

Treatment with levodopa and other dopaminergic agents temporarily addresses the motor symptoms. However, this does not reverse, slow, or halt pathological processes related to the disease. As the disease progresses, these drugs become less effective at controlling the symptoms.

[006] Patients who take these medications often develop side effects such as motor complications (e.g., response oscillations, wearing off phenomena, and drug-induced dyskinesias), as well as nausea, daytime somnolence, sleep attacks, orthostatic hypotension, or impulse control disorders. Symptomatic treatment of non-motor symptoms of PD (e.g., sleep disturbances, anxiety, and depression) are also available. However, to date, there are no approved treatments that have demonstrated protection of neurons or modification of the disease course. There is an urgent need for new therapies that target the underlying cause of Parkinson's disease and, unlike symptomatic therapies, slow its relentless progression.

SUMMARY

[006a] In one aspect, disclosed herein is the use of Prasinezumab in the manufacture of a medicament for maintaining or slowing decline in motor function in a subject having Parkinson's disease or at risk of Parkinson's disease,

wherein the maintaining comprises reducing Parkinson's disease progression as demonstrated by delaying time to progression of at least a 5-point progression in MDS-UPDRS Part III, and the slowing decline comprises at least one of the following:

- (a) slowing decline the patient's MDS-UPDRS Part III motor examination score,
- (b) slowing decline in one or more of speech, facial expression, rigidity, finger tapping, hand movements, pronation-supination movements of hands, toe tapping, leg agility, arising from chair, gait, freezing of gait, postural stability, posture, tremor of hands, rest tremor amplitude, constancy of rest tremor, or Hoehn and Yahr Stage;
- (c) improving bradykinesia;

and wherein the medicament comprises 1000-5000 mg of Prasinezumab and is to be administered at intervals of 3 to 5 weeks.

[006b] In another aspect, disclosed herein is the use of Prasinezumab in the manufacture of a medicament for maintaining or increasing cerebral blood flow in a subject having Parkinson's disease or at risk of Parkinson's disease, wherein the medicament comprises 1000-5000 mg of Prasinezumab and is to be administered at intervals of 3 to 5 weeks.

[006c] In another aspect, disclosed herein is the use of Prasinezumab in the manufacture of a medicament for improving cognitive function in a subject having Parkinson's disease or at

risk of Parkinson's disease wherein the medicament comprises 1000-5000 mg of Prasinezumab and is to be administered at intervals of 3 to 5 weeks.

[006d] In another aspect, disclosed herein is the use of Prasinezumab in the manufacture of a medicament for treating Parkinson's disease or a subject at risk of Parkinson's disease, wherein the treating comprises

(a) reducing Parkinson's disease progression as demonstrated by delaying time to progression of at least a 5-point progression in MDS-UPDRS Part III, or

(b) slowing decline in motor function comprising at least one of the following

i. slowing decline the patient's MDS-UPDRS Part III motor examination score;

ii. slowing decline in one or more of speech, facial expression, rigidity, finger tapping, hand movements, pronation-supination movements of hands, toe tapping, leg agility, arising from chair, gait, freezing of gait, postural stability, posture, tremor of hands, rest tremor amplitude, constancy of rest tremor, or Hoehn and Yahr Stage;

iii. improving bradykinesia,

and

wherein the medicament comprises 1000-5000 mg of Prasinezumab and is to be administered at intervals of 3 to 5 weeks.

[007] In ~~one aspect another example, the invention provides~~disclosed herein is a method for maintaining or slowing decline in motor function in a subject having Parkinson's disease or at risk of Parkinson's disease comprising administering to the subject a regimen of Prasinezumab, wherein the maintaining comprises reducing Parkinson's disease progression as demonstrated by delaying time to progression of at least a 5-point progression in MDS-UPDRS Part III, and

the slowing decline comprises at least one of the following:

(a) slowing decline the patient's MDS-UPDRS Part III motor examination score,

(b) slowing decline in one or more of speech, facial expression, rigidity, finger tapping, hand movements, pronation-supination movements of hands, toe tapping, leg agility, arising from chair, gait, freezing of gait, postural stability, posture, tremor of hands, rest tremor amplitude, constancy of rest tremor, or Hoehn and Yahr Stage; or

(c) improving bradykinesia;

wherein the regimen of Prasinezumab comprises 1000-5000 mg of Prasinezumab at intervals of 3 to 5 weeks.

