Long-acting Cabotegravir plus Rilpivirine in the first group of virologically suppressed adolescents living with HIV-1 to receive an every 8-week, all-injectable regimen in a multicenter, multinational study: IMPAACT 2017 Week 48 Outcomes

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Summary – Week 48 IMPAACT 2017/MOCHA study

AIDS 2024

What is your main question?

What is the safety, antiviral activity, pharmacokinetics (PK), and participant experience of long-acting (LA) cabotegravir (CAB LA) plus rilpivirine (RPV LA) in **adolescents** (12 to < 18 years of age) living with HIV who are virologically suppressed.

What did you find?

Through **Week 48**, in adolescents receiving CAB LA + RPV LA there were no unexpected safety signals, virologic suppression was maintained, PK was comparable to adults and participant experience, good.

Why is it important?

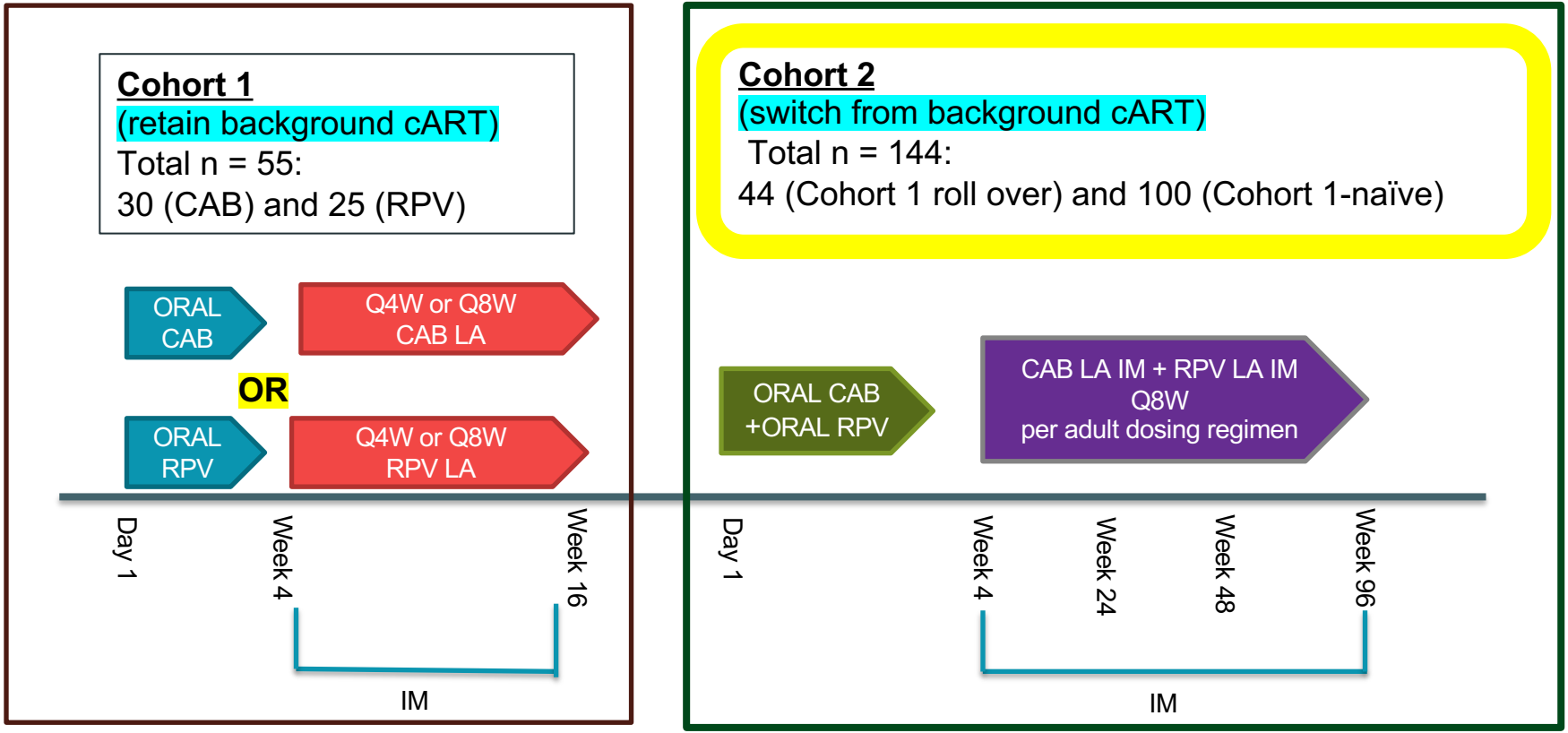
This longest described experience to date from this first cohort of adolescents to receive the first all injectable HIV treatment regimen ahead of the anticipated global use of this regimen helps inform both clinical practice and regulatory submissions.

