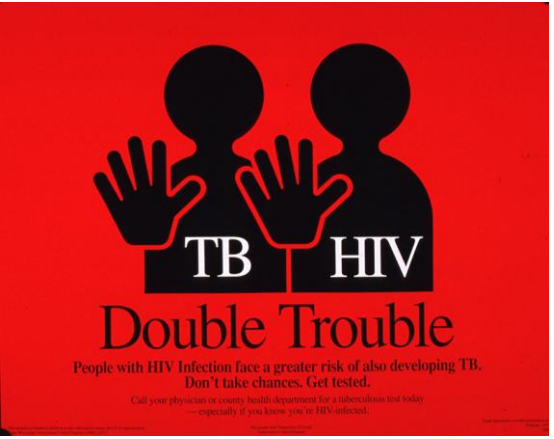
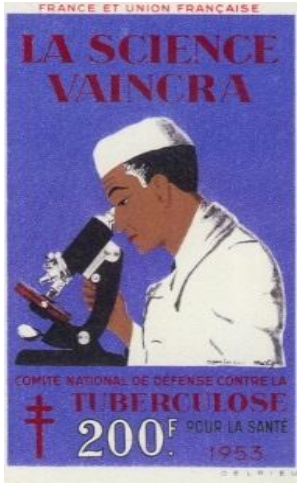




Particularités de la co-infection VIH-tuberculose Focus sur formes graves et traitement antirétroviral

PRE NATHALIE DE CASTRO

DMIT LARIBOISIÈRE SAINT-LOUIS

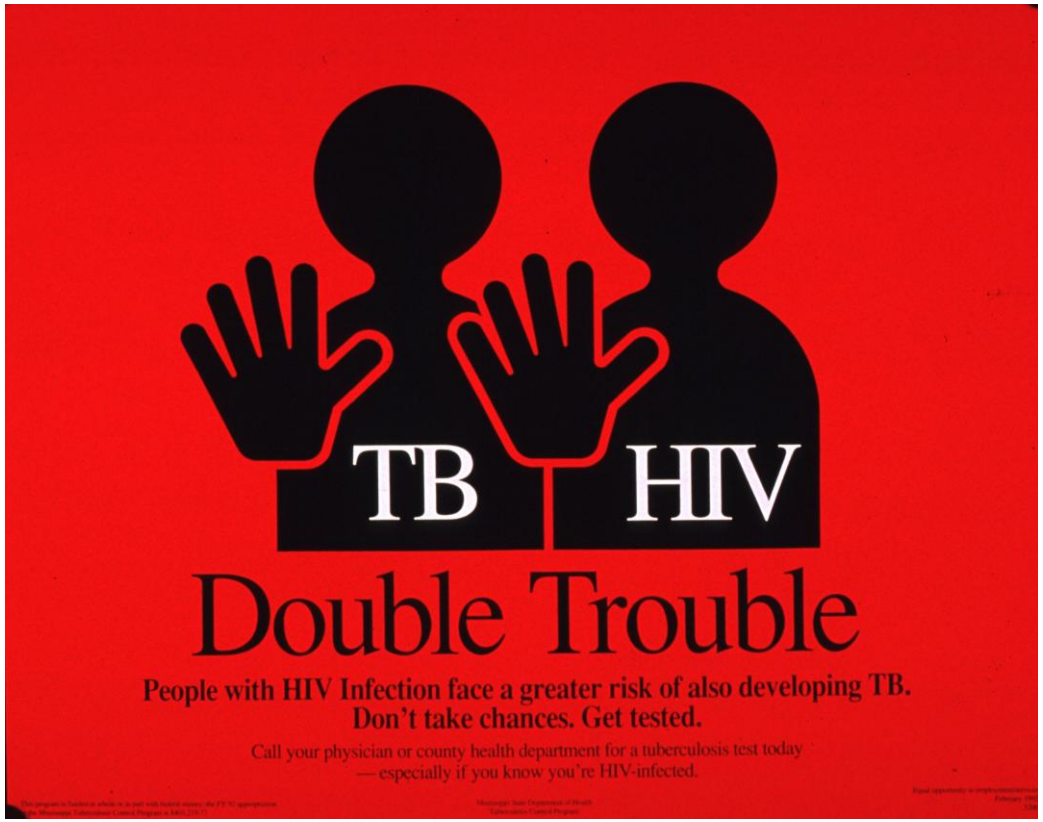
SÉMINAIRE NATIONAL DES DE MALADIES INFECTIEUSES

27 MARS 2026

Sommaire

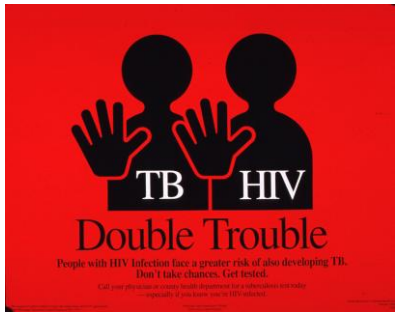
- Epidémiologie
- Prévention de la TB chez les PVVIH
- Les défis
- Principales recommandations
- TARV INSTI et Rifamycines: quelles données?
- Formes sévères : faut-il intensifier? Corticoïdes?
- Conclusion et perspectives

NB : IRIS=> cours spécifique



Mississippi State Dept. of Health, Tuberculosis Control Program, 1992

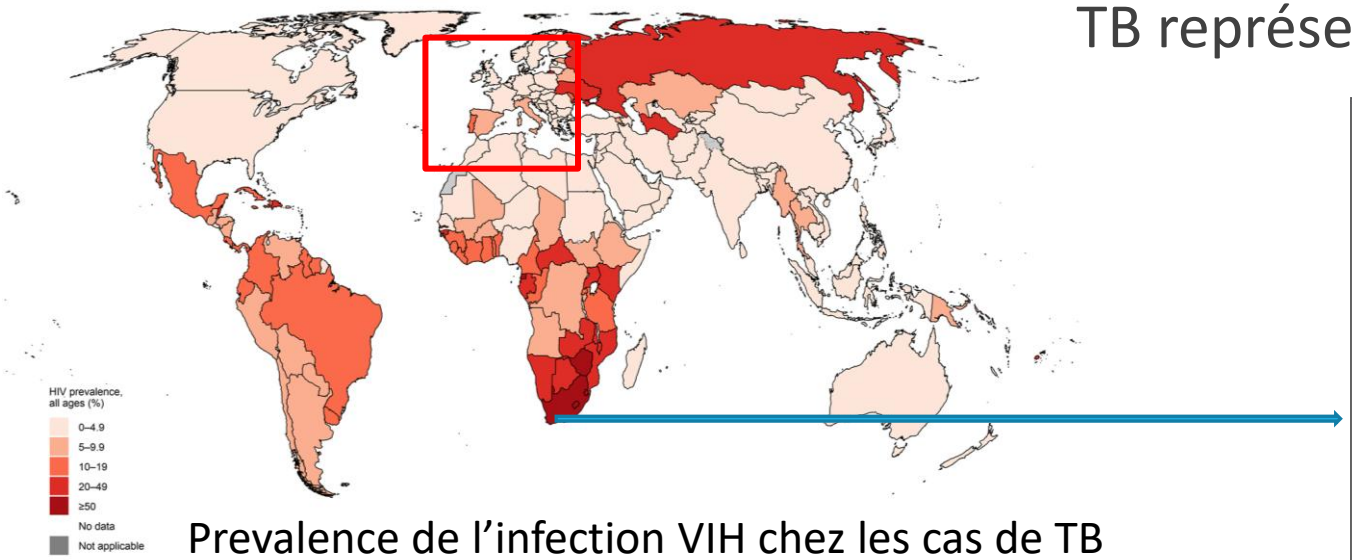
VIH et tuberculose
Toujours un couple mortel



Globalement :

10.7 millions de personnes avec TB

1.3 millions de décès liés à la (12%)



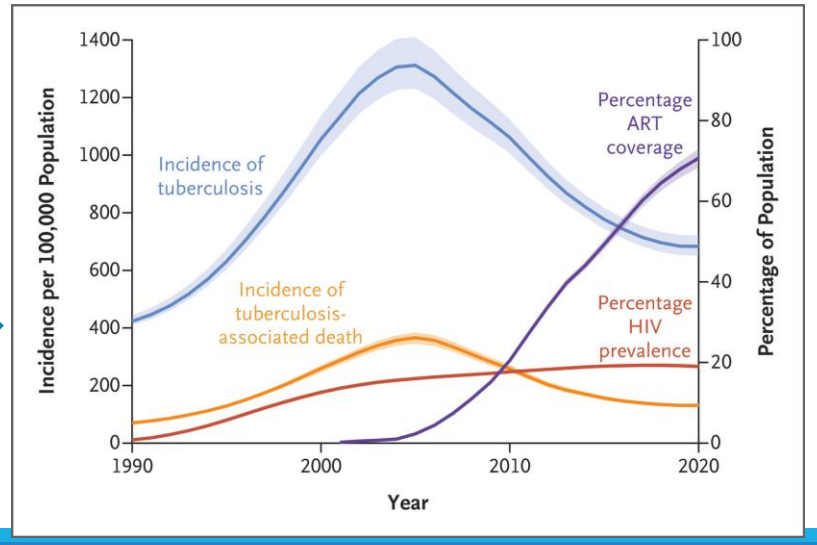
Prevalence de l'infection VIH chez les cas de TB

Chez les PVVIH

640 000 PVVIH avec TB (5,8%)

150 000 PVVIH sont décédées de TB

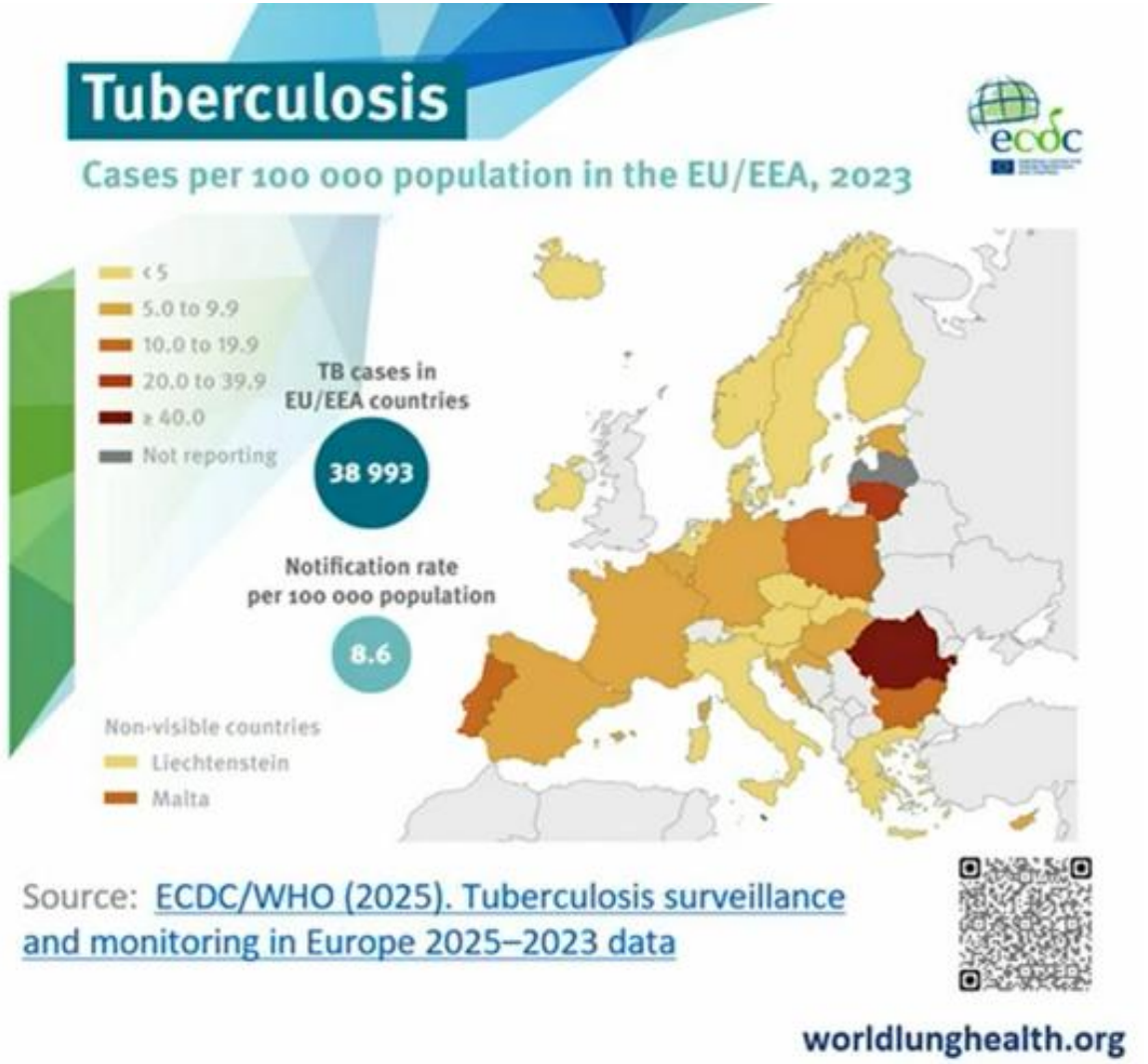
TB représente # 25% des décès liées au VIH

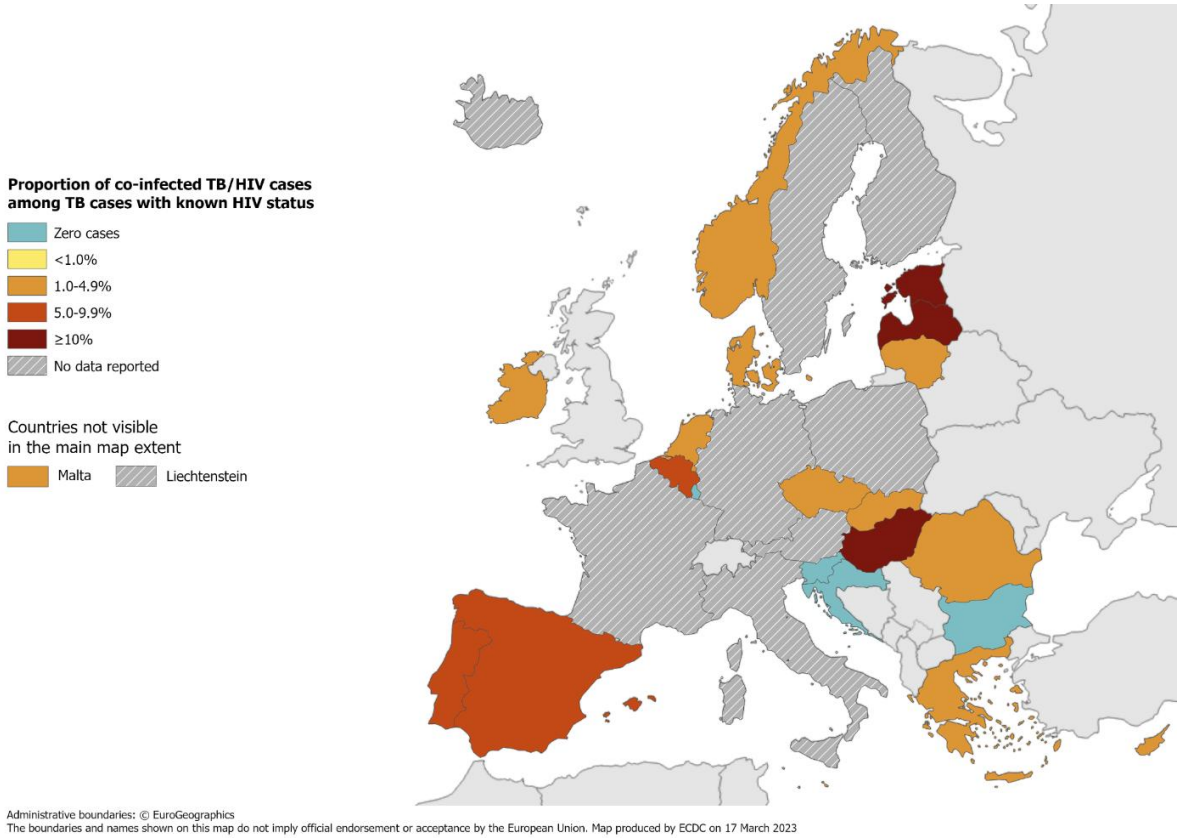


WHO Global TB report, 2025

N Engl J Med 2024;391:343-355
DOI: 10.1056/NEJMra2308181

Tuberculose et co-infection TB/VIH EU/EEA



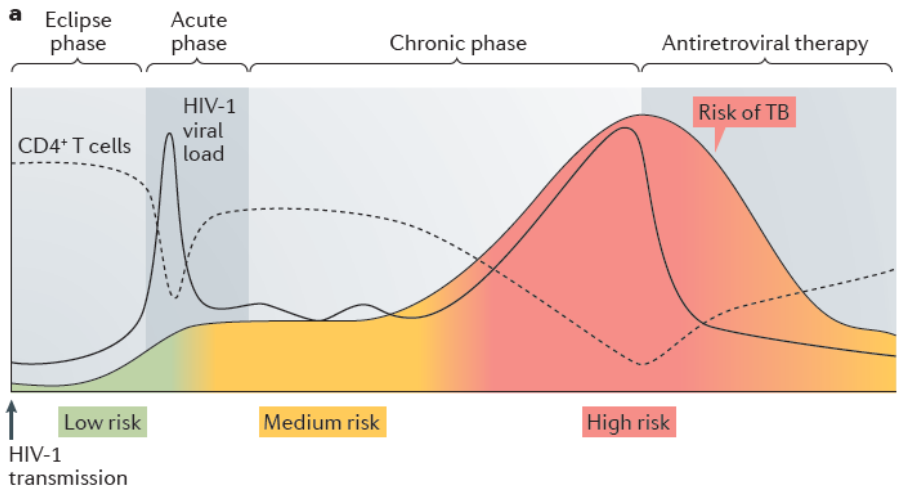


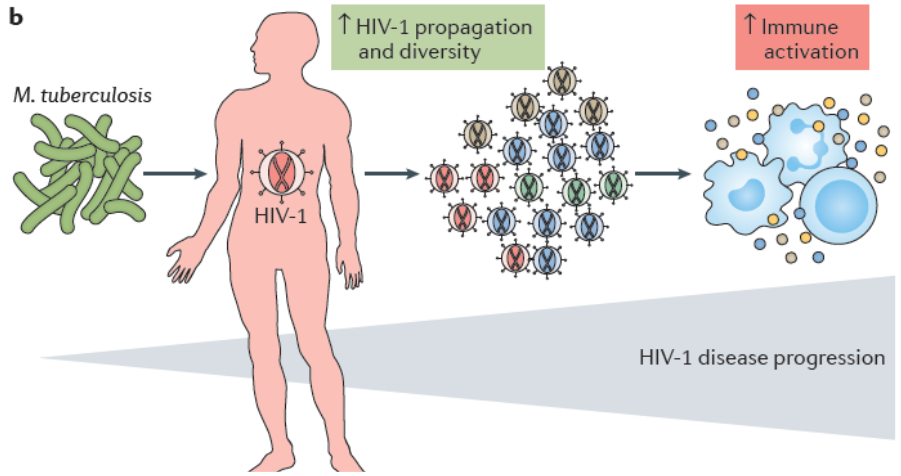
620 (4,1%) HIV-positive TB cases were notified by 21 EU/EEA countries in 2022

VIH et tuberculose
VIH favorise la TB et vice-versa

- Risque de TB chez les PVVIH
  - Augmente dès la primo-infection
  - Atteint un pic quand CD4 <200/mm^3
  - Diminue mais persiste sous TARV

- TB contribue à la progression de l'infection VIH
  - Augmente la réplication du VIH
  - Activation immunitaire
  - Inflammation chronique





Bell et *al*. Nat Rev Microbiol 2018

***N Engl J Med* 2024;391:343-355**
DOI: 10.1056/NEJMra2308181

VIH et tuberculose
Prévention de la tuberculose :recommandations internationales

Table 2. Regimens Currently Recommended for the Prevention of HIV-Associated Tuberculosis.

