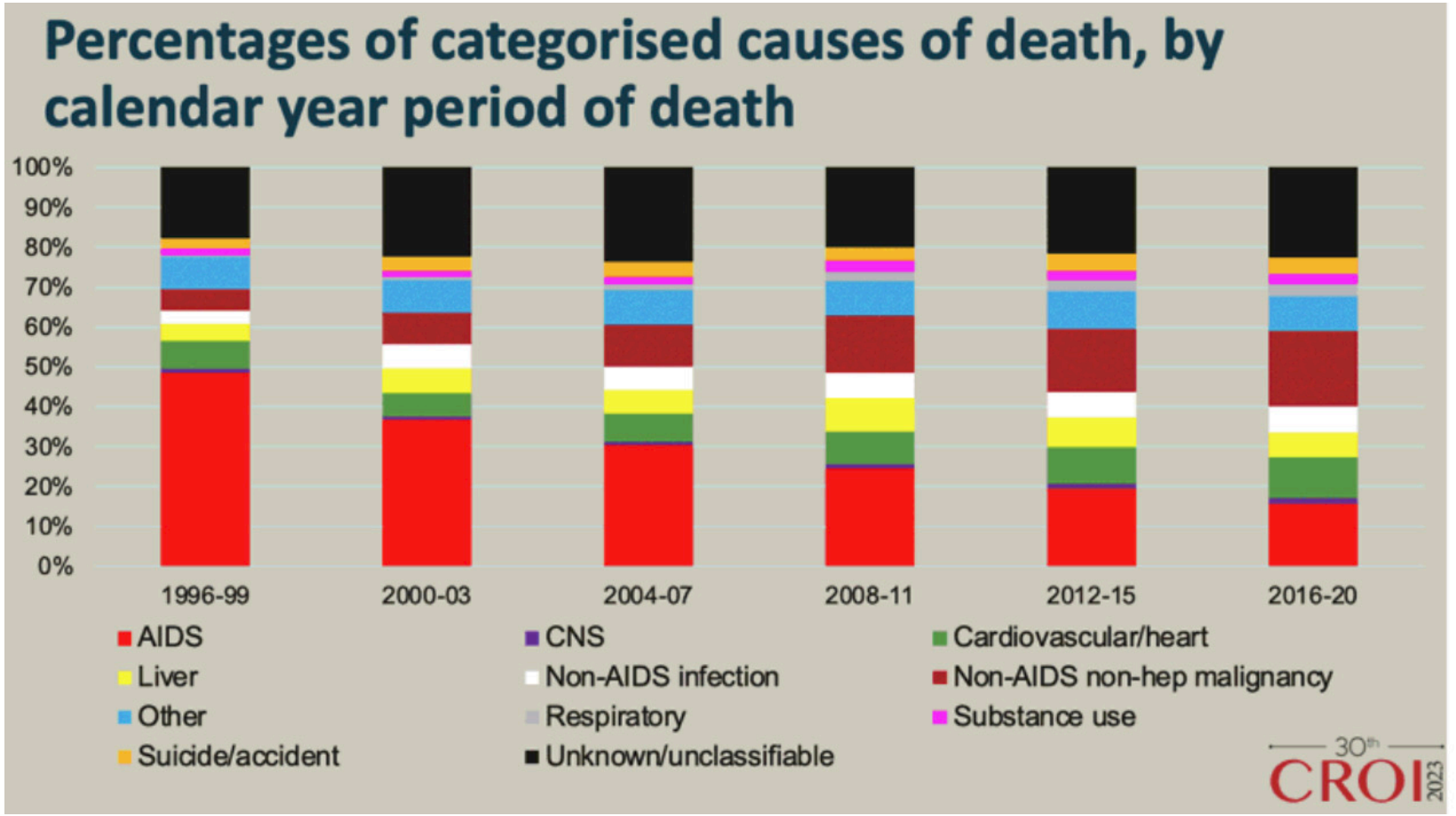
Opportunistic Infections: What's new ?

