Pharmaceutical Challenges in Prolonged Neuroprotective Infusion Therapy

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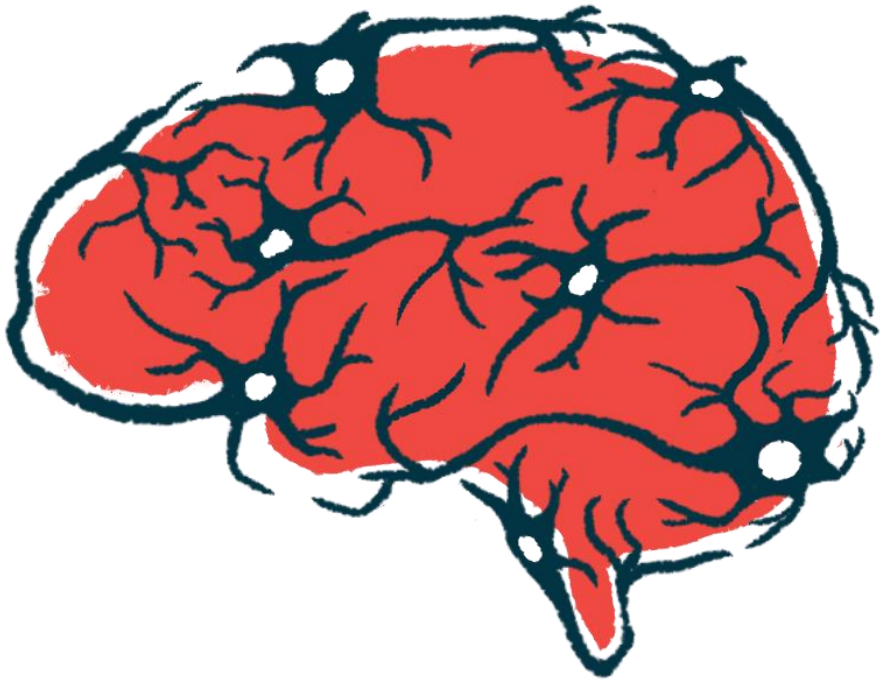
BON SECOURS MERCY HEALTH

Introduction

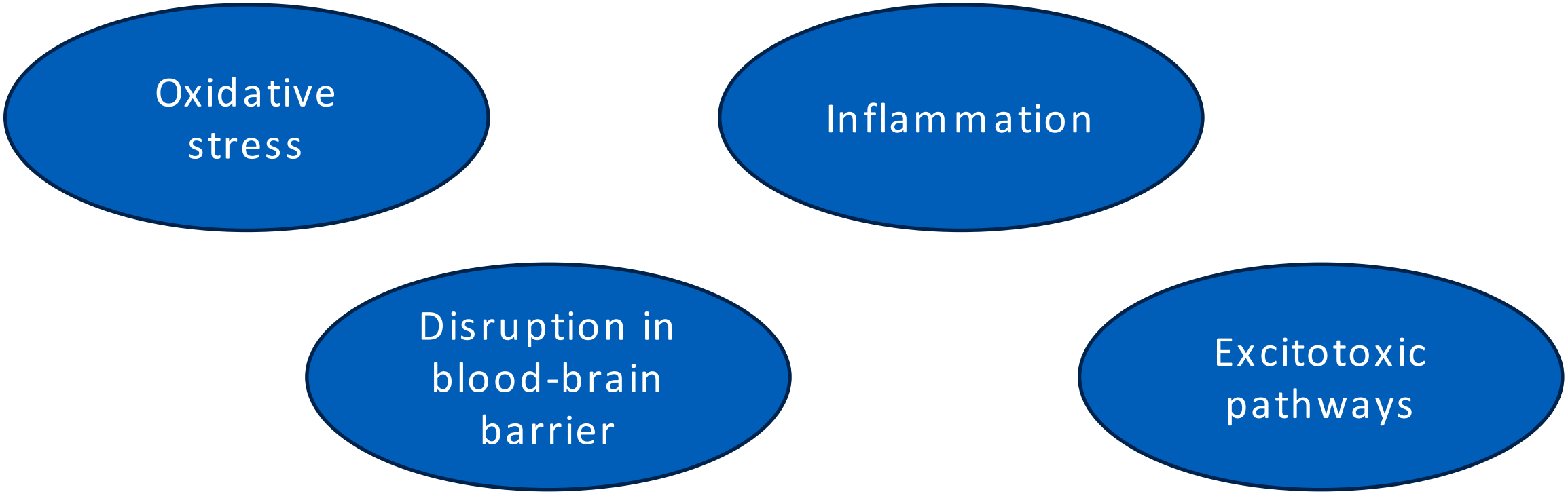
- Advancements in stroke care
- Reperfusion therapy
  - Thrombectomy
  - Thrombolytic therapy

