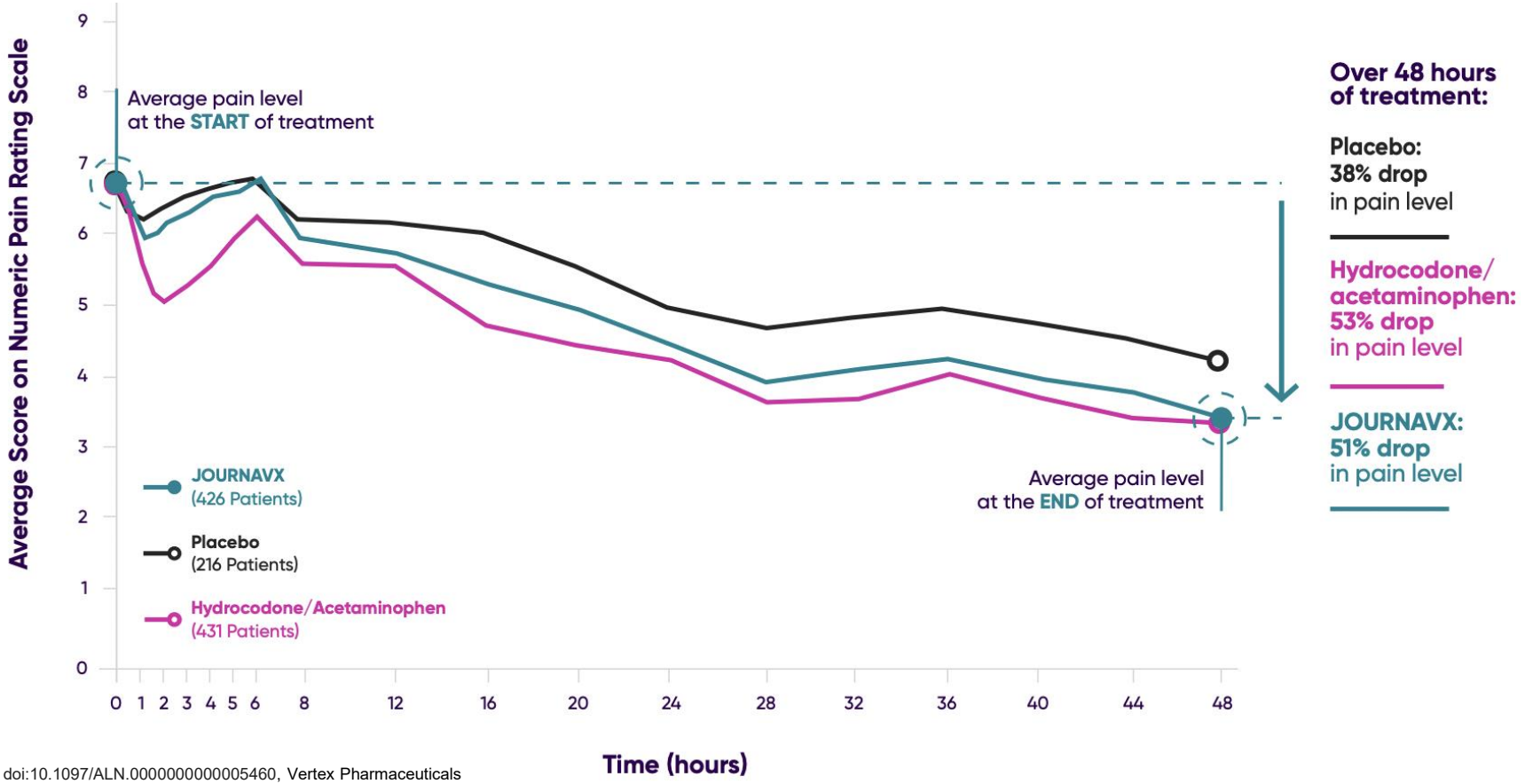
Bertoch T, doi:10.1097/ALN.0000000000005460

