New and Investigational ART Drugs and Strategies

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Financial Relationships With Ineligible Companies (Formerly Described as Commercial Interests by the ACCME) Within the Last 2 Years

Dr Currier has served as a consultant to Merck & Co., Inc. (Updated 08/17/22)

Slide 2

New Drugs Here and on the Horizon

Recently approved Agents
- Long acting Cabotegravir and Rilpivirine

New Drugs on the Horizon
- Islatravir
- Lenacapravir
- GSK 3640254 (aka GSK "254)

Current Antiretroviral Guidelines for Initial ART regimens

World Health Organization 2019	2020	DHHS 2021	IAS–USA 2020	
DTG plus TDF + 3TC (or FTC)	BIC/TAF/FTC	BIC/TAF/FTC	BIC/TAF/FTC	2NRTI Plus InSTI
	DTG or RAL + TDF/FTC or TAF/FTC or TDF/3TC	DTG + TDF/FTC or TAF/FTC	DTG + TDF/FTC or TAF/FTC or TDF/3TC	
	DTG/ABC/3TC	DTG/ABC/3TC		
	DTG/3TC	DTG/3TC	DTG/3TC	1 NRTI plus InSTI

DTG-dolutegravir, TDF-tenofovir disoproxil fumarate, 3TC-lamivudine, FTC-emtricitabine, ABC-abacavir, BIC-bictegravir, RAL-raltegravir.

Slide 5

Long Acting Cabotegravir and Rilpivirine

- Long acting cabotegravir and rilpivirine approved for use in patients with **viral suppression** and **no prior resistance** in an every 4 week dosing schedule in US and Canada. January 21, 2021 and for every 8 week dosing in Feb 2022
- Approved in both an oral formulation cabotegravir 30 mg and rilpivirine and in the sustained release injection to be initiated after an oral lead in.
- Roll out in clinic settings has been very slow due to logistics of drug acquisition and dispensing.
- ATLAS 2M trial examined whether dosing could be given every 8 weeks and whether people could go straight to injections without the oral lead in.

ATLAS-2M: Background

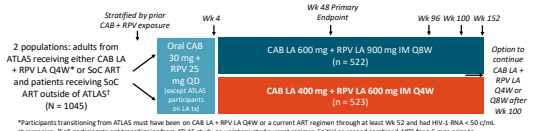
- CAB and RPV approved as the first long-acting, injectable regimen for maintenance of virologic suppression in patients with HIV
  - Monthly or every-2-mo dosing intervals may address challenges of daily oral ART, such as stigma, pill burden/fatigue, drug–food interactions, and adherence
- Wk 48 and 96 results of ATLAS-2M showed that switch to injectable CAB LA + RPV LA **Q8W** was noninferior to switch to IM CAB LA + RPV LA **Q4W in virologically suppressed patients**[1]

1. Overton. CROI 2020. Abstr 34. 2. Jaeger. CROI 2021. Abstr 401.

Slide credit: clinicaloptions.com

ATLAS-2M: Study Design

- Multicenter, randomized, open-label phase IIIb noninferiority trial



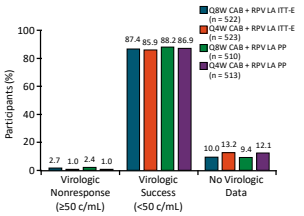
*Participants transitioning from ATLAS must have been on CAB LA + RPV LA Q4W or a current ART regimen through at least Wk 52 and had HIV-1 RNA < 50 c/mL at screening. †SoC participants not transitioning from ATLAS study on uninterrupted current regimen (initial or second combined ART) for ≥ 6 mos prior to screening and documented evidence of ≥ 2 plasma HIV-1 RNA < 50 c/mL in 12 mos prior to screening (one 6-12 mos and one within 6 mos prior to screening). Participants excluded if history of VF or if prior genotype results show any major INSTI or NNRTI mutations (except K103N).

