PHRAMONGKUTKLAO HOSPITAL
PHRAMONGKUTKLAO COLLEGE OF MEDICINE

21st HIV/AIDS WORKSHOP 2022

Challenging Cases in ART Initiation Interactive-case Discussion

21st HIV/AIDS Workshop, Virtual Conference, 27th August 2022

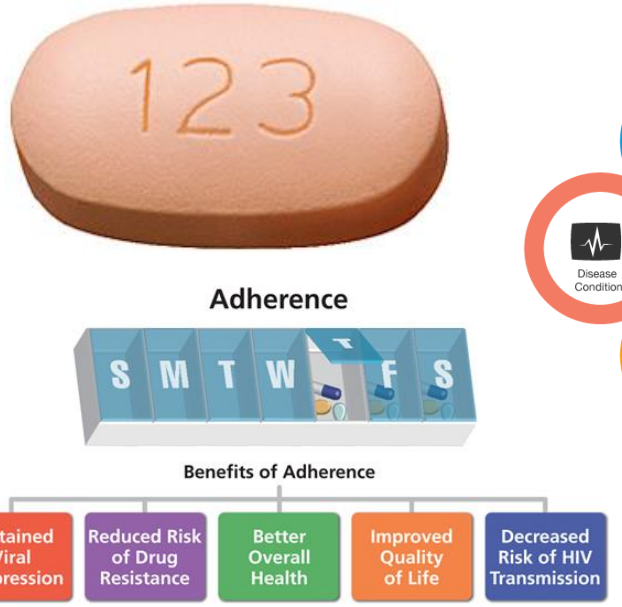
Major Worapong Nasomsong, MD

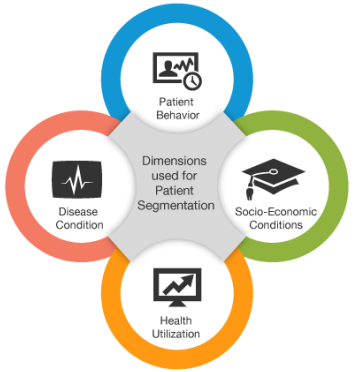
Assistant Professor

Division Infectious Disease

Department of Internal Medicine

Phramongkutklao Hospital and College of Medicine





Panel Discussants

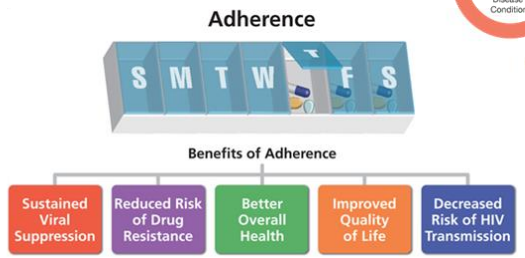
Asst. Prof. Thanomsak Anekthananon, M.D.

Assoc. Prof. Piroon Mootsikapun, M.D.

Asst. Prof. Pansachee Damronglerd, M.D.

Case 1

A young Thai female with chronic cough



Case 1: A young Thai female with chronic cough

Case 25 yrs., female, convenient store staff (night shift), live in Bangkok

Chief complaint: non-productive cough for 4 weeks

Present illness

- 4 wks. PTA she had non-productive cough, accompanied with low-grade fever, malaise and significant weight loss.
- 1 week PTA she visited TB clinic and diagnosed of smear positive pulmonary TB. CXR revealed RUL cavitation and sputum AFB was positive (3+).
- She received standard regimen anti-TB drugs (HRZE)
- Anti-HIV: reactive
- **Past history**: no U/D, no history of significance medical or surgical illness
- **Personal history**: Unprotected SI (last 2 wks.) with temporary partner, no illicit drug use
- **Occupation**: convenient store staff (night shift; 24.00 – 8.00), **Health scheme**: Social Security

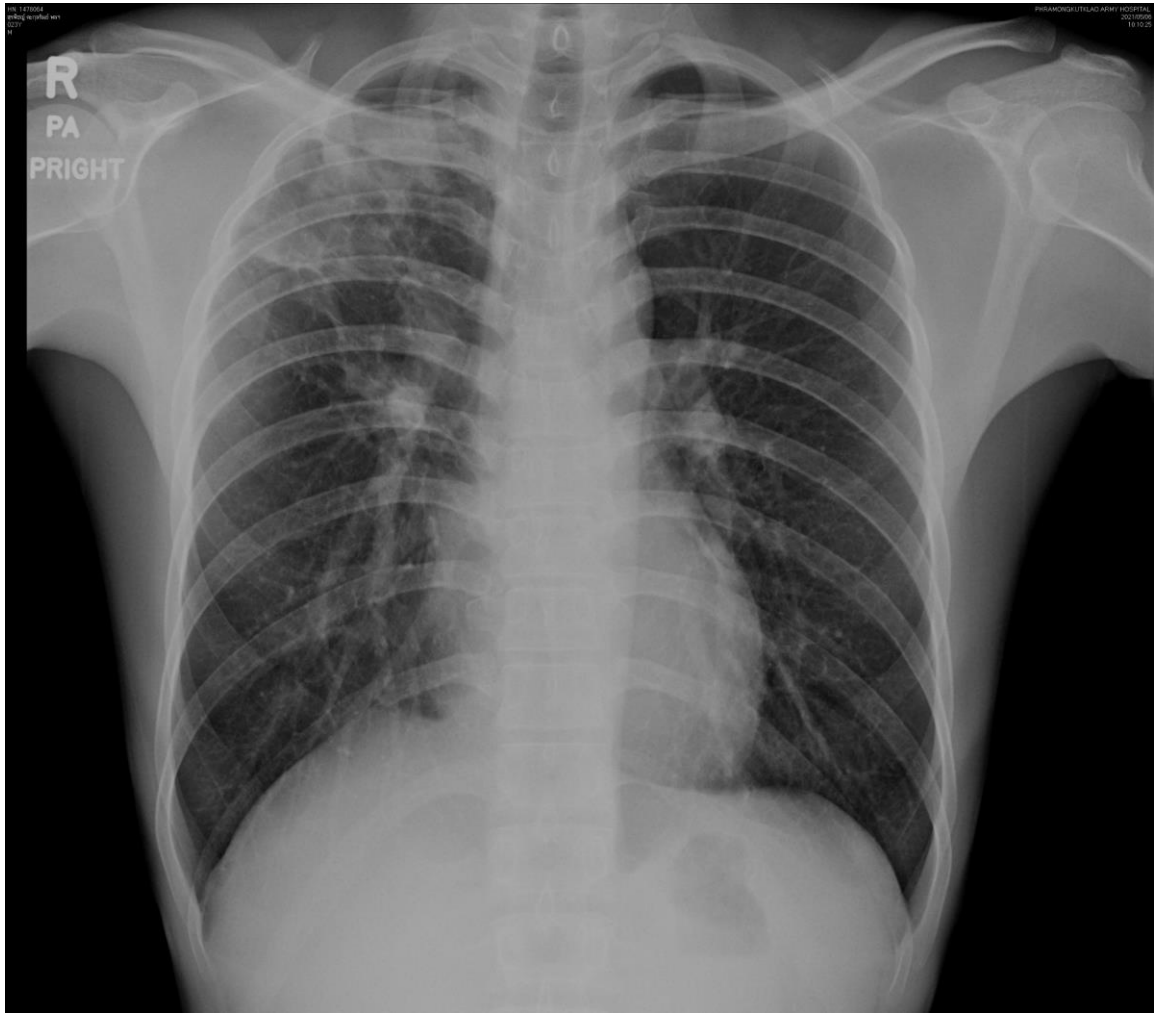
Case 1: A young Thai female with chronic cough

- Vital signs : BT : 36.5^{o}C, RR : 18 /min HR : 70 /min BP : 120/80 mmHg, Weight : 45 kg. Height : 155 cm.
- GA: a young Thai female, normosthenic build, drowsiness, no pallor, no signs of chronic liver disease
- HEENT: not pale conjunctivae, anicteric sclerae, no conjunctival injection, no thyroid gland enlargement, no oral ulcer, no oral thrush
- Heart & Lungs: normal
- Abdomen: normal, liver span 10 cm. no splenic dullness
- Extremity & skin: no edema, no rash, no ulcer, no eschar
- Lymph node: can’t be palpated

Case 1: A young Thai female with chronic cough

Initial laboratory assessment

- Anti-HIV: reactive
- CD4+ T cell: 327 cell/µL (18.9%)
- HBsAg: non-reactive
- Anti-HBS: negative
- Anti-HCV: negative
- RPR : non-reactive, TPHA: negative
- Cr. 0.55 mg/dL (eGFR: 109mL/min/1.73 m^2)



Case 1: Initiation of Antiretroviral Therapy, When and What to start?

