CORTEXYME

GAIN Trial Top-Line Results

Investor Presentation

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Phase 2/3 GAIN Trial Top-Line Results Mark Major Milestone in Alzheimer's

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GAIN Trial demonstrated relationship of reduction of *P. gingivalis* infection and slowing of Alzheimer's disease progression

- Major milestones achieved in advancing our understanding of Alzheimer's disease and profile of atuzaginstat
- Overall cohort did not meet statistical significance in co-primary cognitive (ADAS-Cog11) and functional (ADCS-ADL) endpoints
- 57% slowing (p=0.02) of cognitive decline in pre-specified subgroup with *P. gingivalis* detected in saliva (n=242, 37% of participants) as measured by ADAS-Cog11.
- Similar results seen in prespecified subgroup of participants with high serum anti-*P. gingivalis* antibodies (n=316, 50% of participants)
- Prespecified correlations analysis: reduction of *P. gingivalis* at 24 weeks significantly correlated with benefits at the end of treatment on ADAS-Cog11, CDR-SB, MMSE, and a beneficial trend on ADCS-ADL
- Differentiated mild to moderate population, oral administration and safety profile

GAIN baseline demographics: population and stratification equivalent across groups

Parameter	Placebo	40 mg BID	80 mg BID
n	217	212	214
Mean Age at Informed Consent (years)	69.5	68.6	69.3
Sex			
Male	92 (42%)	89 (42%)	97 (45%)
Female	125 (58%)	123 (58%)	117 (55%)
Race and Ethnicity			
Black or African American	17 (8%)	12 (6%)	13 (6%)
Hispanic or Latino	25 (12%)	18 (9%)	35 (16%)
White, Not Hispanic/Latino	187 (86%)	188 (89%)	174 (81%)
Other	2 (1%)	6 (3%)	1 (1%)

Parameter	Placebo	40 mg BID	80 mg BID
MMSE*			
Moderate >=12 to <=18	110 (51%)	107 (51%)	107 (50%)
Mild >=19 to <=24	107 (49%)	105 (50%)	107 (50%)
ADAS-Cog Mean	23.9	23.5	23.7
ADCS-ADL Mean	60.4	60	59.9
ApoE4 Carriers*	140 (65%)	137 (65%)	137 (64%)
Non-Carriers	77 (36%)	75 (35%)	77 (36%)

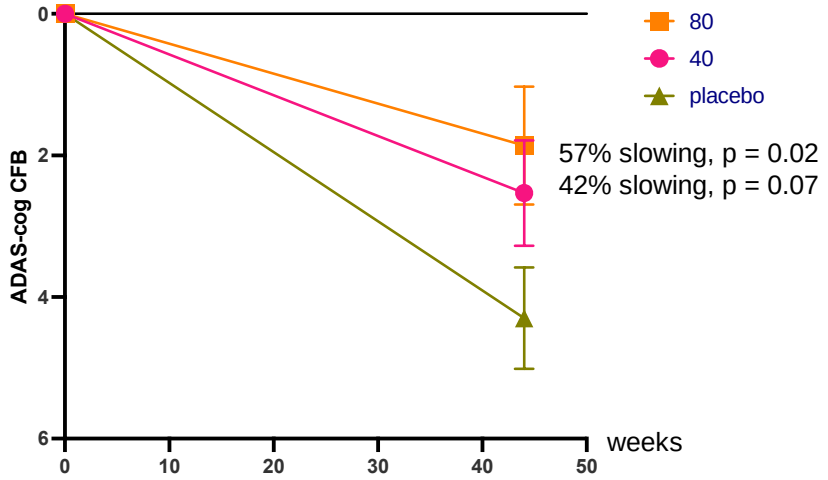
*Randomization stratified by Mild/Moderate and ApoE4 carriers +/-

ADAS-Cog benefits in prespecified subgroups based on *P. gingivalis* infection

MMRM Parametric

Interaction p value = 0.02

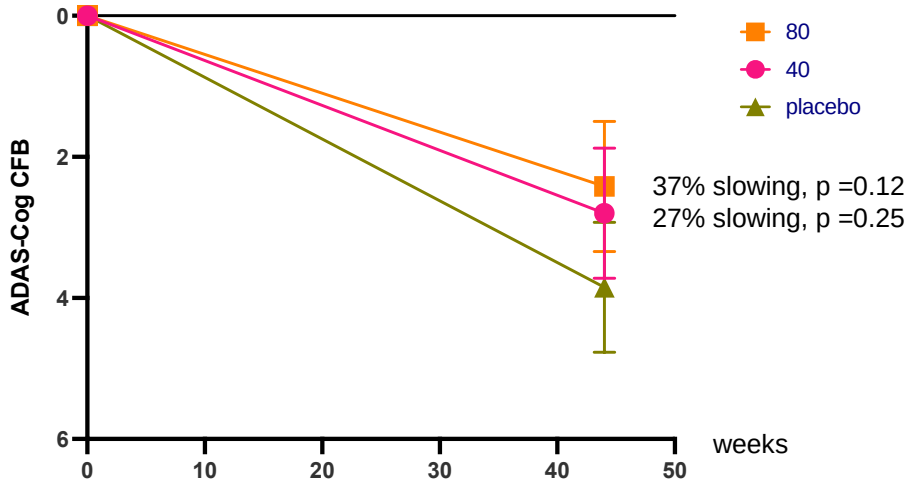
Pg-Detectable in Saliva (37%)



