THE ROLE OF INTEGRASE STRAND TRANSFER INHIBITORS IN HIV CARE
A SELF-STUDY MODULE
EDITION 10

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TARGET AUDIENCE
Physicians, physician assistants, pharmacists, nurse practitioners, nurses, and other interested medical providers

LEARNING OBJECTIVES
After reading this self-study module, you should be able to:
1. Discuss recent changes regarding the use of integrase inhibitors in treatment-naive patients, as stated in the Department of Health and Human Services Guidelines.
2. Describe the role of raltegravir, elvitegravir, and dolutegravir in the management of HIV treatment-naive subjects.
3. List common side effects and potential drug interactions associated with raltegravir, elvitegravir, and dolutegravir.
4. Review the role of integrase inhibitors for the management of post-exposure prophylaxis.

AUTHOR
John J. Faragon, PharmD, BCPS, AAHIV-P
Regional Pharmacy Director,
NY/NJ AIDS Education & Training Center
Pharmacist,
Albany Medical Center
Albany, New York

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John J. Faragon, PharmD, BCPS, AAHIV-P, Cynthia Miller, MD, Carl Koenigsmann, MD, Sarah Walker, MS, Jim Ybarra and Jennifer Price.
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Albany Medical College
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Go to the menu on the right and select The Role of Integrase Inhibitors Paperwork

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Introduction

The management of human immunodeficiency (HIV) infection has changed dramatically since the mid-1990s with the advent of highly active antiretroviral therapy (HAART). Since then, numerous medications have been approved by the FDA, now totaling 24 different medications, many of which are also available as combination tablets. More recently, the FDA has approved single tablet regimens (STRs), where an entire daily regimen for HIV is contained in one tablet aimed at improving adherence and minimizing pill burdens for patients with HIV infection. [1-3] Compared to multiple tablets and capsules that patients needed to manage HIV in the late-1990s, reduced pill burdens have made the management of HIV much easier for most patients.

Guidelines for treating HIV infection from the Department of Health and Human Services (DHHS) have been available to assist providers in managing HIV infection. [4] An update to the most recent version of the guidelines was released in October 2013 to include the addition of newer integrase strand transfer inhibitors (INSTIs), elvitegravir and dolutegravir, to the list of preferred initial regimens, in addition to raltegravir. [5] Raltegravir, in combination with tenofovir/emtricitabine, for the management of HIV post-exposure prophylaxis (PEP), was also added as the preferred regimen by both the New York State Department of Health AIDS Institute and the United States Public Health Service Guidelines. [6-8] This overview will focus specifically on the role of INSTIs in HIV care as it relates to initial therapy for HIV infection and their role in managing PEP.

Department of Health and Human Services Guidelines

In the October 2013 update to the DHHS Guidelines, the panel expanded the preferred regimens for the initial management of HIV infection in the INSTI class to include the following: [4,5]

- Elvitegravir/cobicistat/tenofovir/emtricitabine (Stribild®)
- Dolutegravir (Tivicay®) with either abacavir/lamivudine (Epzicom®) or tenofovir/emtricitabine (Truvada®)
- Raltegravir (Isentress®) with tenofovir/emtricitabine (Truvada®)

While the INSTI-based regimens were changed with this update, other preferred medications remained unchanged. As in previous versions, other preferred regimens include efavirenz/tenofovir/emtricitabine (Atripla®) or either ritonavir-boosted atazanavir (Reyataz® + Norvir®) or darunavir (Prezista® + Norvir®) in combination with tenofovir/emtricitabine (Truvada®). [4]

Table 1 summarizes the current preferred regimens on DHHS Guidelines. [4,5]