Problem List

- **Smear positive cavitating pulmonary tuberculosis**
- **HIV infection [CD4+ T cell: 327 cell/µL (18.9%)]**
- **High-risk sexual behavior**

Occupation: convenient store staff (night shift; 24.00 – 8.00), **Health scheme**: Social Security

Tuberculosis/HIV Coinfection

Rifampicin can be co-administered with following ARV

ARV	THAI 2021-2022	DHHS2022	EASC 2021
NNRTI			
EFV	- **EFV** dose at 600 mg q.d[a+b]	- **EFV** dose at 600 mg q.d[a+b]	- **EFV** dose at 600 mg q.d[a+b]
NVP	- **NVP** 200 mg bid (without lead in)	- Do not coadminister	- Do not coadminister
PIs	Not recommended	Not recommended	Not recommended
INSTIs			
RAL	- **RAL** 800 mg bid[a+b]	- **RAL** 800 mg bid, instead of 400 mg bid (do not use 1200mg OD) [a+b]	- **RAL** 400 or 800 mg bid[a+b]
DTG	- **DTG** 50 mg bid (Without INSTI resistance) [a+b]	- **DTG** 50 mg bid (without INSTI resistance) [a+b]	- **DTG** 50 mg bid (without INSTI resistance) [a+b]
NRTI			
TAF	N/A	Do not coadminister unless benefits outweigh risks. (possible reduce TAF level)	N/A

a = pharmacokinetic study/ b= clinical study

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV:USDHSSS 2022
European AIDS Clinical Society guideline 2021
Thai HIV/AIDS national guidelines 2021-2022

Opportunistic Infections and Optimal Time of ARV Initiation

Opportunistic infections	THAI 2021-2022	DHHS2022	EASC 2021
Tuberculosis (except TB meningitis)	Within 2 weeks not exceed 4 weeks	CD4 counts <50 : within 2 weeks CD4 counts ≥50: within 8 weeks	As soon as possible within 2 weeks of starting TB treatment, regardless of CD4 count
Tuberculous meningitis	Defer ARV for 4 weeks after treatment	Expert consultation	ART should be delayed for 4 weeks, but can be initiated within the first 2 weeks if CD4 < 50
Cryptococcal meningitis	4-6 weeks after treatment	4-6 weeks after treatment	At least 4 weeks after treatment
Non-CNS Cryptococcosis	2-4 weeks after treatment	2 weeks after treatment	N/A
Cerebral toxoplasmosis	2-4 weeks after treatment	2-3 weeks after treatment	As soon as possible within 2 weeks after starting treatment for the OIs
Cytomegalovirus	Defer ARV for 4 weeks after treatment esp. chorioretinitis and encephalitis	Within 2 weeks	
Other OIs	Within 2 weeks	Within 2 weeks	

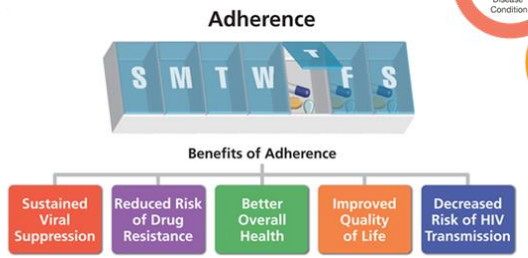
Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV:USDHSSS 2022
European AIDS Clinical Society guideline 2021
Thai HIV/AIDS national guidelines 2021-2022

Case 1: A young Thai female with chronic cough

Date	Treatment
March-2020	- Cavitating pulmonary tuberculosis TB: 2HRZE/4HR
April-2020	- HIV infection: TDF/FTC/EFV at 11.00 AM
October-2020	- HIV infection: VL < 20 copies/mL, CD4+ T cell: 503 cell/µL (22%) - Pulmonary TB: complete treatment
November-2020	- HIV infection: switch regimen to TDF/FTC+RPV
September-2021	- ART: TDF/FTC+RPV - HIV infection: VL < 20 copies/mL, CD4+ T cell: 453 cell/µL (25%)

Case 2

A middle-aged Thai female with HIV-positive partner



Case 2: A middle-aged Thai female with HIV-positive partner

Case 40-year-old female, Self-employed, live in Northern Thailand

Chief complaint: consultation for HIV treatment

Present illness

- She lived with her HIV infection couple for 5 years.
- She recently recognized of her husband had HIV infection, thus she visited a private hospital and anti – HIV was performed.
- At private hospital, anti-HIV was reactive. She denied any abnormal symptoms.
- **Past history**: no history of significance medical or surgical illness
- **Personal history**: Unprotected SI with her husband (3-4 times/ month), no illicit drug use
- **Occupation**: Self-employed, **Health scheme**: civil servant medical benefit

Case 2: A middle-aged Thai female with HIV-positive partner

- Couple history: A 45-year-old male, government officer, live in Bangkok

Date	Treatment/Comment
May -2011	- ITP, First diagnosis HIV infection - ART: TDF+3TC+EFV
January-2012	- ART: TDF+3TC+EFV, VL < 20 copies/mL
April-2018	- Poor adherence, virologic failure, genotypic resistance: M184V, K103N - Change ART: TDF/FTC + ATV/r + enhance adherence counselling
September-2018	- ART: TDF/FTC + ATV/r + enhance adherence counselling - Good adherence, VL < 20 copies/mL, CD4+ T cell: 205 cell/µL (9%)
February-2021	- Change ART to STR : TDF/3TC/DTG - Good adherence, VL < 20 copies/mL, CD4+ T cell: 235 cell/µL (12%)

Case 2: A middle-aged Thai female with HIV-positive partner

- Vital signs : BT : 37^{o}C, RR : 18 /min HR : 70 /min BP : 120/80 mmHg, Weight : 50 kg. Height : 155 cm.
- GA: a young Thai female, normosthenic build, drowsiness, no pallor, no signs of chronic liver disease
- HEENT: not pale conjunctivae, anicteric sclerae, no conjunctival injection, no thyroid gland enlargement, no oral ulcer, no oral thrush
- Heart & Lungs: normal
- Abdomen: normal, liver span 10 cm. no splenic dullness
- Extremity & skin: no edema, no rash, no ulcer, no eschar
- Lymph node: can’t be palpated

Case 2: A middle-aged Thai female with HIV-positive partner

Initial laboratory assessment

- Anti-HIV: reactive
- HBsAg: non-reactive, Anti-HBS: negative
- RPR : non-reactive, TPHA: negative
- CD4+ T cell: 522 cell/µL (28%)
- Anti-HCV: negative
- Cr. 0.85 mg/dL (eGFR: 85 mL/min/1.73 m^2)

Case 2: Initiation of Antiretroviral Therapy, When and What to start?

Problem List

- **Asymptomatic HIV infection [CD4+ T cell: 522 cell/µL (28%)]**
- **Partner diagnosed with drug resistance HIV infection**

Case 2: A middle-aged Thai female with HIV-positive partner

Date	Treatment/Comment
February 2020	At private hospital: start ART: TDF/FTC/EFV
June 2020	At PMK: VL: 3,040 copies/mL; Genotypic resistance: M184V, K103N Change ART: TDF/3TC/DTG
December 2020	VL: 32 copies/mL, Good adherence
October 2021	VL: <20 copies/mL, Good adherence

HIV Drug Resistance

"HIV drug resistance is caused by changes in the genetic structure of HIV that affect the ability of medicines to block the replication of the virus."

Pretreatment HIV drug resistance or Transmitted HIV drug resistance

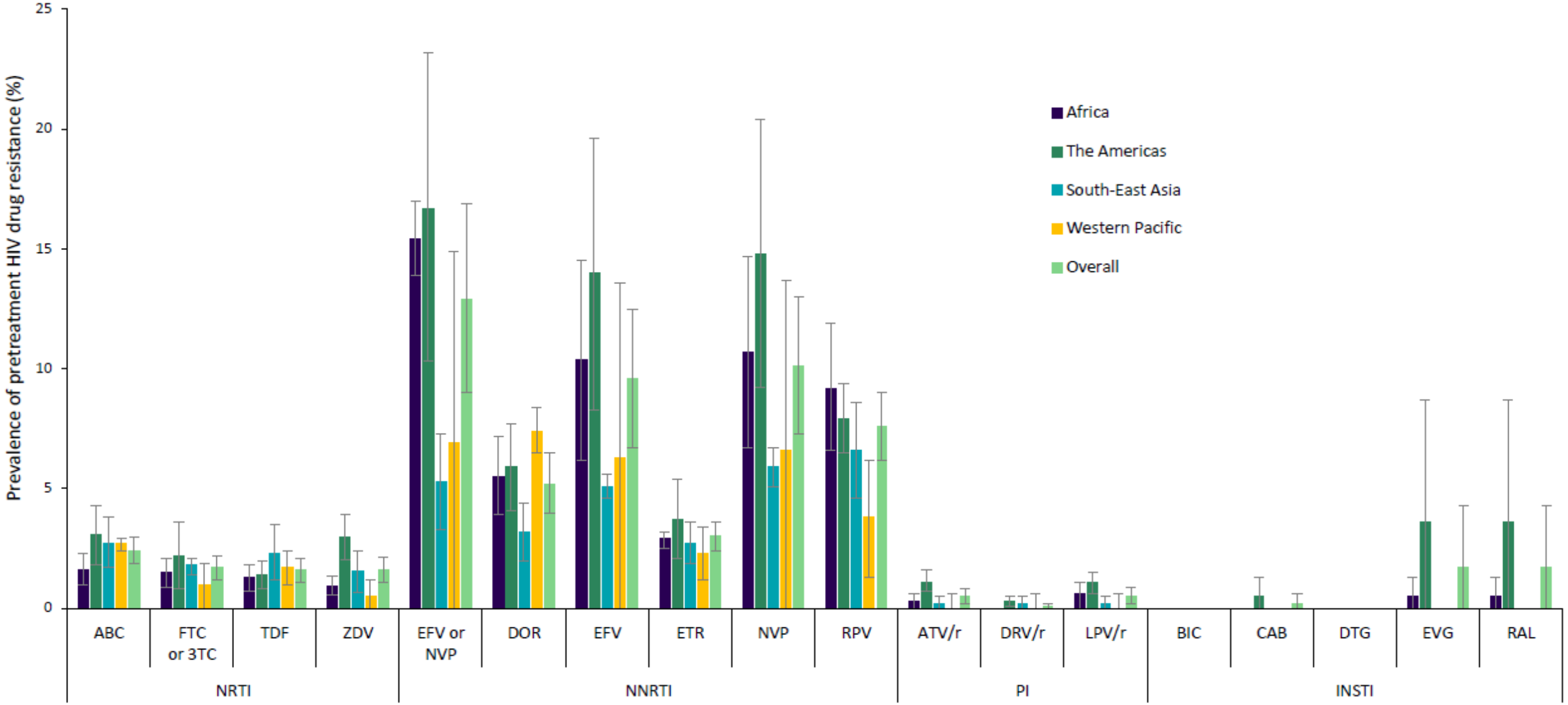
- Resistance detected in ARV drug-naive people initiating ART or people with prior ARV drug exposure initiating or reinitiating first-line ART