BACKGROUND

- The CAB LA + RPV LA regimen was approved for treatment of HIV-1 in virologically suppressed adults by the US FDA:
  - In January 2021 as a once-monthly treatment;
  - In February 2022 for every-2-month dosing

- IMPAACT 2017 Cohort 1 data informed FDA approval for CAB LA + RPV LA once-monthly or every-2-months (dose similar to in adults) in virologically suppressed adolescents (≥12 years and weighing ≥35 kg) in March 2022

STUDY DESIGN



18 IMPAACT 2017 sites enrolled in Cohort 2

2 Botswana
4 South Africa
3 Thailand
2 Uganda
7 US

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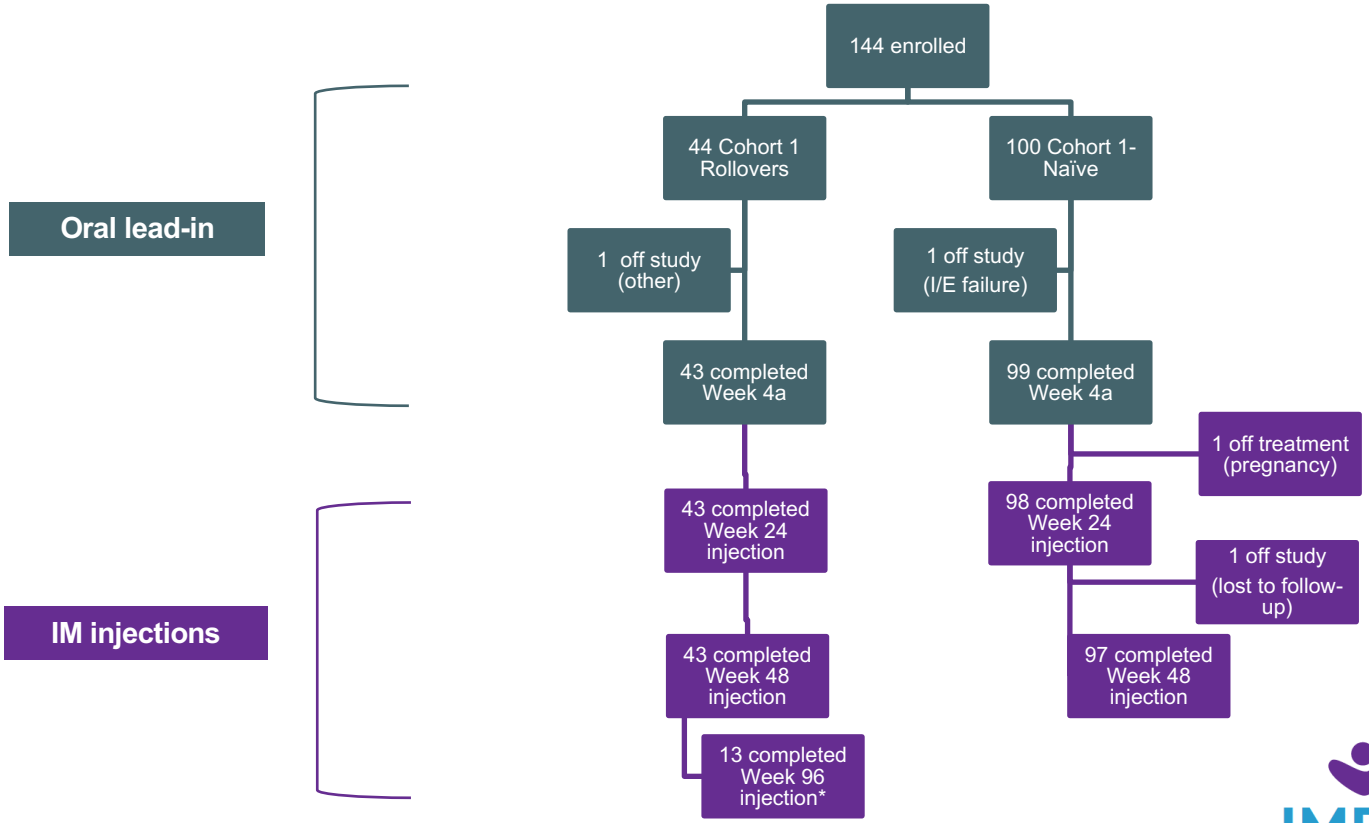
COHORT 2: ACCRUAL AND STUDY STATUS*



