



PRIMARY CARE MANAGEMENT OF HIV: WHY TLD FIRST?

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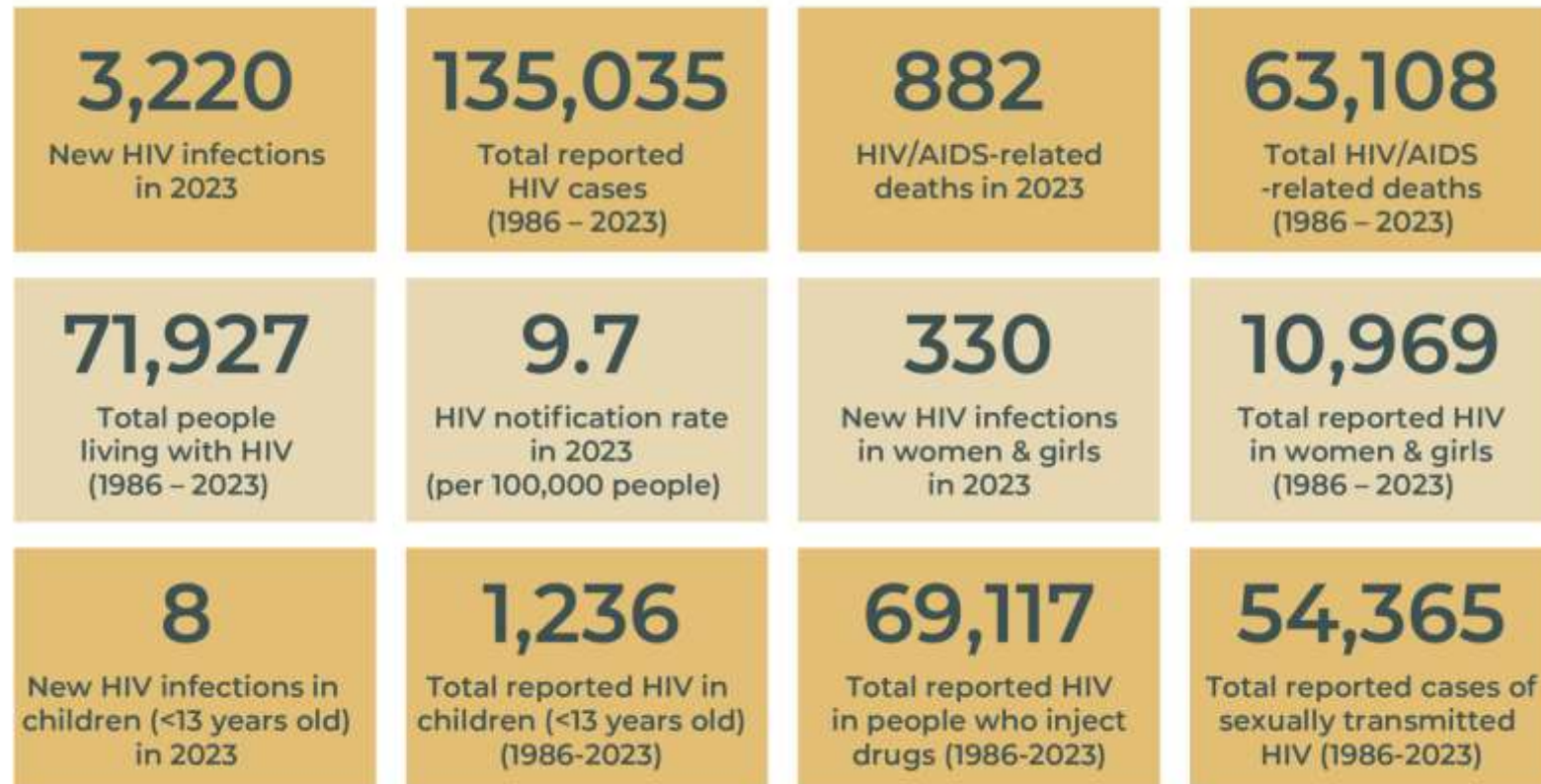
Infectious Disease Phys

Hospital Sultanah Aminah

CME series 2/26: 26/5/2



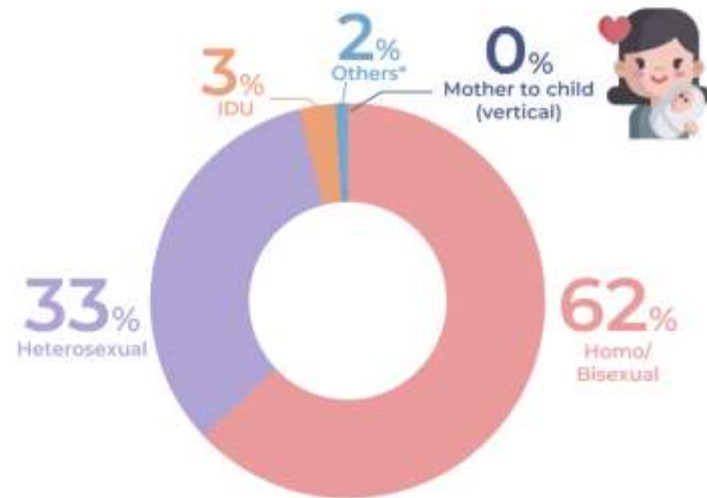
Overview of the HIV & AIDS Epidemic in Malaysia



HIV Transmission by Gender (1986-2023)



HIV Transmission by Risk Factor (2023)



