Phase 1 Results for the Selection of a New Long-Acting Rilpivirine Formulation to Support Dosing Three Times a Year

P039

Eileen Castronova,[1] Ronald D'Amico,[2] Jörg Sievers,[3] Randa Hareedy,[4] Gilda Bontempo,[5] Lisa Morgan,[1] Shawn L. Searle,[6] Katherine Sides,[7] Jeremy Roberts,[8] Herta Crauwels,[9] Kati Vandermeulen,[9] Lorant Leopold,[10] Eileen Birmingham,[11] Rodica Van Solingen-Ristea,[9] Jon Collins,[2] Lionel Tan[3]

[1]GSK, Collegeville, PA, USA; [2]ViiV Healthcare, Durham, NC, USA; [3]ViiV Healthcare, London, UK; [4]GSK, London, UK; [5]ViiV Healthcare, Branford, CT, USA; [6]Trialmed, Las Vegas, NV, USA; [7]Trialmed, Austin, TX, USA; [8]GSK, Mississauga, ON, Canada; [9]Johnson & Johnson, Beerse, Belgium; [10]Johnson & Johnson, Titusville, NJ, USA; [11]Johnson & Johnson, Raritan, NJ, USA

Please scan the QR code for additional resources

Key Takeaways

- **Long-acting cabotegravir plus rilpivirine (CAB+RPV LA), an established injectable regimen, delivers durable virologic suppression with dosing 6 times a year**
- **New CAB and RPV formulations have been developed to explore extending the dosing interval to 3 times a year, offering the convenience of fewer clinic visits**
- **A phase 1 safety and pharmacokinetics (PK) and population pharmacokinetic modeling study support a CAB regimen dosed 3 times a year as part of a viable dosing strategy for HIV-1 treatment**
- **Safety and PK data for new RPV formulations designed to support dosing 3 times a year are explored**

Plain Language Summary

- Long-acting cabotegravir plus rilpivirine (CAB+RPV LA) is an injectable treatment for people with HIV-1 and offers the convenience of dosing 6 times a year instead of daily pills
- New CAB and RPV dosing options are being studied that could reduce dosing to 3 times a year
- This study shows the safety and pharmacokinetic (how the medicine moves through the body) results of the new RPV options

Introduction

- Cabotegravir (CAB) + rilpivirine (RPV) is the first and only complete long-acting (LA) injectable regimen approved for people with HIV-1 who have suppressed viral loads, and is currently administered 6 times a year[1-4]
- Phase 1 safety, pharmacokinetics (PK), and population pharmacokinetic (PopPK) modeling data have been previously reported to support a CAB formulation dosed 3 times a year, offering the convenience of fewer clinic visits[5]
  - CAB PK demonstrated a rapid rise to concentrations associated with clinical efficacy and a terminal half-life >25 weeks, supporting an extended dosing interval with a safety profile consistent with the approved regimen dosed 6 times a year[5]
- Here, we present results from a phase 1 study exploring the safety and PK data for new RPV formulations designed to support dosing 3 times a year

Methods

Study Design

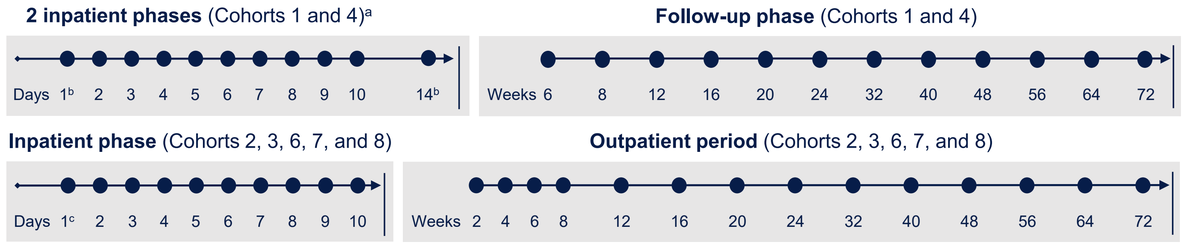
- Adults without HIV aged 18 to 55 years received single or repeat intramuscular (IM) injections of 2 RPV formulations in 7 cohorts in this ongoing phase 1 study (NCT05418868)
- Participants received a single injection of formulation 1 or 2 (12 people per cohort), or 2 injections of formulation 1 on Day 1 and Week 4 (6 people per cohort; Table 1); PK sampling is shown in Figure 1
- To optimize IM gluteal injection delivery, formulation, volume, and needle length were adapted across cohorts (Table 1)
- Results of this phase 1 study were used to establish an RPV dosing regimen to support 3-times-a-year dose selection for a phase 3 study (NCT07650916)[6]