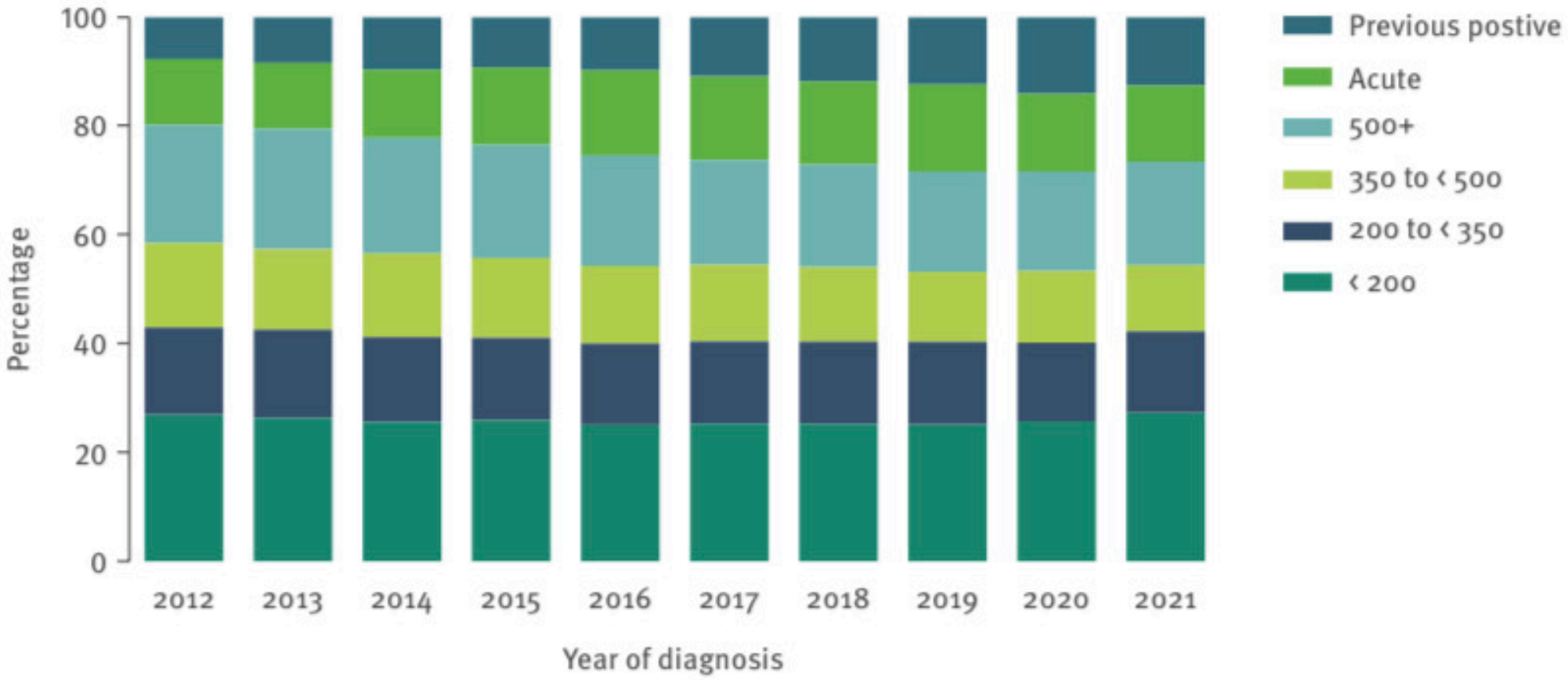
Prof. S. De Wit

Causes of mortality amongst PWH on ART: Europe and North America



CROI 2023:abstract 156

Proportion with late presentation



ECDC/WHO: HIV/AIDS Surveillance in Europe 2022
https://www.ecdc.europa.eu/en/publications-data/hiv-aids-jo surveillance-2021-data

IID INSTITUTE OF INFECTIOUS DISEASES

Outline

- Tuberculosis
- Cryptococcosis
- Histoplasmosis
- Pneumocystosis
- Mpox
- Toxoplasmosis
- Leishmaniosis