<table>
<thead>
<tr>
<th>Class of Regimen</th>
<th>Preferred Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Nucleoside Reverse Transcriptase Inhibitor-Based Regimen</td>
<td>• Efavirenz/tenofovir/emtricitabine (Atripla®)</td>
</tr>
<tr>
<td>Protease Inhibitor-Based Regimen</td>
<td>• Atazanavir + ritonavir + tenofovir/emtricitabine (Reyataz® + Norvir® + Truvada®)</td>
</tr>
<tr>
<td></td>
<td>• Darunavir + ritonavir + tenofovir/emtricitabine (Prezista® + Novir® + Truvada®)</td>
</tr>
<tr>
<td>Integrase Strand Transfer Inhibitor-Based Regimen</td>
<td>• Elvitegravir/cobicistat/tenofovir/emtricitabine (Stribild®)</td>
</tr>
<tr>
<td></td>
<td>• Dolutegravir + tenofovir/emtricitabine (Tivicay® + Truvada®)</td>
</tr>
<tr>
<td></td>
<td>• Dolutegravir + abacavir/lamivudine (if HLA*B5701 negative) (Tivicay® + Epzicom®)</td>
</tr>
<tr>
<td></td>
<td>• Raltegravir + tenofovir/emtricitabine (Isentress® + Truvada®)</td>
</tr>
</tbody>
</table>
INSTI-Based Regimens – Treatment Naïve Patients Overview

The integrase enzyme is essential to the HIV viral life cycle, as it is required for incorporating the HIV viral genome into the host cell DNA within the nucleus of the CD4 cell. By using an INSTI, this integration of the HIV viral genome into the infected host cell is blocked. The use of INSTI-based regimens in HIV treatment-naïve subjects has led to high rates of virologic suppression and acceptable tolerability, with relatively low pill burdens compared to regimens from the mid-1990s. [9-17] In trials of INSTIs when they were combined with nucleoside/nucleotide reverse transcriptase inhibitors, results have demonstrated more rapid reductions in viral load and improved CD4 cell counts when compared to non-nucleoside or protease inhibitor-based regimens. [9, 11-14, 16, 17] In the United States, there are three integrase inhibitors approved by the FDA, raltegravir, elvitegravir (combined with cobicistat, tenofovir and emtricitabine), and dolutegravir. Table 2 provides a comparison of the three INSTIs approved by the FDA. [3,18,19]

**Raltegravir**

Raltegravir is an INSTI that is FDA approved for the management of HIV infection. Its approval in treatment-naïve patients was based on the results of a large, double-blind, placebo-controlled trial comparing raltegravir 400mg twice daily with tenofovir/emtricitabine once daily, compared to efavirenz 600mg with tenofovir/emtricitabine all given once daily. [9] This trial, called the STARTMRK study, was conducted in over 500 HIV treatment-naïve subjects. At 48 weeks, the percentage of subjects who achieved undetectable viral loads was similar, 86% for the raltegravir arm compared to 82% in the efavirenz arm, meeting the predefined non-inferiority criteria. In addition to providing excellent virologic efficacy, the CD4 counts on average increased by 189 cells/mm³ in the raltegravir arm compared to 163 cells/mm³ in those receiving an efavirenz-based regimen. Additional data on this trial out to 156 weeks have demonstrated similar outcomes with no additional safety concerns arising in this study. [20] The DHHS Guidelines have included raltegravir + tenofovir/emtricitabine on their preferred list of ARV regimens for treatment-naïve patients since the 2012 version of the guidelines, not only due to the durable efficacy of raltegravir, but also because of its favorable safety profile and convenience. [4,5]

Despite its efficacy when used twice daily, raltegravir is not approved for use as a once-daily regimen. In the QDMRK study, raltegravir was compared to tenofovir/emtricitabine and efavirenz once daily, with the raltegravir arm achieving 86% suppression compared to 82% for the efavirenz arm, meeting the predefined non-inferiority criteria. In this study, the once-daily raltegravir regimen (given as 800mg daily) did not meet the statistical criteria to be considered non-inferior to the twice daily regimen. Therefore, caution is warranted when using once-daily raltegravir, as this is outside the current FDA labelling for the medication. [10,18] Given its relatively low barrier to resistance, missed doses of this medication may result in integrase resistance mutations, as shown in the trials involving raltegravir. [9,10,18]

