

2 SYNOPSIS

Abbreviations are defined in the list of abbreviations located at the end of the Synopsis. This list serves as first use in text.

SPONSOR: Merck Sharp & Dohme LLC, Rahway, NJ, USA (hereafter called the Sponsor or MSD)

COMPOUND NAME: MK-2214

PROTOCOL TITLE: A Multiple Ascending Dose Clinical Trial to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of MK-2214 in Adults with Mild Cognitive Impairment or Mild-to-Moderate Alzheimer's Disease

The following terms may be used interchangeably in this report:

- Participant and subject
- Intervention and treatment and medication and drug
- Study and trial
- AUC0-28 and AUC0-28d

STUDY IDENTIFIERS:

IND: 154578	EudraCT: Not applicable	WHO/UTN: Not applicable	NCT: NCT05466422
jRCT: Not applicable	EU CT: Not applicable		

STUDY PHASE: Phase 1

INDICATION: Dementia Alzheimer's type

STUDY CENTERS: This study was conducted at 12 centers in 1 country.

STUDY STATUS: This study is complete.

First Participant First Visit	20-SEP-2022
Last Participant Last Visit	03-JUL-2025
Database Lock Date	22-AUG-2025

METHODOLOGY:

This was a randomized, placebo-controlled, single-period, sequential-panel, double-blind, multicenter study in participants with MCI or mild-to-moderate AD (Part 1, Panels A to D). Optional panels in Part 2 (Panels E and F, healthy older participants and/or participants with MCI or mild-to-moderate AD) were not conducted based on the results of Part 1.

Because this was a Phase 1 assessment of MK-2214 in humans, the PK, pharmacodynamic, and safety profiles of the compound were still being elucidated. The protocol was therefore written with flexibility to accommodate the inherent dynamic nature of Phase 1 clinical studies. The actual study conduct is provided below.

Part 1 of this study included 4 panels of 8 participants who each received three 4-weekly doses of MK-2214 administered as IV infusion of 30 or 6 minutes. Each participant was assigned to 1 panel and participated in a single treatment period. Participants were randomized to receive MK-2214 (n=6) or placebo (n=2) in a double-blinded fashion. Doses were administered on Days 1, 29, and 57 in the clinic [Figure 1].

MK-2214 PK was evaluated in both serum and CSF. In addition, pS413 tau was assessed in CSF. Serial PK samples were collected on Days 1, 29, and 57. Additional PK samples were collected throughout the study up to Day 297 (the Poststudy Visit). CSF was collected at baseline for all participants. For 3 participants in Panel A, postdose CSF was collected on Days 29 and 85. After these 3 participants, the number of lumbar punctures was reduced from 3 to 2 to reduce participant burden and to enhance recruitment. That is, for 50% of participants in Panels A, B and C the postdose CSF sample was collected on Day 29, for the other 50% on Day 85. The postdose CSF sample was collected on Day 29 for Panel D. Blood samples for ADA assessment (n=9) were collected throughout the study from all participants. Participants were confined to the clinic from the day before dosing until 30 h after each dose administration. Before implementation of Protocol Amendment 1, participants were confined until 24 h (Days 1 and 57) or 8 h (Day 29) after dosing.

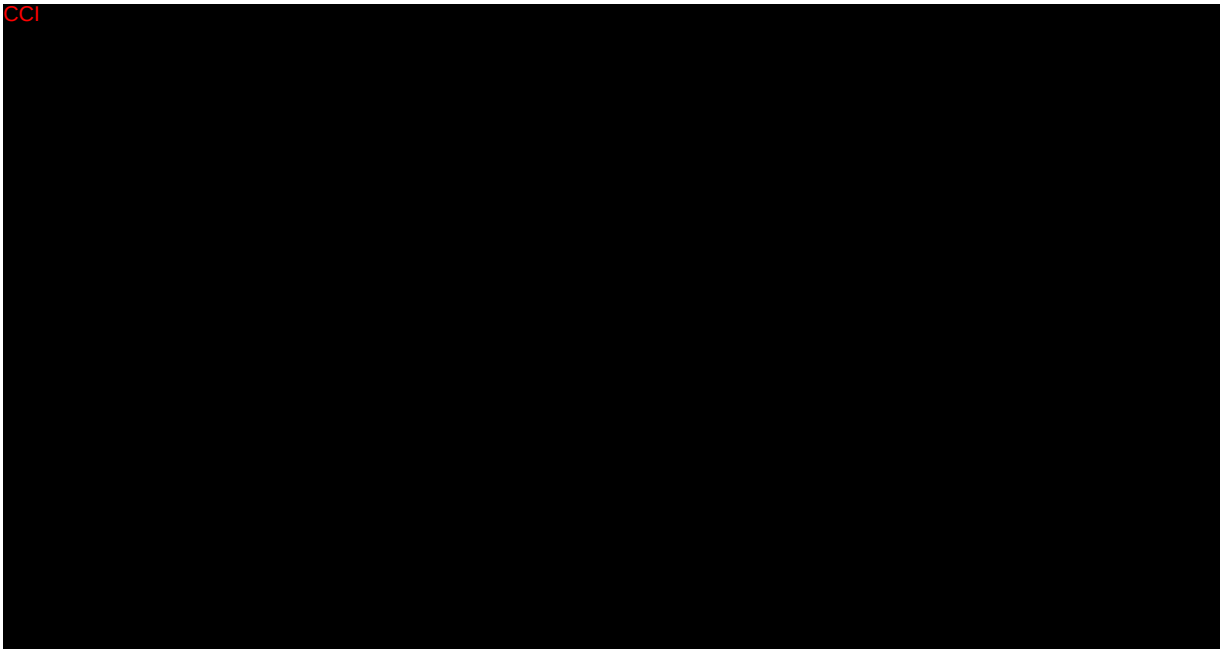
Available safety data from each participant through at least approximately 7 days following the first dose were reviewed by the investigator before the second dose was administered to that participant.

Dose escalation decisions in Part 1 were based on review of key safety variables including AEs, vital signs, 12-lead ECGs, laboratory safety tests, neurological and physical examinations, C-SSRS, and local infusion site and systemic reactions through at least approximately 7 days following the second dose (Day 36) from at least 5 participants in the previous panel, as well as other available safety data. Additionally, serum PK through at least approximately 7 days following the first dose (Day 8) from at least 5 participants in Panel A and Panel B were reviewed before dosing in Panel C and Panel D, respectively. Doses administered are provided in the table below.

CCI

[REDACTED]

Figure 1



Arm Name	Intervention Name	Unit Dose Strength(s)	Dosage Level(s)	Route of Administration	Regimen/Treatment Period	Use
Active	MK-2214	CCI	CCI	IV infusion	CCI	Test product
Placebo	Placebo	0 mg/mL	0 mg	IV infusion	Same as active	Placebo

IV=intravenous; PK=pharmacokinetic

The planned dose for Panel D (2000 mg) was decreased to 4 mg to obtain additional PK and pharmacodynamic data at lower exposures.

Placebo for MK-2214 is diluent alone (5% dextrose).

ELIGIBILITY CRITERIA:

Participants with MCI or mild-to-moderate AD of any sex/gender of nonchildbearing potential from 50 to 80 years of age, inclusive, with a BMI of ≥ 18.5 and ≤ 35 kg/m², inclusive, and an MMSE score >12 as well as an MHIS score <4 .

OBJECTIVES AND ENDPOINTS:

Primary Objectives	Primary Endpoints
Objective: To evaluate the safety and tolerability of multiple ascending doses of MK-2214.	Adverse events and participant discontinuations due to adverse events adverse events.
Objective: To estimate the serum PK profile (eg, AUC ₀₋₂₈ , C _{max} , T _{max} , t _{1/2}) of multiple ascending doses of MK-2214.	Serum AUC ₀₋₂₈ , C _{max} , T _{max} , t _{1/2} (after the third dose)
Objective: To estimate cerebrospinal fluid exposure (eg, cerebrospinal fluid concentration at Day 85) of multiple ascending doses of MK-2214. Hypothesis (Part 1 only): At a generally well tolerated dose level, the true geometric mean concentration at Day 85 of MK-2214 in cerebrospinal fluid is CC1 .	Cerebrospinal fluid concentration at Day 85
Objective: To evaluate the free phospho-tau in cerebrospinal fluid.	Free phospho-tau in cerebrospinal fluid
Secondary Objectives	Secondary Endpoints
There are no secondary objectives in this trial.	Not applicable
Tertiary/Exploratory Objectives	Tertiary/Exploratory Endpoints
Objective: To estimate cerebrospinal fluid exposure relative to serum (eg, cerebrospinal fluid to serum ratio) of multiple ascending doses of MK-2214	Cerebrospinal fluid /serum MK-2214 concentrations
Objective: To evaluate the development of antidrug antibodies after multiple ascending doses of MK-2214.	Serum antidrug antibody

NUMBER OF PARTICIPANTS (planned and analyzed):

The planned enrollment total for Part 1 of this study was 32 participants. As of the last participant last visit:

- 34 participants were randomized (25 to MK-2214, 9 to placebo)
- All 34 participants were included in the All Participants as Treated population for safety analysis
- 25 participants were included in the Per-Protocol population for PK analysis (all participants who received MK-2214) and all 34 participants in the Per-Protocol population for pharmacodynamic analyses

STATISTICAL AND ANALYSIS METHODS:

The planned analyses and determination of sample size are included in the protocol.

