HIV: *novità dai Congressi*

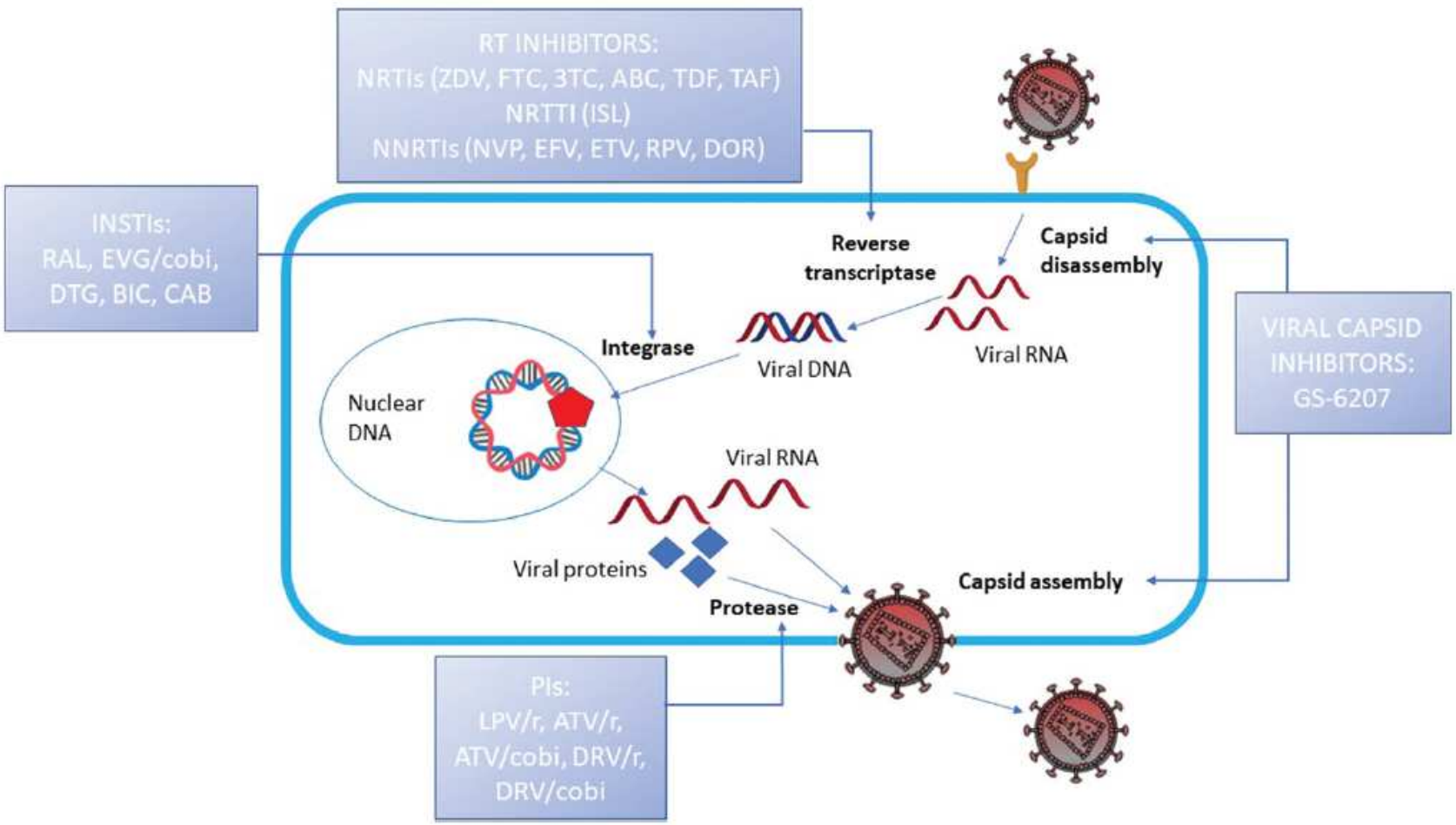
Stefano Rusconi
DIBIC "Luigi Sacco" - UNIMI
U.O. Malattie Infettive Legnano

COIs

ViiV Healthcare, Gilead Sciences, Janssen-Cilag, MSD, Mylan

MEDICI CON L'AFRICA CUAMM

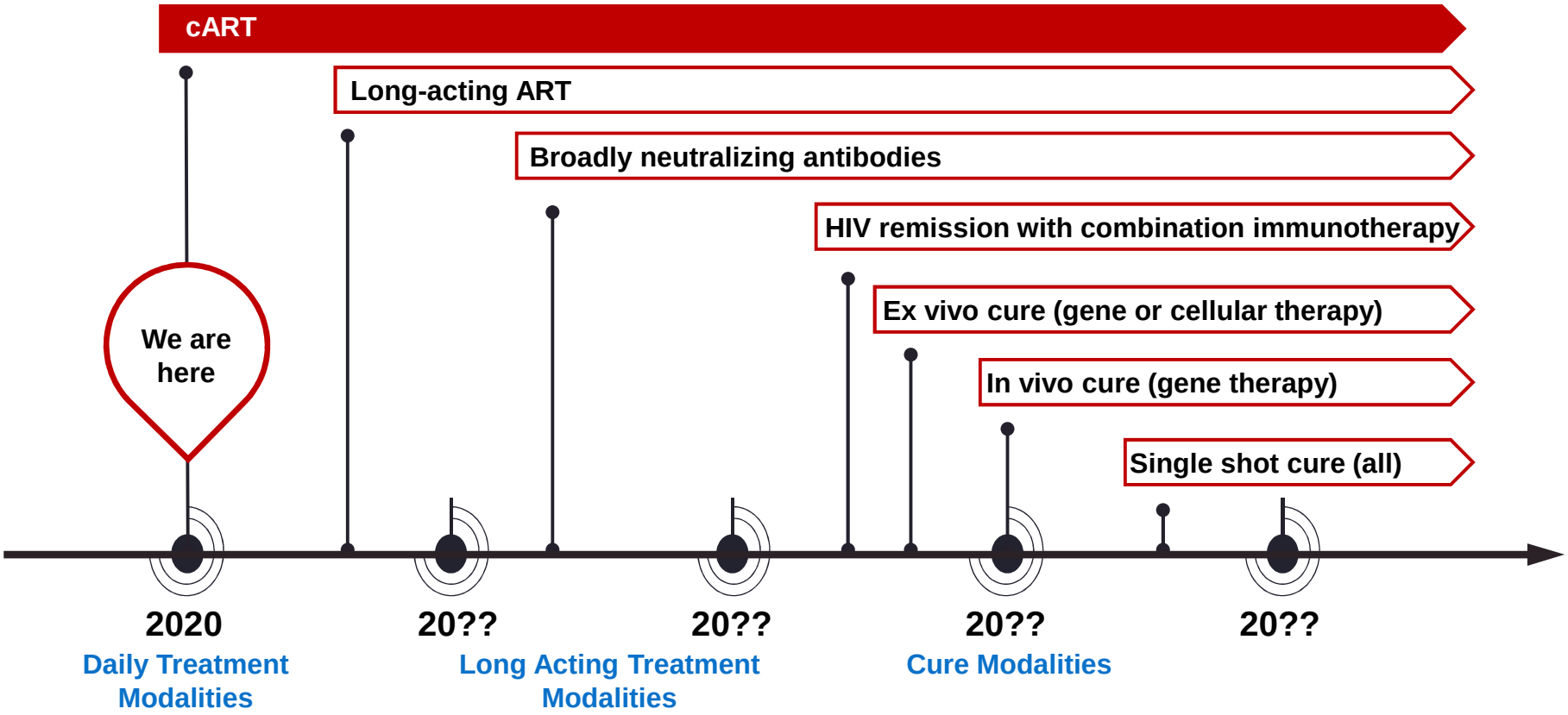
HIV-1 enzymatic steps and antiviral compounds



Andrea Giacomelli, Laura Pezzati & Stefano Rusconi (2020): The crosstalk between antiretrovirals pharmacology and HIV drug resistance, Expert Review of Clinical Pharmacology, DOI: 10.1080/17512433.2020.1782737

Landscape of HIV Treatment

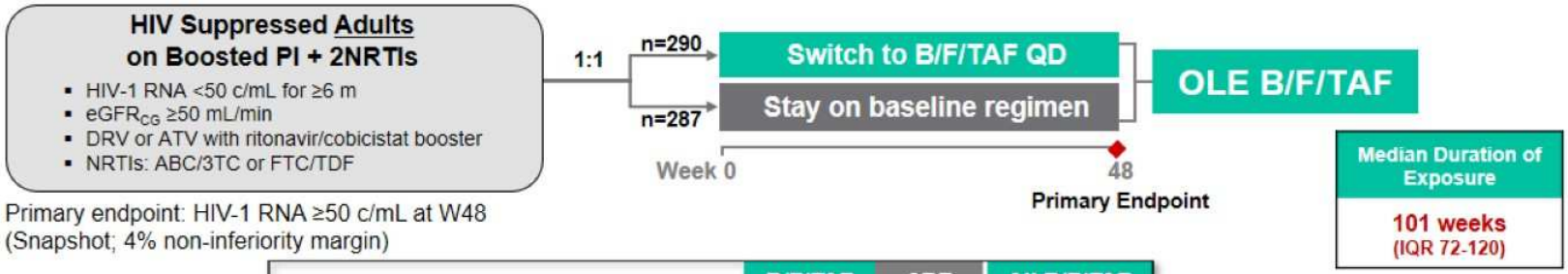
Current and Future



Lewin S. CROI 2020. Boston, MA. Plenary PL-01

Study Design

Phase 3, randomized, open-label, multicenter, active-controlled study



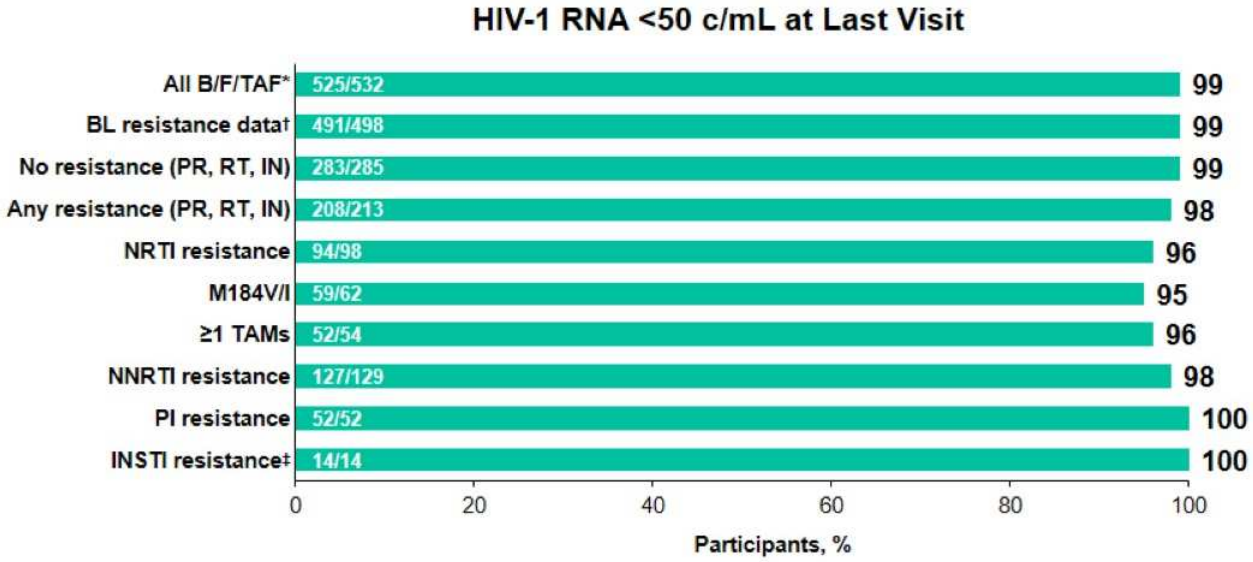
Primary endpoint: HIV-1 RNA ≥50 c/mL at W48
(Snapshot; 4% non-inferiority margin)

Baseline Characteristics	B/F/TAF n=290	SBR n=244	All B/F/TAF N=534
Median age, y	48	48	48
Male, %	84	81	82
Black or African descent, %	27	25	26
Hispanic/Latino, %	21	18	20
Median CD4 count, cells/μL	617	630	624
Median $eGFR_{CG}$, mL/min	106	106	106
Baseline ARV regimen, %			
FTC/TDF, ABC/3TC	85, 16	86, 14	85, 15
DRV, ATV	57, 43	52, 48	54, 46

CG, Cockcroft-Gault. OLE, open-label extension

Rockstroh J, et al. HIV Drug Therapy 2020. Glasgow. P036

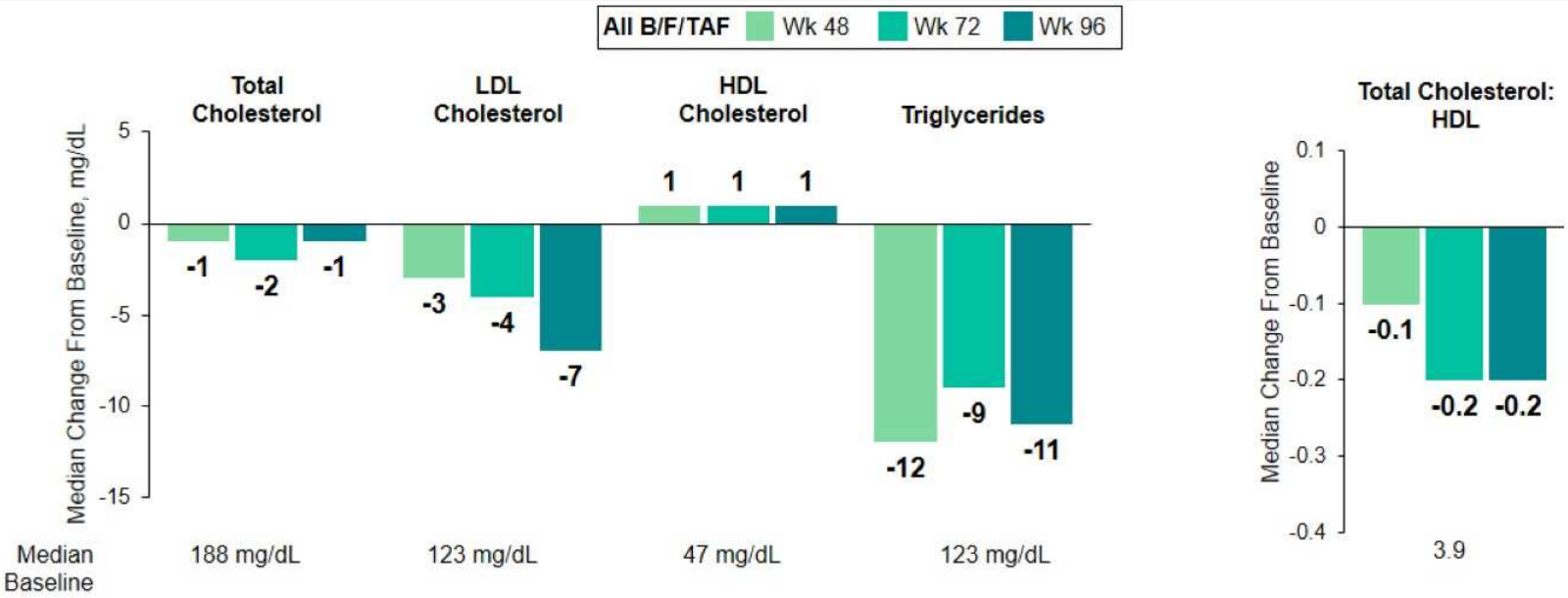
Virologic Outcome by Baseline Resistance