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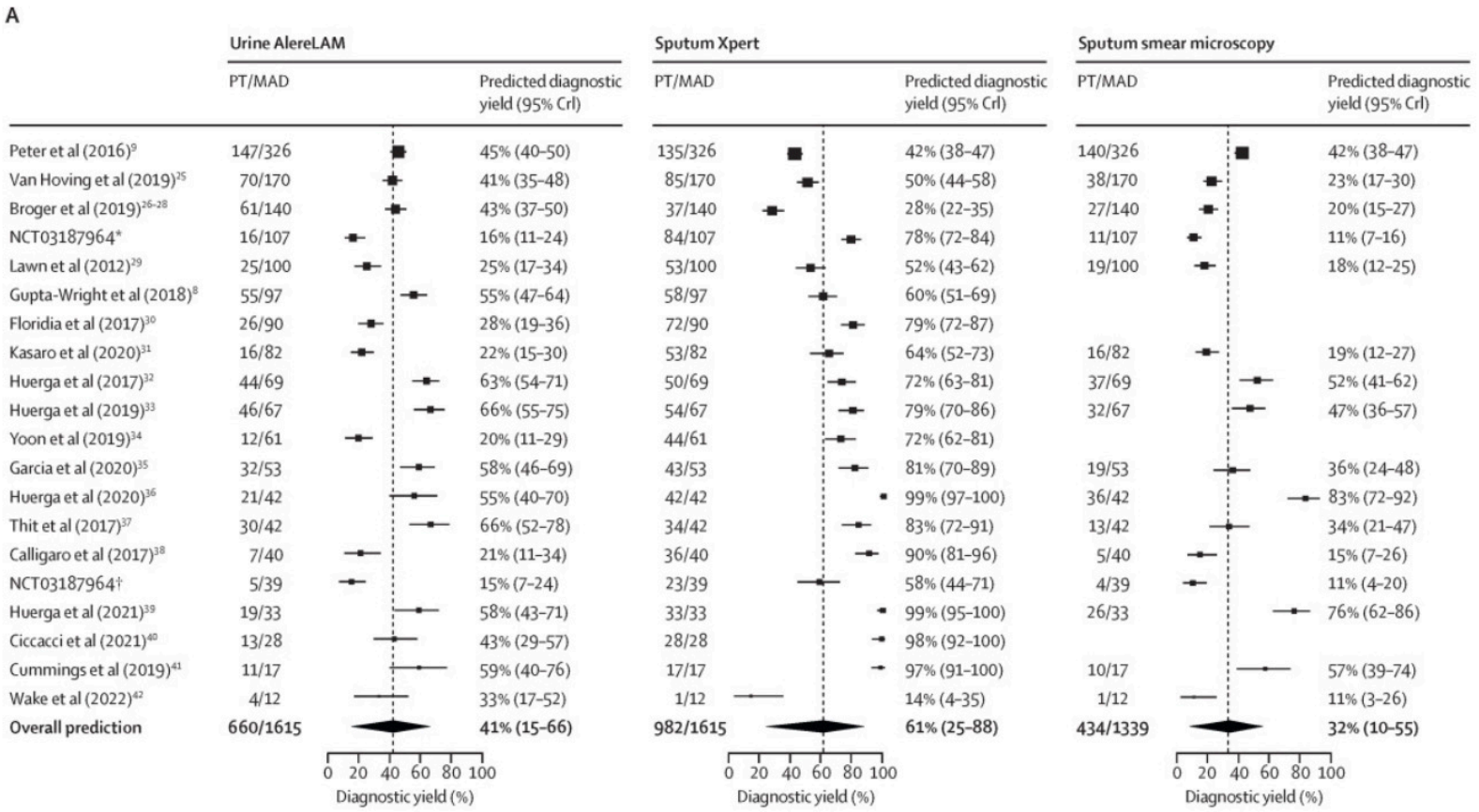
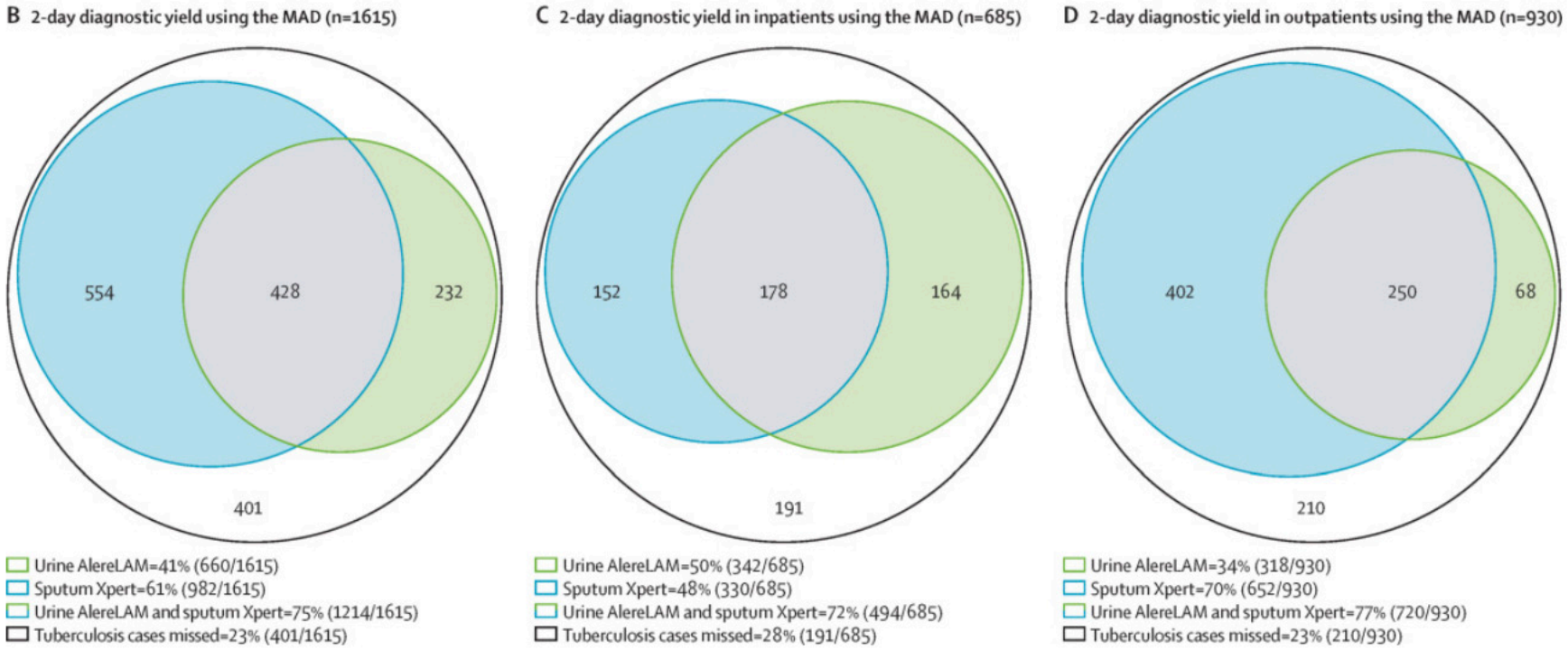
Euroguidelines