Table 1. RPV Dose Cohorts

Formulation/Dose level	RPV total dose	Administration	Needle length
Formulation 1			
Cohort 1	2400 mg	1200 mg IM on Day 1 and on Week 4	1 inch
Cohort 2	1200 mg	1200 mg IM on Day 1	1 inch
Cohort 3	1800 mg	1800 mg IM on Day 1	1 inch
Cohort 4	3600 mg	1800 mg IM on Day 1 and on Week 4	1 inch
Formulation 2			
Cohort 6	1800 mg	1800 mg IM on Day 1	1 inch
Cohort 8[a]	1800 mg	1800 mg IM on Day 1	1.5 inches
Cohort 7	2760 mg	2760 mg IM on Day 1	1.5 inches

[a]Cohort 8 was a repeat from Cohort 6 with longer needle length (1.5 inches vs 1 inch) and was conducted before Cohort 7.

Figure 1. PK Sampling Schedule



[a]A second 10-day inpatient period occurred after Week 4, when they received dose 2. [b]Outpatient visits also occurred at Week 2 between the 2 inpatient phases and at Weeks 2 and 4 after the second inpatient period. [c]Day 1: ≤1 h pre-dose, 1, 2 , 4, and 8 h post-dose.

Results

Participant Demographics

- A total of 72 participants received 84 RPV injections
- As expected, given the small number of participants in each cohort, there was some variability in demographic characteristics across cohorts (Table 2)
  - The median age ranged from 27.0 to 37.5 years, and sex at birth varied greatly across cohorts, with the proportion of male participants ranging from 33% to 75%

Table 2. Participant Demographics

Parameter, n (%)[a]	Formulation 1				Formulation 2		
	2400 mg (n=6)	1200 mg (n=12)	1800 mg (n=12)	3600 mg (n=6)	1800 mg (n=12)	1800 mg (n=12)	2760 mg (n=12)
Sex at birth							
Male	2 (33)	9 (75)	5 (42)	2 (33)	4 (33)	7 (58)	6 (50)
Female	4 (67)	3 (25)	7 (58)	4 (67)	8 (67)	5 (42)	6 (50)
Age, median (IQR), y	30.0 (27.0-32.0)	32.0 (28.5-41.5)	27.0 (25.0-36.0)	31.5 (27.0-37.0)	35.5 (28.0-46.0)	35.5 (33.5-44.5)	37.5 (31.5-42.0)
Race							
Black or African American	1 (17)	3 (25)	3 (25)	3 (50)	6 (50)	3 (25)	5 (42)
White	5 (83)	6 (50)	6 (50)	3 (50)	5 (42)	7 (58)	6 (50)
Asian	0	3 (25)	0	0	0	0	0
Other races	0	0	3 (25)	0	1 (8)	2 (17)	1 (8)
Weight, median (IQR), kg	79.8 (65.7-88.7)	82.0 (75.8-90.4)	73.5 (67.9-75.7)	77.7 (64.2-85.8)	73.6 (66.0-88.5)	74.6 (66.0-83.7)	70.3 (61.7-74.8)
BMI, median (IQR), kg/m^2	26.9 (24.7-29.6)	27.5 (26.0-30.5)	26.4 (23.6-27.7)	28.6 (23.8-30.2)	27.1 (24.3-29.7)	25.3 (23.4-27.1)	24.1 (22.7-27.3)

BMI, body mass index; IQR, interquartile range. [a]Unless otherwise indicated.

