Triple therapy: A new dawn in treatment for cystic fibrosis

Cystic fibrosis (CF) is an autosomal recessive condition, which affects ~80 000 people worldwide. It is due to a mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene, which results in defective function of an anion channel in epithelial cells, leading to poor chloride transport. This causes the accumulation of mucus in the respiratory and gastrointestinal tract as well as other organs.[1]

The Food and Drug Administration in the USA has just approved trikafta, a combination of 1 potentiator and 2 correctors, consisting of elexacaftor, ivacaftor and tezacaftor for the treatment of CF. It is approved for patients 12 years old or more with at least one F508del mutation in the *CFTR* gene, which is thought to encompass 90% of the cystic fibrosis population in the USA.

Trikafta was analysed in two phase-3 trials in which the primary endpoint was an increase in the percent-predicted forced expiratory volume in 1 second ($ppFEV_1$). The first trial was a 24-week, randomised, double-blind, placebo-controlled trial involving 403 patients who had an F508del mutation and a mutation on the second allele that results in either no CFTR protein or a CFTR protein that is not responsive to ivacaftor or tezacaftor/ivacaftor alone. In this trial, the mean $ppFEV_1$ increased by 13.8% from baseline compared with placebo. There were also improvements in sweat chloride, number of pulmonary exacerbations and body mass index compared with placebo.[2]

The second trial was a 4-week randomised, double-blind, active-controlled trial involving 107 patients who had 2 identical F508del mutations comparing triple therapy with tezacaftor/ivacaftor combination. There was an increased mean $ppFEV_1$ of 10% from baseline in the triple-therapy group. There was also an improvement in the sweat chloride concentrations as well as in the number of exacerbations.[3]

The most common adverse reactions reported were headache, upper respiratory tract infection, abdominal pain, diarrhoea, rash, increased liver enzymes, nasal congestion, rhinorrhea, influenza, sinusitis and increased blood bilirubin.

This novel breakthrough is a great step for the treatment of CF; however, the cost of the drug may be a limiting factor as it is USD311 000 (~ZAR4.6m) for a year's supply. This will be a great impediment for those in developing countries.

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