Regimen*	U.S. Guidelines[73]	WHO Guidelines[82]
Isoniazid (900 mg) with rifapentine (900 mg) weekly for 3 mo	Preferred	Strong recommendation
Isoniazid (300 mg) with rifampin (600 mg) daily for 3 mo	Preferred	Strong recommendation
Isoniazid (300 mg) daily for 6–9 mo	Alternative	Strong recommendation
Rifampin (600 mg) daily for 4 mo	Alternative	Conditional recommendation
Isoniazid (300 mg) with rifapentine (600 mg) daily for 1 mo	Alternative	Conditional recommendation
Isoniazid (300 mg) daily for ≥36 mo	Not recommended	Conditional recommendation in settings with high tuberculosis transmission

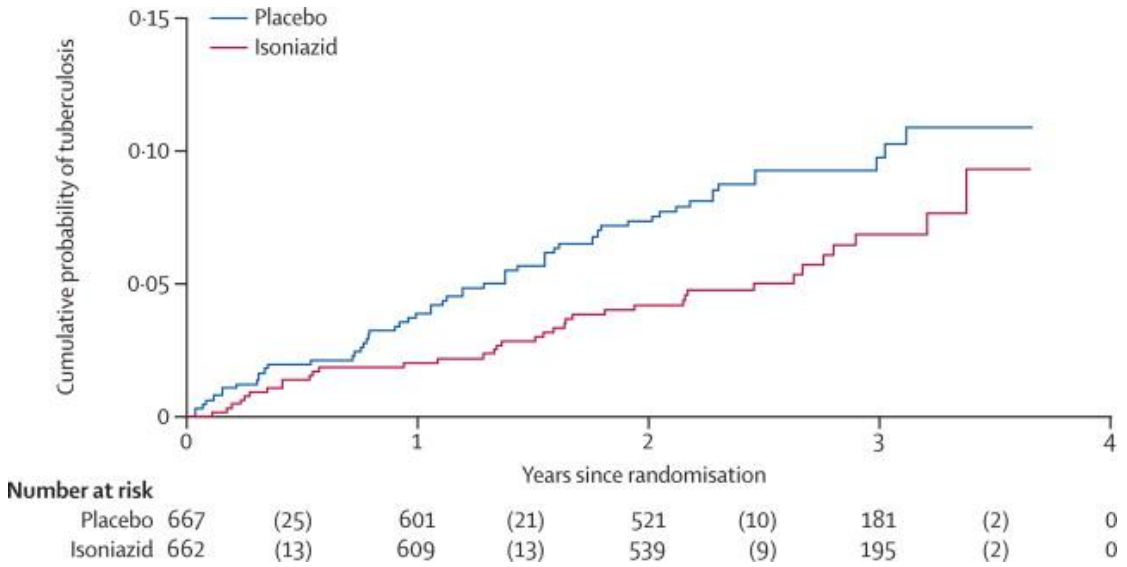
* Doses shown are for adults with a body weight of more than 50 kg.

Yanes-Lane M et al 2021; PLoS Med . 2021;18(9):e1003738. doi: 10.1371/journal.pmed.1003738.
N Engl J Med 2024;391:343-355 DOI: 10.1056/NEJMra2308181

VIH et tuberculose

TB preventive therapy : 9-12 H (daily) or 3 HP (weekly)

Supériorité INH vs placebo



37% lower rate of incident TB in INH arm vs placebo)
No significant difference in mortality
More pts receiving INH stopped study therapy due to grade ≥ 3 ALT

Rangaka et al.The Lancet 2014; 384:682-90

Non-INf 9 INH vs 3HP

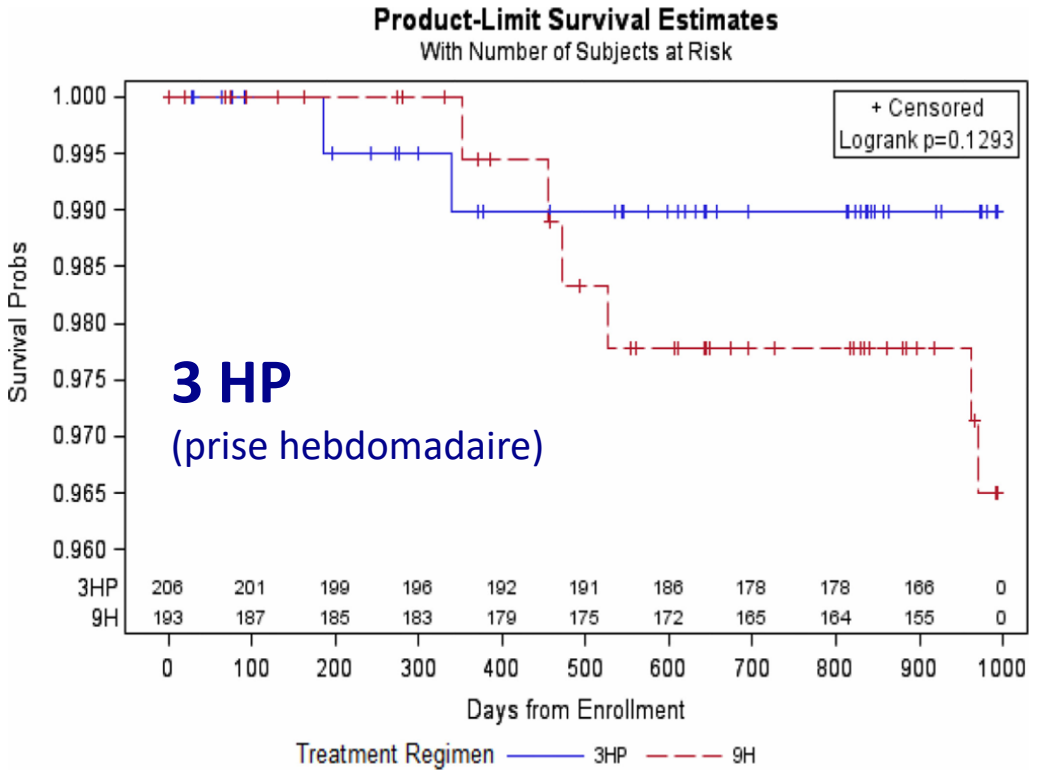


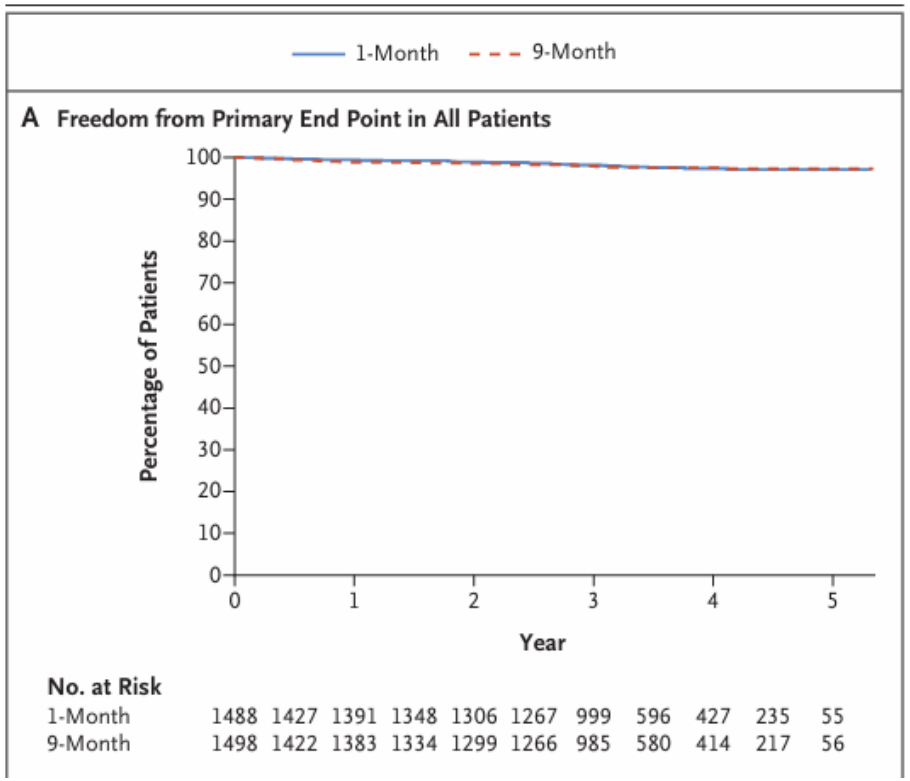
Figure 1. Kaplan-Meier curve of time to tuberculosis by study arm in the MITT study population
The number of persons at risk at 100-day increments from enrollment are provided.

Sterling et al. AIDS 2016; 30:1607-15
https://doi.org/10.1097/qad.0000000000001098

VIH et tuberculose

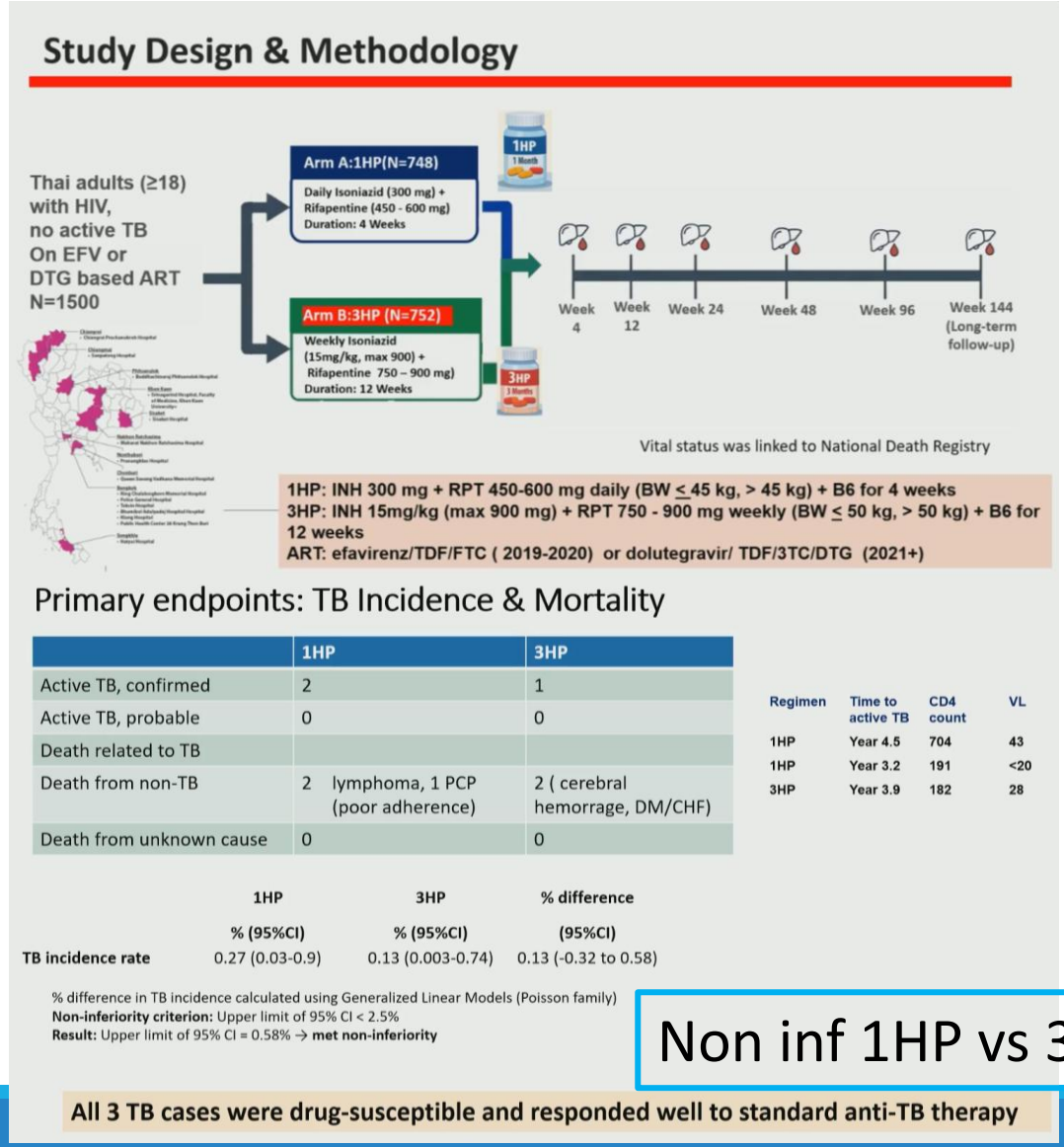
TB preventive therapy : 1 HP (daily) or 3 HP (weekly)

Non inf 1HP vs INH



Treatment completion :
1HP 97% vs 9H 90%

Swindells et al. NEJM 2019; 380:1001-11
https://doi.org/10.1056/nejmoa1806808



Non inf 1HP vs 3 HP

Avihingsanon et al. CROI 2026

VIH et tuberculose
Prévention de la tuberculose en France


HAS anrs CNS

RECOMMANDER LES BONNES PRATIQUES

FICHE

Prise en charge des complications infectieuses associés à l'infection par le VIH

Validée par le Collège le 27 juin 2024

Dépistage de la tuberculose infection (tuberculose latente)

- Ciblé en priorité sur les populations les plus à risque : sujets originaires de zones géographiques de forte endémie et/ou vivant en situation de précarité
- Par test de détection d'interféron gamma (IGRA) de préférence, ou intradermo réaction (IDR) à la tuberculine, et radiographie thoracique
- Si CD4 <200/µL : recherche de tuberculose maladie par radiographie +/- TDM thoracique

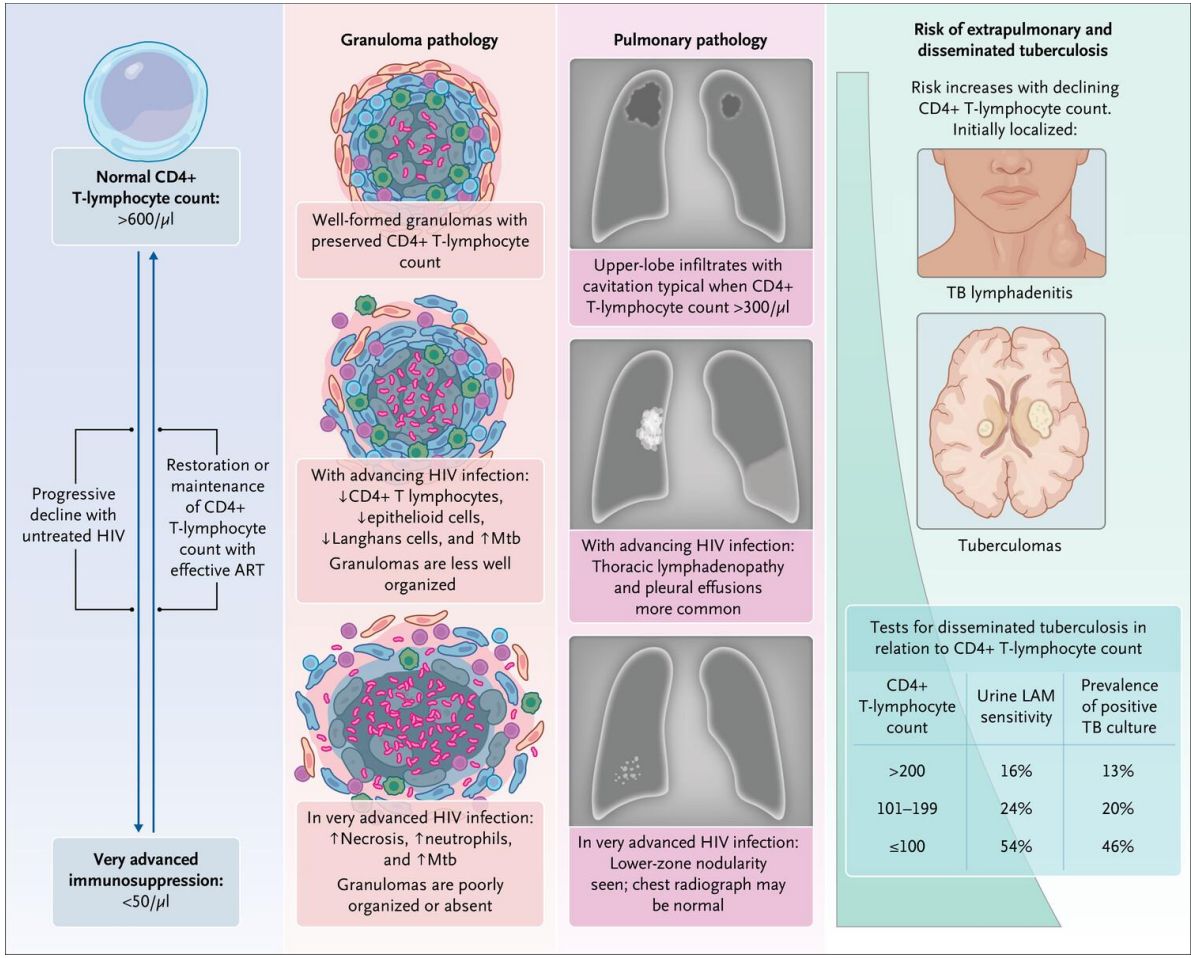
Traitement de la tuberculose infection (tuberculose latente)

