Management of

OIs & Co-infections

2016

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Contents

- HBV co-infection
- HCV co-infection
- OIs
  - timing of ART
  - proper ARV regimen
  - adjunctive treatment

HIV and HBV, HCV coinfections

กลุ่มผู้ป่วยที่มีระดับ CD4 > 500 cells/mm^3 ร่วมกับอาการทางคลินิกตามต่อไปนี้ จะมีประโยชน์ของการเริ่มยาต้านไวรัสเร็ว

ประโยชน์รายบุคคล (Individual benefits)

- TB/HIV co-infection
- HBV/HIV co-infection with cirrhosis
- HCV/HIV co-infection with cirrhosis
- HIV-associated nephropathy (HIVAN)
- Acute/recent HIV infection

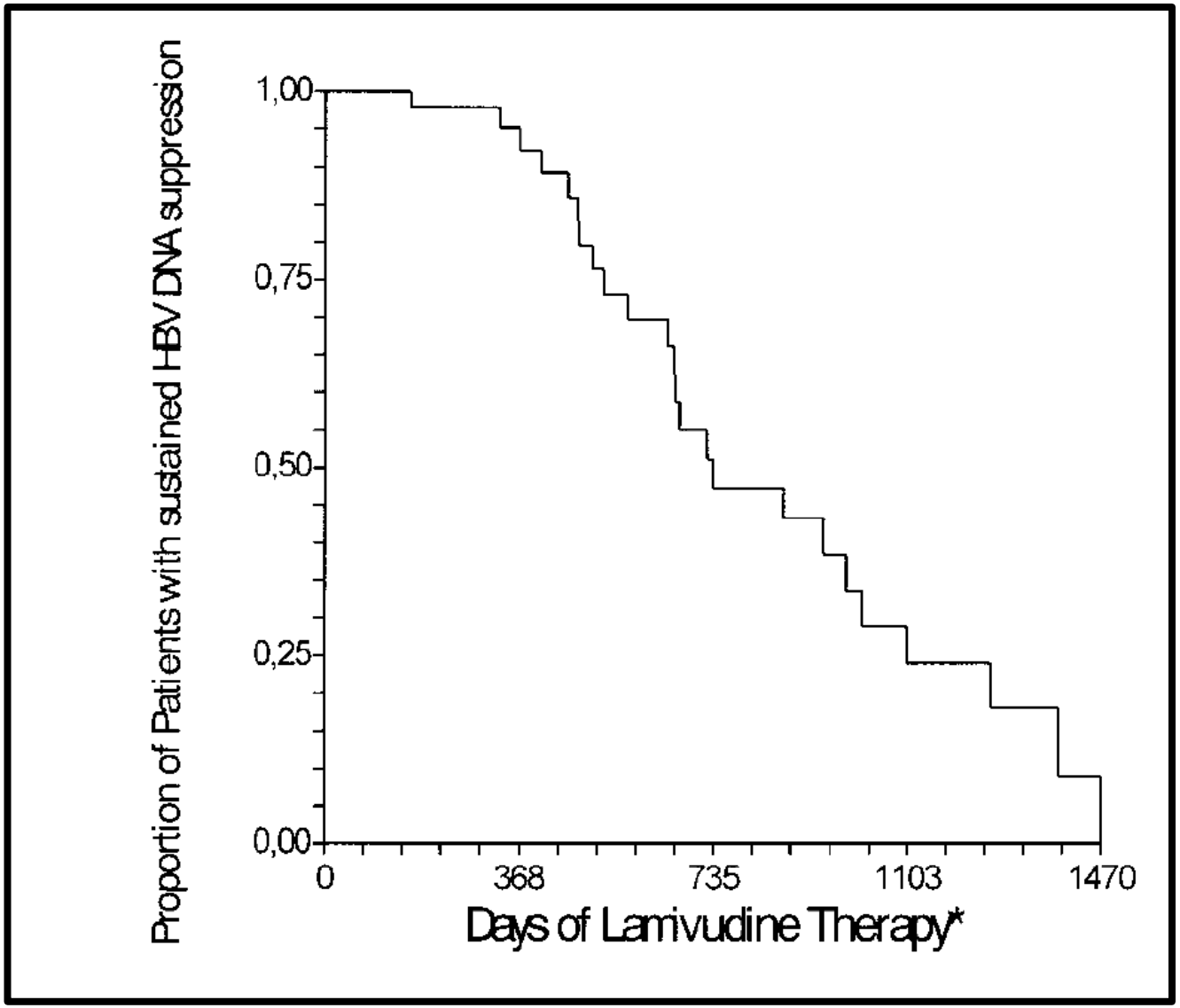
ประโยชน์ต่อการสาธารณสุข (Public health benefits)

- คู่ผลเลือดต่าง (Serodiscordant couples)
- ตั้งครรภ์
- TB/HIV co-infection
- Acute HIV infection

HIV and HBV coinfection

- ใช้ยาต้านไวรัสสูตรที่มี TDF + 3TC หรือ TDF/FTC
- ไม่ควรใช้ยาต้านไวรัสสูตรที่มี 3TC โดยที่ไม่มี TDF

HBV resistance to 3TC in HIV Patients



Benhamou Y, Bochet M, Thibault V, et al. Long-term incidence of hepatitis B virus resistance to lamivudine in humanimmunodeficiency virus-infected patients. Hepatology 1999;30(5):1302-6

การปรับขนาดยาตามการทำงานของไต

ตารางที่ 3.13 ขนาดยาปกติและการปรับขนาดยาต้านไวรัสในผู้ป่วยที่การทำงานของไตบกพร่อง

	eGFR หรือ CrCl (mL/min)[1]					Hemodialysis
	ขนาดปกติต่อวัน	≥ 50	30-49	10-29	< 10	
NRTIs						
3TC	300 mg ทุก 24 ชม. หรือ 150 mg ทุก 12 ชม.		150 mg ทุก 24 ชม.	100 mg ทุก 24 ชม.[2]	50-25 mg ทุก 24 ชม.[2]	50-25 mg ทุก 24 ชม.[2] AD[3]
TDF[4]	300 mg ทุก 24 ชม.		300 mg ทุก 48 ชม.	300 mg สัปดาห์ละ 2 ครั้ง	ไม่แนะนำ	300 mg ทุก 7 วัน AD[3]
TDF/FTC	1 เม็ด ทุก 24 ชม.		ทุก 48 ชม.	ไม่แนะนำ	ไม่แนะนำ	ไม่แนะนำ

หญิง 62 ปี บัตรทอง

HIV & HBV, on TDF 3TC LPV/r

ส่งตัวมารักษามะเร็งเต้านม

Baseline Cr 1.7, BW 41 kg

(Hx of NNRTI resistance, TAMs, M184V)

HBV:HBs Ag

Order date
04-03-14
11:50

Orderable Item	Value	Units	H/L	Ref Range	Perf. Lab
Result	**Positive**		*		**20**

	17-12-13 09:30	04-03-14 09:52	01-04-14 09:46
Glucose (NaF)			**102**
Creatinine	**1.81**	**1.95**	**2.06**
**eGFR(CKD-EPI equation)	29.54	27	25.26

	17-12-13 09:30	04-03-14 09:52	01-04-14 09:46
pH	6.5	6.0	6.0
Sp.Gr.(Refractometer)	1.005	1.016	1.019
Protein	NEG	++	++
Sugar	NEG	+++	+
Ketone	NEG	NEG	NEG

หญิง 62 ปี บัตรทอง

HIV & HBV, on TDF 3TC LPV/r

ส่งตัวมารักษามะเร็งเต้านม

Baseline Cr 1.7, BW 41 kg

(Hx of NNRTI resistance, TAMs, M184V)

Next ARV regimen?