- Primary endpoint: HIV-1 RNA ≥ 50 copies/mL at Wk 48 by FDA snapshot in ITT-E
- Secondary/other endpoints: plasma HIV-1 RNA ≥ 50 or < 50 copies/mL at Wk 152 by FDA snapshot in ITT-E, safety and tolerability, VF in patients with CVF

Overton. CROI 2022. Abstr 479.

Slide credit: clinicaloptions.com

ATLAS-2M: Wk 152 Virologic Outcomes



- 2 additional participants (both male at birth, BMI <30 kg/m²) in Q8W arm met CVF criteria between Wk 96 and 152 (Wk 112, 120)
  - At BL, neither had RAMs; participant with A6 subtype had L74I integrase polymorphism

	Baseline	At Failure		
Country	HIV-1 Subtype	HIV-1 RNA (c/mL)	RPV RAMs	INI RAMs
Germany	B	24,221	E138A+ M230M/L	Q148R
Russia	A6*	59,467	E138A+ Y181Y/C	Q148R

*Originally classified as A1; later reclassified as A6 upon reanalysis

- Through Wk 152, 13 participants had CVF: Q8W, n = 11 (2%); Q4W, n = 2 (<1%)
  - None with injection >7 days late

Overton. CROI 2022. Abstr 479.

Slide credit: clinicaloptions.com

ATLAS-2M: ISRs and Treatment Satisfaction Through Wk 152

injection-site reactions	Q8W (n = 522)	Q4W (n = 523)
Participants who received ≥1 injection, n (%)	516 (99)	517 (99)
Number of injections	20,563	39,478
ISR events, n ▪ Injection site pain, n (% of injections) ▪ Injection site nodule, n (% of injections)	4168 3189 (16) 259 (1)	5494 4180 (11) 457 (1)
Grade 3, n (% of ISR events)	54 (1)	50 (1)
Median duration, days (IQR)	3 (2-5)	3 (2-5)
Participants withdrawing for injection-related reasons, n (%)	8 (2)	13 (3)

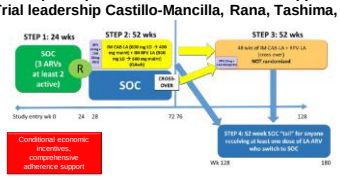
- HIV treatment satisfaction questionnaire scores from participants without prior CAB
  - Total mean scores significantly improved from BL to Wk 152 for both groups
  - Adjusted mean change from BL significantly favored Q8W dosing at Wk 24, 48, and 152

Overton. CROI 2022. Abstr 479.

Slide credit: clinicaloptions.com

Long Acting Cabotegravir and Rilpivirine for people who are NOT suppressed: Research in Progress

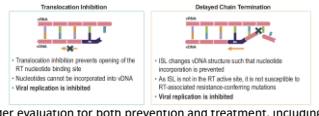
- **LATTITUDE: a randomized controlled trial of LA-cabotegravir and rilpivirine in participants who are unable to be suppressed on oral ART (Trial leadership Castillo-Mancilla, Rana, Tashima, Landovitz)**



Slide 11

Islatravir

- **Other Names:** EFdA, ISL, MK-8591
- **Drug Class:** Nucleoside Reverse Transcriptase Translocation Inhibitors



- Was under evaluation for both prevention and treatment, including both a pill formulation and an implant.
- For treatment: Phase 3 trials combined as a single tablet with Doravirine.
- Half life of intracellular active tri-phosphate is up to 128 hours
- Under study as daily, once weekly and once monthly dosing strategies for treatment and prevention. Implant also under study.

Islatravir

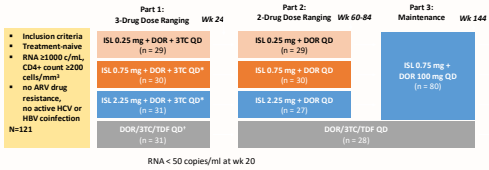
Media > News releases > News release

Merck Announces Clinical Holds on Studies Evaluating Islatravir for the Treatment and Prevention of HIV-1 Infection

The FDA's clinical hold is based observations of decreases in total lymphocyte and CD4+ T-cell counts in some participants receiving islatravir in clinical studies.

