PERSATUAN PERUBATAN HIV MALAYSIA
MALAYSIAN SOCIETY FOR HIV MEDICINE (MASHM)
No Pendaftaran: PPM-001-10-23071997

MyHIV FORUM 2022

15-16 October 2022 | Faculty of Medicine, UiTM, Sungai Buloh, Selangor.

Date: 1 September 2022

Invitation as Speaker in the MyHIV Forum 2022: Getting PrEPped For 2030

Dear Dr Ummu Afeera,

It is with great pleasure to announce that the Malaysian Society for HIV Medicine (MASHM) in collaboration with the Malaysian AIDS Council (MAC), Malaysian AIDS Foundation (MAF), Centre of Excellence for Research in AIDS (CERIA), and Pertubuhan Paramedik Penyakit Berjangkit Se Malaysia (PRISMA) will be organizing *the* ***MyHIV Forum 2022: Getting PrEPped For 2030, at the Faculty of Medicine, UiTM, Sungai Buloh on the 15th- 16th of October 2022.***

2. Our goal is to bring together healthcare professionals and key population representatives who are actively involved in HIV care to have an in depth discussion on the latest HIV care, treatment and prevention strategies.

3. The organising committee would like to formally invite you to join us as a speaker at this conference. We believe your expertise and experience would be an excellent addition to our programme. The programme of the whole forum is attached for your reference. Your session will be as follows:

Date: 16th October 2022
Session: Symposium 10
Theme: Rapid Fire: Top Papers in HIV
Topic: Injectables (CAB/RPV): ATLAS and FLAIR
Time: 2:35pm – 2:50pm

4. Lastly, kindly provide us with a one-page biography of yourself and fill up the speaker details sheet. A template of the biography and the speaker details sheet is attached here.

We look forward to your participation in this event. Thank you.

Yours sincerely,

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Dr Leong Chee Loon
Organizing Chairman
MyHIV Forum 2022

MASHM
MYHIV FORUM 2022

RAPID FIRE:
TOP PAPERS IN HIV

INJECTABLES
CABOTEGRAVIR & RILPIVIRINE

Ummu Afeera Zainulabid

CASE STUDY

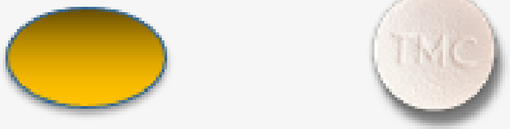
40-year-old male with long standing stable RVD complaining to you about pill fatigue.

POTENTIAL ADVANTAGES OF LA ARV

- Address suboptimal adherence
- Less frequent dosing
- Avoidance of pill fatigue
- Avoidance of HIV related stigma

INJECTABLES
NEW HORIZONS IN THERAPY

Optional Lead-In Oral Components

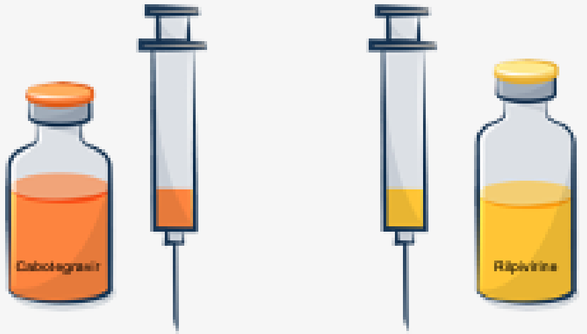


Cabotegravir + Rilpivirine

30 mg — 25 mg

INSTI — NNRTI

Intramuscular Injection Components



Cabotegravir + Rilpivirine

200 mg/mL — 300 mg/mL

INSTI — NNRTI

- **Integrase Strand Transfer Inhibitor (INSTI)**
- **Non-nucleoside reverse transcriptase inhibitor (NNRTI)**

SUMMARY OF KEY STUDIES

CABOTEGRAVIR AND RILPIVIRINE LONG-ACTING INJECTABLE

Phase 3 Trials in Treatment Naïve

- FLAIR: IM CAB + IM RPV monthly versus oral DTG-ABC-3TC: 48 weeks
- FLAIR: IM CAB + IM RPV monthly versus oral DTG-ABC-3TC: 96 weeks
- FLAIR: IM CAB + IM RPV with or without oral lead in: 124-week extension

Phase 3 Trials in Treatment Experienced

- ATLAS: Switch to monthly IM CAB + IM RPV or continue 3-drug oral ART
- ATLAS-2M: switch to IM CAB + IM RPV taken every 1 or 2 months: 48 weeks
- ATLAS-2M: switch to IM CAB + IM RPV taken every 1 or 2 months: 96 weeks