Side effects associated with a raltegravir-based regimen are minimal, and this continues to be one of the best tolerated regimens of those on the preferred list from DHHS Guidelines. Rare cases of creatine kinase elevations and rhabdomyolysis have been reported. Skin reactions, including systemic hypersensitivity reactions, can occur. [18] However, alterations in lipid parameters are unlikely to occur with raltegravir, making this an option in patients at risk for or with concurrent cardiovascular disease. From a drug interaction perspective, raltegravir is metabolized by UGT1A1 and not CYP450 and is therefore unlikely to cause significant drug interactions that are often associated with other classes of HIV medications. [4,18]

**TABLE 2: Integrase Inhibitor Comparison in Treatment-Naïve Subjects [3,18,19]**

<table>
<thead>
<tr>
<th>Medications</th>
<th>Dosing and Pill Burden</th>
<th>Drug Interaction Potential Risk</th>
<th>Food Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raltegravir (Isentress®)</td>
<td>400mg orally twice daily</td>
<td>Low, metabolized via UGT1A1</td>
<td>None</td>
</tr>
<tr>
<td>Elvitegravir (with cobicistat/tenofovir/emtricitabine) (Stribild®)</td>
<td>One tablet orally once daily</td>
<td>High, metabolized predominantly via CYP3A4, minor UGT1A1/3 pathway</td>
<td>Take with a meal</td>
</tr>
<tr>
<td>Dolutegravir (Tivicay®)</td>
<td>50mg orally once daily</td>
<td>Moderate, predominantly via UGT1A1, minor CYP3A4 pathway</td>
<td>None</td>
</tr>
</tbody>
</table>
Elvitegravir/cobicistat/tenofovir/emtricitabine

Elvitegravir is an INSTI contained in the STR that also includes cobicistat (a pharmacokinetic booster for elvitegravir), tenofovir and emtricitabine (Stribild®). [3,11-14] Elvitegravir/cobicistat/tenofovir/emtricitabine was approved in HIV treatment-naïve subjects based upon two large, phase 3 studies that compared this regimen to either efavirenz/tenofovir/emtricitabine or atazanavir/ritonavir + tenofovir/emtricitabine. [3,11-14] When elvitegravir/cobicistat/tenofovir/emtricitabine was approved by the FDA, it was initially placed on the DHHS Guidelines as an alternative regimen. However, recent data published and presented at national conferences has demonstrated the durability and efficacy of this regimen out to 96 and 144 weeks, which resulted in this regimen being classified as a preferred regimen on the current DHHS Guidelines. [3,5,12,14] When efavirenz/tenofovir/emtricitabine was compared to the elvitegravir/cobicistat/tenofovir/emtricitabine, the elvitegravir/cobicistat/tenofovir/emtricitabine regimen was shown to be non-inferior to efavirenz/tenofovir/emtricitabine, with 88% and 84% of patients achieving undetectable HIV viral loads, respectively, thus meeting pre-defined, non-inferiority criteria. [3,12,13] In the second study comparing elvitegravir/cobicistat/tenofovir/emtricitabine to ritonavir-boosted atazanavir with tenofovir/emtricitabine, 90% versus 87% of subjects achieved an undetectable viral load, respectively – again meeting pre-defined, non-inferiority criteria. [3,11,14] The results of these studies demonstrated that the elvitegravir/cobicistat/tenofovir/emtricitabine performed similarly to two DHHS-preferred regimens – an NNRTI-based and a ritonavir-boosted, PI-based regimen. [3-5,11-14]

