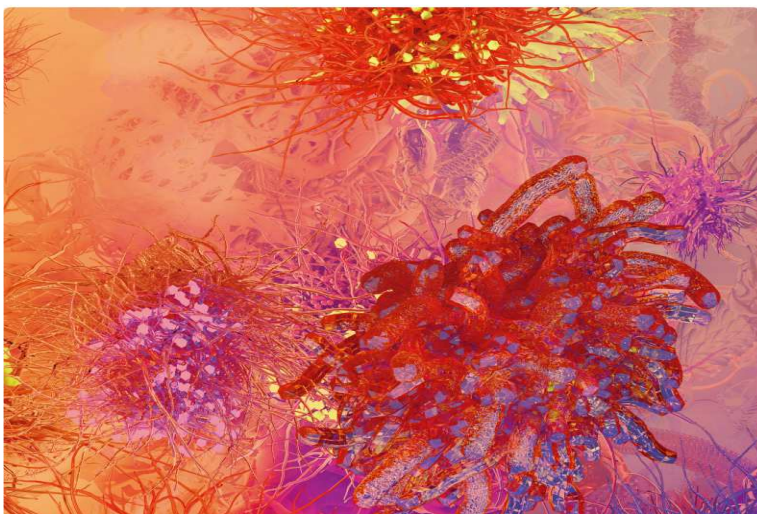


JORNADAS 2018

Actualización y Futuro en VIH

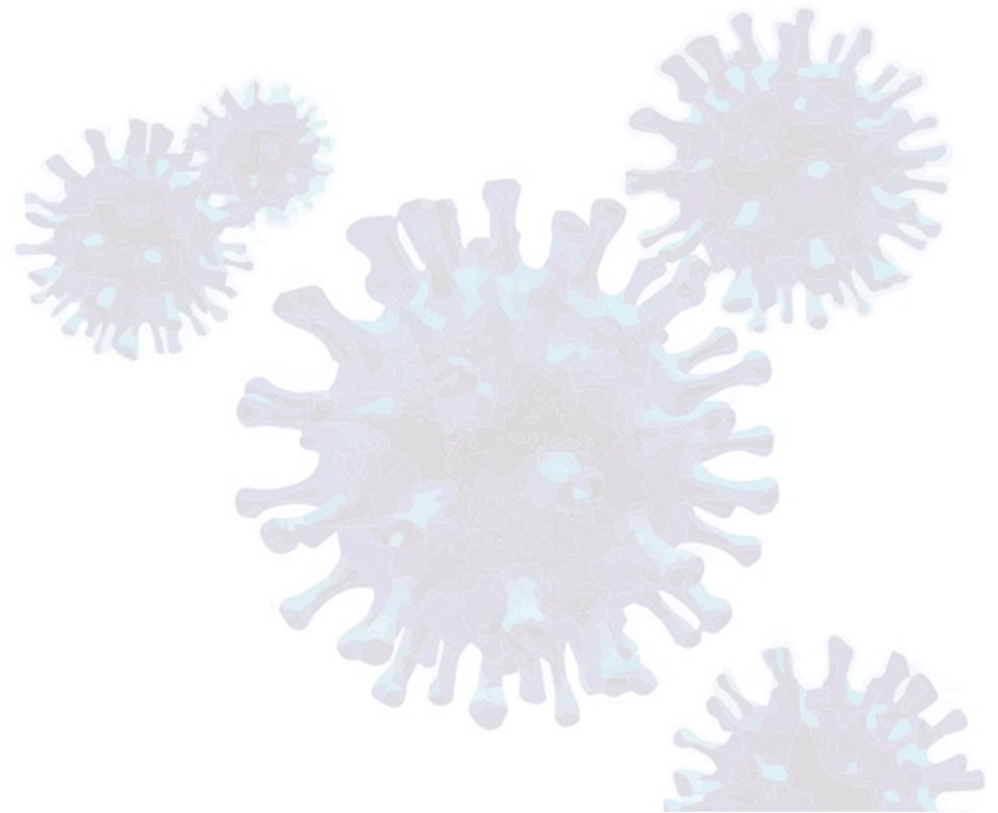


Dr. Santiago Moreno
Servicio de Enfermedades Infecciosas
Hospital U. Ramón y Cajal.
Universidad de Alcalá. IRYCIS.
Madrid



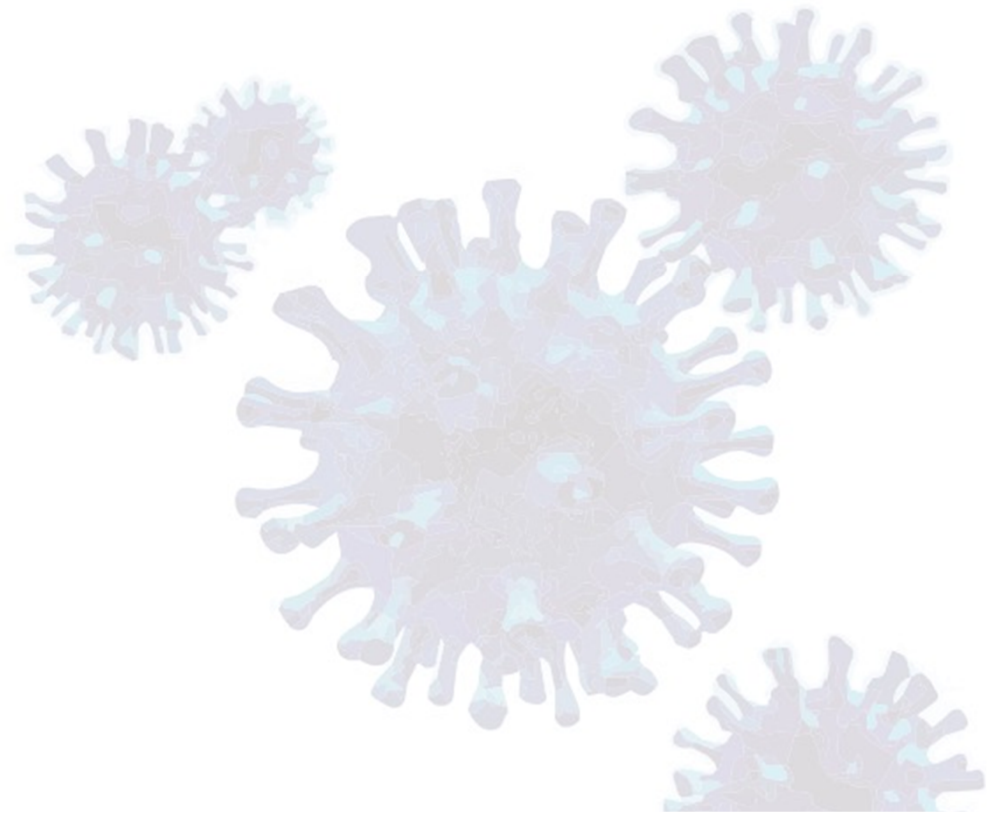
Agenda

- Control of the HIV-epidemic
- Coinfections
- Antiretroviral therapy



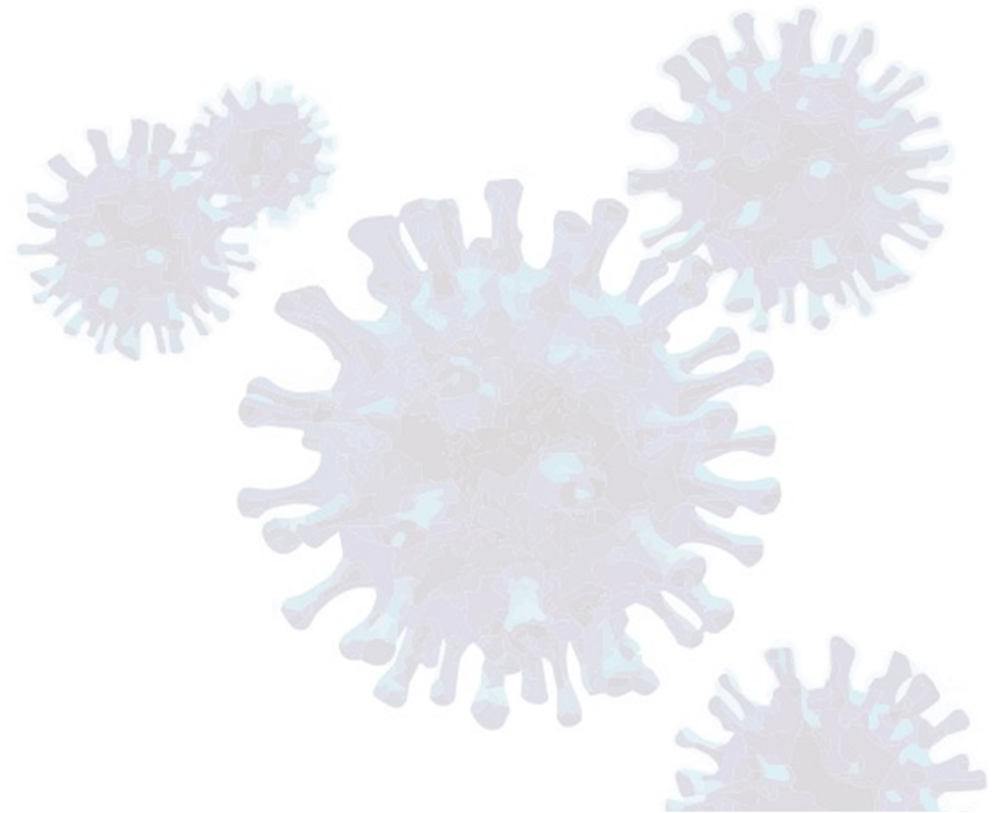
Agenda

- Control of the HIV-epidemic
 - In the world
 - In Europe
- Coinfections
 - Tuberculosis
 - Hepatitis C
- Antiretroviral therapy
 - Guidelines 2017
 - New drugs
 - New strategies



