CYSTIC FIBROSIS Western Australia

CF Fact
cystic fibrosis fact sheet

CFTR Modulator Therapies

Conventional medications for CF focus on treating the symptoms of CF. Cystic fibrosis transmembrane conductance regulator (CFTR) modulators are a new drug therapy that differ from other therapies because they aim to improve or restore the function of the defective CFTR protein made by the CFTR gene.

These therapies are mutation specific and aim to treat the cause of CF and slow the decline in lung function. Different mutations cause different defects in the CFTR protein.

The individual modulators act in different ways depending on how the mutant protein affects the cell. It is important to remember that different therapies are suited to different people depending on their mutation and their medical problems. It is necessary to match the right combination of drugs to each individual.

The CFTR protein controls the flow of water and chloride in and out of the cells lining the airways of the lungs and many other organs. Depending on the mutation, the CFTR protein can be present in small amounts or absent completely. The lack of CFTR protein results in sticky mucus in the lungs, damage to the pancreas and problems in other parts of the body.

Is is important to note that current modulator therapies may not work for everyone, even in those with the specific gene mutation.

This may be due to the inability to tolerate the medication or due to side effects experienced. It is hoped that 90% of all CF gene mutations will be able to be treated with a specific combination of modulators very soon.

CFTR Modulators

Kalydeco® (Ivacaftor)
Indicated for those who have a gating (class III) mutation in their CFTR gene such as: G551D, G1244E, G178R, and G5515. Kalydeco® binds to the defective protein, helping to open the channel so that more chloride and water can move in and out of the cells, thinning the mucus in the lungs and other organs. Available to those eligible over 12 months of age.

Orkambi® (Lumacaftor/Ivacaftor)
A combination corrector therapy that works for people with two copies of the F508 del mutation. Lumacaftor helps the CFTR protein to become the right shape, move to the cell surface and remain there longer. Used with Ivacaftor (Kalydeco®) this allows more chloride and water to flow and reduces the symptoms of CF. This is available to those eligible two years of age and over.

Symdeko® (Tezacaftor/Ivacaftor and Ivacaftor)
A combination therapy for people with two copies of F508 del mutation or who have at least one mutation in the CFTR gene that is responsive to Symdeko® based on laboratory testing and/or clinical evidence. Tezacaftor increases the amount of mature CFTR protein delivered to the cell surface. Available to those eligible age 12 years and older.

Trikaftor® – (Elexacaftor/Ivacaftor/Tezacaftor)
Is the first triple combination therapy indicated for people with an F508 del mutation and one minimal function mutation. Approved by the U.S. Food and Drug Administration in October 2019 for those 12 years and older. Not currently approved by the Australian Therapeutic Goods Administration but available for some who fit strict eligibility criteria on compassionate grounds. The exciting thing about this drug is that is has the potential to treat approximately 90% of the CF population!

How to Get Involved

Each trial has guidelines about who can participate. They also have inclusion and exclusion criteria which refers to the standards used to decide eligibility. If you are interested in being involved in a trial, please talk to your CF team.

Useful Resources

- Kalydeco® (Health Direct)
- Orkambi® (Health Direct)
- Symdeko® (Health Direct)
- Kalydeco® (Vertex- US site)
- Orkambi® (Vertex- US site)
- Symdeko® (Vertex- US site)
- Research Stories (CFWA)
- CFWA Factsheets

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