*As of database freeze on Nov 15, 2023 by which last participant completed Week 48

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BASELINE (N = 144)

Variable	Value
Age (median [min, max])*	15 years (12, 17)
Female	51%
Black or African American	74%
Acquired HIV vertically/perinatally	92%
Body Mass Index (median [min, max])	19.5 kg/m^2 (16, 34)
Weight (median [min, max])	48 kgs (35, 101)

* Age at study enrollment, which is Cohort 1 entry for Cohort 1 rollovers

Cohort 2 Safety, Participant Experience, PK, Antiviral Activity

Shown in the All Treated analysis set

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SAFETY

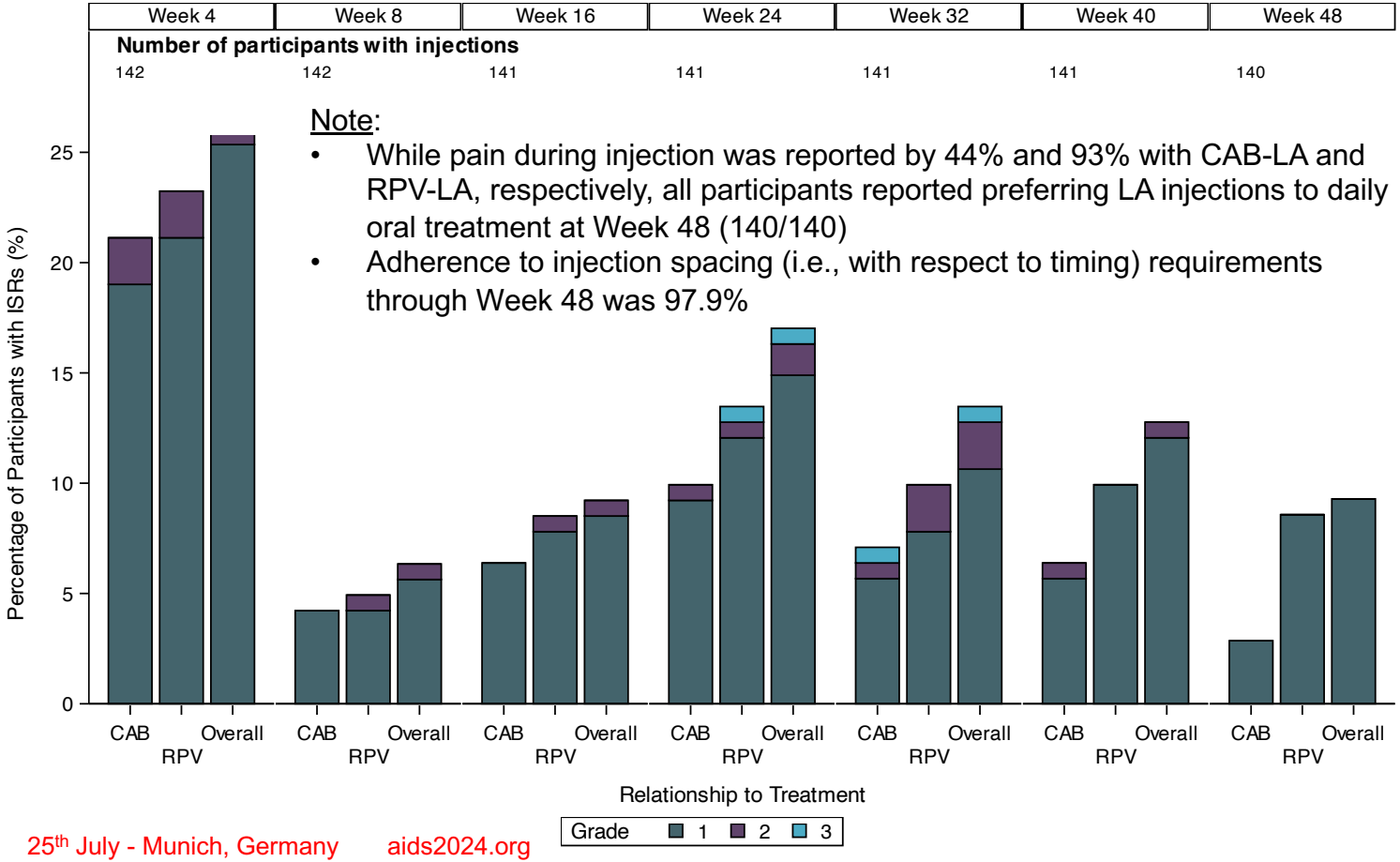
- Most participants received ≥1 injection (142/144) and completed the Week 48 visit (97%; 140/144).

