

## COMMON PITFALLS IN HIV/AIDS MANAGEMENT: A CASE-BASED APPROACH

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### A 41 Year-old Male

- Jul 14: This patient was transferred from OSH with a symptom of chronic headache for 2 weeks with alteration of consciousness. CT scan of the brain showed diffuse leptomeningeal enhancement without mass. Serum CRAG was positive. Upon admission, PE revealed oral candidiasis and hepatosplenomegaly. He had sluggish response to command and stiff neck was positive. Anti-HIV was positive.
- CBC: Hct 21%, WBC 2,500/ml, N58 %, Plt 54,000/UL. BUN/Cr: 30/1.4.
- *Amphotericin B* was started and he was transferred to BIDI.
- CSF finding: WBC 3-5 cells/HPF, positive india ink 3-5 cells/HPF, AFB-ve, CSF C/S: *Cryptococcus neoforman*

## Outline

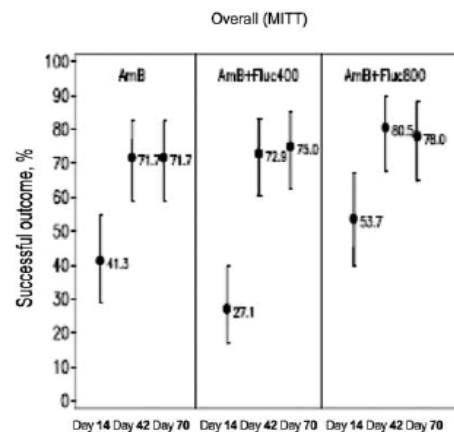
- Considerations for antiretroviral use in patients with coinfections
- Concerning and how to manage drug-drug interactions
  - ARV-other drugs
  - ARV-ARV drugs
- Developing ARV resistance and management

### Q1: What anti-fungal regimen would you start?

1. Amphotericin B
2. Fluconazole
3. Amphotericin B + fluconazole
4. Amphotericin B + flucytosine
5. Something else

# Treatment in HIV-Infected Pts

## Amphotericin B plus Fluconazole 800 mg/day



Successful outcomes at day 14

41% in **AmpB** alone

27% in **AmpB+Flu 400** mg/day

54% in **AmpB+Flu 800** mg/day

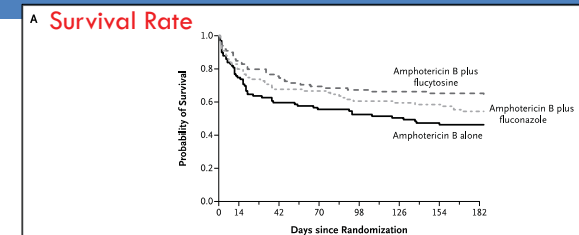
A trend towards better outcomes in the combination therapy arms was seen at days 42 and 70

Efficacy end point was a composite end :1. CSF conversion to negative culture results, 2. stable neurological function, and 3. survival at day 14.

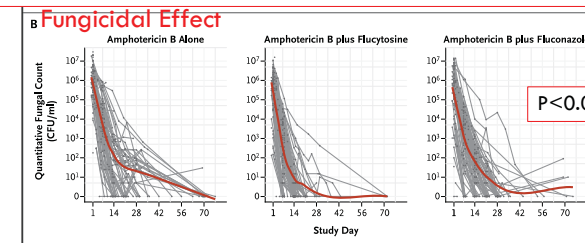
Pappas P, et al. Clin Infect Dis 2009; 48:1775–83.

# Combination Antifungal Therapy for Cryptococcal Meningitis:

## Amp B vs. Amp B + Flucytosine vs. Amp B + Fluconazole



For mortality at 70 days,  $P=0.04$  for the comparison of amphotericin B plus flucytosine with amphotericin B monotherapy, and  $P=0.13$  for the comparison of amphotericin B plus fluconazole with amphotericin B monotherapy.

