

# Exploration of the Efficacy of Pabinafusp-alfa (JR-141) on Neurocognitive Development in Hunter Syndrome (MPS-II): 52-and 104-week Data from Clinical Trials in Japan and Brazil

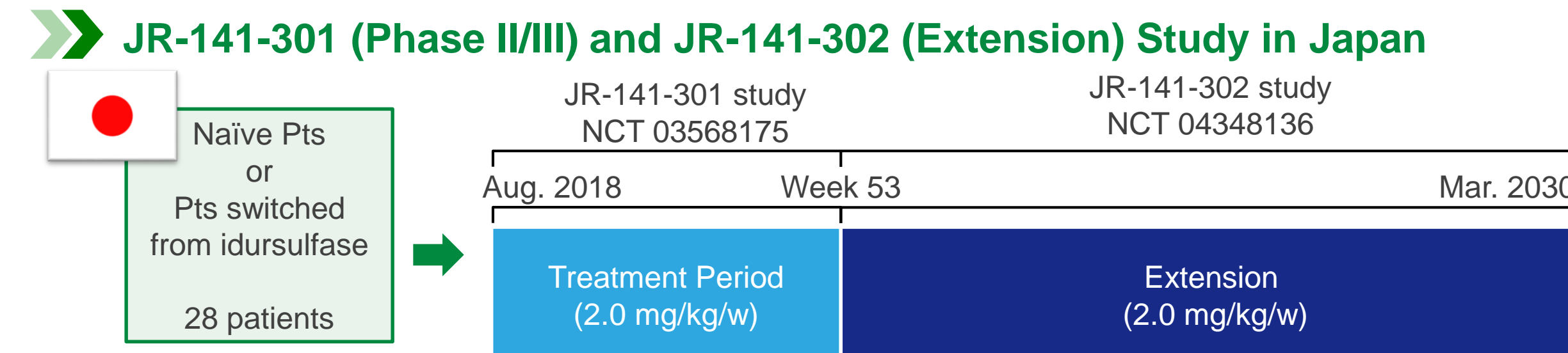
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## Introduction

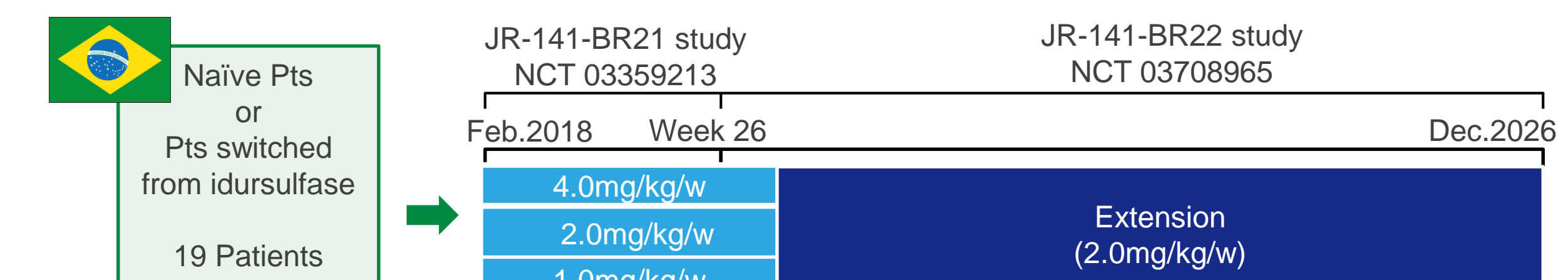
- Mucopolysaccharidosis II (MPS II) is an X-linked recessive lysosomal storage disease caused by mutations in the iduronate-2-sulfatase (IDS) gene.
- Pathological accumulation of glycosaminoglycans in the lysosomes results in a broad spectrum of symptoms, including CNS signs and symptoms.
- Current ERT is not effective for the CNS signs and symptoms because the enzyme does not cross the blood-brain barrier (BBB).
- JR-141 (pabinafusp alfa) is a recombinant fusion protein of an anti-transferrin receptor antibody and IDS. It is designed to cross the BBB and thereby address both the somatic and neurologic signs and symptoms of MPS II.
- Phase II and II/III studies have demonstrated that JR-141 stabilizes or improves the neurological disease burden in subjects with MPS II, suggesting it may prevent progressive neurodegeneration in severe MPS II subjects.
- In this poster we present collective data from a phase II study in Brazil and a phase II/III study in Japan on the changes in neurocognitive and adaptive function upon treatment with JR-141.