HIV-1 RNA <50 c/mL maintained at Week 96, including in those with preexisting resistance

IN, integrase. OLE, open-label extension. PR, protease. RT, reverse transcriptase. TAMS, thymidine analog mutations
*With ≥1 HIV-1 RNA value post-B/F/TAF switch; †Historical and/or proviral genotypes; ‡T97A (n=7), E92G (n=3), S147G (n=2), N155H (n=1), Q148H (n=1)
Rockstroh J, et al. HIV Drug Therapy 2020. Glasgow. P036

Fasting Lipids Over Time



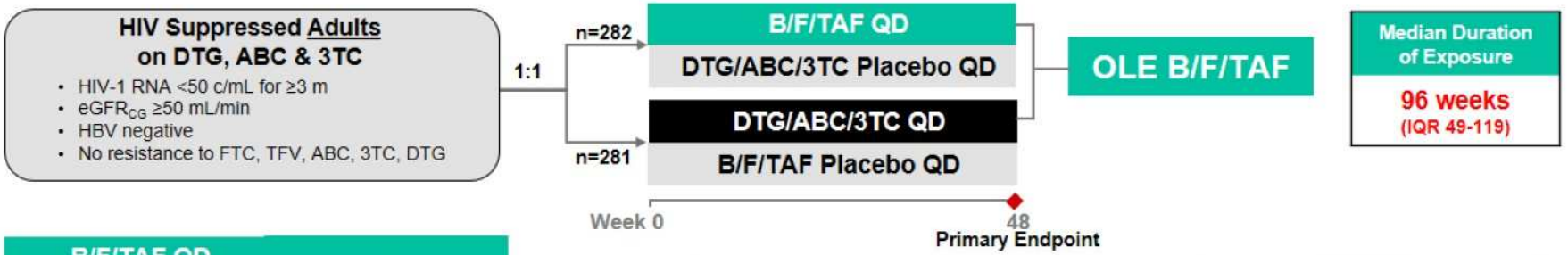
- Lipid lowering agent use at baseline: B/F/TAF 16% and SBR 16%, P=0.91
- Lipid lowering agent initiation during randomized phase: B/F/TAF 3% and SBR 3%, P=0.64

Changes in lipid parameters after switching from boosted PI regimen to B/F/TAF were not clinically relevant

OLE, open-label extension
Rockstroh J, et al. HIV Drug Therapy 2020. Glasgow. P036

Study Design

Phase 3, randomized, double blind, multicenter, active-controlled study



Primary endpoint:

- HIV-1 RNA ≥50 c/mL at W48 (Snapshot; 4% non-inferiority margin)

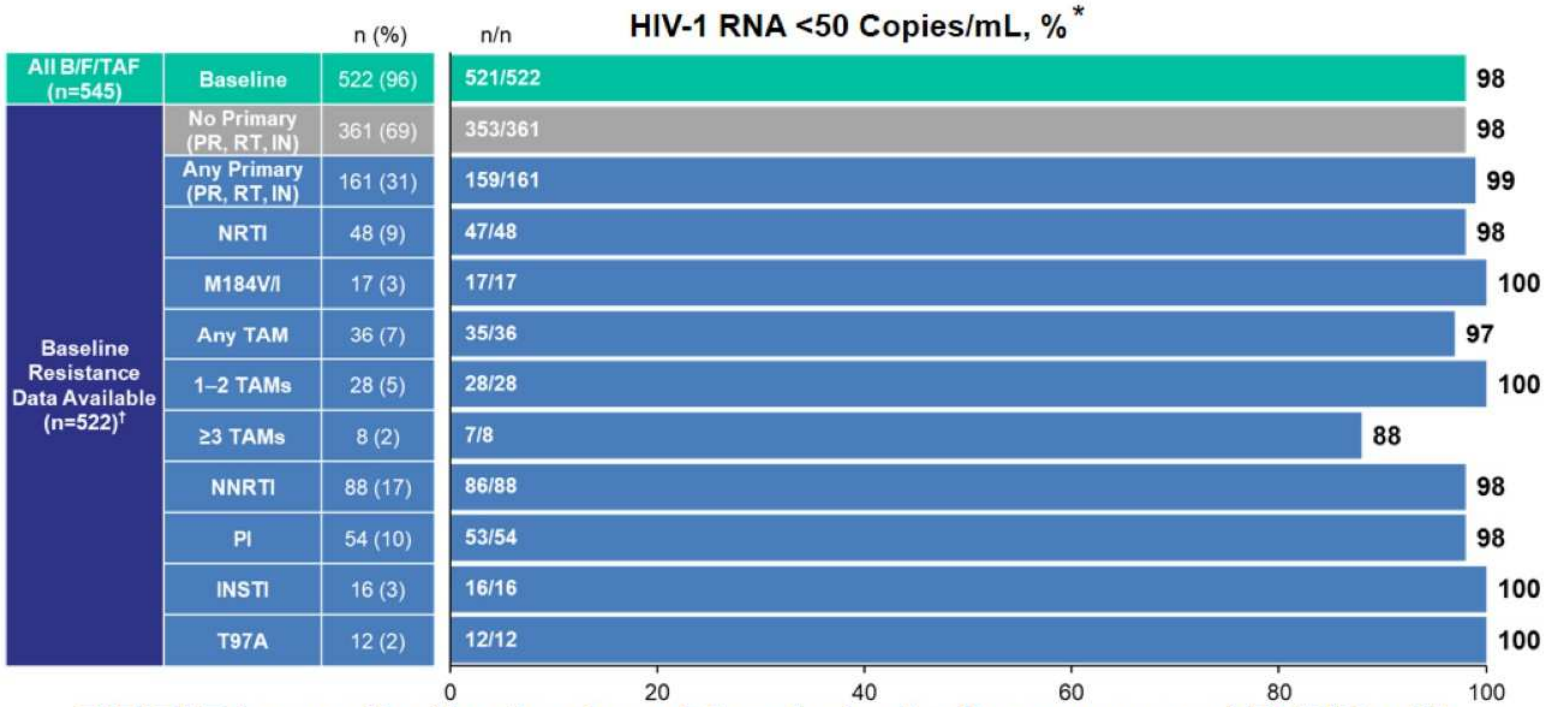
Baseline Characteristics for OLE Participants*		B/F/TAF N=547
Age, y		47 (21–71)
Female at birth		58 (11)
Race/Ethnicity	White	397 (73)
	Black or African descent	116 (21)
	Hispanic/Latino	96 (18)
CD4 count, cells/μL		709 (536, 905)
$eGFR_{CG}$, mL/min		98 (83, 118)
Body mass index, kg/m^2		26 (24, 29)

*Data are n (%) or median (IQR), except age, which is median (range).

$eGFR_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault; OLE, open-label extension

Brar I, et al. IDWeek 2020. Poster #1028

Virologic Suppression by Resistance - LOCF

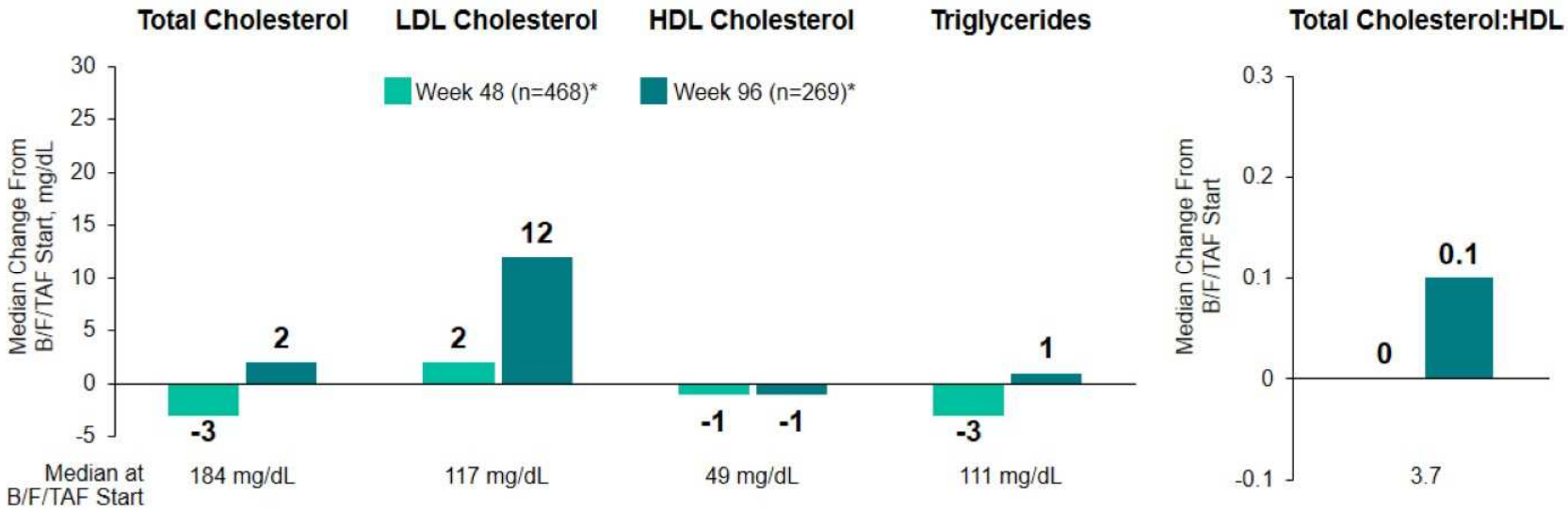


B/F/TAF is an effective treatment for virologically suppressed PLWH with or without preexisting resistance, including M184V/I

LOCF, Last observation carried forward
* 1 participant with ≥3 TAMs (also counted in NRTI-R and Any TAM categories) had 56 copies/mL at last visit & resuppressed on commercial B/F/TAF
† Baseline data derived from cumulative historical and/or proviral genotypes

Brar I, et al. IDWeek 2020. Poster #1028

Changes From Baseline in Fasting Lipids for All B/F/TAF



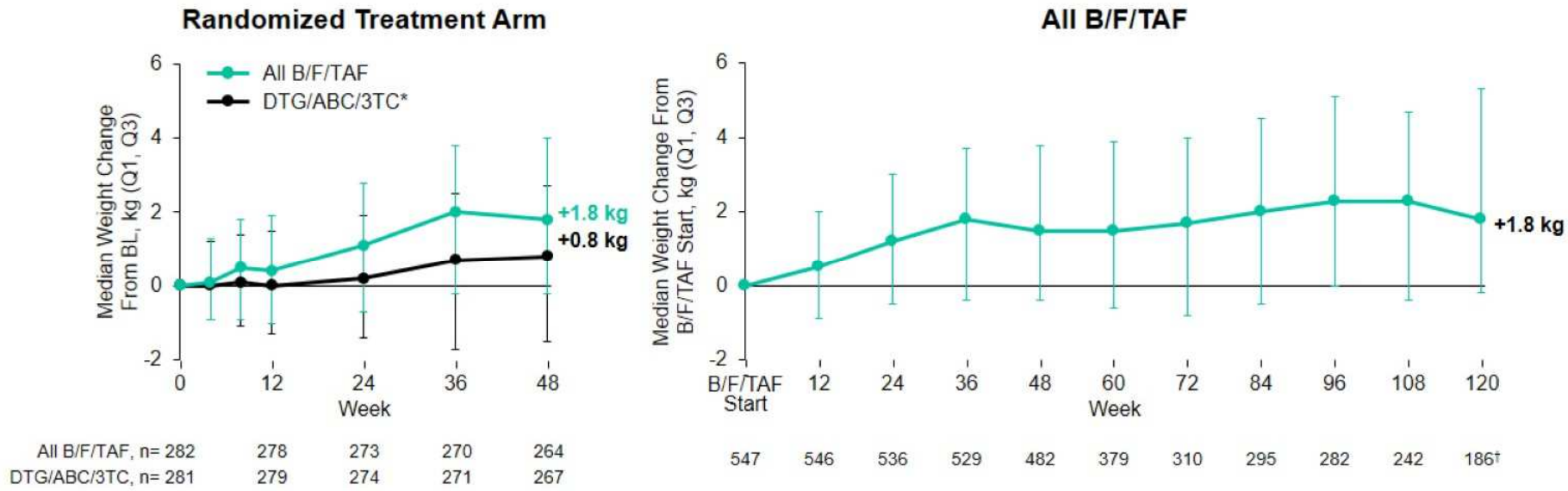
- 17 participants (3%) initiated lipid-modifying agents during the study

Fasting lipids were generally stable, with slight increases in LDL among virologically suppressed adults switched to B/F/TAF

*Weeks after switch to B/F/TAF. HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Brar I, et al. IDWeek 2020. Poster #1028

Change From Baseline in Weight



Weight change from baseline was not clinically different between B/F/TAF and comparator through W48 and remained stable through W120

OLE, open-label extension
*Shown for reference; †Low participant numbers out to Week 168 (n=12); median change at Week 168=+2.1 kg.

Brar I, et al. IDWeek 2020. Poster #1028

Study Design

Phase 3b, multicenter, open-label, single arm study

HIV-Suppressed Adults ≥65 Years

- Stable ART for ≥3 months
- Prior enrollment in studies 1823 or 1826 or on E/C/F/TAF or FTC/TDF + 3rd agent
- $eGFR_{CG}$ ≥30 mL/min

N = 86 → **B/F/TAF**

Week 0 | Week 24 (Primary Endpoint) | Week 48 | Week 72 | Week 96

(ClinicalTrials.gov NCT03405935)

Study locations: Belgium, France, Italy, Spain, and UK

Primary endpoints:

- HIV-1 RNA <50 c/mL at Week 24 defined by FDA Snapshot

Secondary endpoints:

- HIV-1 RNA <50 c/mL at Weeks 48, 72 and 96
- Safety and tolerability of B/F/TAF at Weeks 24, 48, and 96

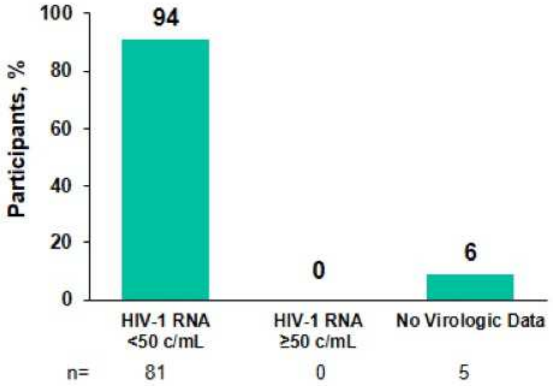
Baseline Characteristics % (n) or Median (range or Q1, Q3)	**B/F/TAF n = 86**
Age, yrs	69 (65 – 80)
Weight, kg	78 (49, 110)
Female	13% (11)
Black race	1% (1)
CD4 count, cells/mm³	676 (132-1385)
eGFR, mL/min	76 (40-130)
E/C/F/TAF regimen	92% (79)

Baseline Chronic Medication, % (n)	**B/F/TAF n = 86**
Cardiovascular	64% (55)
Gastrointestinal	63% (54)
Nervous system	44% (38)
Blood and blood forming organs	27% (23)
Musculoskeletal	23% (20)
Genitourinary system and sex hormones	21% (18)

Maggiolo F, et al. HIV Glasgow. P038

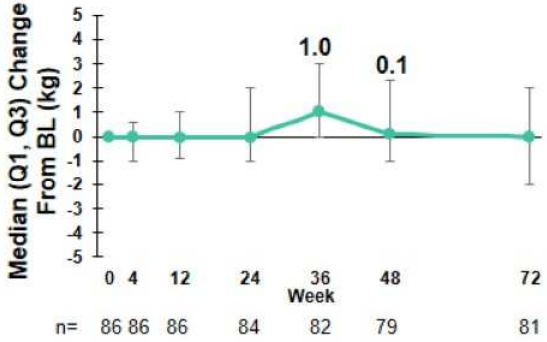
Efficacy, Weight Change and Safety through Week 72

