VOCABRIA + REKAMBYS AP

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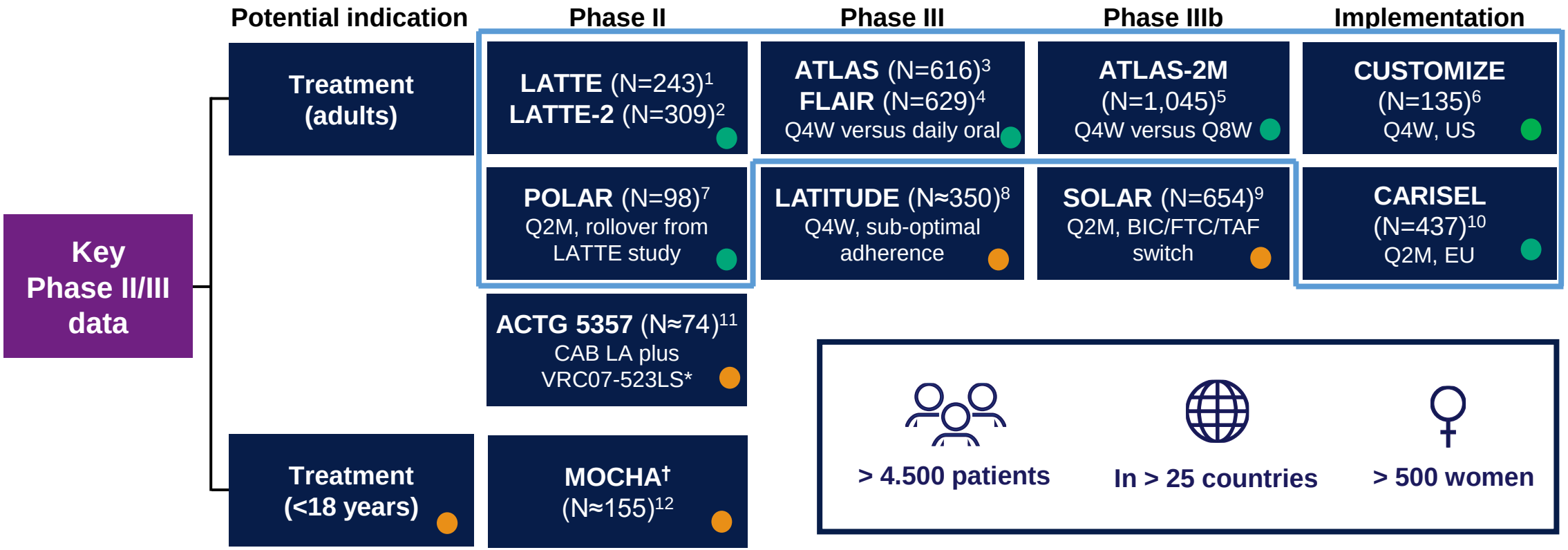
CAB + RPV LA clinical development program



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 December 2022). 7. POLAR (209035). https://clinicaltrials.gov/ct2/show/NCT03639311 (accessed December 2022). 8. LATITUDE (ACTG 5359). Available at: https://clinicaltrials.gov/ct2/show/NCT03635788 (accessed December 2022). 9. SOLAR (213500). Available at: https://clinicaltrials.gov/ct2/show/NCT04542070 (accessed December 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 December 2022).12. MOCHA (IMPAACT 2017). Available at: https://clinicaltrials.gov/ct2/show/NCT03497676 (accessed December 2022)

Efficacy of CAB + RPV LA has been demonstrated through a program of Phase III clinical trials

MONTHLY DOSING vs **DAILY ORAL ART**

FLAIR[1] (N=566)

Treatment-naïve adults with HIV-1 virologically suppressed* for 20 weeks on daily oral ARV therapy

ATLAS[2] (N=616)

Adults with HIV-1 virologically suppressed* for ≥6 months on daily oral ARV therapy

EVERY 2-MONTH DOSING vs **MONTHLY DOSING**

ATLAS-2M[3] (N=1045)

Adults with HIV-1 virologically suppressed* for ≥6 months on daily oral ARV therapy or monthly dosing

Established non-inferiority of long-acting investigational therapy compared with daily HIV regimens; every 2-month dosing non-inferior to monthly dosing[1–3]

*HIV-1 RNA <50 copies/mL

1. Orkin C, et al. N Engl J Med 2020;382:1124–351. 2. Swindells S, et al. N Engl J Med 2020;382:1112–23. 3. Overton ET, et al. Lancet 2021: 396;1994-2005