- Neuroprotection
  - Ongoing effort
  - **Future of stroke care?**



Broderick JP. Stroke. 2026 Jan;57(1):275-284.

Mechanism of Neuronal Injury



Farrell D, et al. Curr Anesthesiol Rep. 2018; 8(3), 279–289.

Medication Review

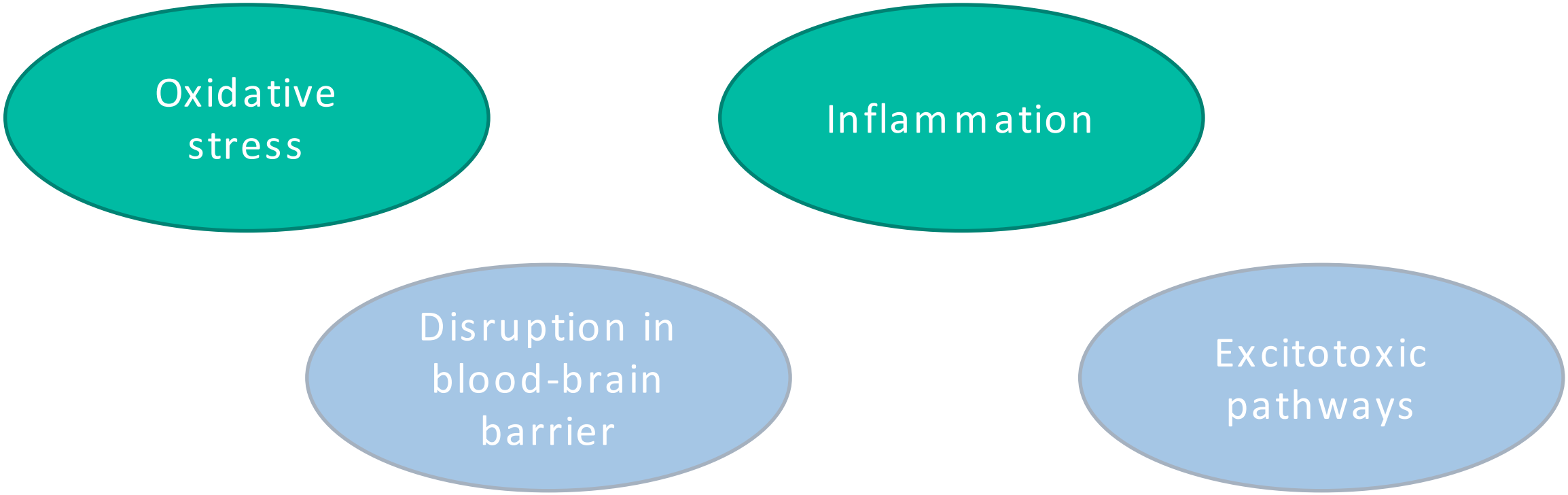
Edaravone

Loberamisal

Medication Review

Edaravone

Edaravone



Xu J, et al. Stroke. 2021 Mar;52(3):772-780.

