GemVax

Research and Development of

GemVax & KAEL

A Multi-center, Randomized, Double-blind, Placebo-controlled, Parallel Design, Prospective, Phase II Clinical Trial to Evaluate the Safety and Efficacy of GV1001 0.56 mg/day and 1.12 mg/day Administered Subcutaneously for the Treatment of Moderate to Severe Alzheimer's Disease

Study overview

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1) Clinical Trial No.: **KG6/2016**

2) Sponsor: **GemVax&KAEL Co. Ltd.**
58, Techno 11-ro, Tuseoung-gu, Daejeon, Korea

3) Medical center and Principal Investigator:
Prof. Seong-Ho Koh
Department of Neurology, Hanyang University Guri Hospital

4) Ministry of Food and Drug Safety:
MFDS ID No.: 201600610 (2016. 12. 22)
5) IRB (Hanyang University Guri Hospital):
IRB ID No.: 2017-03-019 (2017. 04. 26)
7) ClinicalTrials.gov ID No: **NCT03184467**
8) First Patient In: 2017.09.05
9) Last Patient Out: 2019.09.19

Colleagues who participated in this trial

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Sangjae KIM	GemVax&KAEL Co. Ltd.

Introduction

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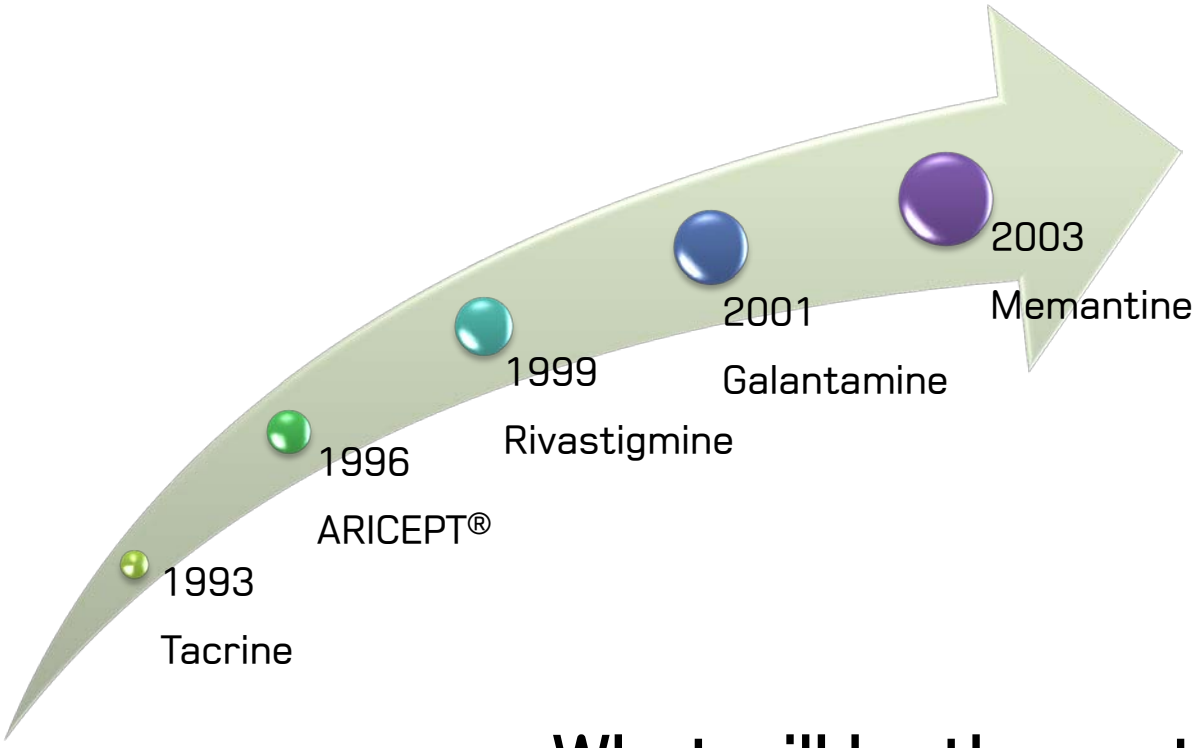
Introductions

South Korea became an aged society in 2017.