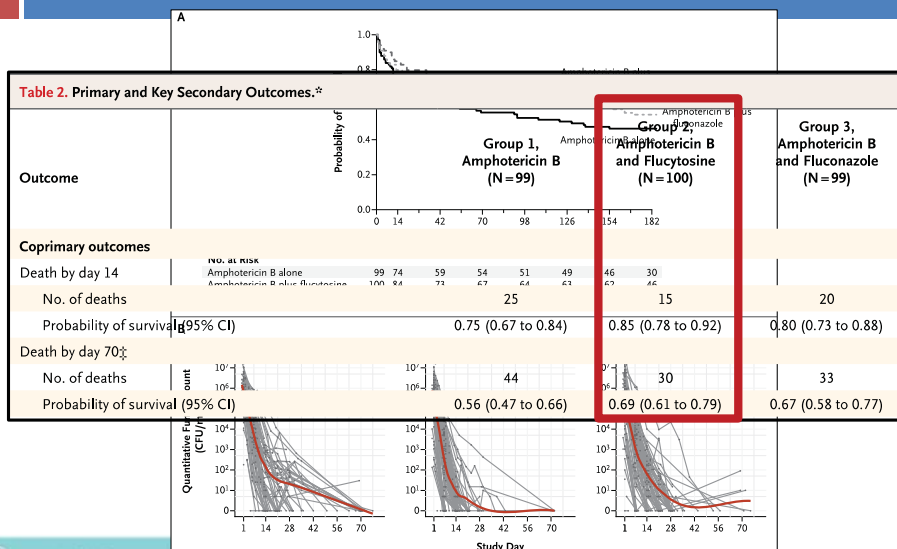


$P<0.001$  for all comparisons

Jeremy D, et al. N Engl J Med 2013;368:1291-302.

# Combination Antifungal Therapy for Cryptococcal Meningitis:

## AmB vs. AmB + Flucy vs. AmB + Fluco



Jeremy D, N Engl J Med 2013;368:1291-302.

# Induction Phase: 2 weeks

IDSA 2010	Thai 2014	WHO 2011	CDC 2013
<b>Preferred Regimens</b> -AmB 0.7-1.0 + FC -Lipo AmB 3-4 + FC	<b>Preferred Regimens</b> -AmB 1.0 -AmB 0.7-1.0 + Flu 800	<b>Preferred Regimens</b> -AmB 0.7-1.0 + FC -AmB 0.7-1.0 + Flu 800	<b>Preferred Regimens</b> -Lipo AmB 3-4 + FC
<b>Alternative Regimens</b> -AmB + Flu -Flu +FC -Flu -Itra	<b>Alternative Regimens</b> -Flu 1200	<b>Alternative Regimens</b> -AmB 0.7-1.0 (5-7 d) + Flu 800 (2 wk) -Flu 1200 + FC -Flu 1200	<b>Alternative Regimens</b> -ABLC 5 + Flu -AmB 0.7-1.0 + FC -Lipo AmB 3-4 + Flu 800 -AmB 0.7-1.0 + Flu 800
FC intolerance (4-6wk) - AmB 0.7-1.0 - Lipo AmB 3-4 - ABLC 5			

## Induction Phase: 2 weeks

IDSA 2010	Thai 2014	WHO 2011	CDC 2013
Preferred Regimens -AmB 0.7-1.0 + FC -Lipo AmB 3-4 + FC	Preferred Regimens -AmB 1.0 -AmB 0.7-1.0 + Flu 800	Preferred Regimens -AmB 0.7-1.0 + FC -AmB 0.7-1.0 + Flu 800	Preferred Regimens -Lipo AmB 3-4 + FC

Four considerations for AmB, lipo AmB, FC, Fluco	Efficacy	Adverse events
1. AmB vs. Lipo AmB	=	>
2. With FC vs. without FC	> (CSF sterilization & survival benefit)	>
3. With Flu vs. without Flu	> (Only CSF sterilization)	> (minimal)
4. FC vs. Flu	>	>

## Consolidation Phase: 8 weeks

IDSA 2010	Thai 2014	WHO 2011	CDC 2013
Preferred Regimens -Flu 400	Preferred Regimens -Flu 400-800	Preferred Regimens -Fluconazole 400-800 (after 2-wk AmB) -Fluconazole 800 (after 1-wk AmB of Flu)	Preferred Regimens -Flu 400
	Alternative Regimens -Itra 400		Alternative Regimens -Itra 400

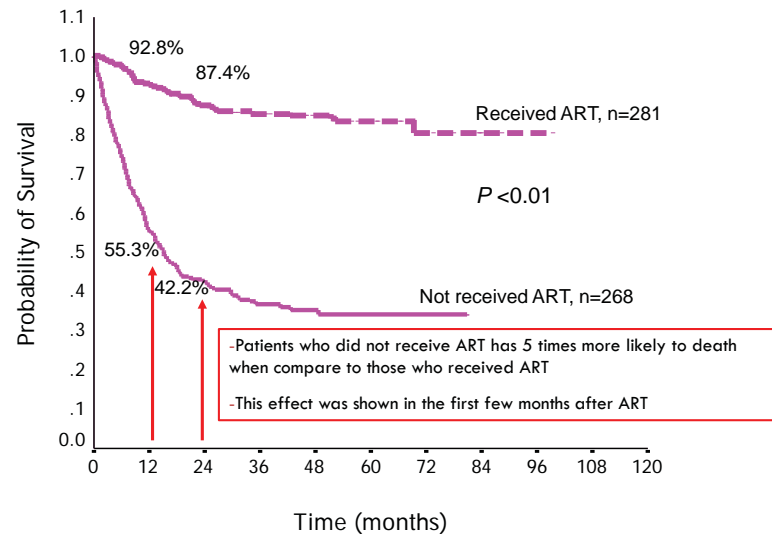
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- Amphotericin B + Fluconazole were given.
- Bone marrow Biopsy: Normocellular marrow, No granuloma, No organism
- HBsAg-positive but anti-HCV-negative

