JORNADAS DOCENTES RIS

"VIH/Sida en 2022: avances en ciencia básica y clínica"
Coordinación: Santiago Moreno, Félix Gutiérrez y Pepe Alcamí

Presente y futuro del TAR: el cambio desde el STR a las pautas long-acting

4 de octubre de 2022

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50 ANOS HOSPITAL PÚBLICO A CORUÑA

SERVIZO GALEGO DE SAÚDE

ÁREA SANITARIA DA CORUÑA E CEE

inibic instituto de investigación biomédica de a coruña

BIOBANCO A Coruña

CONFLICTO DE INTERESES

- En los últimos cinco años he recibido honorarios como ponente y/o recibido ayudas para la investigación de:
  - Abbvie
  - Gilead
  - Janssen
  - MSD
  - Viiv

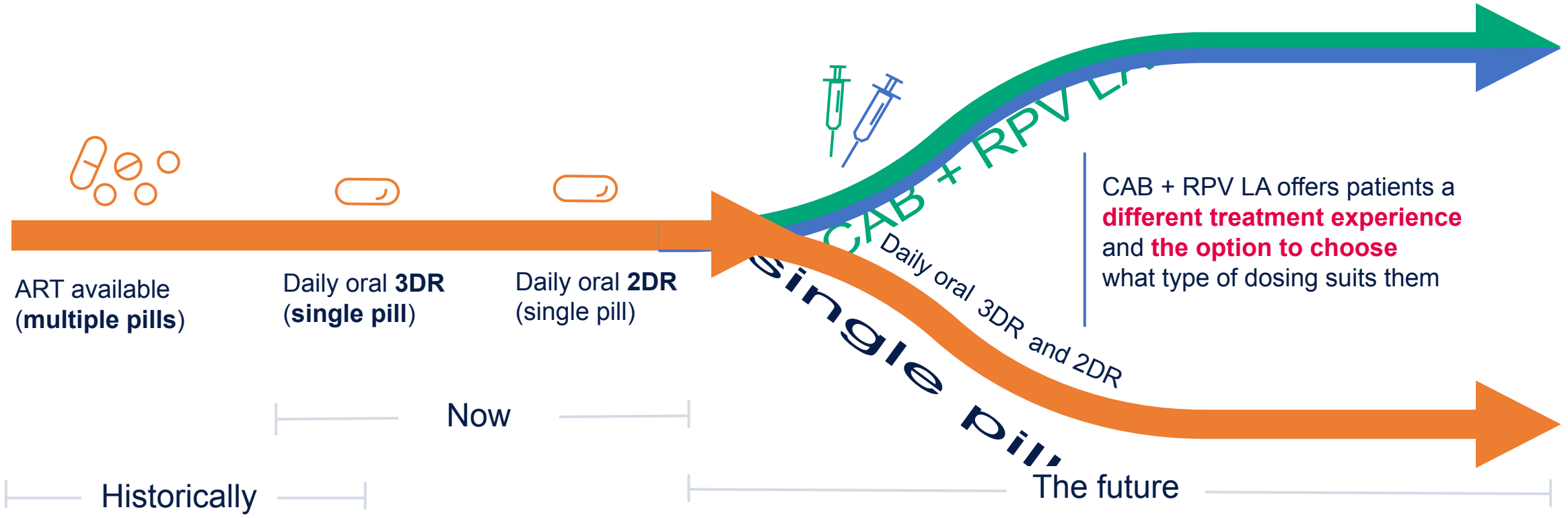
- No tengo ningún conflicto de intereses en esta exposición.
- Recibo honorarios por esta actividad.

TAR actual

- **Eficacia:** >90-95% con el objetivo de CV indetectable. ¿Otros objetivos?
- **Sencillo y cómodo:**
  - Varios STR, comprimidos pequeños.
  - Varios con pocos o nulos requerimientos dietéticos.
  - Pocas interacciones y bien conocidas. (www.hiv-druginteractions.org)
- **Muy Robusto:** pocos fracasos y con pocas consecuencias.
- **Tolerancia:** discontinuaciones de los TAR modernos por EA 0-5%.

TAR actual

Evolución de la Terapia Antirretroviral (TAR)



2DR, 2-drug regimen; **3DR,** 3-drug regimen

Trezza C, et al. Curr Opin HIV AIDS 2015;10:239–45

¿Por qué es importante explorar nuevas formas de administración del TAR?

- **Eficacia del tratamiento** depende de la adherencia.
  - ✔ Para el paciente.
  - ✔ Tratamiento como prevención (TasP: “Treatment as Prevention”).

- Se precisan **altos niveles de adherencia** para que el tratamiento “funcione” (objetivo: carga vírica indetectable).

- **Barreras para una buena adherencia**: salud mental, abuso de sustancias, efectos secundarios, capacidad del paciente para manejar su medicación, …

Chesney MA. Factors affecting adherence to antiretroviral therapy. Clin Infect Dis. 2000;30(Supplement 2):S171–S176176
Kagee A, Remien RH, Berkman A, Hoffman S, Campos L, Swartz L. Structural barriers to ART adherence in Southern Africa: challenges and potential ways forward. Global public health. 2011;6(1):83–97.
Reda AA, Biadgilign S. Determinants of adherence to antiretroviral therapy among HIV-infected patients in Africa. AIDS Res Treat. 2012;2012:574656.

¿Necesitamos más?

Anthony Fauci

Barriers to Daily Pill-Taking

- Substance use
- Housing insecurity
- Food insecurity
- Mental illness
- Forgetfulness
- Stigma
- “Pill fatigue”
- Other structural barriers

