

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;