Elvitegravir/cobicistat/tenofovir/emtricitabine is not recommended in patients with a baseline, pre-treatment creatinine clearance of 70 mL/min or less. [3] This is because the cobicistat contained in the tablet has been shown to actively secrete creatinine in the renal tubules, resulting in small, but measurable, increases in serum creatinine. As a result, the calculated creatinine clearance will be decreased. However, data demonstrate that while there were calculated creatinine clearance changes, no changes in true glomerular function occurred, despite the increases in creatinine. In addition to the increases creatinine associated with cobicistat, tenofovir itself has also been shown in studies to cause renal impairment that can include tubulopathy and Fanconi syndrome. Therefore, when using this regimen the challenge for providers is to discern the increased creatinine associated with cobicistat from the potential renal dysfunction that may occur with tenofovir. The FDA label for Stribild® contains specific guidance to assist providers; patients who experience an increase in serum creatinine of greater than 0.4 mg/dL from baseline should be evaluated for evidence of tenofovir-associated tubulopathy, while increases in serum creatinine of less than 0.4mg/dL from baseline are likely due to cobicistat’s effect on the tubular secretion of creatinine. Serum creatinine should also be measured at baseline prior to initiating the regimen, and then repeated one month after starting therapy; this one month creatinine measure should be used as the “new” baseline creatinine. Any significant change in serum creatinine from that point forward is unlikely to be from the active tubular secretion associated with cobicistat, but rather renal toxicity either from tenofovir or from some other cause.

When patients are receiving elvitegravir/cobicistat/tenofovir/emtricitabine and their estimated creatinine clearance falls to less than 50ml/min, they should stop the medication and be switched to an alternative regimen. Additional common adverse events from elvitegravir/cobicistat/tenofovir/emtricitabine include nausea and diarrhea. [3]

Since cobicistat is a known CYP3A4 inhibitor, elvitegravir/cobicistat/tenofovir/emtricitabine must be used carefully when patients are receiving other medications. [3,4] The drug interaction profile for cobicistat is very similar to ritonavir. [3,4,21] Therefore, most medications that an HIV provider would avoid or use with caution with a ritonavir-boosted PI should likely be avoided with elvitegravir/cobicistat/tenofovir/emtricitabine. Finally, Table 3 lists medications that are contraindicated with elvitegravir/cobicistat/tenofovir/emtricitabine. Providers are encouraged to review medication lists for potential drug interactions prior to initiating this regimen.

INSTI-associated mutations were also detected in patients who failed elvitegravir/cobicistat/tenofovir/emtricitabine, and some even conferred cross-resistance to raltegravir. [3,11-14] In previous ritonavir-boosted PI studies (including atazanavir + ritonavir compared to elvitegravir/cobicistat/tenofovir/emtricitabine), boosting with ritonavir in treatment-naïve patients has been shown to prevent the emergence of primary protease resistance. [11,14] However, data with cobicistat boosting demonstrated that when subjects failed this regimen, despite boosting elvitegravir with cobicistat, resistance mutations may still occur. [3,11-14]
**Dolutegravir**

Dolutegravir is the most recent medication approved for HIV infection, available in the United States in August of 2013. [19] Its approval in treatment-naïve subjects was based upon three large, randomized trials that included the use of dolutegravir 50mg daily in combination with two nucleoside reverse transcriptase inhibitor combinations, either tenofovir/emtricitabine or abacavir/lamivudine. [15-17, 22] In each of the treatment-naïve studies, dolutegravir-containing regimens were compared to the preferred regimens on the DHHS guidelines. The first study compared dolutegravir 50mg daily to raltegravir 400mg twice daily when combined with either tenofovir/emtricitabine or abacavir/lamivudine. [15] At weeks 48 and 96, the dolutegravir arm of the study was found to be non-inferior to the raltegravir arm. [15,22] Two additional studies in treatment-naïve subjects compared dolutegravir-based regimens combined with tenofovir/emtricitabine or abacavir/lamivudine to either darunavir/ritonavir or efavirenz-containing regimens. [16,17] In these latter studies, the dolutegravir arms of the studies were found to be superior to both darunavir/ritonavir and efavirenz containing regimens. Dosing recommendations for dolutegravir are as follows:

