NUTRICIA

Souvenaid®

For Healthcare Professional use only – not for distribution to the general public

Clinical Trials with Souvenaid®

2025

SOUVENAID® IS A FOOD FOR SPECIAL MEDICAL PURPOSES FOR THE DIETARY MANAGEMENT OF EARLY ALZHEIMER'S DISEASE AND MUST BE USED UNDER MEDICAL SUPERVISION. SOUVENAID® DOES NOT CURE OR ALLEVIATE ALZHEIMER'S DISEASE

Note:This page has been intentionally left blank

Introduction

Alzheimer's disease (AD) is the most common form of dementia. There were more than 421,000 Australians in 2024 living with dementia. This number is projected to rise to more than 812,000 by 2054.
It is estimated that in 2024 more than 1.6 million people in Australia are involved in the care of a person with dementia and two thirds of people with dementia are living in the community[1]

AD is distinguished by brain atrophy in both brain cell death and synapse loss.
The physiological hallmarks of AD are well documented and include presence of neuronal fibrillary tau tangles and amyloid plaque (Figure 1). While aggregates of amyloid and tau have been associated with neuronal loss, they are not well correlated to cognitive decline. The strongest correlate of cognitive decline in AD and mild cognitive impairment (MCI) is synaptic loss[2].
There is evidence that these pathophysiological changes of Alzheimer's Disease precede changes in cognition and often the diagnosis of AD (Figure 2). And this preclinical phase allows opportunity for therapeutic intervention[3].

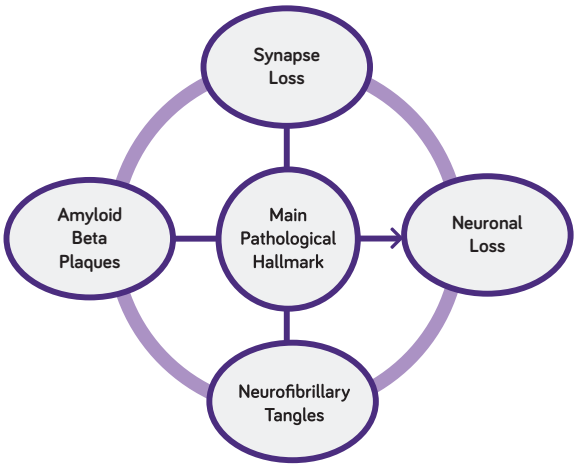


Figure 1: Main pathological hallmarks of Alzheimer's Disease[3]

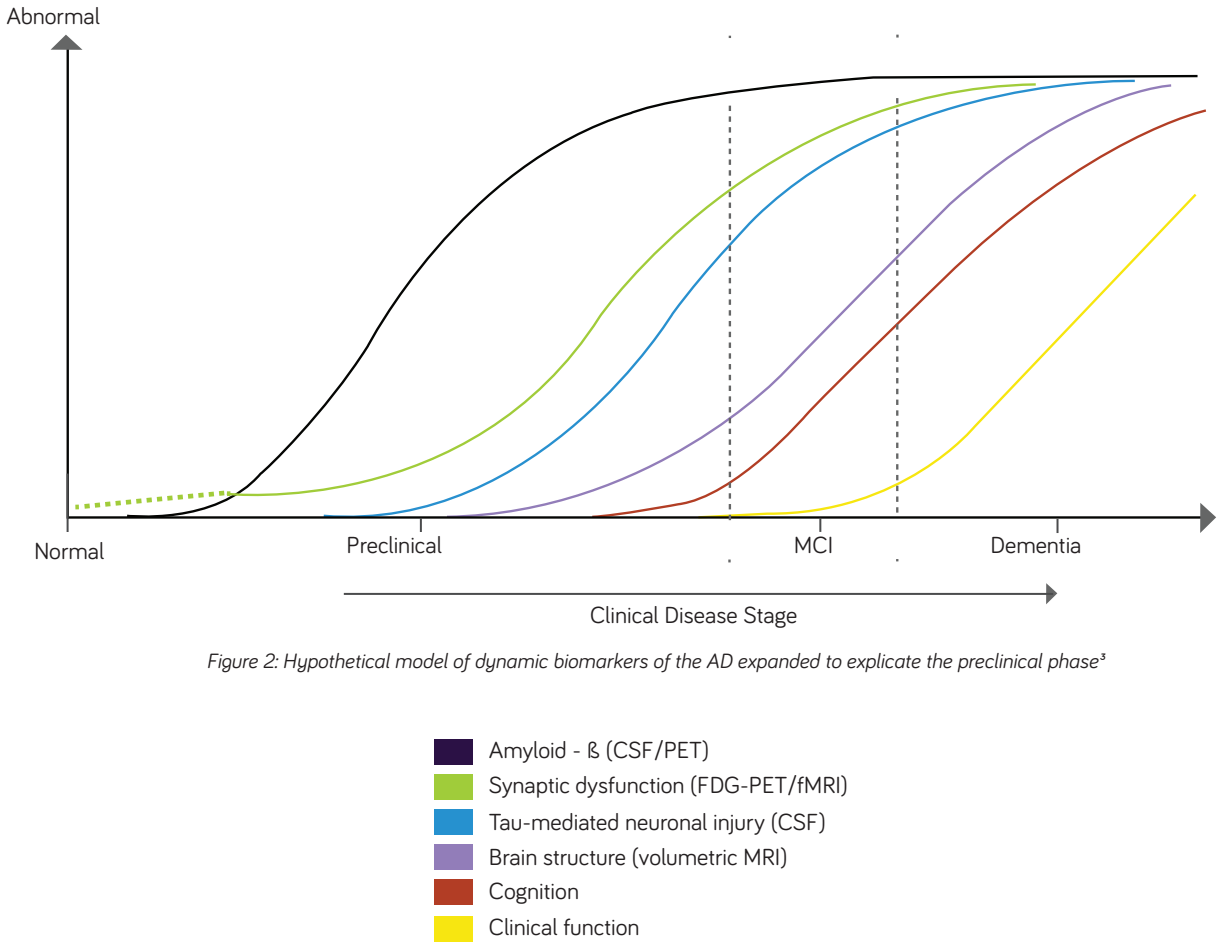


Figure 2: Hypothetical model of dynamic biomarkers of the AD expanded to explicate the preclinical phase[3]

Synapses are continuously being remodelled and their formation depends on the production of neuronal membranes. Neuronal membranes are formed via the Kennedy pathway (Figure 3). This pathway is dependent on nutritional coenzymes which act as rate limiting elements. Shortage of one of these elements deems the pathway inactive[4]. Fortasyn® Connect, the nutrient combination in Souvenaid®, has been developed to specifically meet the nutritional needs of the Kennedy pathway.

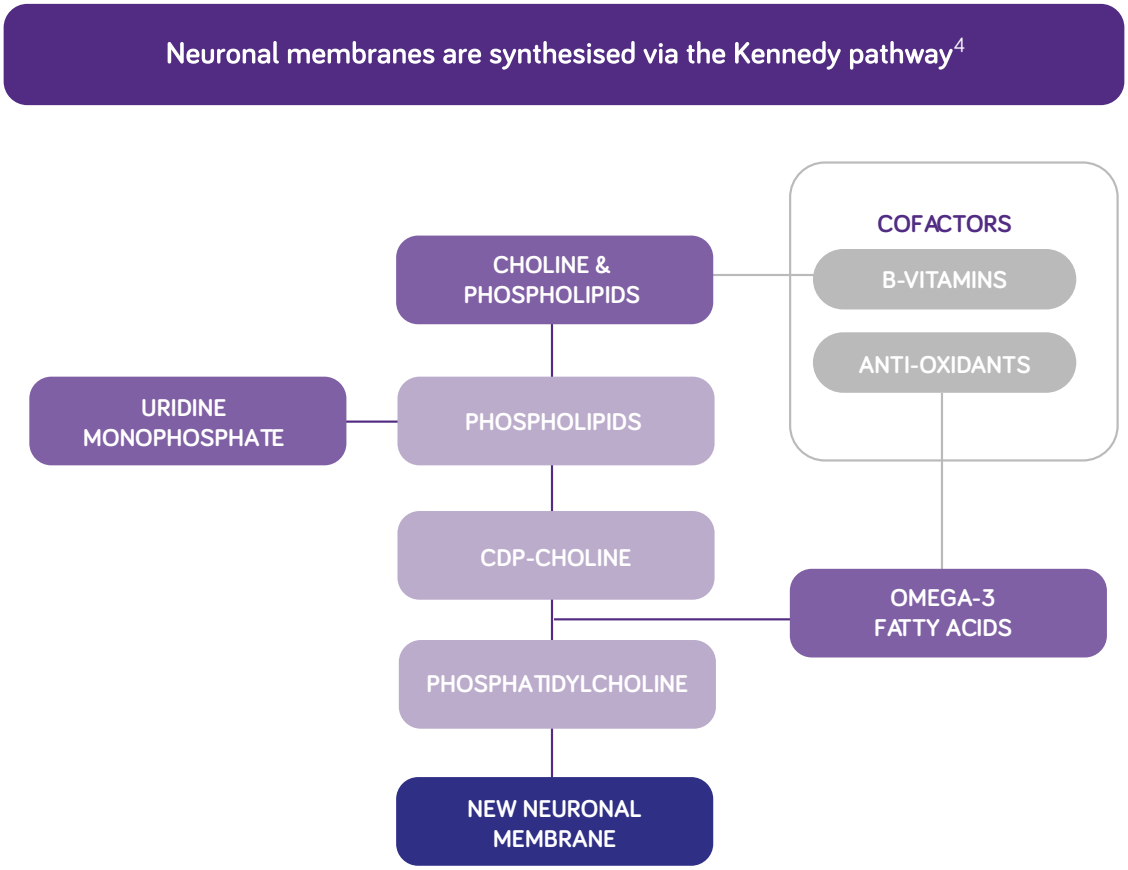
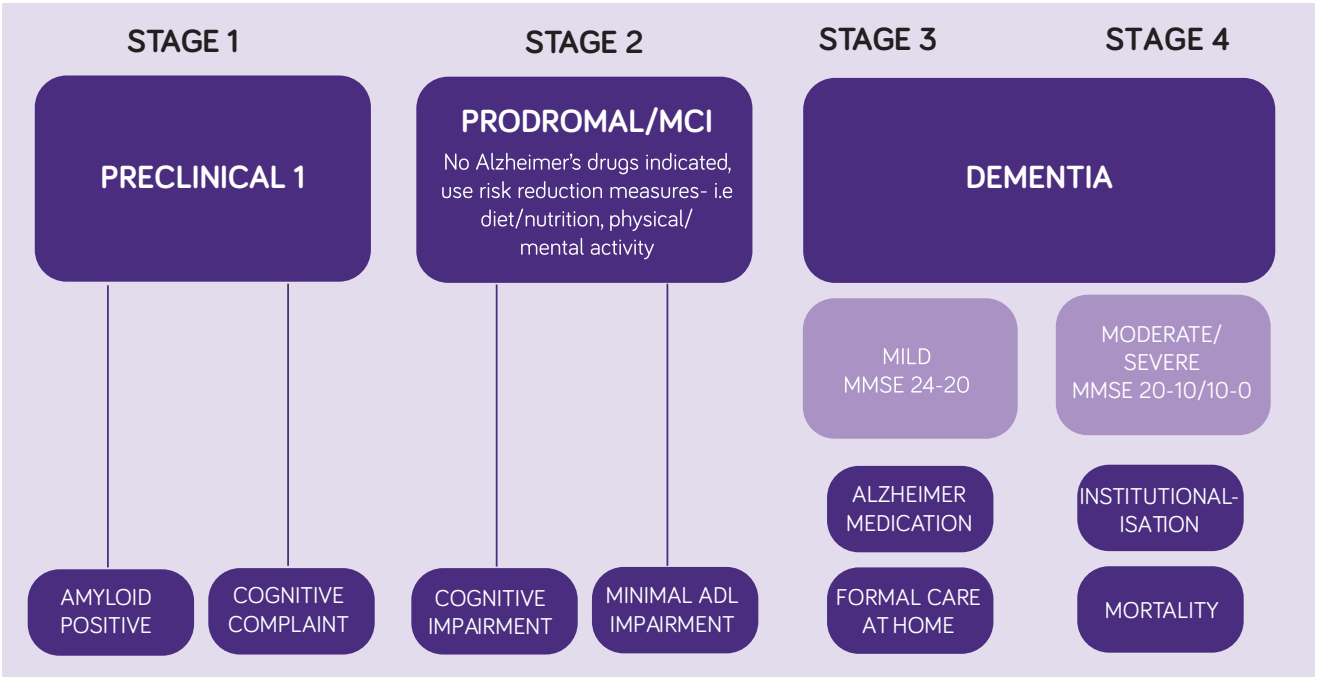