With aging population, the number of Alzheimer's disease (AD) patients has been sky-rocketing and the burden for AD patients has become a big problem in Korea.

Introductions

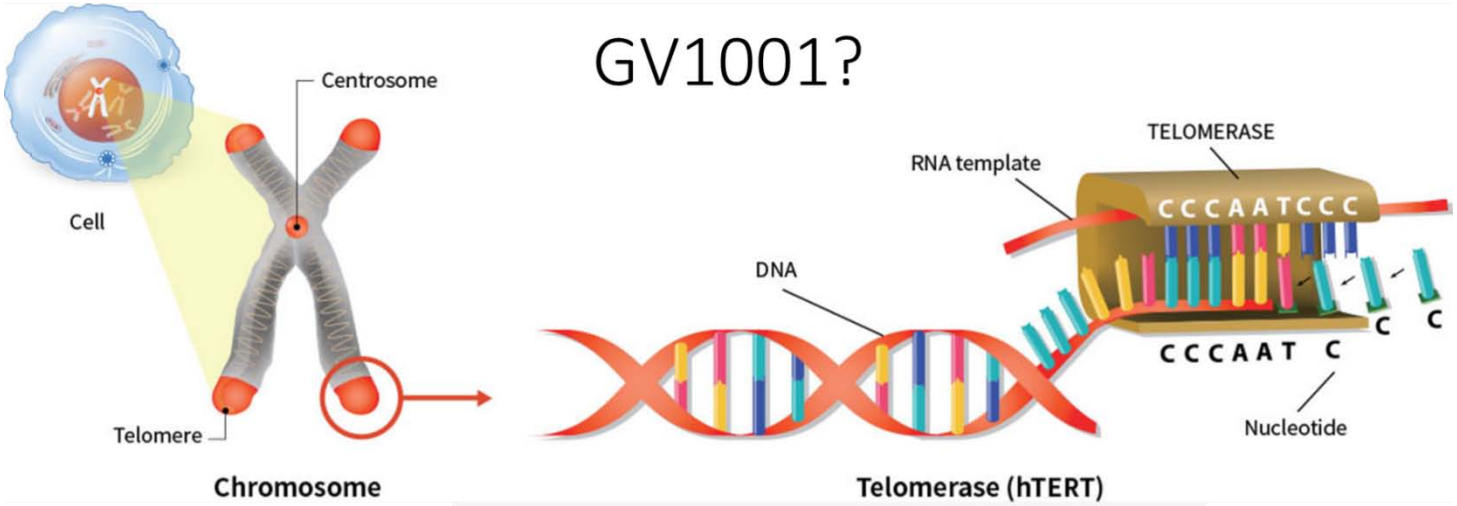
History of Approved Therapies in AD

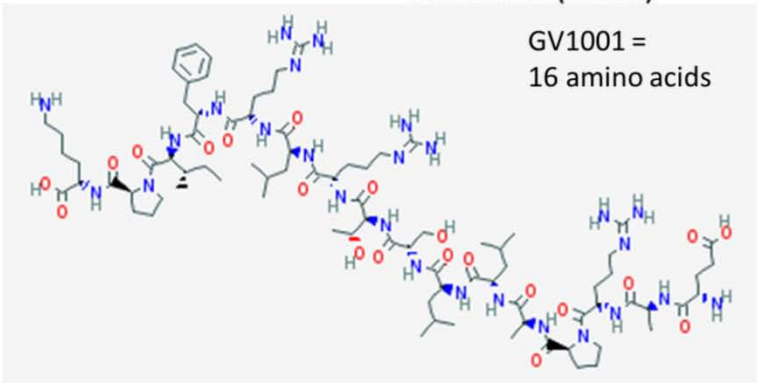


What will be the next ones?