Efficacy



- No treatment emergent resistance to any of the regimen components

Weight Change



Safety

Adverse Events, % (n)	B/F/TAF n = 86
Study drug-related AEs (grades 2, 3 or 4)	**4.7% (4)**
Study drug-related AEs (grades 3 or 4)	**2.3% (2)**
Any study drug-related serious AE	**0**
AE leading to study drug discontinuation	**4.7% (4)**
Drug-related	**2.3% (2)**
Renal AEs leading to study drug discontinuation	**0**
Death	**2***

*1) 77 yo male with pre-existing depressive disorder led to suicide via a benzodiazepine overdose (study day 427), 2) 72 yo male developed and succumbed to pneumonia secondary to COVID-19 infection (study day 672); Neither death study drug-related

B/F/TAF was an effective and well-tolerated treatment with no virologic failure and no treatment emergent resistance in virologically suppressed adults ≥65 years through W72

Maggiolo F, et al. HIV Drug Therapy 2020. Glasgow. P038

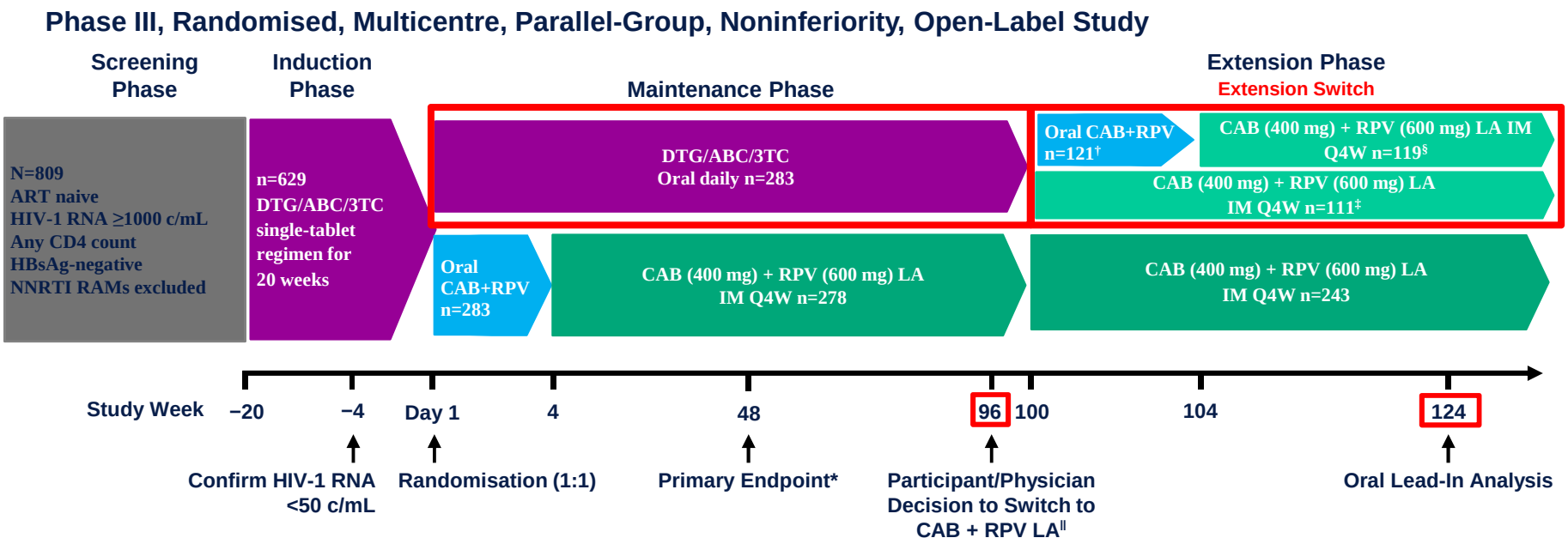
SAFETY AND EFFICACY OF CABOTEGRAVIR + RILPIVIRINE LONG-ACTING WITH AND WITHOUT ORAL LEAD-IN: FLAIR WEEK 124 RESULTS

Ronald D'Amico[1], Chloe Orkin[2], Enrique Bernal Morell[3], Darrell H. S. Tan[4], Harold Katner[5], Yashna Singh[6], Hans-Jürgen Stellbrink[7], Elena Belonosova[8], Rebecca DeMoor[9], Sandy Griffith[1], Shanker Thiagarajah[9], Rodica Van Solingen-Ristea[10], Herta Crauwels[10], Susan L. Ford[11], Parul Patel[1], Amy Cutrell[1], Kimberly Y. Smith[1], Kati Vandermeulen[10], David A. Margolis[1], Marty St. Clair[1], William R. Spreen[1]

[1]ViiV Healthcare, Research Triangle Park, NC, United States; [2]Queen Mary University, London, United Kingdom; [3]Hospital General Universitario Reina Sofía, Murcia, Spain; [4]Division of Infectious Diseases, St. Michael's Hospital, Toronto, Canada; [5]Mercer University Medical School, Macon, GA, United States; [6]Desmond Tutu HIV Foundation, Cape Town, South Africa; [7]ICH Study Center, Hamburg, Germany; [8]Orel Regional Center for AIDS, Orel, Russia; [9]GlaxoSmithKline, London, United Kingdom; [10]Janssen Research and Development, Beerse, Belgium; [11]GlaxoSmithKline, Research Triangle Park, NC, United States

HIV Drug Therapy Glasgow; 5–8 October, 2020; Virtual

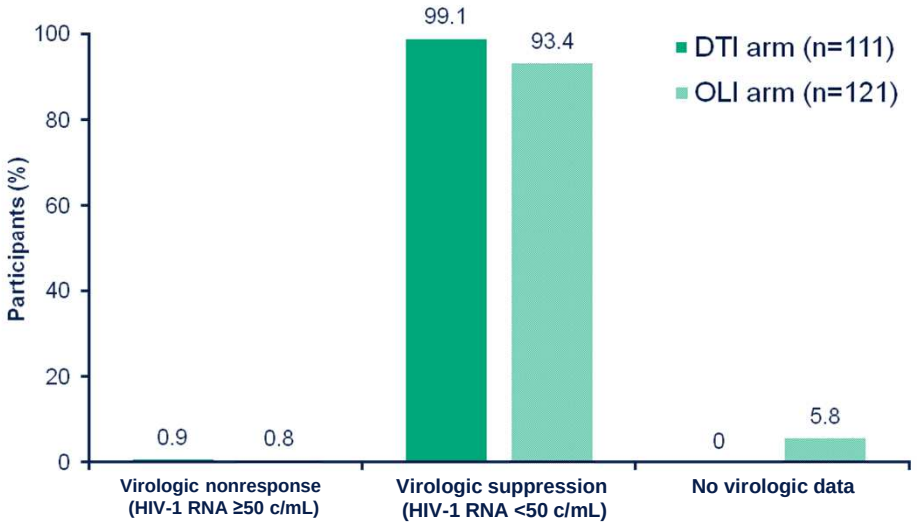
FLAIR OLI: Study Design



*Proportion of participants with HIV-1 RNA ≥50 copies/mL at Week 48 as per the Food and Drug Administration (FDA) Snapshot algorithm.
†Two discontinuations during OLI: 1 subject relocation, 1 pregnancy.
‡For participants in the DTI arm, the last dose of CAR and first loading injections of CAB (600 mg) + RPV (900 mg) LA were administered at Week 100. This was followed by CAB 400 mg + RPV 600 mg LA Q4W.
§For participants in the OLI arm, daily oral CAB (30 mg) + RPV (25 mg) was initiated at Week 100 and continued for ≥4 weeks. Participants received their last dose of oral CAB + RPV and their first loading injections of CAB (600 mg) + RPV (900 mg) LA at Week 104. This was followed by CAB 400 mg + RPV 600 mg LA Q4W.
‖Participants, in consultation with their physician, elected to receive CAB + RPV LA either with an OLI or DTI at Week 96. The new treatment regimen began at Week 100.

3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; CAB, cabotegravir; CAR, current antiretroviral therapy; DTI, direct to inject; DTG, dolutegravir; HBsAg, hepatitis B surface antigen; IM, intramuscular; LA, long-acting; NNRTI, non-nucleoside reverse transcriptase inhibitor; OLI, oral lead-in; Q4W, every 4 weeks; RAM, resistance-associated mutation; RPV, rilpivirine.

FLAIR OLI: Snapshot Virologic Outcomes at Week 124 (Extension Switch)



Outcome, n (%)	DTI arm n=111	OLI arm n=121
HIV-1 RNA <50 copies/mL	110 (99.1)	113 (93.4)
HIV-1 RNA ≥50 copies/mL	1 (0.9)	1 (0.8)
Data in window not below threshold	0	1 (0.8)*
Discontinued for lack of efficacy	1 (0.9)†	0
Discontinued for other reason while not below threshold	0	0
Change in background therapy	0	0
No virologic data	0	7 (5.8)
Discontinued due to AE	0	2 (1.7)‡
Discontinued due to death	0	0
Discontinued study for other reason	0	5 (4.1)§
On study but missing data in window	0	0

*Participant had HIV-1 RNA of 57 copies/mL at Week 124.
†Participant met the CVF criterion at Week 112.
‡Two participants discontinued due to AEs of injection site pain and weight gain.
§Five participants discontinued due to other reasons, which included burden of travel, prohibited medication use, participant relocation, burden of procedures/intolerability of injections and pregnancy.

- Only 1 participant (0.4%) met the CVF criterion in the Extension Switch population
  - The participant was in the DTI arm and met the CVF criterion on the 12th week of LA therapy. No INSTI or NNRTI resistance-associated mutations were detected at baseline and no INSTI resistance-associated mutations were detected at the timepoint of suspected virologic failure (NNRTI mutations could not be generated)

AE, adverse event; CVF, confirmed virologic failure; DTI, direct to inject; INSTI, integrase strand transfer inhibitor; LA, long-acting; NNRTI, non-nucleoside reverse transcriptase inhibitor; OLI, oral lead-in.

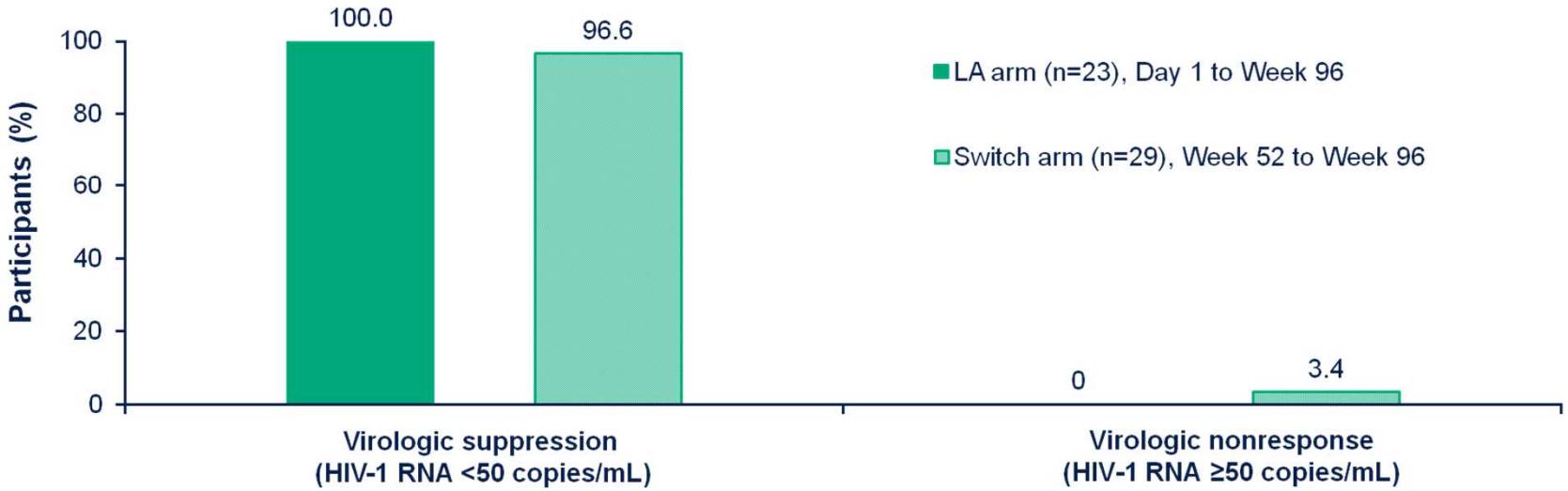
CABOTEGRAVIR + RILPIVIRINE LONG-ACTING AS HIV-1 MAINTENANCE THERAPY: ATLAS WEEK 96 RESULTS

Susan Swindells[1], Thomas Lutz[2], Lelanie Van Zyl[3], Norma Porteiro[4], Paul Benn[5], Jenny O. Huang[6], Conn M. Harrington[7], Kai Hove[8], Susan L. Ford[6], Christine L. Talarico[7], Vasiliki Chounta[5], Herta Crauwels[9], Rodica Van Solingen-Ristea[9], Simon Vanveggel[9], David A. Margolis[7], Kimberly Y. Smith[7], Kati Vandermeulen[9], William R. Spreen[7]

[1]University of Nebraska Medical Center, Omaha, NE, United States; [2]Infektiologikum, Frankfurt, Germany; [3]Syzygy Clinical Research Services, Pretoria, South Africa; [4]Fundación IDEAA, Buenos Aires, Argentina; [5]ViiV Healthcare, Brentford, United Kingdom; [6]GlaxoSmithKline, Research Triangle Park, NC, United States; [7]ViiV Healthcare, Research Triangle Park, NC, United States; [8]GlaxoSmithKline, London, United Kingdom; [9]Janssen Research and Development, Beerse, Belgium

HIV Drug Therapy Glasgow; 5–8 October, 2020; Virtual

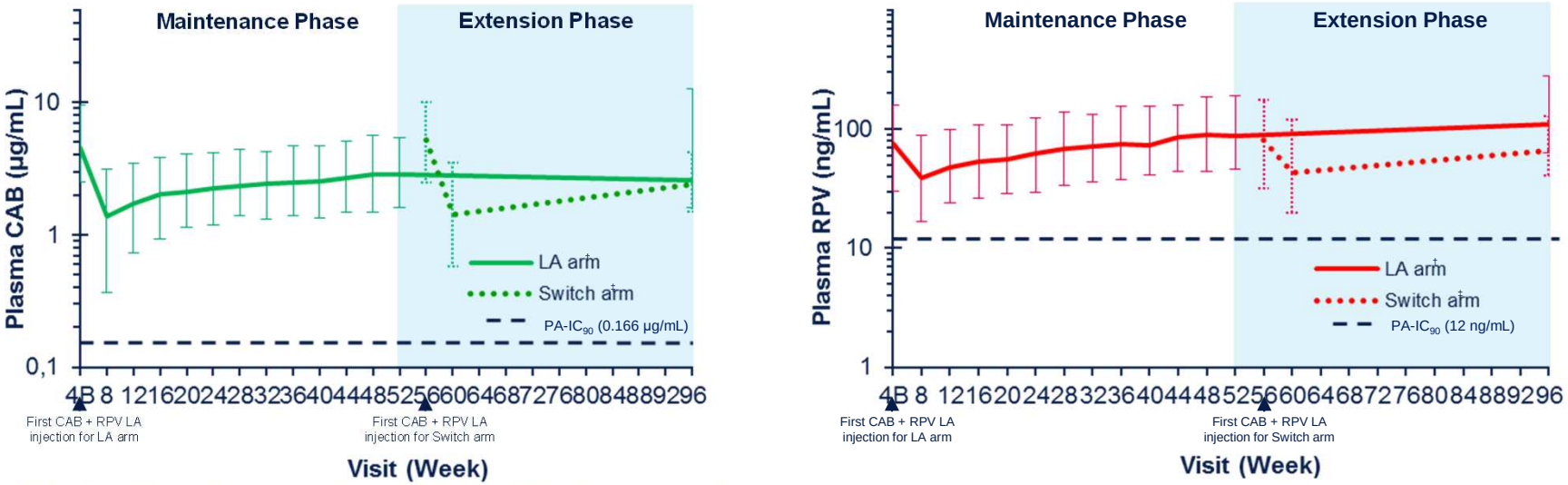
ATLAS Week 96: Virologic Outcomes



- The majority of participants who entered the Extension Phase and remained in the study through the Week 96 analysis maintained virologic suppression with CAB + RPV LA
  - Only 1 participant in the Switch arm had HIV-1 RNA ≥50 copies/mL at the Week 96 data analysis (HIV-1 RNA of 173 copies/mL at Week 92)*
- Furthermore, no participants in either treatment arm met the CVF criterion during the Extension Phase

*Participant discontinued at Week 92 and was included in the Week 96 data analysis.
CAB, cabotegravir; CVF, confirmed virologic failure; LA, long-acting; RPV, rilpivirine.