Agenda

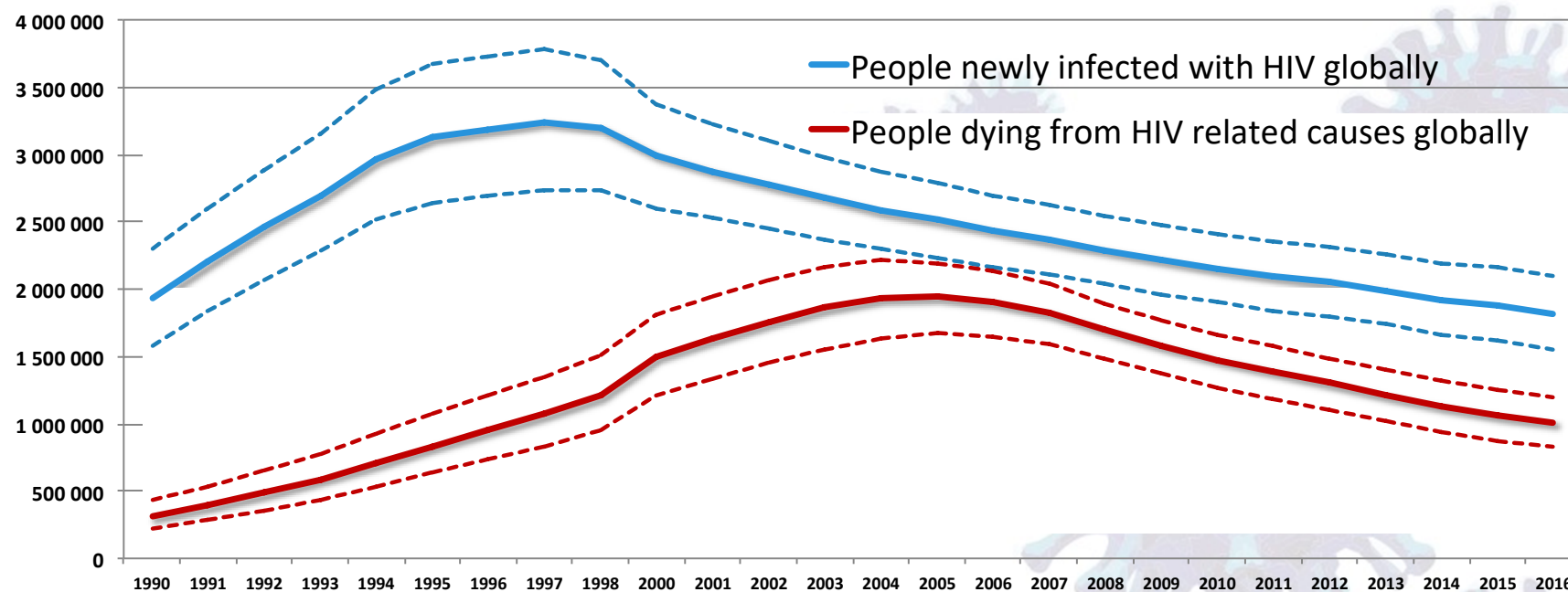
- Control of the HIV-epidemics
 - In Europe
 - In the world
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The HIV Epidemic: The world

Current situation of the HIV epidemic

Decrease in the incidence and mortality of HIV infection over time

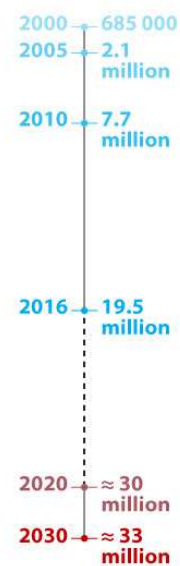
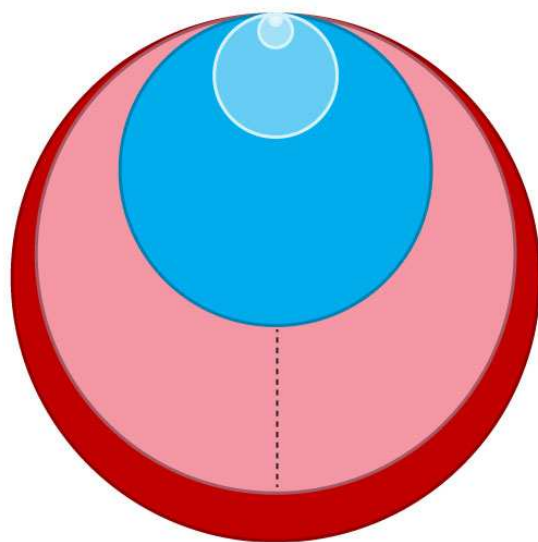


UNAIDS/WHO estimations. www.who.int

The HIV Epidemic: The world

Current situation of the HIV epidemic

Number of people on antiretroviral treatment

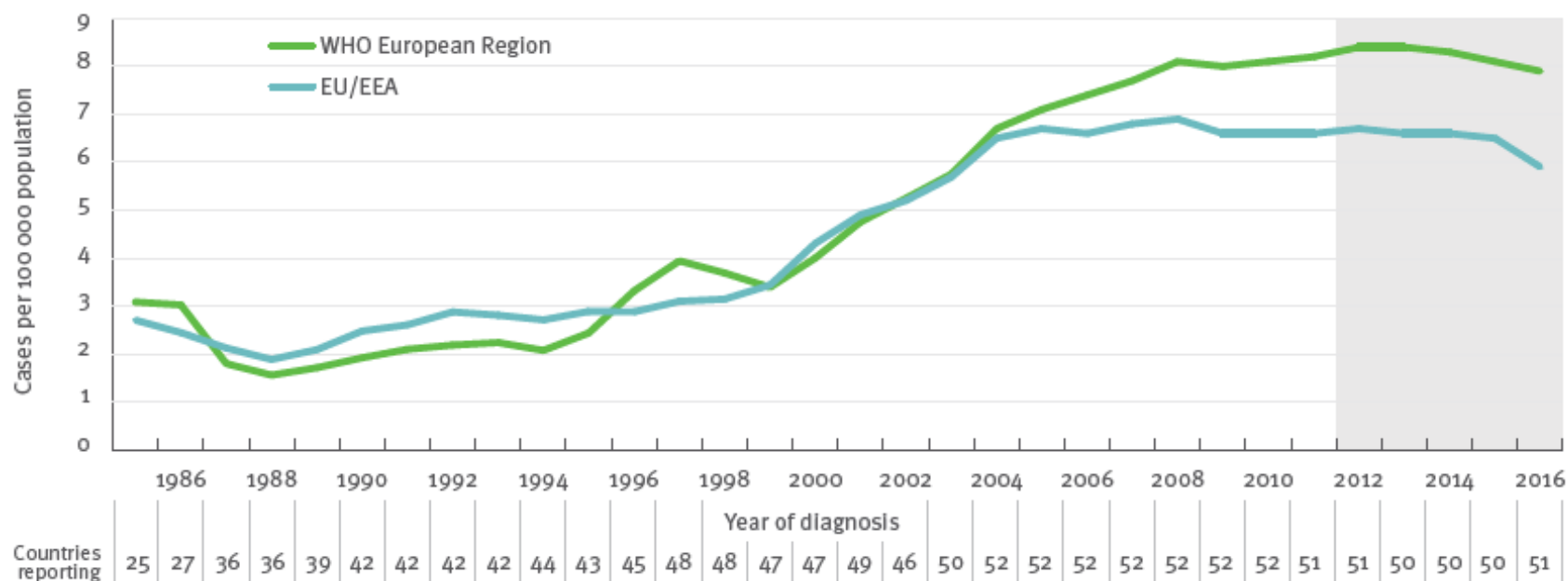


Future
Objectives

The HIV Epidemic: Europe

Current situation of the HIV epidemic

Rate of new HIV diagnoses per 100,000 population in Europe

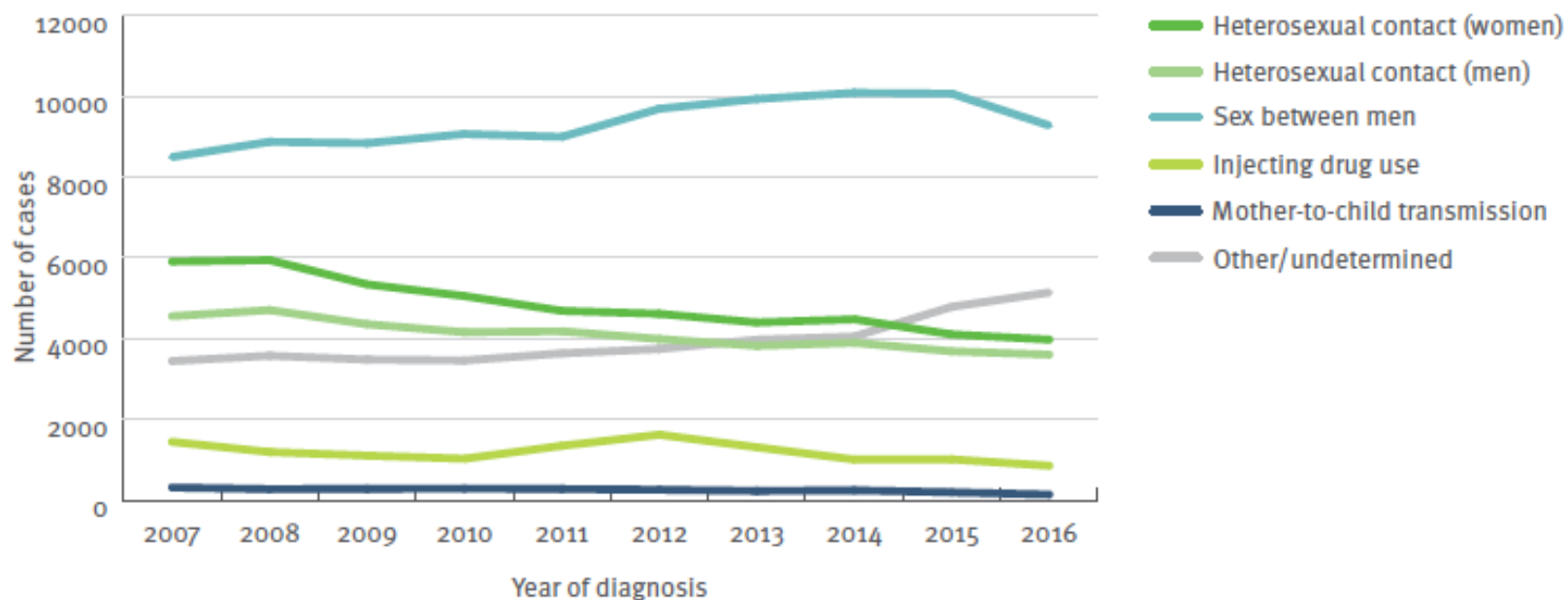


European CDC. HIV/AIDS surveillance in Europe 2017 – 2016 data. Stockholm: ECDC; 2017.

The HIV Epidemic: Europe

Current situation of the HIV epidemic

Number of HIV diagnoses per route of transmission, 2007-2016



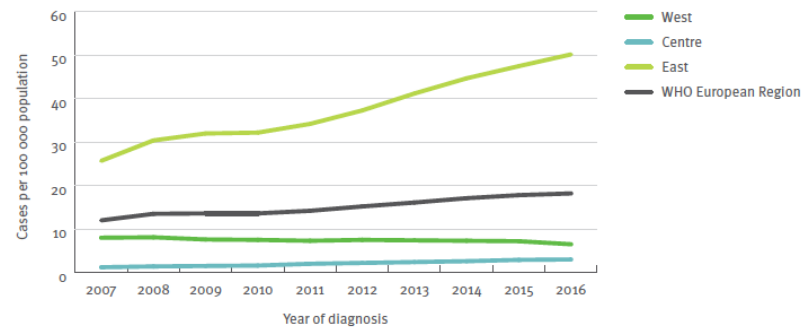
European CDC. HIV/AIDS surveillance in Europe 2017 – 2016 data. Stockholm: ECDC; 2017.

