AURORA: A PHASE 3 VX-445 TRIPLE COMBINATION REGIMEN CYSTIC FIBROSIS CLINICAL TRIAL PROGRAM

Vertex is conducting the global **AURORA Phase 3 clinical trial program** to evaluate VX-445 in triple combination with tezacaftor and ivacaftor for certain people with cystic fibrosis. The program currently consists of two trials, AURORA F/MF and AURORA F/F. Additional studies are planned as part of this clinical trial program.

ABOUT AURORA F/MF

AURORA F/MF

PATIENT POPULATION

Patients with one *F508del* mutation and one minimal function mutation (F/MF).

Minimal function mutations are clinically severe mutations that result in little-to-no functioning cystic fibrosis transmembrane conductance regulator (CFTR) protein and are not responsive to tezacaftor, ivacaftor or the combination of tezacaftor and ivacaftor.

For a list of the minimal function mutations currently included in this study, click here.

AGES ELIGIBLE FOR THE STUDY

12
YEARS OF AGE AND OLDER

NUMBER OF PATIENTS

360
PATIENTS

PRIMARY ENDPOINT

Absolute change in percent predicted forced expiratory volume in one second ($ppFEV_1$) from baseline at Week 4.

SELECTED SECONDARY ENDPOINTS

- Absolute change in $ppFEV_1$ from baseline through Week 24.
- Number of pulmonary exacerbations through Week 24.
- Absolute change in sweat chloride from baseline at Week 4 and through Week 24.
- Absolute change in Cystic Fibrosis Questionnaire - Revised (CFQ-R) respiratory domain score from baseline at Week 4 and through Week 24. CFQ-R is a validated patient-reported outcome measure.
- Absolute change in body mass index (BMI) from baseline at Week 24.
- Safety and tolerability assessments.

TRIAL DESIGN

TRIPLE COMBINATION REGIMEN

180
PATIENTS

MORNING	EVENING
VX-445 200 mg	**Ivacaftor** 150 mg
Tezacaftor 100 mg	
Ivacaftor 150 mg	

TRIPLE PLACEBO REGIMEN

180
PATIENTS

MORNING	EVENING
Placebo 0 mg	**Placebo** 0 mg
Placebo 0 mg	
Placebo 0 mg	

24 WEEKS OF TREATMENT

4 WEEK PRIMARY EFFICACY ENDPOINT

24 WEEK SECONDARY ENDPOINTS

All eligible patients who complete the AURORA F/MF study may roll over into a 96-week open-label extension trial where they will receive the VX-445 triple combination regimen.

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ABOUT AURORA F/F

AURORA F/F

PATIENT POPULATION

Patients with two copies of the *F508del* mutation (F/F).

AGES ELIGIBLE FOR THE STUDY

12 YEARS OF AGE AND OLDER

NUMBER OF PATIENTS

100 PATIENTS

PRIMARY ENDPOINT

Absolute change in percent predicted forced expiratory volume in one second ($ppFEV_1$) from baseline at Week 4.

SELECTED SECONDARY ENDPOINTS

- Absolute change in sweat chloride from baseline at Week 4.
- Absolute change in CFQ-R respiratory domain score from baseline at Week 4.
- Safety and tolerability assessments.

TRIAL DESIGN

RUN-IN PERIOD

TEZACAFTOR + IVACAFTOR

100 PATIENTS

MORNING	EVENING
Tezacaftor 100 mg	Ivacaftor 150 mg
Ivacaftor 150 mg	

TREATMENT PERIOD

TRIPLE COMBINATION REGIMEN

50 PATIENTS

MORNING	EVENING
VX-445 200 mg	Ivacaftor 150 mg
Tezacaftor 100 mg	
Ivacaftor 150 mg	

PLACEBO + TEZACAFTOR + IVACAFTOR

50 PATIENTS

MORNING	EVENING
Placebo 0 mg	Ivacaftor 150 mg
Tezacaftor 100 mg	
Ivacaftor 150 mg	

4 WEEK RUN-IN PERIOD → 4 WEEKS OF TREATMENT

4 WEEK PRIMARY AND SECONDARY ENDPOINTS

All eligible patients who complete the AURORA F/F study may roll over into a 96-week open-label extension trial where they will receive the VX-445 triple combination regimen.

ABOUT THE VX-445 TRIPLE COMBINATION REGIMEN

In CF patients with certain types of mutations in the *CFTR* gene, the CFTR protein is not processed and moved through the cell normally, resulting in little-to-no CFTR protein at the cell surface. VX-445 and tezacaftor are designed to increase the amount of mature protein at the cell surface by targeting the processing and trafficking defect of the *F508del* CFTR protein. Ivacaftor is designed to enhance the function of the CFTR protein once it reaches the cell surface.

The initiation of the AURORA Phase 3 program, together with the ongoing Phase 3 ECLIPSE VX-659 triple combination program, brings Vertex one step closer to the goal of developing a triple combination regimen for up to 90 percent of all people with CF, including F/MF patients, the largest group of patients who do not have a medicine to treat the underlying cause of their disease.

For additional information on this clinical study program, please visit www.clinicaltrials.gov.

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