Diagnostic yields of urinary AlereLAM



Lancet Global Health 2023 Jun;11 (6):e903-e916

2-day diagnostic yield of Urinary AlereLAM

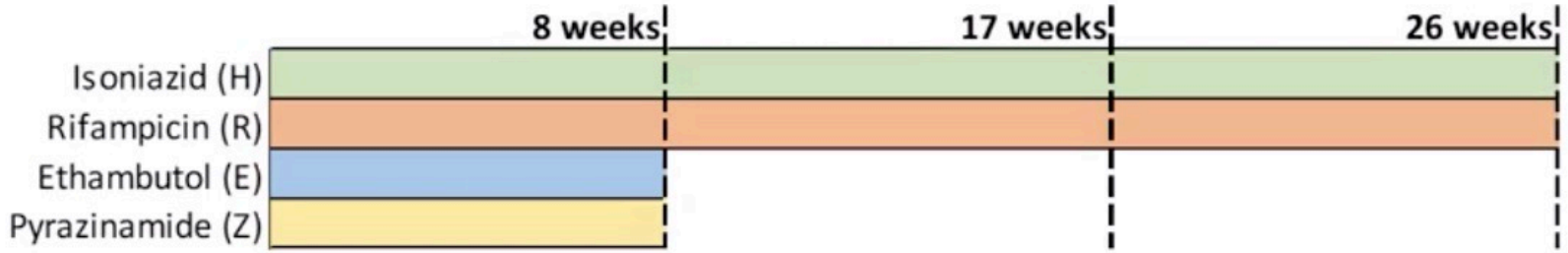


Lancet Global Health 2023 Jun;11(6):e903-e916

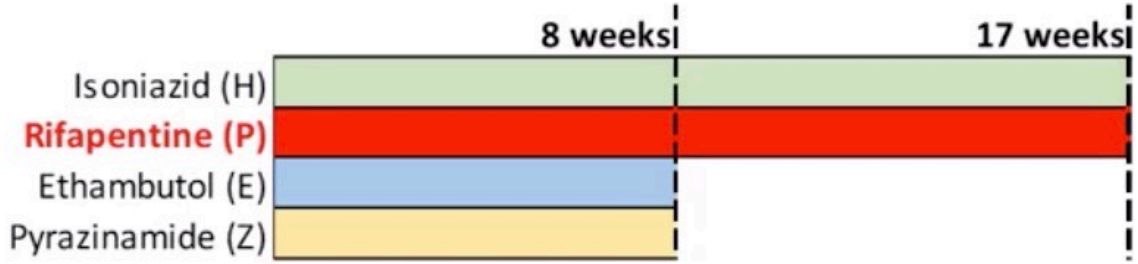
IID INSTITUTE OF INFECTIOUS DISEASES

Can we shorten the duration of HIV/DS-PTB?