Introductions

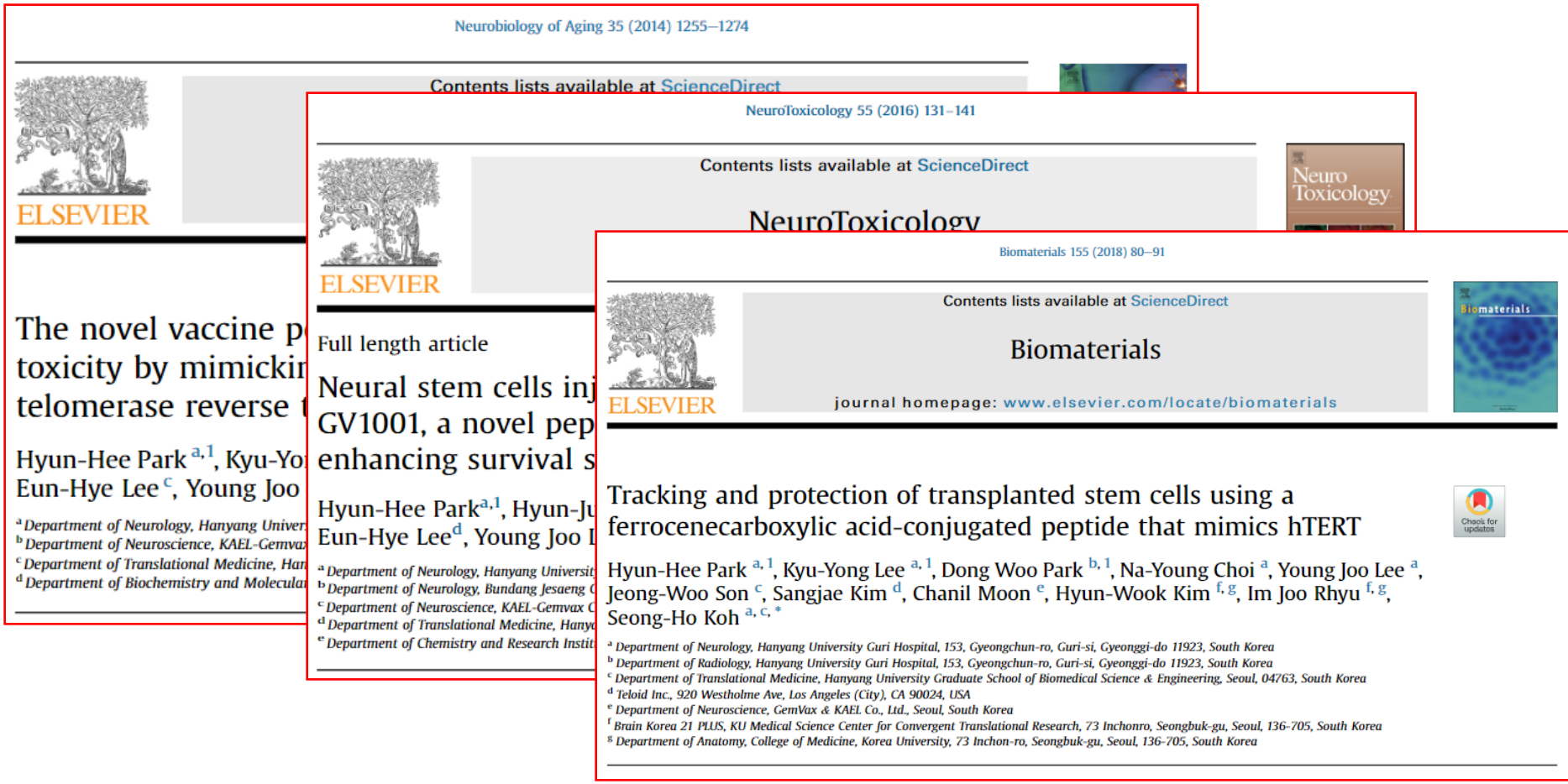
The active compound of GV1001 is a single peptide consisting of 16 amino acids. The peptide corresponds to a fragment from the catalytic site of the enzyme telomerase.





Introductions

GV1001 has been shown to inhibit neurotoxicity, apoptosis, and the production of reactive oxygen species induced by amyloid beta or other stresses in neural cells.