- En l'absence d'arguments pour une tuberculose maladie et en l'absence de notion de traitement antérieur :
- Traitement de toute tuberculose infection chez les PVVIH originaires de zones de forte endémie, en particulier si migration ou contage récent (<2 ans) et/ou si CD4 <200/µL
- Schémas thérapeutiques possibles (selon risque d'hépatotoxicité et d'interactions avec le traitement antirétroviral) :
  - isoniazide 3-5 mg/kg/j (ou 300 mg/j), associé à de la vitamine B6, 6 mois
  - isoniazide 3-5 mg/kg/j (ou 300 mg/j), associé à de la vitamine B6 + rifampicine 10 mg/kg/j (ou 600 mg/j), 3 mois
  - rifampicine 10 mg/kg/j (ou 600 mg/j), 4 mois

https://www.has-sante.fr/jcms/p_3529162/fr/prise-en-charge-des-complications-infectieuses-associees-a-l-infection-par-le-vih#toc_1_1_11

VIH et tuberculose
La présentation clinique de la TB est différente

- Pas d'excavations (CD4<200)
- Plus de formes disséminées et/ou sévères
- Diagnostics différentiels+++



N Engl J Med 2024;391:343-355 DOI: 10.1056/NEJMra2308181

VIH et tuberculose
Le diagnostic de TB est plus difficile chez les PVVIH

- Faible sensibilité des techniques standard réalisées sur les expectorations : BAAR négatif> 50%, en particulier si CD4 bas
- Plus grande fréquence des formes extra-pulmonaires, prélèvements souvent BAAR négatifs/cultures négatives.
- Dans les pays de forte endémie TB, pas de cultures => TB non confirmée dans un grand nombre de cas avec traitement présomptifs.

VIH et tuberculose
La révolution des tests d'amplification génique

GenXpert® MTB-RIF Ultra

Recommendations on Xpert MTB/RIF and Xpert Ultra as initial tests in adults and children with signs and symptoms of pulmonary TB

1. In adults with signs and symptoms of pulmonary TB, Xpert MTB/RIF should be used as an initial diagnostic test for TB and rifampicin-resistance detection in sputum rather than smear microscopy/culture and phenotypic DST.
   (Strong recommendation, high certainty of evidence for test accuracy; moderate certainty of evidence for patient-important outcomes[6])
2. In children with signs and symptoms of pulmonary TB, Xpert MTB/RIF should be used as an initial diagnostic test for TB and rifampicin-resistance detection in sputum, gastric aspirate, nasopharyngeal aspirate and stool rather than smear microscopy/culture and phenotypic DST.
   (Strong recommendation, moderate certainty for accuracy in sputum; low certainty of evidence for test accuracy in gastric aspirate, nasopharyngeal aspirate and stool)

WHO 2021 https://www.who.int/publications/i/item/9789240029415

VIH et tuberculose

Tests rapides « point of care » : lipoarabinomanan (LAM)

Utilisation du LAM réduit la mortalité chez les patients avec CD<50

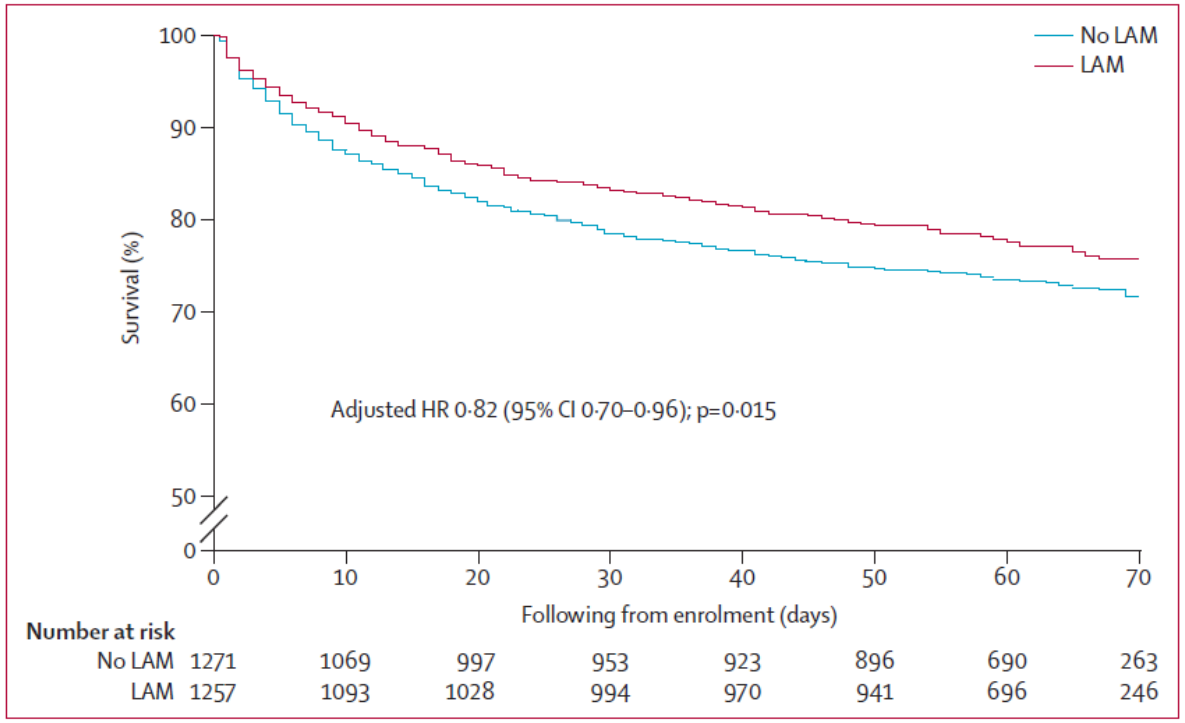


Figure 2: Time to 8-week all-cause mortality
HR=hazard ratio. LAM=lipoarabinomannan. Data are overall HRs and p values for study groups adjusted for country.

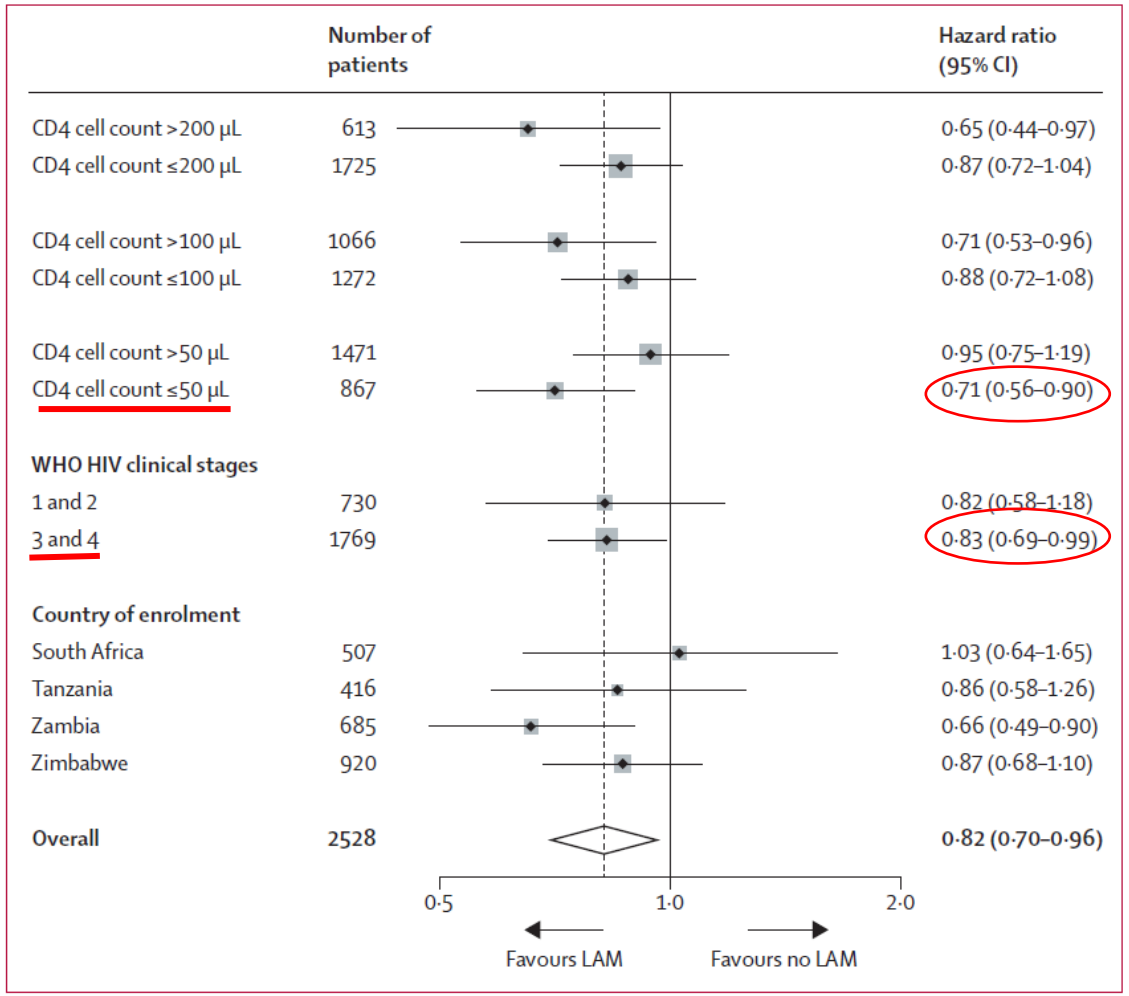


Figure 3: Effect sizes for 8-week all-cause mortality
LAM=lipoarabinomannan. Data are shown for clinical and country-specific subgroups. For each subgroup, the point estimate of the hazard ratio and 95% CI is shown. Number of deaths are shown in the appendix. Lines or CI not including 1 show p values <0·05 when viewed against the relevant baseline.

Peter *et al.* Lancet 2016

VIH et tuberculose
Diagnostic de la TB en France 2024

Examen direct
24h

PCR
M.tuberculosis

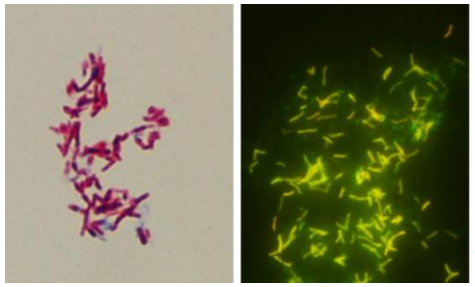
Si BAAR – et forte suspicion : demander PCR+++

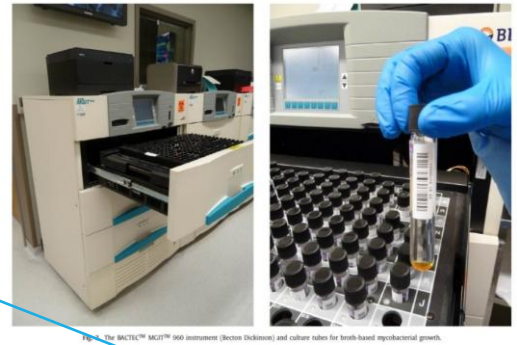
Culture liquide
7-10 j

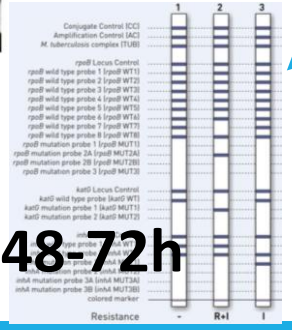
Culture solide
4-6 semaines

Antibiogramme

Diagnostic de résistance 6-8 semaines



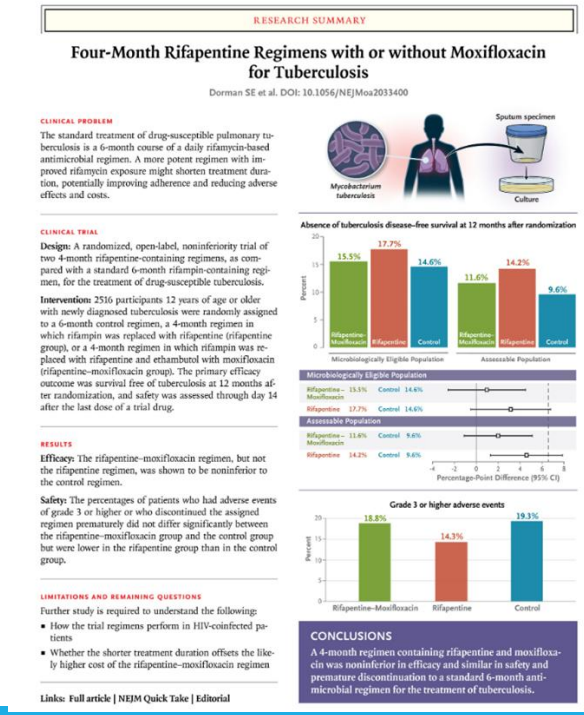




Diagnostic de résistance 48-72h

VIH et tuberculose
Durée du traitement anti-TB

- Traitement standard, mêmes durées que pour les TB hors infection VIH
- Traitement court de 4 mois associant Rifapentine, moxifloxacine, isoniazide, Pyrazinamide recommandé par OMS et USA mais
  - Rifapentine non disponible en Europe
  - Critères d'exclusion de l'essai :
    - Tuberculoses extra-pulmonaires et formes graves de TB
    - CD4<100
    - Femmes enceinte



RESEARCH SUMMARY

Four-Month Rifapentine Regimens with or without Moxifloxacin for Tuberculosis

Dorman SE et al. DOI: 10.1056/NEJMoa2033400

CLINICAL PROBLEM

The standard treatment of drug-susceptible pulmonary tuberculosis is a 6-month course of a daily rifamycin-based antimicrobial regimen. A more potent regimen with improved rifamycin exposure might shorten treatment duration, potentially improving adherence and reducing adverse effects and costs.

CLINICAL TRIAL

Design: A randomized, open-label, noninferiority trial of two 4-month rifapentine-containing regimens, as compared with a standard 6-month rifampin-containing regimen, for the treatment of drug-susceptible tuberculosis.

Intervention: 2516 participants 12 years of age or older with newly diagnosed tuberculosis were randomly assigned to a 6-month control regimen, a 4-month regimen in which rifampin was replaced with rifapentine (rifapentine group), or a 4-month regimen in which rifampin was replaced with rifapentine and ethambutol with moxifloxacin (rifapentine–moxifloxacin group). The primary efficacy outcome was survival free of tuberculosis at 12 months after randomization, and safety was assessed through day 14 after the last dose of a trial drug.

RESULTS

Efficacy: The rifapentine–moxifloxacin regimen, but not the rifapentine regimen, was shown to be noninferior to the control regimen.

Safety: The percentages of patients who had adverse events of grade 3 or higher or who discontinued the assigned regimen prematurely did not differ significantly between the rifapentine–moxifloxacin group and the control group but were lower in the rifapentine group than in the control group.

LIMITATIONS AND REMAINING QUESTIONS

Further study is required to understand the following:

- How the trial regimens perform in HIV-coinfected patients
- Whether the shorter treatment duration offsets the likely higher cost of the rifapentine–moxifloxacin regimen

Links: Full article | NEJM Quick Take | Editorial

CONCLUSIONS

A 4-month regimen containing rifapentine and moxifloxacin was noninferior in efficacy and similar in safety and premature discontinuation to a standard 6-month antimicrobial regimen for the treatment of tuberculosis.

Dorman et al. *N Engl J Med* 2021;384:1705-18.

