Optimizing the use of Integrase inhibitors in practice

Ghassan Wali, MD

Infectious Disease Consultant - HIV / AIDS
King Faisal Specialist Hospital And Research Center Jeddah
University of British Columbia
Objectives

- Review the use of INSTIs for one of our HIV naïve patients.

- How to fit the INSTI into a patient’s regimen when switching a virologically suppressed patient.

- Managing the potential toxicities of the current INSTIs.

- Two vs. three drugs: promising new options

- Options for the treatment experienced patients
Clinical vignette

- 40 years MSM presents with fever and sore throat and generalized body rash for 1 week. Recent new sexual partner.
- No other medical conditions. Exam normal.
- HIV Ab/Ag positive; HIV differentiation Ab positive
- HIV RNA 500k copies/ml
- CD4 cell count 180
- Creatinine 60
- genotype pending; HLA-B5701 pending.
Case#1

- He says he’s willing to start treatment. What do you start?

A. Dolutegravir + lamivudine
B. Elvitegravir/cobi + FTC/tenofovir AF
C. Dolutegravir + TAF/FTC
D. Darunavir/cobi /+ FTC/tenofovir AF
E. Dolutegravir + abacavir/lamuvidine
DHHS, IAS-USA Guidelines: Recommended Regimens for First-line ART in Most Patients With HIV Infection

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>INSTI</td>
<td>▪ BIC/FTC/TAF*</td>
<td>▪ BIC/FTC/TAF*</td>
</tr>
<tr>
<td></td>
<td>▪ DTG/ABC/3TC*</td>
<td>▪ DTG/ABC/3TC*</td>
</tr>
<tr>
<td></td>
<td>▪ DTG + FTC/(TAF or TDF)</td>
<td>▪ DTG + FTC/TAF</td>
</tr>
<tr>
<td></td>
<td>▪ RAL + FTC/(TAF or TDF)</td>
<td></td>
</tr>
</tbody>
</table>
Recommendations basis

- baseline HIV-1 RNA, CD4+ cell count
- CrCl, eGFR
- HLA-B*5701 status
- HBsAg status,
- osteoporosis status
- pregnancy status
- No pharmacologic-boosting agent
# Summary of the Anti-Retroviral Treatment in HIV positive naïve patients in Saudi Arabia

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Preferred treatment</th>
<th>Alternative treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Integrate Inhibitors</strong></td>
<td>TAF / FTC / ELV / C ABC / 3TC / DTG TAF / FTC / BIC TAF / FTC + DTG ABC / 3TC + DTG TAF / FTC + RAL TDF / FTC + DTG TDF / FTC + RAL</td>
<td>TAF / FTC ABC / 3TC + RAL</td>
<td>- Negative HLA B57/K1 prior to ABC &amp; ABC containing regimen's use. - Aged 3TC use in HIV/HBV infection. - TDF is preferred over TAF in HIV/TB on Rifampicin.</td>
</tr>
<tr>
<td><strong>Boosted Protease Inhibitors</strong></td>
<td>TAF / FTC + DRV / C TDF / FTC + DRV / C ABC / 3TC + DRV / C TAF / FTC + ATV / R</td>
<td>TAF / FTC + DRV / R TDF / FTC + DRV / R ABC / 3TC + DRV / C TAF / FTC + ATV / R</td>
<td>Not recommended in HIV/TB co-infection on Rifampicin</td>
</tr>
<tr>
<td><strong>NNRTI</strong></td>
<td>TAF / FTC / RPV TDF / FTC / RPV</td>
<td></td>
<td>Not recommended if HIV Viral load ≥ 100,000 copies/ml and/or CD4 count &lt; 200 cells/μL</td>
</tr>
</tbody>
</table>
## Choosing Among Integrase Inhibitors for First-line Therapy