RPV Plasma Concentrations

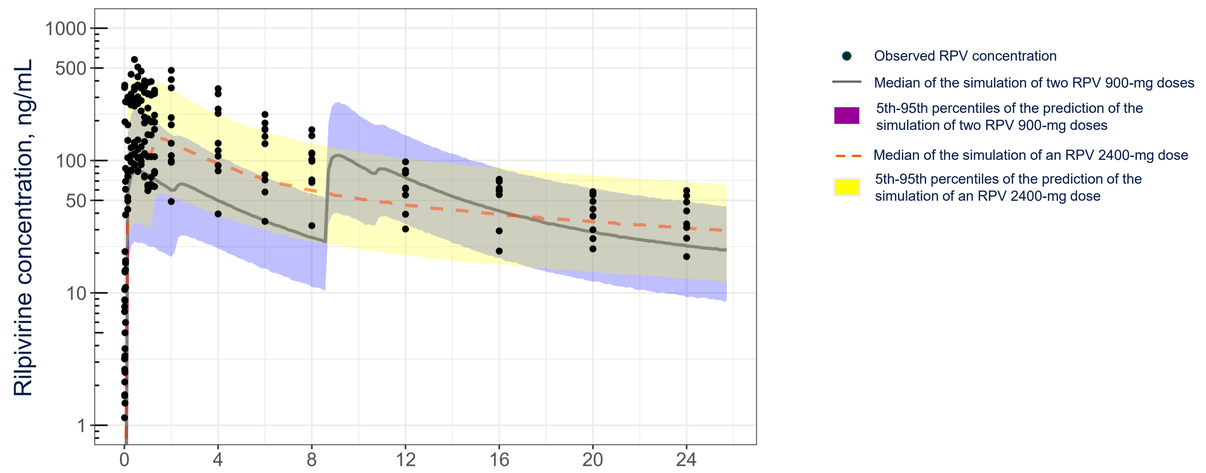
- Maximum RPV concentration was typically reached within 6 weeks post-dose; observed RPV plasma concentrations at Week 16 are supportive of dosing 3 times a year (Table 3)
- Based on the observed RPV concentrations with the new formulations, model simulations suggest that a 2400-mg dose can achieve RPV concentrations over a 4-month interval in range with those for two 900-mg doses every 2 months (Figure 2)

Table 3. Mean RPV Plasma Concentrations

Parameter	Formulation 1				Formulation 2		
	2400 mg (n=6)	1200 mg (n=12)	1800 mg (n=12)	3600 mg (n=6)	1800 mg (n=12)	1800 mg (n=12)	2760 mg (n=12)
Geometric mean C_{max} (%CV[a]), ng/mL	35.2 (50)	ND[a]	87.3 (90)	ND[a]	89.7 (56)	151 (60)	227 (75)[b]
Geometric mean concentration at Week 16 (%CV), ng/mL	15.6 (45)[c]	42.4 (17)	31.4 (54)	39.3 (83)[d]	28.2 (50)	26.5 (41)	48.8 (41)[c]

C_{max}, maximum concentration; CV, coefficient of variation; ND, not determined. [a]Cmax is not reported for multiple-injection cohorts. [b]C_{max} was calculated for the n=10 participants who did not have partial intravenous RPV administration (high RPV concentrations within 1 hour of dosing); these events were not associated with adverse events. [c]n=11. [d]n=5.