The HIV Epidemic: Europe

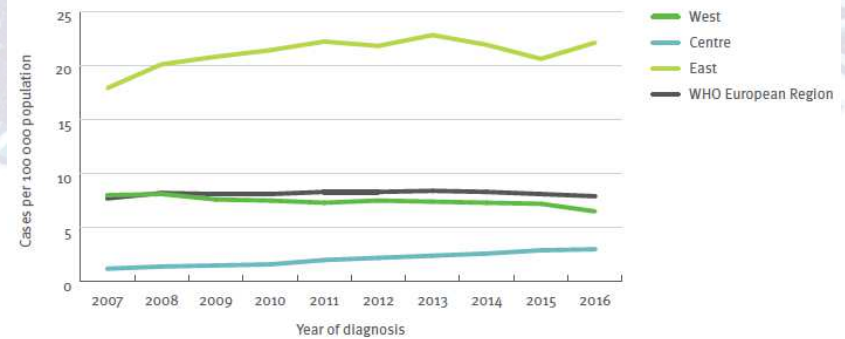
Current situation of the HIV epidemic

Rate of new HIV diagnoses including Russia (A) and excluding Russia (B) 2007-16

A



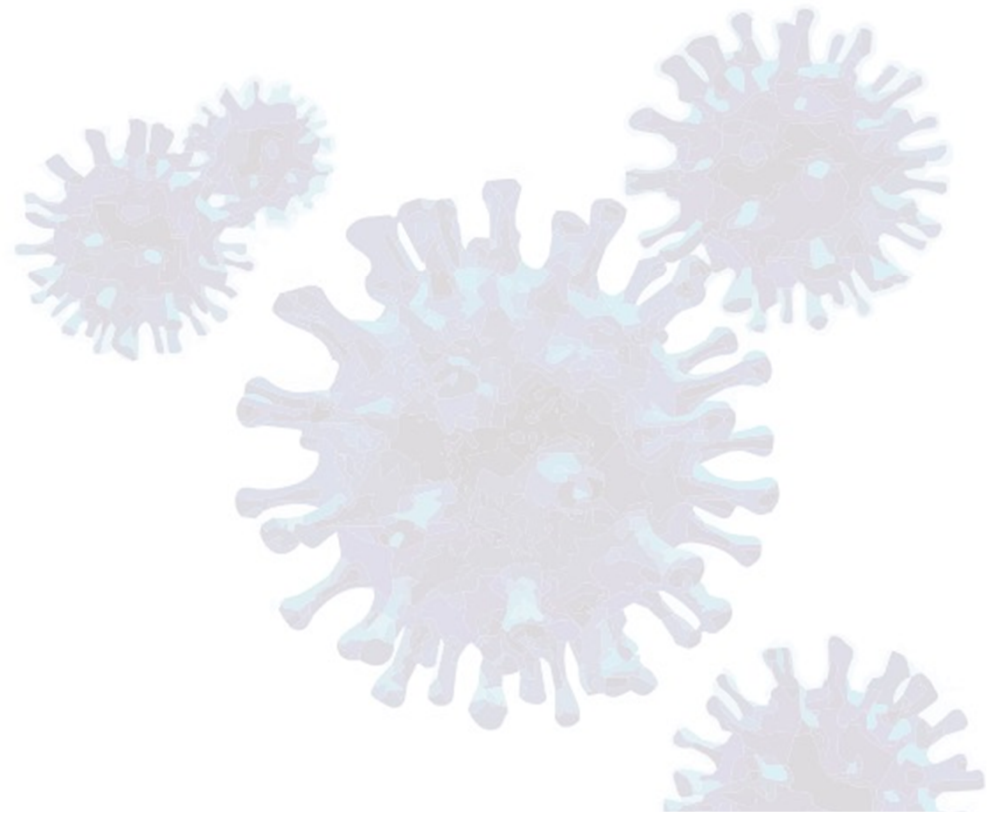
B



European CDC. HIV/AIDS surveillance in Europe 2017 – 2016 data. Stockholm: ECDC; 2017.

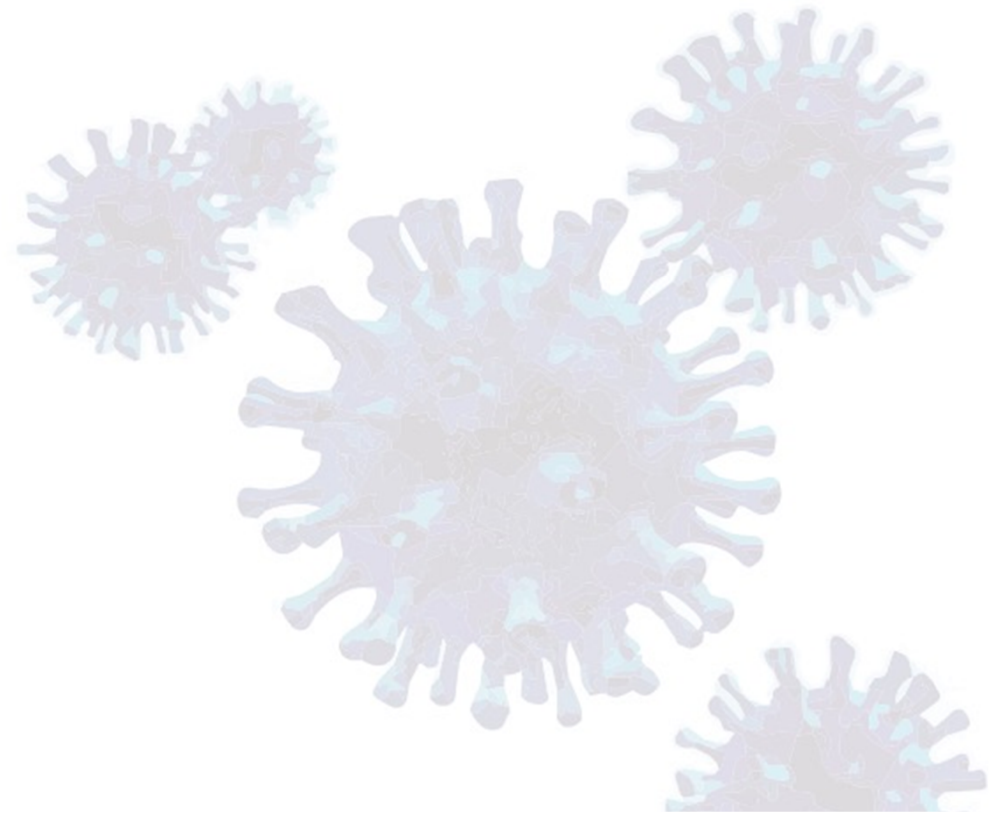
Agenda

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Coinfections: Tuberculosis

One month of rifapentine/isoniazid to prevent TB in People with HIV

Brief-TB/A5279 Randomized Clinical Trial: Study Regimens

Weeks	Control Arm 9H	Experimental Arm 1HP
1 – 4	➤ Isoniazid daily (300 mg)*	➤ Rifapentine 450 mg (<45 kg) or ➤ Rifapentine 600 mg (≥45 kg) plus INH daily (300 mg)*
5 – 36	➤ Isoniazid daily (300 mg)*	No treatment
37 to end of follow-up	No treatment	No treatment

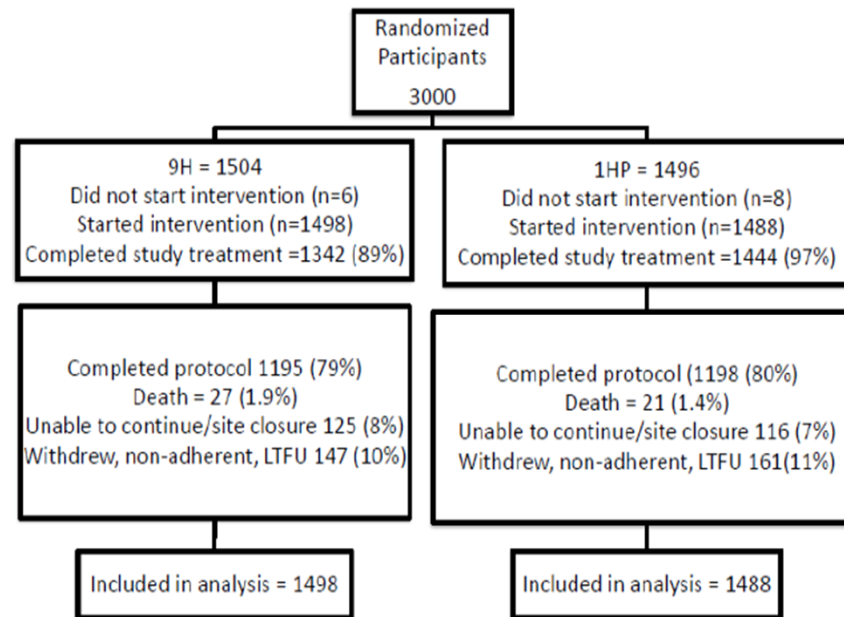
3 years of follow up after last participant enrolled

Swindells S, et al. CROI; Boston, MA; March 4-7, 2018. *Abstract 37LB*

Coinfections: Tuberculosis

One month of rifapentine/isoniazid to prevent TB in People with HIV

Brief-TB/A5279 Randomized Clinical Trial: Consort Diagram



Swindells S, et al. CROI; Boston, MA; March 4-7, 2018. *Abstract 37LB*

Coinfections: Tuberculosis

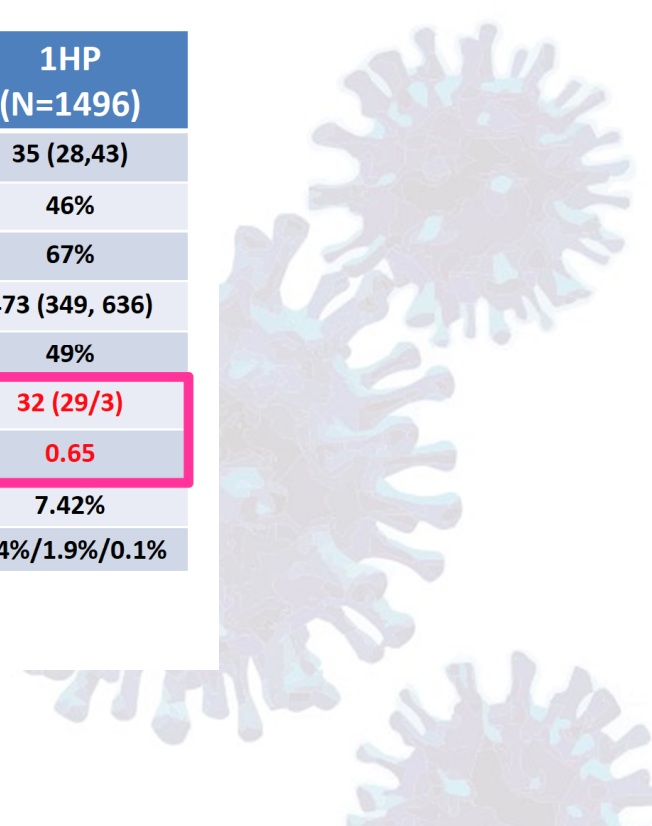
One month of rifapentine/isoniazid to prevent TB in People with HIV

Brief-TB/A5279 Randomized Clinical Trial: Main Results

	9H (N=1504)	1HP (N=1496)
Age (median, IQR) years	35 (28,43)	35 (28,43)
Male gender	46%	46%
Black, non-Hispanic race	66%	67%
CD4 (IQR) cells/mm ³	469 (341, 633)	473 (349, 636)
ART at entry	50%	49%
Events (TB/Death)	33 (24/9)	32 (29/3)
Incidence x 100 Patients-Year*	0.67	0.65
Any Adverse Event	8.97%	7.42%
Any Hematological/Liver /Neurological	1.2%/2.8%/2.0%	2.4%/1.9%/0.1%

*IRR Difference (95% Confidence Interval): 0.023 (-0.35,0.35)

