


Clinical Development

CNP520

CCNP520A2202J / NCT03131453

A randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of CNP520 in participants at risk for the onset of clinical symptoms of Alzheimer's Disease (AD)

Statistical Analysis Plan (SAP)

Author:  Trial Statistician

Document type: SAP Documentation

Document status: Final Addendum 4

Release date: 11-Jan-2021

Number of pages: 107

Document History – Changes compared to previous final version of SAP

Date	Time point	Reason for update	Outcome for update	Section and title impacted (Current)
12-Feb-2020	Prior to DB Lock	Finalizing amendment 1 for CSR	Updated for abbreviated CSR reporting based on the DMC MAP and internal discussions with clinical team, and incorporating the comments from clinical team	
18-Mar-2020	Prior to DB Lock	Creation of Amendment 2	<p>Demographic and baseline characteristics tables with by subgroups genotype and amyloid status not needed for aCSR.</p> <p>Worsening in cognition and reversibility tables and figures with by subgroups genotype, amyloid status and their combination not needed for aCSR.</p> <p>Note added for source of genotype data for disclosure analysis and safety analysis.</p> <p>Cross tabulation for RBANS and CDR-SOB changes not needed for aCSR.</p> <p>In-text tables streamlined as per discussion from data review meeting.</p> <p>SAF definition updated to include the participants who received medication. mSAF definition updated: SAF with atleast 3 months exposure duration</p> <p>VolMRI, RBANS Index scores added for baseline comparability, added Centiloid in baseline characteristics.</p> <p>Added note on source and derivation of Amyloid Status in section 2.3.2, 2.3.3.</p>	
29-Apr-2020 to 27-May-2020				

28-May-2020	Prior to DB Lock		<p>PET SUVR summary table removed, added listing. Added note in section 2.8.1 for consideration on missing information AE relationship Updated censoring rule for TTE in section 2.5.5. Added note in section 2.5 to explain rationale of having worsening in cognition and reversibility before primary endpoint. Mentioned in section 4 VolMRI in place of hippocampal for correlation with RBANS. Document header updated to Amendment 2.</p>	
29-May-2020	Prior to DB Lock		<p>Added a rule to impute missing study treatment end date in section 5.1.1. Updated the censoring rule 3 in section 2.5.5. In section 5.3, added a 30 days window for AEs for liver event criteria (ALT or AST > 3×ULN). In section 5.3, added a 30 days window for injury before the hematuria criteria.</p>	
01-Jul-2020	Post DB Lock	Creation of addendum 1	<p>Updated the derivation of Annualized percent change for Volumetric MRI reporting in section 2.5.2 Updated label for “Centiloid” to “Amyloid PET Centiloid” To include MMSE, CDR-SOB and Amyloid PET Centiloid in baseline comparability, the language for baseline comparability paragraph in section 2.3.3 made more generic and flexible</p>	
12-Jul-2020	Post DB Lock	Creation of addendum 1	<p>Added the need for analysis of Time to first change in diagnosis classification when participants are</p>	2.5.4, 2.5.5

				on treatment, Time to first decrease in RBANS Total Score of \geq 14 points when participants are on treatment.	
				Updated wording in definition of last on treatment for clarity in section 2.1.1.	
21-Jul-2020	Post Lock	DB	Creation of addendum 2	Included effect size and CIs for APCC score in section 2.5.1, 2.5.2.	2.5.1, 2.5.2,
				Censoring rule clarified for time to first decrease in RBANS \geq 14 points in section 2.5.5.	2.5.5
				Minor edits in section 4	
23-Jul-2020	Post Lock	DB		A β 1-42/ A β 1-40 ratio added to CSF biomarker reporting in section 2.7.1, 2.7.2.	2.7.1, 2.7.2
29-Jul-2020	Post Lock	DB		Added a note “summaries of distribution of “last on treatment” and “last off treatment” will be presented in CSR Appendix 16.1.9” in section 2. Added section 5.4.2 for additional SAS outputs in Appendix 5 to be used for CSR Appendix 16.1.9	2, 5
30-Jul-2020	Post Lock	DB		Updated section 5.4.2 to include the raw SAS outputs for all the TTE analyses, minor edits.	
				Updated language in section 2 for the note on appendix 16.1.9	
02-Dec-2020	Post Lock	DB	Creation of addendum 3	In section 2.5.1 added additional criteria for change in cognition; improvement (increase) from previous visit by at least 7 points , no change from baseline (change between -6 and 6), no change from previous visit (change between -6 and 6)	2.5.1

11-Jan-2021	Post Lock	DB	Creation of addendum 4	Plasma A β 1-40 summary added to section 2.7.1 under Biomarkers in blood
-------------	-----------	----	------------------------	--

Table of contents

Table of contents	6
List of abbreviations.....	8
1 Introduction	12
1.1 Study design	12
1.1.1 Study Design Summary	12
1.1.2 Planned Number of Participants	13
1.1.3 Randomization and Stratification	13
1.1.4 Primary Analysis Time Point.....	14
1.1.5 Interim Analyses	15
1.2 Study objectives and endpoints	15
2 Statistical methods	17
2.1 Data analysis general information.....	17
2.1.1 General definitions.....	18
2.2 Analysis sets.....	21
2.2.1 Group for specific analysis	21
2.3 Patient disposition, demographics and other baseline characteristics.....	21
2.3.1 Patient disposition.....	22
2.3.2 Analysis of impact of Disclosure (Genetic Disclosure and Amyloid Disclosure).....	22
2.3.3 Background and demographic characteristics	27
2.4 Treatments (study treatment, rescue medication, concomitant therapies, compliance)	29
2.4.1 Study treatment / compliance	29
2.4.2 Prior, concomitant and non-drug therapies.....	29
2.5 Analysis of the primary objective	29
2.5.1 Worsening in cognition and reversibility	29
2.5.2 Volumetric MRI.....	31
2.5.3 Primary endpoint	32
2.5.4 Statistical hypothesis, model, and method of analysis	34
2.5.5 Handling of missing values/censoring/discontinuations	35
2.5.6 Supportive analyses	36
2.6 Analysis of the key secondary objective	36
2.6.1 Key secondary endpoint	36
2.6.2 Statistical hypothesis, model, and method of analysis	36

2.6.3	Handling of missing values/censoring/discontinuations.....	36
2.7	Analysis of secondary efficacy objective(s).....	37
2.7.1	Secondary endpoints.....	37
2.7.2	Statistical hypothesis, model, and method of analysis.....	41
2.7.3	Handling of missing values/censoring/discontinuations.....	42
2.8	Safety analyses.....	42
2.8.1	Adverse events (AEs).....	43
2.8.2	Deaths.....	44
2.8.3	Laboratory data.....	44
2.8.4	Other safety data.....	45
2.9	Pharmacokinetic endpoints.....	48
2.10	PD and PK/PD analyses.....	48
2.11	Patient reported outcomes.....	48
2.12	Biomarkers.....	48
2.13	Other Exploratory analyses.....	48
2.14	Interim analysis.....	48
3	Sample size calculation.....	49
4	Change to protocol specified analyses.....	51
5	Appendix.....	52
5.1	Imputation rules.....	52
5.1.1	Study drug.....	52
5.1.2	AE date imputation.....	52
5.1.3	Concomitant medication date imputation.....	52
5.2	AEs coding/grading.....	53
5.3	Laboratory parameters derivations.....	53
5.4	Statistical models.....	55
5.4.1	Primary analysis.....	55
5.4.2	Additional SAS outputs.....	55
5.5	Rule of exclusion criteria of analysis sets.....	56
5.6	Notable and abnormality criteria.....	57
5.7	Data collection for roll-over and re-screened participants.....	59
5.8	Analysis windows rules.....	60
5.9	RBANS Index tables.....	69
6	References.....	106

List of abbreviations

A β	Amyloid-beta
AD	Alzheimer's Disease
AE	Adverse event
AESI	Adverse Event of Special Interest
ALT	Alanine Aminotransferase
AmD	Amyloid Disclosure
ANOVA	Analysis of Variance
APOE4	Apolipoprotein E ϵ 4 allele
APCC	API Preclinical Composite Cognitive Battery
API	Alzheimer's Prevention Initiative
APOE	Apolipoprotein E
APP	Amyloid Precursor Protein
ARIA	Amyloid Related Imaging Abnormalities
ARIA-E	Amyloid Related Imaging Abnormality - edema
ARIA-H	Amyloid Related Imaging Abnormality - hemorrhages
AST	Aspartate Aminotransferase
ATC	Anatomic Therapeutic Chemical classification
AUC	Area Under the Curve
BACE	Beta-site-APP Cleaving Enzyme
Bid	bis in diem/twice a day
BMI	Body Mass Index
BSI	Boundary Shift Integral
CDR	Clinical Dementia Rating
CDR-SOB	Clinical Dementia Rating Sum of Boxes
CFR	US Code of Federal Regulations
ChEIs	Cholinesterase-Inhibitors
CI	Confidence Interval
CM	Concomittant Medication
CNS	Central Nervous System
CRF	Case Report/Record Form (paper or (e)electronic)
CSF	Cerebrospinal fluid
CSR	Clinical Study report
C-SSRS	Columbia Suicide Severity Rating Scale
CTC	Common Toxicity Criteria

CTCAE	Common Terminology Criteria for Adverse Events
DDI	Drug-Drug-Interaction
DMC	Data Monitoring Committee
DMAG	Disclosure Advisory Monitoring Group
DRM	Dose Regimen Modification
ECG	Electrocardiogram
ECog	Everyday Cognition scale
EDC	Electronic Data Capture
EoS	End of Study
██████████	██
FAS	Full Analysis Set
FDG	Fluorodeoxyglucose
GCP	Good Clinical Practice
GD	Genetic Disclosure
██████	██
Hb	Hemoglobin
HM(s)	Homozygote(s)
HT(s)	Heterozygote(s)
IA	Interim Analysis
IB	Investigator's Brochure
i.m	Intramuscular
i.v.	Intravenous
ICF	Informed Consent Form
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
IEC	Independent Ethics Committee
IgG	Immunoglobulin G
IGT-AD	Impact of Genetic Testing for Alzheimer's Disease
IRB	Institutional Review Board
IRT	Interactive Response Technology
LDH	Lactate Dehydrogenase
LDR	Lower Dose Regimen
LFT	Liver Function Test
LLOQ	Lower Limit of Quantification

LOAD	Late Onset Alzheimer's Disease
MAP	Master Analysis Plan
MAR	Missing at Random
MCI	Mild Cognitive Impairment
MedDRA	Medical Dictionary for Drug Regulatory Affairs
mSAF	Modified Safety Analysis Set
MMSE	Mini-Mental State Examination
MMRM	Mixed Model Repeated Measure
MRI	Magnetic Resonance Imaging
non-HMs	non-Homozygotes, i.e. Heterozygotes or non-carriers
NFL	Neurofilaments
█	████████████████████
NYHA	New York Heart Association
o.d.	Once Daily
OC/RDC	Oracle Clinical/Remote Data Capture
OS	Overall Survival
p.o.	Oral (per os)
PAC	Progression Adjudication Committee
█	████████████████████
PDS	Programming Dataset Specifications
PET	Positron Emission Tomography
█	████████████████████
PPS	Per-Protocol Set
PPW	Premature Participant Withdrawal
PRO	Participant Reported Outcomes
PT	Preferred Term
q.d.	Quoque die (once each day)
Qd	Qua'que di'e / once a day
█	████████████████████
█	████████████████████
QTcF	Fridericia QT correction formula
RAP	Report and Analysis Process
RAS	Randomized Analysis Set
RBANS	Repeatable Battery for the Assessment of Neuropsychological Status
REVEAL	Risk Evaluation & Education for Alzheimer's Disease

ROI	Region of Interest
SAE	Serious Adverse Event
SAF	Safety Analysis Set
SAP	Statistical Analysis Plan
SAS	Statistical Analytics System(or Software)
SE	Standard Error
SMQ	Standardized MedDRA Query
SOC	System Organ Class
██████	████████████████████
SUVR	Standardized Uptake Ratio
SD	Standard Deviation
TBL	Total Bilirubin
TE	Target Engagement
TEAE	Treatment-emergent Adverse Event
TEC	Treatment Epoch Completion
TLFs	Tables, Listings and Figures
TTE	Time-To-Event
ULN	Upper Limit Of Normality
WHO-DD	World Health Organization Drug Dictionary
γ-GT	Gamma-Glutamyl Transferase

1 Introduction

This Statistical Analysis Plan (SAP) describes main efficacy and safety analyses of clinical trial CCNP520A2202J. This SAP also describes analysis strategy for the impact of genetic and amyloid disclosure in a dedicated [Section 2.3.2](#). The study CNP520A2202J has been terminated prematurely after a regular DMC review in July 2019. Hence, only abbreviated Clinical Study Report (CSR) will be created for this study.

The content of this SAP is based on the final amendment version 3.0 of protocol CCNP520A2202J.

1.1 Study design

1.1.1 Study Design Summary

The study uses a randomized, double-blind, placebo-controlled, parallel group design with variable treatment duration in cognitively unimpaired participants aged 60 to 75 years, with at least one APOE4 allele (Homozygotes (HMs) or Heterozygotes (HTs)) and if HTs, with evidence of elevated brain amyloid. Overall approximately 2000 participants were planned to be randomized into the study, with a sample size of 800 for the selected dose of CNP520 and placebo, respectively, thereby achieving a 1:1 ratio for the selected CNP520 dose vs placebo. Due to early termination of the study the original planned number of participants will not get enrolled into the study.

The various epochs in the study are specified as follows (see below [Figure 1-1](#)):

Screening Epoch

Treatment Epoch

Follow-up Epoch

Right after signing the Informed Consent (ICF#B), the screening epoch starts. The screening epoch consists of two parts: Screening I and Screening II. In Screening part I, less invasive assessments are performed and genotype is disclosed. Participant may take a few days to reflect on this information before continuing to Screening part II. Screening II includes safety assessments, various cognitive and neuropsychological scales, brain MRI scan, and mandatory amyloid PET scan or a lumbar puncture to verify eligibility of HTs based on brain amyloid status. Amyloid status will subsequently be disclosed. Although HMs are eligible regardless of their brain amyloid status (elevated/not elevated), they will also undergo a PET scan or a lumbar puncture during screening (HMs can opt out of amyloid disclosure). Another reflection period may take place after amyloid disclosure. Altogether, the screening period from signature of ICF#B (part I and part II, including reflection periods when required) is expected to last about 12 weeks.

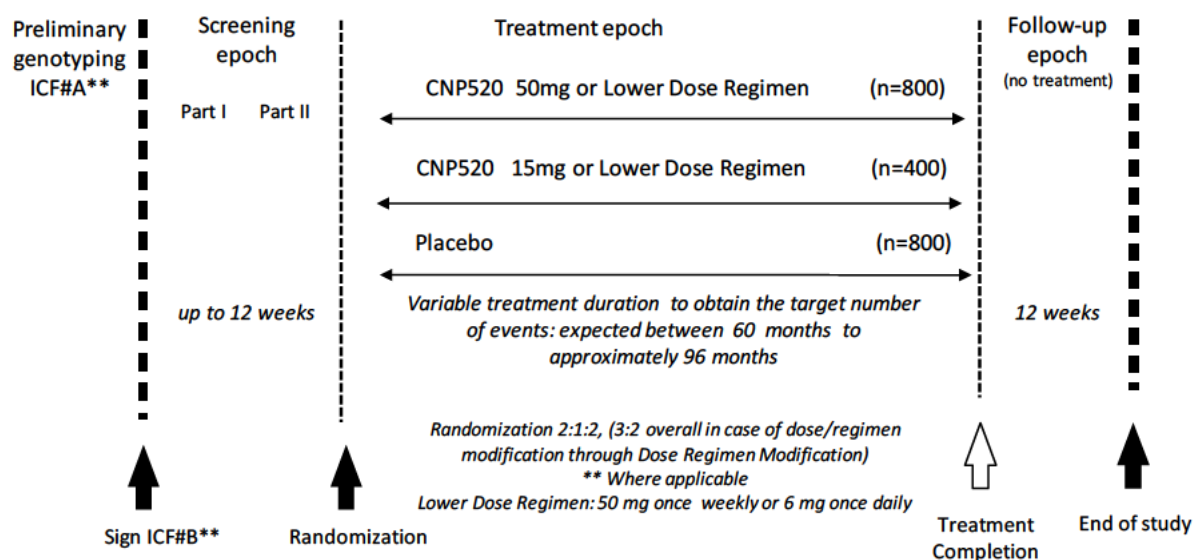
The Treatment Epoch follows a randomized, double-blind, placebo-controlled, parallel group design in which participants receive the investigational treatments or placebo. Participants will be initially randomized to one of the treatment arms in the ratio 2:1:2 (CNP520 50 mg: 15 mg: placebo). The initial regimen is a once daily dose of 50 mg, 15 mg, or placebo throughout

the full treatment epoch. If it is determined that the current doses do not provide a suitable benefit/risk profile, a single Lower Dose Regimen (LDR) will be implemented for both active treatment arms through Dose Regimen Modification (DRM) process described in the study protocol Section 5.1.1 and Section 5.2. This process may be triggered based on DMC recommendation and/or new data for CNP520 or other BACE inhibitors.

The treatment duration for individual participants will be variable, based on when the end of treatment epoch criteria are met, i.e. when (1) all ongoing participants have completed their Week 260_(M 60) assessment and (2) the overall targeted number of events of 498 has been reached, whichever is later. The expected maximal duration for an individual participant is 84 months (7 years).

The Follow-up visit will be scheduled 12 weeks after the last study drug intake.

Figure 1-1 Study Design



1.1.2 Planned Number of Participants

The trial will involve the assessment of efficacy for two doses of the investigational treatment. The primary analysis will compare each active dose of the investigational treatment arm with placebo. A total of up to 2000 participants will be randomized into the study, with a sample size of 800 for the selected dose of CNP520 and placebo, respectively, thereby achieving a 1:1 ratio for the selected CNP520 dose vs placebo (see Section 3 for the full details of the sample size calculation).

1.1.3 Randomization and Stratification

All eligible participants will be randomized via Interactive Response Technology (IRT) to one of the treatment arms.

The study will initially be conducted with a randomization ratio of 2:1:2 (CNP520 50 mg: 15 mg: placebo).

The initial regimen is a once daily dose of 50 mg, 15 mg, or placebo throughout the full treatment epoch. If it is determined that the current doses do not provide a suitable benefit/risk profile, a single Lower Dose Regimen (LDR) will be implemented for both active treatment arms through Dose Regimen Modification (DRM) process (see Section 5.1.1 and Section 5.2 of the protocol). This process may be triggered based on DMC recommendation and/or new data for CNP520 or other BACE inhibitors.

In case of DRM, the LDR will consist of a single lower dose regimen selected - either a 50 mg once weekly dose or a 6 mg once daily dose. Both dose regimens are expected to have a similar safety profile. The selection of the dose regimen will be based on both the timing of the DRM decision, as this may restrict options based on availability of supplies, and any further information available at that time, including PK/PD modeling, external data, etc.

The DRM activation will follow the allocation of 2:1:2 across the three treatment arms, resulting in an overall randomization ratio of 3:2 for CNP520 (arm #1 and #2) vs placebo.

The planned total number of randomized participants will not exceed $n = 2000$.

Randomization across treatment arms will be stratified by age group (60 to 64 years, 65 to 75 years), genotype (HM and HT), method used to determine brain amyloid elevation in HT (PET, CSF) and geographic region (North America, Europe, Asia, Other). In case both methods were used, the one indicating elevated amyloid will be captured. If both results indicate elevated amyloid, then the PET method will be used for stratification.

The stratification by age is using age at randomization, not age at screening. Participants who were 75 years old at screening and reached age 76 at randomization due to the long screening time are still eligible and will be randomized into age stratum ≥ 65 .

1.1.4 Primary Analysis Time Point

After the target overall number of events of 498 has been reached and after all participants have completed their Week 260_(M 60) visit or PPW, the team will agree on the exact cut-off date/point for the final analysis. The final TTE analysis will include data until this cut-off point. Any data collected after this cut-off point will not be used for the primary analysis of TTE. That means specifically that only confirmed events collected up to the data cut-off point will be counted. Confirmation information collected after the cut-off point to confirm an earlier (meaning before the cut-off point) adjudicated diagnosis of MCI or AD due to dementia will not be taken into consideration.

There are two primary endpoint variables: time to first diagnosis of MCI due to AD or dementia due to AD (TTE), and the APCC test score. TTE will be analyzed only after the target number of events has been observed. The APCC score is analysed after all participants have completed PPW or the Week 260_(M 60) visit.

The time required to observe the target number of events is estimated to be close to the 60-month duration required for the APCC test score primary outcome.

1.1.5 Interim Analyses

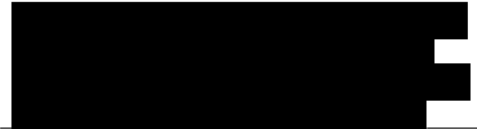

Three IAs have been planned in total for this study. All IAs will be conducted by an independent DMC based on unblinded data. It will be described in a separate DMC MAP and will describe the following:

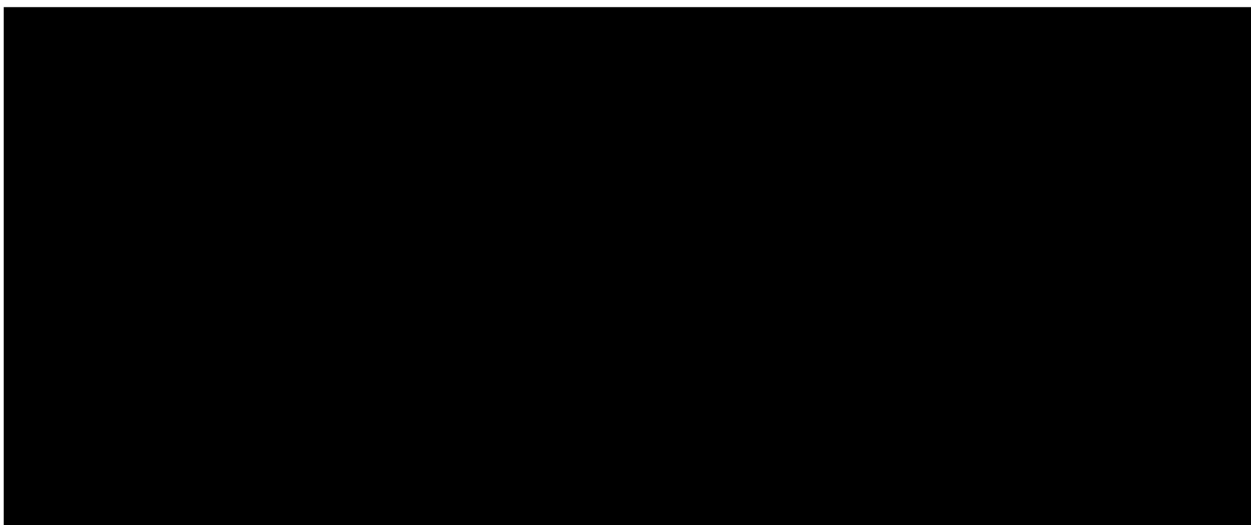
- Regular safety reviews (semi-annually, with an increased frequency as needed to appropriately evaluate the safety/tolerability profile of the current doses of CNP520 and the recommendation to maintain or modify the dose regimen via DRM): Safety and tolerability parameter evaluation including the assessment of potential worsening of cognition on active study drug based on selected clinical endpoints (RBANS and CDR-SOB). The initial regular safety reviews during the recruitment period will also serve the purpose of potential design adaptation.
- Two Interim analyses to assess:
 - Futility based on CNS activity using the following biomarkers:
 - a. Volumetric MRI: hippocampal volume
 - b. CSF: A β , tau, p-tau
 - c. PET : tau tangles
 - Primary efficacy parameters (TTE and APCC test score) to assess futility or early stopping due to overwhelming efficacy.

1.2 Study objectives and endpoints

Table 1-1 Study objectives and Endpoints

Objectives	Endpoints
Primary	
To demonstrate the effect of CNP520 vs placebo on time to diagnosis of MCI due to AD or dementia due to AD, whichever occurs first during the course of the study.	Time to the first event with event defined as the first confirmed diagnosis of MCI due to AD or of dementia due to AD.
To demonstrate the effect of CNP520 vs placebo on cognition using APCC	Change from baseline to Week 260 _(M 60) in APCC score.
Key Secondary	
To demonstrate the effects of CNP520 vs placebo on global clinical status	Change from baseline to Week 260 _(M 60) in Clinical Dementia Rating Scale - Sum of Boxes (CDR-SOB) score.
Secondary	
To demonstrate the safety and tolerability of CNP520 vs placebo	Frequencies, changes from baseline, Kaplan Meier estimates, when applicable, of: <ul style="list-style-type: none"> • Adverse events • Skin events based on a centralized dermatological monitoring • Safety findings from brain structural MRI central reader

Objectives	Endpoints
	<ul style="list-style-type: none"> • Laboratory tests • Vital signs • ECGs findings • Prospective suicidality assessment (behaviors and ideations) from eC-SSRS
To demonstrate the effects of CNP520 vs placebo on cognition using Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)	Change from baseline to Week 260 _(M 60) in total RBANS score and individual neurocognitive domain index scores
To demonstrate the effects of CNP520 vs placebo on function	Change from baseline to Week 260 _(M 60) in total score of the Everyday Cognitive (ECog) scale: ECog-subject and ECog-informant.
	
To demonstrate the effects of CNP520 vs placebo on brain atrophy	Change from baseline to Week 260 _(M 60) on volume of brain regions as measured by volumetric MRI
To demonstrate the effects of CNP520 vs placebo on AD-related biomarkers	<p>Change from baseline to Week 26_(M 6) and Week 260_(M 60) on:</p> <ul style="list-style-type: none"> • neurofibrillary tangle burden as measured by standardized uptake ratio (SUVR) of PET scans with tau tracer • amyloid deposition as measured by SUVR of tracer PET scans • CSF levels of Aβ₄₀, Aβ₄₂ • neurodegeneration as measured by CSF levels of total tau and phosphorylated tau <p>Collected only in participants who consented to additional voluntary procedures</p>



2 Statistical methods

Due to the early termination of the clinical trial, most of the primary, key secondary and the secondary objectives cannot be addressed with the data collected until termination. The originally planned inferential statistical analyses comparing efficacy readouts at Month 60 across treatment groups will not be conducted, but data collected on primary and secondary variables will be reported descriptively.

