Oral lead in and suboptimal compliance to injections

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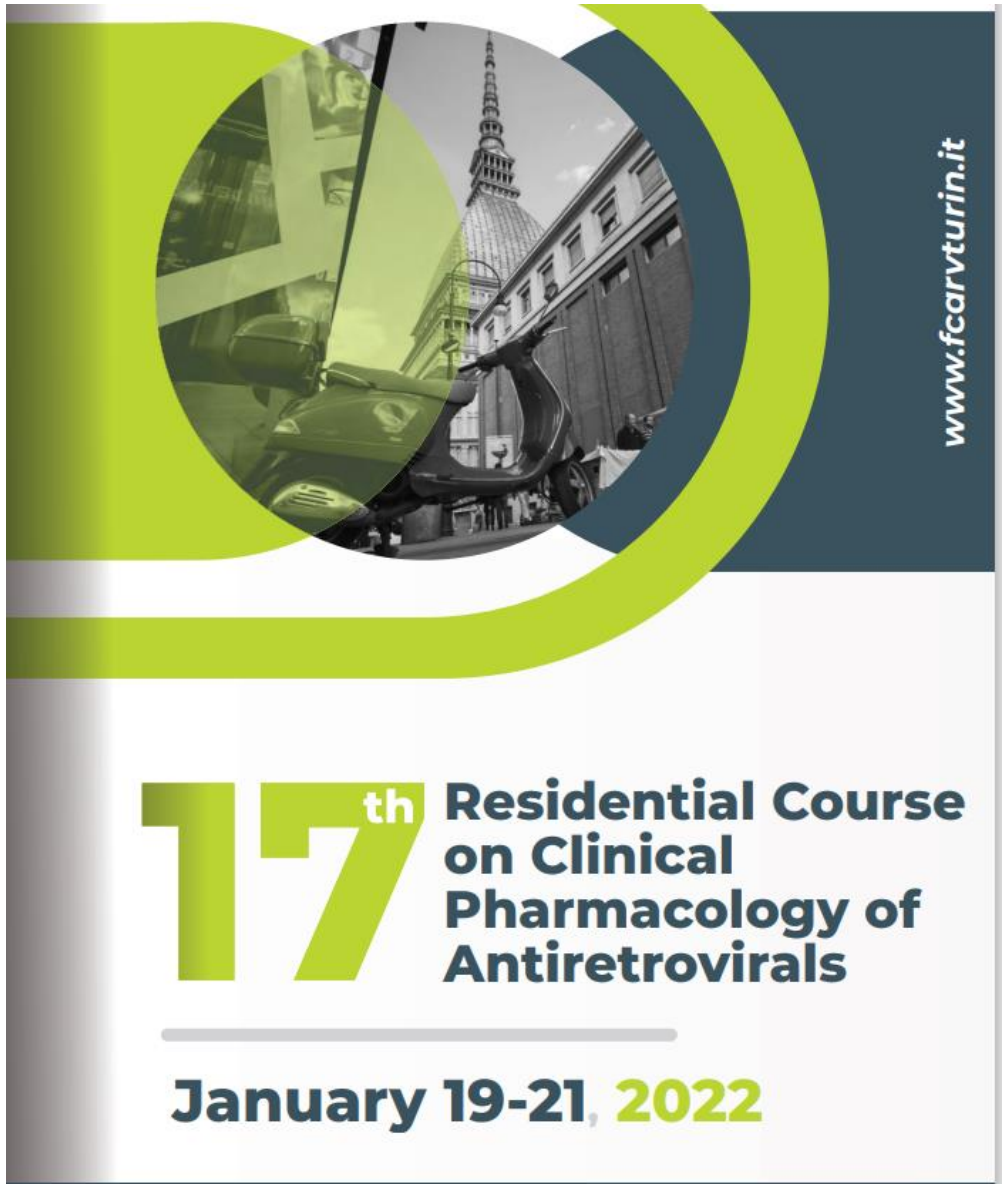

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Outline

-Management of oral lead in of long acting CAB + RPV

-Management of missed or delayed long acting doses

Outline

-Management of oral lead in of long acting CAB + RPV

-Management of missed or delayed long acting doses

Management of switching to LA CAB+ RPV: optional OLI

Previous HAART

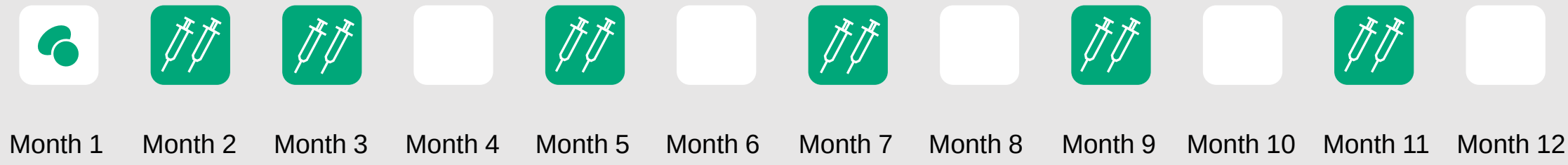
Oral lead in = OLI
CAB + RPV for 4 weeks

Long Acting = LA
CAB + RPV

OLI (oral lead in) could be started before initiation of CAB + RPV LA injections

Every 2 months dosing schedule with OLI[1,2]

1. OLI
2. First IM injections
3. Injections every 2 months



- Prior to the initiation of injections, oral CAB together with oral RPV could be taken for approximately 1 month (at least 28 days) to assess tolerability to CAB and RPV[1,2]
- One CAB 30 mg tablet should be taken with one RPV 25 mg tablet, QD[1,2]

IM, intramuscular

1. Vocabria EU SmPC. Jul 2021
2. Rekambys EU SmPC. Jul 2021

Pooled ATLAS, FLAIR, and ATLAS-2M: OLI phase safety summary

- No drug-related SAEs were reported during OLI[1]
- The most frequently reported AEs during OLI included headache, nasopharyngitis, fatigue, diarrhea, and vitamin D deficiency[2,3]
- AEs leading to withdrawal during OLI in ATLAS-2M included increased transaminases, asthenia, fatigue, depression, and skin lesions[3]

OLI safety summary*[1]

AE, n (%)	Pooled CAB + RPV LA (Q4W/Q8W) N=1,245
Any AE	396 (32)
Any Grade 3–5 AE	15 (1)
Drug-related Grade 3–5 AEs	5 (<1)
Drug-related AEs	102 (8)
AEs leading to withdrawal	10 (<1)
Any SAE	9 (<1)
Drug-related SAEs	0
Fatal SAEs	0

No drug hypersensitivity reactions or other SAEs occurred during OLI that prohibited transition to CAB + RPV LA therapy[1–3]

*ATLAS, FLAIR, and ATLAS-2M Phase III studies included an OLI phase in which daily oral CAB + RPV was prescribed for ≥4 weeks prior to initiation of LA dosing

AE, adverse event; **Q4W,** every 4 weeks; **Q8W,** every 8 weeks; **SAE,** serious adverse event

1. de los Rios P, et al. EACS 2021. Abstract PE2/75
2. Rizzardini G, et al. J Acquir Immune Defic Syndr 2020;85:498–506
3. Overton ET, et al. Lancet 2021;396:1994–2005 (and suppl. appendix)

ATLAS and FLAIR pooled: Common AEs and AEs leading to withdrawal during the OLI period

