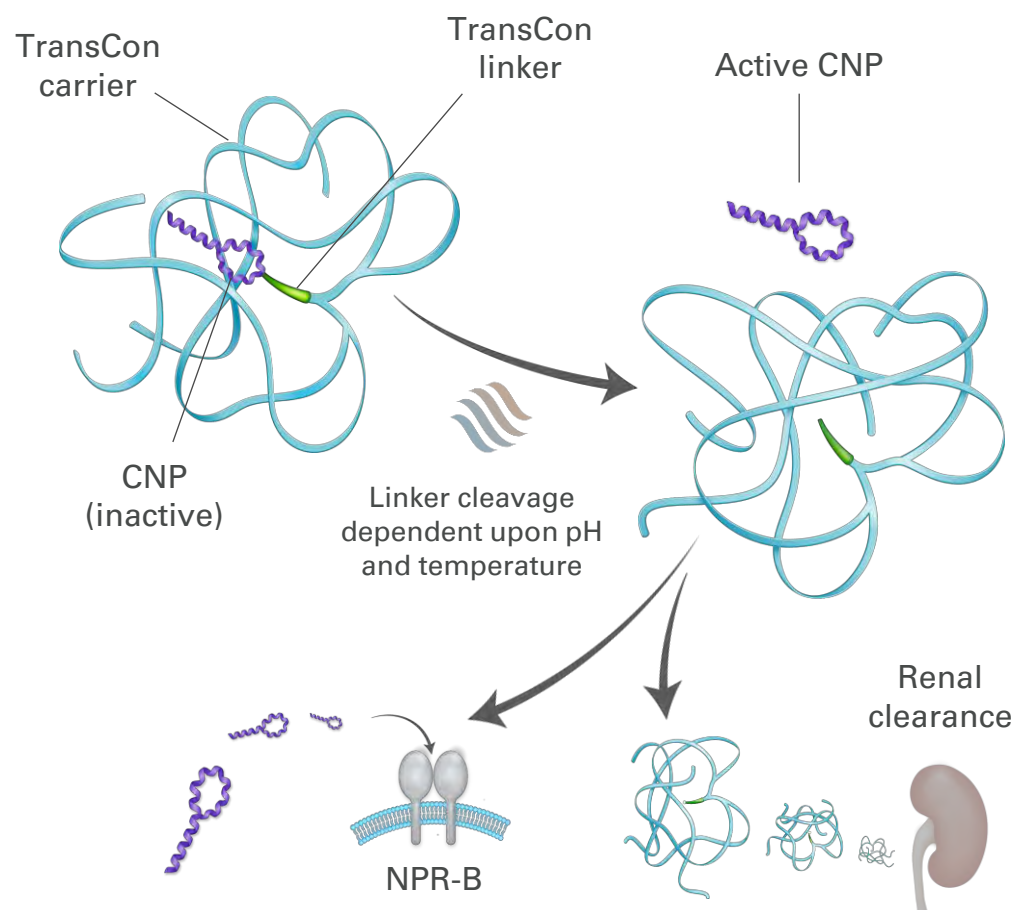


Improved Growth and Physical Functioning in Children with Achondroplasia Treated with Navepegritide in the ApproaCH Trial Open-Label Extension

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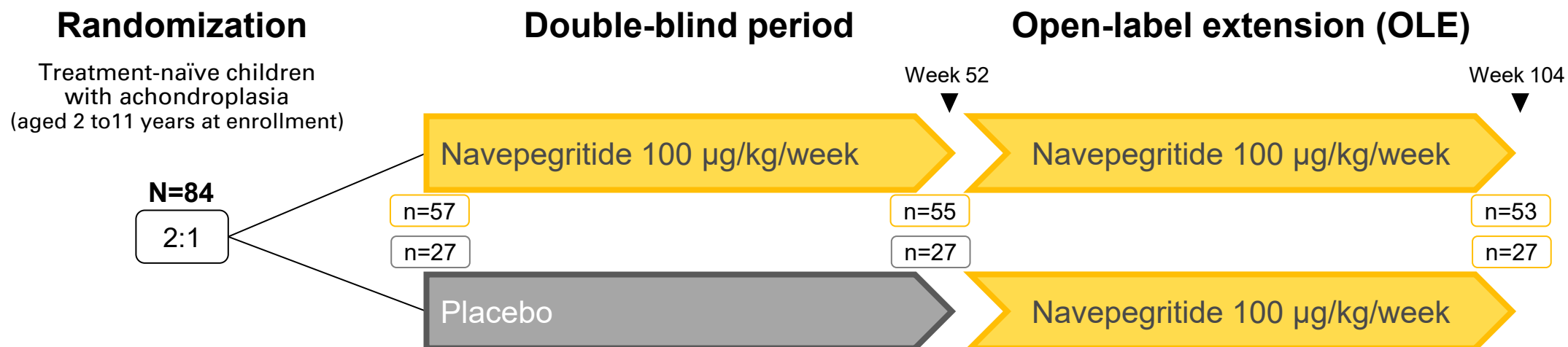
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Navepegritide (TransCon[®] CNP)



