Futuro del Tratamiento Antirretroviral: Nuevos Fármacos, Nuevas Formulaciones

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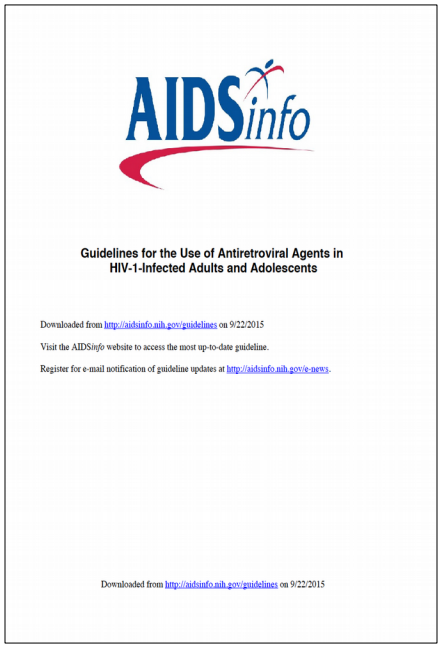
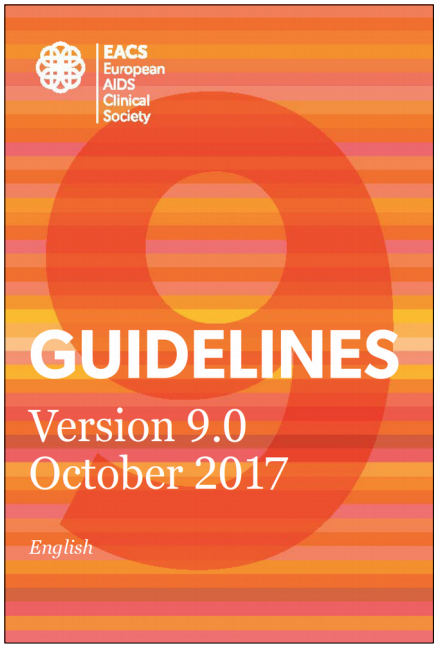
1 Tratamiento Antirretroviral Actual

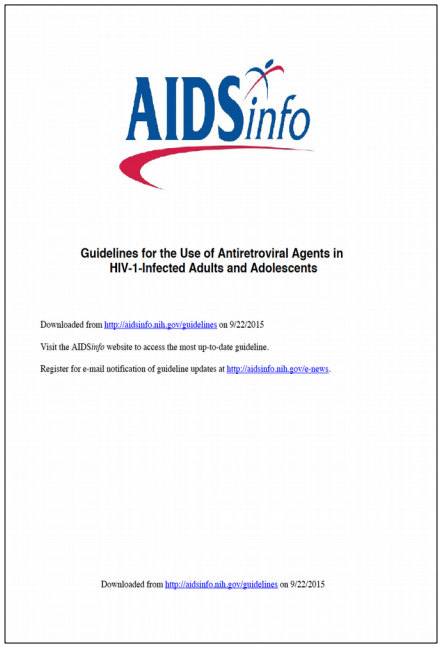
HIV Guidelines
When to Start. What to start.

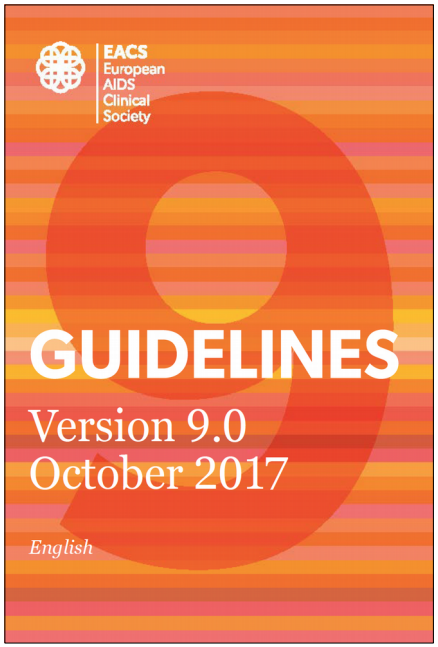




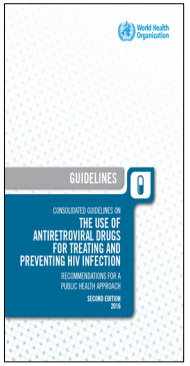
HIV Guidelines
When to Start

All HIV-infected patients, irrespective of CD4 count





WHO Clinical Guidelines 2016: Antiretroviral Therapy

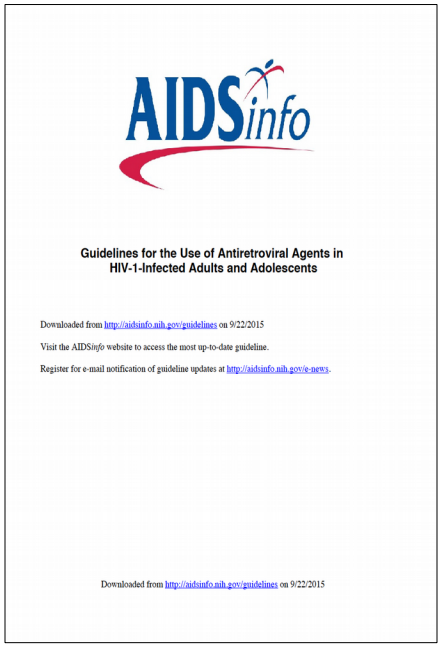


When to Start ART

NEW 4.3.1 When to start ART in adults (>19 years old)	ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count (strong recommendation, moderate-quality evidence).
	As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with a CD4 count ≤350 cells/mm^3 (strong recommendation, moderate-quality evidence).
NEW 4.3.2 When to start ART in pregnant and breastfeeding women	ART should be initiated in all pregnant and breastfeeding women living with HIV, regardless of WHO clinical stage and at any CD4 cell count and continued lifelong (strong recommendation, moderate-quality evidence).

WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, June 2016

HIV Guidelines
What to start.


AIDSinfo

Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

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Visit the AIDS*info* website to access the most up-to-date guideline.

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Clinical Review & Education

Special Communication

Antiretroviral Treatment of Adult HIV Infection
2014 Recommendations
of the International Antiviral Society-USA Panel

Huldrych F. Günthard, MD; Judith A. Aberg, MD; Joseph J. Eron, MD; Jennifer F. Hoy, MBBS, FRACP; Amalio Telenti, MD, PhD; Constance A. Benson, MD; David M. Burger, PharmD, PhD; Pedro Cahn, MD, PhD; Joel E. Gallant, MD, MPH; Marshall J. Glesby, MD, PhD; Peter Reiss, MD, PhD; Michael S. Saag, MD; David L. Thomas, MD, MPH; Donna M. Jacobsen, BS; Paul A. Volberding, MD

IMPORTANCE New data and antiretroviral regimens expand treatment choices in resource-rich settings and warrant an update of recommendations to treat adults infected with human immunodeficiency virus (HIV).

OBJECTIVE To provide updated treatment recommendations for adults with HIV, emphasizing when to start treatment, what treatment to start, the use of laboratory monitoring tools, and managing treatment failure, switches, and simplification.

DATA SOURCES, STUDY SELECTION, AND DATA SYNTHESIS An International Antiviral Society–USA panel of experts in HIV research and patient care considered previous data and reviewed new data since the 2012 update with literature searches in PubMed and EMBASE through June 2014. Recommendations and ratings were based on the quality of evidence and consensus.

RESULTS Antiretroviral therapy is recommended for all adults with HIV infection. Evidence for benefits of treatment and quality of available data increase at lower CD4 cell counts. Recommended initial regimens include 2 nucleoside reverse transcriptase inhibitors (NRTIs; abacavir/lamivudine or tenofovir disoproxil fumarate/emtricitabine) and a third single or boosted drug, which should be an integrase strand transfer inhibitor (dolutegravir, elvitegravir, or raltegravir), a nonnucleoside reverse transcriptase inhibitor (efavirenz or rilpivirine) or a boosted protease inhibitor (darunavir or atazanavir). Alternative regimens are available. Boosted protease inhibitor monotherapy is generally not recommended, but NRTI-sparing approaches may be considered. New guidance for optimal timing of monitoring of laboratory parameters is provided. Suspected treatment failure warrants rapid confirmation, performance of resistance testing while the patient is receiving the failing regimen, and evaluation of reasons for failure before consideration of switching therapy. Regimen switches for adverse effects, convenience, or to reduce costs should not jeopardize antiretroviral potency.

CONCLUSIONS AND RELEVANCE After confirmed diagnosis of HIV infection, antiretroviral therapy should be initiated in all individuals who are willing and ready to start treatment. Regimens should be selected or changed based on resistance test results with consideration of dosing frequency, pill burden, adverse toxic effect profiles, comorbidities, and drug interactions.

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Author Affiliations: Author affiliations are listed at the end of this article.

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JAMA. 2014;312(4):410-425. doi:10.1001/jama.2014.8722

410

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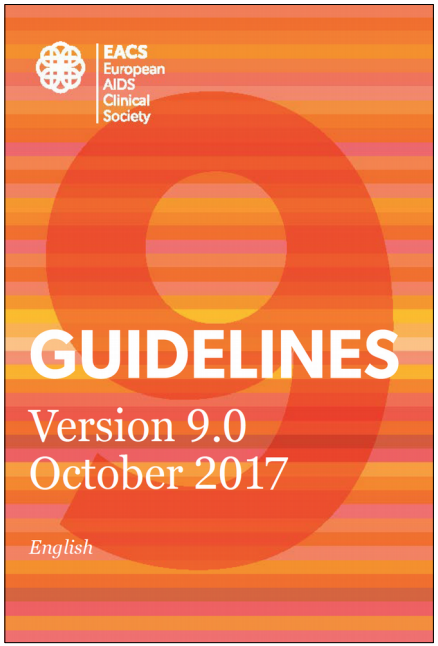
EACS
European
AIDS
Clinical
Society

GUIDELINES

Version 9.0
October 2017

English


Documento de consenso de GeSIDA/Plan Nacional sobre el Sida respecto al tratamiento antirretroviral en adultos con infección por el virus de la inmunodeficiencia humana

(Actualización enero 2015)

Panel de expertos de GeSIDA y Plan Nacional sobre el Sida*

GeSIDA
GRUPO DE ESTUDIO DEL SIDA-SEIMC

GOBIERNO DE ESPAÑA
MINISTERIO DE SANIDAD, SERVICIOS SOCIALES E IGUALDAD

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- Stavudine
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- Zidovudine

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- Etravirine
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- Rilpivirine

- Atazanavir
- Darunavir
- Fosamprenavir
- Indinavir
- Lopinavir
- Nelfinavir
- Ritonavir
- Saquinavir
- Tipranavir

- Raltegravir
- Dolutegravir
- Elvitegravir

- Enfuvirtide

CCR5 Inhibitors

- Maraviroc

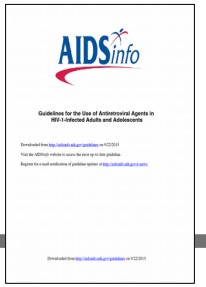
- Ritonavir
- Cobicistat

- Atripla
- Eviplera
- Odefsey
- Stribild
- Genvoya
- Triumeq
- Symtuza

NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PK, pharmacokinetic; STR, single tablet regimens

Adapted from http://www.aidsmeds.com/list.shtml and each product's eMC SPC available at http://www.medicines.org.uk/emc/search

¿Con qué empezar?
Recomendaciones DHHS, 2017



- The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) classifies the following regimens as Recommended Initial Regimens for Most People with HIV (in alphabetical order):
  - Dolutegravir/abacavir/lamivudine[a]—**only** for patients who are HLA-B*5701-negative (**AI**)
  - Dolutegravir plus tenofovir/emtricitabine[a,b] (**AI**)
  - Elvitegravir/cobicistat/tenofovir/emtricitabine[b] (**AI**)
  - Raltegravir plus tenofovir/emtricitabine[a,b] (**AI** for tenofovir disoproxil fumarate, **AII** for tenofovir alafenamide)[a,b]

EACS Guidelines. V 9. October 2017.

¿Con qué empezar? IAS-USA Guidelines, 2018

Generally Recommended:

- BIC/TAF/FTC
- DTG/ABC/3TC
- DTG-TAF/FTC

Other recommended

- DRV/c/TAF (or TDF)/FTC
- DRV/r/TAF (or TDF)/FTC
- EFV/TDF/FTC
- EVG/c/TAF (or TDF)/FTC
- RAL-TAF (or TDF)/FTC
- RPV/TAF (or TDF)/FTC

- Rapid start (including same day as diagnosis) ART
- NNRTIs and abacavir should not be used for rapid ART start
- Recommendations against routine use of MAC prophylaxis
- CD4 cell counts every 6 months until counts >250/μL for at least 1 year with concomitant viral suppression
- 2-1-1 PrEP

Saag MS, Benson CA, Gandhi RT, et al. Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults2018 Recommendations of the International Antiviral Society–USA Panel. JAMA. 2018;320(4):379–396. doi:10.1001/jama.2018.8431.

¿Con qué empezar?
Recomendaciones GESIDA, 2017

3er Fármaco	Pauta†	Comentarios‡
Preferentes. *Pautas aplicables a la mayoría de los pacientes y que en ensayos clínicos aleatorizados han mostrado una eficacia superior frente a otras o mostrando no-inferioridad presentan ventajas adicionales en tolerancia, toxicidad o un bajo riesgo de interacciones farmacológicas.*		
INI	DTG/ABC/3TC	- ABC está contraindicado en pacientes con HLA-B*5701 positivo
	DTG+FTC/TAF	
	RAL+FTC/TAF	- RAL puede administrarse indistintamente como 1 comprimido de 400 mg cada 12 horas, o 2 comprimidos de 600 mg (nueva formulación) cada 24 horas*.

2 Futuro: Nuevos Fármacos, Viejas Familias

Antiretrovirals available in 2018 in Europe

NRTIs

- Abacavir
- Didanosine
- Emtricitabine
- Lamivudine
- Stavudine
- Tenofovir
- Zidovudine

- Delavirdine
- Efavirenz
- Etravirine
- Nevirapine
- Nevirapine XR
- Rilpivirine

- Atazanavir
- Darunavir
- Fosamprenavir
- Indinavir
- Lopinavir
- Nelfinavir
- Ritonavir
- Saquinavir
- Tipranavir

- Raltegravir
- Dolutegravir
- Elvitegravir

- Enfuvirtide

CCR5 Inhibitors

- Maraviroc

- Ritonavir
- Cobicistat

- Atripla
- Eviplera
- Odefsey
- Stribild
- Genvoya
- Triumeq
- Symtuza

NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PK, pharmacokinetic; STR, single tablet regimens

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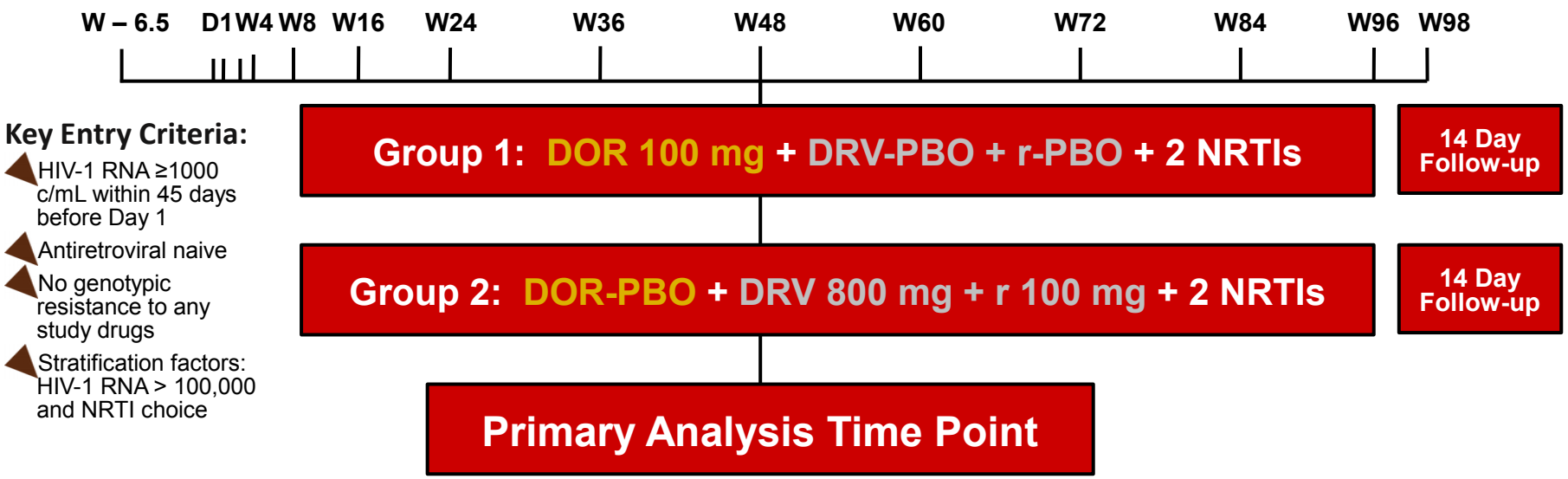
Doravirine