December 13, 2021 5:00 pm ET

Islatravir: P011 Study Design: from 3 to 2 drugs, 3 doses



RNA < 50 copies/ml at wk 20

Key findings: 1 Serious drug related AE in the ISL +DOR part 3 arm, No discontinuations for safety events after week 48

Most common AE in ISL + DOR groups: **headache** (6.5%) ; most common AE in DOR/3TC/TDF group: **diarrhea** (19%)

Similar Incidence of both at Weeks 48 and 96

Cunningham. IAS 2021. Abstr OAB0304.

Islatravir: Safety Data Laboratory (P011 Study)

Laboratory abnormality in ≥ 2 participants in any group, n/N (%)	ISL 0.25 mg + DOR QD	ISL 0.75 mg + DOR QD	ISL 2.25 mg + DOR QD	DOR/ 3TC/ TDF QD
Fasting triglycerides (mg/dL) **Grade 3: > 500-1000**	2/29 (6.9)	0/30 (0)	1/29 (3.4)	0/26 (0)
Alanine aminotransferase (IU/ L) • **Grade 3: 5.0 to < 10.0 x ULN**	0/29 (0)	1/30 (3.3)	2/31 (6.5)	1/31 (3.2)
Creatinine kinase (IU/L) • **Grade 3: 10.0 to < 20.0 x ULN** • **Grade 4: ≥20.0 x ULN**	4/29 (13.8) 1/29 (3.4)	0/30 (0) 2/30 (6.7)	0/31 (0) 3/31 (9.7)	1/31 (3.2) 1/31 (3.2)

No apparent dose related changes in grade 3 and 4 AE's

Cunningham. IAS 2021. Abstr OAB0304.

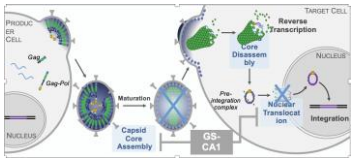
Islatravir: Efficacy at 96 weeks

	ISL (0.25 mg) + DOR QD	ISL (0.75 mg) + DOR QD	ISL (2.25 mg) + DOR QD	ISL Combined	DOR/ 3TC/ TDF QD
	N=29	N=30	N=31	N=90	N=31
Outcome (FDA Snapshot Approach)					
HIV-1 RNA < 50 copies/ mL, n (%)	25 (86.2)	27(90.0)	21(67.7)	73(81.1)	25(80.6)
HIV-1 RNA ≥ 50 copies/ mL, n (%)	2 (6.9)	2 (6.7)	5 (16.1)	9 (10.0)	2 (6.5)
No virologic data at Week 96 window , n (%)	2 (6.9)	1 (3.3)	5 (16.1)	8 (8.9)	4 (12.9)
Reasons for no virologic data in window					
Discontinued due to death or AE* , n (%)	0	0	2 (6.5)	2 (2.2)	1 (3.2)
Discontinued for other reasons, n (%)	1 (3.4)	1 (3.3)	3 (9.7)	5 (5.6)	3 (9.7)
On treatment but missing data, n (%)	1 (3.4)	0	0	1 (1.1)	0

Molina JM et al. HIV Glasgow 2020, abstract O415.
Orkin C et al. HIV Glasgow 2020, abstract P047.