## Q2: When would you start ART after starting fungal treatment in this patient?

- ☐ 1 week
- ☐ 2 weeks
- ☐ 4 weeks
- ☐ 8 weeks
- ☐ Others

## ART Improved Survival Rate in Patients with CM



Chottanapund S, Manosuthi W, et al. J Med Assoc Thai 2007;90:2104.

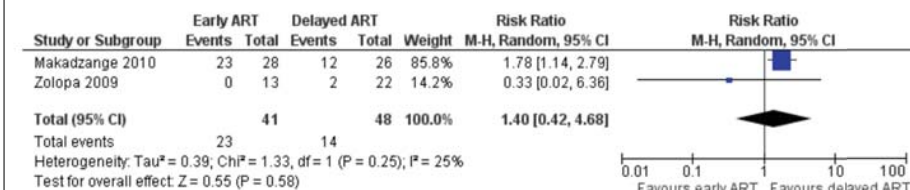
## Potential Advantages and Disadvantages of “Starting ART early in CNS OIs”

Potential advantages of early initiation of ART	
Prevent progressive immunodeficiency	Yes
More rapid immune recovery	Yes
More rapid resolution of OI	Yes
Rapid reduction in mortality risk	No No
Prevention of further OIs and other morbidity	Yes

Potential disadvantages of early initiation of ART	
High pill burden	Yes
Co-toxicity	Yes Yes
Pharmacokinetic drug interactions	Yes
Immune reconstitution disease	Yes Yes (and serious)
More difficult to identify drug causing toxicity	Yes

## Optimal timing for ART initiation in patients with HIV infection and concurrent CM

Figure 4. Forest plot of comparison: I Early ART initiation versus delayed ART initiation, outcome: I. Death.



- Insufficient evidence in support of either early or late initiation of ART.
- Because of the high risk IRIS in patients with cryptococcal meningitis, we recommend that ART initiation should be delayed

•Njei B, et al. Cochrane Database Syst Rev. 2013.

The NEW ENGLAND JOURNAL of MEDICINE

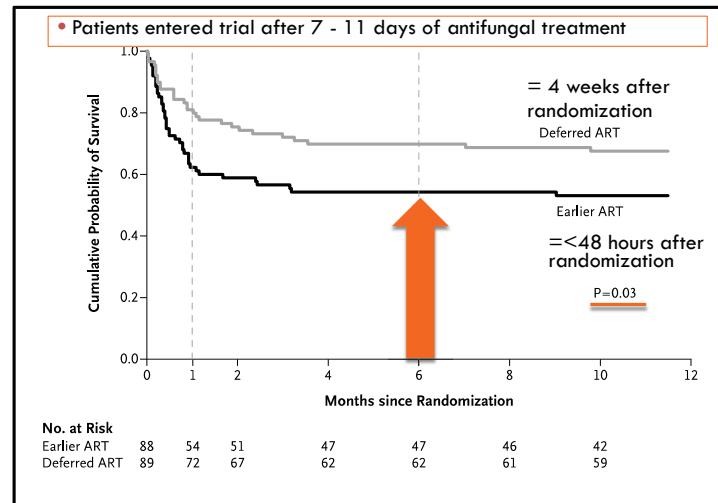
### ORIGINAL ARTICLE

## Timing of Antiretroviral Therapy after Diagnosis of Cryptococcal Meningitis

David R. Boulware, M.D., M.P.H., David B. Mehta, M.Med., Conrad Muzoor, M.Med., Melissa A. Rolfes, Ph.D., Katherine Huppler Hullsiek, Ph.D., Abdu Musubire, M.Med., Kabanda Taseera, M.Med., Henry W. Nabeta, M.B., Ch.B., Charlotte Schutz, M.B., Ch.B., M.P.H., Darlisha A. Williams, M.P.H., Radha Rajasingham, M.D., Joshua Rhein, M.D., Friedrich Thienemann, M.D., Ph.D., Melanie W. Lo, M.D., Kirsten Nielsen, Ph.D., Tracy L. Bergemann, Ph.D., Andrew Kambugu, M.Med., Yukari C. Manabe, M.D., Edward N. Janoff, M.D., Paul R. Bohjanen, M.D., Ph.D., Graeme Meintjes, M.B., Ch.B., Ph.D., for the COAT Trial Team\*