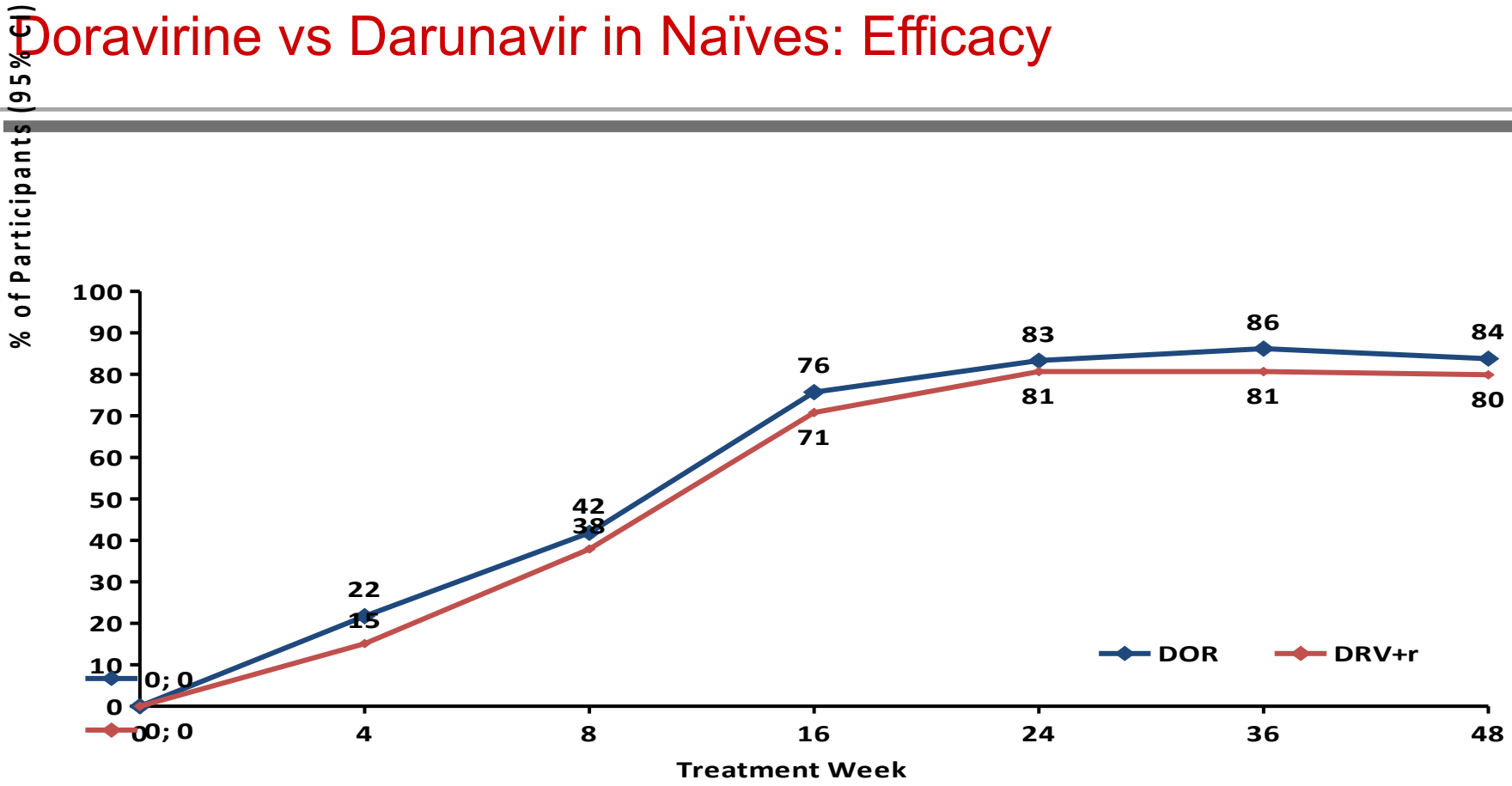
- Doravirine is a novel NNRTI
- **High *in vitro* potency** vs broad panel of isolates including common NNRTI-resistant variants[4]
- **Primary metabolism by CYP3A4**; not an inducer or inhibitor[5]
- **Once daily dosing** (without regard to food)
- **No interactions expected with proton pump inhibitors**

Doravirine vs Darunavir in Naïves: Design



Source: Molina JM, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 45LB.

Doravirine vs Darunavir in Naïves: Efficacy

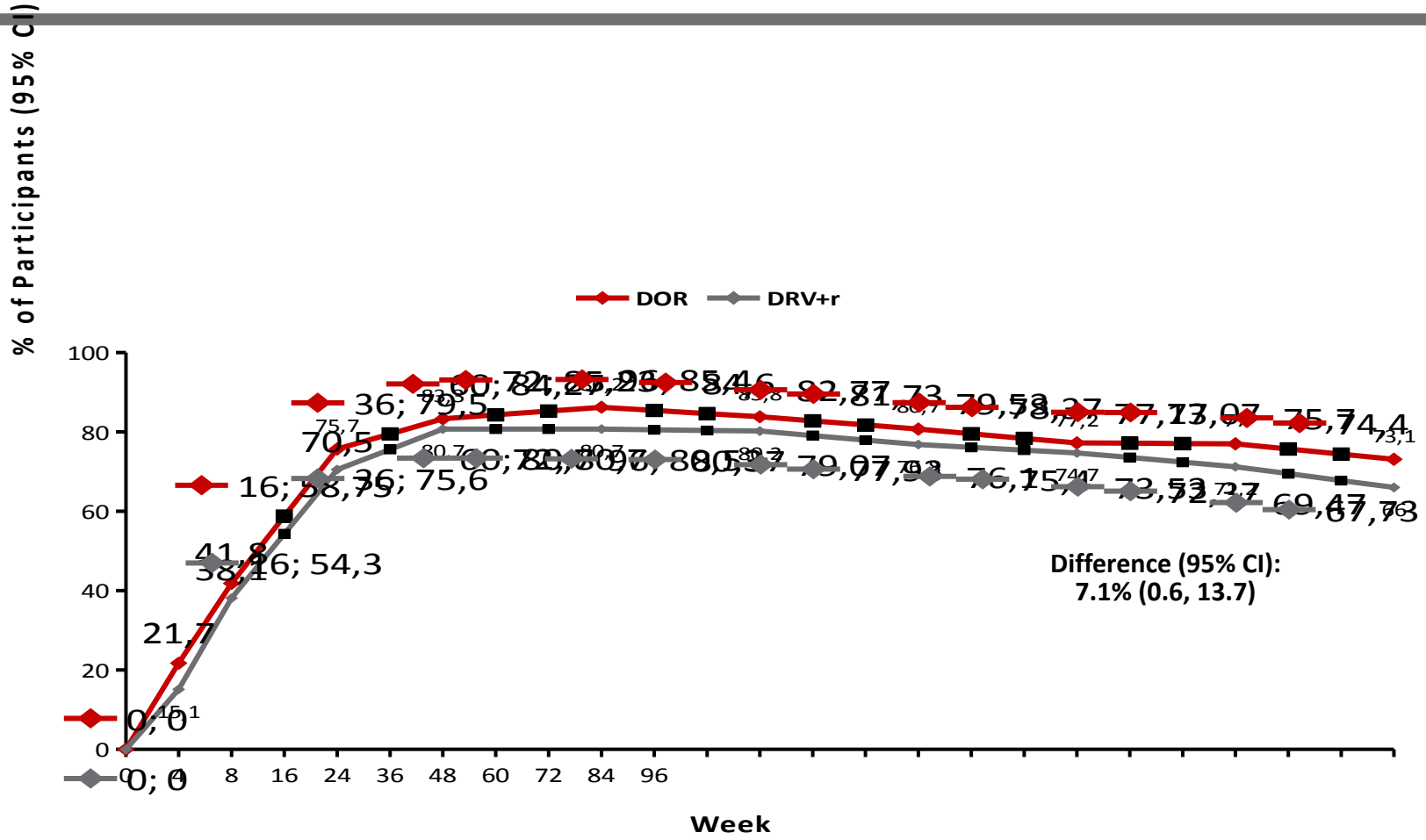


Difference (95% CI): 3.9% (-1.6%, 9.4%)

† FDA Snapshot Approach

Source: Molina JM, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 45LB.

DRIVE-FORWARD Study:
Doravirine vs Darunavir in naïve at 96 weeks



- 2/383 (0.5%) participants on doravirine developing resistance to any study drug

Molina JM, et al. AIDS 2018; Amsterdam, the Netherlands; July 23-27, 2018; Abst. LBPEB017.

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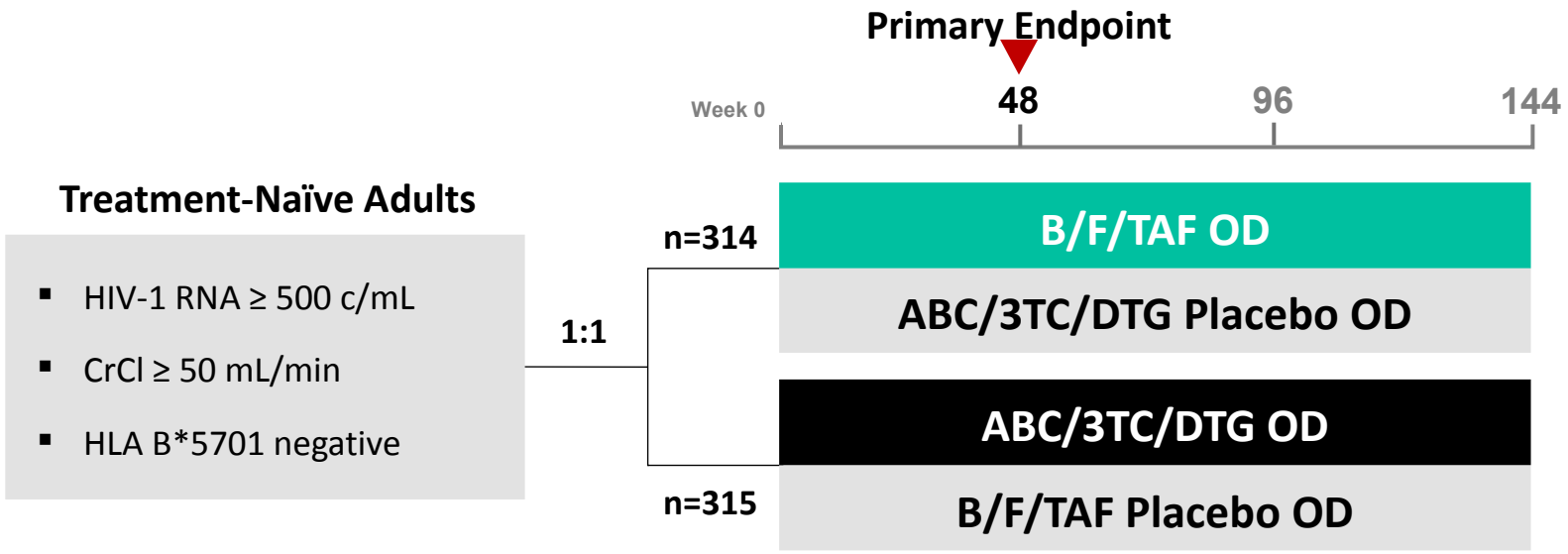
BICTEGRAVIR

- Bictegravir is a novel specific inhibitor of HIV-1 integrase strand transfer activity[1]
- Structurally related to Dolutegravir. Unboosted
- Active against diverse subtypes of wild-type HIV-1 clinical isolates and HIV-2[2]
- Low cytotoxicity in multiple non-target human cell lines and in primary human hepatocyte[2]
- Average human T1/2 of ~19 hours, allowing for once daily dosing[3]
- Close to clinic.

Source: 1. Lazerwith S, et al. ASM 2016; Boston, MA. Poster #414
2. Tsiang M, et al. ASM 2016; Boston, MA. Poster #416
3. Gallant J, et al. ASM 2016. Boston, MA. Poster #415

Phase 3 Randomized Controlled Clinical Trial of Bictegravir in a Fixed Dose Combination, B/F/TAF, vs DTG/ABC/3TC in Treatment-Naïve Adults at Week 48

Study Design

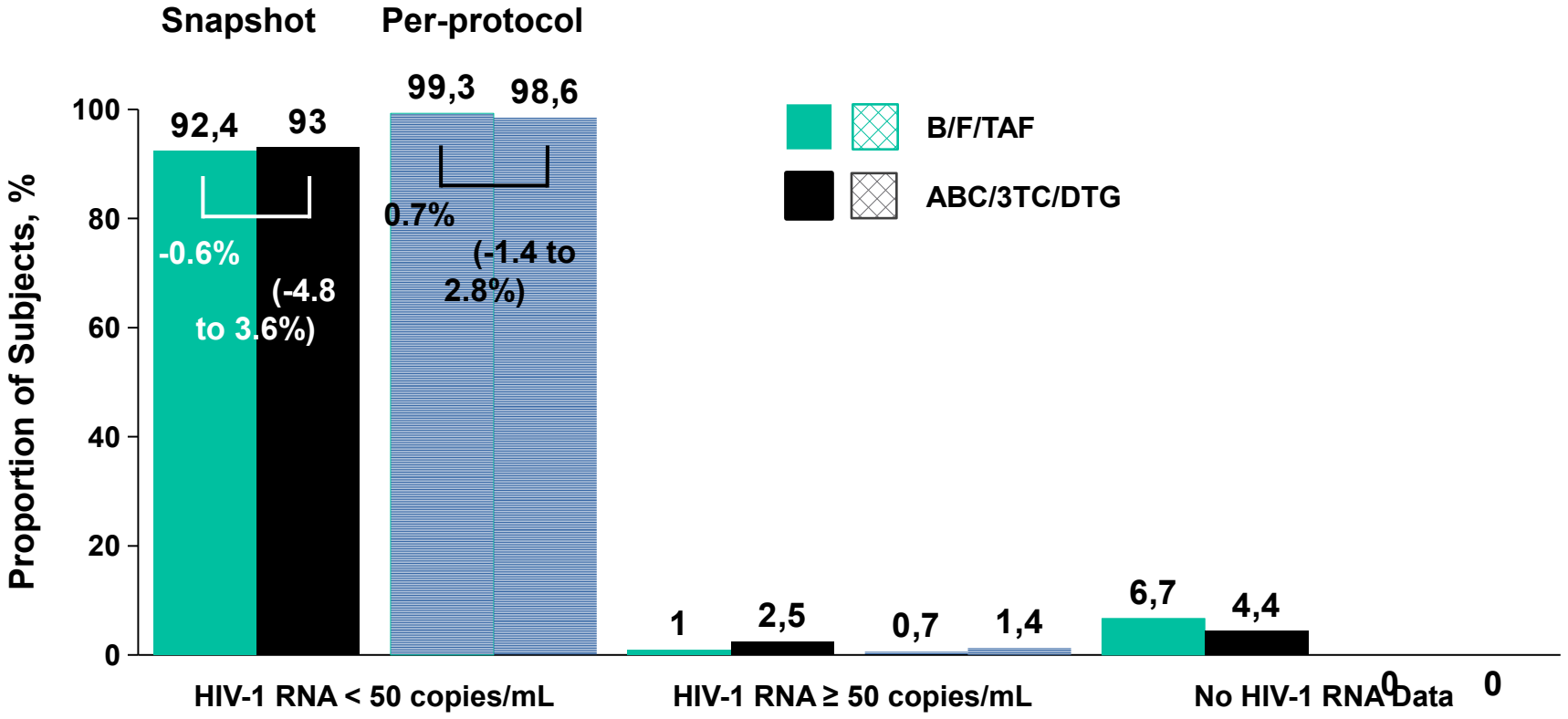


- Phase 3, randomized, double-blind, active-controlled study (ClinicalTrial.gov NCT02607930)
  - Stratified by HIV-1 RNA, CD4 cell count, geographic region
  - North America and Europe
  - Chronic hepatitis C virus infection allowed
- Treatment-naïve, HIV-1-infected adults were randomized 1:1 to receive B/F/TAF 50/200/25 mg or ABC/3TC/DTG 600/300/50 mg with matching placebo once daily
- **Primary endpoint**: HIV-1 RNA < 50 copies/mL at Week 48 by FDA Snapshot algorithm (12% NI margin)

Gallant J, et al. IAS 2017. Paris, France. Oral #MOAB0105LB

CrCl, creatinine clearance. NI, non-inferiority.