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Contents lists available at ScienceDirect

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The novel vaccine p
toxicity by mimickin
telomerase reverse t

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NeuroToxicology 55 (2016) 131–141

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NeuroToxicology

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Full length article

Neural stem cells inj
GV1001, a novel pep
enhancing survival s

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Biomaterials 155 (2018) 80–91

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Biomaterials

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Tracking and protection of transplanted stem cells using a ferrocenecarboxylic acid-conjugated peptide that mimics hTERT

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Clinical Trial Results

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Objectives

The main objective of the current study is to see the feasibility of GV1001 for the treatment of moderate to severe Alzheimer's disease (AD).

Therefore, this study had been conducted to evaluate the safety and efficacy of GV1001 (0.56 mg and 1.12 mg) administered subcutaneously as a treatment for moderate to severe AD.

Primary objectives and endpoints

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Primary objectives	Primary endpoints
• To compare the efficacy of GV1001 (0.56 mg and 1.12 mg) with placebo in participants with AD by evaluating cognitive function, as measured by the change from baseline of the SIB score	• Change from baseline in SIB score at Week 24
• To compare the safety of GV1001 (0.56 mg and 1.12 mg) with placebo in participants with AD	• Adverse events (AEs), laboratory test results, electrocardiogram (ECG) findings, and vital sign measurements

SIB: Severe Impairment Battery

Secondary objectives and endpoints

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Secondary objectives	Secondary endpoints
• To compare the efficacy of GV1001 (0.56 mg and 1.12 mg) with placebo in participants with AD by evaluating cognitive and functional abilities, as measured by the change from baseline in • CIBIC Plus score, • CDR-SB score, • ADCS-ADL score, • NPI score, • MMSE score, and • GDS score	• Secondary efficacy endpoints: Change from baseline in • CIBIC-Plus score, • CDR-SB score, • ADCS-ADL score, • NPI score, • K-MMSE score, and • GDS score at Week 24.

CIBIC: Clinical Dementia Rating, Global Deterioration Scale
CDR-SB: Clinical Dementia Rating Sum of Box
GDS: global deterioration scale
ADCS-ADL: Alzheimer's Disease Cooperative Study-activity of daily living
NPI: Neuropsychiatric Inventory
MMSE: mini-mental state examination

Inclusion criteria

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1) Participants between 55 and 85 years of age
2) Participants who are clinically diagnosed with probable AD as defined in the National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association (NINCDS–ADRDA) criteria
3) Participants must also meet Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM–V) criteria
4) Participants with a K–MMSE score ≤ 19 during the screening visit
5) Participants rated as grade 5 to 6 of Global Deterioration Scale (GDS)
6) Participants who have no other diseases to cause dementias other than AD as a result of MRI or CT scan within 12 months from the screening visit
7) Participants who are able to undergo cognitive and other tests by walking on their own or visiting hospitals using an assist device on an outpatient basis or for hospitalization.
8) Participants with a guardian who is able to accompany the subject for all visits, supervise the subject's compliance with the procedures specified in the clinical trial protocol and the investigational drug, and provide detailed information of the subject
9) Participants or legally representatives, as well as, the caregivers who voluntarily agree to participate in this clinical trial and sign the subject consent form
10) Participants stably taking 10 mg Aricept® for more than 3 months before screening etc.

Exclusion criteria-01

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1) Any other cause of dementia shown by MRI/CT findings and neurological examination within 12 months of randomization.
    - Possible, probable, or definite vascular dementia according to the National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherché et l'Enseignement en Neurosciences (NINDS-AIREN) criteria.
    - Evidence of significant abnormality that would suggest another potential etiology for dementia (eg, evidence of cerebral contusion, encephalomalacia, aneurysm, vascular malformation, >5 microhemorrhages, macrohemorrhage, single infarct >1cm^3).
    - Other central nervous system diseases that may cause cognitive impairment (eg, cerebrovascular disease including cerebrovascular dementia, Parkinsonism, Huntington's disease, subdural hematoma, normal pressure hydrocephalus, brain tumor, Creutzfeldt-Jakob disease).
2) Concurrent or history of clinically significant psychiatric conditions (eg. Schizophrenia or bipolar affective disorder) that in the Investigator's opinion prevents the participant from participating, or is likely to confound interpretation of drug effect or affect cognitive assessments.