Primary Endpoint



Bertoch T, doi:10.1097/ALN.0000000000005460, Vertex Pharmaceuticals

Primary Endpoint



Bertoch T, doi:10.1097/ALN.0000000000005460, Vertex Pharmaceuticals

Secondary Endpoint

SPID48 Compared to HB/APAP

	Abdominoplasty		Bunionectomy	
	Suzetrigine N=447	HB/APAP N=448	Suzetrigine N=426	HB/APAP N=431
With Rescue Imputation (monotherapy)				
LS mean (SE)	118.4 (4.3)	111.8 (4.3)	99.9 (4.5)	120.1 (4.5)
LS mean difference from HB/APAP	6.6	--	-20.2	--
95% CI	(-5.4, 18.7)	--	(-32.7, -7.7)	--
P value vs. HB/APAP	0.2781	--	0.0016	--
Without Rescue Imputation (representative of multimodal therapy in real-world setting)				
LS mean (SE)	153.0 (4.5)	141.0 (4.5)	128.8 (4.7)	140.6 (4.7)
LS mean difference from HB/APAP	12.0	--	-11.8	--
95% CI	(-0.5, 24.4)	--	(-24.8, 1.2)	--
Nominal *P* value vs. HB/APAP*	0.0595	--	0.0752	--

Bertoch T, doi:10.1097/ALN.0000000000005460

Secondary Endpoint

Time to ≥ 2 Point Reduction in NPRS from Baseline Compared to Placebo

	Abdominoplasty		Bunionectomy	
	Suzetrigine N=447	Placebo N=223	Suzetrigine N=426	Placebo N=216
With Rescue Imputation (monotherapy)				
Median time (minutes)	119	480	240	480
95% CI	(90, 180)	(477, 705)	(117, 477)	(476, 716)
Nominal *P* value vs. placebo* (Log rank test)	<0.0001	--	0.0016	--
Without Rescue Imputation (representative of multimodal therapy in real-world setting)				
Median time (minutes)	91	180	122	180
95% CI	(89, 116)	(175, 235)	(115, 177)	(120, 245)
Nominal *P* value vs. placebo† (Log rank test)	<0.0001	--	0.0353	--

ADVOCATE HEALTH

Bertoch T, doi:10.1097/ALN.0000000000005460

Safety Endpoint

Abdominoplasty

	Suzetrigine (n=448)	HB/APAP (n=448)	Placebo (n=222)
Participants with AE's, n(%)	224 (50.0)	272 (60.7)	125 (56.3)
Nausea	85 (19.0)	147 (32.8)	56 (25.2)
Constipation	47 (10.5)	39 (8.7)	24 (10.8)
Headache	19 (4.2)	32 (7.1)	11 (5.0)
Dizziness	18 (4.0)	24 (5.4)	17 (7.7)
Hypotension	11 (2.5)	16 (3.6)	15 (6.8)
Vomiting	10 (2.2)	18 (4.0)	3 (1.4)

Bunionectomy

	Suzetrigine (n=426)	HB/APAP (n=431)	Placebo (n=216)
Participants with AE's, n(%)	132 (31.0)	180 (41.8)	76 (35.2)
Nausea	35 (8.2)	62 (14.4)	23 (10.6)
Constipation	15 (3.5)	22 (5.1)	9 (4.2)
Headache	21 (4.9)	45 (10.4)	20 (9.3)
Dizziness	15 (3.5)	23 (5.3)	11 (5.1)
Hypotension	0	0	1 (0.5)
Vomiting	7 (1.6)	19 (4.4)	6 (2.8)

Bertoch T, doi:10.1097/ALN.0000000000005460

Conclusions

- Suzetrigine was evaluated in two large phase 3 randomized controlled trials for treatment of **acute pain**
  - Bunionectomy and abdominoplasty
- Statistically significant results **against placebo**
  - Proved to be effective as monotherapy/multimodal therapy
- Suzetrigine did not prove to be better than HB/APAP
- Generally safe and well tolerated with lower incidence of AEs compared to HB/APAP

Limitations of Navigate 1/2

- Subjective in nature
- SPID48 is not a validated scoring tool
- Difference in baseline pain between the two procedures
- Patients were permitted to use ibuprofen as a rescue medication
- Numerous exclusions in the supplemental material

Phase 3 Single-Arm Study for Surgical or Non-Surgical Acute Pain

Inclusion: ages 18-80 with mod-severe acute pain on VRS and ≥ 4 on NPRS following surgical procedures or after presenting to a medical facility with non-surgical pain of new origin