Acquired HIV drug resistance or Secondary Resistance

- A drug-resistant strain of HIV emerges while a person is on antiretroviral therapy (ART) for the treatment of HIV infection

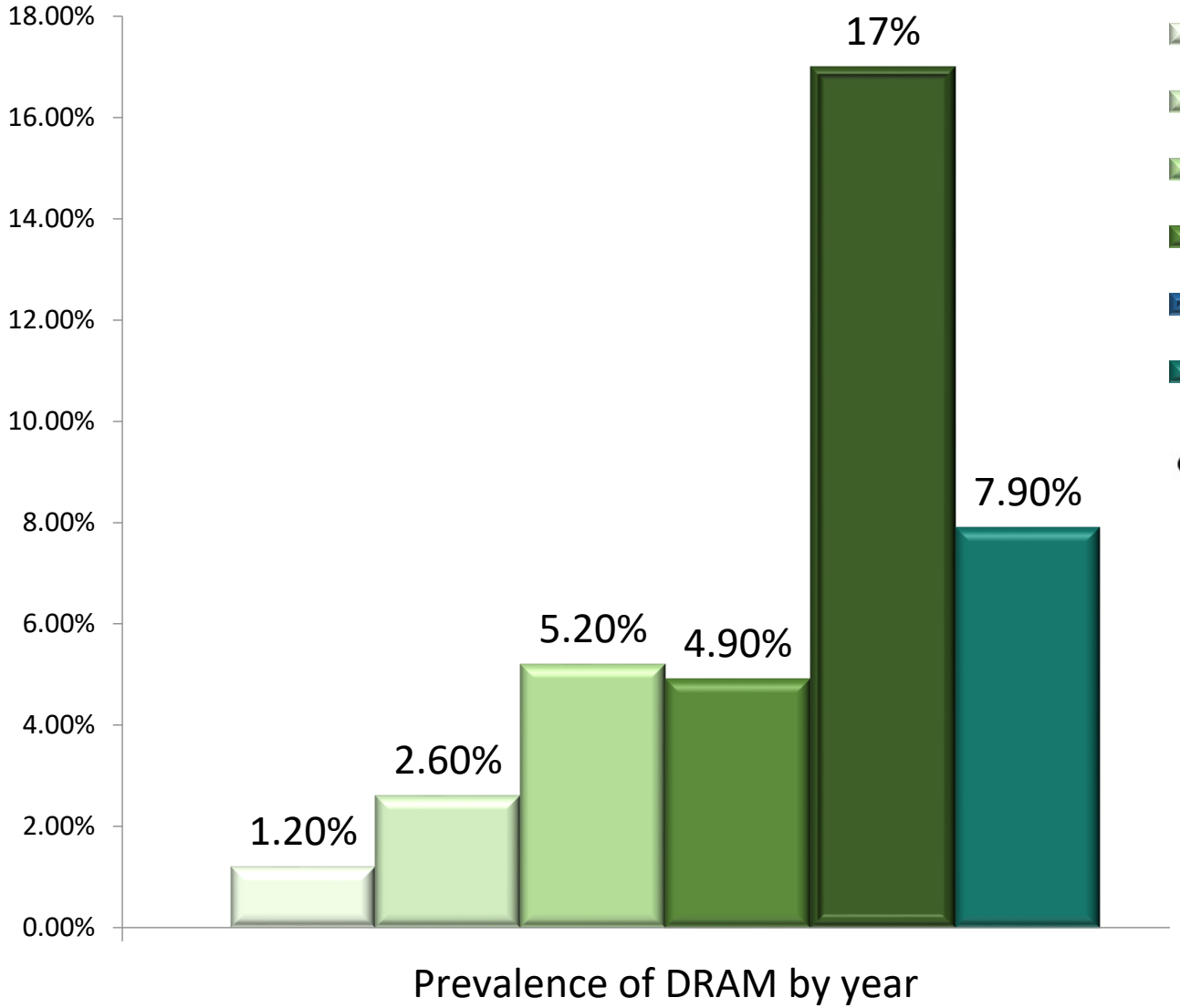
1. Fokam J, Takou D, Teto G, Nforbih SE, Kome OP, Santoro MM, et al. Pre-treatment drug resistance and HIV-1 genetic diversity in the rural and urban settings of Northwest-Cameroon. PLoS ONE. 2022. 15(7): e0235958.
2. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV:USDHSSS 2022

Prevalence of pretreatment HIV drug resistance among adults initiating ART,2014-2020



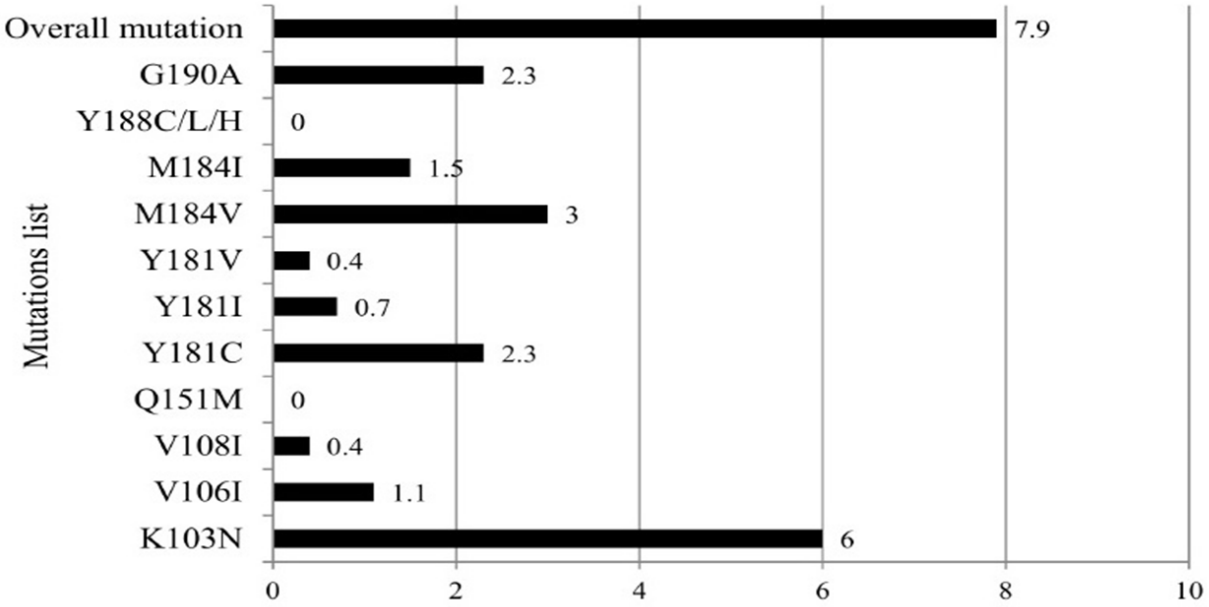
HIV drug resistance report 2021. Geneva: World Health Organization; 2021.

Prevalence of Pretreatment HIV Drug Resistance in Thailand



Prevalence of Primary HIV Drug Resistance in Thailand

- Prospective cohort study of total of 265 naïve HIV-infected patient during 2011-2014.
- Detected by Short Reverse Transcriptase Genotypic Resistance Assay.