Swindells S, et al. CROI; Boston, MA; March 4-7, 2018. *Abstract 37LB*



Coinfections: Tuberculosis

One month of rifapentine/isoniazid to prevent TB in People with HIV

Brief-TB/A5279 Randomized Clinical Trial: Conclusions

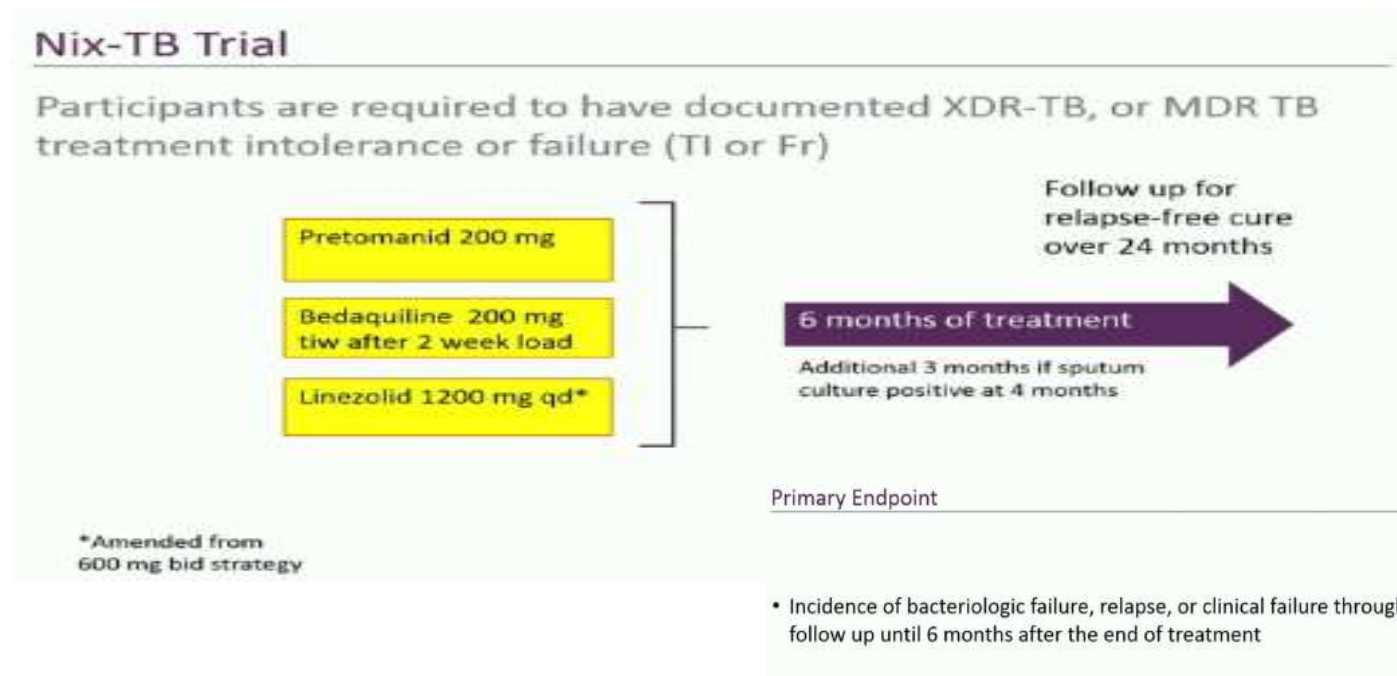
- 1HP is non-inferior to 9H for preventing TB, TB death or death from unknown cause in adults and adolescents with HIV infection
- Rates of TB were higher in those with +TST/IGRA or CD4 $\leq$ 250
- Rates of endpoints were higher in 1HP recipients with CD4 $\leq$ 250 vs 9H
- Safety was good and similar in both arms, with more hematologic toxicity with 1HP and more liver and neuro- toxicity with 9H
- Completion of treatment was excellent in both arms but better with 1HP
- 1HP provides a highly-effective, ultra-short course regimen for the prevention of TB in people with HIV
- 1HP could contribute to improvements in global control of TB and should be studied in other high-risk groups



Coinfections: Tuberculosis

Pretomanid, bedaquiline and linezolid to treat XDR-TB

The NIX-TB trial: Design



Conradie F, et al. CROI; Seattle, Washington; February 13-17, 2017. *Abstract LB80*

Coinfections: Tuberculosis

Pretomanid, bedaquiline and linezolid to treat XDR-TB

The NIX-TB trial: Participant demographics n=72

Age (Mean)	34.7 years	
Gender	M 39	54%
	F 33	46%
Race	Black 56	78%
	White 1	1%
	Mixed 15	21%
HIV infected	37	51%
Types of TB	XDR 47	65%
	MDR TI 8	11%
	MDR TF 17	24%
Chest X-ray Cavities	None 9	13%
	Unilateral 36	50%
	Bilateral 26	36%
	Missing 1	1%

Conradie F, et al. CROI; Seattle, Washington; February 13-17, 2017. *Abstract LB80*

Coinfections: Tuberculosis

Pretomanid, bedaquiline and linezolid to treat XDR-TB

The NIX-TB trial: Main results

Time to Culture Conversion

- All surviving patients were culture negative at 4 months.
- 26 (74%) negative at 8 weeks as of December 2016.
- 4 participants died within the first 8 weeks of therapy

Treatment-Emergent Adverse Events (TEAE)

- The expected linezolid toxicities of peripheral neuropathy (PN) and myelosuppression (MSPN) were common but manageable.
- 49 patients (71%) of participants had at least one linezolid dose interruption
- 14 (22%) due to MSPN
- 20 (28%) due to PN
- There were no cases of optic neuritis

Coinfections: Tuberculosis

Pretomanid, bedaquiline and linezolid to treat XDR-TB

The NIX-TB trial: Conclusions

Conclusion

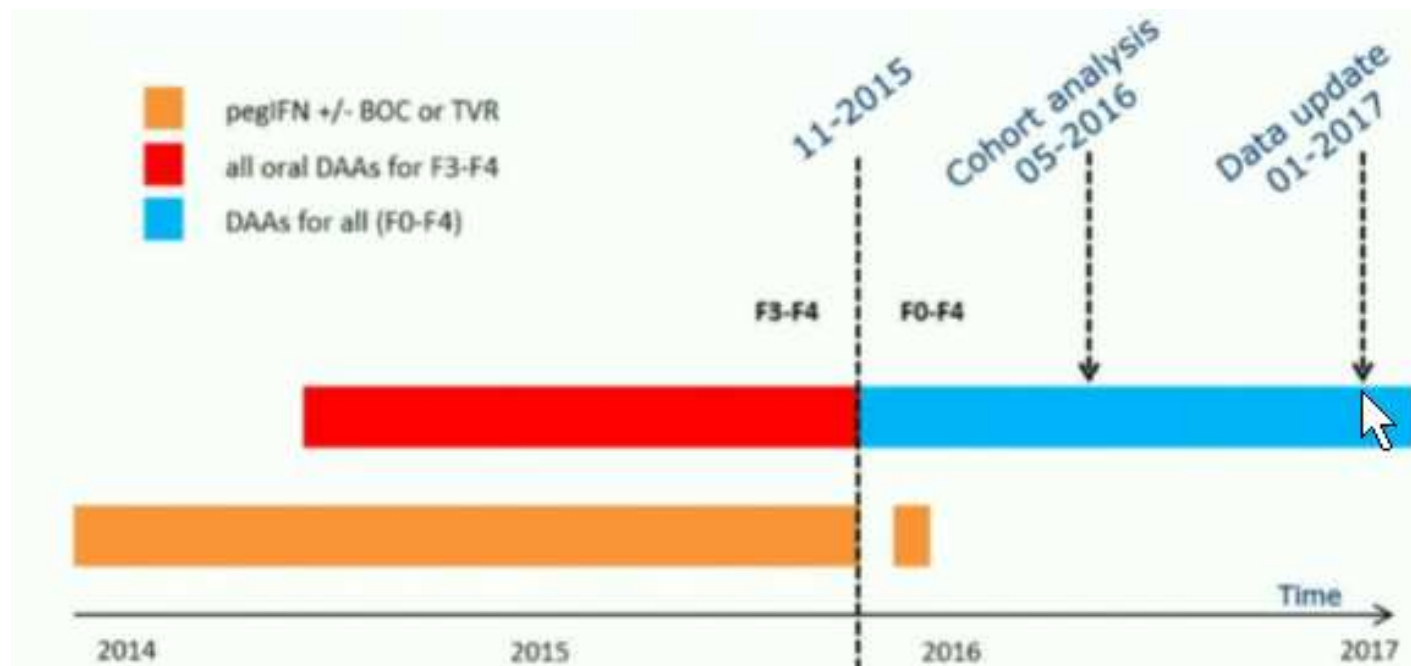
- Current results of this greatly simplified and shortened all-oral regimen for drug resistant TB are encouraging in terms of both efficacy and safety
- Mortality is less than 6%
- There has been only one XDR TB relapse
- No participant has had to have extended treatment

Conradie F, et al. CROI; Seattle, Washington; February 13-17, 2017. *Abstract LB80*

Coinfections: Hepatitis C

Substantial decline in acute HCV infections among Dutch HIV+MSM after DAA roll out

DAA treatment for HCV in the Netherlands



Boerekamps A et al. Clin Infect Dis. 2017 Nov 23.

Coinfections: Hepatitis C

Substantial decline in acute HCV infections among Dutch HIV+MSM after DAA roll out

2014

- Acute hepatitis N= 93
 - Geno 1 = 75 (81%)
 - Geno 4 = 18 (19%)
- Patient/years follow-up: 8,290
- Incidence: 11.2/1000 patients/year (CI 95% 9-14)
- 1.1% anual



RR 0,49
IC 95% 0,34-0,69

2016

- Acute hepatitis N= 49
 - Geno 1 = 34 (69%)
 - Geno 4 = 15 (31%)
- Patient/years follow-up: 8,961
- Incidence 5.5/1000 patients/year (CI 95% 4-7)
- 0.55% anual

Coinfections: Hepatitis C

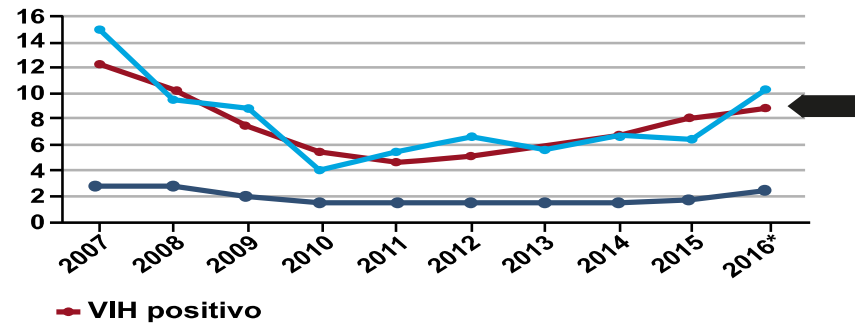
Substantial decline in acute HCV infections among Dutch HIV+MSM after DAA roll out

The decline is not explained by changes in sexual behaviours

Syphilis among MSM in STI clinics in The Netherlands:

- First semester 2015: 446 new diagnoses
 - First semester 2016: 629 new diagnoses
- 41% increase

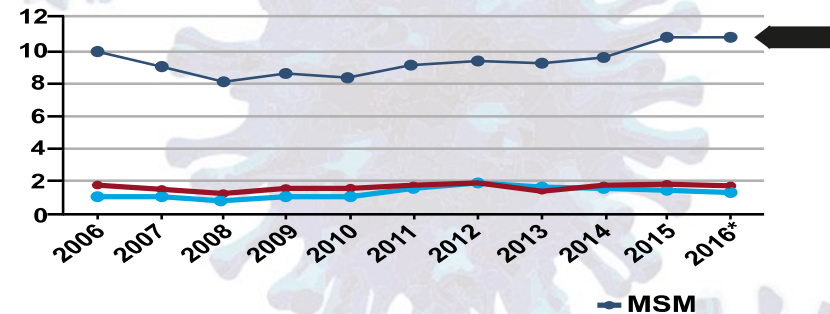
Syphilis in HIV+MSM



Boerekamps A et al. Clin Infect Dis. 2017 Nov 23.