- Navepegritide is a prodrug of CNP administered once weekly and designed to provide continuous exposure to active CNP (amino acid sequence identical to endogenous CNP [89-126])¹
- Active CNP released from navepegritide binds to NPR-B throughout the body to counteract the constitutively active FGFR3 signaling in achondroplasia¹
- Navepegritide (YUWEL[®]) is approved in the United States to increase linear growth in children 2 years and older with achondroplasia with open epiphyses²

ApproaCH trial design, disposition, and demographics



Primary endpoint

- Annualized growth velocity (AGV) at Week 52

Growth assessments

- AGV through Week 104
- Change from baseline in ACH-specific & CDC-based height Z-scores

HRQoL

- Achondroplasia Child Experience Measure (ACEM)

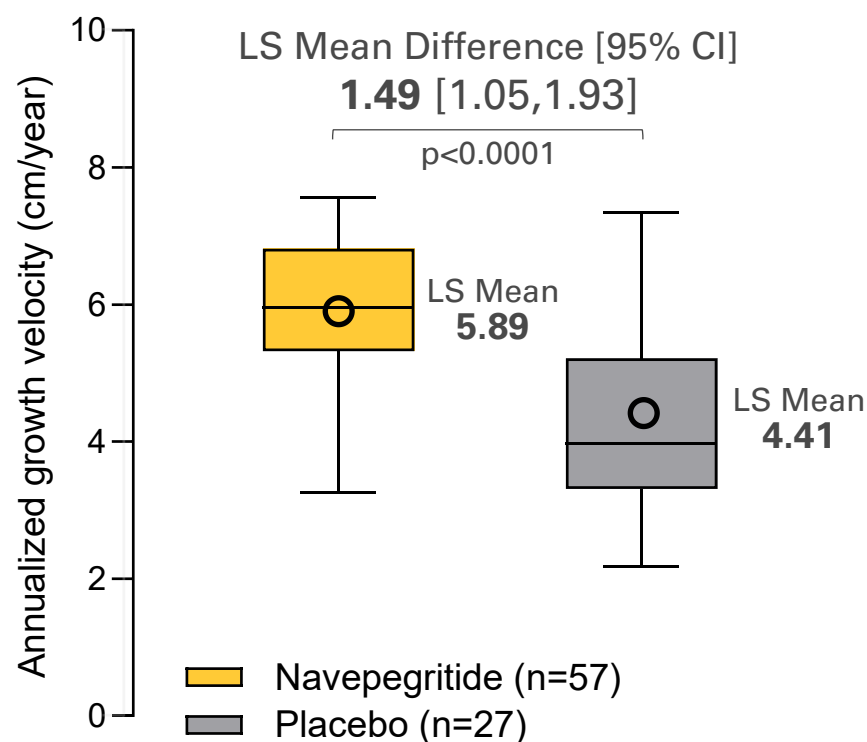
Safety

- Treatment emergent adverse events (AEs)
- Tolerability

Baseline characteristics	Navepegritide n=57	Placebo n=27
Age, years; mean (SD) [min, max]	5.6 (2.6) [2.0, 11.9]	6.0 (2.7) [2.1, 12.0]
Sex, male; n (%)	31 (54.4)	14 (51.9)
ACH-specific height Z-score; mean (SD)	0.18 (0.92)	-0.11 (0.73)