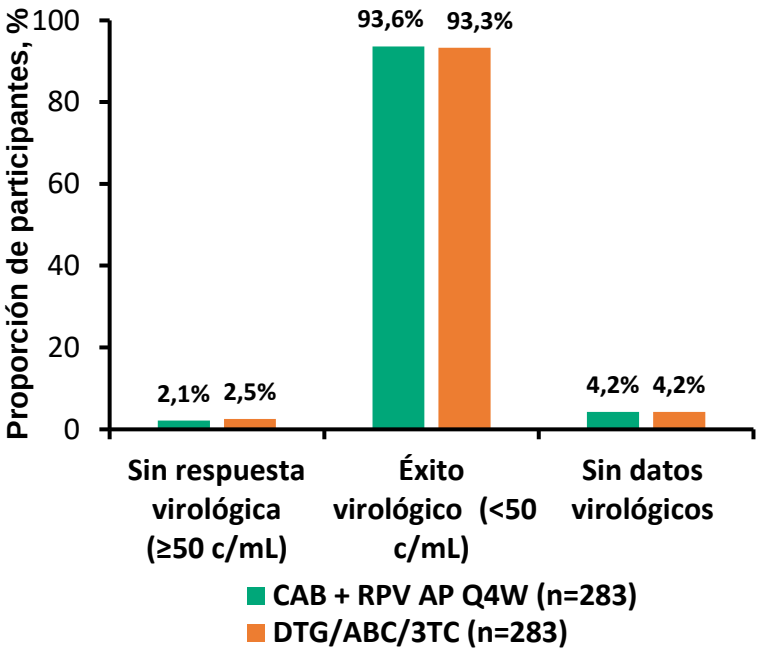
Respuesta virológica a semana 48 de CAB + RPV AP mensual (Q4W) y cada dos meses (Q8W)

Objetivo primario: no inferioridad (ARN del VIH-1 ≥50 c/mL) versus brazo comparador

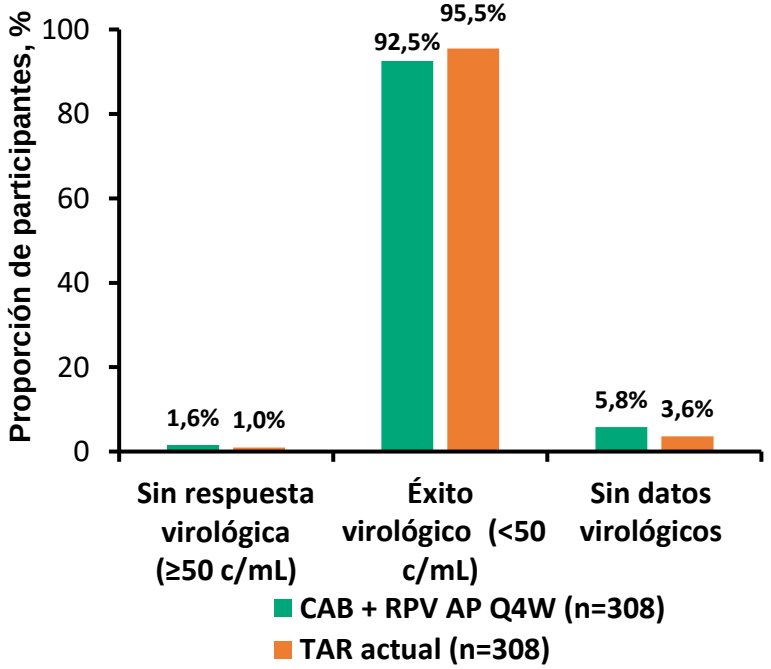
Objetivo secundario principal: no inferioridad (ARN del VIH-1 <50 c/mL) versus brazo comparador

Snapshot de la FDA a semana 48 (ITT-E)*

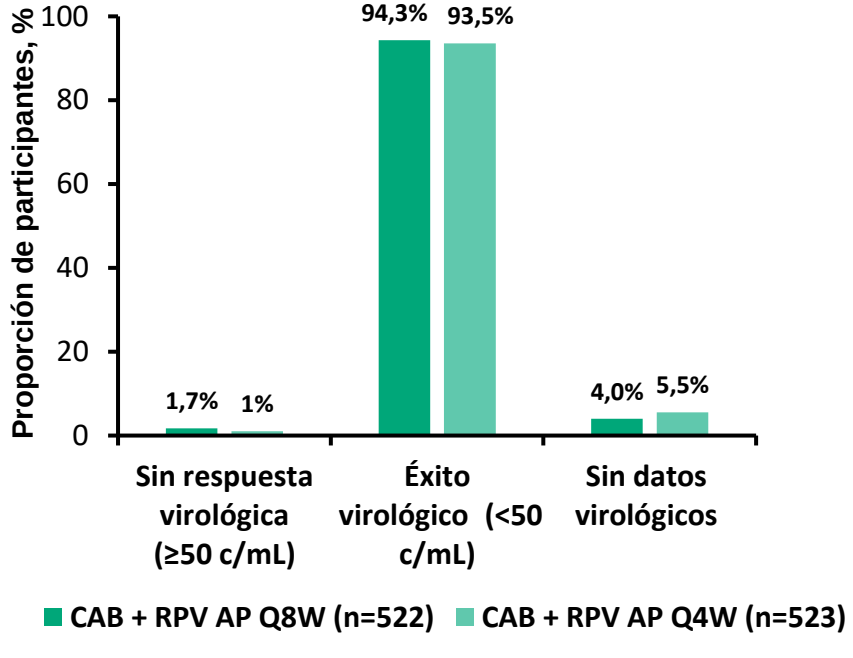
FLAIR[1]



