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- In the Phase 3 portion of ARTISTRY-1, the majority of participants were on a complex regimen (CR) containing a boosted protease inhibitor (PI) and/or integrase strand transfer inhibitor (INSTI)
- Potential drug-drug interactions (DDIs) identified for bicitegravir/lenacapavir (BIC/LEN) were fewer compared with commonly prescribed CRs, all containing a pharmacokinetic (PK) booster
 - This is likely due to strong inhibition of cytochrome P450 3A4 (CYP3A) and P-glycoprotein (P-gp) by PK boosters cobicistat and ritonavir
- This analysis, along with ARTISTRY-1 Phase 2 efficacy and safety findings, highlights the potential of BIC/LEN as a single tablet regimen (STR) for treatment optimization in people with HIV (PWH) who are virologically suppressed (VS) on a CR

- Some people who have human immunodeficiency virus (HIV) need to take several tablets each day for their HIV because existing single tablet treatments do not work for them, might not be safe for them to take, or cause side effects
 - Taking several treatments a day for the same disease is called a "complex regimen"
- People with HIV are likely to be taking medicines to treat other health problems, so it is important to know how HIV treatments affect these medicines
- The ARTISTRY-1 study looked to see if two HIV medicines, bictegravir (BIC) and tenacapavir (LEN), taken together are effective and safe for people with HIV who switch from a complex HIV regimen
- In this analysis, researchers looked at how complex regimens or BIC/LEN might interact with other medicines that are frequently taken by people in the US for other health problems
- Researchers found that BIC/LEN is expected to have fewer interactions with frequently used medicines than some of the other commonly used combinations of HIV medicines
- Taking a single tablet that combines both BIC and LEN once a day may be of benefit to some people with HIV because BIC/LEN has a lower chance of interacting with other medicines compared with complex regimens

Many PWs are unable to benefit from guideline-recommended STRs due to drug resistance, tolerance, contraindications, or DDIs, and are required to take complex antiretroviral therapy (ART) regimens comprising ≥ 2 core antiretroviral classes, ≥ 2 pills/day, and/or requiring more than 10 pills/day.

- CRs commonly include PIs coadministered with PK boosters, which inhibit drug-metabolizing enzymes, including CYP3A5⁶
- CRs can create numerous challenges for PWH, including pill burden, suboptimal adherence, and reduced quality of life^{7,8}

PWH also often take concomitant medications to treat comorbidities¹⁰⁻¹²

It is important to evaluate these medications for potential DDIs, which are frequently reported to be associated with CRs, to avoid toxicity and maintain efficacy of all medications¹³

ARTSTRY-1 (NCT05050341) is an ongoing randomized, open-label, multicenter, active-controlled phase 2/3 study evaluating the safety and efficacy of switching to a BICLEN STR in PWs who are ≥ 18 years on CR¹⁴

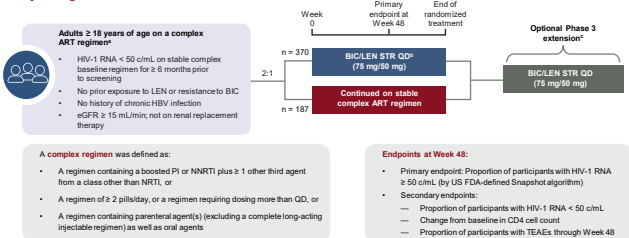
- BIC, a guideline-recommended INSTI, is primarily metabolized by CYP3A and UDP glucuronosyltransferase 1A1 (UGT1A1),^{1,2,5} with similar contribution from these pathways
- LEN, a first-in-class capsid inhibitor, is a substrate of CYP3A, UGT1A1, and P-gp, a moderate inhibitor of CYP3A, and a weak inhibitor of P-gp and breast cancer resistance protein¹⁴⁻¹⁶
- In the previous portion of ARTSTRY-1, a BIC LEN first-in-class, capsid inhibitor, was well tolerated and maintained virologic suppression through Week 48 in participants switching from a CR¹⁷

In Phase 3 of ARTSTRY-1, a BIC 75 mg/mL 50 mg STR is being assessed

- To assess the DDI profile of BIC/LEN and representative CRs being used in the Phase 3 portion of ARTISTRY-1, in the context of frequently prescribed medications in the US

- ARTISTRY-1 (NCT05502341) is an ongoing randomized, open-label, multicenter, active-controlled Phase 2/3 study

Study Design of Phase 3 of ARTISTRY-1



Due to the wide viral resistance, intolerance or contraindication to existing STRs, the use of NNRTIs is increasing in our country, especially on Day 1 of treatment. Patients who search for a CR in the externalization phase are the only leading cause of LEN. **Abbreviations:** CR, complete remission; CCR, complete remission in CR; CCRs, complete remissions; eGFR, estimated glomerular filtration rate; FDA, Food and Drug Administration; HIV, hepatitis B virus; LEN, lenvatinib; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; PI, protease inhibitor; QD, once daily; T4, thyroxine; single regimen, single-drug regimen; STR, single-drug resistance.

