De vele gezichten van de ziekte van Parkinson

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Indeling

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Inleiding

- NL 50000 Parkinson patiënten
- Verdubbeling in de komende 20 jaar
- Opleiding neurologie: “de Parkinsonpatiënt”

Inleiding

- Parkinson is een heterogeen beeld
- Parkinson kan binnen een patiënt wisselen
- Parkinson wordt door iedere patiënt anders ervaren
- Behandeling afstemmen op/met de individuele patiënt

Literatuur

- Motor fenotype (tremor dominant-akinetisch rigide-PIGD (posturele instabiliteit en gangstoornissen)
- Leeftijd van begin (vroeg versus laat)
- Niet motore verschijnselen op de voorgrond
- Genetische vormen

Literatuur

- Parkinson is een verzameling van onderliggende aandoeningen, elk met unieke genetische, biologische en moleculaire afwijkingen
- Het klinisch beeld, de progressie en behandelrespons zijn bij iedere patiënt anders

Parkinson op Maat

- Big data studie, gestart 2017
- 500+ mensen 2 jaar volgen
- Radboud UMC
- Co-design met patiënten

parkinson op maat

Parkinson op Maat

- biomarkers: kliniek, beeldvorming, biochemie en genetica
- valideren van bestaande biomarkers
- identificeren van nieuwe biomarkers
- voorspellen van verschillen in prognose en behandelrespons tussen patiënten
- secundaire doelstelling: Verily study watch

Parkinson op Maat

- richting meer gepersonaliseerde zorg
- meer maatwerk in de behandeling en begeleiding toegesneden op de individuele kenmerken van iedere patiënt

parkinson op maat

Parkinson op Maat

TABEL 1. In- en exclusiecriteria van de Parkinson Op Maat-studie.
Inclusiecriteria
Ziekteduur ≤5 jaar, gedefinieerd als de tijd sinds de diagnose is gesteld door een neuroloog
≥18 jaar
In staat Nederlands te lezen en begrijpen
Bereid, competent en in staat om te voldoen aan alle aspecten van het protocol
Bereid om schriftelijk 'informed consent' te tekenen
Exclusiecriteria
Comorbiditeit die de interpretatie van de parkinsonsymptomen belemmert
Contra-indicaties voor MRI
Zwangerschap of borstvoeding
Nikkelallergie (omdat componenten van de smartwatch nikkel bevatten)

Parkinson op Maat

FIGUUR 1. Overzicht van alle metingen binnen de Parkinson Op Maat-studie.

Parkinson op Maat

- Klinische beoordeling (inclusief NPO)
- Biospecimens (feces, bloed, *liquor*)
- MRI brein
- ECG/Holter
- Smartwatch 2 jaar dragen
- Thuis vragenlijsten

Parkinson op Maat

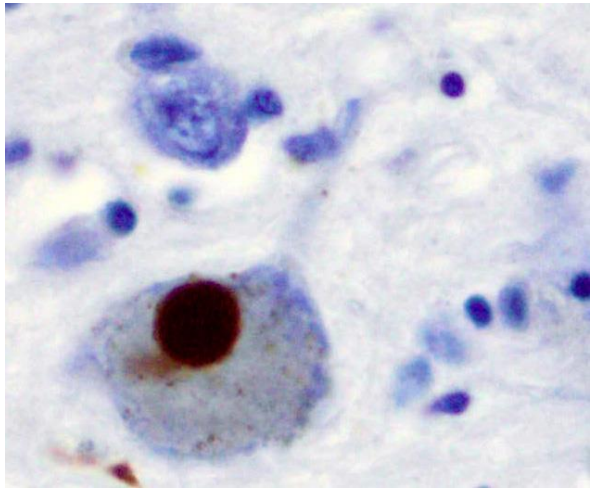
- november 2017 eerste deelnemer, inclusie afgerond
- augustus 2020: Parkinson de novo (<2 jaar), geen parkinsonmedicatie

Parkinson op Maat

- En nu afwachten…

Ander nieuws

- 2 grote studies met MABs bij vroeg PD: negatief
- Orchestra studie loopt



- Background: Parkinson's disease (PD) and its progression are thought to be caused and driven by misfolding of α-synuclein (ASYN). UCB0599 is an oral, small-molecule inhibitor of ASYN misfolding, aimed at slowing disease progression.