ATLAS[2]



ATLAS-2M[3]



*ITT-E, para la población por intención de tratar expuesta

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
4. Quercia R, et al. EACS 2019; Oral PS1/1 available at: http://resourcelibrary.eacs.cyim.com/mediatheque/media.aspx?mediaId=78023&channel=28172 (acceso julio 2021).

Seguridad a 48 semanas: Estudios ATLAS and FLAIR (excluye EA en zona inyección)

n (%)	CAB + RPV LA (N=591)	CAR (N=591)
Any AE	**506 (86)**	**444 (75)**
Any Grade 3/4/5 AE*	**44 (7)**	**35 (6)**
Any drug-related AE	**165 (28)**	**35 (6)**
Any Grade 3/4/5 drug-related AE*	**8 (1)**	**1 (<1)**
Any AEs leading to withdrawal†	**17 (3)**	**9 (2)**
Any serious AE	**24 (4)**	**25 (4)**
Serious AEs related to study treatment	**1 (<1)**	**1 (<1)**
Common AEs (≥5%)		
Nasopharyngitis	108 (18)	90 (15)
Headache	73 (12)	38 (6)
Upper respiratory tract infection	70 (12)	53 (9)
Diarrhea	54 (9)	40 (7)
Back pain	43 (7)	23 (4)
Influenza	42 (7)	34 (6)
Pyrexia	43 (7)	13 (2)
AEs of special interest		
Anxiety	27 (5)	20 (3)
Depression	16 (3)	14 (2)
Suicidal ideation/behavior	4 (<1)	5 (<1)

La mayoría de los EA fueron Grado 1 o 2, de leves a moderados.

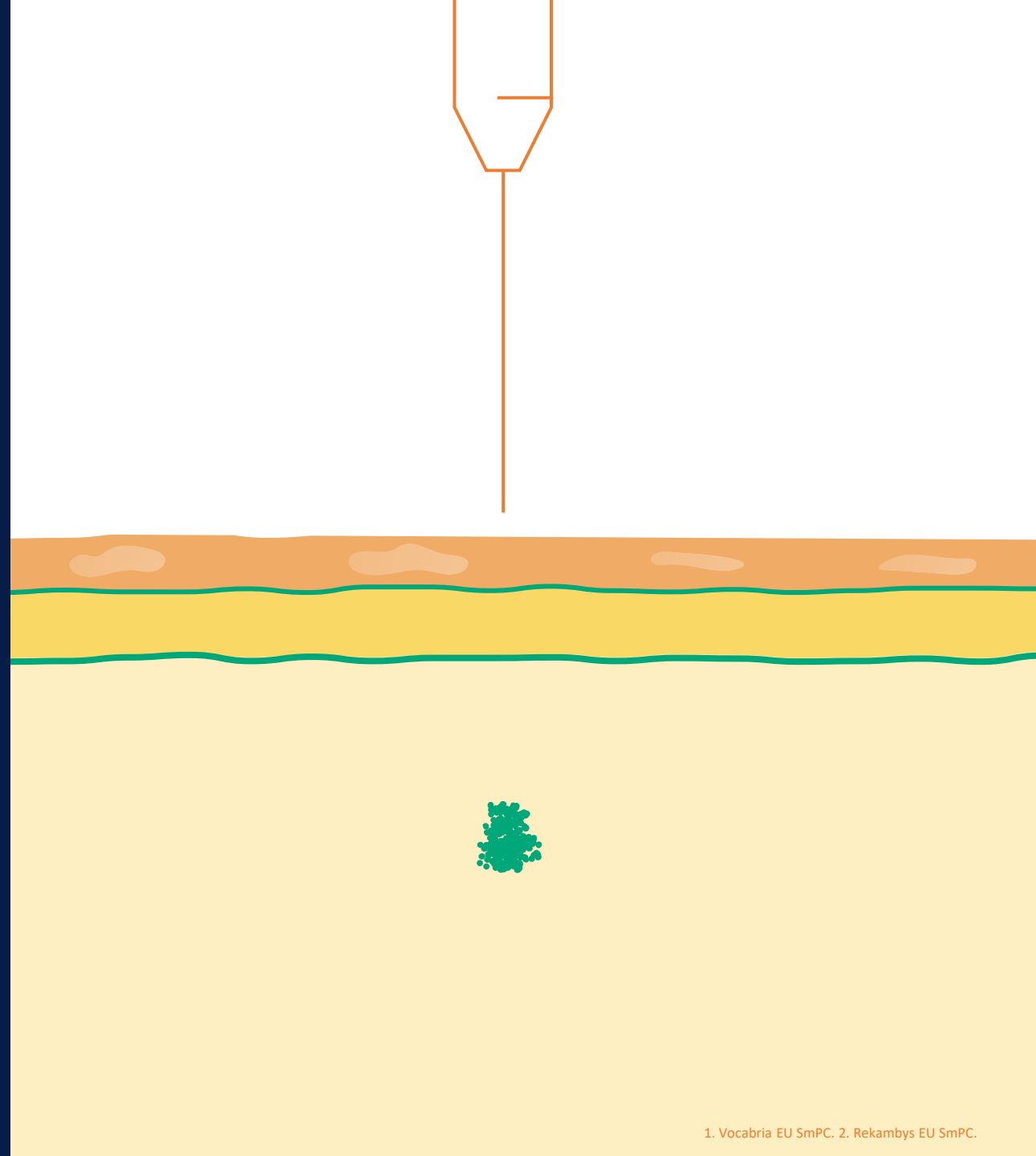
*There was only one (<1%) participant with Grade 5 AE in the CAR arm