All the efficacy and biomarker endpoints except from events and TTE itself will be summarized using descriptive statistics by treatment groups (including active total, i.e., CNP520 Total) as follows

- Raw values by visit including the “last on treatment”, “last off treatment”, TEC and the EoS follow-up visit
- Change from baseline by visit including “last on treatment”, “last off treatment”, TEC and EoS
- Change from “last on treatment” visit to TEC, change from “last on treatment” to “last off treatment”, change from “last on treatment” visit to EoS and change from TEC to EoS

Note: Time of “last on treatment” and “last off treatment” will be discussed in CSR statistical Appendix 16.1.9, specifications will be described in the TFL shells document in Section 16.1.9.

All the safety data will be summarized using descriptive statistics by treatment groups (including active total, i.e., CNP520 Total).

Analysis of genetic disclosure follow-up and amyloid disclosure follow-up will be summarized using descriptive statistics by genotype and/or amyloid status groups as described in [Section 2.3.2](#).

2.1 Data analysis general information

The statistical analysis will be performed by Novartis internal statisticians and programmers.

Unless otherwise stated, summary tables/listings/figures will be presented by treatment group in the respective analysis set. Tables showing only baseline data will also include a total column.

Categorical data will be summarized as frequencies and percentages. Percentages will be calculated as below:

- For population level summaries (like Demographic, AEs, Medical history...etc.), percentages will be calculated using number of participants in each reporting group as the denominator.
- For by visit summaries, percentages will be calculated using the number of participants in the analysis set with an assessment at the specified visit as the denominator.
- For specific event based summaries, the denominator will only include the subset of the analysis population of participants at risk at a specific point in time (Kaplan-Meier approach).

Continuous data will be summarized by presenting the number of non-missing observations, mean, standard deviation (SD), median, minimum and maximum, both for raw (absolute) values and for changes from baseline. Summary tables will be presented wherever applicable by visit if not otherwise specified.

Specified parameters of interest will be listed by treatment group, records will be ordered by country/center/participant and time of assessment.

General information on treatment group labels, decimal places and other output related information will be specified in the specification document for tables, figures and listing (TFLs) shells accompanying this analysis plan.

Statistical analysis will be performed using SAS[®] statistical software (SAS Institute, Cary, NC, USA.) version 9.4 or higher.

2.1.1 General definitions

Study Drug

Study drug refers to CNP520 50 mg, CNP520 15 mg, or placebo.

Date of First Study Drug Administration (Day 1)

Day 1 is defined as the first day of randomized study drug administration. All other days will be labelled relative to Day 1. For event dates on or after Day 1, study day for an event date is calculated as (event date – first dose date + 1) which could be Day 2, Day 3 etc. For event dates before Day 1, study day for an event date is calculated as (event date – first dose date), which could be Day -1, Day -2, etc., referring to one day, two days, etc., before Day 1, respectively. Thus, Day -1 is the day preceding Day 1. Day 0 is not defined.

Date of Last Study Drug Administration

The date of last study drug administration is the day of intake of the last dose of study drug.

Baseline

A baseline value refers to the last (most recent) evaluable measurement prior to Day 1. Typically, baseline values will be the values obtained on the day of randomization. If the Baseline visit is missing or the assessment was not done at Baseline, the last assessment of an earlier visit

(scheduled or unscheduled) which is closest to the Baseline visit will be used as Baseline value. In case an assessment is repeated at a later visit during the screening epoch, the latest one will be used as Baseline value.

Note: Assessments at the day of randomization are assumed to have been taken as per protocol, i.e. if the assessment should be performed before dosing, the assessment will be treated as pre-dose as per protocol. Practically, i.e. that the time part of the date/time entry (when collected) will be ignored. Exception: In case there is a protocol deviation or a comment that specifically indicates that the assessment has been taken post-dose, the assessment will not be handled as pre-dose.

Post-baseline

For safety and efficacy evaluations all assessments after Day 1 are defined as post-baseline assessments.

Roll-over participants

Participants from API015A2201J study (Generation study 1; GS1) may roll over to be enrolled into CNP520A2202J study (Generation study 2; GS2). These participants have been genotyped and disclosed in GS1.

Roll-over participants in GS2 have signed the GS2 Informed Consent Form (ICF/ICF#B), and GS2 inclusion/exclusion criteria were verified. The participant received a new subject identifier in GS2. Some of the screening assessments for these participants will be repeated in GS2, and for some assessments, data obtained in GS1 will be re-entered. More details on data collection for roll-over participants is outlined in [Appendix 5.7](#).

Note: For roll-over participants, data collected in GS1 and skipped in GS2 are expected to be mapped (re-entered) from the GS1 to the GS2 database. Hence, there is no programming effort expected to map the data from GS1 to GS2.

Re-screened participants

Participants who screen-failed due to a temporary condition (e.g. physical, concomitant medications, etc.) or due to administrative reasons may be re-screened after resolution. The participant will receive a new subject identifier at re-screening. The latest screening assessment will be considered for reporting at screening visit. Assessments (like genotype, volumetric MRI, etc.) that are not repeated, will be carried over. This is based on mapping the old subject identifier to the new subject identifier.

In general, all data collected under the old subject identifier is kept after mapping to the new subject identifier. This comprises for instance AEs, vital signs, ECG, and laboratory data. In case of missing values under the new subject identifier, the latest available value from the old subject identifier will be used. In study GS2, the earliest consent date is kept, if the subject is re-screened

Prior and Concomitant Medication

Prior medication will be defined as any medication taken prior to the first dose of the study drug, irrespective of whether the medication continued into the treatment period.

Any medication administered at least once between Day 1 and end of the study is defined as concomitant medication.

Visit Windows

In general, by-visit analyses will include data from scheduled as well as un-scheduled visits using visit windows for scheduled visits except for TEC/PPW and EoS. In general, the lower and upper bound of a visit window will be defined as the midpoint between scheduled visits. The visit window rules for efficacy and safety parameters are defined in [Appendix 5.8](#).

For efficacy parameters: In case of competing assessments within a visit window, the assessment value closest to the scheduled visit day will be used. In case of equal distances, the earliest assessment value will be used. Visit window will not be applicable for TEC and EoS.

For safety parameters: In case of competing assessments within a visit window, the worst assessment value within the visit window will be used. This rule also applies for worsening in cognition as a safety measure.

Listings will include all assessments, sorted by date of assessment, flagging unscheduled visits. The listings will include analysis windows and corresponding flags to indicate the assessment's inclusion in the analysis.

Treatment Epoch Completion (TEC) and End of Study (EoS) and other points in time of interest

TEC is the end of treatment phase visit (i.e., visit 299) that will be completed for all participants after discontinuation of treatment. The same visit will also be completed in case of PPW. PPW is the premature study withdrawal.

EoS is a Follow-up visit scheduled after TEC/PPW, per urgent safety measure (USM) on 11-Jul-2019, and its follow-up letter dated 12-Dec-2019, Modified EoS visits can be scheduled anytime after receipt of this notification but no later than 15-Mar-2020. (i.e. the requirement from 11 July 2019 USM for the 6 month timeframe between modified TEC and mEoS visits is no longer required.).

Participants who were attending study visits (i.e., continuing in the study) but already off-treatment at time of USM were to come for EoS straight (no TEC required).

An assessment will be on treatment if it is before or at last day on study drug + 31 days. The last assessment before or at last day on study drug + 31 days will be referred to as "last on treatment" assessment. The last assessment after last day on study drug + 31 days will be referred to as "last off treatment" assessment. For deriving "last on treatment" or "last off treatment", last assessment date of RBANS will be used. That means, to derive the last on treatment and last off treatment for all the parameters, regardless of their actual assessment

dates, RBANS last assessment date will be used as reference date. Note: the “last on treatment” and “last off treatment” flag will be created for each participant at visit level (not at the individual assessment level). If there is missing RBANS assessment at the specific visit, then date of the first day corresponding to that visit (i.e. non-missing assessment of that parameter under consideration) will be used to derive the “last on/off treatment” assessment.

Note: On treatment is a period from first dose to last dose + 31 days.

For example:

1. If a participant has the last dose on 13-Jul-2019, then “on treatment” period would span from first dose to 13-Jul-2019 + 31 days.
2. If a participant has the last dose on 09-Apr-2019, then “on treatment” period would span from first dose to 09-Apr-2019 + 31 days.

2.2 Analysis sets

The following analysis sets will be used.

The **Randomized analysis set (RAS)** will consist of all participants who received a randomization number, regardless of receiving study medication.

The **Safety analysis set (SAF)** will consist of all participants who received study medication.

Note: The above SAF definition is different from the protocol defined SAF definition which restricts to include only those participants in SAF if they have had at least one safety assessment after first dose administration.

The **modified SAF (mSAF)** will consist of all participants of the SAF with at least 3 months exposure duration.

All efficacy analyses (except worsening in cognition and reversibility) and safety analyses will be conducted on the SAF.

In addition, the following sets of participants will be used to understand the composition of analysis sets and disposition of participants.

The **Screened set** will consist of all participants completing any Screening visit. This set should comprise all participants who underwent any screening assessment.

2.2.1 Group for specific analysis

Analysis of worsening in cognition and assessing reversibility of worsening in cognition will be performed on the mSAF.

2.3 Patient disposition, demographics and other baseline characteristics

Summary tables for demographic variables and other baseline characteristics as well as relevant medical history will include an active total (pooled across active treatment arms) and a total column in addition to the treatment arms.

The impact of genetic and amyloid disclosure for the participants assessed for genetic disclosure and amyloid disclosure during the screening period will also be reported by genotype groups.

2.3.1 Patient disposition

The number and percentage of participants in each analysis set described above will be presented including all participants that started screening. Primary reason for screen failure will be summarized for all participants.

Participant disposition will be summarized for the RAS showing the flow of participants through the treatment epoch and completing the End of Study disposition page. The disposition summary will show the number and proportion of participants who discontinued treatment epoch and End of Study status along with the reason for discontinuation. The number and proportion of participants with missing End of Study assessment will also be reported. The primary reasons for premature discontinuation of study treatment will also be summarized. Listings will be provided showing the primary reason for premature discontinuation of study and of study treatment.

All the important protocol deviations (PDs) reported during the study will be summarized in the following five categories:

- Selection criteria not met
- Participant not withdrawn as per protocol
- Treatment deviation
- Prohibited concomitant medication
- Other deviations (important deviations that do not fall in the above four categories)

Important PDs are defined as subset of PDs that may significantly impact a subject's rights, safety, and well being or the completeness, accuracy, and/or reliability of the study data. The PD codes to identify the above categories are listed in [Table 5-4](#) in the Appendix.

2.3.2 Analysis of impact of Disclosure (Genetic Disclosure and Amyloid Disclosure)

Background

The intention of this section is to summarize the main safety evaluation of Genetic and Amyloid Disclosure follow-up in CNP520A2202J. No inferential statistical analyses will be reported. Disclosure assessment scales, baseline characteristics and all other safety assessment related to disclosure will be reported descriptively as appropriate.

Safety assessments will include disclosure scales, eC-SSRS, adverse events (AEs), and serious adverse events (SAEs) if related to genetic disclosure. The statement that a participant had no adverse event or findings also constitutes a safety assessment.

Summary statistics for categorical data will typically include frequencies and percentages per selected group.

Assessment period for impact of Disclosure

The Screening Epoch of study CNP520A2202J includes several visits, separable into two parts: screening part I and screening part II. Screening part I will have APOE genotype assessed. After genetic counseling and disclosure, participant may take a few days to reflect on this information, before continuing to screening part II. A follow up will take place two to seven days post genetic disclosure. Screening part II starts after the reflection period, and contains MRI scan, amyloid PET scan or a lumbar puncture to verify eligibility of HTs based on brain amyloid status (HTs can opt out of amyloid disclosure). Another reflection period may take place after amyloid disclosure. A follow up will take place two to seven days post disclosure

Throughout the disclosure follow-up periods of CNP520A2202J, an independent Disclosure Monitoring Advisory Group (DMAG) is responsible for monitoring the safety of the participants in relation to the Genetic and Amyloid disclosure. DMAG review the disclosure data twice a year to ensure that any outstanding safety concerns would be properly addressed. A separate analysis plan specifies the analyses to be performed for the DMAG reviews. This genetic and amyloid disclosure CSR will be largely overlapping the DMAG.

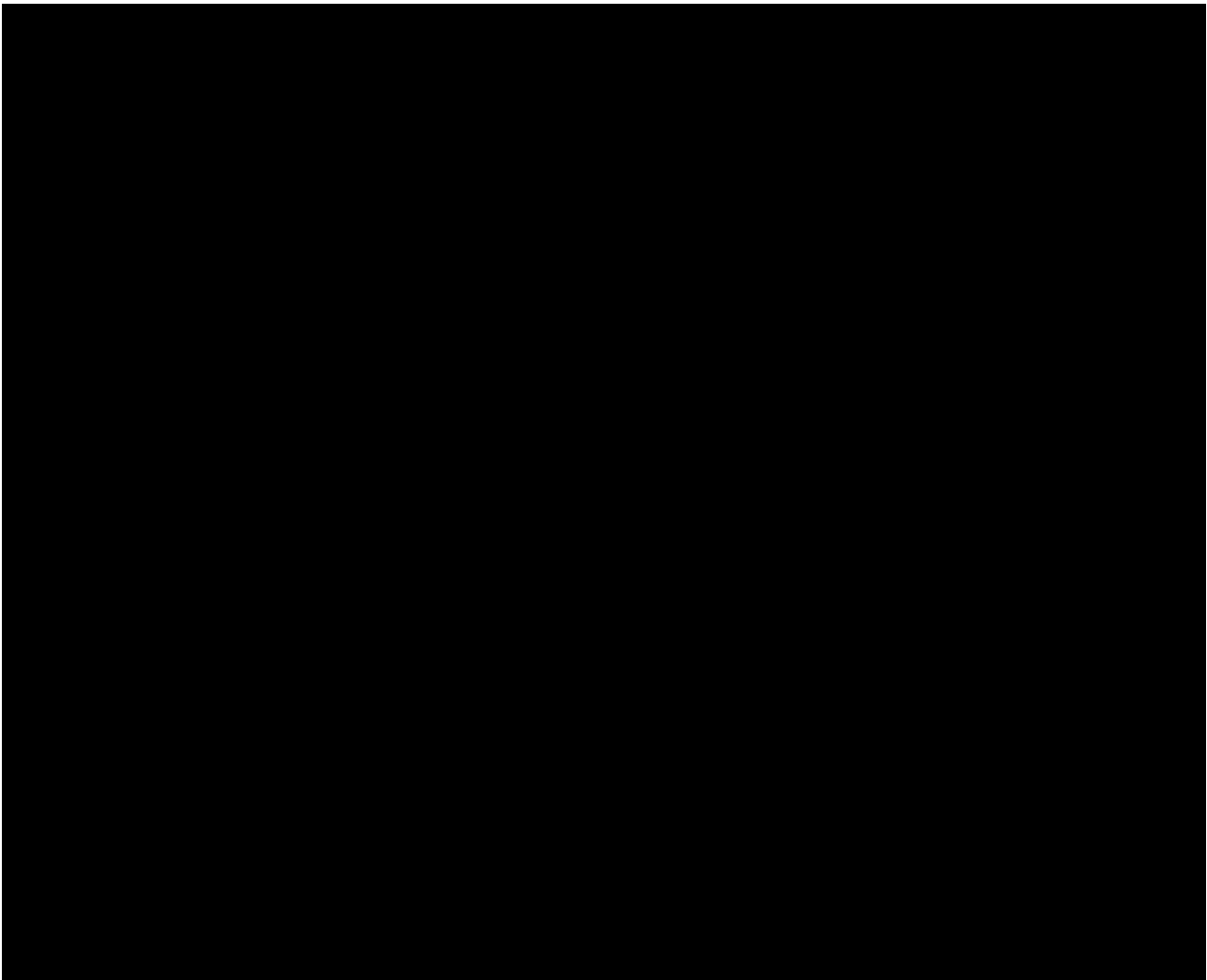
The impact of genetic disclosure is assessed 2-7 days after the genetic disclosure (GD). The

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]



Analysis strategy

Data for impact of GD and AmD will typically be reported based on the corresponding Follow-up set by APOE4 genotype and/or Amyloid status.

Note: In database, APOE genotype data is collected from two sources; CRF and vendor (Covance) load. CRF data is for initial genotyping and vendor load is for genotype confirmation. For reporting of genetic disclosure analysis, CRF data will be used to derive the genotype. However, if the CRF data is missing, the corresponding vendor load data will be used.

Amyloid status will be Elevated/Not-Elevated as derived by vendor result (including a visual examination of the scan).

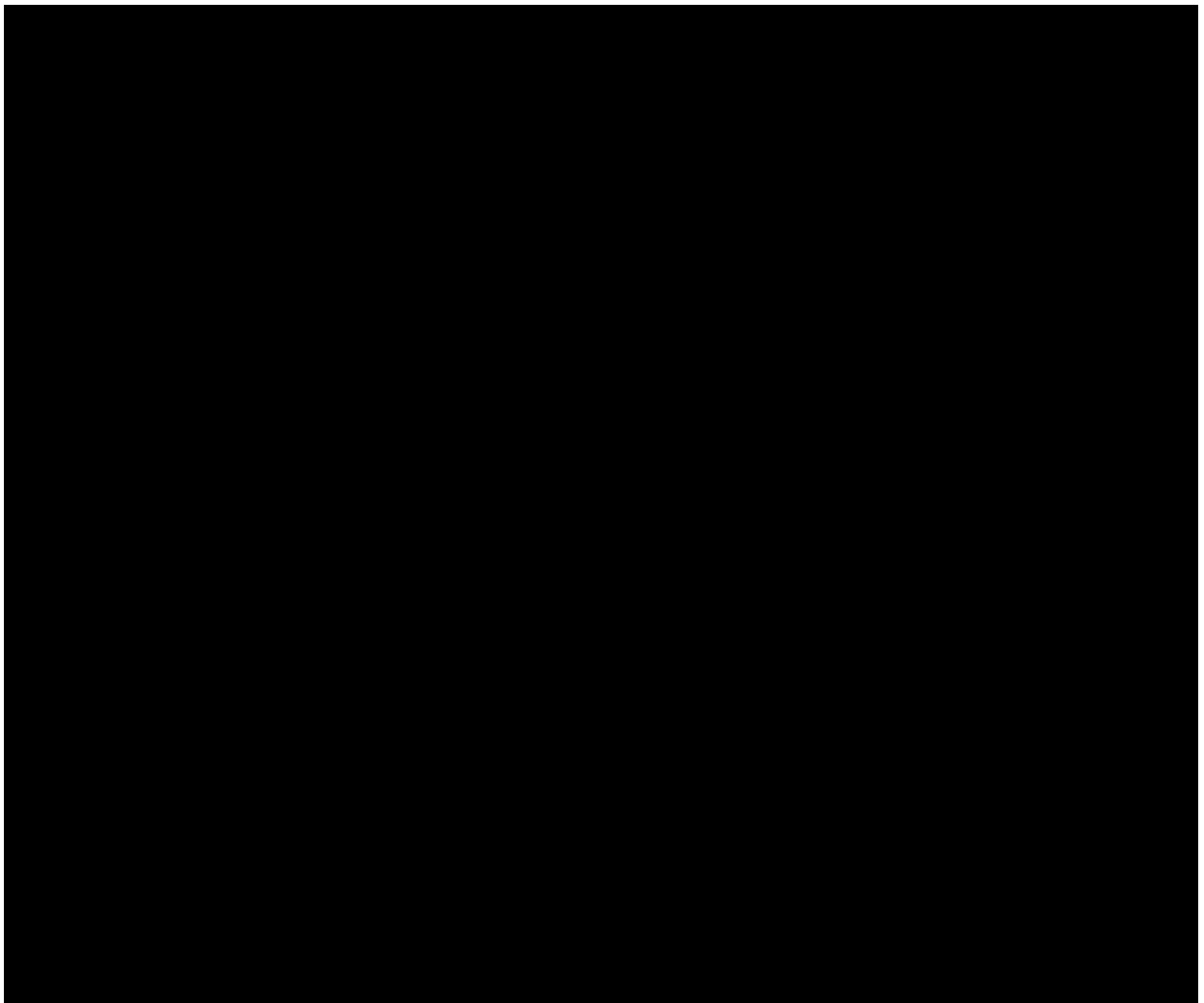
The reference visit for change from “baseline” for impact of GD questionnaires will be the Screening 1 Visit 101 (pre-GD assessment) for reports on the impact of GD. The corresponding reference value is defined as the last value collected before GD, i.e. the value collected at the Screening 1 visit. The Screening 3 Visit 103 (Day 2-7 after GD) will be the reference visit for

reports on the impact of AmD. Nevertheless, the reference value can also stem from an earlier visit. The reference value is defined as the last value collected before AmD, i.e. the value from the last assessment from the last visit before or at the reference visit.

Note: For roll over participants whose assessments corresponding to Screening 1 and Screening 3 visits in GS2 are performed in GS1. However, in GS2 at least one assessment is required before amyloid disclosure and it may be recorded under Screening 1 or Screening 3, hence the change from baseline will be derived as described earlier using for reference value the last value collected before AmD, i.e. the value from the last assessment from the last visit before or at the reference visit.

The number and percentage of participants in each analysis set described above will be presented including all participants that started screening. Reason for screen failure will be listed for all screened participants.

Demographic information will be summarized such as age, gender, prior knowledge of genotype, years of education, family history of AD based on the disclosure Follow-up set.



Adverse events (AEs)

AEs and SAEs identified by the investigator as being related to disclosure will be summarized.

In addition, all AEs related to disclosure will be listed as well as concomitant medications of these participants. Results of the impact of disclosure questionnaires will be listed by visit for these participants.

AEs that may be related to genetic or amyloid disclosure may consist of, but not limited to the following:

- Depression per investigator judgment (and GDS total score >10)
- Anxiety per investigator judgment (and score on the six Item Subset of the STAI-AD >19 at any of the Post-Disclosure Follow-up phone calls)
- Increase in levels of distress per investigator judgment (as reported as AE since no specific scale in GS2).
- Suicidality

Participants meeting any of thresholds in [Table 2-2](#) will be referred for additional follow-up with a psychiatrist, corresponding AE will be recorded and any concomitant medication. In case the assessments were administered over the phone, an unscheduled visit to the site is warranted to collect appropriate safety measures.

eC-SSRS

In addition to the above listed specific questionnaires to assess the impact of genetic and amyloid disclosure, suicidality (ideation and behavior) will be collected as part of the “Screening epoch” of CNP520A2202J. The Columbia-Suicide Severity Rating Scale (C-SSRS) is a questionnaire that prospectively assesses Suicidal Ideation and Suicidal Behavior. If, at any time the score is “yes” on item four or item five of the Suicidal Ideation section of the eC-SSRS (and if at Screening, the ideation occurred in the past 6-months) or “yes” on any item of the Suicidal Behavior section, the participants must be referred to a psychiatrist for further assessment and/or treatment if the investigator is not a certified psychiatrist. More details about eC-SSRS can be found in study protocol.

The eC-SSRS data will also be reported using the same strategy as in DMAG.

Two analysis periods will be defined and used as follows:

1. Lifetime history:

Lifetime assessment occurs only once, Screening 1 visit (Visit 101).

2. Post disclosure pre-treatment period:

Assessments after the Screening 1 visit (Visit 103, Visit 107) up to and including the baseline visit ((Visit 201) and unscheduled visit falling into 12-week Screening period).

First assessment of eC-SSRS is SCREENING 1 (V101) in CCNP520A2202J study.

In CNP520A2202J, eC-SSRS is collected in all screened participants and will, hence, be reported based on the Screened set. The number and percentage of participants in each category will be tabulated by visit for categorical data and summary statistics will be presented for continuous data.

2.3.3 Background and demographic characteristics

The following demographic and baseline variables will be summarized on the SAF . No listings will be provided.

Demographic variables:

Continuous variables:

- Age (years)
- Height (cm)
- Weight (kg)
- BMI (kg/m^2) will be calculate as (body weight in kilograms) / (height in meters)²
- Volumetric MRI-Whole Brain (cm^3)
- Volumetric MRI-Hippocampus (cm^3)
- Amyloid PET Centiloid

Categorical variables:

- Age group (≤ 64 , 65-69, ≥ 70)
- Sex (Male, Female)
- Years of education: ≤ 12 years, 13-16 years, ≥ 17 years
- BMI (< 25 vs ≥ 25)
- Race (Caucasian, Black, Asian, Native American, Pacific Islander, Other, Unknown)
- Ethnicity (Hispanic or Latino, Other East Asian, Southeast Asian, South Asian, West Asian, Russian, Japanese, Chinese, Mixed Ethnicity, Other, Unknown, Not reported)
- Genotype (HM/ HT)
Note: In database, APOE genotype data is collected from two sources; CRF and vendor (Covance Central Laboratory) load. CRF data is for initial genotyping and vendor load is for genotype confirmation. For deriving genotype for safety analysis, vendor(Covance Central Laboratory) load will be considered. However if the vendor load data is missing the corresponding CRF data will be used
- Amyloid status (Elevated/ Not-Elevated) in HMs
Note: Amyloid status will be Elevated/Not-Elevated as derived by vendor result or derived by the combination of the two results CSF and PET (whichever is Elevated) as described in [Section 2.7.1](#) in subsection Analysis of positive/negative amyloid levels.

Cognitive scales at baseline

Continuous variables:

- MMSE
- RBANS Total score
- Immediate Memory Index
- Delayed Memory Index
- Visuospatial/constructional Index
- Language Index
- Attention Index
- CDR-SOB

Categorical variables:

- CDR Global (Score = 0, Score = 0.5, Score > 0.5)

Other characteristics

The following categorical referral and Alzheimer's disease characteristics will be summarized on the SAF.