- **Treatment-naïve, treatment-experienced INSTI-naïve**
  - 50 mg once daily

- **Treatment-naïve, treatment-experienced INSTI-naïve when given with efavirenz, fosamprenavir/ritonavir, tipranavir/ritonavir, or rifampin**
  - 50 mg twice daily

- **INSTI-experienced with certain INSTI-associated resistance mutations or INSTI resistance suspected**
  - 50 mg twice daily

Dolutegravir has demonstrated excellent tolerability, with headache and insomnia being the most commonly reported side effects in their studies. [15-17, 19, 22] Rare cases of hypersensitivity reactions have been reported, which may or may not be due to the use of abacavir in these studies. Similar to the effects of cobicistat, dolutegravir can also inhibit the tubular secretion of creatinine, while not affecting glomerular filtration rates. In studies of dolutegravir, the average change in serum creatinine was 0.11mg/dL, which generally occurred within the first four weeks of therapy. [19] From a resistance standpoint, INSTI resistance mutations have not emerged in treatment-naïve patients failing

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**TABLE 3:** Contraindicated Medications with Elvitegravir/cobicistat/tenofovir/emtricitabine [3,4]

<table>
<thead>
<tr>
<th>Drug Class Contraindicated</th>
<th>Drugs within class that are contraindicated</th>
<th>Clinical Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alpha 1-Adrenoreceptor Antagonist</strong></td>
<td>Alfuzosin</td>
<td>Increased alfuzosin concentrations, which can result in hypotension</td>
</tr>
<tr>
<td>Antimycobacterial</td>
<td>Rifampin</td>
<td>Rifampin can significantly decrease elvitegravir and cobicistat levels.</td>
</tr>
<tr>
<td><strong>Ergot Derivatives</strong></td>
<td>Dihydroergotamine, Ergotamine, Methylergonovine</td>
<td>Acute ergot toxicity</td>
</tr>
<tr>
<td>GI Motility Agent</td>
<td>Cisapride</td>
<td>Serious and/or life-threatening events such as cardiac arrhythmias.</td>
</tr>
<tr>
<td><strong>Herbal Products</strong></td>
<td>St. John’s wort (Hypericum perforatum)</td>
<td>Reduced elvitegravir and cobicistat levels</td>
</tr>
<tr>
<td><strong>HMG-CoA Reductase Inhibitors</strong></td>
<td>Lovastatin, Simvastatin</td>
<td>Potential myopathy or rhabdomyolysis</td>
</tr>
<tr>
<td>Neuroleptic</td>
<td>Pimozide</td>
<td>Potential for life-threatening events such as cardiac arrhythmias</td>
</tr>
<tr>
<td><strong>Phosphodiesterase-5 (PDE5) Inhibitor</strong></td>
<td>Sildenafil when used for pulmonary arterial hypertension</td>
<td>Increased sildenafil-associated adverse events</td>
</tr>
<tr>
<td>Sedative/Hypnotics</td>
<td>Triazolam, Orally administered midazolam</td>
<td>Triazolam or orally administered midazolam may cause prolonged respiratory depression.</td>
</tr>
</tbody>
</table>
Role ofRaltegravir in Post-Exposure Prophylaxis
Guidelines for the use of HIV-1 antiretroviral therapy for post-exposure prophylaxis (PEP) in the management of occupational exposure have been updated. With the availability of better tolerated medications, both the New York State Department of Health (NYSDOH) and the United States Department of Health and Human Services (DHHS) Guidelines have changed their preferred regimen. [6-8] The risk of acquiring HIV from a known HIV-infected source depends on many factors, which are described in detail in both the NYSDOH and DHHS Guidelines. [6-8] Table 5 provides an estimated per-act probability of acquiring HIV when the source subject is known to be HIV-infected. Another important aspect of providing PEP is timing of when to provide HIV medication and should be reviewed. The NYSDOH Guidelines recommend that PEP should be initiated ideally within 2 hours, and should be offered even while the initial evaluation is ongoing. [6,7] Beyond 36 hours of suspected exposure, decisions should be made on a case-by-case basis, taking into account that the timing of ARV initiation may affect the efficacy of this intervention. Despite these timing recommendations, the NYSDOH Guidelines state that an absolute time after which PEP should not be administered cannot be stated with any certainty. [6,7] Additional information on the rationale for PEP, timing, and types of exposures can be found in both guidelines. [6,7]

