MATHEUS MARQUES
MAYOCLINIC
Brexanolone and Zuranolone

1. FDA Approval and Pharmacology

- Brexanolone (Zulresso®) – 1st drug FDA approved for postpartum depression (PPD) moderate-severe
  - Exogenous analog of allopregnanolone. Mechanism of action not fully understood. Thought to be related to its positive allosteric modulation of GABA-A receptors
  - Administered intravenously (100% bioavailability).
  - Half-life of approximately 9 hours.

MPS Fall Program, “On Her Shoulders: The Impact of a Woman’s Mental Health”
Saturday, October 1, 2022
2. Phase III studies
- Double-blind, randomized, placebo-controlled, multicenter studies:
  - Women aged 18 to 45 years
  - 6 months or less postpartum
  - PPD 3rd trimester or 4 weeks postpartum.
- Moderate (HAMD score 20-25) or severe PPD (HAMD ≥ 26)
- After 90-h infusion, patients had significantly larger reductions from baseline in LS mean HAMD total scores than patients in the placebo groups.

Meltzer-Brody et al., Lancet 2018

3. Lessons learned
- HAMD scores were collected before/after infusion from 16 patients
- Lessons learned:
  - Can be effective in cases with prolonged depression and when administered after 6 months postpartum
  - Relief with comorbid symptoms

Patterson et al., Journal of the ACLP 2022

4. Why isn’t brexanolone prescribed more often?
- 60h continuous IV infusion requiring hospitalization with continuous oximetry
- Administration requirements
- Cost (approximately $34,000 not including hospital stay)
- Lack of long-term safety and efficacy data
- Stigma
- Challenging for mothers to spend days away from their newborn babies

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5. Zuranolone

- Zuranolone (SAGE-217) investigational oral neuroactive steroid.
- Not FDA approved.
- GABA-A receptor positive allosteric modulator (PAM).
- In development for the treatment of MDD and postpartum depression.
- Expected submission of the NDA by the first half of 2023.
- Phase III trial for PPD (severe):
  - Significant day 15 improvements from baseline vs placebo.
  - Sustained differences favoring zuranolone were observed from day 3 through day 45.

Deligiannidis et al., JAMA Psychiatry 2021

THANK YOU!