Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Traneurocin (NA-831)

Evidence Summary

A small phase 2a clinical trial showed traneurocin improved cognitive functions in patients with mild cognitive impairment and Alzheimer's disease. The company plans to start two phase 3 programs.

Neuroprotective Benefit: A small phase 2a clinical trial showed improvements in cognitive function in people with mild cognitive impairment and mild/moderate Alzheimer's disease. Larger studies are needed to confirm these findings.

Aging and related health concerns: No evidence exists to date on the efficacy of NA-831 in age-related diseases.

Safety: Phase 1 and phase 2a trials reported that traneurocin was well-tolerated with no adverse effects. However, because the detailed results are not published in a peer-reviewed journal, the full safety profile is unclear.

Availability: not available; in clinical development	**Dose**: not established. In a clinical trial, people with mild cognitive impairment received 10 mg/day, while mild and moderate Alzheimer's patients received 30 mg/day, orally.	**Chemical formula:** not disclosed **MW**: not disclosed
Company: manufactured by NeuroActiva, a subsidiary of BioMed Industries, Inc.		
Half-life: serum half-life of ~7 hours	**BBB**: penetrant	
Clinical trials: A phase 2a trial included 56 patients.	**Observational studies**: none available	

What is it? Traneurocin, also known as NA-831, is a small molecule drug manufactured by NeuroActiva Inc., a subsidiary of BioMed Industries, Inc., a biopharmaceutical company. It is designed to promote neuroprotection, neurogenesis, and memory enhancement (NeuroActiva Inc.; Biomed Industries Inc.). Based on the company website, traneurocin restores neurogenesis by activating synaptic glutamate AMPA receptors and increasing the neurotrophic factor BDNF. AMPA receptors are important for controlling synaptic plasticity and memory functions in the hippocampus. Traneurocin crosses the blood-brain-barrier and has good bioavailability. It is also an endogenous compound, present in the human brain.

Traneurocin is under development for the prevention and treatment of Alzheimer's disease (NeuroActiva Inc.; Biomed Industries Inc.).

Neuroprotective Benefit: A small phase 2a clinical trial showed improvements in cognitive function in people with mild cognitive impairment and mild/moderate Alzheimer's disease. Larger studies are needed to confirm these findings.

Types of evidence:

- a phase 2a clinical trial in mild cognitive impairment and Alzheimer's patients

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function:
In a phase 2a double-blind placebo-controlled clinical trial that included 32 people with mild cognitive impairment (and 24 people with mild or moderate Alzheimer's disease), traneurocin treatment (10 mg per day, orally) for 24 weeks showed better cognitive scores (ADAS-Cog13) by an average of 3.4 points compared to the placebo (p=0.01)(2021 NYAS poster abstract; 2019 CTAD abstract). Based on the Brief Cognitive Rating Scale (BCRS), the effects of traneurocin were apparent after 12 weeks of treatment (p=0.001), with improvements in fatigue, anxiety, irritability, affective lability, disturbance to waking, daytime drowsiness, headache, and nocturnal sleep. Also based on the BCRS, after 24 weeks of treatment, significant improvements were seen in the ability to concentrate, short-term memory, long-term memory, ability to self-care, orientation, and cognitive functions (NeuroActiva website). Results of this study have not been published in a peer-reviewed journal, so details of its results cannot be fully evaluated.

Human research to suggest benefits to patients with dementia:
In a phase 2a double-blind placebo-controlled clinical trial that included 24 people with mild or moderate Alzheimer's disease (and 32 people with mild cognitive impairment), traneurocin treatment (30 mg per day, orally) for 24 weeks resulted in better cognitive scores (ADAS-Cog13) by an average of 4.1 points compared to the placebo group (p=0.001)(2021 NYAS poster abstract; 2019 CTAD abstract). A media article from 2019 reported that in Alzheimer's disease patients, there was less decrease in ADAS-Cog scores than those treated with placebo (−4.7 vs −8.6; p=0.001)(PracticalNeurology.com). The Clinician's Interview-Based Impression of Change Plus Caregiver Input (CIBIC-plus) showed that 82.1% of patients improved (p=0.01)(NeuroActiva website). In the placebo group, only 21.7% showed improvement in CIBIC-Plus (PracticalNeurology.com). After 12 weeks of treatment with traneurocin, the Brief Cognitive Rating Scale (BCRS) showed significant effects (p=0.001), with improvements in fatigue, anxiety, irritability, affective lability, disturbance to waking, daytime drowsiness, headache, and nocturnal sleep (2019 CTAD abstract). Also based on the BCRS, after 24 weeks of treatment, significant improvements were seen in the ability to concentrate, short-term memory, long-term memory, ability to self-care, orientation, and cognitive functions (NeuroActiva website). Results of this study have not been published in a peer-reviewed journal, so details of its results cannot be fully evaluated.

