

2009-013400-31 - Summary

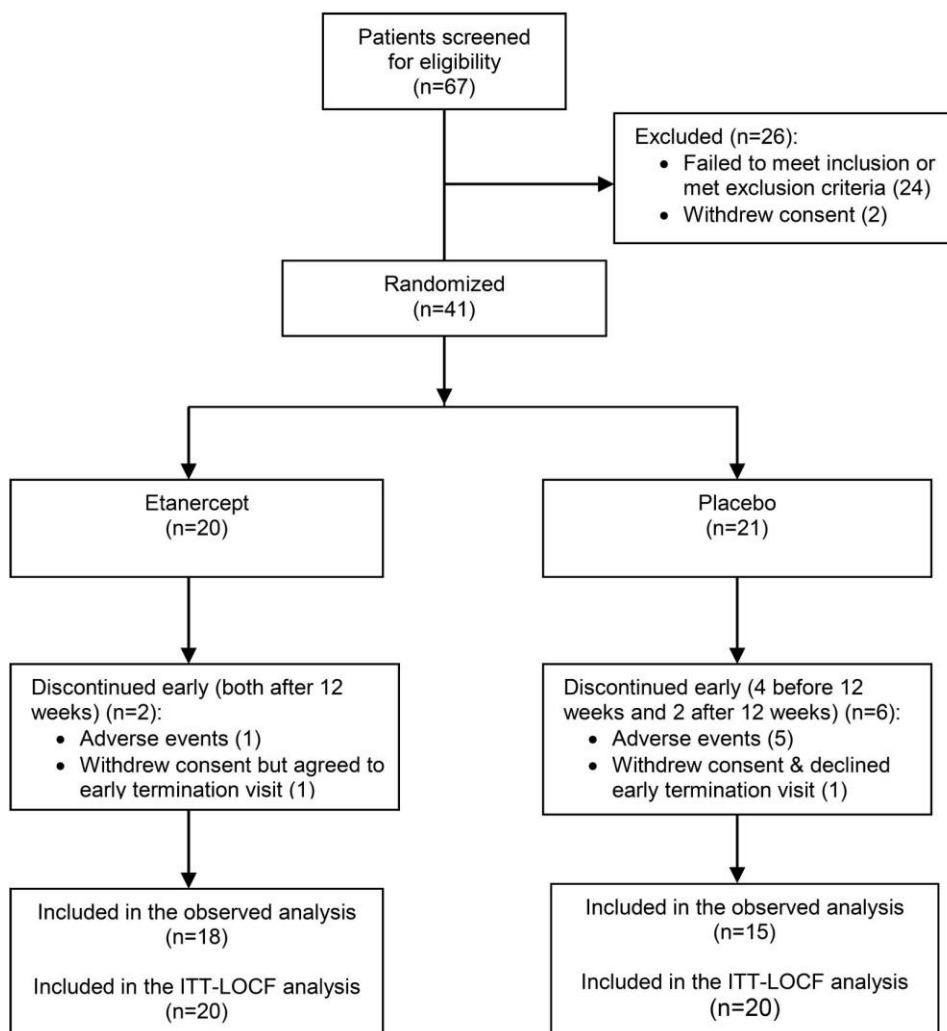
Title: A phase 2, double-blind, placebo-controlled study of the safety and tolerability of etanercept in patients with Alzheimer's disease

Objectives: To determine whether the tumor necrosis factor α inhibitor etanercept is well tolerated and obtain preliminary data on its safety in Alzheimer disease dementia.

Methods: In a double-blind study, patients with mild to moderate Alzheimer disease dementia were randomized (1:1) to subcutaneous etanercept (50 mg) once weekly or identical placebo over a 24-week period.

ClinicalTrials.gov: NCT01068353

1. Participants flow



2. Baseline Characteristic

Treatment	Etanercept 50 mg	Placebo
Number of participants	20	21
Mean age (SE)	72.0 (2.1)	72.9 (2.2)
Men, n (%)	15 (75)	10 (48)
Disease duration, y (SE)	5.1 (0.8)	4.1 (0.4)
ADAS-cog 5 Alzheimer's Disease Assessment Scale– cognitive (SE)	25.8 (2.9)	25.7 (2.5)
Bristol Activities of Daily Living Scale; BADLS pts (SE)	16.5 (3.0)	14.0 (1.7)

