ABNORMAL MOVEMENTS

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Trial of Prasinezumab in Early-Stage Parkinson's Disease

Pagano G et al. DOI: 10.1056/NEJMoa2202867

CLINICAL PROBLEM

Aggregated α-synuclein has a prominent role in the pathogenesis of Parkinson's disease. Prasinezumab, a humanized monoclonal antibody that binds to aggregated α-synuclein, has been proposed as a potential treatment for Parkinson's disease, but clinical trial data are needed.

CLINICAL TRIAL

Design: A phase 2, multinational, double-blind, randomized, placebo-controlled trial examined the efficacy and safety of low- and high-dose prasinezumab in patients with early-stage Parkinson's disease.

Intervention: 316 patients who had not previously received treatment for symptoms of Parkinson's disease or who were receiving stable doses of a monoamine oxidase B inhibitor were assigned to receive intravenous prasinezumab (1500 mg or 4500 mg) or placebo every 4 weeks for 52 weeks. The primary end point was the change from baseline to week 52 in the Movement Disorder Society–sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) total score; scores range from 0 to 236, with higher scores indicating greater symptom severity.

RESULTS

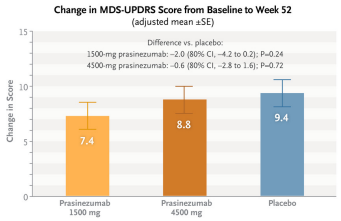
Efficacy: The mean change in the MDS-UPDRS score at week 52 did not differ significantly between either prasinezumab dose and placebo.

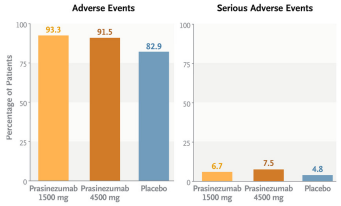
Safety: Infusion reactions were common and were reported most frequently in the 4500-mg group. Serious adverse events occurred more often with prasinezumab than with placebo.

LIMITATIONS AND REMAINING QUESTIONS

- Nearly one third of the participants were excluded from the 52-week efficacy analysis because they had started treatment for symptoms of Parkinson's disease.
- Non-White and non-U.S. or non-European populations were underrepresented in the trial.
- Testing for target engagement of prasinezumab was not performed.

Links: Full Article | NEJM Quick Take | Editorial





CONCLUSIONS

The monoclonal antibody prasinezumab, as compared with placebo, did not slow disease progression in patients with early-stage Parkinson's disease over a 52-week treatment period.

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RESEARCH SUMMARY

Trial of Cinpanemab in Early Parkinson's Disease

Lang AE et al. DOI: 10.1056/NEJMoa2203395

CLINICAL PROBLEM

Existing therapies for Parkinson's disease are limited. The targeting of α-synuclein aggregates has been proposed as a potential disease-modifying strategy. Cinpanemab, a human-derived monoclonal antibody that binds to aggregated α-synuclein, showed promise in a mouse model and in a phase 1 study of Parkinson's disease.

CLINICAL TRIAL

Design: A phase 2, international, double-blind, randomized, placebo-controlled trial examined the efficacy and safety of cinpanemab in persons with early-stage Parkinson's disease.

Intervention: 357 participants who were not receiving treatment for Parkinson's symptoms were assigned to receive intravenous cinpanemab at one of three doses (250 mg, 1250 mg, or 3500 mg) or placebo (control) every 4 weeks for 52 weeks, after which placebo recipients switched to cinpanemab. The primary end points included the change from baseline to weeks 52 and 72 in the total score on the Movement Disorder Society–sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS); scores range from 0 to 236, with higher scores indicating greater symptom severity.

RESULTS

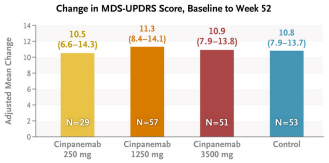
Efficacy: At 52 weeks, the change in MDS-UPDRS total score did not differ significantly between any cinpanemab dose and placebo. Results at 72 weeks, when the trial was stopped early for lack of efficacy, were consistent with the results at 52 weeks.