Lenacapravir: Background

- Lenacapavir: HIV capsid inhibitor that prevents nuclear assembly, virus assembly and release, and capsid assembly. EC_{50} 50 picomolar
  - Retains full activity against NRTI-, NNTRI-, PI-, and INSTI-resistant HIV-1 in vitro[3-5]
  - Oral and SC formulations in development, half life of oral 12 days, SQ (175 d) allows for q 6 month subcutaneous dosing

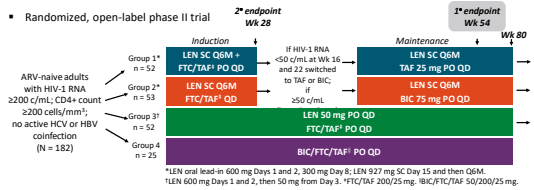


1. Link. Nature. 2020;584:614. 2. Bester. Science. 2020;370:360. 3. Yant. CROI 2019. Abstr 480. 4. Margot. CROI 2020. Abstr 529. 5. VanderVeen. CROI 2021. Abstr 128. 6. Segal-Maurer.CROI 2021. Abstr 127. 7. Molina. IAS 2021. Abstr OALX01B02.

Slide adapted from : clinicaloptions.com

CALIBRATE: Lenacapavir in Treatment-Naive PWH

- Randomized, open-label phase II trial



*LEN oral lead-in 600 mg Days 1 and 2, 300 mg Day 8; LEN 927 mg SC Day 15 and then Q6M.
†LEN 600 mg Days 1 and 2, then 50 mg from Day 3. ‡FTC/TAF 200/25 mg. ‖BIC/FTC/TAF 50/200/25 mg.

- **Primary outcome: proportion with HIV-1 RNA <50 c/mL at Wk 54**
- Secondary outcomes: proportion with HIV-1 RNA <50 c/mL at Wk 28, 38, and 80; change from baseline in log_{10} HIV-1 RNA and CD4+ cell count at Wk 28, 38, 54, and 80

Gupta. CROI 2022. Abstr 138.

Slide credit: clinicaloptions.com

CALIBRATE Primary Analysis: Wk 54 Virologic Outcomes

Virologic Outcome, %	LEN SC + FTC/TAF → TAF (n = 52)	LEN SC + FTC/TAF → BIC (n = 53)	LEN PO + FTC/TAF (n = 52)	BIC/FTC/TAF (n = 25)
FDA Snapshot analysis (ITT)				
▪ HIV-1 RNA <50 c/mL	90	85	85	92
▪ HIV-1 RNA ≥50 c/mL	4*	4*†	6‡	0
▪ No data	6	11	10	8
FDA Snapshot analysis among patients virologically suppressed at Wk 28				
▪ HIV-1 RNA <50 c/mL	94	92	90	92
▪ HIV-1 RNA ≥50 c/mL	4	0	6	0
▪ No data	2	8	4	8

*3 participants (2 in Group 1 and 1 in Group 2) discontinued due to not having HIV-1 RNA <50 c/mL prior to Wk 28. †1 participant discontinued on Day 2.
‡2 of 3 participants with HIV-1 RNA ≥50 c/mL at Wk 54 were suppressed at a subsequent visit.

- In pooled LEN SC cohort (Groups 1 and 2):
  - 88% achieved and maintained virologic suppression at Wk 54
  - 93% of those virologically suppressed at Wk 28 maintained virologic suppression at Wk 54

Gupta. CROI 2022. Abstr 138.

Slide credit: clinicaloptions.com

CALIBRATE: Resistance and Safety

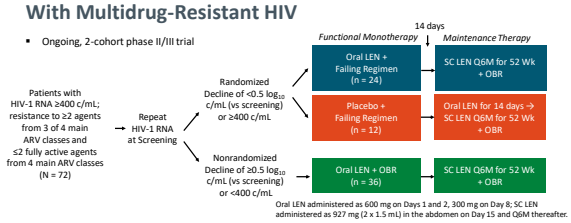
- Emergent LEN resistance observed in 2/157 (1.5%) patients
  - 1 patient receiving **LEN SC + FTC/TAF → BIC** at Wk 10
    - CA: Q67H + K70R (LEN fold change = 20) in CA + M184M/I in RT
    - Pattern suggests incomplete adherence to FTC/TAF
  - 1 patient receiving **LEN PO + FTC/TAF** at Wk 54
    - Q67H (LEN fold change = 7) in CA
    - Nonadherent to FTC/TAF based on pill count, drug levels
- Both later resuppressed on regimen of INSTI + 2 NRTI
- LEN well tolerated with favorable safety profile
  - No SAEs or grade 4 AEs related to study drug
  - Most common AEs: headache and nausea (13% each)
  - GI AEs in SC vs PO LEN
    - Nausea: 14% vs 12%
    - Diarrhea: 7% vs 10%
    - Vomiting: 4% vs 8%
- ISRs mostly grade 1/2; only 1 grade 3 ISR
- 3 discontinuations due to ISRs (due to grade 1 induration or erythema and swelling)