Virologic Outcome at Week 48 by FDA Snapshot Analysis



Mean changes in CD4 cell count (cells/μL) at Week 48: +233 B/F/TAF vs +229 ABC/3TC/DTG (p=0.81)

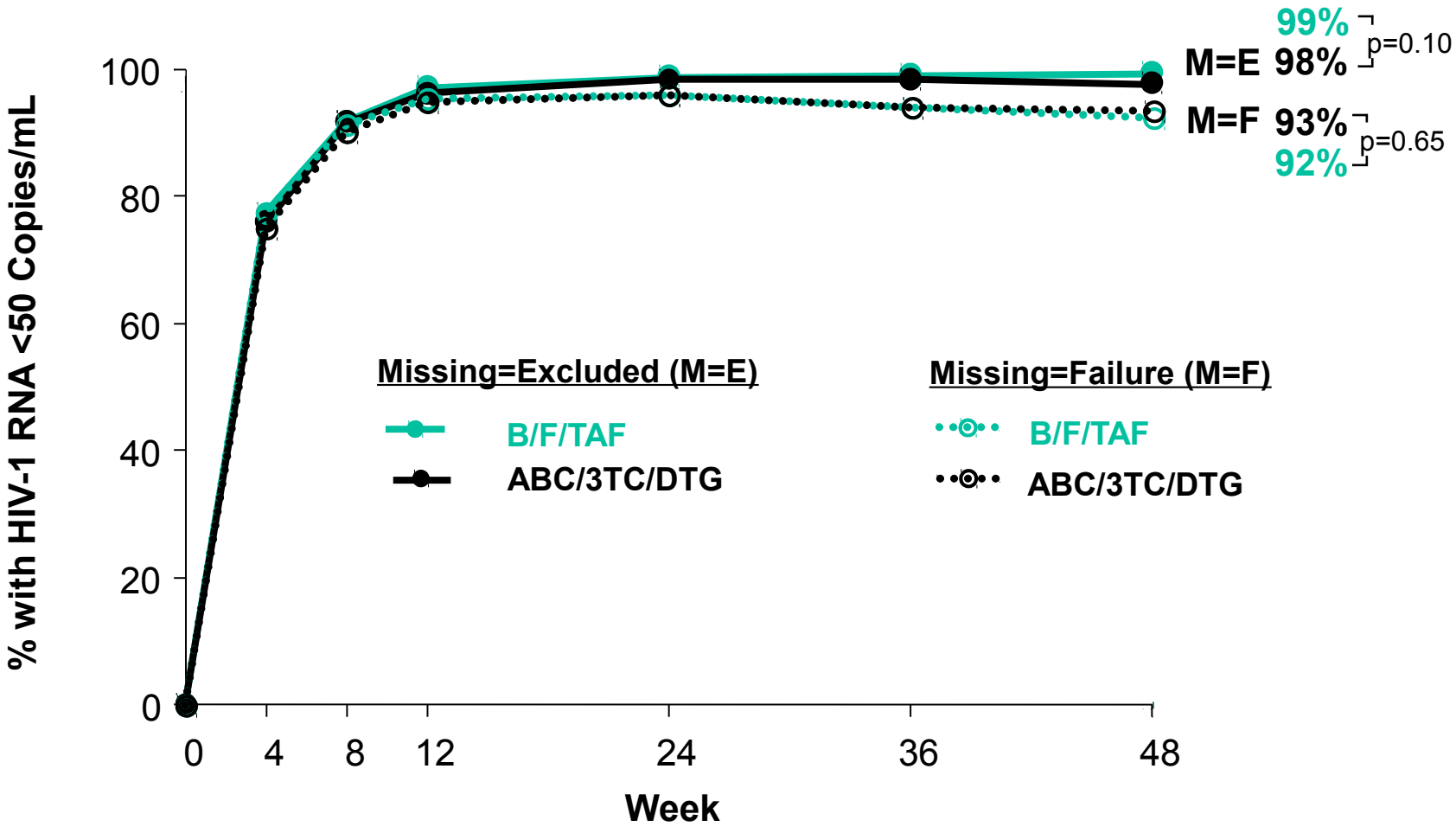
B/F/TAF vs ABC/3TC/DTG: Non-inferior efficacy at Week 48

Confirmed by pre-specified sensitivity analyses (PP, M=E, and M=F)

Gallant J, et al. IAS 2017. Paris, FR. Oral MOAB0105LB.

M=E, missing=excluded. M=F, missing=failure. PP, per-protocol.

Efficacy Through Week 48 (M=E and M=F)

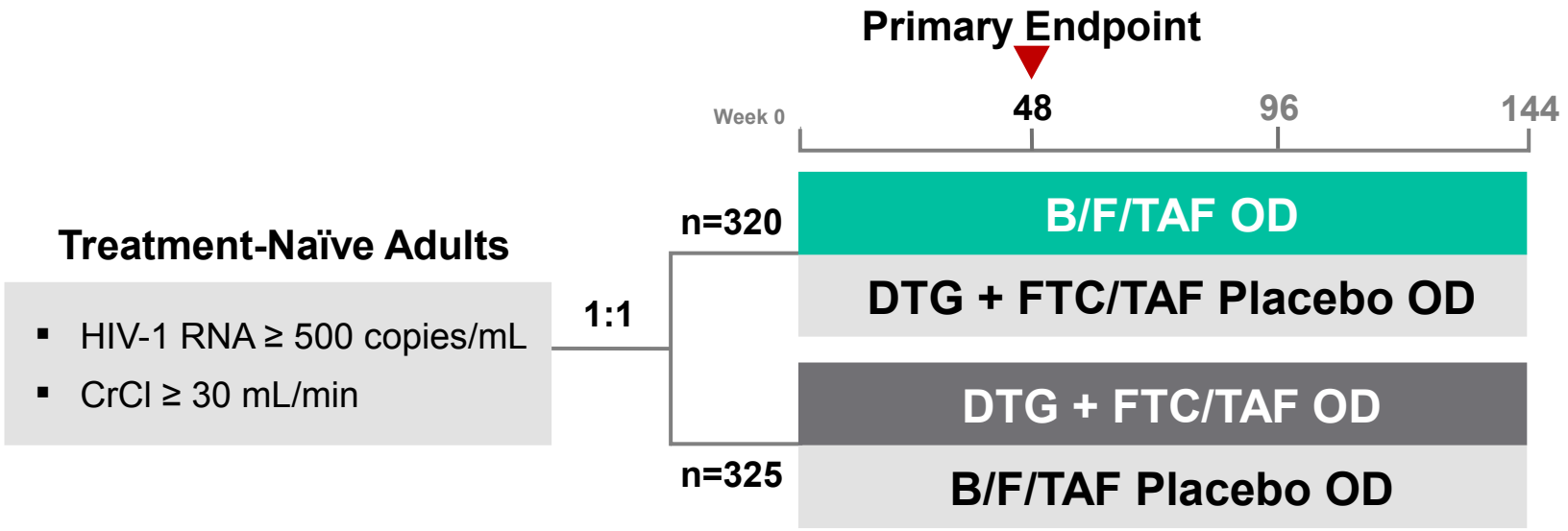


B/F/TAF vs. ABC/3TC/DTG: non-inferior efficacy at Week 48

1. Gallant J, et al. IAS 2017. Paris, FR. Oral MOAB0105LB. 2. Gilead Sciences. Data on file.

Phase 3 Randomized, Controlled, Clinical Trial of Bictegravir Coformulated With FTC/TAF in a Fixed-Dose Combination vs Dolutegravir + FTC/TAF in Treatment-Naïve HIV-1–Positive Adults: Week 48 Results

Study Design

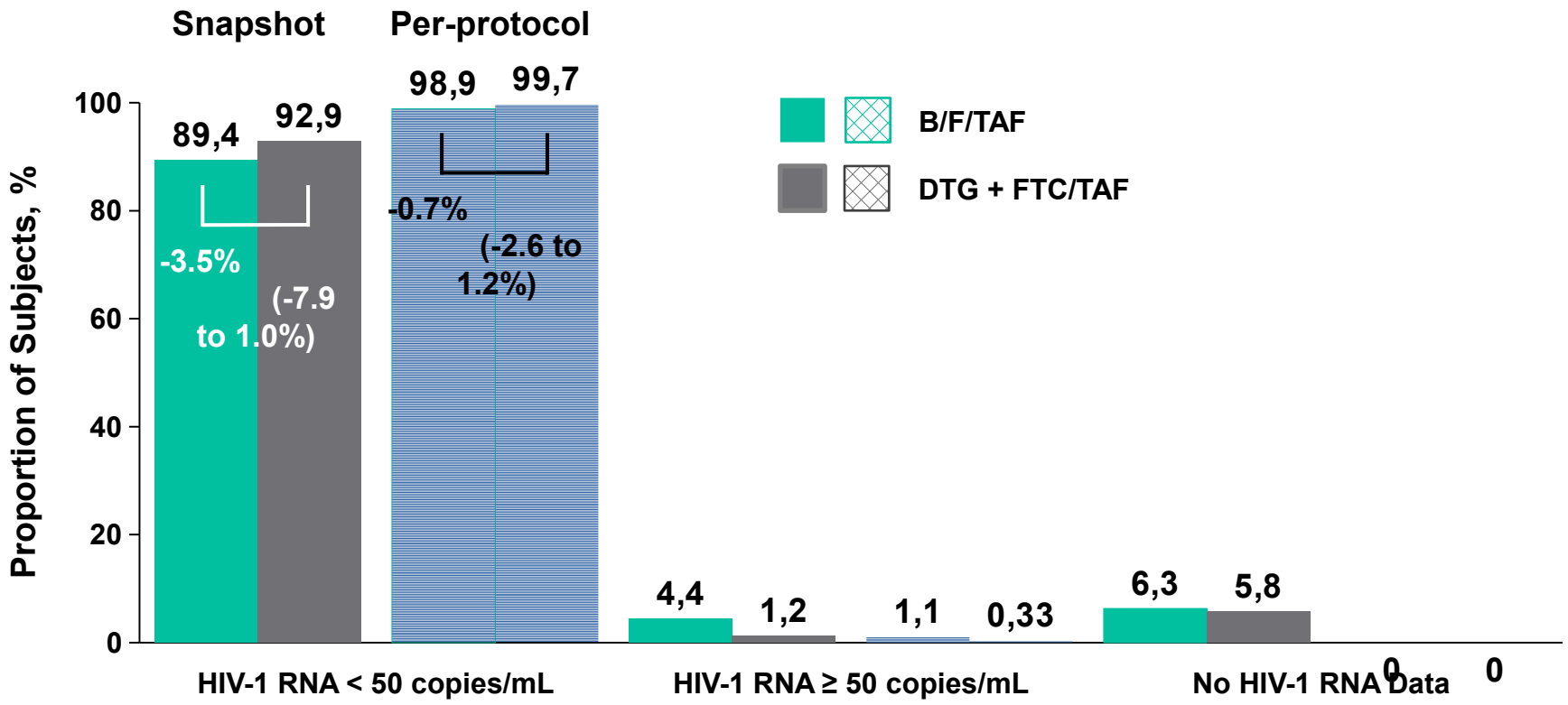


- Phase 3, randomized, double-blind, active-controlled study (ClinicalTrials.gov NCT02607956)
  - Stratified by HIV-1 RNA, CD4 cell count, and geographic region
  - North America, Europe, Australia, and Latin America
  - Chronic hepatitis B and/or C virus infection allowed
- Treatment-naïve, HIV-1-infected adults were randomized 1:1 to receive B/F/TAF 50/200/25 mg or DTG 50 mg + FTC/TAF 200/25 mg with matching placebo once daily
- **Primary endpoint:** HIV-1 RNA < 50 copies/mL at Week 48 by FDA Snapshot algorithm (12% NI margin)

CrCl, creatinine clearance. NI, non-inferiority.

Sax P, et al. IAS 2017. Paris, France. Poster Discussion #TUPDB0201LB.

Virologic Outcome at Week 48 by FDA Snapshot Analysis



Mean changes in CD4 cell count (cells/μL) at Week 48: +180 BIC vs +201 DTG (p=0.10)

BIC vs DTG with FTC/TAF: Non-inferior efficacy at Week 48

Confirmed by pre-specified sensitivity analyses (PP, M=E, and M=F)

M=E, missing=excluded. M=F, missing=failure. PP, per-protocol.

Sax P, et al. IAS 2017. Paris, FR. Poster TUPDB0201LB.

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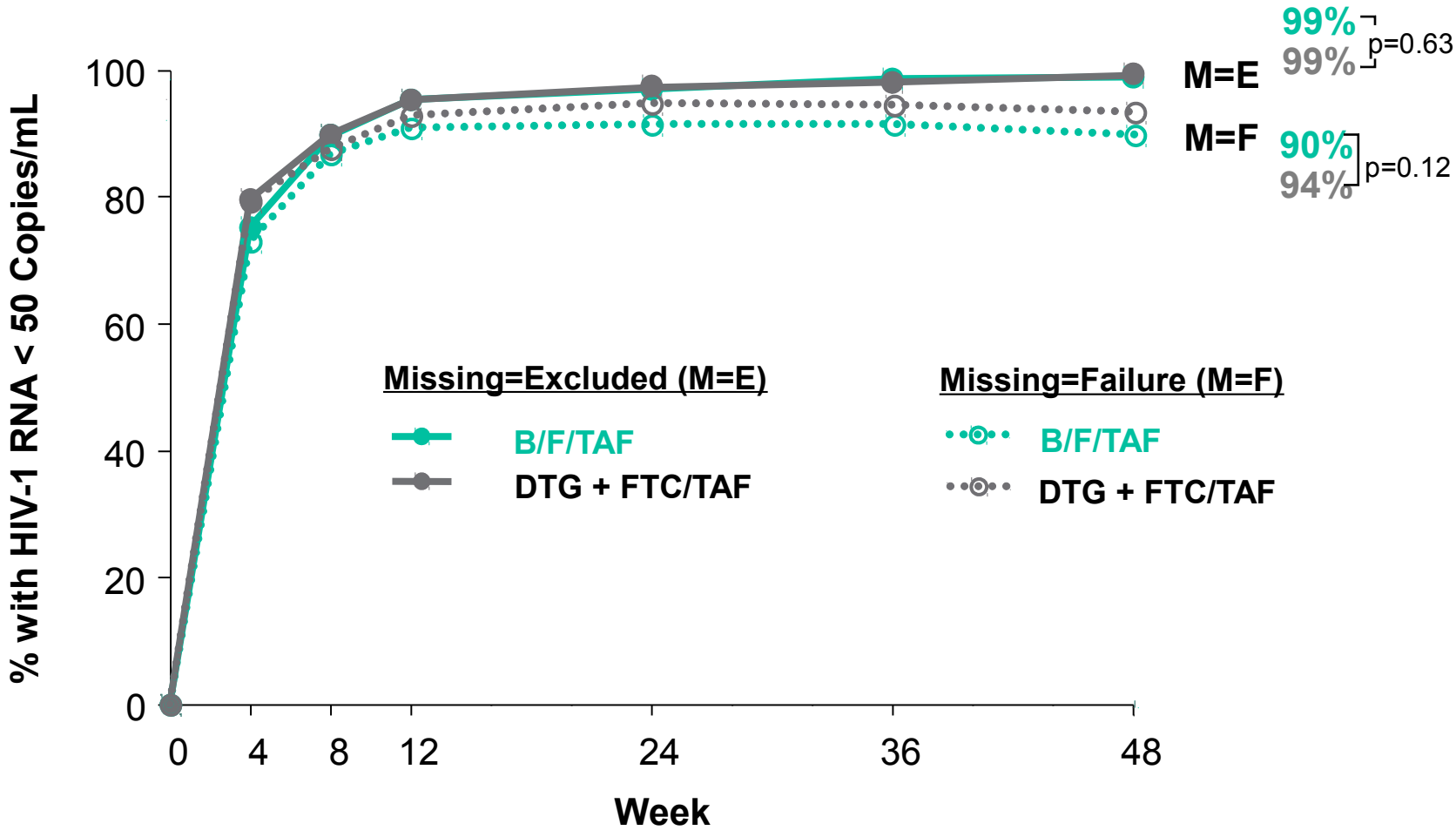

BIC vs. DTG: non-inferior efficacy at Week 48

Sax P, et al. IAS 2017. Paris, FR. Poster TUPDB0201LB.

