The World Congress of Nephrology (WCN) 2023
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Can young children swallow multiple coated mini-tablets? Results from an open-label, single-dose crossover study

Introduction: Iptacopan (LNP023) is an orally administered proximal complement inhibitor that specifically binds factor B and inhibits the alternative complement pathway. It is in clinical development for the treatment of complement-mediated diseases in adults and children. The physicochemical properties of iptacopan present challenges in liquid formulation development for children and require alternative approaches. Coated mini-tablets can overcome this challenge and have proven to be acceptable for infants and children (Klingmann et.al, 2013). This study investigated the acceptability of coated mini-tablets among children aged 1 month to 6 years and their preference for swallowing either several smaller (2.0 mm) or fewer larger (2.5 mm) tablets for the respective age range based on body weight, thus guiding an optimal mini-tablet size selection for pediatric patients.

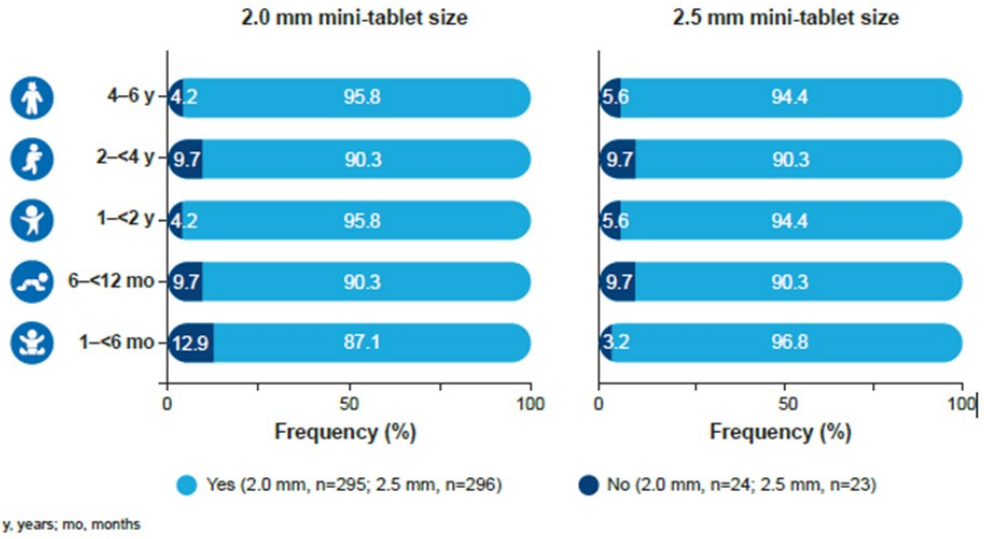
Methods: This open-label, single-dose crossover study recruited 360 children (inpatients or outpatients) at the University Children's Hospital Düsseldorf. The study was performed in five age groups (4–6 years, 2–<4 years, 1–<2 years, 6–<12 months, and 1–<6 months), each with two randomized parallel arms receiving a higher or lower number of mini-tablets in a crossover fashion (N=32–72 per age group; recruitment in 1–<6 months age group was stopped early due to 'swallowing the wrong way/coughing' event in 3 children). The primary objective assessed acceptability derived from swallowability scoring (rated as 'Yes' for swallowability score 1 or 2 and 'No' for swallowability score 3–5). Secondary objectives included palatability (rated as 'pleasant', 'neutral', or 'unpleasant'), acceptability as a composite endpoint derived from palatability and swallowability scores, and safety. All parameters were compared between the two regimens (high number of 2.0 mm versus low number of 2.5 mm mini-tablets) in each age group. Corresponding two-sided 90% confidence intervals (CIs) were calculated for the averaged differences in acceptability and palatability rates between the treatment regimens.

Results: Of the 320 children randomized, 319 completed the study; one child was withdrawn due to coughing. Acceptability rates, based on swallowability, were high and comparable across tablet sizes, quantities, and age groups (averaged difference −0.3%, 90% CI −2.0 to 1.4; p=0.757; Figure). Palatability was rated as 'pleasant' by the majority of children ('neutral' rating in 1-<6 months age group in line with developmental milestones) across all tablet sizes, quantities, and specified age groups (averaged difference 1.0%, 90% CI −0.2 to 2.2; p=0.178). The composite endpoint showed 'high' or 'good' acceptability across all tablet sizes, quantities, and age groups (averaged difference −0.6%, 90% CI −2.6 to 1.3; p=0.588). No adverse events or deaths were reported in the study.

Conclusions: Children aged 6 months to 6 years showed acceptability and tolerability for both a higher number of smaller (2.0 mm) and lower number of larger (2.5 mm) coated mini-tablets. Use of coated mini-tablets in children aged 1 to <6 months warrants careful consideration due to differences in the development of swallowing capabilities in this age group. Coated mini-tablets are potentially suitable formulations for pediatric patients in the iptacopan clinical program.

These data were previously presented at the 2022 IPNA Congress.

Figure: Acceptability rates based on swallowability criteria



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Key words: Iptacopan, mini-tablets, acceptability, palatability, swallowability, pediatric formulation

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Transparency declaration and ethics statement:

This study was conducted according to International Council for Harmonization E6 Guidelines for Good Clinical Practice that have their origin in the Declaration of Helsinki.

Declaration of funding and interests:

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