Gupta. CROI 2022. Abstr 138.

Slide credit: clinicaloptions.com

CAPELLA: Lenacapavir in People With Multidrug-Resistant HIV

- Ongoing, 2-cohort phase II/III trial



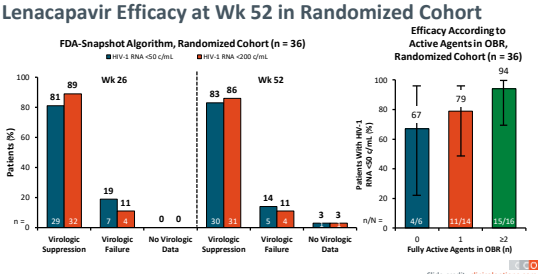
Oral LEN administered as 600 mg on Days 1 and 2, 300 mg on Day 8; SC LEN administered as 927 mg (2 x 1.5 mL) in the abdomen on Day 15 and Q6M thereafter.

- Primary endpoint achieved in prior analysis: ≥0.5 $\log_{10}$ c/mL decline in HIV-1 RNA at Day 14 in randomized cohort
- Secondary endpoints: HIV-1 RNA <50 c/mL, <200 c/mL at Wk 26 and 52 in randomized cohort

Ogbuagu. CROI 2022. Abstr 491.

Slide credit: clinicaloptions.com

CAPELLA Secondary Endpoints: Lenacapavir Efficacy at Wk 52 in Randomized Cohort



Ogbuagu. CROI 2022. Abstr 491.

Slide credit: clinicaloptions.com

CAPELLA: Other Lenacapavir Efficacy and Safety Outcomes in Randomized Cohort

- LEN resistance occurred in 4 patients through Wk 26, but not thereafter
  - All had no fully active drugs in OBR or inadequate adherence to OBR
- Mean change in CD4+ cell count at Wk 52: +83 cells/mm^3
- Incidence of very low CD4+ cell count (<50 cells/mm^3) decreased from 22% (8/36) at baseline to 3% (1/36) at Wk 52
- Incidence of CD4+ cell count ≥200 cells/mm^3 increased from 25% (9/36) at baseline to 60% (21/36) at Wk 52
- ISRs most common AE with SC LEN
  - Most ISRs were grade 1 or 2
  - 2 patients had grade 3 ISRs
  - All nodules were grade 1, except 1 patient with 2 AEs of grade 2 nodules after second and third injections (both resolved in 3 days)
- 1 patient discontinued LEN at Wk 52 due to ISR (nodule; grade 1)

Ogbuagu. CROI 2022. Abstr 491.

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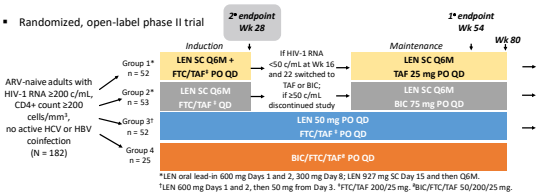
CALIBRATE: Lenacapavir in Treatment-Naive

- Randomized, open-label phase II trial

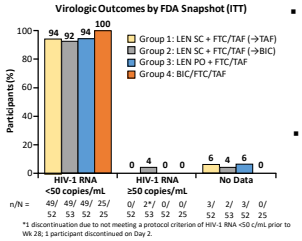


- Participants at baseline: median age 29 yr; 93% male; 52% Black race; 45% Latinx ethnicity
- Primary outcome: proportion with HIV-1 RNA <50 c/mL at Wk 54; **secondary outcomes: proportion with HIV-1 RNA <50 c/mL at Wk 28**, 38, and 80; change from baseline in $\log_{10}$ HIV-1 RNA and CD4+ cell count at Wk 28, 38, 54, and 80

Gupta. IAS 2021. Abstr OALB0302.