ORIGINAL ARTICLE

Trial of Cinpanemab in Early Parkinson's Disease

A.E. Lang, A.D. Siderowf, E.A. Macklin, W. Poewe, D.J. Brooks, H.H. Fernandez, O. Rascol, N. Giladi, F. Stocchi, C.M. Tanner, R.B. Postuma, D.K. Simon, E. Tolosa, B. Mollenhauer, J.M. Cedarbaum, K. Fraser, J. Xiao, K.C. Evans, D.L. Graham, I. Sapir, J. Inra, R.M. Hutchison, M. Yang, T. Fox, S. Budd Haeberlein, and T. Dam, for the SPARK Investigators*

ABSTRACT

BACKGROUND

Aggregated α-synuclein plays an important role in Parkinson's disease pathogenesis. Cinpanemab, a human-derived monoclonal antibody that binds to α-synuclein, is being evaluated as a disease-modifying treatment for Parkinson's disease.

METHODS

In a 52-week, multicenter, double-blind, phase 2 trial, we randomly assigned, in a 2:1:2:2 ratio, participants with early Parkinson's disease to receive intravenous infusions of placebo (control) or cinpanemab at a dose of 250 mg, 1250 mg, or 3500 mg every 4 weeks, followed by an active-treatment dose-blinded extension period for up to 112 weeks. The primary end points were the changes from baseline in the Movement Disorder Society–sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) total score (range, 0 to 236, with higher scores indicating worse performance) at weeks 52 and 72. Secondary end points included MDS-UPDRS subscale scores and striatal binding as assessed on dopamine transporter single-photon-emission computed tomography (DaT-SPECT).

RESULTS

Of the 357 enrolled participants, 100 were assigned to the control group, 55 to the 250-mg cinpanemab group, 102 to the 1250-mg group, and 100 to the 3500-mg group. The trial was stopped after the week 72 interim analysis owing to lack of efficacy. The change to week 52 in the MDS-UPDRS score was 10.8 points in the control group, 10.5 points in the 250-mg group, 11.3 points in the 1250-mg group, and 10.9 points in the 3500-mg group (adjusted mean difference vs. control, −0.3 points [95% confidence interval [CI], −4.9 to 4.3], P=0.90; 0.5 points [95% CI, −3.3 to 4.3], P=0.80; and 0.1 point [95% CI, −3.8 to 4.0], P=0.97, respectively). The adjusted mean difference at 72 weeks between participants who received cinpanemab through 72 weeks and the pooled group of those who started cinpanemab at 52 weeks was −0.9 points (95% CI, −5.6 to 3.8) for the 250-mg dose, 0.6 points (95% CI, −3.3 to 4.4) for the 1250-mg dose, and −0.8 points (95% CI, −4.6 to 3.0) for the 3500-mg dose. Results for secondary end points were similar to those for the primary end points. DaT-SPECT imaging at week 52 showed no differences between the control group and any cinpanemab group. The most common adverse events with cinpanemab were headache, nasopharyngitis, and falls.

CONCLUSIONS

In participants with early Parkinson's disease, the effects of cinpanemab on clinical measures of disease progression and changes in DaT-SPECT imaging did not differ from those of placebo over a 52-week period. (Funded by Biogen; SPARK Clinical Trials.gov number, NCT03318523.)

ORIGINAL ARTICLE

Trial of Prasinezumab in Early-Stage Parkinson's Disease

G. Pagano, K.I. Taylor, J. Anzures-Cabrera, M. Marchesi, T. Simuni, K. Marek, R.B. Postuma, N. Pavese, F. Stocchi, J.-P. Azulay, B. Mollenhauer, L. López-Manzanares, D.S. Russell, J.T. Boyd, A.P. Nicholas, M.R. Luquin, R.A. Hauser, T. Gasser, W. Poewe, B. Ricci, A. Boulay, A. Vogt, F.G. Boess, J. Dukart, G. D'Urso, R. Finch, S. Zanigni, A. Monnet, N. Pross, A. Hahn, H. Svoboda, M. Britschgi, F. Lipsmeier, E. Volkova-Volkmar, M. Lindemann, S. Dziadek, Š. Holiga, D. Rukina, T. Kustermann, G.A. Kerchner, P. Fontoura, D. Umbricht, R. Doody, T. Nikolcheva, and A. Bonni, for the PASADENA Investigators and Prasinezumab Study Group*

ABSTRACT

BACKGROUND

Aggregated α-synuclein plays an important role in the pathogenesis of Parkinson's disease. The monoclonal antibody prasinezumab, directed at aggregated α-synuclein, is being studied for its effect on Parkinson's disease.