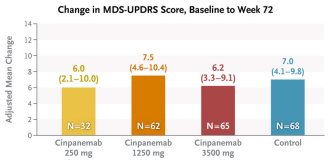
Safety: Adverse events occurred in similar proportions of cinpanemab and placebo recipients and were usually mild to moderate in severity. The most common adverse events with cinpanemab included headache, nasopharyngitis, falls, and back pain.

LIMITATIONS AND REMAINING QUESTIONS

- 40% of the participants were not included in the 52-week analysis because they had started other treatments for Parkinson's symptoms.
- Clearance of α-synuclein in cinpanemab recipients could not be verified.

Links: Full Article | NEJM Quick Take | Editorial





Adverse Events to Week 52

Adverse Event	Cinpanemab 250 mg (N=55)	Cinpanemab 1250 mg (N=102)	Cinpanemab 3500 mg (N=100)	Control (N=100)
Any adverse event	42 (76)	83 (81)	86 (86)	80 (80)
Adverse events occurring in ≥5% of participants				
Headache	6 (11)	19 (19)	21 (21)	18 (18)
Nasopharyngitis	10 (18)	10 (10)	13 (13)	12 (12)
Fall	5 (9)	6 (6)	15 (15)	5 (5)
Back pain	3 (5)	8 (8)	13 (13)	9 (9)

Data are no. of participants (%).

CONCLUSIONS

The monoclonal antibody cinpanemab, as compared with placebo, did not slow progression of Parkinson's disease in patients with early-stage disease.

In these trials involving participants with Parkinson's disease, treatment with cinpanemab or prasinezumab, monoclonal antibodies directed at α-synuclein, showed no evidence of benefit as compared with placebo with regard to clinical, imaging, or quality-of-life measures.

DEMENTIA

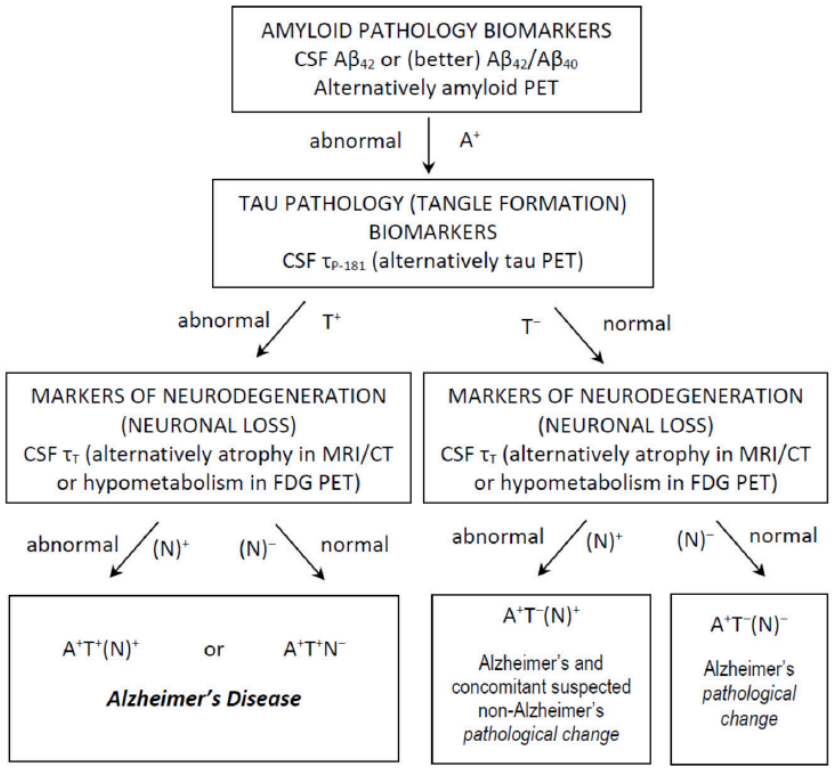


Figure 1. Use of CSF classical biomarkers and the AT(N) classification system in everyday clinical practice, for the diagnosis of Alzheimer's *disease* and Alzheimer's *pathological change*. Other profiles are not compatible with Alzheimer's continuum and are not shown.