ONUSIDA

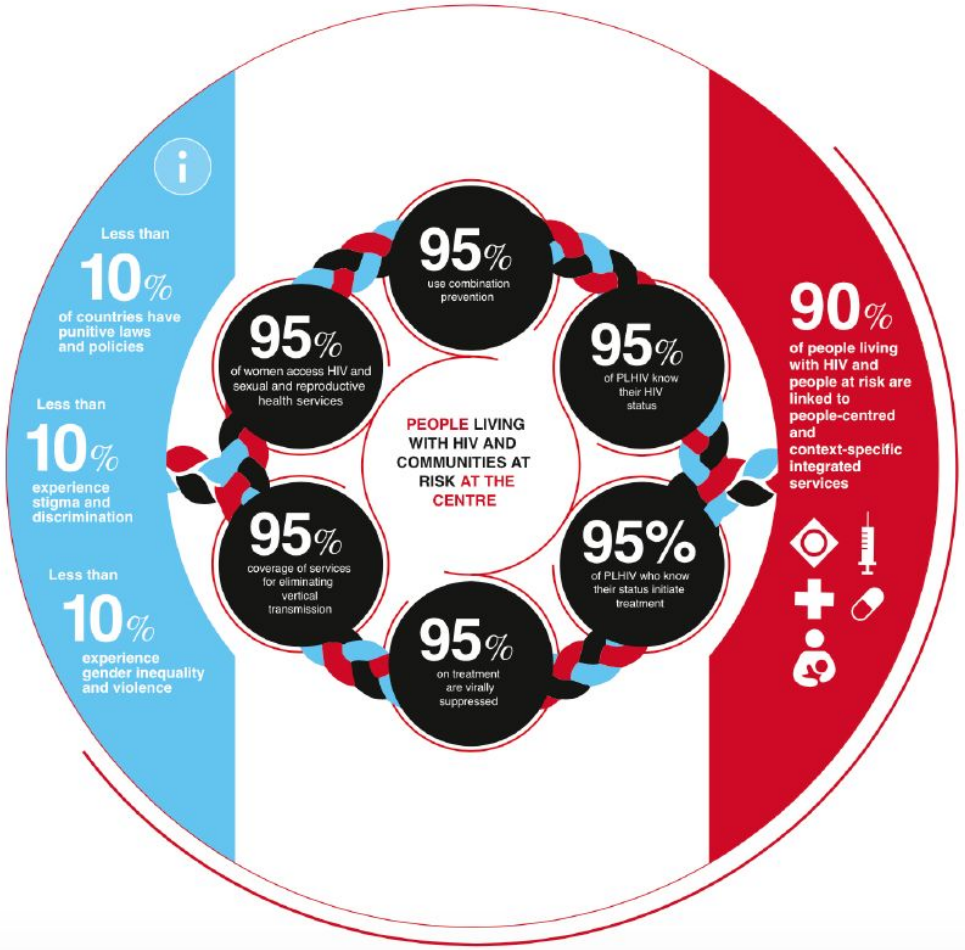
UNAIDS

ABOUT 2025 TARGETS PROCESS DOWNLOAD REPORT

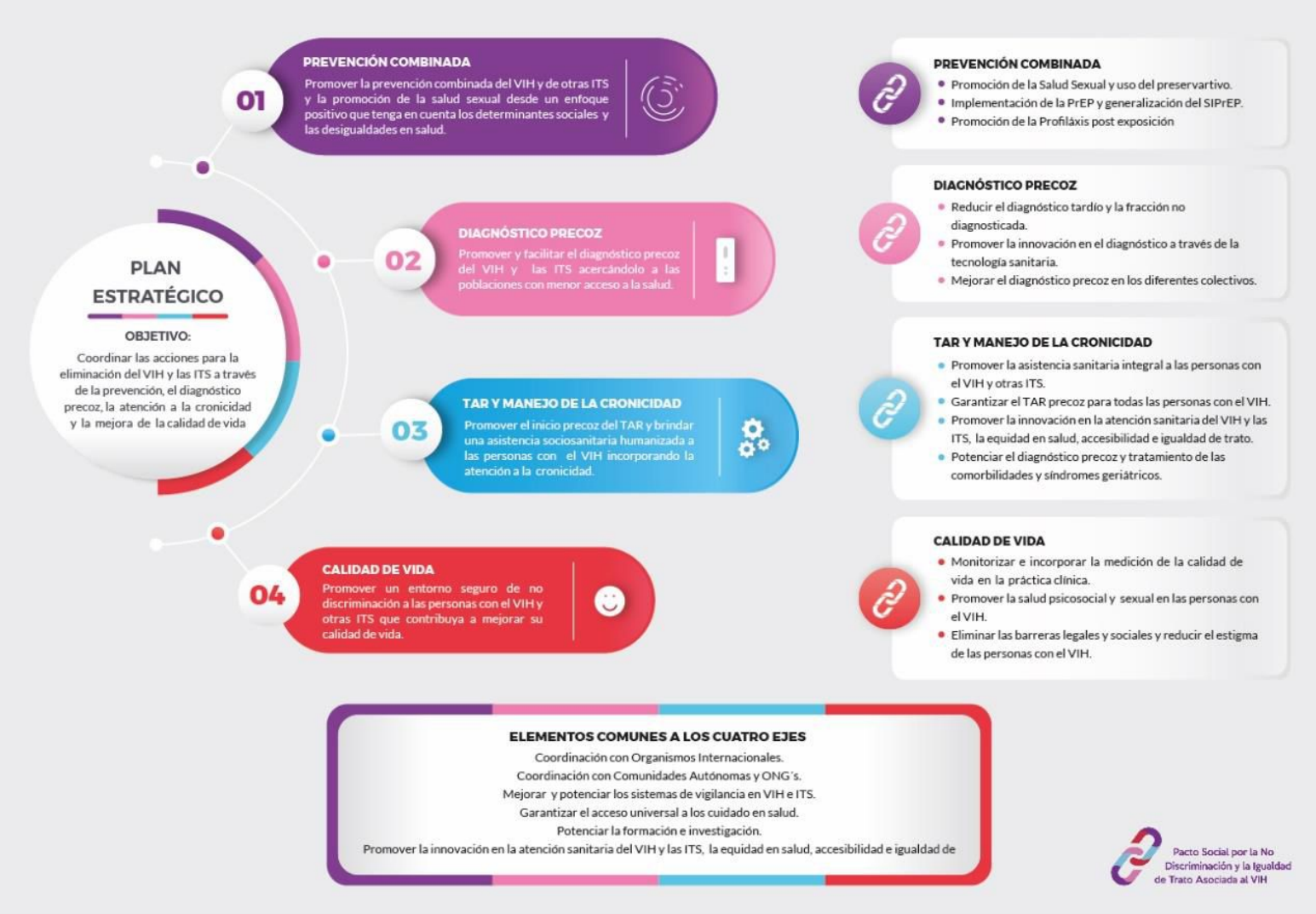
2025 AIDS TARGETS

PUTTING PEOPLE LIVING WITH HIV AND COMMUNITIES AT RISK AT THE CENTRE

THE 10s THE 95s THE INTEGRATION



Plan Nacional SIDA



Calidad de vida

- **RAE: “Conjunto de condiciones que contribuyen a hacer agradable y valiosa la vida”**.
- Va más allá del ámbito sanitario.
- Tiene un componente subjetivo, de percepción.
- Su evaluación probablemente precisa un enfoque múltiple.

Estigma

REAL ACADEMIA ESPAÑOLA

estigma

Del lat. *stigma* 'marca hecha en la piel con un hierro candente', 'nota infamante', y este del gr. στίγμα *stígma*.

1. m. Marca o señal en el cuerpo.

2. m. Desdoro, afrenta, mala fama.

3. m. Huella impresa sobrenaturalmente en el cuerpo de algunos santos extáticos, como símbolo de la participación de sus almas en la pasión de Cristo.

4. m. Marca impuesta con hierro candente, bien como pena infamante, bien como signo de esclavitud.

ESTIGMA SOCIAL:
En sociología, estigma es una **condición, atributo, rasgo o comportamiento que hace que la persona portadora sea incluida en una categoría social hacia cuyos miembros se genera una respuesta negativa y se la vea como inaceptable o inferior.**

El concepto fue acuñado en 1963 por el sociólogo canadiense Erving Goffman, en su reconocido libro del mismo título, en que precisa la noción sociológica del término como pertenencia a un grupo social menospreciado (grupo étnico, religión, nación, etc.).

El estigma puede impactar en todos los escalones de la cascada del cuidado del VIH, afectando la salud de las PVV a largo plazo

Falta de apoyo social y familiar
Rechazo social
Dificultad para acceder a servicios de salud

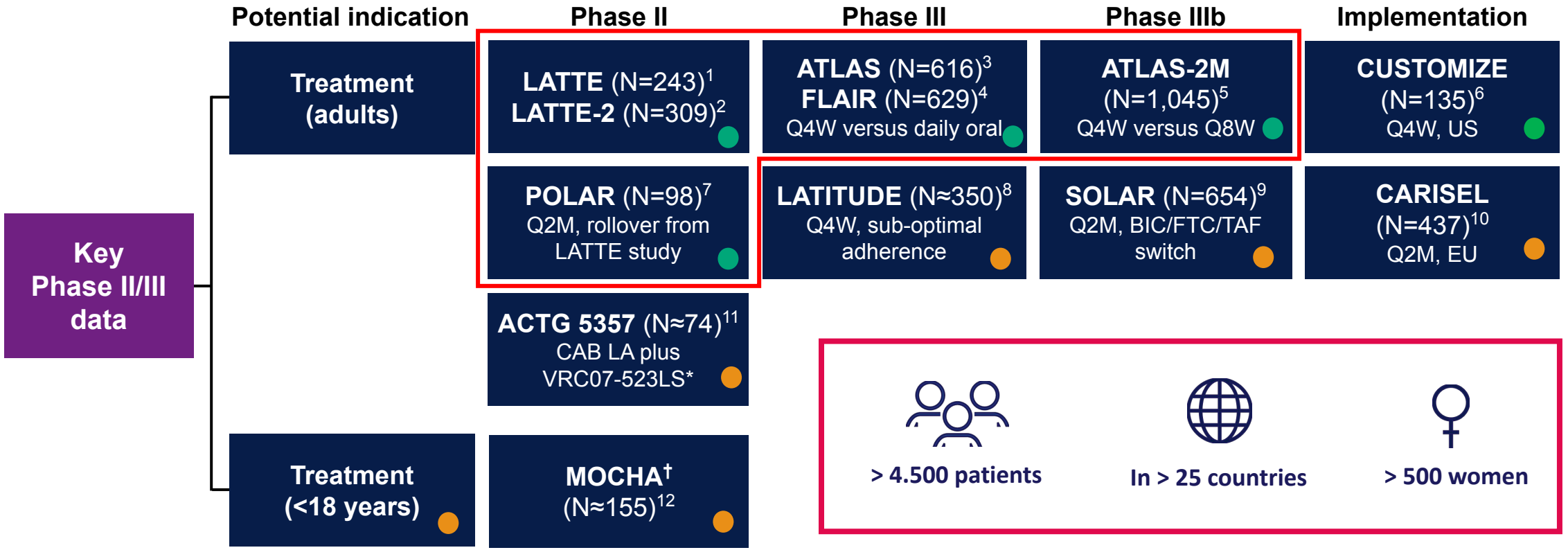
Esquema adaptado de: UNAIDS Confronting discrimination 2017. Available from: https://www.unaids.org/en/resources/documents/2017/confronting-discrimination. Last accessed: July 2020

Referencias: 1. UNAIDS Confronting discrimination 2017. Available from: https://www.unaids.org/en/resources/documents/2017/confronting-discrimination. Last accessed: July 2020; **2.** Mahamboro DB, et al. *Int J Environ Res Public Health* 2020,17:636.

Fármacos de acción prolongada

- **Cabotegravir/Rilpivirina**
- **Islatravir**
- **Islatravir/Doravirina (MK-8591A)**
- **Islatravir/MK-8507**
- **Lenacapavir**
- **Ibalizumab**
- **Implantes**

Programa de desarrollo clínico de CAB + RPV LA



Primary end-point achieved

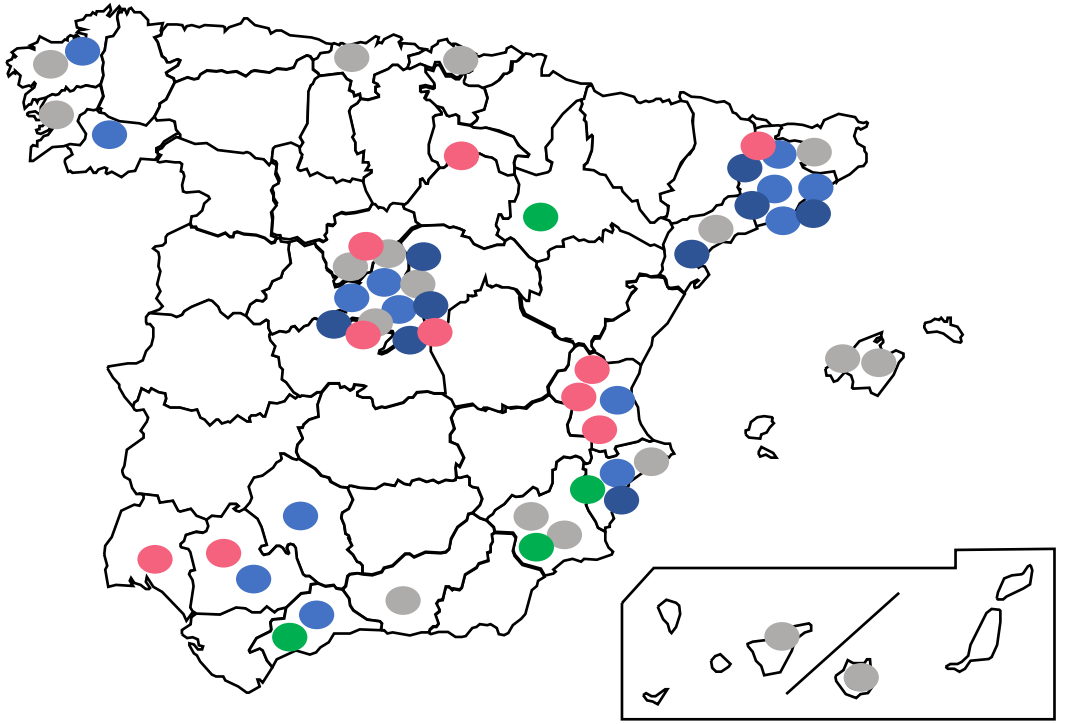
On-going

*CAB LA Q4W IM injection in combination with VRC07-523LS (a broadly neutralizing monoclonal antibody) Q8W IV infusion
†MOCHA (IMPAACT 2017) Phase I/II study will provide supportive information for HIV prevention in adolescents

1. Margolis DA, et al. Lancet Infect Dis 2015;15:1145–55. 2. Margolis DA, et al. Lancet 2017;390:1499–510. 3. Swindells S, et al. N Engl J Med 2020;382:1112–23.4. Orkin C, et al. N Engl J Med 2020;382:1124–35. 5. Overton ET, et al. Lancet. 2021;396:1994-2005.
6. CUSTOMIZE (209493). Available at: https://clinicaltrials.gov/ct2/show/NCT04001803 (accessed April 2022). 7. POLAR (209035). https://clinicaltrials.gov/ct2/show/NCT03639311 (accessed April 2022). 8. LATITUDE (ACTG 5359). Available at: https://clinicaltrials.gov/ct2/show/NCT03635788 (accessed April 2022). 9. SOLAR (213500). Available at: https://clinicaltrials.gov/ct2/show/NCT04542070 (accessed April 2022). 10. Hocqueloux et al. EACS 2021; Virtual and London, UK. Poster PE2/37. 11. ACTG 5357. Available at: https://clinicaltrials.gov/ct2/show/NCT03739996 (accessed April 2022).12. MOCHA (IMPAACT 2017). Available at: https://clinicaltrials.gov/ct2/show/NCT03497676 (accessed April 2022)

