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| **Long-term spirometry follow-up of Cystic Fibrosis patients after compassionate access Elexacaftor-tezacaftor-ivacaftor** |
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| **Introduction/Aim:** Elexacaftor-Tezacaftor-Ivacaftor (ETI) became available in 2019 through an Early Access Program for people with Cystic Fibrosis (CF) and very severe lung disease (FEV1 <30% predicted). In this prospective observational study, interval spirometry was recorded to assess change over long-term follow-up.**Methods:** Twenty-nine adults with CF (n=12 female) were commenced on compassionate access ETI between September 2019 and November 2021. Sixteen were already on a CFTR modulator (n= 11; orkambi, n=1; symdeko, n=4; orkambi to symdeko), 15 were F508del *CFTR* mutation homozygotes. Baseline lung function was assessed prior to ETI initiation and re-assessed at 1-3 months to examine short-term improvements. Thereafter, the best and worst FEV1 values each year were recorded through until 2023 to assess variability and look for evidence of deterioration. Time to best achieved FEV1 over the surveillance period was determined.**Results:** Over the study period one patient died 3.2 years post-initiation, none required transplantation. Median FEV1 prior to ETI was 1.08L (0.96, 1.29) with change from best in the preceding 12-months of -0.22L (-0.35, -0.13). Within 3 months FEV1 improved to median 1.53L (1.38, 1.76) with a change from pretreatment of 0.42L (0.27, 0.62). Best FEV1 over the study period was median 1.7L (1.46, 1.94) with change from pre-treatment of 0.63L (0.42, 0.77) occurring at median 1.09 years (0.26, 2.33) after initiation. Following initiation of therapy there was a continued improvement in FEV1 seen in 60% of eligible patients in the first year, 20% in the second and third year, and 10% in the fourth year. Median patient variability between best and worst FEV1 across the study period was 0.19L (0.13, 0.33) without change with time from ETI initiation.**Conclusion:** For some CF adults with severe lung diseaseETI therapy results in continued FEV1 improvement years after initiation. This persistent improvement may suggest airway remodelling due to ETI therapy.**Grant Support: Nil.** |