Overton ET, et al. IAS 2019. Poster MOPEB257

CAB + RPV LA formulation allows for monthly or every 2-month dosing

CAB LA + RPV LA extended-release suspensions contain finely-milled drug particles suspended in an aqueous vehicle with properties enabling LA dosing

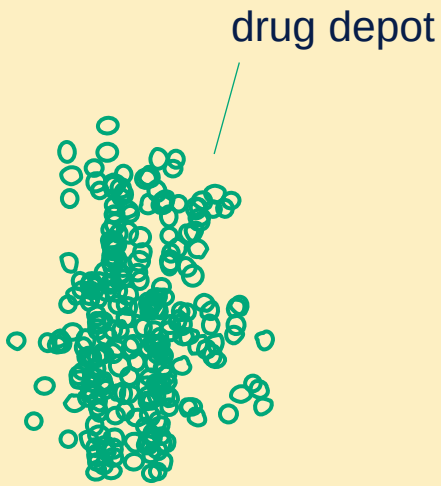
CAB LA and RPV LA are administered as separate gluteal injections[1,2]



1. Vocabria EU SmPC. 2. Rekambys EU SmPC.

CAB + RPV LA formulation allows for monthly or every 2-month dosing

LA suspension forms a drug depot in the muscle

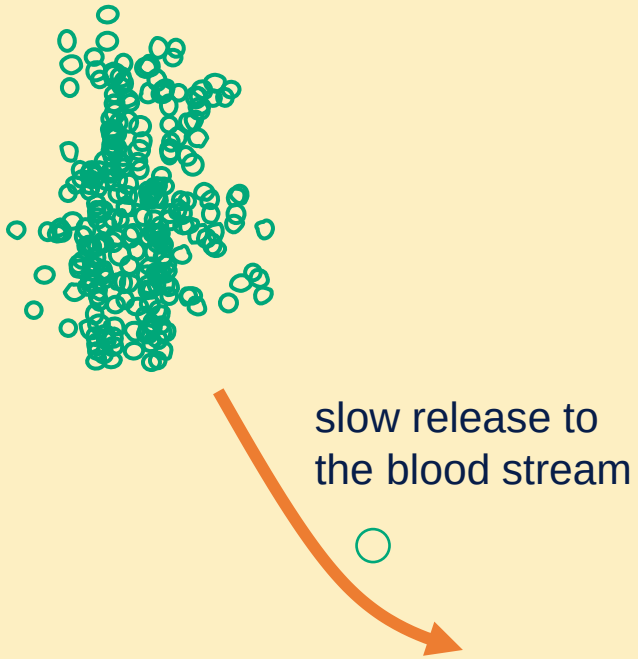


Trezza C, et al. Curr Opin HIV AIDS 2015;10:239–45

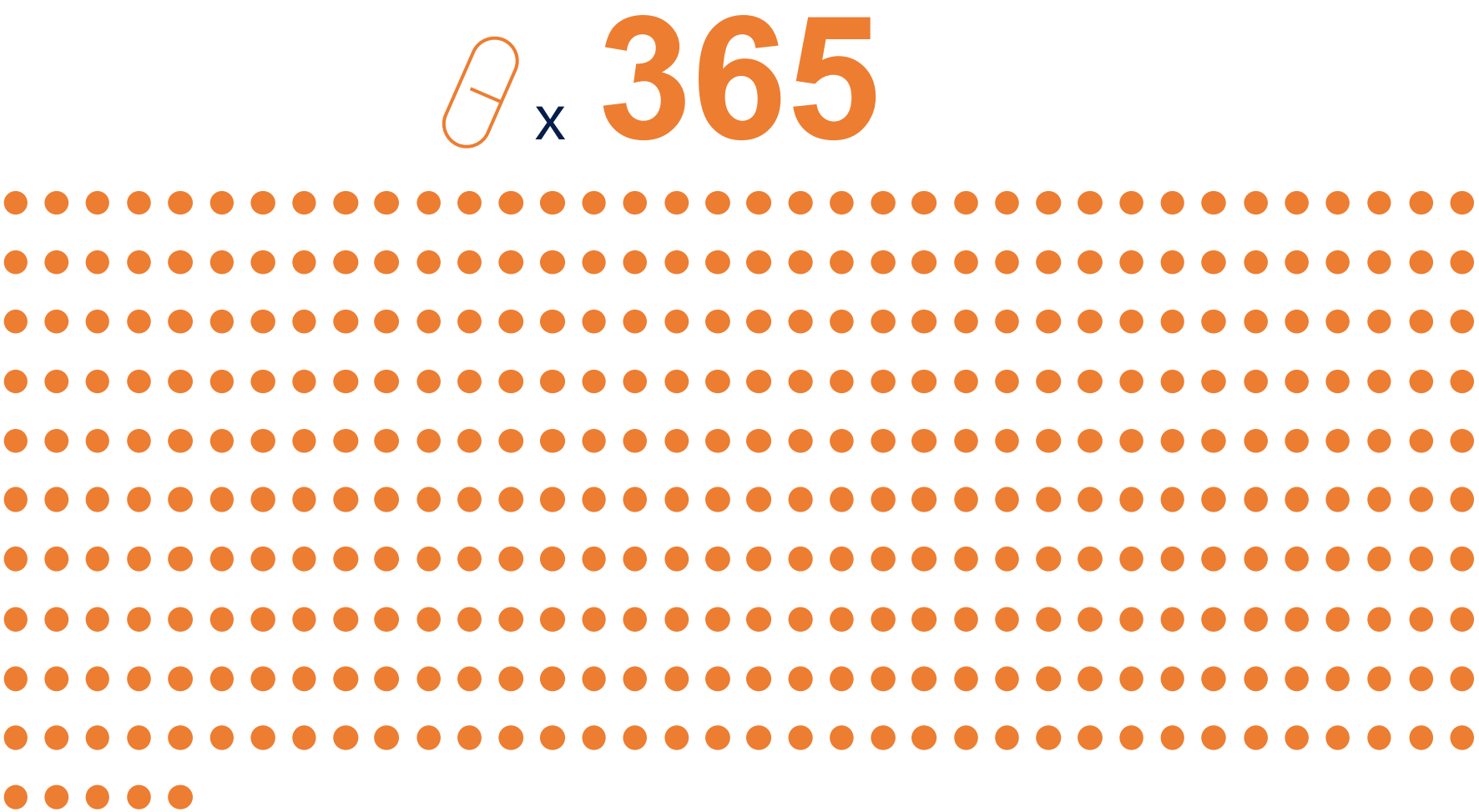
CAB + RPV LA formulation allows for monthly or every 2-month dosing

Drug is slowly absorbed from the depot site into the bloodstream

Formulations allow for continuous drug exposure that lasts over the duration of the dosing interval