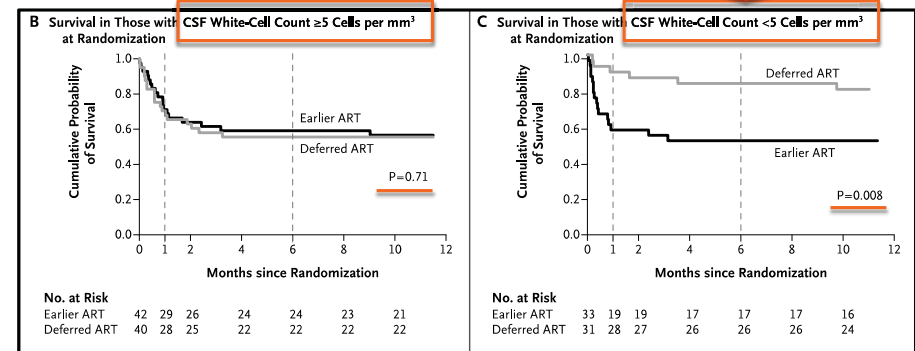
Boulware D, et al. N Engl J Med 2014;26:2487.

## Overall Survival



Boulware D, et al. N Engl J Med 2014;26:2487.

## Survival in Patients with CSF WBC $\geq 5$ and $< 5$ Cells/mm<sup>3</sup> at Randomization



Deferring ART for 5 weeks after diagnosis of cryptococcal meningitis was associated with significantly improved survival, as compared with initiating ART at 1 to 2 weeks, especially among patients with a paucity of white cells in cerebro- spinal fluid

Boulware D, et al. N Engl J Med 2014;26:2487.

Manosuthi et al. AIDS Research and Therapy (2015) 12:12  
DOI 10.1186/s12981-015-0053-z

### REVIEW

### Open Access

## Guidelines for antiretroviral therapy in HIV-1 infected adults and adolescents 2014, Thailand

**Table 2 Recommendations for antiretroviral therapy initiation in Thai HIV-infected adolescents and adults with active major opportunistic infections**

Opportunistic infections	$\leq 50$ cells/mm <sup>3</sup>		$> 50$ cells/mm <sup>3</sup>	
			More severe*	Less severe
Tuberculosis	Within 2 weeks		Within 2 weeks	Between 2–8 weeks
Cryptococcosis	Between 4–6 weeks			
Pneumocystis pneumonia	Between 2–4 weeks			
Mycobacterium avium complex infection				
Others				

Manosuthi W, et al. AIDS Research Therapy 2015;12:12.

## Q3: Would you perform HIV resistance testing before ART initiation in this case?

- ☐ I would
- ☐ I wouldn't
- ☐ Probably

## Q4: What ARV regimen would you prefer in this case?

- ☐ TDF/FTC + EFV
- ☐ TDF/FTC + NVP
- ☐ TDF/FTC + RPV
- ☐ TDF/FC + PI/r



การประเมินผลของการรักษาด้วยยาต้านไวรัส HIV 41 - ผลการประเมินผลของการรักษาด้วยยาต้านไวรัส HIV

## Q5: Would you change your mind to perform HIV resistance testing before ART?

- ☐ I would
- ☐ I wouldn't
- ☐ Probably

- He had a positive HBsAg.
- His additional history is that he had been on HBV treatment for more than one year and he had not taken it for 2 weeks during this illness.



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## HIV Drug Resistance Report

Drug	Viroseq Software v2.8 *	Stanford v6.3.1 **
NRTI	lamivudine, 3TC	Possible Resistance
	emtricitabine, FTC	Possible Resistance
	zidovudine, AZT	None
	didanosine, ddI	Possible Resistance
	stavudine, d4T	None
	abacavir, ABC	Possible Resistance
NNRTI	tenofovir, TDF	Resistance
	efavirenz, EFV	None
	nevirapine, NVP	None
	etravirine, ETR	None
	rilpivirine, RPV	None
	darunavir, DRV/r	None
PI	atazanavir, ATV/r	None
	tipranavir, TPV/r	None
	darunavir, DRV/r	None
	lopinavir, LPV/r	None
	atazanavir, ATV/r	None
	tipranavir, TPV/r	None

Drug resistance Mutation Identification		
Drug	Mutation	Resistance
NRTI	K65R	Susceptible
NNRTI	V106I/V117I	Potential low-level resistance
PI		