Phase 2 Trials

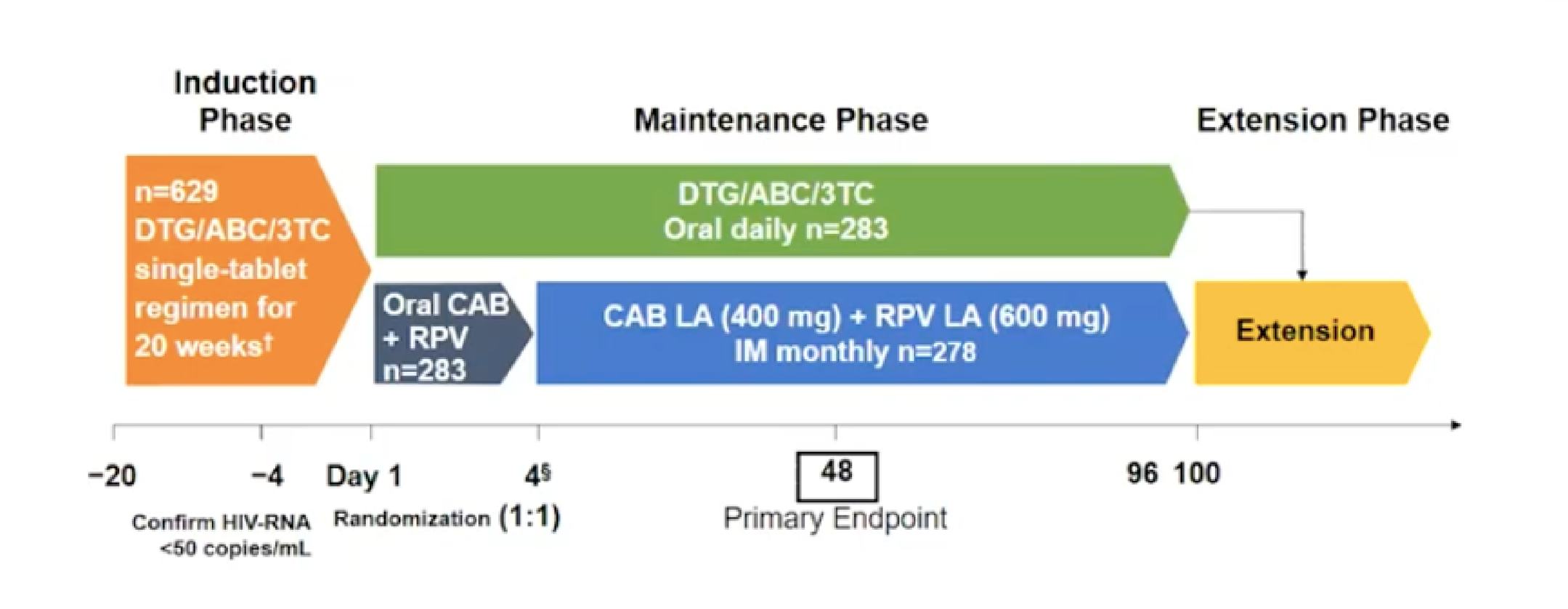
- LATTE: oral CAB + oral RPV daily versus oral EFV plus 2 NRTIs
- LATTE-2: IM CAB + IM RPV every 1 or 2 months versus oral CAB + oral ABC-3TC
- POLAR: every 2-month IM CAB + IM RPV after 5 years or oral CAB + oral RPV

LONG-ACTING IM CABOTEGRAVIR AND IM RILPIVIRINE AFTER ORAL INDUCTION

FLAIR STUDY

LONG-ACTING IM CABOTEGRAVIR AND IM RILPIVIRINE AFTER ORAL INDUCTION

FLAIR STUDY



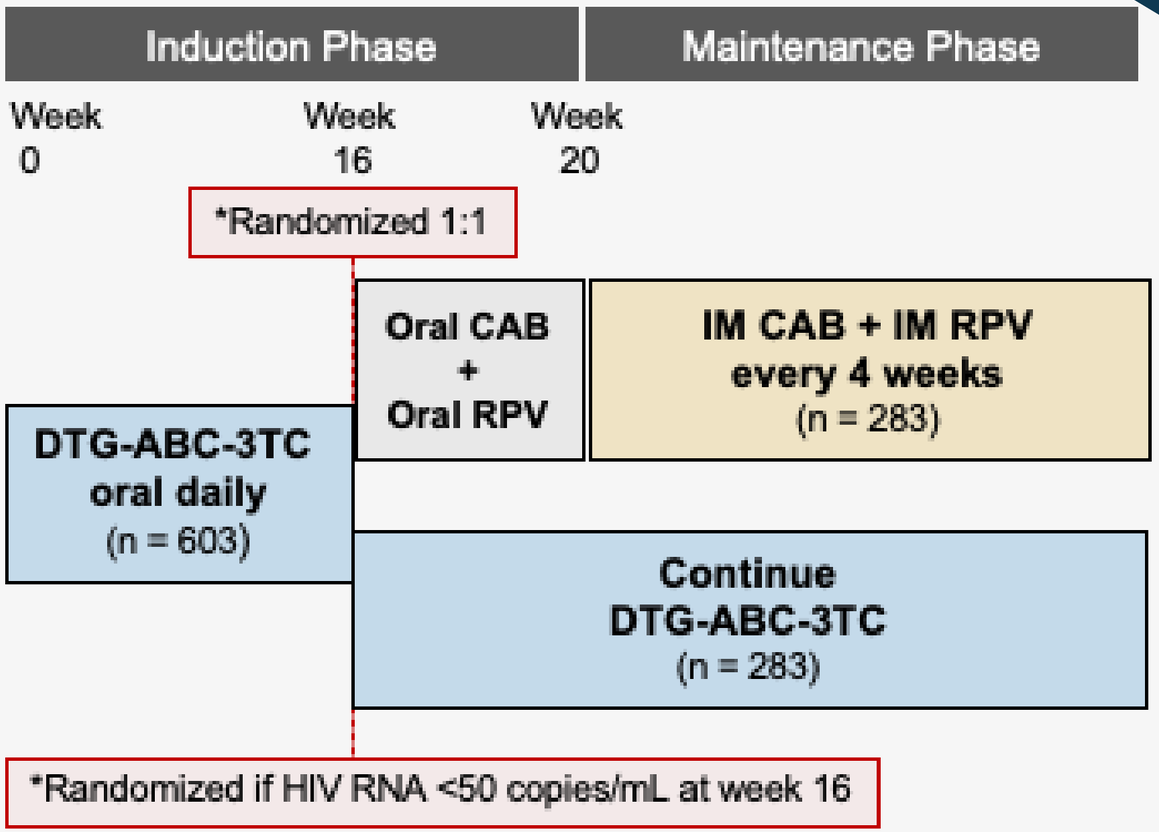
Source: Orkin C, et al. N Engl J Med. 2020;382:1124-35.

LONG-ACTING IM CABOTEGRAVIR AND IM RILPIVIRINE AFTER ORAL INDUCTION

FLAIR STUDY: 48-WEEK DATA

FLAIR STUDY (48-WEEK DATA): DESIGN

- **Background**: Phase 3, randomized, open-label, trial assessing IM CAB + RPV after oral induction for treatment-naïve adults
- **Inclusion Criteria**
  - Age ≥18 years
  - Antiretroviral-naïve
  - HIV RNA ≥1,000 copies/mL
  - Any CD4 cell count
  - No chronic hepatitis B
  - No NNRTI resistance



Oral lead in dosing: cabotegravir 30 mg daily and rilpivirine 25 mg daily x 4 weeks
Loading injections: cabotegravir 600 mg IM and 900 mg rilpivirine IM x 1
Maintenance injections: cabotegravir 400 mg IM and 600 mg rilpivirine IM monthly

Source: Orkin C, et al. N Engl J Med. 2020;382:1124-35.