Safety: AEs reported between the first administration of study intervention up to the Poststudy Visit were tabulated. ECIs were defined as overdose, potential drug-induced liver injury, and suicidal ideation and behavior

Pharmacokinetics:

If ln-transformation was used, the CIs for the means (mean differences) were constructed on the ln-scale and referenced the t-distribution. Exponentiating the least-squares means (mean differences) and lower and upper limits of these CIs yielded estimates for the population GMs (population GMRs) and CIs about the GMs (GMRs) on the original scale.

Model-based Serum PK Summary: Individual PK values for AUC_{0-28d} and C_{max} after the first and third dose from Panels A through D were ln-transformed and analyzed based on a linear mixed effects model containing fixed effects for treatment, day, treatment by day interaction, and a random effect for participant. A 95% CI was constructed for the GMs of MK-2214 AUC_{0-28d} and C_{max} at each day and dose level. The GMR (postdose 3/postdose 1) of AUC_{0-28d} and C_{max} and their 90% CIs were calculated for each dose.

Assessment of Dose Proportionality: The assessment of dose proportionality was conducted for the third dose in Part 1 in an exploratory manner. The primary assessment of dose proportionality for MK-2214 AUC_{0-28d} and C_{max} in serum was performed using the power law model with ln(AUC) as the dependent variable and ln(dose) as an explanatory variable. A point estimate of the slope associated with ln(dose) was provided together with a 95% CI from the power law model.

Target CSF PK Concentration: The primary hypothesis that at a dose level of MK-2214 that is generally well tolerated, the true GM concentration at the surrogate site of action (CSF) at Day 85 (C_{85d}) CCI was tested using a linear fixed effects model having dose as a fixed effect. Individual MK-2214 CSF C_{85d} values from Panels A through D were ln-transformed.

A posterior distribution for the true GM MK-2214 CSF C85d on the log scale was generated for each dose level using flat priors under a normal likelihood assumption. Using the posterior distributions for each dose level, the posterior probability that the true GM MK-2214 CSF C85d ^{CCI} was calculated for each dose. A >80% posterior probability for at least 1 dose level that is also generally well tolerated satisfied the primary PK hypothesis. Point estimates and 95% CIs of MK-2214 CSF C85d GM were provided by dose level.

Serum and CSF Concentration Comparison: Descriptive statistics of the observed CSF concentration, serum concentration, and CSF to serum ratio on common days were reported by dose level and day.

Pharmacodynamics:

Free pS413 tau Level: Descriptive statistics were provided by treatment and day.

Serum ADA data were summarized by dose level.

The protocol-defined imputation for CSF C85d for participants with missing CSF sample on Day 85 was not conducted. No other changes were made to the planned analysis of the study.

RESULTS:

Participant Disposition:

Overall, 34 participants were randomized and received ≥ 1 dose of study intervention (All Participants as Treated population); 30 participants completed study intervention and the study [Table 1].

- One participant in Panel A (MK-2214 ^{CCI}) was lost to follow-up after the first dose of study intervention and discontinued the study. This participant was replaced.
- Three other participants discontinued study intervention and were followed up for safety up to the day of study discontinuation as specified in Protocol Clarification Letters.
 - One participant in Panel A (placebo) discontinued study intervention administration due to an SAE of seizure (last dose was on Day 1). This participant discontinued the study on Day 155 per Sponsor request. This participant was replaced.
 - One participant in Panel C (placebo) discontinued study intervention administration (last dose was on Day 29) as only a partial dose was received on Day 29 due to infusion site extravasation ^{CCI}, and the inability to find another suitable vein to continue the infusion. As this lower dose could impact PK results, administration of the final dose (Day 57) was not warranted. Participant discontinued the study on Day 197 per Sponsor request. This participant was not replaced.

- One participant in Panel D (MK-2214 CCI) discontinued study intervention administration (last dose was on Day 1) as participant would be out of the country for 2 weeks. Participant discontinued the study on Day 141 per Sponsor request. This participant was not replaced.
- All other participants received all planned study intervention.

Demographics and Baseline Characteristics:

Demographics and baseline characteristics are presented in [Table 9]. All participants had an MMSE score of >12, with a median (range) of 22.0 (13.0 to 29.0).

Table 1
Disposition of Participants

	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV	Placebo	Total
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Not Randomized						156
Participants in population	6	7	6	6	9	34
Status for Trial						
Started	6	7	6	6	9	34
Completed	5 (83.3)	6 (85.7)	6 (100.0)	6 (100.0)	7 (77.8)	30 (88.2)
Discontinued	1 (16.7)	1 (14.3)	0 (0.0)	0 (0.0)	2 (22.2)	4 (11.8)
Lost To Follow-Up	0 (0.0)	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.9)
Other	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	2 (22.2)	3 (8.8)
Status for Study Medication in Trial						
Started	6	7	6	6	9	34
Completed	5 (83.3)	6 (85.7)	6 (100.0)	6 (100.0)	7 (77.8)	30 (88.2)
Discontinued	1 (16.7)	1 (14.3)	0 (0.0)	0 (0.0)	2 (22.2)	4 (11.8)
Adverse Event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (11.1)	1 (2.9)
Lost To Follow-Up	0 (0.0)	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.9)

Disposition of Participants

	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV	Placebo	Total
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Status for Study Medication in Trial						
Other	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (11.1)	2 (5.9)
Each participant is counted once for Status for Trial, Status for Study Medication in Trial based on the latest corresponding disposition record. Placebo column is pooled across participants receiving matching placebo in all panels (Panel A, B, C, D). Panel A: MK-2214 CCI IV or placebo administered by 30-minute IV infusion on Days 1, 29, and 57. Panel B: MK-2214 CCI IV or placebo administered by 30-minute IV infusion on Days 1, 29, and 57. Panel C: MK-2214 CCI IV or placebo administered by 30-minute IV infusion on Days 1, 29, and 57. Panel D: MK-2214 CCI IV or placebo administered by 6-minute IV infusion on Days 1, 29, and 57.						

Source: [P002V01MK2214: adam-adsl]

Safety:

MK-2214 was generally well tolerated by participants with MCI or probable mild-to-moderate AD when administered as [REDACTED] CCI. No dose-limiting tolerability issues and no pattern of intervention-related AEs were observed. There were no deaths. Following administration of MK-2214, 1 participant reported an ECI, and 3 participants reported SAEs, none of these AEs were considered related to MK-2214 by the investigator. No participants discontinued due to an AE following administration of MK-2214.

- No deaths were reported in the study. A total of 9 SAEs were reported by 4 participants (1 participant following placebo and 3 participants following MK-2214), and 1 of these participants (placebo) discontinued study intervention due to an SAE. None of the SAEs were considered related to study intervention by the investigator [Table 2, Table 10]. One of the participants with an SAE also had an ECI (suicidal ideation, not related).
- Most AEs were mild in intensity, some were moderate and 4 were severe (all 4 were also SAEs, see below). Most AEs resolved at study end, most of the AEs that were either resolving or not resolved at study end are mentioned below.
- A total of 76.5% (26/34) of participants reported AEs: 76.0% (19/25) following administration of MK-2214 and 77.8% (7/9) following placebo [Table 11].
- The most frequently (>1 participant) reported AEs for MK-2214 were headache (n=7, 28.0%), back pain, dizziness (each n=3, 12.0%), and arthralgia (n=2, 8.0%). For placebo they were urinary tract infection and headache (n=2, 22.2%) [Table 11].
- A total of 20.6% (7/34) of participants reported AEs that were considered related to study intervention by the investigator: 24.0% (6/25) following administration of MK-2214 and 11.1% (1/9) following placebo [Table 12].
- The only study intervention-related AEs that was reported by >1 participant was headache (MK-2214, n=4, 16.0%) [Table 12].
- Nine SAEs were reported by 4 participants (1 participant following MK-2214 [REDACTED] CCI, 2 following [REDACTED] CCI, and 1 following placebo) [Table 10], and 1 of these 4 participants also reported an ECI (following MK-2214 [REDACTED] CCI). The SAEs and the ECI were all considered not related to study intervention by the investigator.
 - One participant in Panel B, MK-2214 [REDACTED] CCI, experienced 5 SAEs, portal vein thrombosis and hepatic lesion (severe intensity), sepsis (moderate intensity), and pleural effusion and dehydration (mild intensity), together with nonserious AEs of normocytic anemia and parvimonas infection ~ 5 months after completion of study intervention resulting in hospitalization. The participant was hospitalized due to dehydration. The parvimonas infection resolved with antibiotics. The SAEs of portal vein thrombosis and hepatic lesion were ongoing when the participant completed the study; all other SAEs resolved.
 - One participant in Panel C, MK-2214 [REDACTED] CCI, developed symptoms of cholelithiasis (mild intensity) ~5 months after the final dose of study intervention. The diagnosis of