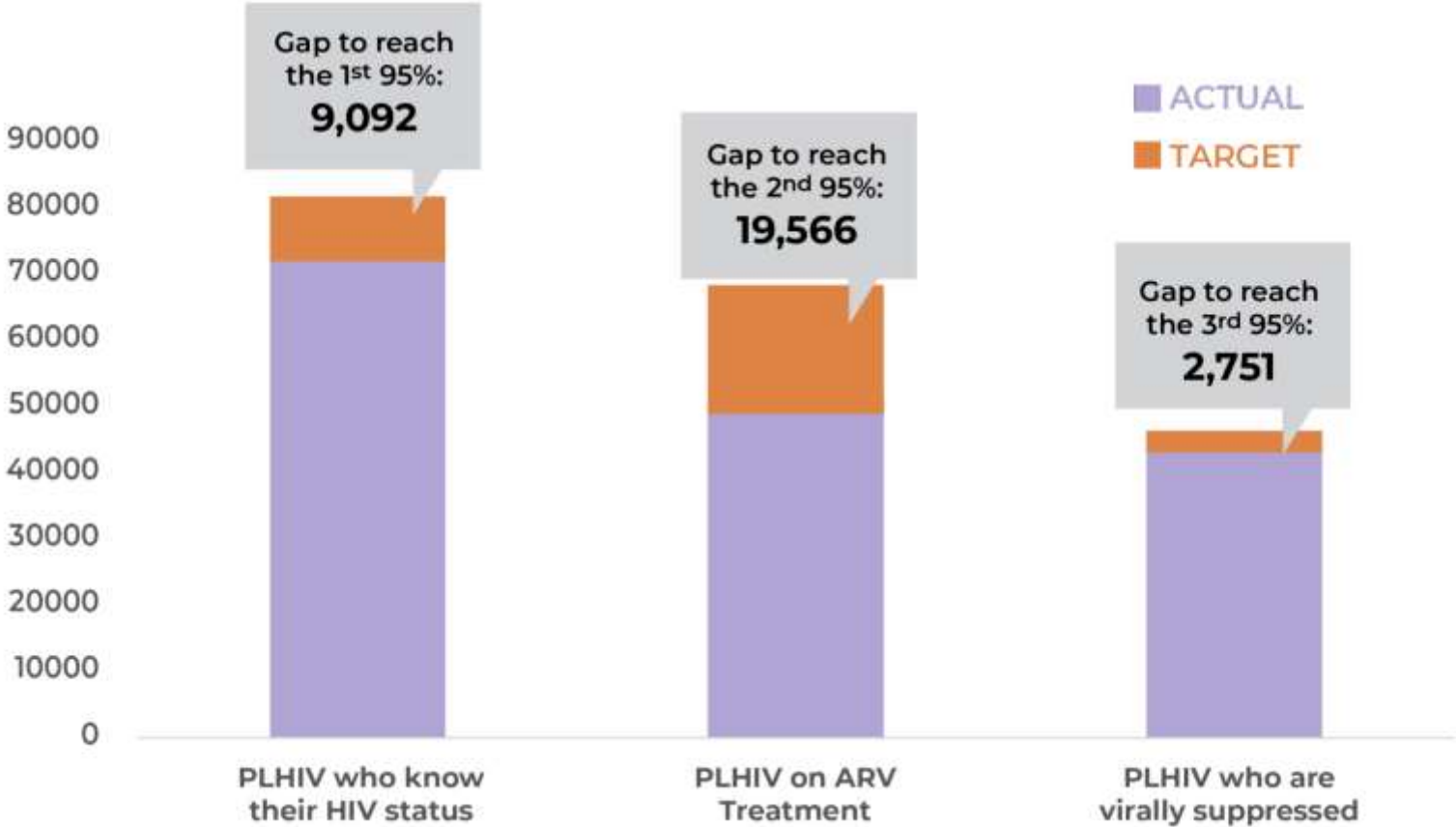
Source: HIV/STI Section, Division of Disease Control, Ministry of Health Malaysia

HIV Transmission by Age (2023)