FLAIR STUDY (48-WEEK DATA): CONCLUSION

CONCLUSION

"Therapy with long-acting cabotegravir plus rilpivirine was noninferior to oral therapy with dolutegravir–abacavir–lamivudine with regard to maintaining HIV-1 suppression. Injection-site reactions were common."

Source: Orkin C, et al. N Engl J Med. 2020;382:1124-35.

LONG-ACTING IM CABOTEGRAVIR AND IM RILPIVIRINE AFTER ORAL INDUCTION

FLAIR STUDY: 96-WEEK DATA

FLAIR STUDY (96-WEEK DATA): CONCLUSION

CONCLUSION

"The 96-week results reaffirm the 48-week results, showing long-acting cabotegravir and rilpivirine continued to be non-inferior compared with continuing a standard care regimen in adults with HIV-1 for the maintenance of viral suppression. These results support the durability of long-acting cabotegravir and rilpivirine, over an almost 2-year-long period, as a therapeutic option for virally suppressed adults with HIV-1."

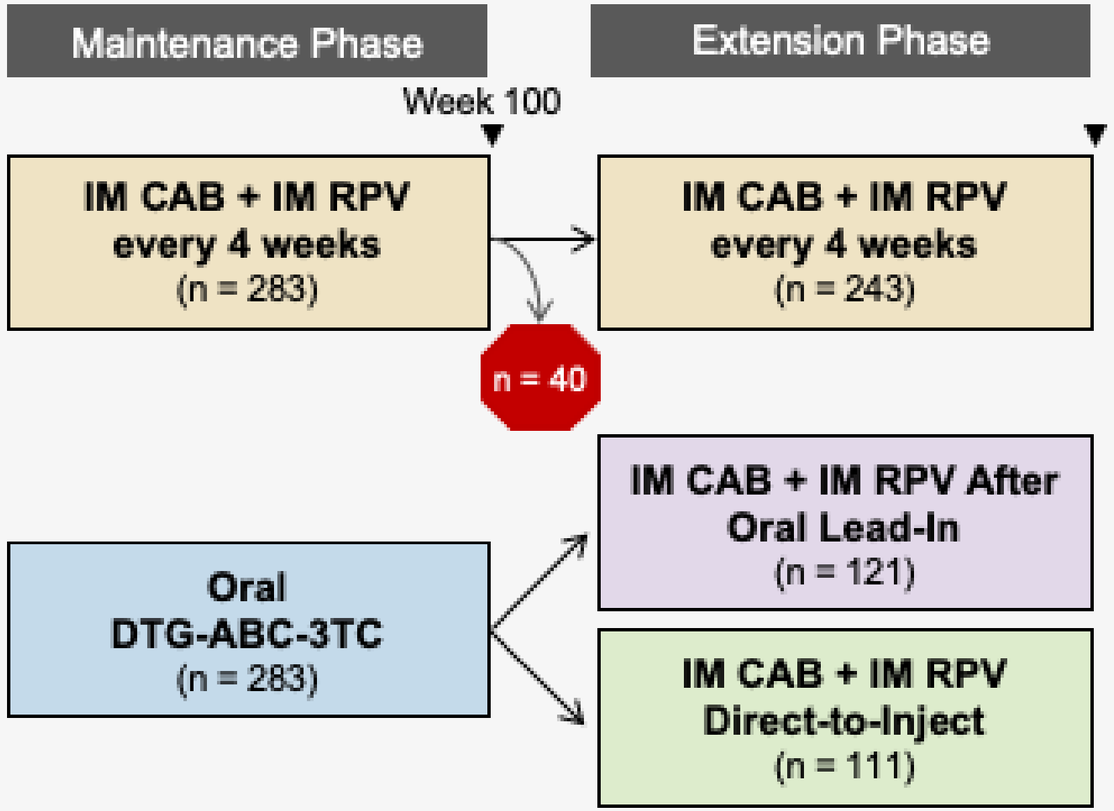
Source: Orkin C, et al. Lancet HIV. 2021;8:e185-e196.

LONG-ACTING IM CABOTEGRAVIR AND IM RILPIVIRINE AFTER ORAL INDUCTION

FLAIR STUDY: WEEK 124 EXTENSION PHASE

FLAIR STUDY (124-WEEK EXTENSION): DESIGN

- **Background**: Extension of phase 3, randomized, open-label trial assessing IM CAB + IM RPV compared to DTG-ABC-3TC for treatment-naïve adults
- **Inclusion Criteria**: After 100-week maintenance phase, participants receiving IM CAB + IM RPV every 4 weeks could choose to continue (*Continuation Group*) or withdraw; those assigned to oral ART could choose to transition (*Switch Group*) to IM CAB + IM RPV after oral lead in or without oral lead in ("direct to inject")



Oral lead in dosing: cabotegravir 30 mg daily and rilpivirine 25 mg daily x 4 weeks
Loading injections: cabotegravir 600 mg IM and 900 mg rilpivirine IM x 1
Maintenance injections: cabotegravir 400 mg IM and 600 mg rilpivirine IM monthly

Source: Orkin C, et al. Lancet HIV. 2021;8:e185-e196.