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- Rilpivirine

PIs

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- Indinavir
- Lopinavir
- Nelfinavir
- Ritonavir
- Saquinavir
- Tipranavir

INSTIs

- Raltegravir
- Dolutegravir
- Elvitegravir

Fusion Inhibitors

- Enfuvirtide

Entry Inhibitors

- Maraviroc
- Fostemsavir
- Ibalizumab
- Pro140
- UB-421

PK Enhancers

- Ritonavir
- Cobicistat

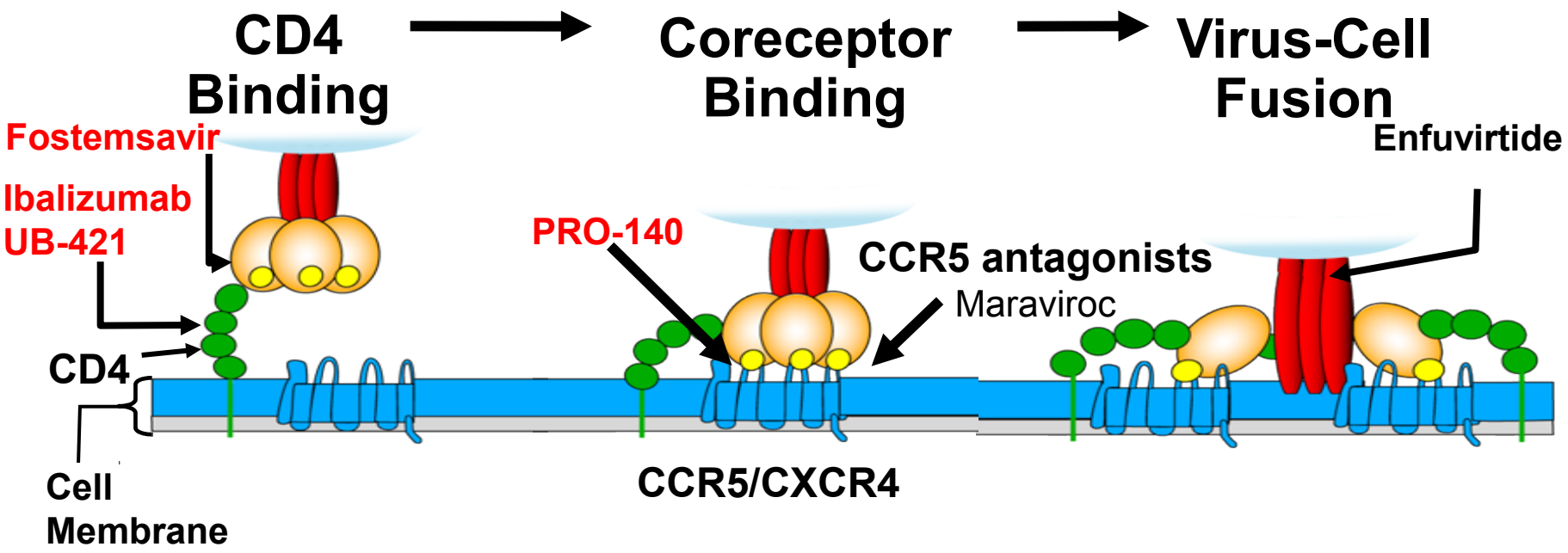
STRs

- Atripla
- Eviplera
- Odefsey
- Stribild
- Genvoya
- Triumeq
- Symtuza

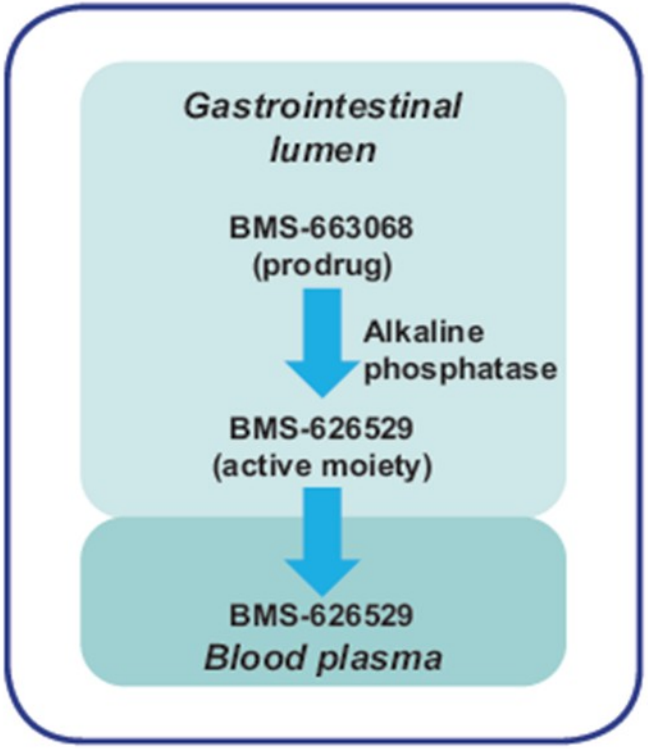
NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PK, pharmacokinetic; STR, single tablet regimens

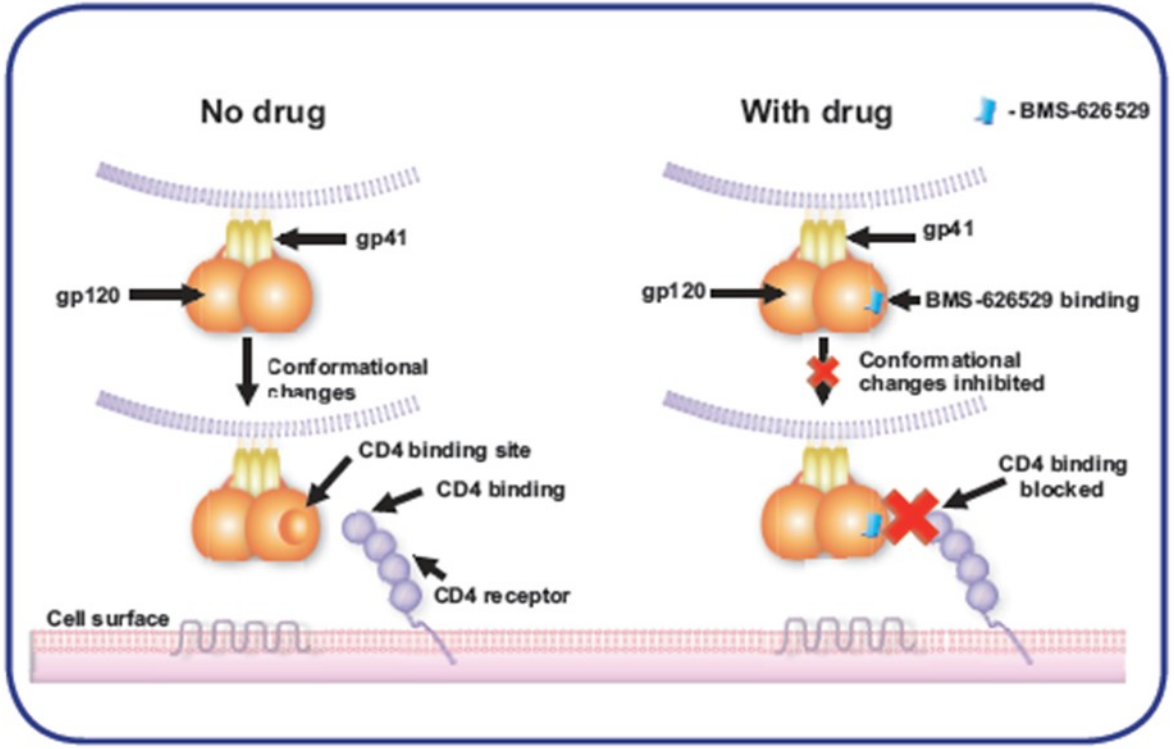
Adapted from http://www.aidsmeds.com/list.shtml and each product's eMC SPC available at http://www.medicines.org.uk/emc/search

Entry Inhibitors



Fostemsavir: Inhibidor del acoplamiento



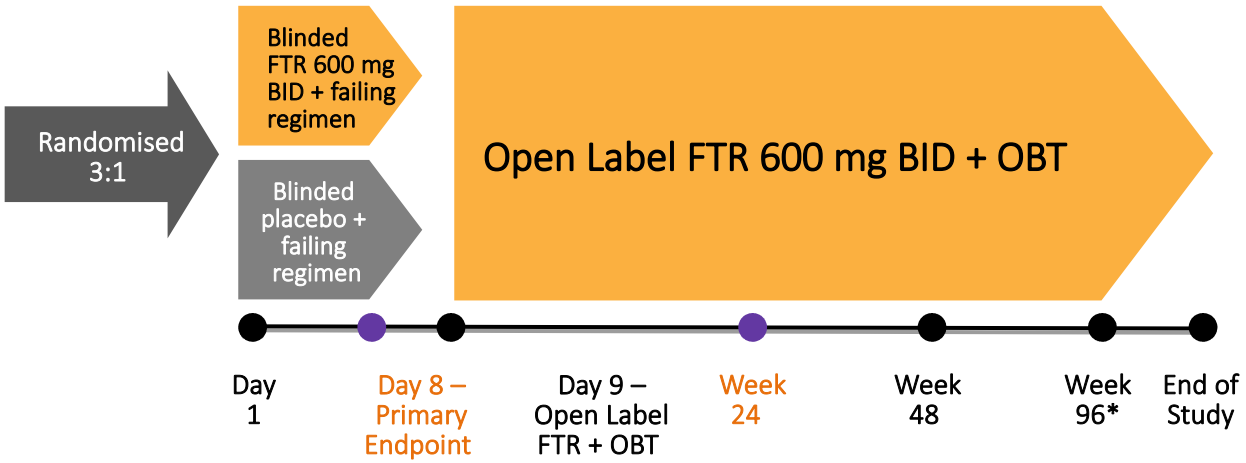


BRIGHTE study: FOSTEMSAVIR in HIGHLY TREATMENT EXPERIENCED PATIENTS

Randomised Cohort :

HTE participants failing current regimen with confirmed HIV-1 RNA ≥ 400 c/mL and:

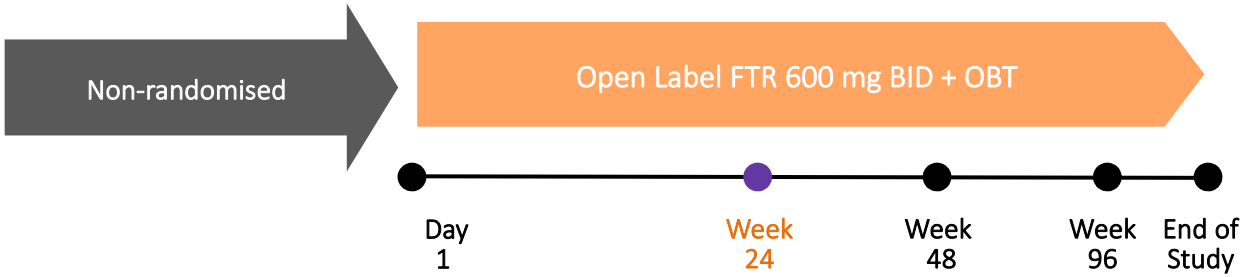
- 1 or 2 ARV classes remaining & ≥1 fully active & available agent per class
- Unable to construct viable regimen from remaining agents



Non-randomised Cohort :

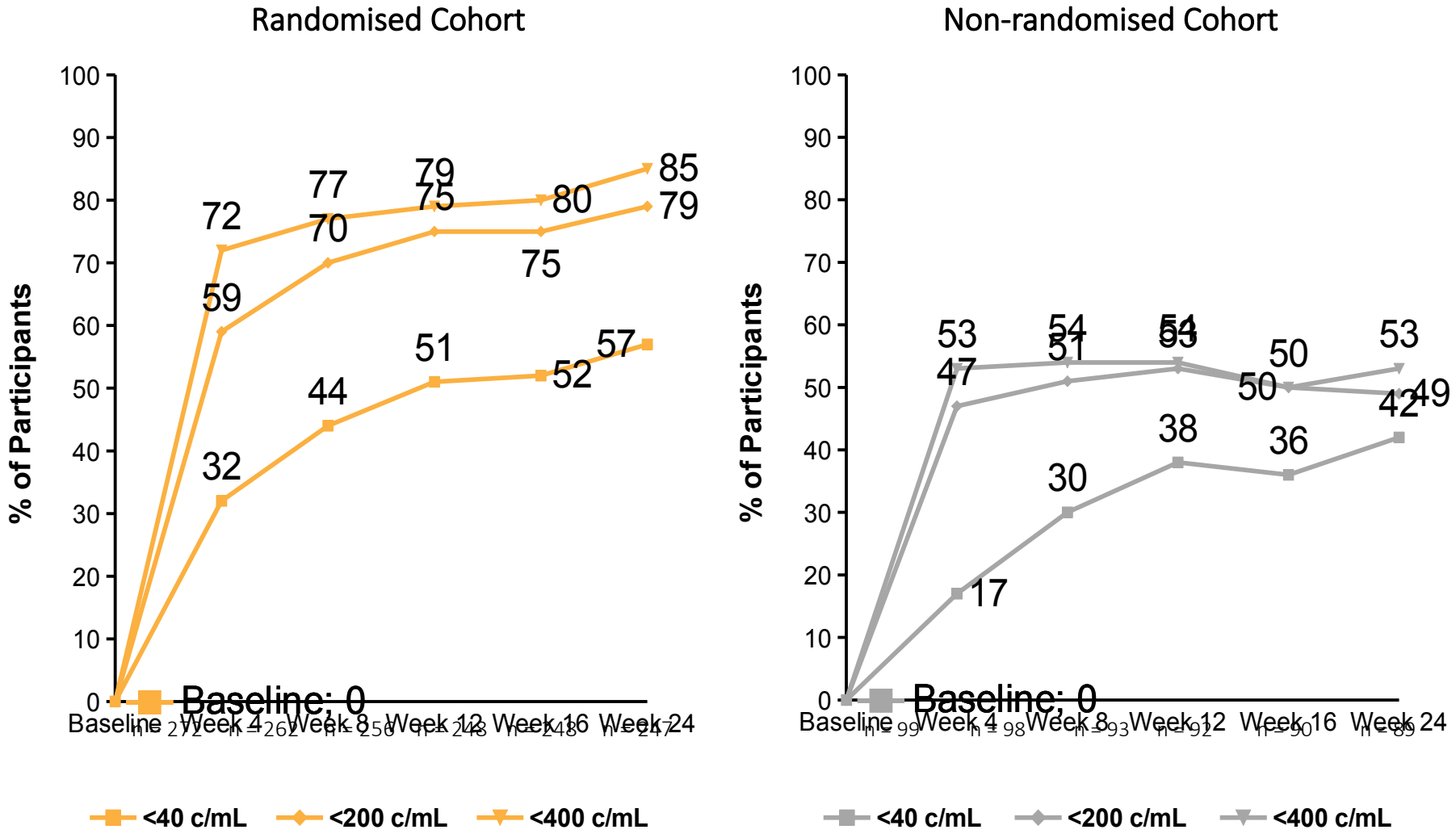
HTE participants, failing current regimen with confirmed HIV-1 RNA ≥400 c/mL and:

- 0 ARV classes remaining and no remaining fully active approved agents



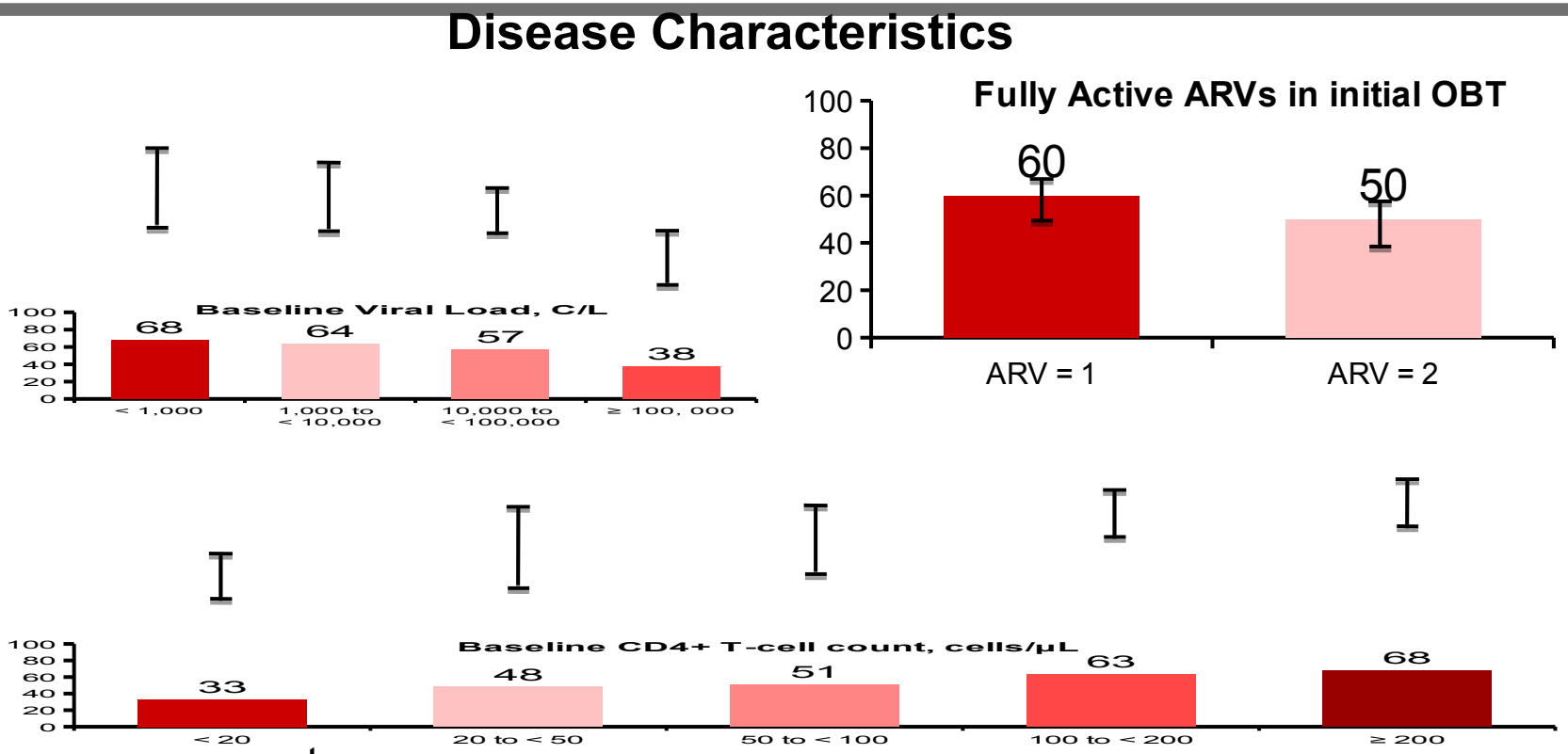
Pialoux G, et al. AIDS 2018; Amsterdam, the Netherlands; July 23-27, 2018; Abst. THPEB045.

BRIGHTE study: Results



Lataillade M, et al; 16th EACS, Milan, Italy, October 25-27, 2017; Abst. PS8/5.

