

primary studies - published RCT

VO(2max) as an exercise tolerance endpoint in people with cystic fibrosis: Lessons from a lumacaftor/ivacaftor trial.

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

Multisite Phase 4 trial

Participants

Subjects ≥ 12 years of age with CF homozygous for F508del-CFTR (n=70).

Interventions

Participants were randomized to receive lumacaftor/ivacaftor (n = 34) or placebo (n = 36).

Outcome measures

The primary endpoint was relative change from baseline in maximum oxygen consumption (VO(2max)) during cardiopulmonary exercise testing (CPET) at Week 24. The key secondary endpoint was relative change from baseline in exercise duration during CPET at Week 24. Other secondary endpoints included changes in other indices of exercise tolerance and changes in CF assessments; safety and tolerability were assessed as an endpoint.

Main results

The least-squares mean difference for lumacaftor/ivacaftor versus placebo in relative change in VO(2max) from baseline at Week 24 was -3.2% (95% CI: -9.2, 2.9; P=0.3021); the least-squares mean difference in relative change from baseline in exercise duration at Week 24 was -3.2% (95% CI: -8.0, 1.6). Safety results were consistent with the known lumacaftor/ivacaftor safety profile.

Authors' conclusions

Definitive conclusions regarding the impact of lumacaftor/ivacaftor on exercise tolerance cannot be drawn from these results; however, multicenter studies using CPETs can be reliably performed with multiple time points and conventional methods, provided that calibration can be achieved. Future studies of exercise tolerance may benefit from lessons learned from this study.

<http://dx.doi.org/10.1016/j.jcf.2020.12.006>

See also

J Cyst Fibros. 2021 May;20(3):499-505. doi: 10.1016/j.jcf.2020.12.006. Epub 2020 Dec 24.

Keywords

Child; Aminophenols; CFTR Modulators; Genetic Predisposition to Disease; Orkambi; pharmacological_intervention; VX-770; ivacaftor; lumacaftor; VX-809;