ART-PRO Trial

#485

LONG-TERM DTG+3TC SWITCH EFFICACY IN PATIENTS WITH ARCHIVED 3TC RESISTANCE

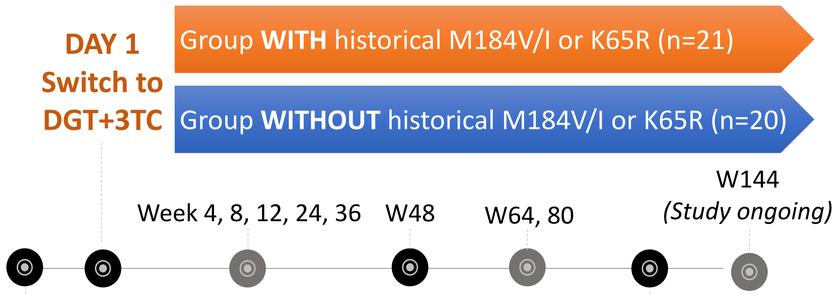
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BACKGROUND: At 48-weeks, DTG+3TC was effective in maintaining virologic control despite history of 3TC resistance and persistence of archived 3TC mutations detected by next-generation sequencing (NGS) (EACS2019 #PS7/5). Long term data to confirm durability of these results are needed.

STUDY DESIGN:

Pilot, single-arm, phase IIa, open label clinical trial conducted at 2 sites.



INCLUSION

- CD4> 350 cel/µL and VL < 50 c/mL for 12 months (1 blip allowed)
- Stable ART for 3 months
- FTC or 3TC in past/present treatment
- INSTI naïve

EXCLUSION

- M184V/I or K65R in baseline proviral DNA Sanger genotype
- HBAgS +
- Pregnant/women wishing to conceive

In this pilot trial, **DTG+3TC was effective at 96 weeks** in maintaining long-term virologic control **despite history of 3TC resistance** and **presence of archived 3TC mutations** detected by NGS.

No case of virologic failure occurred after 2 years of follow-up.

WEEK 96 RESULTS (FDA-SNAPSHOT):	Historical 3TC resistance (n=21)	No historical 3TC resistance (n=20)
HIV-1 RNA ≤50 copies/mL	**18 (85.7)**	**19 (95)**
Virologic failure or HIV-1 RNA ≥50 copies/mL	**0 (0)**	**0 (0)**
No virologic data at Week 96	**3 (14.3)**	**1 (5)**
Discontinuation due to an adverse event	1 (4.8)	0 (0)
Discontinuation for other reasons and last available HIV-1 RNA <50 copies/mL	2 (9.5) *(Protocol Violation)*	1 (5) *(Declined to continue study)*

STUDY POPULATION	Historical 3TC resistance (n=21)	No historical 3TC resistance (n=20)
Male sex, n (%)	16 (76.2)	16 (80)
Age (years), median (IQR)	53.4 (47.1-57.6)	50.8 (42.9-55.3)
Time since HIV diagnosis (years), median (IQR)	21.5 (17.5-23.5)	16.9 (12-27.4)
CD4 count (cells/mm³), median (IQR)		
Nadir	160 (99-216)	259 (70-314)
Baseline	705 (531-871)	647 (530-800)
ART duration (years), median (IQR)	18.8 (17.2-21)	13.1 (7.9-21.6)
Duration of HIV RNA suppression (yrs), median (IQR)	7.7 (4-12)	5.3 (3-8.9)
No. of previous ART regimens, median (IQR)	7 (5-10)	4 (2-7)
Baseline proviral DNA analysis		
M184V (Sanger genotype)♀	2 (9.5)	0 (0)
M184V/I detected by NGS, n (%)		
>20% *	7 (33)	1 (5)
>5% *	14 (66.7)	3 (15)
>1% *	20 (95.2)	7 (35)
K65R/E/N detected by NGS, n (%)		
>20%	1 (4.8)	0 (0)
>5%	2 (9.5)	0 (0)
>1%	3 (14.3)	0 (0)

♀ Protocol violations

**p< 0.05*

ADVERSE EVENTS: There were 30 drug related AEs, only 1 led to discontinuation (insomnia, W8). No related severe AEs.

HYPERMUTATION ANALYSIS: 16/27 of samples with 3TC resistance-associated mutations (RAMs) detected through NGS (>1% threshold) had retrotranscriptase defective viral genomes due to APOBEC-induced mutations.
After removal of reads identified as **hypermutated (18.5%), 3TC RAMs remained present in 22/27 samples.**

TRANSIENT VIRAL REBOUNDS: 14 transient virals rebounds in 12 participants (6 in the group with historical 3TC-resistance). No virologic failures.

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