ApproaCH primary endpoint: Annualized growth velocity (AGV) at Week 52

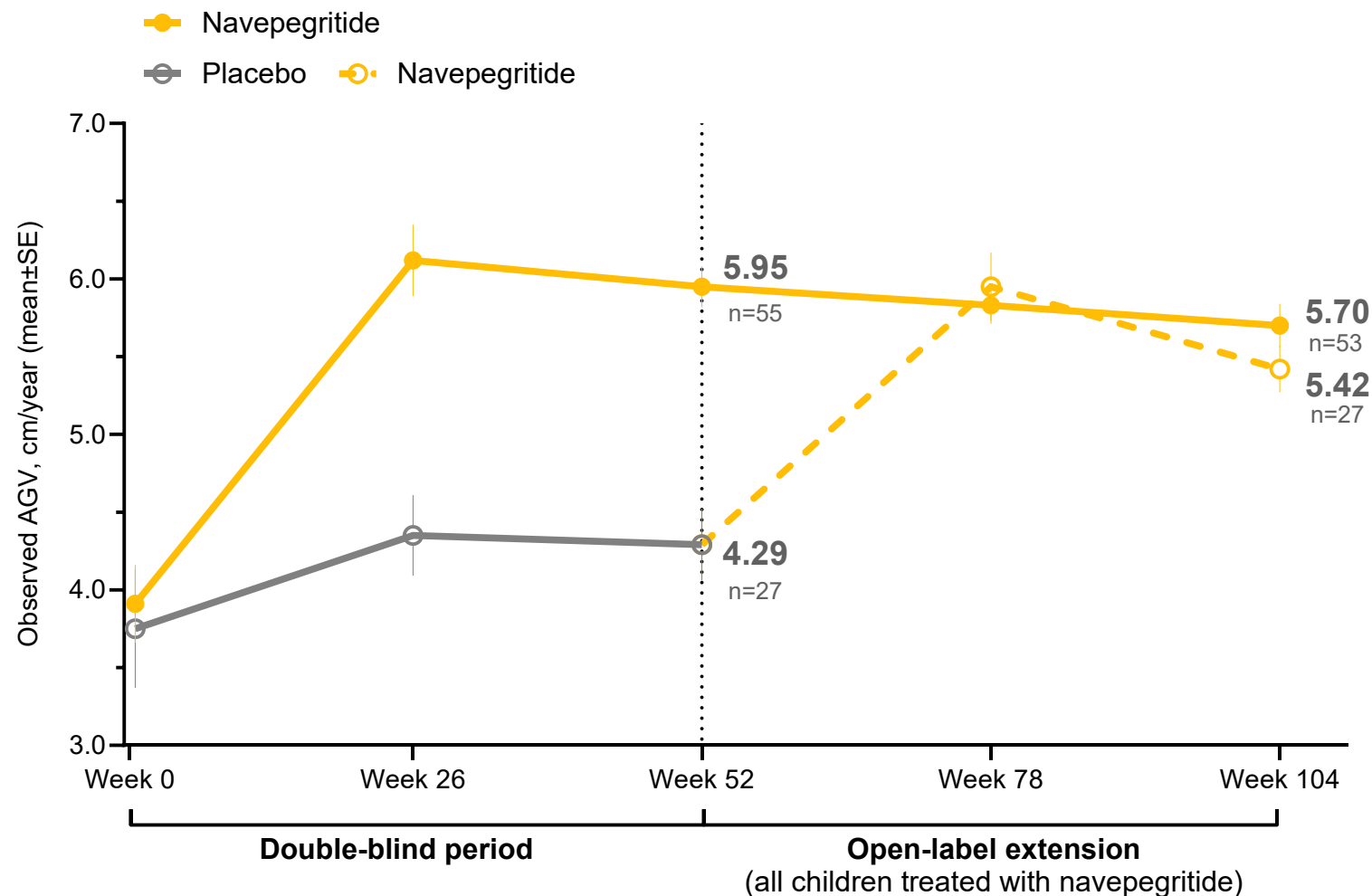
Savarirayan R, et al. Once-weekly navepegritide in children with achondroplasia: The APPROACH randomized trial. *JAMA Pediatrics* 2026.180(1):18-25.