การประเมินผลของการรักษาด้วยยาต้านไวรัส HIV 41 - ผลการประเมินผลของการรักษาด้วยยาต้านไวรัส HIV

## HIV and HBV co-infection

- ☐ “FTC, 3TC, and TDF” have activity against both HIV and HBV
  - If HBV or HIV treatment is needed
    - ART should be initiated with combination of TDF/FTC or TDF/3TC as NRTI backbone
- ☐ If HBV treatment is needed and TDF cannot safely be used
  - Alternative recommended HBV therapy is entecavir in addition to a fully suppressive ARV regimen
  - Other HBV Rx regimens include
    - Peginterferon alfa monotherapy or adefovir in combination with 3TC or FTC
    - Telbivudine in addition to a fully suppressive ARV regimen



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## HIV and HBV co-infection

- “Entecavir”, “3TC or FTC”, and “Tenofovir” have activity against HIV
  - Their uses for HBV treatment without ART in patients with dual infection may result in selection of...
    - M184V: Entecavir, 3TC, FTC
    - K65R: TDF
  - Entecavir must be used in addition to a fully suppressive ARV regimen
  - Entecavir should not be considered to be a part of ARV regimen
- If ART needs to be modified due to HIV virologic failure and patient has adequate HBV suppression
  - ARV drugs active against HBV **should be continued** for HBV treatment in combination with other suitable ARV agents to achieve HIV suppression

DHHS Guideline 2015

## Thai HBV Treatment Guideline 2555

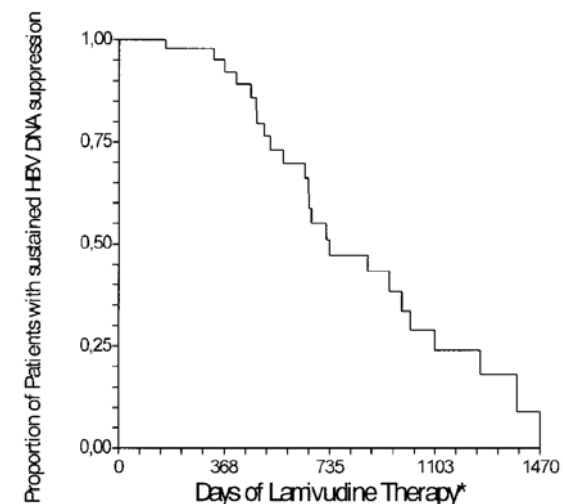
ผู้ป่วยที่ตรวจพบ HBeAg ให้ผลลบ

1. ตรวจพบ HBsAg ในเลือดไม่ต่ำกว่า 6 เดือน
2. ปริมาณ HBV DNA ในเลือดมากกว่าหรือเท่ากับ 2,000 IU/ml
3. ระดับซีรัม ALT มากกว่าหรือเท่ากับ 2 เท่าของค่าปกติ อย่างน้อย 2 ครั้ง ในระยะเวลาไม่น้อยกว่า 3 เดือนขึ้นไป
4. ผู้ป่วยที่ตรวจพบหลักฐานว่ามีพังผืดในตับมากแล้ว โดยพบ fibrosis stage 3-4 หรือ มีลักษณะทางคลินิกที่จะเกิดภาวะ hepatic decompensation ร่วมกับการตรวจพบ HBV DNA ในเลือด ควรให้การรักษาแม้พบระดับซีรัม ALT อยู่ในเกณฑ์ปกติ
5. ผู้ป่วยที่ตรวจพบระดับซีรัม ALT สูงผิดปกติแต่มีน้อยกว่า 2 เท่าของค่าปกติ ควรมีการตรวจหาพยาธิสภาพของตับด้วยการตรวจชิ้นเนื้อตับหรือวิธีอื่นๆ เพื่อยืนยันว่าภาวะตับอักเสบมีสาเหตุจากการติดเชื้อไวรัสตับอักเสบ บี ร่วมกับมีลักษณะทางพยาธิวิทยาบ่งชี้ว่ามีการเปลี่ยนแปลงภายในเนื้อเยื่อในระหว่างที่ควรให้การรักษา โดยพบมีการอักเสบทำลายเนื้อตับ (necroinflammation) ตามระบบ HAI มากกว่าหรือเท่ากับ 4 หรือ ระบบ Metavir มากกว่าหรือเท่ากับ 2 หรือมีลักษณะพังผืดในเนื้อตับโดยพบพังผืดในเนื้อตับ (significant fibrosis) ตามระบบ Metavir มากกว่าหรือเท่ากับ 2 หรือ ระบบ Ishak มากกว่าหรือเท่ากับ 3 หรือตรวจพบความยืดหยุ่นของตับสูงกว่า 7 kPa
6. ผู้ป่วยที่ตรวจพบระดับซีรัม ALT อยู่ในเกณฑ์ปกติ แต่มีปัจจัยเสี่ยงต่อการเกิดโรคตับเรื้อรัง ได้แก่ เป็นผู้ชาย อายุมากกว่า 40 ปี มีประวัติดื่มแอลกอฮอล์เป็นประจำ ตรวจร่างกายพบลักษณะทางคลินิกบ่งชี้โรคตับเรื้อรัง (chronic liver stigmata) ควรตรวจประเมินพยาธิสภาพของตับด้วยการตรวจชิ้นเนื้อตับหรือวิธีอื่นๆ เพื่อยืนยันว่าผู้ป่วยมีโรคตับอยู่ในระยะที่ควรให้การรักษาโดยตรวจพบมีการอักเสบทำลายเนื้อตับตามระบบ HAI มากกว่าหรือเท่ากับ 4 หรือ ระบบ Metavir มากกว่าหรือเท่ากับ 2 หรือมีลักษณะพังผืดในเนื้อตับโดยพบพังผืดในเนื้อตับตามระบบ Metavir มากกว่าหรือเท่ากับ 2 หรือ ระบบ Ishak มากกว่าหรือเท่ากับ 3 หรือตรวจพบความยืดหยุ่นของตับสูงกว่า 7 kPa
7. ตรวจหา HCV Ab, HIV Ab และ HAV Ab ในเลือดก่อนการรักษาทุกราย
8. ผู้ป่วยที่ติดเชื้อไวรัสตับอักเสบ บี ควรคิดค่าเฉลี่ยของผลตอบสนอง