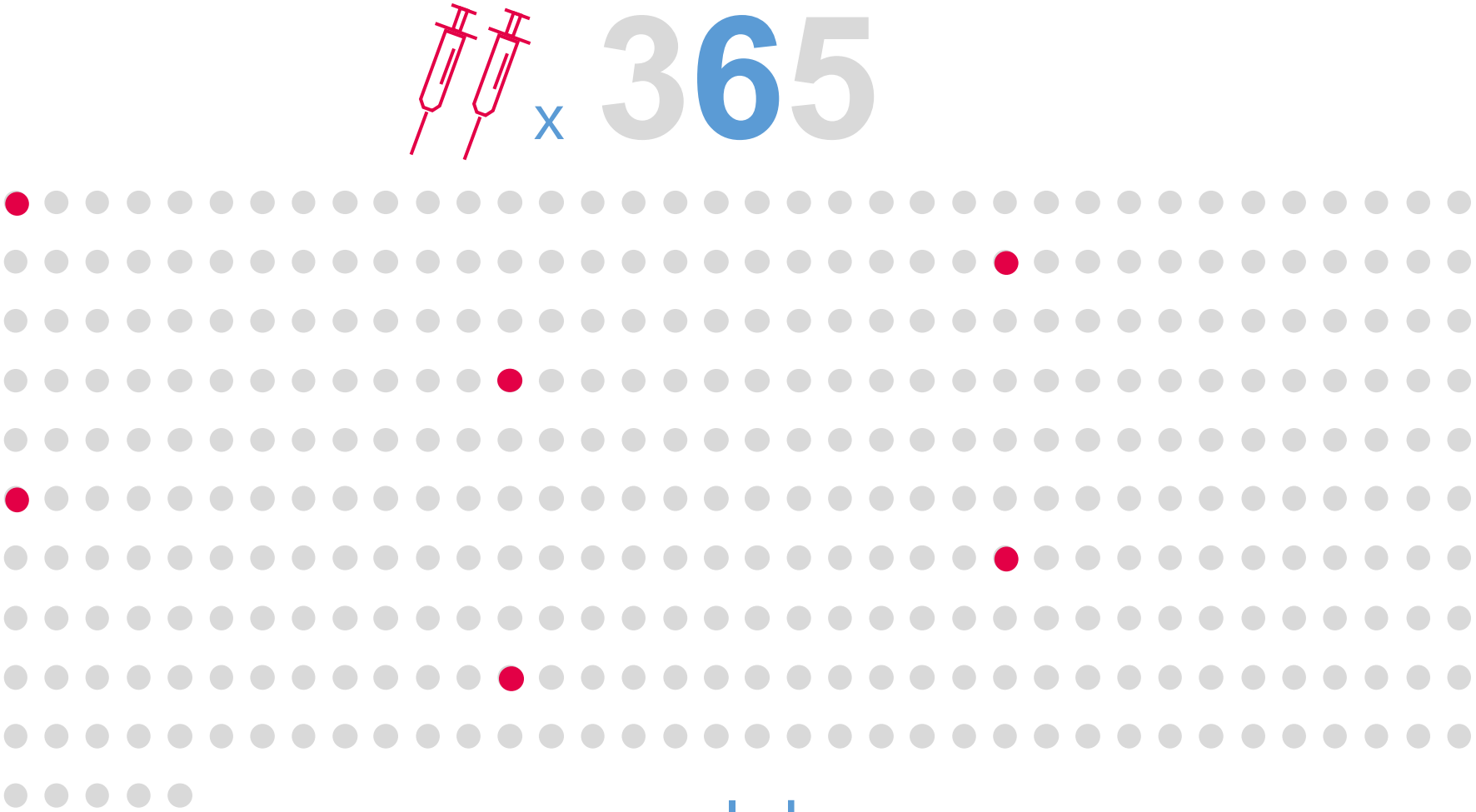


Trezza C, et al. Curr Opin HIV AIDS 2015;10:239–45
Müller RH, et al. Eur J Pharm Biopharm 2011:78;1–9



annual doses
with daily oral regimen*

*Based on once-daily oral dosing of single-tablet regimens as recommended in the corresponding SmPC of GeSIDA recommended regimens for suppressed patients. See slide notes for references



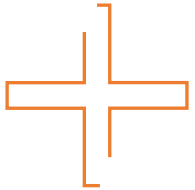
annual doses with CAB + RPV LA*

*These 6 doses do not include the 28 days of optional oral lead-in and the initiation