Apisarnthanarak A. et al.HIV Medicine.2008;9:322–325
Sungkanuparph S.et al.J Int AIDS Soc. 2012.12;15(1):12.
Manosuthi W.et al.J Med Virol. 2013;85(2):194-9.
Kiertiburanakul S.PLoS One. 2016;11(2):e0147945

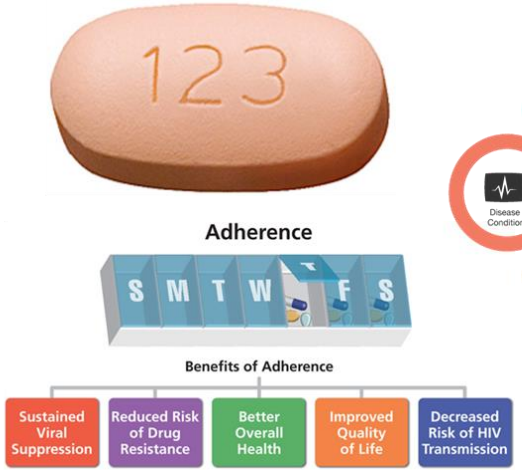
Drug-Resistance Testing

Guidelines	Recommendation
DHHS 2022	HIV drug-resistance testing is recommended at entry into care for persons with HIV to guide selection of the initial antiretroviral therapy (ART) regimen
EACS 2021	Genotypic resistance testing is recommended prior to initiation of ART, ideally at the time of HIV diagnosis. Genotypic testing should not delay ART initiation
Thai 2021-2022	กรณีสงสัยมีคู่ที่มีประวัติเชื้อดื้อยาและในผู้ที่ได้ PrEP

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV:USDHSSS 2022
European AIDS Clinical Society guideline 2021
Thai HIV/AIDS national guidelines 2021-2022

Case 3

A middle-aged Thai male with CKD and OIs



Case 3: A middle-aged Thai male with CKD and OIs

Case 42 yrs., male, military officer, live in Bangkok

Chief complaint: headache for 4 weeks

Present illness

- 4 wks. PTA he complaint of gradual onset of troubling headache
- 2 wks. He had progressive headache accompanied with low-grade fever, malaise and vomiting
- 1 day PTA he had agitation, confusion and subsequently drowsiness.
- **Past history**: no U/D, no history of significance medical or surgical illness
- **Personal history**: Unprotected SI, MSM, no illicit drug use
- **Occupation**: military officer, **Health scheme**: civil servant medical benefit

Case 3: A middle-aged Thai male with CKD and CAD

- Vital signs : BT : **39**^{o}C, RR : 18 /min HR : 70 /min BP : 120/80 mmHg, Weight : 50 kg. Height : 170 cm.
- GA: a young Thai female, **cachexia, drowsiness**, no pallor, **dry lips**, no signs of chronic liver disease
- HEENT: **markedly pale conjunctivae**, anicteric sclerae, no conjunctival injection, no thyroid gland enlargement, no oral ulcer, no oral thrush
- Heart & Lungs: normal
- Abdomen: normal, liver span 10 cm. no splenic dullness
- Extremity & skin: **PPE at both legs**
- Lymph node: multiple firm, movable, erythema and tender **cervical lymph node enlargement** size 2-3 cm.

Case 3: A middle-aged Thai male with CKD and CAD

Neurological examination

- Mental status: **drowsiness**, **not cooperate**, **not orientation to time, place, person**
- Cranial nerve: pupil 3 mm. react to light both eyes, full EOM, no facial palsy, no nystagmus
- Fundoscopic examination: no papilledema A : V ratio 2:3, no venous pulsation
- Motor power: Grade V both upper and lower extremities
- Sensory: can't be evaluated
- Babinski’s: dorsiflexion both sides clonus: negative both side
- Deep tendon reflex: 2+ all extremities
- **Stiffness of neck: positive**

Case 3: A middle-aged Thai male with CKD and OIs

Admit to Intensive care unit for 4 weeks and transfer to medical unit

Cryptococcal meningoencephalitis and cryptococcal septicemia

Disseminated *mycobacterium gordonae*: multiple cervical lymph node and bone marrow

<u>Medication</u>

Amphotericin B + fluconazole for 2 weeks → fluconazole

Levofloxacin, azithromycin, ethambutol

Complication

- Secondary acquire severe AA due to HIV infection
- Acute tubular necrosis; resolution with residual CKD stage III (eGFR; 50 mL/min/1.73 m2)
- Heart failure preserve EF

Case 3: A middle-aged Thai male with CKD and OIs

Hb (g/L)	7.8
Hct (%)	23.7
Wbc (/ul)	3,000
Pmn (%)	55
Lymp (%)	25
Mono (%)	20
Eo (%)	0
Baso (%)	0
Plt (/ul)	269,000
MCV (fl)	79.4
RDW (%)	17.3
MPV (fl)	8.5
MCH (pg)	26.3
MCHC (g/dl)	32.9

Initial laboratory assessment

- Anti-HIV: reactive, HIV VL: 1,239,000 copies/mL
- CD4+ T cell: 140 cell/µL (10%)
- HBsAg: non-reactive, Anti-HBS: negative
- Anti-HCV: negative
- RPR : non-reactive, TPHA: negative
- HLAB*5701: positive

BUN (mg/dl)	20.2
Cr (mg/dl)	1.85
eGFR (mL/min/1.73 m^2)	44
Sodium (mEq/L)	140
Potassium (mEq/L)	4.3
Chloride (mEq/L)	106.9
Bicarbonate (mEq/L)	21

Albumin (g/dL)	2.65
Globulin (g/dL)	3.9
TB (mg/dl)	0.9
DB (mg/dl)	0.7
AST (U/L)	58
ALT (U/L)	63
ALP (U/L)	225

Case 3: Initiation of Antiretroviral Therapy, When and What to start?

Problem List

- Cryptococcal meningoencephalitis and cryptococcal septicemia
- Disseminated *Mycobacterium gordonae*: multiple cervical lymph node and bone marrow
- Secondary acquire severe AA due to HIV infection
- Acute tubular necrosis; resolution with residual CKD stage III (eGFR; 50 mL/min/1.73 m2)
- Heart failure preserve EF
- HLAB*5701: positive

Antiretroviral Regimen Considerations for Initial Therapy Chronic Kidney Disease

Guidelines	Recommendation

DHHS 2022	- ABC may be used if patient is HLA-B*5701 negative.
	- If HIV RNA is >100,000 copies/mL, do not use ABC/3TC plus EFV or ATV/r.
	- TAF may be used if CrCl >30 mL/min or if patient is on chronic hemodialysis (studied only with EVG/c/TAF/FTC)
	- ART Options When ABC, TAF, or TDF Cannot be Used:
	  - DTG/3TC (if HIV RNA <500,000 copies/mL)
	  - DRV/r plus 3TC
	  - DRV/r plus RAL (if CD4 count >200 cells/mm3 and HIV RNA <100,000 copies/mL)

EACS 2021	- ABC/3TC + DTG: HLA-B*57:01 negative and HBsAg negative - XTC + DTG or 3TC/DTG: HBsAg negative, HIV-VL < 500,000 copies/mL, Not recommended after PrEP failur
Thai 2021-2022	- ABC + 3TC or AZT + 3TC และ DTG หรือ EFV หรือ RPV - DTG+3TC • ใช้ในกรณีไม่สามารถหายาสูตรสามตัวที่เหมาะสมได้ เช่น มีโรคไต ไม่สามารถใช้ TDF หรือ TAF ได้ • พิจารณาใช้ในกลุ่มที่ HBs Ag: negative และ Baseline VL < 500,000 copies/mL หรือ CD4 > 200 cell/mm3 และ ไม่มีการดื้อต่อ 3TC

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV:USDHSSS 2022
European AIDS Clinical Society guideline 2021
Thai HIV/AIDS national guidelines 2021-2022

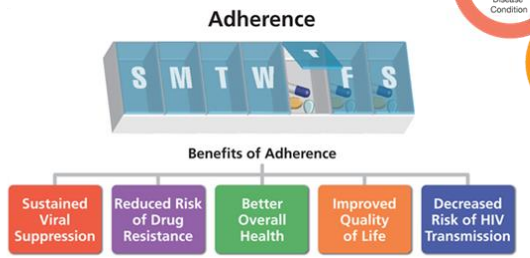
Case 3: A middle-aged Thai male with CKD and OIs

Initiation of Antiretroviral Therapy, When and What to start?

Date	Treatment/Comment
January -2021	- Start ART: 3TC+RAL+DRV/r - Levofloxacin, Ethambutol, Azithromycin
March-2021	- ART: 3TC+RAL+DRV/r, VL 239 copies/mL - Levofloxacin, Ethambutol, Azithromycin
August-2021	- ART: 3TC+RAL+DRV/r, VL < 20 copies/mL - Levofloxacin, Ethambutol, Azithromycin
January -2022	- Change ART to STR: TAF/FTC/BIC - Good adherence, VL < 20 copies/mL, CD4+ T cell: 188 cell/µL (12%) (Cr. 1.63 ;eGFR 50)

Case 4

A young Thai male with progressive headache



Case 4: A young Thai male with progressive headache

- Case 36 yrs., male, military officer, live in Bangkok
- **Chief complaint**: seizure 1 hr. PTA
- **Present illness:** 4 wks. PTA he complaint of gradual onset of diffuse troubling headache without any improvement after receiving pain killer pills.
- 2 wks. PTA He had progressive headache accompanied by low-grade fever, malaise, and weight loss (58 kg → 55 kg in 2 weeks)
- 1 day PTA the headache was worsening. He had near syncope and generalized tonic- clonic seizure for 5 minutes with spontaneous recovery. After recovery he had confusion and drowsiness, thus his colleagues bring him to the hospital.
- **Past history:** no U/D, no history of significance medical or surgical illness
- **Personal history:** Unprotected SI, bisexual, no illicit drug use, social alcohol drinking, no smoking
- **Occupation:** military officer, **Health scheme:** civil servant medical benefit

Case 4: A young Thai male with progressive headache

- Vital signs : BT : **36.5**^{o}C, RR : 18 /min HR : 83 /min BP : 140/110 mmHg, Weight : 55 kg. Height : 173 cm.
- GA: a young Thai male, normosthenic build**, drowsiness**, no pallor
- HEENT: not pale conjunctivae, anicteric sclerae, no conjunctival injection, no thyroid gland enlargement, no oral ulcer, **oral thrush at tongue and both buccal mucosa**.
- Heart & Lungs: normal
- Abdomen: normal, liver span 10 cm. no splenic dullness
- Extremity & skin: **PPE at both legs**
- Lymph node: no enlargement.