Slide credit: clinicaloptions.com

CALIBRATE: Wk 28 Virologic Outcomes



*1 discontinuation due to not meeting a protocol criterion of HIV-1 RNA <50 c/mL prior to Wk 28; 1 participant discontinued on Day 2.

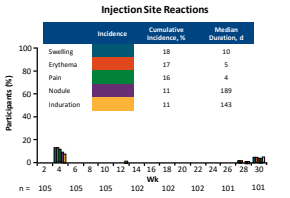
- One participant in LEN SC + FTC/TAF → BIC arm had emergent resistance mutations at Wk 10
  - CA: Q67H + K70R (LEN fold change = 20)
  - RT: M184M/I
- Plasma LEN concentrations consistently in target range

Gupta. IAS 2021. Abstr OALB0302.

Slide credit: clinicaloptions.com

CALIBRATE: Adverse Events and Injection Site Reactions

- LEN was well tolerated with favorable safety profile
  - No SAEs or grade 4 AEs related to study drug
  - Most common AEs: headache and nausea (11% each)
  - GI AEs in SC vs oral LEN:
    - Nausea: 12% vs 8%
    - Diarrhea: 6% vs 8%
- ISRs in 39% of participants; 83% were grade 1 and generally resolved in days
- 2 discontinuations due to ISRs (grade 1 injection site induration)



Gupta. IAS 2021. Abstr OALB0302.

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Lenacapravir: Current status→ on clinical hold

December 21, 2021

Gilead Announces Clinical Hold on Studies Evaluating Injectable Lenacapavir for HIV Treatment and Prevention Due to Vial Quality Concerns

-- Pause Due to Concerns About Compatibility of the Vial Type with the Drug Solution --

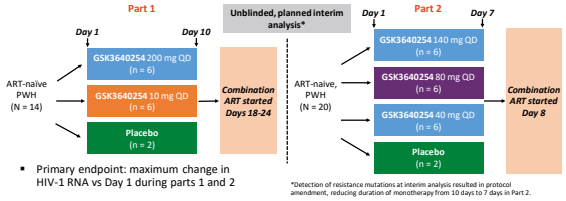
FOSTER CITY, Calif.--(BUSINESS WIRE)-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced that the U.S. Food and Drug Administration (FDA) has placed a clinical hold on the use of injectable lenacapavir in borosilicate vials in all ongoing clinical studies for HIV treatment and HIV pre-exposure prophylaxis (PrEP). The FDA's clinical hold is due to emerging concerns about the compatibility of vials made of borosilicate glass with lenacapavir solution, which could potentially lead to the formation of sub-visible glass particles in the solution of lenacapavir. Dosing of oral formulations of lenacapavir will continue. The company remains confident about the future potential of lenacapavir and is committed to resolving this vial quality issue.

Next Generation Maturation Inhibitor: GSK3640254

- GSK'254
  - Prevents the proteolytic cleavage of specific portions of the Gag protein which prevents processing of the Gag-Pol polyprotein in late stage of HIV replication.
  - Pre-existing mutations at the cleavage site led to termination of development of an earlier maturation inhibitor (bevirimat).
  - Phase 2 A results of a two part study of GSK '254 presented at CROI 2021.

