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| **Long-term safety and efficacy of elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) in people with cystic fibrosis (CF) and at least one F508del allele: an open-label, 192-week extension study** |
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| **Introduction/Aim:** To evaluate long-term safety and efficacy of ELX/TEZ/IVA in people with CF aged ≥12 years and ≥1 F508del-CFTR allele who completed ELX/TEZ/IVA pivotal studies 445-102 or 445-103.**Methods:** Primary endpoint was safety and tolerability; secondary endpoints included absolute changes in percent predicted FEV1 (ppFEV1), sweat chloride, CF Questionnaire-Revised (CFQ-R) respiratory domain score, and number of pulmonary exacerbations (PEx). Annualized rate of change in ppFEV1 was an ad hoc analysis.**Results:** 506 participants (*F508del*/minimal function [*F*/MF], n=399; *F508del/F508del* [*F/F*], n=107) were enrolled and dosed (mean [SD] exposure 172.6 [41.9] weeks); 356 participants (70.4%) completed treatment. Overall, 99.6% of participants had an AE, which for most were mild (12.8%) or moderate (60.7%) in severity. Exposure-adjusted rates of AEs and serious AEs (601.97 and 22.89 events/100 patient-years) were lower than in the treatment arm of the 24-week parent study 445-102 (1096.01 and 36.93 events/100 patient-years). Eighteen participants (3.6%) had AEs leading to treatment discontinuation. Mean (SE) changes in ppFEV1 from parent study baseline at Week 192 were 15.3 (0.8; n=136) and 13.8 (0.8; n=133) percentage points in those with *F*/MF genotypes originally assigned to placebo and ELX/TEZ/IVA in parent study and 10.9 (1.3; n=32) and 10.7 (1.3; n=36) percentage points in those with *F/F* genotype originally assigned to TEZ/IVA and ELX/TEZ/IVA, respectively. Estimated PEx rates (95% CI) per 48 weeks were 0.21 (0.17, 0.25; *F*/MF genotypes) and 0.18 (0.12, 0.25; *F/F* genotype). Absolute changes at Week 192 in sweat chloride and CFQ-R respiratory domain score were comparable to parent studies. Mean (95% CI) annualized rate of change in ppFEV1 was 0.02 (-0.14, 0.19) for all participants.t**Conclusion:** ELX/TEZ/IVA was generally safe and well tolerated. Sustained improvements in lung function, respiratory symptoms, and CFTR function over the 192-week treatment period confirm the broad, durable clinical benefits of ELX/TEZ/IVA.**Grant Support:** N/A |