VIH et tuberculose
Complexité du co-traitement

- Co-administration du TARV, anti-TB, cotrimoxazole ou traitements autres IO
  - Effets secondaires (rash, hepatotoxicité) et interruptions de traitement
  - Nombre de comprimés et difficultés pour adhésion au traitement

- Interactions médicamenteuses entre ARV et anti-TB
  - Rifampicin est un inducteur puissant des CYP450 et UGT1
  - ↘ AUC : IP/rito 57%-75%, efavirenz 26%, raltegravir ↘ 40%, dolutegravir ↘ 54%, Bictegravir ↘ 75%,

- Syndrome de restauration immunitaire (IRIS)
  - Fréquence 15-18%; facteurs de risque CD4<50/mm^3 TB disséminée
  - Pronostic vital rarement en jeu mais lésions compressives

Dean *et al* AIDS 2002
Teed *et al* BMC Pulm Med 2019
Namale *et al* Future Microbiol 2015
Müller *et al* Lancet ID 2010
Abulfathi *et al* Clin Pharmacokinet 2019

Drug-drug Interactions between Anti-tuberculosis Drugs and ARVs

Anti-tuberculosis drugs		ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	DOR	EFV	ETV	NVP	RPV	FTR	MVC	LEN	BIC	CAB/ RPV	DTG	EVG/c	RAL	TAF	TDF
First line and second line drugs	amikacin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔ a
	bedaquiline	↑ b	↑ b	↑	↑	↑62% b	↔	↓18%	↓	↑3%	↔ b	↔ b	↔	↑ c	↔	↔ b	↔	↑	↔	↔	↔
	capreomycin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑ d	↔	↔	↔	↑ E a
	clofazimine	↔	↔	↔	↔	↔	E	↔	↔	↔	E	E	E	↔	E	E	↔	↔	↔	↔	↔
	cycloserine	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	delamanid	e	e	e	e	e	↔	↔ f	↔	↔	↔ g	↔ g	↔	h	↔	↔ g	↔	e	↔	↔	↔
	ethambutol	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	ethionamide	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	isoniazid	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	kanamycin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔ a
	linezolid	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	moxifloxacin	↑ b	↓ b	↔	↓	↓ b	↔	↓	↓	↔	↔ b	↔ b	↔	↔	↔	↔ b	↔	↔	↔	↔	↔
	para-aminosali-cylic acid	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔	↑E
	pretomanid	↓ b	↓ b	↓	↓	↓17% b	↔	↓35%	↓	↓	↔ b	↔ b	↔	↔	↔	↔ b	↔	↓	↔	↔	↔
	pyrazinamide	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	rifabutin	↑ D i	↑ j	↑ D i	↑ j	↑ j	D50% k	↓38% l	D37%	↑17%	D42% m	D30%	n	D #	D38%	D	↔	↑ D i	E19%	D o	↔
	rifampicin	D	D72%	D	D57%	D75% p	D82%	D26% q	D	D58%	D80%	D82%	D r	D82% #	D75%	D	D54% s	D	D40% t	D o	D12%
	rifapentine	D	D	D	D	D	D	D	D	D	D	D	D r	D #	D	D	D u	D	D	D o	↔
	streptomycin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔ a

Double dose INI

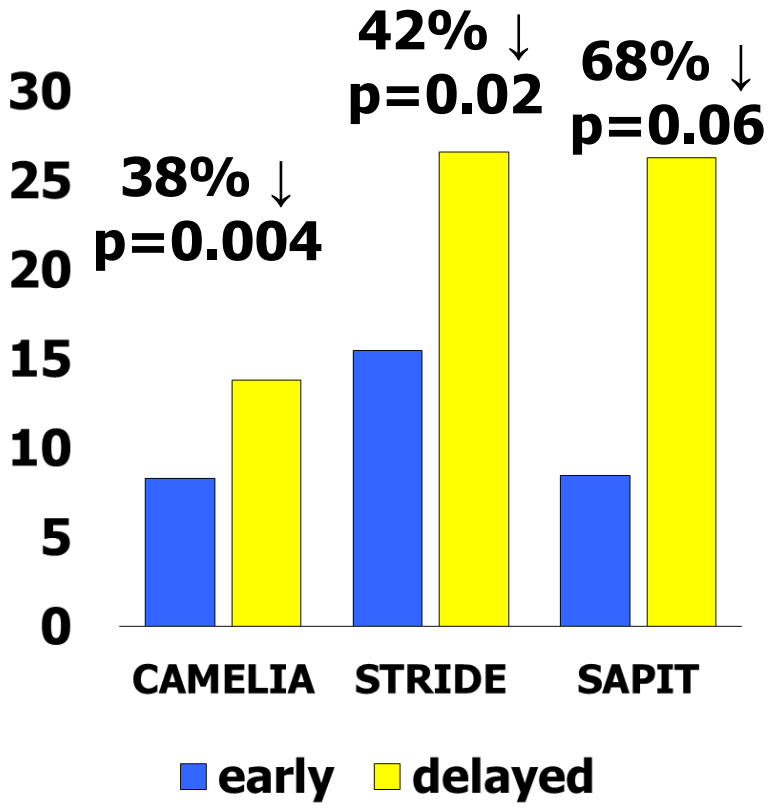
The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 OCTOBER 20, 2011 VOL. 365 NO. 16

VIH et tuberculose

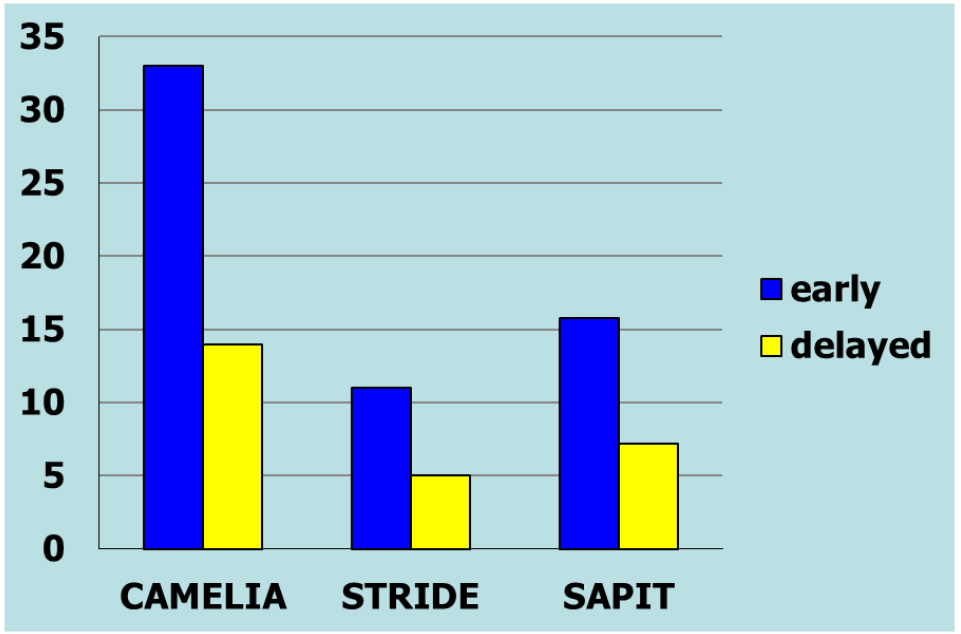
Quand introduire les ARV : Sapit, Stride, Camélia

si CD4 < 50

Réduction SIDA/mortalité



Augmentation des IRIS si traitement précoce



Blanc, NEJM 2011; Havlir NEJM 2011; Abdool Karim NEJM 2011

VIH et tuberculose
Recommandations OMS

Recommandation OMS	**PVVIH sans TB**	**PVVIH avec TB**
Avant 2018 NNRTI	**Co-formulation TLE** **T**enofovir **L**amivudine **E**favirenz 600 mg	**Pas d'ajustement de la dose** Prise 1x/j
Depuis 2018 Inhibiteurs d'intégrase	**Co-formulationTLD*** **T**enofovir **L**amivudine **D**olutegravir 50 mg	**Double dose Dolutegravir:** TLD + Dolutegravir 50 mg Prise 2x/j

*STR de TFX/XTC/DTG non disponible en Europe

WHO updated recommendations 2019
WHO consolidated guidelines 2021
WHO Key facts 2022

TARV en cas de tuberculose : **Recommandations EACS 2023**

Regimen	Main requirements	Footnotes (Additional guidance)
Recommended regimens with rifampicin		
2 NRTIs + INSTI		
TXF/XTC + DTG bid		I (tenofovir salts) II (DTG: dosing)
2 NRTIs + NNRTI		
TXF/XTC + EFV or TDF/FTC/EFV	At bed time or 2 hours before dinner	I (tenofovir salts) III (EFV: suicidality. HIV2 or HIV-1 group 0, dosing)
ABC/3TC + EFV	HLA-B*57:01 negative HBsAg negative HIV-VL < 100,000 copies/mL At bed time or 2 hours before dinner	IV (ABC: HLA-B*57:01) III (EFV: suicidality. HIV-2 or HIV-1 group 0, dosing)
Alternative regimens with rifampicin		
2 NRTIs + INSTI		
TXF/XTC + RAL bid		I (tenofovir salts) V (RAL: dosing)
ABC/3TC + RAL bid	HBsAg negative HLA-B*57:01 negative	IV (ABC: HLA-B*57:01) V (RAL: dosing)

Préférentiel : EFV ou DTG
RAL = alternative

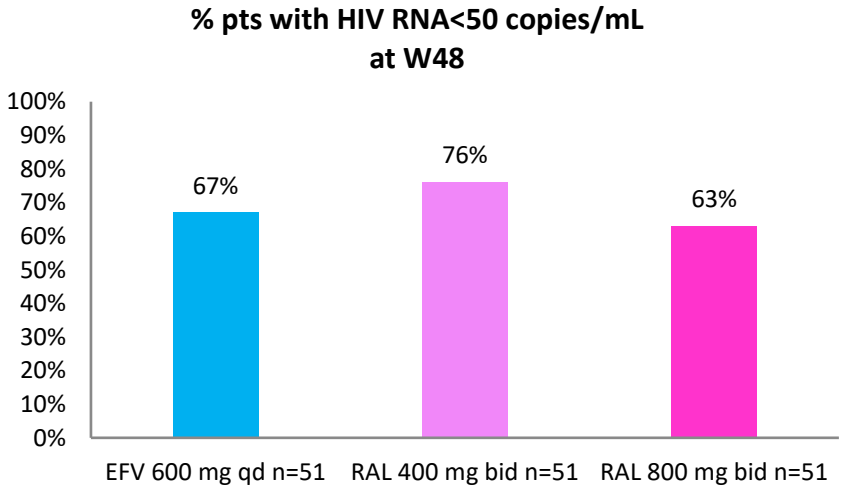
Guidelines EACS. Novembre 2024 online https://eacs.sanfordguide.com/

VIH et tuberculose
Raltegravir et TB

Grinsztejn *et al.* Lancet HIV 2014

Raltegravir for the treatment of patients co-infected with HIV and tuberculosis (ANRS 12 180 Reflate TB): a multicentre, phase 2, non-comparative, open-label, randomised trial

*Beatriz Grinsztejn, Nathalie De Castro, Vincent Arnold, Valdiléa G Veloso, Mariza Morgado, José Henrique Pilotto, Carlos Brites, José Valdez Madruga, Nêmora Tregnago Barcellos, Breno Riegel Santos, Carla Vorsatz, Catherine Fagard, Marilia Santini-Oliveira, Olivier Patey, Constance Delaugerre, Geneviève Chêne, Jean-Michel Molina, for the ANRS 12 180 Reflate TB study group**

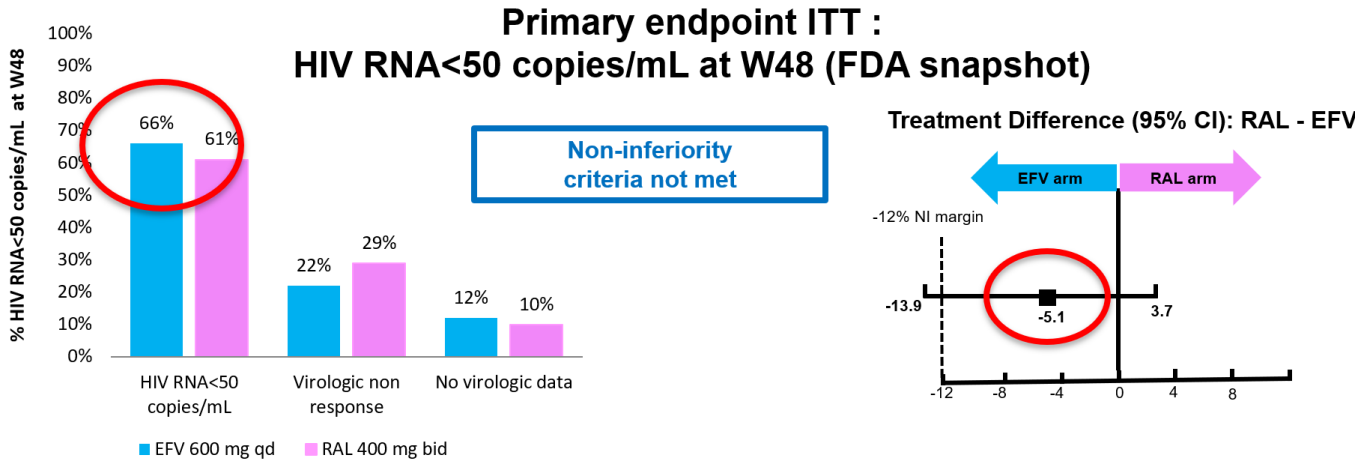


De Castro *et al.* Lancet HIV 2021

Standard dose raltegravir or efavirenz-based antiretroviral treatment for patients co-infected with HIV and tuberculosis (ANRS 12 300 Reflate TB 2): an open-label, non-inferiority, randomised, phase 3 trial

Nathalie De Castro, Olivier Marcy*, Corine Chazallon, Eugène Messou, Serge Eholié, Jean-Baptiste N'takpe, Nilesh Bhatt, Celso Khosa, Isabel Timana Massango, Didier Laureillard, Giang Do Chau, Anaïs Domergue, Valdilea Veloso, Rodrigo Escada, Sandra Wagner Cardoso, Constance Delaugerre, Xavier Anglaret, Jean-Michel Molina, Beatriz Grinsztejn, for the ANRS 12300 Reflate TB2 study group†*

Summary

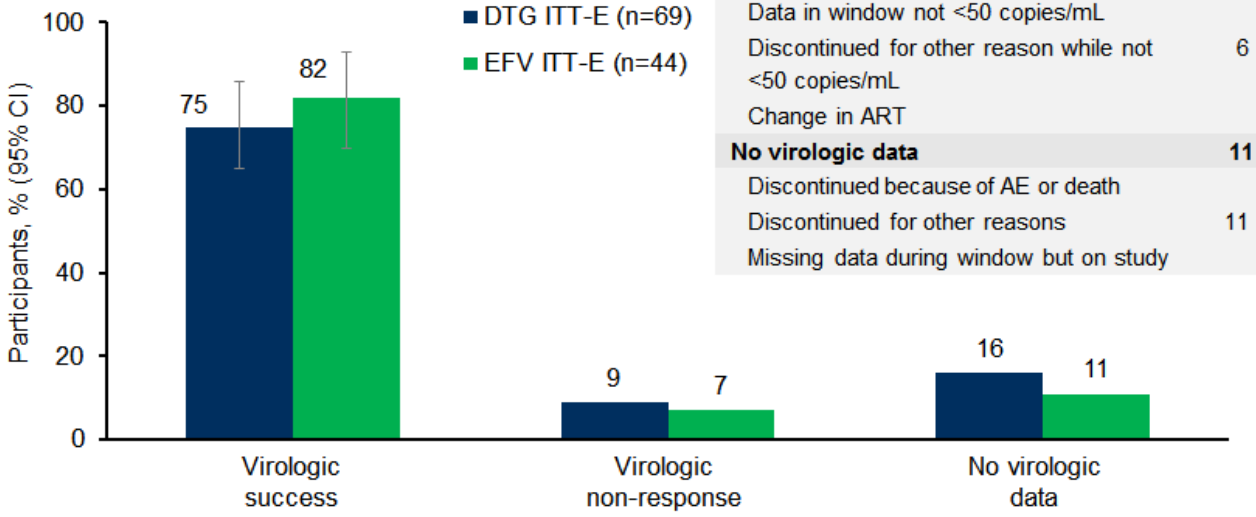


Interaction entre RAL et RIF plus faible qu'observe chez les volontaires sains

Tolérance globalement bonne mais 2 épisodes d'hepatite sévère sous raltegravir 800 mg arm

Grinsztejn *et al.* Lancet HIV 2014
Taburet e*t al*. CID 2015

Dolutegravir et tuberculose
INSPIRING Study

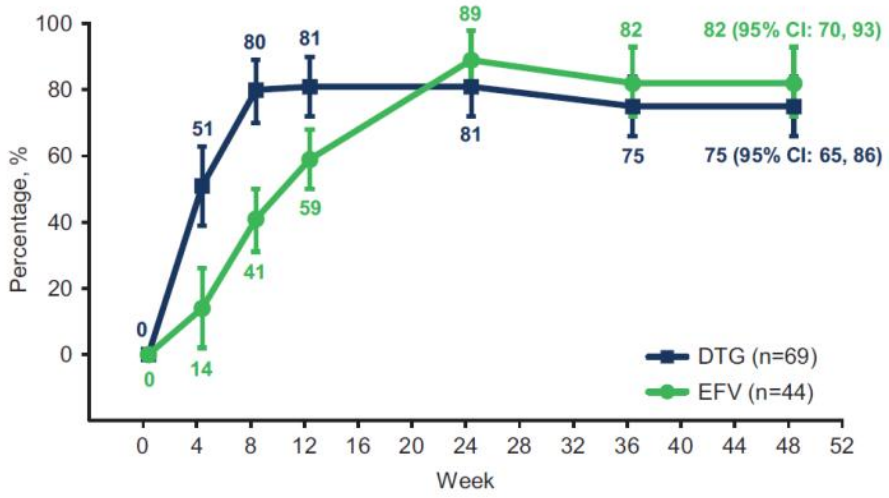


n (%)	DTG (n=69)	EFV (n=44)
Virologic success (HIV-1 RNA <50 copies/mL)	**52 (75)**	**36 (82)**
Virologic nonresponse	**6 (9)**	**3 (7)**
Data in window not <50 copies/mL	0	2 (5)
Discontinued for other reason while not <50 copies/mL	6 (9)[a]	1 (2)[b]
Change in ART	0	0
No virologic data	**11 (16)**	**5 (11)**
Discontinued because of AE or death	0	2 (5)[c]
Discontinued for other reasons	11 (16)[d]	3 (7)[e]
Missing data during window but on study	0	0

[a]DTG: discontinued for other reasons while not <50 copies/mL: 3 lost to follow-up; 2 withdrawal of consent; 1 pregnancy.
[b]EFV: discontinued for other reasons while not <50 copies/mL: 1 lost to follow-up.
[c]EFV: discontinued due to AE: 1 EFV hypersensitivity; 1 increased gamma-glutamyltransferase.
[d]DTG: No virologic data/Discontinued for other reasons: 7 lost to follow-up; 2 pregnancies; 1 physician decision; 1 withdrawal of consent.
[e]EFV: No virologic data/Discontinued for other reasons: 2 lost to follow-up; 1 withdrawal of consent (patient relocated).