Figure 3: Neuronal membranes are synthesized by the Kennedy pathway[4]

This booklet will present the current evidence of Souvenaid® and its role in AD (including MCI)



AD - Alzheimer's Disease; **MCI** - mild cognitive impairment; **MMSE**- mini mental

CONTENTS

PUBLICATIONS

Note: Some studies refer to Souvenaid® and others refer to Fortasyn® Connect. Fortasyn® Connect is the nutritional engine that is in Souvenaid®. Souvenaid® and Fortasyn® Connect have been used interchangeably throughout this evidence book.

Abbreviations and Acronyms

AChEI	Acetylcholinesterase Inhibitor
AD	Alzheimer's Disease
ADAS-cog	Alzheimer Disease Assessment Scale – Cognitive Subscale
BAYER-S	Bayer Activities of Daily Living Scale
BHM	Bayesian Hierarchical Modelling
BLS-D	Blessed Dementia Scale
BNT	Boston Naming Test
BPSD	Behavioural and Psychological Symptoms of Dementia
CDR—SB	Clinical Dementia Rating – Sum of Boxes
CERAD	Consortium to Establish a Registry for Alzheimer's Disease
DBRCT	Double Blind Randomised Controlled Trial
DHA	Docosahexaenoic Acid
EEG	Electroencephalography (EEG)
GDS	Geriatric Depression Scale
GST	Global Statistical Test
GTCT	Global Time Component Test
MCI	Mild Cognitive Impairment
MMSE	Mini Mental State Examination (MMSE)
MRI	Magnetic Resonance Imaging (MRI)
NPI	Neuropsychiatric Inventory
NTB	Neuropsychological Test Battery
PVFT	Phonemic Verbal Fluency Test
RAVLT	Rey Auditory Verbal Learning Test
RCT	Randomised Controlled Trial (RCT)
RDRS2	Rapid Disability Rating Scale 2
SDMT	Symbol Digit Modalities Test
SVFT	Semantic Verbal Fluency Test
TMT	Trail Making Test
TCT	The Component
WMS-r	Wechsler Memory Scale – Revised

Efficacy of a medical food in mild Alzheimer's disease: A randomized controlled trial[5]

Scheltens et al 2010

Souvenir I

12 weeks
Double-blind RCT
Mild AD

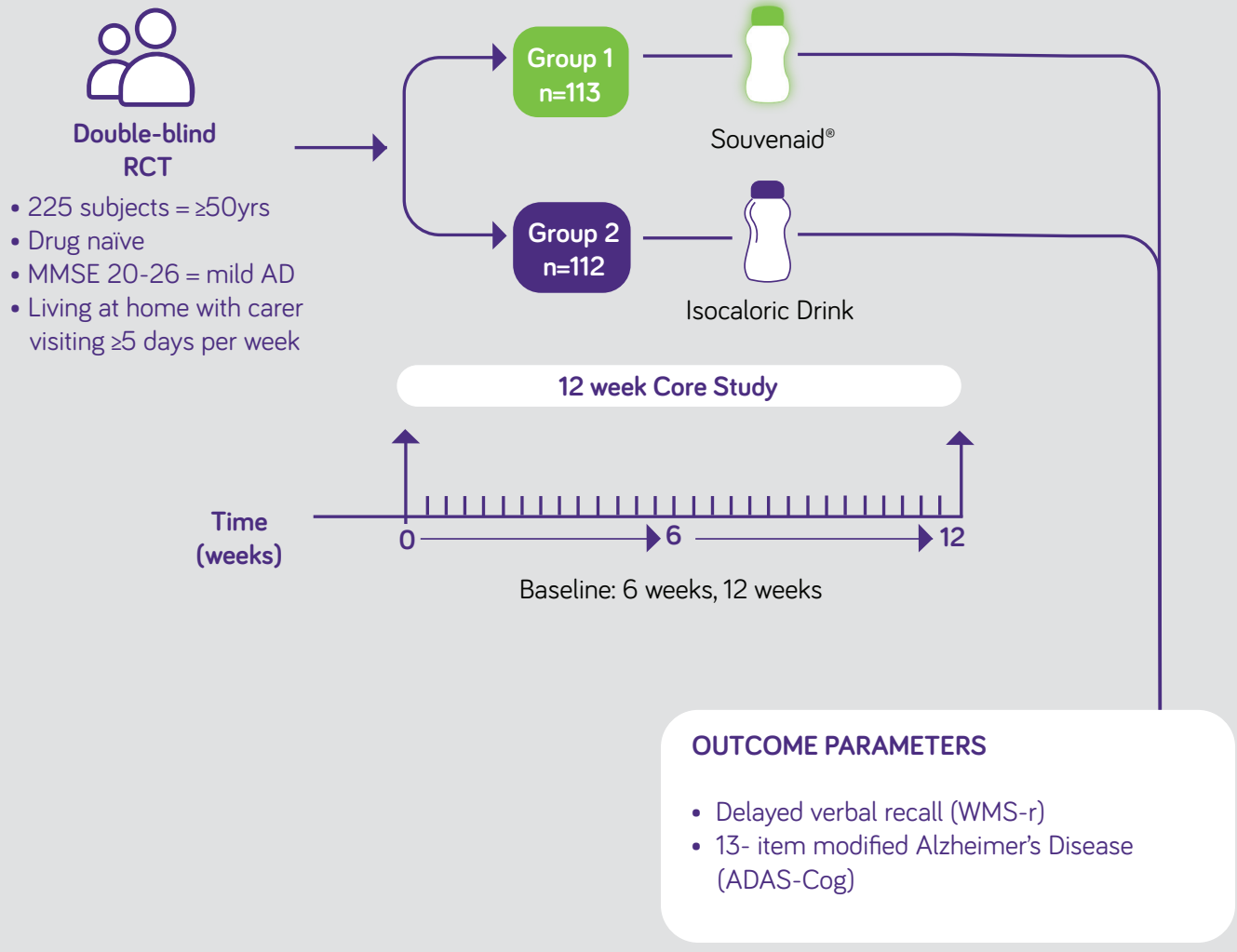
Memory

Cognition

BACKGROUND:

Preclinical studies indicate treatment focusing on restoration of synapses, due to synaptic loss, are well correlated with the changes to cognition, specifically in the hippocampus and cortices. These novel approaches include supplementation of rate limiting precursors to synaptic synthesis including nucleotide uridine, omega 3 polyunsaturated fatty acids and choline, of which Souvenaid® contains.
This RCT, was a proof-of-concept study designed to investigate the impact of Souvenaid® on cognitive function in subjects with mild AD who were not taking any AD medication.