ATLAS Week 96: Plasma CAB and RPV Trough Concentrations*



*Median (5th and 95th percentile) concentration–time data for CAB (left) and RPV (right) following monthly LA administration. Values for Week 4B for the LA arm and Week 52 for the Switch arm represent oral dosing concentrations.
†Timepoint, n (CAB/RPV): Week 4B, n=259/258; Week 8, n=252/251; Week 12, n=261; Week 16, n=248/247; Week 20, n=233; Week 24, n=234/231; Week 28, n=232; Week 32, n=219/218; Week 36, n=209; Week 40, n=209/208; Week 44, n=221/223; Week 48, n=217/216; Week 52, n=215/214; Week 96, n=19.
†Timepoint, n (CAB/RPV): Week 56, n=149; Week 60, n=127; Week 96, n=24.

- Week 96 median CAB concentrations were comparable between the LA and Switch arms, consistent with an achievement of steady state for CAB after 44 weeks of injections
- Week 96 median RPV concentrations were higher in the LA arm (after 23 IM injections) than the Switch arm (after 10 IM injections). This suggests some limited further accumulation of RPV in the second year of injections, in line with the half-life of RPV LA

CAB, cabotegravir; IM, intramuscular; LA, long-acting; PA-IC_{90}, protein-adjusted concentration required for 90% inhibition; RPV, rilpivirine.

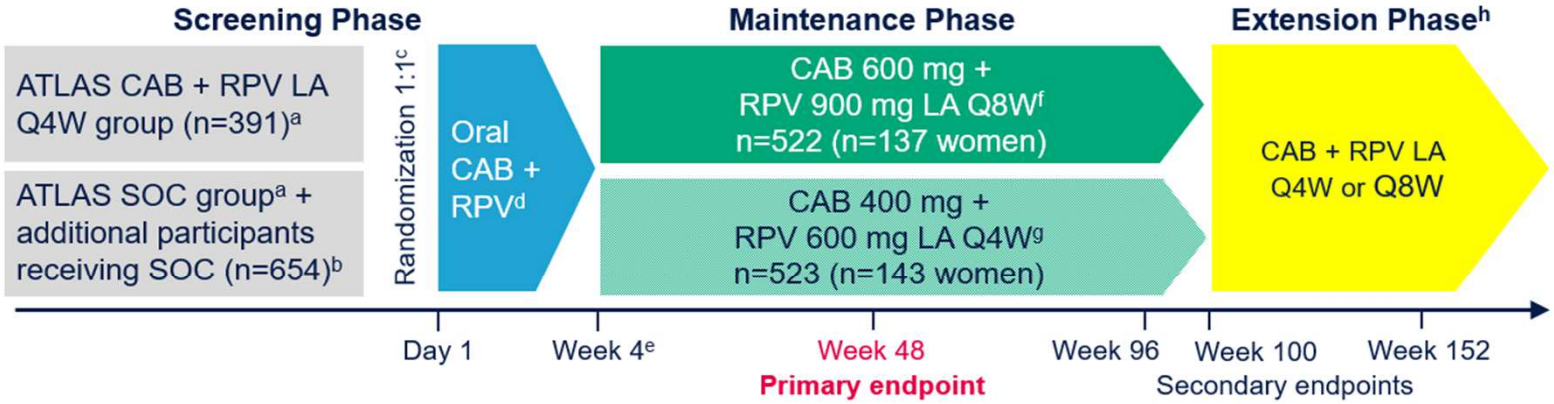
OUTCOMES FOR WOMEN RECEIVING LONG-ACTING CABOTEGRAVIR + RILPIVIRINE MONTHLY AND EVERY 2 MONTHS: ATLAS-2M STUDY WEEK 48 RESULTS

Paul Benn,[1] Romina Quercia,[1] Krischan Hudson,[2] Yuanyuan Wang,[3] Vasiliki Chounta,[1] Christine Talarico,[2] Susan Ford,[2] Amy Cutrell,[2] David A. Margolis,[2] Rodica Van Solingen-Ristea,[4] Simon Vanveggel,[4] Veerle Van Eygen,[4] Joseph W. Polli,[2] Annemiek de Ruiter,[1] Kimberly Smith,[2] William R. Spreen[2]

[1]ViiV Healthcare, Brentford, UK; [2]ViiV Healthcare, Research Triangle Park, NC, USA; [3]GlaxoSmithKline, Collegeville, PA, USA;
[4]Janssen Research & Development, Beerse, Belgium

ATLAS-2M Study Design

- Subgroup analyses were performed on the primary and secondary endpoints of the ATLAS-2M study by sex at birth
  - Differences between Q8W and Q4W groups for women and men in snapshot analyses were based on Cochran–Mantel–Haenszel stratified analysis and adjusted for prior exposure to CAB + RPV

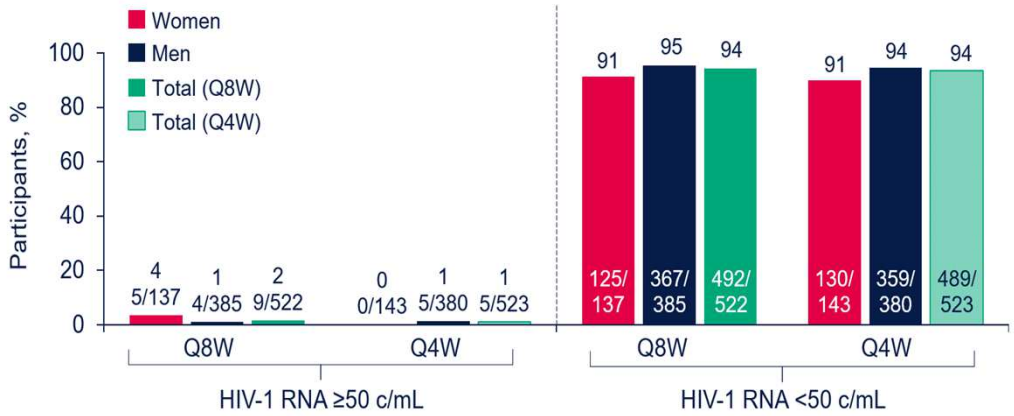


[a]Participants from ATLAS must have been taking CAB + RPV LA Q4W or a current ART regimen through at least Week 52 with HIV-1 RNA <50 c/mL at screening. [b]Participants receiving SOC not from ATLAS must have been taking an uninterrupted ART regimen ≥6 mo prescreening with ≥2 HIV-1 RNA measurements <50 c/mL in the 12 mo prescreening (one between 12 and 6 mo and one ≤6 mo of screening). Exclusion criteria: history of virologic failure or evidence of viral resistance. [c]Randomization stratified by prior CAB + RPV exposure. [d]Except those from ATLAS on LA therapy. [e]Tolerability in participants on oral lead-in ART assessed at Week 4. [f]After oral lead-in period, participants in the Q8W group received intramuscular injections at Weeks 4 and 8, then Q8W thereafter. [g]In participants in the Q4W group with oral lead-in, first LA dose was CAB 600 mg + RPV 900 mg. [h]Optional extension phase to continue randomized CAB + RPV LA Q4W or Q8W at Week 100.

Benn et al. HIV Glasgow 2020; Virtual. Poster P017.

Virologic Snapshot Outcomes at Week 48 (ITT-E Population)

- Proportions of women and men with HIV-1 RNA ≥50 c/mL were similar between groups (adjusted differences [95% CI], 3.5% [0.4 to 6.6] for women and −0.3% [−1.8 to 1.3] for men
- HIV-1 RNA <50 c/mL was maintained in the majority of women and men in each group (adjusted differences [95% CI], 0.4% [−6.2 to 7.1] for women and 0.8% [−2.3 to 4.0] for men)



Other Virologic Outcomes

- The proportion of women and men with HIV-1 RNA <2 c/mL was similar at baseline and at Week 48 across both groups
  - At baseline, 81% (109/135) Q8W and 83% (116/139) Q4W of women and 74% (281/379) Q8W and 73% (276/377) Q4W of men had HIV-1 RNA <2 c/mL, respectively. At Week 48, 81% of women (Q8W, 96/119; Q4W, 105/129) and 76% of men (Q8W, 277/364; Q4W, 267/352) in both arms had HIV-1 RNA <2 c/mL

Benn et al. HIV Glasgow 2020; Virtual. Poster P017.

Women Receiving CAB + RPV LA Q8W with CVF[a] at Week 48

Country (HIV-1 subtype)	SVF, wk	VL at SVF/CVF, c/mL	Baseline RAM[1] (PBMC/HIV-1 DNA; Day 1)		SVF timepoint RAM[1] (HIV-1 RNA)		Drug sensitivity at SVF, FC[b]		
			RT	IN	RT	IN	RPV	CAB	DTG
South Africa (Complex)	8	267/2355	V108V/I Y181Y/C H221H/Y	None	K103N	None	2.4	1.1	0.9
South Africa (C)	16	938/2374	Y/188Y/F/H/ L	G140G/R	Y188L	Q148Q/R N155N/H	6.8	2.6	1.3
Russia (A1)	16	141,132/19,099	None	None	K101E	Q148R	4.7	9.1	1.6
Canada (A1)	24	16,205/874	Y188L P225H	None	Y188L P225H	NA[c]	15.0	NA[c]	NA[c]
Russia (A)	24	211,639/38,015	E138E/A	None	K101E E138A	N155H	2.6	7.0	2.2

FC, fold-change; RAM, resistance-associated mutation; RT, reverse transcriptase; SVF, suspected virologic failure. [a]CVF=2 consecutive plasma HIV-1 RNA levels ≥200 c/mL after prior suppression to <200 c/mL. [b]Monogram biologic/clinical cutoffs: RPV=2.0, CAB=2.5, DTG=4.0. [c]Integrase analysis failed.

1. Wensing et al. *Top Antivir Med*. 2019;27:111-121.

Benn et al. HIV Glasgow 2020; Virtual. Poster P017.

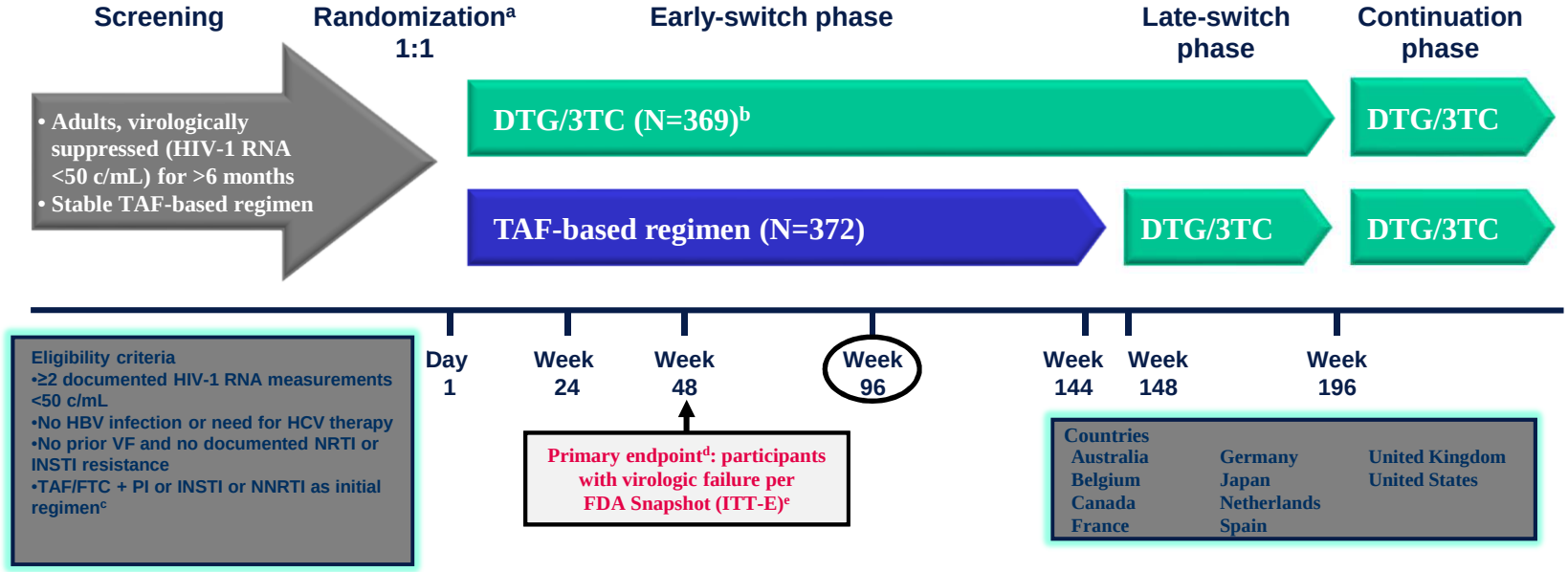
SWITCHING TO DTG/3TC FIXED-DOSE COMBINATION (FDC) IS NON-INFERIOR TO CONTINUING A TAF-BASED REGIMEN (TBR) IN MAINTAINING VIROLOGIC SUPPRESSION THROUGH 96 WEEKS (TANGO STUDY)

J van Wyk,[1] F Ajana,[2] F Bisshop,[3] S De Wit,[4] O Osiyemi,[5] J Portilla,[6] J-P Routy,[7] C Wyen,[8] M Ait-Khaled,[1] M-C Nascimento,[1] KA Pappa,[9] R Wang,[9] J Wright,[10] B Wynne,[9] M Aboud,[1] KY Smith[9]

[1]ViiV Healthcare, Brentford, UK; [2]Centre Hospitalier de Tourcoing, Tourcoing, France; [3]Holdsworth House Medical Brisbane, Queensland, Australia; [4]CHU St-Pierre, Brussels, Belgium; [5]Triple O Research Institute PA, West Palm Beach, FL, USA; [6]Hospital General Universitario de Alicante, Alicante Spain; [7]McGill University Health Center, Montreal, QC, Canada; [8]Praxis am Ebertplatz, Cologne, Germany;
[9]ViiV Healthcare, Research Triangle Park, NC, USA; [10]GlaxoSmithKline, Stockley Park, UK

TANGO Phase III Study Design

Randomized, open-label, multicenter, parallel-group, non-inferiority study



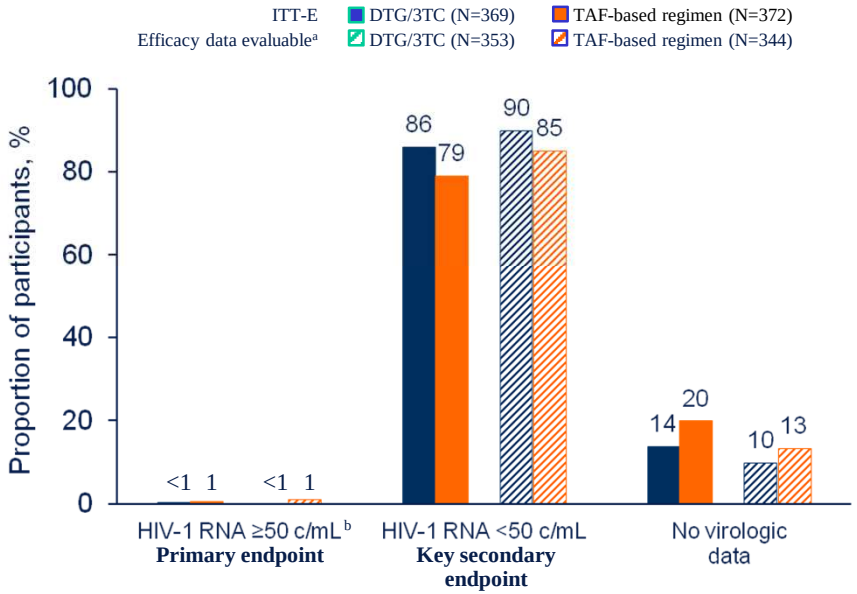
[a]Stratified by baseline third agent class (PI, INSTI, or NNRTI). [b]2 patients excluded who were randomized but not exposed to study drug. [c]Participants with initial TDF treatment who switched to TAF ≥3 months before screening, with no changes to other drugs in their regimen, were also eligible. [d]4% non-inferiority margin. [e]Includes participants who changed a background therapy component or discontinued study treatment for lack of efficacy before Week 48, or who had HIV-1 RNA ≥50 c/mL in the 48-week window.

van Wyk et al. *Clin Infect Dis*. 2020;ciz1243.