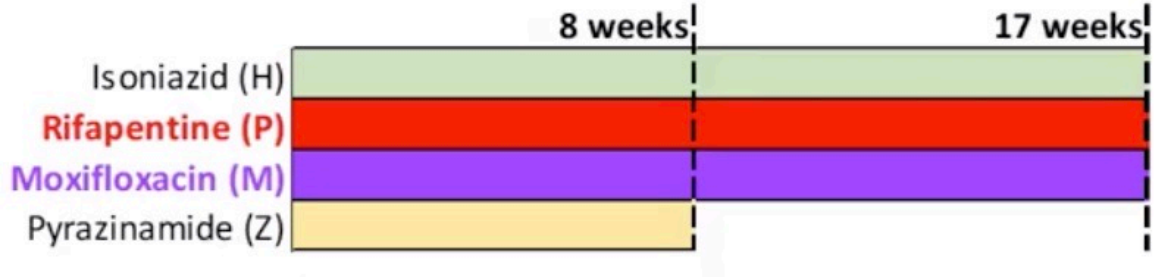
2HRZE + 4HR
"Control"



2HPZE + 2HP
"RPT"

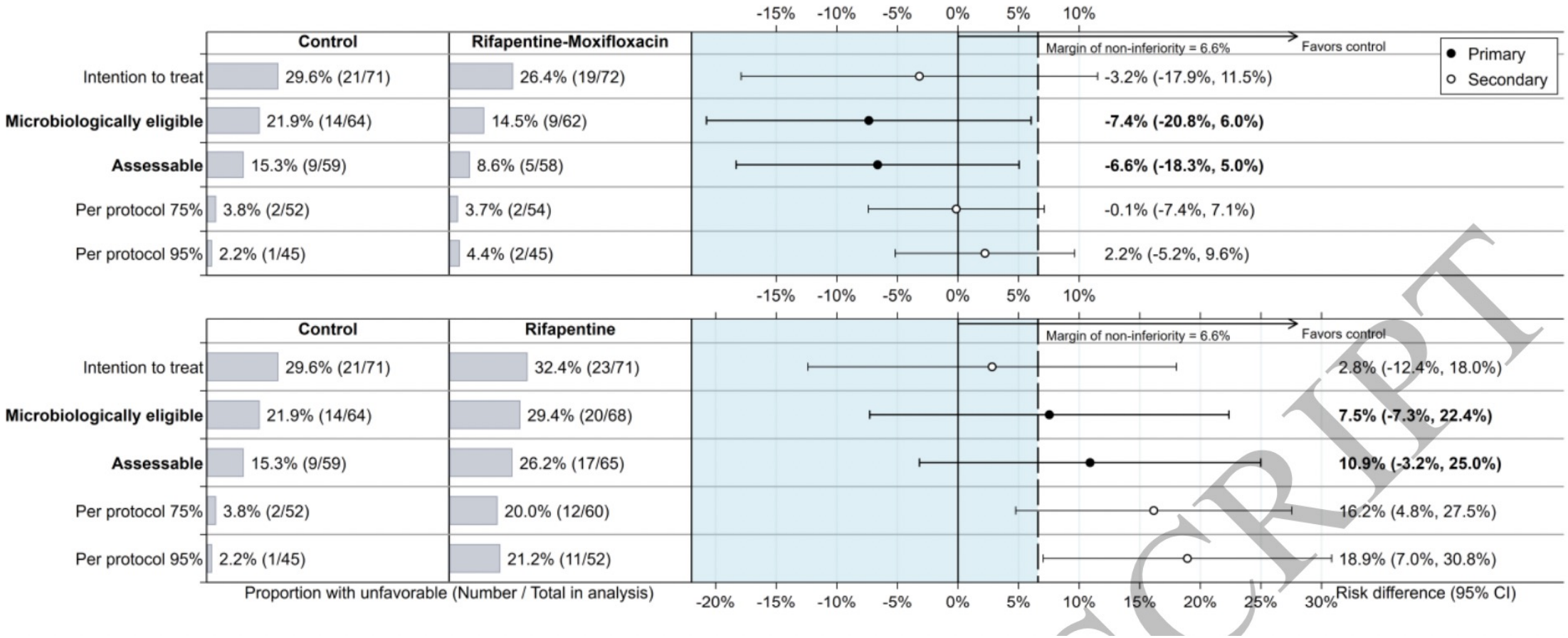


2HPZM + 2HPM
"RPT-MOX"