Desarrollo clínico en España

44 DIFFERENT CENTERS INVOLVED IN THE CLINICAL DEVELOPMENT OF CAB + RPV LA

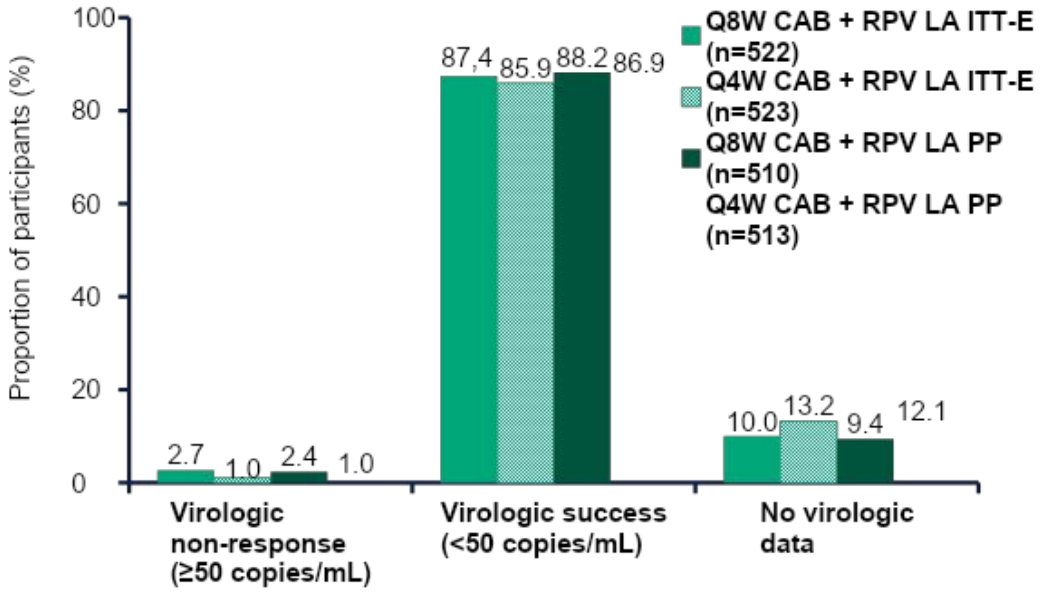


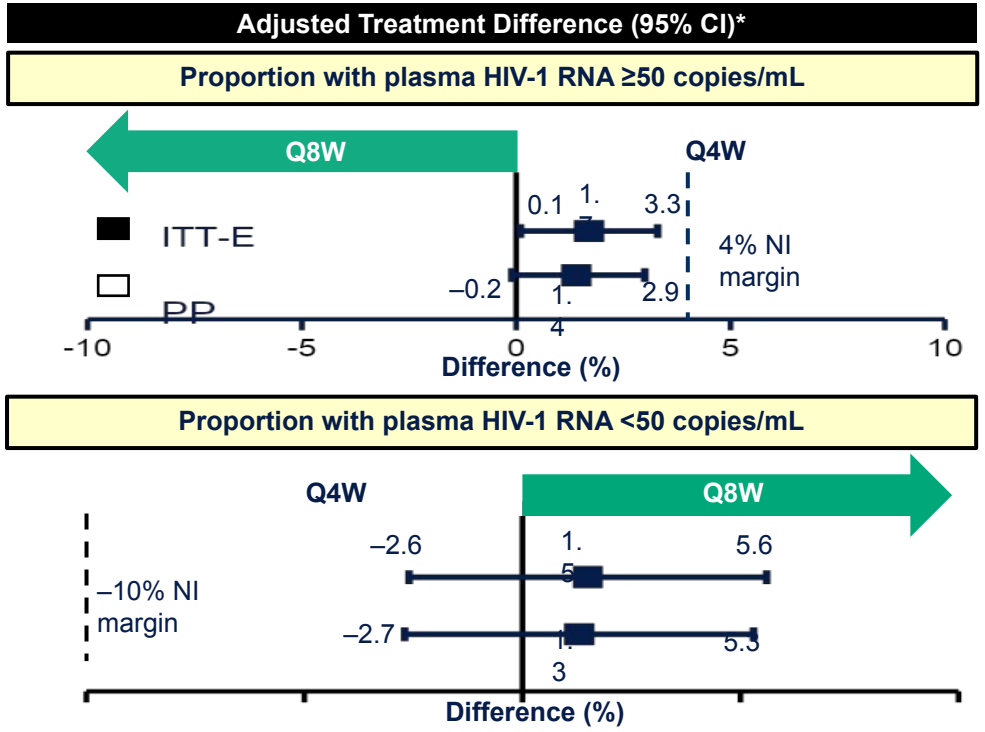
- LATTE-2[1]
- ATLAS-2M & ATLAS[4,2]
- FLAIR[3]
- CARISEL[5]
- SOLAR[6]

Spain contribution to CAB + RPV LA CT	
CAB + RPV LA studies	CENTERS
Phase II	9
Phase III (FLAIR, ATLAS, ATLAS-2M, CARISEL and SOLAR)	42

1. Margolis DA, et al. Lancet 2017;390:1499–510. 2. Swindells S, et al. N Engl J Med 2020;382:1112–23. 3. Orkin C, et al. N Engl J Med 2020;382:1124–35. 4. Overton ET, et al. Lancet. 2021;396:1994-2005. 5. CARISEL (213199). Available at: https://clinicaltrials.gov/ct2/show/NCT04399551 (accessed April 2022) 6. SOLAR (213500). Available at: https://clinicaltrials.gov/ct2/show/NCT04542070 (accessed April 2022)

ATLAS-2M: eficacia a 152 semanas





- Baseline characteristics were similar between arms; 27% (n=280) of participants were female at birth, median (range) age was 42 (19–83), 20% (n=211) had a BMI ≥30 kg/m^2, and 37% (n=391) had prior CAB + RPV exposure[1]
- Noninferiority between Q8W and Q4W was confirmed for pre-specified analyses of HIV-1 RNA ≥50 and <50 copies/mL
- Results for the pre-specified per-protocol population were consistent with those for the ITT-E population

*Based on CMH stratified analysis adjusting for the following baseline stratification factor: prior exposure to CAB + RPV (0 weeks, 1–24 weeks, >24 weeks).
CAB, cabotegravir; CI, confidence interval; CMH, Cochran–Mantel–Haenszel; ITT-E, intention-to-treat exposed; LA, long-acting; NI, noninferiority; PP, per protocol; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine.

1. Overton et al. *Lancet*. 2020;396:1994-2005.

ATLAS-2M: seguridad a 152 semanas

Parameter, n (%)	Q8W (n=522)	Q4W (n=523)
Any AE	469 (90)	490 (94)
Drug-related AEs	142 (27)	167 (32)
Any Grade ≥3 AE	66 (13)	63 (12)
Drug related*	10 (2)	10 (2)
Leading to withdrawal	17 (3)	20 (4)
Drug related	6 (1)	13 (2)
Any serious AE	48 (9)	44 (8)
Drug related	3 (<1)	3 (<1)

- Safety profiles at Week 152 were consistent with the previous analyses, with no new significant safety information observed
- Since Week 96, excluding ISRs, there were two participants with drug-related AEs leading to withdrawal (both Q4W, lipoatrophy and pyrexia) and no drug-related serious AEs

- *One drug-related AE in each arm was Grade 4 (Q8W, acute pancreatitis [n=1]; Q4W, increased blood creatine phosphokinase [n=1]); none were Grade 5.
AE, adverse event; ISR, injection site reaction; Q4W, every 4 weeks; Q8W, every 8 weeks.

Overton et al. CROI 2022; Virtual. Poster 479.

ATLAS-2M: seguridad a 152 semanas

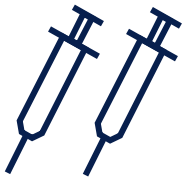
	Q8W (n=522)	Q4W (n=523)
Participants who received ≥1 injection, n (%)	516 (99)	517 (99)
Number of injections	20,563	39,478
ISR events, n*	4168	5494
Injection site pain, n (% of injections)†	3189 (16)	4180 (11)
Injection site nodule, n (% of injections)†	259 (1)	457 (1)
Grade 3, n (% of ISR events)‡	54 (1)	50 (1)
Median duration, days (IQR)	3 (2, 5)	3 (2, 5)
Participants withdrawing for injection-related reasons, n (% of participants with injections)	8 (2)	13 (3)

- ISRs were the most common AEs; most were mild to moderate in severity (99%, n=9555/9662), short-lived (median duration 3 days), with few participants discontinuing due to injection-related reasons
- Three participants withdrew due to injection-related reasons between Week 96 and Week 152 (Q8W, n=1; Q4W, n=2)

*Each ISR event was counted separately. A participant may have had multiple ISR events following a single injection. †Those occurring with ≥1% of injections in either treatment arm are shown.
‡There were no Grade 4 or Grade 5 ISRs. AE, adverse event; IQR, interquartile range; ISR, injection site reaction; Q4W, every 4 weeks; Q8W, every 8 weeks.

Seguridad

95% of drug-related AEs were mild-to-moderate in severity[1–3]



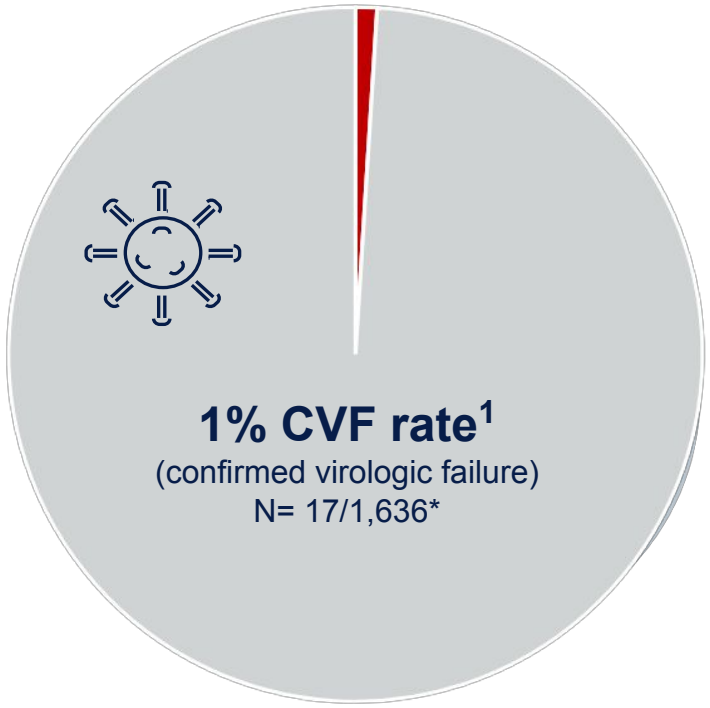
Safety and tolerability was similar between monthly and every-two-month dosing[3]

Only 2% of participants withdrew due to AEs while on CAB + RPV LA (N=1,636*)[1–3]

*ATLAS n=308; FLAIR n=283; ATLAS-2M n=1,045

1. Orkin C, et al. N Engl J Med 2020;382:1124–35. 2. Swindells S, et al. N Engl J Med 2020;382:1112–23. 3. Overton ET, et al. Lancet 2021: 396;1994-2005.

