HTA - - Health Technology Assessment Report

Effects of Lumacaftor/Ivacaftor on Cystic Fibrosis Disease Progression in Children 2 through 5 Years of Age Homozygous for F508del-CFTR: A Phase 2 Placebo-controlled Clinical Trial.

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

HTA review of the clinical effectiveness and cost-effectiveness

Participants

CF adults and children (>/= 6 years) with at least one G551D mutation were eligible.

Interventions

Ivacaftor (Kalydeco((R)), Vertex Pharmaceuticals) is the first of a new class of drugs that target the underlying protein defect in cystic fibrosis (CF).

Outcome measures

utility values, annual decline in percentage predicted forced expiratory volume in 1 second (FEV1), and the baseline exacerbation rate; relation between costs, age and percentage predicted FEV1. Estimates of treatment effect of ivacaftor came from the clinical effectiveness review.

Main results

Three studies were included: a randomised controlled trial (RCT) in adults (n = 167) (>/= 12 years), a RCT in children (n = 26) (6-11 years), and an open-label extension study of the two RCTs. Both RCTs reported significantly greater changes from baseline in all measures of lung function in patients receiving ivacaftor than in those receiving placebo. The mean difference in change in percentage predicted FEV1 was 10.5 [95% confidence interval (CI) 8.5 to 12.5] percentage points in the adults' study and 10.0 (95% CI 4.5 to 15.5) percentage points in the children's study at 48 weeks. Improvements in lung function were seen across all subgroups investigated (age, sex, study region and lung function). There were significantly greater improvements in the ivacaftor group than in the placebo group for all outcomes assessed (exacerbations, quality of life, sweat chloride and weight) with the exception of quality of life in children. Improvements were maintained in the open-label trial. Adverse events were mainly minor and comparable across treatment groups. Both RCTs reported more withdrawals in the placebo group than in the ivacaftor group. The incremental cost-effectiveness ratio varied between pound 335,000 and pound 1,274,000 per quality-adjusted life-year gained. The total additional lifetime costs for all eligible CF patients in England ranged from pound 438M to pound 479M; the lifetime cost for standard care only was pound 72M.

Authors' conclusions

The available evidence suggests that ivacaftor is a clinically effective treatment for patients with CF and the G551D mutation; the high cost of ivacaftor may prove an obstacle in the uptake of this treatment. The main priority for further research is the long-term effectiveness of ivacaftor. STUDY REGISTRATION: This study is registered as PROSPERO CRD42012002516. SOURCE OF FUNDING: The National Institute for Health Research Health Technology Assessment programme.

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See also

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Keywords

Aminophenols; CFTR Modulators; Genetic Predisposition to Disease; pharmacological_intervention; VX-770; ivacaftor; G551D-CFTR;