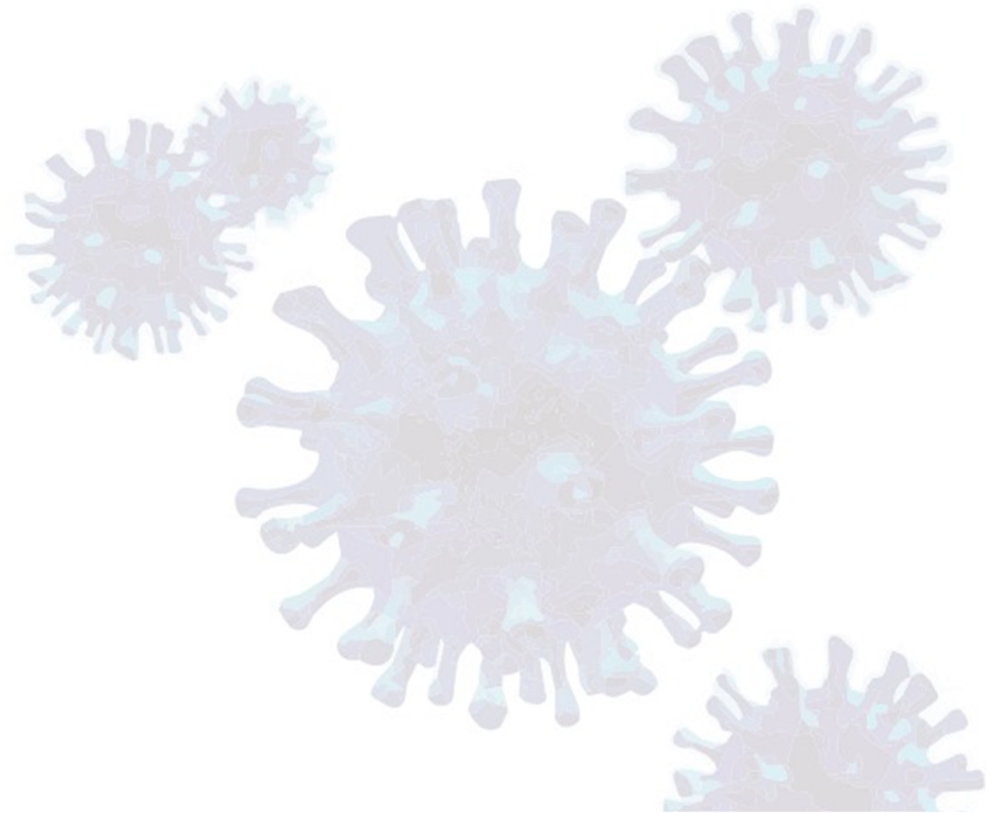
<http://www.rivm.nl> Thermometer seksuele gezondheid nov 2016

LGV in MSM



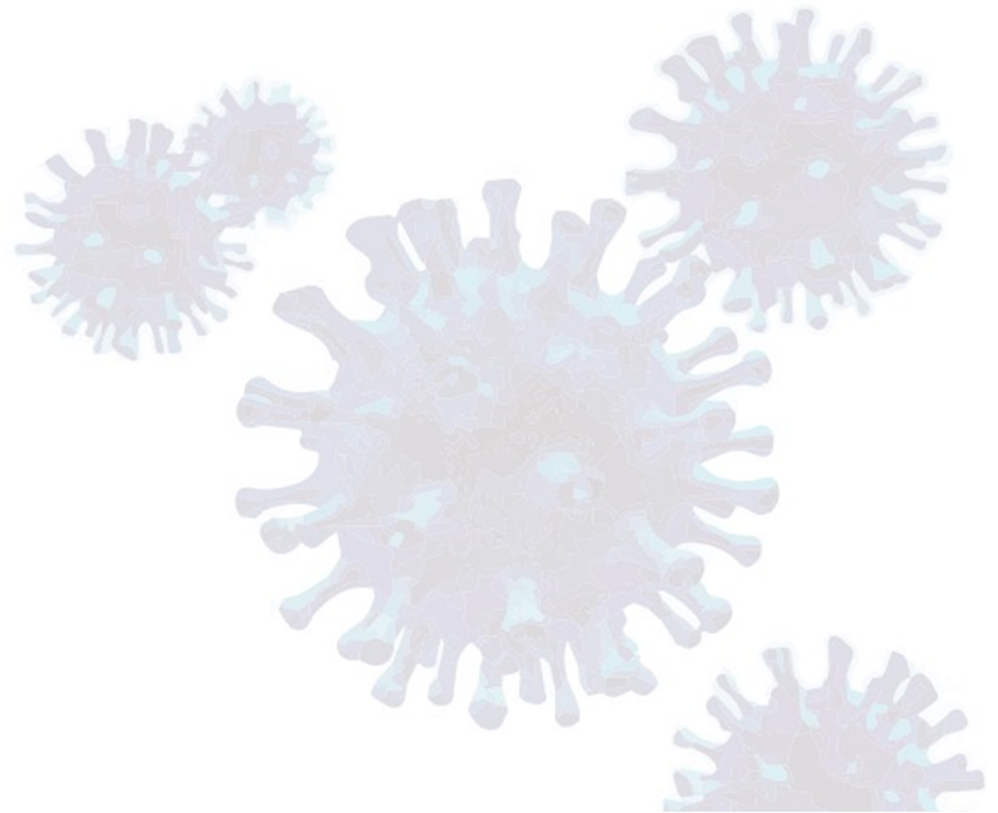
Agenda

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 - In the world
 - In Europe
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 - Tuberculosis
 - Hepatitis C
- Antiretroviral therapy
 - Guidelines 2017
 - New drugs
 - New strategies



Agenda

- Control of the HIV-epidemics
 - In Europe
 - In the world
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- **Antiretroviral therapy**
 - Guidelines 2017
 - New drugs
 - New strategies



Guidelines 2017

HIV Guidelines.

When to Start.

All HIV-infected patients, irrespective of CD4 count



Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

Downloaded from <https://aidsinfo.nih.gov/guidelines> on 4/16/2018

Visit the AIDSinfo website to access the most up-to-date guideline.

Register for e-mail notification of guideline updates at <https://aidsinfo.nih.gov/e-news>.

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Clinical Review & Education

Special Communication

Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults
2016 Recommendations of the International Antiviral Society-USA Panel

Hallbyrd F, Garfield M, Michael S, Song M, Costanza A, Benson M, Carle del Rio M, Joseph J, Eron M, Joffe C, Cabot MC, Wyles D, et al. 2016. *Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults*. 2016 Recommendations of the International Antiviral Society-USA Panel. *Ann Intern Med*. 2016;164(10):695-703.

IMPORTANCE: New data and therapeutic options warrant updated recommendations for the use of antiretroviral drugs (ARVs) to treat or to prevent HIV infection in adults.

OBJECTIVE: To provide updated recommendations for the use of antiretroviral therapy in adults (aged ≥18 years) with established HIV infection, including when to start treatment, initial regimens, and changing regimens, along with recommendations for using ARVs for preventing HIV among those at risk, including preexposure and postexposure prophylaxis.

EVIDENCE REVIEW: A panel of experts in HIV research and patient care convened by the International Antiviral Society-USA reviewed data published in peer-reviewed journals, presented by regulatory agencies, or presented as conference abstracts at peer-reviewed scientific conferences since the 2014 report. For new data or evidence that would change previous recommendations or their ratings, comprehensive literature searches were conducted in the PubMed and the Cochrane Inequalities and Reviews (CINA) databases. Recommendations were by consensus, and each recommendation was rated by strength and quality of the evidence.

FINDINGS: Newer data support the widely accepted recommendation that antiretroviral therapy should be started in all individuals with HIV infection with detectable viremia, regardless of CD4 cell count. Recommended optimal initial regimens for most patients are 2 nucleoside reverse transcriptase inhibitors (NRTIs) plus an integrase strand transfer inhibitor (INSTI). Other effective regimens include nonnucleoside reverse transcriptase inhibitors or boosted protease inhibitors with 2 NRTIs. Recommendations for special populations and in the settings of opportunistic infections and comorbid conditions are provided. Reasons for switching therapy include convenience, tolerability, simplification, and optimization of potential new drug interactions, pregnancy or plans for pregnancy, elimination of food restrictions, virologic failure, or drug toxicity. Laboratory assessments are recommended before treatment, and monitoring during treatment is recommended to assess response, adverse effects, and adherence. Approaches are recommended to improve linkage to and retention in care are provided. Daily tenofovir disoproxil fumarate/emtricitabine is recommended for use as preexposure prophylaxis to prevent HIV infection in persons at high risk. When indicated, postexposure prophylaxis should be started as soon as possible after exposure.

CONCLUSIONS AND RELEVANCE: Antiretroviral agents remain the cornerstone of HIV treatment and prevention. All HIV-infected individuals with detectable plasma virus should receive treatment with recommended initial regimens consisting of an INSTI plus 2 NRTIs. Preexposure prophylaxis should be considered as part of an HIV prevention strategy for at-risk individuals. When used effectively, currently available ARVs can sustain HIV suppression and can prevent new HIV infection. With these treatment regimens, survival rates among HIV-infected adults who are retained in care can approach those of uninfected adults.

JAMA. 2016;316(10):1191-1201. doi:10.1001/jama.2016.0000

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

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Ann Arbor, MI 48106-0616.
Email: fahall@umich.edu

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October 2017
English

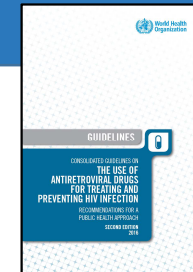
Documento de consenso de Gesida/Plan Nacional sobre el Sida respecto al tratamiento antirretroviral en adultos infectados por el virus de la inmunodeficiencia humana (Actualización enero 2018)

Panel de expertos de Gesida y Plan Nacional sobre el Sida



WHO Clinical Guidelines 2016: Antiretroviral Therapy

When to Start ART



 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/mm³ (strong recommendation, moderate-quality evidence).
 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).

Guidelines 2017

What to Start.

The logo for AIDSinfo features the word "AIDS" in a large, bold, blue sans-serif font, followed by "info" in a smaller, blue, lowercase sans-serif font. A stylized red and blue graphic element, resembling a ribbon or a stylized 'X', is positioned above the 'i' in "info". A thick, curved red swoosh underlines the entire text.

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

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Visit the AIDSinfo website to access the most up-to-date guideline.

Register for e-mail notification of guideline updates at <http://aidsinfo.nih.gov/e-news>.

