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Background

- Vosoritide is the first and only targeted treatment currently licensed for use in achondroplasia from infancy until growth plate closure.
- Clinical trials have shown its impact on growth and quality of life in children with achondroplasia across different ages.
- This study explored the impact of vosoritide on wider health and functional outcomes based on clinical expert experiences.

Methods

- Clinical experts involved in the vosoritide clinical trials participated in a modified Delphi study.
 - Panel members were clinicians involved in at least one of the vosoritide Phase 2 clinical trials (111-202/205 or 111-206/208) due to their long-term experience with vosoritide (up to 9.3 years follow-up), and experience with patients starting vosoritide <5 years of age (up to 5.4 years follow-up) respectively.
- The study consisted of two phases:
 - A structured explorative phase to determine the most significant outcomes of patients with achondroplasia beyond height, based on experience with both untreated and treated patients.
 - An anonymous voting of statements that were developed based on the results of the explorative phase (Figure 1).

Figure 1. Study design

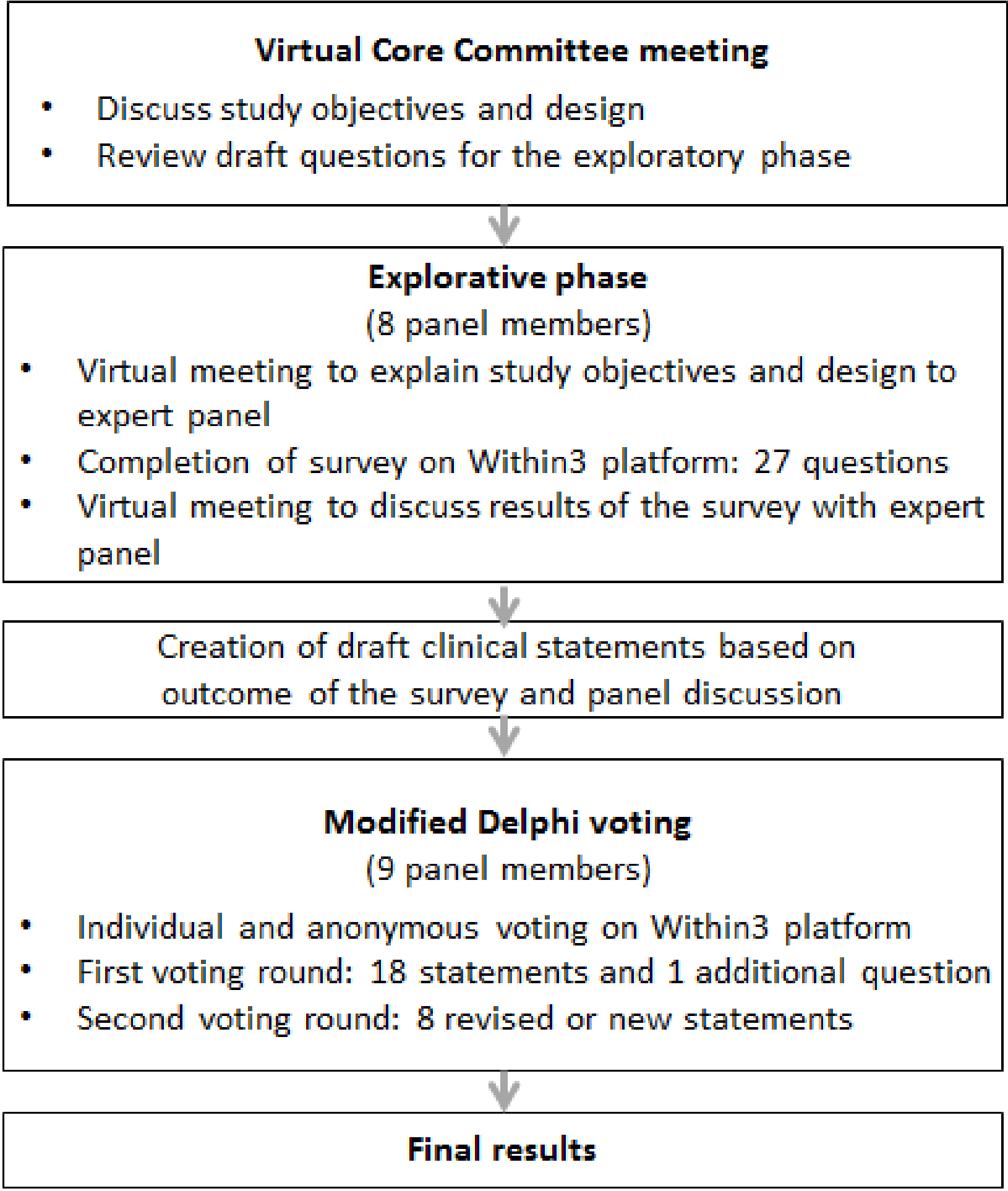


Table 1. Modified Delphi voting results of clinical experts: achondroplasia burden (N=9 panel members)