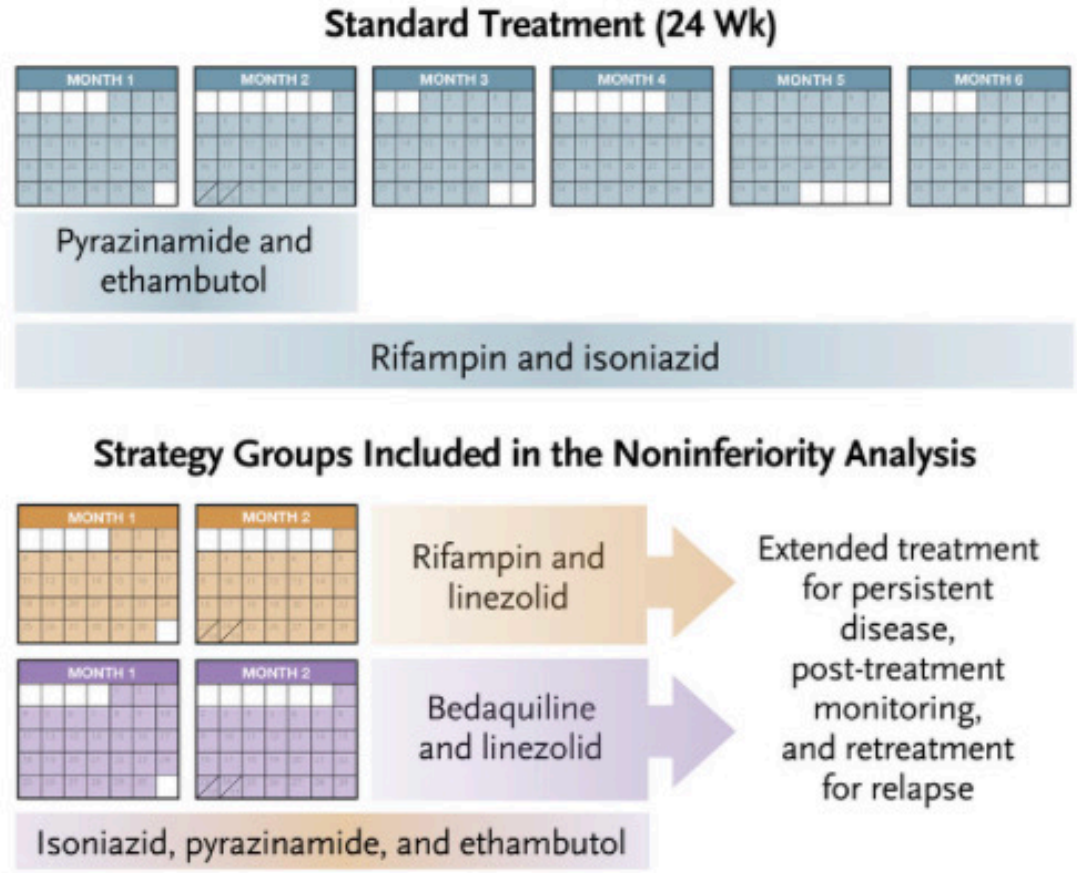
Clin Infect Dis 2023 Feb 8;76(3):e580-e589

RPT-MOX non-inferior to control



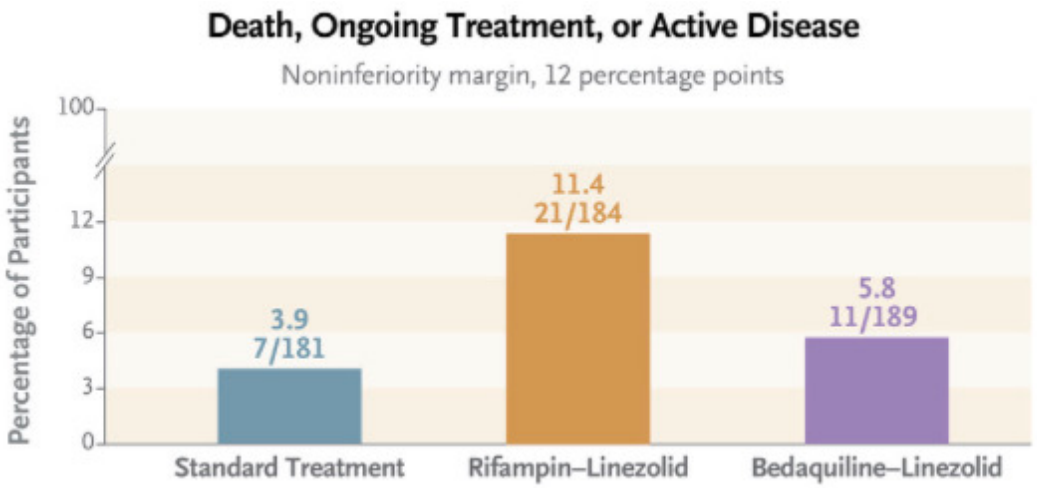
Clin Infect Dis 2023 Feb 8;76(3):e580-e589