<table>
<thead>
<tr>
<th>Agent</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
</table>
| **Bictegravir** | ▪ STR once daily with FTC/TAF  
▪ Few drug or food interactions  
▪ High barrier to resistance | ▪ Least amount of data  
▪ Only available as an STR  
▪ No safety data in pregnancy |
| **Dolutegravir** | ▪ Single agent (eg, with FTC/TAF or FTC/TDF)  
▪ STR once daily with 3TC or ABC/3TC  
▪ Few drug or food interactions  
▪ High barrier to resistance  
▪ A preferred option in pregnancy guidelines during second and third trimester | ▪ Increases metformin levels  
▪ Recent concerns regarding conception/early pregnancy safety |
| **Elvitegravir** | ▪ STR once daily with COBI plus FTC/TAF                                    | ▪ Numerous drug–drug interactions  
▪ Do not use during pregnancy |
| **Raltegravir**  | ▪ Longest experience  
▪ Few drug or food interactions  
▪ A preferred option in pregnancy guidelines | ▪ Multiple pills  
▪ No STR  
▪ Limited safety data at conception |
Studies of Recommended INSTIs as First-line ART Regimens

<table>
<thead>
<tr>
<th>Trial</th>
<th>INSTI Regimen</th>
<th>Comparator</th>
<th>Wks</th>
<th>Outcome vs Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>GS-1489[1]</td>
<td>BIC/FTC/TAF</td>
<td>DTG/ABC/3TC</td>
<td>96</td>
<td>Noninferior</td>
</tr>
<tr>
<td>SINGLE[3]</td>
<td>DTG + ABC/3TC</td>
<td>EFV/FTC/TDF</td>
<td>144</td>
<td>Favors INSTI</td>
</tr>
<tr>
<td>FLAMINGO[4]</td>
<td>DTG + 2 NRTIs</td>
<td>DRV + RTV + 2 NRTIs</td>
<td>96</td>
<td>Favors INSTI</td>
</tr>
<tr>
<td>SPRING-2[5]</td>
<td>DTG + 2 NRTIs</td>
<td>RAL + 2 NRTIs</td>
<td>96</td>
<td>Noninferior</td>
</tr>
<tr>
<td>ARIA[6]</td>
<td>DTG/ABC/3TC</td>
<td>ATV + RTV + FTC/TDF</td>
<td>48</td>
<td>Favors INSTI</td>
</tr>
<tr>
<td>ACTG A5257[7]</td>
<td>RAL + FTC/TDF</td>
<td>ATV or DRV + RTV + FTC/TDF</td>
<td>96</td>
<td>Favors INSTI*</td>
</tr>
<tr>
<td>STARTMRK[8]</td>
<td>RAL + FTC/TDF</td>
<td>EFV + FTC/TDF</td>
<td>240</td>
<td>Favors INSTI</td>
</tr>
</tbody>
</table>
GEMINI-1 and -2: DTG + 3TC in ART-Naive Adults

- Parallel, international, randomized, double-blind phase III noninferiority studies
- Secondary endpoints at Wk 96: HIV-1 RNA < 50 copies/mL (FDA Snapshot and TRDF analyses); AEs; resistance; changes from BL in bone, renal, and lipid parameters

**Stratified by HIV-1 RNA (≤ vs > 100,000 copies/mL), CD4+ cell count (≤ vs > 200 cells/mm³)**

ART-naive adults with HIV-1 RNA 1000-500,000 copies/mL, ≤ 10 days on previous ART, no major RT or PI resistance mutations, no HBV infection or HCV requiring therapy (N = 1433)

Screening within 28 days of study start; studies double-blinded until Wk 96, open-label until Wk 144.