- cholelithiasis was confirmed via ultrasound, and the participant underwent an elective cholecystectomy with full resolution.
- One participant in Panel C, MK-2214 CCI, experienced an SAE of foot osteomyelitis (severe intensity) ~ 3 weeks after the second dose of study intervention resulting in hospitalization for treatment. The participant had a history of foot osteomyelitis. The osteomyelitis was treated with antibiotics and was resolving when the participant completed the study. The participant was followed by an infectious disease specialist. This participant also experienced an ECI of suicidal ideation (without intent, mild in intensity, duration 4 h) ~2 weeks after the final dose of study intervention. The participant was assessed in clinic, determined to be stable, and discharged. The C-SSRS did not indicate any signal of suicidal thoughts/ideation.
 - One participant in Panel A, placebo, experienced 2 SAEs of seizure resulting in brief hospitalizations. The first seizure (moderate intensity, lasting 1.15 h) occurred 1 day after the first dose of study intervention; the participant recovered from the seizure, and study intervention was discontinued. Concomitantly with the seizure, the following AEs were diagnosed: cerebral microhemorrhage (moderate intensity), encephalomalacia, gliosis, mitral and pulmonary valve incompetence, spinal and subclavian artery stenosis (all mild intensity); all continued at study end. The second seizure (severe intensity, lasting 1 h) occurred ~ 4 months after dosing (leukocytosis of moderate intensity, lasting 3 days, was diagnosed as well); the participant recovered from the seizure.
 - None of the clinically meaningful findings (ie, reported as AEs) noted in routine laboratory safety, vital signs, ECGs or physical examination assessments were considered related to study intervention by the investigator [[Table 11](#); [Table 12](#)]
 - No clinically meaningful trends were noted in routine blood chemistry panels, hematology, urinalysis, ECG, vital signs, physical examinations, or C-SSRS. There were no local or systemic infusion/injection reactions.

Table 2
Adverse Event Summary
All Participants as Treated Population

	MK-2214 CCl IV	MK-2214 CCl IV	MK-2214 CCl IV	MK-2214 CCl IV	MK-2214 Total	Placebo	Total
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Participants in population	6	7	6	6	25	9	34
with one or more adverse events	5 (83.3)	5 (71.4)	5 (83.3)	4 (66.7)	19 (76.0)	7 (77.8)	26 (76.5)
with no adverse event	1 (16.7)	2 (28.6)	1 (16.7)	2 (33.3)	6 (24.0)	2 (22.2)	8 (23.5)
with drug-related ^a adverse events	2 (33.3)	1 (14.3)	2 (33.3)	1 (16.7)	6 (24.0)	1 (11.1)	7 (20.6)
with non-serious adverse events	5 (83.3)	5 (71.4)	5 (83.3)	4 (66.7)	19 (76.0)	7 (77.8)	26 (76.5)
with serious adverse events	0 (0.0)	0 (0.0)	1 (16.7)	2 (33.3)	3 (12.0)	1 (11.1)	4 (11.8)
with serious drug-related ^a adverse events	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
who died	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
who died due to a drug-related ^a adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
discontinued drug due to an adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (11.1)	1 (2.9)
discontinued drug due to a drug-related ^a adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
discontinued drug due to a serious adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (11.1)	1 (2.9)

Adverse Event Summary All Participants as Treated Population

	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 Total	Placebo	Total
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
discontinued drug due to a serious drug-related ^a adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

^a Determined by the investigator to be related to any drug.

MK-2214 Total column is pooled across participants receiving active MK-2214 doses in all panels (Panel A, B, C, D).

Placebo column is pooled across participants receiving matching placebo in all panels (Panel A, B, C, D).

Total column is pooled across all participants in all panels (Panel A, B, C, D).

Panel A: MK-2214 CCI IV or placebo administered by 30-minute IV infusion on Days 1, 29, and 57.

Panel B: MK-2214 CCI IV or placebo administered by 30-minute IV infusion on Days 1, 29, and 57.

Panel C: MK-2214 CCI IV or placebo administered by 30-minute IV infusion on Days 1, 29, and 57.

Panel D: MK-2214 CCI IV or placebo administered by 6-minute IV infusion on Days 1, 29, and 57.

Adverse event terms are from MedDRA Version 28.0

Source: [P002V01MK2214: adam-adsl; adae]

Pharmacokinetics:

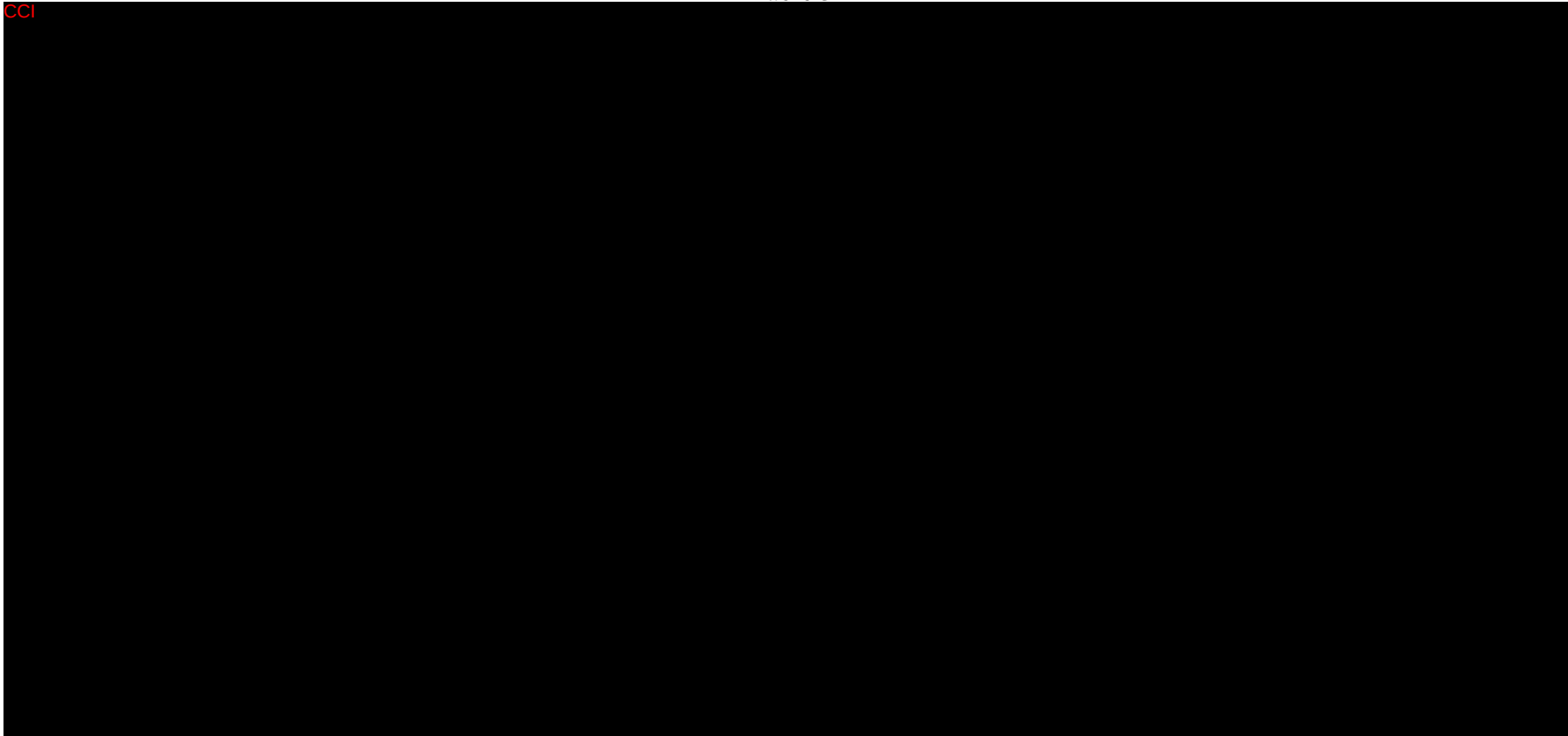
MK-2214 was administered as IV infusion [REDACTED] for doses of [REDACTED]. Tmax was calculated from the start of infusion.

For participants who received MK-2214, postdose CSF was collected on Days 29 and 85 for 3 participants in Panel A ([REDACTED]; only 1 Day 85 sample had analysis results). Postdose CSF was collected on Day 29 only for 2 participants in Panel A ([REDACTED]), 3 participants each in Panels B ([REDACTED] and C ([REDACTED]), and 6 participants in Panel D (4 mg). Postdose CSF was collected on Day 85 only for 2 participants in Panel A ([REDACTED]), 2 participants in Panel B ([REDACTED]), 3 participants in Panel C ([REDACTED] and no participants in Panel D.

- MK-2214 serum Cmax was reached at a median of [REDACTED].
- Compared to the first dose, Cmax [REDACTED] and AUC0 [REDACTED].
- The GM Cmax and AUC0-28 in serum were found to be approximately dose proportional after [REDACTED] MK-2214 [Table 4, Figure 2, Figure 3].
- The posterior probability that the true GM CSF C85d of MK-2214 [REDACTED] was >80% (97%) for the generally well-tolerated dose of [REDACTED] MK-2214. Since the posterior probability exceeded the 80% prespecified threshold, the primary hypothesis is supported [Table 5].
- The GMRs for the MK-2214 CSF/serum concentrations on Days 29 and 85 were [REDACTED] [Table 6].