- Through Week 48, 53/144 (37%) participants experienced a drug-related adverse event (AE). There were no drug related SAEs.
  - 2 (1%) were ≥ Grade 3 AE – *both participants continued study treatment*:
    - 1 participant experienced injection site [IS] pain and abscess
    - 1 participant experienced IS abscess

- After Week 48, 1 participant experienced a Grade 4 anaphylaxis reaction – *participant discontinued study treatment*
  Note: *An independent assessment of the event details by the IMPAACT 2017 Clinical Management Committee noted the event as not consistent with an anaphylactic event and most consistent with a post-injection reaction.*

- Through Week 48, 48/142 (34%) participants with at least one injection reported injection site reaction(s) (ISR), most ISRs were Grade 1 (90%) and resolved within 7 days (89%)

INJECTION SITE REACTIONS



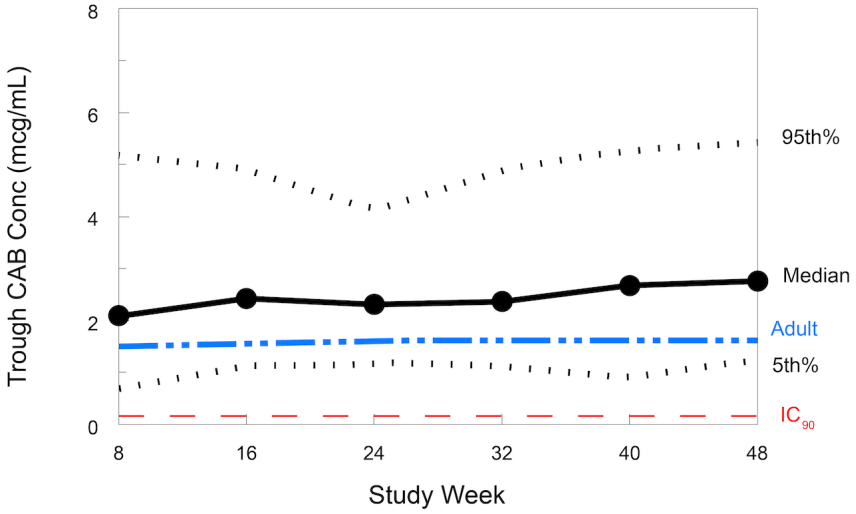
Note:

- While pain during injection was reported by 44% and 93% with CAB-LA and RPV-LA, respectively, all participants reported preferring LA injections to daily oral treatment at Week 48 (140/140)
- Adherence to injection spacing (i.e., with respect to timing) requirements through Week 48 was 97.9%

PARTICIPANT EXPERIENCE

- More participants reported “no hurt” for the CAB injection at Week 48 (79/140 [56.4%]) as compared with Week 4b (52/142 [36.6%]), Week 8 (47/142 [33.1%]) and Week 24 (61/141 [43.3%]).
- A similar number of participants reported “no hurt” for the RPV injections across visits (14/142 [9.9%], 10/142 [7.0%], 10/141 [7.1%], 10/140 [7.1%] at Week 4b, Week 8, Week 24, and Week 48, respectively).
- Participants reported high health-related quality of life across physical, emotional, social, and school domains at Entry, Week 4, Week 8, Week 24, and Week 48.
- All 140 participants who responded to Preference Questionnaire at Week 48 preferred LA injections to daily oral treatment

PHARMACOKINETICS



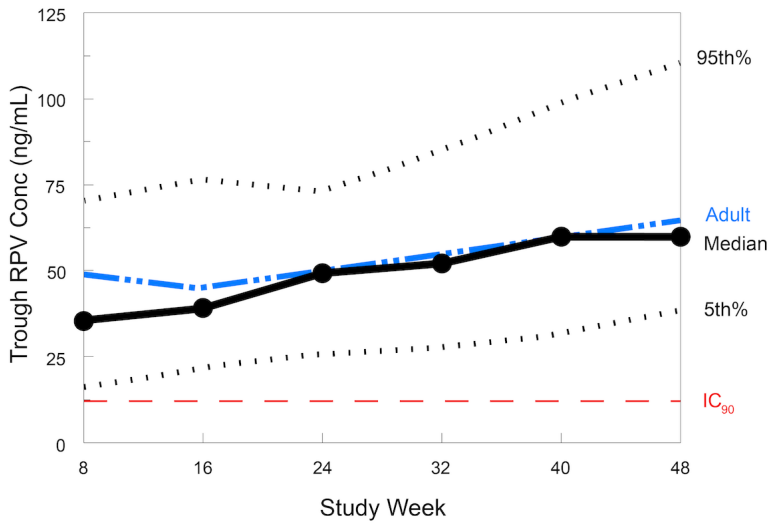


Figure: IMPAACT 2017 CAB and RPV troughs (Black lines – medians [solid] with 5th% - 95th% [dashed]) compared to adults (blue lines) from Latte 2/ATLAS-2M studies and protein adjusted IC_{90}s (red lines)

Median (Q1-Q3) Week-48 observed pre-dose concentrations for CAB (2.77 µg/mL [1.99-3.55]) and RPV (67.9 ng/mL [52.8-82.4]) approximated those in adults and were well above the respective protein-adjusted IC_{90}

ANTIVIRAL ACTIVITY

- All participants in Cohort 2 with a viral load assessment at Week 48 (n = 140) were virologically suppressed (plasma HIV-1 RNA <50 copies/mL). Per the FDA snapshot, 97.2% (93.9%, 99.2%) were virologic success.

- There were no confirmed virologic failures (2 consecutive plasma HIV-1 RNA ≥200 copies/mL) on CAB LA + RPB LA treatment.

Conclusions based on Week 48 data from Cohort 2 of the IMPAACT 2017 study

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At Week 48, in this first group of virologically suppressed adolescents who switched to CAB LA + RPV LA every 2 months

- There were no unexpected safety events.
- CAB and RPV trough levels were similar to those in adults; while CAB appears to be at steady-state by Week 48, the time to reach steady-state for RPV remains to be determined.
- Virologic suppression was maintained.
- Despite reported injection site pain, all participants indicated preference for long-acting injections over oral medications.

In summary

- IMPAACT 2017 data continue to support using CAB LA + RPV LA, given once-monthly or every-two-months, per the adult-dosing regimens, in virologically suppressed adolescents ≥12 years and weighing ≥35 kg.

- Ongoing CAB LA + RPV LA administration for study participants through Week 96 continues.

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