Phase IIa Study of GSK3640254: Study Design

- Multicenter, randomized, double-blind (sponsor-unblinded), placebo-controlled trial



- Primary endpoint: maximum change in HIV-1 RNA vs Day 1 during parts 1 and 2
- Secondary endpoints: resistance, PK, safety

*Detection of resistance mutations at interim analysis resulted in protocol amendment, reducing duration of monotherapy from 10 days to 7 days in Part 2.

Spinner. CROI 2021. Abstr 126.

Slide adapted from: clinicaloptions.com

Phase IIa Study of GSK3640254: Baseline Characteristics

Characteristic	GSK3640254					Placebo (n = 4)	Total (N = 34)
	10 mg* (n = 6)	40 mg† (n = 6)	80 mg† (n = 6)	140 mg† (n = 6)	200 mg* (n = 6)		
Mean age, yrs (SD)	32.7 (8.3)	27.7 (6.9)	32.8 (6.2)	33.2 (8.2)	29.3 (3.9)	36.5 (9.3)	31.8 (7.2)
Male, n (%)	6 (100)	5 (83)	6 (100)	5 (83)	6 (100)	4 (100)	32 (94)
Mean BMI (SD)	25.3 (3.7)	23.9 (4.3)	24.8 (3.7)	23.4 (1.6)	22.6 (2.2)	23.0 (1.3)	23.9 (3.0)
Race, n (%)							
▪ White	2 (33)	5 (83)	4 (67)	5 (83)	5 (83)	3 (75)	24 (71)
▪ Black	0	1 (17)	2 (33)	1 (17)	0	0	4 (12)
▪ Other	4 (67)	0	0	0	1 (17)	1 (25)	6 (18)
Mean HIV-1 RNA, $\log_{10}$ copies/mL (SD)	4.19 (0.311)	4.67 (0.233)	4.43 (0.510)	4.53 (0.577)	4.82 (0.476)	4.25 (0.417)* 4.25 (0.417)†	4.47 (0.489)* 4.57 (0.592)†

*Part 1. †Part 2.

Spinner. CROI 2021. Abstr 126.

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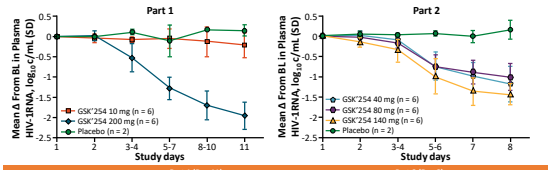
Phase IIa Study of GSK3640254: Antiviral Activity



Mean Change in HIV-1 RNA vs BL, log_{10} copies/mL (SD)	Part 1 (Day 11)			Part 2 (Day 8)			
	GSK3640254 10 mg (n = 6)	GSK3640254 200 mg (n = 6)	Placebo (n = 2)	GSK3640254 40 mg (n = 6)	GSK3640254 80 mg (n = 6)	GSK3640254 140 mg (n = 6)	Placebo (n = 2)
Primary endpoint	-0.22 (0.309)	-1.96 (0.337)	0.14 (0.134)	-1.18 (0.436)	-1.02 (0.330)	-1.45 (0.235)	0.15 (0.226)
Maximum change	-0.36 (0.252)	-2.01 (0.329)	-0.21 (0.262)	-1.18 (0.436)	-1.02 (0.330)	-1.49 (0.267)	-0.03 (0.127)

Spinner. CROI 2021. Abstr 126. Reproduced with permission.

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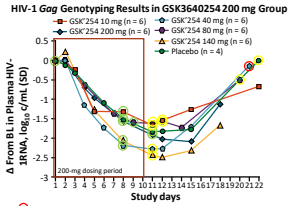
Phase IIa Study of GSK3640254: Resistance

- Resistance mutation A364A/V detected in 4 of 6 patients receiving GSK3640254 200 mg QD at Day 11 in part 1
  - Full conversion and phenotypic resistance in 1 of 4
- No resistance in 10 mg QD group
- Protocol amendment reduced duration of monotherapy from 10 days to 7 days in Part 2
- No resistance detected at any dose in part 2 (140 mg, 80 mg, or 40 mg)