Edaravone

- Timeline
  - Japan – approved in 2001 (small studies and stroke registries)
  - China – widely used
  - USA – approved in 2017 – Amyotrophic lateral sclerosis (ALS)

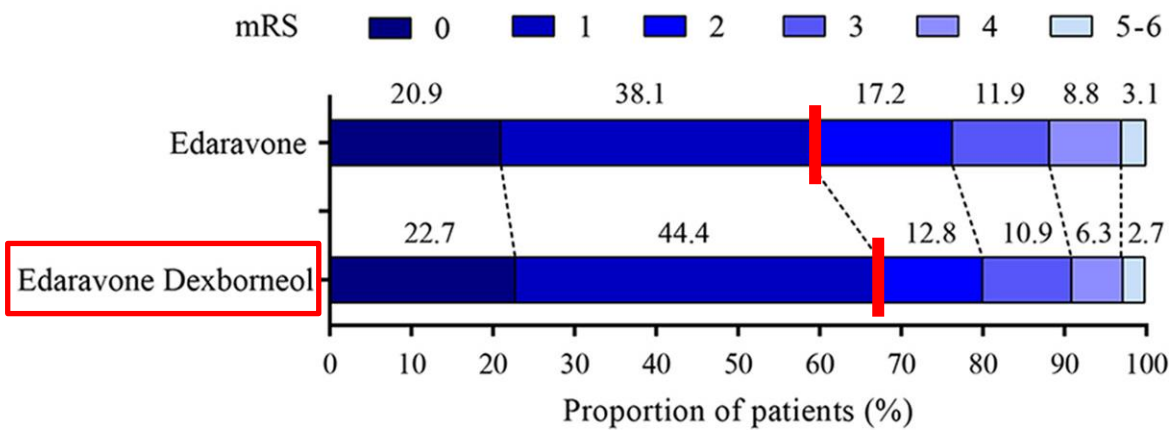
Miyaji Y, et al. NeurolMed Chir. 2015; 55(3):241-247

Edaravone

TASTE Trial 2021

Edaravone dexborneol IV

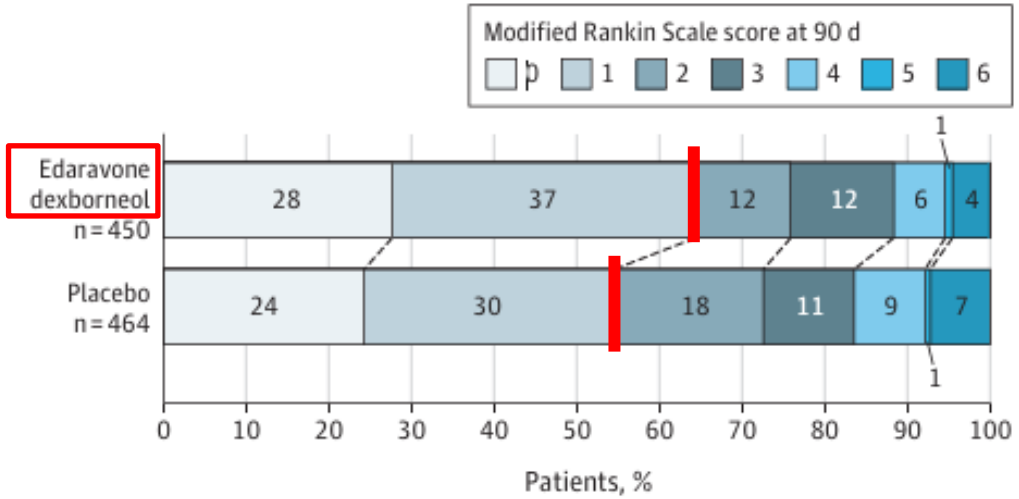
- 37.5 mg IV every 12 hours for 14 days



TASTE-SL 2024

Edaravone dexborneol SL

- 36 mg SL every 12 hours for 14 days



Xu J, et al. Stroke. 2021 Mar;52(3):772-780.; Fu Y, et al. JAMA Neurol. 2024 Feb 19;81(4):319–26.