[008] improvement of at least 18%, 24%, 25%, 33%, 35%, or 45% compared to a placebo after one year of treatment.

[009] In another ~~aspect example, the invention provides~~disclosed herein is a method for maintaining or increasing cerebral blood flow in a subject having Parkinson's disease or at risk of Parkinson's disease comprising administering to the subject a regimen of Prasinezumab comprising 1000-5000 mg of Prasinezumab at intervals of 3 to 5 weeks.

[0010] In some ~~methods~~examples, cerebral blood flow is maintained or increased in the putamen.

[0011] In some ~~methods~~ examples, cerebral blood flow is maintained or increased in the pallidum.

[0012] In some ~~methods~~ examples, wherein cerebral blood flow is maintained or increased in the premotor cortex.

[0013] In some ~~methods~~ examples, blood flow is assessed by changes in magnetic resonance-arterial spin labeling (MRI-ASL).

[0014] In yet another ~~aspect~~ example, the invention provides a method for improving cognitive function in a subject having Parkinson's disease or at risk of Parkinson's disease comprising administering to the subject a regimen of Prasinezumab comprising 1000-5000 mg of Prasinezumab at intervals of 3 to 5 weeks.

[0015] In some ~~methods~~ examples, the subject does not have an impairment in cognitive function.

[0016] In some ~~methods~~ examples, the improvement of cognitive function is measured by Montreal Cognitive Assessment (MoCA), and wherein the improvement is at least 0.2 on a MoCa scoring scale.

[0017] In another ~~aspect~~ example, ~~the invention provides~~ disclosed herein is a method for maintaining or slowing decline in motor function in a subject having Parkinson's disease or at risk of Parkinson's disease comprising administering to the subject a regimen of Prasinezumab, wherein the maintaining comprises reducing Parkinson's disease progression as demonstrated by delaying time to progression of at least a 5-point progression in MDS-UPDRS Part III, and the slowing decline comprises at least one of the following:

- (a) slowing decline the patient's MDS-UPDRS Part III motor examination score,
- (b) slowing decline in one or more of speech, facial expression, rigidity, finger tapping, hand movements, pronation-supination movements of hands, toe tapping, leg agility, arising from chair, gait, freezing of gait, postural stability, posture, tremor of hands, rest tremor amplitude, constancy of rest tremor, or Hoehn and Yahr Stage; or
- (c) improving bradykinesia;

wherein the regimen of Prasinezumab comprises 1000-5000 mg of Prasinezumab at intervals of 3 to 5 weeks.

[0018] In some ~~methods~~ examples, the subject has been diagnosed as a mild motor-predominant subtype, a diffuse-malignant subtype, or an intermediate subtype of Parkinson's, and in some ~~methods~~ examples, the subject has been diagnosed as a diffuse-malignant subtype of Parkinson's disease.

| [0019] In some ~~methods~~ examples, the slowing decline of the patient's motor examination score comprises an improvement of at least 4%, 17%, 18%, 24%, 25%, 33%, 35%, 39%, 45%,

52%, 63%, 64%, 68%, 71%, 74%, 76%, or 109% compared to a placebo after one year of treatment.

[0020] In some ~~methods~~ examples, the Prasinezumab is administered intravenously.

[0021] In some ~~methods~~ examples, the method further comprises administering to the subject a MAO-B inhibitor.

[0022] In some ~~methods~~ examples, the subject is treatment naïve, was diagnosed as having PD in the last two years, or was previously treated with a MAO-B inhibitor.

[0023] In some ~~methods~~ examples, the subject has a weight greater than 65 kg and is administered a dose of 4500 mg Prasinezumab once every 4 weeks.

