Supplementary Online Content

Porsteinsson AP, Drye LT, Pollock BG, et al. Effect of citalopram on agitation in Alzheimer disease: the CitAD randomized controlled trial. *JAMA*. doi:10.1001/jama.2014.93

eAppendix . Clinic by Treatment
eTable. Serious Adverse Events

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Clinic by Treatment

Controlling for clinic (as either a fixed effect or random effect) made very little difference in the citalopram effect estimates. To see if the treatment effects differed by clinic, we tested for a treatment by clinic by linear time interaction using the longitudinal mixed model and it was not significant ($p = 0.42$); however, that test is poorly powered. So we also looked at the estimate of the citalopram minus placebo difference at week 9 at all clinics using the mixed effects means model to look for qualitative differences in the effect estimate. The smallest estimated difference at week 9 by clinic was -0.8 and the largest was -1.2 (compared to the overall difference of -0.9) so we believe that the treatment effects were similar across clinics and the estimates were not driven by clinic interactions

eTable. Serious Adverse Events

	Total	Citalopram	Placebo	
Total serious adverse events (SAEs)	15	8	7	

Serious adverse events for citalopram (8 SAEs)

SR #	Event	Weeks since rz	Age	Gender	Outcome
1	Change in mental status	1	85	M	Hospitalized; patient continued study treatment
2	Cellulitis	1	71	F	Hospitalized treated with antibiotics
	SR #2 update: Sepsis	--	71	F	Hospitalized; patient found to be hyponatremic which normalized; discontinued study drug
4	Adverse reaction to IV contrast	8	77	M	Hospitalized; patient discontinued study drug
	SR #4 update: Pneumonia	--	77	M	Patient diagnosed with pneumonia and treated with antibiotics; discharged from hospital
5	Surgical removal of infected plate in left wrist	5	82	F	Hospitalized; patient continued study treatment
6	Increased agitation	2	74	M	Hospitalized; patient continued study treatment

eTable. Serious Adverse Events

SR #	Event	Weeks since rz	Age	Gender	Outcome
7	Fall	4	80	F	Hospitalized; became more agitated and was treated with haldol and cogentin; study drug compliance unclear
	SR #7 update: Syncope	--	80	F	Hospitalized
8	Syncope/ Hypotension	2	78	F	Hospitalized; study medication dose reduced
12	Chest pain	8	72	F	Hospitalized; study drug stopped and restarted; evaluated for myocardial infarction; Possible Gastroesophageal reflux disease; discharged

Serious adverse events for placebo (7 SAEs, including 1 death)

SR#	Event	Weeks since rz	Age	Gender	Outcome
3	Cancer-lung	1	75	M	Cancer metastasized throughout body; hospice notified
	SR #3 update: death	--	75	M	Death
9	Change in mental status	8	81	F	Hospitalized; medical work-up negative; diagnosis given “end stage AD”; placement in long-term hospice

eTable. Serious Adverse Events

10	Abdominal pain	8	84	M	Hospitalized; undergoing evaluation
	SR#10 update: Acute back pain	--	84	M	Study treatment terminated; medical work-up negative; discharged on Seroquel and Tylenol
11	Skin rash and itching; increased behavioral lack of control	3	81	M	Hospitalized; stopped study medication; found to have UTI; received antibotics and sertraline and seroquel; discharged
13	Increased agitation	<1	82	M	Hospitalized, study drug continued; lorazepam also used as needed
14	Altered mental status	3	76	F	Hospitalized; study drug terminated; seroquel administered; stabilized; discharged to nursing home
15	Broken hip	2	86	F	Fell at home; required surgery; hospitalized; study drug terminated

eTable. Serious Adverse Events

Scales used in CitAD:

Activities of Daily Living (ADCS-ADL)

- **ADL** – ADCS-ADL score (range 0-78 where higher scores indicate less functional impairment).

Clinical Global Impression of Change (ADCS-CGIC)

- **CGIC_Overall** – overall clinical score (range 1-7 where 1 indicates marked improvement and 7 indicates marked worsening from baseline).
- **CGIC_Agitation** – agitation subscore (range 1-7 where 1 indicates marked improvement and 7 indicates marked worsening from baseline).

Cohen-Mansfield Agitation Inventory Scale (CMAI)

- **CMAI –** overall score (range 14-70 where higher scores indicate more severe symptoms).

Get Up and Go (GUG)

- **GUG_performance** – performance rated on the basis of fall risk during test (range 1-5 where 1 is normal and 5 is severely abnormal).
- **GUG_record** – the ability to walk for the GUG test (1 = Yes, 0 = No).
- **GUG_time** – time to complete the GUG test (in seconds).

Mini-Mental State Examination (MMSE)

- **MMSE –** overall score (range 0-30 where higher scores indicate better functioning).

Neurobehavioral Rating scale (NBRS)

- **NBRS** – overall score (range 0-168 where higher scores indicate more severe symptoms).
- **NBRS-Agitation** – agitation subscore (range 0-18 where higher scores indicate more severe symptoms).

Neuropsychiatric Inventory (NPI)

- **TotalNPI –** overall score (range 0-144 where higher scores indicate more severe symptoms).
- **NPI_AberrantMotor –** aberrant motor behavior subscale score (range 0-12 where higher scores indicate more severe symptoms).

eTable. Serious Adverse Events

- **NPI_Agitation –** agitation/aggression subscale score (range 0-12 where higher scores indicate more severe symptoms).
- **NPI_Anxiety –** anxiety subscale score (range 0-12 where higher scores indicate more severe symptoms).
- **NPI_Apathy –** apathy/indifference subscale score (range 0-12 where higher scores indicate more severe symptoms).
- **NPI_Appetite –** appetite and eating disorders subscale score (range 0-12 where higher scores indicate more severe symptoms).
- **NPI_Delusion –** delusions subscale score (range 0-12 where higher scores indicate more severe symptoms).
- **NPI_Depression –** depression/dysphoria subscale score (range 0-12 where higher scores indicate more severe symptoms).
- **NPI_Disinhibition –** disinhibition subscale score (range 0-12 where higher scores indicate more severe symptoms).
- **NPI_Elation –** elation/euphoria subscale score (range 0-12 where higher scores indicate more severe symptoms).
- **NPI_Hallucination –** hallucinations subscale score (range 0-12 where higher scores indicate more severe symptoms).
- **NPI_Irritability –** irritability/liability subscale score (range 0-12 where higher scores indicate more severe symptoms).
- **NPI_NonMood –** non-mood domain score (range 0-12 where higher scores indicate more severe symptoms).
- **NPI_Sleep –** sleep and nighttime behavior disorders subscale score (range 0-12 where higher scores indicate more severe symptoms).

Caregiver Distress

- **Distress** – NPI caregiver distress score (range 0-60 where higher scores indicate greater caregiver distress).