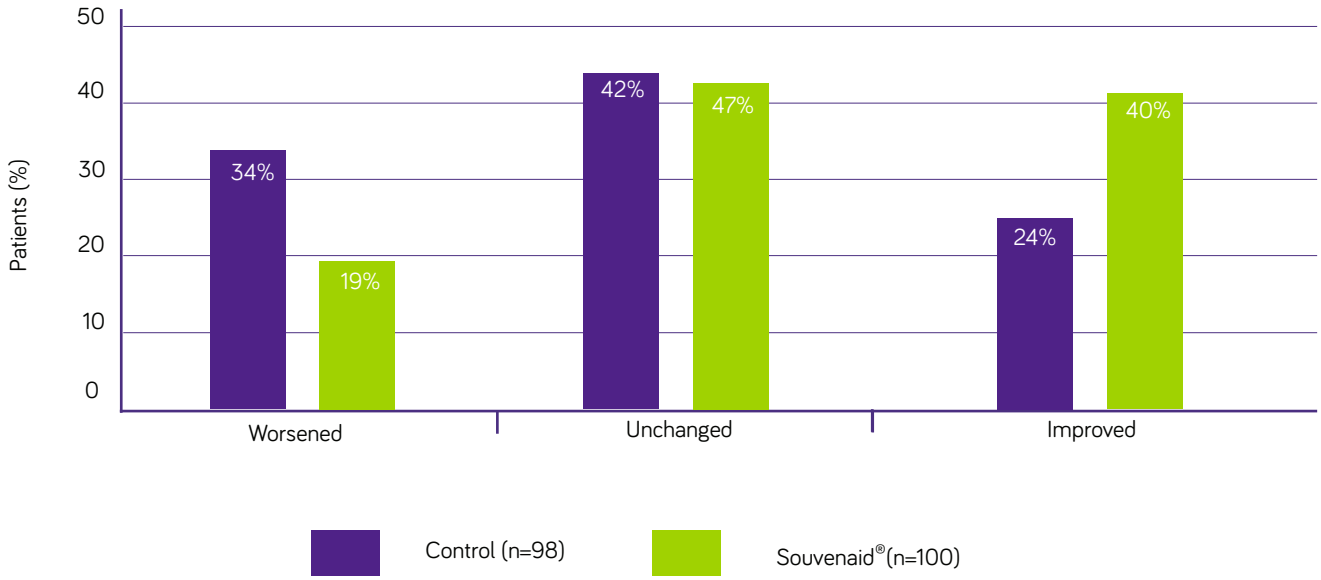
STUDY METHODOLOGY:



OUTCOME PARAMETERS

- Delayed verbal recall (WMS-r)
- 13- item modified Alzheimer's Disease (ADAS-Cog)

RESULTS:



Change in Wechsler Memory Scale revised delayed verbal recall after 12 weeks of supplementation with Souvenaid®. (p = 0.021)

KEY FINDINGS:

- Patients with mild AD who consumed Souvenaid® experienced a significant improvement in WMS-r–delayed verbal recall score at 12 weeks compared to controls.
- There was no difference between the groups for the other co-primary outcome measure (ADAS-cog), which was unchanged in both groups at 12 weeks.
- Compliance was high (95%) and the product was well tolerated.

CONCLUSIONS:

- After 12 weeks, use of Souvenaid® once daily showed an improvement in memory in patients with mild AD.
- Souvenaid® is well tolerated in patients with mild AD.

Efficacy of Souvenaid® in mild Alzheimer's Disease: results from a randomized controlled trial[6]

Scheltens et al 2012

Souvenir II

24 weeks
Double-blind RCT
Mild AD

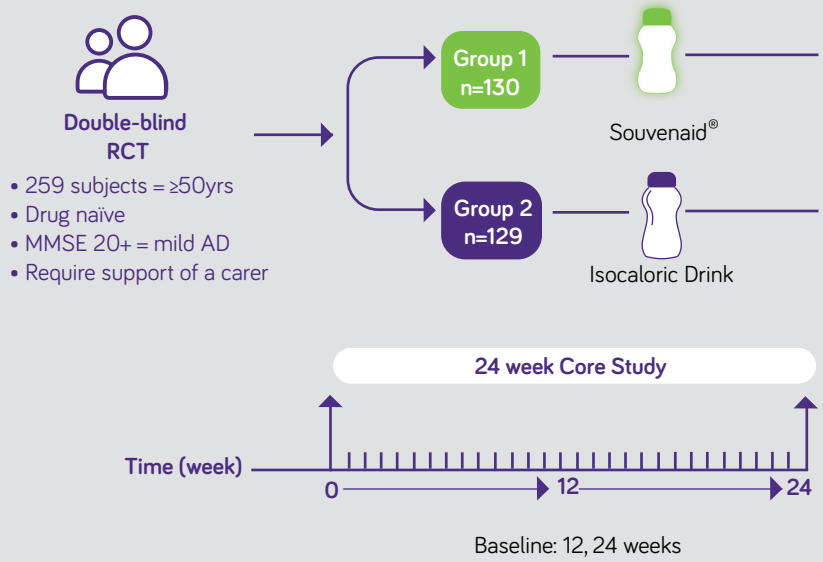
Memory

Brain Connectivity

BACKGROUND:

Souvenir II study was a follow on study from Souvenir I which was based on the hypothesis that supplementation with nutrient precursors of phosphatides in neuronal membranes, may decrease the rate at which synaptic loss occurs.
In this RCT, a potentially more sensitive tool (compared to the tool used in Souvenir I) was used to assess memory function, and the study also included biomarkers of synaptic activity to gain an understanding of the potential mechanism of action of Souvenaid®.

STUDY METHODOLOGY:



Baseline: 12, 24 weeks

OUTCOME PARAMETERS

Primary outcome: Memory function domain score(z -score) of NTB including:

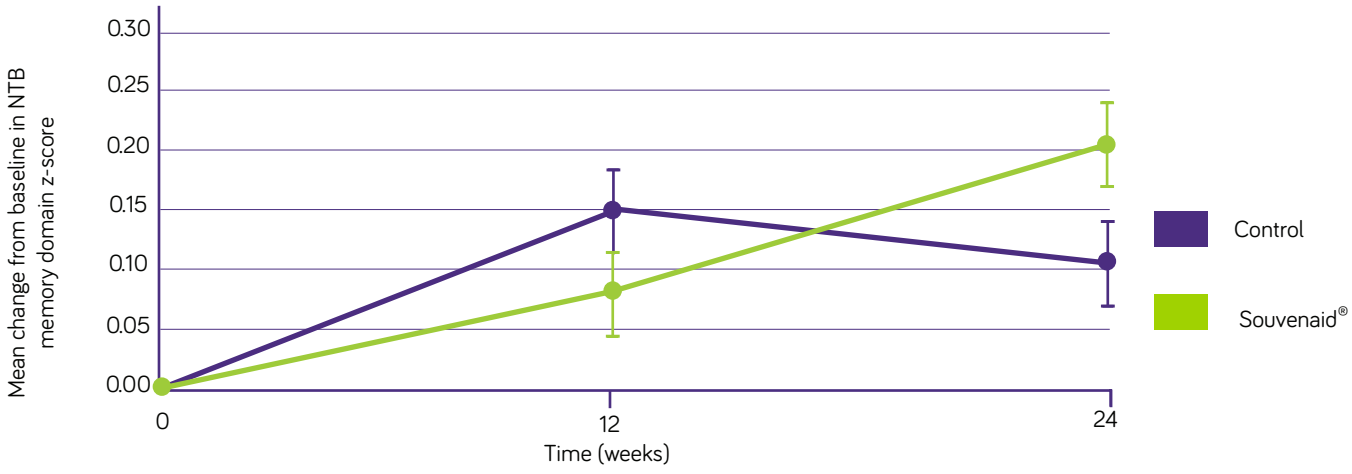
- (RAVLT) Immediate recall, delayed recall and recognition performance
- (WMS-r) verbal paired associates immediate and delayed recall

Secondary outcome

- Executive function domain score (z-score)
- Total NTB composite score
- Individual item score NTB
- Assessment of functional ability (Disability Assessment for Dementia scale)
- EEG data (as a marker of synaptic activity)
- Nutritional measures (blood nutritional markers indicating uptake)

RESULTS:

Sample size (n)	12 weeks	24 weeks
Souvenaid®	107	103
Control	100	103



Mean change from baseline in NTB memory domain score after supplementation of Souvenaid®. The difference in trajectories over time between active and control groups during the 24-week intervention period: p = 0.023

KEY FINDINGS:

- Souvenaid® has a beneficial effect on memory function in mild AD, as evidenced by the NTB memory domain Z-score which was significantly increased in the Souvenaid® versus the control group over the 24-week intervention period.
- The results from this follow-up study confirm the earlier finding that Souvenaid® improved memory performance in individuals with mild AD.
- EEG measures of functional connectivity were significantly different in trajectory over 24 weeks between study groups in favour of the Souvenaid® group.
- These findings suggest that Souvenaid® has an effect on brain functional connectivity, supporting the hypothesis that the intervention enhances synapse formation and function.
- Compliance was very high (96.6% [control] and 97.1% [Souvenaid®]).