[0024] In some ~~methods~~ examples, the subject has a weight less than 65 kg and is administered a dose of 3500 mg Prasinezumab once every 4 weeks.

[0025] In some ~~methods~~ examples, the subject is administered a dose of 1500 mg antibody every 4 weeks.

[0026] In some ~~methods~~ examples, the subject receives Prasinezumab once every 4 weeks for at least 52 weeks.

[0027] In some ~~methods~~ examples, the subject is male.

[0028] In another ~~aspect example~~, the invention provides disclosed herein is a method of treating a subject having Parkinson's disease or at risk of Parkinson's disease comprising administering to the subject a regimen of Prasinezumab, wherein the treating comprises

(a) reducing Parkinson's disease progression as demonstrated by delaying time to

progression of at least a 5-point progression in MDS-UPDRS Part III, or

(b) slowing decline in motor function comprising at least one of the following:

(i) slowing decline the patient's MDS-UPDRS Part III motor examination score;

(ii) slowing decline in one or more of speech, facial expression, rigidity, finger tapping, hand movements, pronation-supination movements of hands, toe tapping, leg agility, arising from chair, gait, freezing of gait, postural stability, posture, tremor of hands, rest tremor amplitude, constancy of rest tremor, or Hoehn and Yahr Stage;

(iii) improving bradykinesia,

wherein the regimen of Prasinezumab comprises 1000-5000 mg of Prasinezumab at intervals of 3 to 5 weeks.

[0029] In some ~~methods~~ examples, the subject has been diagnosed as a mild motor-predominant subtype, a diffuse-malignant subtype, or an intermediate subtype of Parkinson's, and in some

~~methods~~examples, the subject has been diagnosed as a diffuse-malignant subtype of Parkinson's disease.

[0030] In some ~~methods~~ examples, the slowing decline of the patient's motor examination score comprises an improvement of at least 4%, 17%, 18%, 24%, 25%, 33%, 35%, 39%, 45%, 52%, 63%, 64%, 68%, 71%, 74%, 76%, or 109% compared to a placebo after one year of treatment.

[0031] In some ~~methods~~ examples, the Prasinezumab is administered intravenously.

[0032] In some ~~methods~~ examples, the method further comprises administering to the subject a MAO-B inhibitor.

[0033] In some ~~methods~~ examples, the subject is treatment naïve, was diagnosed as having PD in the last two years, or was previously treated with a MAO-B inhibitor.

[0034] In some ~~methods~~ examples, the subject has a weight greater than 65 kg and is administered a dose of 4500 mg Prasinezumab once every 4 weeks.

[0035] In some ~~methods~~ examples, the subject has a weight less than 65 kg and is administered a dose of 3500 mg Prasinezumab once every 4 weeks.

[0036] In some ~~methods~~ examples, the subject is administered a dose of 1500 mg antibody every 4 weeks.

[0037] In some ~~methods~~ examples, the subject receives Prasinezumab once every 4 weeks for at least 52 weeks.

[0038] In some ~~methods~~ examples, the subject is male.

BRIEF DESCRIPTION OF THE DRAWINGS

[0039] **FIG. 1** shows the change in total MDS-UPDRS score (Parts I, II, and III) from baseline to Week 52. Patients who started symptomatic PD treatment contribute until the last visit before symptomatic PD treatment is started. The results show that change from baseline in the MDS-UPDRS total score (Parts I, II, and III) at 52 weeks in each treatment group versus the placebo group was not met (pooled dose levels: -14.0%, -1.30, 80% CI=(-3.18, 0.58); low dose level: -21.5%, -2.02, 80% CI=(-4.21, 0.18); and high dose level: -6.6%, -0.62, 80% CI=(-2.82, 1.58)). Bars represent 80% CI. MDS-UPDRS, Movement Disorder Society Unified Parkinson's Disease Rating Scale.

[0040] **FIG. 2** shows improvement in the MoCA score from baseline to Week 52. MoCA (Montreal Cognitive Assessment) is a 30 point-scale and a higher score indicates better cognitive performance. On average, prasinezumab-treated patients were in the cognitively