## Q6: What ARV regimen would you prefer in this case?

- TDF/FTC + NNRTI
- TDF/FTC + NNRTI + PI/r
- 3TC + NNRTI + PI/r
- NNRTI + PI/r
- Something else

## HBV resistance to 3TC in HIV Patients



Hepatology 1999;30:1302-6.



## Case 2: SK 37 year-old male

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- **Aug 09:** Presented with fever, shortness of breath and weight loss in 2 weeks. Chest X-ray showed bilateral interstitial infiltrations. PCP was diagnosed and cotrimoxazole was given. His baseline ALT was 37 U/L and Cr 0.6 mg/dL. HBs Ag and HBeAg were positive but anti-HCV was negative.
- **Sep 09:** CD4 was 102 (8%). AZT/3TC/EFV was initiated.
- **Mar 10:** CD4 was 211 (14%).
- **Oct 10:** CD4 was 113 (7%) and plasma HIV-1 RNA was 4.1 log. Genotypic resistant test showed K103N, M184V, and D67N. ART was changed to TDF/AZT/LPV/r. **rtv.**

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**Q7: Any concern raised at this moment?**

1. No, it should be fine
2. There are some issues

## H2 antagonist and PPI to ATV/r

	RTV-boosted PIs	
	ATV/r	↓ ATV
H <sub>2</sub> receptor antagonists	DRV/r, LPV/r	No significant effect
	ATV	↓ ATV
PIs without RTV		
	ATV	↓ ATV
	FPV	APV AUC ↓ 30%; no significant change in APV C <sub>max</sub>

H<sub>2</sub> receptor antagonist dose should not exceed a dose equivalent to famotidine 40 mg BID in ART-naïve patients or 20 mg BID in ART-experienced patients.

Give ATV 300 mg + RTV 100 mg simultaneously with and/or ≥10 hours after the H<sub>2</sub> receptor antagonist.

If using TDF and H<sub>2</sub> receptor antagonist in ART-experienced patients, use ATV 400 mg + RTV 100 mg.

H<sub>2</sub> receptor antagonist single dose should not exceed a dose equivalent of famotidine 20 mg or total daily dose equivalent of famotidine 20 mg BID in ART-naïve patients.

Give ATV at least 2 hours before and at least 10 hours after the H<sub>2</sub> receptor antagonist.

Give FPV at least 2 hours before H<sub>2</sub> receptor antagonist if concomitant use is necessary. Consider boosting with RTV.