DIAGNOSIS: biomarkers

The so-called **AT(N) system** (A for amyloid load, T for tau accumulation and N for neurodegeneration) has been proposed by the National Institute of Aging and Alzheimer's Association (NIA–AA) Research Framework group

In Alzheimer's disease, CSF biomarker changes may become evident 10–20 years prior to the symptomatic stage

Jack, C.R et al. A/T/N: An unbiased descriptive classification scheme for Alzheimer disease biomarkers. Neurology 2016, 87, 539–547

DEMENTIA

FDA NEWS RELEASE

FDA Converts Novel Alzheimer's Disease Treatment to Traditional Approval

Action Follows Confirmatory Trial to Verify Clinical Benefit

Anti-CGRP MABs for HEADACHE

JAMA | Original Investigation

Effect of Fremanezumab Compared With Placebo for Prevention of Episodic Migraine
A Randomized Clinical Trial

David W. Dodick, MD; Stephen D. Silberstein, MD; Marcelo E. Bigal, MD, PhD; Paul P. Yeung, MD, MPH; Peter J. Goadsby, MD, PhD; Tricia Blankenbiller, MA; Melissa Grozinski-Wolff; Ronghua Yang, PhD; Yuju Ma, MS; Ernesto Aycardi, MD

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Fremanezumab for the Preventive Treatment of Chronic Migraine

Stephen D. Silberstein, M.D., David W. Dodick, M.D., Marcelo E. Bigal, M.D., Ph.D., Paul P. Yeung, M.D., M.P.H., Peter J. Goadsby, M.D., Ph.D., Tricia Blankenbiller, M.A., Melissa Grozinski-Wolff, B.S., Ronghua Yang, Ph.D., Yuju Ma, M.S., and Ernesto Aycardi, M.D.

Original Article

Cephalalgia

International Headache Society

Efficacy and safety of galcanezumab for the prevention of episodic migrai
Results of the EVOLVE-2 Phase
randomized controlled clinical t

Vladimir Skljarevski[1], Manjit Matharu[2], Brian A
Michael H Ossipov[3], Byung-Kun Kim[4] and Jyun

Cephalalgia
0(0) 1–13
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Galcanezumab in chronic migraine
The randomized, double-blind, placebo-controlled REGAIN study

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Neurology® 2018;91:e1-e11. doi:10.1212/WNL.0000000000006640

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Controlled Trial of Erenumab for Episodic Migraine

Peter J. Goadsby, M.D., Ph.D., Uwe Reuter, M.D., Yngve Hallström, M.D., Gregor Broessner, M.D., Jo H. Bonner, M.D., Feng Zhang, M.S., Sandhya Sapra, Ph.D., Hernan Picard, M.D., Ph.D., Daniel and Robert A. Lenz, M.D., Ph.D.