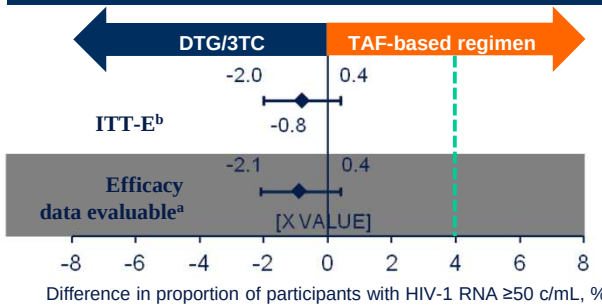
van Wyk et al. HIV Glasgow 2020; Virtual. Slides O441.

DTG/3TC Is Non-Inferior to TAF-Based Regimen at Week 96

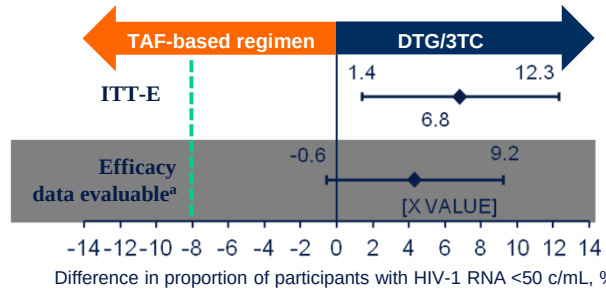
Virologic outcomes (Snapshot analysis)



Adjusted treatment difference (95% CI)[c]



HIV-1 RNA ≥50 c/mL
DTG/3TC is non-inferior to TAF-based regimen at Week 96 based on a 4% non-inferiority margin



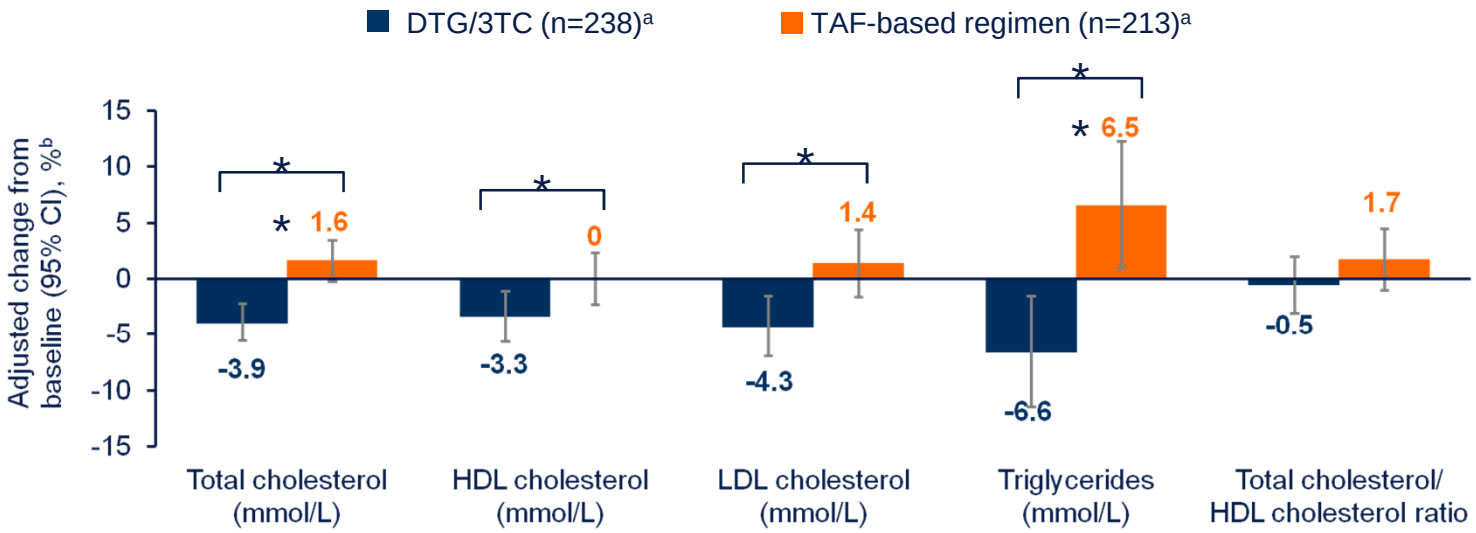
HIV-1 RNA <50 c/mL
DTG/3TC is non-inferior to TAF-based regimen at Week 96 based on a −8% non-inferiority margin

- In the per-protocol population,[d] superiority was demonstrated with 0/348 participants in the DTG/3TC group and 4/351 (1%) in the TAF-based regimen group with HIV-1 RNA ≥50 c/mL at Week 96 (adjusted difference, −1.1%; 95% CI, −2.3% to −0.0%)

[a]Sensitivity analysis excluding 16 and 28 participants in the DTG/3TC and TAF-based regimen groups, respectively, because of no Week 96 HIV-1 RNA data due to effects of the COVID-19 pandemic. [b]Primary endpoint (Snapshot virologic non-response, ITT-E). [c]Based on Cochran-Mantel-Haenszel stratified analysis (DTG/3TC − TAF-based regimen) adjusting for baseline third agent class. [d]Sensitivity analysis.

van Wyk et al. HIV Glasgow 2020; Virtual. Slides O441.

Change in Serum Lipids From Baseline at Week 96: Safety Population



- Changes in total cholesterol, LDL cholesterol, and triglycerides significantly favored the DTG/3TC group; changes in HDL cholesterol favored the TAF-based regimen group

[a]n = number of participants with non-missing fasting lipid data at baseline and Week 96, removing those with lipid-modifying agent administered at baseline (lipid data collected after initiation of a lipid-modifying agent were censored and a last observation carried forward method was applied). Use of lipid-modifying agents at baseline was similar between treatment groups (DTG/3TC, 13%; TAF-based regimen, 15%). [b]Percent change from baseline based on adjusted ratio (Week 96 to baseline) in each group calculated from a repeated measures model applied to change from baseline in $\log_e$-transformed data adjusting for the following: treatment, visit, baseline third agent class, CD4+ cell count, $\log_e$-transformed baseline value, treatment-by-visit interaction, and baseline value-by-visit interaction, with visit as the repeated factor. *P<0.05. **P<0.001.

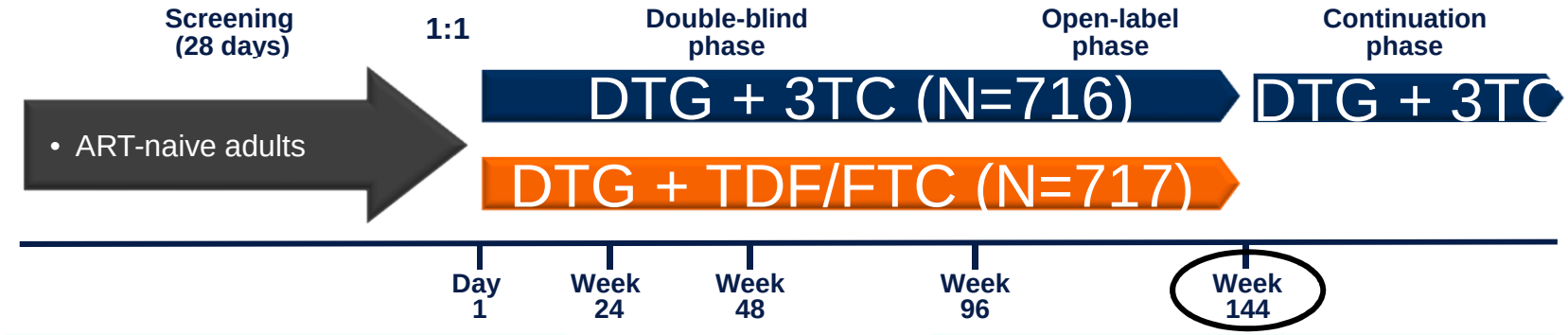
van Wyk et al. HIV Glasgow 2020; Virtual. Slides O441.

DURABLE EFFICACY OF DOLUTEGRAVIR (DTG) PLUS LAMIVUDINE (3TC) IN ANTIRETROVIRAL TREATMENT–NAIVE ADULTS WITH HIV-1 INFECTION— 3-YEAR RESULTS FROM THE GEMINI STUDIES

P Cahn,[1] J Sierra Madero,[2] JR Arribas,[3] A Antinori,[4] R Ortiz,[5] AE Clarke,[6] C-C Hung,[7] JK Rockstroh,[8] P-M Girard,[9] J Sievers,[10] CY Man,[11] R Urbaityte,[12] M Underwood,[11] KA Pappa,[11] KY Smith,[11] M Gartland,[11] M Aboud,[10] J van Wyk,[10] B Wynne[11]

[1]Fundación Huésped, Buenos Aires, Argentina; [2]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico; [3]Hospital La Paz, Madrid, Spain; [4]Istituto Nazionale per le Malattie Infettive Lazzaro Spallanzani, Rome, Italy; [5]Bliss Healthcare Services, Orlando, FL, USA; [6]Royal Sussex County Hospital and Brighton & Sussex Medical School, Brighton, UK; [7]National Taiwan University Hospital, Taipei, Taiwan; [8]Rheinische Friedrich-Wilhelms Universität, Bonn, Germany; [9]Hôpital Saint Antoine, Paris, France; [10]ViiV Healthcare, Brentford, UK;
[11]ViiV Healthcare, Research Triangle Park, NC, USA; [12]GlaxoSmithKline, Stockley Park, UK

GEMINI-1 and GEMINI-2 Study Design



Eligibility criteria
- VL 1000-500,000 c/mL at screening
- ≤10 days of prior ART
- No major RT or PI resistance mutations
- No HBV infection or need for HCV therapy

Primary endpoint at Week 48: participants with HIV-1 RNA <50 c/mL (ITT-E Snapshot)[a]

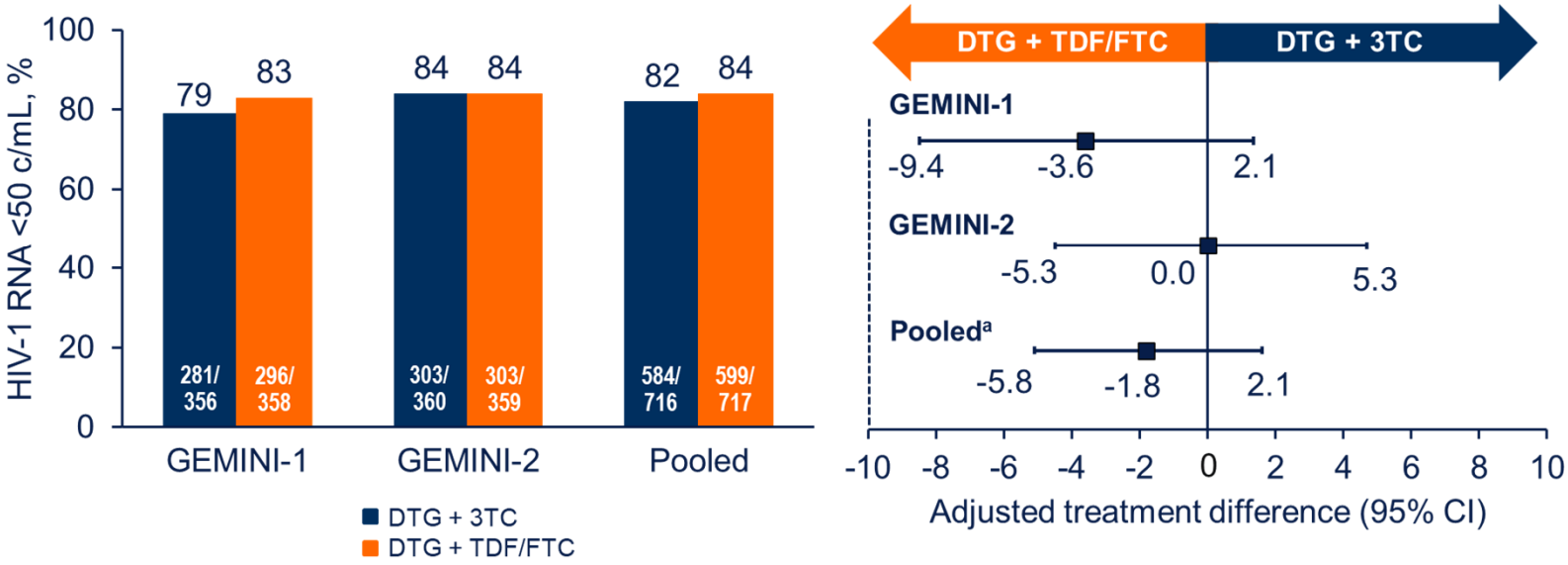
Countries

Argentina	Australia	Belgium
Canada	France	Germany
Italy	Republic of Korea	Mexico
Netherlands	Peru	Poland
Portugal	Romania	Russian Federation
South Africa	Spain	Switzerland
Taiwan	United Kingdom	United States

[a]–10% non-inferiority margin for individual studies.

Cahn et al. HIV Glasgow 2020; Virtual. Poster P018.