Case 4: A young Thai male with progressive headache

Neurological examination

- Mental status: **drowsiness**, **not cooperate**, **not orientation to time, place, person**
- Cranial nerve: pupil 3 mm. react to light both eyes, full EOM, no facial palsy, no nystagmus
- Fundoscopic examination: no papilledema A : V ratio 2:3, no venous pulsation
- Motor power: Grade V both upper and lower extremities
- Sensory: can't be evaluated
- Babinski's: dorsiflexion both sides clonus: negative both side
- Deep tendon reflex: 2+ all extremities
- **Stiffness of neck: positive**

Case 4: A young Thai male with progressive headache

- **Problem list** : Chronic meningoencephalitis with first episode seizure in suspected immunocompromised patient. [DDX: TB meningitis, Cryptococcal meningitis]
- **Initial investigation and management**
- CT brain with CM: leptomeningeal enhancement along right parietal sulci,
- interpenducular cistern, and bilateral cerebellar folia.
- Lumbar puncture was performed.
- Open pressure: 60 cmH_2O, close pressure 19 cmH_2O

Color	WBC	PMN	Mononuclear	Glucose mg/dL	Glucose ratio	Protein mg/dL
Slightly turbid	651 /m^3	4%	96%	38	0.34	47

Case 4: A young Thai male with progressive headache

Hb (g/L)	13.6
Hct (%)	41
Wbc (/ul)	5,100
Pmn (%)	79.5
Lymp (%)	14.6
Mono (%)	5.8
Eo (%)	0
Baso (%)	0
Plt (/ul)	253,000
MCV (fl)	83.3
RDW (%)	17.3
MPV (fl)	9.9
MCH (pg)	27.7
MCHC (g/dl)	33.2

Initial laboratory assessment

- Anti-HIV: reactive
- CD4+ T cell: 40 cell/µL (5.4%)
- HBsAg: non-reactive, Anti-HBS: negative
- Anti-HCV: negative
- RPR : non-reactive, TPHA: negative
- Serum & CSF Cryptococcal Ag : positive

BUN (mg/dl)	8.7
Cr (mg/dl)	0.61
eGFR (mL/min/1.73 m^2)	128.13
Sodium (mEq/L)	135
Potassium (mEq/L)	3.63
Chloride (mEq/L)	98.4
Bicarbonate (mEq/L)	23.5

Albumin (g/dL)	3.75
Globulin (g/dL)	4.71
TB (mg/dl)	0.52
DB (mg/dl)	0.32
AST (U/L)	36
ALT (U/L)	42
ALP (U/L)	61

Hemoculture:

Cryptococcus neoformans

CSF culture:

Cryptococcus neoformans

Case 4: Initiation of Antiretroviral Therapy, When and What to start?

Problem List

- **Cryptococcal meningoencephalitis and cryptococcal septicemia with provoked seizure**
- **Acquired immune deficiency syndrome (AIDS)**
- **Treatment:**
  - Medication: AmBd (1.0 mg/kg/day) plus flucytosine (100 mg/kg /day) for 1 wk. then fluconazole 1,200 mg/day for 1 wk. then fluconazole 800 mg/day.
  - Levetiracetam (200) 2x2 O pc
  - TMP/SMX (400/80) 2x1 O pc
  - Intracranial pressure management: temporary external lumbar drainage (10 days)

Opportunistic Infections and Optimal Time of ARV Initiation

Opportunistic infections	THAI 2021-2022	DHHS2022	EASC 2021
Tuberculosis (except TB meningitis)	Within 2 weeks not exceed 4 weeks	CD4 counts <50 : within 2 weeks CD4 counts ≥50: within 8 weeks	As soon as possible within 2 weeks of starting TB treatment, regardless of CD4 count
Tuberculous meningitis	Defer ARV for 4 weeks after treatment	Expert consultation	ART should be delayed for 4 weeks, but can be initiated within the first 2 weeks if CD4 < 50
Cryptococcal meningitis	4-6 weeks after treatment	4-6 weeks after treatment	at least 4 weeks after treatment
Non-CNS Cryptococcosis	2-4 weeks after treatment	2 weeks after treatment	N/A
Cerebral toxoplasmosis	2-4 weeks after treatment	2-3 weeks after treatment	As soon as possible within 2 weeks after starting treatment for the OIs
Cytomegalovirus	Defer ARV for 4 weeks after treatment esp. chorioretinitis and encephalitis	Within 2 weeks	
Other OIs	Within 2 weeks	Within 2 weeks	

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV:USDHSSS 2022
European AIDS Clinical Society guideline 2021
Thai HIV/AIDS national guidelines 2021-2022

Case 4: A young Thai male with progressive headache

Progression

Date	Progression
17 September – 1 October 2021	- Cryptococcal meningoencephalitis and cryptococcal septicemia with provoked seizure - LOS 15 days - Clinical improve and repeat CSF C/S no growth after 5 days of treatment
26 October 2021	- Start ARV : TDF/3TC/DTG 1 tab OD - Current medication - Fluconazole 800 mg/day - Levetiracetam (200) 2x2 O pc - TMP/SMX (400/80) 2x1 O pc

Case 4: A young Thai male with progressive headache

Progression

Date	Progression
4 December 2021	- Progressive headache 7 days PTA, no N/V, blur vision, or fever - PE: no focal neurological deficit - Repeat LP: open pressure 32, close pressure 18 cmH_2O

Color	WBC	PMN	Mononuclear	Glucose mg/dL	Glucose ratio	Protein mg/dL
Clear	4 /m^3	0%	100%	51	0.56	44

- CSF India ink preparation: negative, CSF Culture: no growth
- CT brain with CM: moderate communicating hydrocephalus

Case 4: A young Thai male with progressive headache

- CD4+ T cell: 40 cell/µL (5.4%) [SEP 2021] → 405 cell/µL (14.3%) [7 DEC 2021]
- HIV-1 VL: 71 copies/mL [7 DEC 2021]

- **Diagnosis:** Paradoxical Cryptococcal Meningitis immune reconstitution inflammatory syndrome

What is the most appropriate management?

- Treatment of IRIS
- ARV adjustment, necessary or not?

Cryptococcal Immune Reconstitution Inflammatory Syndrome

- Prevalence of cryptococcal meningitis IRIS is 10-30% after initiation or re-initiation of effective ART
- **Minimize risk of IRIS**
  - Achieving CSF culture sterility before starting ART
  - Using fluconazole 800 mg per day as consolidation therapy
  - Deferring ART initiation for 4 to 6 weeks from the start of antifungal therapy
- **Distinguishing paradoxical IRIS from treatment failure**
  - Paradoxical IRIS: culture negative
  - Treatment failure: culture positive
  - Negative CSF PCR test has a high predictive value for predicting sterile CSF cultures and can be diagnostically useful to distinguish paradoxical IRIS

Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV 2022. Available at https://clinicalinfo.hiv.gov/en/ guidelines/adult-and-adolescent-opportunistic-infection.

Cryptococcal Immune Reconstitution Inflammatory Syndrome

- **Management strategy for IRIS**
  - Continue both ART and antifungal therapy (AII)
  - Reduce elevated ICP (AII)
  - While diagnostic tests are pending, escalating antifungal therapy is appropriate, such as restarting amphotericin B therapy or increasing the fluconazole dose to 1,200 mg per day (BIII).
- **Severe symptoms of IRIS**
  - Tapering doses of corticosteroids start at 1.0 mg/kg per day of prednisone (BIII)
- At hospital discharge, restarting fluconazole therapy at consolidation therapy doses to be continued for 8 weeks is recommended (BIII).

Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV 2022. Available at https://clinicalinfo.hiv.gov/en/ guidelines/adult-and-adolescent-opportunistic-infection.

