CDNF in the First-in-Human Clinical Trial

12 months clinical data on the monthly infusions of CDNF directly into a targeted area of the brain of people living with Parkinson's

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And

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TreatER Webcast

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The Clinical Trial

The primary endpoint of this First-in-Human study was safety and tolerability

- secondary endpoints included evaluation of efficacy of CDNF

17 patients with Parkinson's disease

The clinical trial was conducted at 3 clinical sites and 2 PET centers in Finland and Sweden

- Karolinska University Hospital, Stockholm, Sweden
- Skåne University Hospital, Lund, Sweden
- Helsinki University Hospital, Finland
- Karolinska Institute PET centre, Sweden
- Turku PET centre, Finland

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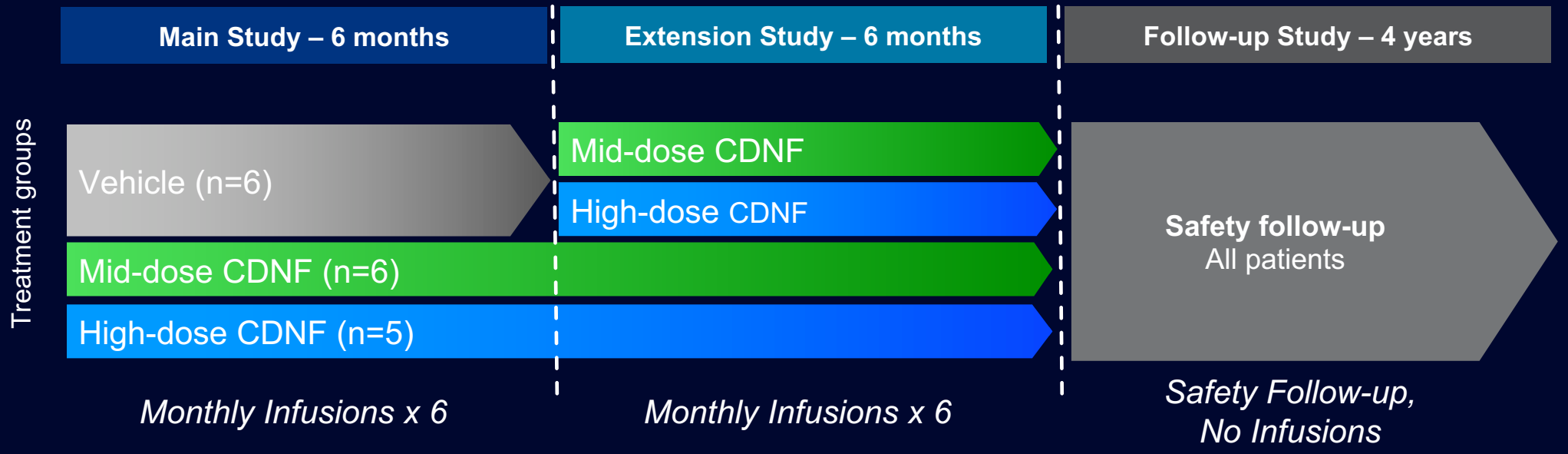
The Clinical Trial Design and Characteristics



Characteristic	**Placebo** n=6	**CDNF** (low-mid-mid) n=6	**CDNF** (low-mid-high) n=5
Age (years)	63.8 ± 6.4	63.2 ± 8.9	57.8 ± 6.7
Disease duration since first motor symptoms (years)	10.5 ± 2.7	10.7 ± 3.1	10.8 ± 2.3

OFF-symptoms more than 4 hours average per day

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Clinical Trial Procedures

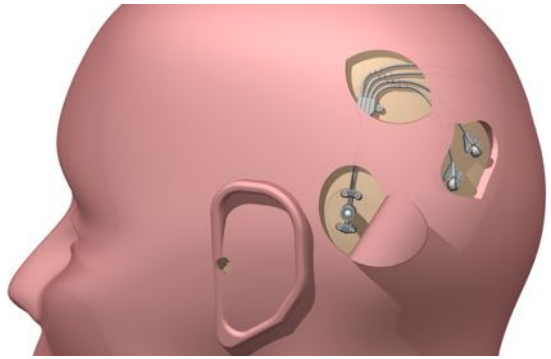
Altogether 26 Visits Over A Period Of 16 Months
- 12 treatment infusions, once every month

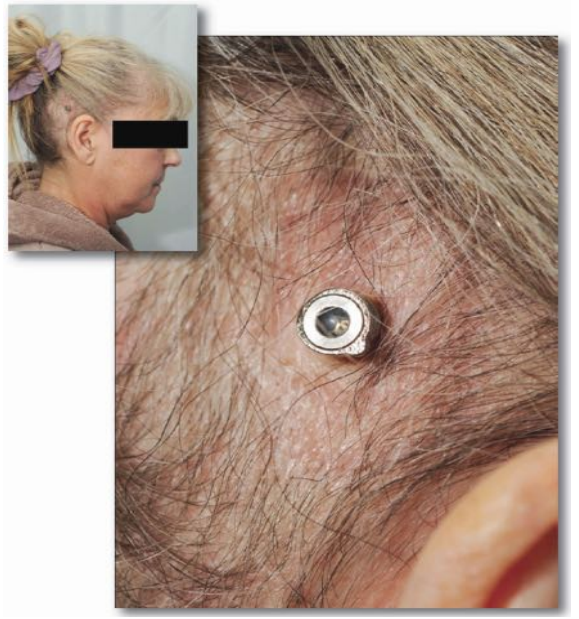
Many Scans Taken For Surgical Planning And Safety

Neurosurgical Implantation Of The Drug Delivery Device

Several Off-medication Session With Stay Overnight, Travel to PET-Centre, Diary to Maintain, etc.