- Adjusted dose TDF, 3TC LPV/r
- 3TC, d4T, LPV/r
- 3TC, LPV/r
- 3TC, LPV/r, RPV

HBV:HBs Ag

Order date
04-03-14
11:50

Orderable Item	Value	Units	H/L	Ref Range	Perf. Lab
Result	Positive	*			20

HIV-1:Viral load

Order dat
18-02-16
09:13

Orderable Item	Value	Units	H/L	Ref Range
SPECIMEN	Blood (EDTA)			
Result	< 40	copies/mL		

MOLECULAR DIAGNOSIS

Order dat
18-02-16

Orderable Item	Value	Units	H/L	Ref Rang
HBV Viral load				
HBV Viral load	< 20 IU/mL	IU/mL		

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    - timing of ART
    - proper ARV regimen
    - adjunctive treatment

Contents

- HBV co-infection
- HCV co-infection
- **OIs**: TB, Cryptococcosis
  - timing of ART
  - proper ARV regimen
  - adjunctive treatment

TB

- timing of ART
- proper ARV regimen
- adjunctive treatment

Potential Advantages of "Starting ART early in Non-CNS OIs vs. CNS OIs"

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

Potential Disadvantages of "Starting ART early in Non-CNS OIs vs. CNS OIs"

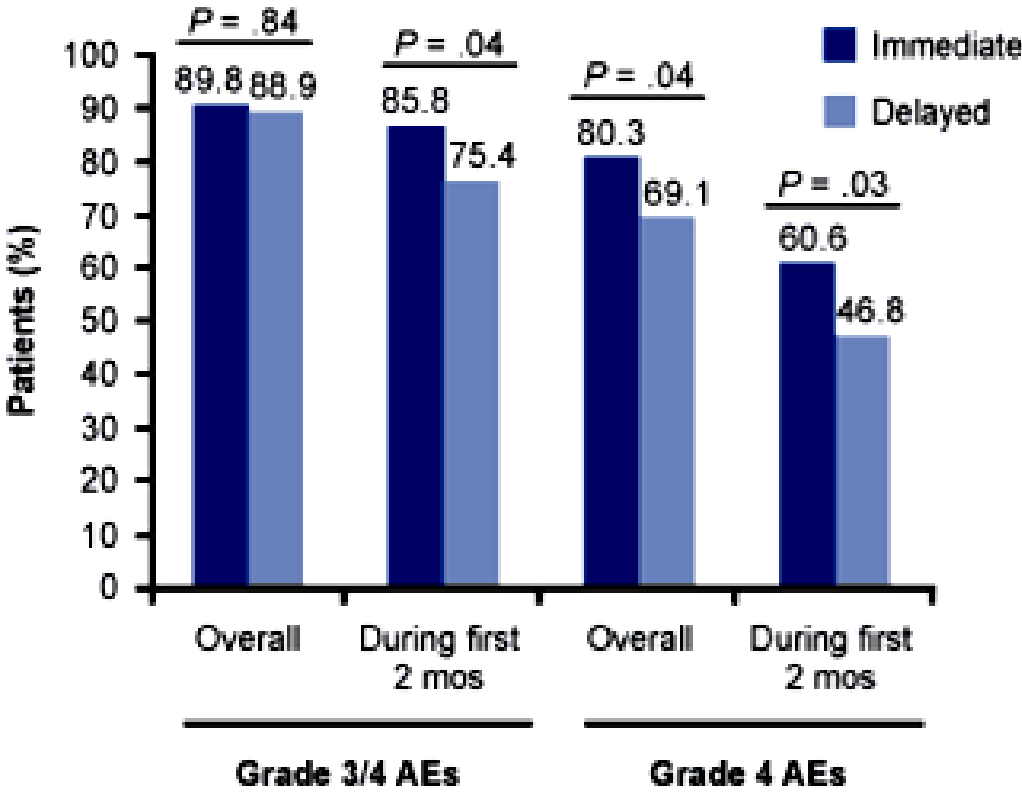
Potential **disadvantages** of early initiation of ART	Non-CNS OIs	CNS OIs
High pill burden	Yes	Yes
Co-toxicity	Yes	Yes
Pharmacokinetic drug interactions	Yes	Yes
Immune reconstitution disease	Yes	Yes, serious
More difficult to identify drug causing toxicity	Yes	Yes

Summary of RCTs between Early vs. Delay ART

Study	TB characteristic	CD4	Study arms	Mortality difference	Country	ARV regimen
1A. SAPIT 1 Abdool S, et al. NEJM 2010	Smear +ve Pul TB	150	Integrated vs. sequential	- 5 vs. 12 deaths/100 PYs - 56% lower in integrated arm	South Africa	ddI, 3TC, EFV
1B. SAPIT 2 Abdool S, et al. NEJM 2011	Smear +ve Pul TB	150	4 vs. 8-12 wks	- No differences of AIDS/death - Lower in only CD4<50 - 8 vs. 26 deaths/100 PYs	South Africa	ddI, 3TC, EFV
2. CAMELIA Blanc FX, et al. NEJM 2011	Smear +ve Pul TB	25	2 vs. 8 wks	- 15% vs. 26% - 38% lower in 2-wk arm	Cambodia	d4T, 3TC, EFV
3. STRIDE Havlir D, et al. NEJM 2011	Confirmed or probable Pul TB	77	<2 vs. 8-12 wks	- No differences of mortality - Lower in only CD4<50 - 15% vs. 27%	Multi-national	TDF/FTC, EFV
4. TOROK Torok E, et al. CID2011	TB meningitis	41	<2 vs. 8 wks	- No differences of time to death	Vietnam	AZT, 3TC, EFV
5. TIME Manosuthi W, et al. JAIDS 2012	Confirmed or probable any TB	43	4 vs. 12 wks	- Have a tendency in CD4<50 -10 vs. 14 deaths/100 PYs	Thailand	TDF, 3TC, EFV
6. TB-HAART *Mfinanga* S, et al. Lancet ID 2014	culture-confirmed TB	367	≤ 2 wks vs. 6 m	- No diff. between early and late ART on composite endpoint of death, tuberculosis treatment failure, and recurrence	South Africa, Uganda, Zambia, Tanzania	AZT, 3TC, EFV

Timing for ART Initiation: TB Meningitis

- 127 patients in immediate arms and 126 in deferred arms (2 mths)
- 1^{ry} end point: Death at 9 mths
- ART: AZT, 3TC and EFV
- Immediate ART was not associated with reduced 9-month mortality vs. deferred Rx
  - HR: 1.12 (95% CI: 0.81-1.55; *P* = .52)



- Incidence of grade 3/4 AEs significantly higher in immediate vs. deferred antiretroviral therapy arm during first 2 months of treatment
- Grade 4 AEs significantly more frequent in immediate vs. deferred antiretroviral therapy arm both overall and during first 2 months of treatment

Torok E, et al, et al. Clin Infect Dis. 2011 Jun;52(11):1374-83.

Optimal Timing to Initiate ART During TB: Guideline Summary

US CDC Guideline 2013	WHO Guideline 2013

What if “TB meningitis”?

- **BHIVA 2011:**
  - Although there was a greater incidence of severe adverse events in the early arm. How this translates to UK clinical practice remains unclear
- **US CDC 2013:**
  - Caution in early ART initiation is warranted in patients with TB meningitis
- **DHHS 2016:**
  - Many experts feel that ART should be initiated as for other HIV/TB-coinfected patients **(CIII)**
- **THAI 2014:**
  - กรณีวินิจฉัยวัณโรคเยื่อหุ้มสมองพิจารณารอเริ่มยาต้านไวรัสหลังรักษาวัณโรคแล้วนาน 2 สัปดาห์

Optimal Timing to Initiate ART During TB: Guideline Summary

US CDC Guideline 2013	
CD4	Recommendation
<50	Within 2 weeks
≥ 50	Within 8-12 weeks

WHO Guideline 2013	
CD4	Recommendation
Any CD4 level	As soon as possible

DHHS Guideline 2015	
CD4	Recommendation
<50	Within 2 weeks
≥50, severe TB	Within 2-4 weeks
≥50, less severe TB	Within 8-12 weeks

Thai Guideline 2014	
CD4	Recommendation
≤50	Within 2 weeks
>50	Severe TB: within 2 wks Not severe TB: 2-8 wks

BHIVA Guideline 2011	
CD4	Recommendation
<100	As soon as practical
100-350	As soon as practical, can wait until completing 2 m
> 350	Physician's discretion

Thai Guideline 2014

ART and anti-TB Initiation (Not include TB Meningitis)

- **การเริ่มยาต้านไวรัสขณะที่ผู้ป่วยกำลังได้ยาวัณโรค**
- เริ่มยาต้านไวรัสในผู้ป่วยเอชไอวีทุกรายที่กำลังรับการรักษาวัณโรค
- ระยะเวลาเริ่มยาต้านไวรัสที่เหมาะสมพิจารณาจากปริมาณเม็ดเลือดขาวซีดีสี่และความรุนแรงของโรคดังตาราง

Thai Guideline 2014	
CD4	Recommendation
≤50	Within 2 weeks
>50	Severe TB: within 2 wks Not severe TB: 2-8 wks

Thai Guideline 2016 (draft):

ART and anti-TB Initiation (Not include TB Meningitis)