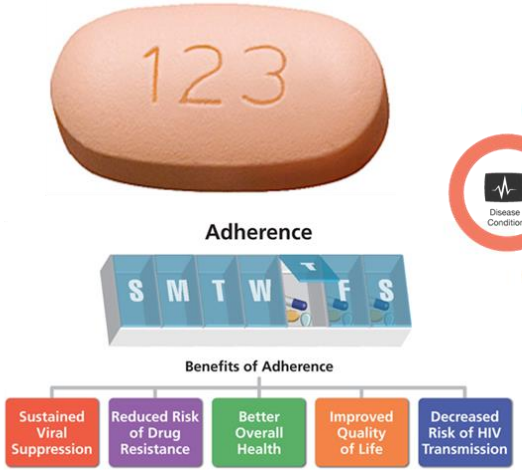
Case 4: A young Thai male with progressive headache

Progression; Paradoxical Cryptococcal Meningitis immune reconstitution inflammatory syndrome

Date	Progression
7 December 2021	- Neurosurgeon performed ventriculoperitoneal (VP) shunt - Resolution of headache and D/C in 7 days later
14 January 2022	- OPD ID: doing well, no headache - TDF/3TC/DTG 1 tab OD - Fluconazole 200 mg/day - Levetiracetam (200) 2x2 O pc
27 June 2022	- OPD ID: doing well, no headache - HIV-1 VL: <20 copies/mL, CD4+ T cell: 390 cell/µL (11.4%) - TDF/3TC/DTG 1 tab OD

Case 5

A young man with acute fever



Case 5: A young man with acute fever

Case 30 yrs., male, military officer, live in Bangkok

Chief complaint: Fever for 7 days

Present illness

- 7 days PTA he developed a high-grade fever with myalgia and then visited a private clinic, where he received antipyretic and amoxicillin without any improvement. He denied other organ specific symptoms.
- 2 days PTA he noticed an enlarged bilateral cervical and groin lymph node.
- 1 day PTA the symptoms were not improved, thus he came to the hospital
- **Past history**: no U/D, no history of significance medical or surgical illness
- **Personal history**: Unprotected SI [last 1 month], heterosexual, no illicit drug use, no history of travelling outside Bangkok within 3 months
- **Occupation**: military officer, **Health scheme**: civil servant medical benefit

Case 5: A young man with acute fever

- Vital signs : BT : **39.5**^{o}C, RR : 18 /min HR : 110 /min BP : 130/80 mmHg, Weight : 65 kg. Height : 175 cm.
- GA: a young Thai male, normosthenic build**,** alert, no pallor
- HEENT: not pale conjunctivae, anicteric sclerae, no conjunctival injection, no thyroid gland enlargement, no oral ulcer, no oral thrush, **dry lips**
- Heart & Lungs: normal
- Abdomen: normal, liver span 10 cm. no splenic dullness
- Extremity & skin: no rash, no eschar, no petechiae
- Lymph node: **bilateral cervical and inguinal lymph node enlargement, size 1-2 cm. in diameter, firm, moveable, not tender.**
- Neurological examination: within normal limit.

Case 5: A young man with acute fever

Hb (g/L)	15.5
Hct (%)	45.5
Wbc (/ul)	3,400
Pmn (%)	68
Lymp (%)	22.7
Mono (%)	9
Eo (%)	0
Baso (%)	0.3
Plt (/ul)	137,000
MCV (fl)	83.3
RDW (%)	13
MPV (fl)	11.2
MCH (pg)	26.4
MCHC (g/dl)	34.2

Initial laboratory assessment

- Dengue NS1Ag: negative, dengue IgM: negative, dengue IgG: positive
- IFA for murine and scrub typhus: negative
- UA: Sp.gr. 1.020, ketone 2+, WBC 0-1, RBC 0-1, erythrocyte negative

BUN (mg/dl)	10.8
Cr (mg/dl)	1.09
eGFR (mL/min/1.73 m^2)	91.24
Sodium (mEq/L)	135
Potassium (mEq/L)	3.63
Chloride (mEq/L)	94.4
Bicarbonate (mEq/L)	25.5

Albumin (g/dL)	4.64
Globulin (g/dL)	2.92
TB (mg/dl)	0.35
DB (mg/dl)	0.18
AST (U/L)	58
ALT (U/L)	44
ALP (U/L)	45

Case 5: A young man with acute fever

Initial laboratory assessment

- Anti-HIV: inconclusive
- 4^{th} generation ELISA [p24Ag ; positive, HIV Ab; negative x 2 technique, HIV immunochromatographic test: negative]
- CD4+ T cell: 752 cell/µL (30.6%)
- HBsAg: non-reactive, Anti-HBS: positive [40 IU/mL], Anti-HCV: negative
- RPR : non-reactive, TPHA: negative
- HIV VL > 10,000,000 copies/mL

Case 5: Initiation of Antiretroviral Therapy, When and What to start?

- Problem lists:

"**Acute retroviral syndrome**"

Early (Acute and Recent) HIV Infection

Acute HIV infection

- Describes the period immediately after infection with HIV when an individual is viremic and has detectable p24 antigen or has HIV RNA without diagnostic HIV antibodies.

Recent infection

- Generally used to describe the 6-month period after infection occurs.

Early infection

- May refer to acute or recent infection, after which infection is defined as chronic.

Suspicion of Acute HIV Infection

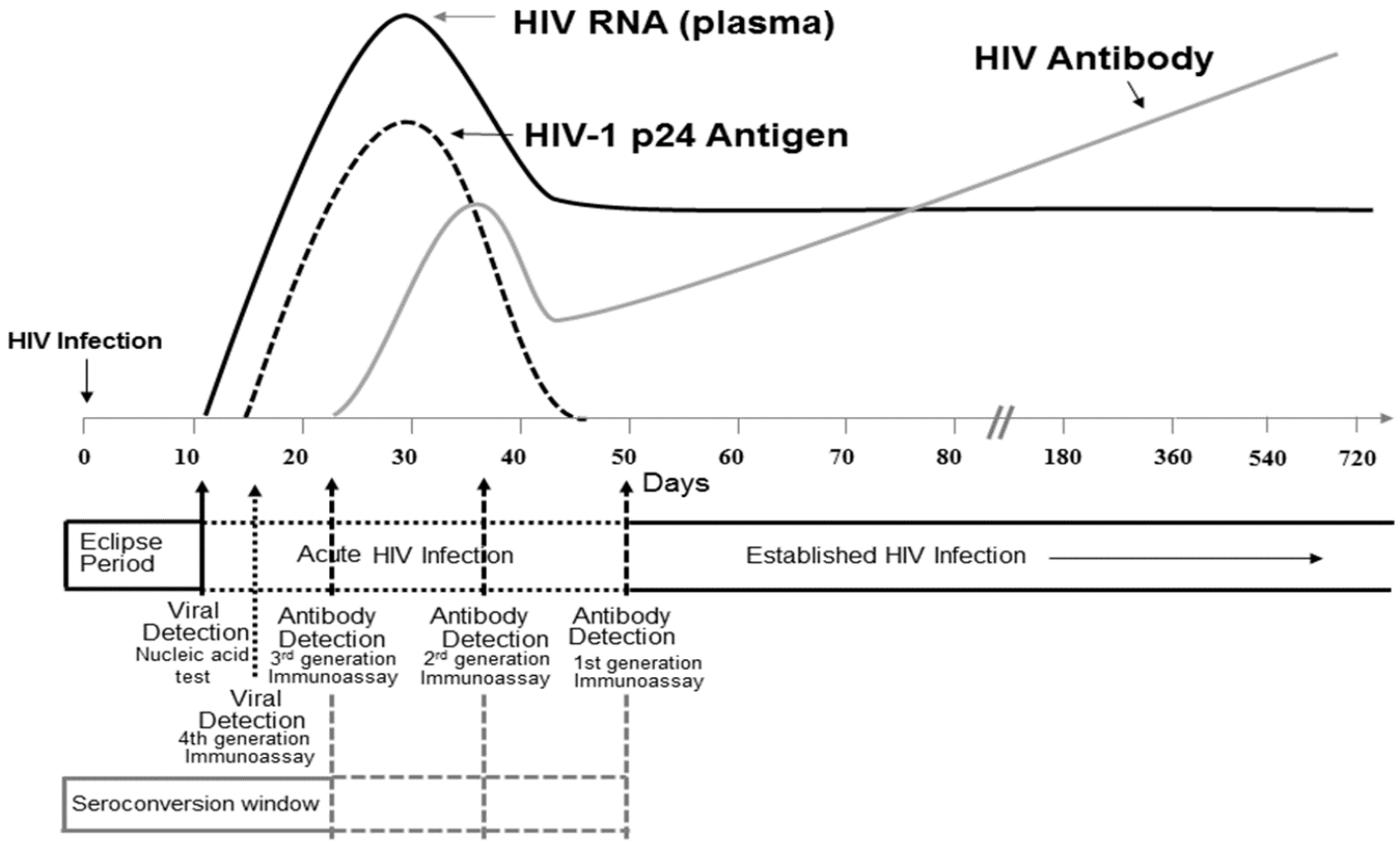
- Individuals with the signs, symptoms, or laboratory findings described below and in asymptomatic individuals with a possible recent (within 2–6 weeks) exposure to HIV
- High-risk exposures include sexual contact; sharing needles; or any exposure in which an individual's mucous membranes or any breaks in the skin come in contact with bodily fluid that potentially carries HIV.
- Signs, symptoms, or laboratory findings of acute HIV infection may include, but are not limited to, one or more of the following: **fever, lymphadenopathy, skin rash, myalgia, arthralgia, headache, diarrhea, oral ulcers, leucopenia, thrombocytopenia, and transaminase elevation**.

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV:USDHSSS 2022

Early (Acute and Recent) HIV Infection

Testing to Diagnose/Confirm Acute HIV Infection

- Detectable **HIV RNA or p24 Ag** in the setting of a **negative or indeterminate HIV Ab** test result.
- A positive result on a quantitative or qualitative plasma HIV RNA test (>100,000 copies/mL) in the setting of a negative or indeterminate antibody test result indicates that acute HIV infection is highly likely. In this case, the diagnosis of HIV infection should be confirmed by **subsequent of HIV Ab seroconversion.**



Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV:USDHSSS 2022

Treatment of Early (Acute and Recent) HIV Infection

Guidelines	Recommendation
DHHS 2022	- If available, the results of ARV drug-resistance testing or the resistance pattern of the source person's virus should be used to guide selection of the regimen. - **DTG** with FTC or 3TC plus TDF or TAF - **BIC**/TAF/FTC - Boosted **DRV** with FTC or 3TC plus TAF or TDF
EACS 2021	- **DTG** with FTC or 3TC plus TDF or TAF - **BIC**/TAF/FTC - Boosted **DRV** with FTC or 3TC plus TAF or TDF
Thai 2021-2022	- **DTG** with FTC or 3TC plus TDF or TAF

Benefits of Treatment AHI

- Virological: decrease of the HIV-VL set-point and size of the viral reservoir; reduction of viral genetic evolution
- Immunological: decrease of immune activation and inflammation; preservation of immune function and integrity of lymphoid tissue;
- Possibly neurological and gut protection; possibly enhancement of post-treatment control and response to future eradication strategies
- Potential benefits of treatment for the community: reduced risk of transmission.