FLAIR STUDY (124-WEEK EXTENSION): CONCLUSION

CONCLUSION

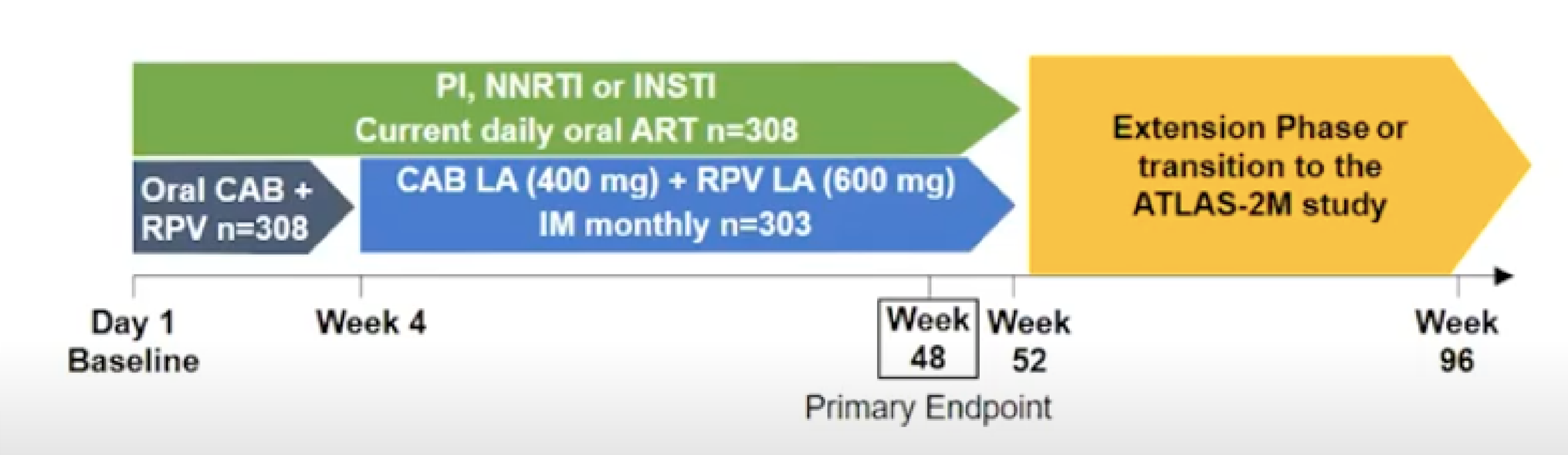
"After 24 weeks of follow-up, switching to long-acting treatment with or without an oral lead-in phase had similar safety, tolerability, and efficacy, supporting future evaluation of the simpler direct-to-injection approach. The week 124 results for participants randomly assigned originally to the long-acting therapy show long-acting cabotegravir plus rilpivirine remains a durable maintenance therapy with a favourable safety profile."

Source: Orkin C, et al. Lancet HIV. 2021;8:e185-e196.

LONG-ACTING IM CABOTEGRAVIR AND IM RILPIVIRINE FOR HIV MAINTENANCE

ATLAS STUDY

ATLAS STUDY: DESIGN

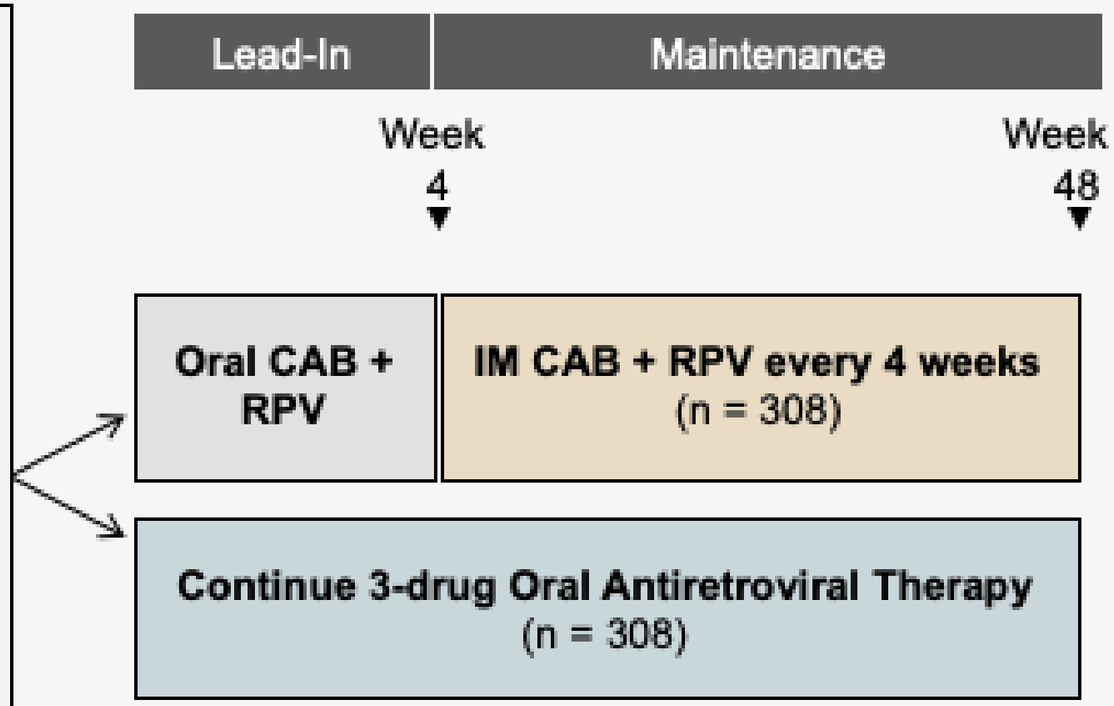


Source: Swindells S, et al. N Engl J Med. 2020;382:1112-23.

ATLAS STUDY: DESIGN

- **Background**: Phase 3, randomized, open-label trial assessing IM cabotegravir plus IM rilpivirine after oral induction for adults taking a 3-drug oral antiretroviral therapy regimen

- **Inclusion Criteria**
  - Age ≥18 years
  - Taking 2NRTIs+INSTI, NNRTI, or PI
  - Stable ARV regimen ≥6 months
  - HIV RNA <50 copies/mL ≥6 months
  - No history of virologic failure
  - No INSTI or NNRTI resistance, except that K103N mutation allowed
  - No chronic hepatitis B



Abbreviations: CAB = cabotegravir; RPV = rilpivirine

Source: Swindells S, et al. N Engl J Med. 2020;382:1112-23.

ATLAS STUDY: CONCLUSIONS

CONCLUSION

“Monthly injections of long-acting cabotegravir and rilpivirine were noninferior to standard oral therapy for maintaining HIV-1 suppression. Injection-related adverse events were common but only infrequently led to medication withdrawal.”