GEMINI-1 and -2: Virologic Response

- DTG + 3TC met criteria for noninferior efficacy vs DTG + FTC/TDF at Wk 96
- No treatment-emergent resistance observed in patients with CVW

**Table:**

<table>
<thead>
<tr>
<th>Endpoint, % (n)</th>
<th>DTG + 3TC (n = 716)</th>
<th>DTG + FTC/TDF (n = 717)</th>
<th>Difference, * % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responders</td>
<td>86.0 (616)</td>
<td>89.5 (642)</td>
<td>-3.4 (-6.7 to 0)</td>
</tr>
</tbody>
</table>

*Adjusted for BL HIV-1 RNA, BL CD4+ cell count, and study.

Cahn. IAS 2019. Abstr WEAB0404LB.
Do we still have to use Boosted PIs?

Pros
▪ before availability of resistance data
▪ Patients with poor adherence

Cons
▪ Drug–drug interactions
▪ GI intolerance
▪ Hyperlipidemia
▪ CV risk with some PIs

### Do we still have to use NNRTIs?

**Pros**
- Adverse events of INSTIs
- In women desiring pregnancy
- If pt experiencing weight gain with INSTIs

**Cons**
- Low barrier to resistance at VF with EFV, RPV
- Neuropsychiatric AEs with EFV
- Higher rates of VF in RPV patients with HIV-1 RNA > 100,000 copies/mL and CD4+ cell counts < 200 cells/mm³
- RPV must be taken with a meal
- Fixed-dose combination with DOR includes TDF not TAF
- Lipid increases with EFV

---

Case#1

- He says he’s willing to start treatment. What do you start?

A. Dolutegravir + lamivudine
B. Elvitegravir/cobi + FTC/tenofovir AF
C. Dolutegravir + TAF/FTC
D. Darunavir/cobi + FTC/tenofovir AF
E. Dolutegravir + abacavir/lamuvudine
Case#2: managing INSTI toxicities and potential drug interactions

- 50 year old male with long standing HIV is taking DTG, ABC, 3TC.
- He remain virologically suppressed on this regimen for 3 years.
- He is complaining of tremendous weight gain (9 kilos) that’s uncontrolled with diet and lifestyle modifications.
- He has vitamin D deficiency, GERD and osteopenia.
- His HBA1C is 8; he gets started on metformin.
- He wants to change his regimen but demands one pill, do you agree?
Liverpool HIV iChart

Providing summary data of HIV drug interactions. Full details available at www.hiv-druginteractions.org

Search For Drug Interactions

Sponsors  Privacy  Disclaimer
Potential Interaction

Dolutegravir

Metformin

Quality of evidence: Low

Coadministration of metformin (500 mg twice daily) was studied with dolutegravir (50 mg once or twice daily) in 15 subjects. Coadministration with once daily dolutegravir increased metformin Cmax and AUC by 66% and 79%, whereas coadministration with twice daily dolutegravir increased metformin Cmax and AUC by 111% and 145%. A dose adjustment of metformin should be considered when

Quality of evidence: Moderate

Simultaneous coadministration of calcium carbonate (1200 mg) and dolutegravir (50 mg single dose) to fasting subjects decreased dolutegravir Cmax, AUC and Cmin by 37%, 39% and 39%, respectively. Simultaneous coadministration to fed subjects increased dolutegravir Cmax, AUC and Cmin by 7%, 9% and 8%, respectively. Coadministration of calcium carbonate 2 h
NAMSAL and ADVANCE: Study Design

- Multicenter, randomized, open-label phase III trials\(^{1-3}\)

NAMSAL - Cameroon
ART-naive adults with HIV-1 RNA > 1000 c/mL (N = 613)

ADVANCE - South Africa
ART-naive patients (≥ 12 yrs) with HIV-1 RNA ≥ 500 c/mL (N = 1053)

Primary Endpoint (Both Trials)
HIV-1 RNA < 50 c/mL at Wk 48 by FDA Snapshot in ITT population (noninferiority margin: -10%)\(^{4,5}\)