Results from the double-blind period demonstrated superiority of once-weekly navepegritide over placebo for AGV at Week 52

Note: Box-and-whisker plots derived using observed data at Week 52 and display the 75th and 25th percentile (box edges), IQR (colored area), median (midline), and minimum and maximum observed values; labeled circles represent least squares mean values. Missing height data at Week 52 for 2 participants in the navepegritide group were imputed using the multiple imputation method. AGV, annualized growth velocity; CI, confidence interval; IQR, interquartile range; LS, least squares

Annualized growth velocity (AGV) through Week 104

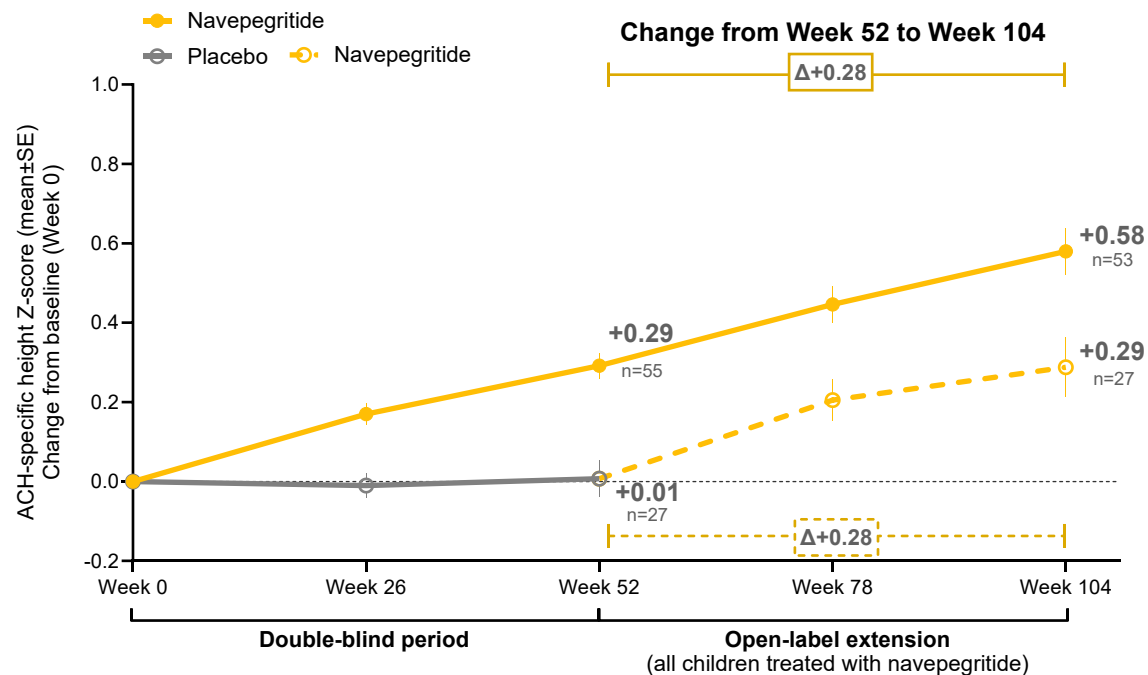


Children continuing navepegritide in the open-label extension maintained AGV through 104 weeks

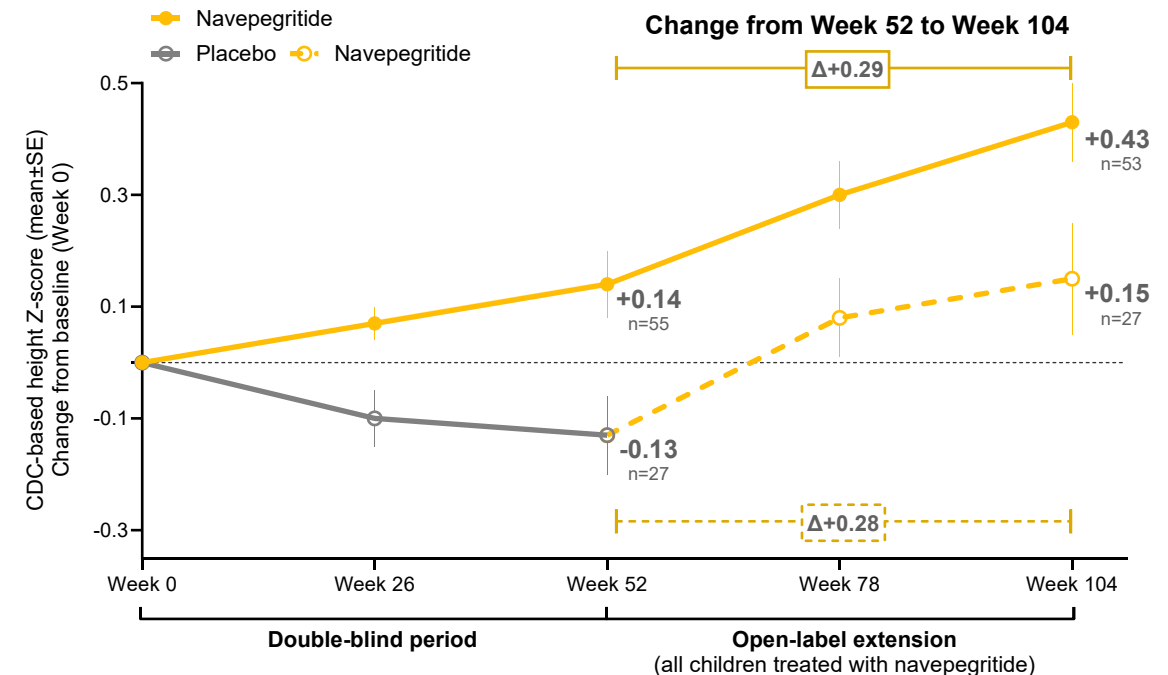
Children who switched from placebo to navepegritide at Week 52 had increased AGV at Week 104, comparable to navepegritide-related gains observed in the double-blind period