International Guidelines

Japanese Stroke Guidelines (2021)

- In patients with acute ischemic stroke **Edaravone** is reasonable *(Grade B, LOE Moderate)*

Chinese Stroke Guidelines (2023)

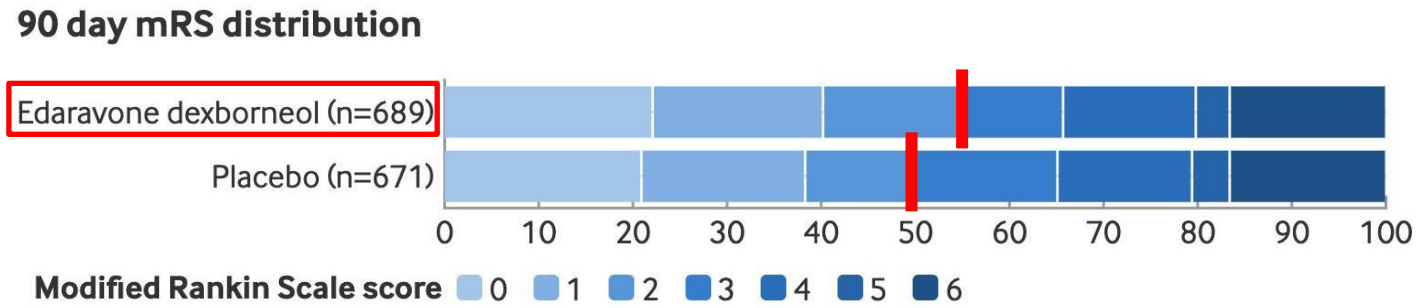
- **Edaravone dexborneol** may improve clinical outcomes in patients with acute ischemic stroke *(IIa, LOE B)*

Miyamoto S, et al. Int J Stroke. 2022 Oct;17(9):1039-1049.; Liu L, et al. Stroke Vasc Neurol. 2023 Dec 29;8(6):e3.

Edaravone

- Limitations
  - Data in Chinese patient population, limited external validity
  - Low median NIHSS (6-7)
  - Exclusion of thrombectomy and/or thrombolysis

- **TASTE 2 Trial (2026)**
  - Targeting patients undergoing thrombectomy (TICI 2b-c in 95%)
  - N=1360
  - 67 yo, NIHSS 15, ASPECTS 9
  - 36% with thrombolytic
  - **Numerical improvement only**



Wang C, et al. BMJ. 2026 Jan 7;392:e086850.

