

# Single Day Event

## Cognitive health monitoring through RShiny

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Novo Nordisk



# Disclaimer

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# Introduction

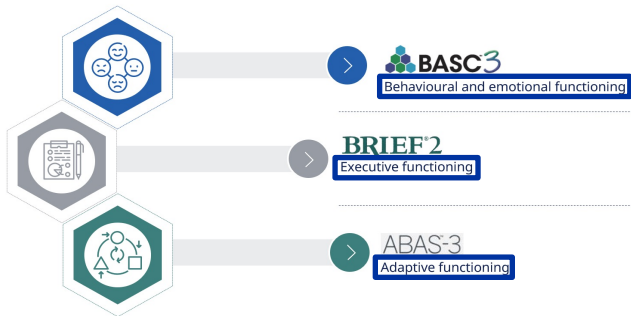
In haemophilia, an inherited bleeding disorder, coagulation factors are used for the management and prevention of bleeds

For approval of a new recombinant pegylated coagulation factor product, health authorities requested assessment of neurodevelopment in paediatric participants

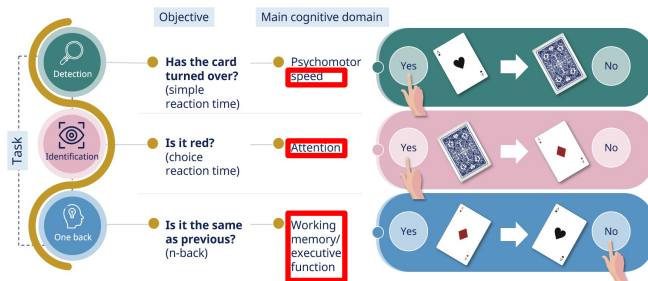
To study this, Several assessments were implemented and evaluated by an external expert panel

# Neurocognitive assessment

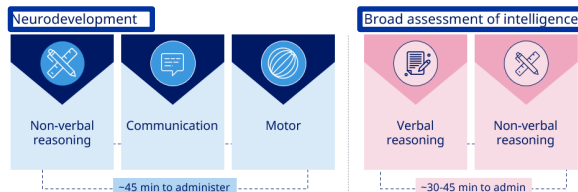
## Parent/caregiver and self-report ratings



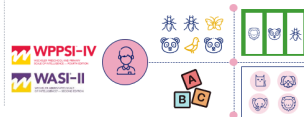
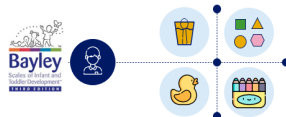
## Computerized Performance Test (Cogstate) – research tool



## Standardized Performance-Based Tests (Psychologist)



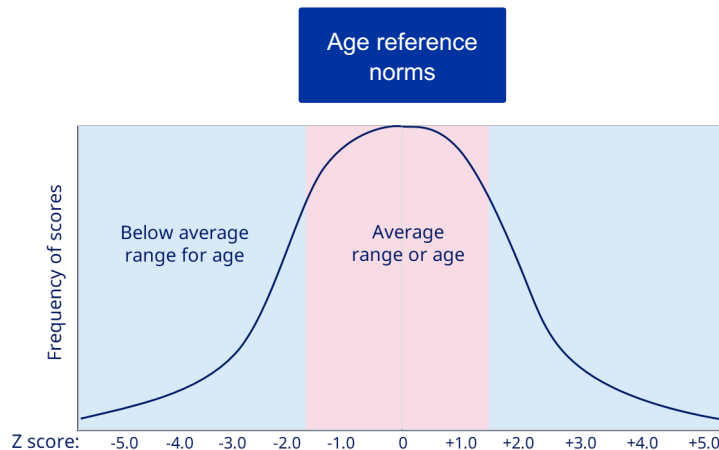
Choice of instruments depends on patient's age and language



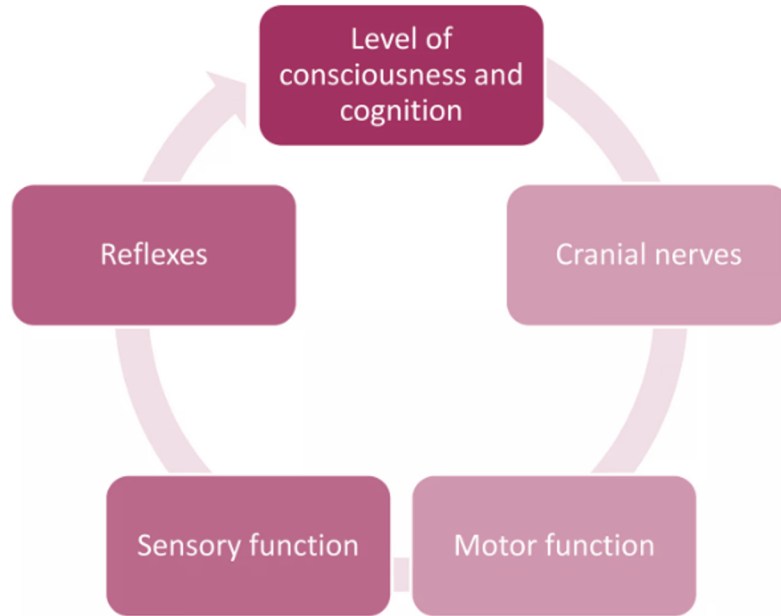
# Normalization of scores

- A separate study was performed to find a baseline in a corresponding population
- To make scores comparable to the base group z-scores were calculated considering above mentioned study as base group

$$\text{Z-score} = \frac{x - \mu}{\sigma}$$



# Neurological Examinations



- General
- Cranial nerves
- Coordination and fine motor function
- Reflexes
- Sensory function
- Gait
- Strength
- Tone

