POSTER: A-IAS2021-00717

Efficacy and safety of long-acting HIV fusion inhibitor albuvirtide in treatment-experienced HIV-1 infected patients: Week 48 analysis from the randomized controlled phase 3 TALENT study

Hao Wu[1*], Cheng Yao[2], Tong Zhang[1], Qingxia Zhao[3], Weiping Cai[4], Min Wang[5], Hongzhou Lu[6], Hui Wang[7], Yun He[7], Yuhuang Zheng[8], Biao Zhu[9], Jianhua Yu[10], Yongtao Sun[11], Min Zhao[12], Wenhui Lun[13], Wei Xia[1], Lijun Sun[1], Lili Dai[1], Taiyi Jiang[1], Qingshan Zheng[14], Haiyan Peng[15], Yao Wang[15], Rongjian Lu[2], Jianhua Hu[2], Meixia Wang[1], Fujie Zhang[13], Dong Xie[2*], for the TALENT Study Team [*] Corresponding authors: Dr. Hao Wu: whdoc@sina.com Dr. Dong Xie: dxie@frontierbiotech.com

BACKGROUND

- There has been significant development of long-acting injectable therapy in recent years. And we are now entering an era of 2 drug regimen due to high potency of the newly developed antiretrovirals.
- Albuvirtide (ABT) is the **first and only long-acting injectable available as dual therapy** for treatment-experienced patients with HIV-1 replication. ABT targets the glycoprotein, gp41 on the surface of HIV.
- In 2018, NMPA granted **expedited marketing approval in China** based on the positive interim result of this **phase 3 TALENT (Test Albuvirtide in Experienced Patients) study.**
- We are now presenting the full result of TALENT study.

METHODS

- TALENT is a phase 3, randomized, controlled, open-label, multicenter non-inferiority study (ClinicalTrials.gov, NCT02369965).
- Eligible subjects **failed the WHO first-line ART therapy with plasma viral load > 1000 copies/mL** were randomly assigned (1:1) to receive **320 mg albuvirtide (once weekly) plus ritonavir-boosted lopinavir (albuvirtide group) or 2 NRTIs plus ritonavir-boosted lopinavir (2 NRTIs group).**
- The primary endpoint was the **proportion of patients with plasma viral load less than 50 copies/mL at 48 weeks by FDA snapshot algorithm**.
- Non-inferiority was pre-specified with a margin of 12%. A modified intention-to-treat analysis was carried out. **FAS** is defined as all subjects who received at least one dose of study drug and having at least one evaluation after dosing. **PPS** is defined as all subjects who completed the treatment regimen and follow up as **per protocol**.

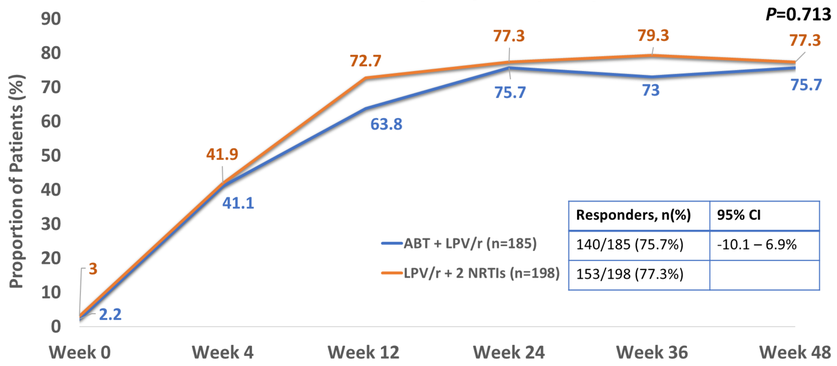
RESULTS

Baseline characteristics (FAS):