BRIGHTE study:
Results by Baseline Characteristics



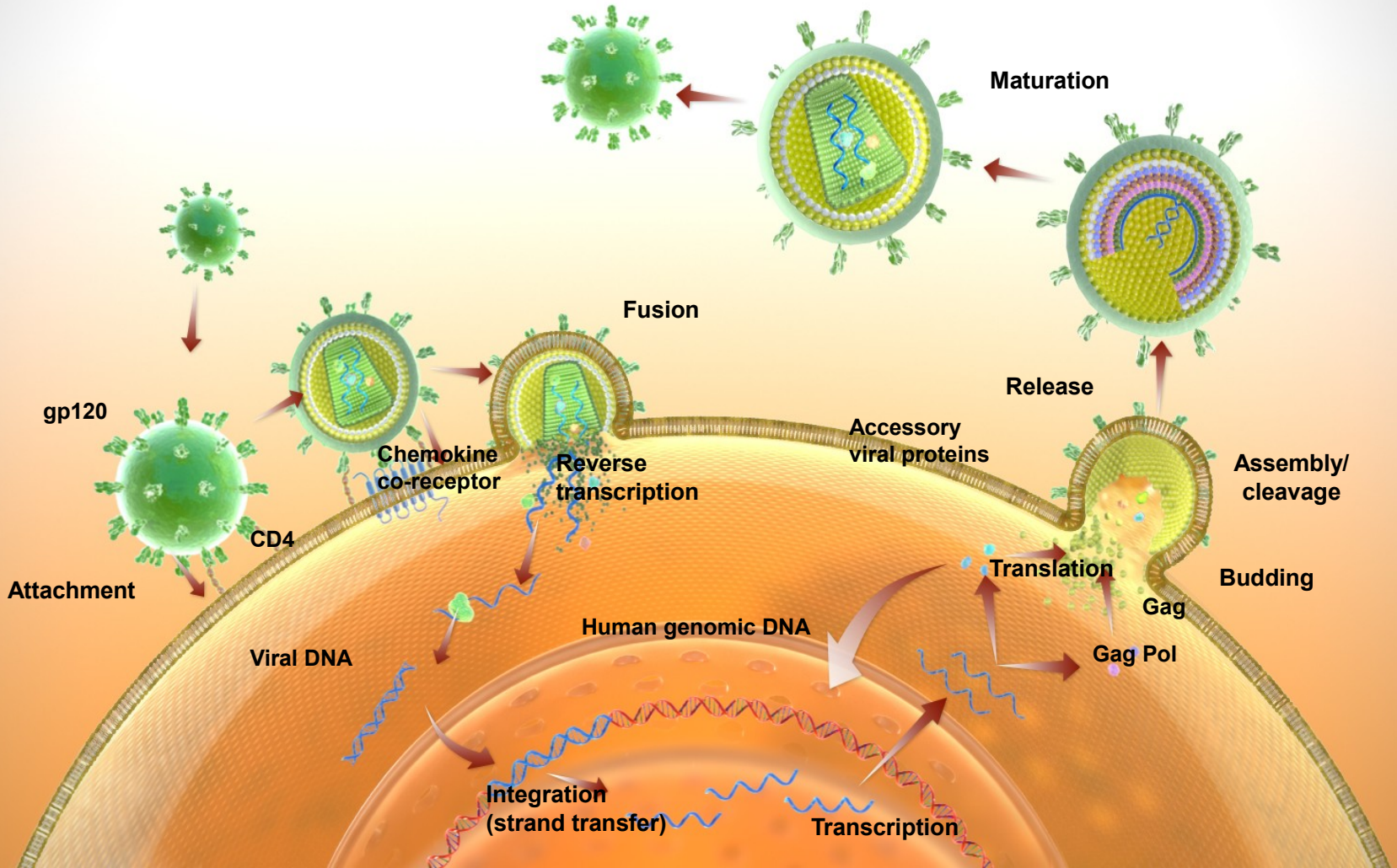
- Higher response rates:
  - Participants with a baseline VL <100,000 c/mL (60%) vs baseline VL≥100,000 c/mL (38%)
  - Participants with a baseline CD4+ T-cell counts of ≥50 cells/µL (63%) vs baseline CD4+ T-cell counts of <50 cells/µL (37%)
- No difference in response by age, gender, race, and region subgroups

a Analysis performed using FDA snapshot algorithm

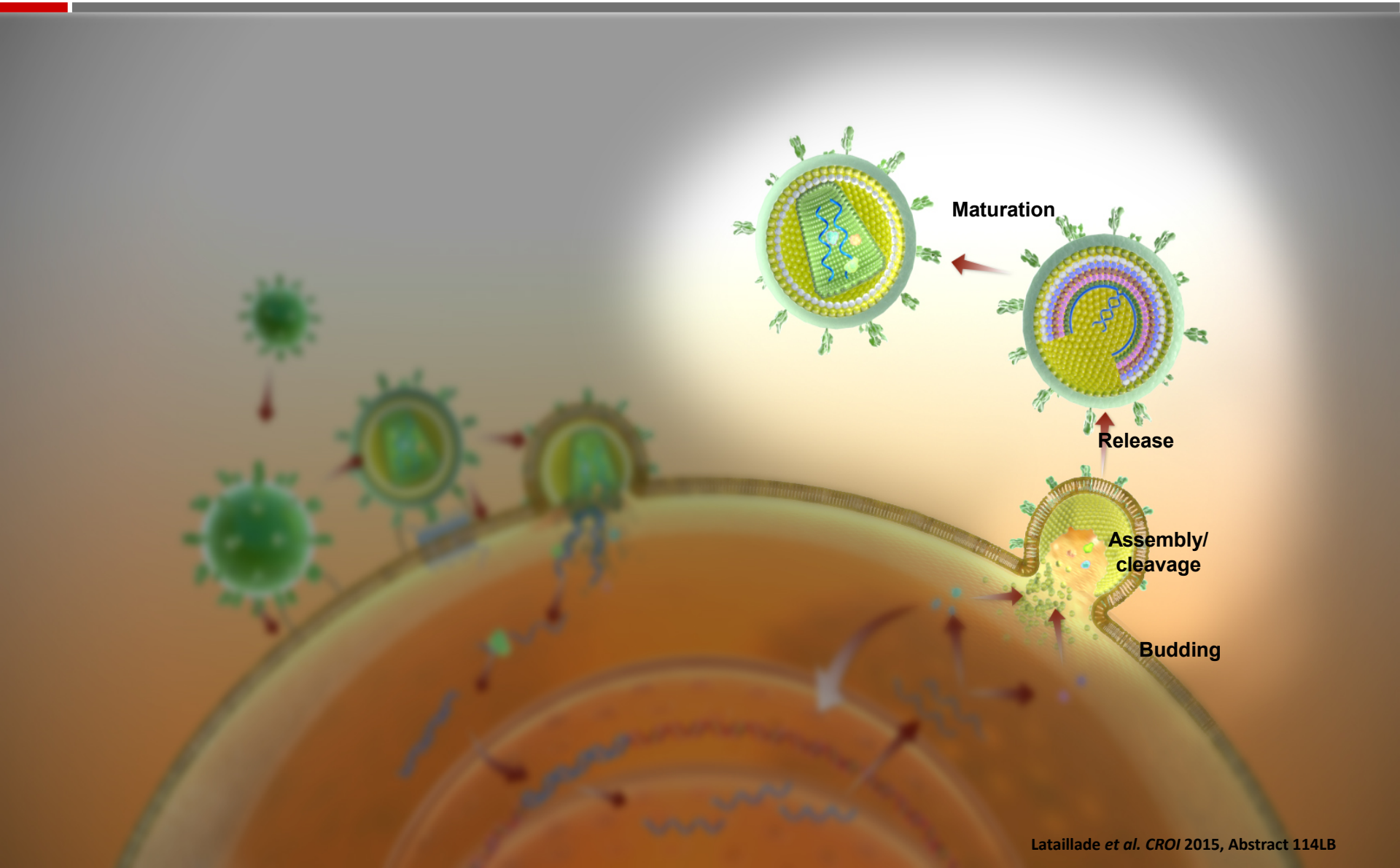
Pialoux G, et al. AIDS 2018; Amsterdam, the Netherlands; July 23-27, 2018; Abst. THPEB045.

3 Futuro: Nuevas Familias

Maturation Inhibitors (MIs): BMS-955176 HIV-1 Lifecycle

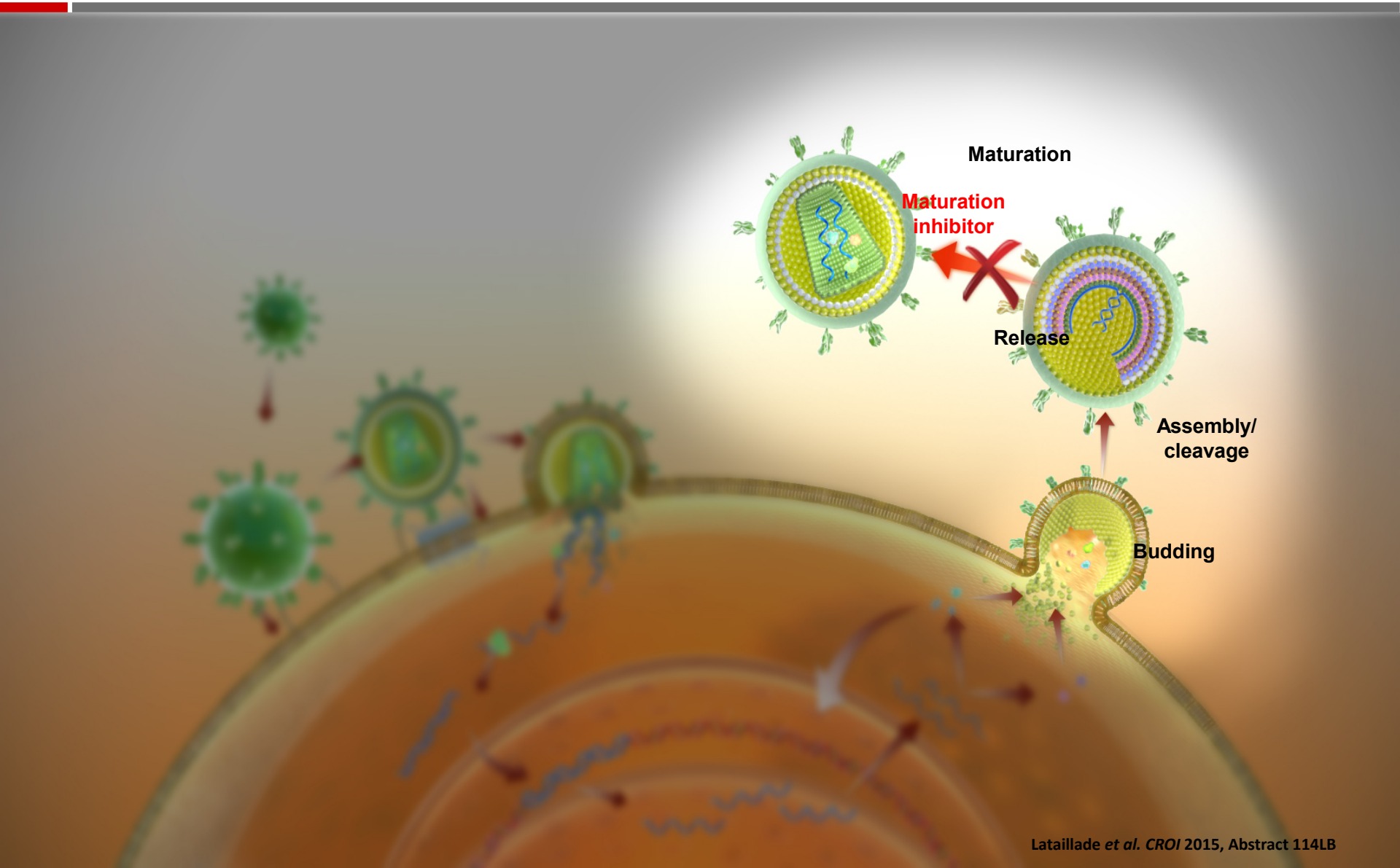


Maturation Inhibitors (MIs): BMS-955176 HIV-1 Lifecycle



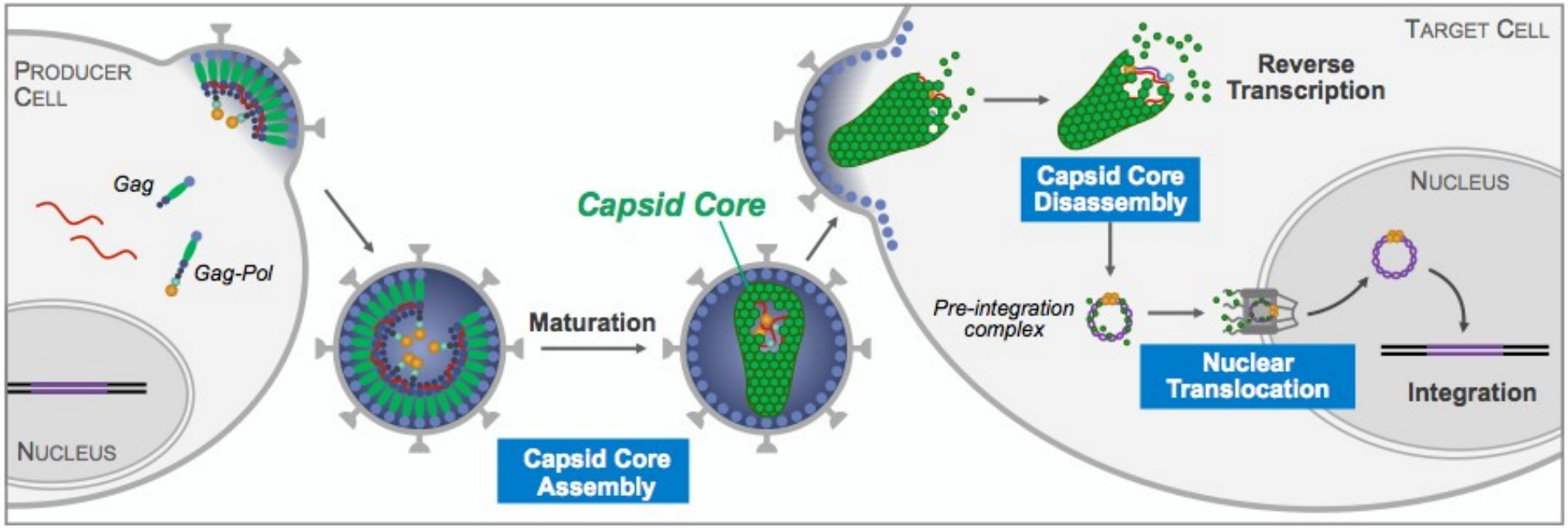
Lataillade *et al. CROI* 2015, Abstract 114LB

Maturation Inhibitors (MIs): BMS-955176 HIV-1 Lifecycle



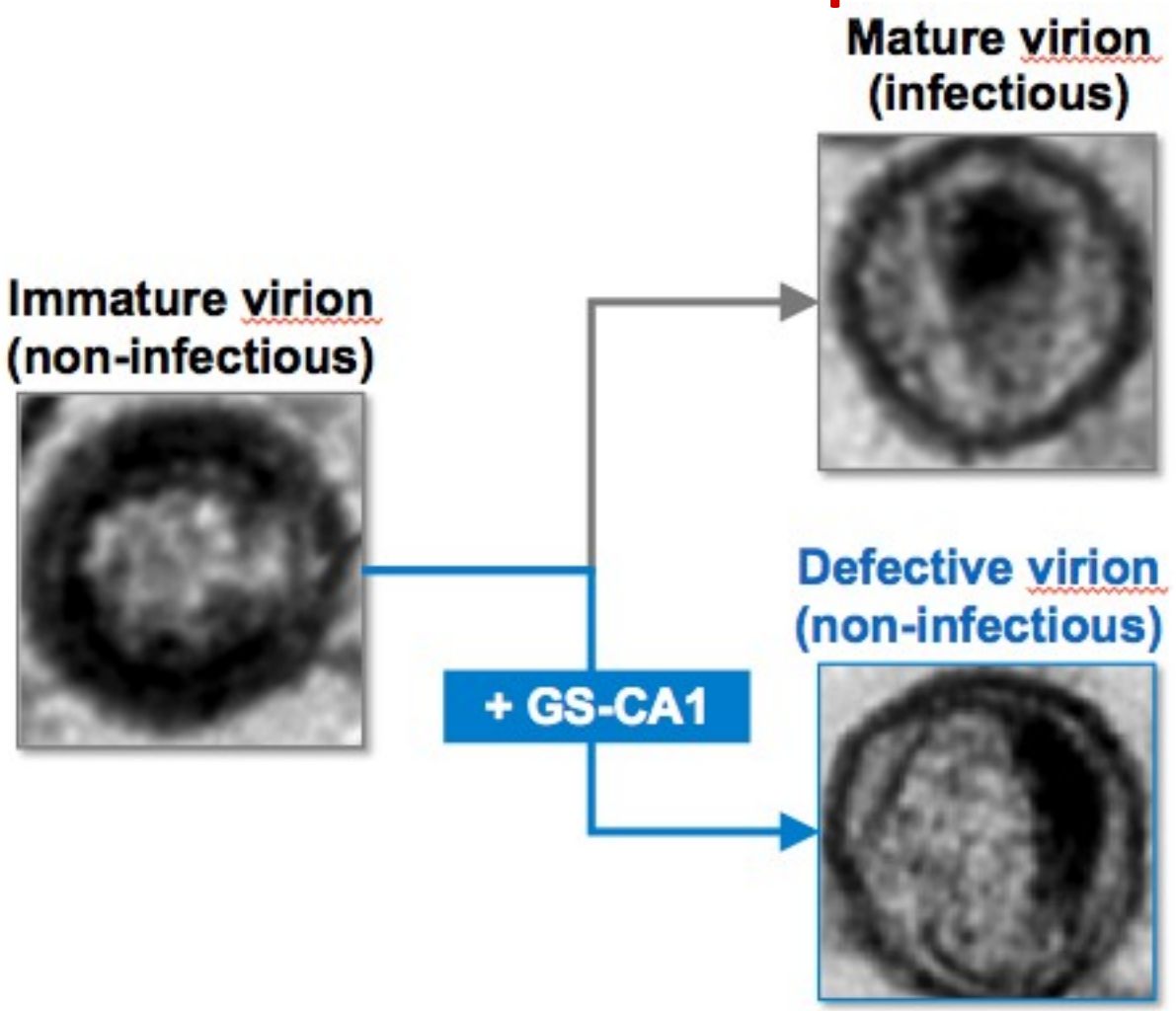
Lataillade *et al. CROI* 2015, Abstract 114LB