## H2 antagonist and PPI to ATV/r

RTV-boosted PIs			
H <sub>2</sub> receptor antagonists	ATV/r	↓ ATV	H <sub>2</sub> receptor antagonist dose should not exceed a dose equivalent to famotidine 40 mg BID in ART-naïve patients or 20 mg BID in ART-experienced patients.  Give ATV 300 mg + RTV 100 mg simultaneously with and/or ≥10 hours after the H <sub>2</sub> receptor antagonist.  If using TDF and H <sub>2</sub> receptor antagonist in ART-experienced patients, use ATV 400 mg + RTV 100 mg.
	DRV/r, LPV/r	No significant effect	
PIs without RTV			
Proton pump inhibitors (PPIs)	ATV	↓ ATV	H <sub>2</sub> receptor antagonist single dose should not exceed a dose equivalent of famotidine 20 mg or total daily dose equivalent of famotidine 20 mg BID in ART-naïve patients.  Give ATV at least 2 hours before and at least 10 hours after the H <sub>2</sub> receptor antagonist.
	FPV	APV AUC ↓ 30%; no significant change in APV C <sub>max</sub>	Give FPV at least 2 hours before H <sub>2</sub> receptor antagonist if concomitant use is necessary. Consider boosting with RTV.
Proton pump inhibitors (PPIs)	ATV	↓ ATV	PPIs are not recommended in patients receiving unboosted ATV. In these patients, consider alternative acid-reducing agents, RTV boosting, or alternative PIs.
	ATV/r	↓ ATV	PPIs should not exceed a dose equivalent to omeprazole 20 mg daily in PI-naïve patients. PPIs should be administered at least 12 hours prior to ATV/r.  PPIs are not recommended in PI-experienced patients.

Guidelines for the Use of Antiretroviral January 2012. <http://www.aids>

## Case 1: SK 37 year-old male

- Aug 09: Presented with fever, shortness of breath and weight loss in 2 weeks. Chest X-ray showed bilateral interstitial infiltrations. PCP was diagnosed and cotrimoxazole was given. His baseline ALT was 37 U/L and Cr 0.6 mg/dL.
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- 2 weeks later: Fever and cervical lymphadenitis occurred. TB cervical lymphadenitis was diagnosed. IRZE was started

กรมรณรงค์ลดเชื้อไวรัส HIV 41 กรุงเทพมหานคร

## Case 1: SK 37 year-old male

- Aug 11: plasma HIV-1 RNA was 4.8 log. Genotypic resistant test showed **multiple RAMs**.

Resistance associated RT Mutations: M41L, E44D, D67N, V75M, V106A, V118I, M184V, G190A, L210W, T215Y, K219R, F227L	
Nucleoside and Nucleotide RT Inhibitors	Resistance Interpretation
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didanosine (ddI)	Resistance
lamivudine (3TC)/emtricitabine (FTC)	Resistance
stavudine (d4T)	Resistance
tenofovir (TDF)	Resistance
zidovudine (AZT)	Resistance
NonNucleoside RT Inhibitors	Resistance Interpretation
efavirenz (EFV)	Possible Resistance
etravirine (ETR)	No Evidence of Resistance
nevirapine (NVP)	Resistance
Resistance associated PR Mutations: L10I, K20R, M36I, M46I, L76V, I84V	
Protease Inhibitors	Resistance Interpretation
atazanavir (ATV)	Resistance
ATV/r **	Resistance
darunavir + ritonavir (DRV/r)	No Evidence of Resistance
fosamprenavir (FPV)	Resistance
FPV/r **	Resistance
indinavir (IDV)	Resistance
IDV/r **	Resistance
lopinavir + ritonavir (LPV/r)	Resistance
nefinavir (NFV)	Resistance
saquinavir + ritonavir (SQV/r)	Resistance
tipranavir + ritonavir (TPV/r)	No Evidence of Resistance

\*\* Protease inhibitors administered with low-dose ritonavir for pharmacological boosting

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Q8: What is the most likely cause of treatment failure in this patients?

- Poor adherence
- Adverse events
- Others

กรมรณรงค์ลดเชื้อไวรัส HIV 41 กรุงเทพมหานคร

## Rifampicin markedly decreases blood levels of all protease inhibitors

PI	Effect of rifampicin
Saquinavir	↓ 80%
Ritonavir	↓ 35%
Indinavir	↓ 90%
Nelfinavir	↓ 82%
Amprenavir	↓ 81%
Lopinavir/ritonavir	↓ 75%

- Boosted PI cannot be given with rifampicin, since PI levels are reduced by ~90%
- Combination of saquinavir (400 mg twice daily) and ritonavir (400 mg twice daily) or doubling of the usual dose of lopinavir/ritonavir can be considered; however, increase risk of hepatotoxicity<sup>1-3</sup>

<sup>1</sup> Veldkamp AI, et al. CID 1999;29;1586.

<sup>2</sup> Gray A, et al. AIDS 2006;20;302. <sup>3</sup> La Porte CJ, et al. AAC2004;48;1553.

