LONG-TERM EFFICACY AND SAFETY OF TWO DOSES OF NORDITROPIN® (SOMATROPIN) IN NOONAN SYNDROME: A 4-YEAR RANDOMISED, DOUBLE-BLIND, MULTICENTRE TRIAL IN JAPANESE PATIENTS[1]

OBJECTIVES AND TRIAL DESIGN

This 4-year randomised, double-blind, multicentre trial investigated the growth-promoting effect of GH in patients with short stature due to NS.

32 ♂ **19** ♀

HSDS <-3 at baseline for both cohorts

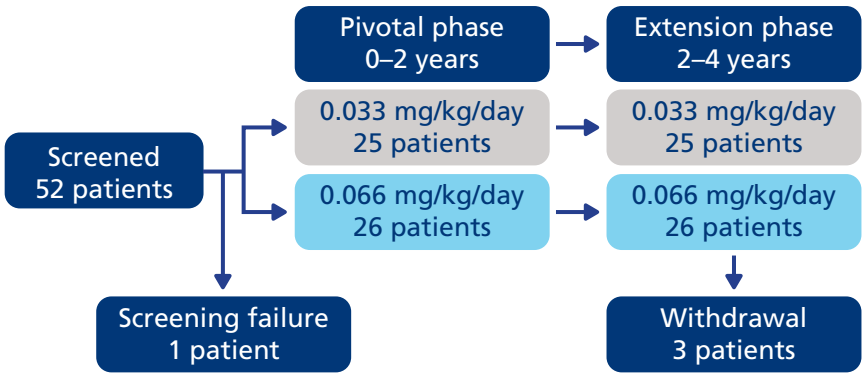
55% have a confirmed mutation in the *PTPN11* gene

Primary objective

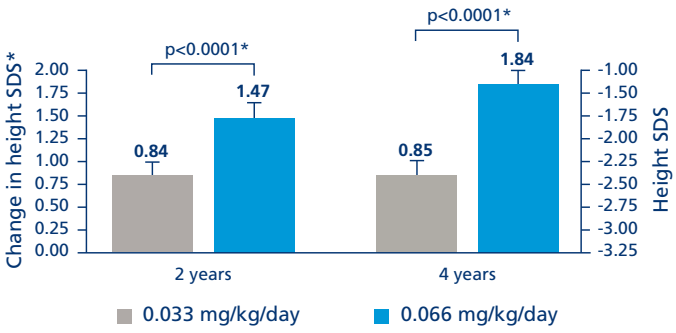
To evaluate the change in height SDS from baseline to 2 years of treatment

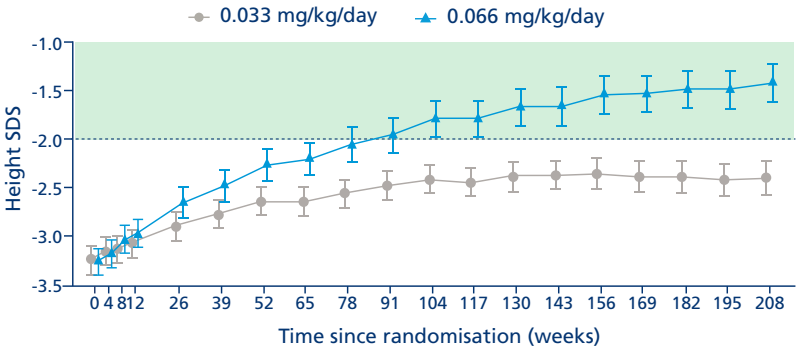
Secondary objective

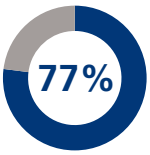
To evaluate the change in height SDS from baseline to 4 years of treatment



EFFICACY IN PROMOTING GROWTH[1,2]

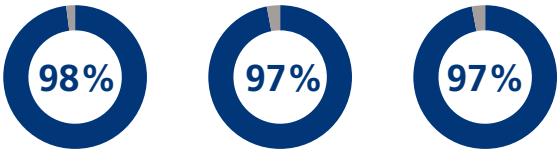






of patients in the higher dose group reached a height in the normal range compared to 32% in the lower dose group

TREATMENT EMERGENT ADVERSE EVENTS



Non-serious | **Mild in severity** | **Unlikely related to GH**

No evidence of negative effect on cardiac function

No deaths

No malignancies

Incidence of TEAEs similar between dose regimens

KEY TAKE-HOME MESSAGES

GH increases height SDS in children with short stature due to NS

0.066 mg/kg/day — Considerably greater height gain with higher dose

No new safety concerns

Earlier treatment initiation is associated with better treatment outcomes

1. Horikawa R, Ogata T, Matsubara Y, et al. Long-term efficacy and safety of two doses of Norditropin® (somatropin) in Noonan syndrome: A 4-year randomized, double-blind, multicenter trial in Japanese patients. *Endo Journal.* doi:10.1507/endocrj.EJ19-0371.
2. Ozono K, et al. *Endocr J.* 2018;65:159-174.