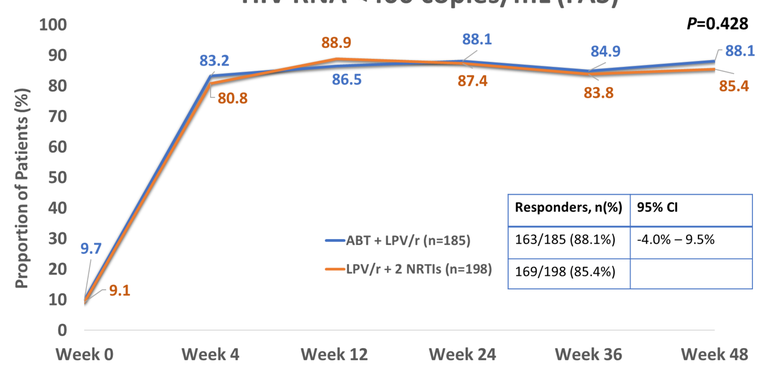
- **More than 20% female** were recruited in both arms,
- **More than 20% participants had CD4+ cells <100** and **~15% had viral load ≥100,000** copies/mL.
- **More than 70% participants** had **at least 2 ARV classes resistance** at baseline.
- Of 374 subjects, the dominant viral subtypes were B (ABT group 49.5% vs. 2 NRTIs group 47.4%), CRF01_AE (32.4% vs. 36.5%), and CRF07_BC (8.2% vs. 3.1%).

	ABT+LPV/r (N=185)	LPV/r + 2 NRTIs (N=198)
Median age, years	41.0	40.0
Sex, n(%)		
Male	139 (75.1)	143 (72.2)
Female	46 (24.9)	55 (27.8)
Race, n(%)		
Chinese- Han	181 (97.8)	193 (97.5)
Others	4 (2.2)	5 (2.5)
Plasma HIV-1 RNA (copies/mL), n(%)		
<100,000	157 (84.9)	167 (84.3)
≥100,000	28 (15.1)	31 (15.7)
CD4 T-cell count (cells/μL), n(%)		
<100	47 (25.4)	47 (23.7)
≥100	138 (74.6)	151 (76.3)
Time on first treatment (months, range)	28.8 (1.5-148.3)	27.0 (1.7-149.2)
Baseline resistance mutation, n(%)		
≥2 classes (NRTI/NNRTI/PI)	131 (72.0)	144 (75.0)
Any 1 class (NRTI/NNRTI/PI)	148 (81.3)	161 (83.9)
NRTIs selected for use at study entry, n(%)		
TDF and 3TC		120 (60.6)
ZDV and 3TC		74 (37.4)
ABC and 3TC		3 (1.5)
TDF, ZDV and 3TC		1 (0.5)

HIV RNA <50 copies/mL (FAS)



HIV RNA <400 copies/mL (FAS)



- At Week 48, 11 participants (6%) in the ABT+LPV/r group and 15 (8%) in the LPV/r +2NRTIs group had HIV-RNA >400 copies/mL, defined as virological failure.
- **No gp41 resistance associated mutation (RAM) observed in all 11 participants** in the ABT+LPV/r group. **1/11 (9%)** had 1 new NRTI RAMs (K103S, G190A) at failure, but **remains sensitive to NRTI and PI classes**. **9/11 (81.8%) do not have new RAMs**. Missing baseline drug resistance data in 1 participant, who had K103N, P225H and V82A at failure.
- **4/15 (26.7%) participants** in the LPV/r+2NRTIs group **had new NRTIs, PIs and/or NNRTIs RAMs** at failure. **11/15 (73.3%) do not have new RAMs.**

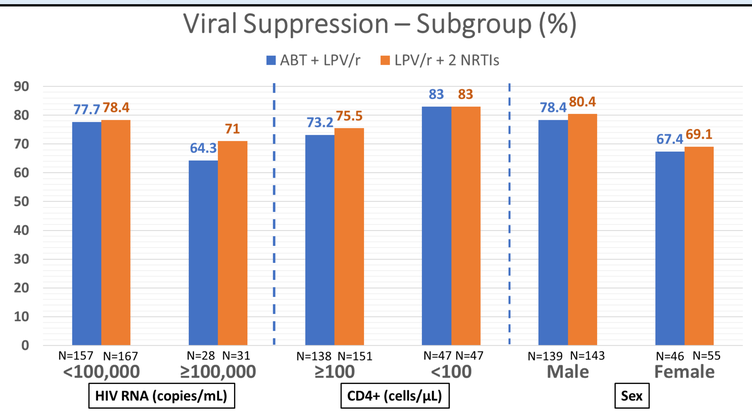
Secondary endpoints:

	ABT + LPV/r	LPV/r + 2 NRTIs	*P* value
Week 48 (FAS)			
Mean Changes of HIV RNA log_{10} copies/mL	-2.2±1.0	-2.1±1.2	0.628
Mean Changes of CD4+ cell/μL	139.1±142.3	142.3±127.6	0.818

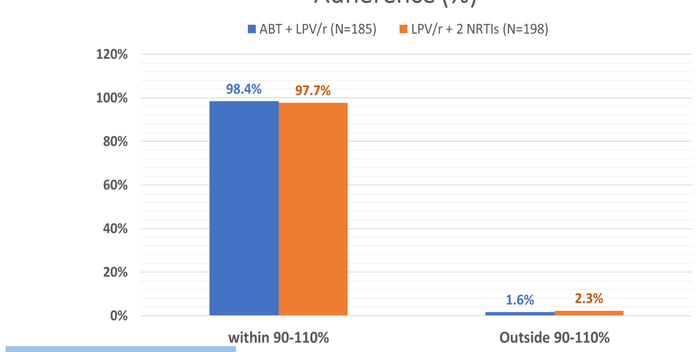
Overall safety:

AE, n (%)	ABT + LPV/r (N=195)	LPV/r + 2 NRTIs (N=206)	*P* value
Any Adverse Events	177 (90.8)	176 (85.4)	0.100
Grade 3 or 4 AEs	35 (17.9)	29 (14.1)	
Drug related AEs	125 (64.1)	127 (61.7)	0.612
Grade 3 or 4 DRAEs	25 (12.8)	20 (9.7)	
Drug related adverse events occurring in ≥2% of participants in either group			
Diarrhea	19 (9.7)	24 (11.7)	
Nausea	3 (1.5)	5 (2.4)	
Gastrointestinal diseases	1 (0.5)	6 (2.9)	
Anemia	0 (0)	5 (2.4)	
Grade 3 or 4 laboratory abnormalities in in ≥2% of participants in either group			
Blood triglycerides increased	10 (5.1)	9 (4.4)	
Blood cholesterol increased	5 (2.6)	2 (1.0)	
Hyperlipidemia	4 (2.1)	1 (0.5)	
AEs leading to withdrawal from the study	2 (1.0)	2 (1.0)	>0.999
Serious AE	12 (6.2)	12 (5.8)	0.890
Injection site reaction	0 (0)		
Drug related serious AE	0 (0)	2 (1.0)	0.499
Death	0 (0)	1 (0.5)	

Viral Suppression – Subgroup (%)



Adherence (%)



CONCLUSION

- HIV RNA suppression rates of 2 drug regimen **(ABT+ LPV/r) at 48 weeks are non-inferior to standard second line 3-drug regimen.**
- Thanks to **high genetic barrier to resistance of ABT+LPV/r that developed no further resistance that may compromise future regimens** for virologically failed patients.
- **Overall safety were comparable** between two groups.
- **First and only injectable ABT and Lopinavir/r dual therapy for 2nd line** treatment shows **high barrier to resistance, good adherence with no injection site reaction**.

Affiliations:[1] Beijing You'an Hospital, Capital Medical University,[2] Frontier Biotechnologies Inc.,[3] Infectious Disease Hospital of Henan Province,[4] The Eighth People's Hospital of Guangzhou,[5] The First Hospital of Changsha ,[6] Shanghai Public Health Clinical Center,[7] The Third People's Hospital of Shenzhen,[8] The Second Xiangya Hospital of Central South University,[9] The First Affiliated Hospital, Zhejiang University,[10] Xixi Hospital of Hangzhou ,[11] Tangdu Hospital of the Fourth Military Medical University,[12] 302 Military Hospital of China,[13] Beijing Ditan Hospital, Capital Medical University,[14] Center for Drug Clinical Research, Shanghai University of Traditional Chinese Medicine,[15] Beijing Co-CRO Medical Development Co., Ltd.