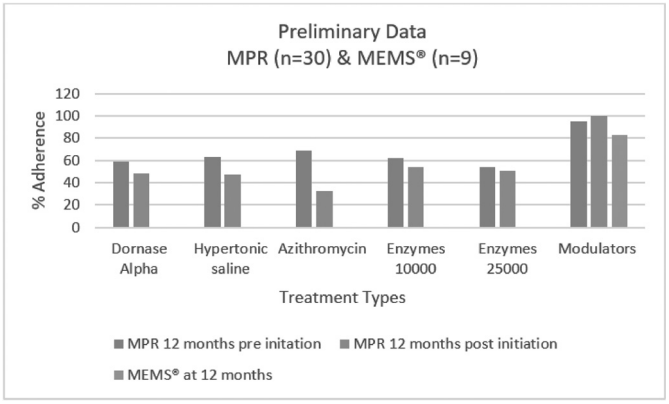

Figure 1. Preliminary medication possession ratio (MPR) data before and after introduction of elexacaftor/tezacaftor/ivacaftor and Medication Electronic Monitoring System (MEMS) data for overall adherence at 12 months

Conclusions: ELX/TEZ/IVA adherence may be overestimated in SRQ and MPR data. Adherence to routine CF therapies is poor, and initiation of ELX/TEZ/IVA may contribute to further reductions with some treatments. Data collection is ongoing for this cohort. Additional data will be available for presentation at the conference.

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Two-year respiratory culture and pulmonary function outcomes in patients on elexacaftor/tezacaftor/ivacaftor

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Background: Elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA), a combination cystic fibrosis (CF) transmembrane conductance regulator modulating medicine, has been widely available to patients in the United States for the past 2 to 3 years. Multiple studies have reflected the improvement in respiratory symptoms and measurements that clinicians have noted while caring for these patients. Previous modulator therapies found similar improvements in respiratory measurements, yet patients were found to have return of baseline *Pseudomonas aeruginosa* densities at 2 years [1]. We investigated whether similar findings would occur with ELX/TEZ/IVA therapy after 2 years and whether improvements in pulmonary function testing measurements would persist as well.

Methods: A retrospective, single-center study was performed using patient data from the adult CF program at the University of Missouri. Fifty patients were included in the analysis, with each patient having completed a pulmonary function test and respiratory culture before and after starting therapy with ELX/TEZ/IVA and again approximately 2 years later.

Results: Significant improvement was found in percentage predicted forced expiratory volume in 1 second (FEV_1pp), percentage predicted forced vital capacity (FVCpp), and absolute change in forced expiratory volume in 1 second (FEV_1 L) and forced vital capacity (FVC L) soon after starting ELX/TEZ/IVA, as well as continued improvement at 2 years in FEV_1pp (mean difference 95% CI, 0.24–5.75, $p = 0.03$) and FVCpp (mean difference 95% CI, 2.6–7.76, $p < 0.001$). There was a significant reduction in percentage of positive respiratory cultures for *P. aeruginosa* soon after starting ELX/TEZ/IVA that persisted at 2 years (mean difference 95% CI, −3.05 to −32.95, $p = 0.01$) (Figure 1A). Unlike *P. aeruginosa*, the percentage of positive respiratory cultures for *Staphylococcus aureus* was not significantly different soon after starting therapy but was found to be significantly lower at 2 years (mean difference 95% CI, −12.5 to −43.5, $p < 0.001$) (Figure 1B). Like *S. aureus*, a significant reduction in percentage of positive respiratory cultures for *Aspergillus* species was found at 2 years that was not seen right after starting therapy (mean difference 95% CI, −2.02 to −25.98, $p = 0.02$) (Figure 1C). No significant difference was noted at 2 y ears in cultures positive for *Candida* species after starting ELX/TEZ/IVA, although a trend toward significance was found at 2 years despite most cultures being obtained via throat swab cultures (before vs 2 years, mean difference 95% CI 3.5 to −39.5, $p = 0.12$) (Figure 1D).

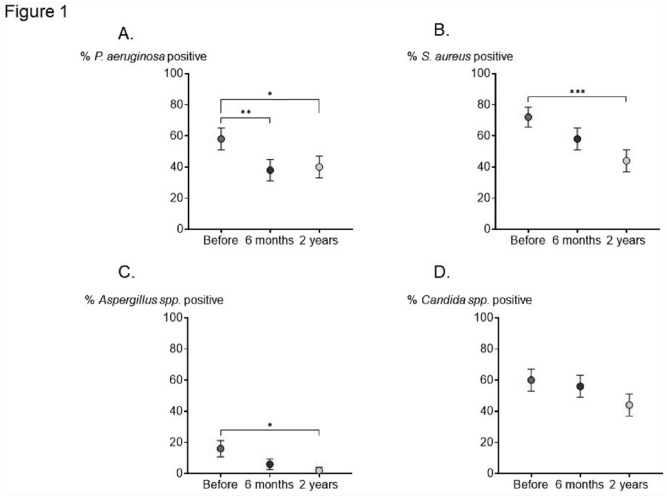

Figure 1. Percentage of respiratory cultures positive for (A) *Pseudomonas aeruginosa,* (B) *Staphylococcus aureus,*(C) *Aspergillus* spp., and (D) *Candida* spp. before, 6 months after, and 2 years after starting elexacaftor/tezacaftor/ivacaftor

Conclusions: Unlike previously seen return-to-baseline bacterial colonization densities at 2 years with early modulator therapies, patients at our center continue to have a reduction in percentage positive respiratory cultures for *S. aureus*, *P. aeruginosa* and *Aspergillus* species 2 years after starting ELX/TEZ/IVA. Continued improvement in pulmonary function testing measurements were also found at 2 years, warranting further investigation.

Reference

[1] Kidd T. Pseudomonas aeruginosa infection after CFTR restoration. One step back, one step forward. *Am J Respir Crit Care Med* 2017;195:1550–1552.

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Results from APPLAUD phase 2 study with pro-resolution drug candidate LAU-7b in adults with cystic fibrosis

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Background: LAU-7b (oral fenretinide) is a novel drug candidate that acts on membrane lipids to modulate inflammation signaling and protein trafficking. Membrane lipid imbalance is believed to play a role in aberrant pulmonary inflammation in individuals with cystic fibrosis (CF), leading to irreversible lung damage over time. Fenretinide was shown to correct the levels of certain membrane phospholipids and sphingolipids in multiple in vitro and in vivo models of CF, improving resolution of inflammation and increasing functional CFTR expression, even under cellular stress conditions. A phase 2 clinical trial (APPLAUD) was conducted in adults with CF to evaluate the safety of LAU-7b and its effect on preservation of lung function by reducing inflammation and restoration of homeostasis.