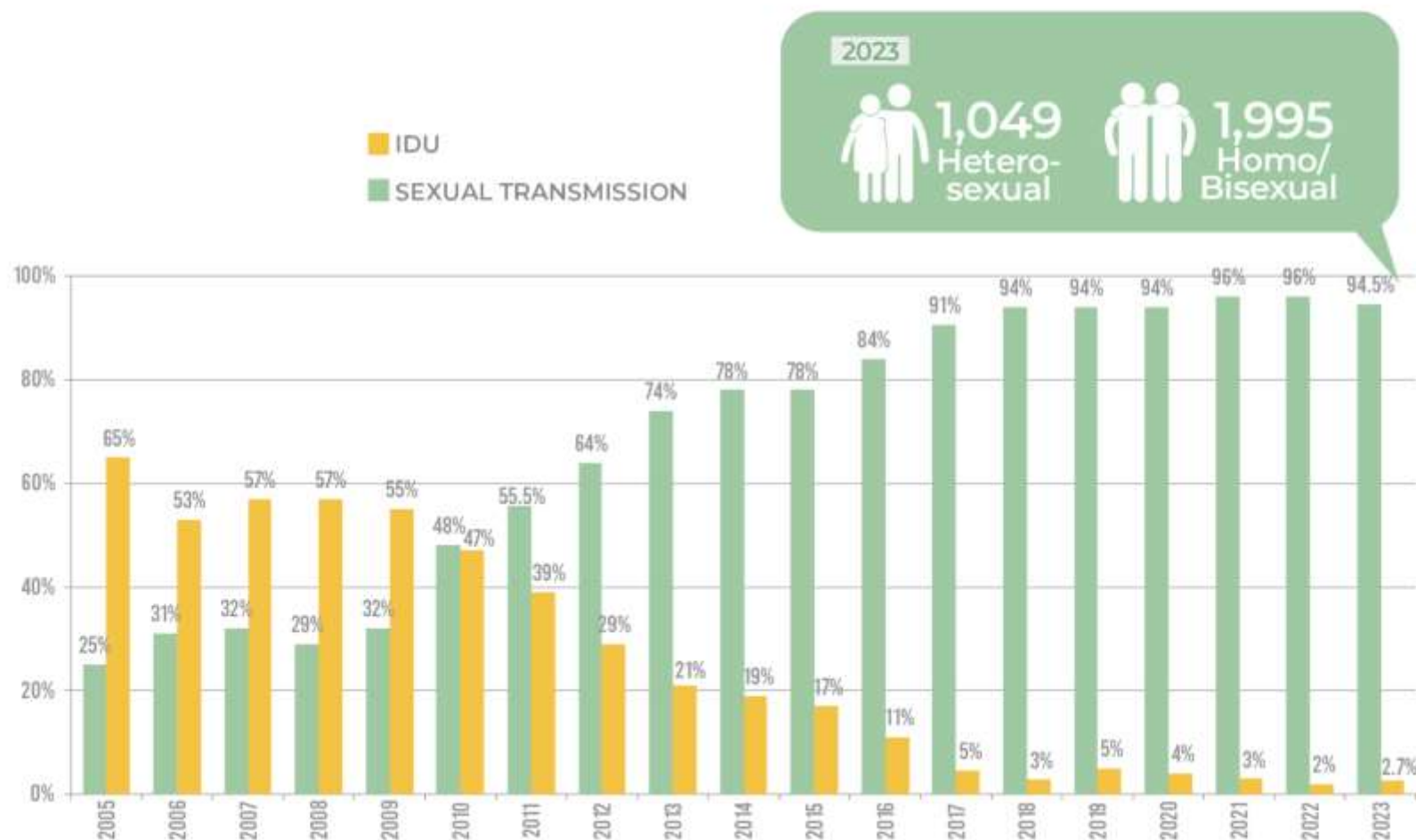


Source: HIV/STI Section, Division of Disease Control, Ministry of Health Malaysia

HIV Testing & Treatment Cascade (2023)



Comparison of New HIV Infections Between Injecting Drug Users (IDU) & Sexual Transmission (2005 - 2023)



Background of TLD as 1st line ART



In **2018**, WHO started to recommend dolutegravir (DTG)-containing regimens as the preferred first- and second-line ART regimens for PLHIV.

Table 1. Preferred and alternative first-line ART regimens

Population	Preferred first-line regimen	Alternative first-line regimen	Special circumstances
Adults and adolescents	TDF + 3TC (or FTC) + DTG ^a	TDF + 3TC + EFV 400 mg ^b	TDF + 3TC (or FTC) + EFV 600 mg ^b AZT + 3TC + EFV 600 mg ^b TDF + 3TC (or FTC) + PI/r ^b TDF + 3TC (or FTC) + RAL TAF ^c + 3TC (or FTC) + DTG ABC + 3TC + DTG ^a
Children	ABC + 3TC + DTG ^d	ABC + 3TC + LPV/r ABC + 3TC + RAL ^e TAF + 3TC (or FTC) + DTG ^f	ABC + 3TC + EFV (or NVP) AZT + 3TC + EFV ^g (or NVP) AZT + 3TC + LPV/r (or RAL)
Neonates	AZT + 3TC + RAL ^h	AZT + 3TC + NVP	AZT + 3TC + LPV/r ⁱ

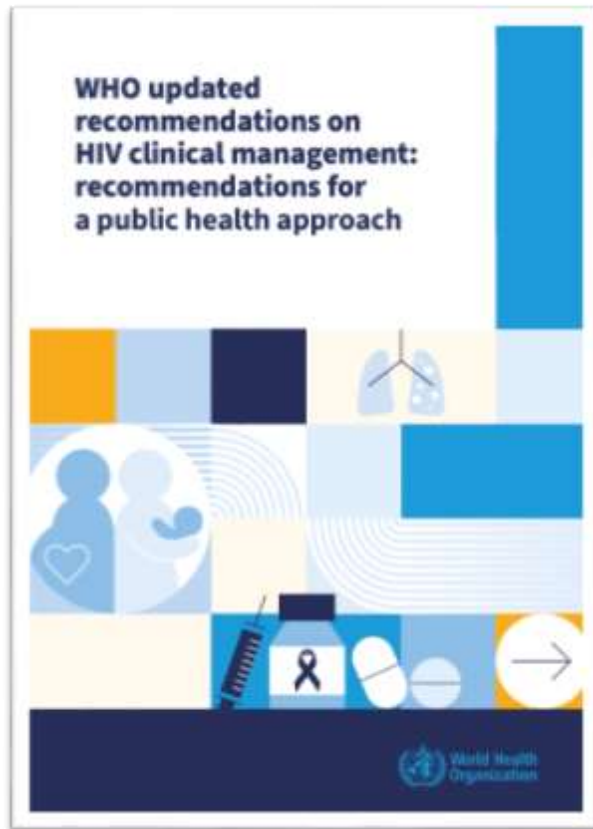


Table 3.2 Preferred and alternative initial regimens in adults, adolescents, children and neonates

Populations	Preferred initial regimen	Alternative initial regimen	Special circumstances
Adults and adolescents	TDF (or TAF) + 3TC (or FTC) + DTG	TDF + 3TC + EFV 400mg ^a	TDF (or TAF) + 3TC (or FTC) + EFV 600 mg ^a AZT + 3TC + EFV 600 mg ^a ABC + 3TC + DTG TDF (or TAF ^b) + 3TC (or FTC) + DRV/r (or ATV/r or LPV/r)
Children	ABC + 3TC + DTG	TAF + 3TC (or FTC) + DTG ABC + 3TC + DRV/r ^c (or ATV/r or LPV/r ^e)	ABC (or AZT) + 3TC + EFV ^d (or NVP) AZT + 3TC + DRV/r ^c (or ATV/r or LPV/r ^e)
Neonates	ABC + 3TC + DTG ^g	AZT + 3TC + NVP	AZT (or ABC) + 3TC + LPV/r ^f

- In **2025**, WHO updated guideline has included TAF as an alternative to TDF in 1st line ART



- As of June **2021**, 110 low to middle income countries have transitioned to DTG with an estimated 22 million people receiving DTG based ART.
- However, the relatively high cost of DTG presents a significant burden and hindrance for its wide usage in Malaysia.

