Vertex Trial VX-661-113

Phase: Phase 3
Treatment: This was a 2 part study of Dual combination modulators (Tezacaftor and Ivacaftor) with the primary objective of assessing the safety and tolerability of Tezacaftor and Ivacaftor.
Population: Children with CF whose genotype included either two copies of the Phe508del or one copy of Phe508del and a residual function gene which is responsive to Ivacaftor
Age: 6 – 11 years
Duration: 24 weeks

Results:

Part A, assessed the safety and tolerability of tezacaftor/ivacaftor over 14 days in 13 children and measured the level of drug in the blood. The data determined the tezacaftor/ivacaftor dose regimens studies in Part B. In Part B, children weighing <40 kg at baseline received tezacaftor 50 mg QD and ivacaftor 75 mg q12h; those weighing ≥40 kg at baseline received tezacaftor 100 mg QD and ivacaftor 150 mg q12h for 24 weeks.

In Part B, 70 children were enrolled. 87% of the children enrolled had two copies of phe508del. Plasma blood levels at 4, 8 and 16 weeks showed that the children were reaching the same target range for the drugs tezacaftor/ivacaftor as for children over 12 years of age. 65 of the 70 children in Part B had at least one adverse event during the study. Most of these related to CF and included; cough; respiratory exacerbation; fever; nasal congestion and abdominal pain. There were no life threatening adverse events. 10% of the children experienced mild elevation of their liver enzymes, but none had to discontinue the study. No clinically meaningful trends were observed in vital signs, ECGs, other blood markers, urinalysis, pulse oximetry, physical or ophthalmologic examination.

Efficacy results from Part B showed that treatment with tezacaftor/ivacaftor reduced (i.e., improved) Sweat Chloride concentrations, indicating enhanced CFTR function by an average of −14.5 mmol/L. Tezacaftor/ivacaftor treatment also resulted in a percentage change in lung function as measured by Forced Expiratory Volume in one second (FEV_1) of 0.9 percentage points. The average change in the Cystic Fibrosis Questionnaire Revised (CFQ-R) respiratory domain child version score was 3.4 (a 4 point change is significant). Mean growth parameters (weight, height, and BMI) were close to normal for age at baseline, and normal growth for age was maintained throughout the study

Tezacaftor/ivacaftor was generally safe and well tolerated, and improved CFTR function in children aged 6 through 11 years with CF with two copies of Phe508del or one copy of Phe508del and a residual function mutation, supporting the use of tezacaftor/ivacaftor in this age group.

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