KURZPROTOKOLL
Envision

Öffentlicher Titel	Phase III/IV Studie zu Aducanumab bei Alzheimer
Wissenschaftl. Titel	A Phase 3b/4 Multicenter, randomized, double-blind, placebo-controlled, parallel-group study to verify the clinical benefit of Aducanumab in Participants with Alzheimer's Disease
Kurztitel	Envision
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, Pharma-Studie, doppelblind, zweiarmig
Studienphase	Phase III/IV
Erkrankung	Psyche: Demenz
Einschlusskriterien	- The participant and/or his/her legally authorized representative (e.g., parent, spouse, or legal guardian, where local regulations and institutional practices permit) must be able, as appropriate and applicable, to understand the purpose and risks of the study, to provide signed and dated informed consent, and to authorize the use of confidential health information in accordance with national and local privacy and ethics regulations - The participant must be 60 to 85 years old, inclusive, at the time of informed consent - All women of childbearing potential must practice effective contraception during the study and for 5 times the half-life or 24 weeks (whichever is longer) after their last dose of study treatment. For further details of contraceptive requirements for this study, refer to Section 11.5 - The participant must have a minimum of 9 years of education or vocational training or the equivalent education/vocational training until the age of 15 or, per Investigator judgment, work experience that indicates a lack of mental deficits other than early-stage dementia - The participant must have confirmed amyloid beta pathology by CSF (historical CSF test results not allowed) or amyloid PET. If providing only a screening amyloid PET scan for amyloid positivity, a historical, amyloid PET scan obtained within 18 months of Screening Visit 2 is permissible. Sponsor-approved tracers must be used and scans must be submitted to the central imaging vendor to confirm that study inclusion criteria are met. In the case of discordant results between CSF and PET, PET results will be used to assess eligibility - The participant must have a history of subjective memory decline with gradual onset and slow progression over the last 6 months before Screening, confirmed by study partner - The participant must meet all of the following clinical criteria for MCI due to Alzheimer's disease or mild Alzheimer's disease according to NIA-AA criteria [Albert 2011; McKhann 2011]: • Have an MMSE score between 22 and 30 inclusive • Have a CDR memory score >= 0.5 • Have a CDR-GS of 0.5 or 1.0 • Have an RBANS score of 85 or lower indicative of objective cognitive impairment (based upon the DMI score) - The participant must be in good health, apart from a clinical diagnosis of early Alzheimer's disease, as determined by the Investigator based on medical history and screening assessments - The participant must consent to ApoE genotyping

- The participant must have 1 informant/care partner who, in the Investigator's opinion, has frequent and sufficient contact with the participant (at least 10 hours/week in person or by phone) as to be able to provide accurate information about the participant's cognitive and functional abilities over time. The informant/care partner ideally has known the participant prior to their cognitive decline to have a reference point for change across time. The informant/care partner must be available by phone to provide information to the Investigator and study staff about the participant as well as agree to attend in-person clinic visits that require partner input for scale completion. The informant/care partner must be literate and provide informed consent and should be available for the duration of the study. The same informant/care partner is required to be consistent across all study visits except under rare, unavoidable circumstances (e.g., unexpected informant health crisis) that are approved by the Investigator and Sponsor