Chronology of getting TLD as 1st line ART in KKM

2023	Perbincangan mengenai TLD, melibatkan pelbagai program dan bahagian di KKM, Medicine Patent Pool (MPP), UNAIDS, WHO, Third World Organisation, MAC
Jan-April 2024	• Mengkaji dan membuat analisa keperluan / justifikasi & implikasi kewangan rawatan TLD • Pengukuhan Rawatan dan Pencegahan HIV menggunakan ubat TLD sbg regimen utama
Mac 2024	Kelulusan daripada TKPK Kesihatan Awam
17 Mei 2024	Pembentangan dalam Mesyuarat Khas KPK Bil. 4/2024 Keputusan : bersetuju dengan kertas dasar yang dibentangkan dan seterusnya diangkat di peringkat Jawatankuasa Dasar dan Perancangan Kementerian Kesihatan (JDPKK).
27 Jun 2024	Mesyuarat Jawatankuasa Dasar Dan Perancangan Kementerian Kesihatan (JDPKK) Bil. 3/ 2024 Keputusan : bersetuju terhadap cadangan "Pengukuhan Rawatan dan Pencegahan HIV Menggunakan Ubat TLD Sebagai Regimen Utama" tetapi tertakluk kepada peruntukan sedia ada.

Chronology and Approval

KRONOLOGI & KELULUSAN

Sasaran	:	ODHA yang menerima rawatan ARV (sedia ada & baru) (2025 : 35,000 2026 : 39,087 2027 : 43,110)
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Tempat	:	Semua hospital dan klinik kesihatan yang memberikan rawatan ART
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Tempoh Masa	:	2025 – 2027 (untuk peralihan besar-besaran. Ini adalah bagi membolehkan negara mendapat harga yang terbaik iaitu USD15 – USD20 sebulan (RM 71.00 – RM 95.00 sebulan). Semakan semula akan dibuat untuk tempoh 2028 – 2030.
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Pelaksana	:	Pakar Perubatan Penyakit Berjangkit & Pakar Perubatan Keluarga
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KETUA PENGARAH KESIHATAN MALAYSIA
Kementerian Kesihatan Malaysia
Aras 12, Blok E7, Kompleks E
Pusat Pentadbiran Kerajaan Persekutuan
62590 PUTRAJAYA

Tel.: 03-8000 8000

Ruj. Kami : KKM.600-40/2/1 Jld. 2 (16)
Tarikh : 29 April 2026

SEPERTI SENARAI EDARAN

YBfg. Datuk Seri/ Dato' Sri/ Datuk/ Dato' Indera / Dato'/ Datin / Tuan / Puan,

SURAT PEKELILING KETUA PENGARAH KESIHATAN MALAYSIA
BIL. 14 / 2026 : PELAKSANAAN PERKHIDMATAN RAWATAN
TLD (TENOFVIR/ LAMIVUDINE/ DOLUTEGRAVIR) SEBAGAI REGIMEN
UTAMA BAGI RAWATAN HIV DI FASILITI KEMENTERIAN KESIHATAN
MALAYSIA (KKM).

1. TUJUAN

Surat pekeliling ini bertujuan untuk memaklumkan pelaksanaan perkhidmatan rawatan TLD (Tenofovir/Lamivudine/Dolutegravir) sebagai regimen utama bagi rawatan HIV di fasiliti Kementerian Kesihatan Malaysia (KKM). Inisiatif ini adalah sebahagian daripada usaha mencapai matlamat Mengakhiri AIDS (Ending AIDS) menjelang tahun 2030.

2. LATAR BELAKANG

- 2.1 Kementerian Kesihatan Malaysia (KKM) komited dalam memperkukuhkan akses kepada rawatan HIV yang efektif, selamat dan berkualiti selaras dengan saranan Pertubuhan Kesihatan Sedunia (WHO) ke arah mencapai sasaran kawalan epidemik HIV.
- 2.2 Pelaksanaan penggunaan regimen TLD sebagai rawatan antiretroviral (ARV) barisan pertama bagi pesakit HIV dilihat berperanan penting dalam usaha untuk meningkatkan liputan rawatan dan mencegah penularan jangkitan.



- Circular **29/4/2026** - implementation of the TLD as the primary regimen for HIV treatment in KKM facilities.

