Other Reviews - - Other Review

Comparative efficacy and safety of CFTR modulators for people with cystic fibrosis with phe508del mutation: a systematic review and bayesian network meta-analysis.

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

Systematic review with Network Meta-Analysis

Participants

People with cystic fibrosis who have a phe508del mutation.

Interventions

Cystic fibrosis transmembrane conductance regulator (CFTR) modulators (correctors and potentiators)

Outcome measures

Primary outcomes were efficacy (change in percent predicted forced expiratory volume (ppFEV(1)), sweat chloride) and safety (frequency of serious adverse events).

Main results

Of the 3473 studies identified through our literature search, 29 studies involving 6450 patients examining 34 treatment combinations were included. For adults treated over 4-8 weeks, vanzacaftor 10 mg-tezacaftor 100 mg-deutivacaftor 150 mg combination therapy had a significant improvement over placebo in improving ppFEV(1) (MD: 15.9; 95% CrI: 7.2-24.2 [high certainty]) with a SUCRA of 92% suggesting the highest probability of effectiveness. Moreover, the vanzacaftor 20 mg-tezacaftor 100 mg-deutivacaftor 150 mg showed a significant reduction in sweat chloride levels (MD: -49.3 mmol/L; 95% CrI: -67.2 to -31.7 [high certainty]) and improved the CFQ-R scores (MD: 39; 95% CrI: 21.2-56.9; [high certainty]) when compared to placebo after 4-8 weeks of treatment. Our findings also highlighted that the triple combination therapies of vanzacaftor 20 mg-tezacaftor 100 mg-deutivacaftor 250 mg and elexacaftor 200 mg-tezacaftor 100 mg-ivacaftor 150 mg provided clinically meaningful improvements across all measured outcomes in adults treated for more than 8 weeks. Confidence in the estimates ranged from high to low, and safety analyses were limited by the low serious adverse event rates.

Authors' conclusions

These findings indicate that vanzacaftor-tezacaftor-deutivacaftor and elexacaftor-tezacaftor-deutivacaftor emerged as the most effective treatment options in adults. However, these results should be interpreted cautiously due to limited data and the low quality of existing evidence. FUNDING: None.

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See also

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Keywords

CP-656; Aminophenols; CFTR Modulators; deutivacaftor; elexacaftor; ivacaftor; ivacaftor+lumacaftor; ivacaftor+tezacaftor; ivacaftor+tezacaftor+elexacaftor; lumacaftor; Orkambi; pharmacological_intervention; Symdeko; Symkevi; tezacaftor; Trikafta; vanzacaftor; VX-121; VX-152; VX-371; VX-440; VX-445; VX-561; VX-659; VX-661; VX-770; VX-809; kaftrio;