## NAMSAL and ADVANCE: Progressive Weight Gain and Clinical Obesity

<table>
<thead>
<tr>
<th>Outcome</th>
<th>NAMSAL</th>
<th>ADVANCE</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean Δ in weight, kg</strong></td>
<td>DTG + 3TC/TDF (n = 293)</td>
<td>EFV + 3TC/TDF (n = 278)</td>
<td>P Value</td>
</tr>
<tr>
<td>Wk 48</td>
<td>+5 NA</td>
<td>+3 NA</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Wk 96</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td><strong>Mean Δ in BMI at Wk 48</strong></td>
<td>+1.7</td>
<td>+1.2</td>
<td>&lt; .001</td>
</tr>
<tr>
<td><strong>Treatment-emergent overweight (BMI 25-29.9), %</strong></td>
<td>16 NA</td>
<td>17 NA</td>
<td>NS</td>
</tr>
<tr>
<td>Wk 48</td>
<td>16 NA</td>
<td>17 NA</td>
<td>NS</td>
</tr>
<tr>
<td>Wk 96</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td><strong>Treatment-emergent obesity (BMI ≥ 30), %</strong></td>
<td>12 NA</td>
<td>5 NA</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>Wk 48</td>
<td>12 NA</td>
<td>5 NA</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>Wk 96</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

Hill. IAS 2019. Abstr MOAX0102LB.
## Switching From Suppressive ART to an STR: Key Studies With Contemporary Regimens

- Noninferior efficacy for all switch regimens vs baseline regimen; all FDA approved to treat virologically suppressed patients

<table>
<thead>
<tr>
<th>Key Studies</th>
<th>Switch From</th>
<th>Switch to</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWORD 1 &amp; 2[^4^]</td>
<td>Third agent + 2 NRTIs</td>
<td>DTG/RPV</td>
</tr>
<tr>
<td>STRIIVING[^5^]</td>
<td>Third agent + 2 NRTIs</td>
<td>DTG/ABC/3TC</td>
</tr>
</tbody>
</table>

Most recent FDA approvals: for BIC/FTC/TAF and DTG/RPV, must have no history of treatment failure and no resistance to regimen components; for DRV/COBI/FTC/TAF, must have no resistance to DRV, TDF.

SWORD-1 and -2: Switch to DTG + RPV vs Continuation of Baseline ART in Virologically Suppressed Adults

- Parallel, randomized, open-label, multicenter phase III noninferiority studies[^1,^2]

**Early Switch Phase**

**Primary Endpoint**

- Switch to DTG + RPV (n = 513)
- Continue Baseline ART (n = 511)

**Late Switch Phase**

**Current Analysis**

- Wk 48: Switch to DTG + RPV
- Wk 52: Continue DTG + RPV
- Wk 100: Continue DTG + RPV
- Wk 148: Switch to DTG + RPV

**Virologic Response With DTG + RPV by FDA Snapshot**

- (HIV-1 RNA < 50 copies/mL at Wk 100)
  - 89%
  - 93%

**Adults on stable ART** (INSTI, NNRTI, or PI + 2 NRTIs) with HIV-1 RNA < 50 copies/mL for ≥ 6 mos at screening; no previous VF or current HBV infection; no resistance to DTG or RPV (N = 1024)

**Primary endpoint:** HIV-1 RNA < 50 copies/mL maintained in 95% of patients in each arm at Wk 48; adjusted treatment difference: -0.2% (95% CI: -3.0 to 2.5)[^2]

**SWORD-1 and -2: Resistance**

- 10/990 (1%) confirmed virologic withdrawals through Wk 100
  - Treatment-emergent NNRTI resistance mutations documented in 3/10, all from early switch arm*

<table>
<thead>
<tr>
<th>Time of Failure</th>
<th>Previous Regimen</th>
<th>Mutations at Baseline</th>
<th>Mutations at Confirmed Virologic Withdrawal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wk 36</td>
<td>EFV/TDF/FTC</td>
<td>None</td>
<td>K101K/E</td>
</tr>
<tr>
<td>Wk 88</td>
<td>DTG/ABC/3TC</td>
<td>None</td>
<td>E138E/A</td>
</tr>
<tr>
<td>Wk 100</td>
<td>EFV/TDF/FTC</td>
<td>K101E, E138A</td>
<td>K101E, E138A, M230M/L Assay failure</td>
</tr>
</tbody>
</table>