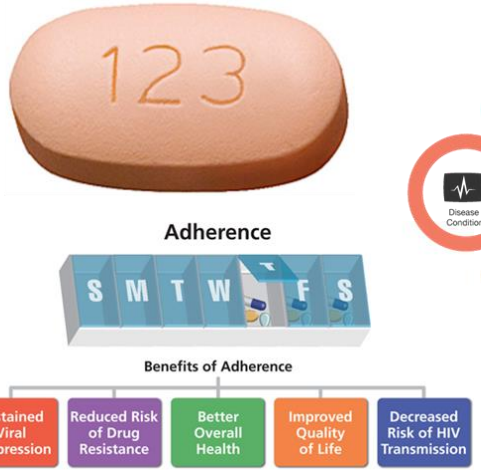
Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV:USDHSSS 2022
European AIDS Clinical Society guideline 2021
Thai HIV/AIDS national guidelines 2021-2022

Case 5: A young man with acute fever

Date	Progression
November 2020	- Start ARV: TDF/FTC/EVG/c 1 tab OD - Advice & counselling
March 2021	- OPD ID: doing well, good adherence - ARV: TDF/FTC/EVG/c 1 tab OD - VL < 20 copies/mL
October 2021	- OPD ID: doing well, good adherence - Switch ARV : TDF/FTC/EVG/c 1 tab OD → TDF/3TC/DTG 1 tab OD
December 2021	- OPD ID: doing well, good adherence - ARV: TDF/3TC/DTG 1 tab OD - VL < 20 copies/mL

Case 6

A young Thai female with teenage pregnancy



Case 6: A young Thai female with teenage pregnancy

Case 22-year-old female, Housewife, live in Bangkok

Chief complaint: consultation for HIV treatment

Present illness

- 3 months PTA: A 22-year-old pregnant woman presented with in-labor without ANC (G2P1001). At labor room, anti-HIV result revealed reactive (2 samples) without any abnormal symptoms. She was discharged home and made the appointment for ID clinic; however, she was loss to followed up.
- 2 months PTA: She complained dyspnea on exertion accompanied with pedal edema
- 1 week PTA: She complained orthopnea and paroxysmal nocturnal dyspnea. The pedal edema was worsening accompanied with generalized edema and abdominal discomfort. Thus, she came to visit ED.

Case 6: A young Thai female with teenage pregnancy

Case 22-year-old female, Housewife, live in Bangkok

- **Past history**: no history of significance medical or surgical illness.
- **Personal history**:
- She had unprotected SI with multiple sexual partner since she was 14 (sex worker).
- She had a history of illicit amphetamine use (inhale) since she was 14, which ceased after imprisonment (5 year ago).
- She was jailed at the age of 18 for drug possession.
- She had a small tattoo on her back which tattooing by a friend in the prison.
- Her first child was born to her ex-husband, a healthy two years old boy.
- **Occupation**: Housewife, **Health scheme**: universal coverage, **Care giver**: husband (self employed)

Case 6: A young Thai female with teenage pregnancy

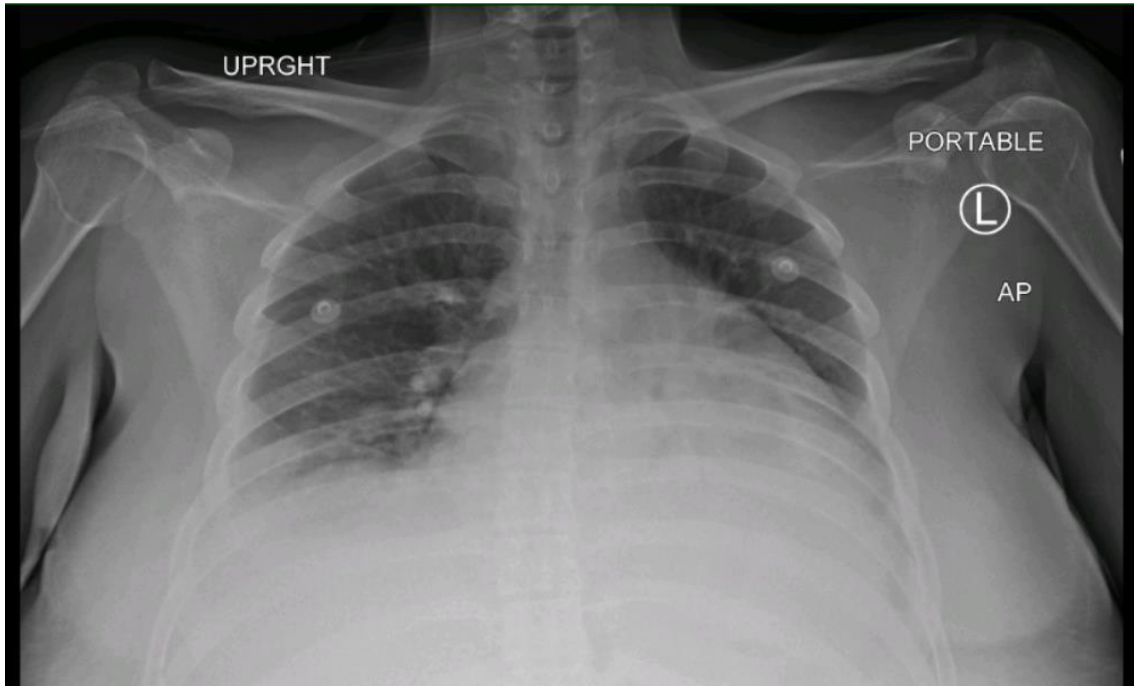
- Vital signs : BT : **36.5**^{o}C, RR : 18 /min HR : 130 /min BP : 130/80 mmHg, Weight : 60 kg. Height : 153 cm.
- GA: a young Thai female, normosthenic build**,** alert, no pallor
- HEENT: not pale conjunctivae, anicteric sclerae, no conjunctival injection, no thyroid gland enlargement, no oral ulcer, no oral thrush
- Heart: **JVP up to mandible**, **PMI at 6th ICS 2 cm. lateral to MCL**, no heaving, no thrill, **soft S1**, normal S2 no murmur, nS3 gallop
- Lungs: **tachypnea, rapid shallow breathing**, trachea in midline, normal chest expansion, resonance on percussion both lungs, normal breath sound, **bilateral fine crepitation at both lower lungs.**
- Abdomen: **mild abdominal distention, mild tender at RUQ abdomen**, normal bowel sound, no shifting dullness, **liver span 14 cm.**, no splenic dullness
- Extremity & skin: **bilateral pitting edema 3+**, no rash, no eschar, no petechiae, no PPE, no needle mark
- Lymph node: no lymphadenopathy
- Neurological examination: within normal limit.

Case 6: A young Thai female with teenage pregnancy

Hb (g/L)	9.8
Hct (%)	30.6
Wbc (/ul)	10,200
Pmn (%)	77.4
Lymp (%)	17.6
Mono (%)	3.7
Eo (%)	1.1
Baso (%)	0.2
Plt (/ul)	240,000
MCV (fl)	72.3
RDW (%)	15.7
MPV (fl)	12.8
MCH (pg)	23.2
MCHC (g/dl)	32

BUN (mg/dl)	11.8
Cr (mg/dl)	0.6
eGFR (mL/min/1.73 m^2)	91.24
Sodium (mEq/L)	137
Potassium (mEq/L)	3.68
Chloride (mEq/L)	106.5
Bicarbonate (mEq/L)	15

Albumin (g/dL)	2.56
Globulin (g/dL)	4.1
TB (mg/dl)	1.2
DB (mg/dl)	1.1
AST (U/L)	43
ALT (U/L)	18.4
ALP (U/L)	82



Echocardiogram: Dilated LV, severely impaired LV systolic function with global hypokinesia LVEF 30-35%

Dilated RV, Mild MR, Mild AR, mild TR

Case 6: A young Thai female with teenage pregnancy

Screening for drugs and drugs of abuse

- Amphetamine/metabolites: detected
- Benzodiazepine /metabolites: detected
- Nicotine /metabolites: detected

Initial laboratory assessment

- Anti-HIV: reactive (2 samples)
- CD4+ T cell: 700 cell/µL (37.8%)
- HBsAg: non-reactive, Anti-HBS: negative
- Anti-HCV: negative
- RPR : non-reactive, TPHA: negative

Case 6: A young Thai female with teenage pregnancy

Problem list

- Dilated cardiomyopathy with biventricular heart failure
    - Ddx: Post-partum cardiomyopathy, amphetamine induced cardiomyopathy
- Illicit drug use; amphetamine
- Acute kidney injury; cardiorenal types 1
- Asymptomatic HIV infection