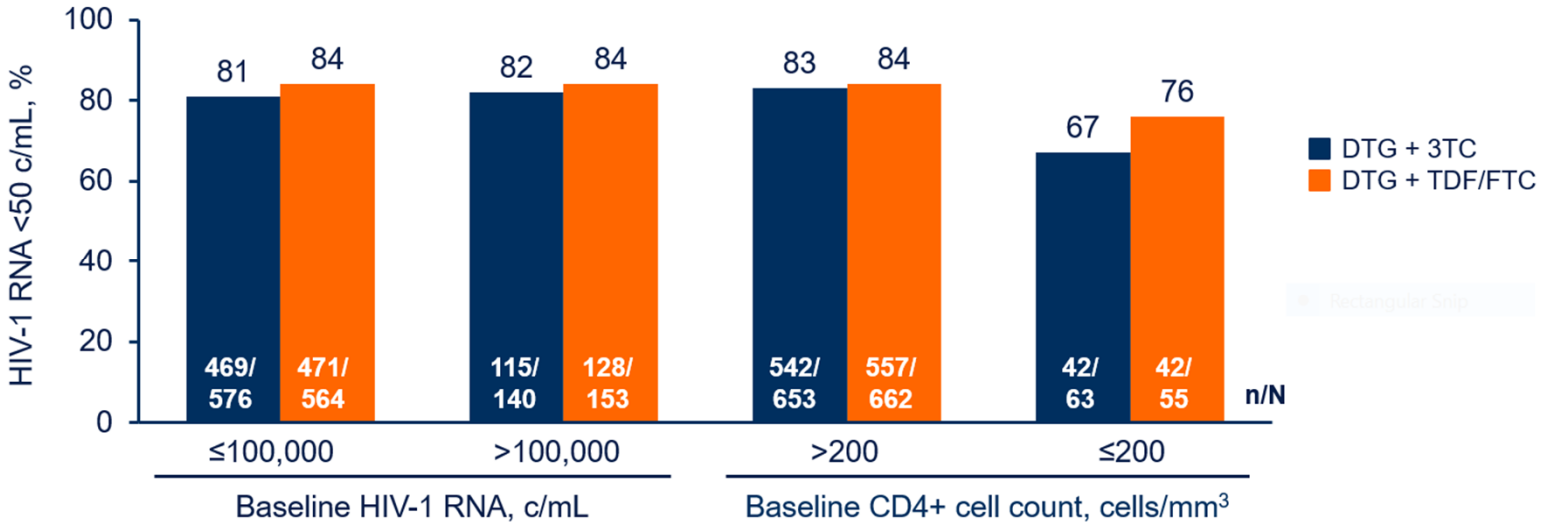
Snapshot Analysis of the Proportion of Participants With Plasma HIV-1 RNA <50 c/mL Through Week 144 in the GEMINI-1, GEMINI-2, and Pooled ITT-E Populations



[a]Based on Cochran-Mantel-Haenszel stratified analysis adjusting for baseline plasma HIV-1 RNA (≤100,000 vs >100,000 c/mL), baseline CD4+ cell count (≤200 vs >200 cells/mm^3), and study (GEMINI-1 vs GEMINI-2).

Cahn et al. HIV Glasgow 2020; Virtual. Poster P018.

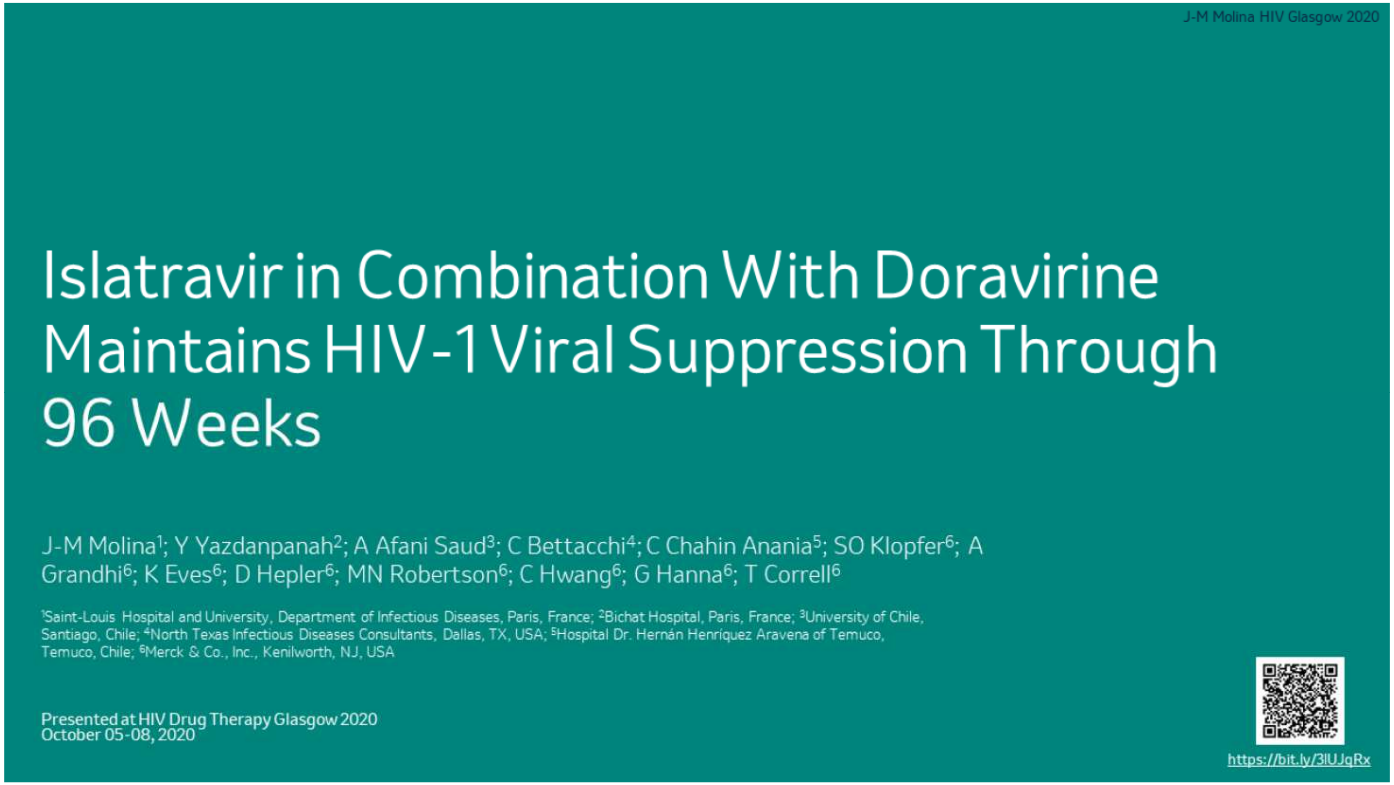
Proportion of Participants With HIV-1 RNA <50 c/mL by Baseline Viral Load and CD4+ Cell Count at Week 144: Snapshot Analysis for the Pooled Population



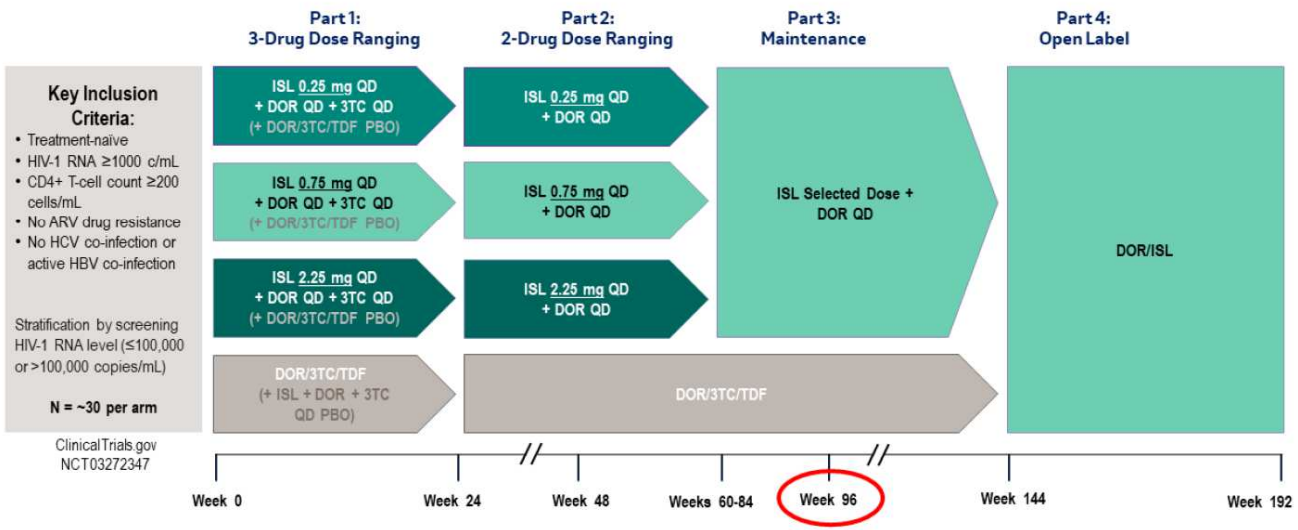
- At Week 144, in participants with baseline HIV-1 RNA >100,000 c/mL, 82% and 84% in the DTG + 3TC and DTG + TDF/FTC groups, respectively, achieved HIV-1 RNA <50 c/mL; among participants with baseline CD4+ cell count ≤200 cells/mm^3, 67% in the DTG + 3TC group and 76% in the DTG + TDF/FTC group achieved HIV-1 RNA <50 c/mL
- The corresponding proportions were 81% and 84%, respectively, for those with baseline HIV-1 RNA ≤100,000 c/mL and 83% and 84%, respectively, for those with baseline CD4+ cell count >200 cells/mm^3

Cahn et al. HIV Glasgow 2020; Virtual. Poster P018.

Islatravir + Doravirina

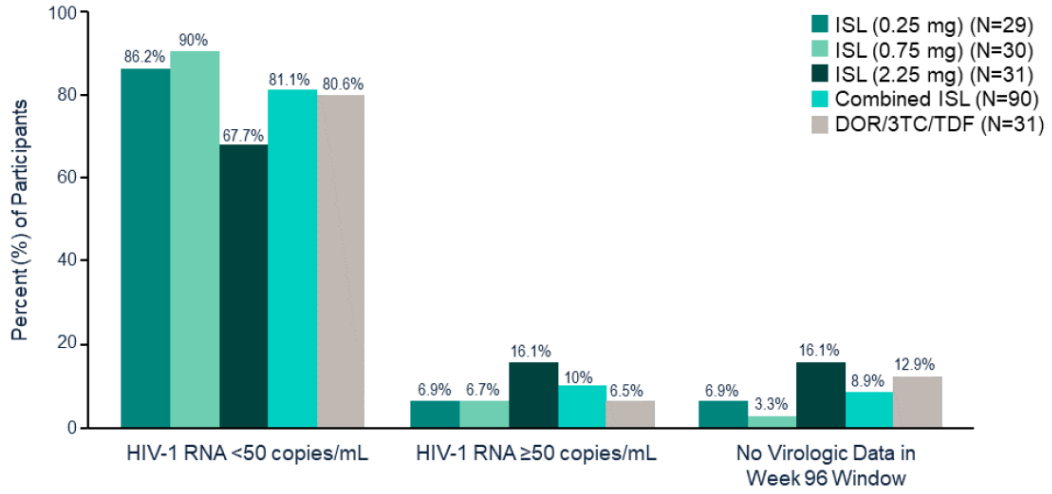


Protocol 011: Phase 2 Dose Ranging Trial of ISL+DOR



After 24 weeks of dosing in Part 1, participants who are virologically suppressed (HIV-1 RNA <50 copies/mL) at the Week 20 visit and have not met any viral failure criteria are eligible to switch to Part 2 of the trial at Week 24. Participants with HIV-1 RNA levels ≥50 copies/mL at Week 20 will remain in Part 1 until the HIV-1 RNA is <50 copies/mL and they have not met any of the viral failure criteria, at which point they transition to Part 2 at their next visit.

Virologic Outcomes at Week 96 (FDA Snapshot Approach)



The numerically lower response rates for ISL (2.25 mg) + DOR group was largely driven by discontinuations through Week 48.

Protocol-Defined Virologic Failure (PDVF) at Week 96

	ISL (0.25 mg) + DOR[a] QD	ISL (0.75 mg) + DOR[a] QD	ISL (2.25 mg) + DOR[a] QD	ISL Combined	DOR/3TC/TDF QD
	N=29	N=30	N=31	N=90	N=31
Protocol-Defined Virologic Failure					
Nonresponder[b], n (%)	0 (0)	0 (0)	1 (3.2)	1 (1.1)	0 (0)
Rebounder with HIV-1 RNA >50 copies/mL, n (%)	2 (6.9)	2 (6.7)	1 (3.2)	5 (5.5)	1 (3.2)
Rebounder with HIV-1 RNA >200 copies/mL, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

- All participants with PDVF had confirmatory HIV-1 RNA levels <80 copies/mL
- No participants met the criteria for resistance testing
- Only one additional participant discontinued with PDVF (rebounder in 2.25 mg group) between weeks 48 and 96
- Five of seven participants with PDVF had a baseline HIV-1 RNA level of >100,000 copies/mL
- Five of seven participants with PDVF had an additional HIV-1 RNA level of <50 prior to changing to a new regimen

[a]Participants initially received ISL+DOR+3TC and switched to ISL+DOR during Part 2 of the study.
[b]Protocol-defined virologic failure (PDVF) for this study is defined as one of the following: 1. Rebounder: Confirmed (two consecutive measures at least 1 week apart) HIV-1 RNA ≥50 copies/mL after initial response of HIV-1 RNA <50 copies/mL at any time during the study, or confirmed HIV-1 RNA >1 log (two consecutive measures at least 1 week apart) increase from the HIV-1 RNA nadir after a >1 log decrease in HIV-1 RNA from baseline at any time during the study; or 2. Nonresponder: Confirmed (two consecutive measures at least 1 week apart) HIV-1 RNA ≥200 copies/mL at any time from week 24 through week 48, or confirmed (two consecutive measures at least 1 week apart) HIV-1 RNA ≥50 copies/mL at week 48.

MK-8507 is a Novel NNRTI in Clinical Development for HIV-1 Treatment

- MK-8507 preclinical data indicate:
  - Favorable safety profile in the anticipated clinical dose range
  - High antiviral potency (IC_{50} = ~50 nM)
  - Activity against common NNRTI resistance-associated mutations
- MK-8507 single and multiple ascending dose clinical trials show:
  - MK-8507 is generally well tolerated up to 1200 mg (single dose) and up to 400 mg (3 x once weekly)
  - PK supports once-weekly oral administration
- This trial evaluated the antiviral efficacy, PK, and safety of single oral doses of 40, 80, and 600 mg MK-8507 in treatment-naive PLWH

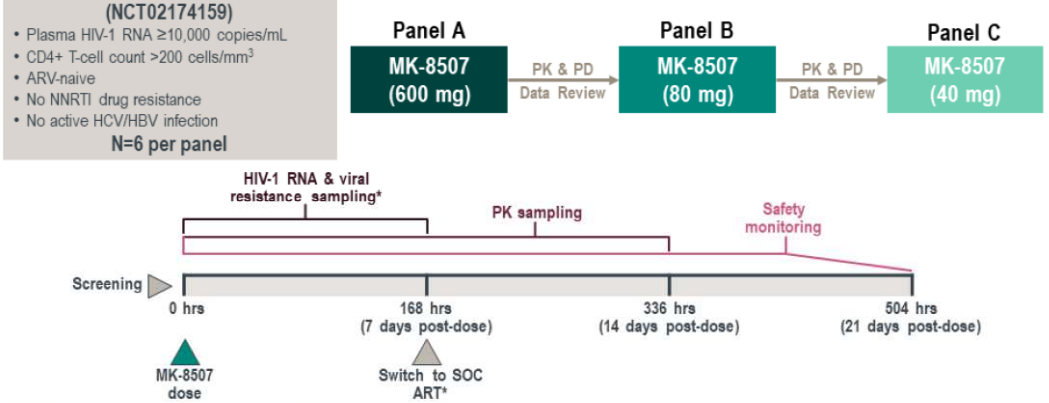
IC_{50}, half-maximal inhibitory concentration; NNRTI, non-nucleoside reverse transcriptase inhibitor; PK, pharmacokinetics; PLWH, people living with HIV.