CVF and resistance with CAB + RPV LA at Week 48 (FLAIR, ATLAS and ATLAS-2M)



	ATLAS & FLAIR[2]		ATLAS-2M[3]	
n (%)	CAB + RPV LA Q4W N=591	Daily oral ARV N=591	CAB + RPV LA Q8W n=522	CAB + RPV LA Q4W n=523
Participants with CVF	6† (1)	7 (1)	8 (<2)	2 (<1)

- INI mutation pattern: Q148R/Q, G140R, N155H, E138E/K[2–5]
- NNRTI mutation pattern: E138E/A/K/T, K101E, K103N, Y188L, V108I, M230L[2–5]
- 50% (8/16) came from Russian sites where:[2–5]
  - A1/A6 subtype is common[6,7]
  - L74I is a common polymorphism[7]

*ATLAS n=308; FLAIR n=283; ATLAS-2M n=1,045[1,3]
†An additional participant in FLAIR was excluded because CVF occurred prior to receiving LA injection (withdrawn to false-positive pregnancy test)[2,4]

1. Cutrell AG, et al. AIDS 2021;35:1333–42. 2. Rizzardini G, et al. J Acquir Immune Defic Syndr 2020;85:498–506. 3. Overton ET, et al. Lancet 2021;396:1994–2005. 4. Orkin C, et al. N Engl J Med 2020;382:1124–35. 5. Swindells S, et al. N Engl J Med 2020;382:1112–23. 6. Hemelaar J, et al. Lancet Infect Dis 2019;19:143–55 (incl. suppl.). 8. Lapovok I, et al. Curr HIV Res 2017;15:318–26.

EPB180

Long-Acting Cabotegravir + Rilpivirine in Older Adults: Pooled Phase 3 Week 96 Results

Emilie R. Elliot[1], Ronald D'Amico[2], Andrew Clark[1], Joseph W. Polli[2], Louise Garside[3], Jeremy Roberts[4], Paul D. Benn[1], Susan L. Ford[5], Simon Vanveggel[6], Bryan Baugh[7], Jean van Wyk[1]

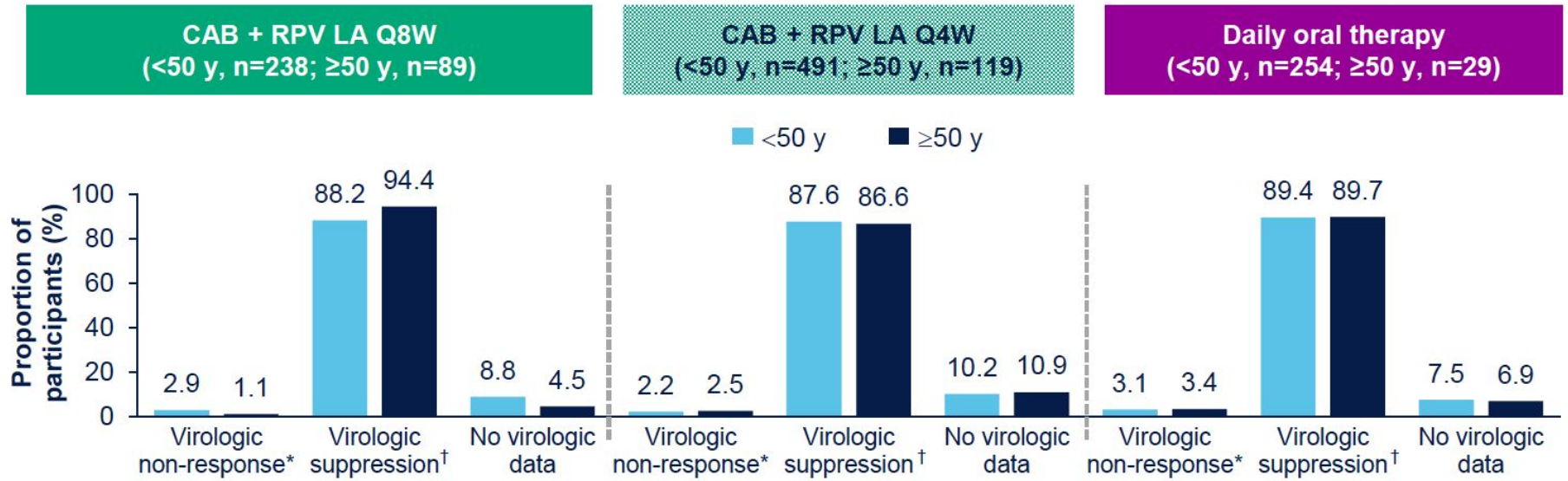
[1]ViiV Healthcare, Brentford, United Kingdom; [2]ViiV Healthcare, Research Triangle Park, NC, United States; [3]PHASTAR, Macclesfield, United Kingdom; [4]GlaxoSmithKline, Mississauga, ON, Canada; [5]GlaxoSmithKline, Research Triangle Park, NC, United States; [6]Janssen Research & Development, Beerse, Belgium; [7]Janssen Research & Development, Titusville, NJ, United States

Key Takeaways

- We present longer-term efficacy, safety, adherence, and treatment satisfaction outcomes through Week 96 for the Phase 3/3b ATLAS-2M and FLAIR studies stratified by age group (<50 years [y] and ≥50 y).
- Efficacy and tolerability were similar across participants aged <50 y and ≥50 y, and support the use of cabotegravir + rilpivirine long-acting (CAB + RPV LA) dosed monthly or every 2 months as a complete regimen for the maintenance of HIV-1 virologic suppression in adults, irrespective of age.

CAB/RPV Adultos >50 años semana 96

Figure 2. Virologic Outcomes at Week 96



*HIV-1 RNA ≥50 copies/mL per FDA Snapshot algorithm.. †HIV-1 RNA <50 copies/mL per FDA Snapshot algorithm.
CAB, cabotegravir; FDA, U.S. Food and Drug Administration; LA, long-acting; Q4W, every 4 weeks; Q8W, every 8 weeks;
RPV, rilpivirine; y, years.

- Virologic outcomes were similar across treatment arms and age groups; rates of virologic suppression were high (87–94%) and rates of non-response were low (1–3%), per the FDA Snapshot algorithm (**Figure 2**).
- CVF rates were similarly low across treatment arms and age groups.
  - Q8W: <50 y, 2.1% (n=5); ≥50 y, 1.1% (n=1); Q4W: <50 y, 0.8% (n=4); ≥50 y, 1.7% (n=2); daily oral therapy: <50 y, 1.6% (n=4); ≥50 y, 0%.

CAB/RPV Adultos >50 años semana 96

Table 2. AE Profiles (Excluding ISRs) Through Week 96

Parameter	CAB + RPV LA Q8W, n (%)		CAB + RPV LA Q4W, n (%)		Daily oral therapy, n (%)	
	<50 y (n=238)	≥50 y (n=89)	<50 y (n=491)	≥50 y (n=119)	<50 y (n=254)	≥50 y (n=29)
Any AE	199 (84)	78 (88)	450 (92)	113 (95)	217 (85)	25 (86)
Drug-related	65 (27)	19 (21)	166 (34)	35 (29)	29 (11)	4 (14)
AEs leading to withdrawal	9 (4)	2 (2)	20 (4)	6 (5)	4 (2)	0
Drug-related	5 (2)*	1 (1)†	11 (2)*	4 (3)†	3 (1)*	0
Any serious AE	13 (5)	8 (9)	29 (6)	11 (9)	18 (7)	4 (14)
Drug-related‡	1 (<1)	0	3 (<1)	1 (<1)	0	0

*Includes: Q8W, headache (n=2), hyperhidrosis, malaise, fatigue, maculopapular rash, osteonecrosis, and pyrexia; Q4W, fatigue (n=2), abnormal dreams (n=2), depression (n=2), discomfort, diarrhea, vomiting, myocardial infarction, dizziness, hypersensitivity, nausea, vertigo, increased transaminases, drug hypersensitivity, chills, disturbance in attention, hyperhidrosis, myalgia, pyrexia, sleep disorder, and insomnia; daily oral therapy, disturbance in attention, dysarthria, amnesia, renal failure, dizziness, fatigue, and nausea. All occurred in one participant each unless specified. More than one reason could have been reported per participant.
†Includes: Q8W, asthenia; Q4W, depression, influenza, headache, hyperhidrosis, nausea, presyncope, disturbance in attention, and sleep disorder. All occurred in one participant each. More than one reason could have been reported per participant.
‡Includes hypersensitivity and suspected (partial) intravenous administration of RPV; drug hypersensitivity; osteonecrosis; right knee monoarthritis; and myocardial infarction. The latter three were not considered drug related by sponsor. All occurred in one participant each.
AE, adverse event; CAB, cabotegravir; ISR, injection site reaction; LA, long-acting; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine; y, years.

- The frequency of drug-related AEs, serious AEs, and AEs leading to withdrawal were broadly comparable between age groups for both LA regimens (**Table 2**).

Weight gain & Lipid changes: ATLAS-2M & FLAIR

Background:

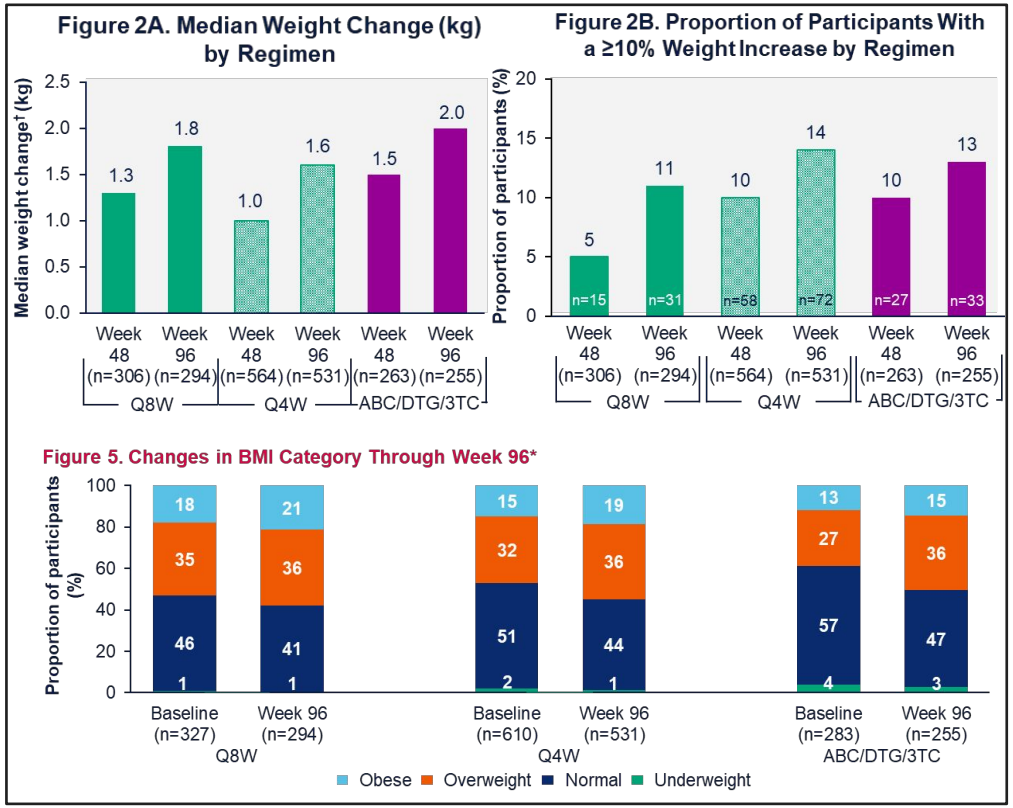
- **Pool de datos de pacientes que recibieron CAB/RPV LA** Q4W o Q8W (n=937) o tratamiento oral ABC/DTG/3TC (n=283) durante 96 semanas en los estudios FLAIR y ATLAS-2M

Resultados:

- **Análisis de los cambios en: TC, HDL, LDL, TG y ratio TC/HDL**. Los resultados son similares entre grupos de tratamiento y de edad.

