6.10 Decreased anti-neutrophil cytoplasmic autoantibodies (ANCA) against bactericidal/permeability-increasing (BPI) post CFTR modulator therapy

Debananda Gogoi [1], Michelle Casey [1,2], Azeez Yusuf [1], Claudie Gabillard-Lefort [1], Cedric Gunaratnam [2], Noel G. McElvaney [1,2] & Emer P. Reeves[1]

[1] Royal College of Surgeons in Ireland, Dublin, Ireland

[2] Beaumont Hospital, Dublin, Ireland

Pseudomonas aeruginosa (P. aeruginosa) is the dominant lung bacteria in patients with cystic fibrosis (PWCF), chronically infecting up to 75% of the adult CF population. Published reports have shown that BPI-ANCA correlate better with lung function impairment and long-time prognosis than anti-*P. aeruginosa* serology, and has similar ability to identify patients with chronic *P. aeruginosa*. Therapeutic interventions specifically targeting defective CFTR protein have improved the outlook for PWCF. Of importance however, there is a gap in our knowledge, and whether the titre of BPI-ANCA declines post CFTR modulator therapy is unknown. Accordingly, the aim of this study was to assess the impact of modulator therapy, elexacaftor/tezacaftor/ivacaftor (ETI), on titres of BPI-ANCA.Plasma samples were collected from patients receiving ETI, post 6 (n=18) or 12 months (n=12) treatment, and healthy controls (n=3). Anti BPI-IgG autoantibodies were measured by ELISA. Results demonstrate that plasma levels of anti BPI-IgG autoantibodies post ETI therapy were significantly reduced at 6 months (p=0.0001) and 12 months (p <0.0001), as compared to pre-modulator therapy samples. The association between *P. aeruginosa* colonization and anti-BPI antibodies is complex, and our findings are the first to demonstrate reduced BPI-IgG autoantibodies post CFTR modulator therapy. Further work is underway to determine whether anti-BPI-IgA and anti-pseudomonas serology similarly decrease post CFTR modulator therapy.

Conflict of Interest: *None to declare*