- Overall, 187 (32%) subjects in the CAB + RPV group had at least one AE[1]
- No drug-related SAEs[2]
- The most frequently reported AEs during OLI were headache (n=17, 3%), nasopharyngitis (n=16, 3%), and vitamin D deficiency (n=16, 3%)[1]
- Drug-related AEs (see red box) leading to withdrawal were asthenia, myalgia, headache, and depression suicidal[2]

AEs leading to withdrawal during OLI[2]

AE, n	CAB + RPV N=591
Any AE, n (%)	187 (32)
Participants with AEs leading to withdrawal	6
AEs leading to withdrawal	7
Hepatitis C	1
Hepatitis A	1
Transaminases increased	1
Asthenia	1
Myalgia	1
Headache	1
Depression suicidal	1

Few participants discontinued CAB + RPV during OLI due to drug-related AEs and no cases of DILI or HSR occurred during OLI[2]

DILI, drug-induced liver injury; **HSR,** hypersensitivity reaction

1. Rizzardini G, et al. J Acquir Immune Defic Syndr 2020;85:498–506
2. ViiV Healthcare, Module 2.7.4, Summary of Clinical Safety for CAB + RPV 2-drug regimen. Version 01, 2019

ATLAS-2M: Common AEs and AEs leading to withdrawal during the OLI period

- No drug-related SAEs were reported during OLI[1]
- AEs primarily consisted of mild/moderate (Grade 1 or 2) events[1]
- Four subjects had AEs leading to withdrawal[1]

AEs leading to withdrawal during OLI[1,2]

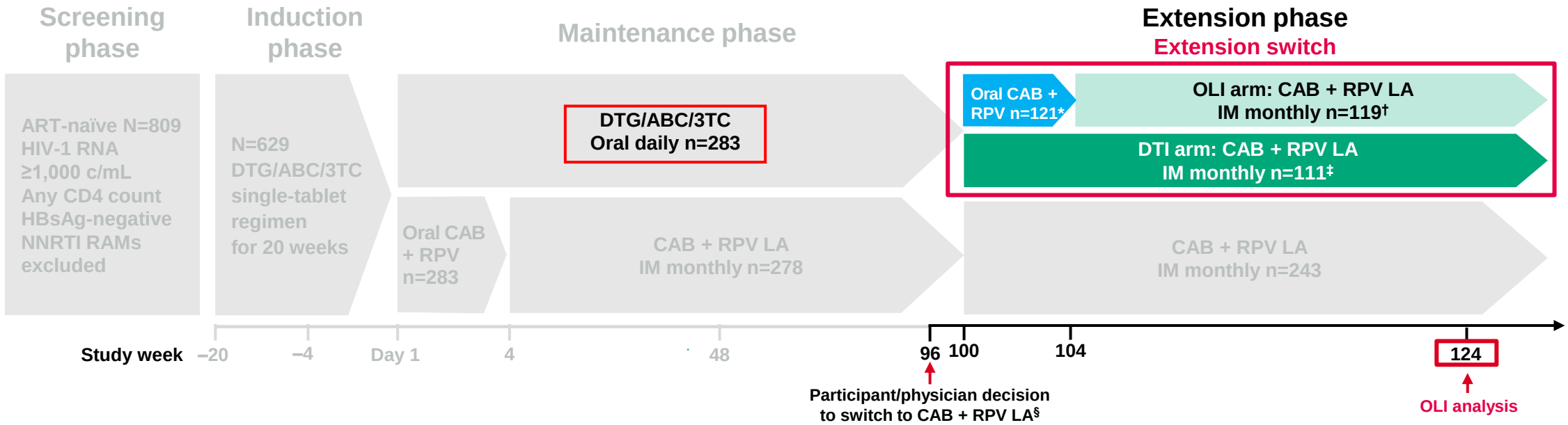
AE, n (%)	CAB + RPV Q8W arm N=328	CAB + RPV Q4W arm N=327
Any AE	91 (28)	118 (36)
AEs leading to withdrawal	2 (<1)	2 (<1)
Asthenia	1 (<1)	0
Fatigue	0	1 (<1)
Transaminases increased	0	1 (<1)
Depression	0	1 (<1)
Skin lesion	1 (<1)	0

Overall, AEs and AEs leading to withdrawal during OLI in ATLAS-2M were similar in frequency and type compared with the OLI period in ATLAS and FLAIR[1,2]

1. Overton ET, et al. Lancet 2021;396:1994–2005 (and suppl. appendix)
2. ViiV Healthcare. Data on File. ATLAS-2M (207966) Week 48 CSR. 19 Dec 2019. Table 3.23

FLAIR extension phase: Optional OLI for participants switching from daily oral ART to CAB + RPV LA

Phase III, randomized, multicenter, parallel-group, non-inferiority, open-label study



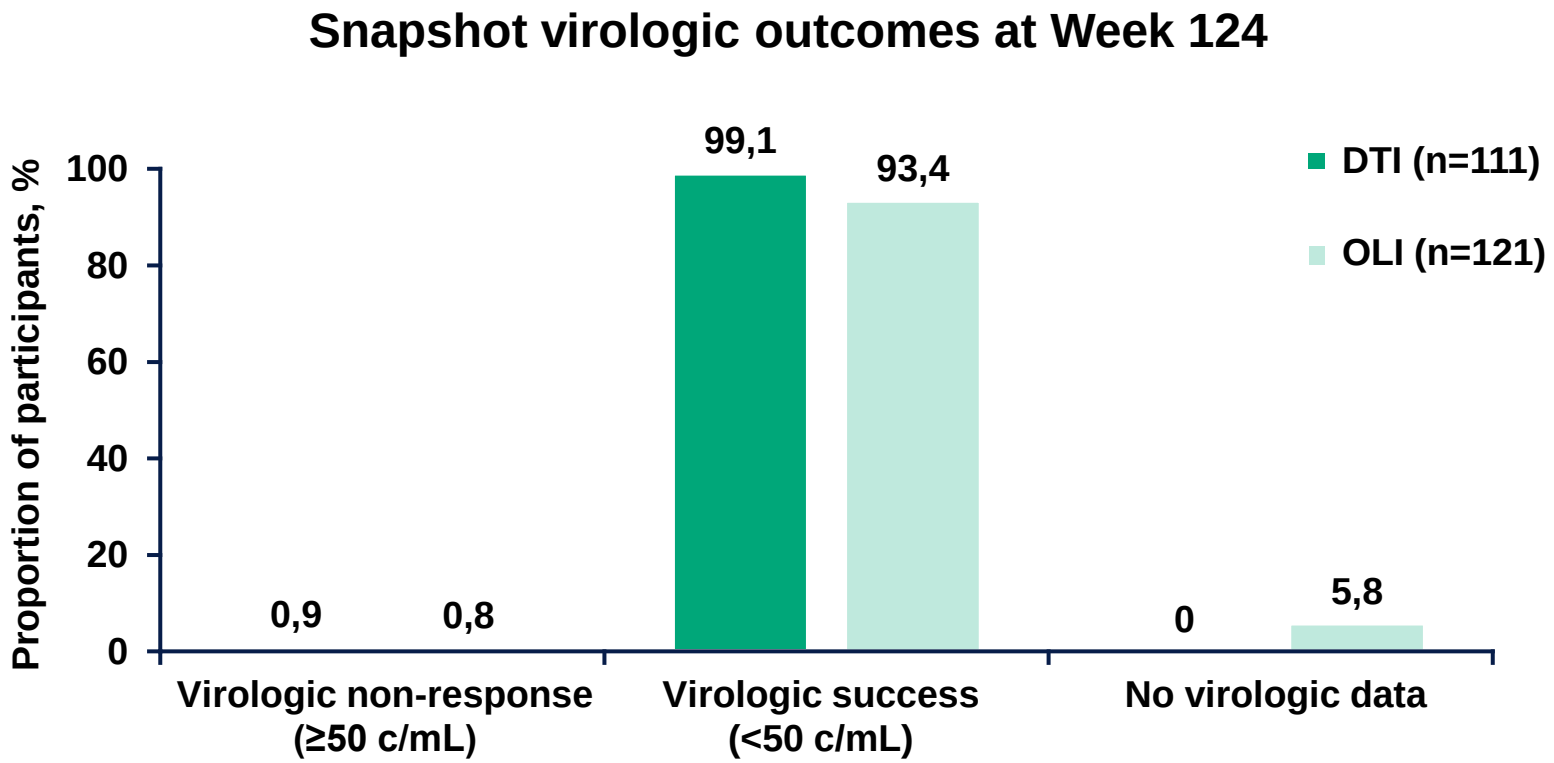
Endpoints assessed at Week 124 for the extension switch population:

- Proportion of participants with HIV-1 RNA ≥50 c/mL at Week 124 per the FDA Snapshot algorithm
- Proportion of participants with HIV-1 RNA <50 c/mL at Week 124 per the FDA Snapshot algorithm
- Incidence of PDVF
- Incidence and severity of AEs and laboratory abnormalities
- Proportion of participants who discontinue treatment due to AEs
- PK of CAB + RPV LA in the context of no OLI

*Two discontinuations during OLI: 1 participant relocation, 1 pregnancy; †Daily oral CAB (30 mg) + RPV (25 mg) was initiated at Week 100 and continued for ≥4 weeks. Participants received their last dose of oral CAB + RPV and their first loading injections of CAB (600 mg) + RPV (900 mg) LA at Week 104, followed by CAB 400 mg + RPV 600 mg LA Q4W
‡Last dose of CAR and first loading injections of CAB (600 mg) + RPV (900 mg) LA were administered at Week 100, followed by CAB 400 mg + RPV 600 mg LA Q4W
§Participants, in consultation with their physician, elected to receive CAB + RPV LA either with an OLI or DTI at Week 96. The new treatment regimen began at Week 100
3TC, lamivudine; **ABC,** abacavir; **ART,** antiretroviral therapy; **c/mL,** copies/mL; **CAR,** current antiretroviral regimen; **CD4,** cluster of differentiation 4; **DTG,** dolutegravir
DTI, direct to injection; **FDA,** US Food and Drug Administration; **HBsAg,** hepatitis B surface antigen; **NNRTI,** non-nucleoside reverse transcriptase inhibitor
PDVF, protocol-defined virologic failure; **RAM,** resistance-associated mutation

D'Amico R, et al. HIV Glasgow 2020. Oral O414

FLAIR extension phase: Efficacy with optional OLI



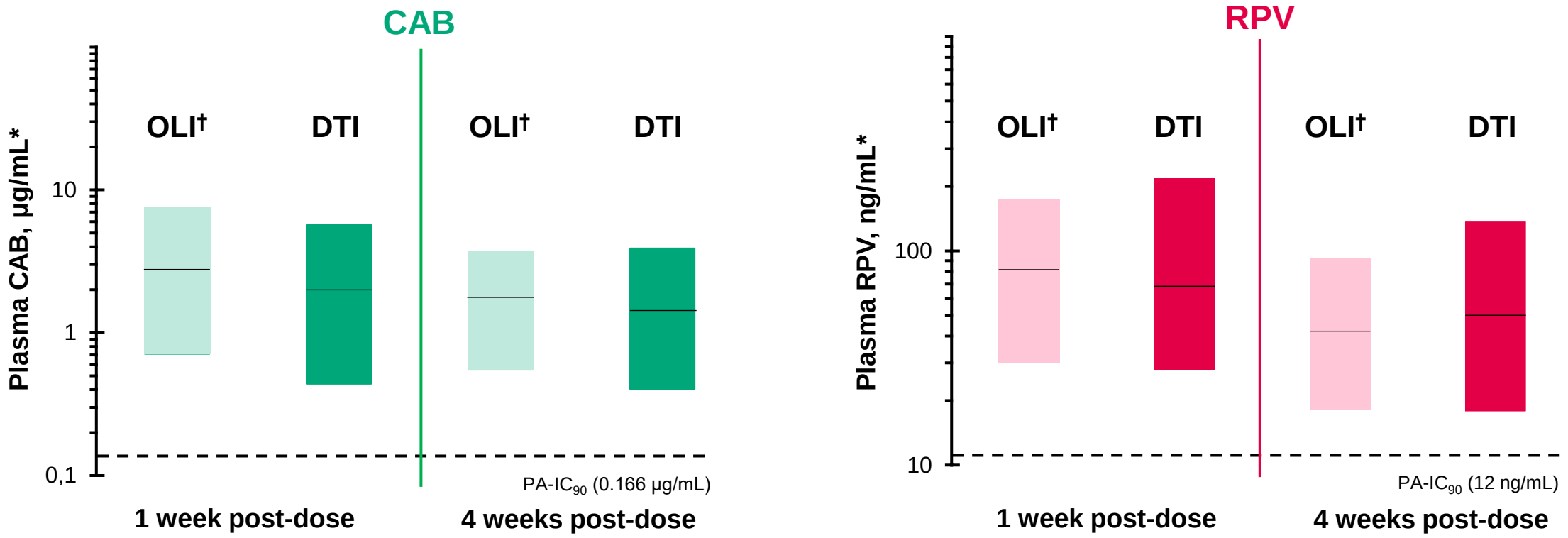
Efficacy was high in participants started directly on injections and those receiving OLI; one participant who started directly on injections (0.4%) met the CVF criterion*†

***Two consecutive plasma HIV-1 RNA measurements of ≥200 c/mL
†The participant was in the DTI arm and met the CVF criterion on the 12th week of LA therapy. No INI or NNRTI RAMs were detected at BL and no INI RAMs were detected at the time point of SVF (NNRTI mutations could not be generated)
BL, baseline; **CVF,** confirmed virologic failure; **INI,** integrase inhibitor; **SVF,** suspected virologic failure

D'Amico R, et al. HIV Glasgow 2020. Oral O414

FLAIR extension phase: PK with optional OLI

CAB and RPV concentrations assessed 1 week post-loading dose injections



No clinically meaningful differences in median CAB and RPV concentrations were observed between participants receiving an OLI and those starting without an OLI

*5th percentile, median, and 95th percentile values 1 week and 4 weeks after LA administration (OLI, LA arm: Week 5, n=262 [CAB]/263 [RPV]; Week 8, n=250 [CAB]/251 [RPV]; no OLI, DTI arm: Week 101, n=104; Week 104, n=79)
†Historical data: participants who were randomized to CAB + RPV LA in the maintenance phase
PA-IC_{90}, protein-adjusted 90% inhibitory concentration

D'Amico R, et al. HIV Glasgow 2020. Oral O414

FLAIR extension phase: Summary of safety data with optional OLI

Summary of AEs (excluding ISRs)

Parameter, n (%)	DTI arm n=111	OLI arm n=121
Any AE	88 (79)	85 (70)
Any Grade 3–4 AEs	4 (4)	5 (4)
Drug-related AEs	22 (20)	23 (19)
Drug-related Grade 3–4 AEs	1 (<1)*	0
AEs leading to withdrawal	1 (<1)*	1 (<1)†
Any SAEs	4 (4)	5 (4)
Drug-related SAEs	1 (<1)*	0
Fatal SAEs	0	0

Common AEs and drug-related AEs (excluding ISRs)