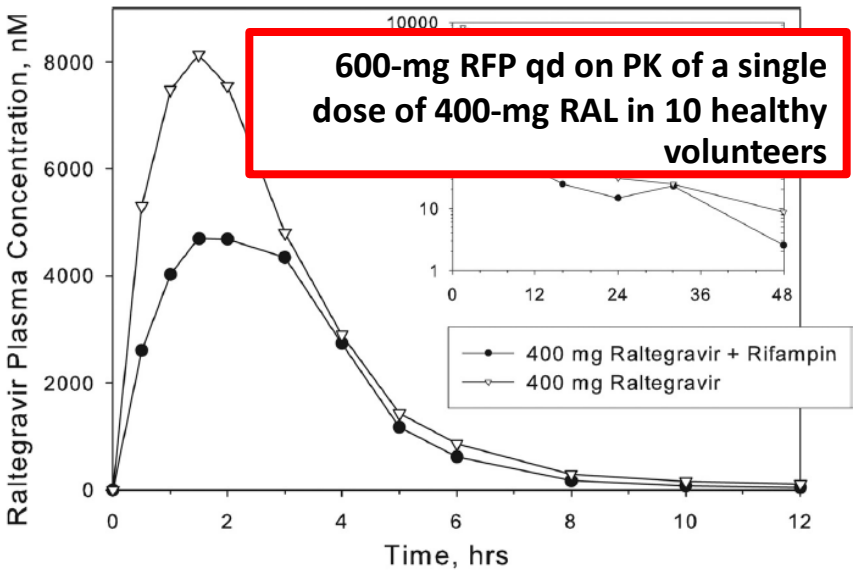
ปริมาณเม็ดเลือดขาว CD4	คำแนะนำการเริ่มยาต้านไวรัสหลังเริ่มยาวัณโรค
<50 cells/mm^3	เริ่มภายใน 2สัปดาห์อย่างช้าไม่เกิน 4 สัปดาห์
50-350cells/mm^3	ถ้าอาการวัณโรครุนแรง*เริ่มภายใน 2สัปดาห์อย่างช้าไม่เกิน 4 สัปดาห์ ถ้าอาการวัณโรคไม่รุนแรงเริ่มระหว่าง2สัปดาห์อย่างช้าไม่เกิน 8 สัปดาห์
>350 cells/mm^3	เริ่มภายใน 2 สัปดาห์- 6 เดือน

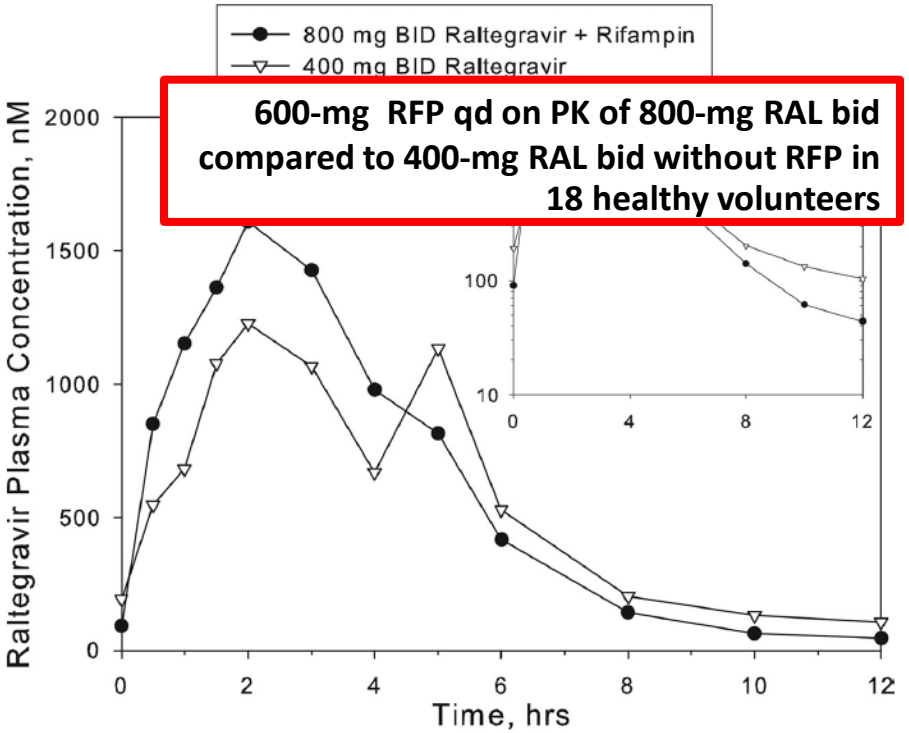
Thai Guideline 2014: ART and anti-TB Initiation

- กรณีที่ไม่มี rifampicin ในสูตรยารักษาวัณโรค ให้พิจารณาเริ่มสูตรยาต้านไวรัสตามปกติ
- กรณีที่มี rifampicin ในสูตรยารักษาวัณโรคให้พิจารณาดังนี้

1. Efavirenz ในขนาด 600 มก.ต่อวัน
2. Nevirapine 200 มก.วันละ 2 ครั้งโดยไม่ต้อง lead-in
3. Raltegravir ขนาด 400 มก.วันละ 2 ครั้ง
4. Maraviroc ขนาด 200 มก.วันละ 2 ครั้ง

Effect of Rifampicin on PK of Raltegravir





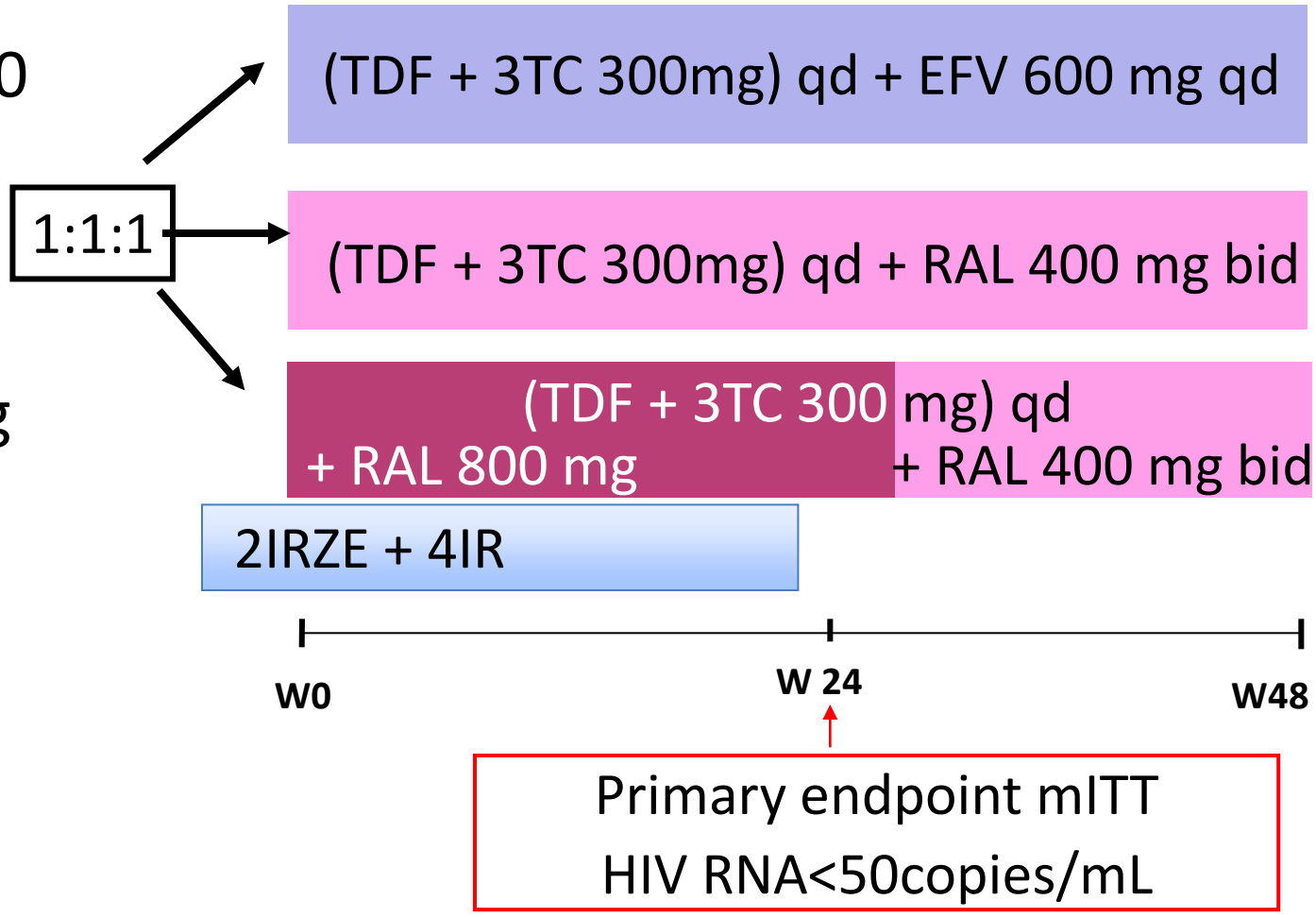
- RAL co-administered with RFP resulted in lower RAL concentration (61% Ctrough reduction)
- Doubling RAL to 800 mg when co-administered with RFP
  - Compensates for effect of RFP on RAL AUC, not overcome effect on C12
- No serious AE reported

Wenning L, et al. Antimicrob Agents Chemother 2009; 53: 2852–2856.