Statement	Agreement ^a	Can't judge
Functional outcomes		
Functional limitations are estimated to be prevalent in untreated patients with achondroplasia, with toileting, reaching for door handles/lights and accessibility to toilets/sinks being most frequently affected, particularly in young children and decreasing with age	100%	0%
Mobility limitations		
Difficulty to climb stairs is a frequent issue in untreated patients with achondroplasia*	100%	0%
Difficulty running is a frequent issue in untreated patients with achondroplasia*	100%	0%
Emotional and social limitations		
Frustration due to physical limitations and poor self-confidence are estimated to be prevalent among untreated patients with achondroplasia, particularly during childhood and adolescence	89%	0%
Impact on parents/caregivers		
Worry about complications has a (relatively) high impact on caregivers/families of untreated children with achondroplasia*	78%	0%
Worry about future challenges and social acceptance, as well as stress/burden of providing daily assistance to untreated children with achondroplasia have a (relatively) high impact on their caregivers/families*	89%	0%
Impact of achondroplasia on caregivers is most apparent during infancy, childhood and adolescence*	100%	11%

Revised and new statements accepted in the second voting round are indicated with an asterisk (*).
^a% of panel members (N=9) agreeing or strongly agreeing with the assumption, excluding "can't judge" votes.

Results

- Clinical experts (N=9) reached ≥75% agreement on 19 final statements, with ten achieving 100% agreement.
- They agreed that vosoritide can positively impact functional outcomes (e.g., accessibility to toilets/sinks, reaching door handles/lights), mobility (e.g., improved stairclimbing, running), emotional/social limitations (e.g., self-confidence), leg bowing, and caregiver burden (e.g., worry about complications, future challenges, and societal acceptance).
- Age at treatment initiation and treatment duration are considered important determinants of treatment impact.

Table 2. Modified Delphi voting results of clinical experts: vosoritide treatment impact (N=9 panel members)

Statement	Agreement ^a	Can't judge
Functional outcomes		
Current experience in the phase II clinical studies suggests that vosoritide can improve accessibility for toilets/sinks, reaching for door handles/lights, and toileting	100%	0%
Age at treatment initiation and treatment duration influence the impact of vosoritide on functional outcomes	89%	0%
Mobility limitations		
Current experience in the phase II clinical studies suggests that vosoritide can have a positive impact on stair climbing and ability to run	89%	0%
Age at treatment initiation and treatment duration influence the impact of vosoritide on mobility outcomes	100%	0%
Emotional and social limitations		
Current experience in the phase II clinical studies suggests that vosoritide can improve self-confidence and ability to participate in activities, and reduce frustration due to physical limitations	100%	0%
Age at treatment initiation and treatment duration influence the impact of vosoritide on emotional/social limitations	89%	0%
Complications of achondroplasia		
Current experience in the phase II clinical studies suggests that vosoritide can have a positive impact on leg bowing, especially in early-treated children	78%	0%
Age at treatment initiation and treatment duration influence the impact of vosoritide on leg bowing*	100%	0%
No negative impact of vosoritide on complications has been observed so far	89%	0%
Impact on parents/caregivers		
Current experience in the phase II clinical studies suggests that vosoritide can have a positive impact on worry about complications, future challenges and society acceptance, as well as stress/burden of providing daily assistance to patients*	100%	0%
Age at treatment initiation and treatment duration influence the impact of vosoritide on burden on parents/caregivers	89%	0%
Additional factors that can influence the impact of vosoritide on burden on parents/caregivers include access to and support by the clinic and services, geographic distance from the treatment center, motivation to adhere to treatment, therapeutic education, socioeconomic status, family structure/ dynamics, community (including church), psychosocial, emotional, developmental and educational factors*	100%	11%

Conclusions

- The results of this study provide valuable new insights regarding the impact of vosoritide on outcomes of achondroplasia beyond height, including functional outcomes, mobility, emotional and social outcomes, complications, and impact on caregivers.
- The findings also underscore the critical role of age at treatment initiation and treatment duration in influencing these outcomes.
- Given the current lack of prospectively collected data for most of these outcomes, clinical expert opinions can provide important first-hand information for clinicians.

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