Common (≥5% in either arm) AEs, n (%)	DTI arm n=111	OLI arm n=121
Nasopharyngitis	20 (18)	13 (11)
Upper respiratory tract infection	10 (9)	7 (6)
Pyrexia	9 (8)	4 (3)
Diarrhea	2 (2)	10 (8)
Dizziness	8 (7)	4 (3)
Gastroenteritis	7 (6)	3 (2)
Headache	7 (6)	3 (2)
Common (≥3% in either arm) drug-related AEs, n (%)		
Pyrexia	6 (5)	2 (2)
Dizziness	3 (3)	2 (2)

- Incidence of Grade 3 or 4 emergent chemistry toxicities (13 vs 5)‡ and rash (4 vs 2; all Grade 1 or 2)§ was higher in the DTI versus OLI arm

No liver monitoring/stopping events, confirmed hypersensitivity reactions, or other significant dermatological manifestations were observed in either treatment arm

*Grade 4 drug-related SAE leading to withdrawal in the DTI arm was Hodgkin's disease mixed cellularity; †One participant discontinued from the OLI arm due to AE of weight gain (8 kg)
‡DTI arm: Grade 3 AST, CPK, GFR, lipase, and phosphate toxicities and Grade 4 CPK and lipase toxicities; OLI arm: Grade 3 CPK and lipase toxicities and Grade 4 CPK toxicities
§One AE of rash pruritic (Grade 1), reported during the OLI period in the OLI arm, and was considered related to study drugs
AST, aspartate aminotransferase; **CPK,** creatine phosphokinase; **GFR,** glomerular filtration rate; **ISR,** injection site reaction

Management of switching to LA CAB+ RPV: optional OLI

Previous HAART

Oral lead in = OLI
CAB + RPV for 4 weeks

Long Acting = LA
CAB + RPV

CAB + RPV LA: Optional OLI overview

- CAB + RPV LA currently could require an OLI as a tolerability check, which consists of oral CAB + RPV taken daily for approximately 1 month (at least 28 days) prior to the first injection[1,2]
- No major safety signals were identified during the OLI in over 1,200 PLHIV that received CAB + RPV LA treatment in Phase III trials, providing the rationale to investigate direct administration of CAB + RPV LA without an OLI[3–5]
- The FLAIR 124-week extension phase compared OLI versus starting patients directly on injections of CAB + RPV LA; there were no meaningful differences over 24 weeks in outcomes including maintenance of virologic suppression, safety, tolerability, and PK[5]
- Optional OLI is being further evaluated in the SOLAR study for CAB + RPV LA treatment, and during the open-label extension phases of both HPTN 083 and HPTN 084 for CAB LA PrEP[6–8]
- Optional OLI aims to increase flexibility and choice for HCPs and PLHIV

CAB, cabotegravir; **HCP,** healthcare provider; **LA,** long-acting; **OLI,** oral lead-in; **PK,** pharmacokinetics **PLHIV,** people living with HIV; **PrEP,** pre-exposure prophylaxis; **RPV,** rilpivirine

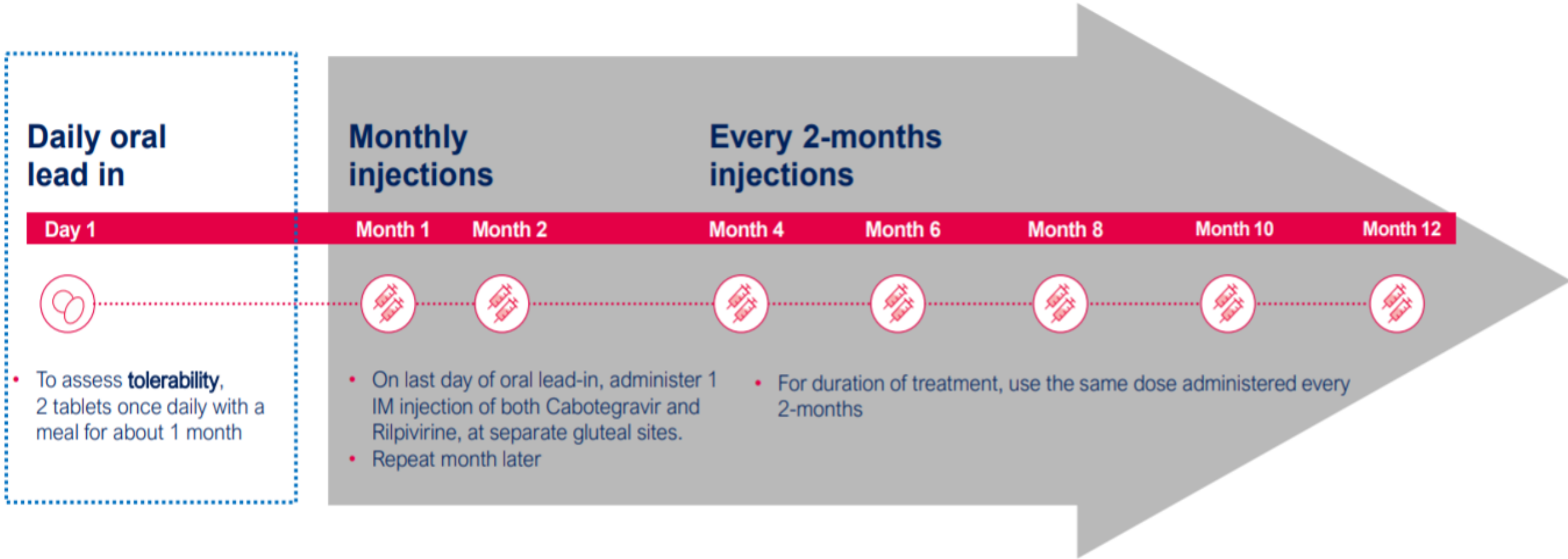
1. Vocabria EU SmPC. Jul 2021; **2.** Cabenuva US PI. Jan 2021; **3.** Rizzardini G, et al. J Acquir Immune Defic Syndr 2020;85:498–506
4. Overton ET, et al. Lancet 2021;396:1994–2005; **5.** D'Amico R, et al. HIV Glasgow 2020. Oral O414
6. SOLAR (NCT04542070). Available at: https://clinicaltrials.gov/ct2/show/NCT04542070 (accessed Sep 2021)
7. HPTN 083 Protocol V4. Feb 2021. Available at: https://drive.google.com/file/d/12Z98Hew8LDlT0iRnFYx-XeZrlUWExJI0/view (accessed Sep 2021)
8. HPTN 084 Protocol V3.0. Aug 2021. Available at: https://www.hptn.org/sites/default/files/inline-files/HPTN%20084%20Prot%203.0%2C%20FINAL%2012Aug2021.pdf (accessed Sep 2021)