*For these 3 patients, HIV-1 RNA at last measurement: < 50 copies/mL, 55 copies/mL, 300 copies/mL, respectively.
TANGO: Switch to DTG/3TC vs Continuing TAF-Based 3-Drug Regimen

- International, randomized, open-label phase III noninferiority study

**Primary Analysis**

- Wk 48
- Wk 148
- Wk 196

Stratified by BL 3rd agent class

- Switch to DTG/3TC (n = 369)
- Continue TAF-Based Regimen (n = 372)
- DTG/3TC

Continuation of DTG/3TC permitted

Adults with HIV-1 RNA < 50 c/mL for > 6 mos on stable TAF-based ART*; no prior VF, NRTI or INSTI resistance, HBV infection or HCV requiring tx (N = 741)

*Initial regimen of FTC/TAF + PI, NNRTI, or INSTI, or TDF switched to TAF ≥ 3 mos prior to screening with no other regimen changes.

- Primary endpoint: virologic failure at Wk 48 by FDA Snapshot analysis (ITT-E)
  - Noninferiority margin: 4%

- Secondary endpoint: safety

TANGO: Virologic Outcomes by FDA Snapshot at Wk 48

- No CVW in DTG/3TC arm, CVW in 1 (< 1%) patient in TAF-based ART arm; no resistance detected at failure
- All 7 patients (4 in DTG/3TC group, 3 in TAF-based ART group) with proviral M184V/I mutation at baseline maintained HIV-1 RNA < 50 c/mL at Wk 48

Primary Endpoint (HIV-1 RNA ≥ 50 c/mL)
DTG/3TC noninferior to continued TAF-based ART

4% NI margin

Key Secondary Endpoint (HIV-1 RNA < 50 c/mL)
DTG/3TC noninferior to continued TAF-based ART

*Adjusted for baseline third agent class.
Case#3

- Present history: DM, GERD and hyperlipidemia
- HIV history:
  - Diagnosed in 1994 (after blood transfusion)
  - Started on ART in 1999: saquinavir, 3TC and AZT
  - Nadir CD4: 60, currently ranges from 400-550
  - Viral load ranges from 5000-22000 c/ml
  - Because he never had a suppressed virus he received multiple regimens
## Continue case presentation

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRTI</td>
<td>DDI, D4T, AZT, and tenovir</td>
</tr>
<tr>
<td>NNRTI</td>
<td>Efavirenz</td>
</tr>
<tr>
<td>PI</td>
<td>Saquinavir, Nelfinavir, Indinavir, Lopinavir/ritonavir, Darunavir</td>
</tr>
<tr>
<td>INSTI</td>
<td>Raltegravir</td>
</tr>
</tbody>
</table>
HIV-1 Genotypic Drug Resistance, P

<table>
<thead>
<tr>
<th>Drug</th>
<th>Genotype/Resist</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine</td>
<td>PR</td>
<td></td>
</tr>
<tr>
<td>Test Note: L74V, K103N, V108I, V118I, V179E, M184V, T215Y mutations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Didanosine</td>
<td>RESIST</td>
<td></td>
</tr>
<tr>
<td>Test Note: L74V mutation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamivudine</td>
<td>RESIST</td>
<td></td>
</tr>
<tr>
<td>Test Note: M184V mutation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emtricitabine</td>
<td>RESIST</td>
<td></td>
</tr>
<tr>
<td>Test Note: M184V mutation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stavudine</td>
<td>PR</td>
<td></td>
</tr>
<tr>
<td>Test Note: M184V, T215Y mutations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abacavir</td>
<td>RESIST</td>
<td></td>
</tr>
<tr>
<td>Test Note: L74V, M184V, T215Y mutations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir</td>
<td>SUSC</td>
<td></td>
</tr>
<tr>
<td>Nevirapine</td>
<td>RESIST</td>
<td></td>
</tr>
<tr>
<td>Test Note: K103N, V108I, V179E mutations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Efavirenz</td>
<td>RESIST</td>
<td></td>
</tr>
<tr>
<td>Test Note: K103N, V108I, V179E mutations</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Protease Mutations

