Clinical Trial Report: Evaluation of ND-300 for Type 3 Diabetes Management

Introduction:
This clinical trial assesses the potential of a novel drug, ND-300, in managing Type 3 diabetes or diabetes secondary to Alzheimer's disease (AD). Type 3 diabetes is characterized by insulin resistance and impaired glucose metabolism in the brain, often accompanying AD. ND-300 is a unique formulation designed to enhance cerebral insulin sensitivity and improve cognitive function. This randomized, controlled trial aims to determine ND-300's efficacy in improving glycemic control and cognitive symptoms associated with Type 3 diabetes.

Methods:
Study Design:
The study enrolled 160 participants diagnosed with mild to moderate Alzheimer's disease and concomitant Type 3 diabetes. Participants were randomized in a 1:1:1 ratio to receive ND-300 at a low dose, ND-300 at a high dose, or a placebo once daily for a period of 52 weeks. The double-blind, placebo-controlled trial evaluated the drug's impact on glycemic control, cognitive function, and brain imaging outcomes.

Inclusion Criteria:
• Age between 50 and 85 years
• Diagnosis of Alzheimer's disease and Type 3 diabetes
• Mini-Mental State Examination (MMSE) score between 16 and 26
• HbA1c level ranging from 5.7% to 10.0%

Exclusion Criteria:
• History of other types of dementia or significant neurological disorders
• Uncontrolled hypertension or cardiovascular disease
• Renal or hepatic impairment
• Pregnancy or breastfeeding

Outcome Measures:
The primary outcome measure was the change in insulin sensitivity in the brain, assessed by positron emission tomography (PET) imaging of cerebral glucose metabolism, from baseline to Week 52. Secondary outcome measures included glycemic control as indicated by HbA1c levels, cognitive function evaluated using the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-COG), and brain volumetric analysis using MRI. Safety assessments included adverse event monitoring, vital sign measurements, and clinical laboratory tests.

Results:
Primary Outcome:
Both doses of ND-300 significantly improved cerebral insulin sensitivity compared to the placebo group. The low dose of ND-300 resulted in a mean increase in cerebral glucose metabolism of 12.8%, while the high dose showed a 16.2% increase, both achieving statistical significance ($p<0.001$).

Secondary Outcomes:
• HbA1c levels demonstrated a dose-dependent reduction with ND-300 treatment, with the high dose showing a significant decrease of -0.4% from baseline ($p<0.05$).
• ADAS-COG scores improved significantly in both ND-300 groups, indicating potential cognitive benefits ($p<0.01$).
• Brain volumetric analysis revealed that ND-300 slowed the rate of hippocampal atrophy, with a mean change of -0.4% in the low dose group and -0.2% in the high dose group, compared to -1.2% in the placebo group ($p<0.01$).

Safety:
ND-300 was generally safe and well-tolerated. Mild adverse events, including dizziness and sleepiness, were reported in some participants but resolved without intervention. No serious drug-related adverse events or changes in vital signs were observed. Clinical laboratory tests did not reveal any safety concerns.

Conclusion:
ND-300 administration resulted in significant improvements in cerebral insulin sensitivity, glycemic control, and cognitive function in participants with Type 3 diabetes and Alzheimer's disease. Furthermore, ND-300 showed potential in slowing brain atrophy, a key aspect of AD pathophysiology. The drug's safety profile appeared encouraging, with manageable mild adverse events. These findings

highlight ND-300's potential as a novel therapeutic approach for Type 3 diabetes and warrant further investigations in larger datasets.

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