Paul Volberding, MD
Professor - Department of Medicine
Director of the AIDS Research Institute
University of California - San Francisco (UCSF)

Prof. Paul Volberding

Paul A. Volberding, MD, is a professor in the Department of Medicine and director of the Center for AIDS Research at the University of California, San Francisco (UCSF) and the Gladstone Institute of Virology and Immunology; and served until 2012 as vice chair of the Department of Medicine. He was appointed director of the AIDS Research Institute at UCSF and director of research for Global Health Sciences in 2012. Dr. Volberding served as director of the Positive Health Program at San Francisco General Hospital (SFGH) for 20 years. He received his undergraduate and medical degrees at the University of Chicago and the University of Minnesota, respectively, and finished training at the University of Utah and at UCSF, where he studied for two years as a research fellow in the virology laboratory of Dr. Jay Levy, later a co-discoverer of HIV. Dr. Volberding's professional activities centered for many years at SFGH, where he established a model program of AIDS patient care, research, and professional education. His research career began with investigations of HIV-related malignancies, especially Kaposi's sarcoma. His primary research focus, however, shifted to clinical trials of antiretroviral drugs. He has been instrumental in testing many compounds, but is best known for groundbreaking trials establishing standards of care for the use of zidovudine in asymptomatic HIV infection and for continuous service on the two major guidelines panels for antiretroviral therapy. Dr. Volberding has written many research and review articles. He is co-editor in chief of the Journal of Acquired Immune Deficiency Syndromes, is the founder and chair of the board of the International AIDS Society–USA, and has served as president of the International AIDS Society and the HIV Medicine Association. He is the co-editor of Global HIV/AIDS

Medicine, the extensively rewritten follow-up to The Medical Management of AIDS, formerly the most widely used textbook of HIV medicine. He was elected a member of the Institute of Medicine of the National Academy of Sciences in 1999 and is a fellow of the American College of Physicians, the Infectious Diseases Society of America, and the American Association for the Advancement of Sciences.

"Thoughts from CROI about switching: The STRATEGY-PI study (Arribas) stable on boosted PI switch to Gilead QUAD was successful. One pill regimen. Less side effects in switch group, better satisfaction scores. That's the main switch study I recall from CROI".

Coformulated EVG 150 mg, COBI 150 mg, FTC 200 mg, and TDF 300 mg safe, well tolerated, efficacious in comparative studies vs efavirenz-based therapy and atazanavir/ritonavir-based therapy in treatment-naive adults. To date, few data on use of this regimen in switch strategies in virologically suppressed patients. Current study evaluated efficacy and safety of switching virologically suppressed HIV-infected patients to EVG/COBI/FTC/TDF from boosted PI plus FTC/TDF regimens. A separate study evaluated switches from NNRTI-based regimens.
Inclusion criteria were: on RTV-boosted PI plus FTC/TDF with HIV-1 RNA < 50 copies/mL for ≥ 6 months, currently on first or second ART regimen, eGFRCG ≥ 70 mL/min.
Exclusion criteria were: history of virologic failure, resistance to FTC or TDF on historical genotype.
Most patients received their initial regimen at randomization, and majority of patients received atazanavir- or darunavir-based regimens.
Primary endpoint was: subjects maintaining HIV-1 RNA < 50 copies/mL at Week 48 by US Food and Drug Administration "Snapshot" algorithm (12% noninferiority margin; prespecified sequential testing protocol for superiority performed if noninferiority established).
Secondary endpoints were: change in CD4+ cell count, safety, tolerability of each regimen through Week 96 (safety analysis included randomized patients who received at least 1 dose of study drug), and patient-reported health-related quality-of-life outcomes (HIV Symptom Index, HIV Treatment Satisfaction, Short Form-36, Visual Analogue Scale Adherence).
Exploratory subgroup analyses were: fasting lipid profile changes from baseline at Week 48 , and virologic success, difference by percentages.
Resistance analysis criteria were: patients on study drug experiencing virologic rebound (2 consecutive visits with HIV-1 RNA ≥ 50 copies/mL, or second HIV-1 RNA ≥ 400 copies/mL) and patients with HIV-1 RNA ≥ 400 copies/mL at Week 48 or at last visit on study drugs.
Switching to EVG/COBI/FTC/TDF was associated with noninferior virologic suppression at Week 48.
Higher rate of HIV-1 RNA < 50 copies/mL at Week 48 in EVG/COBI/FTC/TDF met criteria for statistical superiority (6.7; 95% CI: 0.4-13.7; P = .025): EVG/COBI/FTC/TDF: 94%, RTV-boosted PI plus FTC/TDF: 87%.
Findings consistent across subgroups: age, race, sex, type of PI, and number of previous regimens.
No treatment-emergent resistance observed.
No patients met protocol-defined criteria for treatment-emergent resistance testing (virologic rebound ≥ 400 copies/mL).
Most AEs grade ½.
No serious AEs reported by more than 1 patient .
AEs leading to discontinuation were rare: no proximal renal tubulopathy in either arm, and 1 isolated decrease in eGFR in the PI-based treatment group.
Safety profile consistent with expectations for EVG/COBI/FTC/TDF.

Elevated indirect bilirubin in 17 patients receiving atazanavir.
No discontinuations due to hepatic, pancreatic, or urinary disorders.
Changes in serum creatinine and creatinine clearance at Week 48 consistent with MATE-1 transporter inhibition by COBI, baseline inhibition of MATE-1 by RTV.
Median change from baseline in serum creatinine at Week 48: EVG/COBI/FTC/TDF: 6.19 μmol/L , and RTV-boosted PI plus FTC/TDF: -0.88 μmol/L.
Lipid changes following switch primarily among patients receiving lopinavir/RTV-based regimens.
Switching from lopinavir/RTV resulted in decreases in total cholesterol, triglycerides, and high density lipoprotein (HDL) cholesterol.
Switching from atazanavir/RTV resulted in decreased triglycerides.
Switching from darunavir/RTV resulted in increased HDL cholesterol.
No significant change in total cholesterol:HDL ratio in any subgroup.
Using HIV Symptom Index, switching from RTV-boosted PI plus FTC/TDF to EVG/COBI/FTC/TDF associated with: less diarrhea and bloating at Week 48 compared with baseline (decreases noted at Week 4, and decreases sustained to Week 48) and higher Week 24 score on HIV Treatment Satisfaction questionnaire (mean: 23 vs 15; range: -30 to 30; $P < .001$).
Among randomized patients, 9% in the switch arm and 19% in the continued RTV-boosted PI arm discontinued therapy before Wk 48 .
Most common reasons were: protocol violation, withdrew consent, AEs, lost to follow-up.
No discontinuations due to lack of efficacy.
Switching to elvitegravir (EVG)/cobicistat (COBI)/emtricitabine (FTC)/tenofovir DF (TDF) noninferior to remaining on ritonavir (RTV)-boosted PI plus FTC/TDF regarding virologic suppression at Week 48.
Significantly higher rates of virologic suppression with switch to fixed-dose integrase inhibitor regimen.
High virologic efficacy across subgroups of age, race, sex, PI use, number of previous regimens.
No treatment-emergent resistance observed.
EVG/COBI/FTC/TDF tolerated well with few discontinuations due to adverse events (AEs).
AEs consistent with existing safety profile for coformulated regimen.
Small decreases in estimated glomerular filtration rate by Cockcroft-Gault formula (eGFRCG) consistent with known inhibition of creatinine secretion by cobicistat.
No proximal renal tubulopathy observed.
Switch associated with lipid improvements, lower rates of diarrhea and bloating.