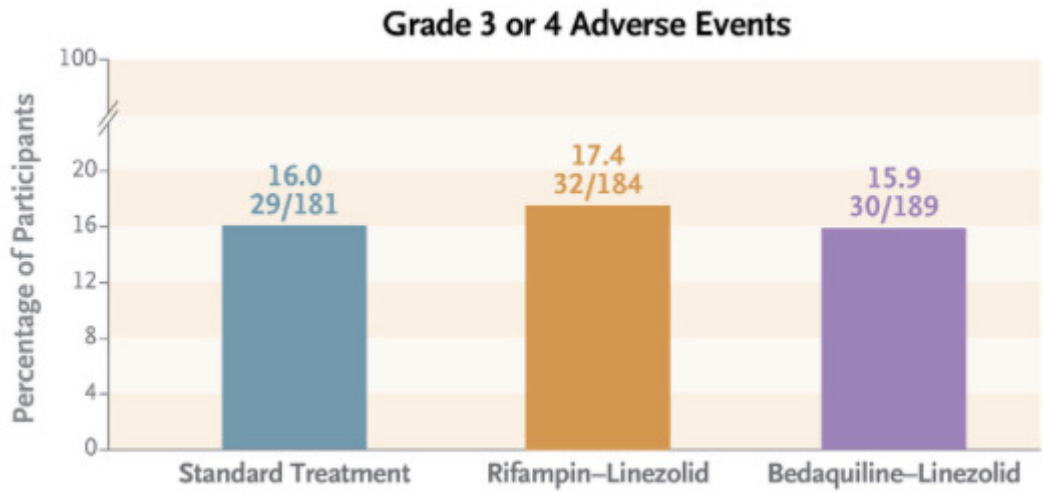
TRUNCATE-TB trial: Short course 8 weeks



N Engl J Med 2023; 388:873-887

TRUNCATE-TB trial: Short course 8 weeks





N Engl J Med 2023; 388:873-887

RADIANT-TB
DTG qd vs bid in HIV/TB treatment

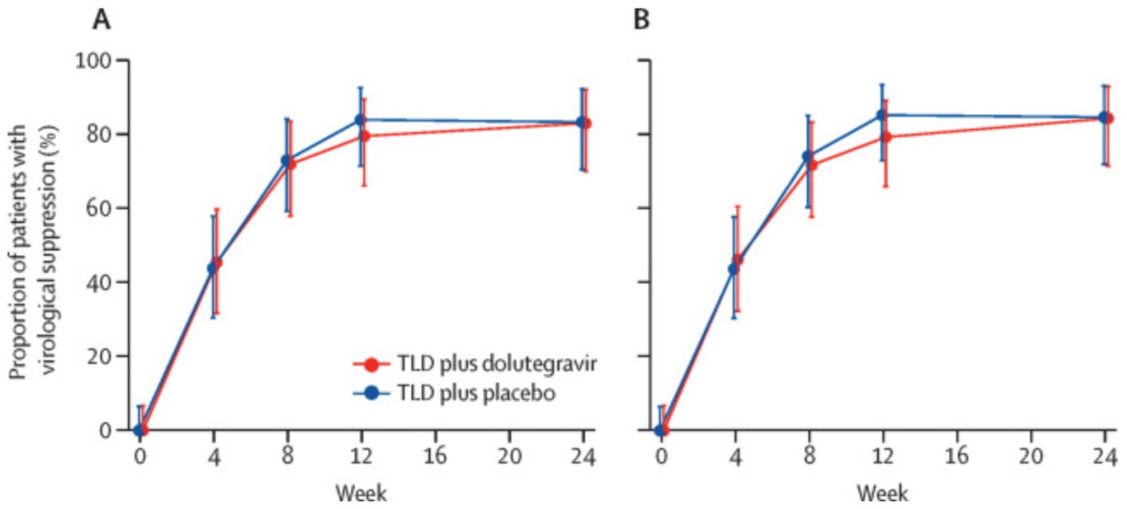
HIV-1>18 yrs
PVL>1000 cps/ml
CD4<200
ARV naïve/interruption
Rifa based ATT < 3 mo's