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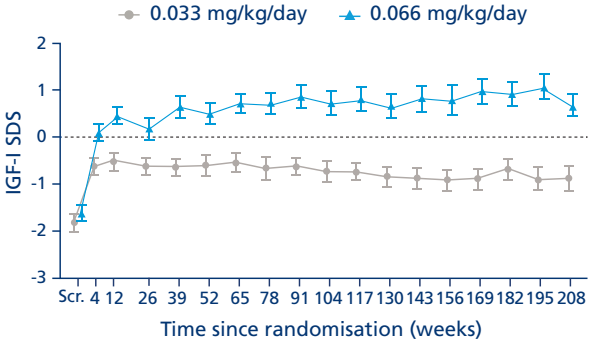
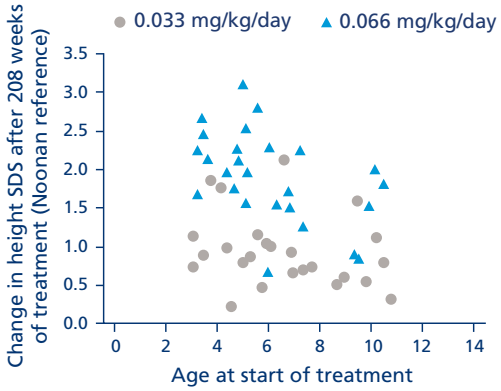
EFFECT ON IGF-I LEVELS

The mean IGF-I SDS remained stable. Overall, two children in the lower and 12 children in the higher dose group had an IGF-I SDS above +2 at some of the visits.

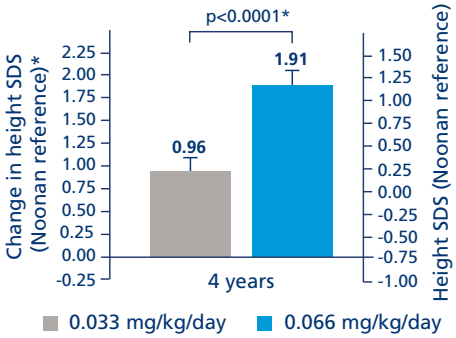


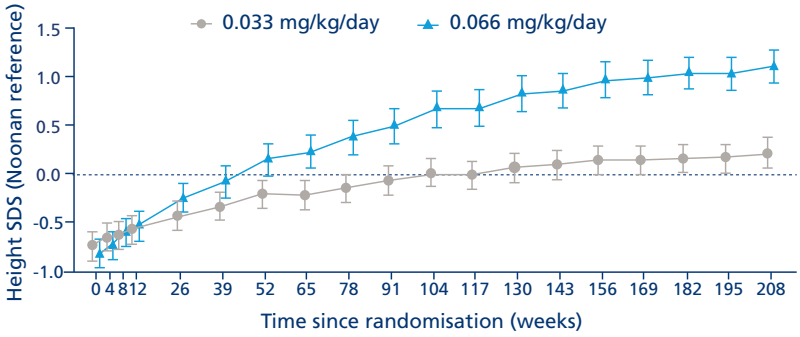
HOW DOES AGE AFFECT TREATMENT RESPONSE?

Initiating treatment at a younger age results in greater change in height SDS



HEIGHT SDS COMPARED WITH NOONAN SYNDROME REFERENCE VALUES

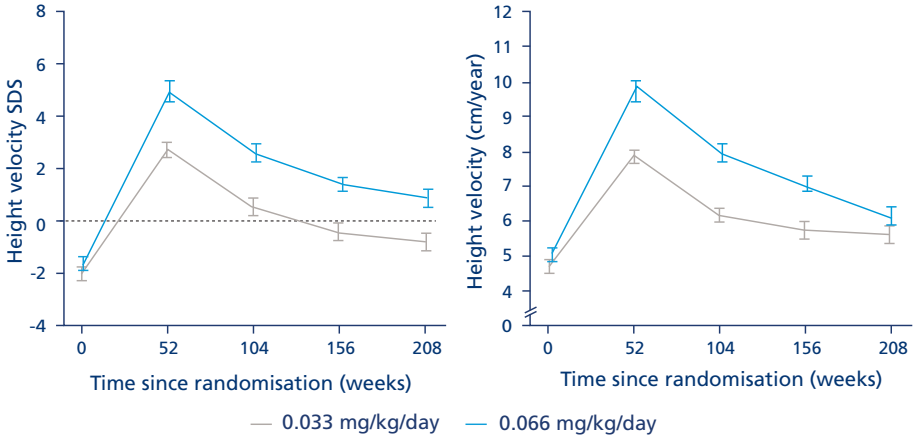




EFFECT ON HEIGHT VELOCITY

Mean height velocity SDS remained above 0 after 2 years of treatment (0.033 mg/kg/day) and after 4 years of treatment (0.066 mg/kg/day).

Height velocity greater than at baseline after 4 years of treatment



Primary reference

1. Horikawa R, Ogata T, Matsubara Y, et al. Long-term efficacy and safety of two doses of Norditropin® (somatropin) in Noonan syndrome: A 4-year randomized, double-blind, multicenter trial in Japanese patients. *Endo Journal.* doi:10.1507/endocrj.EJ19-0371.

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Selected references

1. Romano, A. A., et al. (2010). "Noonan syndrome: clinical features, diagnosis, and management guidelines." *Pediatrics* **126**(4): 746-759.
2. Noonan, J. A. and A. M. Kappelgaard (2015). "The efficacy and safety of growth hormone therapy in children with Noonan syndrome: a review of the evidence." *Horm Res Paediatr* **83**(3): 157-166.
3. Osio, D., et al. (2005). "Improved final height with long-term growth hormone treatment in Noonan syndrome." *Acta Paediatrica* **94**(9): 1232-1237.

Abbreviations
NS, Noonan syndrome; GH, growth hormone; SDS, standard deviation score; HSDS, height standard deviation score; TEAE, treatment emergent adverse event; IGF-I, insulin-like growth factor 1

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