Table 1.

Articles on Liraglutide

Author	Study design	Age (range), y	Diagnosis	Duration	Group, n	Dose range	Scales to measure the clinical outcome	Clinical outcome	Common side effects
Gejl et al[19]	RCT	Liraglutide group = 63.1 (55–70), placebo group = 66.6 (50–80)	Alzheimer disease	26 wk	Liraglutide = 14, placebo = 20	Liraglutide 0.6 mg subcutaneously for 1 wk; thereafter, 1.2 mg daily for 1 wk before finally increasing to 1.8 mg daily	Cognition with the WMS-IV scale, tracer [carbon 11] PIB to measure Aβ load in the brain, [18F] FDG to assess glucose metabolic rate	No significant differences from baseline in total cognitive scores after treatment within or between the 2 groups. Average scores at baseline were 27.1 in the liraglutide group and 27.2 in the placebo group ($P = .99$), and no significant differences were found from baseline in total cognitive score after treatment within or between the 2 groups (liraglutide 0.43, placebo 1.7, $P = .50$)	Transient nausea, weight loss, and reduction in systolic blood pressure were noted after 6 mo of GLP-1 analog treatment
Mansur et al[20]	Open-label study	22–54	Mood disorder	4 wk	19	Liraglutide 0.6 mg for 1st wk, 1.2 mg for the next wk, and 1.8 mg for the final 2 wk	TMTB	Adjunctive liraglutide results in clinically significant weight loss, with corresponding improvement in cognitive function; changes in cognitive function were partially moderated by changes in brain morphometry, underscoring the interrelationship between weight and brain structure/function	Two participants discontinued the study due to severe nausea
O'Neil et al[21]	Post hoc analysis of 5 RCTs	No specific age range	Obesity	One phase 2 trial duration was 2 y, but only 1 y of data were included; 4 phase 3 trials, which were of 3 y, 56 wk, 56 wk, and 32 wk duration, respectively	Liraglutide = 3,384, placebo = 1,941	Liraglutide = 3.0 mg subcutaneous	PHQ-9, C-SSRS	Results of this exploratory pooled analysis provide no cause for concern regarding the neuropsychiatric safety of treatment with liraglutide 3.0 mg in patients similar to those included in the examined trials. Although there was a small numerical imbalance in suicidal ideation with liraglutide through adverse event reporting, no between-treatment imbalances in suicidal ideation/behavior or depression were noted through prospective questionnaire assessments. However, in phase 3a trials, mean baseline PHQ-9 scores of 2.8 ± 3.0 vs 2.9 ± 3.1 for liraglutide vs placebo improved to 1.8 ± 2.7 vs 1.9 ± 2.7, respectively, at treatment end	No side effects were reported

(continued)

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Li et al[22]	Open-label trial	18–65	Cognitive decline in T2DM	12 wk	Initial sample size = 50, 2 patients in control group and 1 patient in GLP-1 group quit the trial. Control group (n = 23), GLP-1 group (n = 24)	Initial liraglutide dose = 0.6 mg/day and a maximum dose = 1.8 mg/day adjusted once a week when hyperglycemia was uncontrolled	MMSE, Digit Span Test (including forward and backward), RAVLT (total learning, long-delay free recall and recognition), TMT, Clock Drawing test, Animal Naming test, Memory and Executive Screening	12 wk of treatment with liraglutide significantly improved the cognitive function in patients with T2DM compared to regular hypoglycemic treatment	No side effects were reported
Mansur et al[23]	Secondary analysis of open-label trial	18–55	MDD and bipolar disorder	4 wk	101 individuals were screened, and of those 19 were enrolled; 17 individuals completed the trial	Initial liraglutide dose = 0.6 mg/day, increased to 1.2 mg/day for the 2nd wk, and then titrated to 1.8 mg/day for the final 2 wk	TMTB, DSST, RAVLT, Stroop test, TMTA, HDRS, YMRS, SHAPS, GAF, CGI-S	The 4-wk trial was associated with significantly improved cognitive performance with increased TMTB standard score from baseline (age and education corrected) (Cohen $d = 0.64$, $P = .009$) and in a composite Z-score comprising multiple cognitive tests (ie, Digit Symbol Substitution Test, Rey Auditory Verbal Learning Test, Stroop test) (Cohen $d = 0.77$, $P < .001$)	Nausea (36.8%), dizziness (10.6%), and indigestion (10.6%). Two participants (10.6%) discontinued liraglutide due to severe nausea
Battini et al[24]	Nested case-noncase study	No specific age range	Depression and T2DM	54 y of data for 1 database, 53 y of data from second database	Database 1 = 121,368; database 2 = 85,267	None	Standardized MedDRA queries	All signal detection methodologies and disproportionality statistics investigating the GLP-1 analogs agreed on its potential antidepressant effect and showed values <1	No side effects were mentioned
Järvinen et al[25]	Case report	20	OCD associated with autism	36 wk	1	Initial liraglutide dose = 0.6 mg/day at week 1, 1.2 mg/day at week 2, 1.8 mg/day at week 4, and gradually increased to 2.4 mg/day during the following 8 wk	OCI-R	Immediate positive response was observed in the patient's food-related behavior manifesting as subsided obsessive food-related thoughts, craving for food, and compulsive eating. Obsessions, compulsions, and behavioral problems not related to food, including aggressive behavior, decreased significantly	No adverse side effects were observed

Abbreviations: CGI-S = Clinical Global Impressions–Severity of Illness, C-SSRS = Columbia-Suicide Severity Rating Scale, FDG = fluorodeoxyglucose, GAF = Global Assessment of Functioning, GLP-1 RA = glucagon-like peptide 1 receptor agonist, HDRS = Hamilton Depression Rating Scale, MedDRA = Medical Dictionary for Regulatory Activities, MMSE = Mini-Mental State Examination, OCD = obsessive-compulsive disorder, OCI-R = Obsessive-Compulsive Inventory-Revised, PDQ = Perceived Deficits Questionnaire, PHQ-9 = 9-item Patient Health Questionnaire, PIB = Pittsburgh Compound B, REY = Rey-Osterreith complex figure test, SHAPS = Snaith-Hamilton Pleasure Scale, TMTA = Trail-Making Test A, TMTB = Trail-Making Test B, WMS-IV = Wechsler Memory Scale, YMRS = Young Mania Rating Scale.