## TB and HIV Co-infection: Drug-Drug Interactions

- Rifamycins should be included in TB regimens
- Many potential drug interactions with rifamycins and ARVs:
  - PIs and NNRTIs:
    - Rifampin may be used only with EFV or NVP
    - Rifampin may not be used with RTV-boosted PIs
    - Rifabutin recommended with NVP, other PIs
      - Dosage adjustment may be necessary
      - Optimal dosage not defined (in patients on PIs + intermittent rifabutin, low rifabutin levels and rifamycin resistance has been reported); monitor drug levels if possible
  - MVC: requires dosage increase when used with rifampin
  - RAL: Can be used with rifampin

## Thai Guideline 2014: ART and anti-TB Initiation

การเริ่มยารักษาโรคในผู้ป่วยกำลังได้ยาด้านไวรัส

- กรณีผู้ป่วยกำลังได้ยาด้านไวรัสสูตร NNRTIs ทั้ง efavirenz และ nevirapine ให้สูตรยารักษาโรคตามปกติ
- กรณีผู้ป่วยกำลังได้ยาด้านไวรัสสูตรที่มี protease inhibitor ให้พิจารณาดังนี้
  - 1. ปรับยา protease inhibitor เป็นสูตรที่มี NNRTIs (พิจารณา ยา efavirenz ก่อน nevirapine) หรือ integrase inhibitor (ได้แก่ raltegravir) เป็นส่วนประกอบแทน และให้สูตรยารักษาโรคตามปกติ ทั้งนี้ตรวจสอบและควรระวังว่าผู้ป่วยไม่เคยมีประวัติแพ้ยาหรือแพ้ยาที่กำลังจะเปลี่ยน
  - 2. ถ้าไม่สามารถใช้ NNRTIs และ integrase inhibitor ได้ ให้พิจารณาปรับสูตรยารักษาโรคเป็น 2IEZ+quinolone/10-16IE+quinolone อาจพิจารณาเพิ่ม streptomycin ในช่วง 2 เดือนแรก

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NonNucleoside RT Inhibitors	Resistance Interpretation
efavirenz (EFV)	Possible Resistance
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nevirapine (NVP)	Resistance

Q9: Does Etravirine remain active?

1. It does
2. It doesn't
3. May be

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NonNucleoside RT Inhibitors	Resistance Interpretation
efavirenz (EFV)	Possible Resistance
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nevirapine (NVP)	Resistance

Q10: Does Rilpivirine remain active?

1. It does
2. It doesn't
3. May be

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zidovudine (AZT)	Resistance
Nucleoside RT Inhibitors	Resistance Interpretation
efavirenz (EFV)	Possible Resistance
etravirine (ETR)	No Evidence of Resistance
nevirapine (NVP)	Resistance

Oct 10: K103N, M184V, and D67N. (On AZT, 3TC, EFV)

Resistance associated RT Mutations: M41L, E44D, D67N, V75M, V106A, V118I, M184V*, G190A, L210W, T215Y*, K219R, F227L	
Nucleoside and Nucleotide RT Inhibitors	Resistance Interpretation
abacavir (ABC)	Resistance
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lamivudine (3TC)/emtricitabine (FTC)	Resistance
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tenofovir (TDF)	Resistance
zidovudine (AZT)	Resistance
Nucleoside RT Inhibitors	Resistance Interpretation
efavirenz (EFV)	Possible Resistance
etravirine (ETR)	No Evidence of Resistance
nevirapine (NVP)	Resistance

## NNRTI RAM: K103N

Nonnucleoside Analogue Reverse Transcriptase Inhibitors (NNRTIs)**	
Efavirenz	100 Y 1 102 106 108 181 188 190 225 230 I N M I C L S A H L
Etravirine	90 98 100 1 136 179 181 190 225 I G I+ A D Cr S A L
Nevirapine	100 Y 1 102 106 108 181 188 190 225 I N A I C C A L L
Rilpivirine	100 Y 1 136 179 181 188 221 227 230 I A C I Y Y C I L

### K103N

- Selected frequent by EFV
- Causes high-level resistance to NVP (~50-fold reduced susceptibility) and EFV (~20-fold reduced susceptibility)
- No effect on ETR and RPV? susceptibility

## Outline

- Considerations for antiretroviral use in patients with coinfections
- Concerning and how to manage drug-drug interactions
  - ARV-other drugs
  - ARV-ARV drugs
- Developing ARV resistance and management

THANK YOU



การประชุมนานาชาติการประติมาตร ครั้งที่ 41 - วิทยาศาสตร์เพื่อชีวิตและสังคม  
ระหว่างปี 25 - 26 พฤษภาคม 2563 ณ โรงแรมอิมพีเรียล แกรนด์ โฮเทล กรุงเทพฯ