- Source of participant's referral (Physician's own practice, Physician referral, Television advertisement, Radio advertisement, Print advertisement, Newsletter/educational material, Advocacy group, ER visit or hospital, Novartis internet site, Non-Novartis internet site, Clinical Trial Registry, Social media, Other)
- Source of the genotyping information (Genematch, 23andMe, Local registry, API015A2201J study, Current study, Other)
- Family history of AD (Father/ Mother, Siblings, Grandparent, Other, None)

Comparability of randomized groups (active versus placebo) at baseline will be assessed via Fisher's exact tests for 2x2 tables or the corresponding Freeman-Halton test for general l x k tables (l, k >= 2) for the selected categorical variables. If Fisher's exact tests are not estimable (e.g. sample size is too large to calculate the statistic) or not adequate, then Chi-squared tests will be performed. Baseline comparability for selected continuous variables will be assessed using t-tests assuming unequal variances in the two groups (active versus placebo). The tests performed together with the p-value will be reported for each baseline variable that has been investigated for comparability. The selected variables for comparisons will be indicated in the TFL shells.

Medical history

Any condition entered as medical history or current medical conditions at baseline will be coded using the MedDRA dictionary effective at the time of the database lock and summarized by system organ class (SOC) and preferred term (PT) on the SAF. No listing will be provided.

2.4 Treatments (study treatment, rescue medication, concomitant therapies, compliance)

2.4.1 Study treatment / compliance

The duration of exposure to study drug is defined as the time (in days) from the first study drug administration to last study drug administration + 31 days.

The duration of exposure will be calculated as

(last dose date + 31 days) – first dose date + 1.

Duration of exposure to CNP520 will be summarized as continuous variable (in days) and categorical variable, using categories ≥ 1 day (any exposure), ≥ 3 months, ≥ 6 months, ≥ 1 year, ≥ 1.5 years.

For each treatment group, the participant-years will be calculated as

(sum of the durations of exposure for all participants in the group)/365.25) and will be summarized.

2.4.2 Prior, concomitant and non-drug therapies

The number and percentage of participants receiving concomitant medications will be summarized on the SAF by ATC class and preferred term (according to the latest World Health Organization drug dictionary (WHO-DD) at the time of database lock, including Anatomical Therapeutic Chemical (ATC) classification code).

The number and percentage of participants receiving significant non-drug therapies will be summarized on the SAF by primary system organ class, preferred term (according to the latest MedDRA dictionary version available at the time of database lock).

2.5 Analysis of the primary objective

Worsening in cognition triggered early termination of the trial and plan is to describe this as rationale for early termination of the trial in CSR before describing the analysis on primary endpoint, hence the below section describes the worsening in cognition and reversibility before the primary endpoint.

2.5.1 Worsening in cognition and reversibility

Worsening in cognition will be assessed based on RBANS, CDR-SOB and APCC for participants in the mSAF.

Tables

The number of participants and the frequency of change (and worsening) in cognition of a specific magnitude (absolute change above specific threshold) will be summarized by visit, including TEC, and EoS as well as last assessment on treatment and last assessment off treatment:

- RBANS decrease (total score and Index scores): ≥ 7 points , and ≥ 14 points from baseline, and from previous visit
- RBANS improvement or increase (total score and Index scores): ≥ 7 points from baseline, and from previous visit
- RBANS no change (change between -6 and 6) from baseline, and from previous visit
- CDR-SOB increase: ≥ 0.5 points, ≥ 1.0 point, and ≥ 1.5 points from baseline, and from previous visit
- CDR-SOB improvement (any decrease) from baseline, and from previous visit
- CDR-SOB no change from baseline, and from previous visit

In addition to the “by visit“ tabulation, the proportion of participants with a clinically relevant worsening from baseline/previous visit will also be shown for

- Either at Week 13 or Week 26 (not at both) – the denominator will be based on participants who have an assessment at both visits;
- Both, at Week 13 and Week 26 – the denominator will be based on participants who have an assessment at both visits;
- At any visit out of Week 13 and Week 26 – the denominator will be based on participants who have an assessment at at least one of the two visits;
- At Any visit up to and including “last on treatment” – the denominator will be based on participants who have an assessment at any post baseline visit (up to and including “last on treatment” assessment).

For the RBANS total score, RBANS index scores and APCC score, effect sizes of change from baseline as well as 80% confidence intervals (CIs) for the effect size will be reported. The effect size (and CI) of change from baseline will be calculated for following post-baseline visits: Week 13 and Week 26, Week 52, TEC, EoS, last assessment on treatment, and last assessment off treatment. The effect size will follow the *Cohen’s d* formula: The raw mean to standard deviation ratio, not model based mean to standard deviation ratio. The effect size will be calculated as the difference between active and placebo in mean change from baseline divided by the pooled standard deviation of the change. Effect sizes and CIs will be calculated (active versus placebo, i.e. the two active CNP520 dose arms will be pooled together without stratification).

Derivation of study specific effect size *d* and corresponding CI

BL = Baseline value; PBL= Post baseline value;

SD = Standard deviation; SE = Standard error; n_1 = Sample size group 1; n_2 sample size group 2; S_1^2 = Variance group 1; S_2^2 = Variance group 2

Numerator: Mean change from BL to PBL active – mean change from BL to PBL control

Denominator: pooled SD defined as

$$SD_{pooled} = \sqrt{\frac{(n_1 - 1)S_1^2 + (n_2 - 1)S_2^2}{n_1 + n_2 - 2}}$$

Where the groups are given by factor treatment (active versus control).

The confidence interval can be derived using the formula proposed by [Hunter and Schmidt 2004](#) and [Nakagawa and Cuthill \(2007\)](#):

$$CI : d \pm z * SE(d)$$

Where z is the 10% Quantile of the normal distribution in case of the 80% CI. The SE(d) is calculated as

$$SE_d = \sqrt{\frac{(n_1 + n_2 - 1)}{(n_1 + n_2 - 3)} \left[\left(\frac{4}{n_1 + n_2} \right) \left(1 + \frac{d^2}{8} \right) \right]}$$

For CDR-SOB, corresponding confidence intervals for the difference between treatment groups will be provided.

Correlation between changes in RBANS total, APCC score and whole brain, hippocampal volume will be reported (correlation coefficient and R square will be reported by treatment group and visit (including also the last assessment on treatment, last assessment off treatment)).

Figures

Graphical presentation (forest plots) of the effect sizes and corresponding confidence intervals for RBANS total, RBANS index scores and APCC score by visit including TEC and EoS, as well as last assessment on treatment and last assessment off treatment.

2.5.2 Volumetric MRI

Screening (baseline) volumetric measurements are performed using FreeSurfer software. This leads to reference volumes for whole brain, ventricles, hippocampus, and intra-cranial.

Volumetric data will be available for the following regions:

- intra-cranial volume (ICV),
- total/whole brain,
- left/right hippocampus,
- lateral ventricles.

In order to assess atrophy rate, volumetric MRI images from follow-up timepoints are compared to those from screening, using the boundary shift integral (BSI) technique in selected brain regions. The technique determines the total volume through which the boundaries of a given cerebral structure have moved, and hence, it aims at quantifying the amount of change in these selected brain regions. The output of the method is a change from baseline in volume (atrophy).

Volume changes in the following regions of interest (ROI) will be reported:

- whole brain,
- hippocampus (sum of left and right),
- lateral ventricles (left and right).

Tables

Summary statistics for absolute change and percent change from Baseline to timepoint will be provided. All statistics will be based on the total volume, i.e. the sum of the respective left and right volumes as applicable. In addition, the annualized percentage change will be calculated as the mean of individual participant annualized percentage change (percentage change per participant / time interval (in days) between current MRI assessment and date of baseline MRI assessment per participant) x 365.25. Time interval (in days) will be derived as date of current MRI assessment – date of baseline MRI assessment + 1.

Raw volumes, as well as changes, % changes, and annualized % changes from baseline will be summarized by visit including TEC, EoS, and last assessment on treatment, last assessment off treatment.

For investigation of worsening (increased atrophy) under treatment and reversibility, these summary statistics will also be provided for the mSAF by visit including TEC, EoS, and last assessment on treatment, last assessment off treatment.

The relationship between percentage change from baseline in hippocampal and whole brain volumes and change in RBANS total score and APCC score will be examined through correlation analysis. This will be done for participants with at least 3 months exposure (mSAF). The Spearman and Pearson correlation coefficients and associated p-values will be reported.

2.5.3 Primary endpoint

There are two primary endpoint variables:

Time-to-event (TTE), with event defined as time to first confirmed diagnosis of MCI due to AD or dementia due to AD (whichever occurs first), and

Change in the API preclinical cognitive composite (APCC), from baseline to Week 260_(M 60)

Time to event (MCI due to AD or dementia due to AD)

Time-to-event (TTE), with event defined as the first confirmed diagnosis of MCI due to AD or dementia due to AD (whichever occurs first). An event is identified as a Progression Adjudication Committee (PAC)-confirmed diagnosis triggered either by an investigator diagnosis or an increase in the CDR global score. The confirmation by the PAC consists of two confirmed adjudications based on data from two consecutive visits.

In case of an identified event, TTE will be calculated as the time from randomization to the first confirmed diagnosis. For each event (confirmed diagnosis), the date of the initial investigator diagnosis will be used to establish the date of the event (neither the date of adjudication, nor the date of the confirmation). In case no confirmed event has been observed for an individual, the

observation will be censored, and the censoring date will be defined as the last date where the diagnosis classification has been assessed. Time to censoring date will be calculated from day of randomization.

The team agreed that the date of 25 August 2019 was the cut-off date/point for the final analysis. The final TTE analysis will include data until this cut-off point. Any data collected after this cut-off point will not be used for the primary analysis of TTE. That means specifically that only confirmed events collected up to the data cut-off point will be counted. Confirmation information collected after the cut-off point to confirm an earlier (meaning before the cut-off point) adjudicated diagnosis of MCI or AD due to dementia will not be taken into consideration. As a consequence, the observation will be censored at the last date prior to cut-off point that the TTE endpoint was evaluated, and the unconfirmed diagnosis will not be counted as an event in the primary analysis.

Due to the early termination of the studies, only a small number of events following the above definition have been observed. Hence, for the abbreviated CSR, the number (%) of participants meeting the following additional situations (change in diagnosis classification) will also be reported:

1. Participants with a change in diagnosis classification from cognitively unimpaired by the principal investigator at any time
 - MCI due to AD,
 - MCI not due to AD,
 - Dementia due to AD,
 - Dementia not due to AD.
2. Participants with an increase in CDR global score from baseline at any time (any increase, increase less than 1, increase of 1 or more);
3. Participants where data was sent for adjudication to PAC (regardless of confirmation at the following visit) split by the result of the adjudication:
 - Cognitively unimpaired,
 - MCI due to AD,
 - MCI not due to AD,
 - Dementia due to AD,
 - Dementia not due to AD,
 - Other (Unable to adjudicate, data not collected, not known).

Note that cut-off date/point (25 August 2019) used for protocol defined event (MCI due to AD or dementia due to AD) will not be applicable for the above defined additional situations. Data up to the the database lock date will be used for the analysis of these additional situations.

APCC score

The APCC test score is defined as a weighted sum of the following test items:

Raven's Progressive Matrices – subset items A2, A4, A8 & B1-B6 (0-9)

MMSE:

- Orientation to Time (0-5)
- Orientation to Place (0-5)

RBANS (Subtest raw scores):

- List Recall (0-10)
- Story Recall (0-12)
- Coding (0-89)
- Line Orientation (0-20)

The range of the APCC test score is from 0 to 100 where higher scores in the APCC correspond to a better cognitive performance. The APCC will be derived based on the test items using the below formula and weights:

APCC test score = $1.360 \times \text{RBANS List Recall} + 1.100 \times \text{RBANS Story Recall} + 1.390 \times \text{Raven's Progressive Matrices (subset items A2, A4, A8, B1-B6)} + 0.321 \times \text{RBANS Coding} + 0.510 \times \text{RBANS Line Orientation} + 2.140 \times \text{MMSE Orientation to Place} + 2.240 \times \text{MMSE Orientation to Time}$.

2.5.4 Statistical hypothesis, model, and method of analysis

Except from the primary objective on the TTE endpoint, the other primary objective (for APCC) aimed to evaluate effects of CNP520 versus Placebo by comparing changes from baseline to Month 60. Due to the early termination of CNP520, no data have been collected at Month 60. Only very few participants have provided data on active treatment with CNP520 beyond one year of follow-up. Hence, the originally planned inferential and model based statistical analyses cannot be performed and are no longer applicable.

Time to event (MCI due to AD or dementia due to AD), Time to first change in diagnosis classification and Time to first decrease in RBANS Total of ≥ 14 points

Tables

Time to Event analysis using Kaplan Meier approach will be presented for time to MCI due to AD or Dementia due to AD (events as per protocol) and for time to first change in diagnosis classification (this is an event regardless of confirmation and adjudication) from cognitively unimpaired by the investigator. Analysis of time to first change in diagnosis classification will also be performed for participants on treatment. In addition, analysis of time to first decrease in RBANS Total Score of ≥ 14 points will be performed for participants on treatment (for on treatment definition, refer [Section 2.1.1](#)). The Kaplan-Meier estimates of the cumulative event rate for each treatment group will be summarized and plotted. To calculate the proportion of participants with events, number of participants at risk will be used as the denominator. "Participant at risk" at a specific time point is defined as the number of participants in the study without an event at up to that time point.

These analyses will only be performed if there are at least five such events.

In addition, the number and percentage of the additional situations ([Section 2.5.3](#)) defined events overall (not by visit) will be summarized by treatment group.

APCC score

Tables

The APCC test score and the seven components (listed above in [Section 2.5.3](#)) will be summarized on the SAF.

2.5.5 Handling of missing values/censoring/discontinuations

Time to event (MCI due to AD or dementia due to AD), Time to first change in diagnosis classification and Time to first decrease in RBANS total \geq 14 points

In general, an observation will be censored if no event has been observed at the TTE analysis cut-off date. The censoring date will be defined as the last date (before cut-off date) where the TTE endpoint has been assessed.

The censoring date for each participant that did not have an event (i.e., a confirmed diagnosis) is defined as follows:

1. For participants ongoing in the study without a confirmed diagnosis at the time of the cut-off: the last day of a diagnosis assessment (the previous visit where a diagnosis assessment occurred prior to the cut-off date).
2. For participants who permanently discontinued from the study prior to the cut-off: The last day of a diagnosis assessment prior to study discontinuation.
3. For participants who had their last diagnosis assessment prior to randomization (i.e. during screening epoch) or do not have any diagnosis assessment post randomization, their randomization date will be used as censoring date.
4. For analysis of time to first decrease in RBANS \geq 14 points, the last RBANS assessment date will be used as censoring date instead of last diagnosis assessment date mentioned in above three points.

Note: For Time to MCI due to AD or dementia due to AD, the cut-off date will be 25 August 2019. Analysis of Time to First change in diagnosis classification, the cut-off date will be database lock date, additional analysis of time to first change in diagnosis classification will be performed for participants on treatment. Also time to first decrease in RBANS \geq 14 points will be performed for participants on treatment.

Further details on derivation of events and censoring will be added to the programming document specifications (PDS).

Other primary efficacy endpoint variable (APCC)

Due to the early termination of the trial, analyses of primary efficacy variable APCC will in general be based on observed cases only, i.e. there will be no imputation of missing data. Exception in primary efficacy variable APCC applies to missing data in subtests of Raven's matrices included in the primary efficacy variable APCC. Missing values for the subtests of Raven's matrices of the APCC may be imputed using the imputation rule defined in [Appendix 5.1.3.3.1](#).

2.5.6 Supportive analyses

Not Applicable.

2.6 Analysis of the key secondary objective

2.6.1 Key secondary endpoint

The key secondary endpoint variable is CDR-SOB.

Clinical Dementia Rating (CDR) global and Sum of Boxes (CDR-SOB)

The CDR is obtained through semi-structured interviews of participants and informants, and cognitive functioning is rated in six domains: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. Each domain is rated on a 5-point scale of functioning as follows: 0, no impairment; 0.5, questionable impairment; 1, mild impairment; 2, moderate impairment; and 3, severe impairment (personal care is scored on a 4-point scale without a 0.5 rating available). The CDR global score ranges from zero to three, with greater scores indicating greater disease severity. The CDR-SOB is defined as the sum of the ratings from the six domains, ranging from 0 to 18 with a minimum increment of 0.5. A higher CDR-SOB score indicates greater disease severity.

2.6.2 Statistical hypothesis, model, and method of analysis

The key secondary objective aimed to evaluate effects of CNP520 versus Placebo by comparing changes from baseline to Month 60. Due to the early termination of CNP520, no data have been collected at Month 60. Only very few participants have provided data on active treatment with CNP520 beyond one year of follow-up. Hence, the originally planned inferential and model based statistical analyses cannot be performed and are no longer applicable.

Tables

CDR-SOB and CDR global will be summarized on the SAF.

2.6.3 Handling of missing values/censoring/discontinuations

Due to early termination of the trial, analyses of CDR-SOB will be based on observed cases only, i.e. there will be no imputation of missing data.

2.7 Analysis of secondary efficacy objective(s)

2.7.1 Secondary endpoints

RBANS Total score and Index scores

The RBANS is comprised of the following five neurocognitive domains, with associated subtests used for Index scores:

- Immediate Memory – List Learning and Story Memory (IMI)
- Visuospatial/Constructional – Figure Copy and Line Orientation
- Language – Picture Naming and Semantic Fluency
- Attention – Digit Span and Coding
- Delayed Memory – List Recognition and Sum of (List Recall, , Story Recall, and Figure Recall; DMI)

The RBANS generates age-adjusted index scores for five neurocognitive domains, which are used to calculate a Total Scale Index score using norm tables for each Index scores in [Appendix 5.9](#). The algorithm (by vendor) to derive index scores is based on the current actual age of the participant at that visit. For longitudinal analyses this approach creates artificial variability. As a consequence, the derived data for index scores will not be used in the analyses, but will be derived from source data using the age at baseline for adjustment for all assessments. The algorithm to derive the Index scores using age at baseline will be described in the programming specifications (PDS) of this study.

A higher RBANS score indicates better cognitive function.

Mini Mental State Examination (MMSE)

The MMSE is a brief, practical clinician reported outcome that examines cognitive status ([Folstein et al., 1975](#)). It evaluates orientation, memory, attention, concentration, naming, repetition, comprehension, and the ability to create a sentence and copy two intersecting pentagons. The test consists of five domains (orientation, registration, attention, recall, and language) with a total score ranging from zero to 30. A higher score indicates better cognitive function. The five sub scores as well as the total score will be recorded.

Raven's Progressive Matrices

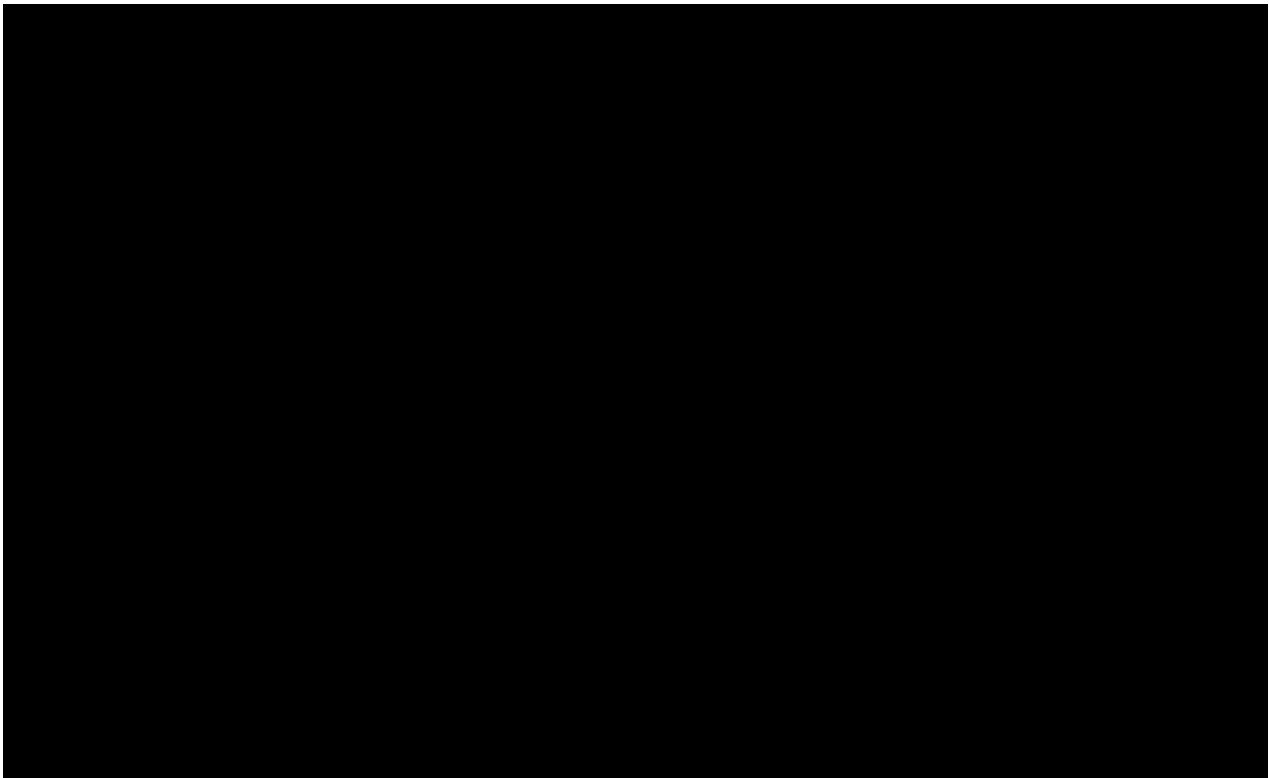
Raven's Progressive Matrices ([Raven et al 2000](#)) is a non-verbal, multiple choice measure of general ability and reasoning using a visual modality. It was designed to be culturally nonbiased, as neither language nor academic skills are required to answer items successfully.

Although all components of the Raven's Progressive Matrices Set A and Set B will be assessed, in order to calculate the APCC test score, only a subset of items from Sets A and B will be used (items A2, A4, A8, B1-B6), with a range from zero to nine.

Everyday Cognition scale (ECog-Subject and ECog-Informant)

The ECog scale measures cognitively-relevant everyday abilities and is comprised of 39 items covering six cognitively-relevant domains: Everyday Memory, Everyday Language, Everyday Visuospatial Abilities, Everyday Planning, Everyday Organization, and Everyday Divided Attention (Farias et al 2008). Within each domain, the ability to perform a specific task is rated on a five-point scale ranging from: 1) no difficulty, 2) mild difficulty, 3) moderate difficulty, 4) severe difficulty, or 5) unable to do. The scale has 2 versions one for patient (PRO) and one for informant (study partner).

The total score for the 39 items ranges from 39 to 195, with greater scores indicating worse daily function.



Biomarkers in Cerebrospinal Fluid (CSF)

The following AD related markers in CSF are analyzed:

- total-tau and phospho-tau (p-tau)
- $A\beta_{1-40}$, $A\beta_{1-42}$ and $A\beta_{1-42}/A\beta_{1-40}$

Biomarkers in blood: serum Light Chain Neurofilaments (NFL)

Available measurements for NFL from serum will be summarized.

Values below the lower limit of quantification (LLOQ) will be set to LLOQ/2 for statistical analysis, values above upper limit of quantification (ULOQ) will be imputed with ULOQ.

LLOQ and ULOQ value may differ across samples according to the dilution factor applied in the specific sample. For statistical analysis, the sample specific LLOQ and ULOQ value should be used.

[REDACTED]

[REDACTED]

Positron Emission Tomography (PET) Standard Uptake Value Ratio (SUVR)

Across the three F¹⁸ amyloid binding radiotracers used Florbetapir (FBP), Florbetaben (FBB) and Flutemetamol (Flute): Centiloids using the agreed formulae

For participants who consent to the voluntary AD-related imaging biomarker evaluations, regional activity concentration and the cortical Standardized Uptake Value (SUV) are measured based on the following brain regions of interest (ROIs):

- Parietal cortex
- Posterior cingulate or Precuneus
- Medial orbitofrontal cortex
- Anterior cingulate
- Temporal cortex

and the whole cerebellum as reference region.

Data for regional activity concentration will not be reported.

The *global* cortical amyloid load will be derived as the unweighted average cortical Standardized Uptake Value Ratio (SUVR) between the cortical ROIs and the reference region.

Standardization of Amyloid PET SUVR values

For Amyloid PET, the baseline load obtained from different tracers (florbetapir (FBP), flutemetamol (Flute) and florbetaben (FBB)) will be converted to a standardized Centiloid scale. The conversion equation for each tracer has been obtained following a non standard analysis method (AVID method) based on level-1 (GAAIN, Klunk et al. Centiloid values) and level-2 (InVicro Centiloid values) as documented in the Image Analysis charter from InVicro:

$$CL = 183.00 * SUVR_{FBP} - 176.97$$

$$CL = 123.90 * SUVR_{Flute} - 114.86$$

$$CL = 156.06 * SUVR_{FBB} - 148.132$$

The reference is [Klunk et al., 2015](#). The % change in SUVR will be calculated as

$$\%SUVR = \frac{(SUVR_{FU} - SUVR_{BL})}{SUVR_{BL}}$$

with $SUVR_{BL}$ as the baseline value and $SUVR_{FU}$ the SUVR value at follow-up visit.

Analysis of positive/negative amyloid levels

Amyloid level (positive/negative) is measured at screening by two methods:

- CSF collection via Lumbar puncture
- Brain Amyloid PET radiotracers (amyloid PET: SUVR)

The studies allow either method for determination of amyloid level. In cases both CSF A β and amyloid PET imaging tests are performed, at least one should be indicative of elevated brain amyloid. CSF samples are collected and analyzed using selected validated assay. The cut-off value to determine the amyloid level as positive/negative will depend on the assay selected. The criteria for positive amyloid level in CSF is based on pTau/Ab42 ratio. The criteria for positive amyloid PET will follow specifications for the specific radiotracer used. Following [Table 2-3](#) describes the cutoffs for both methods.

Table 2-3 Amyloid Level Stratification Criteria

Methods		Positive	Negative
CSF		<ul style="list-style-type: none"> • Elecsys ratio p-Tau/ Aβ1-42 > 0.024 AND <ul style="list-style-type: none"> • Elecsys Aβ1-42 \leq 1700.0 pg/ml (upper limit of the measuring range) 	<ul style="list-style-type: none"> • Elecsys ratio p-Tau/ Aβ1-42 \leq 0.024 OR <ul style="list-style-type: none"> • Elecsys Aβ1-42 > 1700.0 pg/ml (upper limit of the measuring range)
PET	Florbetapir (FBP)	SUVR_FBP \geq 1.1	SUVR_FBP < 1.1
	Flutemetamol (Flute)	SUVR_Flute \geq 1.123	SUVR_Flute < 1.123
	Florbetaben (FBB)	SUVR_FBB \geq 1.105	SUVR_FBB < 1.105

The same criteria will apply to all participants regardless of their genotype. In other words, both HMs and HTs were measured using either one of the methods (or both), and the positivity will be determined using the same rule in [Table 2-3](#). Analysis of Amyloid levels will be derived as Positive/Negative as described in [Table 2-3](#) above. However, in the database, eligibility result for Amyloid status will be Elevated/Not-Elevated as derived by vendor result (including a visual examination of the scan) or by the combination of the two results (whichever is Elevated) and this will be used only to check eligibility criteria for HT participants in this study.