Outline

-Management of oral lead in of long acting CAB + RPV

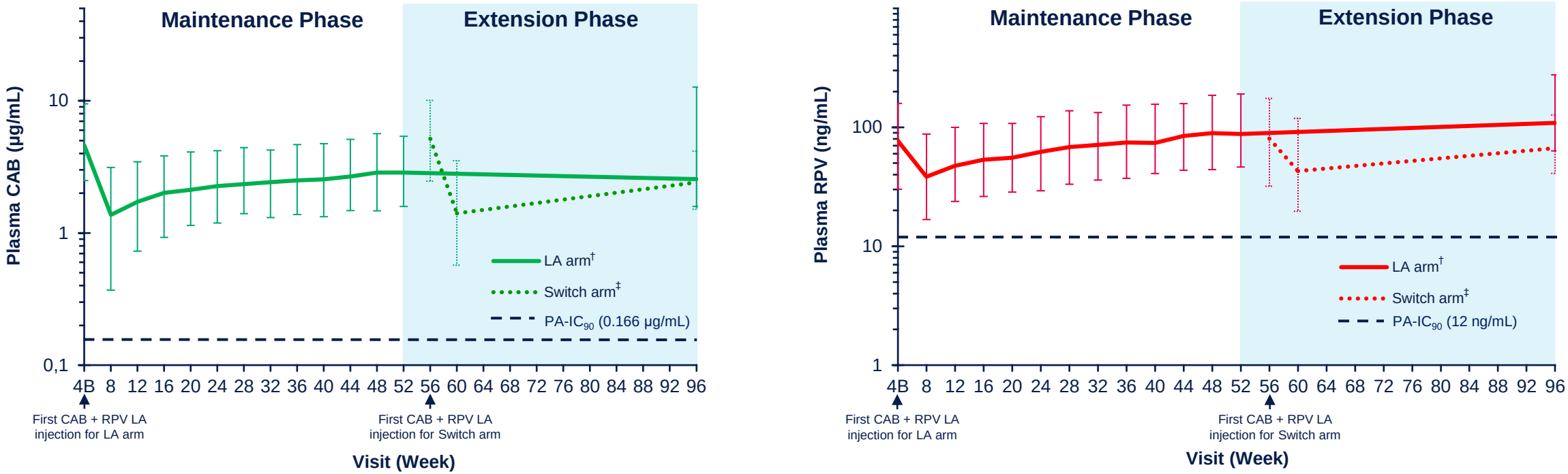
-Management of missed or delayed long acting doses:

CAB and RPV: every 2-months dosing schedule



- **±7-days** dosing window for injections is permitted given minimal impact on CAB and RPV Q2M PK profile
- **Oral CAB + RPV** therapy provides safe and therapeutic exposures for planned interruptions in LA dosing and can be used to cover a planned injection delay for up to one 2-monthly injection cycle

ATLAS Week 96: Plasma CAB and RPV Trough Concentrations*



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

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

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

Outline

-Management of oral lead in of long acting CAB + RPV

-Management of missed or delayed long acting doses:

-1 week delay

Impact of 7-day dosing delays on CAB LA concentrations: Q8W dosing regimen – PK simulations

Percentage of participants above the Phase III benchmark CAB C_{trough}* (target: >95%)

2nd injection delay	Prior to resuming the delayed injection	After resuming the delayed injection
No delay	95	96
1 week	94	95
2–4 weeks	77–91	93–94

4th injection delay	Prior to resuming the delayed injection	After resuming the delayed injection
No delay	95	95
1 week	93	94
2–4 weeks	79–90	93–97

Dosing within 7 days of the target treatment date maintains acceptable CAB and RPV C_{trough} at time of delay

*Simulated 5th percentile C_{trough} following initial injection (0.65 µg/mL)
Interpretations made based on delays of 4th injection are applicable to subsequent injections
C_{trough}, trough concentrations; **PK,** pharmacokinetic

Han K, et al. CROI 2021. Oral 1327

Impact of 7-day dosing delays on RPV LA concentrations: Q8W dosing regimen – PK simulations

Percentage of participants above the Phase III benchmark RPV C_{trough}* (target: >95%)

	Length of delay					
Delayed injection	**No delay**	**1 week**	**2 weeks**	**4 weeks**	**8 weeks**	**12 weeks**
2nd injection	99	99	96	85	49	24
3rd injection	99	97	95	90	76	61
4th injection	99	99	98	96	88	80

Dosing within ±7 days of the target treatment date maintains acceptable RPV C_{trough} at the time of delay

*17.3 ng/mL = Phase III benchmark RPV C_{trough}
Interpretations made based on delays of 4th injection are applicable to subsequent injections

Janssen Research and Development. Data on File. Population PK Report (TMC278 long-acting in study 207966 ATLAS-2M). Dec 2019. Table 12

Target treatment date and ±7-day window for CAB + RPV LA injections: Key principles

- Patients should choose a date and aim to receive their injections **on this date** every month or every two months[1,2]
  - This is known as the **target treatment date**
  - Consider choosing the 1st–28th of the month (not all months have equal number of days)
  - It's important that patients do not miss scheduled injection visits
  - Where this is not possible, injection appointments can be booked up to **7 days before OR 7 days after** the target treatment date*
  - Patients who use the ±7-day window should return to their target treatment date (or as close as possible) for their next injection visit

Example target treatment date of 15th

Sun	Mon	Tue	Wed	Thu	Fri	Sat
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	**15**	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30		

Flexible injection window

*Remain as close to the target treatment date as possible

1. ViiV Healthcare. HCP consultation guide. Available from: https://gskpro.com/content/dam/global/hcpportal/fi_FI/unprotected/pdf/hcp-patient-consultation-guide-finland-42021.pdf (accessed Aug 2021)
2. Cabenuva. Dosing and administration guide. Available from: https://assets.gskstatic.com/pharma/us/viiv/Cabenuva-Dosing-Administration-Guide.pdf (accessed Aug 2021)

-Management of oral lead in of long acting CAB + RPV

-Management of missed or delayed long acting doses:

-1 week delay

-more than 1 week delay (with or without oral bridging):

✓Impact on risk of suboptimal PK

✓Impact on following schedule of injections

Impact of dosing delays on CAB LA concentrations: Q8W dosing regimen – PK simulations

Percentage of participants above the Phase III benchmark CAB C_{trough}* (target: >95%)

2nd injection delay	Prior to resuming delayed injection without OB	Prior to resuming delayed injection with OB	After resuming delayed injection regardless of OB
No delay	95	100	96
1 week	94	100	95
2–4 weeks	77–91	100	93–94
4–8 weeks	33–77	100	92–93 (with resumption)
			96 (with re-initiation)

4th injection delay	Prior to resuming delayed injection without OB	Prior to resuming delayed injection with OB	After resuming delayed injection regardless of OB
No delay	95	100	95
1 week	93	100	94
2–4 weeks	79–90	100	93–94
4–8 weeks	58–79	100	92–93 (with resumption)
			97 (with re-initiation)

*Simulated 5th percentile C_{trough} following initial injection (0.65 µg/mL)
Re-initiating the Q8W regimen means that the resumed delayed injection and the next injection will be 1 month apart instead of 2 months
Interpretations made based on delays of 4th injection are applicable to subsequent injections
OB, oral bridging

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Managing unplanned missed injections (without oral bridging): Q2M

- Dosing beyond the +7-day window should be avoided, especially during initiation phase of the dosing schedule.[1,2] Delays in dosing increase the risk of lower CAB and RPV concentrations and the risk of viral rebound and resistance development in some patients
- Patients who miss a scheduled injection visit by >7 days should be clinically reassessed to ensure resumption of therapy remains appropriate[1,2]

Resumption of injections after unplanned missed injections (without oral bridging)[1,2]

Time since MISSED injection date	Injection dosing recommendation
≤1 month*	Continue with the every 2 month (3 mL, 600 mg CAB and 900 mg RPV) IM injections dosing schedule as soon as possible
>1 month* (and < 2 month)	Re-initiate injections (3 mL, 600 mg CAB and 900 mg RPV): two initiation injections 1 month apart, then every 2 months thereafter

