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Title:

Year in Review (2022): Modulators and COVID-19: the story does on..

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Summary:

This article highlights some of the most important research that has been published in 2022. Studies looking at the effects of COVID-19 confirmed that people with Cystic Fibrosis (pwCF) fared better than expected and infection did not appear to worsen CF related lung disease [1]. Having said this, some pwCF did suffer serious infection and risk factors for this were low lung function, diabetes, being over 40 years old, low body mass index and previous transplant [2, 3].

The role of modulator drugs in the treatment of people with CF is the focus of a new publication: "Standards of Care for CFTR variant-specific therapy" [4]. Research published in 2022 confirmed the positive results of all modulator drugs in eligible patients (including children) both in trial settings and in real world studies [5 - 10]. New evidence also shows that Elexacaftor/ Tezacaftor/ Ivacaftor (ETI) works even in those with advanced lung disease (and low lung function), and there is new data showing its use in people after transplant (both lung and liver) [11 - 13].

The effect of ETI on mental health, which has been a concern for patients and doctors alike, is starting to emerge [14]. Many of the patients affected in this case series had a history of anxiety or low mood suggesting that some people may be at greater risk of developing mental health side effects.

Lung infections, and the best way to treat them, remain an important area of investigation. One study demonstrated that people respond better to treatment delivered in hospital [15]. Current guidelines for treating infections in people who culture Pseudomonas suggest using 2 different classes of antibiotic, however, this may not be necessary; using data

from a large, multi-national study, no difference was found in the number of people needing further treatment within 30 days, regardless of the number of antibiotic classes used [16]. A separate study looked at the effect of changing antibiotics, due to a poor response, during treatment for an infection. No difference was found implying that some patients may have a slow response to treatment regardless of antibiotic choice [17].

Several articles focussed on early lung disease in pwCF. Viruses do not appear to lead to a worsening of CF lung disease (as detected on CT scans) [18]. Two separate studies looked at the effect of Azithromycin and Hypertonic saline on lung damage, as assessed by CT scanning. Long term treatment with azithromycin was not associated with lower rates of lung damage on CT scan, but did reduce the number of antibiotics required [19]. On the other hand Hypertonic saline led to improvements that could be detected on CT imaging [20].

An emerging problem in pwCF is the shift from people being underweight to being overweight or obese, shown using data from the US CF registry (2000 - 2019) [21], which is prior to the introduction of modulators. However, more recent evidence suggests that modulator drugs are only going to exacerbate this trend [22]. With an aging CF population, this means we may see an increase in heart disease, which has previously been rare in pwCF.

Finally, there are several novel approaches being pursued to find treatment for the 15 - 20% individuals not able to benefit from modulator drugs. The hope is that over the next few years we will start to see results that will lead to highly effective treatment for all pwCF.

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