Table 3

CCI



CCI

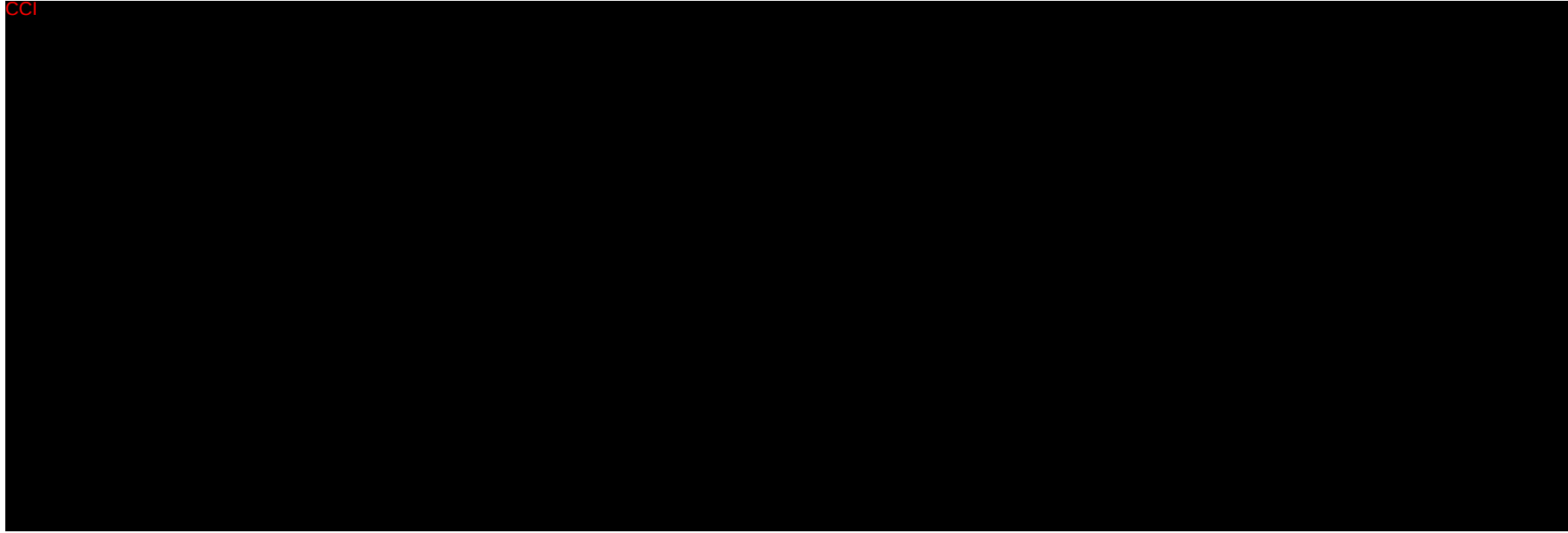


Table 4
Assessment of Dose Proportionality of Serum MK-2214 Following Administration of 3 Monthly IV Doses of MK-2214 to
Participants with Mild Cognitive Impairment or Mild-to-Moderate Alzheimer's Disease (N=5 to 6 per dose level)
Per-Protocol Population

Pharmacokinetic Parameter	Dose Range	Slope Estimate (95% CI) ^a	Predicted Fold- Change (95% CI) ^b	Expected Fold- Change with Perfect Dose-Proportionality ^c
CCI				
CI = Confidence interval, IV = intravenous. ^a A true slope of 1.0 indicates perfect dose proportionality. ^b Least squares estimate and confidence interval from linear fixed effects model including ln-dose as a continuous effect, performed on natural log-transformed values. ^c Fold change for highest dose/lowest dose.				

Source: [P002V01MK2214: adam-adpp]

Table 5

CCI

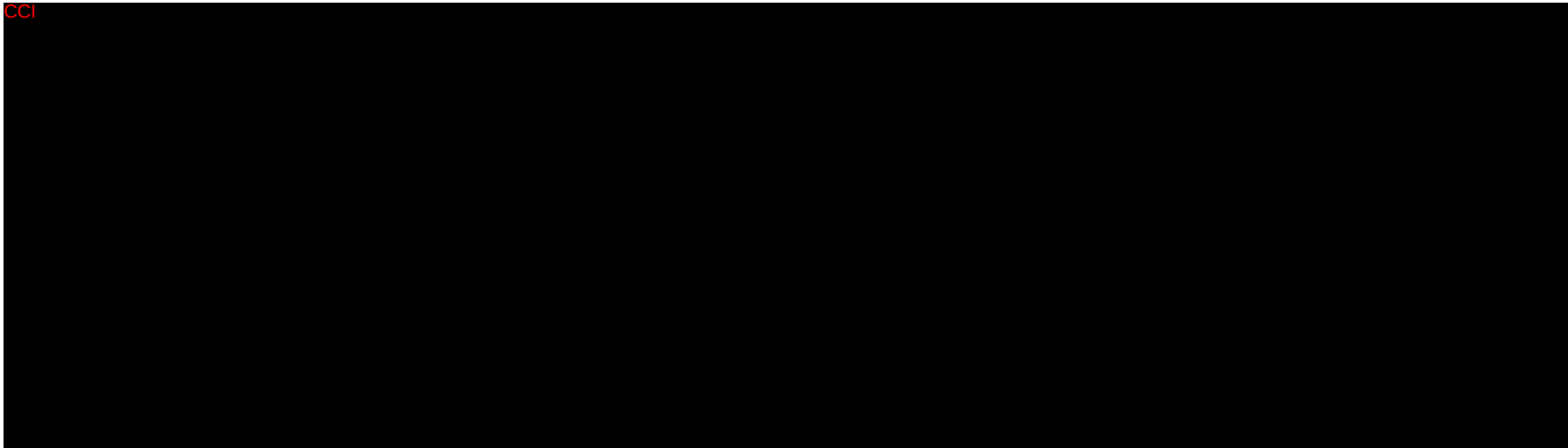
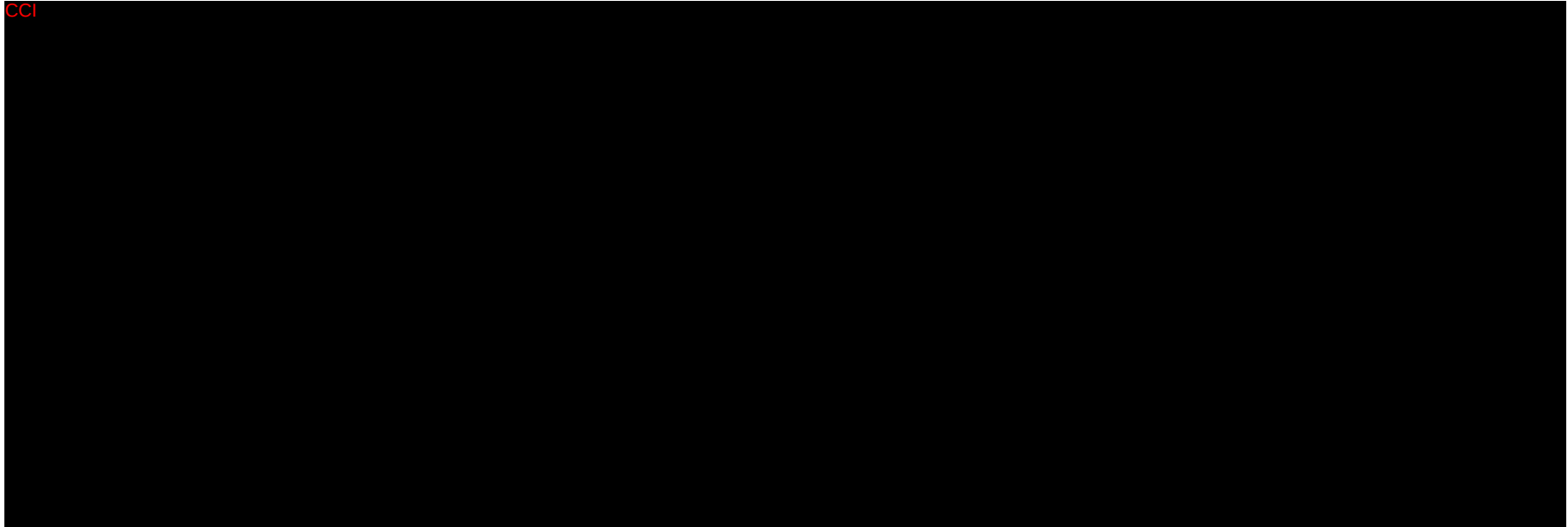


Table 6

CCI



Pharmacodynamics:CSF Free pS413-Tau

- The mean postdose ^{CCI} concentrations in participants receiving MK-2214 ^{CCI}

[Table 7].

ADA

- All 25 participants who received MK-2214 were evaluable for the MK-2214 ADA assessment [Table 8].
- ^{CCI}
- There did not appear to be any trend in ADA incidence with dose level. There did not appear to be any effect on the safety or PK profiles in ADA-treatment-emergent positive participants as compared to ADA-negative participants.