Single Oral Dose Proof-of-Concept Trial in Treatment-Naive PLWH

Key Inclusion Criteria (NCT02174159)

- Plasma HIV-1 RNA ≥10,000 copies/mL
- CD4+ T-cell count >200 cells/mm^3
- ARV-naive
- No NNRTI drug resistance
- No active HCV/HBV infection

N=6 per panel



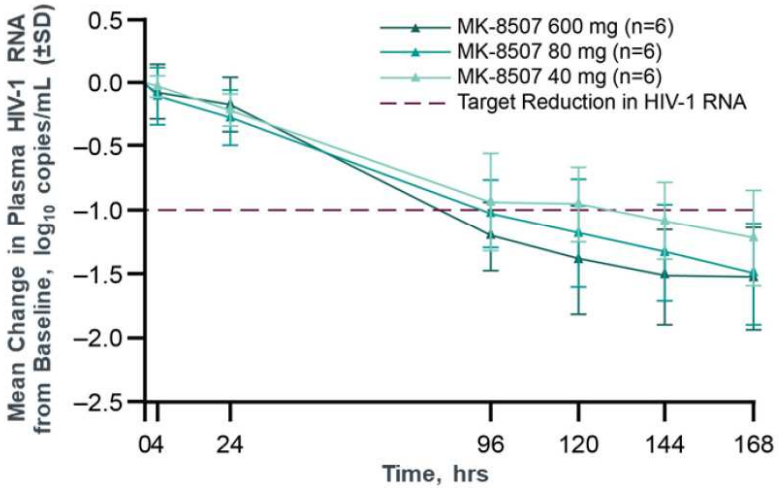
- **HIV-1 RNA reduction target:** Change from baseline ≥1 $\log_{10}$ copies/mL relative to historical placebo data[1]

*3 participants in Panel A were assessed for PK and HIV-1 RNA through 336 hr (14 days post-dose), initiating SOC ART immediately thereafter. 1 participant in Panel C declined SOC ART; PK and HIV-1 RNA samples were therefore analyzed through 336 hr.

ART, antiretroviral therapy; ARV, antiretroviral; HBV, hepatitis B virus; HCV, hepatitis C virus; NNRTI, non-nucleoside reverse transcriptase inhibitor; PD, pharmacodynamic; PK, pharmacokinetic; PLWH, people living with HIV; SOC, standard of care.

1. Xu Y, et al. *Clin Transl Sci*. 2016;9:192–200.

Single Oral Doses of MK-8507 Reduced HIV-1 RNA Levels for at Least 1 Week



LS Mean Change in Plasma HIV-1 RNA from Baseline at 7 Days Post-Dose, log_{10} copies/mL (95% CI)		
MK-8507 (600 mg) Slide6	MK-8507 (80 mg)	MK-8507 (40 mg)
n=6	n=6	n=6
−1.53 (−1.84, −1.23)	−1.50 (−1.80, −1.19)	−1.22 (−1.52, −0.91)

- Single oral doses of MK-8507 as low as 40 mg achieved the 7-day HIV-1 RNA reduction target with >99% posterior probability

CI, confidence interval; LS, least squares; SD, standard deviation.

Viral Resistance Analysis

- 0 of 14 participants initiating SOC ART at 7 days post-dose exhibited viral rebound
- 1 of 4 participants initiating SOC ART after 14 days post-dose exhibited viral rebound
  - The RT resistance mutation F227C was first detected using Sanger sequencing 10 days post-dose (MK-8507 600 mg) in the participant exhibiting viral rebound
- F227C is an uncommon resistance mutation that is susceptible to other classes of ARVs[1], the emergence of this mutant after 10 days of monotherapy is not considered to be clinically relevant in the context of combination ART administered weekly
- No other NNRTI resistance was detected

ARV, antiretroviral; ART, antiretroviral therapy; NNRTI, non-nucleoside reverse transcriptase inhibitor; RT, reverse transcriptase; SOC, standard of care.

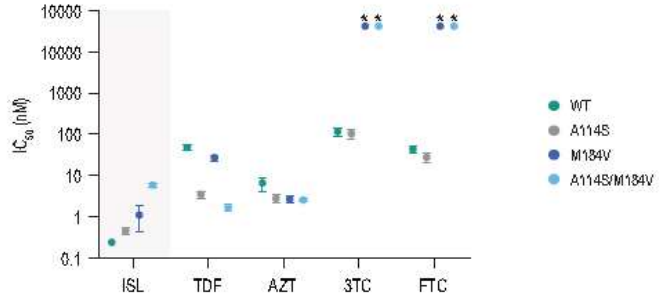
1. Stanford University. HIV drug resistance database. Essential Data on NNRTI DRMs. 2016. Available at: https://hivdb.stanford.edu/pages/POC_NNRTIDRMs_Summary.html. Accessed September 2020.

Islatravir Selects for HIV-1 Variants in MT4-GFP Cells That Profoundly Reduce Replicative Capacity in Peripheral Blood Mononuclear Cells

Tracy Diamond[1]; Winnie Ngo[1]; Min Xu[2]; Shih Lin Goh[2]; Silveria Rodriguez[2]; Ming-Tain Lai[1]; Ernest Asante-Appiah[1]; Jay Grobler[1]

[1]Infectious Disease and Vaccines, [2]Quantitative Biosciences, Merck & Co., Inc., Kenilworth, NJ, USA

Figure 2A. Potency (IC_{50}) of ISL and NRTIs Against RT Variants in PBMCs



*IC_{50} >42000nM

- ISL displays similar or greater potency against A114S, M184V, and A114S/M184V compared to TDF, AZT, 3TC, and FTC against WT

Figure 2B. Fold Change in IC_{50} From WT for ISL and NRTIs Against RT Variants in PBMCs

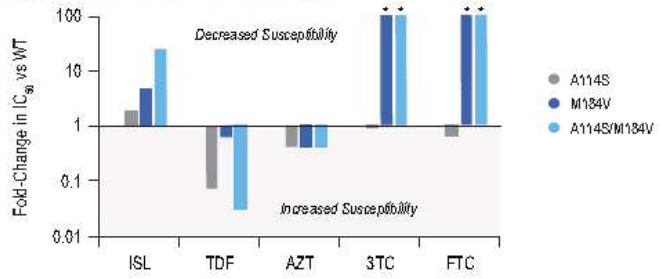
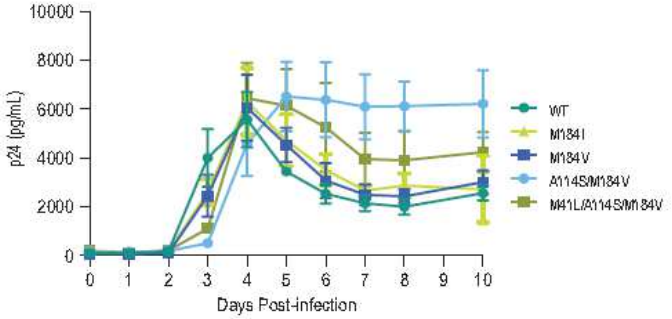
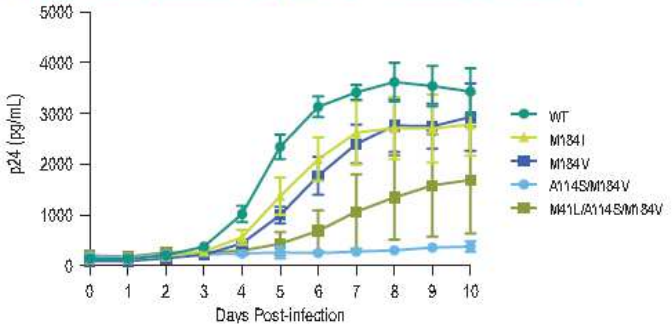


Figure 4A. Replicative Capacity of Viruses in MT4-GFP Cells



- All viruses replicated to some extent in MT4-GFP cells as monitored by GFP (data not shown) and p24

Figure 4B. Replicative Capacity of Viruses in PBMCs



#1008

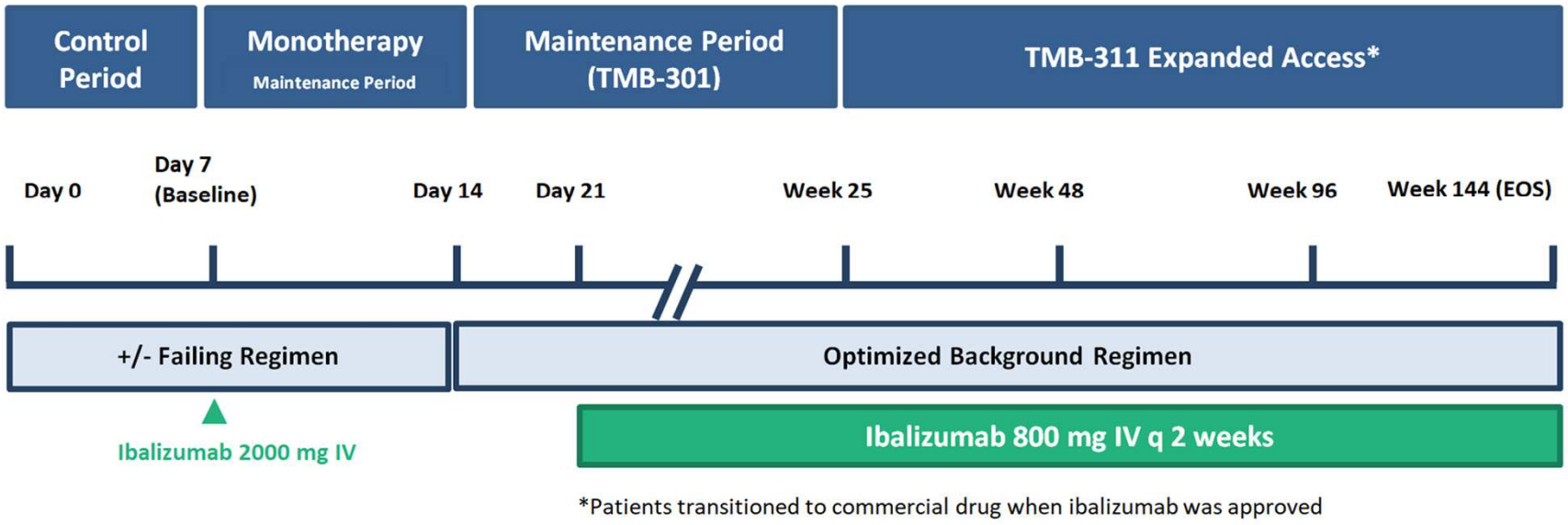
DISEASE SEVERITY IMPACT ON LONG-TERM VIROLOGIC RESPONSE TO IBALIZUMAB IN EXPANDED ACCESS PROTOCOL (TMB-311)

P. KUMAR[1], J. LEIDER[2], J. SLIM[3], G. MOYLE[4], M. LEONARD[5], R.B. CASH[6], S. WEINHEIMER[7], P. MESQUITA[6]

[1]Georgetown University, Washington DC; [2]Jacobi Medical Center, Bronx, NY; [3]Saint Michael's Medical Center, Newark, NJ; [4]Chelsea & Westminster Hospital, London, UK; [5]Theratechnologies Europe LTD, Dublin, Ireland; [6]Theratechnologies Inc., Montreal, QC, Canada; [7]TaiMed Biologics, Irvine, CA

THERA technologies

STUDY DESIGN



*Patients transitioned to commercial drug when ibalizumab was approved

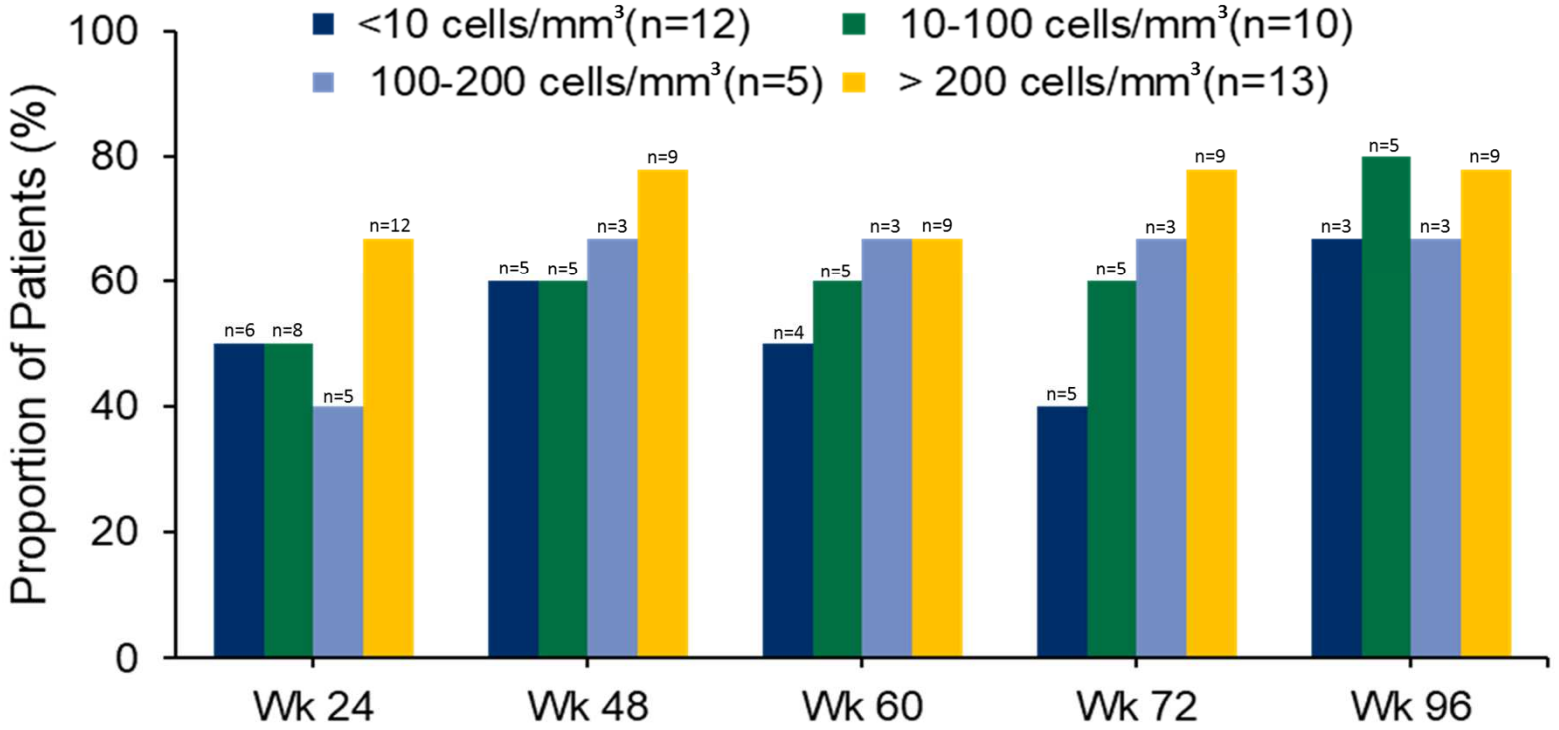
DISEASE SEVERITY IMPACT ON LONG-TERM VIROLOGIC RESPONSE TO IBALIZUMAB IN EXPANDED ACCESS PROTOCOL (TMB-311)