2.7.2 Statistical hypothesis, model, and method of analysis

RBANS Total score and Index scores

Tables

RBANS total score and RBANS Index scores will be summarized on the SAF.

MMSE

Tables

MMSE total score and the sub-scores on each of the five domains (orientation, registration, attention, recall, and language) will be summarized on the SAF.

Raven's Progressive Matrices

Tables

Raven's total score (sum of all items from Sets A and B) and the sub-score included in the APCC (sum of items A2, A4, A8, B1-B6) will be summarized on the SAF.

Everyday Cognition scale (ECog-Subject and ECog-Informant)

Tables

ECog total score will be summarized on the SAF for participants as well as for informants.

[REDACTED]

[REDACTED]

[REDACTED]

Biomarkers in CSF

Tables

All available AD related markers will be summarized for actual values as well as for change from baseline.

Baseline ratios for p-Tau/A β 1-42 were used to determine Elevated /Not elevated brain Amyloid status and results will be reported as described in [Section 2.7.1](#).

Figures

Box-plots for CSF parameters (Total tau, p-tau, A β 1-40 and A β 1-42) and ratio A β 1-42/A β 1-40 over time by treatment group will be provided

Biomarkers in blood: serum Light Chain Neurofilaments (NFL)

Tables

Available measurements for NFL from serum will be summarized for actual values as well as for change from baseline.

Figures

Box-plots for serum NFL over time by treatment group will be provided



PET SUVR

Listing

PET SUVR listing will be reported.

Analysis of positive/negative amyloid levels

Tables

Amyloid levels (Positive/Negative) by method CSF and PET will be summarized as frequencies and percentages.

2.7.3 Handling of missing values/censoring/discontinuations

Due to the early termination of the trial, analyses of secondary efficacy variables will in general be based on observed cases only, i.e. there will be no imputation of missing data. Exception applies to missing data in RBANS Index scores, i.e., missing values for RBANS Index scores may be imputed using the imputation rule defined in [Appendix 5.1.3.3.1](#).

2.8 Safety analyses

Reporting of safety data will be based on the SAF. Safety assessments will include adverse events, serious adverse events, deaths, laboratory data (hematology, blood chemistry, urinalysis), vital signs, ECG, safety MRI, physical and neurological examination, prospective suicidality assessment, dermatology photo report.

Summary statistics for categorical data will typically include frequencies and percentages.

For safety parameters, the summaries will be based on worst available observation in an analysis window. The analysis window and definition of worst value is present in [Appendix 5.8](#).

2.8.1 Adverse events (AEs)

Treatment-emergent AEs (TEAEs) are events that either started after the first dose of study drug or events present prior to the start of study drug but increased in severity since the first dose. Adverse events reported within 31 days (5 half-lives) from study drug discontinuation date (i.e., last dose date) will be considered as TEAE. AEs reported more than 31 days after study drug discontinuation will not be considered treatment emergent (non-TEAE).

TEAEs and non-TEAEs will be summarized separately on the SAF.

Tables

TEAEs, SAEs, deaths and non-TEAEs will be summarized as follows

- TEAEs regardless of relationship to study drug by SOC, PT and maximum severity
- non-TEAEs, regardless of relationship to study drug by SOC and PT
- TEAEs causing study drug discontinuation by SOC, PT and maximum severity
- TEAEs related to study drug by SOC, PT and maximum severity
- TE-SAEs regardless of relationship to study drug by SOC and PT and maximum severity

Note: For missing information on AE relationship to study drug, the most conservative approach will be considered: If information on relationship of the AE to study drug is missing, the AE will be considered as related to study drug for reporting TEAEs.

The above summaries are generally without exposure adjustment, except from TEAEs by SOC and PT: this summary will be presented with exposure adjustment. The exposure-adjusted incidence rate of adverse events is defined as the number of participants with the adverse event divided by total participant years at risk in the treatment group. The time at risk for each participant will differ for each adverse event. For participants with events, only the time until the first event contributes to the total participant years at risk. For participants who do not experience the event, the time at risk will be calculated using the duration of exposure as defined in [Section 2.4.1](#). The exposure-adjusted incident rate will be summarized per 100 participant years. For participants with multiple occurrences of the same event, the event will be counted only once per participant.

Adverse events will be reported according to the latest MedDRA dictionary version available at the time of database lock.

If a participant reported more than one adverse event within the same PT, the adverse event with the greatest severity will be counted. If a participant reported more than one adverse event within the same SOC, the participant will be counted only once with the greatest severity at the SOC level, wherever applicable. Sorting order for the AE summaries will be as follows:

- For summaries by SOC, SOC will be presented in alphabetical order.
- For summaries by SOC and PT, SOC will be presented in alphabetical order; PT will be sorted within system organ class in alphabetical order.

Listings

All AEs will be listed ordered by country/center/participant and event date. Supplementary data for dermatological adverse events will also be listed (i.e., distribution of pruritus, presence, laterality and directionality).

2.8.1.1 Adverse events of special interest / grouping of AEs

An adverse event of special interest (AESI) is a set of adverse events that are of scientific and medical concern specific to a compound. These groupings are defined using MedDRA terms, SMQs (standardized MedDRA queries), HLGs (high level group terms), HLT (high level terms) and PTs (preferred terms).

Customized SMQs (Novartis MedDRA queries, NMQ) may also be used. An NMQ is a customized group of search terms which defines a medical concept for which there is no official SMQ available or the available SMQ does not completely fit the need. It may include a combination of single terms and/or an existing SMQ, narrow or broad.

AESIs as specified in the CNP520-specific Development Safety Profiling Plan (DSPP) are grouped in the corresponding Case Retrieval Sheet (eCRS) and analysed as a specific group along with other risk search terms.

The search criteria for each of the risks and events will be based on MedDRA and will be comprised by the eCRS. The most recent eCRS at the time of database lock will be used to determine the MedDRA search criteria for identification of the adverse events of special interests.

Tables

Number and percentages of participants with treatment emergent adverse events of special interest by risk and MedDRA levels will be summarized on SAF.

2.8.2 Deaths

Tables

Deaths regardless of relationship to study drug by SOC and PT will be summarized on the SAF.

Listings

Deaths will also be listed separately.

2.8.3 Laboratory data

Tables

Number and percentages of participants with newly occurring or worsening laboratory abnormalities meeting the clinically notable criteria at any time post-baseline visit will be summarized for all parameters as specified in [Appendix 5.6](#) of this document.

For a participant to meet the criterion of a newly occurring clinically notable value, the participant needs to have a baseline value that is not clinically notable for that parameter. For a participant to meet the criterion of a worsening clinically notable value, the participant needs to have a baseline value that is clinically notable and also have a worse post-baseline value. For participants with missing baseline value, any post-baseline notable value will be considered as newly occurring.

For each participant, all available post-baseline laboratory tests will be used to compare with the notable criteria. If at least one of the results, for a particular parameter, exceeds the criteria, the value will be considered as clinically notable abnormal for that parameter. A participant can be counted in both, low and high categories.

The upper limit of normal (ULN) for each parameter is available in the lab dataset. All available post-baseline laboratory tests will be used to compare with the criteria specified in [Appendix 5.6](#). If at least one of the results, for a particular parameter, exceeds the criteria, the value will be considered as notable abnormal for that parameter. To categorize the abnormality, use the worst case within a lab parameter for a participant if multiple abnormality occurrences exist for the same lab parameter.

The laboratory parameters will be reported in SI units.

The number and percentage of participants with newly occurring or worsening liver enzyme abnormalities meeting the clinically notable criteria at any time post-baseline visit as specified in [Appendix 5.3](#) will be summarized.

Figures

Box-plots for lab parameters of hematology, biochemistry and urinalysis over time by treatment group will be provided:

2.8.4 Other safety data

2.8.4.1 ECG and cardiac imaging data

12-lead ECGs will be performed at screening and throughout the study in supine position. The ECG values will be interpreted and analyzed centrally. The QT intervals will be corrected according to the formula by Fridericia:

Fridericia's formula: $QTcF = QT/RR^{1/3}$

Tables

The number and percentage of participants with newly occurring or worsening clinically notable ECG abnormalities at any time post-baseline visit will be summarized for all parameters as specified in [Appendix 5.6](#).

Figures

Box plots over time will be presented by ECG parameter and treatment group.

2.8.4.2 Vital signs

Tables

Parameters to be summarized are the following:

- Change from baseline in body weight will be summarized by visit including last assessment on treatment and last assessment off treatment.
- Vital signs: clinically notable changes (Body weight change will also be split by weight loss and weight gain).

The number and percentage of participants with clinically notable vital signs abnormalities at any time post-baseline visit will be summarized. The criteria of clinically notable vital signs are provided in [Appendix 5.6](#).

Clinically notable weight changes of participants will be further investigated with the following summaries:

Frequency table will be presented for clinically notable weight changes (decrease/increase from baseline $\geq 7\%$ from baseline weight) during the treatment phase, by baseline weight categories (<55 kg, 55 - <70 kg, 70 - <84 kg, ≥ 84 kg) and by gender (Male, Female)

Participant demographics and other baseline characteristics with clinically notable weight decrease (loss) will be summarized.

Figures

For the following parameters, box-plots by visit will be created: Heart Rate, Systolic BP, Diastolic BP, body weight.

2.8.4.3 Prospective Suicidality Assessment

The Columbia-Suicide Severity Rating Scale (C-SSRS) is a questionnaire that prospectively assesses Suicidal Ideation and Suicidal Behavior. The electronic version, the eC-SSRS will be administered as described in the visit schedule of the study protocols and may also include unscheduled visits. At the first time of administration of the eC-SSRS, a retrospective assessment of suicidal behavior and ideation will be collected across lifetime. This data will be used to check inclusion/exclusion criteria. At all other scheduled assessments of suicidal behavior and ideation, any occurrence since the last visit will be collected.

The data will be reported by analysis period. The following three periods have been identified to cover lifetime history, the time between collection of lifetime history and start of study drug intake, and the time on study drug.

Tables

The number and percentage of participants pertaining to each of the categories of suicidal ideation and behaviors will be presented by analysis period and treatment.

The analysis periods will be defined as follows

1. Lifetime history: Lifetime assessment occurs only once (Screening 1 visit (Visit 101)).
2. Post disclosure pre-treatment period: assessments after the Screening 1 visit up to and including the baseline visit (Visit 103, Visit 107 and Visit 201 and unscheduled visit falling into this time period)
3. Post baseline: all visits after baseline visit (including unscheduled).

The summaries will show numbers and percentages of participants who have an answer “yes” to a suicidal behavior or ideation category at any time within the corresponding analysis period.

Listings

For participants with any assessment that meets the criteria to trigger the recording of an SAE as specified in the study protocols, a full listing will be presented. The criteria for SAE reporting are as follows:

If, at any time, the score is “Yes” on item 4 or item 5 of the Suicidal Ideation section of the C-SSRS or “Yes”. All such cases regardless of whether there was an SAE reported or not will be listed.

2.8.4.4 Safety MRI

Safety MRI findings will be summarized overall (at any visit) for ARIA-E, ARIA-H and White matter disease findings.

Worsening of white matter disease is defined on the age-related white matter changes rating Scale (ARWMC) which is rated on a 4 point (0-3) scale per region (bilaterally) on the following 5 different brain regions: Frontal Lobe, Parieto-Occipital, Temporal Lobe, Infratentorial area, Basal ganglia. ARWMC composite score is the sum of individual ARWMC scores from the 5 regions and ranges from 0 to 15. The ARWMC composite score will be used to summarize the white matter disease findings.

The definitions of the rating scores is shown in the below [Table 2-4](#).

Table 2-4 The ARWMC Rating Scale for MRI

Score	Definition
White matter lesions	
0	No lesions (including symmetrical, well-defined caps or bands)
1	Focal lesions
2	Beginning confluence of lesions
3	Diffuse involvement of the entire region, with or without involvement of U fibers
Basal ganglia lesions	
0	No lesions
1	1 focal lesion (≥5 mm)
2	>1 focal lesion
3	Confluent lesions

Tables

For ARIA-E, the following parameters will be presented

- Participants with any new ARIA-E (mild, moderate and severe) since Baseline,

For ARIA-H, the following parameters will be presented

- Participants with > 4 new microhemorrhages or any new macrohemorrhage \geq 10 mm in diameter since the Baseline MRI assessment

OR

- Participants with >10 microhemorrhages (new hemosiderin deposits < 10 mm) Or \geq 2 macrohemorrhages or \geq 2 areas of superficial siderosis (large area of hemosiderin deposition \geq 10 mm)

For white matter disease, the following parameters will be presented

- Participants with a white matter disease score increase since Baseline

Listings

Detailed safety MRI listings will be produced for participants with new occurrences or worsening (including Other MRI abnormalities) of identified findings.



The table content is redacted with black boxes.

2.11 Patient reported outcomes

The analysis for the patient reported outcome ECog, along with the Informant (study partner) version, is described within the secondary efficacy variables [Section 2.7](#), and eCSSRS is described in the safety analysis [Section 2.8](#).

2.12 Biomarkers

The biomarkers are described in secondary variables [Section 2.7](#).



The table content is redacted with black boxes.

2.14 Interim analysis

Due to early termination of the studies, the planned IA for CNP520 will not be performed.

3 Sample size calculation

A total of up to 2000 participants will be randomized into the study, with a sample size of 800 for the selected dose of CNP520 and placebo, respectively, thereby achieving a 1:1 ratio for the selected CNP520 dose vs placebo. Sample size calculations were mainly based on reaching a target power of 80% for the test of the elementary hypothesis on the TTE endpoint for the selected dose of CNP520 vs placebo.

Type I Error Rate and Power

The overall significance level will be $\alpha=5\%$ (rate of any false positive decision, i.e., at least one Null-Hypothesis is rejected although all were true). The overall α of 5% will be split between the two primary hypotheses on the two primary endpoints as follows: An alpha of 4% will be chosen to test the hypothesis H₀₁ on the time to first diagnosis of MCI or dementia due to AD; an alpha of 1% will be chosen to test the hypothesis H₀₂ on the APCC score.

A small portion (0.004% and 0.001%, respectively) of the error rates will be spent in a Bonferroni split to account for multiplicity due to the IA on primary endpoints. Since the portion will be very small, this has been ignored for power calculations.

Sample size calculations were mainly driven by power considerations for the primary endpoint time to first diagnosis of MCI or dementia due to AD, based on the planned recruitment time of two years and variable observation period of five to seven years. The power, i.e., the probability to detect a true difference between treatment arms, was set to be at least 80% for this analysis.

The power for the primary analysis does not account for the potential and non-negligible inflation of the type II error due to futility analyses using biomarkers and the primary efficacy endpoints. On the other hand, the potential inflation of the type II error due to the adaptive design is expected to be minimal and hence, has been ignored for the calculations of sample size.

Simulations

The sample size of the trial has been calculated based on simulations. Further details are described in the Sample Size documentation.

Sample Size Calculation based on the Primary Endpoint Time to MCI / Dementia due to AD

The sample size calculation for the TTE endpoint, i.e., for time to first diagnosis of MCI due to AD or dementia due to AD has been based on the following assumptions:

two years accrual period,

five to seven years observation period,

30% of participants experiencing an event in the control group in 60 months observation period,

a hazard ratio of 0.75 in favor of the active treatment arm,

30% drop-out rate over 60 months (corresponding to a yearly drop-out rate of about 6.9%),
 $\alpha = 4\%$, two-sided test.

Power has been investigated for the comparison of the CNP520 high dose versus placebo using a log-rank test under Lakatos approximation. Based on the above-mentioned assumptions, a sample size of 1600 participants (800 participants in the selected CNP520 dose group and placebo, respectively) need to be randomized to achieve at least 80% power. The targeted number of events required to be observed in the active treatment arm is 180 and that placebo group is 228 adding up to a total of 408 target events for the comparison of the primary active arm versus placebo. Assuming the same underlying event rate of 22.5% in the active treatment arms, the targeted number of events in the secondary active arm is calculated as 22.5% of the total number of participants in the arm (i.e. 90 events). Supposing therefore that no adaptation occurred (i.e. 2000 participants randomized), the overall targeted number of events is 498 (= 228 + 180 + 90). The power estimation using the log-rank test provides a conservative estimate and should thus be interpreted as the lower limit of power.

In the simulation setting, the trial data were simulated using models which included certain prognostic factors. This enabled the investigation of different population assumptions and allowed each subject to have its own TTE distribution depending on baseline characteristics. The power estimates based on the adjusted Cox PH model hence were overly optimistic and should be interpreted as the upper limit of power which may only be reached in a best case scenario. Power for the TTE endpoints reached 89% and more in simulations depending on the underlying assumptions on the population.

The above calculation was done using the commercial software PASS 2008.

Power calculations based on the primary endpoint APCC

Power considerations for the APCC have been based on the MMRM model generated from the simulated trials and on standard power calculation based on a t-test. The following assumptions for the power calculations based on the change from baseline to Week 260_(M 60) in APCC were used:

- Statistical test used: t-test (standard) and MMRM (simulations),
- 30% drop-out rate over five years,
- Target power of 80%,
- $\alpha = 1\%$, two-sided test.

The sample size of $n = 800$ participants in the selected CNP520 dose arm and placebo, respectively, is sufficient to detect an effect size of 0.20 with 80% power. Results from simulations indicate that using a longitudinal model and adjusting for prognostic factors will increase power to detect an effect size of 0.20.

Power calculations for APCC using the two-sided t-test have been performed with nQuery Advisor 7.0.

Overall power

The overall power to detect a true treatment effect in at least one of the two endpoints is higher as compared to the power for the single endpoints. The difference in power between the dual and single endpoints is largest when the endpoints are independent and will be small when the endpoints are strongly positively correlated.

4 Change to protocol specified analyses

SAF definition (defined in [Section 2.2](#)) is different from the protocol defined SAF definition.

An additional analysis set, mSAF, has been defined.

The following analysis were defined in the protocol but will not be performed due to early termination of the study:

- Primary analysis for both the primary endpoints
- Sensitivity to the primary analysis
- Supportive analysis to primary endpoints
- MMRM analysis to key secondary endpoint
- MMRM analysis to secondary efficacy endpoints

■ [REDACTED]

The following analysis were not defined in the protocol but will be added:

- All the efficacy analysis (except worsening in cognition and reversibility) will be performed on the SAF
- Worsening in cognition and reversibility as efficacy analysis using mSAF

5 Appendix

5.1 Imputation rules

5.1.1 Study drug

If study treatment end date is missing, then treatment epoch completion date will be considered the last dose date, the rule will be provided in Programming Dataset Specification (PDS) document in details.

5.1.2 AE date imputation

Rules for imputing AE end date or start date will be provided in Programming Dataset Specification (PDS) document in details.

5.1.3 Concomitant medication date imputation

Rules for imputing the CM end date or start date will be provided in Programming Dataset Specification (PDS) document in details.

5.1.3.1 Prior therapies date imputation

Not Applicable.

5.1.3.2 Post therapies date imputation

Rules for imputing the post non-drug therapies end date or start date will be provided in Programming Dataset Specification (PDS) document in details.

5.1.3.3 Other imputations

5.1.3.3.1 Missing values from the same latent variable

For subtests that contribute to the same latent construct variable ([Table 5-1](#)), the following rule for missing subtests will be applied: When less than or equal to 50% of the related subtests within a constructed latent variable is missing, these missing subtests will be imputed from the remaining subtests contributing to its latent variable, standardized so that each subtest contributes the same weight to the construct as it would have if measured.

Table 5-1 Latent construct variables and their corresponding subtests

Latent construct variable	Subtests
Immediate Memory Index score	List Learning and Story Memory
Visuospatial/Constructional Index Score	Figure Copy and Line Orientation
Language Index Score	Semantic Fluency and Picture Naming
Attention Index Score	Coding and Digital Span
Delayed Memory Index Score	List Recall, Story Recall, Figure Recall and List Recognition

Latent construct variable	Subtests
Raven's matrices contributing to APCC	A2, A4, A8, B1-B6

This is done by calculating the total subscale-weight adjusted observed subtests (*i*), divided by the maximum weight-adjusted values possible for the observed subtests (*i*). This will provide the proportion to apply to the missing subtest (*j*) maximum possible value in order to obtain its imputed value as follows:

$$\text{missing subtest}_j = \frac{\sum_{i=1}^n (\text{weight}_i \times \text{observed subtest}_i)}{\sum_{i=1}^n (\text{weight}_i \times \text{observed subtest max}_i)} \times \text{missing subtest}_j \text{ max.}$$

Missing subtests that could not borrow information from observed related subtests and construct variable values which could not be calculated from their underlying observed/imputed values will be regarded as MAR and will not be imputed.

5.2 AEs coding/grading

The MedDRA version which will be available at the time of database lock, will be used for the coding purpose of the adverse events.

5.3 Laboratory parameters derivations

Table 5-2 Liver Event and Laboratory Trigger Definitions

	Definition/ threshold
LIVER LABORATORY TRIGGERS	3×ULN < ALT / AST ≤ 5×ULN 1.5×ULN < TBL ≤ 2×ULN
LIVER EVENTS	ALT or AST > 5 × ULN ALP > 2×ULN (in the absence of known bone pathology) TBL > 2×ULN (in the absence of known Gilbert syndrome) ALT or AST > 3×ULN and INR > 1.5 Potential Hy's Law cases (defined as ALT or AST > 3×ULN and TBL > 2×ULN [mainly conjugated fraction] without notable increase in ALP to > 2×ULN) Any clinical event of jaundice (or equivalent term) ALT or AST > 3×ULN accompanied# by (general) malaise, fatigue, abdominal pain, nausea, or vomiting, or rash with eosinophilia Any adverse event potentially indicative of a liver toxicity *

*These events cover the following: hepatic failure, fibrosis and cirrhosis, and other liver damagerelated conditions; the non-infectious hepatitis; the benign, malignant and unspecified liver neoplasms

#Consider these adverse events in a window from 30 days before the liver event criteria (ALT or AST > 3×ULN) to 30 days after the liver event criteria (ALT or AST > 3×ULN).

ALP = alkaline phosphatase; ALT = Alanine aminotransferase; AST = Aspartate aminotransferase TBL: total bilirubin; ULN: upper limit of normal

Table 5-3 Specific renal alert criteria and actions

	Definition/ threshold
Serum event	Serum creatinine increase 25 – 49% compared to baseline Acute Kidney Injury: Serum creatinine increase \geq 50% compared to baseline
Urine event	New dipstick proteinuria \geq 1+ Albumin- or Protein-creatinine ratio increase \geq 2-fold ACR \geq 30 mg/g or \geq 3 mg/mmol; PCR \geq 150 mg/g or $>$ 15 mg/mmol New dipstick glycosuria \geq 1+ not due to diabetes New dipstick hematuria \geq 1+ not due to trauma*

ACR = Albumin-creatinine ratio; PCR = Protein-creatinine ratio

*Consider adverse event (injury) in a window from 30 days before the hematuria criteria.

5.4 Statistical models

SAS codes for all statistical methodology described in this section will be included as programming note in TFL Shells.

5.4.1 Primary analysis

Kaplan Meier approach for TTE

The Kaplan-Meier estimates of the survival functions for each treatment will be plotted. The plot will include the number of participants at risk for each treatment group at pre-specified timepoints. Median time to event and quartiles including 95% confidence intervals, if estimable, will be provided for each treatment group using the SAS procedure LIFETEST. The confidence intervals will be based on log-log transformation. For each treatment group and time interval: participants at risk, participants with event, participants with event divided by participants at risk, cumulative participants with event and cumulative event probability including 95% confidence interval will be provided.

5.4.2 Additional SAS outputs

For the below mentioned analyses, additional (raw) SAS outputs resulted from SAS/STAT procedures or statistical derivations will be presented and used for CSR Appendix 16.1.9:

- Effect Size and 80% Confidence Intervals for APCC score, RBANS Total, RBANS Index scores
- Time to event (TTE) analyses:
 - Time to first confirmed diagnosis of MCI due to AD or Dementia due to AD-SAF
 - Time to first change in diagnosis classification-SAF
 - Time to first change in diagnosis classification when participants are on treatment-SAF

- Time to first change in diagnosis classification when participants are on treatment-mSAF
- Time to first decrease in RBANS Total \geq 14 points when participants are on treatment-SAF
- Baseline comparability

Further details for these additional SAS outputs will be described in the programming notes of the respective shells in the TFL shells Section 16.1.9.

5.5 Rule of exclusion criteria of analysis sets

The important protocol deviations are defined in below [Table 5-4](#) with deviation ID, deviation code and it's corresponding text description.

Rule of exclusion criteria from analysis sets due to important protocol deviations (if any) will be included prior to database lock in a separate document in CREDI.

The Non-PD criteria for exclusion from analysis sets is explained in below [Table 5-5](#).