An important aspect of providing PEP is which regimen to select. In July 2012, the NYSDOH Guidelines changed their preferred regimen for occupational PEP from zidovudine + lamivudine + tenofovir to an INSTI-based regimen, raltegravir + tenofovir/emtricitabine. [6] In 2013, the NYSDOH Guidelines for non-occupational PEP were also changed to this regimen. [7] The rationale for the updated guideline was the favorable side effect profile and fewer potential drug interactions with an INSTI-based regimen.

<table>
<thead>
<tr>
<th>Class of Regimen</th>
<th>Preferred Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etravirine</td>
<td>Do not coadminister with dolutegravir unless patient is also on atazanavir/ritonavir, darunavir/ritonavir or tipranavir/ritonavir.</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>Increase dolutegravir to 50mg twice daily in treatment-naive, treatment-experienced, or INSTI-naive patients.</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>Do not coadminister with dolutegravir.</td>
</tr>
<tr>
<td>Fosamprenavir/ritonavir, tipranavir/ritonavir</td>
<td>Increase dolutegravir to 50mg twice daily in treatment-naive, treatment-experienced, or INSTI-naive patients. Consider alternatives to rifampin if INSTI resistance suspected.</td>
</tr>
<tr>
<td>Oxcarbazepine, phenytoin, phenobarbital, carbamazepine</td>
<td>Do not coadminister with dolutegravir.</td>
</tr>
<tr>
<td>Antacids/laxatives (cation-containing), sucralfate, oral iron supplements, oral calcium supplements, buffered medications</td>
<td>Dolutegravir should be administered 2 hours before or 6 hours after taking medications containing polyvalent cations.</td>
</tr>
<tr>
<td>Metformin</td>
<td>Increased metformin concentrations may occur. Dose adjustment of metformin may be required.</td>
</tr>
<tr>
<td>Rifampin</td>
<td>Increase dolutegravir to 50mg twice daily in treatment-naive, treatment-experienced, or INSTI-naive patients. Consider alternatives to rifampin if INSTI resistance suspected.</td>
</tr>
</tbody>
</table>

Dolutegravir Drug Interactions
Conclusion

The role of FDA-approved INSTIs has expanded with the updated DHHS Guidelines now recommending all three available INSTIs as preferred regimens. [4,5] The role of raltegravir has also expanded since the NYSDOH and USPHS Guidelines have changed to include this medication in current PEP regimens. [6-8] Raltegravir remains a preferred INSTI on DHHS Guidelines because of extensive clinical trial data and durable potency. Elvitegravir is combined in a single-tablet regimen that needs to be given with food. Because this regimen also includes cobicistat, it has increased potential for drug interactions. Dolutegravir, the most recent INSTI, can be given once or twice daily and has been shown to be superior to preferred efavirenz-based and darunavir/ritonavir- based regimens. An STR with dolutegravir and abacavir/lamivudine is in development. [23]
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EVALUATION