Conclusiones:

- **Cambios de peso de carácter menor**
- Los aumentos de peso ≥10% y cambios de IMC fueron infrequentes y sin cambios lipídicos significativos asociados.
- Aumento peso: Black/African American > Mujeres > Pacientes menores de 50 años.



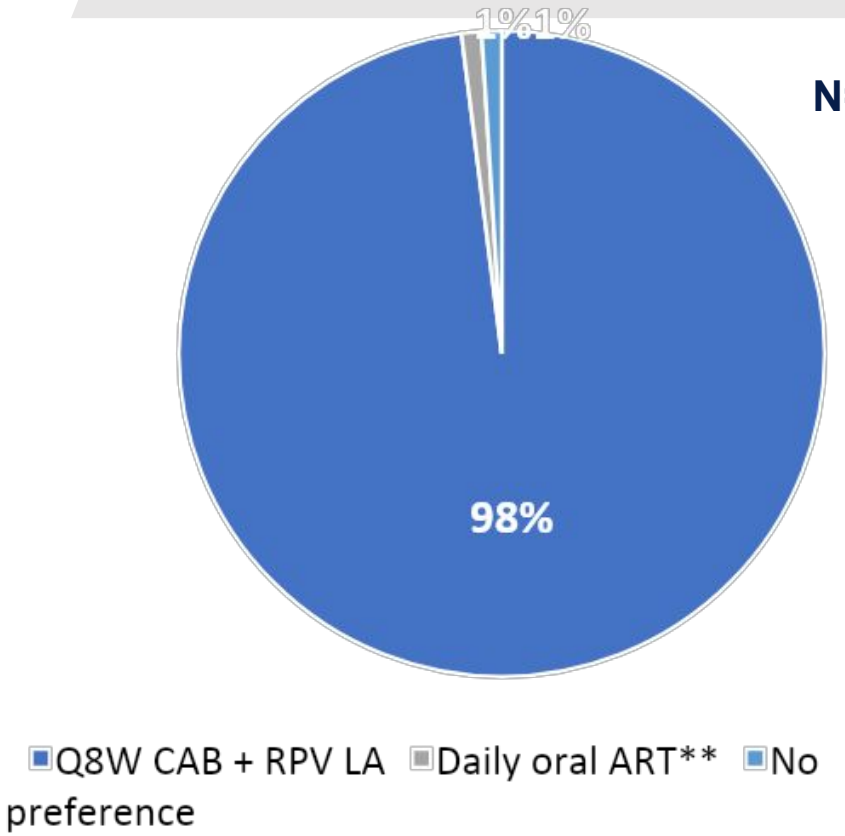
TAKE HOME MESSAGES:

- Primeros datos Provides long term weight gain and lipid data for CAB + RPV LA through 96 weeks
- El aumento peso es similar al de Symtuza a las 96 semanas en el EMERALD (1.8 kg) y AMBER (2.0 kg)

Patel. AIDS 2022 Abstract #EPB183

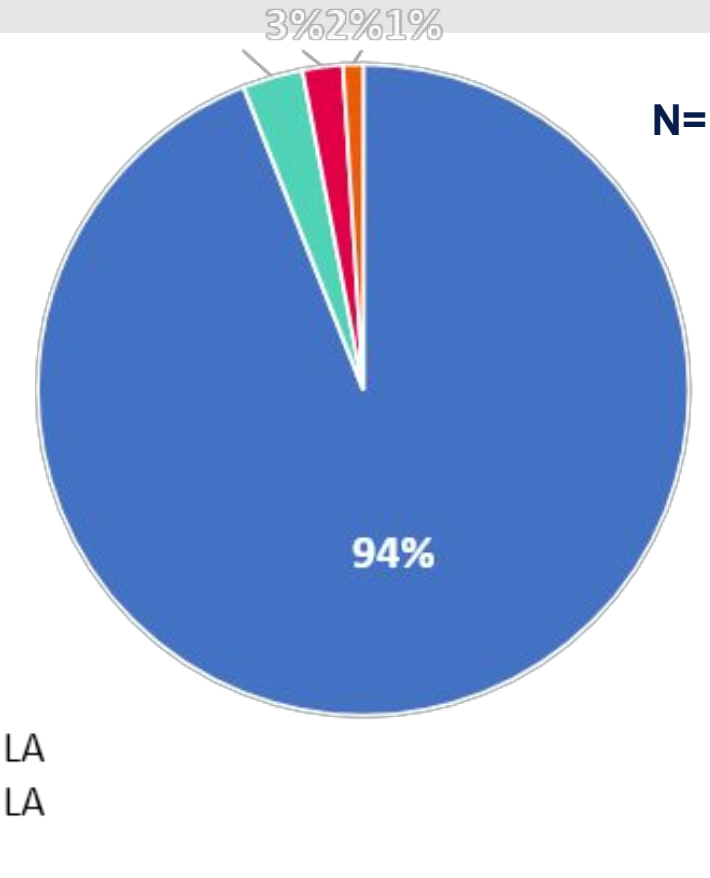
Most participants preferred CAB + RPV LA Q8W dosing over daily oral ART and Q4W dosing in the ATLAS-2M study

Participants on Q8W arm from oral ART (no prior Q4W experience)*



N=306

Participants on Q8W arm with prior Q4W experience in ATLAS*



N=191

*Percentages are calculated out of those participants with recorded response to the preference question
**Daily oral ART refers to CAB + RPV received during the OLI period during either ATLAS-2M or ATLAS

1.Chounta et al. AIDS 2020: Virtual. Poster PEB0261. Available at: https://programme.aids2020.org/PAGMaterial/PPT/3379_2494/PEB0261_Chounta_AIDS%202020_ATLAS-2M%20PRO.pptx (accessed April 2022)

But the injection is a whole other situation. It's just one quick moment and then it's over. You don't have to deal with it every day …like you do with the pills….and in some ways that just makes you have to continue to think about it each time.–Spain, Male trial participant

I love it because I don't have to take a daily medication, so that's just one less thing on my plate that I have to worry about… I definitely feel there's less pressure. I like the injection because it's not a daily, in my face, I have to do this.–U.S., Female trial participant

One day is nothing…it's as if you have a day with a headache. You take ibuprofen and that's it. You put up with it. It's temporary.–Spain, Male trial participant

It might be painful, but it's better than pills.–U.S., Male trial participant

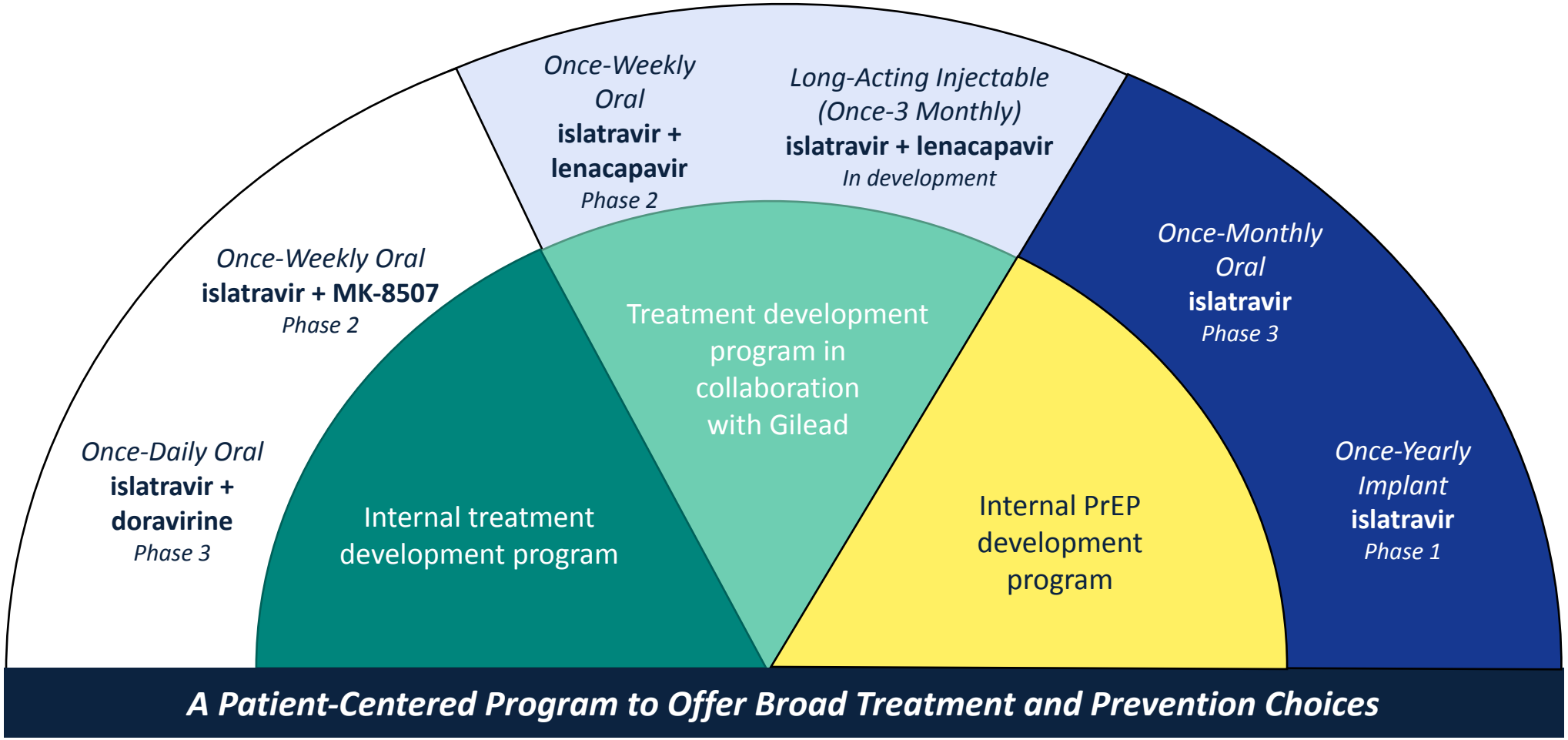
It seems to me that it's much better because you simply don't have to worry about anything. If you go on a trip, you don't have to bring your pills or take anything at all along. You follow your 'normal life.' You come once a month. You get the shot and it's over. You don't have to be thinking everyday … oh I forgot to take the pill. Or …when did I take it last… You just don't worry about anything. In reality, taking the pill everyday keeps it [HIV] present …and the shot is just once a month…you remember it when you come in and the rest of the time you can basically forget it.–Spain, Male trial participant

