Supplementary Information

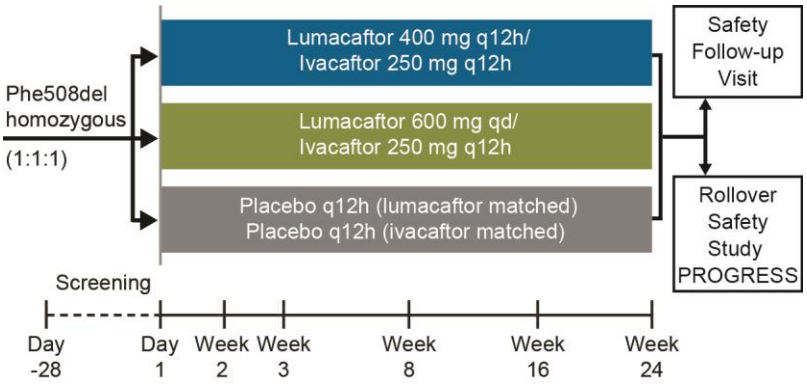
Study design and patients

The TRAFFIC and TRANSPORT studies were Phase 3, multinational, randomised, double-blind, placebo-controlled, parallel-group studies conducted from April 2013 through April 2014.[1] The study protocols were identical except that ambulatory electrocardiography was measured only in the TRAFFIC study, and pharmacokinetic assessments were made in a subgroup of adolescent patients only in the TRANSPORT study. Key inclusion criteria were age 12 years or older with a confirmed diagnosis of cystic fibrosis (CF), homozygous for the Phe508del *CFTR* mutation, a percent predicted forced expiratory volume in 1 second ($ppFEV_1$) of 40 to 90 at the time of screening, stable disease, and a willingness to remain on a specified CF treatment regimen for 24 weeks. Some patients had $ppFEV_1$ levels that reduced to below 40 between the screening and baseline visits (≤4 weeks). Key exclusion criteria were an acute upper or lower respiratory tract infection or change in therapy (including antibiotics) for pulmonary disease occurring within 4 weeks before the first dose of study drug, colonization with organisms associated with a more rapid decline in pulmonary status (eg, *Burkholderia cenocepacia, Burkholderia dolosa*, and *Mycobacterium abscessus*), history of solid organ or haematologic transplantation, or use of strong inhibitors or moderate or strong inducers of cytochrome P450 3A within 14 days before the first dose of study drug.

Procedures

Patients were randomly assigned in a 1:1:1 ratio to treatment with LUM 600 mg qd/IVA 250 mg q12h, LUM 400 mg q12h/IVA 250 mg q12h, or matched placebo q12h, stratified by age (<18 vs ≥18 years), sex, and $ppFEV_1$ at screening (<70 vs ≥70). Patients continued to take their prestudy medications throughout the study period. The study design schematic is shown in Supplementary Figure 1. Patients initiated study treatment within 4 weeks of screening; clinic visits during the 24-week treatment period were scheduled on days 1 (baseline) and 15, and at weeks 4, 8, 16, and 24. Patients who completed all visits during the treatment period, regardless of whether or not they discontinued study treatment, were eligible to enroll in a treatment or observational cohort of a rollover extension study (PROGRESS; ClinicalTrials.gov number, NCT01931839). A safety follow-up visit was scheduled at 4 weeks after completion of the week 24 visit but was not required for patients who chose to enroll in the extension study.

Supplemental Figure 1: TRAFFIC and TRANSPORT study design[1]



Reference

1. Wainwright CE, Elborn JS, Ramsey BW, et al. Lumacaftor-ivacaftor in patients with cystic fibrosis homozygous for Phe508del *CFTR*. *N Engl J Med* 2015; **373:** 220-31.