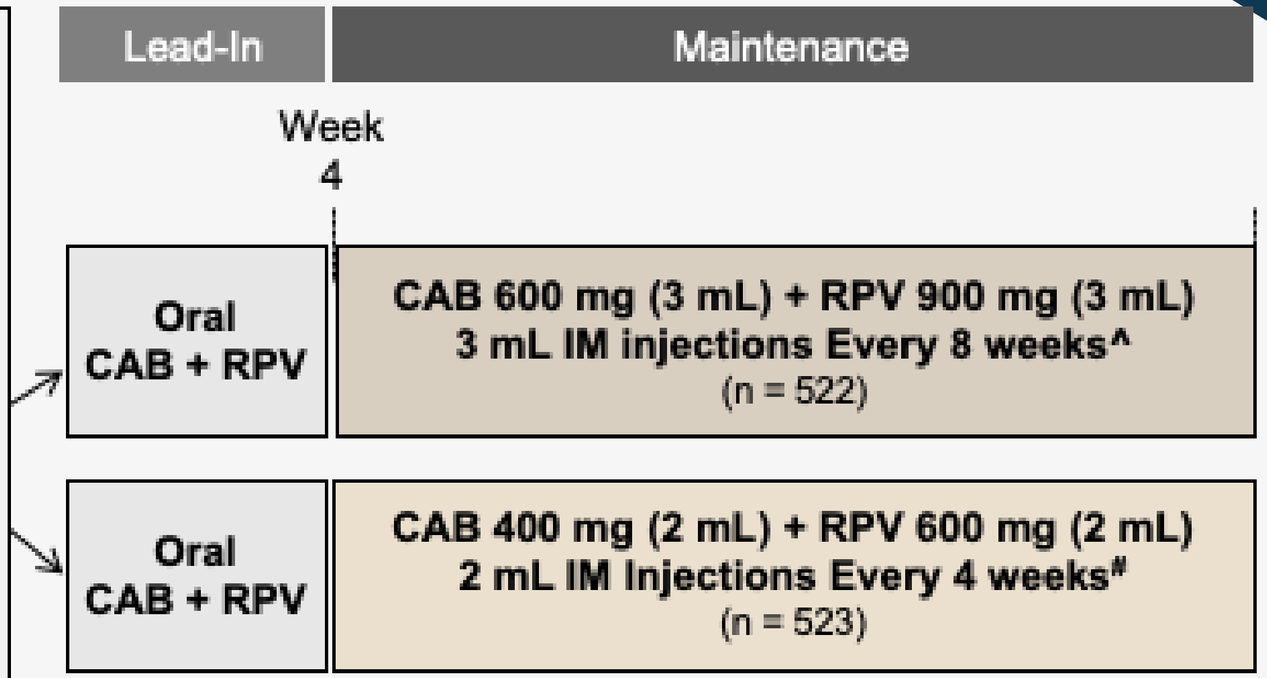
Source: Swindells S, et al. N Engl J Med. 2020;382:1112-23.

LONG-ACTING IM CABOTEGRAVIR AND IM RILPIVIRINE FOR HIV MAINTENANCE

ATLAS-2M

ATLAS-2M STUDY: DESIGN

- **Background**: Phase 3, randomized, open-label trial assessing IM CAB plus IM RPV maintenance ART administered every 8 weeks versus every 4 weeks
- **Inclusion Criteria**
  - Age ≥18 years
  - Taking an uninterrupted first or second oral standard of care ART regimen for ≥6 months
  - HIV RNA <50 copies/mL ≥6 months at screening and >2x in prior year
  - No history of virologic failure
  - No INSTI or NNRTI resistance, except that K103N mutation allowed



*Some individuals enrolled from ATLAS trial; those already receiving IM CAB + RPV through ATLAS did not require oral lead-in for ATLAS-2M

^Participants first received loading doses of CAB 600 mg (3 mL) + RPV 900 mg (3 mL) 3 mL IM injections given at study weeks 4 and 8

#Participants first received loading dose of CAB 600 mg (3 mL) + RPV 900 mg (3 mL) 3 mL IM injections given at study week 4

Source: Overton ET, et al. Lancet. 2020:396:1994-2005.

ATLAS-2M STUDY

CONCLUSION

“The efficacy and safety profiles of dosing every 8 weeks and dosing every 4 weeks were similar. These results support the use of cabotegravir plus rilpivirine long-acting administered every 2 months as a therapeutic option for people living with HIV-1.”

Source: Overton ET, et al. Lancet. 2020:396:1994-2005.

LONG-ACTING IM CABOTEGRAVIR AND IM RILPIVIRINE FOR HIV MAINTENANCE

ATLAS-2M: 96-WEEK RESULTS

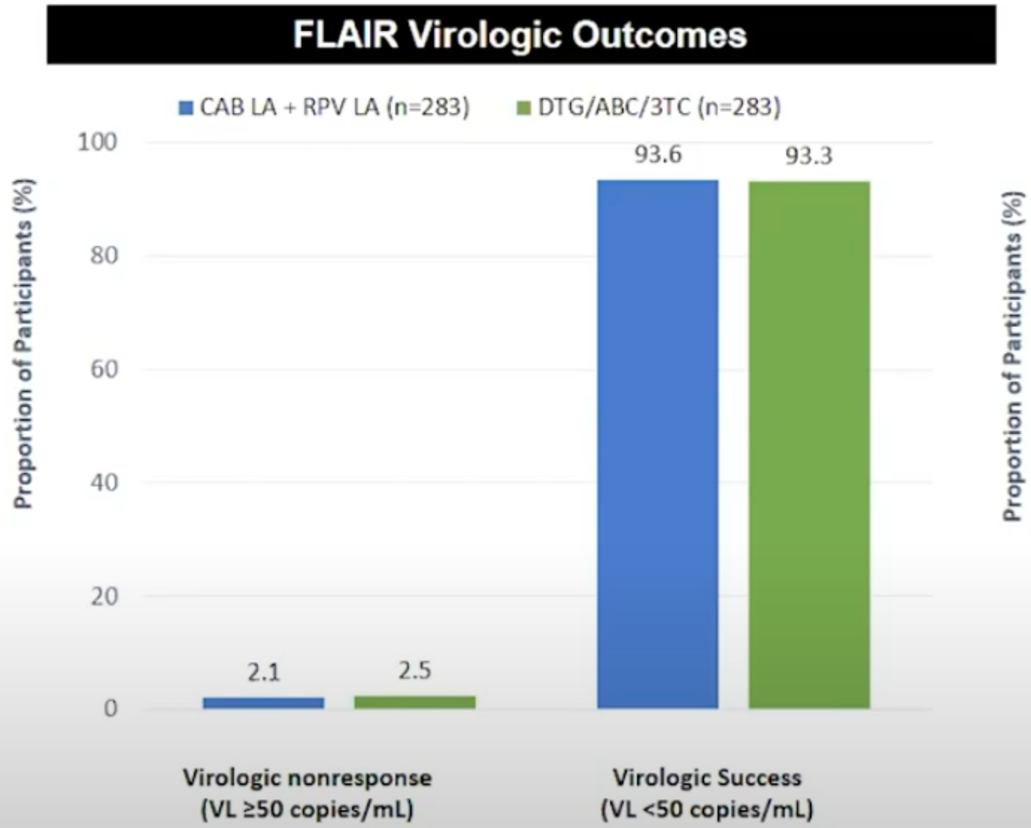
ATLAS-2M STUDY: RESULTS (WEEK 96)

