TRIKAFTA - FAST FACTS

1. **Lung function**
   a. F508/F508del increased by 10% after 4 weeks. Trial participants had been taking Symdeko
   b. F508/minimal increased by 13.8% at 4 weeks and 14.3% versus placebo after 24 weeks
   c. Preservation of lung function … maintain lung health … halts further decline
   d. Relative Fev1 increase ... a sustained improvement
   e. Declining lung function is a key indicator of morbidity and death

2. **Exacerbations**
   a. F508/F508del continues to decrease
   b. F508/minimal saw a 63% decrease over 24 weeks
   c. Awaiting data for F508/residual and F508/gating mutations

3. **Hospitalisations** reduced

4. **Antibiotic use** reduced

5. **Sweat Chloride**
   a. F508/F508del sweat chloride reduced by 45 mmol per litre
   b. F508/minimal mean sweat chloride concentration at week 24 was 57.9 mmol per litre, relative to 102.4 mmol per litre in the placebo group

6. **Nutritional status**
   a. F508/F508 continues to improve
   b. F508/minimal BMI improved significantly at week 24 with a mean difference of 1.04 to placebo
   c. Awaiting data for F508/residual and F508/gating mutations
   d. Increased BMI
   e. Less likelihood of diabetes or less severe symptoms

7. **Mental health** (CFQR)
   a. F508/F508 improved by 14.3%
   b. F508/minimal 20.1%
   c. Awaiting data for F508/residual and F508/gating mutations
   d. Social inclusion, employment, school and reduced' late effects'
   e. Less personal and family stress resulting in less depression and anxiety for patients, parents and support networks

8. **Life years** extended

9. **PBAC Check List**
   - Trikafta trials proved clinical effectiveness & safety

- Trikafta changes health outcomes and extends lives
- Trikafta cannot be compare to other treatments … it is a first!
- Australian's with CF need access to life changing drugs like Trikafta

10. **CF symptoms**
    a. Persistent cough and some difficulty in breathing or wheezing
    b. Salt loss in hot weather resulting in muscle weakness and muscle cramps
    c. Tiredness, lethargy or impaired exercise ability
    d. Poor appetite, frequent bowel motions and malnutrition

11. **Safety – F508del homozygous and F508del/Minimal Function trial**
    a. A favourable safety profile and the triple combination regimen was well tolerated
    b. Most adverse events were mild or moderate. Rash in 10% of patients; hypertension in a patient with pre-existing cirrhosis; elevated levels of creatine kinase and blood-pressure changes
    c. There were no discontinuations in patients F508del homozygous
    d. Adverse events leading to discontinuation in 1% of the patients F508del + minimal function

12. **Conclusions**
    a. Elexacaftor–tezacaftor–ivacaftor was efficacious in patients with cystic fibrosis with two copies of F508del and one F508del + a minimal function genotype
    b. CFTR modulators treat the underlying cause of disease and have improved clinical outcomes in persons with at least one copy of F508del
    c. The small-molecule 'correctors' increase cell-surface expression by improving the processing and trafficking of CFTR. A second corrector overcomes the multiple folding issues by working at a different point. Of CFTR
    d. The small molecule 'potentiators' augment the chloride channel

LINKS

https://www.nejm.org/doi/full/10.1056/NEJMoa1908639

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)32597-8/fulltext?dgcid=raven_jbs_etoc_email