CONCLUSIONS:

- Souvenaid® is well tolerated in patients with mild AD.
- Souvenaid® improved memory function in patients with mild AD.
- Souvenaid® has a suggested beneficial effect on brain functional connectivity

The S-Connect Study: results from a randomized controlled trial of Souvenaid® in mild-to-moderate Alzheimer's disease[7]

Shah et al 2013

S-Connect

24 weeks
Double-blind RCT
Mild-Moderate AD

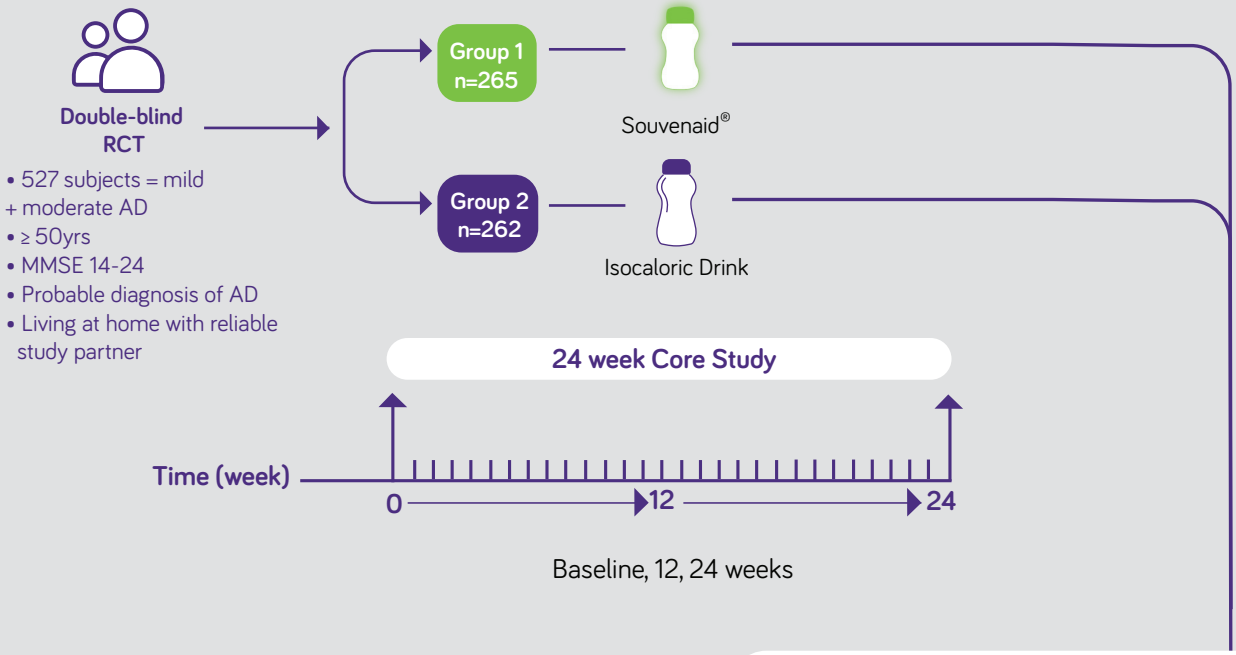
Cognition

Safety

BACKGROUND:

Early studies (Souvenir I & II) demonstrated a beneficial effect of Souvenaid® on memory performance in patients with mild AD who were not taking any AD medication. The S-connect study followed those 2 studies but in a slightly different population: individuals with mild – moderate AD who were also taking medication to manage their AD (cholinesterase inhibitors and/or memantine). This study used a more sensitive measure of change in moderate AD.

STUDY METHODOLOGY:



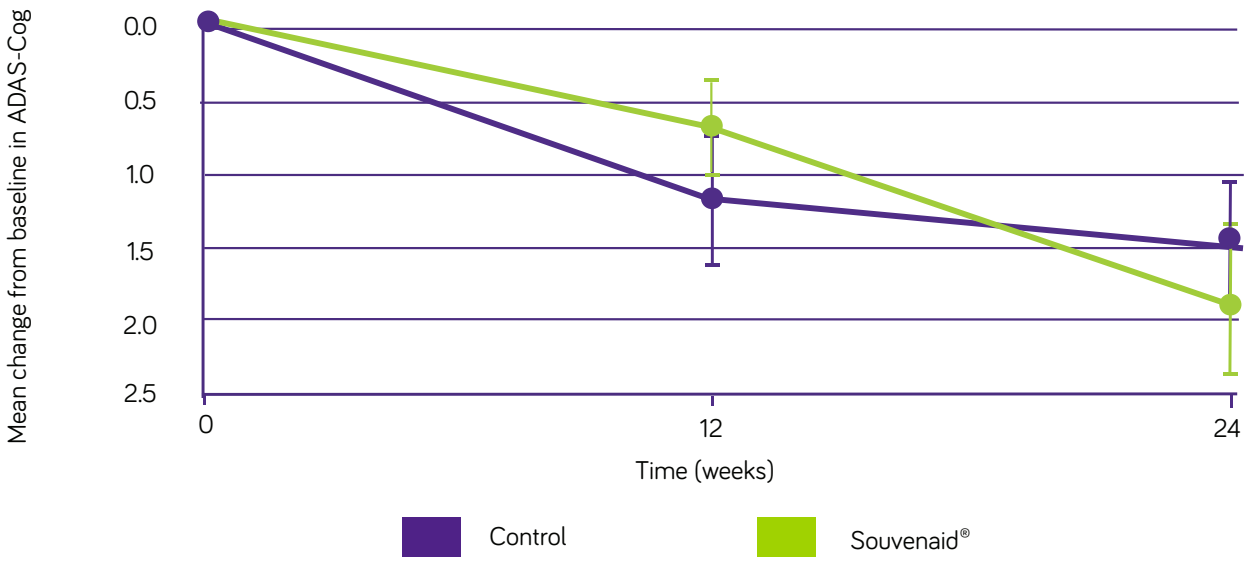
OUTCOME PARAMETERS

Primary outcome:
- 11 item Alzheimer's Disease Assessment Scale - Cognitive Subscale (ADAS-Cog)

Secondary outcome:
- Cognition
- Nutritional measures (blood nutritional markers indicating uptake)
- Functional abilities
- Global clinical impression
- Safety

RESULTS:

Sample size (n)	12 weeks	24 weeks
Souvenaid®	230	218
Control	228	207



Mean change from baseline in ADAS-Cog after 24 weeks of supplementation with Souvenaid® in patients with mild-moderate AD. P=0.513

KEY FINDINGS:

- Both the treatment and control groups showed a moderate increase of ADAS-cog scores, with no significant difference between study groups.
- Souvenaid® is safe and well tolerated when used in combination with standard medication for Alzheimer's disease.
- Compliance was high (94.1% [Souvenaid®]and 94.5% [control]).
- There was a predicted change in peripheral nutritional blood biomarkers.

CONCLUSIONS:

- Souvenaid® did not slow overall cognitive decline in patients with mild to moderate Alzheimer's disease.
- Souvenaid® is safe to be taken with AD medication
- Souvenaid® is well tolerated in patients with mild-moderate AD

Effectiveness of a specific nutritional supplement on cognitive, behavioural and functional symptoms in mild cognitive impairment and Alzheimer's dementia: caregivers judgments. Results of an observational survey[8]

Bianchetti et al 2018

Memento

6 months
Observational Study
4 months average supplementation

Cognition

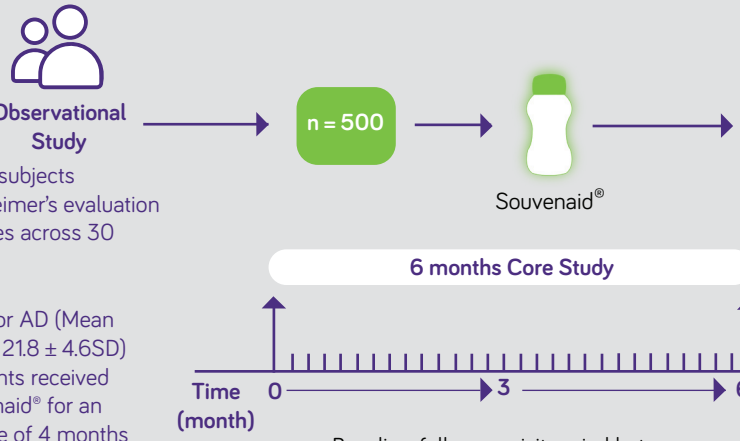
Memory

Functional ability

BACKGROUND:

In real world settings the opinions and judgements of caregivers is important in collection of patient clinical history particularly in monitoring of changes in the behaviour and functional abilities. Despite this, this opinion is not often considered in effectiveness of treatment. However it is important and can give a personalised dimension of treatment and disease progression.
This observational study was conducted to obtain patient and caregiver judgment about changes in cognition, behaviour and function.

STUDY METHODOLOGY:



- 500 subjects
- Alzheimer's evaluation centres across 30 Italian sites
- MCI or AD (Mean MMSE 21.8 ± 4.6SD)
- Patients received Souvenaid® for an average of 4 months
- Assessments were aligned with the follow up appointments, usually after 3 or 6 months

OUTCOME PARAMETERS

- Subjective judgement of patients and caregivers through responses to a structured interview to standardised questions using a hierarchical scale on cognitive, behavioural and functional areas of life.

KEY FINDINGS:

Results from evaluation at follow up visit (timeline varied between patients, usually 3 or 6 months) which explored cognitive, behavioural and functional domains in real life situations.

- Both patients and caregivers provided an overall positive opinion about the effectiveness of the dietary supplementation on cognitive, behavioural and functional domains explored using "real life" situations;
- The level of satisfaction was higher for patients with higher MMSE score and in those with MCI compared to AD
- Patients with higher duration of treatment reported higher benefit from the treatment.
- The findings also support that Souvenaid® be used early in the progression of disease and for a prolonged period of time.