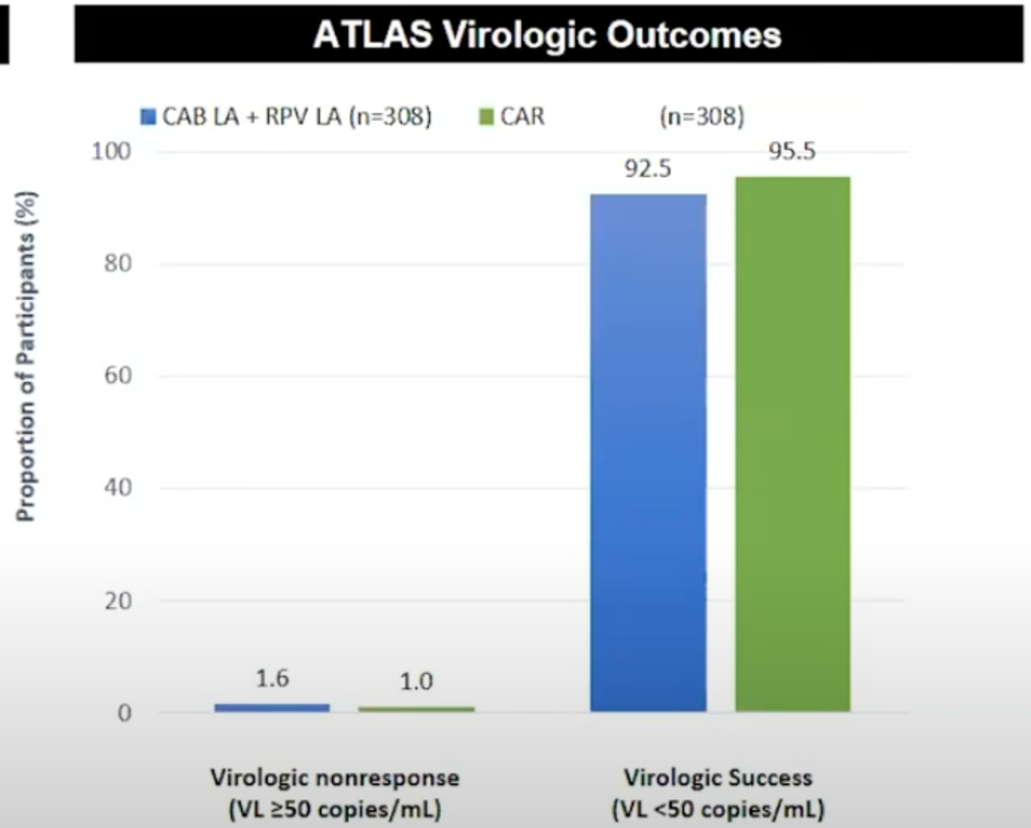
INTERPRETATION

“Long-acting cabotegravir and rilpivirine dosed every 8 weeks had non-inferior efficacy compared with that of every 4 weeks through the 96-week analysis, with both regimens maintaining high levels of virological suppression. These results show the durable safety, efficacy, and acceptability of dosing long-acting cabotegravir and rilpivirine monthly and every 2 months as maintenance therapy for people living with HIV-1.

Source: Jaeger H, et al. Lancet HIV. 2021;8:e679-e689.