In the OLE, ACH-specific and CDC-based height Z-scores increased with navepegritide

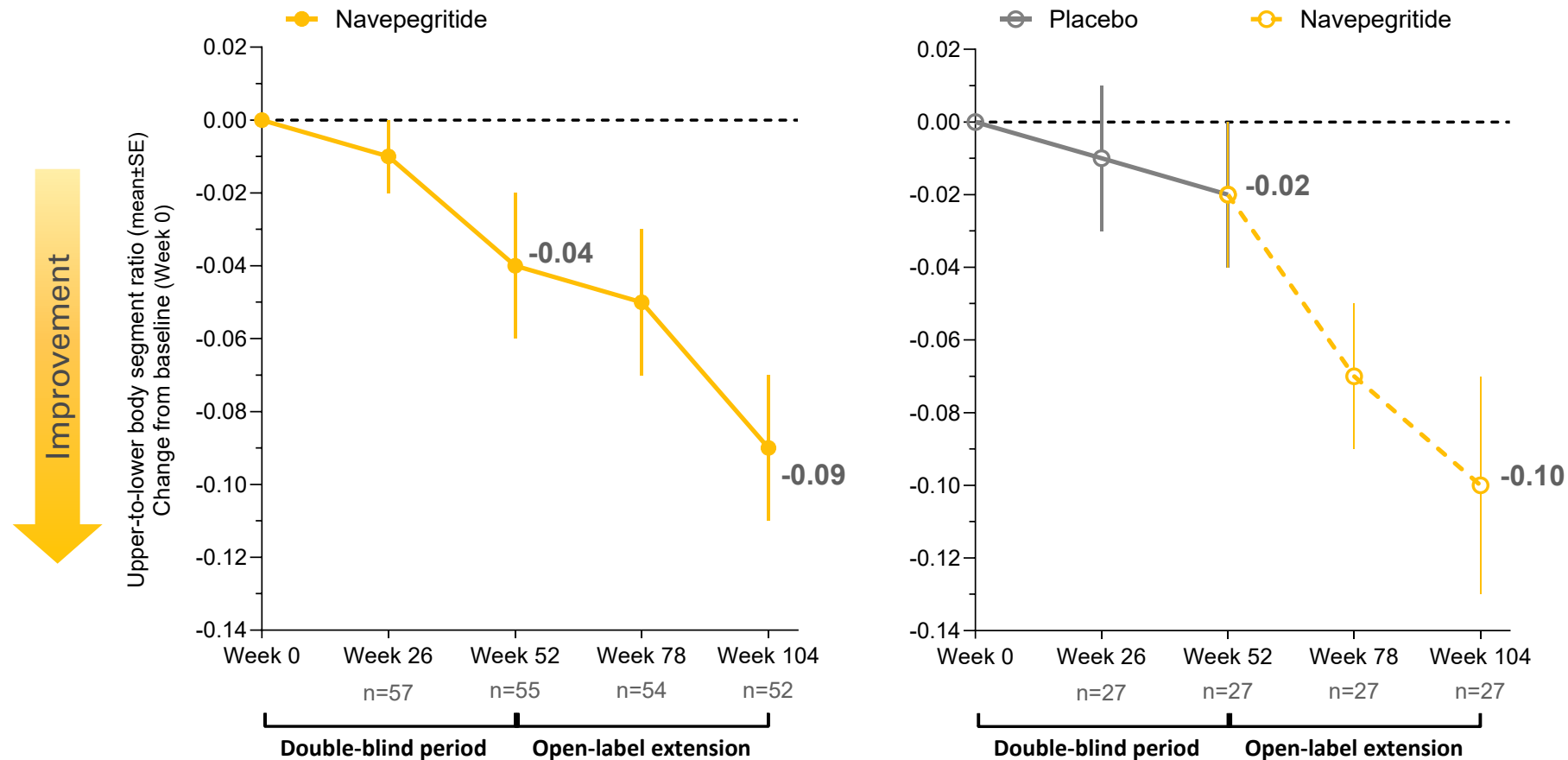
Change in ACH-specific height Z-score



Change in CDC-based height Z-score



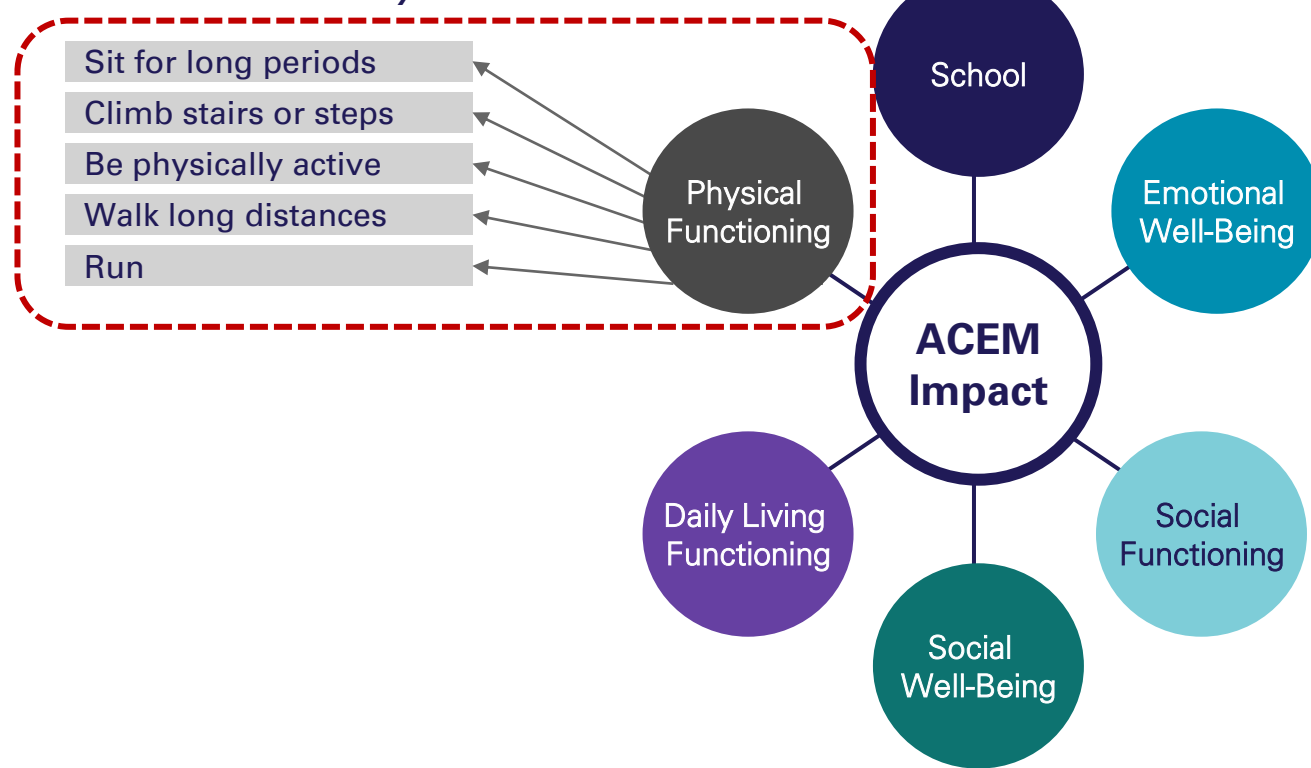
Upper-to-lower body segment ratio improved with navepegritide treatment, indicating promotion of proportional growth



Condition-specific clinical outcome assessments: Achondroplasia Child Experience Measure (ACEM)