- Part of the efforts to achieve the goal of **Ending AIDS by the year 2030.**

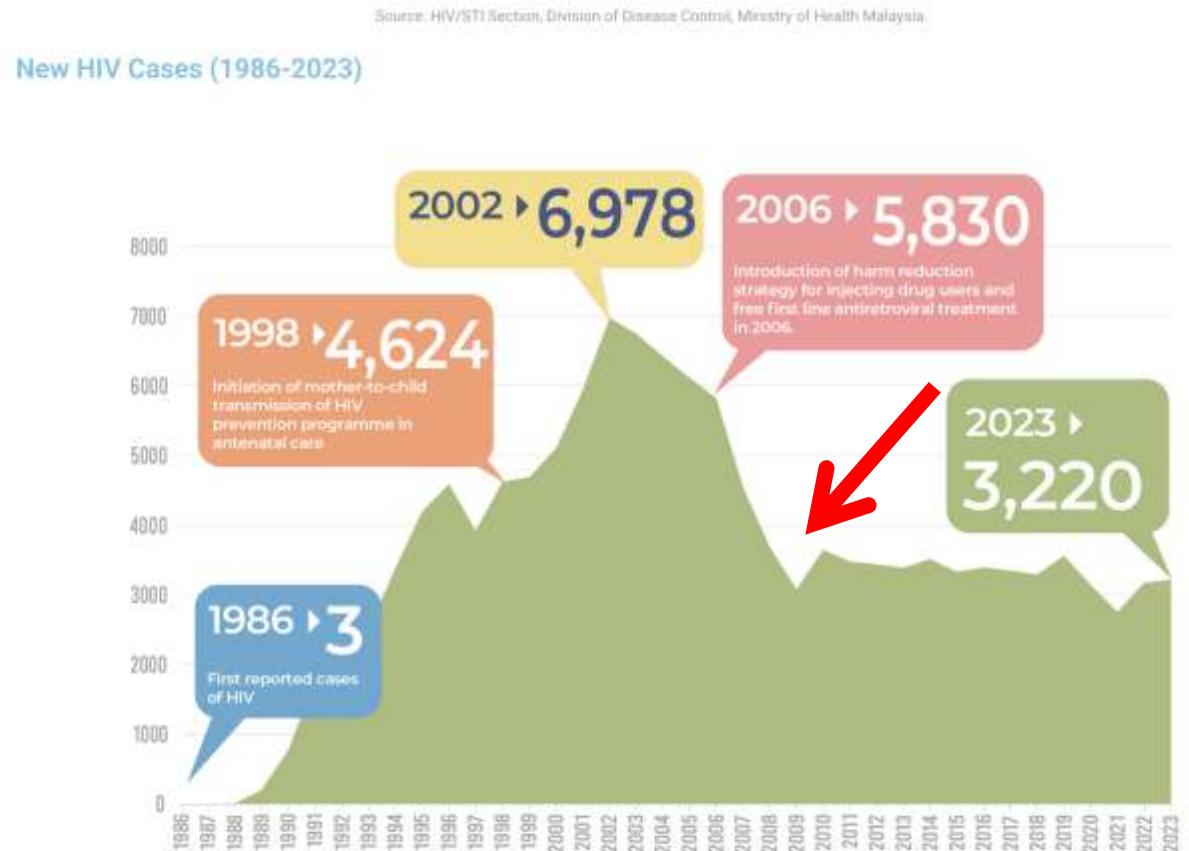


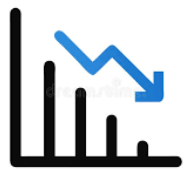
- strengthening access to **effective, safe, and quality** HIV treatment in line with the recommendations of the WHO.

- The implementation of the **TLD regimen as a first-line ARV** plays an important role in efforts to increase treatment coverage and prevent the transmission of infection.

Justification to implement ILD as 1st line treatment in Malaysia

- **Notification of HIV new cases did not show any decline since 2010**, with estimation of around 3,300 new cases reported each year.
- Estimated 282,817 key population (MSM, FSW, TG, PWID) were identified to be high risk but HIV negative (PSE 2018 & 2022)
- HIV prevalence remains high among key population: MSM (12.9%), TG (5.9%) (IBBS 2022)





More Potent:
High virological
efficacy



Better Tolerated:
Good safety
profile and high
patient tolerance

***Advantages of
TLD***

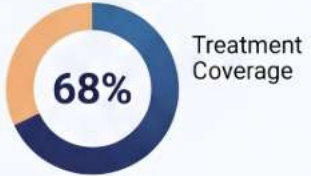


More Durable:
Higher drug
resistance barrier



More Convenient: A
once-daily dosing
regimen that
improves treatment
adherence

2022 Baseline:
The Starting Point



Treatment
Coverage

Expanding treatment coverage:

Increasing the number of PLHIV receiving ARV treatment from 68% (in 2022) to over **95% by 2030**



Preventing transmission:

Stopping the spread of HIV to meet the goal of ending AIDS by 2030, targeting **fewer than 900 new cases a year by 2030**.

Ending AIDS 2030



Population
Health Impact



Achieving viral suppression:

Accelerating and maintaining viral suppression so patients can reach the **U=U** stage (Undetectable = Untransmittable).

Reducing mortality:

Decreasing the number of deaths caused by HIV



TLD HIV Treatment: National Implementation Roadmap

STRATEGIC ROLLOUT & COVERAGE



Universal MOH Facility Integration

TLD treatment is mandated for implementation across all Ministry of Health facilities nationwide.



The primary objective is to transition over 95% of existing patients to TLD.



Immediate Protocol for New Patients

All newly diagnosed HIV/AIDS patients will receive TLD as their first-line treatment.

CLINICAL EXECUTION & LOGISTICS



Existing
Efavirenz
Patients



Staged Clinical Transition

Medical officers are responsible for identifying and transitioning existing Efavirenz patients in stages.



TLD



Malaysia TLD Transition: Clinical Guidelines for HIV Treatment

TLD Regimen Essentials



The TLD Fixed-Dose Combination

A single tablet containing Tenofovir Disoproxil Fumarate (TDF) 300mg, Lamivudine (3TC) 300mg, and Dolutegravir (DTG) 50mg.



Standard Dosage

The regimen is administered as 1 tablet taken once daily.

Prerequisites & Contraindications

Prerequisites

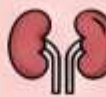


> 40 kg
> 12 years of age

Prerequisite:
Age > 12 years of age

Prerequisite:
Weight ≥ 40 kg

Contraindications



< 50 ml/min

Contraindication:
Renal eGFR < 50 ml/min

Contraindication:
Allergy
Known hypersensitivity to TDF or 3TC

Action Plan by Patient Status

Current Regimen / Patient Status	Proposed Action	Notes
 1. Treatment Naïve	 Start TLD	Apply to all new patients unless contraindicated.
 2. Stable 1st-line (NNRTI)	Switch to TLD	Includes EFV or NVP based regimens.
 3. Failed 1st-line (NNRTI)	Switch to TLD	No viral resistance testing required prior to switch.
 4. Stable PI-based	Switch to TLD	Check for previous Raltegravir exposure; no resistance testing needed.
 5. Stable Dolutegravir-containing	Switch to TLD	Specifically for those on DTG + (AZT/3TC or TDF/FTC).

General Switching Rule

For most scenarios, patients should be switched to TLD unless specific contraindications (like renal issues) are present.

Important Clinical Notes

Viral Load Suppression



**95%
U=U**

STABLE is defined as a viral load < 50 copies/mL for 6+ months; **FAILED** is a persistently detectable viral load > 1000 copies/mL after 6+ months on ARV. TLD is expected to help 95% of patients achieve viral suppression (U=U: Undetectable = Untransmittable).

Adherence Check



For patients with unsuppressed viral loads prior to a TLD switch, clinicians must address adherence and psychosocial factors first.

Clinical Decision Guide: Initiating and Switching to TLD HIV Treatment

Visual protocol for transitioning HIV patients to the TLD (Tenofovir/Lamivudine/Dolutegravir) regimen based on current treatment status.

DEFINITIONS: Stable Treatment Status



Decline in viral load to < 50 copies/mL within 6 months of commencing ARV, sustained thereafter.

DEFINITIONS: Failed Treatment Status



Persistently detectable viral load > 1000 copies/mL after at least 6 months on ARV therapy.

Universal Assumption: These recommendations assume the patient has no contraindications to TLD (e.g., eGFR < 50 ml/min or hypersensitivity).