# Assessments overview by age-groups

| Subject Age       | Examination     | Neurodevelopment<br>General Cognitive<br>Intelligence                             | Attention<br>Processing Speed                                                                                          | Executive Function                                                                                              | Behavioral                                                                                                                     | Adaptive                                                                                                            |
|-------------------|-----------------|-----------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------|
| 12 to 24 months   | Neurologic Exam |  |                                                                                                                        |                                                                                                                 |                                                                                                                                |                                                                                                                     |
| 24 to 42 months   |                 |                                                                                   |                                                                                                                        | 2:0-5:11y Parent<br>         | PRS-P Parent 2-5<br>                        | 0-5y Parent<br>                  |
| 4 to 5:11 years   | Neurologic Exam |  | Custom Battery –<br>Peds (4-9)<br>    |                                                                                                                 | PRS-C Parent 6-11<br>                       |                                                                                                                     |
| 6 to 6:11 years   | Neurologic Exam |                                                                                   |                                                                                                                        |                                                                                                                 | PRS-C Parent 6-11<br>SRP-C 8-11<br>         |                                                                                                                     |
| 7 to 7:11 years   | Neurologic Exam |  | Custom Battery –<br>Adult (10-21)<br> | 5-18y Parent<br>             |                                                                                                                                |                                                                                                                     |
| 8 to 9:11 years   | Neurologic Exam |                                                                                   |                                                                                                                        |                                                                                                                 | PRS-A Parent 12-21<br>SRP-A 12-21<br>       |                                                                                                                     |
| 10 to 10:11 years | Neurologic Exam |                                                                                   |                                                                                                                        |                                                                                                                 |                                                                                                                                | 5-21y Parent<br>                 |
| 11 to 11:11 years | Neurologic Exam |                                                                                   |                                                                                                                        | 5-18y Parent<br>11-17 SR<br> |                                                                                                                                |                                                                                                                     |
| 12-15 years       | Neurologic Exam |                                                                                   |                                                                                                                        |                                                                                                                 | PRS-A Parent 12-21<br>SRP College 18-25<br> |                                                                                                                     |
| 16-17 years       | Neurologic Exam |                                                                                   |                                                                                                                        |                                                                                                                 |                                                                                                                                | 16-29y Parent<br>16-89 Adult<br> |
| 18-21 years       | Neurologic Exam |                                                                                   |                                                                                                                        | 18-90 Adult<br>              |                                                                                                                                |                                                                                                                     |



# External Expert Review Panel



## Panel consists of

- Chair
- Neuropsychologists
- Neurologist
- Haematologist

## Evaluation of subjects

- Each individual profile is reviewed
- Categorisation of evaluation
  - Contributing factors (yes/no)
  - Clinical concern (yes/no)



# Visualization tool

Constructing the app

## Packages

Shiny

shinydashboard

Haven

Plotly



**Reactive app:** output automatically reacts to new user input

## Building the app

- 3 basic components:
  - `ui`: user interface
  - `server`: feed in data for ui
  - `shinyApp`: execution

- Example:

```
ui <- fluidPage(  
  )  
server <- function(input, output, session) {  
  }  
shinyApp(ui, server)
```



# Visualization tool

## EERP: Study 1 and Study 2

**Trial:**

**Subject ID:**

**Assessment:**

**Type of score:**

**Instrument:**

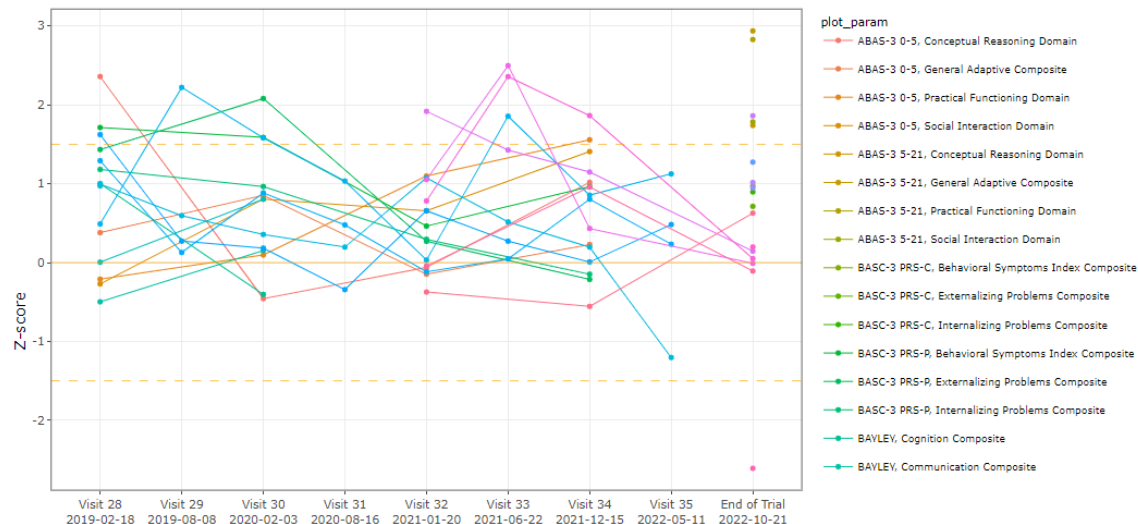
**New data:**

Subject: 10969  
Country: United States of America  
Age at latest neurocognitive assessment: 7.2 years  
Clinical concern at latest evaluation: no  
Contributing factors at latest evaluation: no

[NCA](#) [Subject Information](#) [Medical History](#) [Concomitant Medication](#) [Adverse Events](#) [Neurological Examinations](#)

[NCA overview](#) [All NCAs \(figures\)](#) [All NCAs \(listing\)](#)

### Primary Outcome Measures



Data shown in the app are simulated for demonstration purpose.