- Patients included (N= 256) received suzetrigine 100 mg followed by 50 mg every 12 hours for 14 days or until pain relief

- Permitted to use acetaminophen (650 mg) and ibuprofen (400 mg) every 6 hours as needed for additional pain relief

ADVOCATE HEALTH

McCoun J, doi:10.2147/JPR.S509144

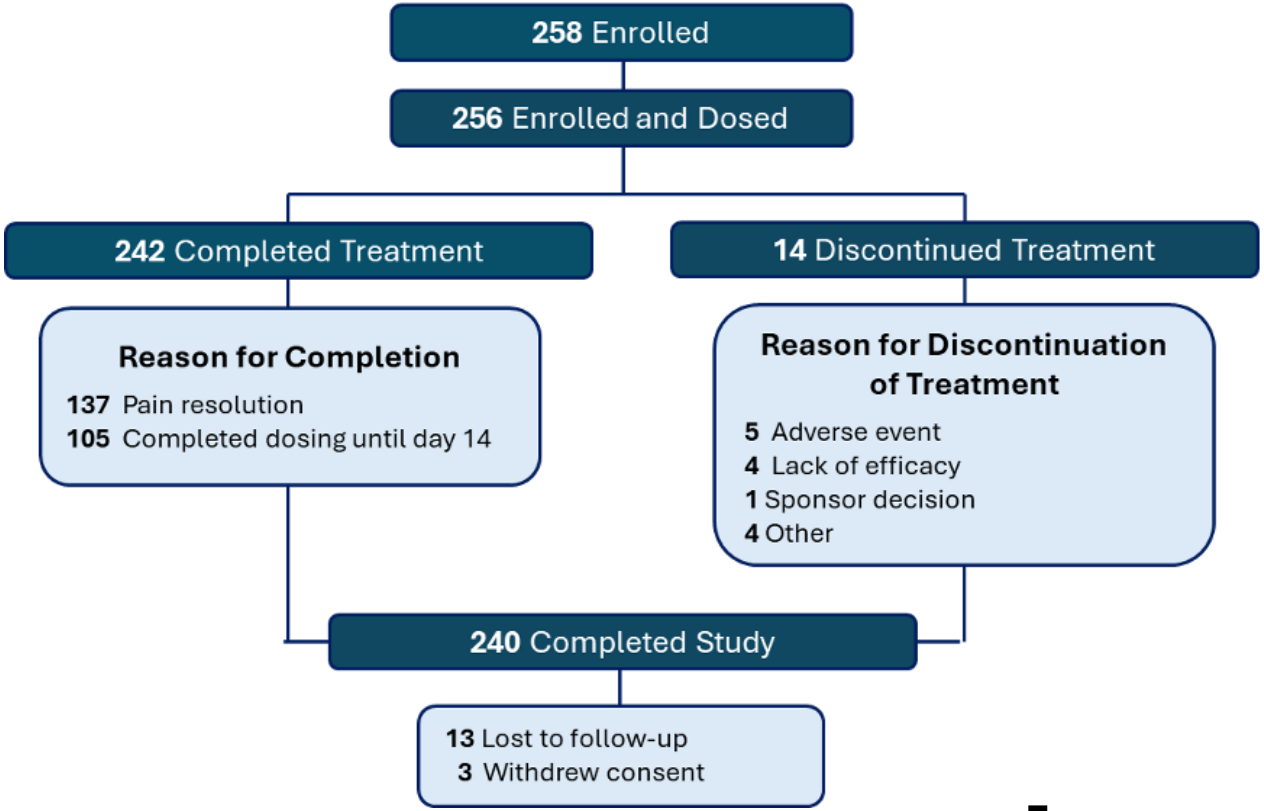
Patient Demographics

	Suzetrigine n=256
Age (years), mean (SD)	43.9 (14.1)
Male, n (%)	83 (32.4)
Female, n (%)	173 (67.6)
White, n (%)	214 (83.6)
African American, n (%)	34 (13.3)
BMI (kg/m2), mean (SD)	29.29 (4.91)
NPRS, mean (SD)	6.7 (1.7)