injections. A single CAB + RPV LA dose consists of two separate gluteal injections administered by a healthcare professional

1. Vocabria EU SmPC. 2. Rekambys EU SmPC.

CAB + RPV LA safety: Frequently reported AEs* at Week 48 (FLAIR, ATLAS and ATLAS-2M)

Headache[1,2]



Pyrexia[1,2]

ISRs[1,2]

<2% (n=23/1,636†) of participants **discontinued** due to injection-related reasons[3,4]

98% (n=9,197/9,322) of ISRs were **mild-to-moderate** and declined over time[3,4]

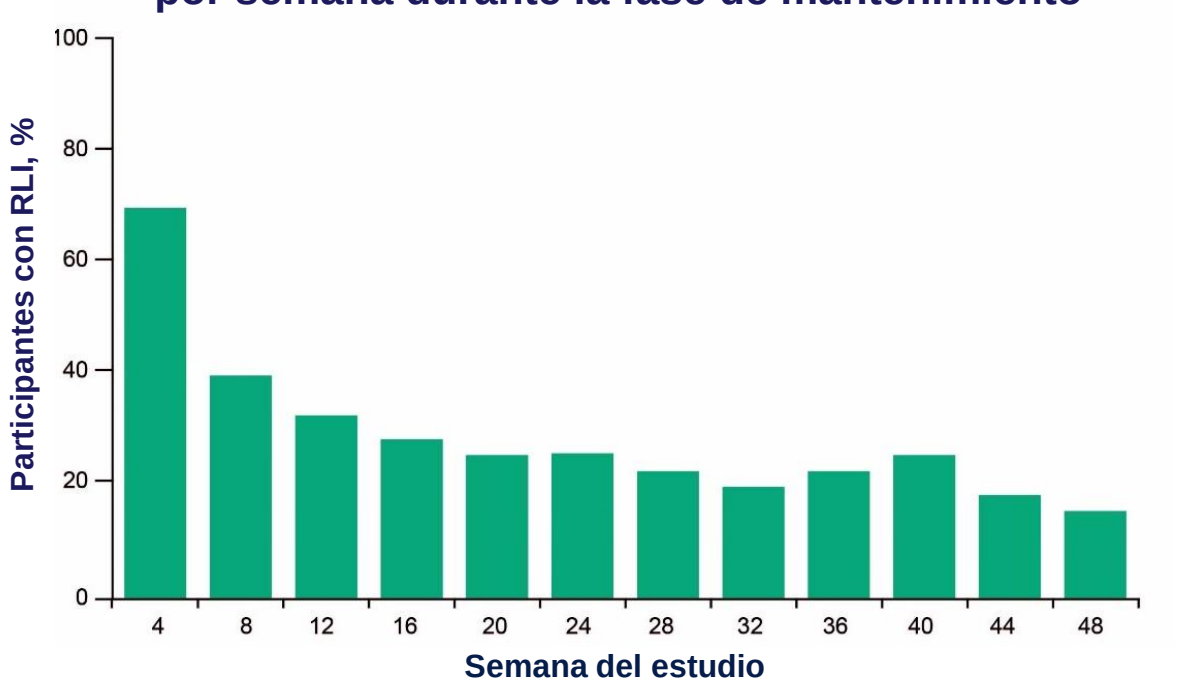
3 days median duration[3,4]