HIV-1 *Gag* Genotyping Results in GSK3640254 200 mg Group



A364V: Full conversion of the mixture and loss of sensitivity to GSK'254
A364A/V: Mixed population of amino acids "A" and "V" with partial resistance to GSK'254
No resistance

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Slide credit: clinicaloptions.com

GSK'254 Summary

- In ART-naive persons with HIV, novel HIV-1 maturation inhibitor, GSK3640254, demonstrated dose-response activity
  - HIV-1 RNA decreased 1.5 log_{10} copies/mL with 140-mg QD dose and 2.0 log_{10} copies/mL with 200-mg QD dose
- GSK3640254 was well-tolerated
  - No grade 3/4 AEs and no AEs leading to d/c
- Investigators conclude these findings support evaluation of GSK3640254 (100 mg QD, 150 mg QD, and 200 mg QD) in combination with 2 NRTIs in phase IIb study

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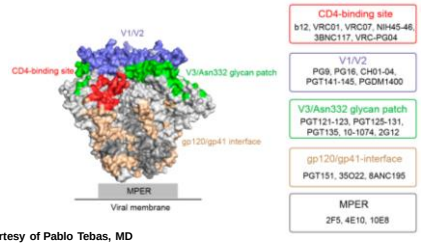
Slide adapted: clinicaloptions.com

Additional Ongoing Studies with GSK' 254

- DOMINO; NCT04493216 **Phase**: 2b
  Purpose: The purpose of this study is to evaluate the safety and efficacy of GSK3640254 (given at three different doses) compared to dolutegravir (brand name: Tivicay), each given in combination with abacavir/lamivudine or emtricitabine/tenofovir alafenamide, in adults who have never taken HIV medicines.
- DYNAMIC; NCT04900038 **Phase**: 2b
  Purpose: The purpose of this study is to evaluate the safety, efficacy, and resistance profile of GSK3640254 (given at three different doses) in combination with dolutegravir, as compared to lamivudine in combination with dolutegravir, in adults who have never taken HIV medicines.

clinicalinfo.hiv.gov/en/drugs/gsk3640254

Broadly Neutralizing Antibodies against HIV



CD4-binding site
b12, VRC01, VRC07, NIH45-46, 3BNC117, VRC-PG04

V1/V2
PG9, PG16, CH01-04, PGT141-145, PGDM1400

V3/Asn332 glycan patch
PGT121-123, PGT125-131, PGT135, 10-1074, 2G12

gp120/gp41-interface
PGT151, 35O22, 8ANC195

MPER
2F5, 4E10, 10E8

Slide **courtesy of Pablo Tebas, MD**

Future Combinations and Approaches in the works

- Long acting cabotegravir and a broadly neutralizing antibodies
  - A5357: A single arm trial of long-acting cabotegravir and VRC07LS (a broadly neutralizing antibody; bNAb) as maintenance ART
  - A5364: A single arm trial of two bNAbs (3BNC117-LS & 10-1074-LS) to prevent relapse of viremia of discontinuation of oral ART
  - A5377, a first-in-human Phase 1 clinical trial of a tri-specific monoclonal antibody (SAR441236) to establish safety, pharmacokinetics, and preliminary antiviral activity
- Ongoing Phase 1 study combined with GS-5423 (AKA 3BNC117-LS) in people with virologic suppression

Summary

- Greater confidence emerging around the use of simplified regimens as initial therapy and for switch of those who are suppressed
  - 2 drug combinations with Integrase inhibitors
  - Long acting injectable cabotegravir and Rilpivirine
    - Investigational approaches with q 8 week dosing, combination with other agents and use in populations that have struggled with adherence in progress.
- New drugs with novel mechanisms of action and less frequent dosing are in development with some on hold currently
  - Islatravir—on hold
  - Lenacapravir-on hold
  - GSK'254 in Phase 2b
  - Broadly neutralizing antibodies- In Phase 2 trials

Question-and-Answer Session