

DISRUPTIVE COMBINATION
AGAINST NEUROLOGICAL DISORDERS

Study THN201-101
Key Results

A Pharmacodynamics,
Safety, and Pharmacokinetics
Study of THN201 Versus Donepezil
in Healthy Male Volunteers

ClinicalTrials.gov : NCT03698695

January 15th, 2020

▲ NEURONAL NETWORK
● GLIAL NETWORK

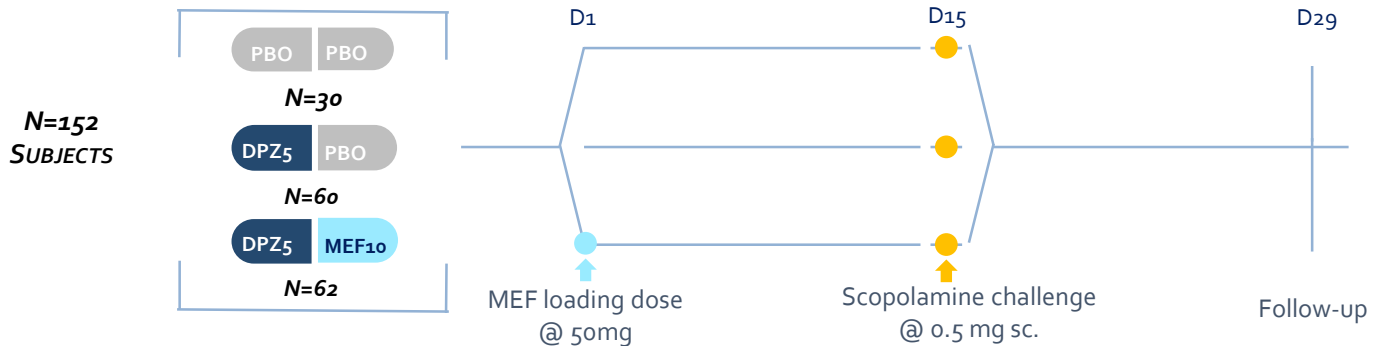




THN201-101 : STUDY DESIGN

A PHARMACODYNAMICS, SAFETY, AND PHARMACOKINETICS STUDY OF THN201 VERSUS DONEPEZIL (DPZ) IN HEALTHY MALE SUBJECTS

A DOUBLE-BLIND, RANDOMIZED, PARALLEL-GROUP, PLACEBO & ACTIVE CONTROLLED STUDY
(10 SITES IN EUROPE - PI: PROF. REGIS BORDET, LILLE)



PHARMACODYNAMIC ENDPOINTS :

COGNITIVE FUNCTION: COGNITIVE DRUG RESEARCH (CDR) COMPUTERIZED ASSESSMENT

EEG: QUANTITATIVE EEG (QEEG), EVENT RELATED POTENTIALS (P300).

SAFETY AND PK ENDPOINTS



THN201-101 : KEY RESULTS

DEMOGRAPHICS

- 152 healthy male subjects randomized (62 THN; 60 DPZ; 30 Placebo)
- 147 subjects completed the study (60 THN201 ; 58 DPZ ; 29 Placebo)
- Small number of drop-outs : 5 drop-outs (2 THN201 ; 2 DPZ ; 1 Placebo)
 - THN201 : 1 discontinuation for adverse event, 1 discontinuation for withdrawal by subject
 - DPZ : 1 discontinuation for adverse event, 1 discontinuation for withdrawal by subject
 - Placebo : 1 discontinuation for adverse event

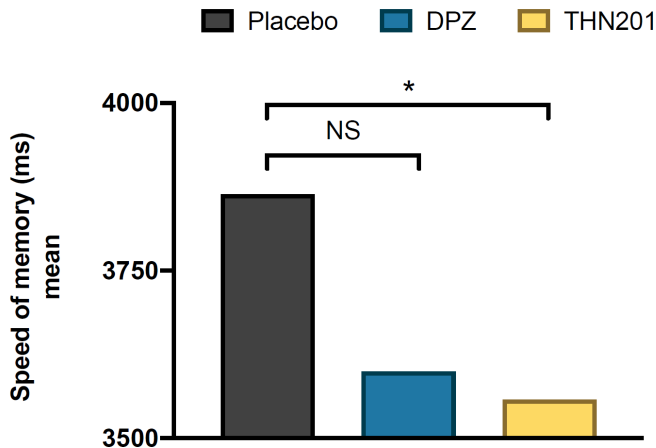


THN201-101 : KEY RESULTS

SPEED OF MEMORY

- « **Speed of memory** » is a composite endpoint of the CDR assessment ; this endpoint is typically considered to be one of the most sensitive to decline in AD patients over time (Wesnes et al, 2010).

Speed of memory
Day 15, 1 hour after scopolamine challenge



* p=0.04, THN201 vs Placebo
NS, non-significant, DPZ vs Placebo
(ANCOVA estimate)

CONCLUSION :

- Significant increase of speed of memory by THN201 vs Placebo (p=0.04) at 1 h post scopolamine challenge
- No significant effect of DPZ vs Placebo