HIV-1 viral load: < 20 copies/mL

Case 6: A young Thai female with teenage pregnancy

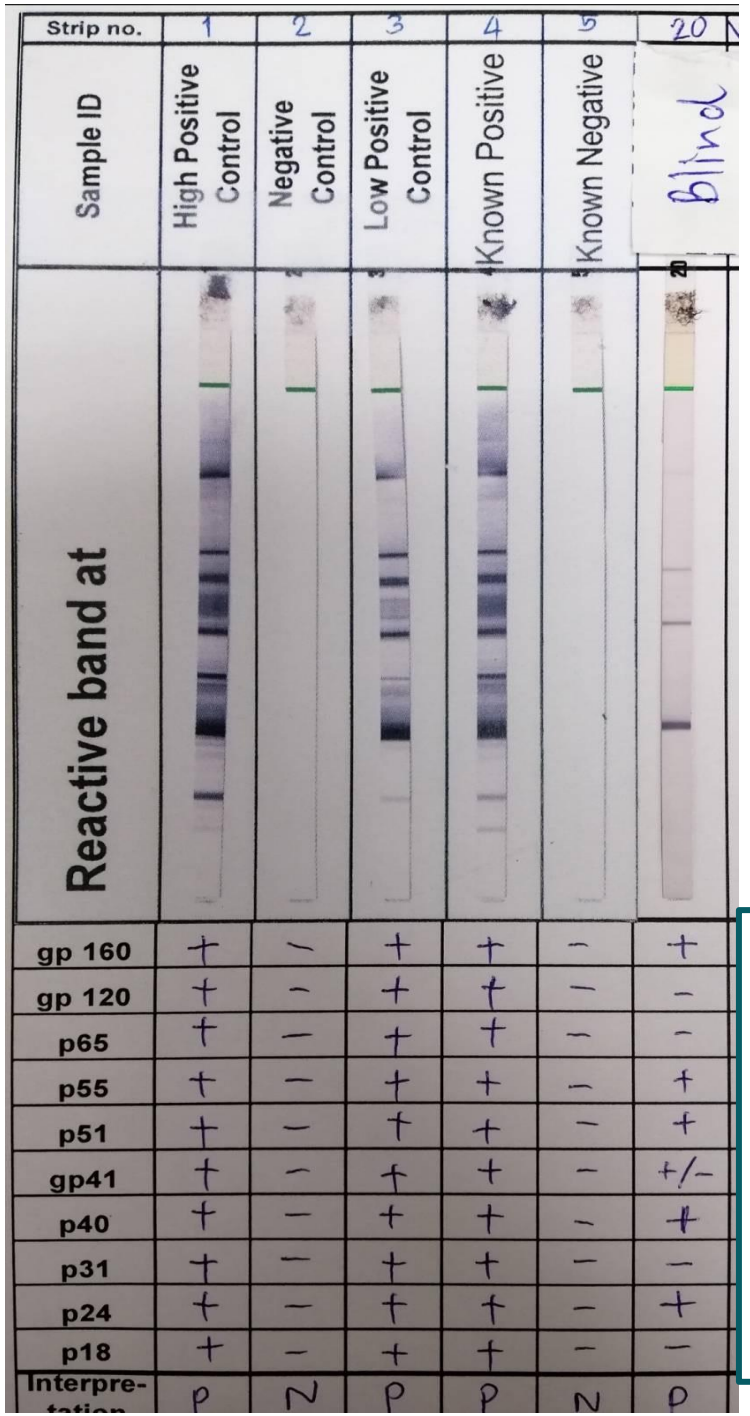
- 4^{th} generation ELISA anti-HIV: Reactive

[OD; 150, p24Ag ; positive, HIV Ab; reactive x 2 technique, HIV immunochromatographic test: positive]

- HIV-1 viral load: < 20 copies/mL

Is she infected with HIV?

Case 6: A young Thai female with teenage pregnancy



gp 160: Positive
gp 120: Negative
p 65: Negative
p55: Positive
pP51:Positive
gp41: +/-
p40: Positive
p31: Negative
p24:Positive
p18: Negative

Suspected HIV-1 infection (elite controller)

"HIV type 1 (HIV-1) elite controllers (ECs) represent a rare group of individuals with an ability to maintain an undetectable HIV-1 viral load overtime in the absence of previous antiretroviral therapy."

Interpretation: **positive HIV-1**

Case 6: Initiation of Antiretroviral Therapy, When and What to start?

- **Problem lists:**
- Suspected elite controller HIV-1 infection
- Dilated cardiomyopathy with biventricular heart failure
  - Ddx: Post-partum cardiomyopathy, amphetamine induced cardiomyopathy
- Illicit drug use; amphetamine
- Teenage pregnancy

Elite HIV Controllers

- HIV type 1 (HIV-1) elite controllers (ECs) represent a rare group (<1%) of individuals with an ability to maintain an undetectable HIV-1 viral load overtime in the absence of previous antiretroviral therapy.
  - Viremic controllers (VCs) were defined as having plasma HIV-1 RNA loads below 2000 copies/mL [≥3 measurements over 12 months without ART]
  - Long-Term Nonprogressors (LTNP): a small group of people with HIV who do not take ART and still maintain CD4 counts in the normal range indefinitely.
- **Clinical outcome in ECs**
  - Increased risk of all causes of hospitalizations esp. cardiovascular and psychiatric disease compared with medically controlled individuals with HIV -1
  - Significantly increased atherosclerotic plaques
  - Significantly higher inflammatory markers (sCD163, sCD14, hsIL6 and CXCL10)
  - May be decreased in CD4+T cell as a result of a reduced thymic output.

1. Gebara NY, El Kamari V, Rizk N. HIV-1 elite controllers: an immunovirological review and clinical perspectives. J Virus Erad. 2019;5(3):163-166.
2. Groves KC, Bibby DF, Clark DA, Isaksen A, Deayton JR, Anderson J, Orkin C, Stagg AJ, McKnight A. Disease Progression in HIV-1-Infected Viremic Controllers. J Acquir Immune Defic Syndr. 2012 ;61(4):407-16.

Elite HIV Controllers

- There are limited data on the benefits of initiating ART in ECs.
- Given that ongoing HIV replication occurs even in elite controllers, **ART is strongly recommended for controllers with evidence of HIV disease progression**, which is defined by declining CD4 counts or the development of HIV-related complications (AIII)
- **If ART is withheld**, elite controllers should be **followed closely**, as some may experience CD4 cell decline, loss of viral control, or complications related to HIV infection.

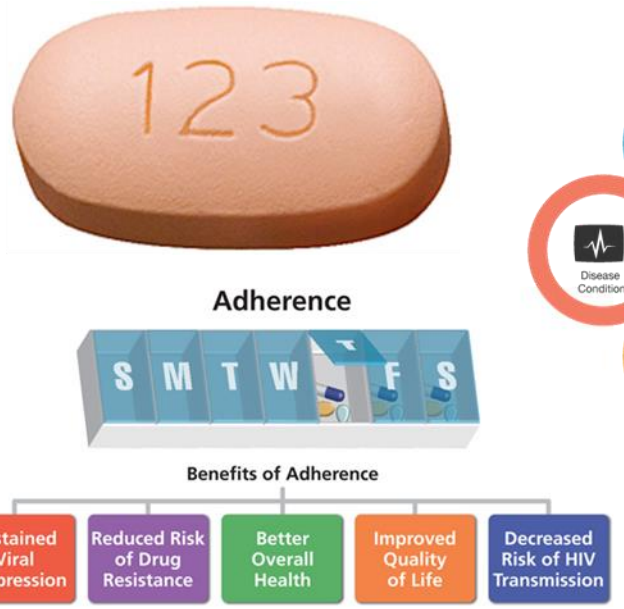
Case 6: A young Thai female with teenage pregnancy

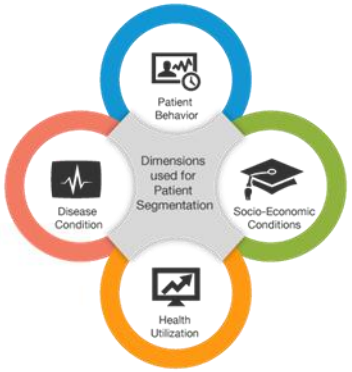
Date	Progression
July 2018	- First diagnosis HIV infection - HIV-1 VL < 20 copies/mL
February 2019	- No ARV - HIV-1 VL 145 copies/mL
August 2019	- OPD ID: DCM, limited activity - HIV-1 VL 55 copies/mL
October 2019	- Visit ED: decompensated heart failure, withdraw consent for continuing treatment.

Q & A

Thank You


HIV TREATMENT
as PREVENTION
A HIGHLY EFFECTIVE STRATEGY TO PREVENT THE SEXUAL TRANSMISSION OF HIV
People living with HIV who take
HIV medication daily
as prescribed
and get and keep an
undetectable viral load
have effectively no risk of
sexually transmitting HIV
to their HIV-negative partners
LEARN MORE AT HIV.GOV/TASP


123
Adherence
S M T W T F S
Benefits of Adherence
Sustained Viral Suppression
Reduced Risk of Drug Resistance
Better Overall Health
Improved Quality of Life
Decreased Risk of HIV Transmission


Patient Behavior
Disease Condition
Dimensions used for Patient Segmentation
Socio-Economic Conditions
Health Utilization