Mechanisms of action for neuroprotection identified from laboratory and clinical research:
Based on the company website, traneurocin restores neurogenesis by activating synaptic glutamate AMPA receptors and increasing the neurotrophic factor BDNF. Based on a 2018 poster abstract, traneurocin promoted neuroprotection, neurogenesis, and cognitive function in aged mice and in a

model of Alzheimer's disease (2018 AAIC poster abstract). Traneurocin also promoted regeneration of human neural stem cells. Because no preclinical or laboratory data regarding traneurocin have been published in a peer-reviewed journal, its effects or precise mechanism of action cannot be fully evaluated.

APOE4 interactions: Unknown.

Aging and related health concerns: No evidence exists to date on the efficacy of NA-831 in age-related diseases.

Types of evidence:

- None

No evidence exists to date on the efficacy of NA-831 in age-related diseases. There are several clinical studies that are ongoing in people with COVID-19 (ClinicalTrials.gov).

Safety: Phase I and phase 2a trials reported that traneurocin was well-tolerated with no adverse effects. However, because the detailed results are not published in a peer-reviewed journal, the full safety profile is unclear.

Types of evidence:

- a phase I study
- a phase 2a clinical trial in mild cognitive impairment and Alzheimer's patients

According to a conference abstract, in phase I studies, NA-831 treatment did not result in adverse effects and it was well-tolerated up to 100 mg/day in healthy volunteers (2021 CTAD abstract). Pharmacokinetics data showed dose-dependent exposure linearity and low variability.

Based on a 2018 conference abstract, the first 2 cohorts of the phase I trial received an oral dose of placebo on day 1, followed by 5 mg of traneurocin on days 2 and 3, then 10 mg on days 4 and 5, then 20 mg on days 6 and 7 (2018 AAIC poster abstract). The second 2 cohorts received placebo on day 1, followed by 30 mg of traneurocin on days 2 and 3; then 40 mg on days 4 and 5, followed by 50 mg on days 6 and 7. Traneurocin was rapidly absorbed with Cmax at 2-3 hours post-dose with linear

pharmacokinetics. The mean serum half-life was approximately 7 hours and consistent across doses. Traneurocin was well-tolerated up to a maximum dosage of 50 mg per day and no adverse effects were reported.

In a phase 2a double-blind placebo-controlled clinical trial that included 32 people with mild cognitive impairment and 24 people with mild or moderate Alzheimer's disease, traneurocin treatment (10 mg/day, orally, for mild cognitive impairment; 30 mg/day, orally, for Alzheimer's patients) for 24 weeks was well-tolerated and no adverse effects were observed (2019 CTAD abstract).

The phase I and phase 2a trial results are not publicly available and have not been published in peer-reviewed journals. While conference abstracts and the company website noted there were no adverse effects observed, it is not clear if there were zero cases of adverse events recorded. If there were some adverse events, it is not evident what types of adverse events occurred and their rates.

Drug interactions: Drug interactions with traneurocin have not been documented.

Sources and dosing: Traneurocin is under development for the prevention and treatment of Alzheimer's disease (NeuroActiva Inc.; Biomed Industries Inc.). In a phase 2a clinical trial, people with mild cognitive impairment received 10 mg/day, orally, while mild and moderate Alzheimer's patients received 30 mg/day, orally (2021 NYAS poster abstract; 2019 CTAD abstract).

Research underway: Based on ClinicalTrials.gov, there are 2 clinical trials investigating traneurocin as part of a combination therapy for the treatment of COVID-19. One is a phase 2/3 trial evaluating 4 treatment strategies for hospitalized COVID-19 patients: traneurocin, traneurocin+atazanavir, traneurocin+dexamethasone, and atazanavir+dexamethasone (NCT04452565). The other is a phase 3 trial evaluating the safety and efficacy of the oral polio vaccine and traneurocin for COVID-19 (NCT04540185).

NeuroActiva plans to conduct two phase 3 trials for traneurocin (neuroactiva.com; 2019 CTAD abstract). The COGNITION Program aims to enroll 375 patients with mild and moderate Alzheimer's disease testing a dose of 30 mg/day, orally, over 12 months. The PREVENTION Program aims to enroll 550 subjects who are high risk but asymptomatic, testing a dose of 10 mg/day, orally, over 24 months.

Search terms:

Pubmed, Google:

- Traneurocin, NA-831

Websites visited for: traneurocin, NA-831

- Clinicaltrials.gov
- NIH RePORTER (0)
- Drugs.com (0)
- WebMD.com (0)
- PubChem (0)
- DrugBank.ca (0)
- Cafepharma (0)
- Pharmapro.com (0)