Table 7

CCI

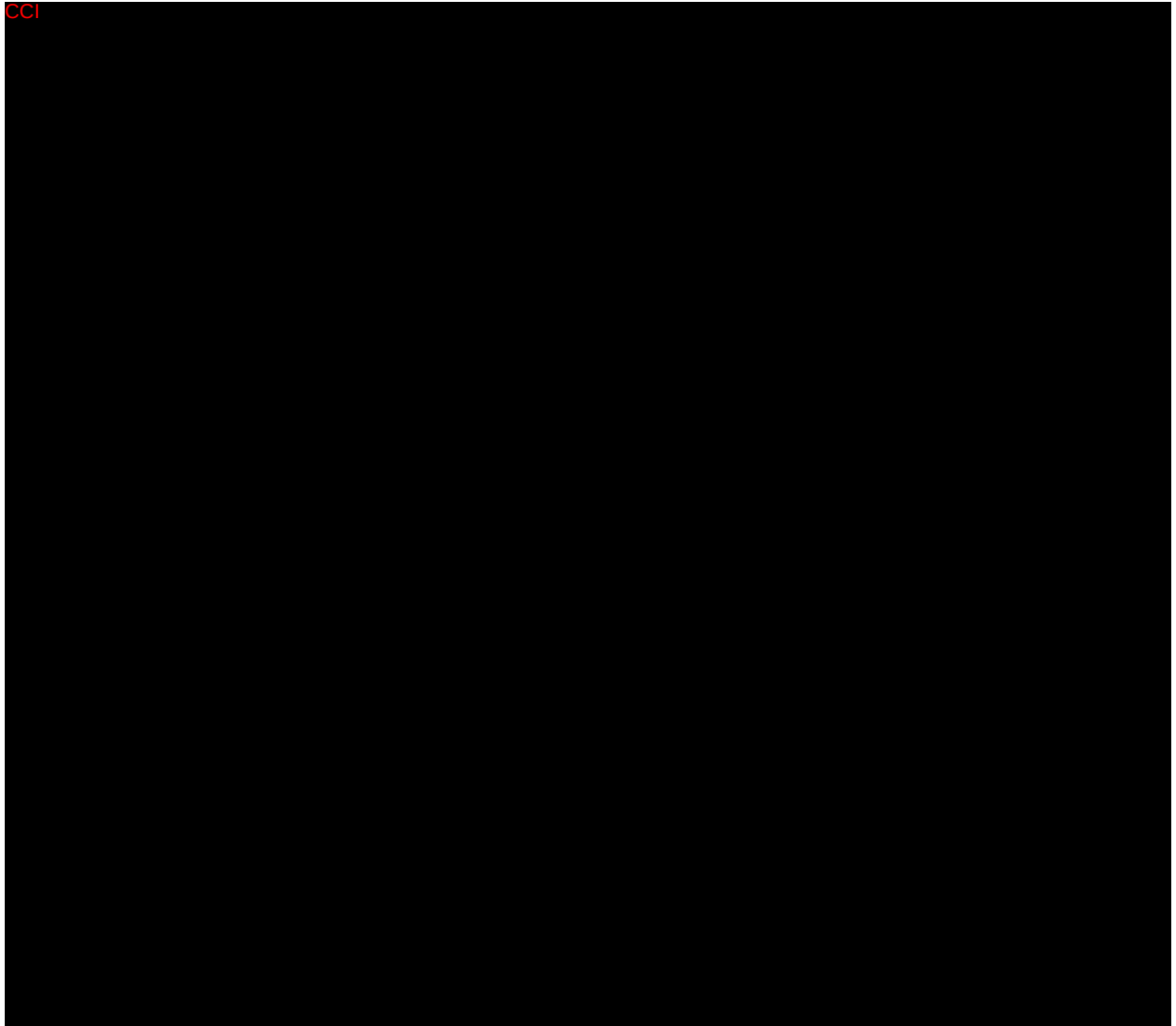


Table 8
Summary of Participants Anti-MK-2214 Antibody Status
All Participants with at Least One ADA Sample Result

	MK-2214 ■ IV n (%)	MK-2214 ■ IV n (%)	MK-2214 ■ IV n (%)	MK-2214 ■ IV n (%)	Total n (%)
Participants in population	6	7	6	6	25
Unevaluable participants	0	0	0	0	0
Evaluable participants ^a	6	7	6	6	25
Immunogenicity Status					
Negative					
Inconclusive ^b					
Predose positive ^c					
Treatment emergent positive ^d					
ADA = antidrug antibody, IV=intravenous.					
^a Participants with at least one ADA result after treatment with MK-2214. The number of participants evaluable per dose group is the denominator of the percentages in the table.					
^b Participants with a drug concentration in the last sample that exceeds the drug tolerance level of the ADA assay or the drug concentration result is missing.					
^c Participants positive at baseline.					
^d Participants who were negative at baseline and positive postdose were considered treatment emergent.					

Source: [P002V01MK2214: adam-adada]

CONCLUSIONS:

Safety Key Results

- MK-2214 was generally well tolerated by participants with MCI or probable mild-to-moderate AD when administered as 3 monthly IV doses up to [REDACTED] CCI. No dose-limiting tolerability issues and no pattern of intervention-related AEs were observed. There were no deaths. Following administration of MK-2214, 1 participant reported an ECI, and 3 participants reported SAEs, none of which were considered related to MK-2214 by the investigator. No participants discontinued due to an AE following administration of MK-2214.
- No clinically meaningful trends were noted in routine blood chemistry panels, hematology, urinalysis, ECGs, vital signs, physical examinations, or C-SSRS. There were no local or systemic infusion/injection reactions.

Pharmacokinetic Conclusion

- [REDACTED] CCI

Pharmacokinetic and Pharmacodynamic Key Results

- [REDACTED] CCI
- The serum C_{max} and AUC₀₋₂₈ increased in an approximately dose-proportional manner [REDACTED] CCI
- Compared to the first dose, C_{max} [REDACTED] CCI [REDACTED]
- The GMRs for the MK-2214 CSF/serum concentrations on Days 29 and 85 were [REDACTED] CCI
- There did not appear to be any trend in ADA incidence with dose level. There did not appear to be any effect on the safety or PK profiles in ADA-treatment-emergent positive participants as compared to ADA-negative participants.

LIST OF ABBREVIATIONS:

Abbreviation/Term	Definition
AD	Alzheimer's Disease
ADA	antidrug antibody
AE	adverse event
AUC0-28(d)	area under the concentration-time curve from time 0 to 28 days
BMI	body mass index
C85d	cerebrospinal fluid concentration at Day 85
CI	confidence interval
Cmax	maximum serum concentration
CSF	cerebrospinal fluid
CSR	clinical study report
C-SSRS	Columbia-Suicide Severity Rating Scale
ECG	electrocardiogram
ECI	event of clinical interest
EU CT	European Union Clinical Trial
EudraCT	European Union Drug Regulating Authorities Clinical Trial
GCP	Good Clinical Practice
GM	geometric mean
GMR	geometric mean ratio
h	hour(s)
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	Independent Ethics Committee
IND	investigational new drug (application)
IV	intravenous
jRCT	Japan Registry for Clinical Trials
ln	natural log
MCI	mild cognitive impairment
MHIS	Rosen-Modified Hachinski Ischemic Scale
MMSE	Mini-Mental State Examination

Abbreviation/Term	Definition
NCT	national clinical trial
PK	pharmacokinetic(s)
CCI	
SAE	serious adverse event
t _{1/2}	half-life
T _{max}	time of maximum serum concentration
UTN	universal trial number
WHO	World Health Organization

PUBLICATION(S): As of the date of this report, there are no publications based on this study.

