SHAREABLE PDF

Long-term safety and efficacy of elexacaftor/tezacaftor/ivacaftor in people with cystic fibrosis and at least one *F508del* allele: 144-week interim results from a 192-week open-label extension study

Cori L. Daines[1,20], Elizabeth Tullis[2,20], Stefano Costa[3], Rachel W. Linnemann[4], Marcus A. Mall[5,6,7], Edward F. McKone[8], Deepika Polineni[9], Bradley S. Quon[10], Felix C. Ringshausen[11,12], Steven M. Rowe[13], Hiran Selvadurai[14], Jennifer L. Taylor-Cousar[15], Nicholas J. Withers[16], Neil Ahluwalia[17], Samuel M. Moskowitz[17], Valentin Prieto-Centurion[17], Yaoyuan Vincent Tan[17], Simon Tian[17], Tanya Weinstock[17], Fengjuan Xuan[17], Yaohua Zhang[17], Bonnie Ramsey[18,21] and Matthias Griese[19,21] for the VX17-445-105 Study Group

[1]University of Arizona, Banner University Medical Center, Tucson, AZ, USA. [2]St Michael's Hospital, Toronto, ON, Canada. [3]University of Messina, Messina, Italy. [4]Emory University, Atlanta, GA, USA. [5]Charité – Universitätsmedizin Berlin, Berlin, Germany. [6]Berlin Institute of Health, Berlin, Germany. [7]German Center for Lung Research (DZL), Associated Partner Site, Berlin, Germany. [8]St Vincent's University Hospital, Dublin, Ireland. [9]Washington University in St Louis, St Louis, MO, USA. [10]UBC and St Paul's Hospital, Vancouver, BC, Canada. [11]Hannover Medical School and German Center for Lung Research (DZL), Hannover, Germany. [12]European Reference Network Respiratory Diseases (ERN-LUNG), Frankfurt/Main, Germany. [13]University of Alabama at Birmingham, Birmingham, AL, USA. [14]The Children's Hospital at Westmead, Westmead, Australia. [15]National Jewish Health, Denver, CO, USA. [16]Royal Devon and Exeter NHS Foundation Trust, Exeter, UK. [17]Vertex Pharmaceuticals Incorporated, Boston, MA, USA. [18]Seattle Children's Hospital, Seattle, WA, USA. [19]Ludwig Maximilian University and German Center for Lung Research (DZL), Munich, Germany. [20]C.L. Daines and E. Tullis contributed equally to this work. [21]B. Ramsey and M. Griese contributed equally to this work.

Corresponding author: Cori L. Daines (cdaines@arizona.edu)

Check for updates

Shareable abstract (@ERSpublications)
This 144-week interim analysis of an open-label extension study in participants who completed the ELX/TEZ/IVA pivotal studies supports the favourable safety profile and durable, disease-modifying clinical benefits of ELX/TEZ/IVA https://bit.ly/3PLRfbD

Cite this article as: Daines CL, Tullis E, Costa S, *et al*. Long-term safety and efficacy of elexacaftor/tezacaftor/ivacaftor in people with cystic fibrosis and at least one *F508del* allele: 144-week interim results from a 192-week open-label extension study. *Eur Respir J* 2023; 62: 2202029 [DOI: 10.1183/13993003.02029-2022].

This article has an editorial commentary: https://doi.org/10.1183/13993003.02026-2023

Received: 19 Oct 2022
Accepted: 27 Sept 2023

Abstract

Background In two pivotal phase 3 trials, up to 24 weeks of treatment with elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) was efficacious and safe in patients with cystic fibrosis (CF) ⩾12 years of age who have at least one *F508del* allele. The aim of this study is to assess long-term safety and efficacy of ELX/TEZ/IVA in these patients.

Methods In this phase 3, open-label, single-arm extension study, participants with *F508del*–minimal function (from a 24-week parent study; n=399) or *F508del–F508del* (from a 4-week parent study; n=107) genotypes receive ELX/TEZ/IVA at the same dose (ELX 200 mg once daily, TEZ 100 mg once daily and IVA 150 mg every 12 h). The primary end-point is safety and tolerability. A prespecified interim analysis was conducted when the last participant reached the Week 144 visit.

Results At the Week 144 interim analysis, mean duration of exposure to ELX/TEZ/IVA in the extension study was 151.1 weeks. Exposure-adjusted rates of adverse events (AEs) (586.6 events per 100 participant-years) and serious AEs (22.4 events per 100 participant-years) were lower than in the ELX/TEZ/IVA treatment group in the 24-week parent study (1096.0 and 36.9 events per 100 participant-years, respectively); most participants had AEs classified as mild (16.4% of participants) or moderate (60.3% of participants) in severity. 14 participants (2.8%) had AEs that led to treatment discontinuation. Following initiation of ELX/TEZ/IVA, participants had increases in forced expiratory volume in 1 s (FEV_1) percentage predicted, Cystic Fibrosis Questionnaire-Revised respiratory domain score and body mass

index, and had decreases in sweat chloride concentration and pulmonary exacerbation rates that were maintained over the interim analysis period. The mean annualised rate of change in FEV_1 % pred was +0.07 (95% CI −0.12–0.26) percentage points among the participants.

Conclusions ELX/TEZ/IVA was generally safe and well tolerated, with a safety profile consistent with the 24-week parent study. Participants had sustained improvements in lung function, respiratory symptoms, CF transmembrane conductance regulator function, pulmonary exacerbation rates and nutritional status. These results support the favourable safety profile and durable, disease-modifying clinical benefits of ELX/TEZ/IVA.