GS-CA1: el primer inhibidor de la cápside



Tse WC et al. CROI 2017; Seattle, WA. Abstract 38

GS-CA1: un nuevo inhibidor de la cápside



Tse WC et al. CROI 2017; Seattle, WA. Abstract 38

GS-CA1: principales características

- Actúa a nivel picomolar
  - EC50 de DTG: 1.200 pM
  - EC50 de GS-CA1: 140 pM
- Unión a región muy conservada
  - Mutantes con escasa capacidad replicativa
- Posibilidad de formulación “long-acting”
  - 1 inyección sc mensual

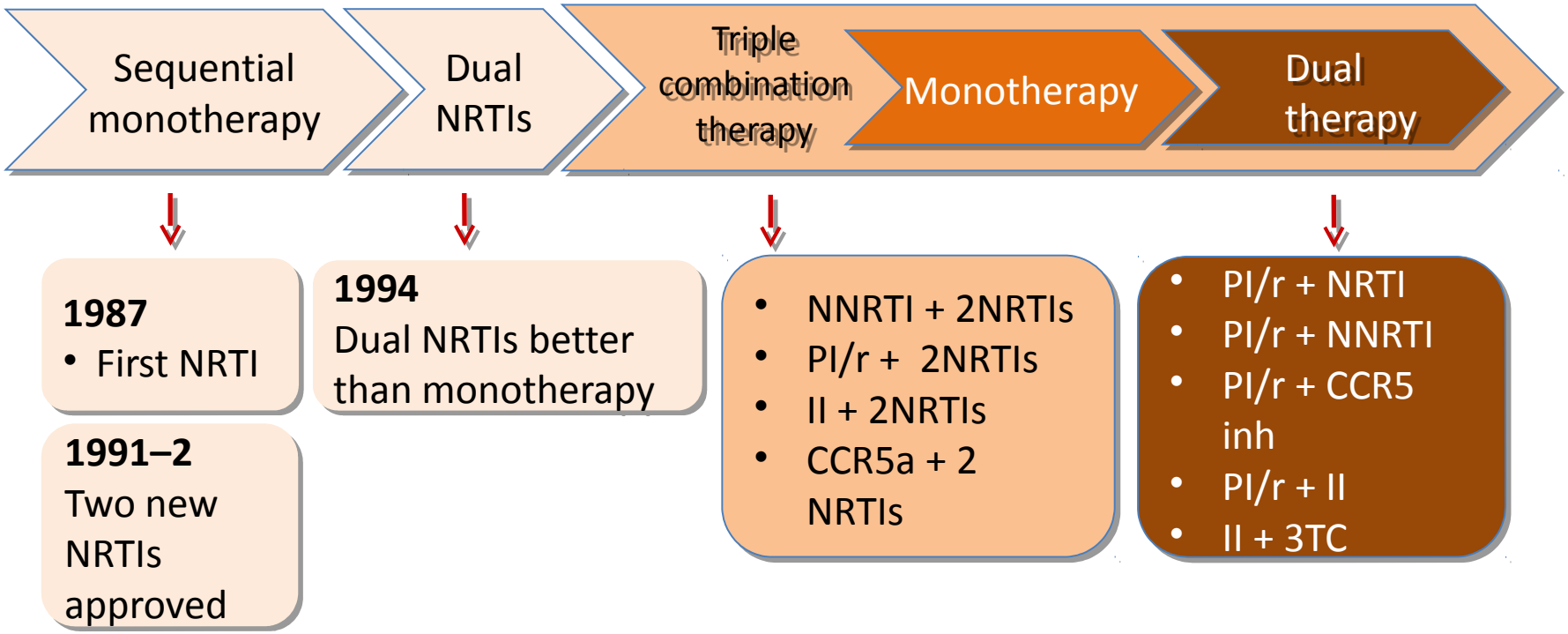
Tse WC et al. CROI 2017; Seattle, WA. Abstract 38

Nuevos Fármacos: Usos Potenciales

- **Doravirina:**
  - Perfil de resistencias distinto, mejor tolerabilidad
  - Tratamiento de inicio, ¿simplificación?, ¿rescate?
- **Bictegravir:**
  - Tratamiento de inicio, simplificación, rescate
  - Nuevo STR
- **Inh. de la entrada:**
  - Tratamiento de rescate.
  - Posibilidad administración prolongada
- **Inh. Maduración:**
  - Interrumpido desarrollo?
- **Inh. Cápside**:
  - Administración prolongada

4 Futuro: Nuevas Estrategias Biterapias

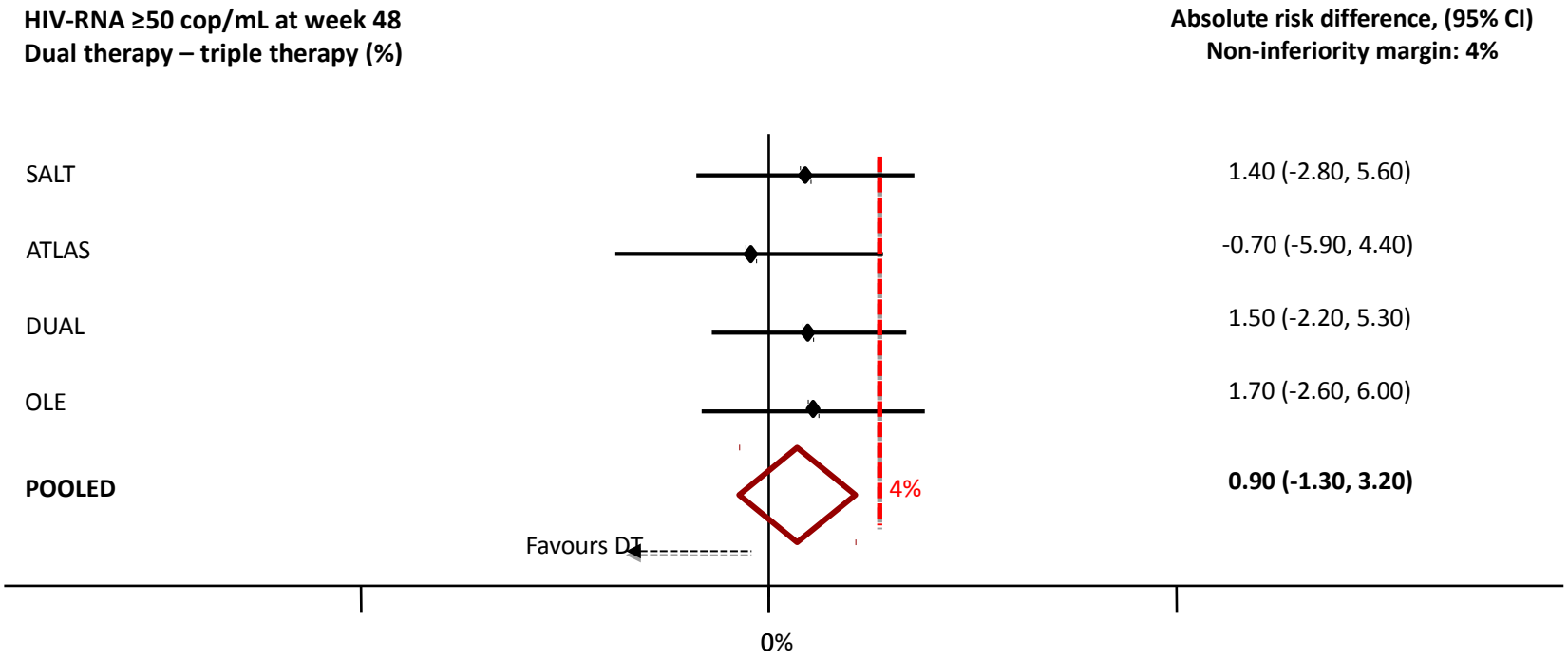
Número de Fármacos: Evolución del TAR



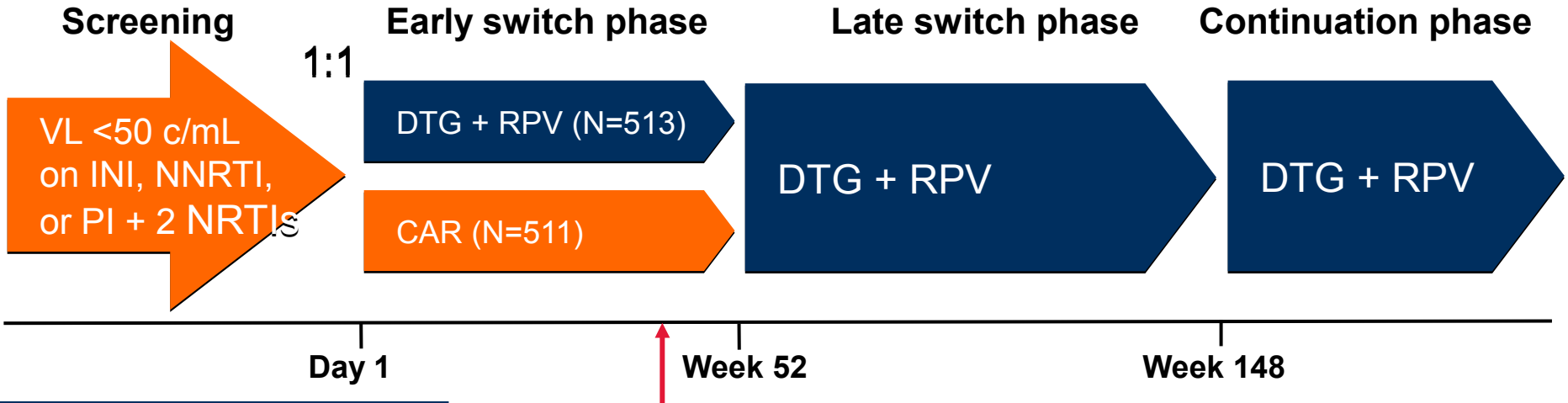
Combinations of bPI + 3TC: Switch in suppressed patients

At 48w, 4% of patients on DT vs. 3.04% on TT had HIV-RNA ≥50 cop/mL

Difference 0.9% (95%CI, -1.3% to 3.2%)



SWORD-1 and SWORD-2 Phase III Study Design



Inclusion criteria

- On stable CAR ≥6 months before screening
- 1st or 2nd ART with no change in prior regimen due to VF
- Confirmed HIV-1 RNA <50 c/mL during the 12 months before screening
- HBV negative

Primary endpoint at 48 weeks: subjects with VL <50 c/mL (ITT-E snapshot)[a]

Countries

Argentina	Australia	Belgium
	Canada	
France	Germany	Italy
	Netherlands	
Russia	Spain	Taiwan
	United Kingdom	
United States		

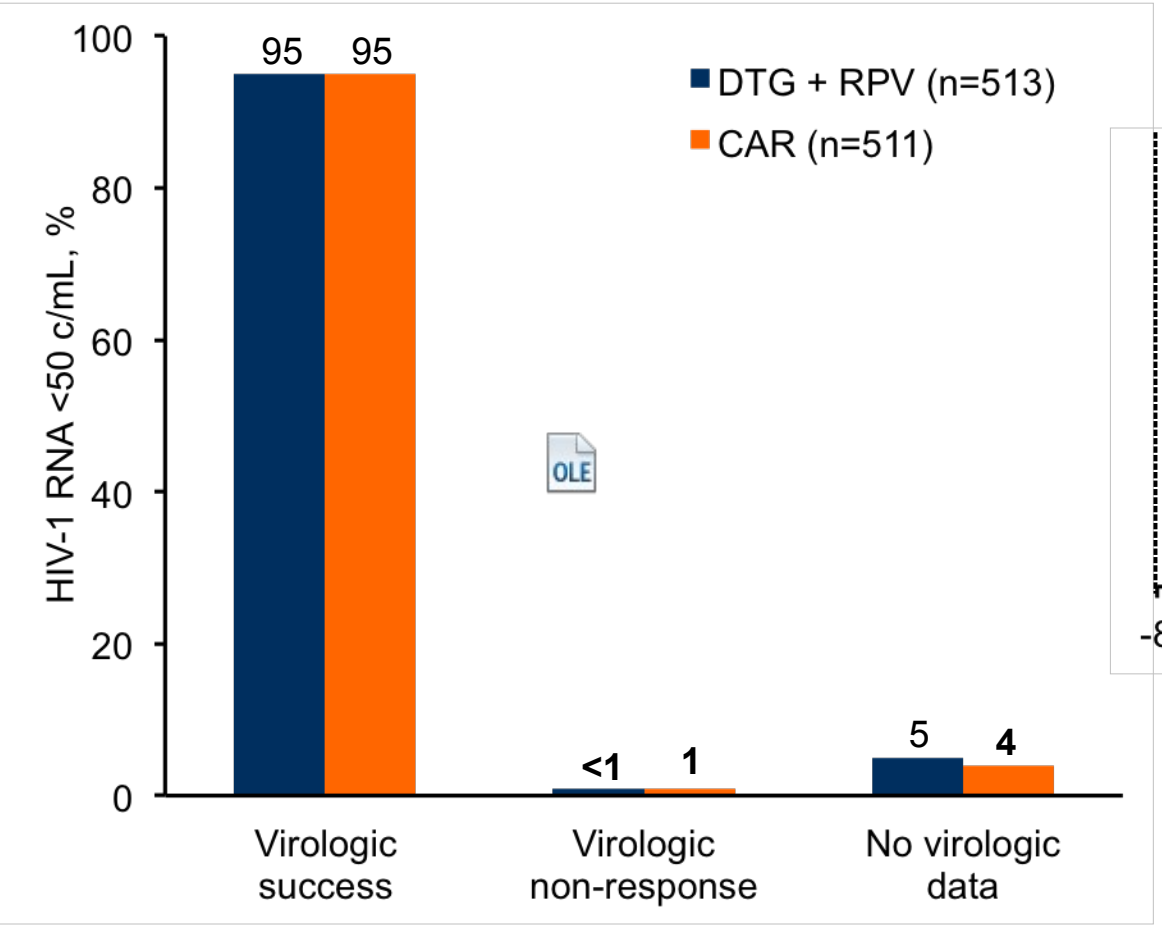
[a]-8% non-inferiority margin for pooled data

-10% non-inferiority margin for individual studies

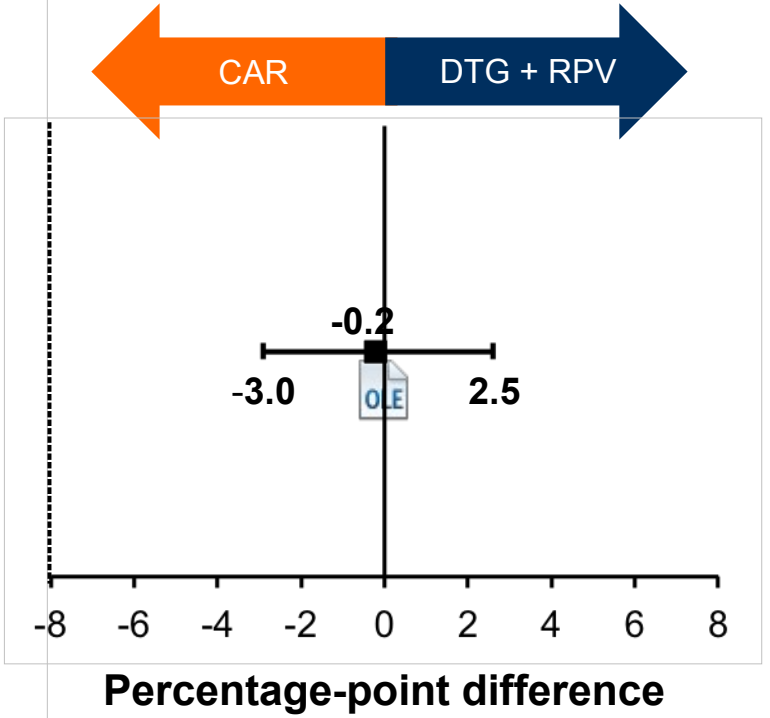
Llibre et al. CROI 2017; Seattle, WA. Abstract 44LB

Snapshot Outcomes at Week 48 (Pooled)

Virologic outcomes



Adjusted treatment difference (95% CI)[a]



DTG + RPV is **non-inferior** to CAR with respect to snapshot in the ITT-E population (<50 c/mL) at Week 48