Dooley et al. 22nd International AIDS Conference; Amsterdam, the Netherlands. Slides TUAB0206.

22nd International AIDS Conference; July 23-27, 2018; Amsterdam, the Netherlands

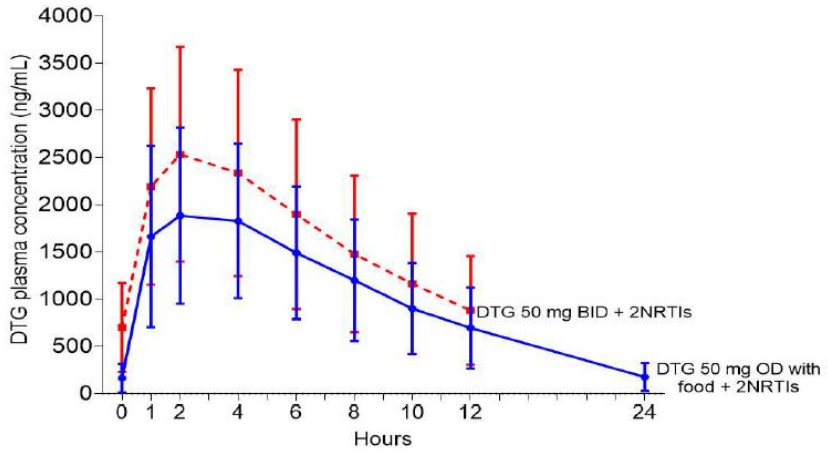


Dooley *et al*. CID 2019

Dolutegravir et tuberculose
Dolutegravir à dose standard ou double dose (LMICs)

HIV NAT 254 (Thailande)

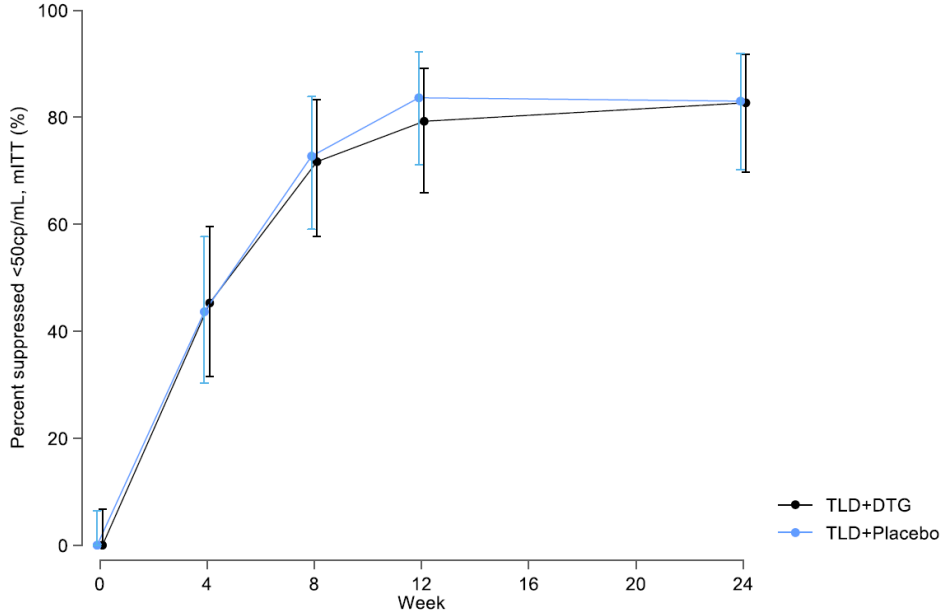
Figure 2. 24 hour pharmacokinetic time-curve of dolutegravir plasma concentrations



Avihingsanon *et al*. AIDS conference 2022

Radiant (Afrique du Sud)

Figure 2: Virological suppression over time (HIV-1 RNA <50 copies/mL) by mITT analysis



Griesel *et al*. Lancet HIV 2023

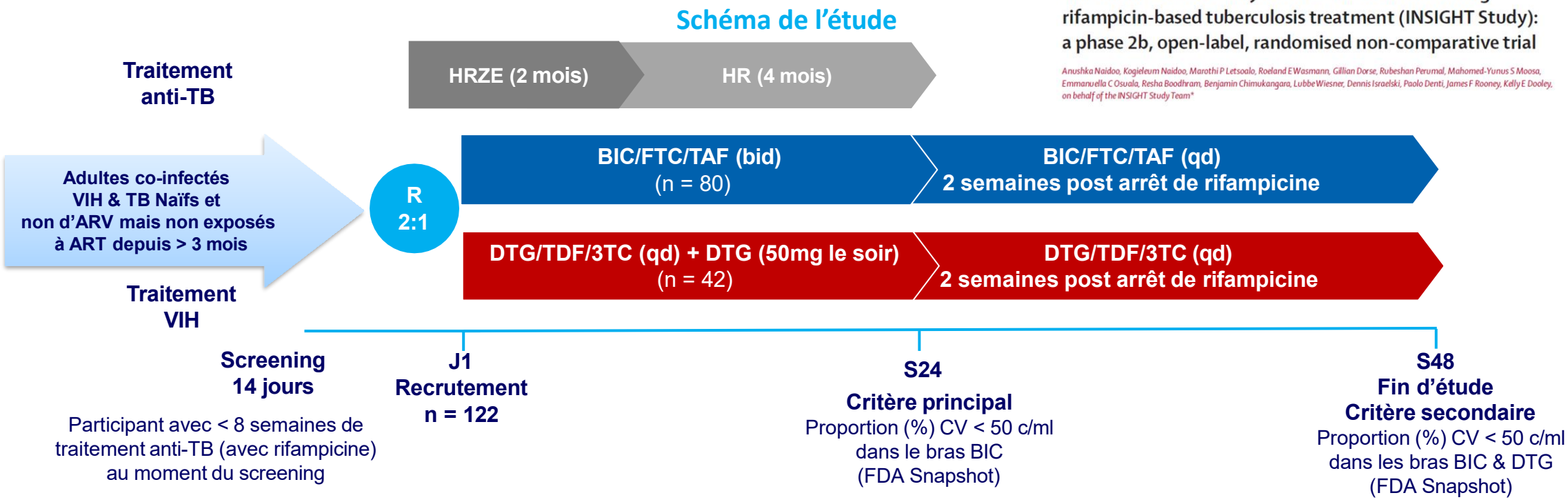
Essai INSIGHT CAPRISA 093 : PK et tolérance de BIC/FTC/TAF bid associé à un traitement anti-TB avec rifampicine (1)

- **Objectif :** efficacité, tolérance et PK d'un schéma en 2 prises quotidiennes de BIC/FTC/TAF chez des adultes co-infectés VIH et TB (**CD4+ >50 cells/µL**), recevant un traitement anti-TB contenant rifampicine

Fixed-dose combination bictegravir–emtricitabine–tenofovir alafenamide twice-daily for treatment of HIV during rifampicin-based tuberculosis treatment (INSIGHT Study): a phase 2b, open-label, randomised non-comparative trial

Anushka Naidoo, Kogieleum Naidoo, Marothi P Letsoalo, Roeland E Wasmann, Gillian Dorse, Rubeshan Perumal, Mahomed-Yunus S Moosa, Emmanuella C Osuala, Resha Boodhram, Benjamin Chimukangara, Lubbe Wiesner, Dennis Israelski, Paolo Denti, James F Rooney, Kelly E Dooley, on behalf of the INSIGHT Study Team*

Schéma de l'étude

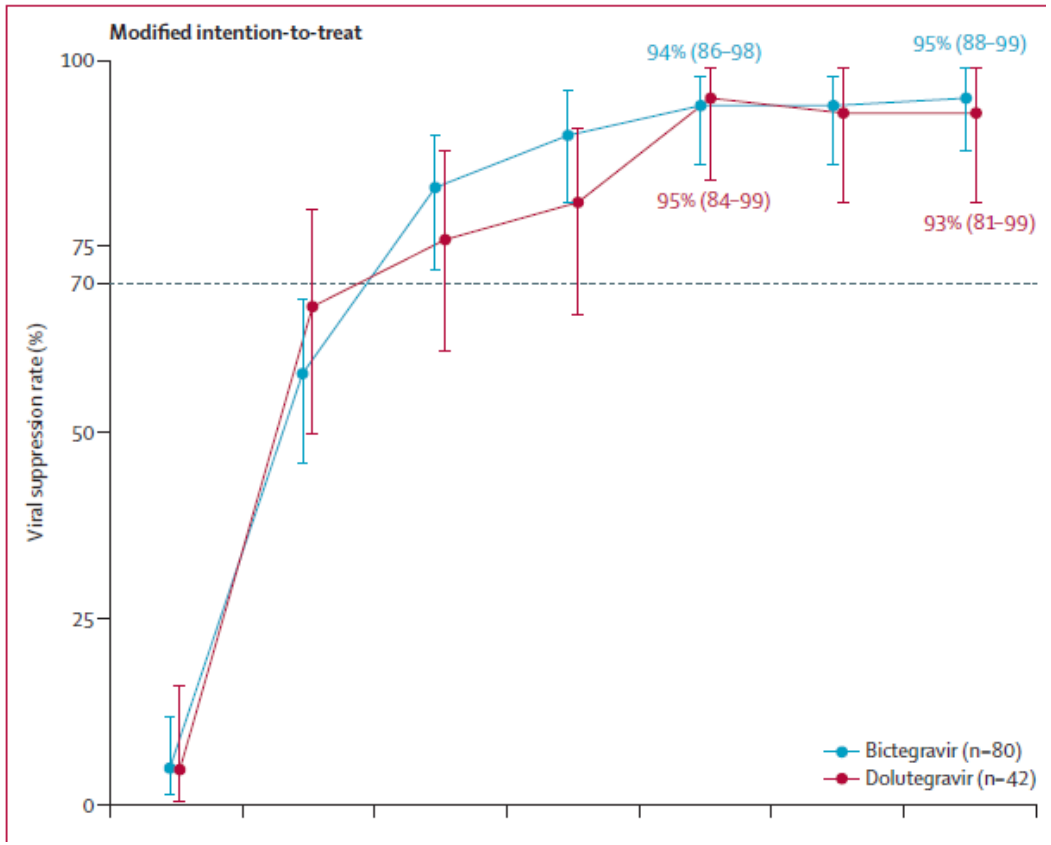


HRZE : isoniazide + rifampicine + pyrazinamide + ethambutol
HR : isoniazide + rifampicine

NNaidoo A, Lancet HIV 2026
https://doi.org/10.1016/s2352-3018(25)00040-2

Essai INSIGHT CAPRISA 093 : PK et tolérance de BIC/FTC/TAF bid associé à un traitement anti-TB avec rifampicine (3)

Critère de jugement principal CV < 50 c/ml à S24 (%) selon le bras de randomisation (FDA snapshot ; IC 95 %)



- **Médiane de changement de CD4 (IQR) /mm³ à S24**
  - BIC : 96 (35 - 137)
  - DTG : 69 (27 - 122)
- **Effets indésirables sévères**
  - BIC : n = 9 (11 %)
  - DTG : n = 3 (7 %)
- **Effets indésirables de grade 3 et 4**
  - Grade 3 : BIC : n = 30 (38 %) et DTG n = 15 (36 %)
  - Grade 4 : BIC : n = 6 (8 %) et DTG n = 6 (14 %)
- **Effets indésirables de grade 3 et 4 (biologiques hépatiques)**
  - Grade 3 : BIC : n = 3 (4 %) et DTG n = 3 (7 %)
  - Grade 4 : BIC : n = 1 (1 %) et DTG n = 0 (0 %)

- La suppression virologique était élevée et similaire à S24 entre les bras BIC/F/TAF bid et DTG/3TC/TDF + DTG qd
- Aucun EI engendrant un arrêt de la stratégie, un retrait de consentement ou un switch des traitements de l'étude

NNaidoo A, Lancet HIV 2026
https://doi.org/10.1016/s2352-3018(25)00040-2

VIH et tuberculose
Formes graves de TB

Quelles stratégies pour diminuer la mortalité?

- Traitement anti-TB préemptif chez patients profondément immunodéprimés sans TB documentée
- Intensification du traitement antibiotique :
  - fortes doses Rifampicine ou Isoniazide
  - Ajout d'une autre molécule : fluoroquinolones, linézolide
- Traitement immunomodulateur (sepsis +/- prévention IRIS)
  - Corticoïdes fortes doses dans TB méningée
  - Corticoïdes doses « modérées » dans TB disséminée
  - Anti-TNF et TB méningée

VIH et tuberculose
Formes graves de TB

- Traitement anti-TB préemptif chez patients

profondément immunodéprimés sans TB documentée

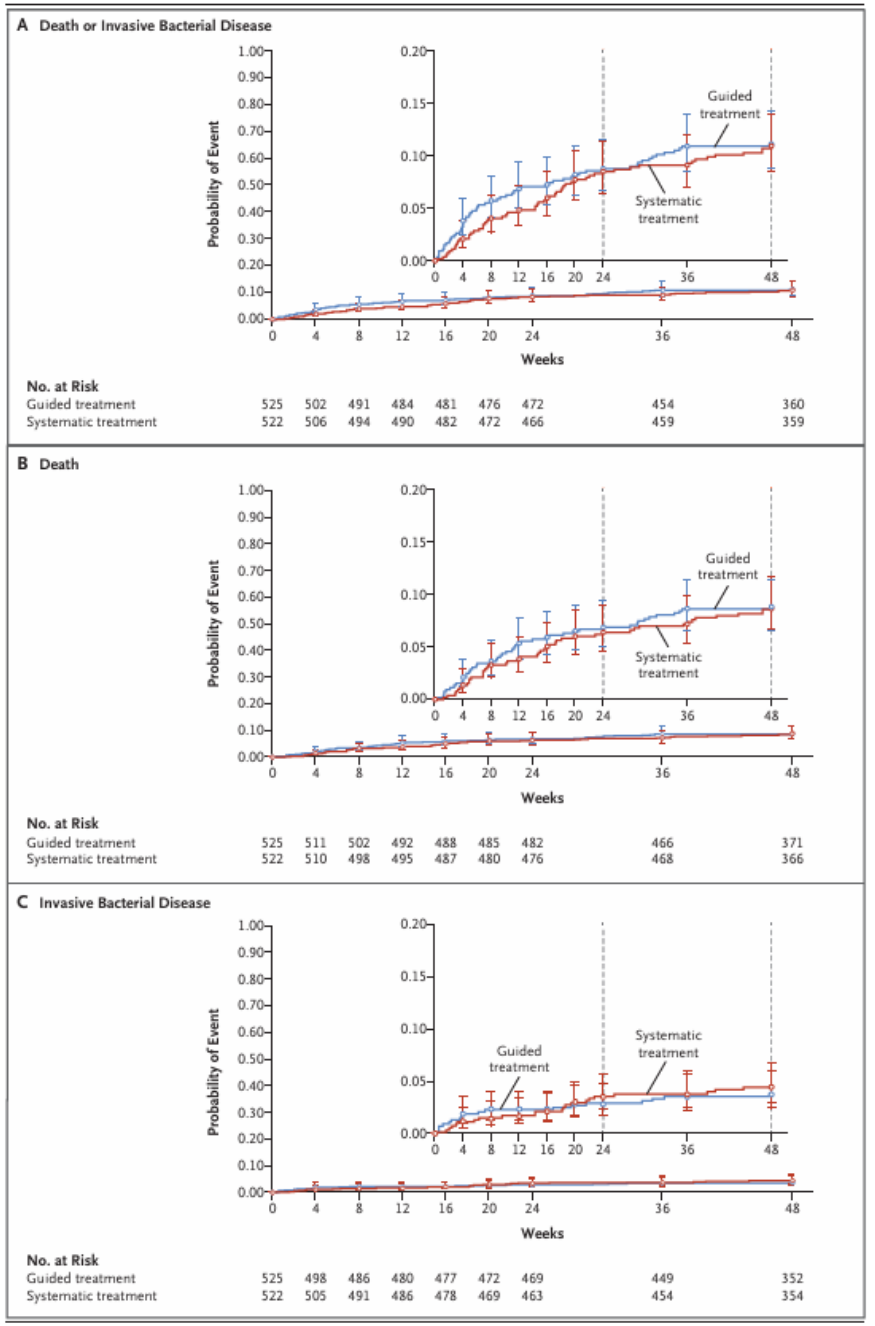
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 18, 2020 VOL. 382 NO. 25

Systematic or Test-Guided Treatment for Tuberculosis in HIV-Infected Adults

F.-X. Blanc, A.D. Badje, M. Bonnet, D. Gabillard, E. Messou, C. Muzoora, S. Samreth, B.D. Nguyen, L. Borand, A. Domergue, D. Rapoud, N. Natukunda, S. Thai, S. Juchet, S.P. Eholié, S.D. Lawn,* S.K. Domoua, X. Anglaret, and D. Laureillard, for the STATIS ANRS 12290 Trial Team†

Pas de différence de mortalité
Diminution du risque de TB mais au prix d'une toxicité hépatique élevée