ADVOCATE HEALTH

McCoun J, doi:10.2147/JPR.S509144

Participants



ADVOCATE HEALTH

McCoun J, doi:10.2147/JPR.S509144

Primary Endpoint

Safety of suzetrigine

	Suzetrigine n=256
Participants with any AEs, n (%)	94 (36.7)
Participants with any AEs by max severity, n (%)	
Mild	71 (27.7)
Moderate	21 (8.2)
Severe	2 (0.8)
Participants with AEs leading to discontinuation, n (%)	5 (2.0)

	Suzetrigine n=256
AEs occurring in ≥2% of participants, n (%)	
Headache	18 (7.0)
Constipation	9 (3.5)
Nausea	8 (3.1)
Fall	6 (2.3)
Rash	5 (2.0)

ADVOCATE HEALTH

McCoun J, doi:10.2147/JPR.S509144

Secondary Endpoint

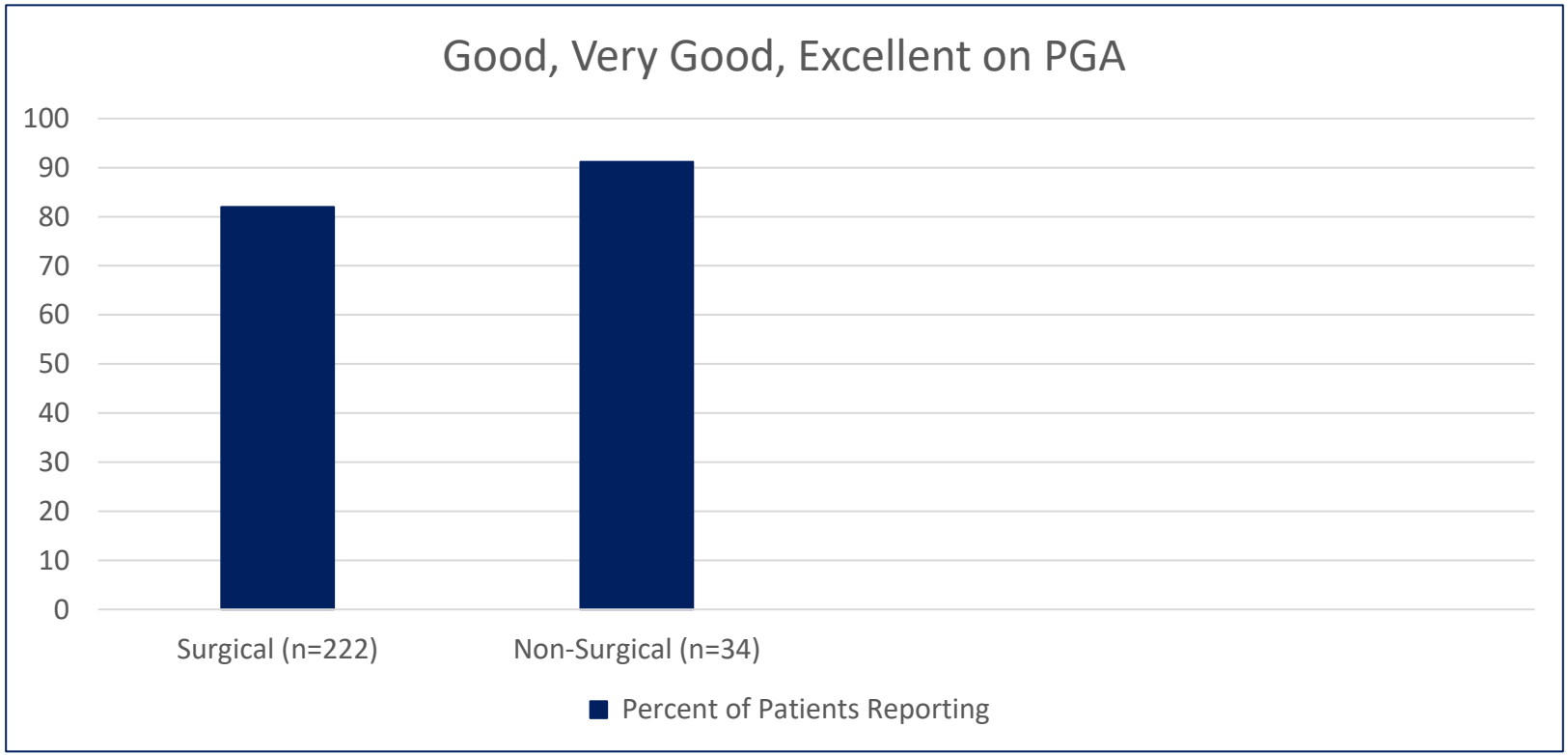
Patient Global Assessment

	Suzetrigine
Reporting good, very good, excellent on the PGA at EOT, n (%)	213 (83.2)
PGA at EOT, n (%)	
Excellent	70 (27.3)
Very Good	92 (35.9)
Good	51 (19.9)
Fair	26 (10.2)
Poor	11 (4.3)
Missing	6 (2.3)

McCoun J, doi:10.2147/JPR.S509144

ADVOCATE HEALTH

Patient Global Assessment



ADVOCATE HEALTH

Conclusions

- Suzetrigine is safe and generally well tolerated
- A high proportion of participants reported good, very good, or excellent on the PGA
- Suzetrigine can be used as monotherapy or with acetaminophen/ibuprofen as part of multimodal therapy

Future Directions

Chronic Pain

Suzetrigine has only been studied in acute pain

Studied in minimally to moderately painful procedures

Need for further studies focusing on related conditions to the MOA of suzetrigine

Ceiling Effect

Only studied at one dose

Can higher doses provide improved analgesia?

Will higher doses cause more side effects?

Outside of Surgical Population

Sample size of nonsurgical patients in McCoun et al.

- 34 out of 256 total patients