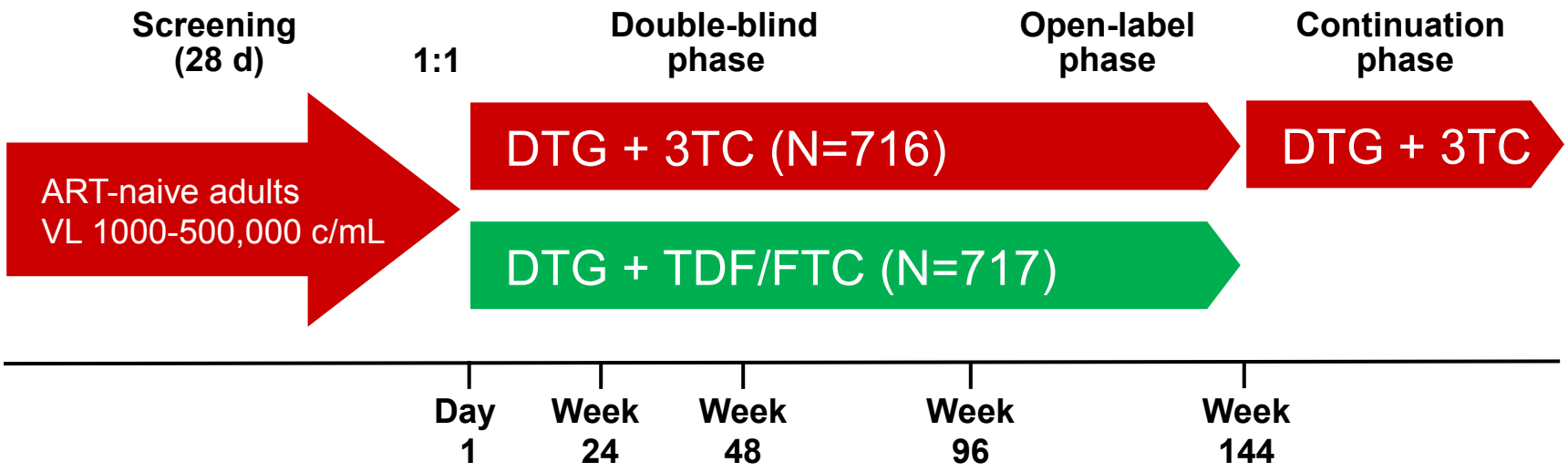
Llibre et al. CROI 2017; Seattle, WA. Abstract 44LB

ACTG A5353: 3TC + Dolutegravir
Primary Objective (snapshot at 24 weeks)

	Baseline viral load		
	> 100,000 cpm N=37	≤ 100,000 cpm N=83	Total N=120
Virological suppression HIV-1 RNA < 50 c/m **[95% CI]**	**33 (89%) [75%,97%]**	**75 (90%) [82%,96%]**	**108 (90%) [83%,95%]**
No suppression	**3 (8%)**	**2 (2%)**	**5 (4%)**
HIV-1 RNA ≥ 50 c/m	3	0	3
Discontinuation with CV > 50 c/m*	0	2	2
No virological data	**1 (3%)**	**6 (7%)**	**7 (6%)**
Discontinuation for other reasons#	1	5	6
In study but without data	0	1	1

** Poor adherence; # Lost of follow-up, pregnancy.*

GEMINI 1 and 2: Study design



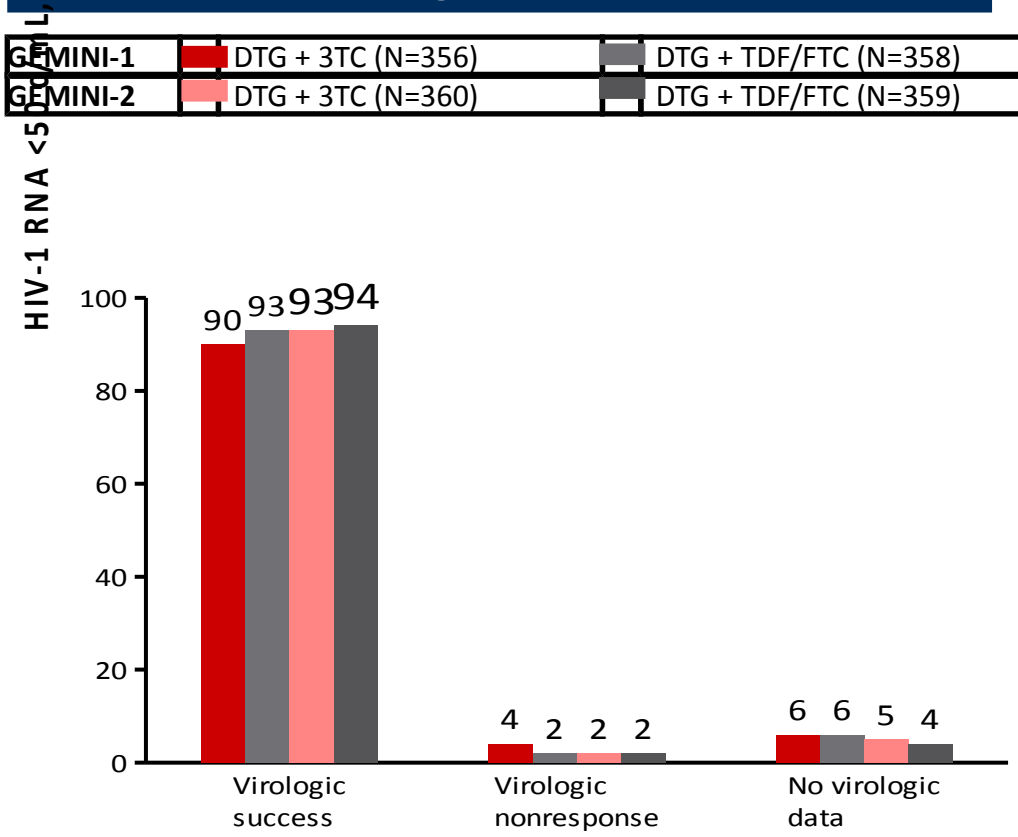
- Eligibility criteria
  - ≤10 days of prior ART
  - No evidence of pre-existing viral resistance based on presence of any major resistance-associated mutation
  - No HBV infection or need for HCV therapy

Cahn P, et al. AIDS 2018; Amsterdam, the Netherlands; July 23-27, 2018; Abst. TUAB0106LB.

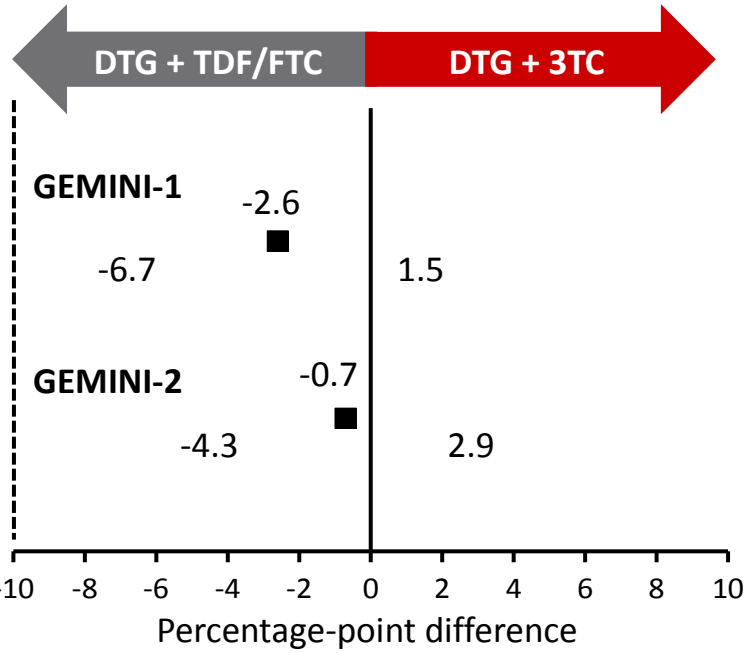
GEMINI 1 and 2: Snapshot Outcomes at Week 48

Virologic outcome

GEMINI-1	DTG + 3TC (N=356)	DTG + TDF/FTC (N=358)
GEMINI-2	DTG + 3TC (N=360)	DTG + TDF/FTC (N=359)

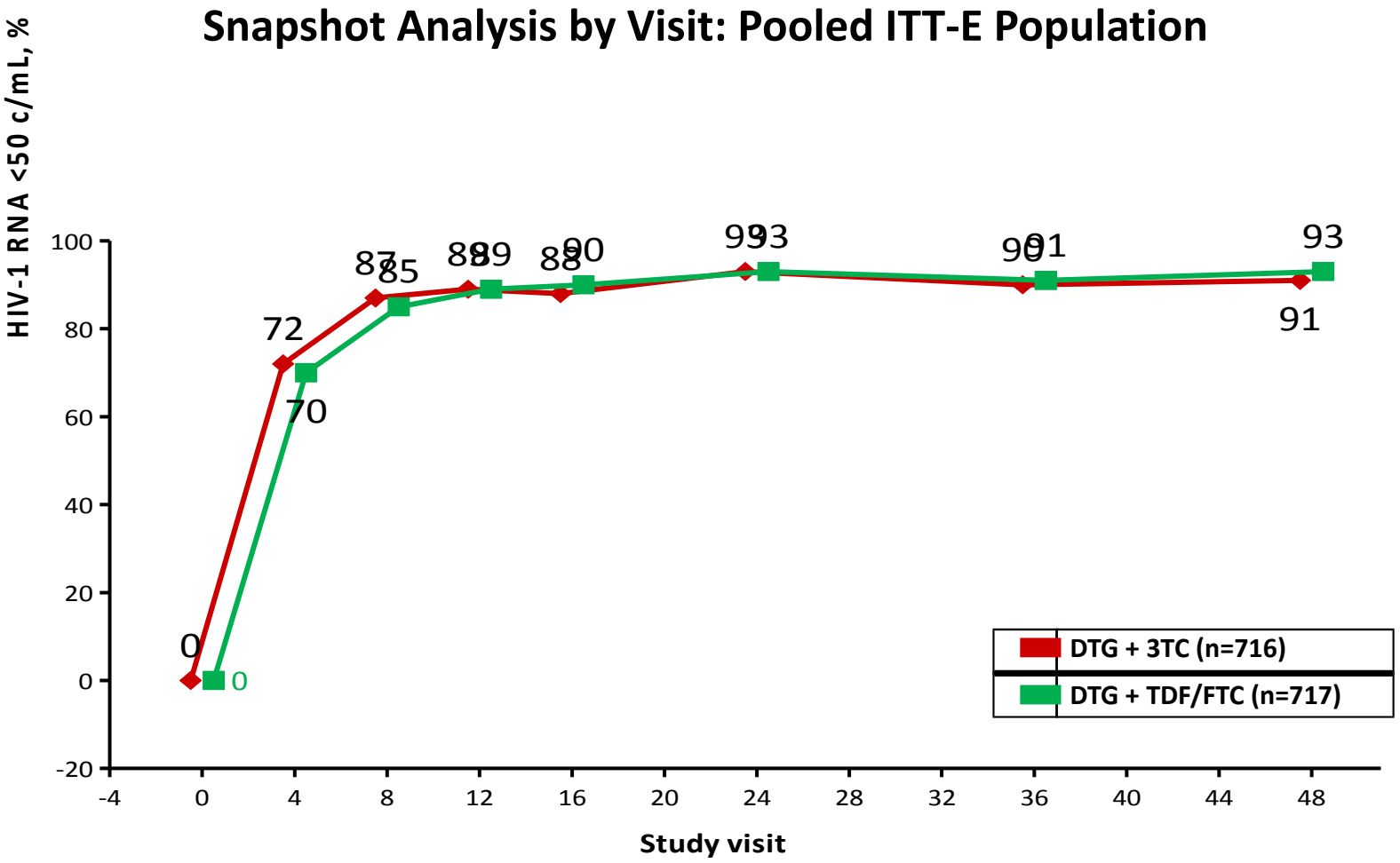


Adjusted treatment difference (95% CI)



Cahn P, et al. AIDS 2018; Amsterdam, the Netherlands; July 23-27, 2018; Abst. TUAB0106LB.

GEMINI 1 and 2: Results



Cahn P, et al. AIDS 2018; Amsterdam, the Netherlands; July 23-27, 2018; Abst. TUAB0106LB.

5

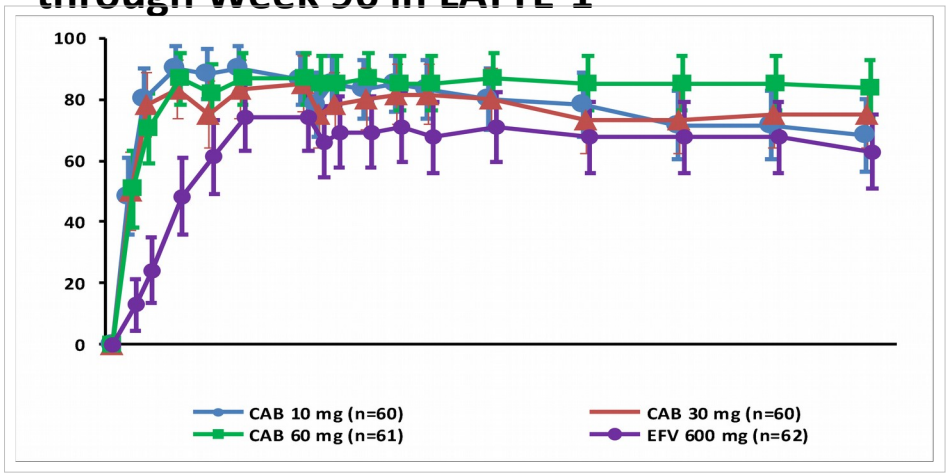
Futuro:
Nuevas Estrategias
Administración Prolongada

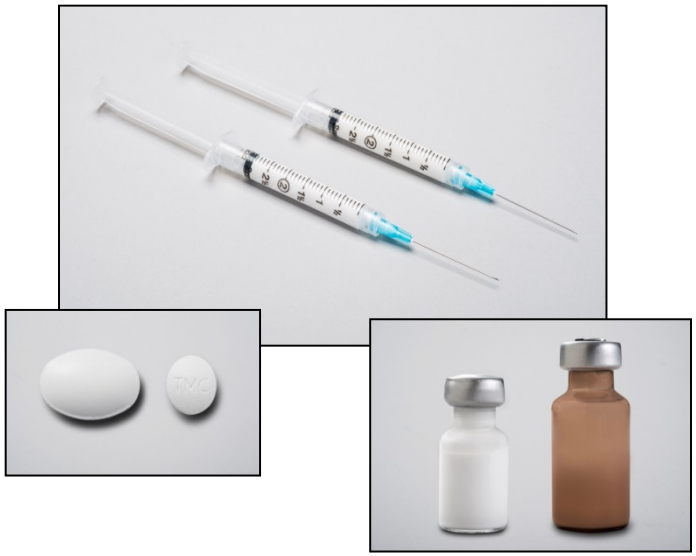
Nuevas Estrategias:
Fármacos de Acción Prolongada

Cabotegravir + Rilpivirine as Long-Acting Maintenance Therapy: LATTE-2 Week 32 Results

Background

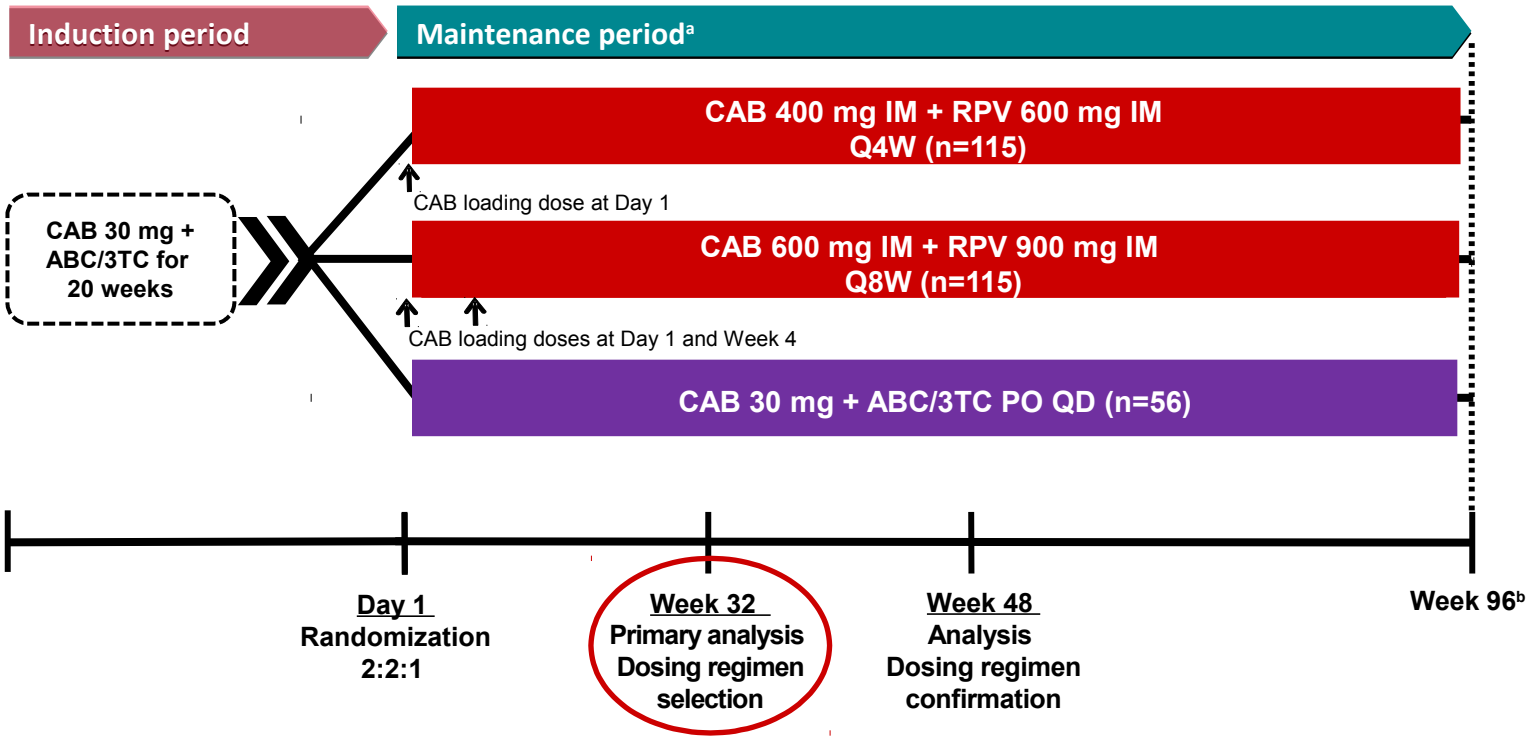
- **CAB** is an HIV-1 integrase inhibitor
  - Oral 30 mg tablet (t½, ~40 hours)
  - **LA nanosuspension 200 mg/mL (t½, ~20-40 days)**
- **RPV** is an HIV-1 NNRTI
  - Oral 25 mg tablet (t½, ~50 hours)
  - **LA nanosuspension 300 mg/mL (t½, ~30-90 days)**
- **Oral 2-drug CAB + RPV proof of efficacy through Week 96 in LATTE-1**





Margolis et al. CROI 2016; Boston, MA. Abstract 31LB.