ANRS 12 180 REFLATE TB

Phase II open label randomized multicenter trial

- HIV RNA>1000
- ART naïve
- Confirmed or probable TB
- RIF containing regimen



Sample size : 50 patients/arm, 80% power to show ≥70% success at W24

Grinsztejn B, et al. CROI 2013. Abstract 853

ANRS 12 180 REFLATE TB

Table 1. Baseline characteristics of patients, ANRS 12 180 REFLATE TB

	EFV		RAL 400		RAL 800	
	N = 51		N = 51		N = 51	
Male, n (%)	39	(76)	35	(69)	38	(75)
Age in years, median [IQR]	35	[29-45]	37	[31-44]	38	[33-43]
BMI in kg/m^2, median [IQR]	21	[19-23]	21	[19-23]	20	[17-23]
CD4+/mm^3, median [IQR]	129	[45-308]	115	[50-213]	166	[80-367]
CD4 ≤ 50/mm^3, n (%)	14	(27)	12	(24)	5	(10)
HIV RNA in log$_{10}$ cp/ml, median [IQR]	5.0	[4.5-5.5]	4.9	[4.4-5.4]	4.9	[4.2-5.4]
HIV RNA ≥ 100,000 cp/ml, n (%)	26	(51)	20	(39)	24	(47)
TB location*, n (%)						
Pulmonary only	20	(39)	23	(45)	23	(45)
Pulmonary and Extrapulmonary	26	(51)	20	(39)	23	(45)
Extrapulmonary only	5	(10)	8	(16)	5	(10)
Bacteriologically confirmed TB*, n (%)	23	(45)	27	(53)	25	(49)
Time between anti-TB and ARV, in weeks [IQR]	5.7	[4.9-6.9]	6.0	[4.9-7.1]	5.9	[5.0-6.7]
Hepatitis B or C co-infection, n (%)	2	(4)	4	(8)	5	(10)

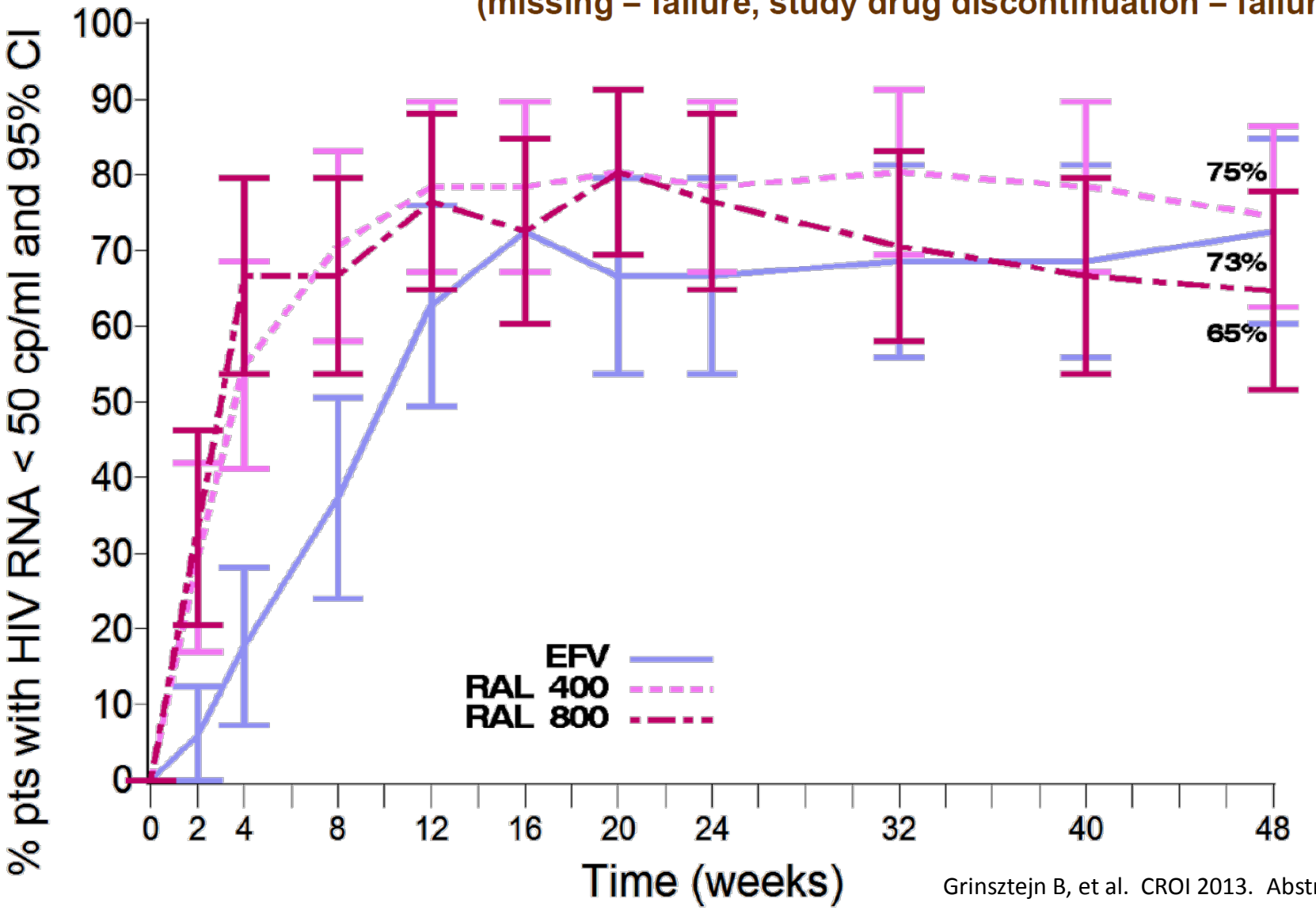
* *One patient had atypical mycobacterium infection and not TB*

Grinsztejn B, et al. CROI 2013. Abstract 853

ANRS 12 180 REFLATE TB

Proportions of patients with HIV-1 RNA < 50cp/ml at each visit

(missing = failure, study drug discontinuation = failure)



Grinsztejn B, et al. CROI 2013. Abstract 853

Rifampicin markedly decreases blood levels of all PIs

PI	Effect of Rifampicin
Saquinavir	↓ 80%
Ritonavir	↓ 35%
Indinavir	↓ 90%
Nelfinavir	↓ 82%
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 [1-3]

[1] Veldkamp AI, et al. CID 1999:29;1586.
[2] Gray A , et al. AIDS 2006:20;302. [3] La Porte CJ, et al. AAC2004:48;1553.

Thai Guideline 2014: ART and anti-TB Initiation

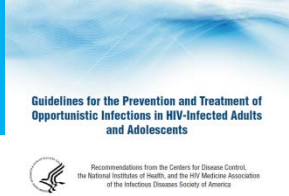
การเริ่มยาวัณโรคขณะที่ผู้ป่วยกำลังได้ยาต้านไวรัส

- กรณีผู้ป่วยกำลังได้ยาต้านไวรัสสูตร NNRTIs ทั้ง EFV และ NVP ให้สูตรยาวัณโรคตามปกติ
- กรณีผู้ป่วยกำลังได้ยาต้านไวรัสสูตรที่มี PIให้พิจารณาดังนี้
  - 1. ปรับยา PI เป็นสูตรที่มี NNRTIs (พิจารณายา EFV ก่อน NVP) หรือ integrase inh. (ได้แก่ raltegravir) เป็นส่วนประกอบแทน และให้สูตรยาวัณโรคตามปกติ ทั้งนี้ตรวจสอบและควรระวังว่าผู้ป่วยไม่เคยมีประวัติดื้อยาหรือแพ้ยาที่กำลังจะเปลี่ยน
  - 2. ถ้าไม่สามารถใช้ NNRTIs และ integrase inh.ได้ ให้พิจารณาปรับสูตรยาวัณโรคเป็น 2IEZ+quinolone/10-16IE+quinolone อาจพิจารณาเพิ่ม streptomycin ในช่วง 2 เดือนแรก

steroid

- TB of non-CNS
- TB of CNS
- For adjunctive treatment
- For treatment of IRIS

Other Considerations in TB Management



- Adjunctive corticosteroid improves survival for patients with HIV-related TB involving the CNS and pericardium **(AI)**

- Dexamethasone has been used for CNS disease with the following dosing schedule:

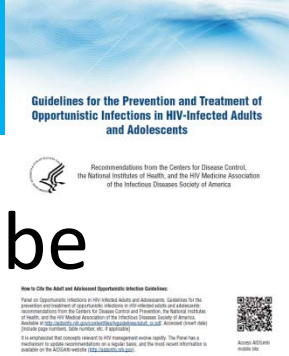
  0.3–0.4 mg/kg/day for 2–4 weeks,
  then taper 0.1 mg/kg per week until 0.1 mg/kg,
  then 4 mg per day and taper by 1 mg/week;
  total duration of approximately 12 weeks

- Prednisolone may be used in pericardial disease

  (e.g. 60 mg PO daily and taper by 10 mg per day weekly;
  total duration approximately 6 weeks)

DHHS Guideline 2013

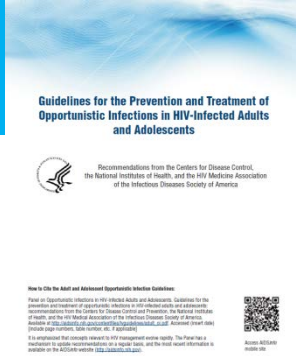
Other Considerations in TB Management



- Paradoxical reaction that is not severe may be treated symptomatically **(CIII)**

- For moderately severe paradoxical reaction, may consider use of corticosteroid, and taper over 4 weeks (or longer) based on clinical symptoms **(BIII)**

Other Considerations in TB Management



Examples of Prednisone Dosing Strategies

- In patients on a RIF-based regimen:

  prednisone 1.5 mg/kg/day x 2 weeks,
  then 0.75 mg/kg x 2 weeks

- In patients on a RFB + boosted PI regimen:

  prednisone 1.0 mg/kg/day x 2 weeks,
  then 0.5 mg/kg/day x 2 weeks

Cryptococcal Meningitis

- timing of ART
- proper ARV regimen
- adjunctive treatment

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 (serious)
More difficult to identify drug causing toxicity	Yes

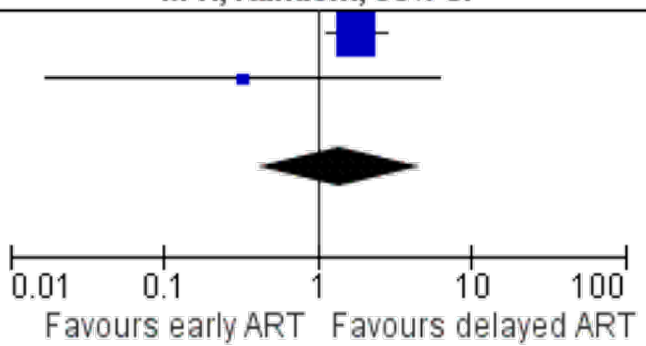
Optimal timing for ART initiation in HIV infn and concurrent CM

Cochrane Library

Study or Subgroup	Early ART Events	Early ART Total	Delayed ART Events	Delayed ART Total	Weight	Risk Ratio M-H, Random, 95% CI
Makadzange 2010	23	28	12	26	85.8%	1.78 [1.14, 2.79]
Zolopa 2009	0	13	2	22	14.2%	0.33 [0.02, 6.36]
Total (95% CI)		**41**		**48**	**100.0%**	**1.40 [0.42, 4.68]**
Total events	23		14			

Heterogeneity: Tau² = 0.39; Chi² = 1.33, df = 1 (P = 0.25); I² = 25%

Test for overall effect: Z = 0.55 (P = 0.58)



Forest plot of comparison: 1 Early ART initiation versus delayed ART initiation, outcome: 1.1 Death.

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

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

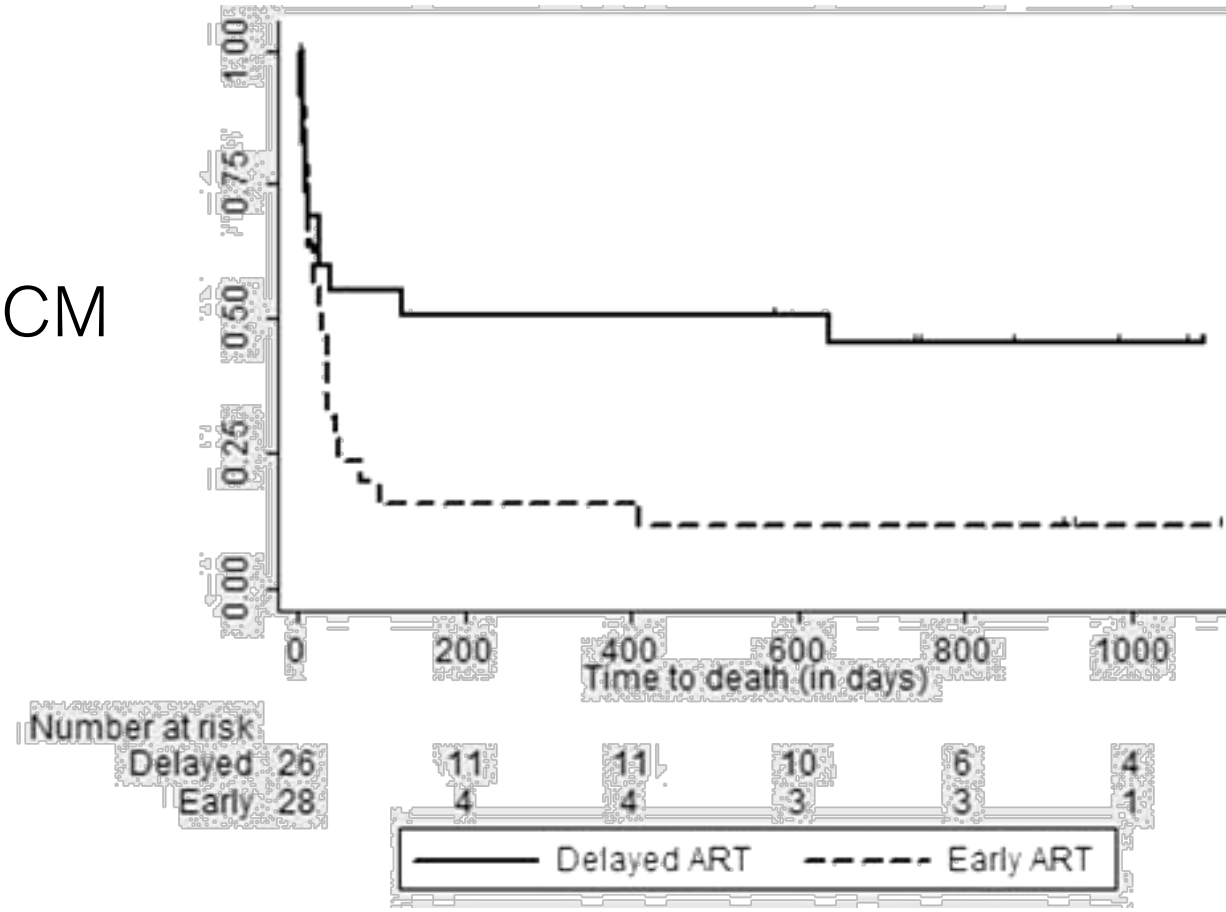
Early versus Delayed Initiation of ART for Concurrent HIV Infection and Cryptococcal Meningitis in Sub-Saharan Africa

54 HIV-infected pt w/ CM

26 pts-delayed ART after 10 wks

28 pts-early ART within 72 hrs

CM was treated initially by Fluco. 800 mg/d



Kaplan-Meier survival estimates by treatment group. Early treatment was asso. with increased mortality and a median survival time of 28 days, compared with delayed with median survival time of 637 days (*P=0.031, by log-rank test)*

Makadzange AT. CID 2010

Early ART reduces AIDS progression/death in individuals with acute OIs
A multicenter randomized strategy trial

