ARV Therapies and Therapeutic Strategies

INDEPENDENT REPORTING ON IAS 2017

COMPREHENSIVE EXPERT REVIEW AND DISCUSSION OF KEY PRESENTATIONS

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DUAL THERAPY WITH DARUNAVIR/RITONAVIR PLUS LAMIVUDINE FOR HIV-1 TREATMENT INITIATION: WEEK 24 RESULTS OF THE RANDOMIZED ANDES STUDY

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Abstract MOAB0106

ANDES: STUDY DESIGN

ARV-naïve patients, from 5 sites in Argentina

- ≥18 years
- HIV-1 RNA >1000 copies/ml
- No IAS-USA defined NRTI or PI resistance at screening
- HB(s)Ag negative

(N=145)

Stratified at screening by HIV-1 RNA (≤ or >100,000 copies/mL)

Wk 24 Interim analysis

Wk 48 Primary endpoint

Dual Therapy
DRV/r 800/100 mg QD + 3TC 300 mg QD (n=75)

Triple Therapy
DRV/r 800/100 mg QD + 3TC/TDF 300/300 mg QD (n=70)

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ANDES STUDY: BASELINE CHARACTERISTICS

	Global (n=145)	DT (N=75)	TT (N=70)
Age	30 (25-39)	30 (24-42)	30 (26-38)
Males	131 (91%)	70 (93%)	61 (88%)
MSM/Bisexual	101 (73%)	53 (76%)	48 (71%)
CDC Stage B*	11 (8%)	6 (8%)	5 (7%)
Viral Load (log_{10})	4.5 (4.0-5.0)	4.6 (4.1-5.1)	4.5 (3.9-5.0)
VL >100,000 c/mL	35 (24%)	20 (27%)	15 (22%)
Median CD4 count (IQR 25-75)	383 (286-562)	419 (290-564)	366.5 (275-544)

Shown are medians (IQR 25-75) for continuous variables or n(%) for categorical variables.
Comparisons were performed by chi-sq test or t-tests.
* No stage CDC C was enrolled

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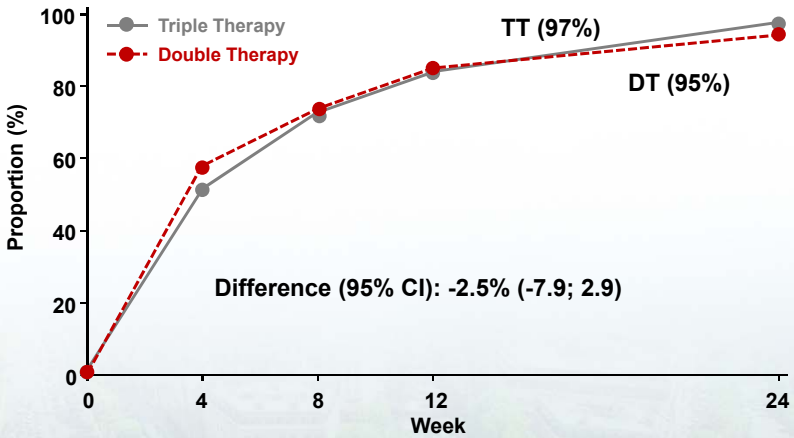
ANDES STUDY: INTERIM 24-WEEK RESULTS



Proportion of patients with plasma HIV-1 RNA less than 400 copies per mL

No virologic failure in dual therapy arm; all patients with baseline HIV RNA >100,000 responded to therapy

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ANDES STUDY: PATIENTS WITH VL<400 C/ML AT WEEK 24

	DT	TT	Difference (95% CI)
ITT Snapshot (n=145)	71/75 (95%)	68/70 (97%)	-2.5% (-7.9; 2.9)
On Treatment (n=140)	**71/71 (100%)**	**68/69 (99%)**	**1.4% (-0.9, 3.8)**
Discontinuations	4*	1**	
Virological Failure	**0**	**1**	

*Withdraw consent (1) ,SAE (1), LTFU (1) , RASH (1)
** LTFU

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ACTG A5353: A PILOT STUDY OF DOLUTEGRAVIR (DTG) + LAMIVUDINE (3TC) FOR INITIAL TREATMENT OF HIV-1-INFECTED PARTICIPANTS WITH HIV-1 RNA <500,000 COPIES/ML

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Abstract TULBPEB21

ACTG 5353: STUDY DESIGN

Phase II, single-arm, 52-week, study of **DTG 50 mg + 3TC 300 mg** in treatment-naïve participants with **VL ≥1000 and <500,000 cpm**

Primary Objective

- To estimate the virologic success rate at week 24

Key Secondary Objectives

- Compare efficacy with baseline VL ≤100,000 vs >100,000 cpm
- Describe emergent integrase and RT resistance during virologic failure
- Evaluate safety and tolerability
- Explore impact of minority drug-resistant variants and drug exposure/adherence on observed outcomes

Taiwo B, et al; 9th IAS, Paris, France, July 23-26, 2017; Abst. MOAB0107LB.

ACTG 5353: BASELINE CHARACTERISTICS

		Baseline HIV-1 RNA Category	
		>100,000 cpm (N=37)	≤100,000 cpm (N=83)
Age (years)	Median (Q1, Q3)	30 (25, 40)	30 (24, 42)
Sex	Male	89%	86%
Race/Ethnicity	White Non-Hispanic Black Non-Hispanic Hispanic	27% 32% 35%	29% 43% 23%
CD Count (cells/mm^3)	Median (Q1, Q3) <200	350 (173, 458) 30%	413 (328, 671) 6%
HIV-1 RNA (log_{10} cpm) (cpm)	Median (Q1, Q3) <10,000 10,000 -99,999 100,000 – 200,000 >200,000	5.23 (5.09, 5.46) -- -- 62% 38%	4.23 (3.82, 4.65) 42% 58% -- --

Taiwo B, et al; 9th IAS, Paris, France, July 23-26, 2017; Abst. MOAB0107LB.

ACTG 5353: RESULTS AT 24 WEEKS

	Baseline HIV-1 RNA		
	>100,000 cpm N=37	≤100,000 cpm N=83	Total N=120
Virologic success HIV-1 RNA <50 cpm **[95% CI]**	33 (89%) [75%, 97%]	75 (90%) [82%, 96%]	108 (90%) [83%, 95%]
Virologic non-success HIV-1 RNA ≥50 cpm Discontinued study treatment for other reasons while HIV RNA ≥50	3 (8%) 3 0	2 (2%)* 0 2	5 (4%) 3 2
No virologic data in window Discontinued study treatment for other reasons On study but missing data in window	1 (3%) 1 0	6 (7%) 5 1	7 (6%) 6 1

*One study subject with poor adherence developed M184V, and R263R/K mixture

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ACTG 5353: CONCLUSIONS

- In this pilot study, DTG+3TC demonstrated potent virologic efficacy with study entry VL up to 500,000 copies/mL
- Virologic failure was uncommon and associated with suboptimal adherence
  - 3 patients met PDVF, one of whom had emergent R263RK mixture and M184V
- Future work in A5353:
  - Investigate baseline and on-treatment RT and INI minority variants in the participants with virologic failure and a matched control group
  - Perform phenotyping on the participant with emergent R263K/R mixture
  - Analysis of pharmacogenetics associations
- Two large randomized studies (GEMINI-1 and GEMINI-2) are underway and will provide more data on the resistance barrier of DTG+3TC

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