## Study Design, Objectives & Methods



Study Design	A phase II/III open-label, single-group, multicenter
Development Assessments (at Week 1/Week 26/ Week 53/Week 105)	<ul style="list-style-type: none"> <li>Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III)</li> <li>Kaufman Assessment Battery for Children, Second Edition (KABC II)</li> <li>Kyoto Scale of Psychological Development 2001 (KSPD2001)</li> <li>Vineland-II Adaptive Behavior Scale (VABS II)</li> </ul>
Disease severity*	Severe (20 patients), Attenuated (8 patients)

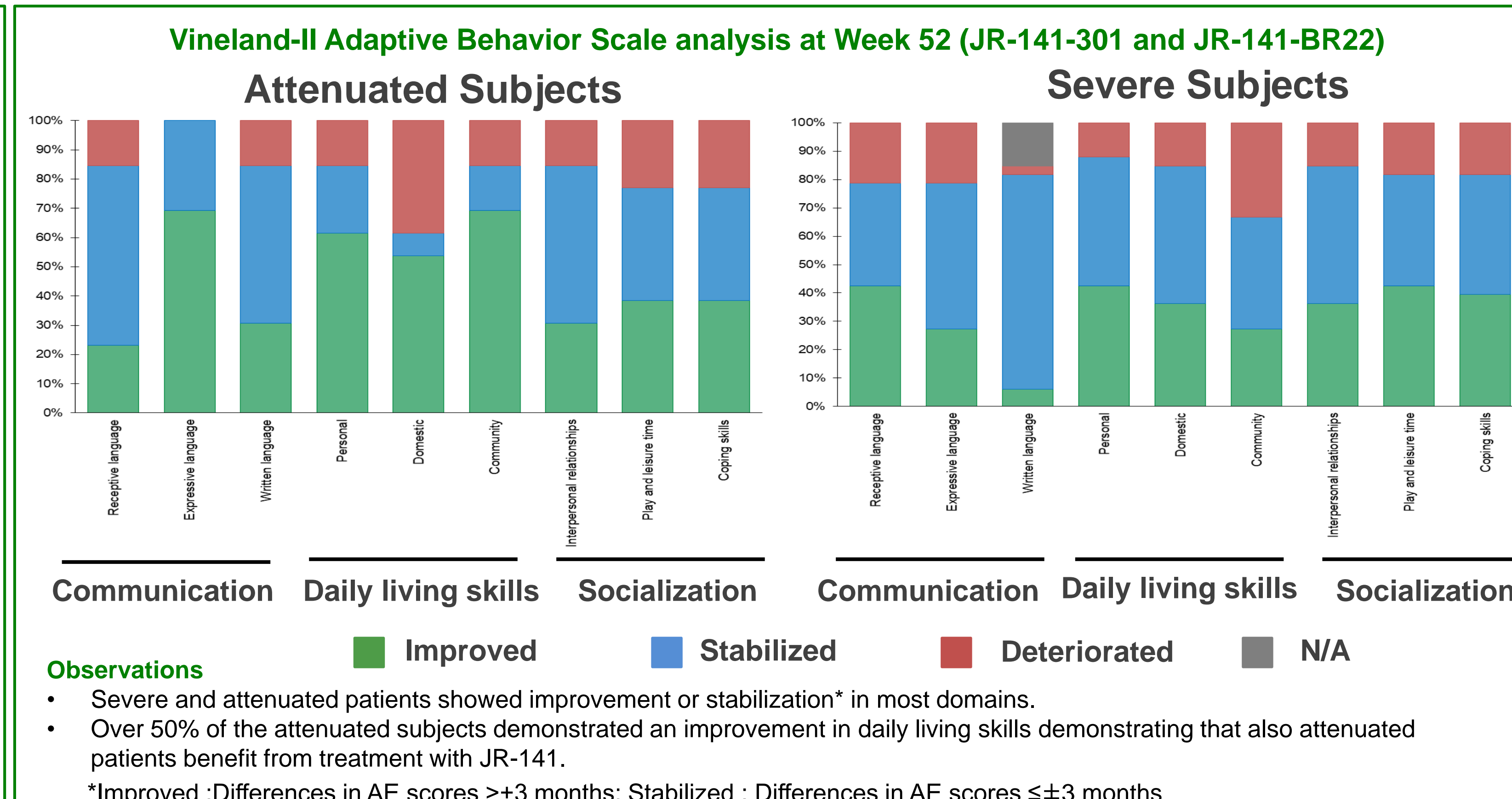
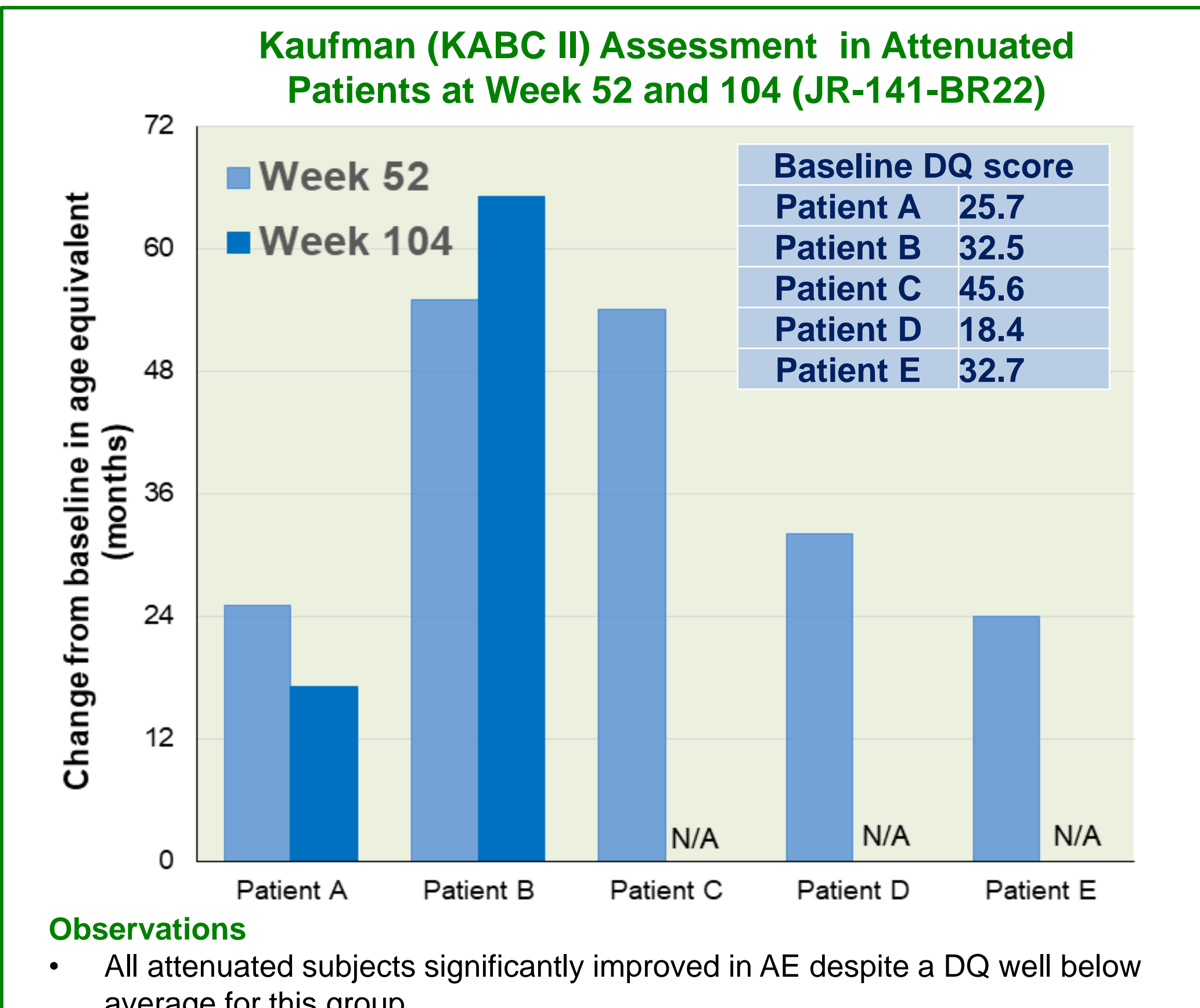