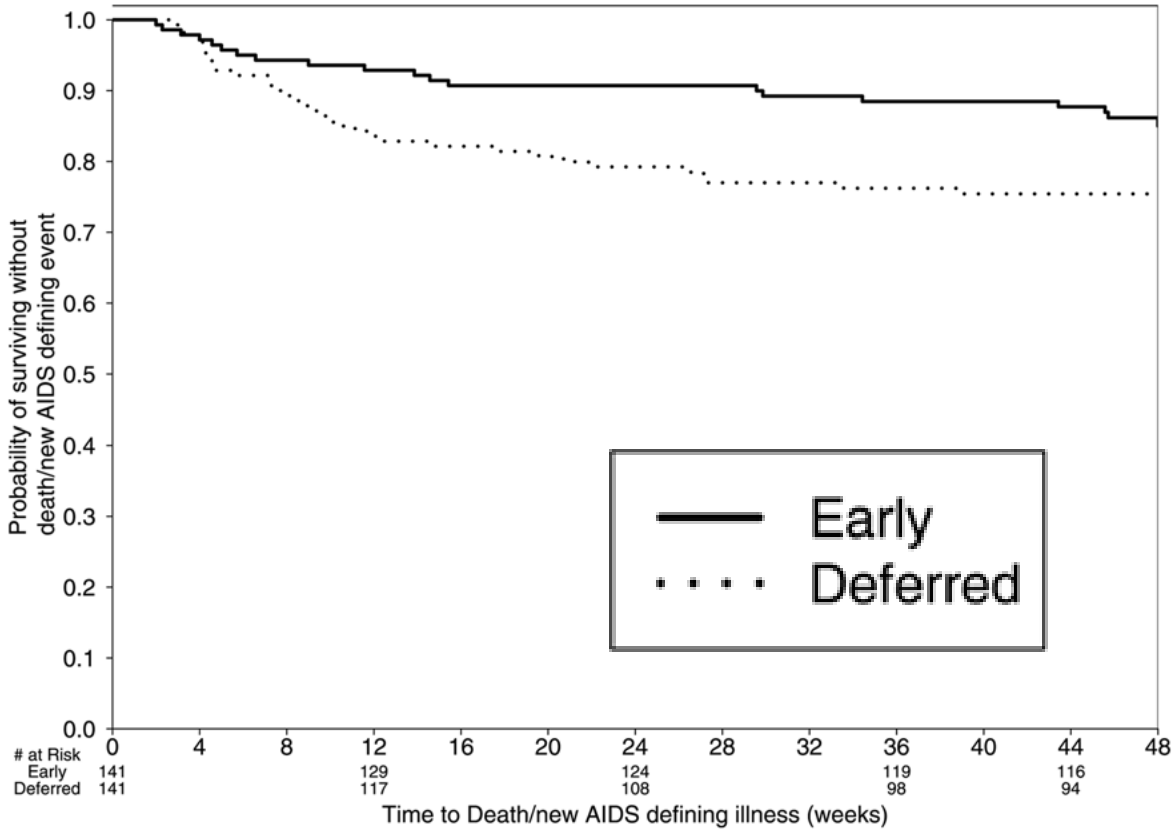
ART initiation after acute OIs Tx

Total of 282 pts

141 pts in early ART, median 12 d

141 pt in delayed ART, after 6-12 wks

CM: 9 pts in early and 16 pts in delayed ART



Time to AIDS progression or death. HR = 0.53 Early versus Deferred ART

[95%CI 0.30–0.92 p = 0.023]

Zolopa AR. PLoS ONE 2009

The NEW ENGLAND JOURNAL of MEDICINE

COAT study

ORIGINAL ARTICLE

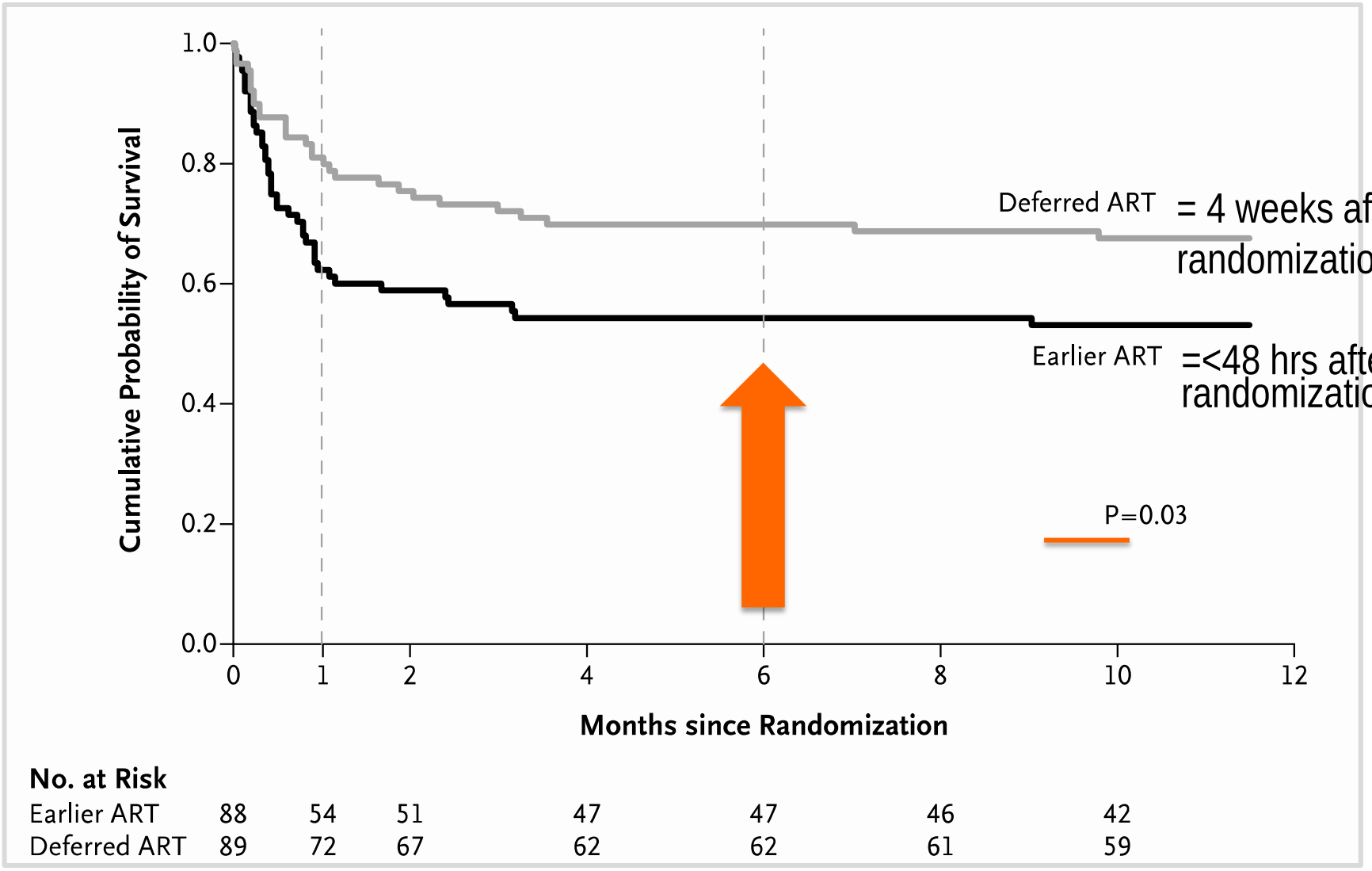
Timing of Antiretroviral Therapy after Diagnosis of Cryptococcal Meningitis

David R. Boulware, M.D., M.P.H., David B. Meya, M.Med., Conrad Muzoora, 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;26:2487-98

