A5359: LATITUDE

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Agenda

1. Protocol Overview
2. Study modifications and enrollment data
3. Challenges and lessons learned

Background and Rationale

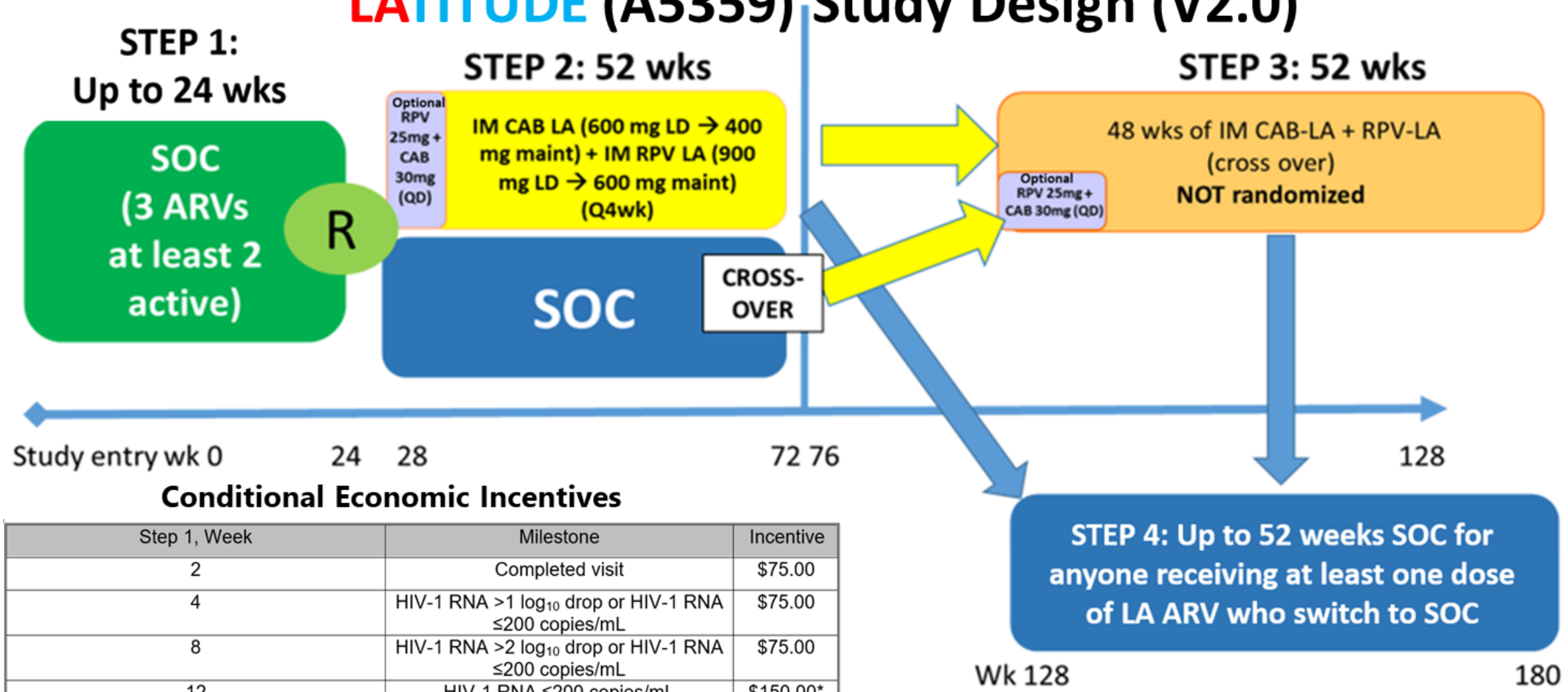
- Achieving virologic suppression remains a challenge for some individuals with HIV infection. Adherence key factor.

- Long acting (LA) ART may improve virologic suppression in non-adherent patients:
  - Infrequent dosing, opportunity to implement DOT.
  - BUT, suppression required prior to transitioning to LA regimen (DHHS Guidelines).
  - Current phase III studies did not evaluate PWH with adherence barriers.

Hypothesis

- After achieving suppression during a 24-week period of incentivized SOC, LA ART consisting of RPV-LA + CAB-LA will be a more successful therapy compared to a SOC regimen in keeping previously non-adherent, HIV-infected individuals on treatment and virologically suppressed.

LATITUDE (A5359) Study Design (V2.0)



Conditional Economic Incentives

Step 1, Week	Milestone	Incentive
2	Completed visit	$75.00
4	HIV-1 RNA >1 $\log_{10}$ drop or HIV-1 RNA ≤200 copies/mL	$75.00
8	HIV-1 RNA >2 $\log_{10}$ drop or HIV-1 RNA ≤200 copies/mL	$75.00
12	HIV-1 RNA ≤200 copies/mL	$150.00*
16 (if needed)	HIV-1 RNA ≤200 copies/mL	$150.00*
20 (if needed) or Confirmation viral load after week 20 (but prior to week 24)	HIV-1 RNA ≤200 copies/mL	$150.00

Step 1 Enrollment

		Total (N=291)
Age, years	Median (Q1, Q3)	40 (32, 51)
	Min, Max	18, 75
	18-24	16 (5%)
	25-30	39 (13%)
	31-40	92 (32%)
	41-50	67 (23%)
	51+	77 (26%)
Sex at Birth	Female	83 (29%)
	Male	208 (71%)
Gender Identity	Cisgender	277 (95%)
	Transgender Spectrum	13 (4%)
	Information Not Collected	1
Race	Black or African American	181 (62%)
	White	80 (27%)
	Asian	2 (1%)
	Multiple	7 (2%)
	Unknown	21 (7%)
Ethnicity	Hispanic or Latino	52 (18%)
	Not Hispanic or Latino	235 (81%)
	Unknown	4 (1%)
History of IV drug use	Currently	14 (5%)
	Previously	36 (12%)
	Never	241 (83%)

A5359 Challenges

Recruitment	• Clinical research sites inexperience with this population • COVID • FDA approval of CAB/RPV and off label use by providers	• Protocol trainings • Outreach worker
Screening	•VL>200 and genotype requirement at screening -40% of all screen failures	• Version 3: VL<200 c/mL and genotype no longer required

Randomization	• Version 1 ~40% of participants failed Step 1:
	  • 50% not suppressed oral ART at randomization timepoint (week 20); of those **<u>75%</u>** had rebounded after initial suppression
	  • 50% due to other reasons (mostly loss to follow-up)
		• Version 2: Week 12
		• Version 3: Week 4

Protocol Evolution

- Version 1:
  - Required suppression for 20 weeks in Step 1.
  - HIV VL <50 copies/mL required to transition to Step 2.
- Version 2:
  - Allow to transition as early as Week 12 in Step 1 if suppressed.
  - HIV VL <200 copies/mL required to transition to Step 2.
- Version 3 (proposed):
  - Allow transition as early as Week 4 in Step 1 if suppressed.
  - Participants with HIV VL <200 copies/mL at screening (who otherwise meet non-adherence criteria) allowed. Genotype at screening not mandatory.

QUESTIONS