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| 1. Program goal: To enable the learner to have the most recent information about Integrase Strand Transfer Inhibitors in HIV Care. | STRONGLY\
| | AGREE | DISAGREE | STRONGLY DISAGREE |
| | | | |
| 2. The knowledge and/or skills gained through this module are directly applicable to my profession. | | | |
| 3. Overall I was satisfied with this module. | | | |
| 4. As a result of attending this learning activity I am able to achieve the following objectives: | A. Discuss recent changes regarding the use of integrase inhibitors in treatment-naïve patients, as stated in the Department of Health and Human Services Guidelines. | | |
| | B. Describe the role of raltegravir, elvitegravir, and dolutegravir in the management of HIV treatment-naïve subjects. | | |
| | C. List common side effects and potential drug interactions associated with raltegravir, elvitegravir, and dolutegravir. | | |
| | D. Review the role of integrase inhibitors for the management of post-exposure prophylaxis. | | |
| 5. The objectives of this learning activity were relevant to the overall goal(s) of the program. | | | |
| 6. The author was effective for this learning activity. John J. Faragon, PharmD, BCPS, AAHIV-P | | | |
| 7. There was no commercial bias in this learning activity. | | | |
| 8. The author identified any off-label (non-approved) use of FDA-approved drugs or devices. | | | |

Additional Comments:

Please proceed to the next page and complete the self-assessment test.
1. Which of the following is a preferred first line regimen for a newly-diagnosed HIV infected patient based upon the most recent version of the DHHS Guidelines?
   A. Lopinavir/ritonavir with zidovudine/lamivudine
   B. Atazanavir/ritonavir with abacavir/emtricitabine
   C. Raltegravir/ritonavir with tenofovir/emtricitabine
   D. Dolutegravir with abacavir/lamivudine (assuming negative HLA b5701)

2. Which of the following is true regarding integrase inhibitor-based regimens according to clinical trials in treatment-naïve subjects?
   A. Raltegravir should only be given once daily.
   B. Elvitegravir/cobicistat/tenofovir/emtricitabine performed similarly to efavirenz/tenofovir/emtricitabine.
   C. Dolutegravir-based regimens (including either tenofovir/emtricitabine or abacavir/lamivudine) proved to be superior to efavirenz and darunavir/ritonavir-based regimen.
   D. All of the above are true.

3. Which of the following is true regarding cobicistat (contained in Stribild®) as it relates to drug interactions?
   A. Cobicistat has a list of contraindicated concurrent medications similar to maraviroc.
   B. Cobicistat is likely to decrease simvastatin levels.
   C. Cobicistat should not be used combined with ergotamine derivatives.
   D. None of the above

4. According to recent New York State Department of Health Guidelines, which of the following would be an appropriate regimen for a needlestick injury, assuming that an HIV specialist has decided that therapy should be initiated?
   A. Tenofovir + lamivudine + zidovudine
   B. Tenofovir + emtricitabine + raltegravir
   C. Darunavir + emtricitabine + dolutegravir
   D. Elvitegravir + darunavir + tenofovir

PLEASE PROCEED TO THE NEXT PAGE AND COMPLETE THE HRSA PARTICIPANT INFORMATION FORM
HRSA AIDS Education and Training Centers
PARTICIPANT INFORMATION FORM

To create your unique ID number, use the month of your birth, the day of your birth, and the last four digits of your social security number. For example, May 29, 123-45-6789 has the ID number 05296789.

Unique ID Number

Please completely fill in the circles (○) when answering the questions.

3. Your Primary Profession/Discipline (Select one)
   ○ 1. Dentist
   ○ 2. Other Dental Professional
   ○ 3. Advanced Practice Nurse
   ○ 4. Nurse
   ○ 5. Pharmacist
   ○ 6. Physician
   ○ 7. Physician Assistant
   ○ 8. Clergy/Faith-Based Professional
   ○ 9. Dietitian/Nutritionist
   ○ 10. Health Educator
   ○ 11. Mental/Behavioral Health Professional
   ○ 12. Other Public Health Professional
   ○ 13. Social Worker
   ○ 14. Substance Abuse Professional
   ○ 15. Community Health Worker
   ○ 16. Other Non-Professional (specify): _______________________________