80	74		48
40	86		62
Placebo	82		74

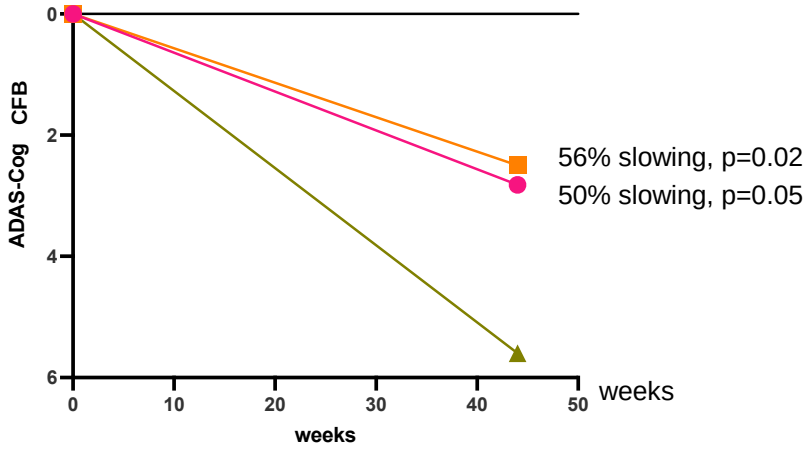
Interaction p value = 0.03

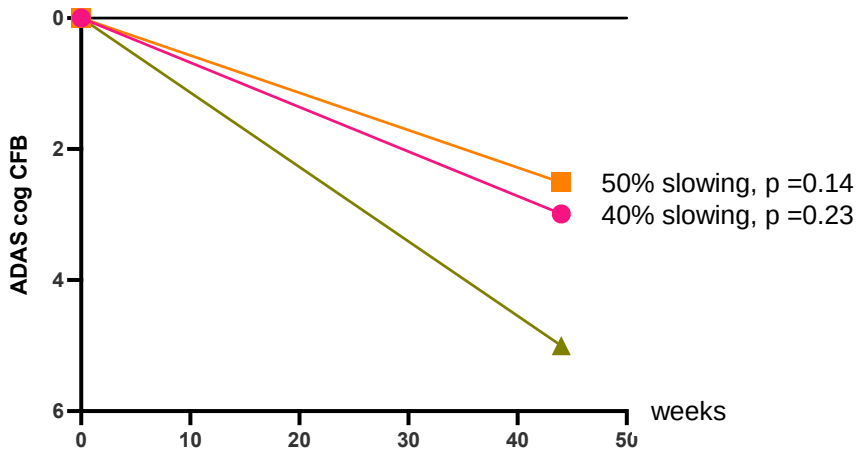
High serum anti-Pg IgG (50%)