Ausschlusskriterien

- Any uncontrolled medical or neurological/neurodegenerative condition (other than Alzheimer's disease) that, in the opinion of the Investigator, might be a contributing cause of the participant's cognitive impairment (e.g., Lewy body dementia, head trauma, substance abuse, frontotemporal dementia, vitamin B12 deficiency, abnormal thyroid function, stroke, or other cerebrovascular condition)
- Clinically significant and/or unstable psychiatric illness within 6 months prior to Screening
- Any documented prior history of chronic schizophrenia
- History of long-term major depression or bipolar affective disorder with an active episode in the past 5 years
- Transient ischemic attack or stroke or any unexplained loss of consciousness within 1 year prior to Screening
- Brain MRI performed at Screening (per centrally read MRI) that shows evidence of any of the following: • Acute or subacute hemorrhage • Prior cerebral hemorrhage > 1 cm in diameter on T2* sequence or prior subarachnoid hemorrhage unless it can be documented that the finding is not due to an underlying structural or vascular abnormality (i.e., finding does not suggest participant is at risk of recurrent hemorrhage) • 4 or more microhemorrhages (defined as <= 1 cm in diameter on T2* sequence) • 1 or more localized superficial siderosis findings • Cortical infarct (defined as > 1.5 cm in diameter irrespective of anatomic location) • > 1 lacunar infarct (defined as <= 1.5 cm in diameter) • History of diffuse white matter disease as defined by a score of 3 on the agerelated white matter changes scale [Wahlund 2001] • Any finding that, in the opinion of the Investigator, might be a contributing cause of participant's dementia, might pose a risk to the participant, or might prevent a satisfactory MRI assessment for safety monitoring
- History of bleeding disorder or predisposing conditions, blood clotting, or clinically significant abnormal results on coagulation profile at Screening as determined by the Investigator
- Presence of diabetes mellitus that, in the judgment of the Investigator, cannot be controlled or adequately managed
- History of unstable angina, myocardial infarction, chronic heart failure (New York Heart Association Class III or IV), or clinically significant conduction abnormalities (e.g., unstable atrial fibrillation) within 1 year prior to Screening
- Clinically significant 12-lead ECG abnormalities as determined by the Investigator
- Uncontrolled hypertension defined as: average of 3 SBP/DBP readings > 165 mmHg and/or > 100 mmHg at Screening (blood pressure measurements exceeding these limits may be repeated as warranted by the Investigator, but values must be within the specified limits for the participant to be eligible for the study); or persistent SBP/DBP readings > 180 mmHg and/or > 100 mmHg 3 months prior to randomization (Day 1) that, in the opinion of the Investigator, are indicative of chronic uncontrolled hypertension

- History of malignancy or carcinoma. The following exceptions may be made after discussion with the Sponsor: • Participants with cancers in remission >= 5 years prior to Screening Visit 1. • Participants with a history of excised or treated basal cell or squamous carcinoma of the skin.• Participants with localized prostate cancer with treatment cycles that completed at least 6 months prior to Screening Visit 1
- History of seizures or new-onset seizures within 10 years prior to Screening
- Indication of impaired liver function as shown by an abnormal liver function profile at Screening (e.g., repeated values of AST and ALT >= 2 × the upper limit of normal)
- History or evidence of an autoimmune disorder considered clinically significant by the Investigator
- Recent history (within 1 year of Screening) of alcohol or substance abuse as determined by the Investigator, or a positive urine drug test (due to a nonprescription drug and without a clear justification of the results according to the Investigator) at Screening
- Within 30 days of Screening, clinically significant systemic illness or infection that requires hospitalization or that, in the opinion of the Investigator, is impacting the patient's usual performance in function or cognition
- History of or known seropositivity for HIV
- Current hepatitis B infection (defined as positive for HBsAg and total anti-HBc). Participants with immunity to hepatitis B from previous natural infection (defined as negative HBsAg, positive anti-HBc, and positive anti-HBs) or vaccination (defined as negative HBsAg, negative anti-HBc, and positive anti-HBs) are eligible to participate in the study
- Current hepatitis C virus infection (defined as positive HCV antibody and detectable HCV RNA). Participants with positive HCV Ab and undetectable HCV RNA are eligible to participate in the study
- History of severe allergic or anaphylactic reactions or of hypersensitivity to any of the inactive ingredients in the drug product. (Refer to the Investigator's Brochure for information on the clinical formulation.)
- Symptoms consistent with SARS-CoV-2 infection, per the judgment of the Investigator, within 14 days prior to Day 1, including but not limited to fever (temperature > 37.5°C), sore throat, new and persistent cough, shortness of breath, diarrhea, muscle aches, or loss of taste or smell
- Any other medical conditions (e.g., renal disease) that are not stable or controlled or, in the opinion of the Investigator, could affect the participant's safety or interfere with the study assessments
- Participation in any active immunotherapy study targeting A unless documentation of receipt of placebo is available
- Participation in any passive immunotherapy study targeting A within 12 months of Screening unless documentation of receipt of placebo is available
- Participation in any study with purported disease-modifying effect in Alzheimer's disease within 12 months prior to Screening unless documentation of receipt of placebo is available
- Current use or previous use of medications with a purported diseasemodifying effect in Alzheimer's disease, outside of investigational studies
- Use of any medications that, in the opinion of the Investigator, may contribute to cognitive impairment, put the participant at higher risk for AEs, or impair the participant's ability to perform cognitive testing or complete study procedures