Downloaded from <http://aidsinfo.nih.gov/guidelines> on 9/22/2015

Clinical Review & Education

Special Communication

Antiretroviral Treatment of Adult HIV Infection 2014 Recommendations of the International Antiviral Society-U.S.A Panel

Hughley A. Gotlib¹, Judith A. Aronoff², Michael J. Bozzette³, Mary Jane Brumby⁴, Eric M. Frigo⁵, Francis Street⁶, MD, Constance A. Sponson⁷, MD, David R. Bangs⁸, PhD, Peter Cahn⁹, MD, PhD, Joel Gelernter¹⁰, MD, Martin Malin¹¹, Carolyn B. Miller¹², Peter Hirschbar, MD, PhD, Michael E. Suga¹³, David L. Thomas III¹⁴, Michael W. Jacobsen¹⁵, Richard A. Volberding¹⁶

IMPORTANCE: New data and antiretroviral regimens expand treatment choices in response to HIV settings and warrant an update of recommendations to adult patients infected with human immunodeficiency virus (HIV).

OBJECTIVE: To provide updated recommendations for adults with HIV, emphasizing where to start treatment, what regimen to choose, the use of laboratory monitoring tools, and managing treatment failure, switches, and amplification.

PATIENTS AND STUDY DESIGN, SETTING, AND DATA SOURCES: An international literature review of U.S.A panel of experts in HIV research in care combined previous data and reviewed new data since the 2012 update with literature searches in PubMed and EMBASE through June 2014. Recommendations and ratings were given by majority 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 T-cell counts. Recommended initial regimens include 2-nucleoside reverse-transcriptase inhibitors (NRTIs), zalcitabine or lamivudine, boosted protease inhibitor(s) and/or a third drug or boosted dolutegravir, which should be an integrase strand-transfer inhibitor (dolutegravir, elvitegravir, or rilpivirine), a nonnucleoside reverse transcriptase inhibitor (efavirenz or etravirine) or a boosted protease inhibitor (darunavir or atazanavir). Alternative regimens are available. Boosted protease inhibitor monotherapy is generally not recommended, but HIV-sparing options may be considered for patients who are unable to tolerate or experience side effects from preferred regimens. 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. Drug–drug interactions for adverse effects, resistance, or in reduce costs should not preclude antiretroviral therapy.

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 effect profiles, comorbidities, and drug interactions.

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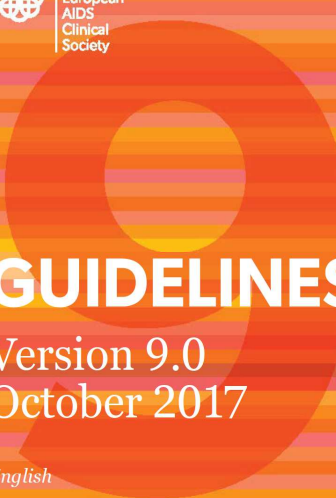
Author Affiliations: Author affiliations are listed at end of this article.

Corresponding Author: Hughley A. Gotlib, MD, University Hospital, Davis, California 95616 (e-mail: [gotlib@ucsf.edu](#)).
[gotlib@ucsf.edu](#)

JAMA. 2014;311(24):3041–45. doi:10.1001/jama.2014.20422

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9

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)**

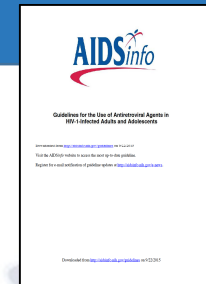
Panel de expertos de GeSIDA y Plan Nacional sobre el Sida*



Guidelines 2017

DHHS Guidelines October, 2017

What to Start: Recommended regimens

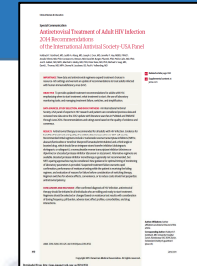


- The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) classifies the following regimens as **Recommended Initial Regimens for Most People with HIV (in alphabetical order)**:
 - Dolutegravir/abacavir/lamivudine^a—**only** for patients who are HLA-B*5701-negative (**AI**)
 - Dolutegravir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

Guidelines 2017

IAS-USA Panel Guidelines 2016

What to Start: Recommended regimens



Regimen	Rating
Dolutegravir/abacavir/lamivudine	A1a
Dolutegravir plus tenofovir alafenamide/emtricitabine ^b	A1a
Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine ^b	A1a
Raltegravir plus tenofovir alafenamide/emtricitabine ^b	A1II

GeSIDA Guidelines 2018

What to Start: Preferred regimens

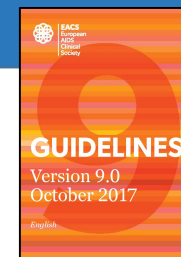


3er Fármaco	Pauta [†]	Comentarios [‡]
Preferentes. Pautas aplicables a la mayoría de los pacientes y que en ensayos clínicos aleatorizados han mostrado una eficacia superior frente a otras o mostrando no-inferioridad presentan ventajas adicionales en tolerancia, toxicidad o un bajo riesgo de interacciones 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*.

Guidelines 2017

EACS Guidelines 2017

What to Start: Recommended regimens



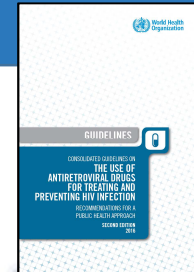
Pauta	Dosis
2 ITIAN + INI	
ABC/3TC/DTG ^(1,6)	ABC/3TC/DTG 600/300/50 mg, 1 comprimido qd
TAF/FTC ⁽⁴⁾ o TDF/FTC ⁽⁶⁾ + DTG	TAF/FTC 25/200 mg, 1 comprimido qd o TDF/FTC 300/200mg, 1 comprimido qd + DTG 50 mg, 1 comprimido qd
TAF/FTC/EVG/c ⁽⁴⁾ TDF/FTC/EVG/c ^(6,8,9)	TAF/FTC/EVG/c 10/200/150/150 mg, 1 comprimido qd o TDF/FTC/EVG/c 300/200/150/150 mg, 1 comprimido qd
TAF/FTC ⁽⁴⁾ o TDF/FTC ⁽⁶⁾ + RAL	TAF/FTC 25/200 mg, 1 comprimido qd o TDF/FTC 300/200mg, 1 comprimido qd + RAL 400 mg, 1 comprimido bid
2 ITIAN + ITINN	
TAF/FTC/RPV ⁽³⁾ TDF/FTC/RPV ⁽³⁾	TAF/FTC/RPV 25/200/25 mg, 1 comprimido qd TDF/FTC/RPV 300/200/25 mg, 1 comprimido qd
2 ITIAN + IP/r	
TAF/FTC ⁽⁴⁾ o TDF/FTC ⁽⁶⁾ + DRV/c ⁽⁴⁾ o + DRV/r ⁽⁴⁾	TAF/FTC 10/200 mg, 1 comprimido qd o TDF/FTC 300/200mg, 1 comprimido qd + DRV/c 800/150 mg, 1 comprimido qd o + DRV 800 mg, 1 comprimido qd + RTV 100 mg, 1 comprimido qd

EACS Guidelines. V 9. October 2017.

Guidelines 2017

WHO Clinical Guidelines 2016: Antiretroviral Therapy

What to Start: First line ART



4.4.1 First-line ART for adults	First-line ART for adults¹ should consist of two nucleoside reverse-transcriptase inhibitors (NRTIs) plus a non-nucleoside reverse-transcriptase inhibitor (NNRTI) or an integrase inhibitor (INSTI): • TDF + 3TC (or FTC) + EFV as a fixed-dose combination is recommended as the preferred option to initiate ART (strong recommendation, moderate-quality evidence). • If TDF + 3TC (or FTC) + EFV is contraindicated or not available, one of the following alternative options is recommended: ◦ AZT + 3TC + EFV ◦ AZT + 3TC + NVP ◦ TDF + 3TC (or FTC) + NVP (strong recommendation, moderate-quality evidence).
NEW 4.4.2 Fixed-dose combinations	NEW TDF + 3TC (or FTC) + DTG or TDF + 3TC (or FTC) + EFV 400 mg/day may be used as alternative options to initiate ART (conditional recommendation, moderate-quality evidence). Fixed-dose combinations and once-daily regimens are preferred for antiretroviral therapy (strong recommendation, moderate-quality evidence).

New Drugs

Antiretrovirals available in 2018 in Europe

NRTIs

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

NNRTIs

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

PIs

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

INIs

- Raltegravir
- Dolutegravir
- Elvitegravir

Fusion inhibitors

- Enfuvirtide

Entry Inhibitors

- Maraviroc

PK Boosters

- Ritonavir
- Cobicistat

STR

- Atripla
- Eviplera
- Stribild
- Triumeq
- Genvoya

NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PK, pharmacokinetic

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

New Drugs

Antiretrovirals available in 2018

NRTIs ■ Abacavir ■ Didanosine ■ Emtricitabine ■ Lamivudine ■ Stavudine ■ Tenofovir ■ Zidovudine	NNRTIs ■ Delavirdine ■ Efavirenz ■ Etravirine ■ Nevirapine ■ Nevirapine XR ■ Rilpivirine ■ Doravirine	PIs ■ Atazanavir ■ Darunavir ■ Fosamprenavir ■ Indinavir ■ Lopinavir ■ Nelfinavir ■ Ritonavir ■ Saquinavir ■ Tipranavir	INIs ■ Raltegravir ■ Dolutegravir ■ Elvitegravir ■ Bictegravir
Fusion inhibitors ■ Enfuvirtide	Entry Inhibitors ■ Maraviroc ■ Fostemsavir ■ Ibalizumab ■ Pro140 ■ IBI-421	PK Boosters ■ Ritonavir ■ Cobicistat	STR ■ Atripla ■ Eviplera ■ Stribild ■ Triumeq ■ Genvoya

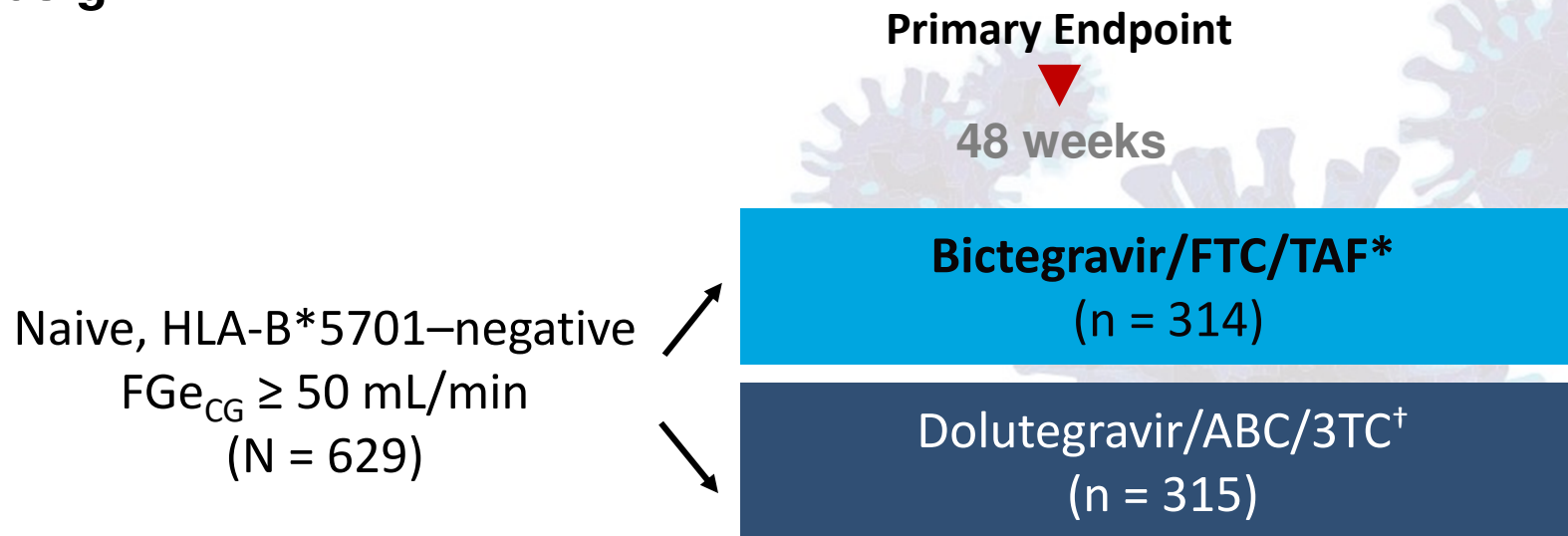
NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PK, pharmacokinetic