FLAIR & ATLAS: Noninferiority Achieved





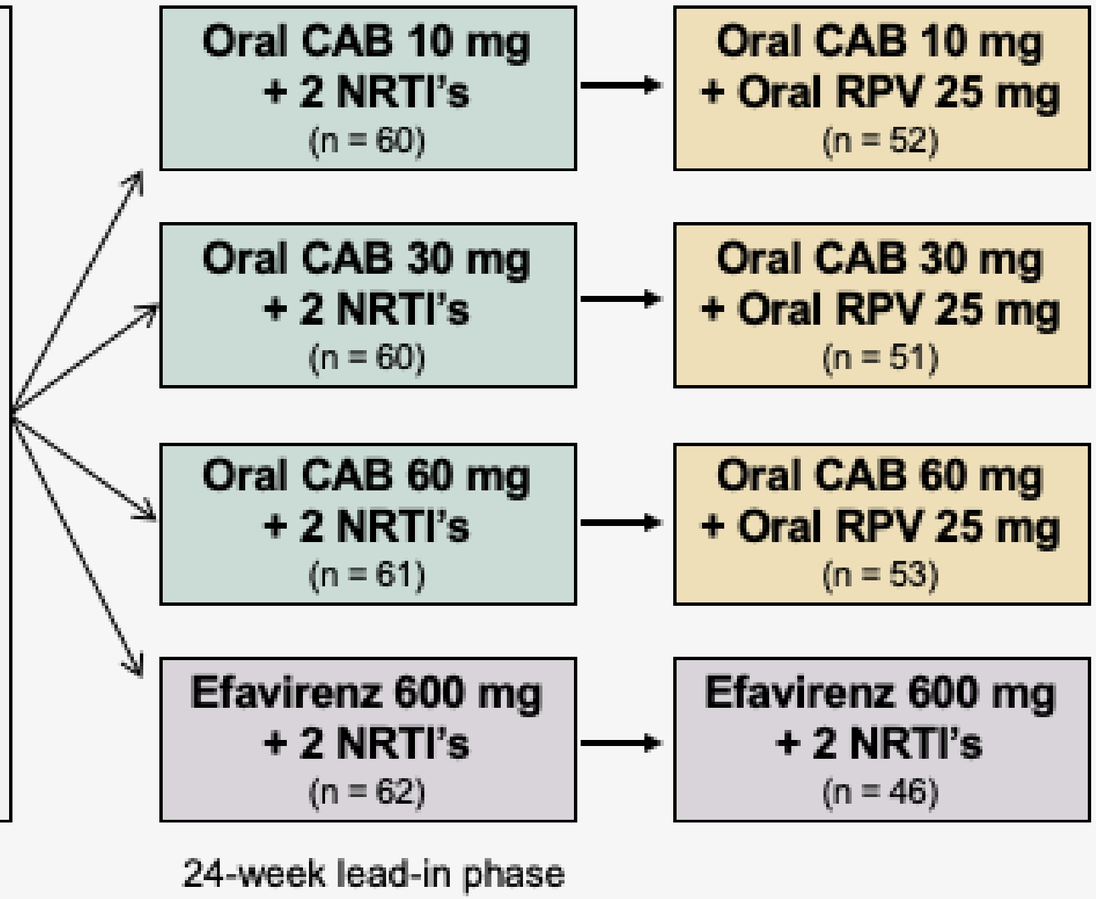
Orkin C, et al. N Engl J Med. 2020;382:1124-35
Swindells S, et al. N Engl J Med. 2020;382:1112-23

ORAL CABOTEGRAVIR + ORAL RILPIVIRINE VERSUS EFAVIRENZ + 2 NRTI’S

LATTE STUDY

LATTE STUDY: DESIGN

- **Background**: Phase 2b, randomized, partially blinded study done at multiple centers in the U.S. and Canada
- **Inclusion Criteria**
  - Age ≥18 years
  - Antiretroviral-naïve
  - HIV RNA >1,000 copies/mL
  - CD4 count >200 cells/mm^3
  - CrCl >50 mL/min
  - No hepatitis B
  - No significant transaminitis



Source: Margolis DA, et al. Lancet Infect Dis. 2015;15:1145-55.

LATTE STUDY

CONCLUSION

"Cabotegravir plus dual NRTI therapy had potent antiviral activity during the induction phase. As a two drug maintenance therapy, cabotegravir plus rilpivirine provided antiviral activity similar to efavirenz plus dual NRTIs until the end of week 96. Combined efficacy and safety results lend support to our selection of oral cabotegravir 30 mg once a day for further assessment. LATTE precedes studies of the assessment of long-acting injectable formulations of both drugs as a two-drug regimen for the treatment of HIV-1 infection."

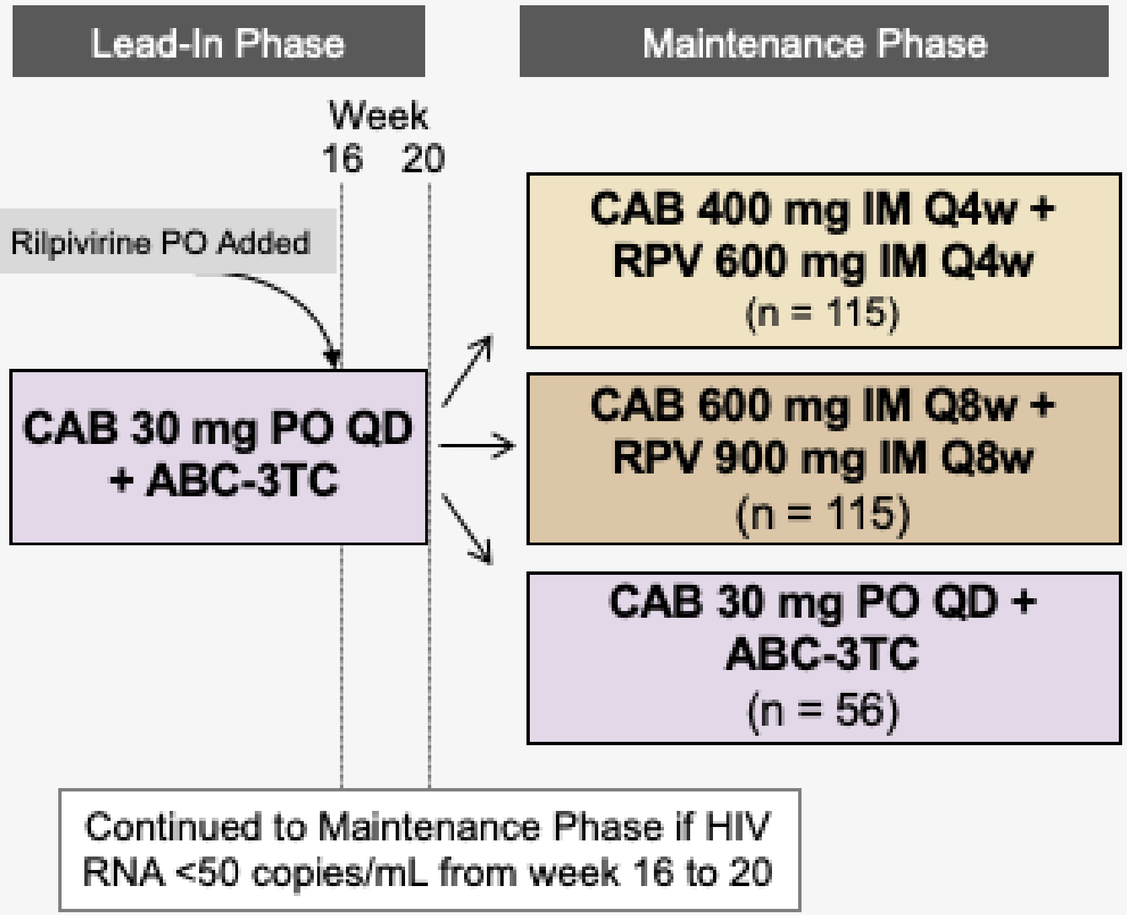
Source: Margolis DA, et al. Lancet Infect Dis. 2015;15:1145-55.