Medication Review

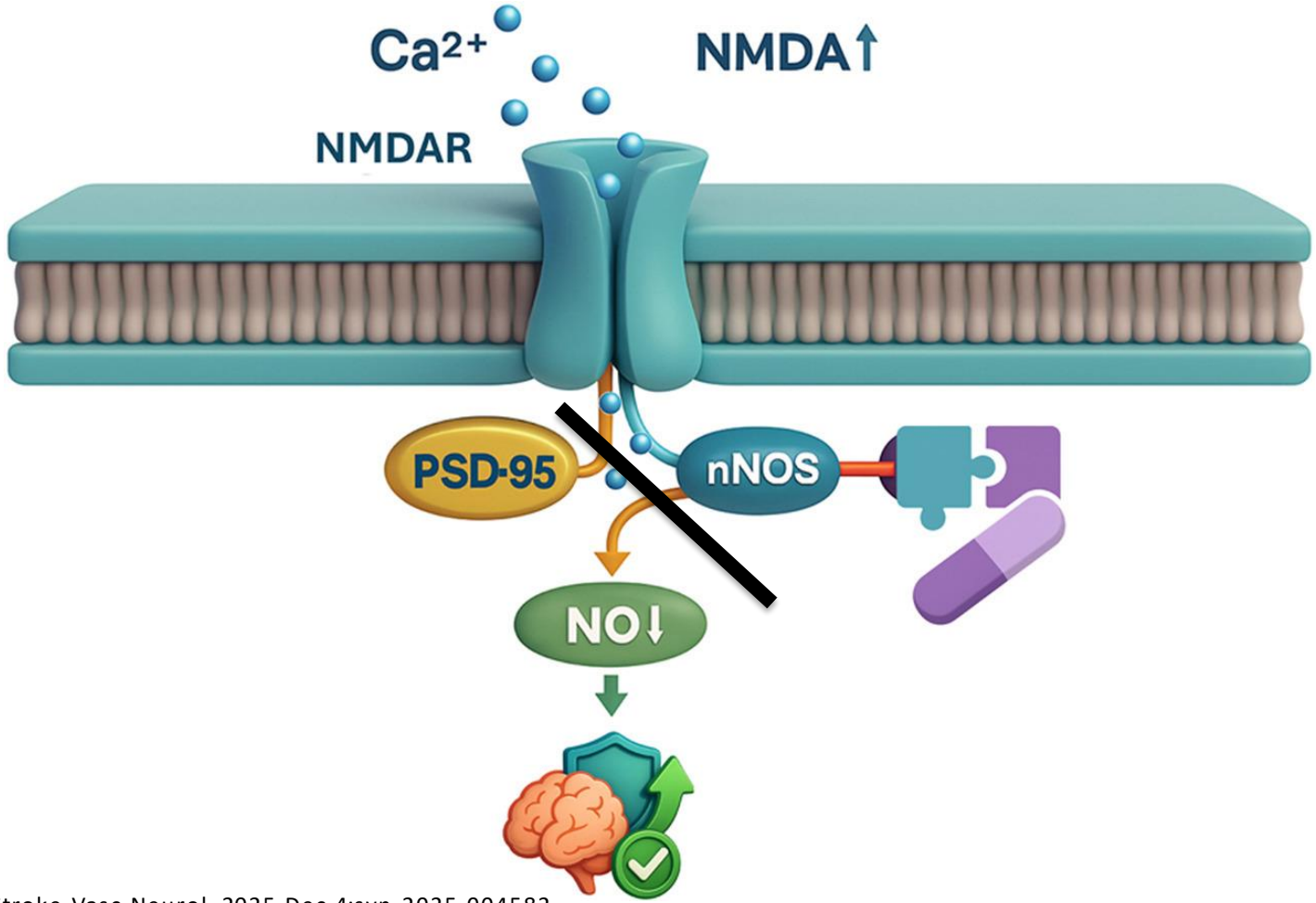
Edaravone

Loberamisal

Medication Review

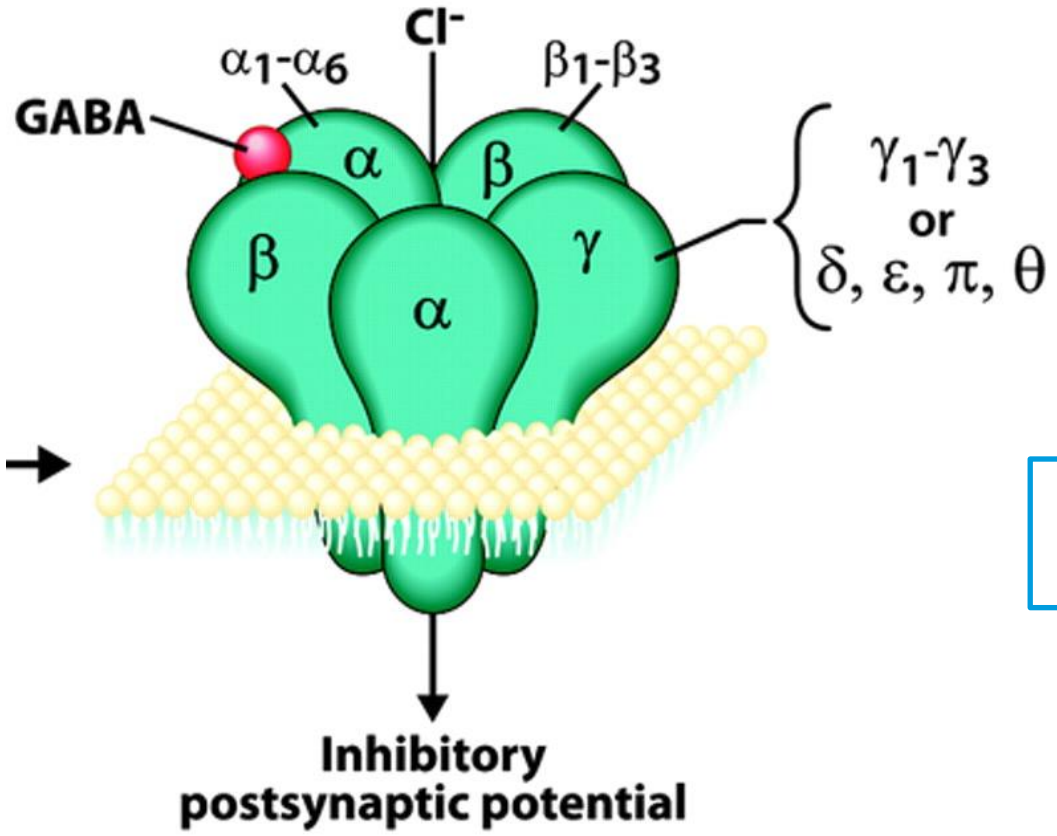
Loberamisal

Excitotoxic pathways



Feng B, et al. Stroke Vasc Neurol. 2025 Nov 10:svn-2025-004581.; Li S, et al. Stroke Vasc Neurol. 2025 Dec 4:svn-2025-004582.

Loberamisal



- Positive allosteric modulator of α2 $GABA_A$ receptors

Treats anxiety and depression

Lack of sedating and amnestic effect

Maintains medication effect

Feng B, et al. Stroke Vasc Neurol. 2025 Nov 10:svn-2025-004581.; Li S, et al. Stroke Vasc Neurol. 2025 Dec 4:svn-2025-004582.

Loberamisal

LAIS Phase III Trial (Publication pending)

- Design
  - Multicenter double blind, placebo-controlled RCT in China
  - Within 48 h of symptom onset, NIHSS 7-20
  - Exclusions: >81 yo, **thrombectomy**, underlying mental disorder, dementia, **depression or anxiety**

Loberamisal 40 mg IV daily over 60 min for 10 days

- Planned sample size of 998 with expected 10% difference

Li S, et al. Stroke Vasc Neurol. 2025 Dec 4:svn-2025-004582.

Loberamisal

LAIS Phase III Trial (Publication pending)

- **Preliminary findings**
  - 13.2% absolute increase in mRS 0-1 at 90 days with loberamisal
  - Reduced rate of depression
  - No difference in rate of side effect
- 17% received thrombolytics

2026, Feb 6, American Stroke Association. [News release]

Loberamisal

- Limitations
  - Data in Chinese patient population, limited external validity
  - Exclusion of thrombectomy and underlying mental disorders
  - Administration duration

Challenges with Neuroprotective Agents

- Lack of sufficient data
- Medication cost
- Hospitalization cost
- Outpatient infusion center
- Alternative formulations
- Widespread use of antidepressant and anxiolytic agents

Conclusions

- AHA/ASA Stroke Guidelines 2026

4.11. Neuroprotective Agents

COR	LOE	Recommendation
3: No Benefit	A	1. At present, in patients with AIS, the use of pharmacological or nonpharmacological neuroprotective treatments is not recommended to improve functional outcome.[1–5]

- TASTE-2 Trial (2026) → Limited benefit
- LAIS Trial (2026) → Promising findings

Prabhakaran S, et al. Stroke. 2026 Jan 26.

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Thank you!

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