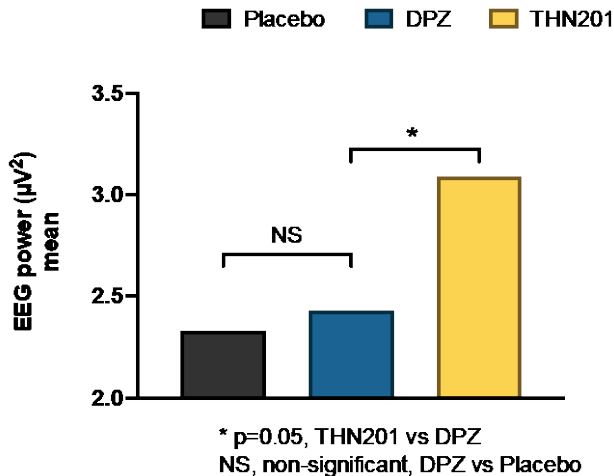


THN201-101 : KEY RESULTS

EEG POWER IN THE GAMMA BAND

- EEG power has been quantified during scopolamine challenge and the gamma band (30-40 Hz) has been extracted.
- **EEG gamma band** is recognized as a marker of cognitive activity (Herrmann et al, 2001 ; Fitzgibbon et al, 2004) ; an increase in this band is considered as beneficial for AD patients (Herrmann et al, 2005).

EEG power in the gamma band [30-40 Hz]
Day 15, 1 hour after scopolamine challenge



CONCLUSION :

- Significant increase of EEG power on gamma band by THN201 vs DPZ (p=0.05) at 1 h post scopolamine challenge
- No significant effect of DPZ vs Placebo

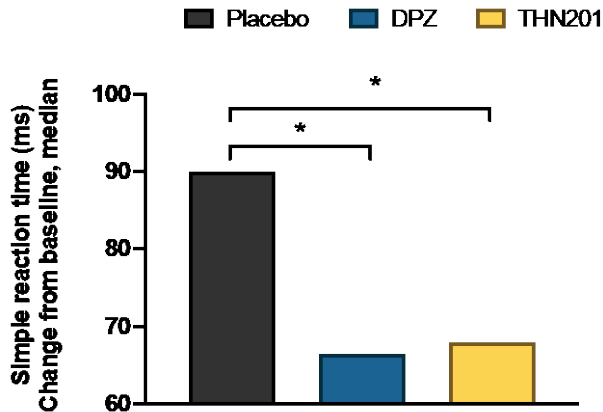


THN201-101 : KEY RESULTS

ATTENTION: SIMPLE REACTION TIME

- Simple Reaction Time is a task used to quantify Attention.

Simple reaction time
Day 15, 1 hour after scopolamine challenge



* $p=0.03$ for THN201 vs Placebo

* $p=0.04$ for DPZ vs Placebo

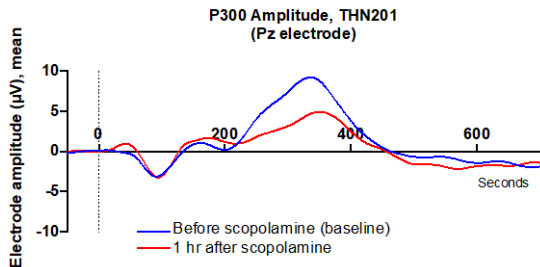
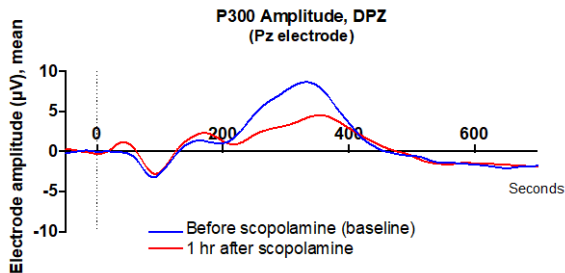
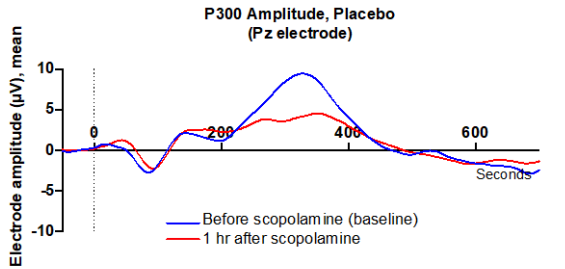
CONCLUSION :

- Significant improvement of Simple Reaction Time by THN201 ($p=0.03$) and DPZ ($p=0.04$) vs Placebo at 1 h post scopolamine challenge



THN201-101 : KEY RESULTS

EVENT RELATED POTENTIALS (P300)



- The **P300 (P3) wave** is an event-related potential (ERP) component linked to attentional processes and decision making.
- P300 is altered during scopolamine challenge.

CONCLUSION :

- P300 is strongly impaired 1 hr after scopolamine challenge
- Similar P300 profiles in all three groups, further analysis may be required



THN201-101 : KEY RESULTS

SAFETY AND TOLERABILITY

- **Adverse events (attributed to treatment):**
 - THN201 : Nausea , headache, fatigue, insomnia
 - DPZ : Nausea , headache, GI symptoms, insomnia, irritability
 - Placebo : Headache, fatigue, irritability

CONCLUSION :

- Overall THN201 very well tolerated.
- Similar TEAE profile for THN201 and DPZ, with mild to moderate intensity, mostly attributable to DZP effects
- No serious adverse event



THN201-101 : KEY RESULTS CONCLUSIONS

- Pharmacological profile of THN201
 - Stronger mnemonic fluidity observed during cognitive tests (CDR Speed of Memory) compared to Donepezil alone
 - Stronger activity in the Gamma band of EEG which is involved in cognitive processes compared to Donepezil alone
 - Similar profile to Donepezil on other pharmacodynamic parameters

Enlargement of the effect of Donepezil by Mefloquine in favour of a reinforcement of executive processes

- The tolerance profile of THN201 is similar to that of Donepezil