START: Patient HIV Treatment Status

PATHWAY 1: Treatment Naive Patients

ARV Initiation for New Patients



Start TLD immediately.
No resistance testing required.
(Regardless of baseline CD4 count or Viral Load).

PATHWAY 2: Switching Stable Patients



Stable 1st-line NNRTI
(e.g., TDF/FTC or AZT/3TC + EFV or NVP)

Switch to TLD.
No resistance testing required.



Stable PI-based Regimen
(e.g., LPV/r or ATV/r)

Switch to TLD.
No resistance testing required.
(Must check for previous Raltegravir exposure).



Stable DTG-containing Regimen
(e.g., AZT/3TC + DTG)

Switch to TLD
(Fixed-Dose Combination tablet).
No resistance testing required.

PATHWAY 3: Switching Failed Patients



Failed 1st-line NNRTI

Switch to TLD immediately.
Critically, there is **NO** need for viral resistance testing.



Failed PI-based Regimen



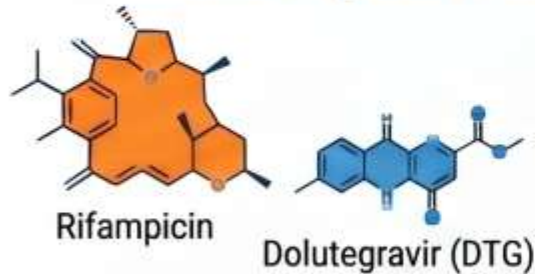
DO NOT switch to TLD automatically.
Refer to an Infectious Disease (ID) Physician for subsequent regimen and send for viral resistance testing.



KEY FINDING: Address Root Causes. For any unsuppressed viral load, clinicians must identify and address adherence issues or psychosocial factors before or during the switch.

Clinical Guide: Special Considerations for TLD (Dolutegravir) Treatment

Rifampicin-based TB Treatment



The Rifampicin Interaction Challenge:

Rifampicin significantly reduces Dolutegravir (DTG) plasma concentrations, which typically necessitates a dose adjustment to maintain viral suppression.

Standard Action: Double Dosing



Most guidelines recommend double dosing of DTG (50mg twice daily) to compensate for the reduction caused by Rifampicin.

Consult ID first

Criteria for Daily Dosing (Standard Dose)



Recent studies show a standard daily dose is adequate **ONLY** if the patient is on 1st line Dolutegravir-based ARV **AND** has a CD4 count > 100 cells/ μ L.

Suggested Clinical Actions



Discuss the case with an Infectious Disease (ID) physician



Wait until TB treatment is completed before initiating or switching to TLD.

Previous INSTI (Raltegravir) Exposure



Raltegravir Status Update

Note that Raltegravir production has been discontinued; however, previous exposure remains a critical factor in current treatment planning.



Risk of Treatment Failure

A history of failure on a Raltegravir-based regimen increases the risk of resistance, which may require double dosing of Dolutegravir.



Required Action: Resistance Testing

A viral resistance test is necessary prior to changing the patient's regimen to TLD if they have a history of INSTI exposure.

Managing Drug-Drug Interactions with Dolutegravir (DTG)

Guidance for Healthcare Providers on Optimizing Malaysia TLD Regimen Efficacy and Safety.

INTERACTING DRUG CLASS	EFFECT ON LEVELS	CLINICAL RECOMMENDATION
ANTICONSULSANTS (Carbamazepine, Phenytoin, Phenobarbital) 	 DECREASE Significant reduction in DTG plasma concentrations, potentially compromising HIV viral suppression.	Avoid Co-administration - Ideally switch to non-interacting alternatives (e.g., Sodium Valproate, Lamotrigine, Levetiracetam, Topiramate). - If no alternative, IMPLEMENT DOUBLE DOSING: 50mg twice daily.
METFORMIN (Diabetes Management) 	 INCREASE Increased metformin concentration; heightens risk of dose-related adverse effects.	Start Low, Limit Dose, Monitor - Initiate at lowest possible dose and titrate carefully. ENSURE TOTAL DAILY DOSE DOES NOT EXCEED 1g. - Vigilant monitoring for signs of Lactic Acidosis, especially in renal impairment.
POLYVALENT CATIONS (Supplements & Antacids) 	 DECREASE Decreased DTG absorption; cations bind to and decrease DTG absorption.	Follow "2 Hours Before or 6 Hours After" Rule - Take DTG AT LEAST 2 hours BEFORE or 6 hours AFTER cation-containing products. Special Considerations: Mg/Al antacids decrease levels regardless of food intake; Ca/Fe supplements specifically decrease levels on an empty stomach.

Based on Malaysia Ministry of Health guidelines for TLD regimen

Side Effects Profile: TLD HIV Treatment Regimen

The TLD fixed-dose combination offers high efficacy and genetic barrier, but each component—Dolutegravir (DTG), Tenofovir (TDF), and Lamivudine (3TC)—has a distinct side effect profile requiring specific clinical attention during treatment.



DTG Central Nervous System Effects

Common symptoms include insomnia, headaches, and vivid dreams, often managed by adjusting medication timing.



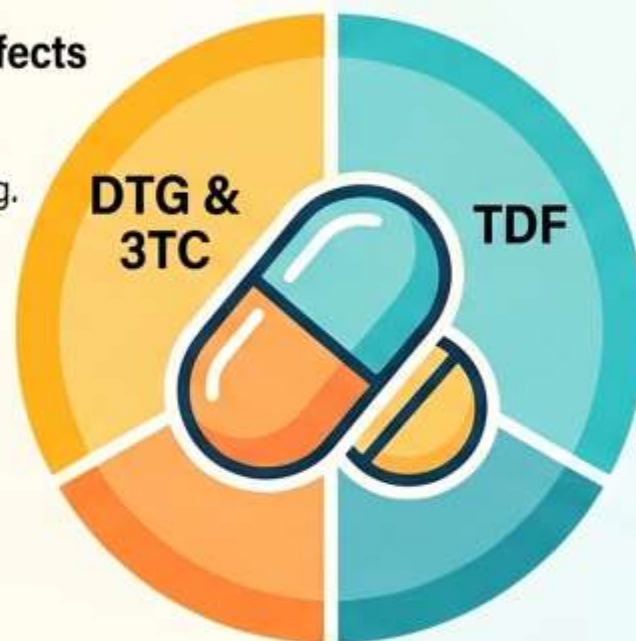
3TC Hepatitis Flare Risk

Severe acute hepatitis flares may occur in HBV co-infected patients who discontinue 3TC.