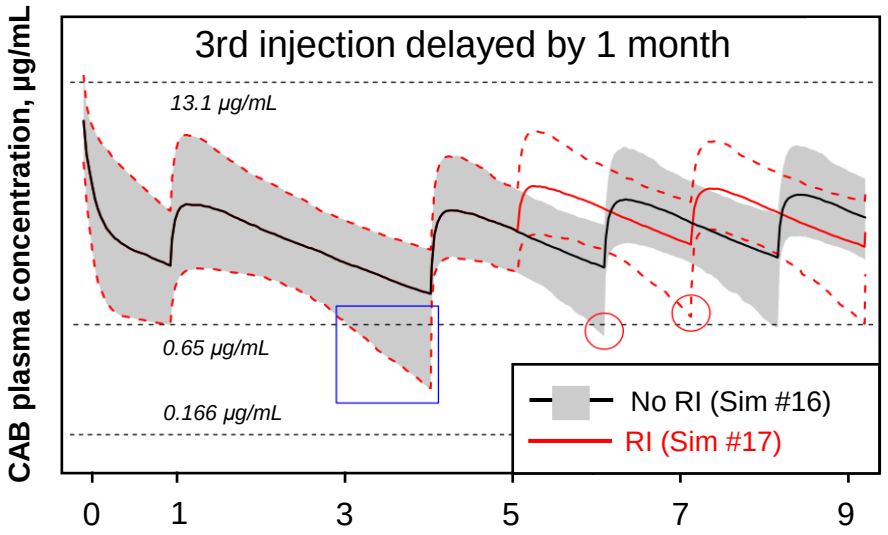
- Assuming it is convenient, patients should return to their target treatment date (or as close as possible)

*1 month = 28 day

1. Vocabria EU SmPC. Jul 2021
2. Rekambys EU SmPC. Jul 2021

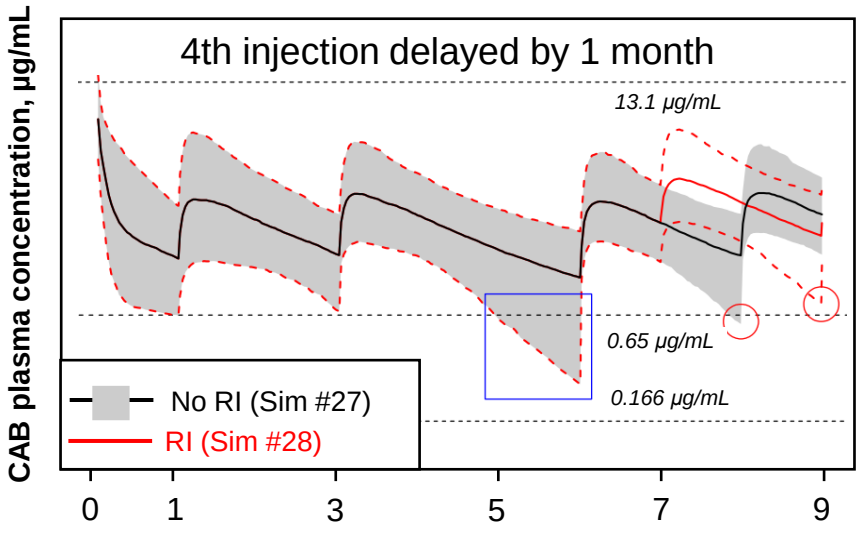
Simulated impact of 3rd and 4th injection dosing delays on CAB PK: Q8W dosing regimen

4-week delay of 3rd injection (with and without re-initiating Q8W regimen)



- Predicted percentage of subjects with CAB C_{trough} above 0.65 µg/mL:
  - **96.6%** versus **93.2%** (with and without re-initiation of Q8W dosing, respectively)

4-week delay of 4th injection* (with and without re-initiating Q8W regimen)



- Predicted percentage of subjects with CAB C_{trough} above 0.65 µg/mL:
  - **96.8%** versus **93.4%** (with and without re-initiation of Q8W dosing, respectively)

Re-initiation of Q2M dosing is recommended for delays >1 month regardless of which visit is delayed and regardless of oral bridging

***Interpretations made based on delays of 4th injection are applicable to subsequent injections
Re-initiation of dosing means giving 2 initiation doses 1 month apart and then 600 mg IM Q8W thereafter
RI, re-initiation

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Impact of dosing delays on CAB LA concentrations: Q8W dosing regimen – PK simulations

Percentage of participants above the Phase III benchmark CAB C_{trough}* (target: >95%)

2nd injection delay	Prior to resuming delayed injection without OB	Prior to resuming delayed injection with OB	After resuming delayed injection regardless of OB
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1 week	94	100	95
2–4 weeks	77–91	100	93–94
4–8 weeks	33–77	100	92–93 (with resumption) 96 (with re-initiation)

4th injection delay	Prior to resuming delayed injection without OB	Prior to resuming delayed injection with OB	After resuming delayed injection regardless of OB
No delay	95	100	95
1 week	93	100	94
2–4 weeks	79–90	100	93–94
4–8 weeks	58–79	100	92–93 (with resumption) 97 (with re-initiation)

*Simulated 5th percentile C_{trough} following initial injection (0.65 µg/mL)
Re-initiating the Q8W regimen means that the resumed delayed injection and the next injection will be 1 month apart instead of 2 months
Interpretations made based on delays of 4th injection are applicable to subsequent injections
OB, oral bridging

Han K, et al. CROI 2021. Oral 1327

Managing planned missed injections (with oral bridging): Q2M

- CAB and RPV oral tablets QD can be used to replace CAB + RPV LA injections for up to 2 months[1,2]
  - For oral therapy durations greater than 2 months, an alternative oral regimen is recommended[1,2]
- The 1st dose of oral therapy should be taken on the target date for injection (±7 days)[1,2]
- It is recommended to resume injection dosing on the target treatment date. Oral dosing completes on the same day as injections restart[3]

IM, intramuscular

1. Vocabria EU SmPC. Jul 2021; **2.** Rekambys EU SmPC. Jul 2021; **3.** ViiV Healthcare. HCP consultation guide. Available from: https://gskpro.com/content/dam/global/hcpportal/fi_FI/unprotected/pdf/hcp-patient-consultation-guide-finland-42021.pdf (accessed Aug 2021)

Managing planned missed injections (with oral bridging): Q2M

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- The 1st dose of oral therapy should be taken on the target date for injection (±7 days)[1,2]
- It is recommended to resume injection dosing on the target treatment date. Oral dosing completes on the same day as injections restart[3]

Resumption of injections after planned missed injections (with oral bridging)[1,2]

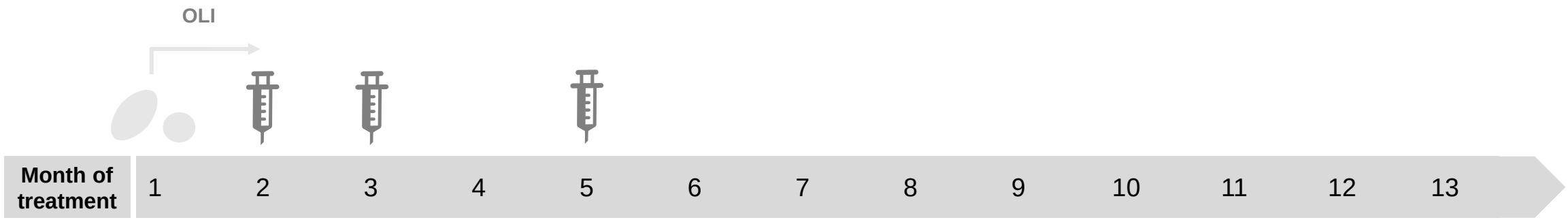
Time since MISSED injection date	Injection dosing recommendation
≤1 month	Continue with every 2 month (3 mL, 600 mg CAB LA and 900 mg RPV LA) IM injections dosing schedule as soon as possible
>1 month	Re-initiate injections (3 mL, 600 mg CAB LA and 900 mg RPV LA): two initiation injections 1 month apart, then every 2 months thereafter

