Switch to dolutegravir/lamivudine (DTG/3TC) in people living with HIV-1 suppressed on bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF): 96-week final analysis from the SOUND study

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Background: DTG/3TC is approved for ART–naive and virologically suppressed people living with HIV-1 with no prior virologic failure or resistance to DTG/3TC. In the SOUND study, virologically suppressed participants who switched from B/F/TAF to DTG/3TC with **unknown resistance** history maintained high rates of virologic suppression at week 48. Here, we present the 96-week final analysis from SOUND.

Methods: SOUND is an open-label, single-center, **pilot study** of people living with HIV-1 who were on B/F/TAF for >24 weeks, with viral load <50 c/mL for >6 months (≥12 months if history of virologic failure), **no prior resistance testing available**, and negative hepatitis B surface antigen. Week 96 endpoints included virologic and immunologic outcomes, safety, and retrospective proviral DNA resistance testing of baseline samples using the Genosure Archive.

Results: Of 40 individuals enrolled, 18 **(45%) identified as female** and 23 **(58%) as Black**; median (range) **time on B/F/TAF was 2.5** (1-3.6) **years** and **mean number of prior ARV regimens was 5 (range 1 – 14)**. **At Week 96, 37 (93%) participants maintained virologic suppression** (HIV-1 RNA <50 c/mL). The remaining **3 participants withdrew**[a] **from the study while virologically suppressed,** with no discontinuations since the 48-week analysis. Serious adverse events[b] were observed in 5 participants (none related to DTG/3TC). No participants discontinued due to laboratory abnormalities. Among the 32 baseline samples available for proviral DNA resistance testing, 6 (19%) had NRTI resistance-associated mutations (RAMs), all with M184V or M184M/V (refer to table1). Two (6%) participants had INSTI RAMs at baseline (S147S/G and Q148Q/R); neither conferred resistance to DTG. Baseline NNRTI and PI RAMs were observed in 8 (25%) and 3 (9%) participants, respectively.

a. All three patients withdrew consent due to not wanting to participate in the study any longer
b. SAEs include acute pyelonephritis, hiatal hernia, endometrial cancer, symptomatic anemia, and pulmonary nodule

Table.
Retrospective Proviral DNA Resistance Analysis on Baseline Samples[a]

RAMs, n (%)	Participants with available baseline samples (N=32)[b]
NRTI	6 (19)[c]
T69N	1 (3)
M184M/V	5 (16)
M184V	1 (3)
INSTI	2 (6)[e]
S147S/G	1 (3)
Q148Q/R	1 (3)
NNRTI	8 (25)[d]
K101Q	1 (3)
K103K/N	6 (19)
K103N	1 (3)
V106I	1 (3)
Y188Y/H	1 (3)
PI	3 (9)[f]
D30D/N	2 (6)
L33L/I	1 (3)
M46M/V	1 (3)
I47I/V	1 (3)
N88S	1 (3)
N88N/S	1 (3)

[a]Mutations are not mutually exclusive, and participants could have >1 mutation. [b]Samples were not available for 8 participants due to participant withdrawal (n=3), sample tubes cracking in transport (n=2), samples unable to be located (n=2), and samples unable to be analyzed (n=1). [c]RAMs were associated with resistance to lamivudine and emtricitabine (n=6). [d]RAMs were associated with resistance to efavirenz and nevirapine (n=8). [e]RAMs were associated with resistance to elvitegravir (n=1) and elvitegravir and raltegravir (n=1). [f]RAMs were associated with resistance to nelfinavir (n=3).

Conclusions: Final results from SOUND support he efficacy and safety of switching to DTG/3TC for people living with HIV-1 who are virologically suppressed on B/F/TAF with unknown resistance history; and would suggest that a larger, multicenter study, should be conducted to that end.

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