Blanc et al. *N Engl J Med* 2020;382:2397-410
10.1056/NEJMoa1910708

VIH et tuberculose

Formes graves de TB

- Intensification du traitement antibiotique et corticoïdes :

Supplemental high-dose rifampicin and levofloxacin for inpatients with disseminated HIV-TB

NewStrat-TB trial

Graeme Meintjes*, Phiona Namale, David Barr, Linda Boloko, Marcia Vermeulen, Bryony Simmons, Andrew Hill, Sean Wasserman, Kate Haigh, Freedom Gumedze, Ayanda Trevor Mnguni, Thomas Crede, Yakoob Vallie, Gary Maartens, Charlotte Schutz on behalf of the NewStrat-TB investigators

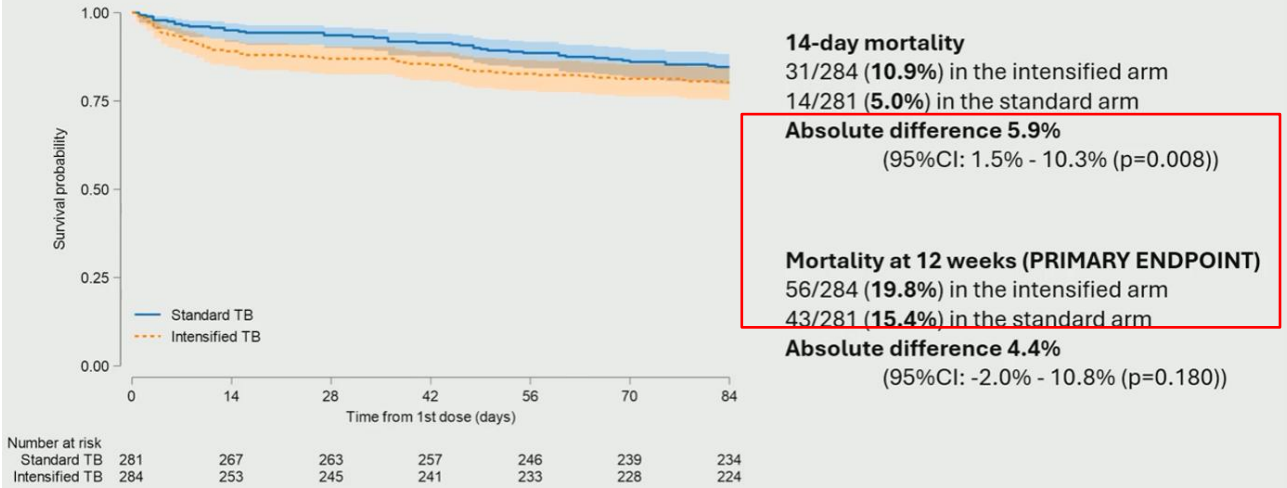
CROI, San Francisco
10 March 2025
Abstract 114

Adjunctive prednisone for inpatients with disseminated HIV-associated TB

Phiona Namale, David Barr, Linda Boloko, Marcia Vermeulen, Bryony Simmons, Andrew Hill, Sean Wasserman, Kate Haigh, Bianca Sossen, Ayanda Trevor Mnguni, Thomas Crede, Yakoob Vallie, Gary Maartens, Charlotte Schutz, Graeme Meintjes, on behalf of the **NewStrat-TB trial** investigators

CROI, Denver, Colorado
23 February 2026
Abstract 124

Mortality at 2 and 12 weeks

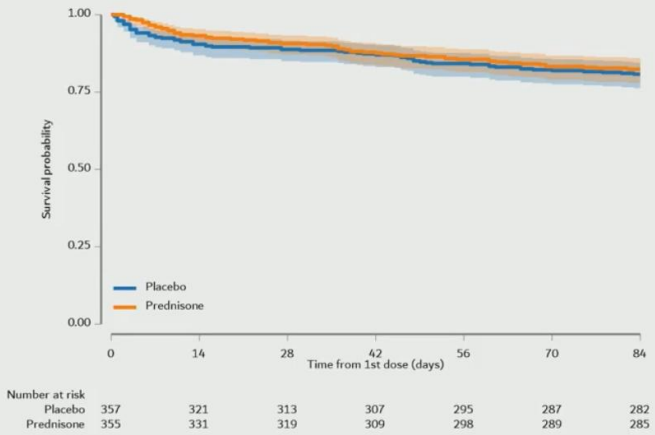


14-day mortality
31/284 (**10.9%**) in the intensified arm
14/281 (**5.0%**) in the standard arm
Absolute difference 5.9%
(95%CI: 1.5% - 10.3% (p=0.008))

Mortality at 12 weeks (PRIMARY ENDPOINT)
56/284 (**19.8%**) in the intensified arm
43/281 (**15.4%**) in the standard arm
Absolute difference 4.4%
(95%CI: -2.0% - 10.8% (p=0.180))

Absolute difference, 95%CI and p-value obtained from KM estimates using bootstrap methodology (1,000 repetitions)

Mortality: Prednisone vs placebo



14-day mortality
24/355 (**6.8% [95%CI 4.6-9.9%]**) in prednisone arm
34/357 (**9.5% [95%CI 6.9-13.1%]**) in placebo arm
Absolute difference -2.8%
(95%CI: -6.9-1.3 (p=0.185))

Mortality at 12 weeks (PRIMARY ENDPOINT)
62/355 (**17.6% [95%CI 14.0-22.0%]**) in prednisone arm
68/357 (**19.2% [95%CI 15.5-23.7%]**) in placebo arm
Absolute difference -1.6%
(95%CI: -7.5-4.2 (p=0.588))

Absolute difference, 95%CI and p-value obtained from KM estimates using bootstrap methodology (1,000 repetitions)

CD4 :40-46/mm^3

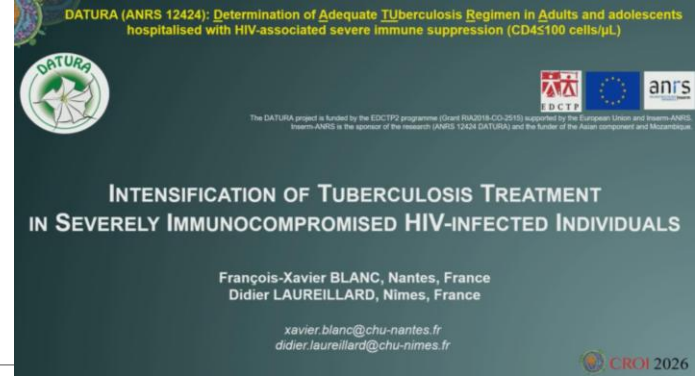
LAM + : 68%; Urine Xpert 81-85%; TB blood culture 20-25%

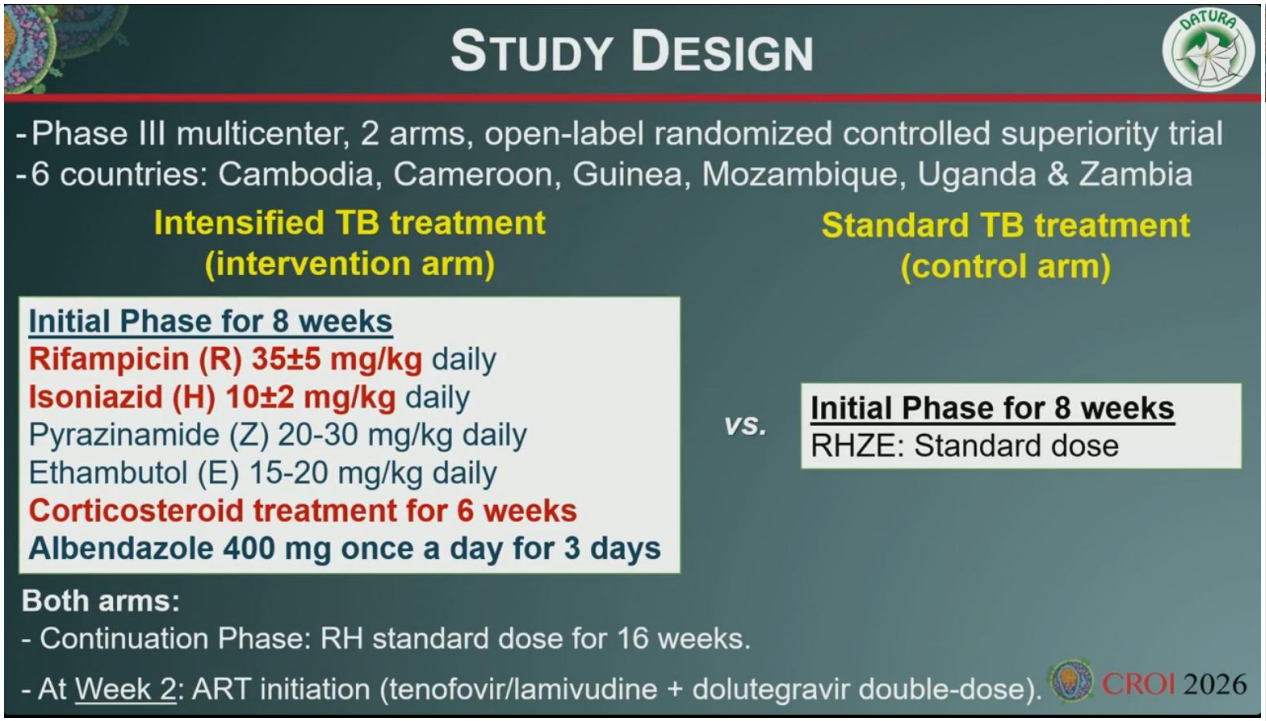
Mentjes et al. CROI 2025; Namale et al. CROI 2026

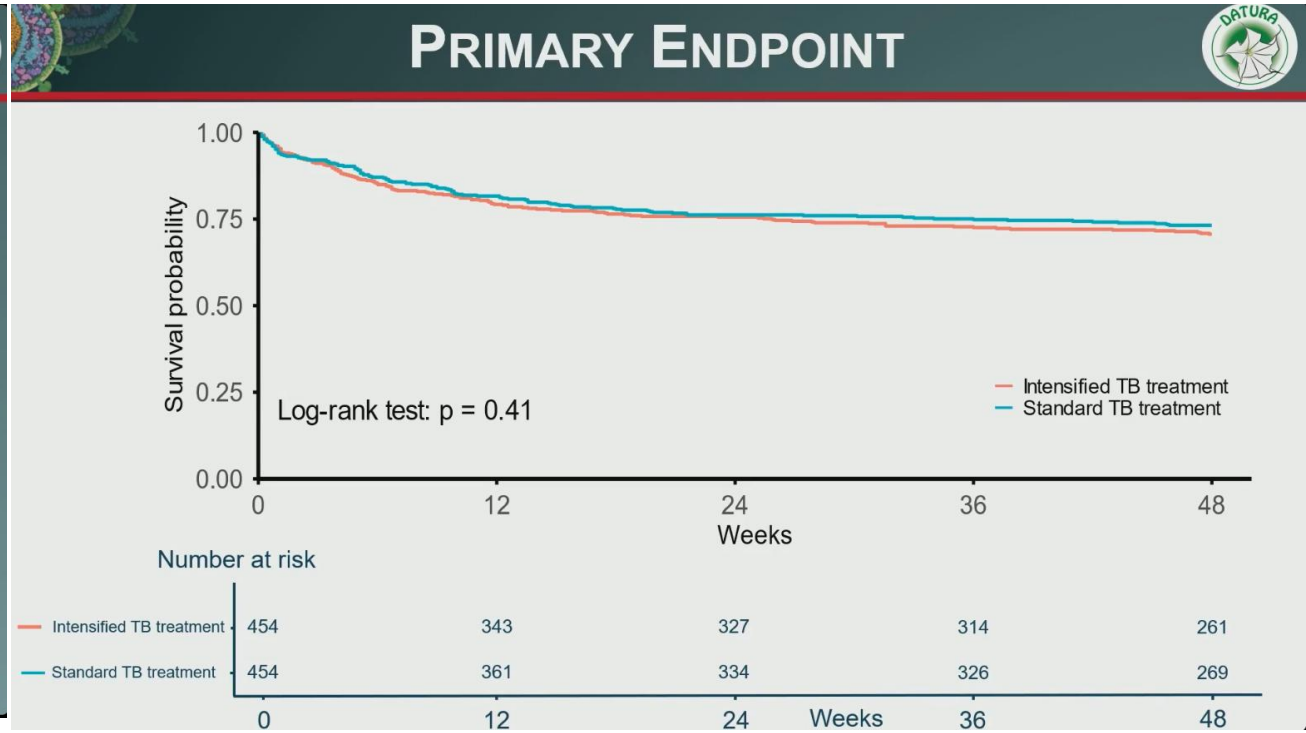
VIH et tuberculose

Formes graves de TB

- Intensification du traitement antibiotique et corticoïdes :







CD4 :44/mm^3

LAM + : 26%

Sputum Xpert + 70%

Blanc FX, CROI 2026

VIH et tuberculose
Formes graves de TB

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 12, 2023 VOL. 389 NO. 15

Adjunctive Dexamethasone for Tuberculous Meningitis in HIV-Positive Adults

Joseph Donovan, Ph.D., Nguyen D. Bang, Ph.D., Darma Imran, M.D., Ho D.T. Nghia, Ph.D., Erlina Burhan, Ph.D., Dau T.T. Huong, M.Sc., Nguyen T.T. Hiep, M.D., Lam H.B. Ngoc, B.Sc., Dang V. Thanh, M.D., Nguyen T. Thanh, M.D., Anna L.S. Wardhani, B.Sc., Kartika Maharani, M.D., Cakra P. Gasmara, M.D., Nguyen H.H. Hanh, M.D., Pham K.N. Oanh, M.D., Riwanti Estiasari, Ph.D., Do D.A. Thu, B.Sc., Ardiana Kusumaningrum, M.D., Le T. Dung, M.D., Do C. Giang, Ph.D., Dang T.M. Ha, Ph.D., Nguyen H. Lan, M.D., Nguyen V.V. Chau, Ph.D., Nguyen T.M. Nguyet, B.Sc., Ronald B. Geskus, Ph.D., Nguyen T.T. Thuong, Ph.D., Evelyne Kestelyn, M.P.H., Raph L. Hamers, Ph.D., Nguyen H. Phu, Ph.D., and Guy E. Thwaites, F.R.C.P., for the ACT HIV Investigators*

TBM prouvée 41% , probable 49%

MRC 2 ou 3 : 62%

70% <100 CD4

52% avec CD4<50

50 % naïfs ARV

/!\ 26% de corticothérapie en ouvert

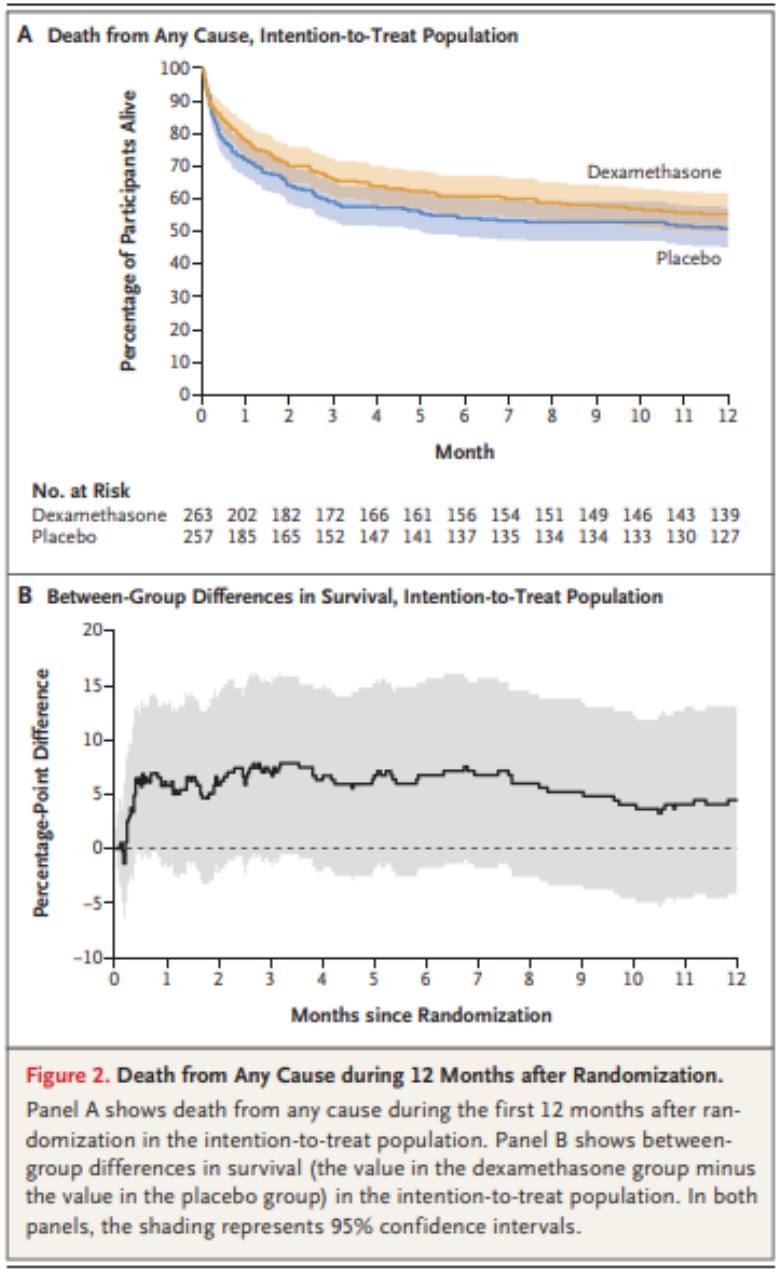


Figure 2. Death from Any Cause during 12 Months after Randomization.
Panel A shows death from any cause during the first 12 months after randomization in the intention-to-treat population. Panel B shows between-group differences in survival (the value in the dexamethasone group minus the value in the placebo group) in the intention-to-treat population. In both panels, the shading represents 95% confidence intervals.