General DTG Tolerability

Occasional reports of hepatotoxicity, rash, and hyperglycaemia, though generally well-tolerated by most.



Renal Health Monitoring

Potential for renal insufficiency and Fanconi syndrome; serious tubular damage occurs in 0.5%.



Bone Density Impact

Long-term use is associated with reduced bone mineral density and osteomalacia.



Common Gastrointestinal Distress

Patients may initially experience nausea, vomiting, flatulence, or diarrhoea.



	Component	Primary Side Effects	Specific Clinical Risks
DTG	Dolutegravir (DTG)	 Insomnia, headache, nausea	 Hepatotoxicity, hyperglycaemia, rash
TDF	Tenofovir (TDF)	 Nausea, vomiting, diarrhoea	 Renal insufficiency, reduced bone density
	Lamivudine (3TC)	 Minimal general toxicity	 Severe hepatitis flare (if HBV co-infected)

Timing of Medications



**Mornin
g**

Recommended if the patient experiences insomnia or vivid dreams as side effects, which some people report when taking it at night.

Some prefer taking it at bedtime to minimize potential dizziness or nausea during the day.

Night



Caution and monitoring

Creatinine

(1 – 3 months post initiation)

- Creat rise < 25% or <30 mmol/L is still acceptable
– Likely DTG related
- **Creat rise > 25%** or >30 mmol/L –
To workout for possible renal disease, **stop TLD** and consider other regimes

LFT

(1 month post initiation)

- DTG has risk of hepatotoxicity
- Lamivudine – severe acute flare of Hep B in HBV coinfecting patient who discontinue lamivudine

Allergic and rashes

- DTG: rare, <1%
- 3TC: rare, 0.7 – 1%
- TDF: 5 –10%

Preferred monitoring schedule

TEST	FREQUENCY
HIV VL	<u>After ARV Initiation / from previous failed regimen</u> : Repeat VL after 4 months <u>After switching (other indications)</u> : Repeat VL after 6 months Thereafter if stable VL suppression achieved - Repeat 6 monthly to yearly VL depending on feasibility
CD4	(to align with VL) CD4 < 200 cells/mm : 3 to 6 monthly CD4 200-350 cells/mm : annually CD4 > 350 cells/mm : (2 occasions 1 yr apart - no further CD4 required)
FBC	Every 4 to 6 months
Renal function	At week 4 then week 12; then 4 to 6 monthly if stable
Liver function	At week 4 then every 4 to 6 months
FSL / FBS	Every 6 to 12 months



Case study:



Case 1

Mr. R, 66-year-old Indian gentleman, smoker, alcohol drinker 4 -5 cans of beer/day

Married with 4 children, unemployed, previously works as guard, staying with family

Recent MVA in March 2026, became weak

RVD diagnosed since 2010,
on ART under
KK Larkin f/up

•Co-morbidity:
asthma,
dyslipidemia

ART:
Tenvir-EM 1/1
ON, Efavirenz
600mg ON

Latest blood
investigations
(13/11/25)
CD4: 834,
VL: Not
Detected

- Brought in by ambulance, informed by daughter that patient was found lying on the bed with alleged Clorox ingestion
- Suicidal attempt as family found out about his illness recently (breach of COC)
- OGDS: + esophagitis, erythematous hemorrhagic gastritis
- CXR: + aspiration pneumonitis
- Also has transaminitis
- ART withheld
- Condition improved gradually with supportive treatment

Which ART regime to restart

1

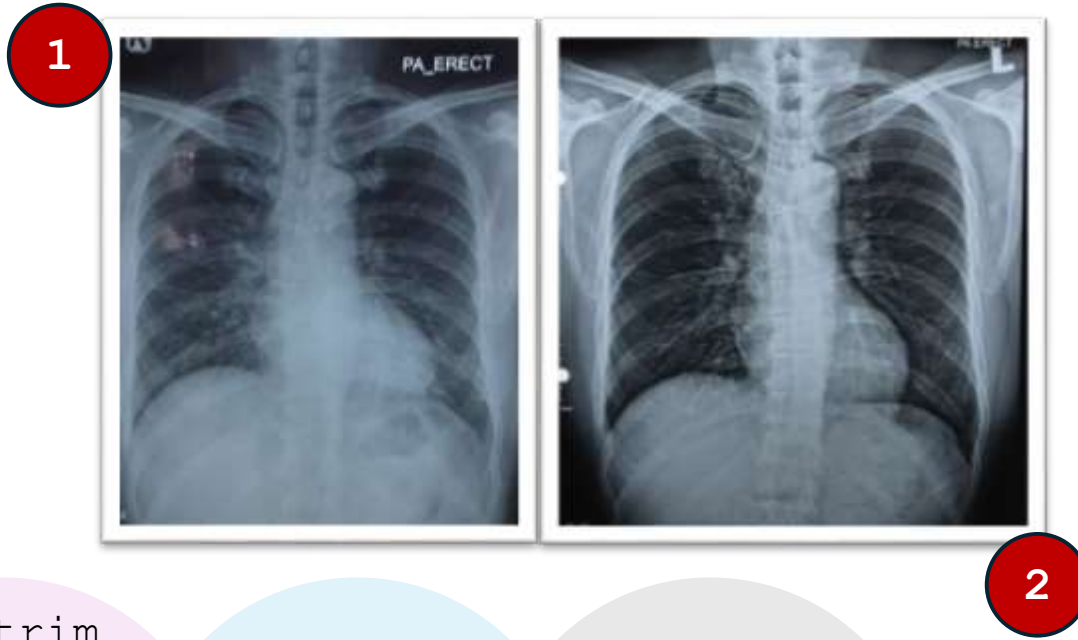


2



Case 2

Mr. S, 49-year-old Malay gentleman



DM, HPT,
dyslipide
mia, h/o
TIA 2020;
under GP
f/up

Newly
diagnosed
RVD, **CD4:**
21, VL:
679,000
(18/5/26)

Cough for
2 weeks
and
shortness
of breath
→ **PCP**

Bactrim
3/3/4
tabs TDS
for 1
week →
transamin
itis +
AKI

Clindamyc
in 600mg
TDS +
primaquin
e 30mg OD

Urine
LAM:
negative

Which ART regime is preferable to start with?