*Very common, ≥10%; please refer to the SmPCs for the full list of adverse reactions
†ATLAS n=308; FLAIR n=283; ATLAS-2M n=104
SmPC, summary of product characteristics

1. Vocabria EU SmPC. 2. Rekambys EU SmPC. 3. Rizzardini G, et al. J Acquir Immune Defic Syndr 2020;85:498–506 4. Overton ET, et al. Lancet 2021;396:1994–2005

ATLAS y FLAIR: la incidencia de las RLI disminuyó con el tiempo

Incidencia de la reacciones en el lugar de inyección por semana durante la fase de mantenimiento



[a]Las barras representan la incidencia de RLI después de cada visita mensual de inyección intramuscular. Los porcentajes se han calculado respecto al numero de participantes en cada visita.

Evento, n (%), ITT-E	CAB + RPV AP N=591
Número de inyecciones	14.682
Número de eventos de RLI (eventos/inyecciones)*	3.663 (25)
Grado 1	3.063 (84)
Grado 2	565 (15)
Grado ≥3 – grave	34 (<1)
Reacciones en el lugar de inyección*	
Dolor	3087 (21)
Nódulo	140 (<1)
Induración	136 (<1)
Hinchazón	86 (<1)
Discontinuaciones por RLI, participantes n (%)	**6 (1)**

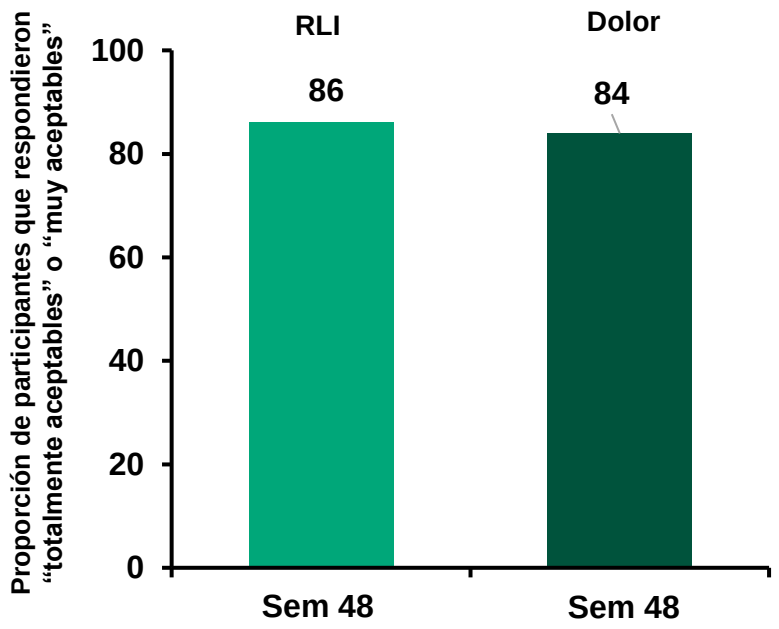
Adaptado de: Rizzardini G, et al. J Acquir Immune Defic Syndr. 2020;85:498-506

Las RLI disminuyeron con el tiempo, con una mediana de duración de 3 días, siendo el dolor la RLI más frecuente