METHODS

In this phase 2 trial, we randomly assigned participants with early-stage Parkinson's disease in a 1:1:1 ratio to receive intravenous placebo or prasinezumab at a dose of 1500 mg or 4500 mg every 4 weeks for 52 weeks. The primary end point was the change from baseline to week 52 in the sum of scores on parts I, II, and III of the Movement Disorder Society–sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS; range, 0 to 236, with higher scores indicating greater impairment). Secondary end points included the dopamine transporter levels in the putamen of the hemisphere ipsilateral to the clinically more affected side of the body, as measured by ^{123}I-ioflupane single-photon-emission computed tomography (SPECT).

RESULTS

A total of 316 participants were enrolled; 105 were assigned to receive placebo, 105 to receive 1500 mg of prasinezumab, and 106 to receive 4500 mg of prasinezumab. The baseline mean MDS-UPDRS scores were 32.0 in the placebo group, 31.5 in the 1500-mg group, and 30.8 in the 4500-mg group, and mean (±SE) changes from baseline to 52 weeks were 9.4±1.2 in the placebo group, 7.4±1.2 in the 1500-mg group (difference vs. placebo, −2.0; 80% confidence interval [CI], −4.2 to 0.2; P=0.24), and 8.8±1.2 in the 4500-mg group (difference vs. placebo, −0.6; 80% CI, −2.8 to 1.6; P=0.72). There was no substantial difference between the active-treatment groups and the placebo group in dopamine transporter levels on SPECT. The results for most clinical secondary end points were similar in the active-treatment groups and the placebo group. Serious adverse events occurred in 6.7% of the participants in the 1500-mg group and in 7.5% of those in the 4500-mg group; infusion reactions occurred in 19.0% and 34.0%, respectively.

CONCLUSIONS

Prasinezumab therapy had no meaningful effect on global or imaging measures of Parkinson's disease progression as compared with placebo and was associated with infusion reactions. (Funded by F. Hoffmann–La Roche and Prothena Biosciences; PASADENA ClinicalTrials.gov number, NCT03100149.)

Ander nieuws

- Positieve kanten van de ziekte van Parkinson?

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COMMENT OPEN

Check for updates

The silver linings of Parkinson's disease

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Parkinson's disease (PD) is a neurodegenerative condition, characterized by motor, non-motor disability, and a reduced quality of life. Stimulated by a question raised by a person with PD, we posted an orienting survey on social media, asking whether there is possibly any "silver lining" (an upside) to having PD. Most respondents identified one or more positive changes, mainly a new focus in life, better coping skills, new activities, healthier lifestyle, and improved relationships with relatives and friends. This ability to perceive a silver lining of disease is in line with the concept of adversarial growth in illness, and positive health, which underscores resilience, self-management, and the ability to adapt. Importantly, not every respondent identified an upside to living with PD, so this is very much an example of personalized medicine. This is a delicate, difficult issue, and discussing the presence of silver linings may feel counterintuitive. However, exploring this issue may help people with PD and caregivers to better deal with the disease, and allow medical professionals to provide better support, to learn about coping strategies, to understand the degree of disease acceptance, and to enhance a healthier lifestyle. Further research should demonstrate whether addressing silver linings may impact positively on the outcome of PD and on the perceived quality of life. To facilitate this process, we have adapted a pre-existing silver lining questionnaire (SLQ-38) in light of the responses provided by people with PD, to offer a simple, feasible tool to further explore this issue in clinical and research settings.

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Table 1. Possible silver linings of Parkinson's disease.