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ADDITIONAL TABLES AND FIGURES:

Table 9
Participant Characteristics

	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV
	n (%)	n (%)	n (%)
Participants in population	6	7	6
Sex			
Male	2 (33.3)	4 (57.1)	2 (33.3)
Female	4 (66.7)	3 (42.9)	4 (66.7)
Age (Years)			
50 to 80	6 (100.0)	7 (100.0)	6 (100.0)
Mean	73.3	73.1	68.3
SD	3.1	9.5	4.3
Median	73.5	78.0	69.5
Range	69 to 77	56 to 80	61 to 73
Race			
Asian	1 (16.7)	0 (0.0)	0 (0.0)
Black Or African American	1 (16.7)	1 (14.3)	2 (33.3)
White	4 (66.7)	6 (85.7)	4 (66.7)
Ethnicity			
Hispanic Or Latino	1 (16.7)	3 (42.9)	3 (50.0)
Not Hispanic Or Latino	5 (83.3)	4 (57.1)	3 (50.0)
Height (cm)			
Participants with data	6	7	6

Participant Characteristics
All Participants as Treated Population

	MK-2214 CCI IV		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	6		9		34	
Sex						
Male	3	(50.0)	5	(55.6)	16	(47.1)
Female	3	(50.0)	4	(44.4)	18	(52.9)
Age (Years)						
50 to 80	6	(100.0)	9	(100.0)	34	(100.0)
Mean	71.2		68.9		70.9	
SD	8.5		8.2		7.2	
Median	73.5		68.0		71.5	
Range	59 to 79		58 to 80		56 to 80	
Race						
Asian	0	(0.0)	0	(0.0)	1	(2.9)
Black Or African American	1	(16.7)	0	(0.0)	5	(14.7)
White	5	(83.3)	9	(100.0)	28	(82.4)
Ethnicity						
Hispanic Or Latino	0	(0.0)	4	(44.4)	11	(32.4)
Not Hispanic Or Latino	6	(100.0)	5	(55.6)	23	(67.6)
Height (cm)						
Participants with data	6		9		34	

Participant Characteristics
All Participants as Treated Population

	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV
	n (%)	n (%)	n (%)
Mean	162.6	167.2	161.7
SD	5.8	6.4	16.1
Median	163.5	168.0	155.2
Range	154.3 to 169.0	159.0 to 177.0	145.0 to 186.7
Weight (kg)			
Participants with data	6	7	6
Mean	74.8	82.3	76.9
SD	11.1	12.2	22.8
Median	72.2	88.2	71.9
Range	63.9 to 89.1	59.6 to 92.3	52.5 to 120.1
BMI (kg/m²)			
Participants with data	6	7	6
Mean	28.0	29.6	28.8
SD	3.3	4.1	5.7
Median	28.0	30.1	30.1
Range	22.5 to 31.4	21.1 to 33.4	20.5 to 34.2
MMSE Score			
Participants with data	6	7	6
Mean	23.0	21.9	21.8
SD	6.0	4.3	3.1
Median	25.5	22.0	20.5

Participant Characteristics
All Participants as Treated Population

	MK-2214 CCI IV	Placebo	Total
	n (%)	n (%)	n (%)
Mean	166.3	162.2	163.9
SD	9.2	9.9	9.7
Median	166.8	165.0	165.0
Range	155.5 to 177.0	149.0 to 179.0	145.0 to 186.7
Weight (kg)			
Participants with data	6	9	34
Mean	72.3	78.4	77.2
SD	9.5	12.0	13.6
Median	73.8	75.9	76.1
Range	59.7 to 82.1	59.0 to 96.9	52.5 to 120.1
BMI (kg/m²)			
Participants with data	6	9	34
Mean	26.1	29.7	28.6
SD	3.6	2.8	3.9
Median	26.4	29.5	29.0
Range	20.2 to 31.5	26.6 to 34.5	20.2 to 34.5
MMSE Score			
Participants with data	6	9	34
Mean	21.2	23.0	22.2
SD	6.9	5.1	4.9
Median	20.5	23.0	22.0

Participant Characteristics
All Participants as Treated Population

	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV
	n (%)	n (%)	n (%)
Range	14.0 to 29.0	15.0 to 28.0	19.0 to 27.0

Participant Characteristics
All Participants as Treated Population

	MK-2214 CCI IV	Placebo	Total
	n (%)	n (%)	n (%)
Range	13.0 to 29.0	15.0 to 29.0	13.0 to 29.0
SD=Standard deviation. BMI = body mass index. IV = Intravenous. MMSE = Mini-Mental State Examination. Placebo column is pooled across participants receiving matching placebo in all panels (Panel A, B, C, D). Panel A: MK-2214 CCI IV or placebo administered by 30-minute IV infusion on Days 1, 29, and 57. Panel B: MK-2214 CCI IV or placebo administered by 30-minute IV infusion on Days 1, 29, and 57. Panel C: MK-2214 CCI IV or placebo administered by 30-minute IV infusion on Days 1, 29, and 57. Panel D: MK-2214 CCI IV or placebo administered by 6-minute IV infusion on Days 1, 29, and 57.			

Source: [P002V01MK2214: adam-adsl]

Table 10
Participants With Serious Adverse Events
(Incidence > 0% in One or More Treatment Groups)
All Participants as Treated Population

	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 Total
	n (%)	n (%)	n (%)	n (%)	n (%)
Participants in population	6	7	6	6	25
with one or more serious adverse events	0 (0.0)	0 (0.0)	1 (16.7)	2 (33.3)	3 (12.0)
with no serious adverse events	6 (100.0)	7 (100.0)	5 (83.3)	4 (66.7)	22 (88.0)
Hepatobiliary disorders	0 (0.0)	0 (0.0)	1 (16.7)	1 (16.7)	2 (8.0)
Cholelithiasis	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	1 (4.0)
Hepatic lesion	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (4.0)
Portal vein thrombosis	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (4.0)
Infections and infestations	0 (0.0)	0 (0.0)	1 (16.7)	1 (16.7)	2 (8.0)
Osteomyelitis	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	1 (4.0)
Sepsis	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (4.0)
Metabolism and nutrition disorders	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (4.0)
Dehydration	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (4.0)
Nervous system disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Seizure	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Participants With Serious Adverse Events
(Incidence > 0% in One or More Treatment Groups)
All Participants as Treated Population

	Placebo		Total	
	n	(%)	n	(%)
Participants in population	9		34	
with one or more serious adverse events	1	(11.1)	4	(11.8)
with no serious adverse events	8	(88.9)	30	(88.2)
Hepatobiliary disorders	0	(0.0)	2	(5.9)
Cholelithiasis	0	(0.0)	1	(2.9)
Hepatic lesion	0	(0.0)	1	(2.9)
Portal vein thrombosis	0	(0.0)	1	(2.9)
Infections and infestations	0	(0.0)	2	(5.9)
Osteomyelitis	0	(0.0)	1	(2.9)
Sepsis	0	(0.0)	1	(2.9)
Metabolism and nutrition disorders	0	(0.0)	1	(2.9)
Dehydration	0	(0.0)	1	(2.9)
Nervous system disorders	1	(11.1)	1	(2.9)
Seizure	1	(11.1)	1	(2.9)

Participants With Serious Adverse Events
(Incidence > 0% in One or More Treatment Groups)
All Participants as Treated Population

	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 Total
	n (%)	n (%)	n (%)	n (%)	n (%)
Respiratory, thoracic and mediastinal disorders	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (4.0)
Pleural effusion	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (4.0)

Participants With Serious Adverse Events
(Incidence > 0% in One or More Treatment Groups)
All Participants as Treated Population

	Placebo		Total	
	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	0	(0.0)	1	(2.9)
Pleural effusion	0	(0.0)	1	(2.9)

Every participant is counted a single time for each applicable row and column.
 MK-2214 Total column is pooled across participants receiving active MK-2214 doses in all panels (Panel A, B, C, D).
 Placebo column is pooled across participants receiving matching placebo in all panels (Panel A, B, C, D).
 Total column is pooled across all participants in all panels (Panel A, B, C, D).
 Panel A: MK-2214 **CCI** IV or placebo administered by 30-minute IV infusion on Days 1, 29, and 57.
 Panel B: MK-2214 **CCI** IV or placebo administered by 30-minute IV infusion on Days 1, 29, and 57.
 Panel C: MK-2214 **CCI** IV or placebo administered by 30-minute IV infusion on Days 1, 29, and 57.
 Panel D: MK-2214 **CCI** IV or placebo administered by 6-minute IV infusion on Days 1, 29, and 57.
 Adverse event terms are from MedDRA Version 28.0.

Source: [P002V01MK2214: adam-adsl; adae]

Table 11
Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
All Participants as Treated Population

	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV
	n (%)	n (%)	n (%)	n (%)
Participants in population	6	7	6	6
with one or more adverse events	5 (83.3)	5 (71.4)	5 (83.3)	4 (66.7)
with no adverse events	1 (16.7)	2 (28.6)	1 (16.7)	2 (33.3)
Blood and lymphatic system disorders	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)
Anaemia	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)
Leukocytosis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Normocytic anaemia	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)
Cardiac disorders	0 (0.0)	1 (14.3)	0 (0.0)	0 (0.0)
Atrioventricular block first degree	0 (0.0)	1 (14.3)	0 (0.0)	0 (0.0)
Mitral valve incompetence	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pulmonary valve incompetence	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastrointestinal disorders	0 (0.0)	0 (0.0)	1 (16.7)	1 (16.7)
Dyspepsia	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)
Nausea	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)
Toothache	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vomiting	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
General disorders and administration site conditions	1 (16.7)	0 (0.0)	1 (16.7)	1 (16.7)
Fatigue	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
All Participants as Treated Population

	MK-2214 Total		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	25		9		34	
with one or more adverse events	19	(76.0)	7	(77.8)	26	(76.5)
with no adverse events	6	(24.0)	2	(22.2)	8	(23.5)
Blood and lymphatic system disorders	1	(4.0)	1	(11.1)	2	(5.9)
Anaemia	1	(4.0)	0	(0.0)	1	(2.9)
Leukocytosis	0	(0.0)	1	(11.1)	1	(2.9)
Normocytic anaemia	1	(4.0)	0	(0.0)	1	(2.9)
Cardiac disorders	1	(4.0)	1	(11.1)	2	(5.9)
Atrioventricular block first degree	1	(4.0)	0	(0.0)	1	(2.9)
Mitral valve incompetence	0	(0.0)	1	(11.1)	1	(2.9)
Pulmonary valve incompetence	0	(0.0)	1	(11.1)	1	(2.9)
Gastrointestinal disorders	2	(8.0)	2	(22.2)	4	(11.8)
Dyspepsia	1	(4.0)	0	(0.0)	1	(2.9)
Nausea	1	(4.0)	0	(0.0)	1	(2.9)
Toothache	0	(0.0)	1	(11.1)	1	(2.9)
Vomiting	0	(0.0)	1	(11.1)	1	(2.9)
General disorders and administration site conditions	3	(12.0)	2	(22.2)	5	(14.7)
Fatigue	1	(4.0)	0	(0.0)	1	(2.9)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
All Participants as Treated Population

