primary studies - published RCT

Long-Term Impact of Lumacaftor/Ivacaftor Treatment on Cystic Fibrosis Disease Progression in Children 2 Through 5 Years of Age Homozygous for F508del-CFTR: A Phase 2, Open-Label Clinical Trial.

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Study design (if review, criteria of inclusion for studies)

Phase 2 trial had two parts: Part 1, a 48-week, randomized, double-blind, placebo-controlled study (previously reported) was followed by a 48-week open-label treatment period

Participants

Children 2 Through 5 Years of Age Homozygous for F508del-CFTR

Interventions

This phase 2 trial had two parts: Part 1, a 48-week, randomized, double-blind, placebo-controlled study of LUM/IVA in children aged 2 through 5 years (previously reported) was followed by a 48-week open-label treatment period where all children received LUM/IVA (Part 2; reported here).

Outcome measures

Endpoints assessed in Part 2 included absolute changes from baseline in chest magnetic resonance imaging (MRI) global score at week 96; weight-for-age, stature-for-age, and body mass index (BMI)-for-age z-scores at week 96; lung clearance index (LCI(2.5)) through week 96; chest MRI morphological score, chest MRI perfusion score, weight, stature, BMI, and microbiology cultures (oropharyngeal swabs) at week 96; sweat chloride, serum levels of immunoreactive trypsinogen, fecal elastase-1 levels, and fecal calprotectin through week 96; and number of pulmonary exacerbations (PEx), time-to-first PEx, and number of CF-related hospitalizations.

Main results

49 children received â‰¥1 dose of LUM/IVA in the open-label period (33 in the LUM/IVA to LUM/IVA group and 16 in the placebo to LUM/IVA group); mean exposure 47.1 (SD, 5.2) weeks. The mean absolute change in MRI global score (negative value = improvement) from baseline at Week 96 was -2.7 (SD 7.0; 95% CI, -5.2 to -0.1) in the LUM/IVA to LUM/IVA group and -5.6 (SD 6.9; 95% CI, -9.2 to -1.9) in the placebo to LUM/IVA group. Improvements in LCI(2.5), sweat chloride concentration, and markers of pancreatic function and intestinal inflammation were also observed in both groups. Growth parameters remained stable in both groups. The majority of children had adverse events (AEs) considered mild (38.8%) or moderate (40.8%). Two (4.1%) children discontinued LUM/IVA treatment due to AEs (distal intestinal obstruction syndrome [n=1] and alanine aminotransferase increase [n=1]).

Authors' conclusions

These findings confirm the potential for early LUM/IVA treatment to alter the trajectory of CF disease progression, including CF lung disease, in children as young as 2 years of age.

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See also

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Keywords

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lumacaftor; VX-809;