ACEM-IMPACT

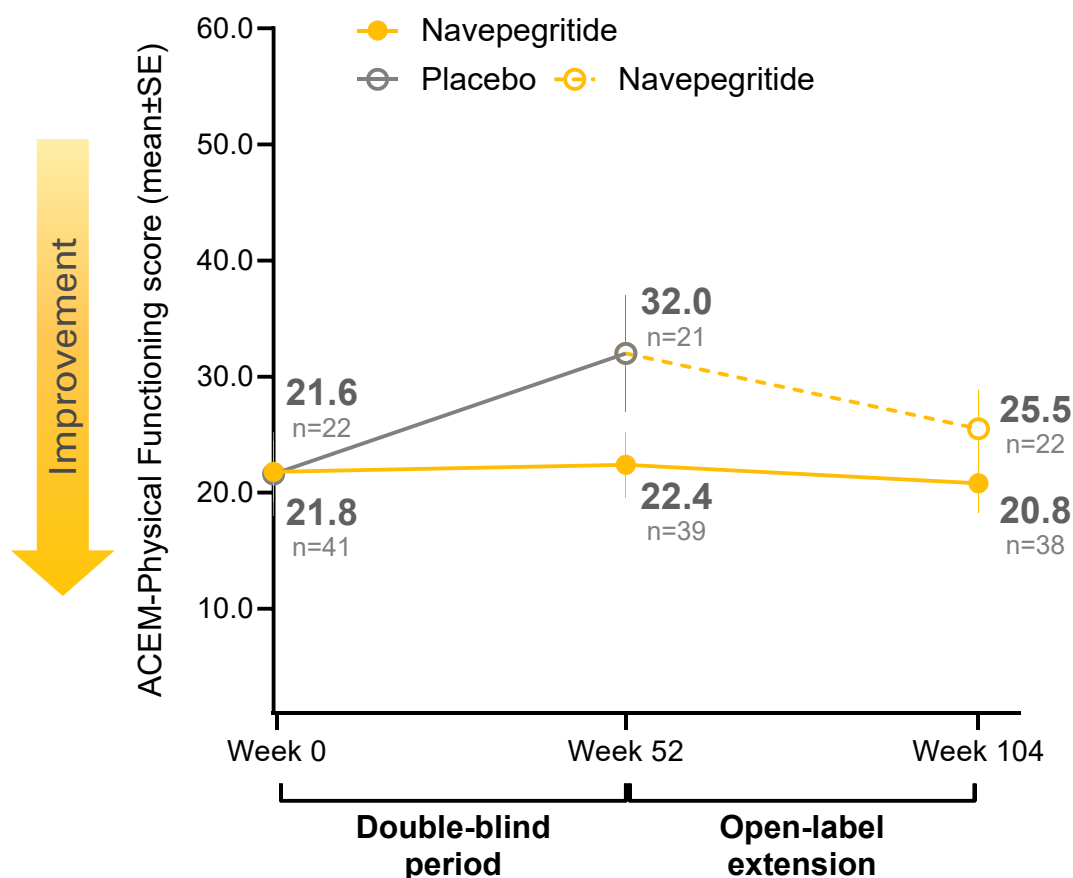
In the past 2 weeks, because of achondroplasia, how difficult was it for your child to:^{1,2}