Table 5-4 Deviation codes description

Deviation code	Text description	Deviation ID
1	SELECTION CRITERIA NOT MET	INCLXX EXCLXX
2	PARTICIPANT NOT WITHDRAWN AS PER PROTOCOL	WITHXX
4	TREATMENT DEVIATION	TRTXX
5	PROHIBITED CONCOMITANT MEDICATION	COMDXX
998	OTHER	OTHXX

Table 5.5 Participant Classification

Analysis Set	PD ID that cause patients to be excluded	Non-PD criteria that cause patients to be excluded
Screened Set	NA	Not having informed consent; Not having screening epoch disposition page
RAS	NA	Not randomized
SAF	NA	No double-blind study drug taken

5.6 Notable and abnormality criteria

Table 5-6 Clinically notable criteria for vital signs

Vital Sign Variable	Notable Criteria
Pulse (beats/min)	> 120bpm or Increase of ≥ 15 bpm from baseline or < 50bpm or Decrease of ≥ 15 bpm from baseline
Systolic BP (mmHg)	>180 mm Hg or Increase of ≥ 20 mm Hg from baseline Or < 90 mm Hg or Decrease of ≥ 20 mm Hg from baseline
Diastolic BP (mmHg)	> 105 mmHg or Increase of ≥ 15 mm Hg from baseline Or < 50 mmHg or Decrease of ≥ 15 mm Hg from baseline
Body weight (kg)	Decrease $\geq 7\%$ from baseline weight Increase $\geq 7\%$ from baseline weight

Table 5-7 Clinically notable criteria for selected hematology tests

Laboratory parameter	SI units		US or other units	
	Lower bound	Upper bound	Lower bound	Upper bound
Hemoglobin	70 (g/L)	200 (g/L)	7 (g/dL)	20 (g/dL)
White Cell count	2 ($\times 10^9/L$)	30 ($\times 10^9/L$)	2 ($\times 10^3/uL$)	30 ($\times 10^3/uL$)

Laboratory parameter	SI units		US or other units	
	Lower bound	Upper bound	Lower bound	Upper bound
Platelets	50 (x10 ⁹ /L)	1000 (x10 ⁹ /L)	50 (x10 ³ /uL)	1000 x10 ³ /uL)

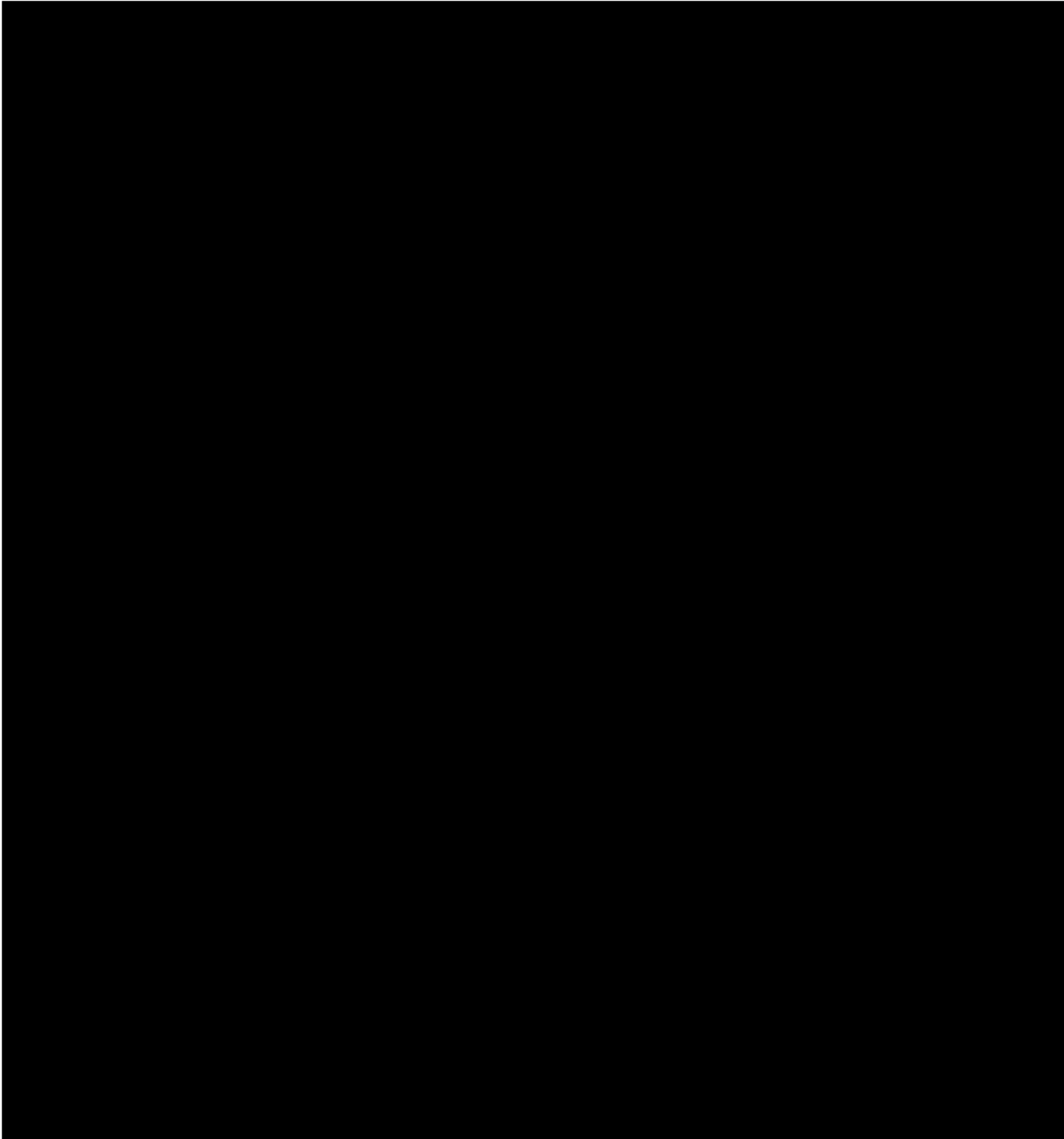
Table 5-8 Clinically notable criteria for selected blood chemistry tests

Laboratory parameter	SI units		US or other units	
	Lower bound	Upper bound	Lower bound	Upper bound
Sodium	125 (mmol/L)	155 (mmol/L)	125 (mmol/L)	155 (mmol/L)
Potassium	3 (mmol/L)	6 (mmol/L)	3 (mmol/L)	6 (mmol/L)
Calcium	1.5 (mmol/L)	3 (mmol/L)	6 (mg/dL)	12 (mg/dL)
Magnesium	0.4 (mmol/L)	1.2 (mmol/L)	1 (mg/dL)	3 (mg/dL)
Bilirubin (Total)	-	41 (umol/L)	-	2.4 (mg/dL)
AST	-	> 3×ULN	-	> 3×ULN
ALT	-	> 3×ULN	-	> 3×ULN
Alkaline Phosphatase (Male)	-	> 2×ULN	-	> 2×ULN
Alkaline Phosphatase (Female)	-	> 2×ULN	-	> 2×ULN
Creatinine	-	increase 25 – 49% compared to baseline increase ≥ 50% compared to baseline	-	increase 25 – 49% compared to baseline increase ≥ 50% compared to baseline

Table 5-9 ECG Abnormality Ranges

ECG Parameter	Abnormality Flags
	Absolute
PR interval	> 250 msec
QRS Interval	> 140 msec
QTcF Interval (Fridericia's correction)	>= 500 msec (All) >= 450 msec (Male) >= 470 msec (Female)

ECG Parameter	Abnormality Flags
	Absolute
QT change from baseline	>60 msec



5.8 Analysis windows rules

Table 5-11 RBANS, Raven's, ██████████ and plasma A β

Visit Number	Scheduled Timepoint	Analysis window*		Visit Label
		Lower	Upper	
201	Baseline (Day 1)	-1	1	Baseline
202	Week 13 (Day 91)	2	136	Week 13
203	Week 26 (Day 182)	137	272	Week 26
204				
205	Week 52 (Day 364)	273	454	Week 52
206				
207	Week 78 (Day 546)	455	636	Week 78
208				
209	Week 104 (Day 728)	637	818	Week 104
210				
211	Week 130 (Day 910)	819	1000	Week 130
212				
213	Week 156 (Day 1092)	1001	1182	Week 156
214				
215	Week 182 (Day 1274)	1183	1364	Week 182
216				
217	Week 208 (Day 1456)	1365	1546	Week 208
218				
219	Week 234 (Day 1638)	1547	1728	Week 234

Visit Number	Scheduled Timepoint	Analysis window*		Visit Label
		Lower	Upper	
220				
221	Week 260 (Day 1820)	1729	1910	Week 260
222				
223	Week 286 (Day 2002)	1911	2092	Week 286
224				
225	Week 312 (Day 2184)	2093	2274	Week 312
226				
227	Week 338 (Day 2366)	2275	2456	Week 338
228				
229	Week 364 (Day 2548)	2457	2638	Week 364
230				
231	Week 390 (Day 2730)	2639	Until EOS	Week 390

Table 5-12 MMSE, CDR, ECog, MCI / Dementia Diagnostic Verification

Visit Number	Scheduled Timepoint	Analysis window*		Visit Label
		Lower	Upper	
201	Baseline (Day 1)	-1	1	Baseline
202				
203	Week 26 (Day 182)	2	272	Week 26
204				
205	Week 52 (Day 364)	273	454	Week 52
206				
207	Week 78 (Day 546)	455	636	Week 78
208				
209	Week 104 (Day 728)	637	818	Week 104

Visit Number	Scheduled Timepoint	Analysis window*		Visit Label
		Lower	Upper	
210				
211	Week 130 (Day 910)	819	1000	Week 130
212				
213	Week 156 (Day 1092)	1001	1182	Week 156
214				
215	Week 182 (Day 1274)	1183	1364	Week 182
216				
217	Week 208 (Day 1456)	1365	1546	Week 208
218				
219	Week 234 (Day 1638)	1547	1728	Week 234
220				
221	Week 260 (Day 1820)	1729	1910	Week 260
222				
223	Week 286 (Day 2002)	1911	2092	Week 286
224				
225	Week 312 (Day 2184)	2093	2274	Week 312
226				
227	Week 338 (Day 2366)	2275	2456	Week 338
228				
229	Week 364 (Day 2548)	2457	2638	Week 364
230				
231	Week 390 (Day 2730)	2639	Until EOS	Week 390

Table 5-13 Physical / Neurological examination, ECG, Laboratory Evaluations

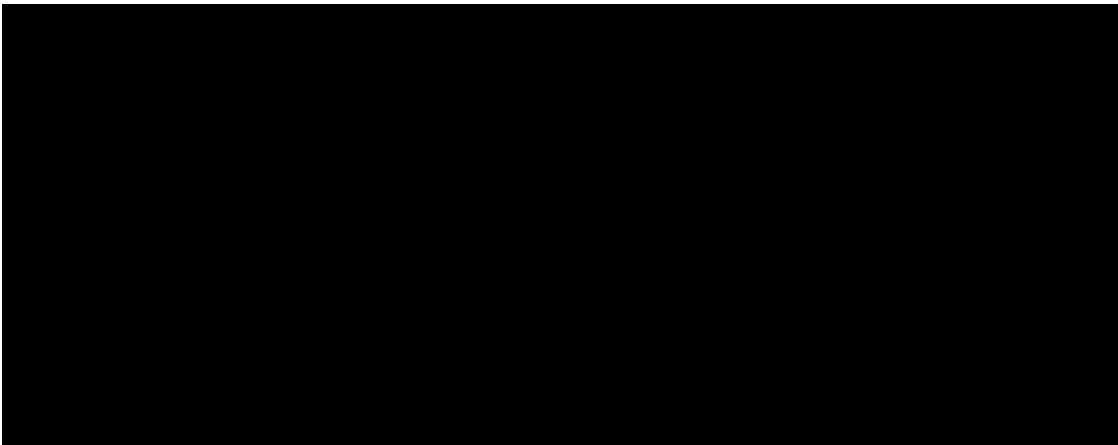
Visit Number	Scheduled Timepoint	Analysis window*		Visit Label
		Lower	Upper	
201	Baseline (Day 1)	-1	1	Baseline
202	Week 13 (Day 91)	2	136	Week 13
203	Week 26 (Day 182)	137	272	Week 26
204				
205	Week 52 (Day 364)	273	454	Week 52
206				
207	Week 78 (Day 546)	455	636	Week 78
208				
209	Week 104 (Day 728)	637	818	Week 104
210				
211	Week 130 (Day 910)	819	1000	Week 130
212				
213	Week 156 (Day 1092)	1001	1182	Week 156
214				
215	Week 182 (Day 1274)	1183	1364	Week 182
216				
217	Week 208 (Day 1456)	1365	1546	Week 208
218				
219	Week 234 (Day 1638)	1547	1728	Week 234
220				
221	Week 260 (Day 1820)	1729	1910	Week 260
222				
223	Week 286 (Day 2002)	1911	2092	Week 286
224				
225	Week 312 (Day 2184)	2093	2274	Week 312

Visit Number	Scheduled Timepoint	Analysis window*		Visit Label
		Lower	Upper	
226				
227	Week 338 (Day 2366)	2275	2456	Week 338
228				
229	Week 364 (Day 2548)	2457	2638	Week 364
230				
231	Week 390 (Day 2730)	2639	Until EOS	Week 390

Table 5-14 Vital Signs

Visit Number	Scheduled Timepoint	Analysis window*		Visit Label
		Lower	Upper	
201	Baseline (Day 1)	-1	1	Baseline
202	Week 13 (Day 91)	2	136	Week 13
203	Week 26 (Day 182)	137	227	Week 26
204	Week 39 (Day 273)	228	318	Week 39
205	Week 52 (Day 364)	319	454	Week 52
206				
207	Week 78 (Day 546)	455	636	Week 78
208				
209	Week 104 (Day 728)	637	818	Week 104
210				
211	Week 130 (Day 910)	819	1000	Week 130
212				
213	Week 156 (Day 1092)	1001	1182	Week 156
214				
215	Week 182 (Day 1274)	1183	1364	Week 182
216				

Visit Number	Scheduled Timepoint	Analysis window*		Visit Label
		Lower	Upper	
217	Week 208 (Day 1456)	1365	1546	Week 208
218				
219	Week 234 (Day 1638)	1547	1728	Week 234
220				
221	Week 260 (Day 1820)	1729	1910	Week 260
222				
223	Week 286 (Day 2002)	1911	2092	Week 286
224				
225	Week 312 (Day 2184)	2093	2274	Week 312
226				
227	Week 338 (Day 2366)	2275	2456	Week 338
228				
229	Week 364 (Day 2548)	2457	2638	Week 364
230				
231	Week 390 (Day 2730)	2639	Until EOS	Week 390



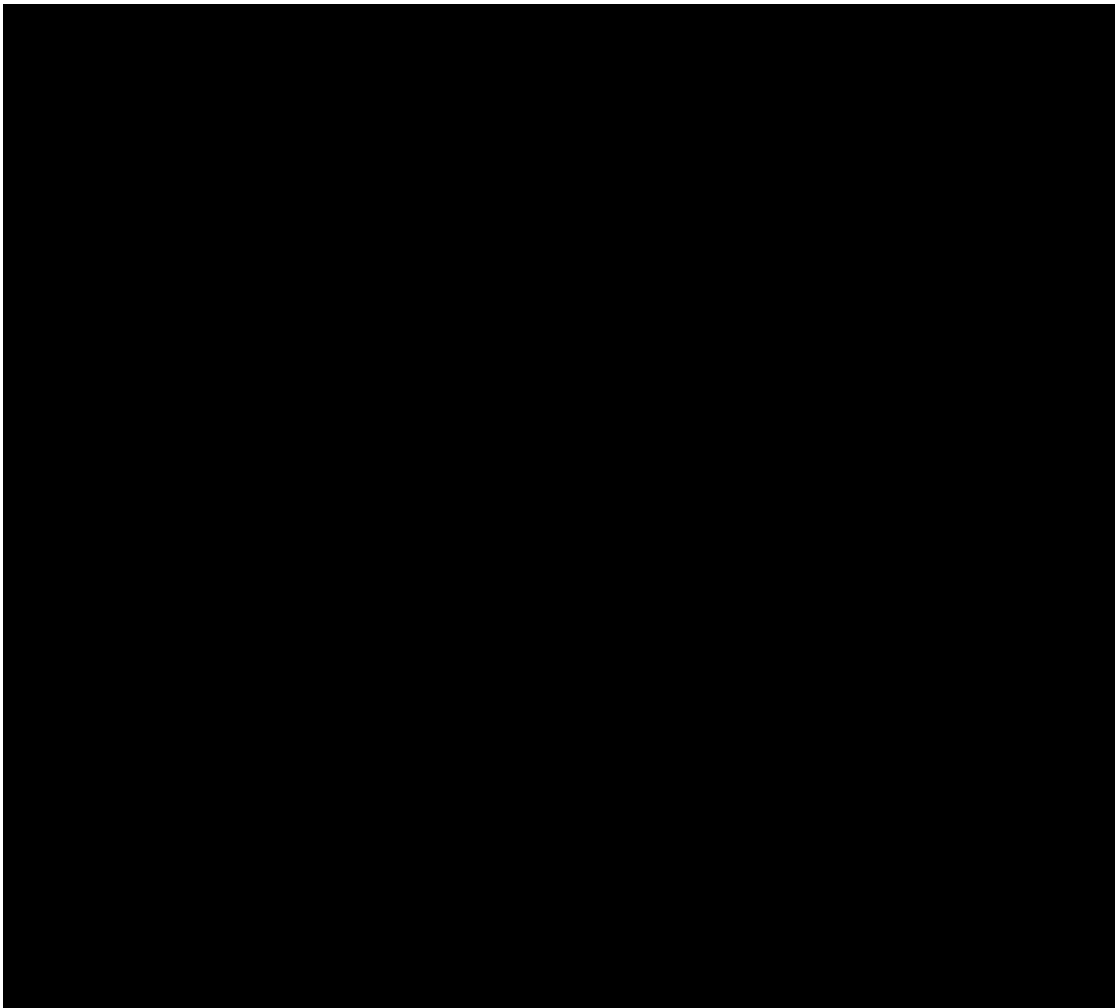


Table 5-16 MRI (Safety, voIMRI, fMRI)

Visit Number	Scheduled Timepoint	Analysis window*		Visit Label
		Lower	Upper	

201	Baseline (Day 1)	-1	1	Baseline
202				
203	Week 26 (Day 182)	2	272	Week 26
204				
205	Week 52 (Day 364)	273	545	Week 52
206				
207				
208				
209	Week 104 (Day 728)	546	909	Week 104
210				
211				
212				
213	Week 156 (Day 1092)	910	1273	Week 156
214				
215				
216				
217	Week 208 (Day 1456)	1274	1637	Week 208
218				
219				
220				
221	Week 260 (Day 1820)	1638	2001	Week 260
222				
223				
224				
225	Week 312 (Day 2184)	2002	2365	Week 312
226				
227				
228				

229	Week 364 (Day 2548)	2366	Until EOS	Week 364
-----	---------------------	------	-----------	----------

Analyses not by Analysis windows

The following domains will not be analysed by analysis window, but according to the scheduled visit and/or visit day as applicable. Analysis windows will not be provided for these.

- Amyloid PET
- Tau PET
- CSF biomarkers
- Blood biomarkers (Serum/Plasma)
- Drug administration
- C-SSRS

5.9 RBANS Index tables

The RBANS index scores are obtained from the following five age adjusted tables corresponding to the respective total subtest scores.

Table 5-17 Immediate Memory Index Score Equivalents of Subtest Raw Score

		Story Memory Total Score																										
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24		
List Learning Total Score	Ages 50-59	0	40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
		1	40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
		2	40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
		3	40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
		4	40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
		5	40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
		6	40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
		7	40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
		8	40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
		9	40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
		10	40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
		11	40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
		12	44	44	44	44	44	49	49	49	53	53	57	57	61	65	65	73	76	81	81	81	81	81	81	85	90	97
		13	44	44	44	44	44	49	49	49	53	53	57	57	61	65	65	73	76	81	81	81	81	81	81	85	90	97
		14	44	44	44	44	44	49	49	49	53	53	57	57	61	65	65	73	76	81	81	81	81	81	81	85	90	97
		15	44	44	44	44	44	49	49	49	53	53	57	57	61	65	65	73	76	81	81	81	81	81	81	85	90	97
		16	49	49	49	49	49	53	53	53	57	57	61	61	65	69	69	76	78	83	83	83	83	83	83	87	94	100
		17	49	49	49	49	49	53	53	53	57	57	61	61	65	69	69	76	78	83	83	83	83	83	83	87	94	100
		18	53	53	53	53	53	57	57	57	61	61	65	65	69	73	73	78	81	85	85	85	85	85	85	90	97	103
		19	53	53	53	53	53	57	57	57	61	61	65	65	69	73	73	78	81	85	85	85	85	85	85	90	97	103
		20	53	53	53	53	53	57	57	57	61	61	65	65	69	73	73	78	81	85	85	85	85	85	85	90	97	103
		21	57	57	57	57	57	61	61	61	65	65	69	69	73	76	76	81	83	87	87	87	87	87	87	94	100	106
		22	61	61	61	61	61	65	65	65	69	69	73	73	76	78	78	83	85	90	90	90	90	90	90	97	103	109
		23	61	61	61	61	61	65	65	65	69	69	73	73	76	78	78	83	85	90	90	90	90	90	90	97	103	109
24	65	65	65	65	65	69	69	69	73	73	76	76	78	81	81	85	87	94	94	94	94	94	94	100	106	112		

		Story Memory Total Score																									
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	
	25	69	69	69	69	69	73	73	73	76	76	78	78	81	83	83	87	90	97	97	97	97	97	103	109	114	
	26	73	73	73	73	73	76	76	76	78	78	81	81	83	85	85	90	94	100	100	100	100	100	106	112	117	
	27	76	76	76	76	76	78	78	78	81	81	83	83	85	87	87	94	97	103	103	103	103	103	109	114	120	
	28	76	76	76	76	76	78	78	78	81	81	83	83	85	87	87	94	97	103	103	103	103	103	109	114	120	
	29	78	78	78	78	78	81	81	81	83	83	85	85	87	90	90	97	100	106	106	106	106	106	112	117	123	
	30	81	81	81	81	81	83	83	83	85	85	87	87	90	94	94	100	103	109	109	109	109	109	114	120	126	
	31	81	81	81	81	81	83	83	83	85	85	87	87	90	94	94	100	103	109	109	109	109	109	114	120	126	
	32	81	81	81	81	81	83	83	83	85	85	87	87	90	94	94	100	103	109	109	109	109	109	114	120	126	
	33	83	83	83	83	83	85	85	85	87	87	90	90	94	97	97	103	106	112	112	112	112	112	117	123	129	
	34	85	85	85	85	85	87	87	87	90	90	94	94	97	100	100	106	109	114	114	114	114	114	120	126	132	
	35	87	87	87	87	87	90	90	90	94	94	97	97	100	103	103	109	112	117	117	117	117	117	123	129	136	
	36	87	87	87	87	87	90	90	90	94	94	97	97	100	103	103	109	112	117	117	117	117	117	123	129	136	
	37	90	90	90	90	90	94	94	94	97	97	100	100	103	106	106	112	114	120	120	120	120	120	126	132	140	
	38	94	94	94	94	94	97	97	97	100	100	103	103	106	109	109	114	117	123	123	123	123	123	129	136	144	
	39	97	97	97	97	97	100	100	100	103	103	106	106	109	112	112	117	120	126	126	126	126	126	132	140	148	
	40	100	100	100	100	100	103	103	103	106	106	109	109	112	114	114	120	123	129	129	129	129	129	136	144	152	
	Ages 60 - 69	0	40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94
		1	40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94
		2	40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94
		3	40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94
4		40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
5		40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
6		40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
7		40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
8		40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
9		40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
10		40	40	40	40	40	44	44	44	49	49	53	53	57	61	61	69	73	78	78	78	78	78	83	87	94	
11		44	44	44	44	44	49	49	49	53	53	57	57	61	65	65	73	76	81	81	81	81	81	81	85	90	97
12		44	44	44	44	44	49	49	49	53	53	57	57	61	65	65	73	76	81	81	81	81	81	81	85	90	97
13	44	44	44	44	44	49	49	49	53	53	57	57	61	65	65	73	76	81	81	81	81	81	81	85	90	97	

		Story Memory Total Score																								
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
	14	44	44	44	44	44	49	49	49	53	53	57	57	61	65	65	73	76	81	81	81	81	81	85	90	97
	15	49	49	49	49	49	53	53	53	57	57	61	61	65	69	69	76	78	83	83	83	83	83	87	94	100
	16	49	49	49	49	49	53	53	53	57	57	61	61	65	69	69	76	78	83	83	83	83	83	87	94	100
	17	49	49	49	49	49	53	53	53	57	57	61	61	65	69	69	76	78	83	83	83	83	83	87	94	100
	18	53	53	53	53	53	57	57	57	61	61	65	65	69	73	73	78	81	85	85	85	85	85	90	97	103
	19	53	53	53	53	53	57	57	57	61	61	65	65	69	73	73	78	81	85	85	85	85	85	90	97	103
	20	53	53	53	53	53	57	57	57	61	61	65	65	69	73	73	78	81	85	85	85	85	85	90	97	103
	21	57	57	57	57	57	61	61	61	65	65	69	69	73	76	76	81	83	87	87	87	87	87	94	100	106
	22	61	61	61	61	61	65	65	65	69	69	73	73	76	78	78	83	85	90	90	90	90	90	97	103	109
	23	61	61	61	61	61	65	65	65	69	69	73	73	76	78	78	83	85	90	90	90	90	90	97	103	109
	24	65	65	65	65	65	69	69	69	73	73	76	76	78	81	81	85	87	94	94	94	94	94	100	106	112
	25	69	69	69	69	69	73	73	73	76	76	78	78	81	83	83	87	90	97	97	97	97	97	103	109	114
	26	73	73	73	73	73	76	76	76	78	78	81	81	83	85	85	90	94	100	100	100	100	100	106	112	117
	27	76	76	76	76	76	78	78	78	81	81	83	83	85	87	87	94	97	103	103	103	103	103	109	114	120
	28	78	78	78	78	78	81	81	81	83	83	85	85	87	90	90	97	100	106	106	106	106	106	112	117	123
	29	78	78	78	78	78	81	81	81	83	83	85	85	87	90	90	97	100	106	106	106	106	106	112	117	123
	30	81	81	81	81	81	83	83	83	85	85	87	87	90	94	94	100	103	109	109	109	109	109	114	120	126
	31	81	81	81	81	81	83	83	83	85	85	87	87	90	94	94	100	103	109	109	109	109	109	114	120	126
	32	81	81	81	81	81	83	83	83	85	85	87	87	90	94	94	100	103	109	109	109	109	109	114	120	126
	33	83	83	83	83	83	85	85	85	87	87	90	90	94	97	97	103	106	112	112	112	112	112	117	123	129
	34	85	85	85	85	85	87	87	87	90	90	94	94	97	100	100	106	109	114	114	114	114	114	120	126	132
	35	87	87	87	87	87	90	90	90	94	94	97	97	100	103	103	109	112	117	117	117	117	117	123	129	136
	36	90	90	90	90	90	94	94	94	97	97	100	100	103	106	106	112	114	120	120	120	120	120	126	132	140
	37	94	94	94	94	94	97	97	97	100	100	103	103	106	109	109	114	117	123	123	123	123	123	129	136	144
	38	94	94	94	94	94	97	97	97	100	100	103	103	106	109	109	114	117	123	123	123	123	123	129	136	144
	39	97	97	97	97	97	100	100	100	103	103	106	106	109	112	112	117	120	126	126	126	126	126	132	140	148
	40	100	100	100	100	100	103	103	103	106	106	109	109	112	114	114	120	123	129	129	129	129	129	136	144	152
Ages 70-79	0	40	40	40	40	44	49	49	49	53	53	57	57	61	65	69	73	73	78	78	78	81	83	87	90	94
	1	40	40	40	40	44	49	49	49	53	53	57	57	61	65	69	73	73	78	78	78	81	83	87	90	94