CABOTEGRAVIR IM + RILPIVIRINE IM EVERY ONE OR TWO MONTHS VERSUS ORAL CAB + ABC-3TC

LATTE-2

LATTE-2 STUDY: DESIGN

- **Background**
  - Phase 2b, randomized, open-label trial assessing dual therapy with long-acting, injectable agents for maintenance
- **Inclusion Criteria**
  - Age ≥18 years
  - Antiretroviral-naïve
  - HIV RNA >1,000 copies/mL
  - CD4 count >200 cells/mm^3
  - CrCl >50 mL/min
- **Exclusions**
  - Major resistance mutations
  - Pregnancy
  - Significant hepatic impairment
  - AIDS-defining condition



Source: Margolis DA, et al. Lancet 2017;390:1499-1510.

LATTE-2 STUDY

CONCLUSION

“The two-drug combination of all-injectable, long-acting cabotegravir plus rilpivirine every 4 weeks or every 8 weeks was as effective as daily three-drug oral therapy at maintaining HIV-1 viral suppression through 96 weeks and was well accepted and tolerated.”

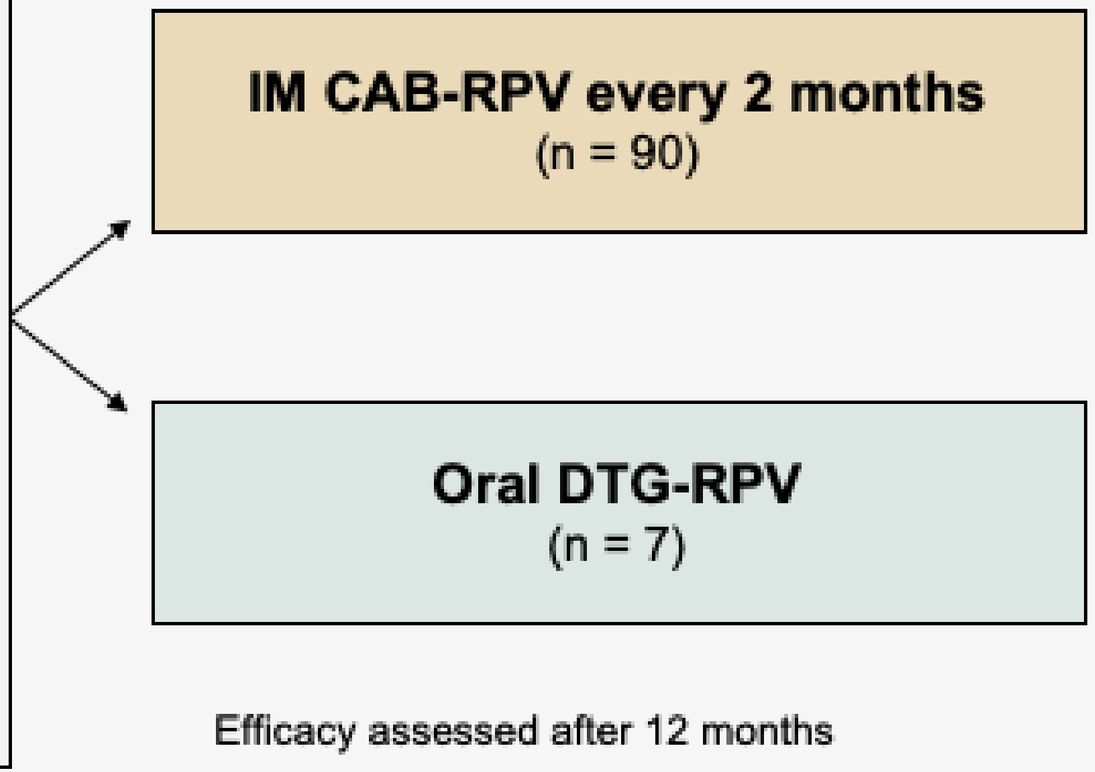
Source: Margolis DA, et al. Lancet 2017;390:1499-1510.

EVERY 2-MONTH IM CAB PLUS IM RPV AFTER 5 YEARS OF ORAL CAB PLUS ORAL RPV

POLAR STUDY

POLAR STUDY: DESIGN

- **Background**
  - Phase 2b, multicenter, non-randomized, rollover study; LATTE participants who completed 300 weeks of oral CAB + oral RPV and had HIV RNA <50 copies/mL were eligible
- **Design**
  - Eligible participants could elect to switch to every 2-month IM CAB-RPV or switch to dolutegravir (DTG) with RPV as 2-drug oral maintenance ART



Source: Mills A, et al. AIDS. 2022;36:195–203.

POLAR STUDY

CONCLUSION

“Cabotegravir plus rilpivirine (CAB + RPV) long-acting maintained virologic suppression in participants who had previously received daily oral CAB + RPV for at least 5 years in LATTE, with a favorable safety profile. Most participants preferred CAB + RPV long-acting to their prior oral CAB + RPV regimen at month 12.”

Source: Mills A, et al. AIDS. 2022;36:195–203.

SUMMARY

- Injectable and implantable ARV therapy have great potential for both HIV treatment
- Patients may face challenges with access and administration but also may prefer this to traditional oral therapy

“My patients [at the University of Nebraska Medical Center in Omaha] say they like not having to take a pill every day and not having to remember their HIV every day. They also felt less stigma with not having to worry about roommates or co-workers finding their pill bottles. It has surprised me how much people do like it.”

Dr Susan Swindells, ATLAS Investigator

MASHM

THANK YOU

LET'S WORK TOGETHER