Exclusion criteria-02

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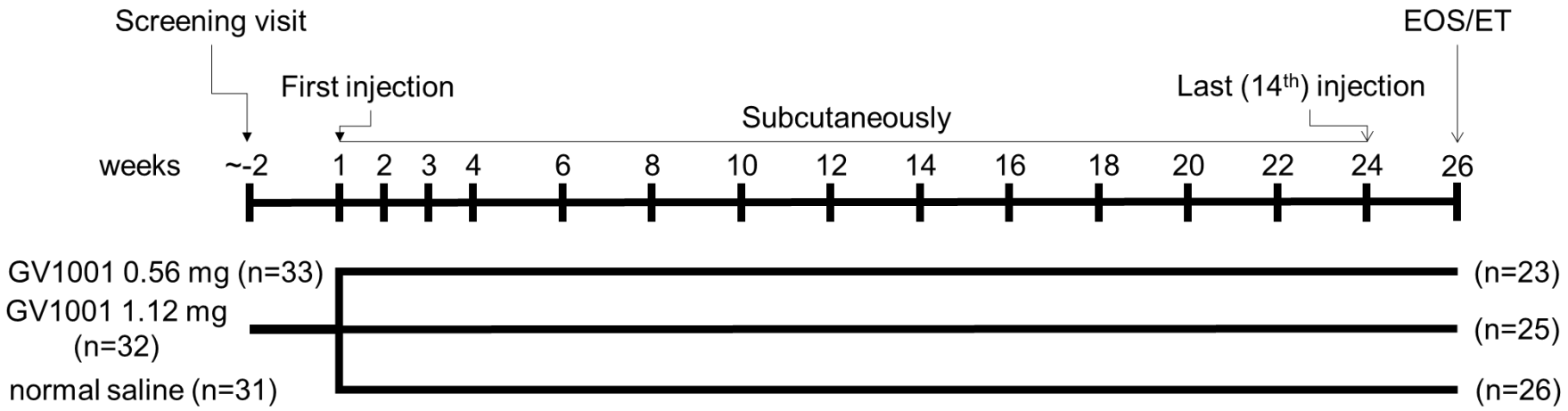
3) Participants with a history of known or suspected seizures, including febrile seizure, or recent loss of consciousness which is not explained, or a history of significant head trauma accompanied by loss of consciousness
4) Participants who have abnormal test results which are considered to contribute to the severity of their dementia or become a cause of dementia in the vitamin B12/folic acid test, the syphilis serology, and the thyroid stimulating hormone (TSH)
5) Participants with acute or unstable cardiovascular disease, active peptic ulcer, or uncontrolled hypertension; uncontrolled diabetes or insulin dependent patients; or patients with any medical condition that may interfere with the completion of clinical trials

Overall Study Design



With Aricept® 10mg

Baseline Evaluation	Midterm Evaluation	Final Evaluation
SIB	SIB	SIB
K-MMSE	K-MMSE	K-MMSE
CIBIC-Plus	CIBIC-Plus	CIBIC-Plus
CDR-SB	CDR-SB	CDR-SB
GDS	GDS	GDS
ADCS-ADL	ADCS-ADL	ADCS-ADL
NPI	NPI	NPI