Overall Survival

Patients entered trial after 7 - 11 days of antifungal treatment

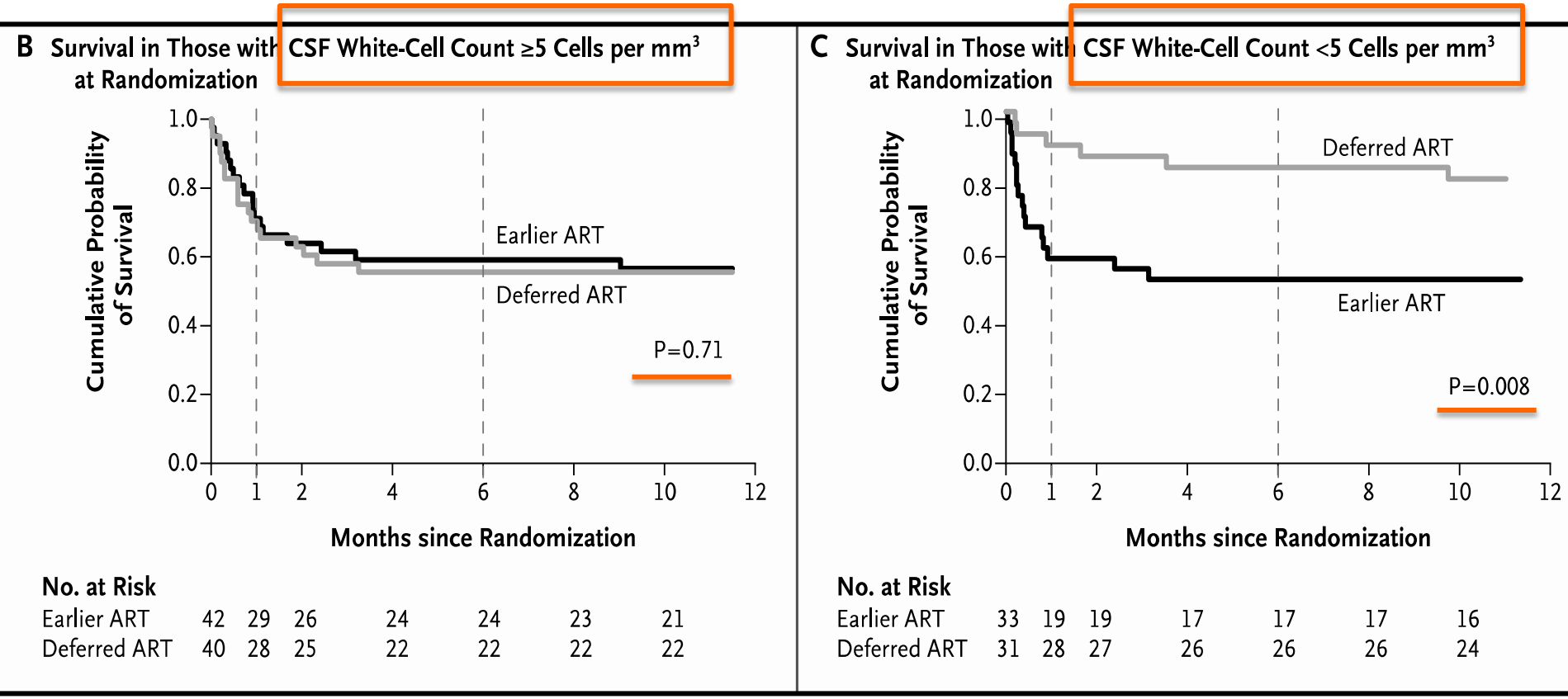


No. at Risk

Earlier ART	88	54	51	47	47	46	42
Deferred ART	89	72	67	62	62	61	59

Boulware D, et al. N Engl J Med 2014;26:2487-98

Survival in Patients with CSF WBC ≥5 and <5 Cells/mm^3



Deferring ART for 5 weeks after diagnosis of CM was associated with sig. improved survival, as compared with initiating ART at 1 to 2 weeks, esp. among patients with a paucity of white cells in CSF

Boulware D, et al. N Engl J Med 2014;26:2487-98

เกณฑ์ระยะเวลาในการเริ่มยาต้านไวรัสภายหลังเริ่มรักษาโรคติดเชื้อฉวยโอกาส

โรคติดเชื้อฉวยโอกาส	ระดับ CD4 (cells/mm^3)		
	≤ 50	> 50	
วัณโรค (Tuberculosis)	ภายใน 2 สัปดาห์	รุนแรง*	ไม่รุนแรง
		ภายใน 2 สัปดาห์	ระหว่าง 2-8 สัปดาห์
Cryptococcosis	ระหว่าง 4-6 สัปดาห์		
PCP/MAC/อื่น ๆ	ระหว่าง 2-4 สัปดาห์		
CMV/PML/Cryptosporidium	ควรพิจารณาเริ่มให้ยาต้านไวรัสกับผู้ป่วยเร็วที่สุดเท่าที่จะทำได้		

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Adjunctive Dexamethasone in HIV-Associated Cryptococcal Meningitis

J. Beardsley, M. Wolbers, F.M. Kibengo, A.-B.M. Ggayi, A. Kamali, N.T.K. Cuc, T.Q. Binh, N.V.V. Chau, J. Farrar, L. Merson, L. Phuong, G. Thwaites, N. Van Kinh, P.T. Thuy, W. Chierakul, S. Siriboon, E. Thiansukhon, S. Onsanit, W. Supphamongkholchaikul, A.K. Chan, R. Heyderman, E. Mwinjiwa, J.J. van Oosterhout, D. Imran, H. Basri, M. Mayxay, D. Dance, P. Phimmasone, S. Rattanavong, D.G. Lalloo, and J.N. Day, for the CryptoDex Investigators*

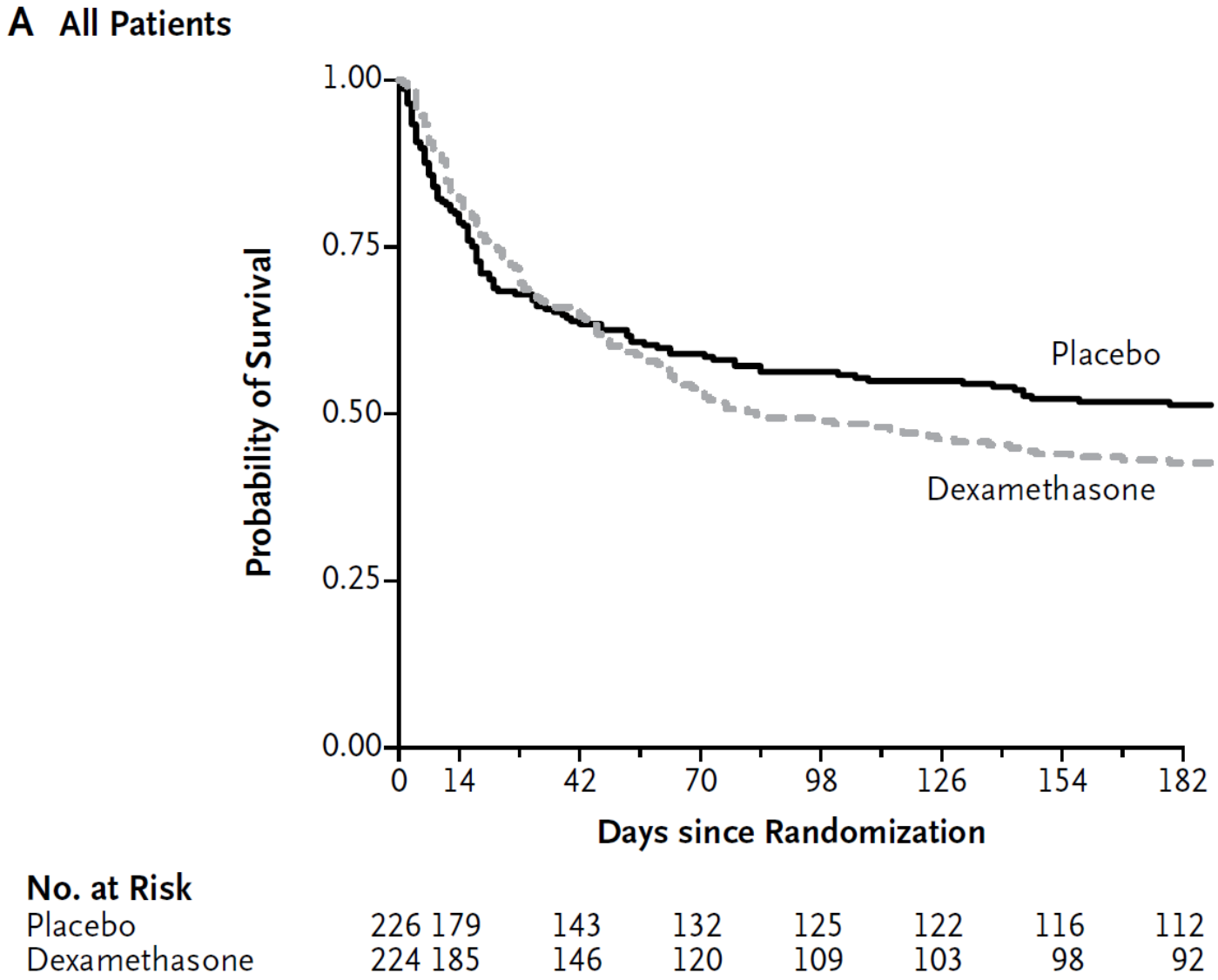
Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Dexamethasone (N = 224)	Placebo (N = 226)
Residence — no. (%)		
Africa	122 (54)	124 (55)
Asia	102 (46)	102 (45)
Male sex — no. (%)	147 (66)	132 (58)
Median age (IQR) — yr	35 (31–41)	35 (30–40)
History of intravenous drug use — no./total no. (%)	17/215 (8)	18/215 (8)
Current antiretroviral-therapy status — no. (%)		
None	135 (60)	133 (59)
≤3 mo duration	41 (18)	46 (20)
>3 mo duration	48 (21)	47 (21)

Beardsley J, et al. NEJM 2016

Characteristic	Dexamethasone (N = 224)	Placebo (N = 226)
Residence — no. (%)		
Africa	122 (54)	124 (55)
Asia	102 (46)	102 (45)
Symptoms — no./total no. (%)		
Headache	217/224 (97)	212/226 (94)
Fever	147/222 (66)	134/223 (60)
Neck stiffness	106/222 (48)	103/219 (47)
Seizures	35/223 (16)	43/225 (19)