Donovan et al. *N Engl J Med* 2023;389:1357-1367
10.1056/NEJMoa2216218

VIH et tuberculose
Formes graves de TB

The NEW ENGLAND JOURNAL of MEDICINE

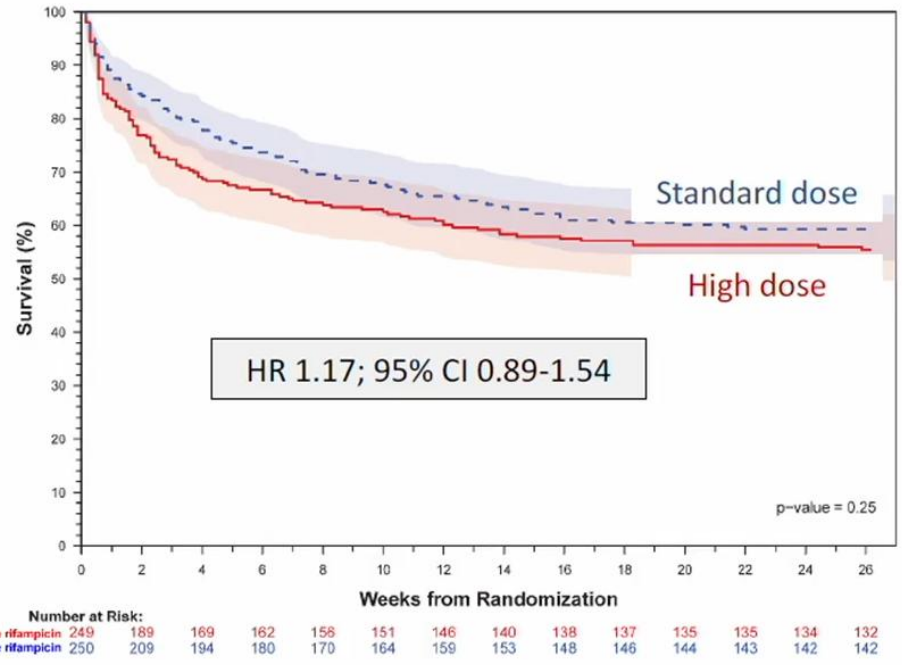
ORIGINAL ARTICLE

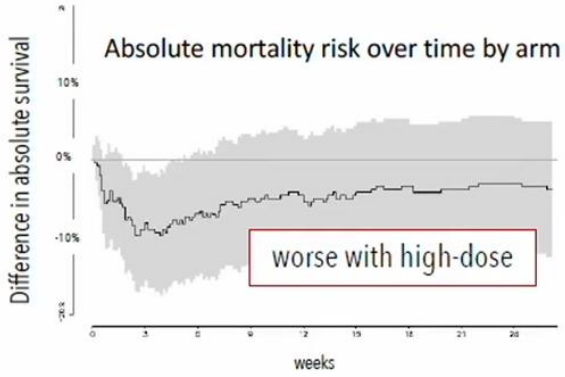
Trial of High-Dose Oral Rifampin in Adults with Tuberculous Meningitis

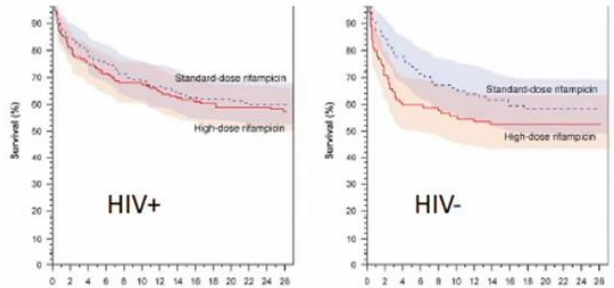
D.B. Meya,[1,2] F.V. Cresswell,[1,3,4] B. Dai,[5] N. Engen,[5] K. Naidoo,[6,7] A.R. Ganiem,[8,9] D. Imran,[10] M. Kabahubya,[1] R.J. Lessells,[6,11] V. Yunivita,[9,12] R. Estiasari,[10] L. Tugume,[1] B. Hlabisa,[6] M.Y. Kurniawati,[13,14] N. Sagita,[15] E. Kagimu,[1] K. Maharani,[10] J. Gakuru,[1] M.N. Gaharu,[16] T. Mugabi,[1] S. Kimuda,[1] S. Namombwe,[1] L. te Brake,[17] R. Aarnoutse,[17] E.M. Svensson,[17,18] A.S. Bangdiwala,[5] S. Namanda,[1] N.C Bahr,[5] A.K. Musubire,[1] M.Y.S. Moosa,[19] R.L. Hamers,[20,21] S. Marais,[22,23] D.R. Boulware,[2] R. van Crevel,[21,24,25] and R. Ruslami,[9,12] for the HARVEST Trial Team*

- Median age 37 (IQR 28-45)
- 44% female
- 80% MRC grade 2/3
- 61% HIV-infected
  (41% on ART, 51% < 100 CD4)
- 47.5% confirmed TB
- 20.5% had < 5 CSF leukocytes
- 70% had received TB drugs at time of randomization (~ 3 days)

No benefit from high-dose rifampicin







Meya et al N Engl J Med 2025;393:2434-46. DOI: 10.1056/NEJMoa2502866

Conclusions et perspectives

En absence d'immunodepression:

- Présentation identiques aux immunocompétents

En cas de deficit immunitaire:

- Formes plus graves et disséminées, diagnostic plus difficile
- IRIS
- Diagnostics différentiels

Durée et type de traitement anti-TB ne diffèrent pas des immunocompétents

Complexité du traitement, même avec ARV "modernes"

Conclusions et perspectives

Efavirenz reste la molecule la mieux évaluée dasn essais de phase III

Pas d'essais de phase III évaluant dolutegravir ou bictegravir

- Risque de diminution de l'adhésion au TARV en cas de prise 2x/jour
- Consequences sur émergence de resistance peu documentées

Traitement pré-emptif, intensification et corticoides dans formes graves: deception...

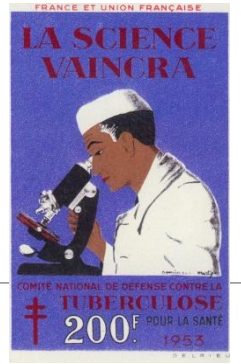
Bictegravir: Pas de données si CD4<50

Perspectives à court/moyen terme

- Traitements sans rifamycines: pas d'interactions significatives entre ARV et bedaquilline/moxiflo/liné/delamanide
- Traitements avec rifapentine: mêmes interactions avec ART que la RIF
- Importance des données vie réelle
- Quelles Nouvelles strategies pour formes graves ???


thank you
danke
рахмат
謝謝
ngiyabonga
teşekkür ederim
spas
Баярлалаа
mersi
kia ora
barka
welalin
tack
mahalo
спасибо
faafetai lava
vinaka
blagodaram
dank je
misaotra
paldies
grazzi
tapadh leat
спасибі
kiitos
dankie
matondo
gracias
хвала
nanni
nandri
dhanyavad
asante
manana
bedankt
bayarlalaa
gràcie
hvala
mauruuru
köszönöm
akun dankon
aciú
obrigada
tenki
murakoze
enkosi
djiere dieuf
tau
mochchakkeram
дякую
mamnun
chokrane
dziękuję
chnorakaloutioun
gratias ago
gràcies
sulpáy
go raibh maith agat
sobodi
dėkuji
obrigado
sagolun
sukriya
kop khun krap
taiku
arigatô
takk
dakujem
trugarez
mėsi
didi madloba
ありがとう
tanemirt
grazie
najis tuke
terima kasih
rahmet
kam sah hamnida
rahmat
diolch
dhanyavadagalu
shukriya
mercé
мерси
তোমাকে ধন্যবাদ
감사합니다
xièxie
ευχαριστώ
merci

INH /immunocompétents : Alaska



ETUDES À BETHEL: INUITS, ALASKA

« HOUSEHOLD CONTACTS »

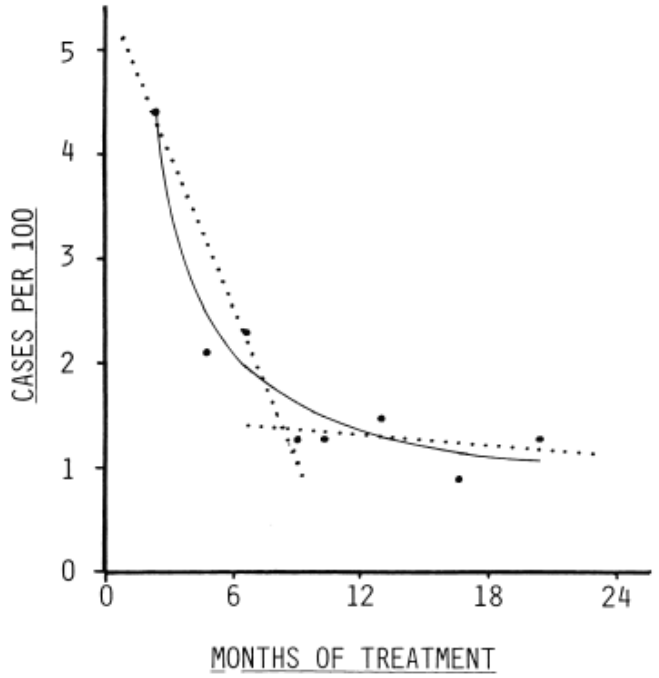


Figure Tuberculosis case rates (%) in the Bethel Isoniazid Studies population according to the number of months isoniazid was taken in the combined programs. Dots represent observed values; thin line, the calculated curve ($y = a + b/x$); and dotted lines, the calculated values based on the first four and last five observations ($y = a + bx$).

1957-1959: ESSAI RANDOMISÉ

INH VS PLACEBO

Contacts de patients avec TB

12 mois de traitement, 5 ans de suivi

60% de réduction de l'incidence effet durable

Risque annuel est passé de 8% à 0,5%

Pas de bénéfice à traitement plus long (12 mois)

Effet similaire si dose prise estimée entre 40 et 100%=>influence sur recommandations ultérieures de 6 mois d'INH

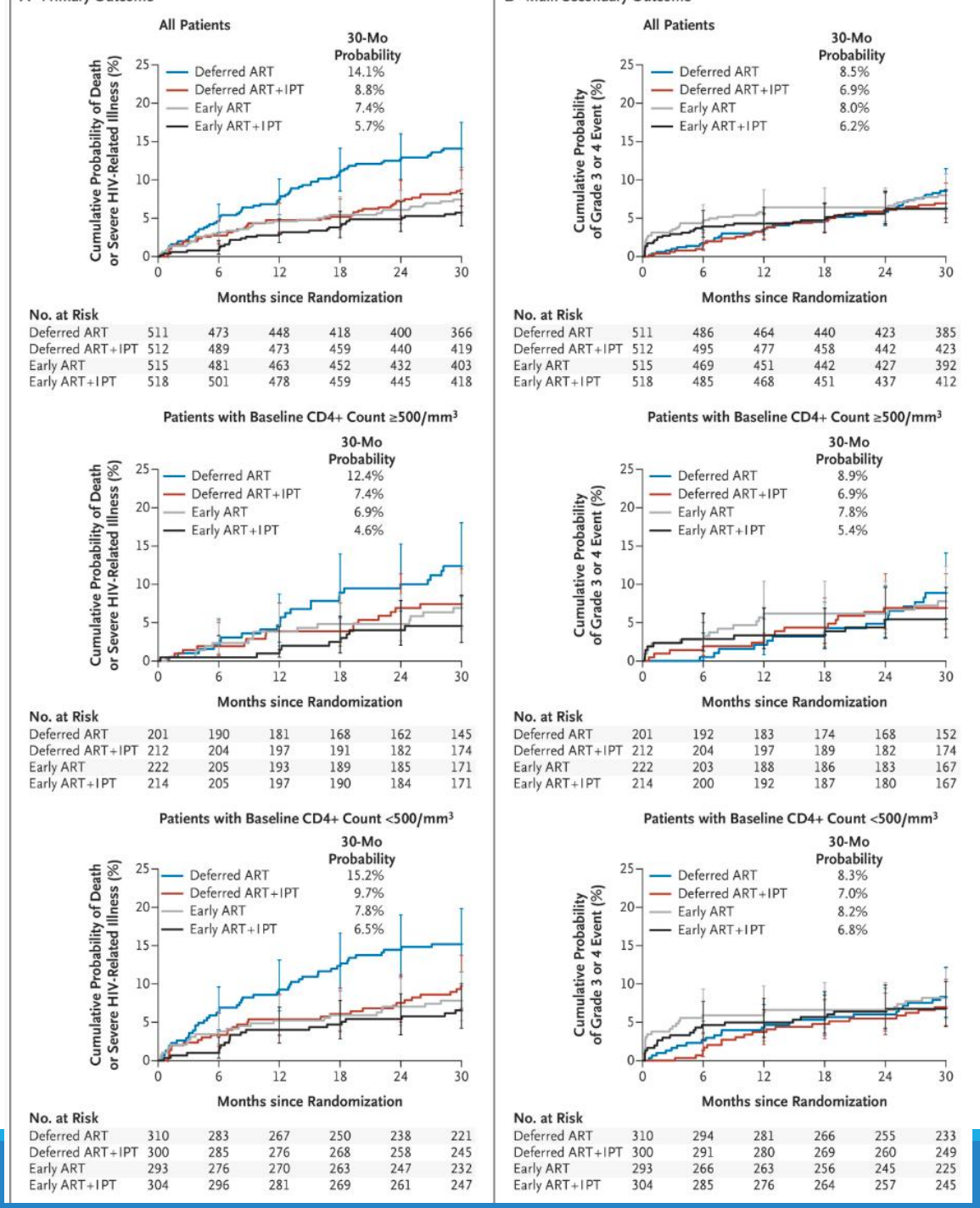
How much isoniazid is needed fr prevention of tuberculosis in immunocompetent adults. Comstock *et al*. Int J Tuberc Lung Dis 1999;3:847-50

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa

The TEMPRANO ANRS 12136 Study Group*



DOI: 10.1056/NEJMoa1507198

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ORIGINAL ARTICLE

A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa

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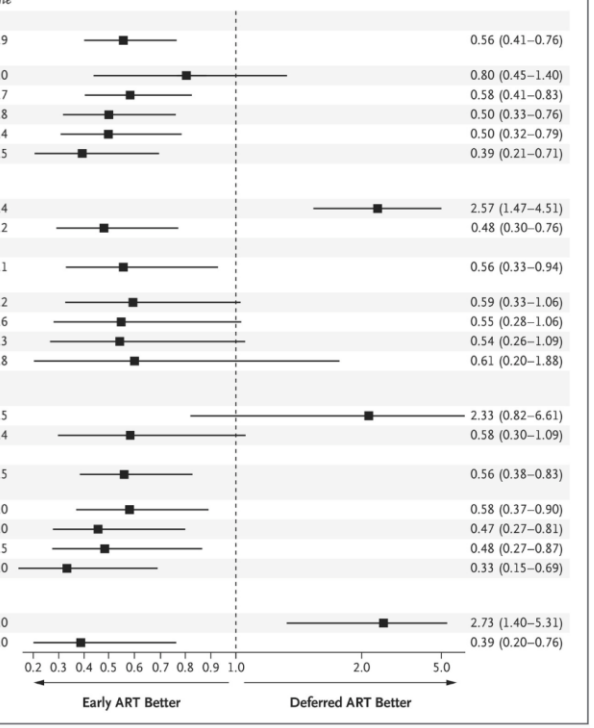
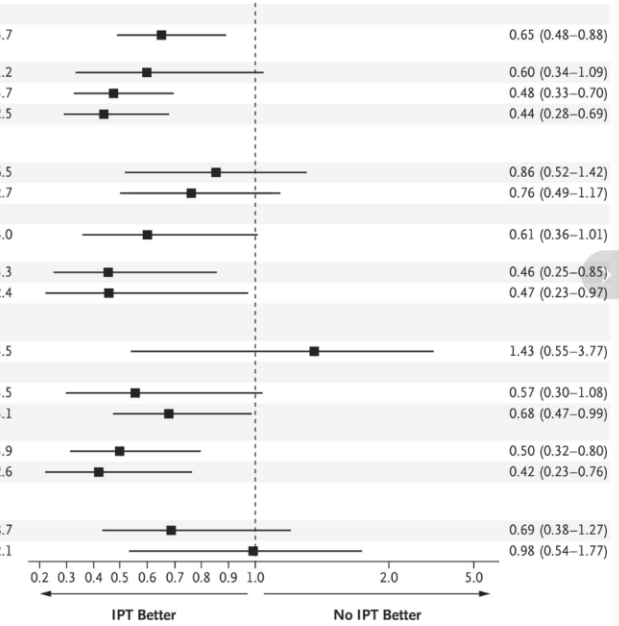
Subgroup	(groups 3 and 4) no. of patients	person-yr	rate	(groups 1 and 2) no. of patients	person-yr	rate	Adjusted Hazard Ratio (95% CI)
All patients							
Death or severe HIV-related illness (primary outcome)	64	2313	2.8	111	2248	4.9	0.56 (0.41–0.76)
Death	21	2520	0.8	26	2502	1.0	0.80 (0.45–1.40)
Death or AIDS	50	2333	2.1	84	2288	3.7	0.58 (0.41–0.83)
AIDS	33	2333	1.4	65	2288	2.8	0.50 (0.33–0.76)
Tuberculosis	28	2337	1.2	55	2298	2.4	0.50 (0.32–0.79)
Invasive bacterial diseases	14	2358	0.6	36	2332	1.5	0.39 (0.21–0.71)
Other grade 3 or 4 adverse event (main secondary outcome)							
<6 mo after randomization	43	489	8.8	17	500	3.4	2.57 (1.47–4.51)
6–30 mo after randomization	27	1775	1.5	57	1798	3.2	0.48 (0.30–0.76)
Patients with baseline CD4+ count ≥500/mm³							
Death or severe HIV-related illness (primary outcome)	23	966	2.4	38	919	4.1	0.56 (0.33–0.94)
Death or AIDS	19	972	1.9	30	930	3.2	0.59 (0.33–1.06)
AIDS	14	972	1.4	24	930	2.6	0.55 (0.28–1.06)
Tuberculosis	12	974	1.2	21	932	2.3	0.54 (0.26–1.09)
Invasive bacterial diseases	5	983	0.5	8	954	0.8	0.61 (0.20–1.88)
Other grade 3 or 4 adverse event (main secondary outcome)							
<6 mo after randomization	12	206	5.8	5	202	2.5	2.33 (0.82–6.61)
6–30 mo after randomization	15	742	2.0	25	727	3.4	0.58 (0.30–1.09)
Patients with baseline CD4+ count <500/mm³							
Death or severe HIV-related illness (primary outcome)	41	1347	3.0	73	1329	5.5	0.56 (0.38–0.83)
Death or AIDS	31	1361	2.3	54	1359	4.0	0.58 (0.37–0.90)
AIDS	19	1361	1.4	41	1359	3.0	0.47 (0.27–0.81)
Tuberculosis	16	1363	1.2	34	1366	2.5	0.48 (0.27–0.87)
Invasive bacterial diseases	9	1375	0.7	28	1379	2.0	0.33 (0.15–0.69)
Other grade 3 or 4 adverse event (main secondary outcome)							
<6 mo after randomization	31	283	10.9	12	299	4.0	2.73 (1.40–5.31)
6–30 mo after randomization	12	1034	1.2	32	1071	3.0	0.39 (0.20–0.76)