	Story Memory Total Score																								
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
2	40	40	40	40	44	49	49	49	53	53	57	57	61	65	69	73	73	78	78	78	81	83	87	90	94
3	40	40	40	40	44	49	49	49	53	53	57	57	61	65	69	73	73	78	78	78	81	83	87	90	94
4	40	40	40	40	44	49	49	49	53	53	57	57	61	65	69	73	73	78	78	78	81	83	87	90	94
5	40	40	40	40	44	49	49	49	53	53	57	57	61	65	69	73	73	78	78	78	81	83	87	90	94
6	40	40	40	40	44	49	49	49	53	53	57	57	61	65	69	73	73	78	78	78	81	83	87	90	94
7	40	40	40	40	44	49	49	49	53	53	57	57	61	65	69	73	73	78	78	78	81	83	87	90	94
8	40	40	40	40	44	49	49	49	53	53	57	57	61	65	69	73	73	78	78	78	81	83	87	90	94
9	40	40	40	40	44	49	49	49	53	53	57	57	61	65	69	73	73	78	78	78	81	83	87	90	94
10	44	44	44	44	49	53	53	53	57	57	61	61	65	69	73	76	76	81	81	81	83	85	90	94	97
11	44	44	44	44	49	53	53	53	57	57	61	61	65	69	73	76	76	81	81	81	83	85	90	94	97
12	44	44	44	44	49	53	53	53	57	57	61	61	65	69	73	76	76	81	81	81	83	85	90	94	97
13	44	44	44	44	49	53	53	53	57	57	61	61	65	69	73	76	76	81	81	81	83	85	90	94	97
14	49	49	49	49	53	57	57	57	61	61	65	65	69	73	76	78	78	83	83	83	85	87	94	97	100
15	49	49	49	49	53	57	57	57	61	61	65	65	69	73	76	78	78	83	83	83	85	87	94	97	100
16	53	53	53	53	57	61	61	61	65	65	69	69	73	76	78	81	81	85	85	85	87	90	97	100	103
17	53	53	53	53	57	61	61	61	65	65	69	69	73	76	78	81	81	85	85	85	87	90	97	100	103
18	57	57	57	57	61	65	65	65	69	69	73	73	76	78	81	83	83	87	87	87	90	94	100	103	106
19	61	61	61	61	65	69	69	69	73	73	76	76	78	81	83	85	85	90	90	90	94	97	103	106	109
20	61	61	61	61	65	69	69	69	73	73	76	76	78	81	83	85	85	90	90	94	97	100	106	109	112
21	65	65	65	65	69	73	73	73	76	76	78	78	81	83	85	87	87	94	94	94	97	100	106	109	112
22	65	65	65	65	69	73	73	73	76	76	78	78	81	83	85	87	87	94	94	94	97	100	106	109	112
23	69	69	69	69	73	76	76	76	78	78	81	81	83	85	87	90	90	97	97	97	100	103	109	112	114
24	73	73	73	73	76	78	78	78	81	81	83	83	85	87	90	94	94	100	100	100	103	106	112	114	117
25	73	73	73	73	76	78	78	78	81	81	83	83	85	87	90	94	94	100	100	100	103	106	112	114	117
26	76	76	76	76	78	81	81	81	83	83	85	85	87	90	94	97	97	103	103	103	106	109	114	117	120
27	78	78	78	78	81	83	83	83	85	85	87	87	90	94	97	100	100	106	106	106	109	112	117	120	123
28	78	78	78	78	81	83	83	83	85	85	87	87	90	94	97	100	100	106	106	106	109	112	117	120	123
29	81	81	81	81	83	85	85	85	87	87	90	90	94	97	100	103	103	109	109	109	112	114	120	123	126
30	81	81	81	81	83	85	85	85	87	87	90	90	94	97	100	103	103	109	109	109	112	114	120	123	126
31	83	83	83	83	85	87	87	87	90	90	94	94	97	100	103	106	106	112	112	112	114	117	123	126	129
32	85	85	85	85	87	90	90	90	94	94	97	97	100	103	106	109	109	114	114	114	117	120	126	129	132

		Story Memory Total Score																								
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
	33	87	87	87	87	90	94	94	94	97	97	100	100	103	106	109	112	112	117	117	117	120	123	129	132	136
	34	87	87	87	87	90	94	94	94	97	97	100	100	103	106	109	112	112	117	117	117	120	123	129	132	136
	35	90	90	90	90	94	97	97	97	100	100	103	103	106	109	112	114	114	120	120	120	123	126	132	136	140
	36	90	90	90	90	94	97	97	97	100	100	103	103	106	109	112	114	114	120	120	120	123	126	132	136	140
	37	94	94	94	94	97	100	100	100	103	103	106	106	109	112	114	117	117	123	123	123	126	129	136	140	144
	38	97	97	97	97	100	103	103	103	106	106	109	109	112	114	117	120	120	126	126	126	129	132	140	144	148
	39	97	97	97	97	100	103	103	103	106	106	109	109	112	114	117	120	120	126	126	126	129	132	140	144	148
	40	100	100	100	100	103	106	106	106	109	109	112	112	114	117	120	123	123	129	129	129	132	136	144	148	152
Ages 80-89	0	40	40	44	44	49	49	49	53	53	57	57	61	69	73	73	76	76	78	81	83	83	85	87	90	94
	1	40	40	44	44	49	49	49	53	53	57	57	61	69	73	73	76	76	78	81	83	83	85	87	90	94
	2	40	40	44	44	49	49	49	53	53	57	57	61	69	73	73	76	76	78	81	83	83	85	87	90	94
	3	40	40	44	44	49	49	49	53	53	57	57	61	69	73	73	76	76	78	81	83	83	85	87	90	94
	4	40	40	44	44	49	49	49	53	53	57	57	61	69	73	73	76	76	78	81	83	83	85	87	90	94
	5	40	40	44	44	49	49	49	53	53	57	57	61	69	73	73	76	76	78	81	83	83	85	87	90	94
	6	40	40	44	44	49	49	49	53	53	57	57	61	69	73	73	76	76	78	81	83	83	85	87	90	94
	7	40	40	44	44	49	49	49	53	53	57	57	61	69	73	73	76	76	78	81	83	83	85	87	90	94
	8	40	40	44	44	49	49	49	53	53	57	57	61	69	73	73	76	76	78	81	83	83	85	87	90	94
	9	44	44	49	49	53	53	53	57	57	61	61	65	73	76	76	78	78	81	83	85	85	87	90	94	97
	10	44	44	49	49	53	53	53	57	57	61	61	65	73	76	76	78	78	81	83	85	85	87	90	94	97
	11	44	44	49	49	53	53	53	57	57	61	61	65	73	76	76	78	78	81	83	85	85	87	90	94	97
	12	44	44	49	49	53	53	53	57	57	61	61	65	73	76	76	78	78	81	83	85	85	87	90	94	97
	13	49	49	53	53	57	57	57	61	61	65	65	69	76	78	78	81	81	83	85	87	87	90	94	97	100
	14	49	49	53	53	57	57	57	61	61	65	65	69	76	78	78	81	81	83	85	87	87	90	94	97	100
	15	53	53	57	57	61	61	61	65	65	69	69	73	78	81	81	83	83	85	87	90	90	94	97	100	103
	16	57	57	61	61	65	65	65	69	69	73	73	76	81	83	83	85	85	87	90	94	94	97	100	103	106
	17	61	61	65	65	69	69	69	73	73	76	76	78	83	85	85	87	87	90	94	97	97	100	103	106	109
	18	61	61	65	65	69	69	69	73	73	76	76	78	83	85	85	87	87	90	94	97	97	100	103	106	109
	19	65	65	69	69	73	73	73	76	76	78	78	81	85	87	87	90	90	94	97	100	100	103	106	109	112
	20	69	69	73	73	76	76	76	78	78	81	81	83	87	90	90	94	94	97	100	103	103	106	109	112	114
	21	73	73	76	76	78	78	78	81	81	83	83	85	90	94	94	97	97	100	103	106	106	109	112	114	117
22	73	73	76	76	78	78	78	81	81	83	83	85	90	94	94	97	97	100	103	106	106	109	112	114	117	

		Story Memory Total Score																								
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
23		76	76	78	78	81	81	81	83	83	85	85	87	94	97	97	100	100	103	106	109	109	112	114	117	120
24		78	78	81	81	83	83	83	85	85	87	87	90	97	100	100	103	103	106	109	112	112	114	117	120	123
25		78	78	81	81	83	83	83	85	85	87	87	90	97	100	100	103	103	106	109	112	112	114	117	120	123
26		81	81	83	83	85	85	85	87	87	90	90	94	100	103	103	106	106	109	112	114	114	117	120	123	126
27		83	83	85	85	87	87	87	90	90	94	94	97	103	106	106	109	109	112	114	117	117	120	123	126	129
28		83	83	85	85	87	87	87	90	90	94	94	97	103	106	106	109	109	112	114	117	117	120	123	126	129
29		85	85	87	87	90	90	90	94	94	97	97	100	106	109	109	112	112	114	117	120	120	123	126	129	132
30		85	85	87	87	90	90	90	94	94	97	97	100	106	109	109	112	112	114	117	120	120	123	126	129	132
31		87	87	90	90	94	94	94	97	97	100	100	103	109	112	112	114	114	117	120	123	123	126	129	132	136
32		87	87	90	90	94	94	94	97	97	100	100	103	109	112	112	114	114	117	120	123	123	126	129	132	136
33		90	90	94	94	97	97	97	100	100	103	103	106	112	114	114	117	117	120	123	126	126	129	132	136	140
34		90	90	94	94	97	97	97	100	100	103	103	106	112	114	114	117	117	120	123	126	126	129	132	136	140
35		94	94	97	97	100	100	100	103	103	106	106	109	114	117	117	120	120	123	126	129	129	132	136	140	144
36		94	94	97	97	100	100	100	103	103	106	106	109	114	117	117	120	120	123	126	129	129	132	136	140	144
37		97	97	100	100	103	103	103	106	106	109	109	112	117	120	120	123	123	126	129	132	132	136	140	144	148
38		97	97	100	100	103	103	103	106	106	109	109	112	117	120	120	123	123	126	129	132	132	136	140	144	148
39		100	100	103	103	106	106	106	109	109	112	112	114	120	123	123	126	126	129	132	136	136	140	144	148	152
40		100	100	103	103	106	106	106	109	109	112	112	114	120	123	123	126	126	129	132	136	136	140	144	148	152

Table 5-18 Visuospatial/Constructional Index Score Equivalents of Subtest Raw Scores

		Line Orientation Total Score																					
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
Figure Copy Total Score	Ages 50-59	0	50	50	50	50	50	50	53	53	56	58	60	60	62	64	64	66	69	72	78	81	84
		1	50	50	50	50	50	50	53	53	56	58	60	60	62	64	64	66	69	72	78	81	84
		2	50	50	50	50	50	50	53	53	56	58	60	60	62	64	64	66	69	72	78	81	84
		3	50	50	50	50	50	50	53	53	56	58	60	60	62	64	64	66	69	72	78	81	84
		4	50	50	50	50	50	50	53	53	56	58	60	60	62	64	64	66	69	72	78	81	84
		5	50	50	50	50	50	50	53	53	56	58	60	60	62	64	64	66	69	72	78	81	84
		6	50	50	50	50	50	50	53	53	56	58	60	60	62	64	64	66	69	72	78	81	84

			Line Orientation Total Score																				
			0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
		7	50	50	50	50	50	50	53	53	56	58	60	60	62	64	64	66	69	72	78	81	84
		8	50	50	50	50	50	50	53	53	56	58	60	60	62	64	64	66	69	72	78	81	84
		9	50	50	50	50	50	50	53	53	56	58	60	60	62	64	64	66	69	72	78	81	84
		10	50	50	50	50	50	50	53	53	56	58	60	60	62	64	64	66	69	72	78	81	84
		11	50	50	50	50	50	50	53	53	56	58	60	60	62	64	64	66	69	72	78	81	84
		12	53	53	53	53	53	53	56	56	58	60	62	62	64	66	66	69	72	75	81	84	87
		13	56	56	56	56	56	56	58	58	60	62	64	64	66	69	69	72	75	78	84	87	89
		14	58	58	58	58	58	58	60	60	62	64	66	66	69	72	72	75	78	81	87	89	92
		15	60	60	60	60	60	60	62	62	64	66	69	69	72	75	75	78	81	84	89	92	96
		16	62	62	62	62	62	62	64	64	66	69	72	72	75	78	78	81	84	87	92	96	100
		17	66	66	66	66	66	66	69	69	72	75	78	78	81	84	84	87	89	92	100	102	105
		18	72	72	72	72	72	72	75	75	78	81	84	84	87	89	89	92	96	100	105	109	112
		19	75	75	75	75	75	75	78	78	81	84	87	87	89	92	92	96	100	102	109	112	116
		20	81	81	81	81	81	81	84	84	87	89	92	92	96	100	100	102	105	109	116	121	126
			Line Orientation Total Score																				
			0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Figure Copy Total Score	Ages 60-69	0	50	50	50	50	50	50	53	56	56	58	60	60	62	64	64	66	69	72	78	81	84
		1	50	50	50	50	50	50	53	56	56	58	60	60	62	64	64	66	69	72	78	81	84
		2	50	50	50	50	50	50	53	56	56	58	60	60	62	64	64	66	69	72	78	81	84
		3	50	50	50	50	50	50	53	56	56	58	60	60	62	64	64	66	69	72	78	81	84
		4	50	50	50	50	50	50	53	56	56	58	60	60	62	64	64	66	69	72	78	81	84
		5	50	50	50	50	50	50	53	56	56	58	60	60	62	64	64	66	69	72	78	81	84
		6	50	50	50	50	50	50	53	56	56	58	60	60	62	64	64	66	69	72	78	81	84
		7	50	50	50	50	50	50	53	56	56	58	60	60	62	64	64	66	69	72	78	81	84
		8	50	50	50	50	50	50	53	56	56	58	60	60	62	64	64	66	69	72	78	81	84
		9	50	50	50	50	50	50	53	56	56	58	60	60	62	64	64	66	69	72	78	81	84
		10	50	50	50	50	50	50	53	56	56	58	60	60	62	64	64	66	69	72	78	81	84
		11	53	53	53	53	53	53	56	58	58	60	62	62	64	66	66	69	72	75	81	84	87
		12	53	53	53	53	53	53	56	58	58	60	62	62	64	66	66	69	72	75	81	84	87

		Line Orientation Total Score																					
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
Ages 70-79	13	56	56	56	56	56	56	56	58	60	60	62	64	64	66	69	69	72	75	78	84	87	89
	14	58	58	58	58	58	58	58	60	62	62	64	66	66	69	72	72	75	78	81	87	89	92
	15	60	60	60	60	60	60	60	62	64	64	66	69	69	72	75	75	78	81	84	89	92	96
	16	62	62	62	62	62	62	62	64	66	66	69	72	72	75	78	78	81	84	87	92	96	100
	17	66	66	66	66	66	66	66	69	72	72	75	78	78	81	84	84	87	89	92	100	102	105
	18	72	72	72	72	72	72	72	75	78	78	81	84	84	87	89	89	92	96	100	105	109	112
	19	75	75	75	75	75	75	75	78	81	81	84	87	87	89	92	92	96	100	102	109	112	116
	20	84	84	84	84	84	84	84	87	89	89	92	96	96	100	102	102	105	109	112	121	126	131
	0	50	50	50	50	50	50	50	53	56	58	58	60	60	62	64	64	66	69	72	78	81	84
	1	50	50	50	50	50	50	50	53	56	58	58	60	60	62	64	64	66	69	72	78	81	84
	2	50	50	50	50	50	50	50	53	56	58	58	60	60	62	64	64	66	69	72	78	81	84
	3	50	50	50	50	50	50	50	53	56	58	58	60	60	62	64	64	66	69	72	78	81	84
	4	50	50	50	50	50	50	50	53	56	58	58	60	60	62	64	64	66	69	72	78	81	84
	5	50	50	50	50	50	50	50	53	56	58	58	60	60	62	64	64	66	69	72	78	81	84
	6	50	50	50	50	50	50	50	53	56	58	58	60	60	62	64	64	66	69	72	78	81	84
	7	50	50	50	50	50	50	50	53	56	58	58	60	60	62	64	64	66	69	72	78	81	84
	8	50	50	50	50	50	50	50	53	56	58	58	60	60	62	64	64	66	69	72	78	81	84
	9	50	50	50	50	50	50	50	53	56	58	58	60	60	62	64	64	66	69	72	78	81	84
	10	50	50	50	50	50	50	50	53	56	58	58	60	60	62	64	64	66	69	72	78	81	84
	11	53	53	53	53	53	53	53	56	58	60	60	62	62	64	66	66	69	72	75	81	84	87
12	56	56	56	56	56	56	56	58	60	62	62	64	64	66	69	69	72	75	78	84	87	89	
13	58	58	58	58	58	58	58	60	62	64	64	66	66	69	72	72	75	78	81	87	89	92	
14	58	58	58	58	58	58	58	60	62	64	64	66	66	69	72	72	75	78	81	87	89	92	
15	60	60	60	60	60	60	60	62	64	66	66	69	69	72	75	75	78	81	84	89	92	96	
16	64	64	64	64	64	64	64	66	69	72	72	75	75	78	81	81	84	87	89	96	100	102	
17	69	69	69	69	69	69	69	72	75	78	78	81	81	84	87	87	89	92	96	102	105	109	
18	72	72	72	72	72	72	72	75	78	81	81	84	84	87	89	89	92	96	100	105	109	112	
19	78	78	78	78	78	78	78	81	84	87	87	89	89	92	96	96	100	102	105	112	116	121	
20	84	84	84	84	84	84	84	87	89	92	92	96	96	100	102	102	105	109	112	121	126	131	

			Line Orientation Total Score																				
			0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Ages 80-89	0	50	50	50	50	50	53	53	56	58	58	60	60	62	64	64	69	72	78	81	84	87	
	1	50	50	50	50	50	53	53	56	58	58	60	60	62	64	64	69	72	78	81	84	87	
	2	50	50	50	50	50	53	53	56	58	58	60	60	62	64	64	69	72	78	81	84	87	
	3	50	50	50	50	50	53	53	56	58	58	60	60	62	64	64	69	72	78	81	84	87	
	4	50	50	50	50	50	53	53	56	58	58	60	60	62	64	64	69	72	78	81	84	87	
	5	50	50	50	50	50	53	53	56	58	58	60	60	62	64	64	69	72	78	81	84	87	
	6	50	50	50	50	50	53	53	56	58	58	60	60	62	64	64	69	72	78	81	84	87	
	7	50	50	50	50	50	53	53	56	58	58	60	60	62	64	64	69	72	78	81	84	87	
	8	50	50	50	50	50	53	53	56	58	58	60	60	62	64	64	69	72	78	81	84	87	
	9	50	50	50	50	50	53	53	56	58	58	60	60	62	64	64	69	72	78	81	84	87	
	10	53	53	53	53	53	56	56	58	60	60	62	62	64	66	66	72	75	81	84	87	89	
	11	53	53	53	53	53	56	56	58	60	60	62	62	64	66	66	72	75	81	84	87	89	
	12	56	56	56	56	56	58	58	60	62	62	64	64	66	69	69	75	78	84	87	89	92	
	13	58	58	58	58	58	60	60	62	64	64	66	66	69	72	72	78	81	87	89	92	96	
	14	60	60	60	60	60	62	62	64	66	66	69	69	72	75	75	81	84	89	92	96	100	
	15	62	62	62	62	62	64	64	66	69	69	72	72	75	78	78	84	87	92	96	100	102	
	16	66	66	66	66	66	69	69	72	75	75	78	78	81	84	84	89	92	100	102	105	109	
	17	72	72	72	72	72	75	75	78	81	81	84	84	87	89	89	96	100	105	109	112	116	
	18	75	75	75	75	75	78	78	81	84	84	87	87	89	92	92	100	102	109	112	116	121	
	19	78	78	78	78	78	81	81	84	87	87	89	89	92	96	96	102	105	112	116	121	126	
20	84	84	84	84	84	87	87	89	92	92	96	96	100	102	102	109	112	121	126	131	136		

Table 5-19 Language Index Score Equivalents of Subtest Raw Scores

			Picture Naming Total Score									
			0	1	2	3	4	5	6	7	8	9-10
Semantic Fluency Total Score	Ages 50-59	0	40	40	40	40	40	44	47	51	57	71
		1	40	40	40	40	40	44	47	51	57	71
		2	40	40	40	40	40	44	47	51	57	71
		3	40	40	40	40	40	44	47	51	57	71
		4	40	40	40	40	40	44	47	51	57	71

	Picture Naming Total Score									
	0	1	2	3	4	5	6	7	8	9-10
5	40	40	40	40	40	44	47	51	57	71
6	40	40	40	40	40	44	47	51	57	71
7	44	44	44	44	44	47	51	54	60	75
8	44	44	44	44	44	47	51	54	60	75
9	47	47	47	47	47	51	54	57	64	79
10	47	47	47	47	47	51	54	57	64	79
11	47	47	47	47	47	51	54	57	64	79
12	51	51	51	51	51	54	57	60	68	82
13	51	51	51	51	51	54	57	60	68	82
14	54	54	54	54	54	57	60	64	71	84
15	57	57	57	57	57	60	64	68	75	87
16	60	60	60	60	60	64	68	71	79	90
17	60	60	60	60	60	64	68	71	79	90
18	64	64	64	64	64	68	71	75	83	94
19	64	64	64	64	64	68	71	75	83	94
20	68	68	68	68	68	71	75	79	87	97
21	71	71	71	71	71	75	79	83	90	99
22	71	71	71	71	71	75	79	83	90	99
23	75	75	75	75	75	79	83	87	92	102
24	75	75	75	75	75	79	83	87	92	102
25	79	79	79	79	79	83	87	90	94	105
26	83	83	83	83	83	87	90	92	96	109
27	83	83	83	83	83	87	90	92	96	109
28	87	87	87	87	87	90	92	94	100	113
29	87	87	87	87	87	90	92	94	100	113
30	90	90	90	90	90	92	94	96	102	117
31	92	92	92	92	92	94	96	100	104	120
32	92	92	92	92	92	94	96	100	104	120
33	94	94	94	94	94	96	100	102	108	124
34	96	96	96	96	96	100	102	104	112	127
35	100	100	100	100	100	102	104	108	116	131

		Picture Naming Total Score									
		0	1	2	3	4	5	6	7	8	9-10
	36+	100	100	100	100	100	102	104	108	116	131
Ages 60-69	0	40	40	40	40	40	44	47	51	57	74
	1	40	40	40	40	40	44	47	51	57	74
	2	40	40	40	40	40	44	47	51	57	74
	3	40	40	40	40	40	44	47	51	57	74
	4	40	40	40	40	40	44	47	51	57	74
	5	40	40	40	40	40	44	47	51	57	74
	6	44	44	44	44	44	47	51	54	60	78
	7	44	44	44	44	44	47	51	54	60	78
	8	44	44	44	44	44	47	51	54	60	78
	9	47	47	47	47	47	51	54	57	64	82
	10	47	47	47	47	47	51	54	57	64	82
	11	47	47	47	47	47	51	54	57	64	82
	12	51	51	51	51	51	54	57	60	68	85
	13	51	51	51	51	51	54	57	60	68	85
	14	54	54	54	54	54	57	60	64	71	87
	15	57	57	57	57	57	60	64	68	75	90
	16	60	60	60	60	60	64	68	71	79	92
	17	60	60	60	60	60	64	68	71	79	92
	18	64	64	64	64	64	68	71	75	83	96
	19	64	64	64	64	64	68	71	75	83	96
	20	68	68	68	68	68	71	75	79	87	98
	21	71	71	71	71	71	75	79	83	90	101
	22	71	71	71	71	71	75	79	83	90	101
	23	75	75	75	75	75	79	83	87	92	104
	24	75	75	75	75	75	79	83	87	92	104
	25	79	79	79	79	79	83	87	90	94	108
	26	83	83	83	83	83	87	90	92	96	111
	27	87	87	87	87	87	90	92	94	100	116
	28	87	87	87	87	87	90	92	94	100	116

		Picture Naming Total Score									
		0	1	2	3	4	5	6	7	8	9-10
	29	90	90	90	90	90	92	94	96	102	120
	30	90	90	90	90	90	92	94	96	102	120
	31	94	94	94	94	94	96	100	102	108	127
	32	94	94	94	94	94	96	100	102	108	127
	33	94	94	94	94	94	96	100	102	108	127
	34	96	96	96	96	96	100	102	104	112	130
	35	100	100	100	100	100	102	104	108	116	134
	36+	100	100	100	100	100	102	104	108	116	134
Ages 70-79	0	40	40	40	40	40	47	47	51	57	74
	1	40	40	40	40	40	47	47	51	57	74
	2	40	40	40	40	40	47	47	51	57	74
	3	40	40	40	40	40	47	47	51	57	74
	4	40	40	40	40	40	47	47	51	57	74
	5	40	40	40	40	40	47	47	51	57	74
	6	44	44	44	44	44	51	51	54	60	78
	7	44	44	44	44	44	51	51	54	60	78
	8	47	47	47	47	47	54	54	57	64	82
	9	47	47	47	47	47	54	54	57	64	82
	10	51	51	51	51	51	57	57	60	68	85
	11	51	51	51	51	51	57	57	60	68	85
	12	54	54	54	54	54	60	60	64	71	88
	13	54	54	54	54	54	60	60	64	71	88
14	57	57	57	57	57	64	64	68	75	90	
15	60	60	60	60	60	68	68	71	79	92	
16	60	60	60	60	60	68	68	71	79	92	
17	64	64	64	64	64	71	71	75	83	96	
18	64	64	64	64	64	71	71	75	83	96	
19	68	68	68	68	68	75	75	79	87	99	
20	71	71	71	71	71	79	79	83	90	101	
21	75	75	75	75	75	83	83	87	92	105	
22	75	75	75	75	75	83	83	87	92	105	