CONCLUSIONS:

- The subjective views of patients and caregivers of the effects of Souvenaid® on memory, behaviour and function, support the findings from clinical trials

LipiDiDiet multinutrient clinical trial in prodromal Alzheimer's disease: Results from 24 and 36 months[9,10]

Soininen H, et al. Alzheimer's Dement. 2021;17:29–40.
Soininen H, et al. Lancet Neurol. 2017;16:965-975

LipiDiDiet

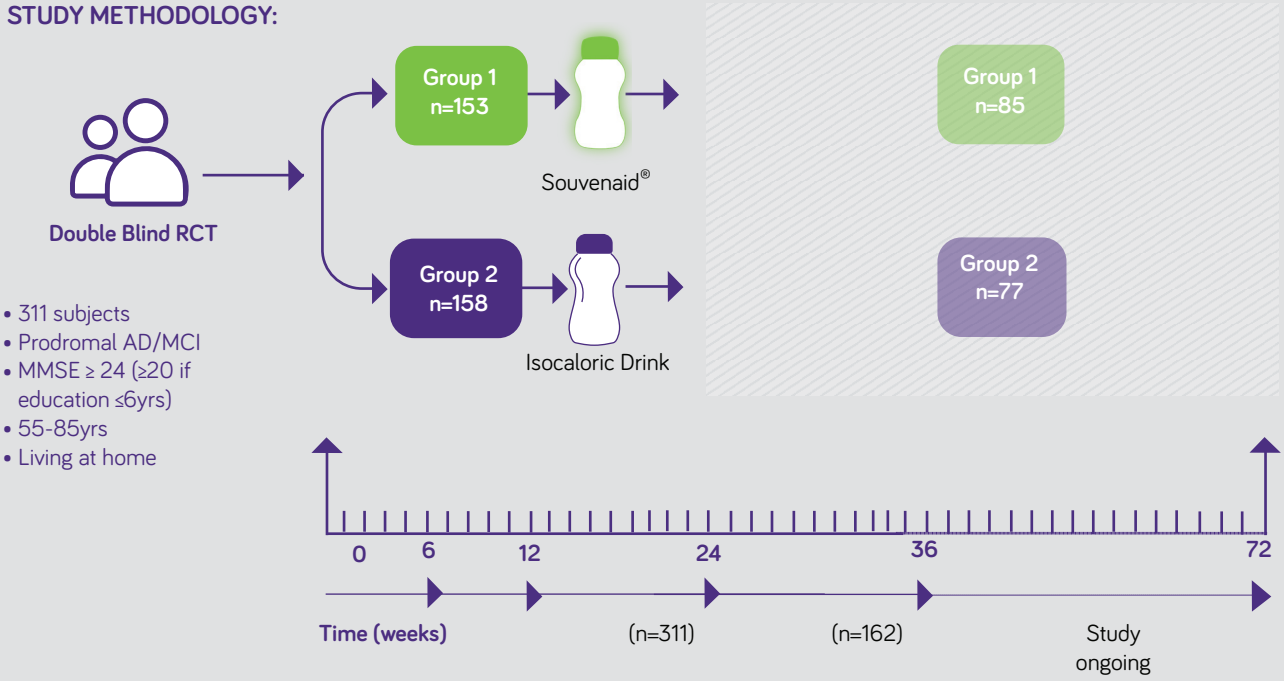
Double-blind RCT
Prodromal AD (MMSE ≥ 24)

- Cognition
- Functional ability
- Brain atrophy

BACKGROUND:

Based on the results of Souvenir I and Souvenir II, an independent European Commission funded a new trial focusing on the long-term use of Souvenaid® (Fortasyn® Connect) for memory and cognitive function in the very early stages of Alzheimer's disease - known as "prodromal AD" or "mild cognitive impairment" (MCI). With patients potentially followed up to 8 years, the LipiDiDiet study is the longest nutrition intervention trial in MCI.
The LipiDiDiet (LDD) study is the first clinical trial to investigate the effects of a medical food in patients with prodromal Alzheimer's disease (AD), often referred to as "Mild Cognitive Impairment" (MCI), and considered early stage AD.

STUDY METHODOLOGY:



- 311 subjects
- Prodromal AD/MCI
- MMSE ≥ 24 (≥20 if education ≤6yrs)
- 55-85yrs
- Living at home

Evaluation at baseline, 6, 12 months, 24 months, 36 months

OUTCOME PARAMETERS

Primary outcome:
- NTB 5-item composite
- Z score

Secondary outcome:
- Episodic memory (3 items: NTB memory domain, NTB executive function domain, NTB total)
- CDR Sum of boxes (CDR-SB)
- MRI brain volumes: hippocampal, whole brain, ventricular
- Executive function
- Total NTB composite (16 items)
- Progression to Alzheimer's disease, dementia
- Biomarkers

MRI = magnetic resonance imaging; **CDR-SB** = clinical dementia rating sum of boxes; **NTB** = neuropsychological battery; **CERAD** = Consortium to Establish a Registry for Alzheimer's Disease

KEY RESULTS:

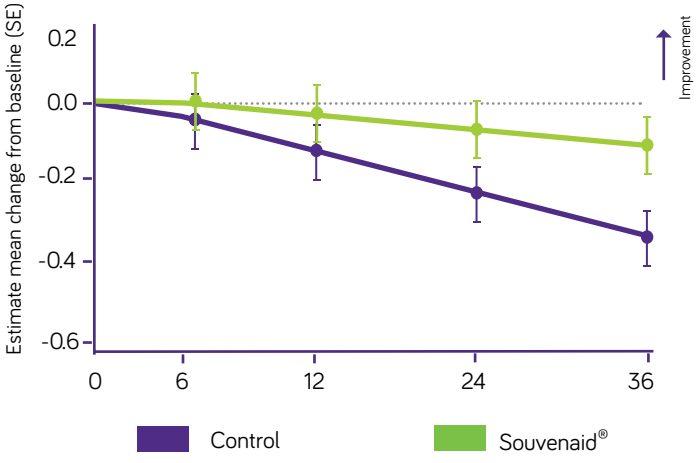
Mean change in baseline for main endpoints at 24 and 36 months of intervention

1) NTB 5-item Composite

(cognition and memory; z-score)

24 months:p=0.116,

36 months:p=0.014 60% reduction



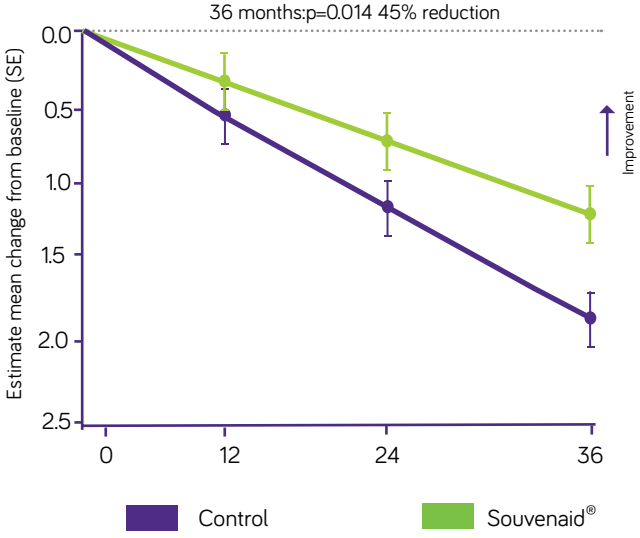
At 36 months: 60% reduction in decline in NTB 5-item Composite favouring the Souvenaid® group.

2) CDR-SB

(cognition and memory; score)

24 months:p=0.005,

36 months:p=0.014 45% reduction



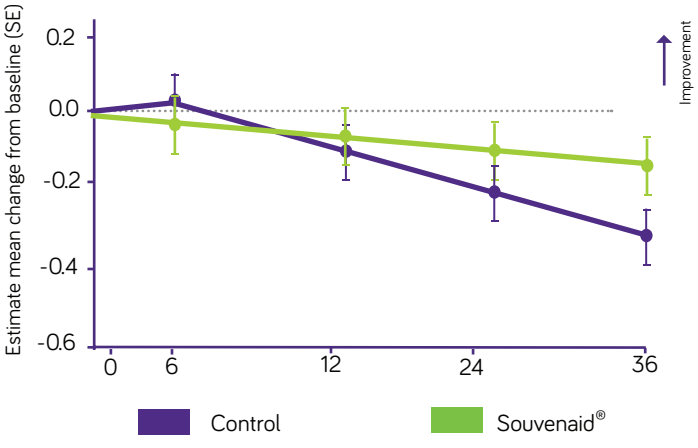
At 36 months: 45% less worsening in CDR-SB was observed for the Souvenaid® group compared to control

3) NTB Memory

(memory; z-score)

24 months:p=0.101,

36 months:p=0.008, 76% reduction



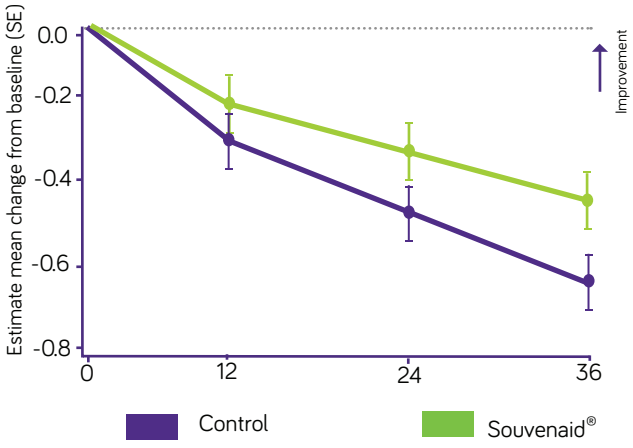
At 36 months: 76% reduction in decline for the Souvenaid® group in NTB memory domain

4) MRI Hippocampal Volume[38]

(MRI; cm^3)

24 months: p=0.005,

36 months: p=0.002, 33% less deterioration



At 36 months: Rate of deterioration in hippocampal volume was 33% less in the Souvenaid® group compared to control.

KEY FINDINGS:

Results from evaluation at follow up visit (timeline varied between patients, usually 3 or 6 months) which explored cognitive, behavioural and functional domains in real life situations.

- Results from the 24 months of intervention published in 2017 showed favourable effects on some secondary outcomes (e.g., CDR-SB and hippocampal atrophy) but not on the primary NTB endpoint. As some effects were observed at 24 months but cognitive decline was less than anticipated in the control group, it was proposed that the longer intervention may lead to more pronounced effects.

- Results from 36 months of the intervention were published in 2021 showing significant positive benefits on cognition, function, and rates of brain atrophy (brain shrinkage) in the active group (Souvenaid®) specifically.

- The rates of deterioration for hippocampal atrophy were significantly less in the Souvenaid® than the control group at 24 and 36 months, showing potential effect on disease pathology. The effect on hippocampal atrophy may be the basis for the memory benefit reported for the active group.