ABSTRACT

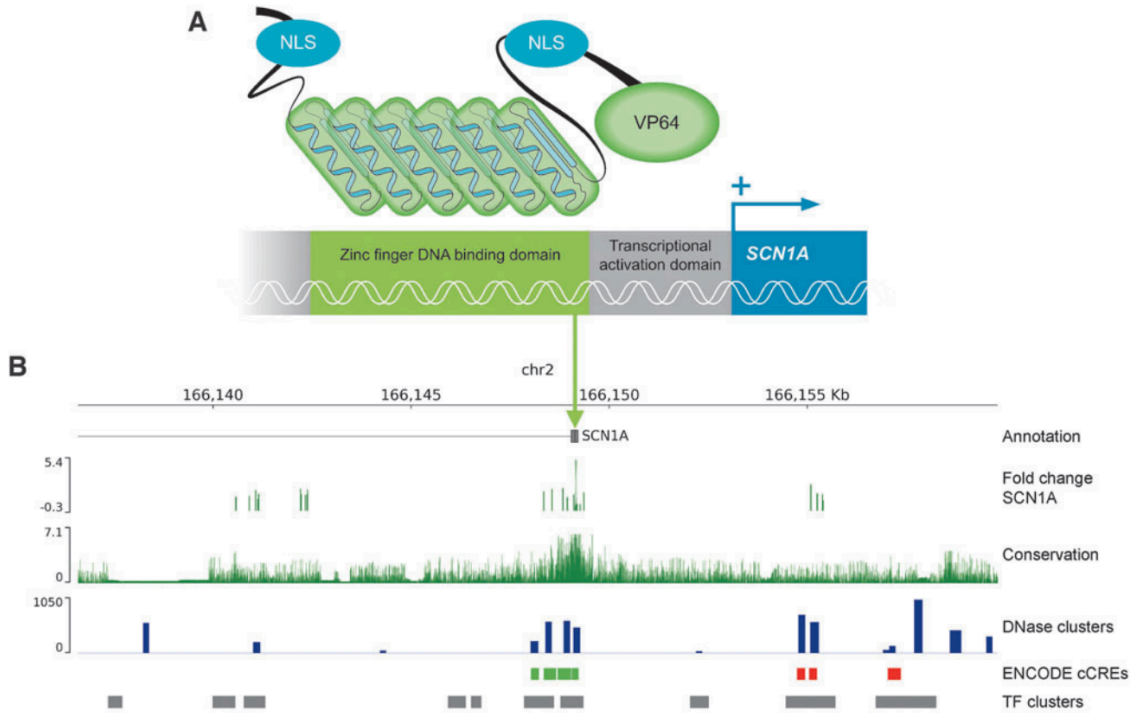
Safety and efficacy of erenumab for preventive treatment of chronic migraine: a randomised, double-blind, placebo-controlled phase 2 trial

Stewart Tepper, Messoud Ashina, Uwe Reuter, Jan L Brandes, David Doležil, Stephen Silberstein, Paul Winner, Dean Leonardi, Daniel Mikol, Robert Lenz

Vall d'Hebron Barcelona Hospital Campus | Neurociències

EPILEPSY

- Increased understanding of the role of astrocytes in epileptogenesis.1 The role of neurons in epileptogenesis has been extensively investigated
- Progress was also made in diagnosis of autoimmune encephalitis by use of a signs and symptoms score. The antibodies contributing focal epilepsy signs and symptoms (ACES) score encompasses six factors: temporal MRI hyperintensities, autoimmune diseases, behavioural changes, autonomic symptoms, cognitive symptoms, and speech problems. An ACES score of at least 2 had a sensitivity of 100% to diagnose seizures of autoimmune origin, and a specificity of 84·9%.



Gene Therapy for Dravet Syndrome

Information regarding the state-of-the-field for disease-modifying therapeutic approaches.

Terapia génica que permite aumentar la esperanza de vida y disminuir la frecuencia de crisis en los pacientes con encefalopatías epilépticas por mutación SCN1A

Front. Neurol. Sec. Pediatric Neurology

i.org/10.3389/fneur.2021.753753

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NEUROMUSCULAR

TABLE. DISEASE-MODIFYING TREATMENTS FOR SPINAL MUSCULAR ATROPHy			
Medication	**Nusinersen**	**Onasemnogene abeparvovec**	**Risdiplam**
Route of delivery	Intrathecal	Intravenous	Oral
Dosing intervals	4 loading doses in 4 months, then maintenance dosing every 4 months	1-time	Once daily
Common side effects	Thrombocytopenia, renal toxicity, coagulation abnormalities	Elevated liver transaminases	Thrombocytopenia, renal toxicity, coagulation abnormalities
Indications	All patients with SMA	SMA ≤2 years old	SMA ≥2 months old
Year approved	2016	2019	2020
Abbreviation: SMA, spinal muscular atrophy.			

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