Trial Profile

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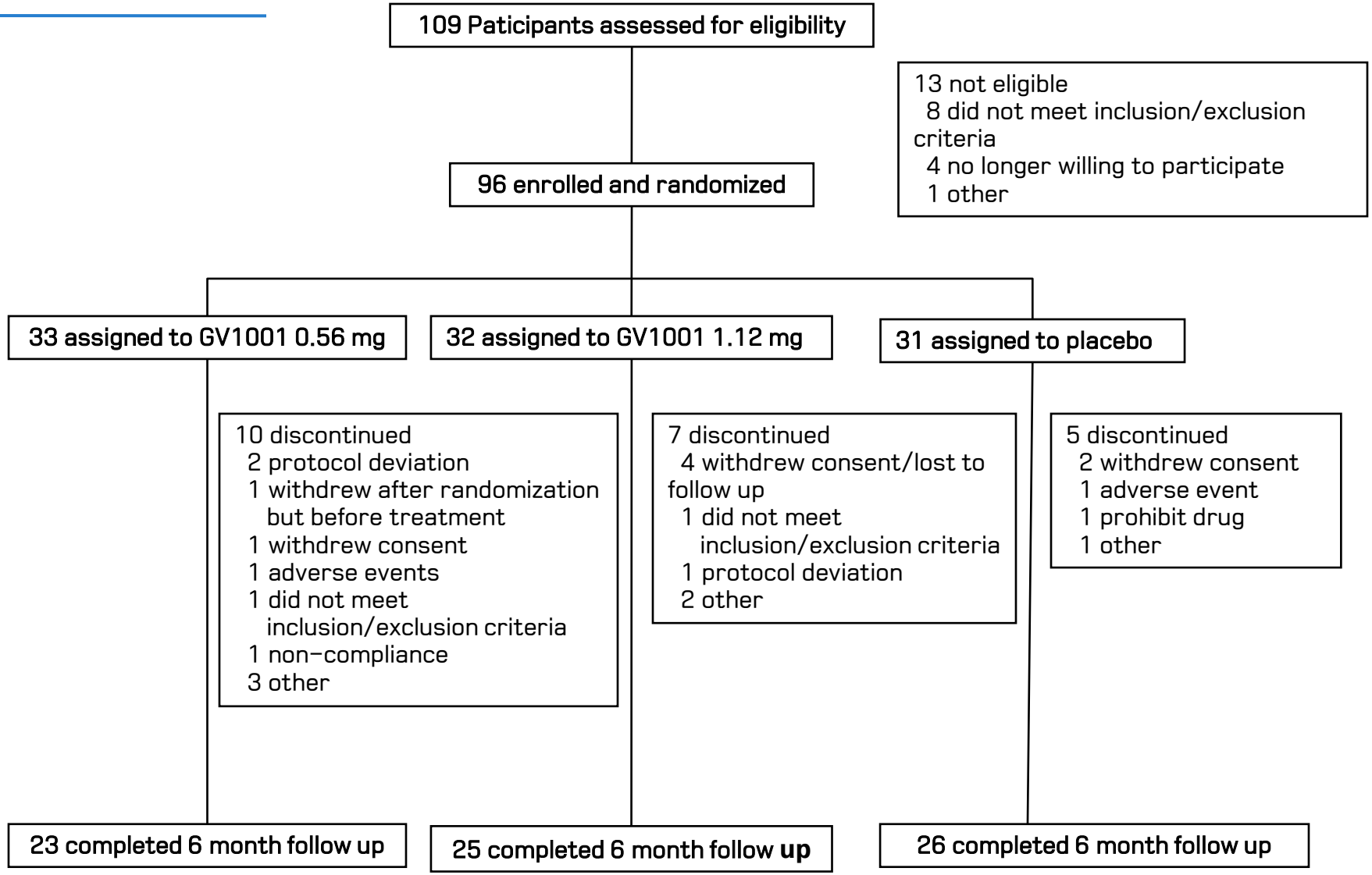

Participant number of each group

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		Study Group 1 (GV1001 0.56 mg)	Study Group 2 (GV1001 1.12 mg)	Placebo	Total
Randomized Set	N	33	32	31	96
Safety Set	N (%)	32(97.0)[1]	32(100.0)	31(100.0)	95(99.0)
FAS	N (%)	26(78.8)	28(87.5)	27(87.1)	81(84.4)
PPS	N (%)	22(66.7)	25(78.1)	26(83.9)	73(76.0)