80	99		67
40	113		75
Placebo	104		92

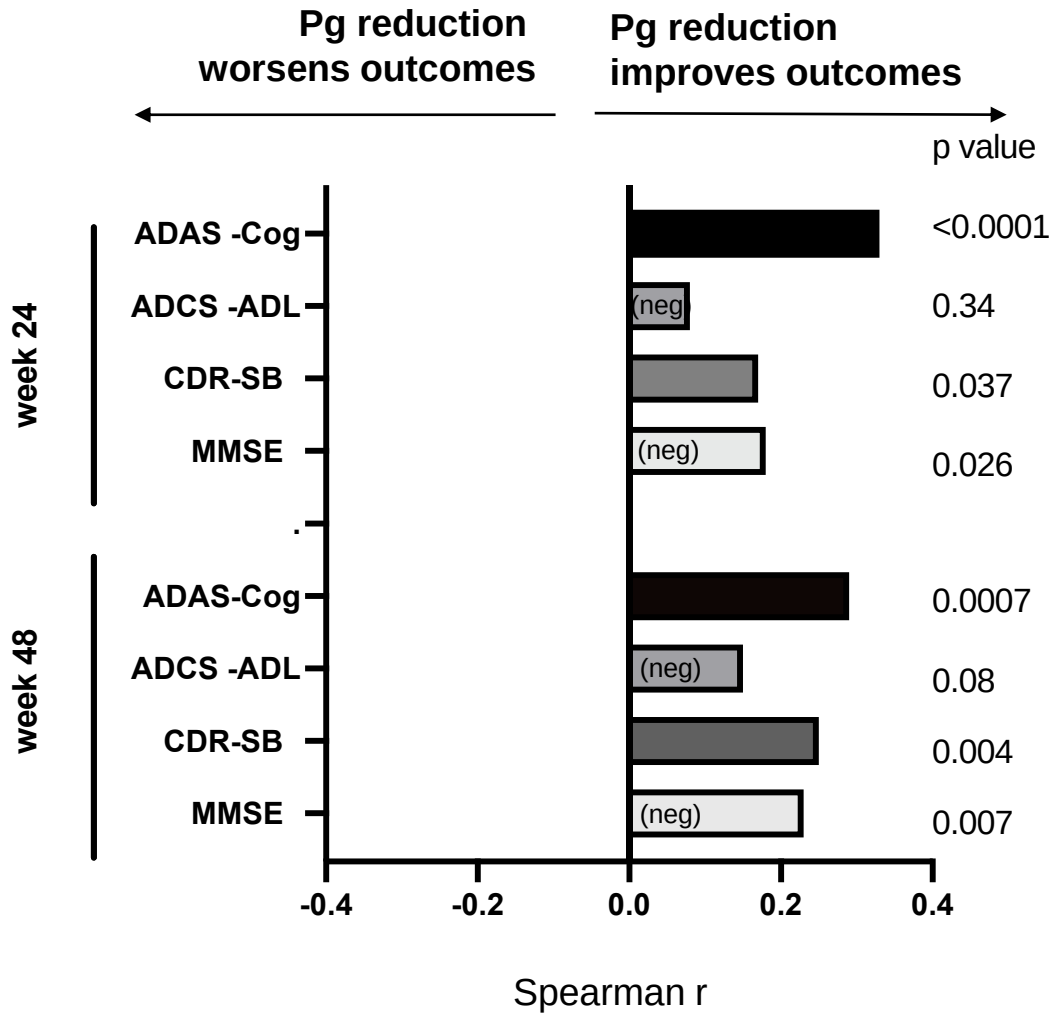
Nonparametric
analysis specified in SAP by non-normality of data





Improvement is up on all scales

Prespecified interaction of target engagement and outcomes
Change in *P. gingivalis* in saliva at 24 weeks correlates to clinical outcomes



Safety summary: Most Common Adverse Events (TEAEs)

	Placebo (n= 217)	40 mg BID (n= 212)	80 mg BID (n= 214)
Any TEAE	147 (67.7%)	170 (80.2%)	164 (76.6%)
Diarrhea	7 (3.2%)	34 (16.0%)	27 (12.6%)
ALT increased	4 (1.8%)	20 (9.4%)	37 (17.3%)
AST increased	3 (1.4%)	20 (9.4%)	34 (15.9%)
Urinary tract infection	21 (9.7%)	16 (7.5%)	28 (13.1%)
Lipase increased	11 (5.1%)	13 (6.1%)	20 (9.3%)
Headache	14 (6.5%)	18 (8.5%)	15 (7%)
Amylase increased	8 (3.7%)	12 (5.7%)	16 (7.5%)
Nausea	4 (1.8%)	13 (6.1%)	13 (6.1%)
Agitation	7 (3.2%)	9 (4.2%)	10 (4.7%)
Decreased appetite	2 (0.9%)	9 (4.2%)	10 (4.7%)
Fall	4 (1.8%)	7 (3.3%)	11 (5.1%)
Abdominal pain	3 (1.4%)	7 (3.3%)	11 (5.1%)
TEAEs potentially of interest with incidence lower than 5%:			
COVID-19	5 (2.3%)	8 (3.8%)	2 (0.9%)

FINDINGS

- Atuzaginstat is well tolerated overall
- Most common drug-associated AE: diarrhea, also associated with some other GI AEs
- Dose dependent liver enzyme elevations, may be mitigated by titration
- Virtually all cases of laboratory abnormalities were not clinically significant and were asymptomatic
- No increase in ARIA (microhemorrhage and edema) or superficial siderosis

Key takeaways

- Co-primary endpoints were not met in the broad intent-to-treat study population
- Randomized, double-blind, placebo-controlled trial results support the extensive research establishing *P. gingivalis* as a root cause of Alzheimer's Disease
- These *Pg*-AD patients are easily identified through saliva or simple blood tests, offering a convenient level of precision medicine atypical in Alzheimer's disease
- Prespecified interaction analysis shows significant interaction of high Pg subgroups with better outcomes
- Pre-specified subgroup with Pg DNA detectable in saliva (PG-DS) showed statistically and clinically significant superiority of atuzaginstat over placebo on cognition.
- Multiple pre-specified statistically and clinically significant correlations between reduction of bacterial load and improved clinical outcomes
- Differentiated safety profile, oral route of administration, patient population (both disease severity and Pg infection) from amyloid-targeted therapeutics