- Souvenaid® was found to be safe, very well tolerated, and compliance at 36 months was very high (means of 91.4% in the active group and 90.8% in the control group)

CONCLUSIONS:

- Souvenaid® slowed the decline in cognition, memory function, brain atrophy and disease progression over a 36 month period in people with prodromal AD.
- These results indicate greater benefit when Souvenaid® is taken over an increased length of time

Evaluation of Clinical Meaningfulness of Fortasyn® Connect in Terms of "Time Saved"[11]

Dickson et al. 2024

24 months

Secondary data analysis

Cognition

Brain atrophy

BACKGROUND:

Assessment of meaningfulness in randomized controlled trials (RCTs) in Alzheimer's disease (AD) is challenging, particularly in early disease. A metric that is easily understood by diverse stakeholders is useful so that the determination of whether an effect is meaningful or not can be widely applied across the varying scenarios. Converting clinical outcomes to disease progression time allows assessment of effects using a metric that is understandable and meaningful: time. The LipiDiDiet RCT was designed to assess the safety and efficacy of Fortasyn® Connect (Souvenaid®). This investigation by Dickson et al used the meta Time Component Test (TCT's) to analyse the 24-month data from the LipiDiDiet RCT in patients with MCI due to AD patients (known as prodromal AD)

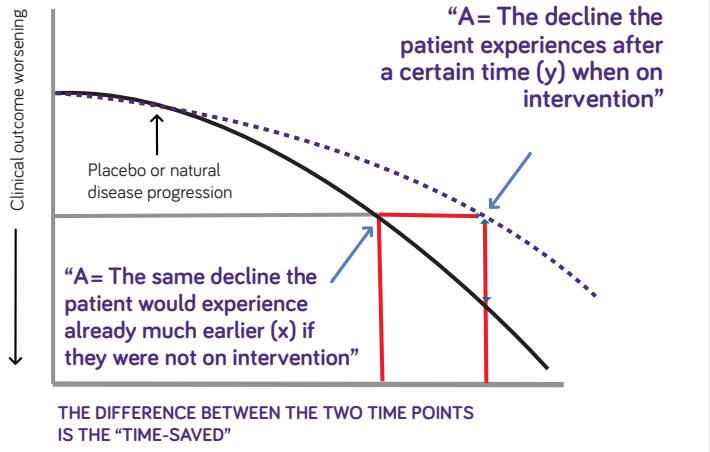
STUDY METHODOLOGY:

This investigation uses the meta Time Component Test (TCT) to determine how cognitive, functional and structural outcomes from the LiPiDiDiet RCT at 24 months can translate into time saved.

Using the LipiDiDiet 24 month dataset, the TCT was applied to the 3 outcomes:

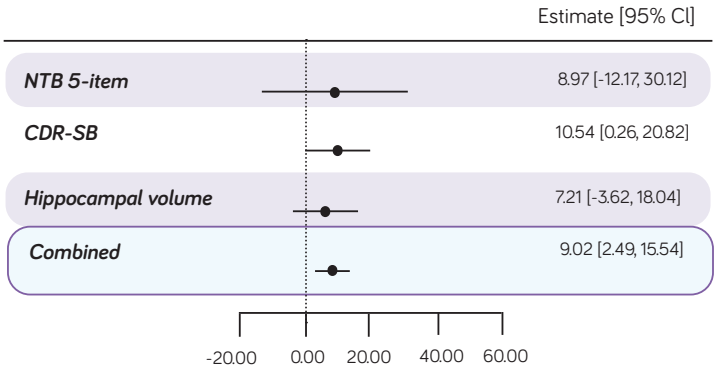
- 5-item NTB composite Z-score
- CDR-SB
- Hippocampal volume

An assessment was also completed to the 3 outcomes combined in an optimised global Time Component Test (gTCT).



Adapted from Dickson, et al. 2023, *Journal of Prevention of Alzheimer's Disease*

Combined analysis of gTCT showed 9 months slowing in disease progression over 24 months of intervention*†.



Based on 24-month datapoint in the LipiDiDiet 2-year dataset. Abbreviations: NTB- neuropsychological test battery; CDR-SB- clinical dementia rating - sum of boxes.

KEY FINDINGS

When using the 2 year data set from the LipiDiDiet[10] RCT:

- The time saving at 2 years of intervention was 9 months (95% CI), 10.5 months (95% CI) and 7.2 months (95% CI), when the meta TCT analysis was applied to each of the three trial outcomes individually: 5-item NTB, CDR-SB and hippocampal volume, respectively.

- The time saving was found to be 9 months*† (95% CI) over 2 years of intervention, when all 3 outcomes were combined in a gTCT analysis (5-item NTB, CDR-SB and hippocampal volume).

- Time saved is an intuitive and relatable metric that aligns with what patients and caregivers want to know.

CONCLUSIONS:

- The gTCT combined analysis of the 2 year data set from the LipiDiDiet RCT, showed that Fortasyn® Connect (Souvenaid®) slowed disease progression by 9 months in people with MCI due to AD.

*In patients with MCI due to AD
†After 2 years of continuous daily use of Souvenaid®, relative to natural (placebo) progression. Results are derived from a global TCT analysis of three 24-month endpoints (5-item NTB, CDR-SB, and hippocampal volume) from the 2-year LipiDiDiet dataset.1,3

Assessment of a potential synergistic effect of Souvenaid® in mild Alzheimer's disease patients on treatment with acetylcholinesterase inhibitors: An observational, non-interventional study[12]

Vinuela et al 2021

6 months
Prospective, non-interventional study

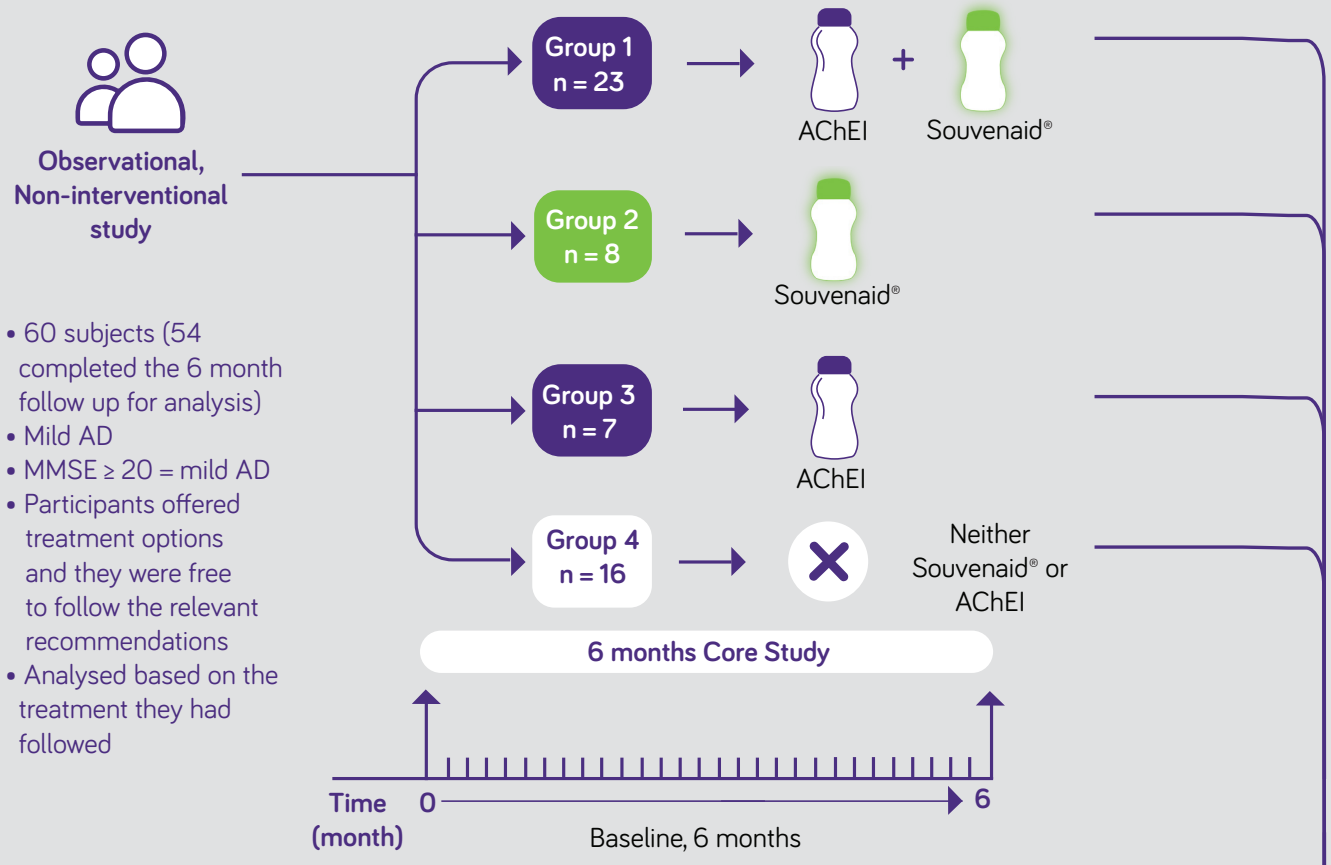
Memory Function

Cognition

BACKGROUND:

In this observational study, patients were offered both Souvenaid® and AChEI in a real life clinical setting. The goal of the study was to evaluate the safety and efficacy of Souvenaid® along with a possible synergistic effect of the combined therapy.