P. KUMAR[1], J. LEIDER[2], J. SLIM[3], G. MOYLE[4], M. LEONARD[5], R.B. CASH[6], S. WEINHEIMER[7], P. MESQUITA[6]

[1]Georgetown University, Washington DC; [2]Jacobi Medical Center, Bronx, NY; [3]Saint Michael's Medical Center, Newark, NJ; [4]Chelsea & Westminster Hospital, London, UK; [5]Theratechnologies Europe LTD, Dublin, Ireland; [6]Theratechnologies Inc., Montreal, QC, Canada; [7]TaiMed Biologics, Irvine, CA

THERA technologies

Proportion of patients with viral loads <50 copies/mL stratified by baseline CD4 (OT Population)



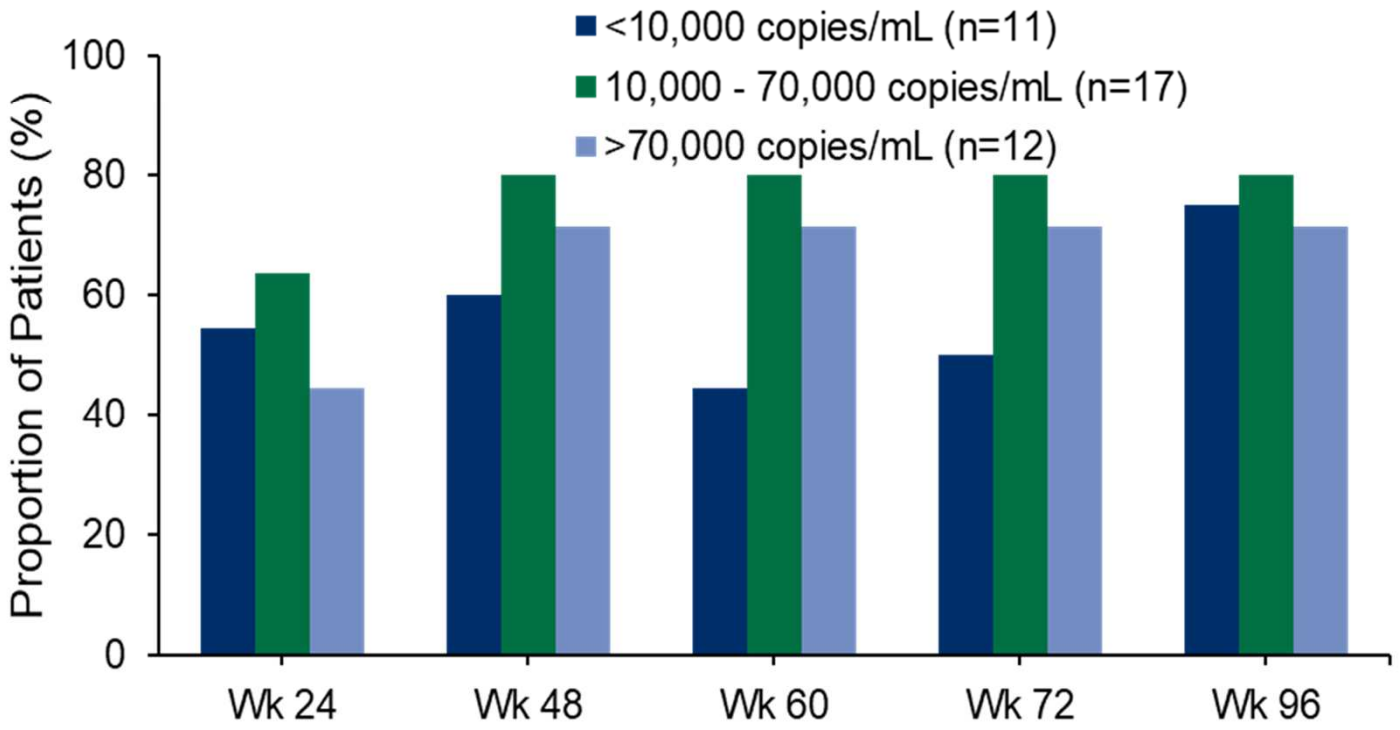
DISEASE SEVERITY IMPACT ON LONG-TERM VIROLOGIC RESPONSE TO IBALIZUMAB IN EXPANDED ACCESS PROTOCOL (TMB-311)

P. KUMAR[1], J. LEIDER[2], J. SLIM[3], G. MOYLE[4], M. LEONARD[5], R.B. CASH[6], S. WEINHEIMER[7], P. MESQUITA[6]

[1]Georgetown University, Washington DC; [2]Jacobi Medical Center, Bronx, NY; [3]Saint Michael's Medical Center, Newark, NJ; [4]Chelsea & Westminster Hospital, London, UK; [5]Theratechnologies Europe LTD, Dublin, Ireland; [6]Theratechnologies Inc., Montreal, QC, Canada; [7]TaiMed Biologics, Irvine, CA

THERA technologies

Proportion of patients with viral loads <50 copies/mL stratified by baseline viral load (OT Population)



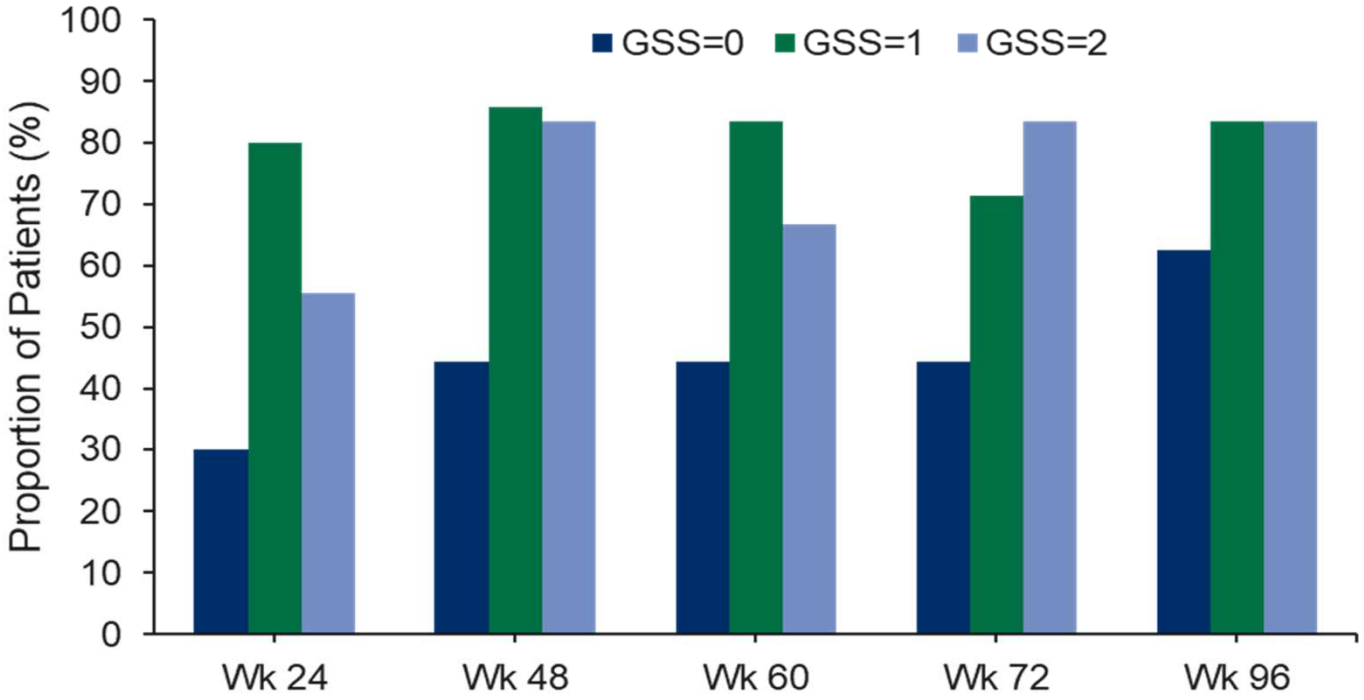
DISEASE SEVERITY IMPACT ON LONG-TERM VIROLOGIC RESPONSE TO IBALIZUMAB IN EXPANDED ACCESS PROTOCOL (TMB-311)

P. KUMAR[1], J. LEIDER[2], J. SLIM[3], G. MOYLE[4], M. LEONARD[5], R.B. CASH[6], S. WEINHEIMER[7], P. MESQUITA[6]

[1]Georgetown University, Washington DC; [2]Jacobi Medical Center, Bronx, NY; [3]Saint Michael's Medical Center, Newark, NJ; [4]Chelsea & Westminster Hospital, London, UK; [5]Theratechnologies Europe LTD, Dublin, Ireland; [6]Theratechnologies Inc., Montreal, QC, Canada; [7]TaiMed Biologics, Irvine, CA

THERA technologies

Proportion of patients with viral loads <50 copies/mL stratified by GSS (OT Population)



Long-term Efficacy, Safety, and Durability of Ibalizumab-based Regimens in Subgroup of TMB-202 Participants

William Towner[1], MD, FACP, FIDSA, Edwin DeJesus[2], MD, FIDSA, Shannon Schrader[3], MD, Jerome de Vente[4], MD, Colleen McGary[5], PhD, Mohammed Zogheib[5], PharmD, MPH, Steven Weinheimer[6], PhD, Pedro Mesquita[7], PhD

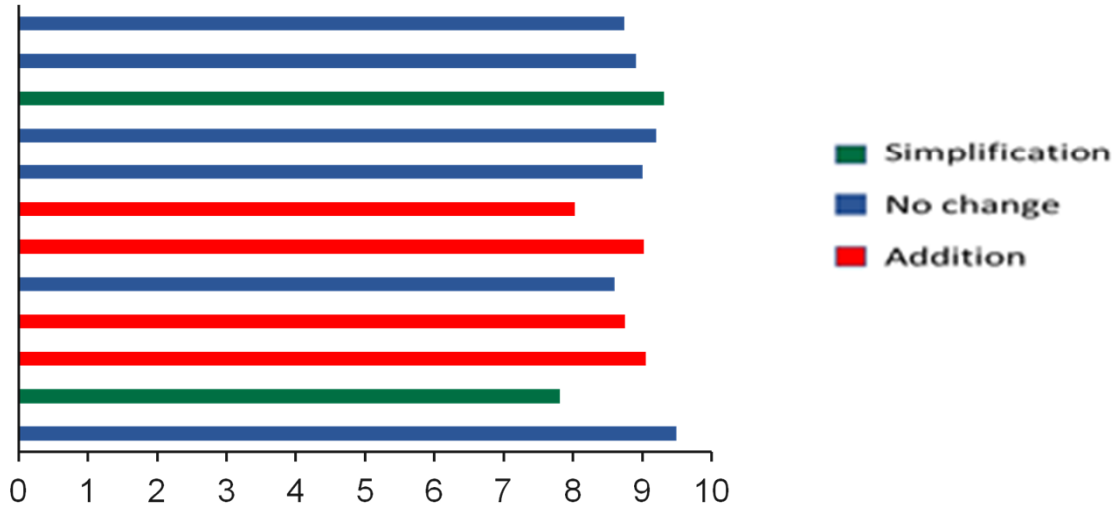
[1]Kaiser Permanente Southern California; Pasadena, CA; [2]Orlando Immunology Center, University of Central Florida College of Medicine; Orlando, FL; [3]Research Access Network; Houston, Texas; [4]Long Beach Education and Research Consultants; Long Beach, California; [5]Syneos Health, Somerset, NJ; [6]Taimed Biologics; Irvine, California; [7]Theratechnologies Inc., Montreal, QC, Canada;

THERA technologies

Results (cont'd)

Durability of Response

- Overall, the 12 patients remained on IBA for an average of 8.9 years (range 7.8-9.5)
- During this period, 8/12 did not require addition of new ARVs to their OBR to maintain suppression.

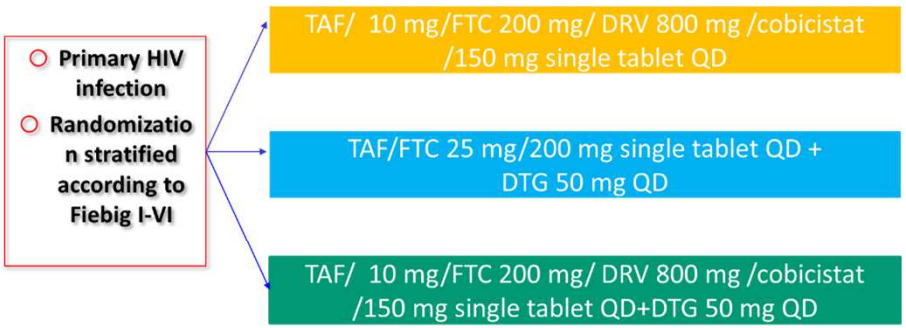


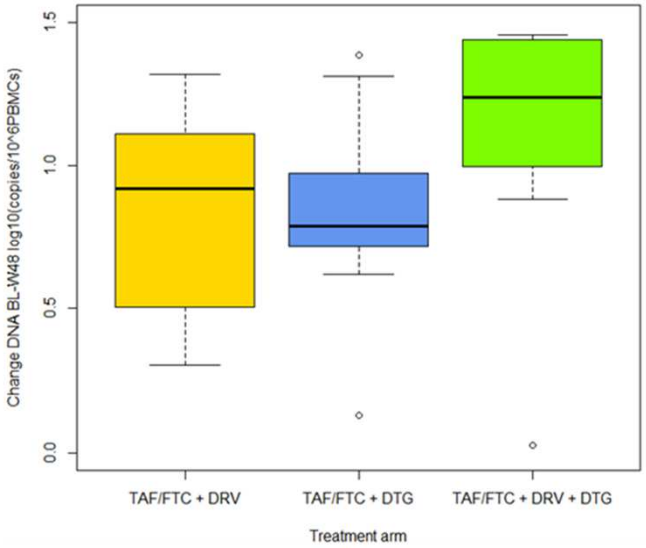
HIV-DNA decrease during treatment in Primary HIV-1 Infection: a randomized clinical trial with 3 different drug regimens.

Nozza S[1], Gabrieli A[2], Bernasconi D[3], Marchetti G[4], Calcagno A[5], Ripamonti D[6], Antinori A[7], Squillace N[8], Cauda R[9], Parisi MR[1], Muscatello A[10], Bandera A[4], Tambussi G[1], Rusconi S[4] on behalf of INACTION Sudy Group.

P024

[1]Department of Infectious Diseases, San Raffaele Scientific Institute, Milano, Italy. [2]Department of Biomedical and Clinical Sciences Luigi Sacco, University of Milan, Milan, Italy.[3]Center of Biostatistics for Clinical Epidemiology, School of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy. 4University of Milan, Milan, Italy. [5]Unit of Infectious Diseases, Department of Medical Sciences , University of Torino , Torino , Italy. [6]Division of Infectious Diseases, ASST Papa Giovanni XXIII, Bergamo, Italy. [7]UOC Immunodeficienze virali, Instituto Nazionale per le Malattie Infettive Lazzaro Spallanzani-IRCCS, Rome, Italy [8]Divisione Malattie Infettive AO S. Gerardo, Monza, Italy.[9] Institute of Infectious Diseases, Catholic University of the Sacred Heart, A. Gemelli Hospital, Roma, Italy. [10] Infectious Disease Unit, Department of Internal Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy.
Corresponding author: **Silvia Nozza nozza.silvia@hsr.it**





MEDICI
CON L'AFRICA
CUAMM

la salute è un diritto, battersi per il suo rispetto è un dovere