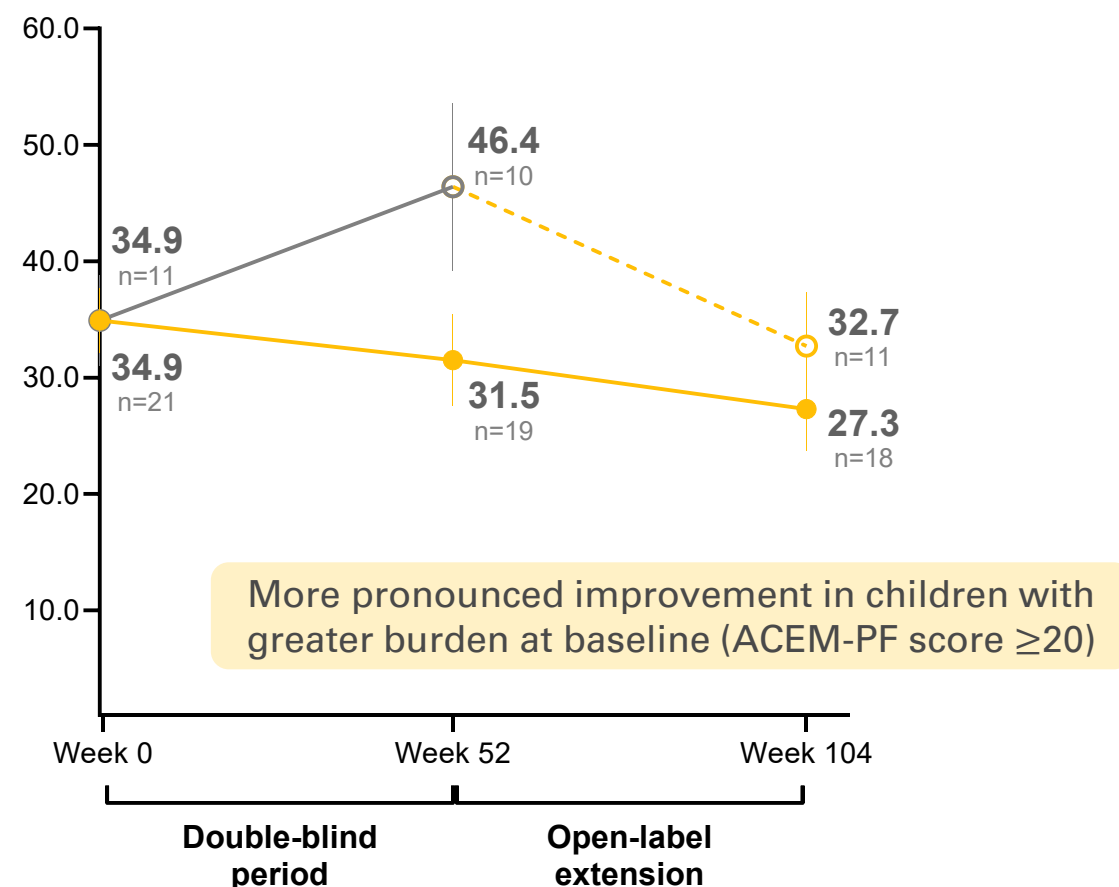
The measure is completed by the caregiver and scored on a 0-100 scale with higher scores indicating greater impairment

Navepegritide treatment positively impacted HRQoL, particularly for the ACEM-Physical Functioning domain

Same respondent analysis



Same respondent, baseline ACEM-PF score ≥ 20



Most AEs in navepegritide-treated children were mild or moderate, with none leading to treatment discontinuation or trial withdrawal

AEs through Week 104	Navepegritide-treated children [†] N=84
Any treatment-emergent AE, n (%)	76 (90.5)
Most frequent AEs (≥15% of children)	
Otitis media	31 (36.9)
Nasopharyngitis	29 (34.5)
Pyrexia	29 (34.5)
Upper respiratory tract infection	19 (22.6)
Headache	17 (20.2)
Vomiting	16 (19.0)
Influenza	13 (15.5)
Injection site reaction (ISR), n (%)	17 (20.2)
ISRs per person-year of exposure	0.35
Symptomatic hypotension, n (%)	0 (0.0)

[†]Cumulative treatment exposure to navepegritide was 137 person-years

- The overall rate of ISRs was low, and all events were mild
 - 0.35 ISRs per person-year of exposure is equivalent to approximately 1 ISR for every 3 years of treatment
- No symptomatic hypotension occurred through 104 weeks of navepegritide treatment
- In the OLE, two children experienced fractures associated with trauma (1 clavicle, 1 forearm); neither fracture included the growth plate

Conclusions

During the ApproaCH trial

- Children who continued treatment with navepegritide maintained elevated AGV through Week 104
- Children who switched from placebo to navepegritide at Week 52 had increased AGV at Week 104, comparable to improvements seen with navepegritide in the double-blind period
- Achondroplasia-specific and CDC-based height Z-scores improved with navepegritide treatment; gains were consistent with those observed with navepegritide in the double-blind period
- Treatment with navepegritide had a positive impact on physical functioning
- Navepegritide was generally well-tolerated, with no new safety signals identified

Results from the ApproaCH trial support the efficacy and safety of navepegritide through 104 weeks of treatment

We would like to thank the children, caregivers,
study staff, and investigators
who participated in this trial

Author Declaration of Conflicts of Interest

Carlos A Bacino: Investigator in clinical trials with Ascendis Pharma

The ApproaCH trial was funded by Ascendis Pharma Growth Disorders A/S