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

New Drugs: Bictegravir

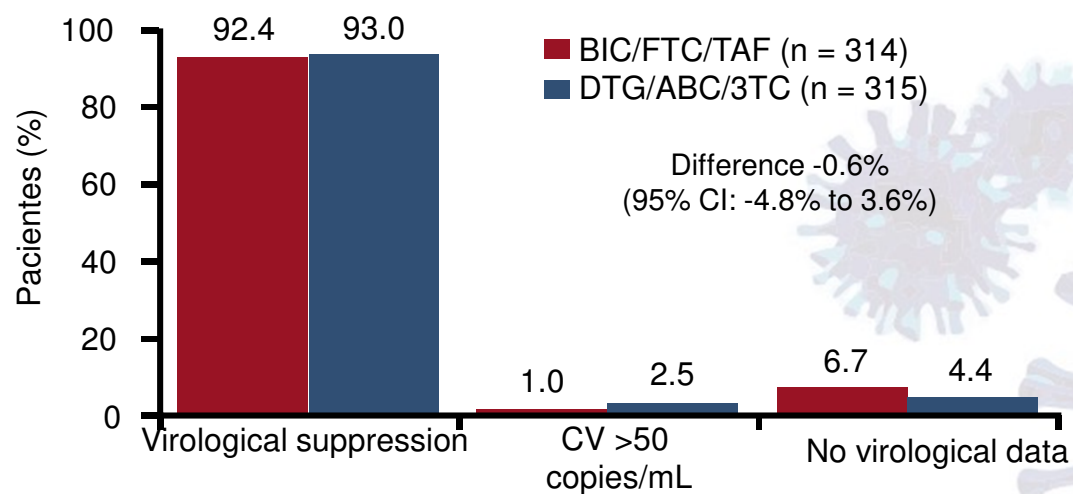
Study 1489: Bictegravir + TAF/FTC vs Dolutegravir + ABC/3TC, both coformulated, in naive patients

Design



New Drugs: Bictegravir

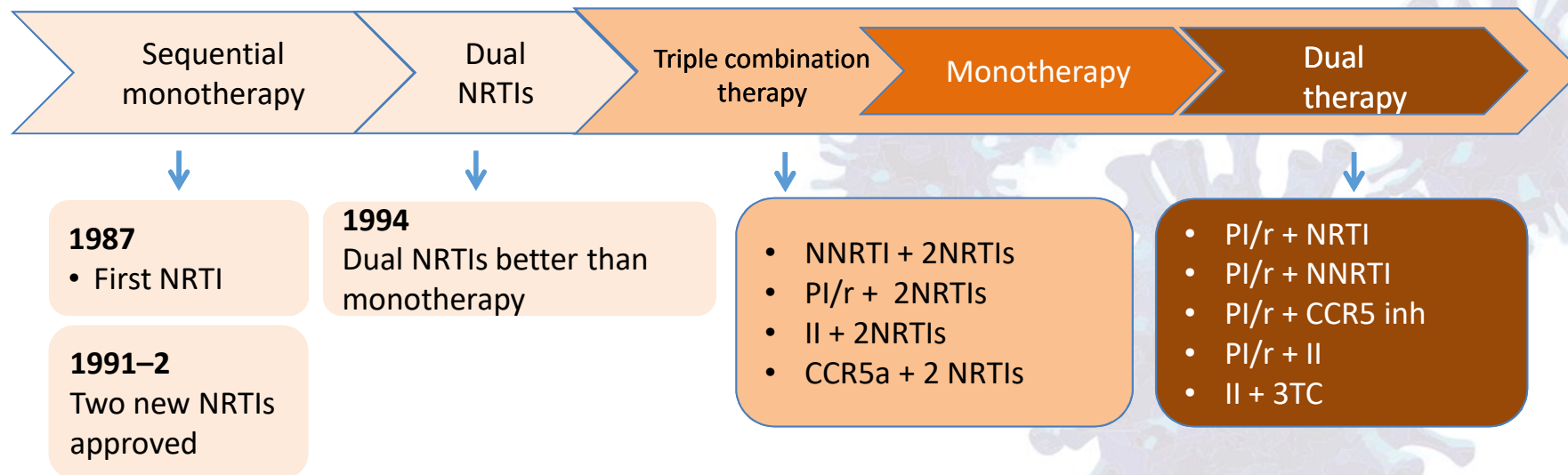
Study 1490: Virological Efficacy (week 48)



- No resistance mutations

New Strategies: 2 Drug-Regimens

Number of drugs: ART Evolution



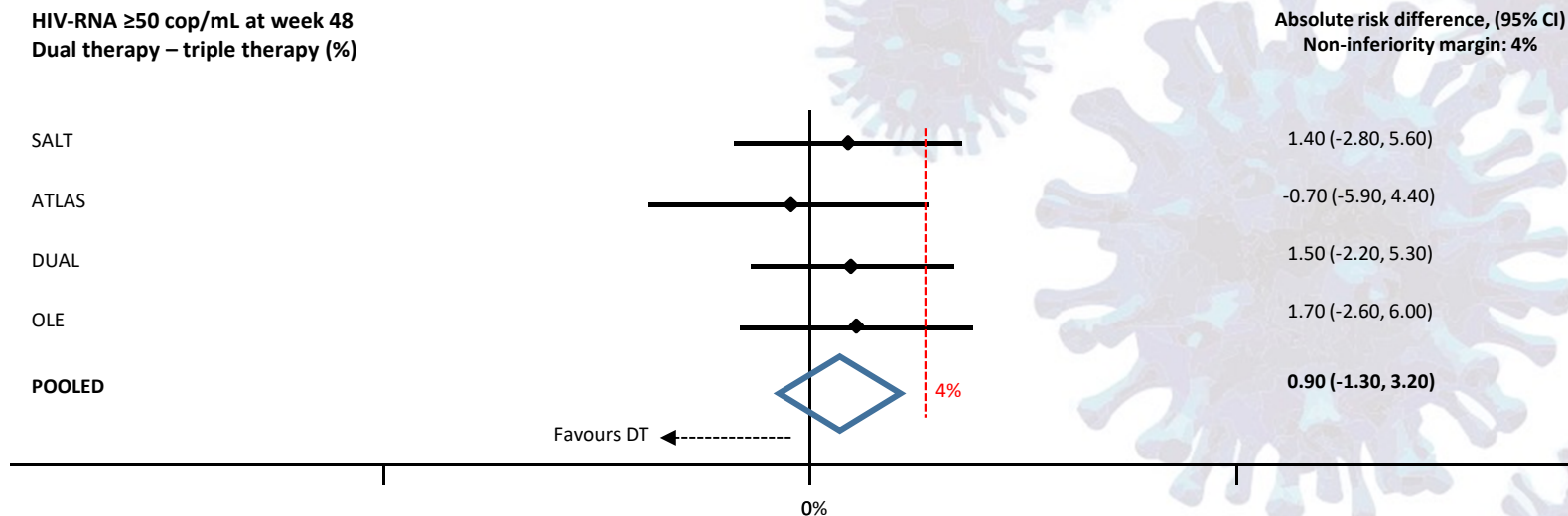
New Strategies: 2 Drug-Regimens

Combinations of bPI + 3TC.

Switch in suppressed patients

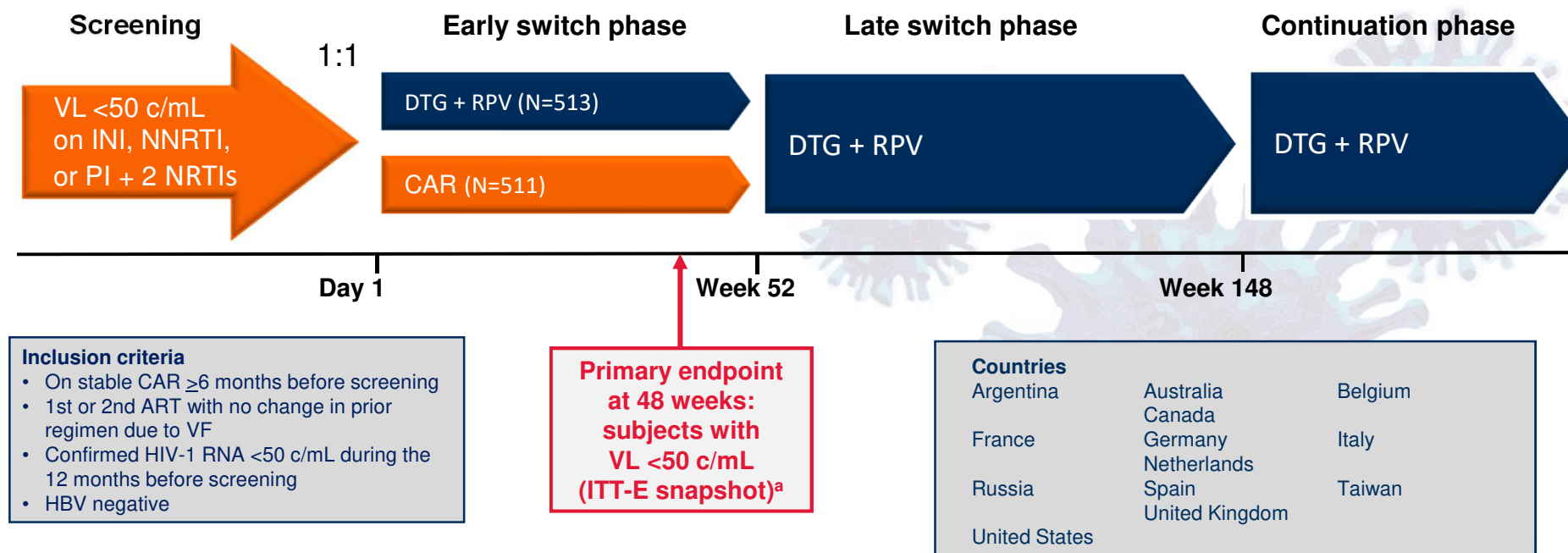
At 48w, 4% of patients on DT vs. 3.04% on TT had HIV-RNA ≥ 50 cop/mL