IM, intramuscular

1. Vocabria EU SmPC. Jul 2021; **2.** Rekambys EU SmPC. Jul 2021; **3.** ViiV Healthcare. HCP consultation guide. Available from: https://gskpro.com/content/dam/global/hcpportal/fi_FI/unprotected/pdf/hcp-patient-consultation-guide-finland-42021.pdf (accessed Aug 2021)

Managing planned missed injections (with oral bridging): Q2M

- If a patient needs to miss an upcoming scheduled injection visit (e.g. due to an extended vacation), oral bridging with CAB and RPV can be used to replace the scheduled injection dose for up to 2 months[1,2]
- For example, a patient uses oral bridging for 2 months:



Full guidance in SmPCs
SmPC, Summary of Product Characteristic

1. Vocabria EU SmPC. Jul 2021
2. Rekambys EU SmPC. Jul 2021

Managing planned missed injections (with oral bridging): Q2M

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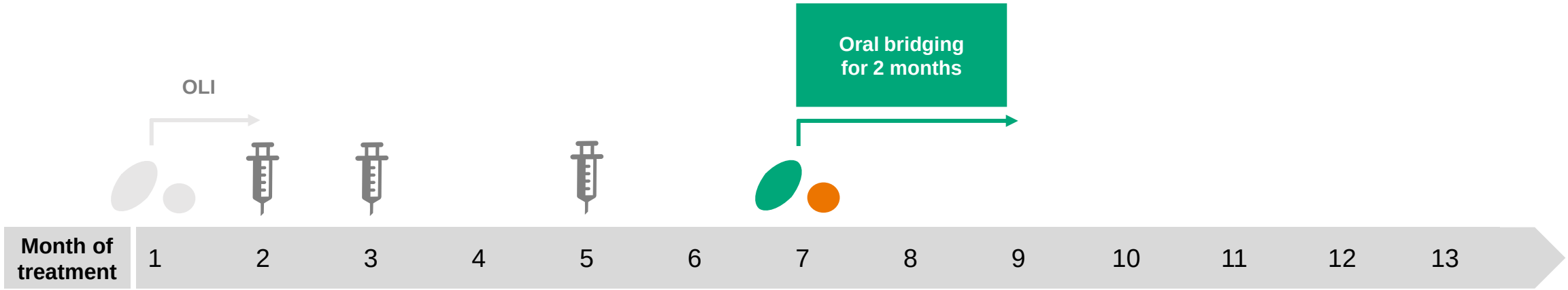

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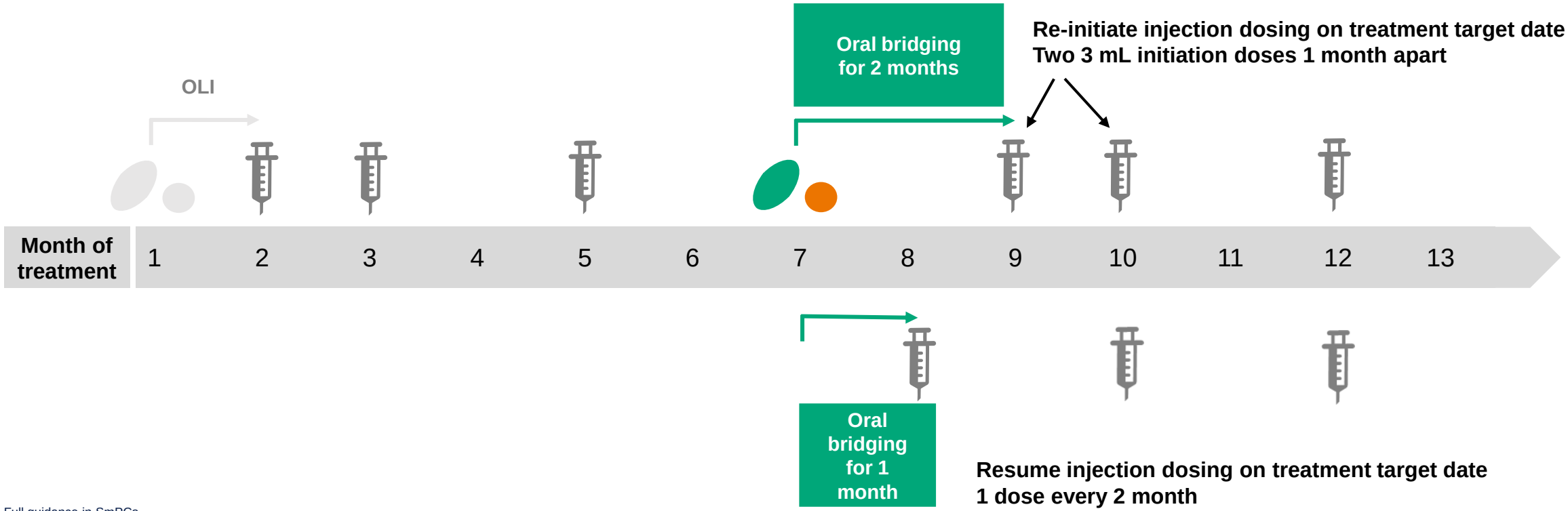
Managing planned missed injections (with oral bridging): Q2M

- Re-initiate injection dosing on treatment target date
- Two 3 mL initiation doses 1 month apart



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Case-based scenario: Missed injections with oral bridging (Q2M)

- A patient has been receiving CAB + RPV LA Q2M injections for 1 year on the 14th of the month
- They receive their February injections, but plan to be away until May 24th (6 weeks after their target date, April 14th). You counsel the patient about oral bridging
- **When should oral bridging be started?**
  a. April 14th (next treatment target date)
  b. February 14th (same day as injections)
  c. May 24th (when the patient returns)