- **Daily Maintenance Of The Skin Around The Port**
- Very intense period for both the patients and the clinic personnel





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Renishaw's Drug Delivery System

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CDNF in the First-in-Human clinical trial

12 Months Primary Endpoint - Safety

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Safety Assessment During the Clinical Trial

Safety Was Assessed At Any Time During The Study:

- By asking the patient if they have experienced **any new adverse events** since the previous visit, also events unrelated to the study treatment

Laboratory Blood And Urine Testing At Every Visit

- Also testing for anti-CDNF antibodies

Physical Examination At Screening, Before Treatment Start And Every Six Months

- Included neurological examination
- ECG

Brain MRI Every Three Months

- Every 3 months completion of **questionnaires** related to cognition, depression and impulsive-compulsive behavior
- **Extra visits for follow-up of adverse events**

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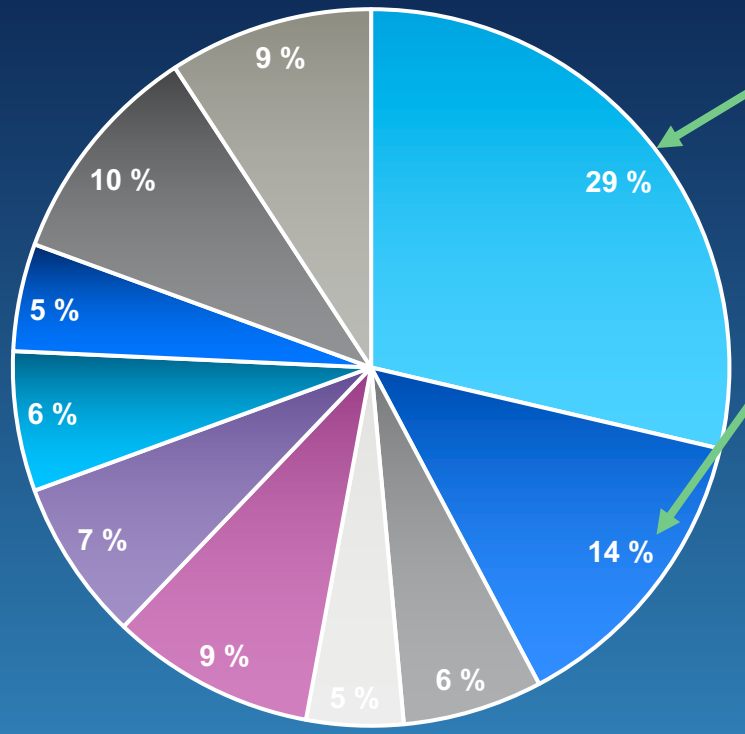
Observed Adverse Events* Profile



- NERVOUS SYSTEM DISORDERS
- GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS
- PSYCHIATRIC DISORDERS
- INJURY, POISONING AND PROCEDURAL COMPLICATIONS
- INFECTIONS AND INFESTATIONS
- GASTROINTESTINAL DISORDERS
- MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS
- SKIN AND SUBCUTANEOUS TISSUE DISORDERS
- INVESTIGATIONS (BLOOD AND URINE TESTING)
- OTHER

* Includes all adverse events after first treatment dosing; both related and unrelated to treatment

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The Most Common Reported Drug-Related Adverse Events

Altogether **68 Drug-related Adverse Events** Were Reported During the 12-Month Treatment Period

Were Mild to Moderate, and Majority Has Recovered:

Central Nervous System Disorders

Dyskinesias, Headache, small air bubbles in brain

General Disorders

Feeling cold, Fever, Tiredness

Other Disorders

Weight loss

Psychiatric Disorders

Impulse-control disorder

Gastrointestinal Disorders

Nausea

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Serious Adverse (Device) Events

Altogether **9 serious adverse (device) events** were reported in the Main and Extension study:

- **1 serious** event occured **prior to surgery** or treatment start – purulent sinusitis
- **5 serious** adverse events occuring **after surgery, prior to treatment start**:
  - Confusion (2x)
  - Infection of the skin around the port
  - Skin tissue decay (necrosis) around the port
  - Wrist fracture after a fall
- **3 serious** adverse events occuring **during treatment**:
  - Brain abscess (2x)
  - General infection, not specified

All Recovered from Serious Adverse (Device) Events

Infectious events:

- Brain abscess occured in Main study during the first 6-month period
- Port skin necrosis in Main study during the first 6-month period

Risk mitigation improvements made to surgical procedure, infusion procedure, device maintenance procedure, and additional training of investigators

After risk mitigation improvements, **87 infusions conducted without** infusion procedure-related infections or other procedure-related **AEs**

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Summary of 12-Month Safety Data

12 Monthly Intracerebral Doses of **CDNF was Safe and Well-Tolerated**

Majority of the Reported Drug-related **Adverse Events Were Mild And all Patients have Recovered**

Similar Safety Profile in Main and Extension Study, Less Reported Adverse Events in Extension

- **No clear difference** in **safety profile** between treatment groups
- **No dose-limiting toxic effects** of the drug were observed

i. CDNF Confirmed Safe & Well Tolerated ⇒ Drug Safety Established

ii. Drug-Device Combination ⇒ Safety Improvements Made During The Study

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