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



New Strategies: 2 Drug-Regimens

SWORD-1 and SWORD-2 Phase III Study Design

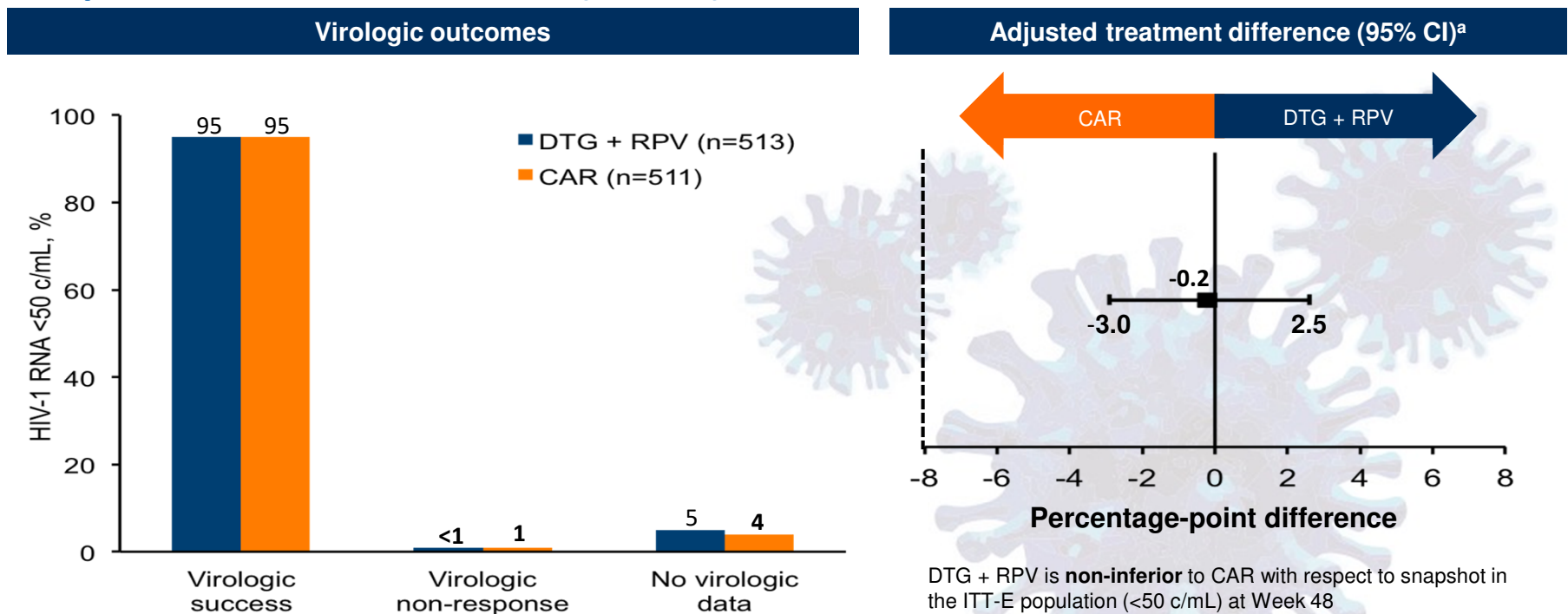


Libre et al. Lancet. 2018;391:839-849.

- ^a-8% non-inferiority margin for pooled data
- 10% non-inferiority margin for individual studies

New Strategies: 2 Drug-Regimens

Snapshot Outcomes at Week 48 (Pooled)



New Strategies: 2 Drug-Regimens

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

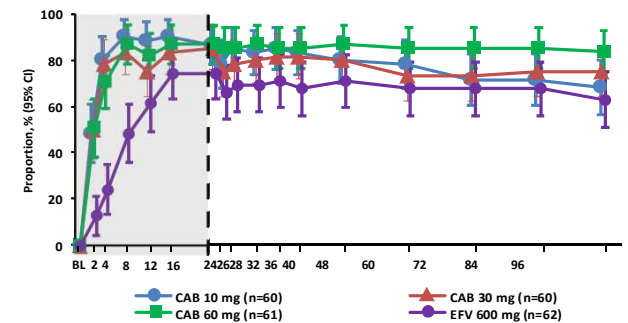
	Baseline viral load		Total N=120
	> 100,000 cpm N=37	≤ 100,000 cpm N=83	
Virological suppression HIV-1 RNA < 50 c/m [95% CI]	33 (89%) [75%,97%]	75 (90%) [82%,96%]	108 (90%) [83%,95%]
No suppression HIV-1 RNA ≥ 50 c/m	3 (8%) 3	2 (2%) 0	5 (4%) 3
Discontinuation with CV > 50 c/m*	0	2	2
No virological data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

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

New Strategies: Long acting regimens

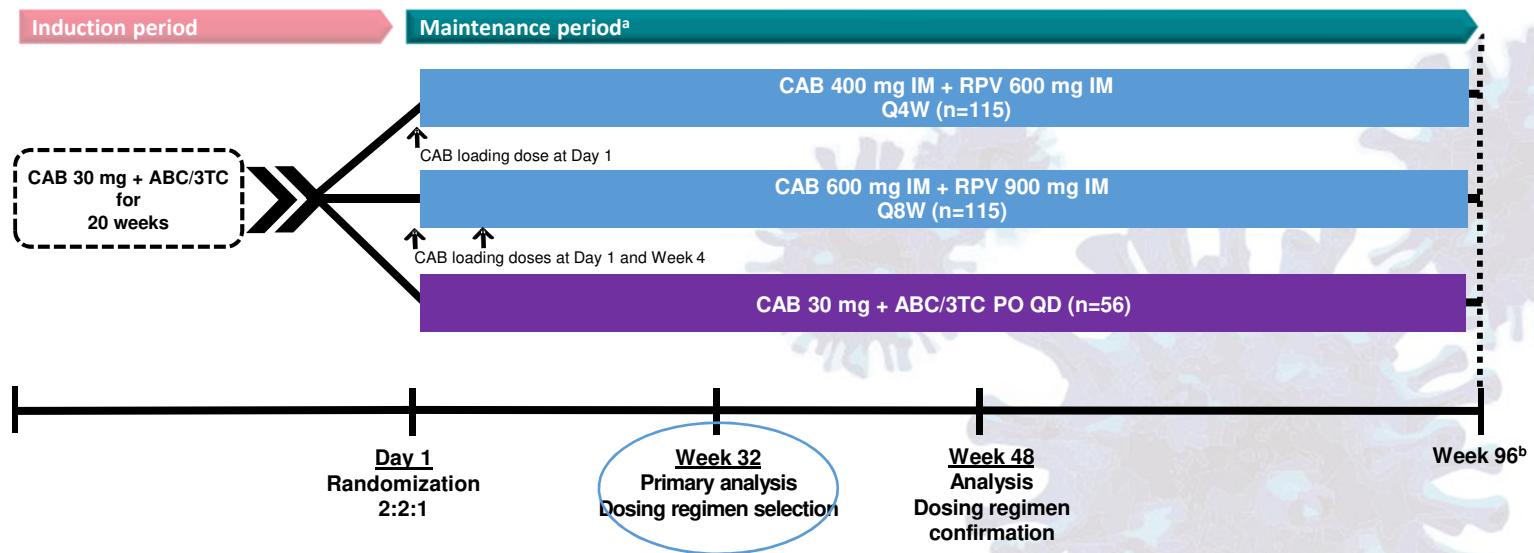
Long-acting antiretrovirals: Cabotegravir + rilpivirine

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



New Strategies: Long acting regimens

Latte-2: Study design

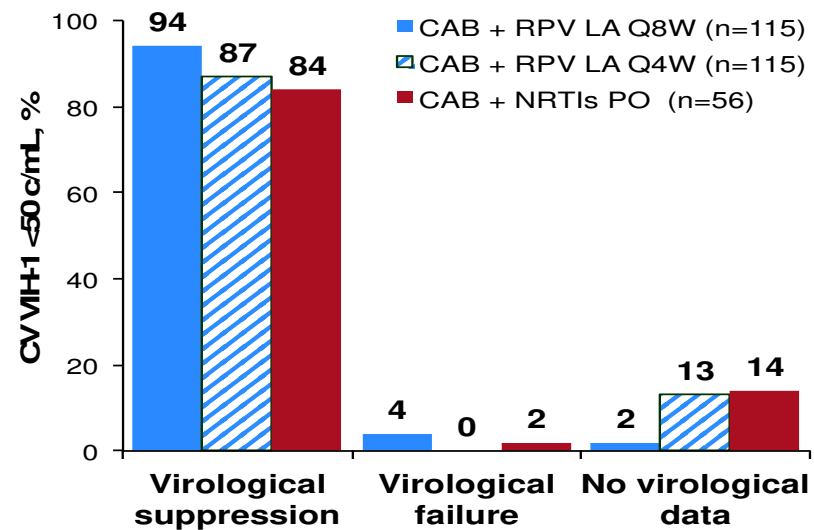


- ABC/3TC, abacavir/lamivudine; ALT, alanine aminotransferase; IM, intramuscular; PO, orally; Q4W, every 4 weeks; Q8W, every 8 weeks; QD, once daily; ULN, upper limit of normal. ^aSubjects who withdrew after at least 1 IM dose entered the long-term follow-up period. ^bSubjects can elect to enter LA Extension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

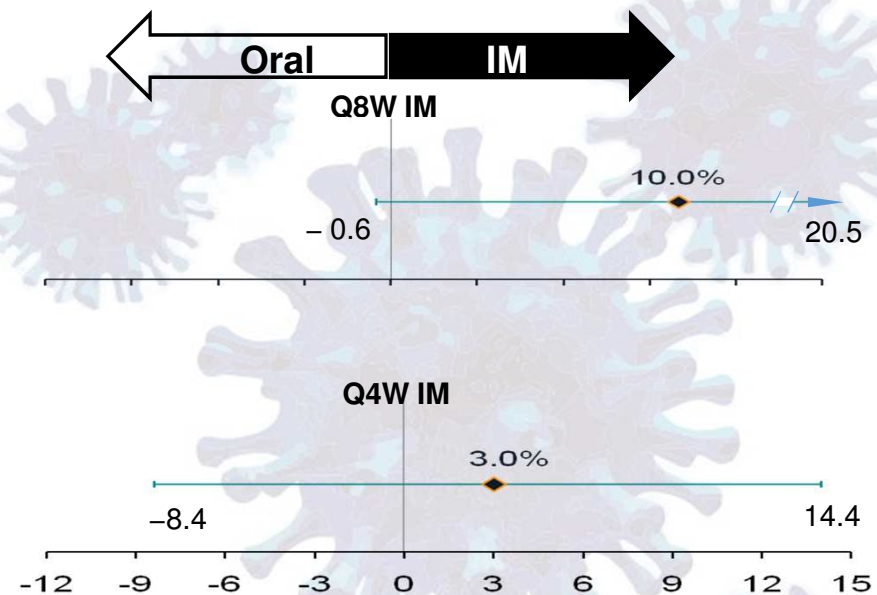
New Strategies: Long acting regimens

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

Virological Response



Differences in treatment (IC 95%)



Conclusions

Year in Infectious Diseases 2017: HIV

- **Control of the HIV-epidemic**
 - Improvement in the overall figures for HIV worldwide
 - Still large differences in Eastern and Western Europe
- **Coinfections**
 - New options for treatment of latent infections and XDR tuberculosis
 - Treatment as prevention proved to be successful in the control of HCV spread
- **Antiretroviral therapy**
 - Guidelines tend to coincide regarding when to start and what to start
 - New drugs in the short-, mid-, and long-term
 - New strategies are being designed to treat HIV