		Picture Naming Total Score										
		0	1	2	3	4	5	6	7	8	9-10	
Ages 80-89	23	79	79	79	79	79	87	87	90	94	108	
	24	79	79	79	79	79	87	87	90	94	108	
	25	83	83	83	83	83	90	90	92	96	112	
	26	83	83	83	83	83	90	90	92	96	112	
	27	87	87	87	87	87	92	92	94	100	117	
	28	90	90	90	90	90	94	94	96	102	120	
	29	92	92	92	92	92	96	96	100	104	124	
	30	92	92	92	92	92	96	96	100	104	124	
	31	94	94	94	94	94	100	100	102	108	128	
	32	94	94	94	94	94	100	100	102	108	128	
	33	96	96	96	96	96	102	102	104	112	131	
	34	100	100	100	100	100	104	104	108	116	134	
	35	100	100	100	100	100	104	104	108	116	134	
	36+	100	100	100	100	100	104	104	108	116	134	
		0	40	40	40	40	40	47	51	54	57	76
		1	40	40	40	40	40	47	51	54	57	76
		2	40	40	40	40	40	47	51	54	57	76
	3	40	40	40	40	40	47	51	54	57	76	
	4	40	40	40	40	40	47	51	54	57	76	
	5	44	44	44	44	44	51	54	57	60	80	
	6	44	44	44	44	44	51	54	57	60	80	
	7	44	44	44	44	44	51	54	57	60	80	
	8	47	47	47	47	47	54	57	60	64	83	
	9	51	51	51	51	51	57	60	64	68	86	
	10	51	51	51	51	51	57	60	64	68	86	
	11	54	54	54	54	54	60	64	68	71	89	
	12	57	57	57	57	57	64	68	71	75	92	
	13	57	57	57	57	57	64	68	71	75	92	
	14	60	60	60	60	60	68	71	75	79	95	
	15	64	64	64	64	64	71	75	79	83	97	
	16	68	68	68	68	68	75	79	83	87	99	

		Picture Naming Total Score									
		0	1	2	3	4	5	6	7	8	9-10
	17	71	71	71	71	71	79	83	87	90	103
	18	71	71	71	71	71	79	83	87	90	103
	19	75	75	75	75	75	83	87	90	92	107
	20	79	79	79	79	79	87	90	92	94	110
	21	83	83	83	83	83	90	92	94	96	113
	22	87	87	87	87	87	92	94	96	100	117
	23	90	90	90	90	90	94	96	100	102	122
	24	90	90	90	90	90	94	96	100	102	122
	25	92	92	92	92	92	96	100	102	104	125
	26	92	92	92	92	92	96	100	102	104	125
	27	94	94	94	94	94	100	102	104	108	129
	28	94	94	94	94	94	100	102	104	108	129
	29	94	94	94	94	94	100	102	104	108	129
	30	96	96	96	96	96	102	104	108	112	133
	31	96	96	96	96	96	102	104	108	112	133
	32	96	96	96	96	96	102	104	108	112	133
	33	100	100	100	100	100	104	108	112	116	137
	34	100	100	100	100	100	104	108	112	116	137
	35	100	100	100	100	100	104	108	112	116	137
	36+	100	100	100	100	100	104	108	112	116	137

Table 5-20 Attention Index Score Equivalents of Subtest Raw Scores

		Digit Span Total Score																	
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	
Coding Total Score	Ages 50-59	0	40	40	40	40	43	46	49	53	56	64	72	75	79	82	85	88	91
		1	40	40	40	40	43	46	49	53	56	64	72	75	79	82	85	88	91
		2	40	40	40	40	43	46	49	53	56	64	72	75	79	82	85	88	91
		3	40	40	40	40	43	46	49	53	56	64	72	75	79	82	85	88	91
		4	40	40	40	40	43	46	49	53	56	64	72	75	79	82	85	88	91
		5	40	40	40	40	43	46	49	53	56	64	72	75	79	82	85	88	91
		6	40	40	40	40	43	46	49	53	56	64	72	75	79	82	85	88	91
		7	40	40	40	40	43	46	49	53	56	64	72	75	79	82	85	88	91
		8	40	40	40	40	43	46	49	53	56	64	72	75	79	82	85	88	91
		9	40	40	40	40	43	46	49	53	56	64	72	75	79	82	85	88	91
		10	40	40	40	40	43	46	49	53	56	64	72	75	79	82	85	88	91
		11	40	40	40	40	43	46	49	53	56	64	72	75	79	82	85	88	91
		12	43	43	43	43	46	49	53	56	60	68	75	79	82	85	88	91	94
		13	43	43	43	43	46	49	53	56	60	68	75	79	82	85	88	91	94
		14	43	43	43	43	46	49	53	56	60	68	75	79	82	85	88	91	94
		15	43	43	43	43	46	49	53	56	60	68	75	79	82	85	88	91	94
		16	43	43	43	43	46	49	53	56	60	68	75	79	82	85	88	91	94
		17	43	43	43	43	46	49	53	56	60	68	75	79	82	85	88	91	94
		18	43	43	43	43	46	49	53	56	60	68	75	79	82	85	88	91	94
		19	46	46	46	46	49	53	56	60	64	72	79	82	85	88	91	94	97
		20	46	46	46	46	49	53	56	60	64	72	79	82	85	88	91	94	97
		21	46	46	46	46	49	53	56	60	64	72	79	82	85	88	91	94	97
		22	46	46	46	46	49	53	56	60	64	72	79	82	85	88	91	94	97
		23	46	46	46	46	49	53	56	60	64	72	79	82	85	88	91	94	97
24	46	46	46	46	49	53	56	60	64	72	79	82	85	88	91	94	97		

	Digit Span Total Score																
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
25	46	46	46	46	49	53	56	60	64	72	79	82	85	88	91	94	97
26	49	49	49	49	53	56	60	64	68	75	82	85	88	91	94	97	100
27	49	49	49	49	53	56	60	64	68	75	82	85	88	91	94	97	100
28	49	49	49	49	53	56	60	64	68	75	82	85	88	91	94	97	100
29	49	49	49	49	53	56	60	64	68	75	82	85	88	91	94	97	100
30	49	49	49	49	53	56	60	64	68	75	82	85	88	91	94	97	100
31	53	53	53	53	56	60	64	68	72	79	85	88	91	94	97	100	103
32	53	53	53	53	56	60	64	68	72	79	85	88	91	94	97	100	103
33	53	53	53	53	56	60	64	68	72	79	85	88	91	94	97	100	103
34	56	56	56	56	60	64	68	72	75	82	88	91	94	97	100	103	106
35	56	56	56	56	60	64	68	72	75	82	88	91	94	97	100	103	106
36	56	56	56	56	60	64	68	72	75	82	88	91	94	97	100	103	106
37	60	60	60	60	64	68	72	75	79	85	91	94	97	100	103	106	109
38	60	60	60	60	64	68	72	75	79	85	91	94	97	100	103	106	109
39	60	60	60	60	64	68	72	75	79	85	91	94	97	100	103	106	109
40	60	60	60	60	64	68	72	75	79	85	91	94	97	100	103	106	109
41	64	64	64	64	68	72	75	79	82	88	94	97	100	103	106	109	112
42	64	64	64	64	68	72	75	79	82	88	94	97	100	103	106	109	112
43	68	68	68	68	72	75	79	82	85	91	97	100	103	106	109	112	115
44	68	68	68	68	72	75	79	82	85	91	97	100	103	106	109	112	115
45	72	72	72	72	75	79	82	85	88	94	100	103	106	109	112	115	118
46	72	72	72	72	75	79	82	85	88	94	100	103	106	109	112	115	118
47	72	72	72	72	75	79	82	85	88	94	100	103	106	109	112	115	118
48	72	72	72	72	75	79	82	85	88	94	100	103	106	109	112	115	118
49	75	75	75	75	79	82	85	88	91	97	103	106	109	112	115	118	122
50	75	75	75	75	79	82	85	88	91	97	103	106	109	112	115	118	122

	Digit Span Total Score																
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
51	79	79	79	79	82	85	88	91	94	100	106	109	112	115	118	122	125
52	79	79	79	79	82	85	88	91	94	100	106	109	112	115	118	122	125
53	79	79	79	79	82	85	88	91	94	100	106	109	112	115	118	122	125
54	82	82	82	82	85	88	91	94	97	103	109	112	115	118	122	125	128
55	82	82	82	82	85	88	91	94	97	103	109	112	115	118	122	125	128
56	82	82	82	82	85	88	91	94	97	103	109	112	115	118	122	125	128
57	85	85	85	85	88	91	94	97	100	106	112	115	118	122	125	128	132
58	85	85	85	85	88	91	94	97	100	106	112	115	118	122	125	128	132
59	85	85	85	85	88	91	94	97	100	106	112	115	118	122	125	128	132
60	85	85	85	85	88	91	94	97	100	106	112	115	118	122	125	128	132
61	88	88	88	88	91	94	97	100	103	109	115	118	122	125	128	132	135
62	88	88	88	88	91	94	97	100	103	109	115	118	122	125	128	132	135
63	91	91	91	91	94	97	100	103	106	112	118	122	125	128	132	135	138
64	91	91	91	91	94	97	100	103	106	112	118	122	125	128	132	135	138
65	94	94	94	94	97	100	103	106	109	115	122	125	128	132	135	138	142
66	94	94	94	94	97	100	103	106	109	115	122	125	128	132	135	138	142
67	94	94	94	94	97	100	103	106	109	115	122	125	128	132	135	138	142
68	97	97	97	97	100	103	106	109	112	118	125	128	132	135	138	142	146
69	97	97	97	97	100	103	106	109	112	118	125	128	132	135	138	142	146
70	97	97	97	97	100	103	106	109	112	118	125	128	132	135	138	142	146
71	97	97	97	97	100	103	106	109	112	118	125	128	132	135	138	142	146
72	100	100	100	100	103	106	109	112	115	122	128	132	135	138	142	146	150
73	100	100	100	100	103	106	109	112	115	122	128	132	135	138	142	146	150
74	100	100	100	100	103	106	109	112	115	122	128	132	135	138	142	146	150
75	100	100	100	100	103	106	109	112	115	122	128	132	135	138	142	146	150
76	100	100	100	100	103	106	109	112	115	122	128	132	135	138	142	146	150

		Digit Span Total Score																
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Ages 60-69	77	100	100	100	100	103	106	109	112	115	122	128	132	135	138	142	146	150
	78	100	100	100	100	103	106	109	112	115	122	128	132	135	138	142	146	150
	79	100	100	100	100	103	106	109	112	115	122	128	132	135	138	142	146	150
	80	100	100	100	100	103	106	109	112	115	122	128	132	135	138	142	146	150
	81	100	100	100	100	103	106	109	112	115	122	128	132	135	138	142	146	150
	82	100	100	100	100	103	106	109	112	115	122	128	132	135	138	142	146	150
	83	100	100	100	100	103	106	109	112	115	122	128	132	135	138	142	146	150
	84	100	100	100	100	103	106	109	112	115	122	128	132	135	138	142	146	150
	85	100	100	100	100	103	106	109	112	115	122	128	132	135	138	142	146	150
	86	100	100	100	100	103	106	109	112	115	122	128	132	135	138	142	146	150
	87	100	100	100	100	103	106	109	112	115	122	128	132	135	138	142	146	150
	88	100	100	100	100	103	106	109	112	115	122	128	132	135	138	142	146	150
89	100	100	100	100	103	106	109	112	115	122	128	132	135	138	142	146	150	
	0	40	40	40	40	43	46	49	53	60	64	72	75	79	85	88	91	91
	1	40	40	40	40	43	46	49	53	60	64	72	75	79	85	88	91	91
	2	40	40	40	40	43	46	49	53	60	64	72	75	79	85	88	91	91
	3	40	40	40	40	43	46	49	53	60	64	72	75	79	85	88	91	91
	4	40	40	40	40	43	46	49	53	60	64	72	75	79	85	88	91	91
	5	40	40	40	40	43	46	49	53	60	64	72	75	79	85	88	91	91
	6	40	40	40	40	43	46	49	53	60	64	72	75	79	85	88	91	91
	7	40	40	40	40	43	46	49	53	60	64	72	75	79	85	88	91	91
	8	40	40	40	40	43	46	49	53	60	64	72	75	79	85	88	91	91
	9	40	40	40	40	43	46	49	53	60	64	72	75	79	85	88	91	91
	10	40	40	40	40	43	46	49	53	60	64	72	75	79	85	88	91	91
	11	43	43	43	43	46	49	53	56	64	68	75	79	82	88	91	94	94
	12	43	43	43	43	46	49	53	56	64	68	75	79	82	88	91	94	94

	Digit Span Total Score																
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
13	43	43	43	43	46	49	53	56	64	68	75	79	82	88	91	94	94
14	43	43	43	43	46	49	53	56	64	68	75	79	82	88	91	94	94
15	43	43	43	43	46	49	53	56	64	68	75	79	82	88	91	94	94
16	43	43	43	43	46	49	53	56	64	68	75	79	82	88	91	94	94
17	43	43	43	43	46	49	53	56	64	68	75	79	82	88	91	94	94
18	46	46	46	46	49	53	56	60	68	72	79	82	85	91	94	97	97
19	46	46	46	46	49	53	56	60	68	72	79	82	85	91	94	97	97
20	46	46	46	46	49	53	56	60	68	72	79	82	85	91	94	97	97
21	46	46	46	46	49	53	56	60	68	72	79	82	85	91	94	97	97
22	46	46	46	46	49	53	56	60	68	72	79	82	85	91	94	97	97
23	46	46	46	46	49	53	56	60	68	72	79	82	85	91	94	97	97
24	49	49	49	49	53	56	60	64	72	75	82	85	88	94	97	100	100
25	49	49	49	49	53	56	60	64	72	75	82	85	88	94	97	100	100
26	49	49	49	49	53	56	60	64	72	75	82	85	88	94	97	100	100
27	49	49	49	49	53	56	60	64	72	75	82	85	88	94	97	100	100
28	53	53	53	53	56	60	64	68	75	79	85	88	91	97	100	103	103
29	53	53	53	53	56	60	64	68	75	79	85	88	91	97	100	103	103
30	53	53	53	53	56	60	64	68	75	79	85	88	91	97	100	103	103
31	53	53	53	53	56	60	64	68	75	79	85	88	91	97	100	103	103
32	56	56	56	56	60	64	68	72	79	82	88	91	94	100	103	106	106
33	56	56	56	56	60	64	68	72	79	82	88	91	94	100	103	106	106
34	56	56	56	56	60	64	68	72	79	82	88	91	94	100	103	106	106
35	56	56	56	56	60	64	68	72	79	82	88	91	94	100	103	106	106
36	60	60	60	60	64	68	72	75	82	85	91	94	97	103	106	109	109
37	60	60	60	60	64	68	72	75	82	85	91	94	97	103	106	109	109
38	60	60	60	60	64	68	72	75	82	85	91	94	97	103	106	109	109

	Digit Span Total Score																
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
39	60	60	60	60	64	68	72	75	82	85	91	94	97	103	106	109	109
40	60	60	60	60	64	68	72	75	82	85	91	94	97	103	106	109	109
41	64	64	64	64	68	72	75	79	85	88	94	97	100	106	109	112	112
42	64	64	64	64	68	72	75	79	85	88	94	97	100	106	109	112	112
43	68	68	68	68	72	75	79	82	88	91	97	100	103	109	112	115	115
44	68	68	68	68	72	75	79	82	88	91	97	100	103	109	112	115	115
45	72	72	72	72	75	79	82	85	91	94	100	103	106	112	115	118	118
46	72	72	72	72	75	79	82	85	91	94	100	103	106	112	115	118	118
47	72	72	72	72	75	79	82	85	91	94	100	103	106	112	115	118	118
48	72	72	72	72	75	79	82	85	91	94	100	103	106	112	115	118	118
49	75	75	75	75	79	82	85	88	94	97	103	106	109	115	118	122	122
50	79	79	79	79	82	85	88	91	97	100	106	109	112	118	122	125	125
51	79	79	79	79	82	85	88	91	97	100	106	109	112	118	122	125	125
52	82	82	82	82	85	88	91	94	100	103	109	112	115	122	125	128	128
53	82	82	82	82	85	88	91	94	100	103	109	112	115	122	125	128	128
54	85	85	85	85	88	91	94	97	103	106	112	115	118	125	128	132	132
55	85	85	85	85	88	91	94	97	103	106	112	115	118	125	128	132	132
56	88	88	88	88	91	94	97	100	106	109	115	118	122	128	132	135	135
57	88	88	88	88	91	94	97	100	106	109	115	118	122	128	132	135	135
58	88	88	88	88	91	94	97	100	106	109	115	118	122	128	132	135	135
59	91	91	91	91	94	97	100	103	109	112	118	122	125	132	135	138	138
60	91	91	91	91	94	97	100	103	109	112	118	122	125	132	135	138	138
61	94	94	94	94	97	100	103	106	112	115	122	125	128	135	138	142	142
62	94	94	94	94	97	100	103	106	112	115	122	125	128	135	138	142	142
63	94	94	94	94	97	100	103	106	112	115	122	125	128	135	138	142	142
64	94	94	94	94	97	100	103	106	112	115	122	125	128	135	138	142	142

		Digit Span Total Score																
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
	65	97	97	97	97	100	103	106	109	115	118	125	128	132	138	142	146	146
	66	97	97	97	97	100	103	106	109	115	118	125	128	132	138	142	146	146
	67	97	97	97	97	100	103	106	109	115	118	125	128	132	138	142	146	146
	68	97	97	97	97	100	103	106	109	115	118	125	128	132	138	142	146	146
	69	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150
	70	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150
	71	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150
	72	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150
	73	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150
	74	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150
	75	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150
	76	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150
	77	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150
	78	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150
	79	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150
	80	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150
	81	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150
	82	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150
	83	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150
	84	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150
85	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150	
86	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150	
87	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150	
88	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150	
89	100	100	100	100	103	106	109	112	118	122	128	132	135	142	146	150	150	
Ag es 70-	0	40	40	40	43	46	49	49	53	60	64	72	75	79	85	88	91	91

	Digit Span Total Score																
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1	40	40	40	43	46	49	49	53	60	64	72	75	79	85	88	91	91
2	40	40	40	43	46	49	49	53	60	64	72	75	79	85	88	91	91
3	40	40	40	43	46	49	49	53	60	64	72	75	79	85	88	91	91
4	40	40	40	43	46	49	49	53	60	64	72	75	79	85	88	91	91
5	40	40	40	43	46	49	49	53	60	64	72	75	79	85	88	91	91
6	40	40	40	43	46	49	49	53	60	64	72	75	79	85	88	91	91
7	40	40	40	43	46	49	49	53	60	64	72	75	79	85	88	91	91
8	40	40	40	43	46	49	49	53	60	64	72	75	79	85	88	91	91
9	40	40	40	43	46	49	49	53	60	64	72	75	79	85	88	91	91
10	40	40	40	43	46	49	49	53	60	64	72	75	79	85	88	91	91
11	43	43	43	46	49	53	53	56	64	68	75	79	82	88	91	94	94
12	43	43	43	46	49	53	53	56	64	68	75	79	82	88	91	94	94
13	43	43	43	46	49	53	53	56	64	68	75	79	82	88	91	94	94
14	43	43	43	46	49	53	53	56	64	68	75	79	82	88	91	94	94
15	43	43	43	46	49	53	53	56	64	68	75	79	82	88	91	94	94
16	43	43	43	46	49	53	53	56	64	68	75	79	82	88	91	94	94
17	46	46	46	49	53	56	56	60	68	72	79	82	85	91	94	97	97
18	46	46	46	49	53	56	56	60	68	72	79	82	85	91	94	97	97
19	46	46	46	49	53	56	56	60	68	72	79	82	85	91	94	97	97
20	49	49	49	53	56	60	60	64	72	75	82	85	88	94	97	100	100
21	49	49	49	53	56	60	60	64	72	75	82	85	88	94	97	100	100
22	49	49	49	53	56	60	60	64	72	75	82	85	88	94	97	100	100
23	53	53	53	56	60	64	64	68	75	79	85	88	91	97	100	103	103
24	53	53	53	56	60	64	64	68	75	79	85	88	91	97	100	103	103
25	56	56	56	60	64	68	68	72	79	82	88	91	94	100	103	106	106
26	56	56	56	60	64	68	68	72	79	82	88	91	94	100	103	106	106

	Digit Span Total Score																
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
27	56	56	56	60	64	68	68	72	79	82	88	91	94	100	103	106	106
28	60	60	60	64	68	72	72	75	82	85	91	94	97	103	106	109	109
29	60	60	60	64	68	72	72	75	82	85	91	94	97	103	106	109	109
30	60	60	60	64	68	72	72	75	82	85	91	94	97	103	106	109	109
31	60	60	60	64	68	72	72	75	82	85	91	94	97	103	106	109	109
32	64	64	64	68	72	75	75	79	85	88	94	97	100	106	109	112	112
33	64	64	64	68	72	75	75	79	85	88	94	97	100	106	109	112	112
34	64	64	64	68	72	75	75	79	85	88	94	97	100	106	109	112	112
35	64	64	64	68	72	75	75	79	85	88	94	97	100	106	109	112	112
36	64	64	64	68	72	75	75	79	85	88	94	97	100	106	109	112	112
37	68	68	68	72	75	79	79	82	88	91	97	100	103	109	112	115	115
38	68	68	68	72	75	79	79	82	88	91	97	100	103	109	112	115	115
39	68	68	68	72	75	79	79	82	88	91	97	100	103	109	112	115	115
40	72	72	72	75	79	82	82	85	91	94	100	103	106	112	115	118	118
41	72	72	72	75	79	82	82	85	91	94	100	103	106	112	115	118	118
42	72	72	72	75	79	82	82	85	91	94	100	103	106	112	115	118	118
43	75	75	75	79	82	85	85	88	94	97	103	106	109	115	118	122	122
44	75	75	75	79	82	85	85	88	94	97	103	106	109	115	118	122	122
45	75	75	75	79	82	85	85	88	94	97	103	106	109	115	118	122	122
46	79	79	79	82	85	88	88	91	97	100	106	109	112	118	122	125	125
47	79	79	79	82	85	88	88	91	97	100	106	109	112	118	122	125	125
48	82	82	82	85	88	91	91	94	100	103	109	112	115	122	125	128	128
49	82	82	82	85	88	91	91	94	100	103	109	112	115	122	125	128	128
50	82	82	82	85	88	91	91	94	100	103	109	112	115	122	125	128	128
51	85	85	85	88	91	94	94	97	103	106	112	115	118	125	128	132	132
52	85	85	85	88	91	94	94	97	103	106	112	115	118	125	128	132	132

	Digit Span Total Score																
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
53	85	85	85	88	91	94	94	97	103	106	112	115	118	125	128	132	132
54	88	88	88	91	94	97	97	100	106	109	115	118	122	128	132	135	135
55	88	88	88	91	94	97	97	100	106	109	115	118	122	128	132	135	135
56	88	88	88	91	94	97	97	100	106	109	115	118	122	128	132	135	135
57	91	91	91	94	97	100	100	103	109	112	118	122	125	132	135	138	138
58	91	91	91	94	97	100	100	103	109	112	118	122	125	132	135	138	138
59	91	91	91	94	97	100	100	103	109	112	118	122	125	132	135	138	138
60	91	91	91	94	97	100	100	103	109	112	118	122	125	132	135	138	138
61	94	94	94	97	100	103	103	106	112	115	122	125	128	135	138	142	142
62	94	94	94	97	100	103	103	106	112	115	122	125	128	135	138	142	142
63	94	94	94	97	100	103	103	106	112	115	122	125	128	135	138	142	142
64	97	97	97	100	103	106	106	109	115	118	125	128	132	138	142	146	146
65	97	97	97	100	103	106	106	109	115	118	125	128	132	138	142	146	146
66	97	97	97	100	103	106	106	109	115	118	125	128	132	138	142	146	146
67	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
68	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
69	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
70	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
71	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
72	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
73	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
74	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
75	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
76	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
77	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
78	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150

		Digit Span Total Score																
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
	79	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
	80	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
	81	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
	82	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
	83	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
	84	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
	85	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
	86	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
	87	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
	88	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150
89	100	100	100	103	106	109	109	112	118	122	128	132	135	142	146	150	150	
Ages 80-89	0	40	40	40	43	46	49	53	56	68	72	79	82	85	88	88	91	94
	1	40	40	40	43	46	49	53	56	68	72	79	82	85	88	88	91	94
	2	40	40	40	43	46	49	53	56	68	72	79	82	85	88	88	91	94
	3	40	40	40	43	46	49	53	56	68	72	79	82	85	88	88	91	94
	4	40	40	40	43	46	49	53	56	68	72	79	82	85	88	88	91	94
	5	40	40	40	43	46	49	53	56	68	72	79	82	85	88	88	91	94
	6	40	40	40	43	46	49	53	56	68	72	79	82	85	88	88	91	94
	7	40	40	40	43	46	49	53	56	68	72	79	82	85	88	88	91	94
	8	40	40	40	43	46	49	53	56	68	72	79	82	85	88	88	91	94
	9	40	40	40	43	46	49	53	56	68	72	79	82	85	88	88	91	94
	10	43	43	43	46	49	53	56	60	72	75	82	85	88	91	91	94	97
	11	43	43	43	46	49	53	56	60	72	75	82	85	88	91	91	94	97
	12	43	43	43	46	49	53	56	60	72	75	82	85	88	91	91	94	97
	13	43	43	43	46	49	53	56	60	72	75	82	85	88	91	91	94	97
14	43	43	43	46	49	53	56	60	72	75	82	85	88	91	91	94	97	