PLoS One. 2018 Jan 5;13(1):e0190487

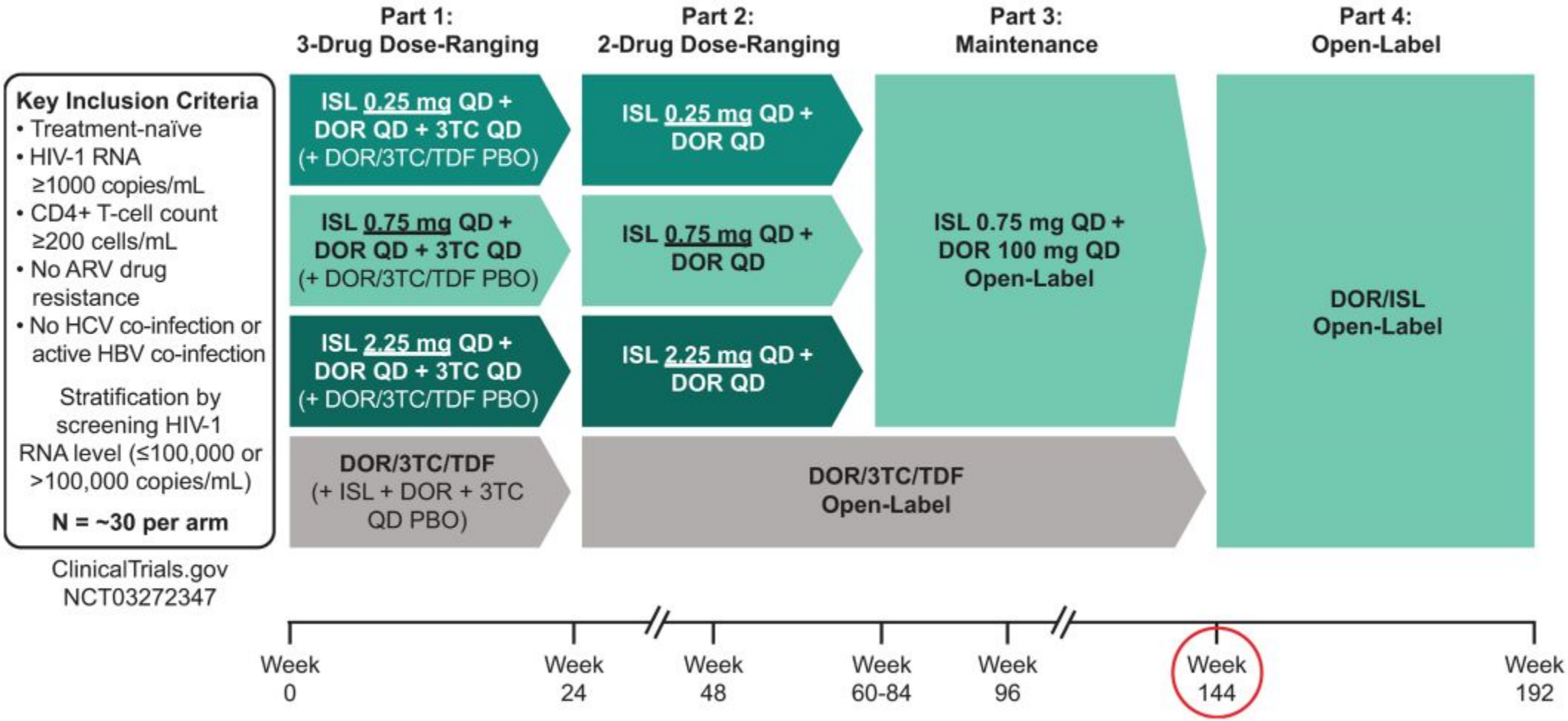
Fármacos de acción prolongada

- Cabotegravir/Rilpivirina
- Islatravir
- Islatravir/Doravirina (MK-8591A)
- Islatravir/MK-8507
- Lenacapavir
- Ibalizumab
- Implantes

Islatravir, desarrollo clínico



MK-8591 Protocol 011: Phase 2 Dose-Ranging Trial of ISL+DOR[a]

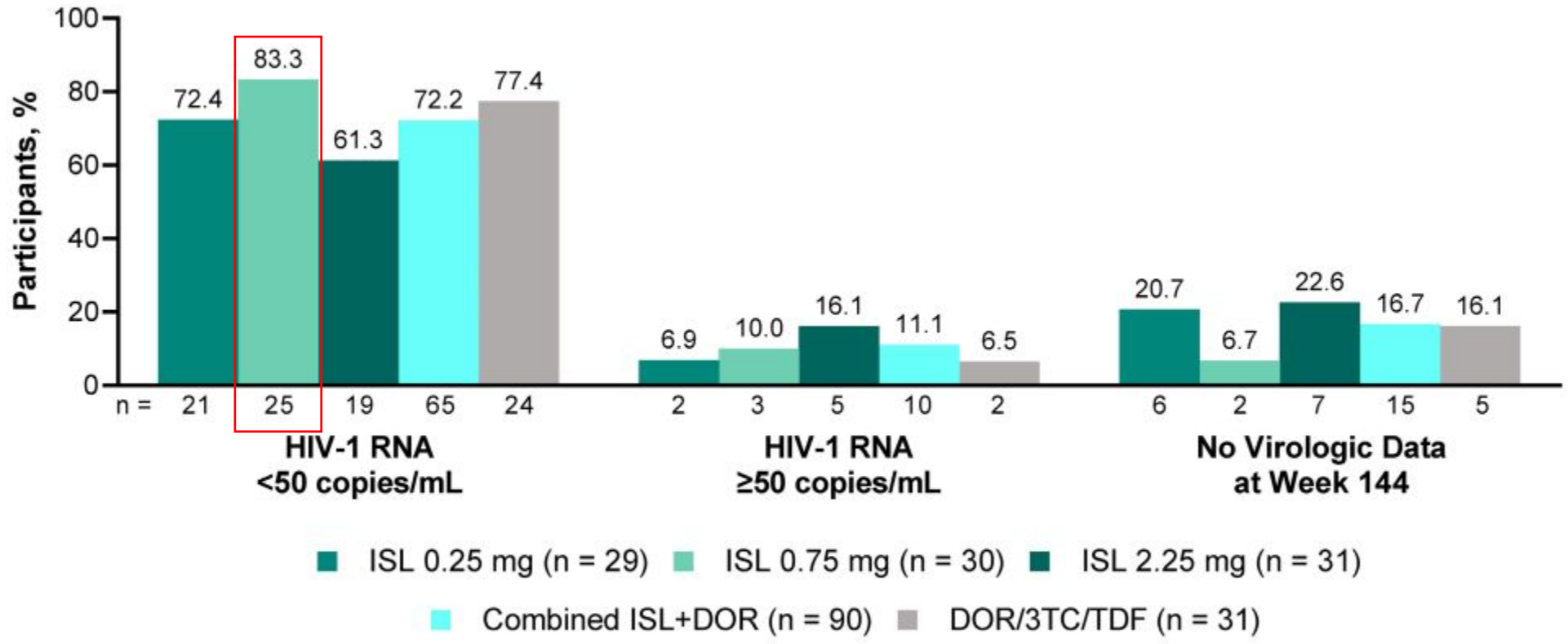


3TC, lamivudine; ARV, antiretroviral; DOR, doravirine; HBV, hepatitis B virus; HCV, hepatitis C virus; ISL, islatravir; PBO, placebo; QD, once daily; TDF, tenofovir disoproxil fumarate.

[a]After 24 weeks of dosing in Part 1 (double-blinded) of the trial, participants who are virologically suppressed (HIV-1 RNA <50 copies/mL) at the Week 20 visit and did not meet any viral failure criteria were eligible to enter Part 2 at Week 24. Participants with HIV-1 RNA levels ≥50 copies/mL at Week 20 remained in Part 1 until their HIV-1 RNA was <50 copies/mL and they did not meet any of the viral failure criteria, at which point they transitioned to Part 2 at their next visit. Part 2 (blinded only to ISL dose) evaluated the 2-drug dose-ranging maintenance phase. Participants receiving ISL+DOR then transitioned to the selected dose (ISL 0.75 mg, open-label) and continued through Week 144 (Part 3). Control group participants received open-label DOR/3TC/TDF from Week 24 through Week 144.

McComsey GA, et al. Abstract presented at: IAS Conference on HIV Science; July 18-21, 2021. Virtual. Abstract # A-IAS2021-01017.

Respuesta virológica 144w (FDA Snapshot)



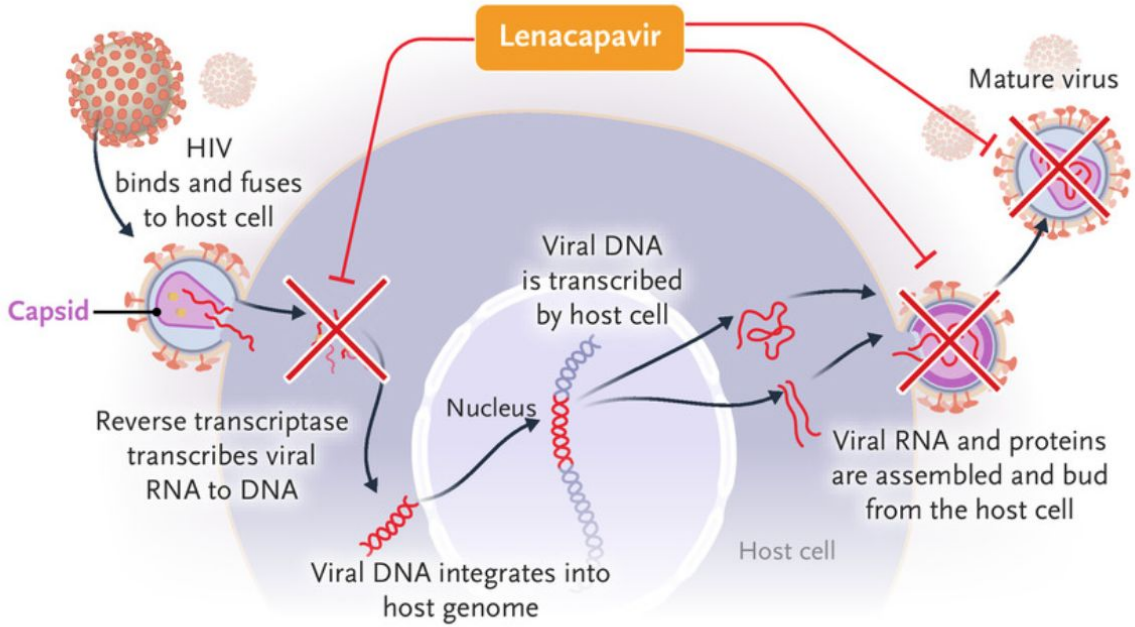
- At Week 144, 72.2% of participants (65/90) in the combined ISL+DOR groups had HIV-1 RNA <50 copies/mL
  - Corresponding values at Week 48 and Week 96 were 85.6% (77/90) and 82.2% of participants (74/90), respectively
- At Week 144, in the ISL 0.75 mg + DOR group (Phase 3 dose), 83.3% of participants (25/30) had HIV-1 RNA <50 copies/mL