3. Outcomes: Changes in psychometric scores compare the baseline to 12 weeks and 24 weeks

	Week 12				Week 24			
	Etanercept (n = 20) (SE)	Placebo (n = 17) (SE)	Mean difference corrected ^a (95% CI)	p Value	Etanercept (n = 18) (SE)	Placebo (n = 15) (SE)	Mean difference corrected ^a (95% CI)	p Value
Observed cases								
sMMSE	−0.6 (0.5)	−0.5 (0.7)	0.004 (−1.9 to 1.9)	1.0	−0.1 (0.5)	−1.9 (1.2)	−2.5 (−5.2 to 0.2)	0.07
ADAS-cog	1.3 (1.4)	1.4 (1.5)	0.2 (−4.3 to 4.6)	0.9	3.2 (1.8)	5.6 (2.0)	1.2 (−5.1 to 7.5)	0.7
BADLS	−1.1 (2.1)	1.2 (0.9)	0.6 (−4.6 to 5.8)	0.8	0.8 (1.2)	6.0 (2.1)	5.6 (0.4 to 10.9)	0.04
NPI	−2.0 (2.7)	3.8 (1.6)	4.4 (−3.0 to 11.7)	0.2	−0.3 (3.3)	10.2 (3.6)	13.2 (2.4 to 24.0)	0.02
Cornell	−0.2 (0.9)	0.1 (1.0)	0.1 (−2.8 to 3.0)	0.9	0.4 (1.0)	1.9 (1.5)	1.6 (−2.3 to 5.5)	0.4
CGI-I	0.4 (0.2)	0.5 (0.2)	0.2 (−0.5 to 0.8)	0.6	0.6 (0.2)	0.9 (0.3)	0.3 (−0.6 to 1.1)	0.3
ITT-LOCF								
sMMSE	−0.6 (0.5)	−0.5 (0.7)	0.05 (−1.7 to 1.9)	0.9	−0.2 (0.5)	−1.4 (1.0)	−1.4 (−3.8 to 1.0)	0.2
ADAS-cog	1.3 (1.4)	1.9 (1.4)	0.6 (−3.6 to 4.8)	0.8	2.9 (1.7)	5.1 (1.6)	1.6 (−3.5 to 6.6)	0.5
BADLS	−1.1 (2.1)	1.4 (0.9)	0.5 (−4.2 to 5.2)	0.8	0.5 (1.2)	4.9 (1.7)	3.7 (−0.9 to 9.3)	0.1
NPI	−2.0 (2.7)	3.7 (1.5)	4.2 (−2.6 to 11.1)	0.2	0.8 (3.1)	6.9 (3.2)	6.5 (−3.4 to 16.5)	0.2
Cornell	−0.2 (0.9)	0.4 (0.8)	0.2 (−2.4 to 2.9)	0.9	0.5 (0.9)	1.9 (1.2)	0.8 (−2.4 to 3.9)	0.6
CGI-I	0.4 (0.2)	0.5 (0.2)	0.1 (−0.5 to 0.7)	0.7	0.7 (0.2)	0.7 (0.3)	0.1 (−0.8 to 0.6)	0.8

Abbreviations: ADAS-cog 5 Alzheimer's Disease Assessment Scale–cognitive; BADLS 5 Bristol Activities of Daily Living Scale; CGI-I 5 Clinical Global Impression–Improvement; CI 5 confidence interval; Cornell 5 Cornell Scale for Depression in Dementia; ITT-LOCF 5 intention to treat–last observation carried forward; NPI 5 Neuropsychiatric Inventory; SE 5 standard error; sMMSE 5 standardized Mini-Mental State Examination.

All p values are 2-sided.

^a Corrected for baseline age, sex, and psychometric score.

4. Number of adverse events by system organ class category

Disorder	Adverse events, no. of events (no. of participants)	
	Etanercept (n = 20)	Placebo (n = 21)
All disorders	42 events	55 events
Blood and lymphatic system (normocytic anemia, benign monoclonal hypergammaglobulinemia)	0 (0)	3 (3)
Cardiac (abnormal heart sounds, angina pectoris, irregular heart rate, atrial fibrillation)	2 (2)	2 (2)
Eye (eye pain)	0 (0)	2 (2)
Ear and labyrinth (wax impaction, deafness)	0 (0)	2 (1)
Gastrointestinal (nausea and vomiting, hematochezia, epigastric discomfort, diarrhea, constipation, colonic polyp)	5 (5)	7 (5)
General fatigue	1 (1)	1 (1)
Injection-site reaction	4 (2)	1 (1)
Infections (gastroenteritis, respiratory tract, urinary tract, pharyngitis, cellulitis)	11 (9)	7 (6)
Injury (falls)	2 (2)	4 (4)
Investigations (DNA antibody positive, increase serum CRP, creatinine, transaminase, colonoscopy)	6 (6)	5 (5)
Metabolic (hyperkalemia, dehydration)	2 (1)	1 (1)
Musculoskeletal (sciatica, osteoarthritis, joint stiffness, back pain, thoracic vertebral fracture, muscle weakness)	1 (1)	5 (3)
Neoplasms	0 (0)	0 (0)
Nervous system (parosmia, headache, parkinsonism, balance disorder)	2 (2)	2 (2)
Psychiatric (poor sleep, confusional state, behavioral symptoms, mood alteration, hallucinations, delusions)	3 (3)	6 (5)
Renal and urinary (urinary frequency, urinary incontinence)	1 (1)	1 (1)
Respiratory (yawning)	1 (1)	0 (1)
Skin (varicose eczema, hyperhidrosis, seborrheic dermatitis, seborrheic keratitis, eczema)	1 (1)	4 (3)
Vascular (hypertension, lymphedema)	0 (0)	2 (2)

5. Publication

<https://pubmed.ncbi.nlm.nih.gov/25934853/>