<table>
<thead>
<tr>
<th>Drug</th>
<th>Genotype/Resist</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saquinavir with Ritonavir</td>
<td>SUSC</td>
<td></td>
</tr>
<tr>
<td>Indinavir</td>
<td>RESIST</td>
<td></td>
</tr>
<tr>
<td>Test Note: M46I mutation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indinavir with Ritonavir</td>
<td>PR</td>
<td></td>
</tr>
<tr>
<td>Test Note: M46I mutation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>PR</td>
<td></td>
</tr>
<tr>
<td>Test Note: M36I, M46I, I54V mutations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fosamprenavir</td>
<td>RESIST</td>
<td></td>
</tr>
<tr>
<td>Test Note: M46I, I54V mutations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fosamprenavir with Ritonavir</td>
<td>PR</td>
<td></td>
</tr>
<tr>
<td>Test Note: M46I, I54V mutations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>洛潘奈韦与司他夫定</td>
<td>PR</td>
<td></td>
</tr>
<tr>
<td>Test Note: K43T, M46I, I54V, L63P, L89M mutations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atazanavir</td>
<td>PR</td>
<td></td>
</tr>
<tr>
<td>Test Note: K20I, M36I, M46I, I54V mutations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atazanavir with Ritonavir</td>
<td>PR</td>
<td></td>
</tr>
<tr>
<td>Test Note: M36I, M46I, I54V mutations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tipranavir with Ritonavir</td>
<td>PR</td>
<td></td>
</tr>
<tr>
<td>Test Note: I13V, M36I, K43T, I54V, M69K mutations</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Testing was done by DNA sequencing method (Trugene HIV-1 Genotyping Kit: Bayer Healthcare LLC), and results were
**Goal:** Fully suppressive ARV regimen

- If **susceptible** to boosted PI → regimen can be similar for those with first line failure.
- If **NOT** susceptible to boosted PI → new regimen should have a minimum of 2 (preferably 3) fully active drugs if possible.

  - Susceptibility to drug predicted from patient treatment history, prior and current resistance and tropism testing, MoA of novel drug class.

- Not recommended to add single agent to failing regimen due to risk of developing resistance to entire regimen.

DHHS : Management of ART Failure of second line ARV failure

DHHS guideline
VIKING-3: STUDY DESIGN (N=183)

Main eligibility criteria:
- HIV-1 RNA ≥500 c/mL
- Screening or documented historic evidence of resistance to RAL and/or EVG and resistance to ≥2 ART classes other than INIs

Functional monotherapy phase
- DTG 50 mg BID and continue falling ART regimen

Optimised phase
- DTG 50 mg BID + OBR with OSS ≥1

Screening visit - Day -35
Screening period up to a maximum of 42 days
Day 1
Day 8
Week 24 analysis
Week 48 analysis

OSS, overall susceptibility score, determined by Monogram Biosciences net assessment. 
Integrase inhibitors are the first line of choice for naïve patients, in absence of genotype testing choose DTG or BIC.

Certain 2-drug regimens appear to be as effective as 3-drug strategies, although long-term data are not yet available.

Switching for toxicities can be done with many safe options.

For treatment experienced patients, use 2 preferably 3 potent drugs.

As more our patients are living longer, the need for a durable regimen with minimal toxicity, high genetic barrier, non-booster single tablet is important.