Studies performed in relatively healthy individuals

- No history of respiratory, cardiovascular, metabolic, hematologic, neurologic, or psychiatric disease
- Food and drug allergies

Conditions included

- Traumatic and atraumatic acute musculoskeletal pain, orofacial pain, burns, and cutaneous and soft tissue pain

Long Term Data

Current studies are limited to short durations

- Bertoch et al. 48 hours of treatment with follow up at 14 days
- McCoun et al. Max 14 days treatment with follow up at 28 days

Studies with longer durations and follow ups are needed to fully characterize the safety and efficacy profile

Assessment Question #3

Patient JS has a PMH of CKD stage III, OUD, and hypertension. He presents for an elective abdominoplasty. Which of the following pain regimens can you consider post-operatively?

a. HB/APAP 10-325 mg every 4-6 hours as needed
b. Tramadol 100 mg every 4-6 hours as needed
c. Suzetrigine 100 mg then 50 mg every 12 hours + Tylenol 500 mg every 4-6 hours as needed
d. Gabapentin 300 mg three times daily + oxycodone 5 mg every 4-6 hours as needed

Assessment Question #4

Which of the following is a limitation in the way that the medication, suzetrigine, was studied in clinical trials?

a. Studied in two surgical populations
b. Studied with concurrent use of rescue medications
c. Studied for a maximum duration of 14 days
d. All of the above

Conclusions

Pain is a complex condition with multiple contributing factors

Effective pain management involves a multimodal approach

Suzetrigine's selective mechanism makes it an appealing addition to a multimodal pain regimen

Additional studies are needed to determine long term use and safety, beyond the scope of acute surgical pain