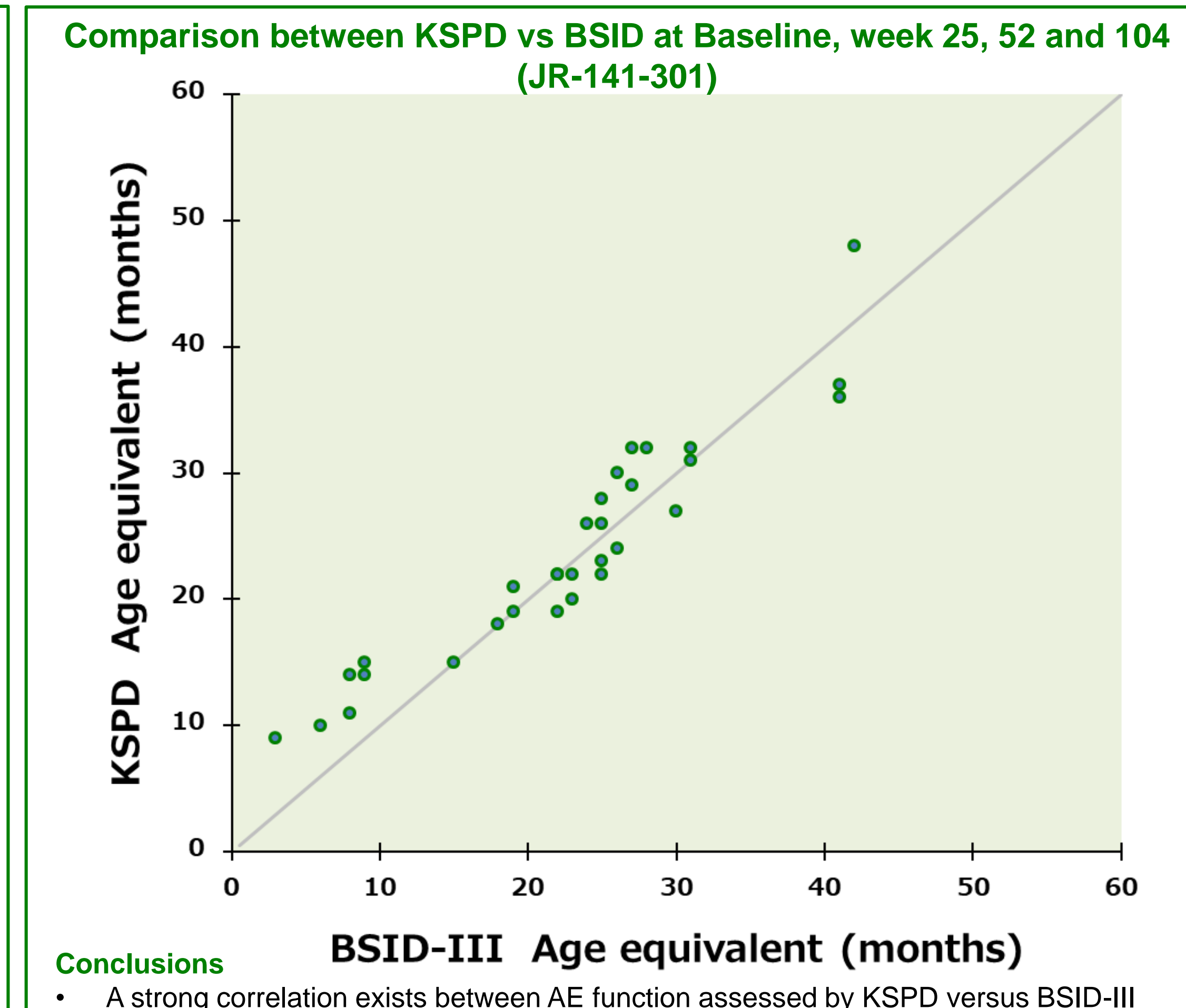
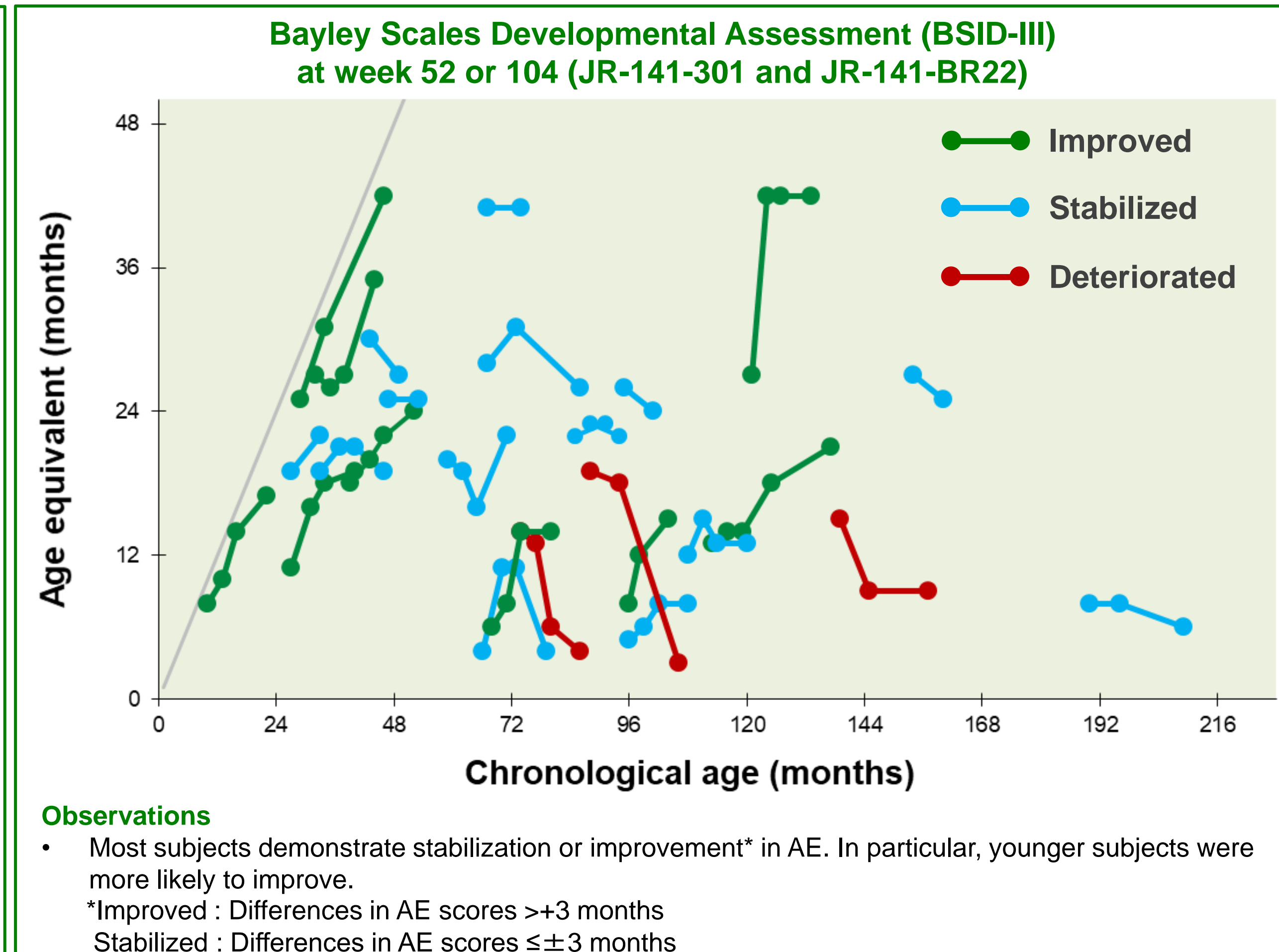
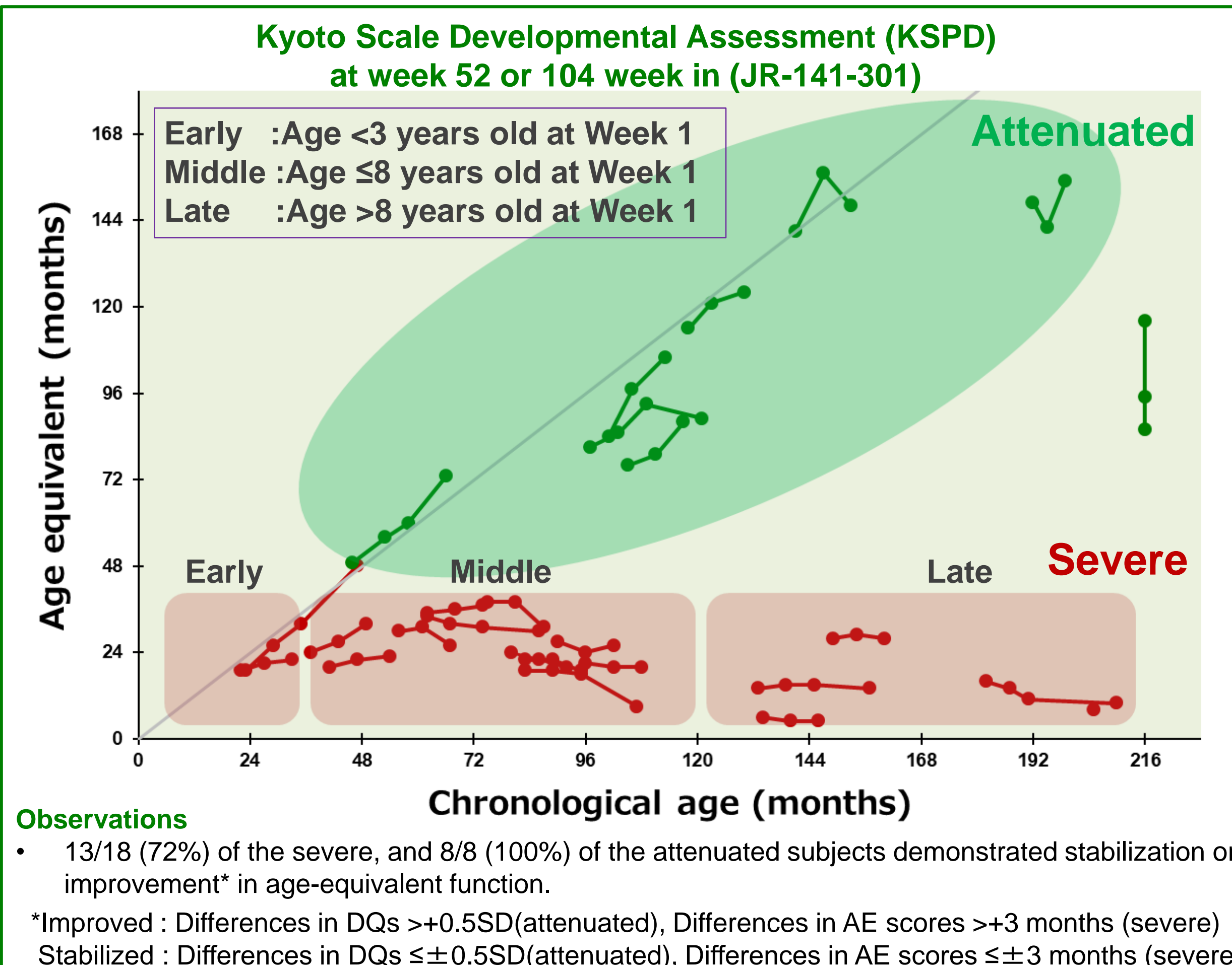
## JR-141-BR21 (Phase II) and JR-141-BR22 (Extension) Study in Brazil