■ The DDl profile of BICLEN and the top 6 most commonly used CRs from Phase 3 of ARTISTRY-1 was assessed with 18 frequently prescribed drugs in the US²⁸

— The top 10 most prescribed medications in the US were identified using the ClinCalc DrugStats Database 2022²⁹: atazanavir, metformin, lisinopril, levothyroxine, amlodipine, metoprolol, albuterol, losartan, omeprazole, gabapentin

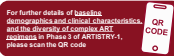
— A further 8 medications were identified from a literature search of commonly prescribed drugs in the elderly population: apixiban, apixiban, celecoxib, dexamethasone, gabapentin, gabapentin, gabapentin, gabapentin

■ DDl profiles were assessed using the Liverpool HD Drug Interactions database³⁰ and/or US drug prescribing information

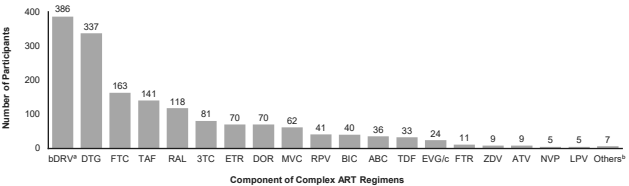
■ The DDl profiles for each of the individual drugs within the ART regimens of interest were combined

Baseline Demographics

- The median (range) age of participants in Phase 3 of ARTISTRY-1 was 60 (22-84) years with a median (range) of 7 (2-29) prior ART regimens
- In total, 96% of participants (n = 533) received ≥ 1 concomitant medication

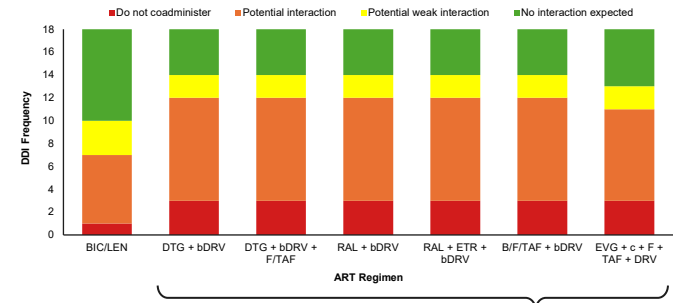


Number of Participants on Individual Antiretroviral Drugs as Part of Their Complex ART Regimen in the Phase 3 Portion of ARTISTRY-1



• Of 557 patients enrolled and treated in Phase 3, the majority were on a CR containing a boosted PI and/or INSTI

DDI Profile of BIC/LEN and Representative^a Complex ART Regimens



Concomitant Medication of Interest	BIC/LEN	Representative Complex ART Regimens
Albuterol		
Gabapentin		
Lisinopril		
Omeprazole		
Losartan		
Metoprolol		
Levothyroxine ^b		When coadministering with DRVr or ETR, close monitoring of thyroid parameters is recommended, and adjustment of the levothyroxine dose may be necessary if clinically indicated
Pravastatin		When coadministering with bDRV or EVG + c + F + TAF, start with the lowest dose and titrate up to the desired clinical effect while monitoring for safety
Atorvastatin		When coadministering with bDRV or EVG + c + F + TAF, start with the lowest dose and titrate carefully while monitoring for safety
Prednisone		Monitoring is recommended when coadministering with bDRV, EVG/c, or ETR
Rosuvastatin		When coadministering with bDRV, start with the lowest dose and titrate up to the desired clinical effect while monitoring for safety
Amlodipine	LEN is expected to increase amlodipine concentrations by 60%; clinical monitoring is advised with dose adjustment if needed	Close monitoring is recommended when coadministering with bDRV or EVG/c. DRVr and EVG/c are expected to increase amlodipine concentrations by ~100%; if coadministration is indicated, consider a dose reduction for amlodipine of 50%. With DRV/c, amlodipine should be started at low doses with careful titration to response
Apixaban	The product label for apixaban indicates that no dose adjustment is required for apixaban when coadministered with drugs that are not strong inhibitors of CYP3A4; monitoring for increased apixaban side effects is recommended	Use of bDRV or EVG/c and this anticoagulant is not recommended, although the US label gives the option to use apixaban at a reduced dose if needed
Metformin	Close monitoring should be considered when starting coadministration of BIC with metformin in those with moderate renal impairment, due to increased risk of lactic acidosis, and a dose adjustment of metformin should be considered if required	Reduction of the metformin dose should be highly considered in those who are taking DTG; careful monitoring and dose adjustment of metformin is recommended in those who are taking DRV/c or EVG + c + F + TAF; close monitoring should be considered when starting coadministration of BIC with metformin in those with moderate renal impairment, due to increased risk of lactic acidosis, and a dose adjustment of metformin should be considered if required
Warfarin	Monitor INR and adjust warfarin dose accordingly	Monitoring of INR is recommended
Fluticasone	Dose titration recommended in those who are taking LEN	
Simvastatin	Dose titration recommended in those who are taking LEN	
Clopidogrel		

The top 6 most commonly used complex ART regimens in the Phase 3 portion of ARTISTRY-1 are shown.

^a† Potential interaction reported for DRV and ETR, but not for DRV or EVG + c + F + TAF + DRV [no interaction expected (green category)].

DDI categories are based on the Liverpool/HIV Drug Interactions database (red: these drugs should not be coadministered; orange: potentially clinically significant interaction that is likely to require additional monitoring, alteration of drug dosage, or timing of administration; yellow: potential interaction likely to be of weak intensity, additional clinical monitoring or dosage adjustment is unlikely to be required; green: no clinically significant interaction expected).¹⁸

Abbreviations: ART, antiretroviral therapy; BIC, bictegravir; DRV, boosted darunavir; c, coformulated C39A; cytochrome P450 3A4; DDI, drug-drug interaction; DRV, darunavir; DTG, dolutegravir; ETR, etravirine; EVG, elvitegravir; F, emtricitabine; INR, international normalized ratio; LEN, lenacapavir; r, ritonavir; RAL, raltegravir; TAF, tenofovir alafenamide.

- A larger number of potential DDIs were identified for ART regimens containing boosted PI than for BIC/LEN due to strong inhibition of the drug-metabolism pathway components CYP3A and P-gp by PK boosters cobicistat and ritonavir compared with moderate CYP3A inhibition and weak P-gp inhibition by LEN

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Disclosures: PA, JMM-R, PS, BG-P, and DDM are employees of, and hold stocks/shares in, Gilead Sciences, Inc.

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