Subgroup	IPT (groups 2 and 4) no. of patients	person-yr	rate	No IPT (groups 1 and 3) no. of patients	person-yr	rate	Adjusted Hazard Ratio (95% CI)
All patients							
Death or severe HIV-related illness (primary outcome)	71	2334	3.0	104	2227	4.7	0.65 (0.48–0.88)
Death	18	2538	0.7	29	2484	1.2	0.60 (0.34–1.09)
Death or tuberculosis	42	2372	1.8	83	2263	3.7	0.48 (0.33–0.70)
Tuberculosis	26	2372	1.1	57	2263	2.5	0.44 (0.28–0.69)
Other grade 3 or 4 adverse event (main secondary outcome)							
<6 mo after randomization	28	500	5.6	32	489	6.5	0.86 (0.52–1.42)
6–30 mo after randomization	37	1818	2.0	47	1755	2.7	0.76 (0.49–1.17)
Patients with baseline CD4+ count ≥500/mm³							
Death or severe HIV-related illness (primary outcome)	24	966	2.5	37	920	4.0	0.61 (0.36–1.01)
Death or tuberculosis	15	975	1.5	31	931	3.3	0.46 (0.25–0.85)
Tuberculosis	11	975	1.1	22	931	2.4	0.47 (0.23–0.97)
Other grade 3 or 4 adverse event (main secondary outcome)							
<6 mo after randomization	10	206	4.9	7	202	3.5	1.43 (0.55–3.77)
6–30 mo after randomization							
Patients with baseline CD4+ count <500/mm³	15	750	2.0	25	718	3.5	0.57 (0.30–1.08)
Death or severe HIV-related illness (primary outcome)	47	1368	3.4	67	1307	5.1	0.68 (0.47–0.99)
Death or tuberculosis	27	1396	1.9	52	1332	3.9	0.50 (0.32–0.80)
Tuberculosis	15	1396	1.1	35	1332	2.6	0.42 (0.23–0.76)
Other grade 3 or 4 adverse event (main secondary outcome)							
<6 mo after randomization	18	295	6.1	25	287	8.7	0.69 (0.38–1.27)
6–30 mo after randomization	22	1068	2.1	22	1036	2.1	0.98 (0.54–1.77)



DOI: 10.1056/NEJMoa1507198

VIH et tuberculose

Formes graves de TB

Supplemental high-dose rifampicin and levofloxacin for inpatients with disseminated HIV-TB

NewStrat-TB trial

Graeme Meintjes*, Phiona Namale, David Barr, Linda Boloko, Marcia Vermeulen, Bryony Simmons, Andrew Hill, Sean Wasserman, Kate Haigh, Freedom Gumedze, Ayanda Trevor Mnguni, Thomas Crede, Yakoob Vallie, Gary Maartens, Charlotte Schutz on behalf of the NewStrat-TB investigators

CROI, San Francisco
10 March 2025
Abstract 114

Adjunctive prednisone for inpatients with disseminated HIV-associated TB

Phiona Namale, David Barr, Linda Boloko, Marcia Vermeulen, Bryony Simmons, Andrew Hill, Sean Wasserman, Kate Haigh, Bianca Sossen, Ayanda Trevor Mnguni, Thomas Crede, Yakoob Vallie, Gary Maartens, Charlotte Schutz, Graeme Meintjes, on behalf of the **NewStrat-TB trial** investigators

CROI, Denver, Colorado
23 February 2026
Abstract 124

- Intensification du traitement antibiotique et corticoïdes :

NewStrat-TB trial: RCT with 2 x 2 factorial design

Hospitalised adults Disseminated HIV-TB

- Standard TB treatment + Prednisone 14 days
- Standard TB treatment + Placebo 14 days
- Intensified TB treatment + Prednisone 14 days
- Intensified TB treatment + Placebo 14 days

3 hospitals in Cape Town
Started 11 August 2021

https://clinicaltrials.gov/study/NCT04951986

Intensified TB treatment
Standard TB treatment with
Rif 35 mg/kg + Levofloxacin
750 mg < 46 kg, 1000 mg ≥ 46 kg

Prednisone 1.5mg/kg/day

From Day 15 - all receive standard TB treatment to 6 months

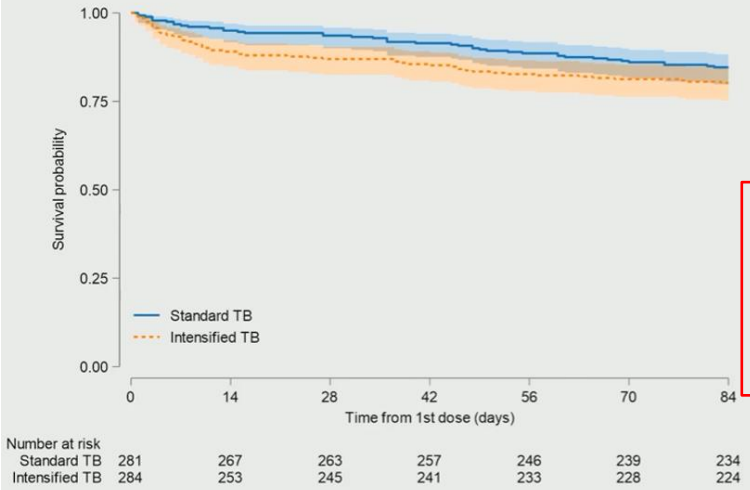
Primary endpoint:
12-week all-cause mortality

Target sample size = 732. Powered to demonstrate relative reduction in mortality of 32% at 12 weeks (28% to 19% absolute reduction)[4]

Mentjes et al. CROI 2025; Namale et al. CROI 2026

VIH et tuberculose
Formes graves de TB

Mortality at 2 and 12 weeks

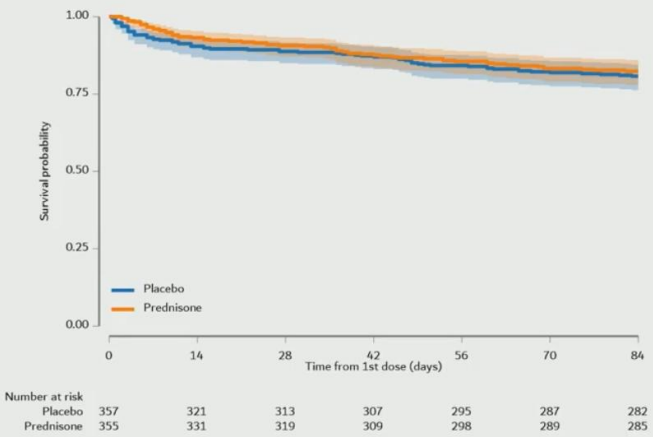


14-day mortality
31/284 (**10.9%**) in the intensified arm
14/281 (**5.0%**) in the standard arm
Absolute difference 5.9%
(95%CI: 1.5% - 10.3% (p=0.008))

Mortality at 12 weeks (PRIMARY ENDPOINT)
56/284 (**19.8%**) in the intensified arm
43/281 (**15.4%**) in the standard arm
Absolute difference 4.4%
(95%CI: -2.0% - 10.8% (p=0.180))

Absolute difference, 95%CI and p-value obtained from KM estimates using bootstrap methodology (1,000 repetitions)

Mortality: Prednisone vs placebo



14-day mortality
24/355 (**6.8% [95%CI 4.6-9.9%]**) in prednisone arm
34/357 (**9.5% [95%CI 6.9-13.1%]**) in placebo arm
Absolute difference -2.8%
(95%CI: -6.9-1.3 (p=0.185))

Mortality at 12 weeks (PRIMARY ENDPOINT)
62/355 (**17.6% [95%CI 14.0-22.0%]**) in prednisone arm
68/357 (**19.2% [95%CI 15.5-23.7%]**) in placebo arm
Absolute difference -1.6%
(95%CI: -7.5-4.2 (p=0.588))

Absolute difference, 95%CI and p-value obtained from KM estimates using bootstrap methodology (1,000 repetitions)

CD4 :40-46/mm^3
LAM + : 68%
Urine Xpert 81-85%
TB blood culture 20-25%

Mentjes et al. CROI 2025; Namale et al. CROI 2026

VIH et tuberculose
Formes graves de TB

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trial of High-Dose Oral Rifampin in Adults with Tuberculous Meningitis

D.B. Meya,[1,2] F.V. Cresswell,[1,3,4] B. Dai,[5] N. Engen,[5] K. Naidoo,[6,7] A.R. Ganiem,[8,9] D. Imran,[10] M. Kabahubya,[1] R.J. Lessells,[6,11] V. Yunivita,[9,12] R. Estiasari,[10] L. Tugume,[1] B. Hlabisa,[6] M.Y. Kurniawati,[13,14] N. Sagita,[15] E. Kagimu,[1] K. Maharani,[10] J. Gakuru,[1] M.N. Gaharu,[16] T. Mugabi,[1] S. Kimuda,[1] S. Namombwe,[1] L. te Brake,[17] R. Aarnoutse,[17] E.M. Svensson,[17,18] A.S. Bangdiwala,[5] S. Namanda,[1] N.C Bahr,[5] A.K. Musubire,[1] M.Y.S. Moosa,[19] R.L. Hamers,[20,21] S. Marais,[22,23] D.R. Boulware,[2] R. van Crevel,[21,24,25] and R. Ruslami,[9,12] for the HARVEST Trial Team*

HARVEST trial design

Double-blinded, placebo controlled

Eligible: **microbiologically confirmed / clinically diagnosed**

Exclusion: confirmed other Dx; > 5 days TB therapy; protease-inh

All receive standard dose H, Z, E + steroids

Intervention: Rifampicin 35mg/kg/day weeks 0-8

(FDC + 4 pills 300 mg Rif if ≥ 38 kg, + 3 pills if < 38 kg)

Control: Rif 10mg/kg/day + placebo

(FDC + 4 pills placebo if ≥ 38 kg, + 3 pills if < 38 kg)

Stratification by site, HIV status and BMRC (severity) grade

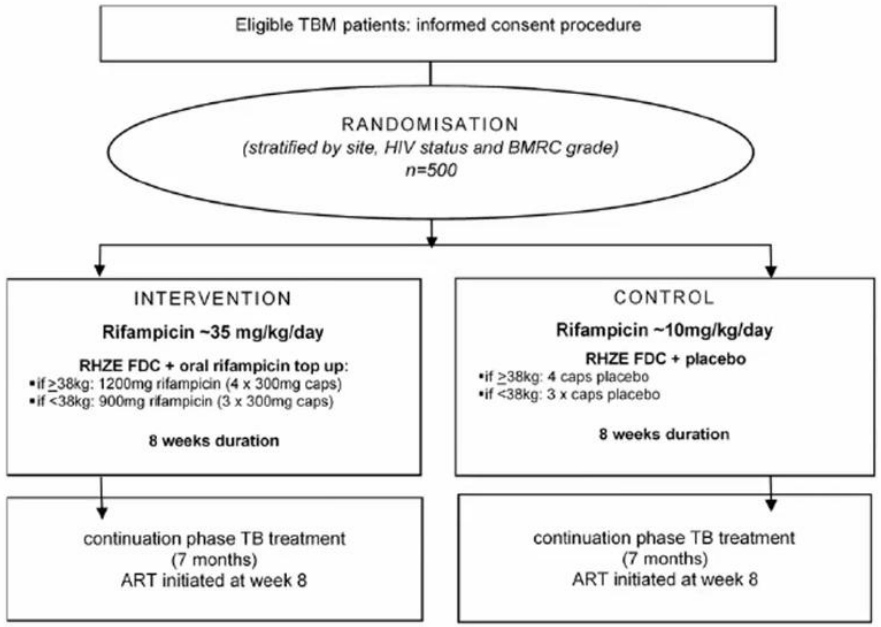
Primary endpoint: 6-month mortality

Powered for 13% absolute survival benefit and 5% LTFU

Secondary endpoints:

12-mth mortality, functional outcomes, safety, days of hospitalization, drug discontinuation, rehospitalization for neurological deterioration, management DILI

other: PK-PD; cost-effectiveness

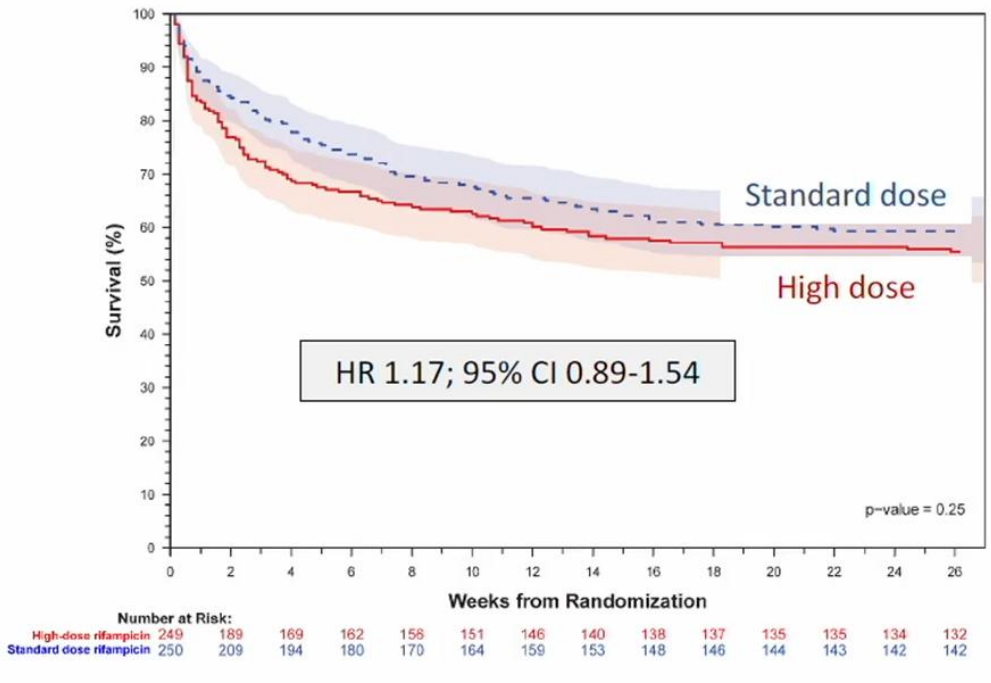


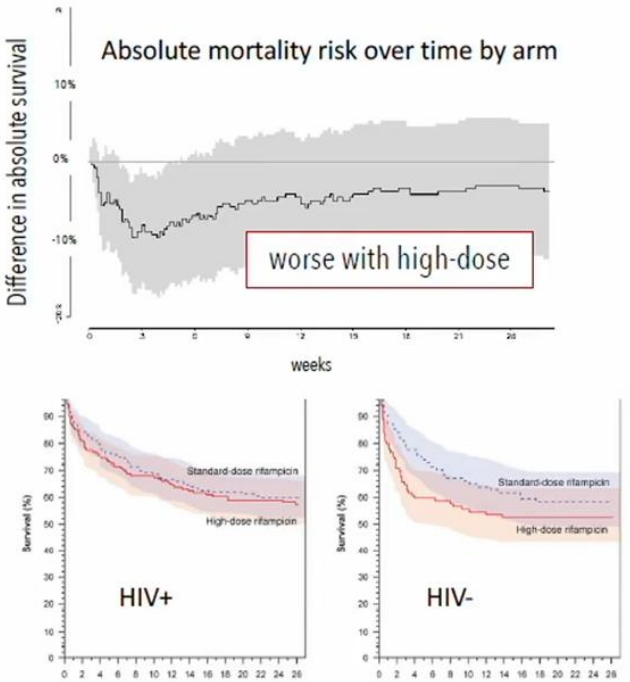
Meya et al N Engl J Med 2025;393:2434-46. DOI: 10.1056/NEJMoa2502866

VIH et tuberculose
Formes graves de TB

- Median age 37 (IQR 28-45)
- 44% female
- 80% MRC grade 2/3
- 61% HIV-infected
  (41% on ART, 51% < 100 CD4)
- 47.5% confirmed TB
- 20.5% had < 5 CSF leukocytes
- 70% had received TB drugs at time of randomization (~ 3 days)

No benefit from high-dose rifampicin





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