	Digit Span Total Score																
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
15	43	43	43	46	49	53	56	60	72	75	82	85	88	91	91	94	97
16	46	46	46	49	53	56	60	64	75	79	85	88	91	94	94	97	100
17	46	46	46	49	53	56	60	64	75	79	85	88	91	94	94	97	100
18	46	46	46	49	53	56	60	64	75	79	85	88	91	94	94	97	100
19	49	49	49	53	56	60	64	68	79	82	88	91	94	97	97	100	103
20	49	49	49	53	56	60	64	68	79	82	88	91	94	97	97	100	103
21	49	49	49	53	56	60	64	68	79	82	88	91	94	97	97	100	103
22	53	53	53	56	60	64	68	72	82	85	91	94	97	100	100	103	106
23	53	53	53	56	60	64	68	72	82	85	91	94	97	100	100	103	106
24	56	56	56	60	64	68	72	75	85	88	94	97	100	103	103	106	109
25	56	56	56	60	64	68	72	75	85	88	94	97	100	103	103	106	109
26	56	56	56	60	64	68	72	75	85	88	94	97	100	103	103	106	109
27	60	60	60	64	68	72	75	79	88	91	97	100	103	106	106	109	112
28	60	60	60	64	68	72	75	79	88	91	97	100	103	106	106	109	112
29	64	64	64	68	72	75	79	82	91	94	100	103	106	109	109	112	115
30	64	64	64	68	72	75	79	82	91	94	100	103	106	109	109	112	115
31	68	68	68	72	75	79	82	85	94	97	103	106	109	112	112	115	118
32	68	68	68	72	75	79	82	85	94	97	103	106	109	112	112	115	118
33	72	72	72	75	79	82	85	88	97	100	106	109	112	115	115	118	122
34	72	72	72	75	79	82	85	88	97	100	106	109	112	115	115	118	122
35	75	75	75	79	82	85	88	91	100	103	109	112	115	118	118	122	125
36	75	75	75	79	82	85	88	91	100	103	109	112	115	118	118	122	125
37	75	75	75	79	82	85	88	91	100	103	109	112	115	118	118	122	125
38	79	79	79	82	85	88	91	94	103	106	112	115	118	122	122	125	128
39	79	79	79	82	85	88	91	94	103	106	112	115	118	122	122	125	128
40	82	82	82	85	88	91	94	97	106	109	115	118	122	125	125	128	132

	Digit Span Total Score																
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
41	82	82	82	85	88	91	94	97	106	109	115	118	122	125	125	128	132
42	85	85	85	88	91	94	97	100	109	112	118	122	125	128	128	132	135
43	85	85	85	88	91	94	97	100	109	112	118	122	125	128	128	132	135
44	88	88	88	91	94	97	100	103	112	115	122	125	128	132	132	135	138
45	88	88	88	91	94	97	100	103	112	115	122	125	128	132	132	135	138
46	91	91	91	94	97	100	103	106	115	118	125	128	132	135	135	138	142
47	91	91	91	94	97	100	103	106	115	118	125	128	132	135	135	138	142
48	91	91	91	94	97	100	103	106	115	118	125	128	132	135	135	138	142
49	94	94	94	97	100	103	106	109	118	122	128	132	135	138	138	142	146
50	94	94	94	97	100	103	106	109	118	122	128	132	135	138	138	142	146
51	94	94	94	97	100	103	106	109	118	122	128	132	135	138	138	142	146
52	94	94	94	97	100	103	106	109	118	122	128	132	135	138	138	142	146
53	97	97	97	100	103	106	109	112	122	125	132	135	138	142	142	146	150
54	97	97	97	100	103	106	109	112	122	125	132	135	138	142	142	146	150
55	97	97	97	100	103	106	109	112	122	125	132	135	138	142	142	146	150
56	97	97	97	100	103	106	109	112	122	125	132	135	138	142	142	146	150
57	97	97	97	100	103	106	109	112	122	125	132	135	138	142	142	146	150
58	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
59	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
60	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
61	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
62	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
63	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
64	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
65	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
66	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154

	Digit Span Total Score																
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
67	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
68	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
69	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
70	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
71	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
72	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
73	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
74	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
75	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
76	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
77	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
78	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
79	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
80	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
81	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
82	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
83	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
84	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
85	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
86	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
87	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
88	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154
89	100	100	100	103	106	109	112	115	125	128	135	138	142	146	146	150	154

Table 5-21 Delayed Memory Index Score Equivalents of Subtest Raw Scores

		List Recognition Total Score																					
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19-20		
Sum of List/Story/ Figure Total Score	Ages 50-59	0	40	40	40	40	40	40	40	40	40	40	40	40	40	44	44	48	48	52	60	77	
		1	40	40	40	40	40	40	40	40	40	40	40	40	40	40	44	44	48	48	52	60	77
		2	40	40	40	40	40	40	40	40	40	40	40	40	40	40	44	44	48	48	52	60	77
		3	40	40	40	40	40	40	40	40	40	40	40	40	40	40	44	44	48	48	52	60	77
		4	40	40	40	40	40	40	40	40	40	40	40	40	40	40	44	44	48	48	52	60	77
		5	40	40	40	40	40	40	40	40	40	40	40	40	40	40	44	44	48	48	52	60	77
		6	40	40	40	40	40	40	40	40	40	40	40	40	40	40	44	44	48	48	52	60	77
		7	40	40	40	40	40	40	40	40	40	40	40	40	40	40	44	44	48	48	52	60	77
		8	44	44	44	44	44	44	44	44	44	44	44	44	44	44	48	48	52	52	56	64	80
		9	44	44	44	44	44	44	44	44	44	44	44	44	44	44	48	48	52	52	56	64	80
		10	48	48	48	48	48	48	48	48	48	48	48	48	48	48	52	52	56	56	60	68	82
		11	48	48	48	48	48	48	48	48	48	48	48	48	48	48	52	52	56	56	60	68	82
		12	48	48	48	48	48	48	48	48	48	48	48	48	48	48	52	52	56	56	60	68	82
		13	52	52	52	52	52	52	52	52	52	52	52	52	52	52	56	56	60	60	64	71	85
		14	52	52	52	52	52	52	52	52	52	52	52	52	52	52	56	56	60	60	64	71	85
		15	56	56	56	56	56	56	56	56	56	56	56	56	56	56	60	60	64	64	68	75	88
		16	60	60	60	60	60	60	60	60	60	60	60	60	60	60	64	64	68	68	71	78	91
		17	60	60	60	60	60	60	60	60	60	60	60	60	60	60	64	64	68	68	71	78	91
		18	60	60	60	60	60	60	60	60	60	60	60	60	60	60	64	64	68	68	71	78	91
		19	60	60	60	60	60	60	60	60	60	60	60	60	60	60	64	64	68	68	71	78	91
		20	60	60	60	60	60	60	60	60	60	60	60	60	60	60	64	64	68	68	71	78	91
		21	64	64	64	64	64	64	64	64	64	64	64	64	64	64	68	68	71	71	75	81	94
		22	64	64	64	64	64	64	64	64	64	64	64	64	64	64	68	68	71	71	75	81	94
23	64	64	64	64	64	64	64	64	64	64	64	64	64	64	68	68	71	71	75	81	94		

		List Recognition Total Score																				
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19-20	
	24	64	64	64	64	64	64	64	64	64	64	64	64	64	68	68	71	71	75	81	94	
	25	68	68	68	68	68	68	68	68	68	68	68	68	68	71	71	75	75	78	84	97	
	26	68	68	68	68	68	68	68	68	68	68	68	68	68	71	71	75	75	78	84	97	
	27	71	71	71	71	71	71	71	71	71	71	71	71	71	75	75	78	78	81	86	99	
	28	71	71	71	71	71	71	71	71	71	71	71	71	71	75	75	78	78	81	86	99	
	29	75	75	75	75	75	75	75	75	75	75	75	75	75	78	78	81	81	84	88	101	
	30	75	75	75	75	75	75	75	75	75	75	75	75	75	78	78	81	81	84	88	101	
	31	78	78	78	78	78	78	78	78	78	78	78	78	78	81	81	84	84	86	91	105	
	32	78	78	78	78	78	78	78	78	78	78	78	78	78	81	81	84	84	86	91	105	
	33	81	81	81	81	81	81	81	81	81	81	81	81	81	84	84	86	86	88	94	108	
	34	81	81	81	81	81	81	81	81	81	81	81	81	81	84	84	86	86	88	94	108	
	35	84	84	84	84	84	84	84	84	84	84	84	84	84	86	86	88	88	91	97	111	
	36	86	86	86	86	86	86	86	86	86	86	86	86	86	88	88	91	91	94	100	115	
	37	88	88	88	88	88	88	88	88	88	88	88	88	88	91	91	94	94	97	102	119	
	38	88	88	88	88	88	88	88	88	88	88	88	88	88	91	91	94	94	97	102	119	
	39	91	91	91	91	91	91	91	91	91	91	91	91	91	94	94	97	97	100	104	124	
	40	91	91	91	91	91	91	91	91	91	91	91	91	91	94	94	97	97	100	104	124	
	41	94	94	94	94	94	94	94	94	94	94	94	94	94	97	97	100	100	102	108	127	
	42	97	97	97	97	97	97	97	97	97	97	97	97	97	100	100	102	102	104	112	131	
	Ages 60-69	0	40	40	40	40	40	40	40	40	40	40	40	40	40	44	48	48	48	56	60	78
		1	40	40	40	40	40	40	40	40	40	40	40	40	40	44	48	48	48	56	60	78
		2	40	40	40	40	40	40	40	40	40	40	40	40	40	44	48	48	48	56	60	78
3		40	40	40	40	40	40	40	40	40	40	40	40	40	44	48	48	48	56	60	78	
4		40	40	40	40	40	40	40	40	40	40	40	40	40	44	48	48	48	56	60	78	
5		40	40	40	40	40	40	40	40	40	40	40	40	40	44	48	48	48	56	60	78	

List Recognition Total Score																				
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19-20
6	40	40	40	40	40	40	40	40	40	40	40	40	40	44	48	48	48	56	60	78
7	44	44	44	44	44	44	44	44	44	44	44	44	44	48	52	52	52	60	64	81
8	44	44	44	44	44	44	44	44	44	44	44	44	44	48	52	52	52	60	64	81
9	44	44	44	44	44	44	44	44	44	44	44	44	44	48	52	52	52	60	64	81
10	48	48	48	48	48	48	48	48	48	48	48	48	48	52	56	56	56	64	68	84
11	48	48	48	48	48	48	48	48	48	48	48	48	48	52	56	56	56	64	68	84
12	48	48	48	48	48	48	48	48	48	48	48	48	48	52	56	56	56	64	68	84
13	52	52	52	52	52	52	52	52	52	52	52	52	52	56	60	60	60	68	71	86
14	52	52	52	52	52	52	52	52	52	52	52	52	52	56	60	60	60	68	71	86
15	56	56	56	56	56	56	56	56	56	56	56	56	56	60	64	64	64	71	75	89
16	60	60	60	60	60	60	60	60	60	60	60	60	60	64	68	68	68	75	78	92
17	60	60	60	60	60	60	60	60	60	60	60	60	60	64	68	68	68	75	78	92
18	60	60	60	60	60	60	60	60	60	60	60	60	60	64	68	68	68	75	78	92
19	64	64	64	64	64	64	64	64	64	64	64	64	64	68	71	71	71	78	81	95
20	64	64	64	64	64	64	64	64	64	64	64	64	64	68	71	71	71	78	81	95
21	64	64	64	64	64	64	64	64	64	64	64	64	64	68	71	71	71	78	81	95
22	64	64	64	64	64	64	64	64	64	64	64	64	64	68	71	71	71	78	81	95
23	68	68	68	68	68	68	68	68	68	68	68	68	68	71	75	75	75	81	84	98
24	68	68	68	68	68	68	68	68	68	68	68	68	68	71	75	75	75	81	84	98
25	68	68	68	68	68	68	68	68	68	68	68	68	68	71	75	75	75	81	84	98
26	71	71	71	71	71	71	71	71	71	71	71	71	71	75	78	78	78	84	86	100
27	71	71	71	71	71	71	71	71	71	71	71	71	71	75	78	78	78	84	86	100
28	75	75	75	75	75	75	75	75	75	75	75	75	75	78	81	81	81	86	88	102
29	75	75	75	75	75	75	75	75	75	75	75	75	75	78	81	81	81	86	88	102
30	75	75	75	75	75	75	75	75	75	75	75	75	75	78	81	81	81	86	88	102

		List Recognition Total Score																			
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19-20
	31	78	78	78	78	78	78	78	78	78	78	78	78	78	81	84	84	84	88	91	106
	32	78	78	78	78	78	78	78	78	78	78	78	78	78	81	84	84	84	88	91	106
	33	81	81	81	81	81	81	81	81	81	81	81	81	81	84	86	86	86	91	94	110
	34	84	84	84	84	84	84	84	84	84	84	84	84	84	86	88	88	88	94	97	112
	35	84	84	84	84	84	84	84	84	84	84	84	84	84	86	88	88	88	94	97	112
	36	86	86	86	86	86	86	86	86	86	86	86	86	86	88	91	91	91	97	100	116
	37	88	88	88	88	88	88	88	88	88	88	88	88	88	91	94	94	94	100	102	121
	38	88	88	88	88	88	88	88	88	88	88	88	88	88	91	94	94	94	100	102	121
	39	91	91	91	91	91	91	91	91	91	91	91	91	91	94	97	97	97	102	104	126
	40	91	91	91	91	91	91	91	91	91	91	91	91	91	94	97	97	97	102	104	126
	41	94	94	94	94	94	94	94	94	94	94	94	94	94	97	100	100	100	104	108	129
	42	97	97	97	97	97	97	97	97	97	97	97	97	97	100	102	102	102	108	112	133
Ages 70-79	0	40	40	40	40	40	40	40	40	40	40	40	40	40	44	48	48	52	56	60	79
	1	40	40	40	40	40	40	40	40	40	40	40	40	40	44	48	48	52	56	60	79
	2	40	40	40	40	40	40	40	40	40	40	40	40	40	44	48	48	52	56	60	79
	3	40	40	40	40	40	40	40	40	40	40	40	40	40	44	48	48	52	56	60	79
	4	40	40	40	40	40	40	40	40	40	40	40	40	40	44	48	48	52	56	60	79
	5	44	44	44	44	44	44	44	44	44	44	44	44	44	48	52	52	56	60	64	82
	6	44	44	44	44	44	44	44	44	44	44	44	44	44	48	52	52	56	60	64	82
	7	44	44	44	44	44	44	44	44	44	44	44	44	44	48	52	52	56	60	64	82
	8	44	44	44	44	44	44	44	44	44	44	44	44	44	48	52	52	56	60	64	82
	9	48	48	48	48	48	48	48	48	48	48	48	48	48	52	56	56	60	64	68	85
	10	48	48	48	48	48	48	48	48	48	48	48	48	48	52	56	56	60	64	68	85
	11	48	48	48	48	48	48	48	48	48	48	48	48	48	52	56	56	60	64	68	85
12	52	52	52	52	52	52	52	52	52	52	52	52	52	56	60	60	64	68	71	87	

List Recognition Total Score																				
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19-20
13	52	52	52	52	52	52	52	52	52	52	52	52	52	56	60	60	64	68	71	87
14	56	56	56	56	56	56	56	56	56	56	56	56	56	60	64	64	68	71	75	90
15	60	60	60	60	60	60	60	60	60	60	60	60	60	64	68	68	71	75	78	93
16	60	60	60	60	60	60	60	60	60	60	60	60	60	64	68	68	71	75	78	93
17	60	60	60	60	60	60	60	60	60	60	60	60	60	64	68	68	71	75	78	93
18	64	64	64	64	64	64	64	64	64	64	64	64	64	68	71	71	75	78	81	95
19	64	64	64	64	64	64	64	64	64	64	64	64	64	68	71	71	75	78	81	95
20	64	64	64	64	64	64	64	64	64	64	64	64	64	68	71	71	75	78	81	95
21	68	68	68	68	68	68	68	68	68	68	68	68	68	71	75	75	78	81	84	98
22	68	68	68	68	68	68	68	68	68	68	68	68	68	71	75	75	78	81	84	98
23	71	71	71	71	71	71	71	71	71	71	71	71	71	75	78	78	81	84	86	101
24	71	71	71	71	71	71	71	71	71	71	71	71	71	75	78	78	81	84	86	101
25	71	71	71	71	71	71	71	71	71	71	71	71	71	75	78	78	81	84	86	101
26	75	75	75	75	75	75	75	75	75	75	75	75	75	78	81	81	84	86	88	103
27	75	75	75	75	75	75	75	75	75	75	75	75	75	78	81	81	84	86	88	103
28	78	78	78	78	78	78	78	78	78	78	78	78	78	81	84	84	86	88	91	107
29	78	78	78	78	78	78	78	78	78	78	78	78	78	81	84	84	86	88	91	107
30	81	81	81	81	81	81	81	81	81	81	81	81	81	84	86	86	88	91	94	110
31	81	81	81	81	81	81	81	81	81	81	81	81	81	84	86	86	88	91	94	110
32	84	84	84	84	84	84	84	84	84	84	84	84	84	86	88	88	91	94	97	113
33	84	84	84	84	84	84	84	84	84	84	84	84	84	86	88	88	91	94	97	113
34	86	86	86	86	86	86	86	86	86	86	86	86	86	88	91	91	94	97	100	117
35	86	86	86	86	86	86	86	86	86	86	86	86	86	88	91	91	94	97	100	117
36	88	88	88	88	88	88	88	88	88	88	88	88	88	91	94	94	97	100	102	122
37	88	88	88	88	88	88	88	88	88	88	88	88	88	91	94	94	97	100	102	122

		List Recognition Total Score																			
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19-20
	38	88	88	88	88	88	88	88	88	88	88	88	88	88	91	94	94	97	100	102	122
	39	91	91	91	91	91	91	91	91	91	91	91	91	91	94	97	97	100	102	104	127
	40	94	94	94	94	94	94	94	94	94	94	94	94	94	97	100	100	102	104	108	130
	41	97	97	97	97	97	97	97	97	97	97	97	97	97	100	102	102	104	108	112	134
	42	100	100	100	100	100	100	100	100	100	100	100	100	100	102	104	104	108	112	115	137
Ages 80-89	0	40	40	40	40	40	40	40	40	40	40	40	40	40	44	48	52	52	56	64	80
	1	40	40	40	40	40	40	40	40	40	40	40	40	40	44	48	52	52	56	64	80
	2	44	44	44	44	44	44	44	44	44	44	44	44	44	48	52	56	56	60	68	82
	3	44	44	44	44	44	44	44	44	44	44	44	44	44	48	52	56	56	60	68	82
	4	44	44	44	44	44	44	44	44	44	44	44	44	44	48	52	56	56	60	68	82
	5	48	48	48	48	48	48	48	48	48	48	48	48	48	52	56	60	60	64	71	85
	6	48	48	48	48	48	48	48	48	48	48	48	48	48	52	56	60	60	64	71	85
	7	48	48	48	48	48	48	48	48	48	48	48	48	48	52	56	60	60	64	71	85
	8	52	52	52	52	52	52	52	52	52	52	52	52	52	56	60	64	64	68	75	88
	9	52	52	52	52	52	52	52	52	52	52	52	52	52	56	60	64	64	68	75	88
	10	56	56	56	56	56	56	56	56	56	56	56	56	56	60	64	68	68	71	78	90
	11	56	56	56	56	56	56	56	56	56	56	56	56	56	60	64	68	68	71	78	90
	12	56	56	56	56	56	56	56	56	56	56	56	56	56	60	64	68	68	71	78	90
	13	60	60	60	60	60	60	60	60	60	60	60	60	60	64	68	71	71	75	81	93
	14	60	60	60	60	60	60	60	60	60	60	60	60	60	64	68	71	71	75	81	93
	15	64	64	64	64	64	64	64	64	64	64	64	64	64	68	71	75	75	78	84	96
	16	64	64	64	64	64	64	64	64	64	64	64	64	64	68	71	75	75	78	84	96
	17	68	68	68	68	68	68	68	68	68	68	68	68	68	71	75	78	78	81	86	98
	18	68	68	68	68	68	68	68	68	68	68	68	68	68	71	75	78	78	81	86	98
19	71	71	71	71	71	71	71	71	71	71	71	71	71	75	78	81	81	84	88	101	

List Recognition Total Score																				
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19-20
20	71	71	71	71	71	71	71	71	71	71	71	71	71	75	78	81	81	84	88	101
21	71	71	71	71	71	71	71	71	71	71	71	71	71	75	78	81	81	84	88	101
22	75	75	75	75	75	75	75	75	75	75	75	75	75	78	81	84	84	86	91	104
23	75	75	75	75	75	75	75	75	75	75	75	75	75	78	81	84	84	86	91	104
24	75	75	75	75	75	75	75	75	75	75	75	75	75	78	81	84	84	86	91	104
25	78	78	78	78	78	78	78	78	78	78	78	78	78	81	84	86	86	88	94	107
26	78	78	78	78	78	78	78	78	78	78	78	78	78	81	84	86	86	88	94	107
27	78	78	78	78	78	78	78	78	78	78	78	78	78	81	84	86	86	88	94	107
28	81	81	81	81	81	81	81	81	81	81	81	81	81	84	86	88	88	91	97	110
29	81	81	81	81	81	81	81	81	81	81	81	81	81	84	86	88	88	91	97	110
30	84	84	84	84	84	84	84	84	84	84	84	84	84	86	88	91	91	94	100	114
31	84	84	84	84	84	84	84	84	84	84	84	84	84	86	88	91	91	94	100	114
32	84	84	84	84	84	84	84	84	84	84	84	84	84	86	88	91	91	94	100	114
33	86	86	86	86	86	86	86	86	86	86	86	86	86	88	91	94	94	97	102	119
34	86	86	86	86	86	86	86	86	86	86	86	86	86	88	91	94	94	97	102	119
35	88	88	88	88	88	88	88	88	88	88	88	88	88	91	94	97	97	100	104	123
36	88	88	88	88	88	88	88	88	88	88	88	88	88	91	94	97	97	100	104	123
37	91	91	91	91	91	91	91	91	91	91	91	91	91	94	97	100	100	102	108	126
38	91	91	91	91	91	91	91	91	91	91	91	91	91	94	97	100	100	102	108	126
39	94	94	94	94	94	94	94	94	94	94	94	94	94	97	100	102	102	104	112	131
40	94	94	94	94	94	94	94	94	94	94	94	94	94	97	100	102	102	104	112	131
41	97	97	97	97	97	97	97	97	97	97	97	97	97	100	102	104	104	108	115	134
42	100	100	100	100	100	100	100	100	100	100	100	100	100	102	104	108	108	112	119	137

The RBANS Total scores (Total Scale of Index scores) corresponds to the Sum of Index scores in the table below.

Table 5-22 Total Scale Index Score Equivalents of Sum of Index Scores

Sum of Index Scores	Total Scale of Index Scores	Percentiles	Sum of Index Scores	Total Scale of Index Scores	Percentiles	Sum of Index Scores	Total Scale of Index Scores	Percentiles
200–207	40	<0.1	427–430	81	10	574–576	122	93
208–215	41	<0.1	431–435	82	12	577–580	123	94
216–223	42	<0.1	436–440	83	13	581–583	124	95
224–231	43	<0.1	441–444	84	14	584–586	125	95
232–239	44	<0.1	445–449	85	16	587–588	126	96
240–247	45	<0.1	450–454	86	18	589–591	127	96
248–255	46	<0.1	455–458	87	19	592–593	128	97
256–263	47	<0.1	459–461	88	21	594–596	129	97
264–271	48	<0.1	462–464	89	23	597–598	130	98
272–279	49	<0.1	465–468	90	25	599–600	131	98
280–287	50	<0.1	469–471	91	27	601–602	132	98
288–295	51	0.1	472–475	92	30	603–604	133	99
296–303	52	0.1	476–479	93	32	605–606	134	99
304–311	53	0.1	480–483	94	34	607–608	135	99
312–319	54	0.1	484–487	95	37	609–610	136	99
320–327	55	0.1	488–490	96	39	611–612	137	99
328–330	56	0.2	491–493	97	42	613	138	99
331–333	57	0.2	494–496	98	45	614–615	139	99.5
334–336	58	0.3	497–499	99	47	616–617	140	99.6
337–339	59	0.3	500–505	100	50	618–619	141	99.7
340–343	60	0.4	506–509	101	53	620–621	142	99.7
344–347	61	0.5	510–513	102	55	622–624	143	99.8

Sum of Index Scores	Total Scale of Index Scores	Percentiles	Sum of Index Scores	Total Scale of Index Scores	Percentiles	Sum of Index Scores	Total Scale of Index Scores	Percentiles
348–351	62	1	514–516	103	58	625–628	144	99.8
352–355	63	1	517–520	104	61	629–632	145	99.9
356–359	64	1	521–523	105	63	633–636	146	99.9
360–363	65	1	524–527	106	66	637–639	147	99.9
364–367	66	1	528–530	107	68	640–651	148	99.9
368–372	67	1	531–533	108	70	652–663	149	99.9
373–376	68	2	534–536	109	73	664–675	150	>99.9
377–380	69	2	537–539	110	75	676–687	151	>99.9
381–384	70	2	540–542	111	77	688–699	152	>99.9
385–387	71	3	543–545	112	79	700–711	153	>99.9
388–391	72	3	546–548	113	81	712–723	154	>99.9
392–394	73	4	549–551	114	82	724–735	155	>99.9
395–398	74	4	552–554	115	84	736–748	156	>99.9
399–402	75	5	555–556	116	86	749–761	157	>99.9
403–405	76	5	557–559	117	87	762–774	158	>99.9
406–409	77	6	560–562	118	88	775–787	159	>99.9
410–414	78	7	563–566	119	90	788–800	160	>99.9
415–419	79	8	567–570	120	91			
420–426	80	9	571–573	121	92			

6 References

Folstein MF, Folstein SE, McHugh PR (1975) A practical method for grading the cognitive state of patients for the clinician. *J. psychiat. Res.*; 12:189-98.

Raven JC (2000) Standard Progressive Matrices-1998 Edition, updated 2000. Manual for Standard Progressive Matrices (Section 3): NCS Person, Inc.; San Antonio.

Farias ST, Mungas D, Reed BR, et al (2008) The measurement of everyday cognition (ECog): Scale development and psychometric properties. *Neuropsychology*; 22(4):531-44.

Klunk et al. The Centiloid Project: Standardizing quantitative amyloid plaque estimation by PET. *Alzheimer and Dementia* 2015 (11): 1-15.

Nakagawa, S., and Cuthill, I. C. (2007). Effect size, confidence interval and statistical significance: a practical guide for biologists. *Biol. Rev.* 82, 591–605.