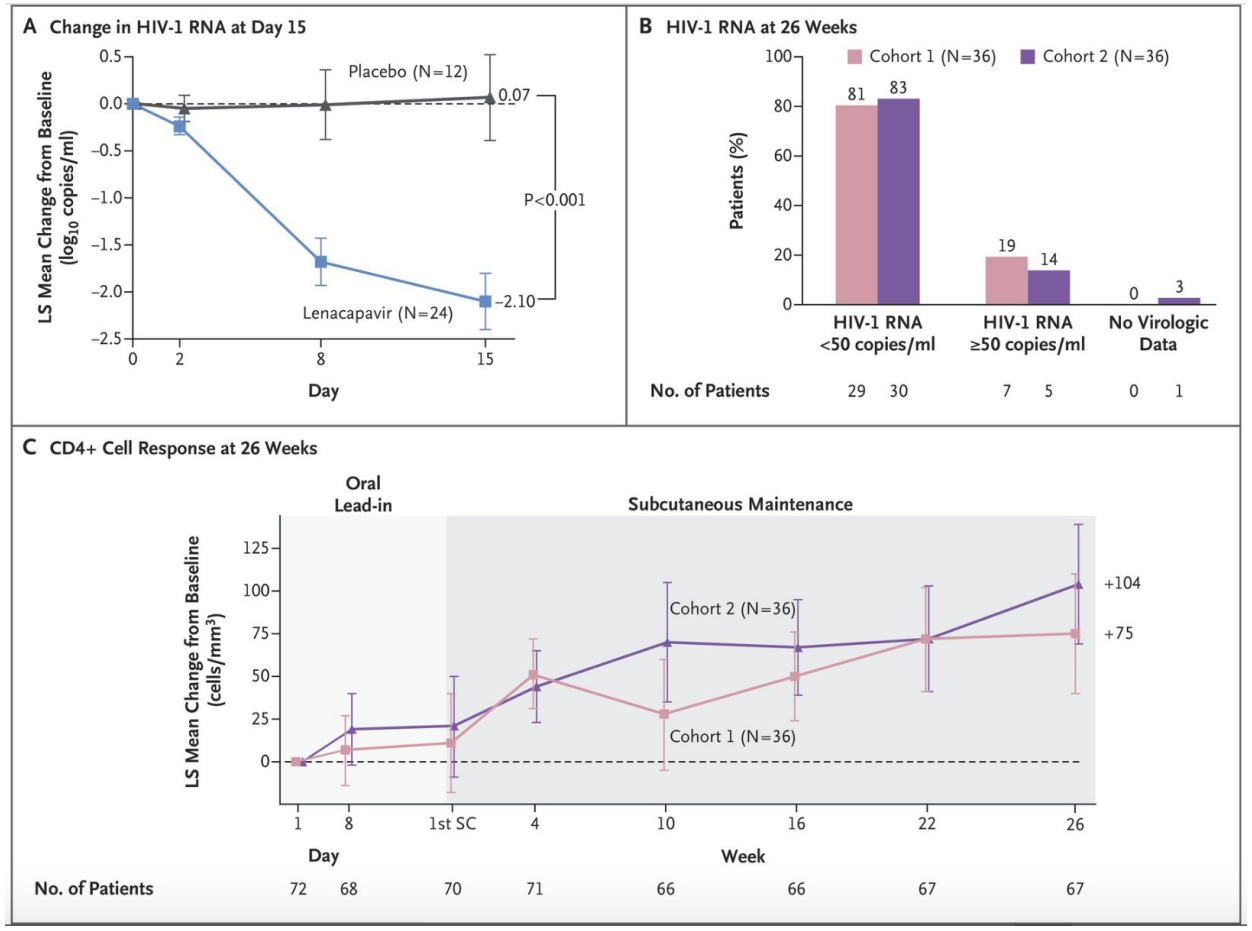
3TC, lamivudine; DOR, doravirine; ISL, islatravir; TDF, tenofovir disoproxil fumarate. NOTE: data shown for 'HIV-1 RNA ≥50 copies/mL' and 'No virologic data at Week 144' reflect corrections made after EACS.

Fármacos de acción prolongada

- Cabotegravir/Rilpivirina
- Islatravir
- Islatravir/Doravirina (MK-8591A)
- Islatravir/MK-8507
- Lenacapavir
- Ibalizumab
- Implantes

Lenacapavir

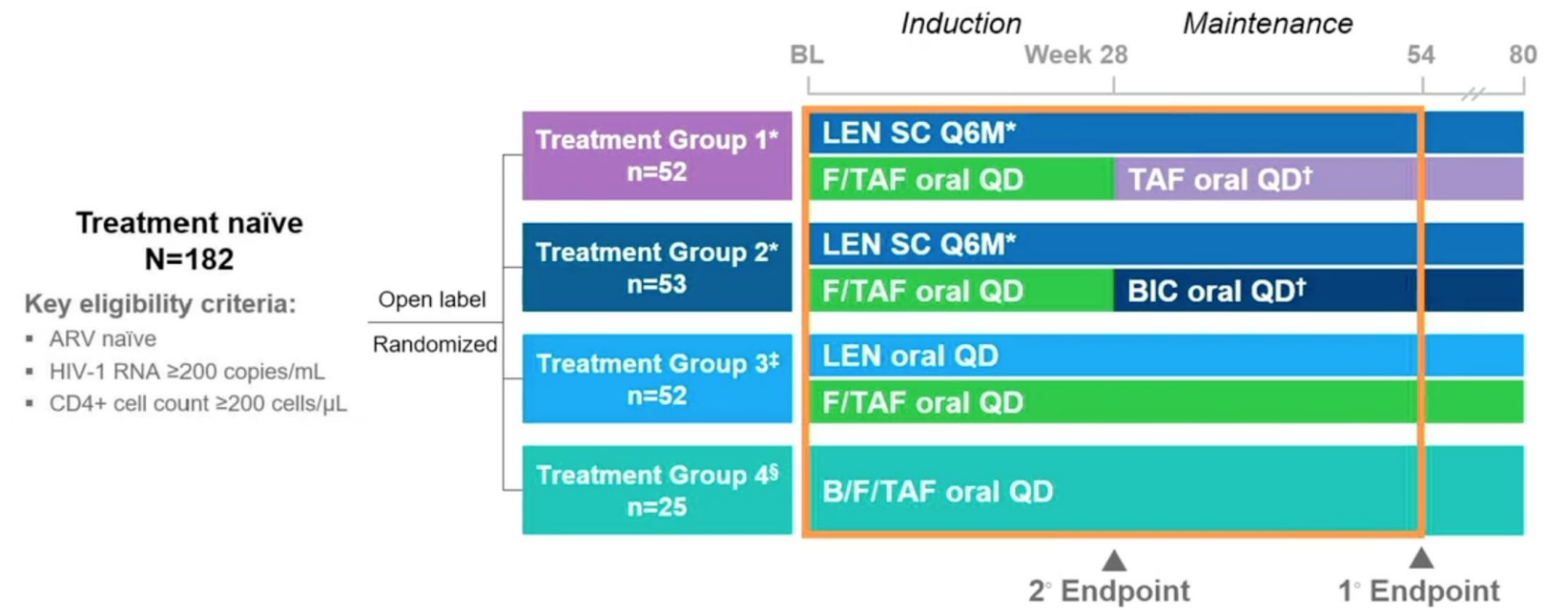




N Engl J Med 2022; 386:1793-1803

Lenacapavir as part of a combination régimen in treatment naive PWH: week 54 results

Study Design



*LEN oral lead-in (600 mg on Days 1 and 2, 300 mg on Day 8) followed by LEN SC 927 mg on Day 15; F/TAF 200/25 mg; †Participants in TG 1 and 2 will need HIV-1 RNA results <50 copies/mL at Weeks 16 and 22 to initiate either TAF 25 mg or BIC 75 mg at Week 28; those with HIV-1 RNA ≥50 copies/mL will discontinue study at Week 28; ‡LEN 600 mg on Days 1 and 2, followed by LEN 50 mg from Day 3; F/TAF 200/25 mg; §B/F/TAF 50/200/25 mg.
ARV, antiretroviral; BIC, B, bictegravir; BL, baseline; QD, once daily; Q6M, every 6 months; SC, subcutaneous; TG, treatment group.

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Lenacapavir as part of a combination régimen in treatment naive PWH: week 54 results

Baseline Characteristics

Calibrate

TG 1: LEN SC + F/TAF to LEN SC + TAF
TG 2: LEN SC + F/TAF to LEN SC + BIC
TG 3: LEN QD + F/TAF
TG 4: B/F/TAF

	LEN Total			B/F/TAF	
	TG 1 n=52	TG 2 n=53	TG 3 n=52	TG 4 n=25	Overall N=182
Age, median (range), years	31 (19, 61)	28 (19, 56)	28 (19, 72)	29 (21, 61)	29 (19, 72)
Sex, % female at birth	10	2	12	0	7
Race, % Black	46	45	60	64	52
Ethnicity, % Hispanic/Latinx	48	40	46	48	45
HIV-1 RNA, median $\log_{10}$ copies/mL	4.27	4.32	4.53	4.37	4.37
Q1, Q3	3.77, 4.63	3.96, 4.74	3.82, 4.83	4.09, 4.77	3.86, 4.74
>100,000 copies/mL, %	10	17	17	16	15
CD4 count, median cells/μL	404	450	409	482	437
Q1, Q3	320, 599	332, 599	301, 600	393, 527	332, 599
<200 cells/μL, %	0	2	6	0	2

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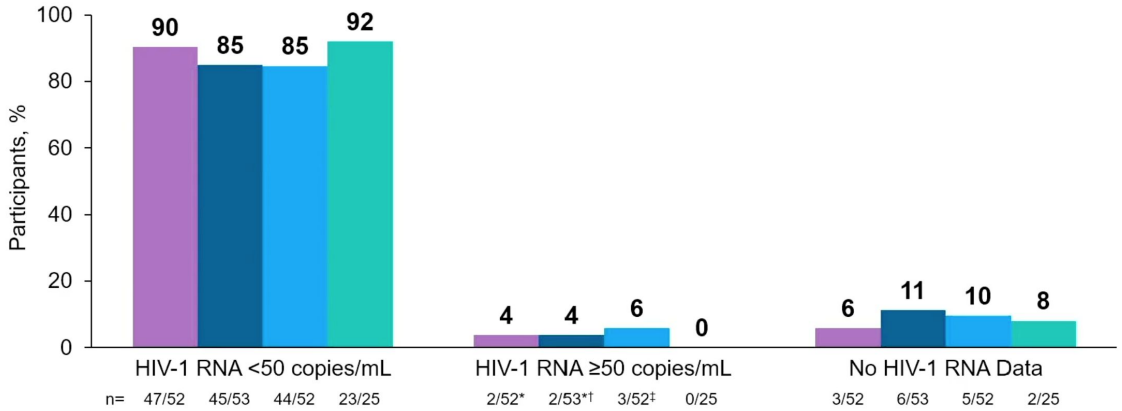
Lenacapavir as part of a combination régimen in treatment naive PWH: week 54 results

Efficacy at Week 54 (FDA Snapshot)

Calibrate

TG 1: LEN SC + F/TAF to LEN SC + TAF
TG 2: LEN SC + F/TAF to LEN SC + BIC
TG 3: LEN QD + F/TAF
TG 4: B/F/TAF



- In the pooled SC LEN group (TG 1+2: initially in combination with F/TAF, then with TAF or BIC), 88% (92/105) achieved and maintained virologic suppression at Week 54