STUDY METHODOLOGY:

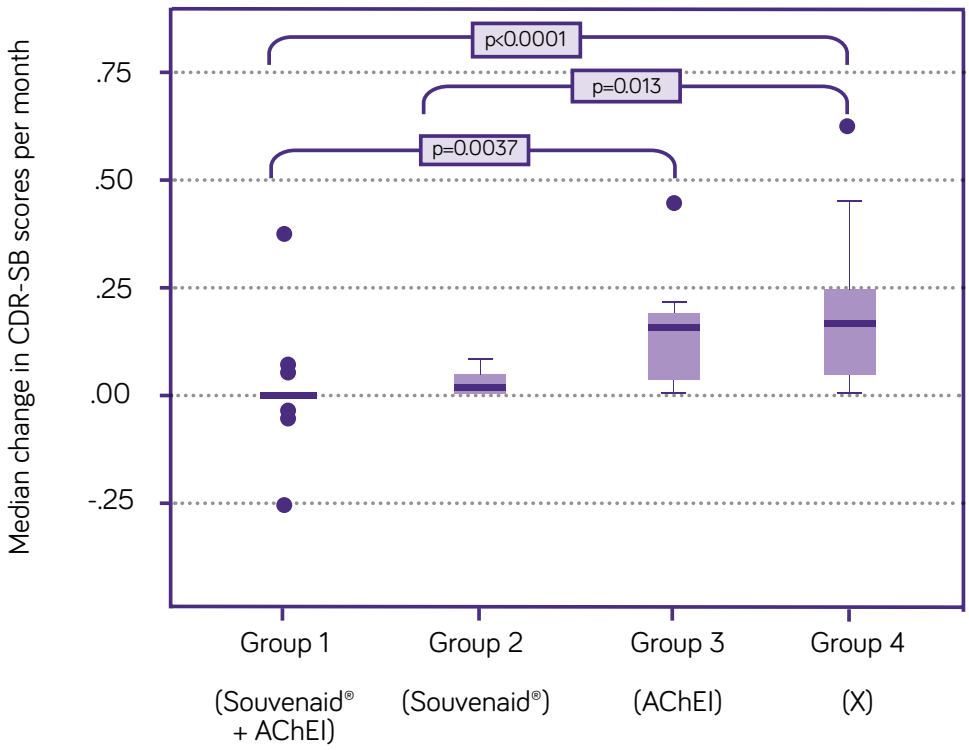


- 60 subjects (54 completed the 6 month follow up for analysis)
- Mild AD
- MMSE ≥ 20 = mild AD
- Participants offered treatment options and they were free to follow the relevant recommendations
- Analysed based on the treatment they had followed

OUTCOME PARAMETERS

- CDR-SB
- Adherence and side effects

RESULTS:



Median monthly change in CDR-SB after 6 months of patient selected treatment option, according to treatment group.

KEY FINDINGS:

6 month follow up results:

- There were statistically significant differences in the changes of the CDR-SB score at the end of the follow up in patients from Group 1 (Souvenaid® + AChEI) as compared with patients from Group 4 (no treatment) (p = 0.003)
- There were no differences between Group 2 (only Souvenaid®) or Group 3 (only AChEI) as compared with Group 4 (no treatment) (p = 0.094 and p = 1.0, respectively)
- Souvenaid® + AChEI was the only statistically significant factor associated to lower CDR-SB changes at the end of the 6 month follow up (p = 0.043)

Monthly changes in CDR scores:

- Monthly increases in CDR-SB scores were significantly lower in patients on treatment with Souvenaid® +AChEI (Group 1) in comparison with those treated only with AChEI (Group 3; p = 0.0037) or no treatment (Group 4; p < 0.0001).
- Patients on Souvenaid® (Group 2) had significantly lower monthly increases in CDR-SB scores in comparison to patients on no treatment (Group 4; p=0.013).

CONCLUSION:

- Souvenaid® is well tolerated in patients with mild AD when consumed with AChEI
- Clinical benefit was mostly attributed to Souvenaid®, and the addition of AChEI did not reduce the positive effect.
- There is a possible synergistic effect of the addition of AChEI when consuming Souvenaid®.

Efficacy of Souvenaid® combined with acetylcholinesterase inhibitors in the treatment of mild Alzheimer's disease[13]

Garcia-Alberca et al 2023

12 months
Retrospective analysis of clinical data

Cognition

Functional ability

BPSD

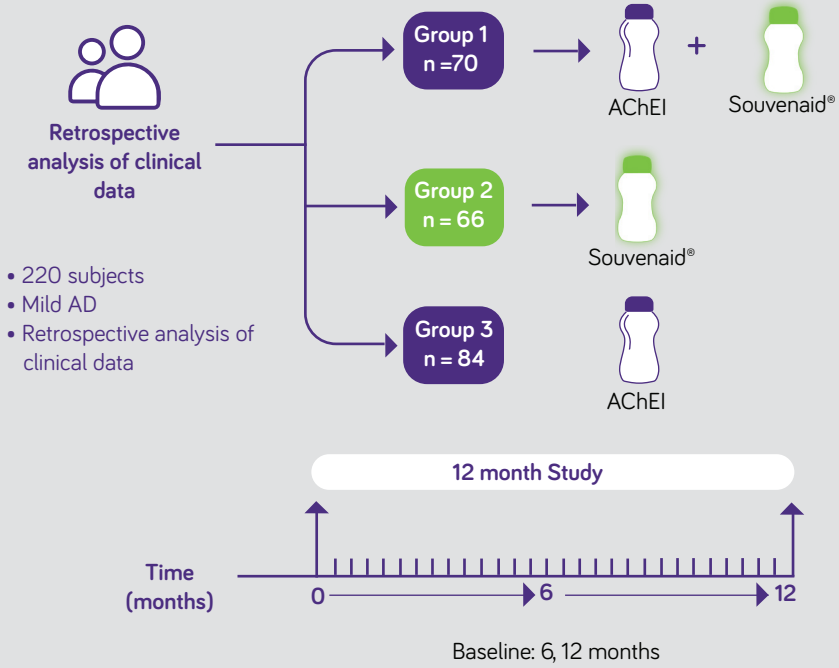
BACKGROUND:

Recently, a prospective, non-interventional research showed that mild AD patients taking Souvenaid® alone and the Souvenaid® plus AChEI combination had significantly lower monthly increases in Clinical Dementia Rating Scale scores[12] than either those patients taking AChEIs alone or those receiving no treatment.

Therefore, since there appears to be a potential usefulness for adding Souvenaid® to usual AChEI treatment in AD, further evidence supporting the use of combination therapy is worthwhile. The objective of this research is to shed light on the potential synergistic effect of the combination of Souvenaid® with AChEI in patients with mild AD in a real-world context.

For this purpose, a review was conducted of data in AD patients who attended a memory clinic over a 12-month period. The results are based on real clinical practice.

STUDY METHODOLOGY:



Baseline: 6, 12 months

OUTCOME PARAMETERS

- Cognitive Function: MMSE, RAVLT, SDMT, BNT, TMT-a; TMT-B, SVFT and PVFT
- Neuropsychiatric symptoms: NPI
- Functional capacity: BAYER-S

Graphs with results are unable to be replicated due to copyright- please refer to published clinical paper.

KEY FINDINGS:

- The combination of Souvenaid® and AChEI (Group 1) showed a statistically significant result compared to AChEI alone (Group 3) in the following tests compared to at 12 months follow up: MMSE, RAVLT, SVFT, PVFT, TMTA, TMTB and NPI, with an improvement already showing at the 6 month mark for MMSE and NPI.
- Souvenaid® + AChE inhibitors (Group1) showed statistically significant improvement in MMSE and NPI after 6 months compared to Souvenaid® (Group2)
- These results aligns with other clinical research showing the efficacy of Souvenaid® in patients with MCI and mild AD in cognitive function.

CONCLUSION:

- Combined treatment of Souvenaid® and AChEI showed benefit performance in cognitive areas including sustained attention, short term memory, verbal episodic memory, working memory, linguistic competence, executive functioning, visuospatial ability and semantic knowledge.
- Combination of Souvenaid® and AChEI was safe and tolerated in patients with mild AD.
- Souvenaid® and AChEI have different pathophysiological mode of action and combining them can lead to greater benefits than if the treatments were used alone.

Fortasyn® Connect improves neuropsychiatric symptoms in patients with mild cognitive impairment and dementia: Results from a retrospective real-world study[14]

Aguilar-Barbera et al 2023

12 months
Retrospective Study

Cognition

BPSD

BACKGROUND:

The effect of Souvenaid® on cognition, brain function and atrophy and disease progression has been studied in the LipiDiDiet clinical trial with positive outcomes. However the impact of Souvenaid® on behavioural and psychological symptoms of dementia (BPSD) needs exploration . This retrospective real world study assesses the effectiveness of Souvenaid® on BPSD using the Neuropsychiatric Inventory (NPI) which is a validated tool based on an interview of the caregivers evaluating delusions, hallucinations, agitation, depression, anxiety, euphoria, apathy, disinhibition, irritability, psychomotor alterations, sleep change, and eating change, as well as caregiver distress.

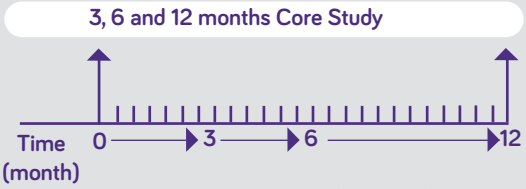
STUDY METHODOLOGY:

Retrospective study

- 236 patients
- with MCI or dementia (any type)
- ≥50years
- had received Fortasyn® Connect for at least 3 months

n = 236

Fortasyn® Connect



Baseline and 12 months

OUTCOME PARAMETERS:

- Neuropsychiatric Inventory (NPI)- to assess BPSD
- MMSE

Cognition
- GDS – depression
- BLS-D & RDRS2- everyday functioning
- GDS - presence and severity of dementia

KEY FINDINGS:

- Total NPI score, caregiver impact, and symptoms of depression, anxiety, apathy, and irritability improved after 3, 6, and 12 months from Fortasyn® Connect initiation ($p < 0.001$).
- NPI decreases were more pronounced when baseline NPI score was higher than > 20 points ($p < 0.001$).
- The benefit of Fortasyn® Connect was independent of gender, age, diagnosis, etiology, or concomitant treatment ($p < 0.0001$), although larger decreases in NPI total score were observed in MCI patients ($p < 0.0001$).
- After 12 months, GDS scores decreased ($p = 0.042$), and MMSE, BLS-D, and RDRS 2 scores remained stable

CONCLUSION:

- Fortasyn®Connect improved BPSD over at least a year in patients with MCI and dementia. Depression, anxiety, apathy, and irritability were the symptoms that improved the most. The benefit was independent of patients' characteristics and treatment but was greater if prescribed early and when baseline NPI scores were higher.