- Use of allowed chronic concomitant medications (see Section 7.7.1.1) at doses that have not been stable for at least 4 weeks prior to Screening Visit 2 and during Screening up to Day 1, or use of Alzheimer's disease medications (including but not limited to donepezil, rivastigmine, galantamine, tacrine, and memantine) at doses that have not been stable for at least 8 weeks prior to Screening Visit 2 and during Screening up to Day 1
- Use of allowed chronic concomitant medications that affect cognition (e.g., antidepressants, anticonvulsants, atypical and typical antipsychotics, short-/medium-acting benzodiazepines; see Section 7.7.1.2.1) at doses that have not been stable for at least 8 weeks prior to Screening Visit 2 and during Screening up to Day 1
- Use of long-acting benzodiazepines (allowed only for sedation prior to MRI/PET scans or LP for participants requiring sedation)
- Use of medications with antiplatelet or anticoagulant properties (acetylsalicyclic acid [aspirin] is allowed at a dose <= 325 mg per day)
- Use of chemotherapeutic agents and checkpoint inhibitors
- Chronic use of systemic immunosuppressive drugs (including systemic corticosteroids) as indicated in Section 7.7.1.2. Local immunosuppressants and local corticosteroids (including inhaled or topical corticosteroids) are allowed; short-term courses of systemic corticosteroids may also be permitted at the Sponsor's discretion
- Use of parenteral immunoglobulin (i.e., IVIG), blood products, plasma derivatives, plasma exchange, or plasmapheresis
- Use of active or passive immunotherapy agents targeting the CNS
- Use of any drug of abuse (prescription or recreational), including but not limited to, amphetamine, cocaine, opiates, methadone, phencyclidine, or barbiturates
- Use of THC-containing cannabinoids (products containing only CBD are allowed)
- Use of opioid medications within 4 weeks prior to Screening Visit 1
- Use of anticholinergics, such as benztropine
- Use of any investigational drug
- Vaccinations (including COVID-19 vaccines and boosters) within 5 days prior to randomization (Day 1)
- Prior exposure to aducanumab either commercially or by participation in a previous study with aducanumab. (Participants are eligible if they did not receive active aducanumab.)
- Contraindications to having a brain MRI (e.g., pacemaker; MRI-incompatible aneurysm clips, artificial heart valves, or other metal foreign body; or claustrophobia that cannot be medically managed)
- Any of the following contraindications to having an amyloid PET scan or LP if CSF testing is used for amyloid confirmation: • Contraindications to PET (e.g., inability to lie flat or still for the duration of the scan) or intolerance to previous PET scans (i.e., previous hypersensitivity reactions to any PET ligand or imaging agent or failure to participate in and comply with previous PET scans); the participant has had or plans to have exposure to experimental radiation within 12 months prior to Screening such that radiodosimetry limits would be exceeded by participating in this study. • Contraindications to having a LP (e.g., presence of risk for increased or uncontrolled bleeding, anatomical factors at or near the LP site). Any symptoms caused by or related to the optional LP during Screening must be resolved prior to randomization (Day 1)
- A negative PET scan result with any amyloid-targeting ligand within 12 months prior to Screening
- Female participants who are pregnant or currently breastfeeding

- Participant currently lives in an organized care facility with extensive intervention and/or support of daily living activities
- Blood donation (>= 1 unit) within 1 month prior to Screening
- Inability to comply with study requirements
- Other unspecified reasons that, in the opinion of the Investigator or Sponsor, make the participant unsuitable for enrollment

Alter 60 - 85 Jahre

Prüfzentren

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Sponsor Biogen

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