References

1. Yam MF, Loh YC, Tan CS, Khadijah Adam S, Abdul Manan N, Basir R. General Pathways of Pain Sensation and the Major Neurotransmitters Involved in Pain Regulation. *Int J Mol Sci*. 2018;19(8):2164. Published 2018 Jul 24. doi:10.3390/ijms19082164
2. Brummett CM, Waljee JF, Goesling J, et al. New Persistent Opioid Use After Minor and Major Surgical Procedures in US Adults. *JAMA Surg*. 2017;152(6):e170504. doi:10.1001/jamasurg.2017.0504
3. Acute Pain Medicine in the United States: A Status Report
4. Acute Pain - International Association for the Study of Pain (IASP)
    - for, A. (2021, July 13). *Acute Pain - International Association for the Study of Pain (IASP)*. International Association for the Study of Pain (IASP). https://www.iasp-pain.org/advocacy/global-year/acute-pain/
5. Osteen JD, Immani S, Tapley TL, et al. Pharmacology and Mechanism of Action of Suzetrigine, a Potent and Selective $Na_V1.8$ Pain Signal Inhibitor for the Treatment of Moderate to Severe Pain. *Pain Ther*. 2025;14(2):655-674. doi:10.1007/s40122-024-00697-0
6. Bertoch T, D'Aunno D, McCoun J, et al. Suzetrigine, a Nonopioid Na V 1.8 Inhibitor for Treatment of Moderate-to-severe Acute Pain: Two Phase 3 Randomized Clinical Trials. *Anesthesiology*. 2025;142(6):1085-1099. doi:10.1097/ALN.0000000000005460
7. McCoun J, Winkle P, Solanki D, et al. Suzetrigine, a Non-Opioid $Na_V1.8$ Inhibitor With Broad Applicability for Moderate-to-Severe Acute Pain: A Phase 3 Single-Arm Study for Surgical or Non-Surgical Acute Pain. *J Pain Res*. 2025;18:1569-1576. Published 2025 Mar 25. doi:10.2147/JPR.S509144
8. Starobova H, Alshammari A, Winkler IG, Vetter I. The role of the neuronal microenvironment in sensory function and pain pathophysiology. *J Neurochem*. 2024;168(11):3620-3643. doi:10.1111/jnc.15724

ADVOCATE HEALTH

References

9. Robinson CL, Schatman ME, Hasoon J, et al. Suzetrigine: Is This What We Have Been Waiting for or Just the Beginning?. *J Pain Res*. 2025;18:2047-2049. Published 2025 Apr 15. doi:10.2147/JPR.S527710

10. Joshi GP. Rational Multimodal Analgesia for Perioperative Pain Management. *Curr Pain Headache Rep*. 2023;27(8):227-237. doi:10.1007/s11916-023-01137-y

11. Nicholas TA 4th, Robinson R. Multimodal Analgesia in the Era of the Opioid Epidemic. *Surg Clin North Am*. 2022;102(1):105-115. doi:10.1016/j.suc.2021.09.003

12. Garland EL. Pain processing in the human nervous system: a selective review of nociceptive and biobehavioral pathways. *Prim Care*. 2012;39(3):561-571. doi:10.1016/j.pop.2012.06.013

13. Waxman SG. Targeting a Peripheral Sodium Channel to Treat Pain. *N Engl J Med*. 2023;389(5):466-469. doi:10.1056/NEJMe2305708

14. Inturrisi CE. Clinical pharmacology of opioids for pain. *Clin J Pain*. 2002;18(4 Suppl):S3-S13. doi:10.1097/00002508-200207001-00002

15. Klimas J, Gorfinkel L, Fairbairn N, et al. Strategies to Identify Patient Risks of Prescription Opioid Addiction When Initiating Opioids for Pain: A Systematic Review. *JAMA Netw Open*. 2019;2(5):e193365. Published 2019 May 3. doi:10.1001/jamanetworkopen.2019.3365

16. Karcz M, Abd-Elsayed A, Chakravarthy K, et al. Pathophysiology of Pain and Mechanisms of Neuromodulation: A Narrative Review (A Neuron Project). *J Pain Res*. 2024;17:3757-3790. Published 2024 Nov 16. doi:10.2147/JPR.S475351

References

17. Baldini A, Von Korff M, Lin EH. A Review of Potential Adverse Effects of Long-Term Opioid Therapy: A Practitioner's Guide. *Prim Care Companion CNS Disord*. 2012;14(3):PCC.11m01326. doi:10.4088/PCC.11m01326

18. Pham A, Yep H, Wozniak S, Javvaji A, Nada E, Bergese S. Beyond Opioids: A Review of Suzetrigine for Acute Pain Management. *Int J Mol Sci*. 2025;26(20):9865. Published 2025 Oct 10. doi:10.3390/ijms26209865

19. Paul AK, Smith CM, Rahmatullah M, et al. Opioid Analgesia and Opioid-Induced Adverse Effects: A Review. *Pharmaceuticals (Basel)*. 2021;14(11):1091. Published 2021 Oct 27. doi:10.3390/ph14111091

Questions?

Maria Hajiharis
maria.hajiharis@aah.org