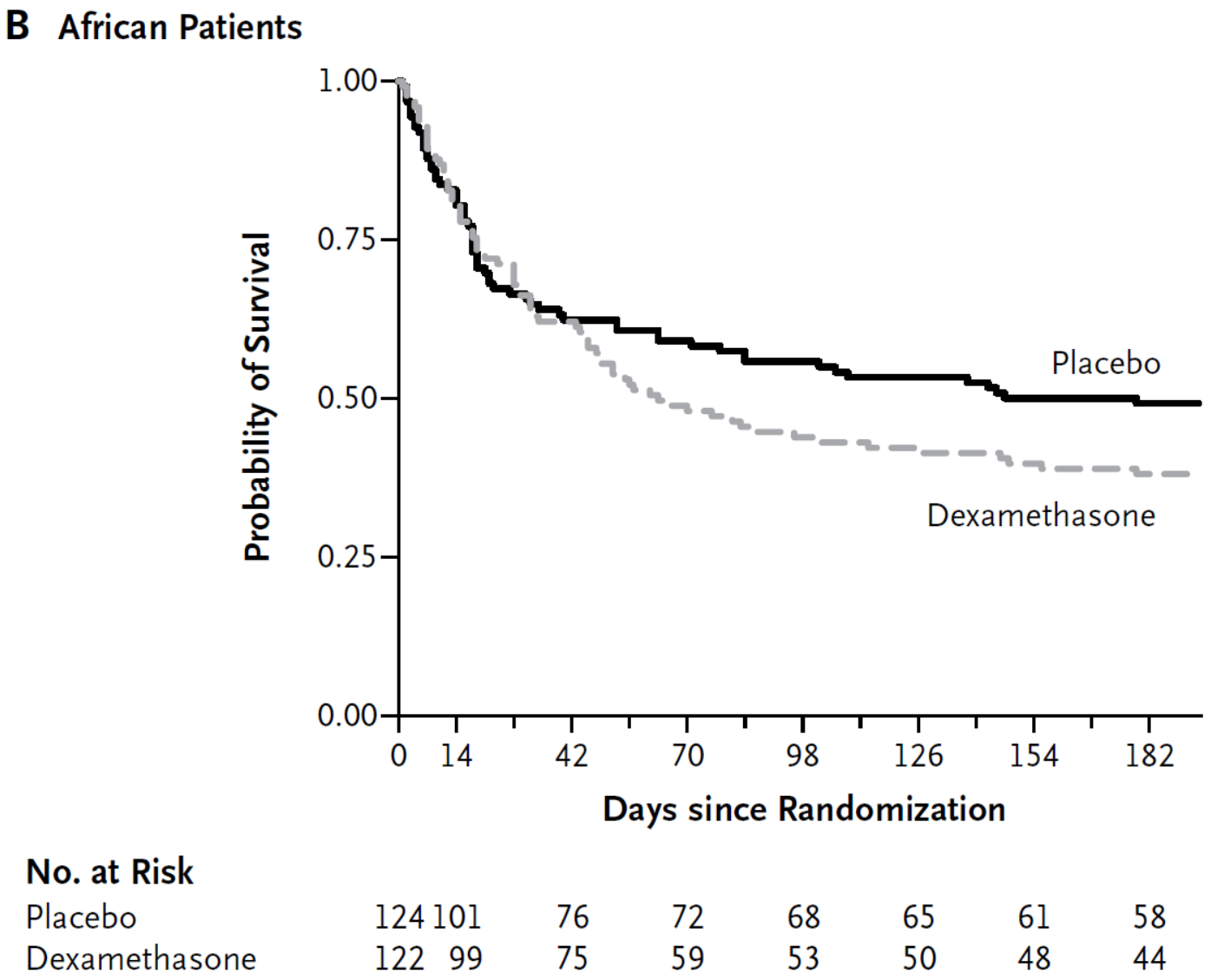
Beardsley J, et al. NEJM 2016



Survival among All Patients and According to Continent.

By10 wks (cutoff for primary outcome), 106 of 224 pts (47%) in the dexa. Gr. and 93 of 226 (41%) in the placebo gr. had died. At 6 mo., the estimated risks of death were 57% and 49%, respectively.

Beardsley J, et al. NEJM 2016



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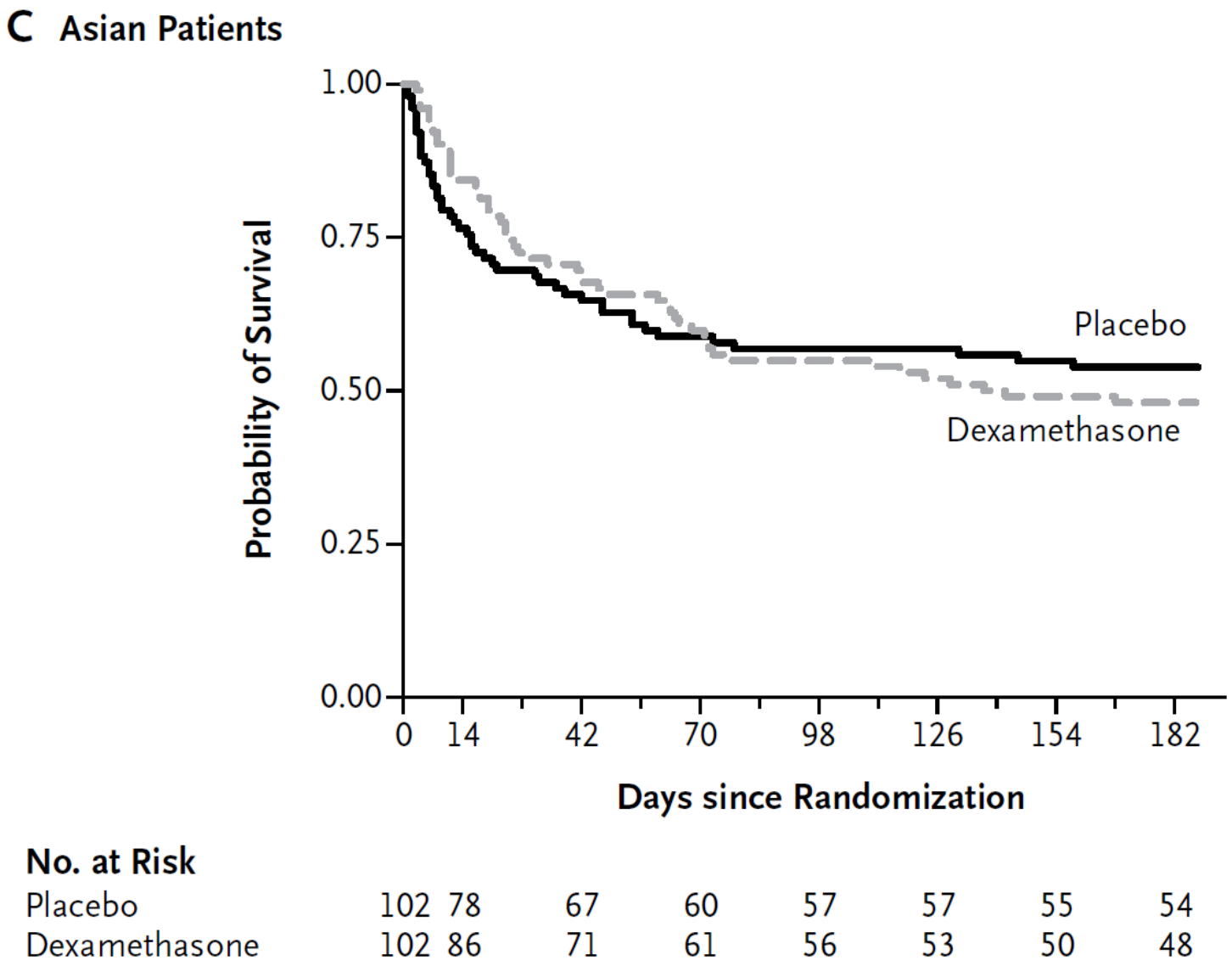

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Beardsley J, et al. NEJM 2016

CONCLUSIONS

- Dexamethasone did not reduce mortality among patients with HIV-associated CM
- Dexamethasone was associated with more adverse events and disability than was placebo.

Worsening of symptoms after ARV initiation sequential to OIs treatment

- Treatment Failure
- Paradoxical IRIS
- Unmasking IRIS
- Medication Adverse Effects

สรุป

การดูแลรักษา HIV, Coinfections, และ OIs มีความซับซ้อน และมีข้อมูลเพิ่มขึ้นตลอดเวลาเพื่อการดูแลผู้ป่วยที่ดีมากขึ้น