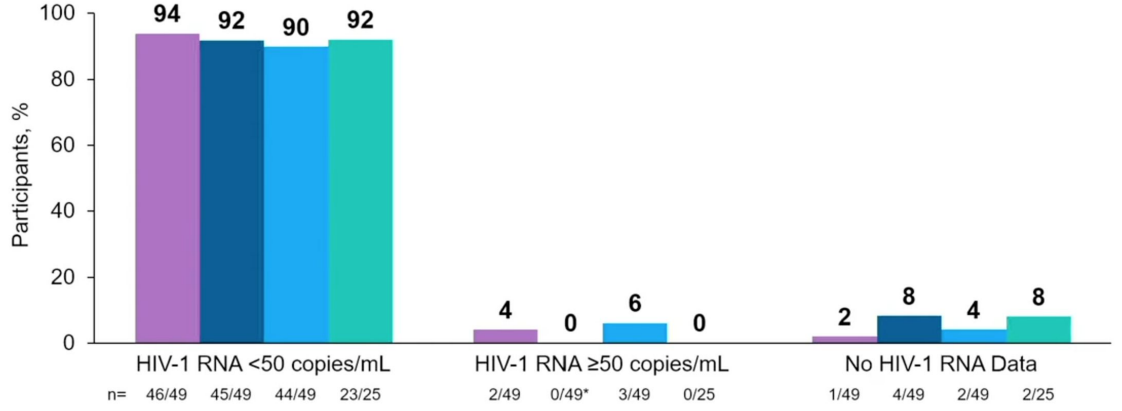
*3 participants (2 in TG 1 and 1 in TG 2) discontinued due to not meeting the protocol criteria of having HIV-1 RNA <50 copies/mL prior to Week 28;
†1 participant discontinued on Day 2; ‡2 of the 3 participants with HIV-1 RNA ≥50 copies/mL at Week 54 were suppressed in subsequent visit.

Efficacy at Week 54 (FDA Snapshot)

Among Participants who were Virologically Suppressed at Week 28

Calibrate

TG 1: LEN SC + F/TAF to LEN SC + TAF
TG 2: LEN SC + F/TAF to LEN SC + BIC
TG 3: LEN QD + F/TAF
TG 4: B/F/TAF



- In the pooled SC LEN group (TG 1+2: initially in combination with F/TAF, then with TAF or BIC), among participants who were virologically suppressed at Week 28, 93% (91/98) maintained virologic suppression at Week 54

*1 participant discontinued due to not meeting the protocol criteria of having HIV-1 RNA <50 copies/mL prior to Week 28; 1 participant discontinued on Day 2.

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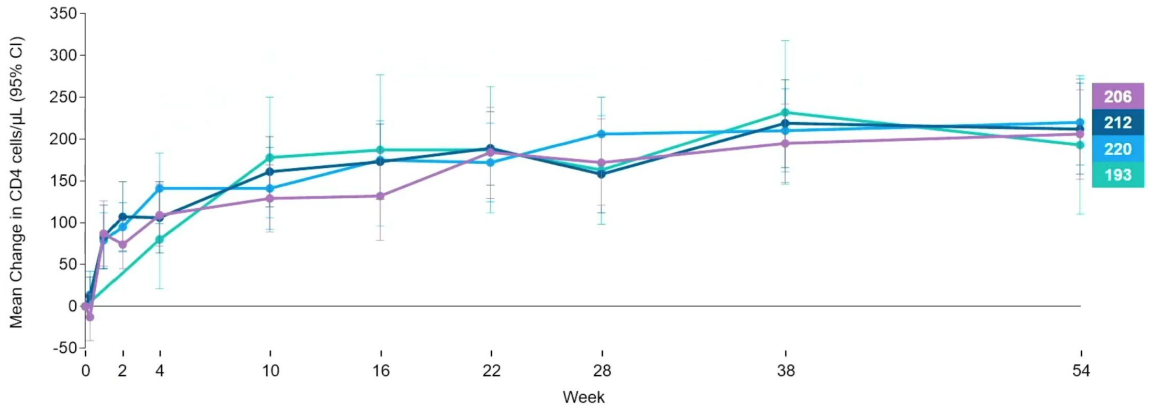
Lenacapavir as part of a combination régimen in treatment naive PWH: week 54 results

Changes in CD4

Calibrate

TG 1: LEN SC + F/TAF to LEN SC + TAF
TG 2: LEN SC + F/TAF to LEN SC + BIC
TG 3: LEN QD + F/TAF
TG 4: B/F/TAF



- Baseline CD4 of the overall study population: median 437 cells/µL

Resistance Analysis*

Calibrate

TG 1: LEN SC + F/TAF to LEN SC + TAF
TG 2: LEN SC + F/TAF to LEN SC + BIC
TG 3: LEN QD + F/TAF
TG 4: B/F/TAF

Participants, n	TG 1 n=52	TG 2 n=53	TG 3 n=52	TG 4 n=25
Participants meeting the resistance testing criteria	1	1	3	1
Emergent LEN resistance	0	1	1	0

- Emergent LEN resistance in 2/157 (1.5%) participants
  - One participant in TG 2 developed Q67H+K70R (LEN fold change=20) in CA at Week 10, preceded by M184M/I in RT (IDWeek 2021)†
    - Pattern of mutation emergence suggests incomplete adherence to F/TAF
  - One participant in TG 3 developed Q67H (LEN fold change=7) in CA at Week 54
    - Nonadherence to F/TAF as assessed by pill count and drug levels
  - Both participants later re-suppressed on a regimen of INSTI + 2 NRTI

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Lenacapavir as part of a combination régimen in treatment naive PWH: week 54 results

Injection Site Reactions

ISR Types*	After 1st SC Dose at Week 1 n=103†	After 2nd SC dose at Week 26 n=95†	Median duration (days)
Swelling	14%	12%	11
Erythema	14%	18%	5
Pain	15%	9%	4
Nodule	11%	8%	195
Induration	9%	6%	202

- Mostly Grade 1 or 2 ISRs
  - One Grade 3 ISR (nodule) after the second SC dose
- Three participants discontinued due to ISRs:
  - Two due to induration (both Grade 1, after the first SC dose)
  - One due to erythema and swelling (Grade 1, after the second SC dose)

Adverse Events (excluding ISRs)

≥10% Participants in LEN total, %	LEN Total TG 1+2+3 n=157	B/F/TAF TG 4 n=25
Headache	13%	12%
Nausea	13%	4%
COVID-19	10%	12%

- No SAEs related to study drug
- No Grade 4 AEs related to study drug
- No discontinuations due to non-ISR AEs
- Gastrointestinal AEs: SC LEN (TG 1+2) vs oral LEN (TG 3)
  - Nausea: 14% vs 12%
  - Diarrhea: 7% vs 10%
  - Vomiting: 4% vs 8%

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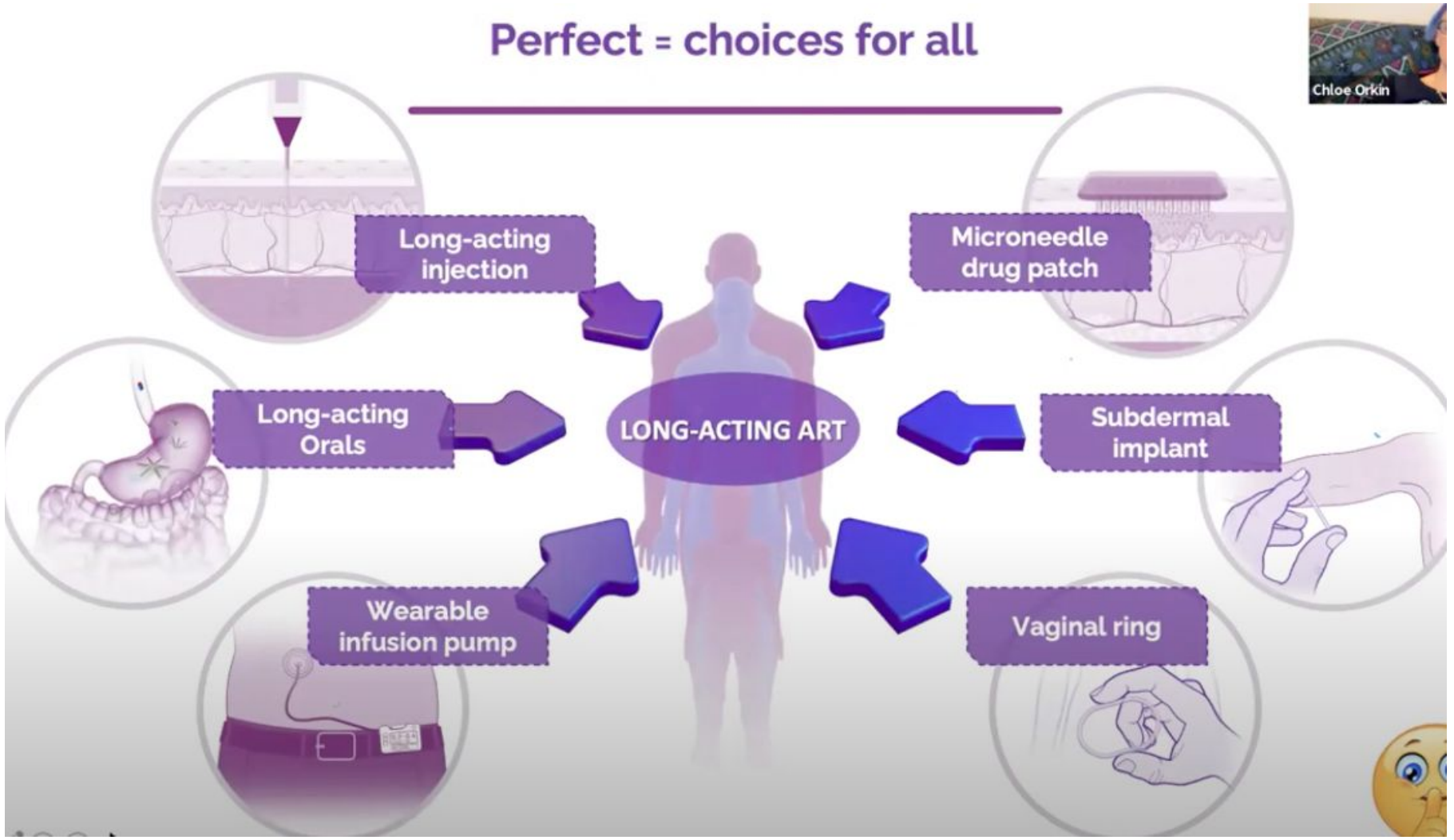
Perfect = choices for all
Chloe Orkin
Long-acting injection
Microneedle drug patch
Long-acting Orals
LONG-ACTING ART
Subdermal implant
Wearable infusion pump
Vaginal ring

Mensajes

- Con los fármacos actuales, eficacia y seguridad son asignaturas superadas.
- La atención a la cronicidad, la mejora de la calidad de vida y el estigma deben ser objetivos prioritarios.
- CAB-RPV LA es eficaz y bien tolerado. Alta satisfacción en los pacientes con su uso.
- Las alternativas LA son una realidad, en el futuro habrá distintos tipos de posibilidades que habrá que individualizar.
- Es necesario incorporar estrategias de medición de PROs, PROMs y PREMs a la práctica clínica.

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