1. One participant(05-S-013) withdrew after randomization but before treatment drug administration

Overall Summary of Treatment-emergent Adverse Events: Safety Set Population

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Category	Group 1 (GV1001 0.56 mg) (n=32)		Group 2 (GV1001 1.12 mg) (n=32)		Control (n=31)		Overall (n=95)		p-value
	n (%)	events	n (%)	events	n (%)	events	n (%)	events	
Patients with any TEAE	18(56.3)	34	15(46.9)	44	16(51.6)	38	49(51.6)	116	0.7545[1]
Patients with any ADR	10(31.3)	16	8(25.0)	15	7(22.6)	19	25(26.3)	50	0.7213[1]
Patients with any SAE	1(3.1)	1	0(0.0)	0	2(6.5)	2	3(3.2)	3	0.3191[2]
Patients with any TEAE leading to study withdrawal	1(3.1)	2	1(3.1)	1	1(3.2)	1	3(3.2)	4	1.0000[2]

Abbreviations: n = Number of patients; TEAE = Treatment-emergent adverse event; SAE=Severe adverse event; ADR = Adverse drug reaction

Note: Study Group 1 = GV1001 0.56 mg; Study Group 2 = GV1001 1.12 mg; Control = Placebo.

[1] Chi-square test; [2] Fisher's Exact test

Most Frequent Treatment–Emergent Adverse Events Which Occurred in > 2 Patient Overall: Safety Set Population

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System Organ Class[a] Preferred Term[a]	Group 1 (GV1001 0.56 mg) (n=32)		Group 2 (GV1001 1.12 mg) (n=32)		Control (n=31)		Overall (n=95)	
	n (%)	events	n (%)	events	n (%)	events	n (%)	events
Infections and infestations								
Nasopharyngitis	2(6.3)	2	1(3.1)	1	3(9.7)	5	6(6.3)	8
Cellulitis	1(3.1)	1	1(3.1)	1	1(3.2)	1	3(3.2)	3
Gastrointestinal disorders								
Diarrhoea	2(6.3)	2	1(3.1)	1	1(3.2)	1	4(4.2)	4
Abdominal pain	1(3.1)	1	1(3.1)	1	1(3.2)	2	3(3.2)	4
Psychiatric disorders								
Anxiety	2(6.3)	2	1(3.1)	1	1(3.2)	1	4(4.2)	4
Delusion	1(3.1)	1	0(0.0)	0	2(6.5)	2	3(3.2)	3
Musculoskeletal and connective tissue disorders								
Back pain	2(6.3)	2	2(6.3)	2	0(0.0)	0	4(4.2)	4
Arthralgia	2(6.3)	2	0(0.0)	0	1(3.2)	1	3(3.2)	3
Metabolism and nutrition disorders								
Decreased appetite	2(6.3)	2	0(0.0)	0	1(3.2)	1	3(3.2)	3
Vascular disorders								
Hypertension	1(3.1)	1	1(3.1)	1	2(6.5)	2	4(4.2)	4

Abbreviations: TEAE = Treatment-emergent adverse event; n = Number of patients.
Note: Study Group 1 = GV1001 0.56 mg; Study Group 2 = GV1001 1.12 mg; Control = Placebo
[a] TEAEs are classified using MedDRA version 22.1

Overall Summary of Treatment-Emergent Adverse Events by Severity: Safety Set Population

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	Group 1 (GV1001 0.56 mg) (n=32)		Group 2 (GV1001 1.12 mg) (n=32)		Control (n=31)		Overall (n=95)	
All TEAEs	**n (%)**	**events**	**n (%)**	**events**	**n (%)**	**events**	**n (%)**	**events**
Mild	13(40.6)	33	10(31.3)	28	12(38.7)	32	35(36.8)	93
Moderate	5(15.6)	7	5(15.6)	10	2(6.5)	4	12(12.6)	21
Severe	0(0.0)	0	0(0.0)	0	2(6.5)	2	2(2.1)	2

Abbreviations: TEAE = Treatment-emergent adverse event; n = Number of patients.
Note: Study Group 1 = GV1001 0.56 mg; Study Group 2 = GV1001 1.12 mg; Control = Placebo.

Conclusions

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The results demonstrated that **GV1001 is safe and well tolerable and has potential beneficial effects in patients with moderate to severe AD.**

Further investigation may be needed to confirm these observations, but the results provide a **predictor of good outcomes** of the next large-scale clinical trial.

Acknowledgements

Clinical trials

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감 사 합 니 다.