	MK-2214 CCI IV		MK-2214 CCI IV		MK-2214 CCI IV		MK-2214 CCI IV	
	n	(%)	n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	1	(16.7)	0	(0.0)	1	(16.7)	1	(16.7)
Generalised oedema	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)
Infusion site extravasation	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Peripheral swelling	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)
Hepatobiliary disorders	0	(0.0)	0	(0.0)	1	(16.7)	1	(16.7)
Cholelithiasis	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)
Hepatic lesion	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)
Portal vein thrombosis	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)
Infections and infestations	0	(0.0)	1	(14.3)	1	(16.7)	3	(50.0)
Influenza	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)
Osteomyelitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)
Parvimonas infection	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)
Pyuria	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Sepsis	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)
Tooth infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)
Upper respiratory tract infection	0	(0.0)	1	(14.3)	0	(0.0)	0	(0.0)
Urinary tract infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)
Injury, poisoning and procedural complications	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
All Participants as Treated Population

	MK-2214 Total		Placebo		Total	
	n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	3	(12.0)	2	(22.2)	5	(14.7)
Generalised oedema	1	(4.0)	0	(0.0)	1	(2.9)
Infusion site extravasation	0	(0.0)	1	(11.1)	1	(2.9)
Pain	0	(0.0)	1	(11.1)	1	(2.9)
Peripheral swelling	1	(4.0)	0	(0.0)	1	(2.9)
Hepatobiliary disorders	2	(8.0)	0	(0.0)	2	(5.9)
Cholelithiasis	1	(4.0)	0	(0.0)	1	(2.9)
Hepatic lesion	1	(4.0)	0	(0.0)	1	(2.9)
Portal vein thrombosis	1	(4.0)	0	(0.0)	1	(2.9)
Infections and infestations	5	(20.0)	3	(33.3)	8	(23.5)
Influenza	1	(4.0)	0	(0.0)	1	(2.9)
Osteomyelitis	1	(4.0)	0	(0.0)	1	(2.9)
Parvimonas infection	1	(4.0)	0	(0.0)	1	(2.9)
Pyuria	0	(0.0)	1	(11.1)	1	(2.9)
Sepsis	1	(4.0)	0	(0.0)	1	(2.9)
Tooth infection	1	(4.0)	0	(0.0)	1	(2.9)
Upper respiratory tract infection	1	(4.0)	0	(0.0)	1	(2.9)
Urinary tract infection	1	(4.0)	2	(22.2)	3	(8.8)
Injury, poisoning and procedural complications	1	(4.0)	1	(11.1)	2	(5.9)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
All Participants as Treated Population

	MK-2214 CCI IV		MK-2214 CCI IV		MK-2214 CCI IV		MK-2214 CCI IV	
	n	(%)	n	(%)	n	(%)	n	(%)
Injury, poisoning and procedural complications	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)
Tongue injury	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Ulna fracture	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)
Wrist fracture	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)
Investigations	0	(0.0)	0	(0.0)	2	(33.3)	0	(0.0)
Blood bilirubin increased	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)
Haemoglobin decreased	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)
Metabolism and nutrition disorders	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)
Decreased appetite	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)
Dehydration	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)
Musculoskeletal and connective tissue disorders	2	(33.3)	3	(42.9)	1	(16.7)	0	(0.0)
Arthralgia	0	(0.0)	1	(14.3)	1	(16.7)	0	(0.0)
Back pain	2	(33.3)	1	(14.3)	0	(0.0)	0	(0.0)
Neck pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Osteoarthritis	0	(0.0)	1	(14.3)	0	(0.0)	0	(0.0)
Spinal stenosis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
All Participants as Treated Population

	MK-2214 Total		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Injury, poisoning and procedural complications	1	(4.0)	1	(11.1)	2	(5.9)
Tongue injury	0	(0.0)	1	(11.1)	1	(2.9)
Ulna fracture	1	(4.0)	0	(0.0)	1	(2.9)
Wrist fracture	1	(4.0)	0	(0.0)	1	(2.9)
Investigations	2	(8.0)	0	(0.0)	2	(5.9)
Blood bilirubin increased	1	(4.0)	0	(0.0)	1	(2.9)
Haemoglobin decreased	1	(4.0)	0	(0.0)	1	(2.9)
Metabolism and nutrition disorders	1	(4.0)	1	(11.1)	2	(5.9)
Decreased appetite	1	(4.0)	1	(11.1)	2	(5.9)
Dehydration	1	(4.0)	0	(0.0)	1	(2.9)
Musculoskeletal and connective tissue disorders	6	(24.0)	3	(33.3)	9	(26.5)
Arthralgia	2	(8.0)	1	(11.1)	3	(8.8)
Back pain	3	(12.0)	0	(0.0)	3	(8.8)
Neck pain	0	(0.0)	1	(11.1)	1	(2.9)
Osteoarthritis	1	(4.0)	0	(0.0)	1	(2.9)
Spinal stenosis	0	(0.0)	1	(11.1)	1	(2.9)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1	(4.0)	0	(0.0)	1	(2.9)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
All Participants as Treated Population

	MK-2214 CCI IV		MK-2214 CCI IV		MK-2214 CCI IV		MK-2214 CCI IV	
	n	(%)	n	(%)	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)
Lipoma	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)
Nervous system disorders	3	(50.0)	1	(14.3)	3	(50.0)	3	(50.0)
Cerebral microhaemorrhage	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Dizziness	2	(33.3)	0	(0.0)	1	(16.7)	0	(0.0)
Encephalomalacia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Gliososis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Headache	2	(33.3)	1	(14.3)	1	(16.7)	3	(50.0)
Lethargy	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)
Presyncope	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)
Seizure	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Tremor	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Psychiatric disorders	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)
Anxiety	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)
Depression	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Suicidal ideation	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)
Renal and urinary disorders	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)
Hypertonic bladder	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
All Participants as Treated Population

	MK-2214 Total		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1	(4.0)	0	(0.0)	1	(2.9)
Lipoma	1	(4.0)	0	(0.0)	1	(2.9)
Nervous system disorders	10	(40.0)	5	(55.6)	15	(44.1)
Cerebral microhaemorrhage	0	(0.0)	1	(11.1)	1	(2.9)
Dizziness	3	(12.0)	1	(11.1)	4	(11.8)
Encephalomalacia	0	(0.0)	1	(11.1)	1	(2.9)
Gliositis	0	(0.0)	1	(11.1)	1	(2.9)
Headache	7	(28.0)	2	(22.2)	9	(26.5)
Lethargy	1	(4.0)	0	(0.0)	1	(2.9)
Presyncope	1	(4.0)	0	(0.0)	1	(2.9)
Seizure	0	(0.0)	1	(11.1)	1	(2.9)
Tremor	0	(0.0)	1	(11.1)	1	(2.9)
Psychiatric disorders	1	(4.0)	1	(11.1)	2	(5.9)
Anxiety	1	(4.0)	0	(0.0)	1	(2.9)
Depression	0	(0.0)	1	(11.1)	1	(2.9)
Suicidal ideation	1	(4.0)	0	(0.0)	1	(2.9)
Renal and urinary disorders	1	(4.0)	0	(0.0)	1	(2.9)
Hypertonic bladder	1	(4.0)	0	(0.0)	1	(2.9)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
All Participants as Treated Population

	MK-2214 CCI IV		MK-2214 CCI IV		MK-2214 CCI IV		MK-2214 CCI IV	
	n	(%)	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	1	(16.7)	0	(0.0)	1	(16.7)	0	(0.0)
Epistaxis	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)
Pleural effusion	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)
Skin and subcutaneous tissue disorders	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Hyperhidrosis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Vascular disorders	1	(16.7)	1	(14.3)	0	(0.0)	0	(0.0)
Hypertension	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)
Subclavian artery stenosis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Thrombophlebitis	0	(0.0)	1	(14.3)	0	(0.0)	0	(0.0)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
All Participants as Treated Population

	MK-2214 Total		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	2	(8.0)	0	(0.0)	2	(5.9)
Epistaxis	1	(4.0)	0	(0.0)	1	(2.9)
Pleural effusion	1	(4.0)	0	(0.0)	1	(2.9)
Skin and subcutaneous tissue disorders	0	(0.0)	1	(11.1)	1	(2.9)
Hyperhidrosis	0	(0.0)	1	(11.1)	1	(2.9)
Vascular disorders	2	(8.0)	1	(11.1)	3	(8.8)
Hypertension	1	(4.0)	0	(0.0)	1	(2.9)
Subclavian artery stenosis	0	(0.0)	1	(11.1)	1	(2.9)
Thrombophlebitis	1	(4.0)	0	(0.0)	1	(2.9)
Every participant is counted a single time for each applicable row and column. MK-2214 Total column is pooled across participants receiving active MK-2214 doses in all panels (Panel A, B, C, D). Placebo column is pooled across participants receiving matching placebo in all panels (Panel A, B, C, D). Total column is pooled across all participants in all panels (Panel A, B, C, D). Panel A: MK-2214 CCI IV or placebo administered by 30-minute IV infusion on Days 1, 29, and 57. Panel B: MK-2214 CCI IV or placebo administered by 30-minute IV infusion on Days 1, 29, and 57. Panel C: MK-2214 CCI IV or placebo administered by 30-minute IV infusion on Days 1, 29, and 57. Panel D: MK-2214 CCI IV or placebo administered by 6-minute IV infusion on Days 1, 29, and 57. Adverse event terms are from MedDRA Version 28.0.						