# Visualization tool

## E EERP: Study 1 and Study 2

Study 1

Subject ID:

10969

Assessment

All

Type of score:

Z-score

Instrument

All

New data:

All

Reset

Age at latest neurocognitive assessment: 1.2 years  
Clinical concern at latest evaluation: no  
Contributing factors at latest evaluation: no

NCA

Subject Information

Medical History

Concomitant Medication

Adverse Events

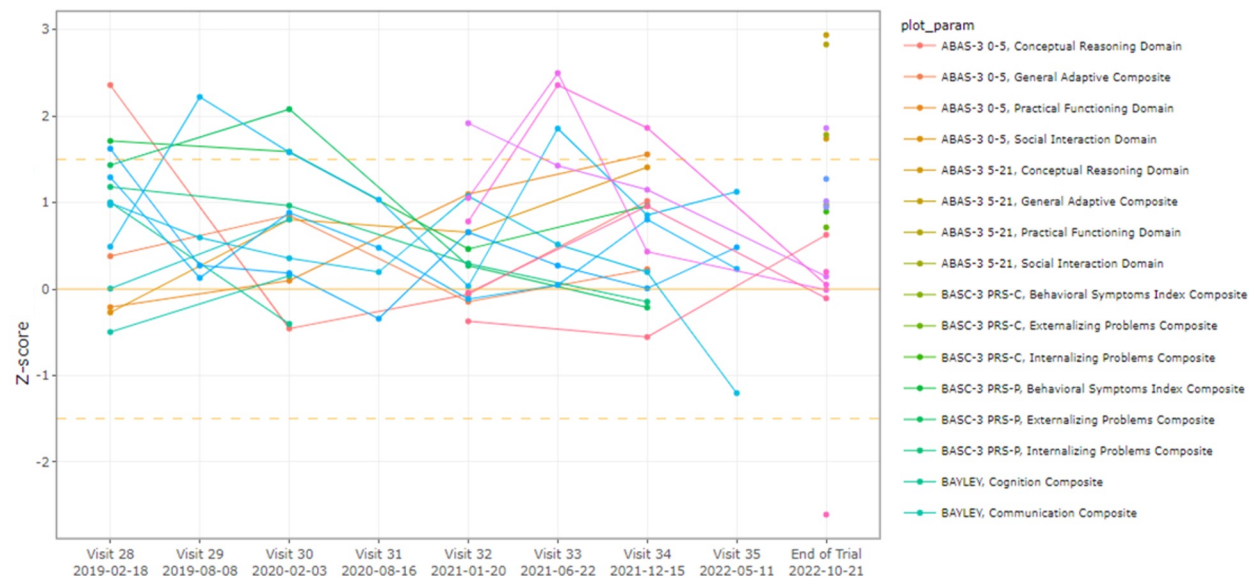
Neurological Examinations

NCA overview

All NCAs (figures)

All NCAs (listing)

### Primary Outcome Measures





# Visualization tool

## EERP: Study 1 and Study 2

Trial:

Study 1

Subject ID:

10969

Assessment

All

Type of score:

Z-score

Instrument

All

New data:

All

Reset

Subject: 10969  
Country: United States of America  
Age at latest neurocognitive assessment: 7.2 years  
Clinical concern at latest evaluation: no  
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NCA

Subject Information

Medical History

Concomitant Medication

Adverse Events

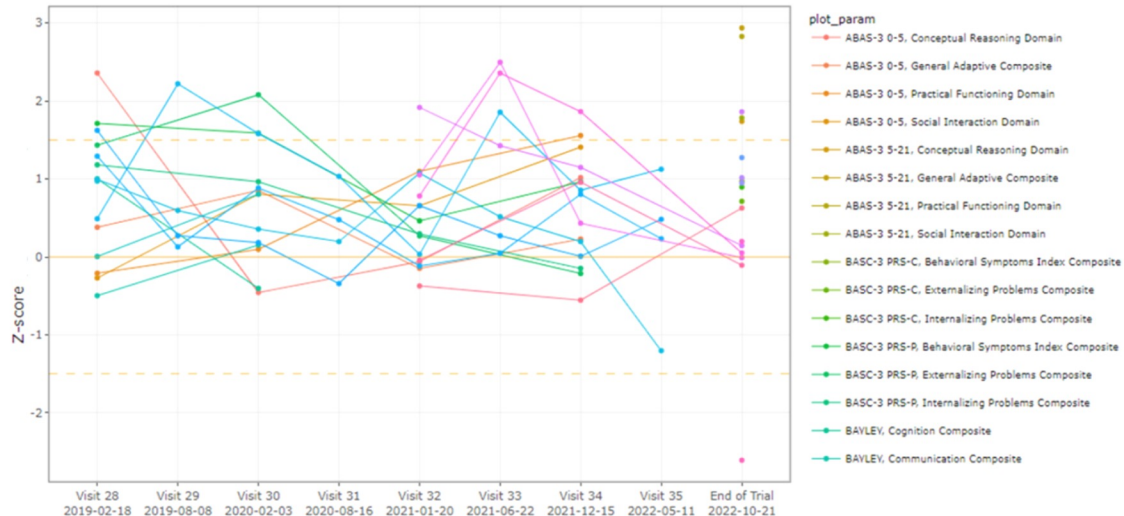
Neurological Examinations

NCA overview

All NCAs (figures)

All NCAs (listing)

### Primary Outcome Measures



# Visualization tool

EERP: Study 1 and Study 2

Trial:

Study 1

Subject ID

10969

Assessment

All

Type of score

Z-score (

Instrument

All

New data:

All

Reset

Trial:

Study 1

Subject ID:

10969

Assessment

All

Type of score:

Z-score

Instrument

All

New data:

All

Reset

America  
re assessment: 7.2 years  
valuation: no  
st evaluation: no

Information

Medical History

Concomitant Medication

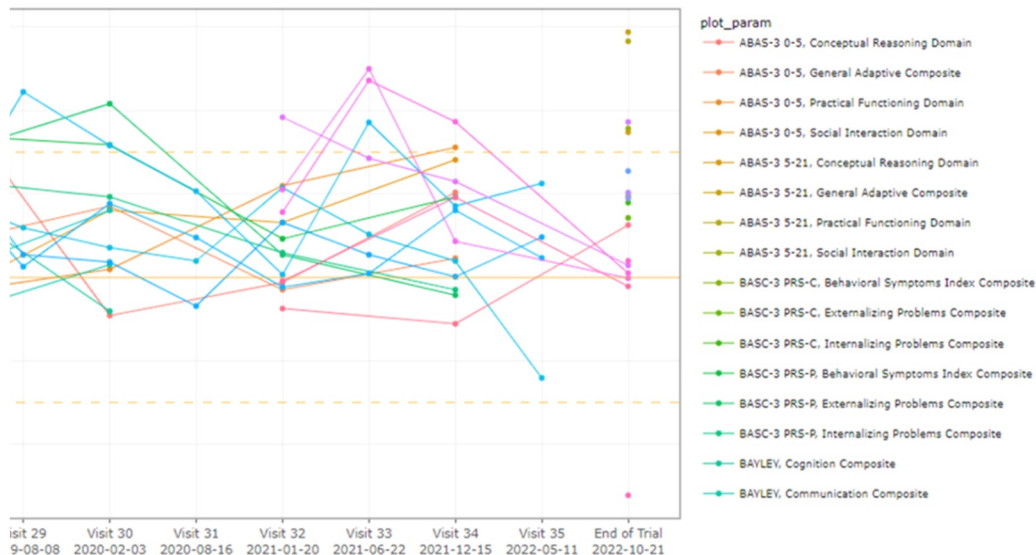
Adverse Events

Neurological Examinations

NCA's (figures)

All NCA's (listing)

Some Measures





# Visualization tool

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Subject ID:

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Assessment

All

Type of score:

Z-score

Instrument

All

New data:

All

Reset

NCA

Subject Information

Medical History

Concomitant Medication

Adverse Events

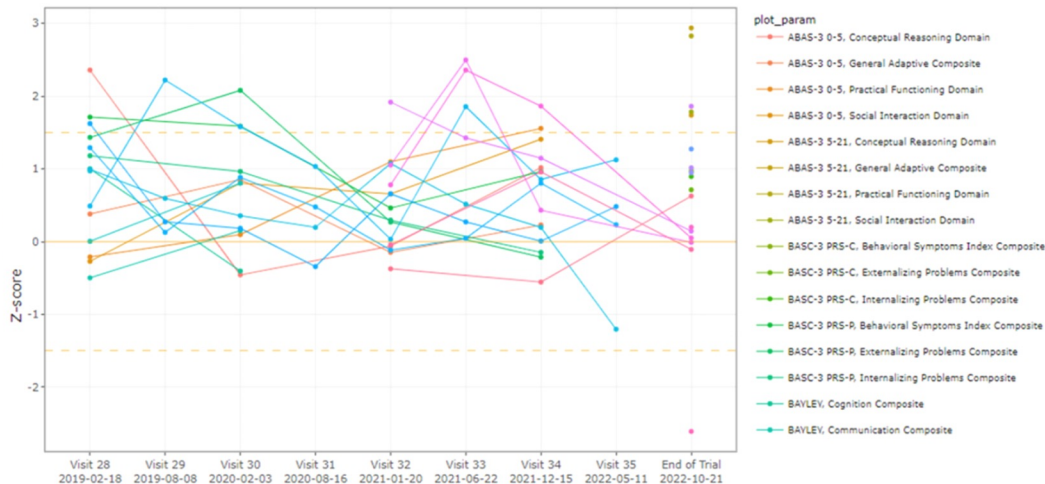
Neurological Examinations

NCA overview

All NCAs (figures)

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### Primary Outcome Measures





# Visualization tool

## EERP: Study 1 and Study 2

Trial:

Study 1

Subject ID:

10969

Assessment

All

Type of score:

Z-score

Instrument

All

New data:

All

Reset

Subject: 10969

Country: United States of America

Subject: 10969

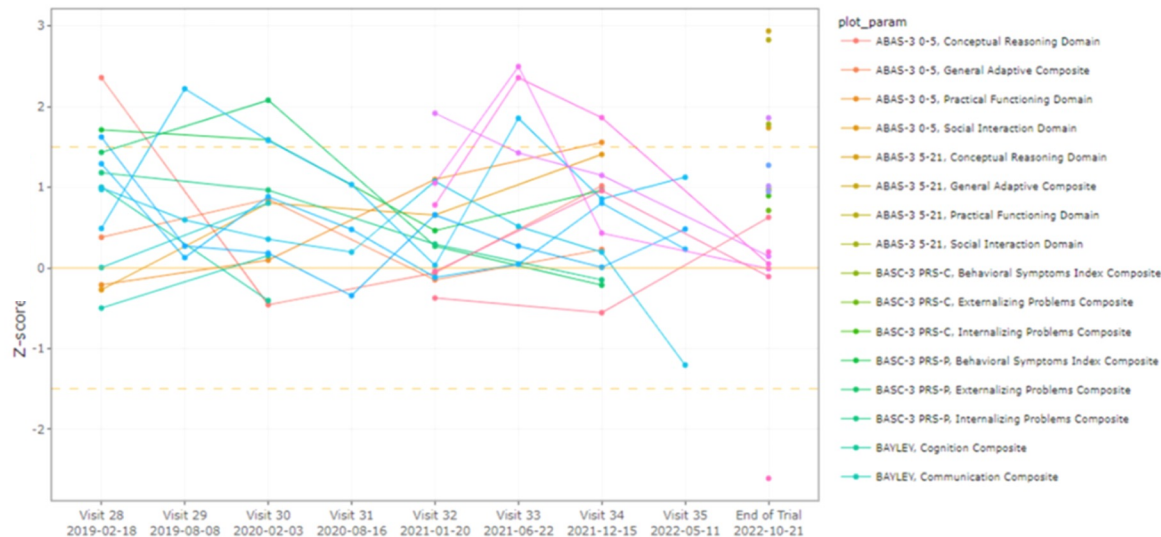
Country: United States of America

Age at latest neurocognitive assessment: 7.2 years

Clinical concern at latest evaluation: no

Contributing factors at latest evaluation: no

nts Neurological Examinations





# Visualization tool

## EERP: Study 1 and Study 2

Trial:

Study 1

Subject ID:

10969

Assessment

All

Type of score:

Z-score

Instrument

All

New data:

All

Reset

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Adverse Events

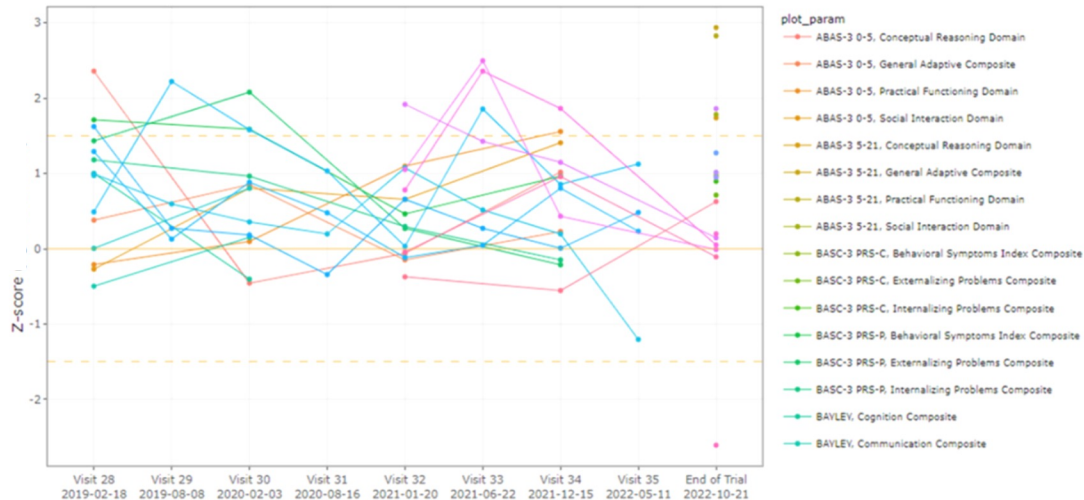
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All NCAs (figures)

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### Primary Outcome Measures





# Visualization tool

## EERP: Study 1 and Study 2

Trial:

Study 1

Subject ID:

10969

Assessment

All

Type of score:

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All

New data:

All

Reset

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NCA

Subject Information

Medical History

Concomitant Medication

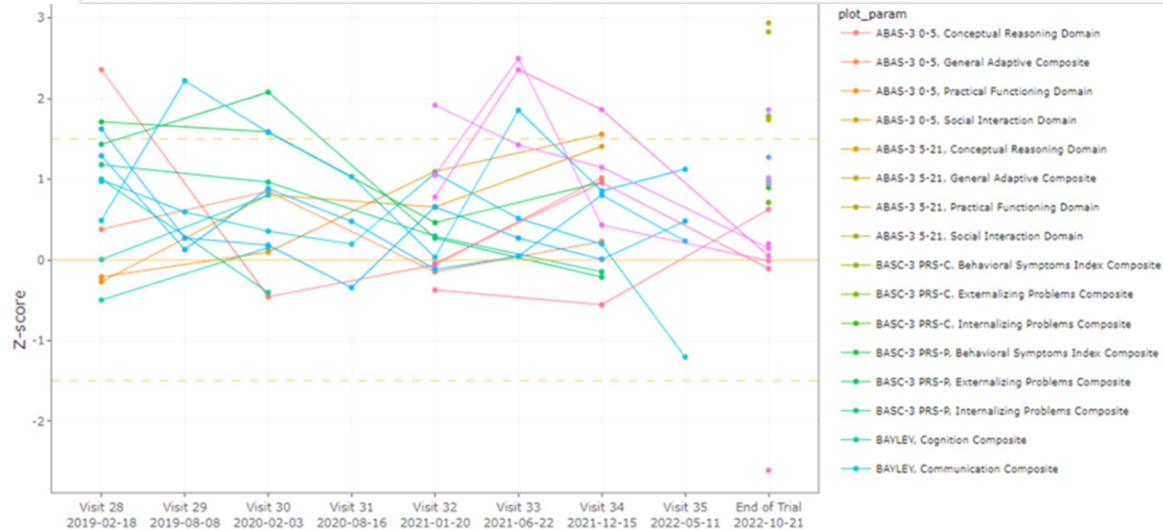
Adverse Events

Neurological Examinations

NCA overview

All NCAs (figures)

All NCAs (listing)