Study Design	A Phase II open-label, randomized, parallel group, 2 sites (Brazil)
Development Assessments (at Week 1/Week 26/ Week 53/Week 105)	BSID III, KABC II and VABS II
Disease severity*	Severe (14 patients), Attenuated (5 patients)

\* Judged by medical monitor, based on the subject's mutation, age, AE and other information (e.g. sibling's phenotypes)

## Results



**Narrative Reports (JR-141-301 and JR-141-BR22)**

The findings from the study in Japan. Clinical behavioral observations collected from subjects' families and investigators:

**Language:**

- 12/18 (67%) of narrative reports from severe subjects in Japan showed an improvement in language.
- Changes generally observed include increased word count, increased number of conversations, and singing.

**Liveliness/Expression:**

- 11/18 (61%) of narrative reports from severe subjects in Japan demonstrated an improvement in liveliness/expression.
- Changes generally observed include increased activity and richer facial expressions.

**The Brazilian study also examined behavioral changes in 19 patients**

- Generally positive changes were found in language, motor skills and liveliness/expression.
- Notably, Pts without marked improvements in language or motor functions showed positive changes in liveliness/expression.

## Summary

- Most subjects in the JR-141-301/302 study showed AE stabilization or improvement on Kyoto Scale Developmental Assessment (KSPD) at 52 and 104 weeks of treatment. One severe subject (JP-08-03) showed normal cognitive development at 104 weeks of treatment.
- Most subjects in the JR-141-301/302 and JR-141-BR21/22 studies showed AE stabilization or improvement on Bayley Scale Developmental Assessment (BSID) at 52 and 104 weeks after first dosing.
- AEs from KSPD correlate well with those from BSID.
- Marketing authorization application for JR-141 for Japan and Brazil have been submitted in 2020.
- A global phase III study of JR-141 in patients with MPS II start in 2021 in Brazil, Europe (Germany, France and UK) and US.

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 Institutions  
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