Source: [P002V01MK2214: adam-adsl; adae]

Table 12
Participants With Drug-Related Adverse Events
All Participants as Treated Population

	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 Total
	n (%)	n (%)	n (%)	n (%)	n (%)
Participants in population	6	7	6	6	25
with one or more drug-related adverse events	2 (33.3)	1 (14.3)	2 (33.3)	1 (16.7)	6 (24.0)
with no drug-related adverse events	4 (66.7)	6 (85.7)	4 (66.7)	5 (83.3)	19 (76.0)
Cardiac disorders	0 (0.0)	1 (14.3)	0 (0.0)	0 (0.0)	1 (4.0)
Atrioventricular block first degree	0 (0.0)	1 (14.3)	0 (0.0)	0 (0.0)	1 (4.0)
Gastrointestinal disorders	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	1 (4.0)
Nausea	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	1 (4.0)
General disorders and administration site conditions	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)
Fatigue	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)
Investigations	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (4.0)
Haemoglobin decreased	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (4.0)
Nervous system disorders	2 (33.3)	0 (0.0)	1 (16.7)	1 (16.7)	4 (16.0)

Participants With Drug-related Adverse Events
(Incidence > 0% in One or More Treatment Groups)
All Participants as Treated Population

	Placebo		Total	
	n	(%)	n	(%)
Participants in population	9		34	
with one or more drug-related adverse events	1	(11.1)	7	(20.6)
with no drug-related adverse events	8	(88.9)	27	(79.4)
Cardiac disorders	0	(0.0)	1	(2.9)
Atrioventricular block first degree	0	(0.0)	1	(2.9)
Gastrointestinal disorders	0	(0.0)	1	(2.9)
Nausea	0	(0.0)	1	(2.9)
General disorders and administration site conditions	0	(0.0)	1	(2.9)
Fatigue	0	(0.0)	1	(2.9)
Investigations	0	(0.0)	1	(2.9)
Haemoglobin decreased	0	(0.0)	1	(2.9)
Nervous system disorders	1	(11.1)	5	(14.7)

Participants With Drug-related Adverse Events
(Incidence > 0% in One or More Treatment Groups)
All Participants as Treated Population

	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 CCI IV	MK-2214 Total
	n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders	2 (33.3)	0 (0.0)	1 (16.7)	1 (16.7)	4 (16.0)
Headache	2 (33.3)	0 (0.0)	1 (16.7)	1 (16.7)	4 (16.0)

Participants With Drug-related Adverse Events
(Incidence > 0% in One or More Treatment Groups)
All Participants as Treated Population

	Placebo	Total
	n (%)	n (%)
Nervous system disorders	1 (11.1)	5 (14.7)
Headache	1 (11.1)	5 (14.7)

Every participant is counted a single time for each applicable row and column.

MK-2214 Total column is pooled across participants receiving active MK-2214 doses in all panels (Panel A, B, C, D).

Placebo column is pooled across participants receiving matching placebo in all panels (Panel A, B, C, D).

Total column is pooled across all participants in all panels (Panel A, B, C, D).

Panel A: MK-2214 CCI IV or placebo administered by 30-minute IV infusion on Days 1, 29, and 57.

Panel B: MK-2214 CCI IV or placebo administered by 30-minute IV infusion on Days 1, 29, and 57.

Panel C: MK-2214 CCI IV or placebo administered by 30-minute IV infusion on Days 1, 29, and 57.

Panel D: MK-2214 CCI IV or placebo administered by 6-minute IV infusion on Days 1, 29, and 57.

Adverse event terms are from MedDRA Version 28.0.

Source: [P002V01MK2214: adam-adsl; adae]

Figure 2
AUC0-28d Dose-Proportionality Plot of Serum MK-2214 Following Administration of
3 Monthly IV Doses of [REDACTED] MK-2214 to Participants With Mild Cognitive
Impairment or Mild-to-Moderate Alzheimer's Disease (N = 5 to 6 /Panel)
Per-Protocol Population

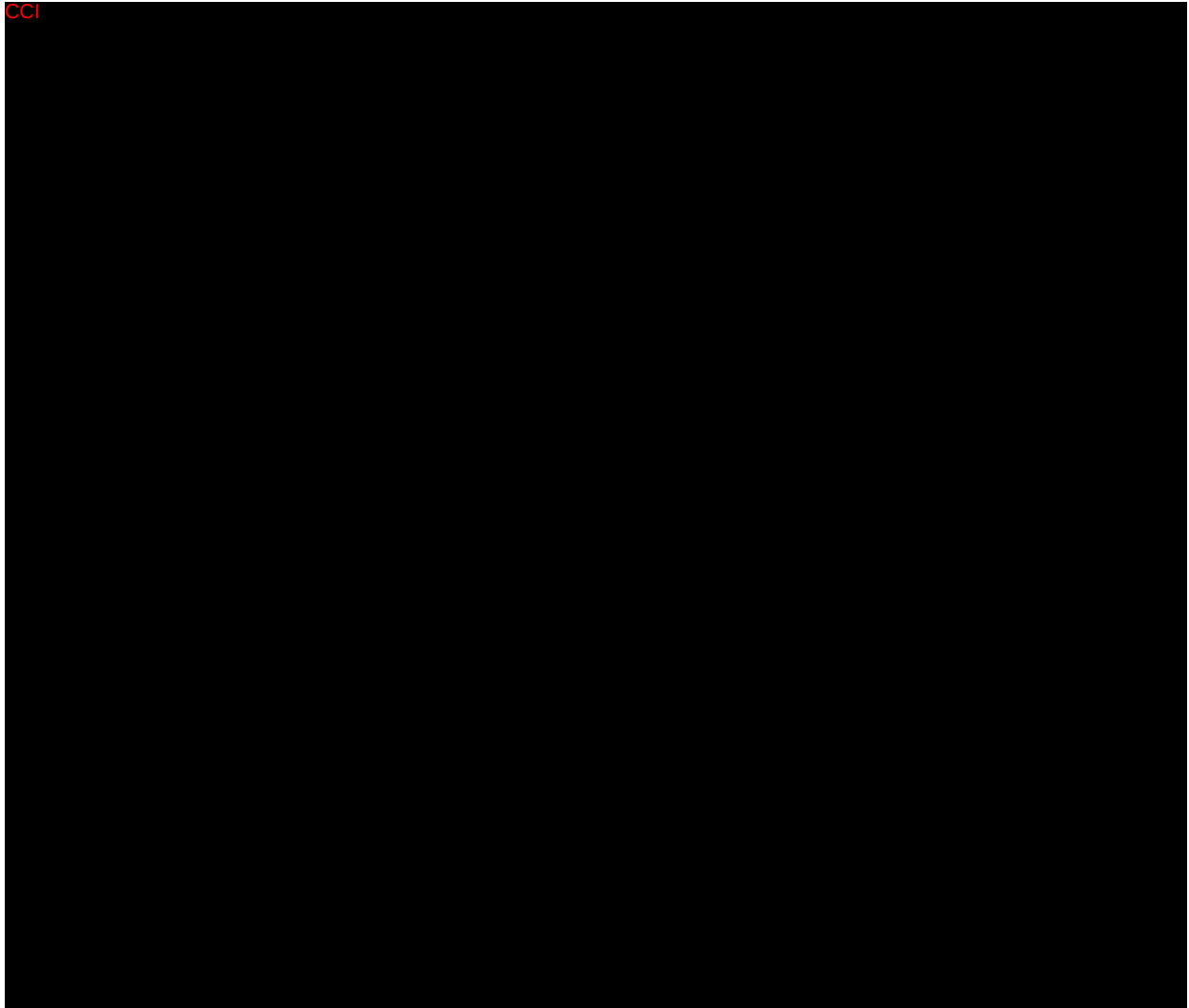


Figure 3
C_{max} Dose-Proportionality Plot of Serum MK-2214 Following Administration of 3 Monthly
IV Doses of [REDACTED] MK-2214 to Participants With Mild Cognitive Impairment or
Mild-to-Moderate Alzheimer's Disease (N=5 to 6 /Panel)
Per-Protocol Population