Rizzardini G, et al. J Acquir Immune Defic Syndr. 2020;85:498-506

FLAIR y ATLAS: CAB + RPV AP tolerabilidad y aceptación de las RLI

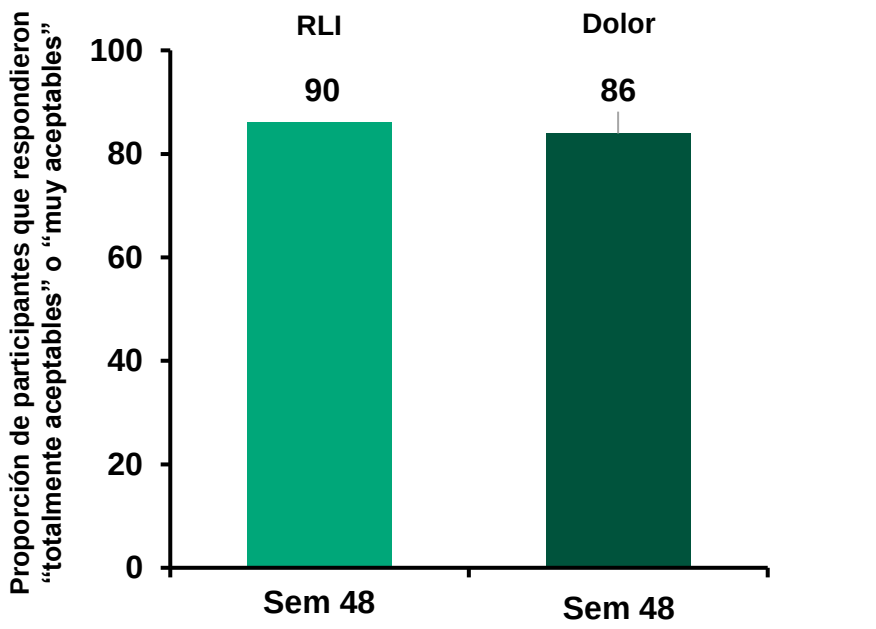
FLAIR



Adaptado de Murray M, AIDS Behav. 2020 Dec;24(12):3533-3544.

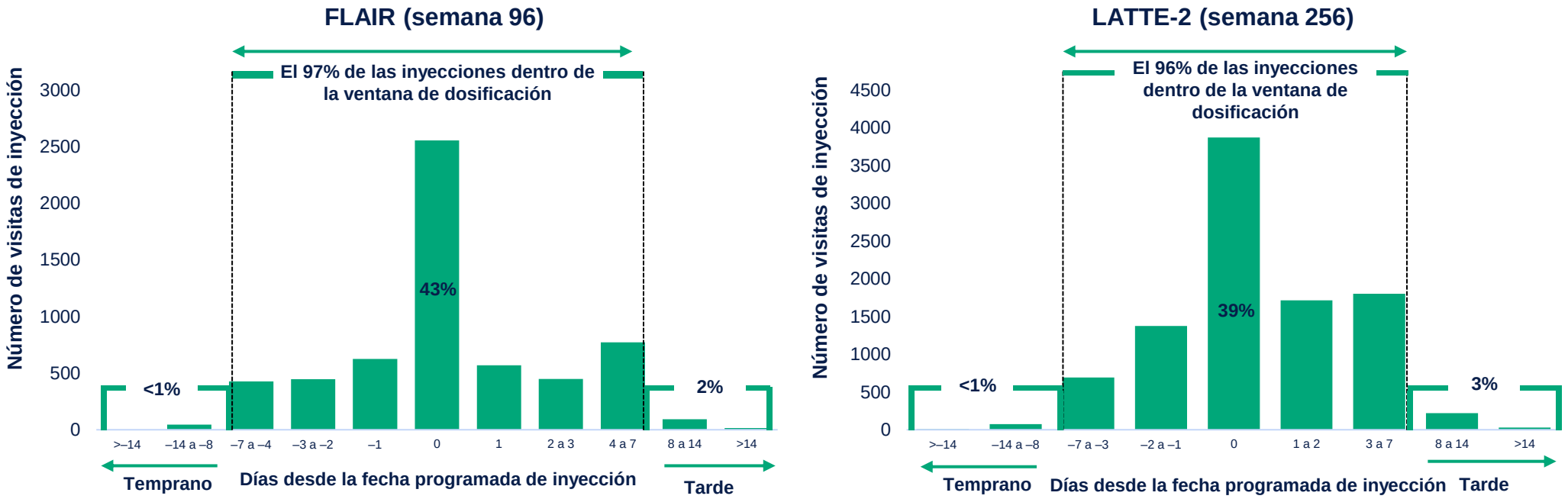
El 86% y 84% de los pacientes en CAB + RPV AP consideraron las RLI y el dolor como "totalmente o muy aceptables" a semana 48

ATLAS



El 90% y 86% de los pacientes en CAB + RPV AP consideraron las RLI y el dolor como "totalmente o muy aceptables" a semana 48

Adherencia a largo plazo a las visitas de inyección



>7 días fuera de la ventana de dosificación: 2% (313/15.808)
1-7 días fuera de la ventana de dosificación: <1% (41/15.808)

En los estudios FLAIR y LATTE-2, **ningún participante** con una visita de inyección fuera del periodo ventana de dosificación de +/-7 días **cumplió criterios de FVC**

Teichner et al. IDWeek 2020™; Virtual. Poster 1029. Available at: https://www.natap.org/2020/IDWeek/IDWeek_51.htm (acceso julio 2021)