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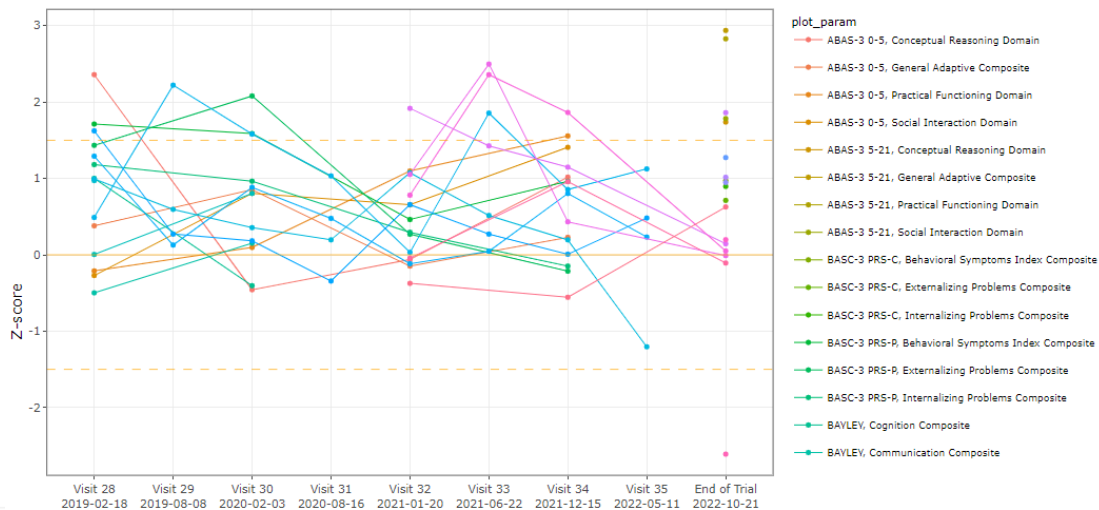
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All

Type of score:

Z-score

Instrument

All

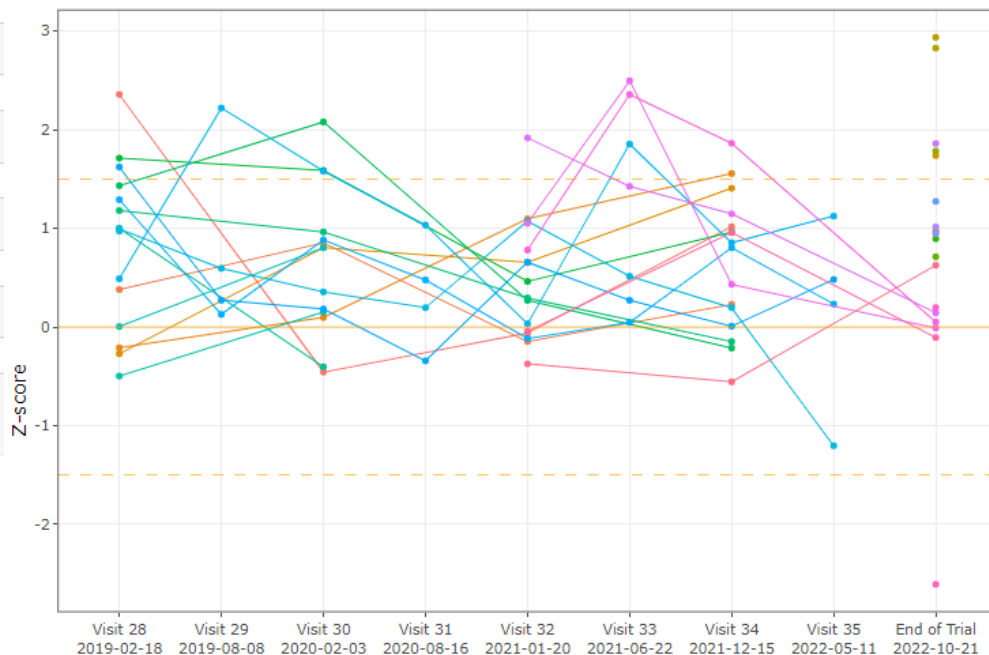
New data:

All

Reset

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Age at latest neurocognitive assessment: 7.2 years  
Clinical concern at latest evaluation: no  
Contributing factors at latest evaluation: no

### Primary Outcome Measures



plot\_param

- ABAS-3 0-5, Conceptual Reasoning Domain
- ABAS-3 0-5, General Adaptive Composite
- ABAS-3 0-5, Practical Functioning Domain
- ABAS-3 0-5, Social Interaction Domain
- ABAS-3 5-21, Conceptual Reasoning Domain
- ABAS-3 5-21, General Adaptive Composite
- ABAS-3 5-21, Practical Functioning Domain
- ABAS-3 5-21, Social Interaction Domain
- BASC-3 PRS-C, Behavioral Symptoms Index Composite
- BASC-3 PRS-C, Externalizing Problems Composite
- BASC-3 PRS-C, Internalizing Problems Composite
- BASC-3 PRS-P, Behavioral Symptoms Index Composite
- BASC-3 PRS-P, Externalizing Problems Composite
- BASC-3 PRS-P, Internalizing Problems Composite
- BAYLEV, Cognition Composite
- BAYLEV, Communication Composite



# Visualization tool

## EERP: Study 1 and Study 2

Trial:

Study 1

Subject ID:

10969

Assessment

All

Type of score:

Z-score

Instrument

All

New data:

All

Reset

Subject: 10969  
Country: United States of America  
Age at latest neurocognitive assessment: 7.2 years  
Clinical concern at latest evaluation: no  
Contributing factors at latest evaluation: no