Case 3

Mr. F, 26-year-old Malay gentleman, MSM (vertical transmission)

RVD
diagnosed
since 2021
at age of
21 years
old during
screening

Started
ART:
Tenvir-EM
1 tab ON,
Efavirenz
600mg ON

Definitely
Died
2021 -
2025 due
to unable
to accept
illness



4/2021



12/2021

1



10/2022

5

RPR: 1:128

Baseline CD4:
240, VL:
268,813

CD4: 284
VL: <40



Returned
to care at
KKSI in,
restarted
ART with
same

VL:

338,000

- Adherent to ART, Blood test 10/4/26, CD4: 229, VL: 85
- However, suffered from mental health issues:
 - Low mood past 4 years
 - Unable to accept his illness
 - Anhedonia
 - Frequent sleep
 - Unable to function at work
 - Feeling worthless
 - + deliberate self harm: punching mirror
 - Anxious in crowded environment



admitted
Which ART regime to restart with?

- + transaminitis (ALT: 188, AST 83), ART withheld

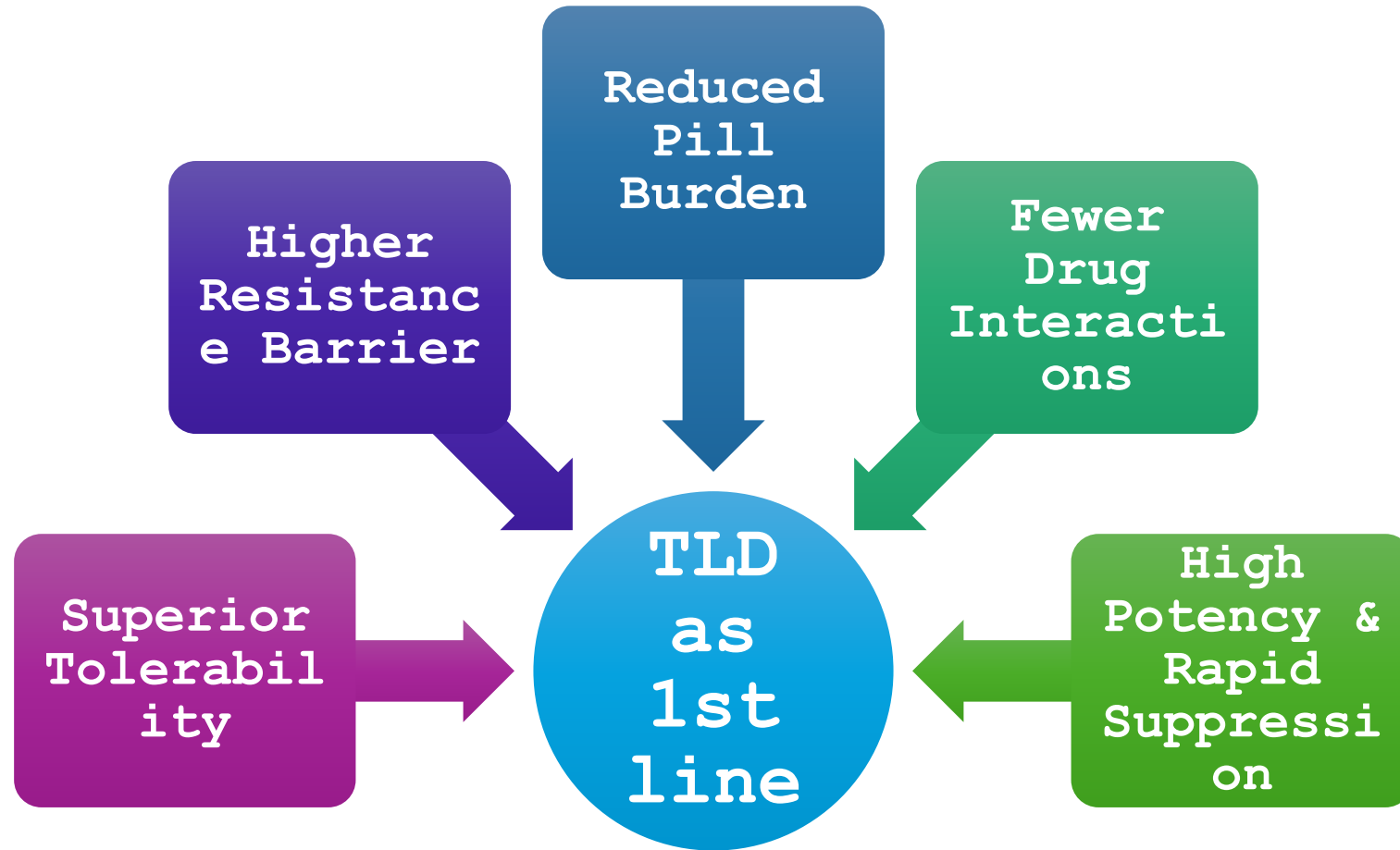
Case 4

Mr. M, 29-year-old Malay gentleman



- Grade 3 rashes
- MPE secondary to Efavirenz
- ART withheld
- **Which ART to restart?**

Summary



FIRST ANNOUNCEMENT



National AIDS Conference (NAC) 2026

Innovating Prevention,
Strengthening Care,
No One Left Behind



18-19 SEPTEMBER 2026



KLANG VALLEY,
MALAYSIA
(To be confirmed)



HIGHLIGHTS

- Innovations in HIV prevention and care
- Optimising management of HIV, including advanced disease
- Person-centered care across the life course
- Addressing stigma and structural barriers
- Strengthening community and research partnerships

Organised by
Malaysian Society for HIV Medicine

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