Silver lining (*n*, %)	Example
Better and improved focus in life, increased awareness (*n* = 73, 65%)	*I have learned the real value of life in all its beauty and complexity. The limitations of movement when Parky is at play, has given me an appreciation and joy of movement and the gratitude of modern medicine and the drugs and medicines, which have made my life possible and often pleasurable. I have learned patience and how to accept the loss of the illusion that I can control all situations. But the most important lesson I have learned is the grace of gratitude for life itself and all I have been given.*
New relationships, activities, interests (*n* = 46, 41%)	*I began to share my PD diagnosis with family, friends and to total strangers through interviews on radio and TV and by sharing my journey through my podcast, "When Life Gives You Parkinson's." I have impacted the world in a more positive way through my podcast and personal connections in three years with Parkinson's than I have in 35 years in radio. I used to have a job, now I have a purpose.*
Engagement with the PD community (*n* = 20, 18%)	*I cycled through the Czech Republic and Slovakia (…), and through the Parkinson's Association I meet other people again (…) I come into contact with numerous people I would never have seen otherwise, and in places I would never have been otherwise.*
Travelling (*n* = 14, 12%)	*When first diagnosed, I heard about 'Parky Perks' —the unexpected good things that come out of having a diagnosis of Parkinson's. For me, they are mainly in the form of the many wonderful people I have met and some fantastic experiences I have had (eg Cycling Vietnam to Cambodia and Land's End to John O'Groats) that I would otherwise not have had.*
Improved relationship with family, friends (*n* = 39, 35%)	*Her husband told her that there are some diseases that you need to follow in love with, and he will just do it with her and for her.*
Better coping skills (*n* = 39, 35%)	*Even beyond Parkinson's, this disease can teach one they're able to handle much more than previously believed. This then can be extended to understand one has substantial control over their response to a situation even with limited control over its occurrence. Not a really advantage, but an opportunity to grow up*
Healthier lifestyle (*n* = 25, 22%)	*I started exercising, eating healthily and more consciously, meditating, and feeling better than I had in years.*
Improved self-esteem (*n* = 24, 21%)	*Developing a sense of self-compassion. More peace in myself, less fighting but letting it happen, I can handle it. I know my limits and how I can and want to deal with them.*
Improved professional life, starting new projects (*n* = 19, 17%)	*So I also found nice (voluntary) work again. And now I am also asked more and more to do other things. I feel very honoured with what I can do now. I have rediscovered a little world (just like the one I used to live in at P&G) in which I can do what I like and which is appreciated. I belong!*
Reduction of time devoted to work (*n* = 16, 14%)	*I am indeed more at home and enjoy my family and certainly my grandchildren more. That's something I would never have done if I hadn't had the disease, because you would have kept working 40 h a week.*
Increased creativity, artistic skills (*n* = 7, 6%)	*I draw more freely and therefore more beautifully than before (…) I can sometimes make good use of the tremor when colouring larger areas.*

The left column depicts the main categories, while the right column provides an example for each category. The number of responses and proportion are shown between parentheses.

Ander nieuws

- Sport en PD
- Leefstijl en PD

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Editorial

Inhibition of Neuroinflammation May Mediate the Disease-Modifying Effects of Exercise: Implications for Parkinson's Disease

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The Association Between Lifestyle Factors and Parkinson's Disease Progression and Mortality

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Abstract

Background: Lifestyle factors may contribute to the development of Parkinson's disease, but little is known about factors that influence progression. The objective of the current study was to examine whether caffeine or alcohol consumption, physical activity, or cigarette smoking is associated with progression and survival among PD patients.

Methods: We assessed lifelong coffee, tea, and alcohol consumption, smoking, and physical activity in a prospective community-based cohort (n = 360). All patients were passively followed for mortality (2001–2016); 244 were actively followed on average ± SD 5.3 ± 2.1 years (2007–2014). Movement disorder specialists repeatedly assessed motor function (Hoehn & Yahr) and cognition (Mini-Mental State Exam). We used Cox proportional hazards models and inverse probability weights to account for censoring.

Results: Coffee, caffeinated tea, moderate alcohol consumption, and physical activity were protective against at least 1 outcome. Smoking and heavy alcohol consumption were associated with increased risks. Coffee was protective against time to Hoehn & Yahr stage 3 (hazard ratio,

Take home message

- De ziekte van Parkinson is heterogeen
- Personalized medicine
- Parkinson op Maat studie
- Studies met MABs helaas negatief
- Belang leefstijl (oa sport)

BEDANKT VOOR UW AANDACHT.

ZIJN ER NOG VRAGEN?

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