Scenario and patient are fictive and only to illustrate concept

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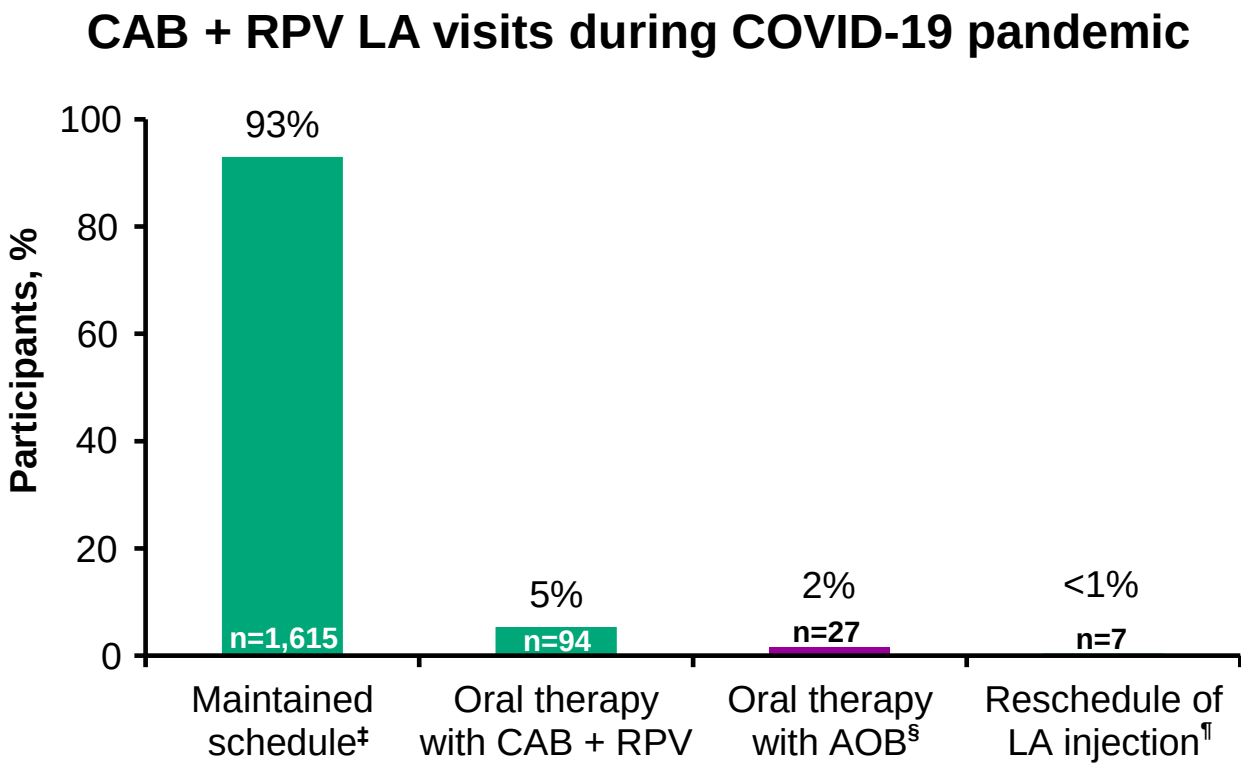
  c. Both a. and b. are reasonable options
- Option b may be preferable for some since A) monthly packs of oral tablets are dispensed B) maintaining an established treatment target date may be easier to manage. In addition, it has been **>1 month** since the missed target date, so regardless of oral bridging, re-initiate injections, with two initiation doses 1 month apart and Q2M thereafter[1,2]

Scenario and patient are fictive and only to illustrate concept

1. Vocabria EU SmPC. Jul 2021
2. Rekambys EU SmPC. Jul 2021

Impact of the COVID-19 pandemic on oral bridging requirements in ongoing Phase II/III CAB + RPV LA clinical trials

- In ongoing CAB + RPV LA clinical studies, most (93%) visits proceeded as planned*
- Few participants had COVID-19-impacted visits; most used temporary oral therapy for bridging to maintain continuous ART†



Despite the impact of the COVID-19 pandemic, there have been no ART interruptions among participants in CAB + RPV LA clinical trials

*LATTE-2, POLAR (both Phase IIb), FLAIR, ATLAS, ATLAS-2M (all Phase III), and CUSTOMIZE (Phase IIIb); †One participant was removed from the study
‡Attended an injection visit within the planned ±7-day window; §Oral SOC: DTG + RPV or DTG/RPV, n=11 (41%); DTG/ABC/3TC, n=10 (37%); EVG/c/TAF/FTC, n=2 (7%); EVG/TDF/FTC, n=1 (4%); BIC/TAF/FTC, n=1 (4%); DRV/r/TDF/FTC, n=1 (4%); DTG + TDF/FTC, n=1 (4%); ¶Attended an injection visit 1 day before or up to 5 days after the treatment window
3TC, lamivudine; **ABC,** abacavir

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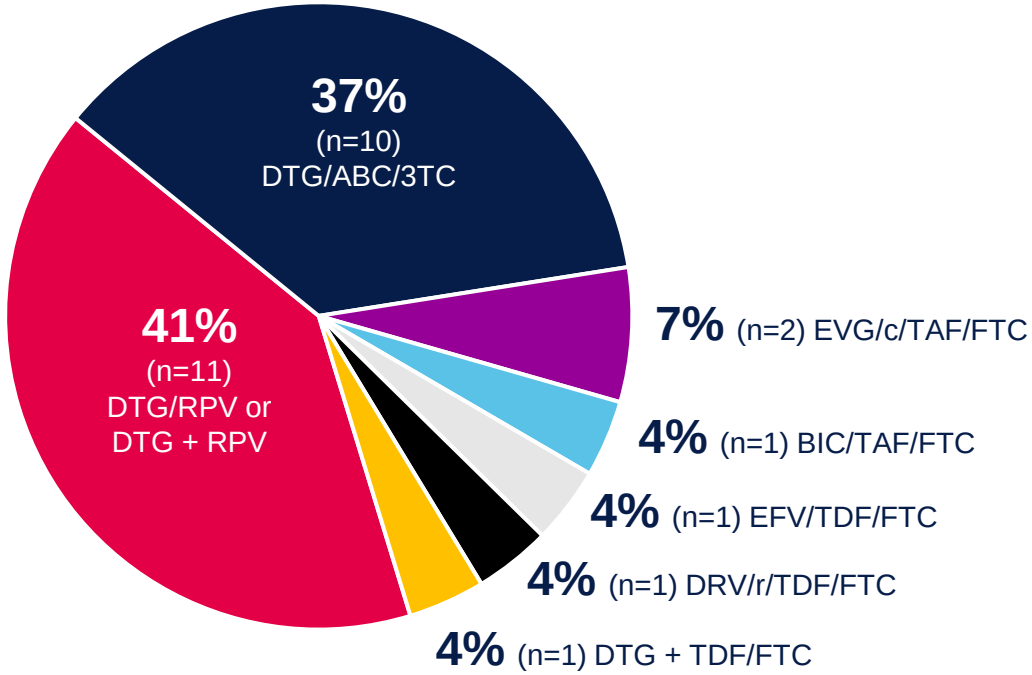
AOB regimens selected for missed CAB + RPV LA injections in ongoing Phase II/III clinical trials

- If oral CAB + RPV was unavailable, physicians were allowed to choose an alternative oral ART
- AOB was used as per CAB + RPV oral bridging guidelines in the current label:
  - Started at time of planned missed LA dose and stopped on day of resumption of LA dosing
- DTG-based regimens were used in 81% of participants

Participants using AOB for COVID-19-impacted visits*



AOB regimens were used in 27 participants across Phase II/III trials in the early stages of the COVID-19 pandemic

*Data from six ongoing CAB + RPV LA studies: LATTE-2, POLAR (both Phase IIb), FLAIR, ATLAS, ATLAS-2M (all Phase III), and CUSTOMIZE (Phase IIIb)

Czarnogorski M, et al. IDWeek 2020. Oral LB-8

Outcomes for participants receiving oral CAB + RPV or AOB for COVID-19-impacted visits in ongoing Phase II/III clinical trials

The median duration of oral therapy to cover the COVID-19-impact visit(s) was **51 days** (IQR: 27–69)*

110 of 121 (91%) of participants who transitioned to temporary oral therapy (CAB + RPV or AOB) have **restarted CAB + RPV LA therapy,** and disposition of remaining participants is in progress†

No SVFs or CVFs have been observed in patients receiving **oral CAB + RPV** or **AOB** as a consequence of COVID-19

Analysis of six CAB + RPV LA studies including LATTE-2, POLAR (both Phase IIb), FLAIR, ATLAS, ATLAS-2M (all Phase III), and CUSTOMIZE (Phase IIIb)
***Data for median duration were available for 103 participants as of September 15, 2020
†As of October 19, 2020
CVF, confirmed virologic failure; **IQR,** interquartile range; **SVF,** suspected virologic failure

Thank you

Edward Jenner, the pioneer of smallpox vaccine, sees off the anti-vaccinators (1868)