NCA

Subject Information

Medical History

Concomitant Medication

Adverse Events

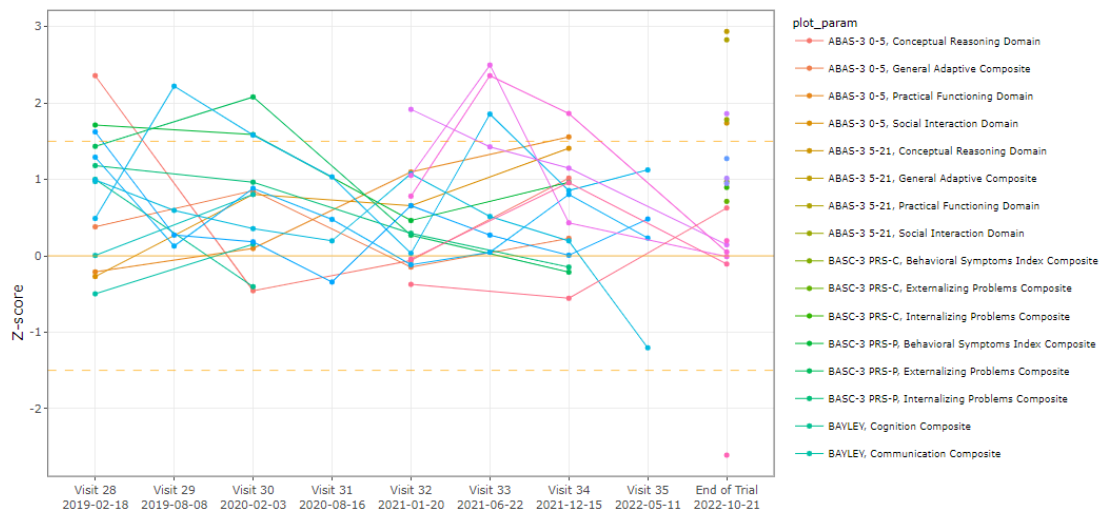
Neurological Examinations

NCA overview

All NCAs (figures)

All NCAs (listing)

### Primary Outcome Measures





# Visualization tool

EERP: Study 1 and Study

NCA Subject Information Medical History Concomitant Medication Adverse Events Neurological Examinations

NCA overview All NCAs (figures) All NCAs (listing)

Trial:

Study 1

Subject ID:

10969

Assessment

All

Type of score:

Z-score

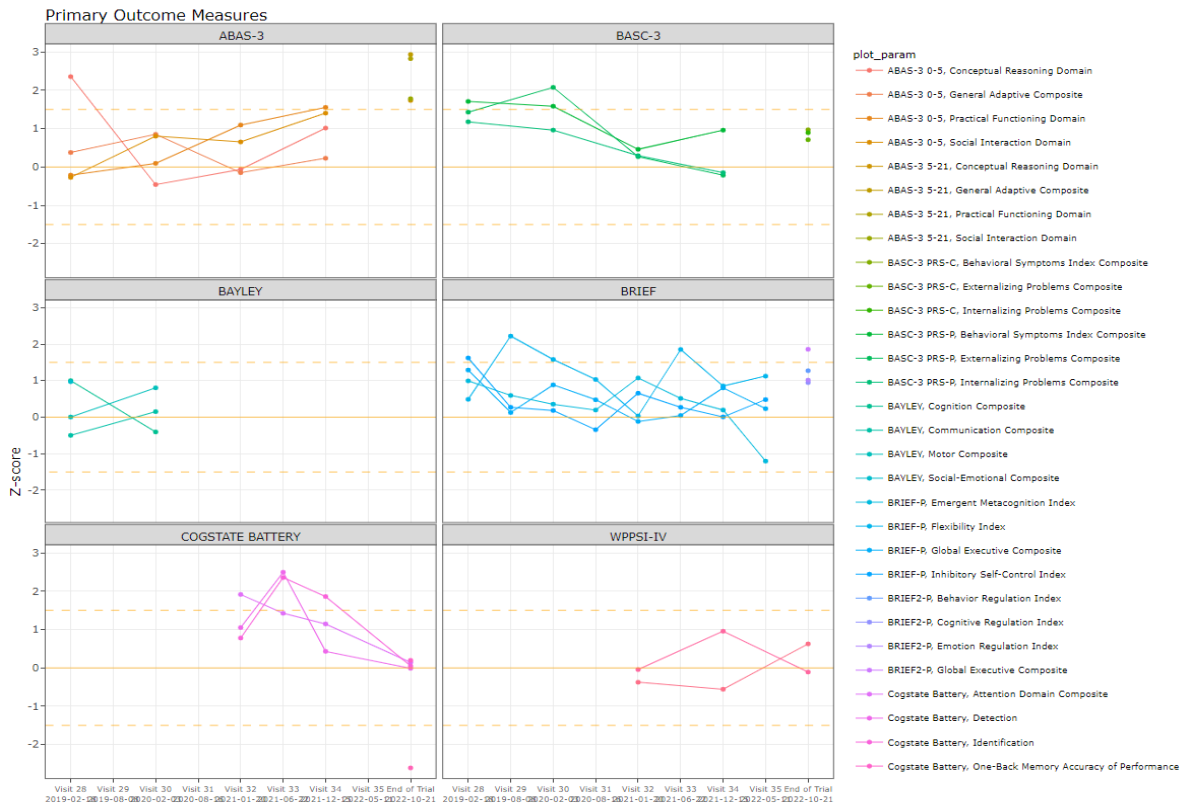
Instrument

All

New data:

All

Reset





# Visualization tool

## EERP: Study 1 and Study 2

Trial:

Study 1

Subject ID:

10969

Assessment

All

Type of score:

Z-score

Instrument

All

New data:

All

Reset

Subject: 10969  
Country: United States of America  
Age at latest neurocognitive assessment: 7.2 years  
Clinical concern at latest evaluation: no  
Contributing factors at latest evaluation: no

NCA Subject Information Medical History Concomitant Medication Adverse Events Neurological Examinations

NCA overview All NCAs (figures) All NCAs (listing)





# Visualization tool

EERP: S

Trial:

Study 1

Subject ID:

10969

Assessment

All

Type of score

Z-score

Instrument

All

New data:

All

Reset

Trial:

Study 1

Subject ID:

10575

Assessment

All

Domain

General

Examination results

All

New data:

All

Reset

Subject: 10575  
Country: United Kingdom  
Age at initial neurocognitive assessment: 2.4 years  
Clinical concern at initial evaluation: yes  
Contributing factors at initial evaluation: yes

