Cochrane Database of Systematic Reviews - - Cochrane Review

Lumacaftor-ivacaftor (Orkambi) for treatment of cystic fibrosis (Structured abstract)

Code: HTA-32016000090 **Year:** 2015 **Date:** 2016 - updated: 21 August 2019 **Author:** HAYES

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

Randomised controlled trials (RCTs), published or unpublished and in any language will be included. Quasi-RCTs will be included if the authors are satisfied that the groups are similar at baseline.

List of included studies (1)

Treggiari 2011

Participants

People with CF, diagnosed clinically or by genetic or sweat testing. Each participant must have had an episode of PA within the last six months which was successfully treated with an eradication regimen. They must remain free of infection with PA between the end of eradication and start of treatment for ongoing prevention.

Interventions

In PWCF in whom PA has been successfully eradicated, a time-limited course of therapy (if this is antimicrobial, it may be oral, inhaled or intravenous or any combination of these) to prevent a recurrent infection with the organism to usual care, placebo or another therapeutic strategy we will compared. Time-limited therapy will include all treatment in which a specific duration is pre-specified. Time-limited therapy will include regimens where the treatment is intermittent but continues at specified intervals for a defined duration. Long-term suppressive therapy, given for an indefinite period, will not be considered.

Outcome measures

Primary outcomes: Time to next isolation of PA (identified by any method, e.g. sputum culture, BAL or OP culture and as defined by the trial investigators). Secondary outcomes: Change in quality of life (QoL); Change (absolute and relative) from baseline for pulmonary function tests; Pulmonary exacerbations; Nutritional parameters; Time to chronic PA infection; Adherence to treatment self-reported measures; Adverse effects of treatment; Mortality; Isolation of resistant bacteria; Cost effectiveness

Main results

One trial (n = 306) included in the review; however, only 253 participants had undergone successful eradication of PA, so fulfilling the inclusion criteria for our review. Information presented relates only to the included subset of participants. The trial recruited children aged one to 12 years (mean (standard deviation (SD)) age of 5.8 (3.5) years), 129 participants (51.0%) were female and the median followâ€•up was 494 days. We compared cycled therapy with tobramycin inhalation solution (TIS), in which participants underwent 28 days of TIS every three months, with cultureâ€•based therapy, in which participants were only prescribed medication when a quarterly sputum sample was positive for PA. Reasons for downgrading the quality of the evidence included applicability (only included children), incomplete outcome data and a small number of participants. The time to next isolation of PA was probably shorter with cycled TIS therapy than with cultureâ€•based therapy, hazard ratio (HR) 2.04 days (95% confidence interval (CI) 1.28 to 3.26) (moderateâ€•quality evidence). This is in contrast to the main publication of the only included trial, which examined rate of PA positivity rather than time to PA infection and included participants not eligible for inclusion in this review. At the end of the trial, there was no difference between the cycled and cultureâ€•based groups in the change from baseline in forced expiratory volume in one second (FEV1) L, mean difference (MD) 0.0 L (95% CI â€•0.09 to 0.09) or in FEV1 % predicted, MD 0.70% (95% CI â€•4.33 to 5.73) (both very lowâ€•quality evidence). There was no difference in the change from baseline for FVC between the groups. There was also no difference in the frequency of pulmonary exacerbations between groups, MD â€•0.18 (95% CI â€•0.51 to 0.14) (moderateâ€•quality evidence). Similarly, there was no difference between groups in the risk of participants developing novel resistant bacteria, RR 1.00 (95% CI 0.67 to 1.5) (moderateâ€•quality evidence). There were more severe adverse events in the cycled group, but the type of treatment probably makes little or no difference to the results, RR 0.65 (95% CI 0.39 to 1.11) (moderateâ€•quality evidence). There was no difference between groups in the change in weight or height from baseline or in rates of adherence to tobramycin or all trial medicines. The included trial did not assess changes in quality of life, the time to chronic infection with PA or the costâ€•effectiveness of treatment.

Authors' conclusions

Cycled TIS therapy may be beneficial in prolonging the time to recurrence of PA after successful eradication, but further trials are required, specifically addressing this question and in both adults and children

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See also

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Keywords

Anti-Bacterial Agents; Bacterial Infections; Infection; Oral; pharmacological_intervention; Pseudomonas aeruginosa; Pseudomonas; Respiratory Tract Diseases; Respiratory Tract Infections; Colonization; Exacerbation;