4. Your Primary Functional Role (Select one)
   ○ 1. Administrator
   ○ 2. Agency Board Member
   ○ 3. Care Provider/Practitioner
   ○ 4. Case Manager
   ○ 5. Client/Patient Educator
   ○ 6. Clinical/Medical Assistant
   ○ 7. Intern/Resident
   ○ 8. Researcher/Evaluator
   ○ 9. Student/Graduate Student
   ○ 10. Teacher/Faculty
   ○ 11. Other (specify): _______________________________

5. Your Principal Employment Setting (Select one)
   ○ 1. Academic Health Center
   ○ 2. Community Health Center
   ○ 3. Family Planning Clinic
   ○ 4. STD Clinic
   ○ 5. HMO/Managed Care Organization
   ○ 6. Hospital-Based Clinic
   ○ 7. Hospital/ER
   ○ 8. Indian Health Services/Tribal Clinic
   ○ 9. Infectious Disease Clinic
   ○ 10. Long-Term Nursing Facility
   ○ 11. Maternal/Child Health Clinic
   ○ 12. Mental/Behavioral Health Clinic
   ○ 13. Rural Health Clinic
   ○ 14. Sexually Transmitted Disease Clinic
   ○ 15. Substance Abuse Treatment Center
   ○ 16. College/University
   ○ 17. Community-Based Organization
   ○ 18. Community/Retail Pharmacy
   ○ 19. Correctional Facility
   ○ 20. Military/VA
   ○ 21. Private Practice
   ○ 22. State/Local Health Department
   ○ 23. Non-Health
   ○ 24. Other Primary Care
   ○ 25. Not Working (skip to Q. #9)

6a. Primary Employment Setting
   ○ Rural ○ Suburban-Urban

6b. Zip Code

7. Is the employment setting a faith-based organization?
   ○ Yes ○ No ○ Don’t Know

8a. Does the employment setting receive Ryan White Program Funding?
   ○ Yes (skip to Q9) ○ No (skip to Q9) ○ Don’t Know (go to Q9b)

8b. If No, please write full name of your agency:

NOTE: Please answer BOTH Question 9 about Hispanic origin and Question 10 about race.

9. Are you of Hispanic, Latin, or Spanish origin?
   ○ Yes ○ No

10. What is your racial background? (Select all that apply)
    ○ American Indian or Alaska Native
    ○ Asian
    ○ Black or African American
    ○ Native Hawaiian or Other Pacific Islander
    ○ White

11. What is your gender?
    ○ Female
    ○ Male
    ○ Transgender

12a. Do you provide services directly to clients/patients?
    ○ Yes ○ No [Stop here. You are done with this form.]

12b. Please estimate the PERCENTAGE of your OVERALL CLIENT/PATIENT population in the past YEAR who were racial-ethnic minorities:
    ○ None/yr. 1-24%/yr. 25-49%/yr. 50-74%/yr. ≥75%/yr.

13. Do you provide services directly to HIV-infected clients/patients?
   ○ Yes ○ No/Don’t know
   (Stop here. You are done with this form.)

14. How many YEARS have you been providing services directly to HIV-infected clients/patients?
   ○ (Round up to the nearest whole year.)

15. Estimate the NUMBER of HIV-infected clients/patients to whom you provide direct services in an average MONTH
   ○ None/yr. 1-9/yr. 10-19/yr. 20-49/yr. 50+/yr.

For questions 16 through 19, estimate the PERCENTAGE of your HIV-infected clients/patients in the past YEAR who were:

16. HIV+ who are racial-ethnic minorities
    None/yr. 1-24%/yr. 25-49%/yr. 50-74%/yr. ≥75%/yr.

17. HIV+ who are co-infected with Hepatitis C
    None/yr. 1-24%/yr. 25-49%/yr. 50-74%/yr. ≥75%/yr.

18. HIV+ who are receiving antiretroviral therapy
    None/yr. 1-24%/yr. 25-49%/yr. 50-74%/yr. ≥75%/yr.

19. HIV+ who are women
    None/yr. 1-24%/yr. 25-49%/yr. 50-74%/yr. ≥75%/yr.