Cystic Fibrosis a fight we must win

Orkambi, the Cystic Fibrosis Trust and the Accelerated Access Review

- Cystic fibrosis (CF) is a genetic condition affecting more than 10,800 people in the UK.
- The gene affected by CF controls the movement of salt and water in and out of cells. People with cystic fibrosis experience a build-up of thick sticky mucus in the lungs, digestive system and other organs, causing a wide range of challenging symptoms affecting the entire body.
- The median age of death in 2015 was 28.
- Precision medicines like Kalydeco and Orkambi are the first treatments that tackle the underlying cause of CF - the genetic defect - rather than just the symptoms.
- These treatments offer long-term preventative stabilization of cystic fibrosis, which the current NICE system – based on 24 weeks of clinical trial data - struggles to measure.
- The Cystic Fibrosis Trust proposes an innovative solution for Orkambi to be provided on a managed access scheme while the UK CF Data Registry gathers crucial real-world data.
- This offers a unique test-bed for the reforms proposed in the Accelerated Access Review (the AAR) and provides a perfect candidate for an Accelerated Access Partnership.

Kalydeco is the first precision medicine for CF. It targets a mutation affecting around 6% of people with CF in the UK. It was approved in 2012, outside of the current NICE process. Long-term data suggests that patients on this drug could expect near normal life expectancy.

Orkambi is the next precision medicine for CF. It targets a mutation affecting around 40% of people with CF in the UK. NICE cited a lack of long-term data in being unable to recommend Orkambi in 2016, acknowledging it as 'an important new therapy for managing CF', with 'significant clinical benefits' as well as 'wider benefits to society for people with CF'.

Data published in October at the North American Cystic Fibrosis Conference, based on 96 weeks of trials, shows that Orkambi slows the decline in lung health by up to 42%. This is comparable with the 47% slow in decline caused by Kalydeco.

This data was unavailable to NICE and clearly illustrates the point that drugs like Orkambi need the chance to prove their worth in the long-term.

Treatments such as Orkambi cannot be accurately assessed under the current the NICE appraisal system. The focus on measuring the benefits of a treatment in terms of quality-adjusted life years massively underestimates the impact drugs like Orkambi have on quality of life over the long term.

With a pipeline of treatments meaning 90% of people with CF could be eligible for a precision medicine within 5 years, we must create a fair and sustainable model for reimbursement.

The CF Trust is therefore proposing a solution under which access to Orkambi is granted while crucial real-world data is gathered on longer-term impact using the UK CF Data Registry. This has been endorsed by NICE and is supported by Vertex and the clinical community. It could provide a template for future appraisals that could be adapted across other conditions.

The UK CF Data Registry is a one-of-a-kind resource. Over 99% of people with CF consent to their anonymised data being collected, which is then used for research, annual reporting, quality improvement, and as the evidence base for the cost of CF care, informing proportionate tariff payments by NHS England. It is relied upon by the European Medicines Agency to evaluate the safety and efficacy of therapies for post-marketing surveillance. It was cited as an exemplar for data gathering in the interim report of the AAR.

The Proposal

New CF medicines should be made available for specialist clinical prescription immediately following marketing authorization, on the condition that an agreed set of data are routinely monitored through UK CF Registry data against the therapies' performance at a population level.

We suggest the therapy should be concurrently evaluated by a UK-wide technology appraisal body, with three options available to the Appraisal Committee at the conclusion of the process:

- Recommended for routine use and funded from the baseline commissioning budget (a drug which thus demonstrates both clinical and cost effectiveness).
- Not recommended for routine use and thus there is no baseline funding (a drug which thus does not demonstrate clinical effectiveness).
- Recommended for use for evaluation within a predetermined period of time (e.g. 12 months evaluation period plus 6 months for data collection and analysis) in order to build both an extended and novel evidence base via the UK CF Registry's patient records.

After this time, an abbreviated appraisal process would be undertaken to formally review the collated data, and issue final guidance regarding the therapy's continued use.

The establishment of any proposed mechanism of novel CF therapy appraisal must be underpinned by an acceptable interim commercial access arrangement, which confirms the cost of the drug to the NHS (agreed between the company and the NHS) and data collection arrangements.

Participation in the data collection exercise should be open to all eligible individuals covered by the EMA's marketing-authorisation guidance to enable assessment of impact at population level, and understand that participants must be informed and provide written consent in advance, agreeing to the time-limited nature of the data collection exercise.

We believe Orkambi is a therapy where this pilot could be initiated with low administrative and infrastructural burden, as the necessary data collection already happens.

Data from the UK CF Registry could support such a pilot, running for a period of 12 to 24 months to provide sufficient time for the publication of the data from the data collection period.

This model could act as a more powerful rollover study that can call upon both cumulative data from the initial trials and historical data stored in the UK CF Registry, while boosting our holistic understanding of the therapy through collection of broader data points.

The Trust can support this with the Clinical Trials Accelerator Platform, a £3 million investment to bring together CF centres to increase participation and improve delivery and access to CF clinical trials in the UK.

This will be vital - as new treatments become available, the population of people with CF eligible to participate in a clinical trials may be less – increasing the likelihood of traditional clinical trial design having insufficient power to assess outcomes of upcoming therapies.