Figure 2. Observed Phase 1 Data Following a Single 2760 mg RPV LA Dose Overlaid on Predicted Exposures After a Simulated Dose of RPV 2400 mg or 2 Simulated Doses of RPV LA 900 mg



ISR

- Injections of RPV formulations were generally well tolerated (Table 4)
- A longer needle length was consistently used in the last 2 cohorts and resulted in fewer and lower-grade injection site reactions (ISRs) compared with earlier formulation 1 dose administrations and cohort 6 (1800 mg) with formulation 2, for which a shorter needle was used for most injections

Table 4. ISR Summary of RPV Formulations

Parameter, n (%)	Formulation 1						Formulation 2		
	2400 mg (n=6)		1200 mg (n=12)	1800 mg (n=12)	3600 mg (n=6)		1800 mg (n=12)	1800 mg (n=12)	2760 mg (n=12)
	Day 1	Day 28[a]			Day 1	Day 28			
Any ISR	6 (100)	6 (100)	10 (83)	12 (100)	5 (83)	3 (60)	10 (83)	9 (75)	11 (92)
Maximum grade 1	6 (100)	6 (100)	4 (33)	7 (58)	3 (50)	0	3 (25)	9 (75)	10 (83)
Maximum grade 2	0	0	6 (50)	1 (8)	0	2 (40)	3 (25)	0	1 (8)
Maximum grade 3	0	0	0	4 (33)	2 (33)	1 (20)	4 (33)	0	0

[a]Administered 1 month after injection 1.

Summary of AEs

- Overall, 83% to 100% of participants had an adverse event (AE), and 83% to 100% had drug-related AEs (Table 5)
- All non-ISR AEs reported were grade 1 or 2
  - 8% to 33% of participants had non-ISR drug-related AEs across cohorts, except for cohort 6, in which no participants experienced any non-ISR drug-related AEs
- No serious AEs were reported

Table 5. Summary of AEs

Preferred term, n%	Formulation 1				Formulation 2		
	2400 mg (n=6)	1200 mg (n=12)	1800 mg (n=12)	3600 mg (n=6)	1800 mg (n=12)	1800 mg (n=12)	2760 mg (n=12)
Any AE	6 (100)	11 (92)	12 (100)	5 (83)	10 (83)	11 (92)	11 (92)
Maximum grade 1	6 (100)	3 (25)	6 (50)	1 (17)	3 (25)	11 (92)	9 (75)
Maximum grade 2	0	8 (67)	2 (17)	1 (17)	3 (25)	0	2 (17)
Maximum grade 3	0	0	4 (33)	3 (50)	4 (33)	0	0
Any drug-related AE	6 (100)	10 (83)	12 (100)	5 (83)	10 (83)	10 (83)	11 (92)
Maximum grade 1	6 (100)	3 (25)	7 (58)	1 (17)	3 (25)	10 (83)	10 (83)
Maximum grade 2	0	7 (58)	1 (8)	1 (17)	3 (25)	0	1 (8)
Maximum grade 3	0	0	4 (33)	3 (50)	4 (33)	0	0

Conclusions

- The new RPV formulations exhibit favorable tolerability and safety, with a PK profile that supports dosing 3 times a year
- These results, along with data on a new formulation of CAB 1600,[5] support the potential for a complete long-acting CAB + RPV regimen dosed 3 times a year, offering greater convenience through fewer clinic visits
- The efficacy, safety, and tolerability of CAB+RPV LA dosed 3 times a year in people with HIV-1 are currently being assessed in CUATRO, a phase 3 study (NCT07650916)[6] comparing the regimen with CAB+RPV LA dosed 6 times a year

Acknowledgments: This study was funded by ViiV Healthcare. Editorial assistance and graphic design support for this poster were provided under the direction of the authors by Fingerpaint Medical and funded by ViiV Healthcare.

References: 1. Vocabria [summary of product characteristics]. ViiV Healthcare; 2025. **2.** Rekambys [summary of product characteristics]. ViiV Healthcare; 2025. **3.** Cabenuva [prescribing information]. ViiV Healthcare; 2025. **4.** Hsu et al. *J Int AIDS Soc*. 2025;28:e70068. **5.** Castronova et al. CROI 2026; Denver, CO. Poster 495. **6.** ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT07650916. Accessed September 29, 2026.

Corresponding author: Eileen Castronova; eileen.b.doyle@gsk.com