LATTE-2 Study Design

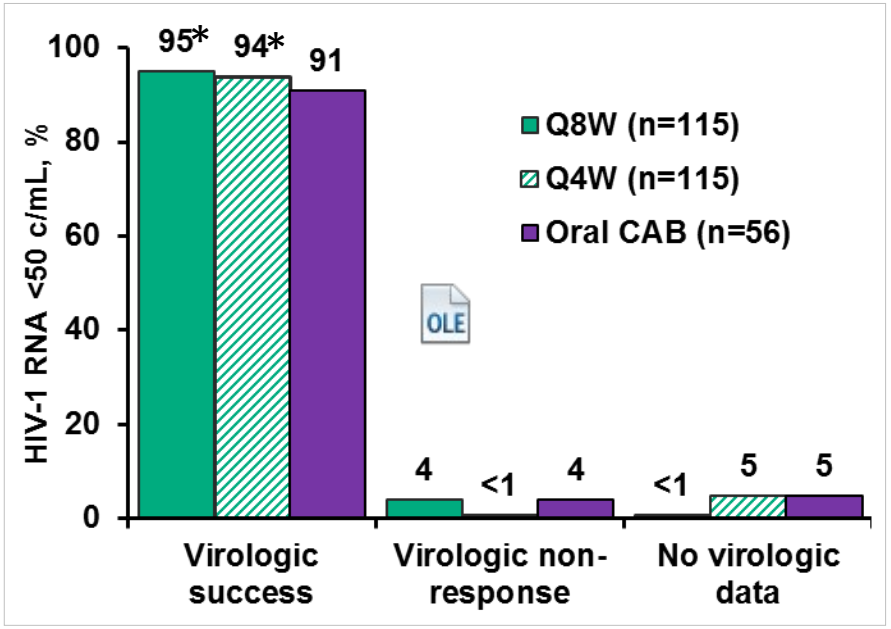


ABC/3TC, abacavir/lamivudine; ALT, alanine aminotransferase; IM, intramuscular; PO, orally; Q4W, every 4 weeks; Q8W, every 8 weeks; QD, once daily; ULN, upper limit of normal. [a]Subjects who withdrew after at least 1 IM dose entered the long-term follow-up period. [b]Subjects can elect to enter LA Extension Phase beyond Week 96.

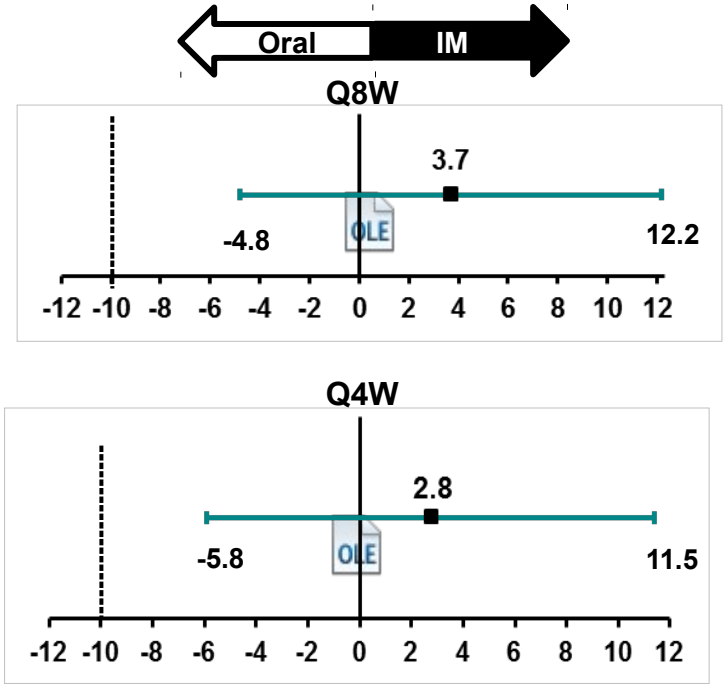
Margolis et al. CROI 2016; Boston, MA. Abstract 31LB.

LATTE-2 Week 32 Primary Endpoint: HIV-1 RNA <50 c/mL by Snapshot (ITT-ME)

Virologic outcomes



Treatment differences (95% CI)



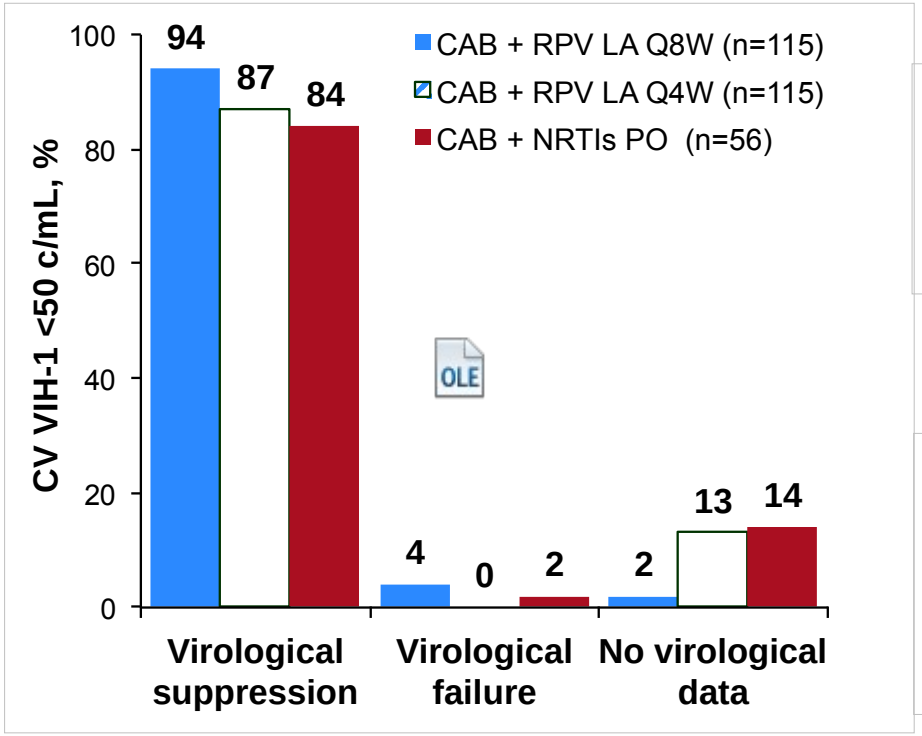
Both Q8W and Q4W comparable to oral CAB at Week 32

*Met pre-specified threshold for concluding IM regimen is comparable to oral regimen (Bayesian posterior probability >90% that true IM response rate is no worse than -10% compared with the oral regimen).

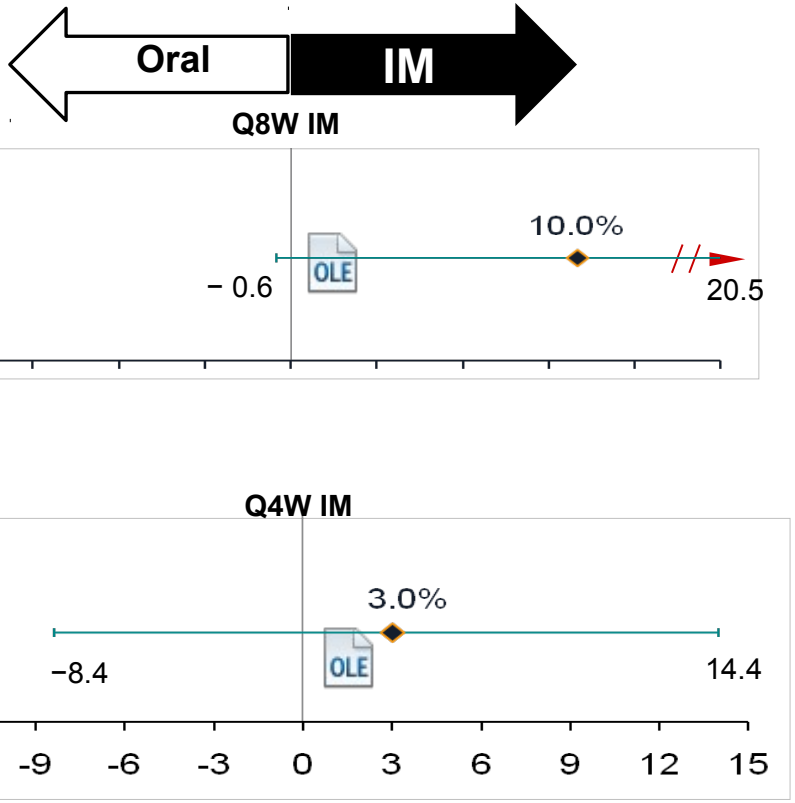
Margolis et al. CROI 2016; Boston, MA. Abstract 31LB.

LATTE-2 : Efficacy at week 96 (ITT-ME Snapshot)

Virological Response



Differences in treatment (IC 95%)

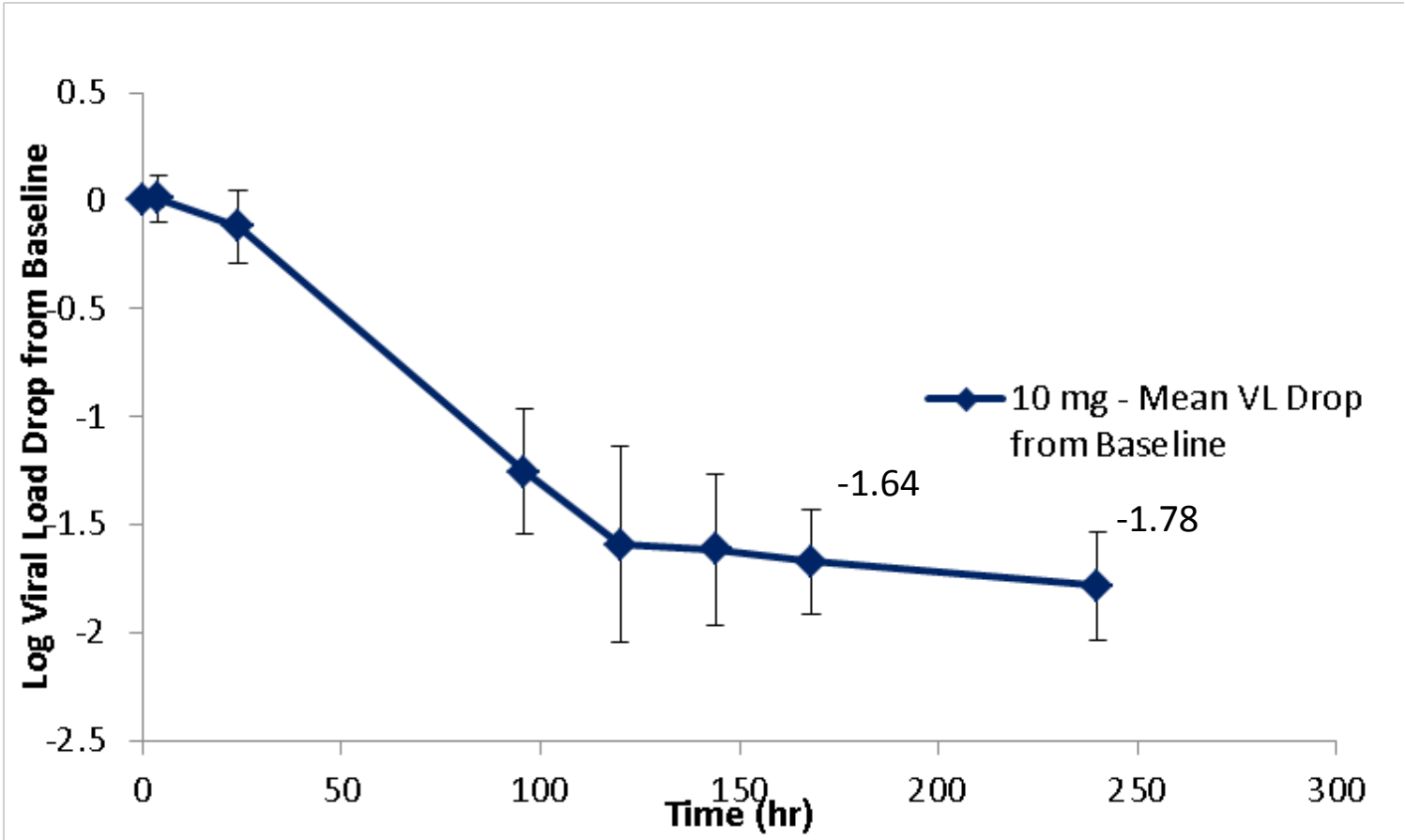


Margolis DA. Lancet. 2017;390:1499-1510.

Nuevas Estrategias:
Fármacos de Acción Prolongada

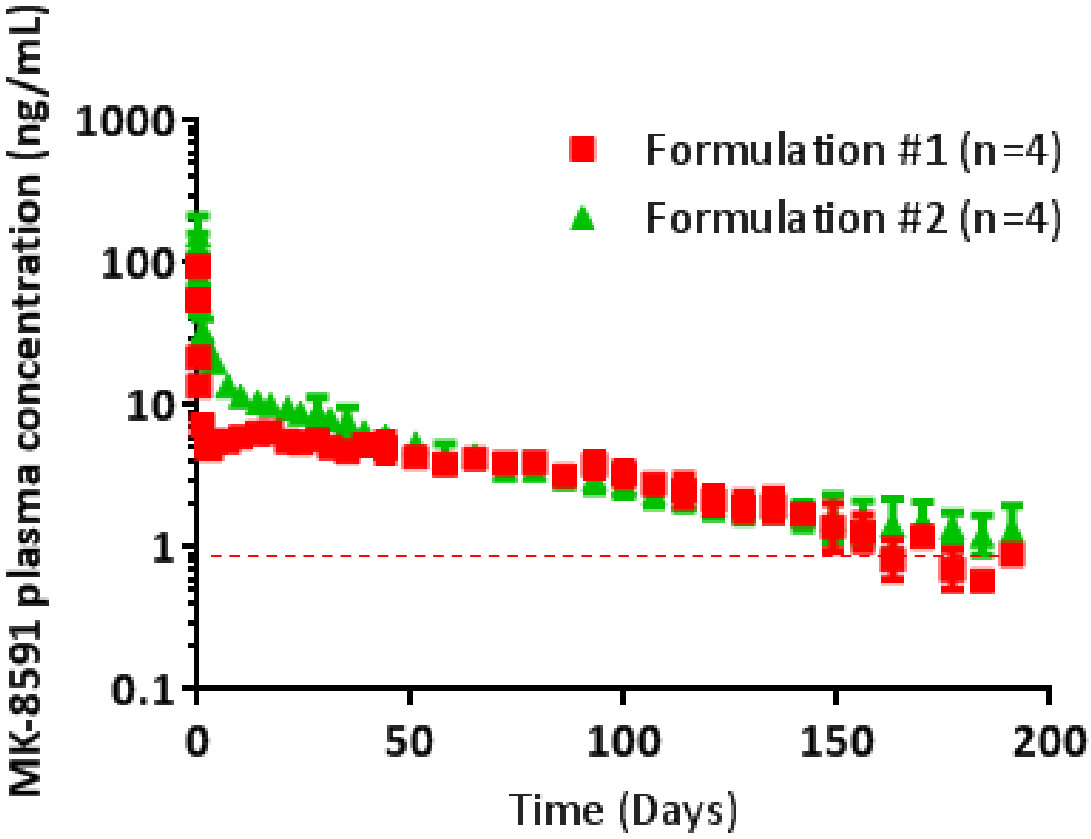
Long-acting Oral and Parenteral Dosing of MK-8591 for HIV Treatment or Prophylaxis

Reducción de C.V. Tras 10 mg (oral)



- Persistent reduction of VL through 10 days with a single 10 mg dose of MK-8591 p.o.
- Low projected daily dose amenable to extended duration parenteral formulation

MK-8591 parenteral formulations release for >180 days



Note:
< 50% drug released after 180 days

>180 day extended release after a single injection in rat

Conclusiones

- **Tratamiento Antirretroviral Actual**
  - Excelencia en todas las características

- **Futuro**
  - Nuevos fármacos de viejas familias y nuevas familias de fármacos para satisfacer las necesidades no cubiertas
  - Fármacos de administración parenteral y de acción prolongada (administración cada 2, 3, 6 o 12 meses)
  - Reducción del número de fármacos