NCA

Subject Information

Medical History

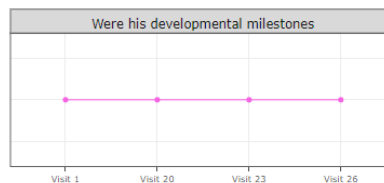
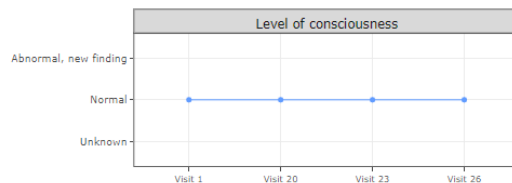
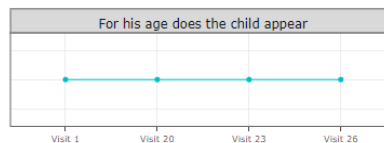
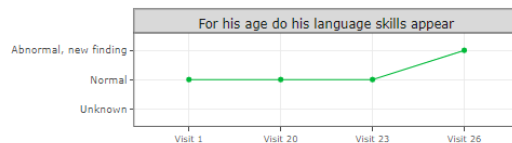
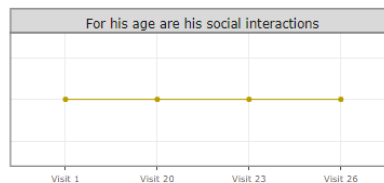
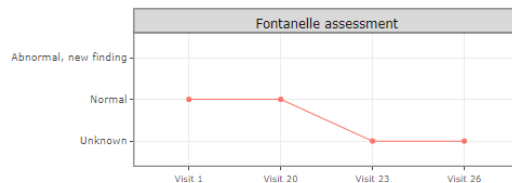
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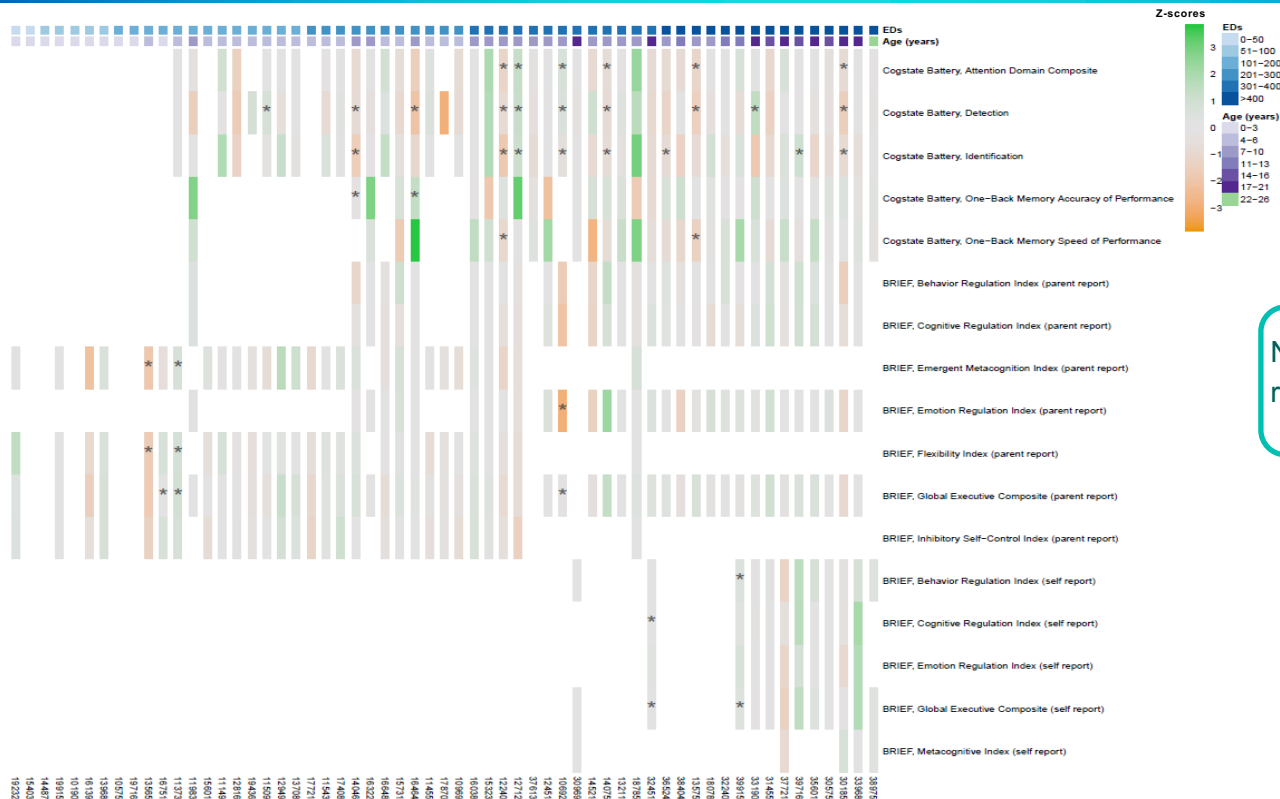
Neurological examinations (listing)

Neurological examinations (figures)





# Pattern in relation to exposure



No obvious pattern in the z-scores in relation to treatment duration

\* Represents mean change in z-scores below -1.5



# Summary

- Importance of understanding the therapeutic area and clinical outcomes
- Use of a visualization tool – an innovative way to make data comprehensible
- Useful to observe if any pattern exists

## **Based on the simulated data shown previously -**

- No overall pattern found in compiled analyses of the cognitive functioning of participants in relation to the treatment



# Acknowledgment

I would like to express my gratitude towards

- Pernille Juul Jørgensen (Senior Statistician), Novo Nordisk
- Pernille Højlund Nielsen (Senior Statistician), Novo Nordisk

# Thank you



**The Global Healthcare  
Data Science Community**

**Contact Channels**

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🌐 [phuse.global](http://phuse.global)

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📘 [/phusebook](https://facebook.com/phusebook)  
▶ [/phusetube](https://youtube.com/phusetube)  
🌐 [/company/phuse](https://linkedin.com/company/phuse)