Integrating a multimodal lifestyle intervention with medical food in prodromal Alzheimer's disease: the MIND-AD$_{mini}$ randomized controlled trial[15]

Thunborg et al. 2024

6 months
Proof-of-concept RCT

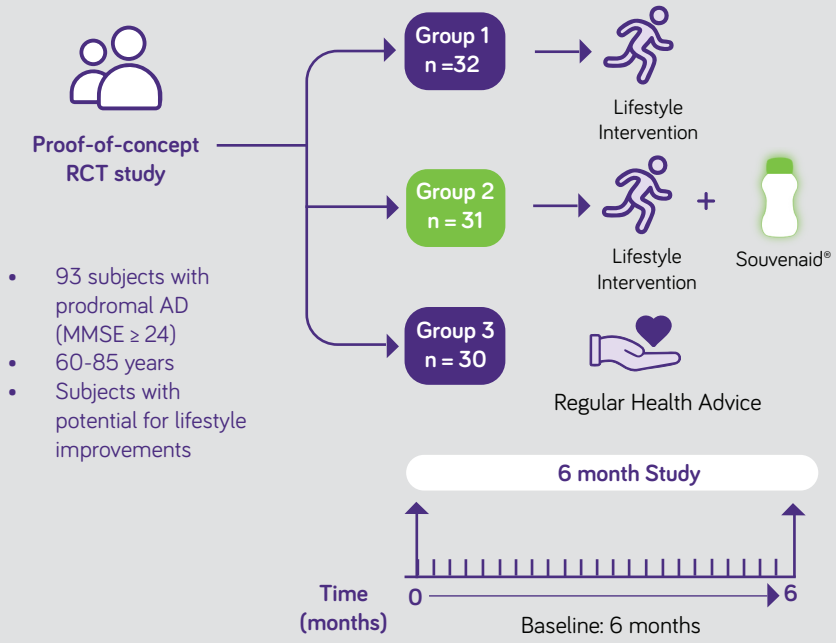
Cognition

Lifestyle

BACKGROUND:

The MIND-AD$_{mini}$ trial aimed to assess the feasibility and potential benefit of adopting a multimodal approach to managing prodromal AD, by introducing lifestyle interventions alongside the use of a medical food (Souvenaid®) to address cognitive and functional symptoms. Prior studies identified the measurable benefits achievable using lifestyle and nutritional interventions respectively. The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) trial highlighted the effectiveness of a multimodal lifestyle intervention approach to AD in high-risk older patients, and the LipiDiDiet study showed the impact of a medical food (Souvenaid®) in prodromal AD.[10] However, the feasibility and efficacy of combining both approaches for patients with prodromal AD remained uncertain.

STUDY METHODOLOGY:



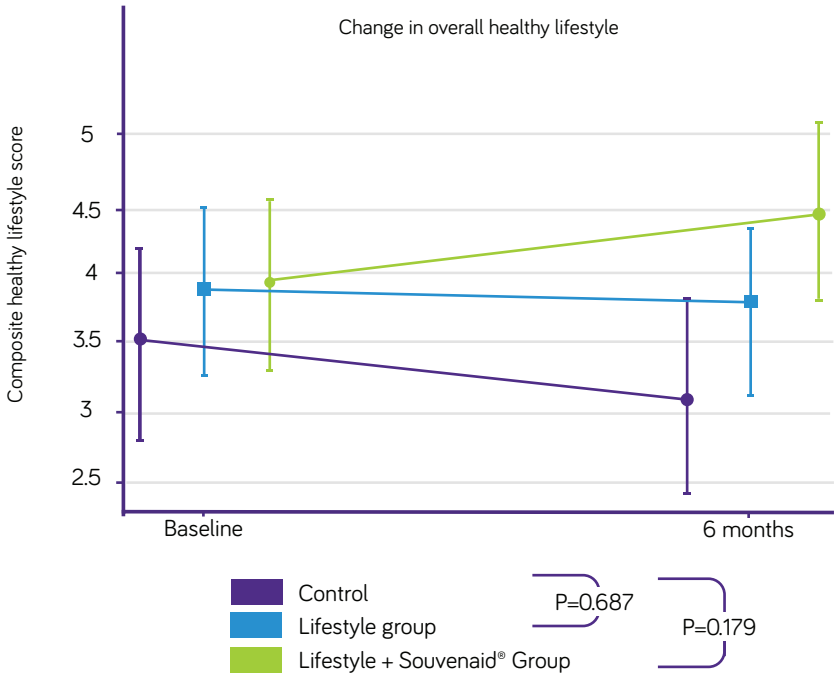
- 93 subjects with prodromal AD (MMSE ≥ 24)
- 60-85 years
- Subjects with potential for lifestyle improvements

OUTCOME PARAMETERS

Primary
- Feasibility of the multimodal intervention

Secondary
- Adherence to lifestyle domains:
  - Nutrition
  - Cognitive
  - Exercise
  - Metabolic Risk Factors
  - Medical Food

Exploratory Assessments
- CDR-SB



Impact of Lifestyle and Medical Food Intervention on Adherence to healthy Behaviours Over 6 months
Adapted from Thunborg et al. Alzheimer's Research & Therapy(2024) 16:118

KEY FINDINGS:

- Overall adherence to intervention was high in both groups (Lifestyle group = 78.1%, Lifestyle + Souvenaid® group = 87.1%)
- Both the Lifestyle Intervention group and the Lifestyle Intervention Group + Souvenaid® had significant increases in healthy dietary intake (P=0.038; P=0.043)
- The Lifestyle + Souvenaid® group had a significant reduction in cardiovascular risk burden vs control (P=0.043).
- The Lifestyle + Souvenaid® group had a significantly lower likelihood for decreasing cognitive- functional level (increasing CDR- SB) compared with control (P<0.05, exploratory analysis).

CONCLUSION:

- For patients with prodromal AD there was good adherence and feasibility of both a lifestyle intervention and lifestyle intervention combined with Souvenaid® over 6 months.
- Further larger-scale research trials investigating the interesting cognitive and health benefit findings would be beneficial.

References

1. Dementia Australia. Dementia facts and figures[Internet]. Dementia Australia 2024, Dementia Statistics, January 2024 [cited 2024 Apr 2]. Available from: https://prod.dementia.org.au/statistics

2. Sheppard C, et al. Alzheimer's Disease: Drug Discovery [Internet]. Brisbane, Australia: Exon Publications; 2020 [cited 2023 Nov 17]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK566126/

3. Sperling RA, et al. Toward defining the preclinical stages of Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimer's Dement. 2011

4. Kennedy EP, Weiss SB. The function of cytidine coenzymes in the biosynthesis of phospholipids. J Biol Chem. 1956;222(1):193–214.

5. Scheltens P, et al. Efficacy of a medical food in mild Alzheimer's Disease: A randomized controlled trial. Alzheimer's Dement. 2010;6:1-10.

6. Scheltens P, et al. Efficacy of Souvenaid® in mild Alzheimer's Disease: Results from a randomized controlled trial. J Alzheimer's Dis. 2014;31:225-236.

7. Shah RC, et al. The S-Connect study: results from a randomized controlled trial of Souvenaid® in mild-to-moderate Alzheimer's Disease. Alzheimer's Res Ther. 2013;5:59.

8. Bianchetti A, et al. Effectiveness of a specific nutritional supplement on cognitive, behavioral and functional symptoms in mild cognitive impairment and Alzheimer's dementia: caregivers' judgements. J Gerontol Geriatr 2018;66:68-74.

9. Soininen H, et al. 24-month intervention with a specific multinutrient in people with prodromal Alzheimer's disease (LipiDiDiet): a randomised, double-blind, controlled trial. Lancet Neurol. 2017;16:965–975

10. Soininen H, et al. 36- month LipiDiDiet multinutrient clinical trial in prodromal Alzheimer's disease. Alzheimer's Dement. 2020; 1-12.

11. Dickson SP, et al. Evaluation of clinical meaningfulness of Fortasyn® Connect in terms of "time saved". J Prev Alz Dis. 2024.11(4):992-7.

12. Vinuela A, et al. Assessment of a Potential synergistic effect of Souvenaid® in mild Alzheimer's disease patients on AChEI treatment: an observational study. J Alzheimer's Dis. 2021;80:1377-82.

13. Garcia-Alberca JM, et al. Efficacy of Souvenaid® combined with Acetylcholinesterase inhibitors in the treatment of mild Alzheimer's Disease. J Alzheimer's Dis. 2023;91:1459-1469.

14. Aguilar-Barbera M, et al. Fortasyn® Connect improves neuropsychiatric symptoms in patients with mild cognitive impairment and dementia: Results from a retrospective real-world study. J Alzheimer's Dis. 2023;93:621-31.

15. Thunborg C, et al. Integrating a multimodal lifestyle intervention with medical food in prodromal Alzheimer's disease: the MIND-AD mini RCT. Alzheimer's Res Ther. 2024;16:118.

Souvenaid® is a food for special medical purposes for the dietary management of early Alzheimer's disease. Must be used under medical supervision

Nutricia Australia Pty Ltd
The Zenith, Tower B, Level 12, 821 Pacific Highway,
Chatswood, NSW, 2067, Australia.

Danone Nutricia NZ Ltd
56-58 Aintree Ave, Airport Oaks, Auckland 2022,
New Zealand.

SHT052419-Sep 2025

Note:This page has been intentionally left blank

Scan here to learn more about Souvenaid®

NUTRICIA CARELINE

For Product and Nutrition advice:

For more information, our Careline team of expert dietitians can provide free product support and general nutrition advice

Email: nutriciacareline@danone.com
Phone: 1800 438 500 (Mon - Fri, 9am to 5pm AEST)