Stratified: ARV naïve and 1st Line ART interruption

TLD + DTG/DTG

TLD + DTG/Placebo

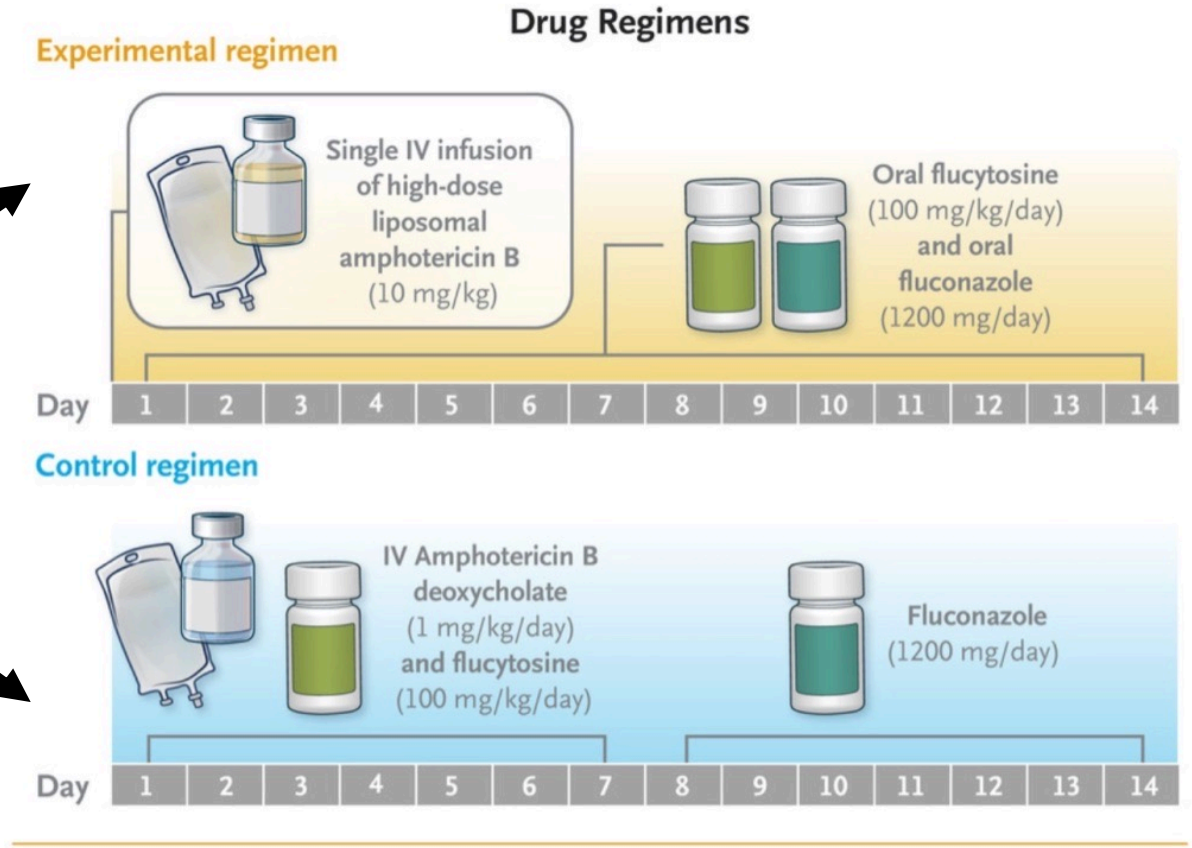
Proportion with PVL<50 Wk 24



Lancet HIV 2023 Jul; 10(7): e433–e441

AMBITION-CM:
single high dose lipo Ampho B for CM

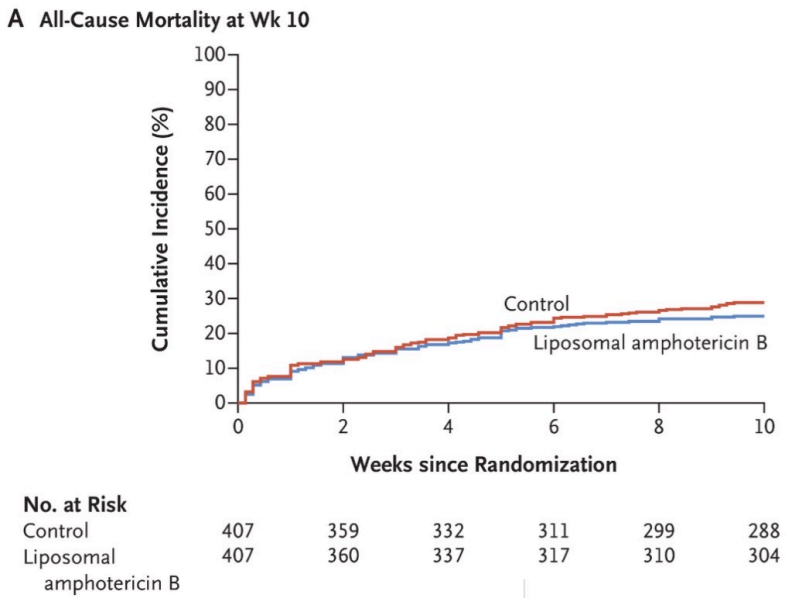
HIV-1
First episode of CM

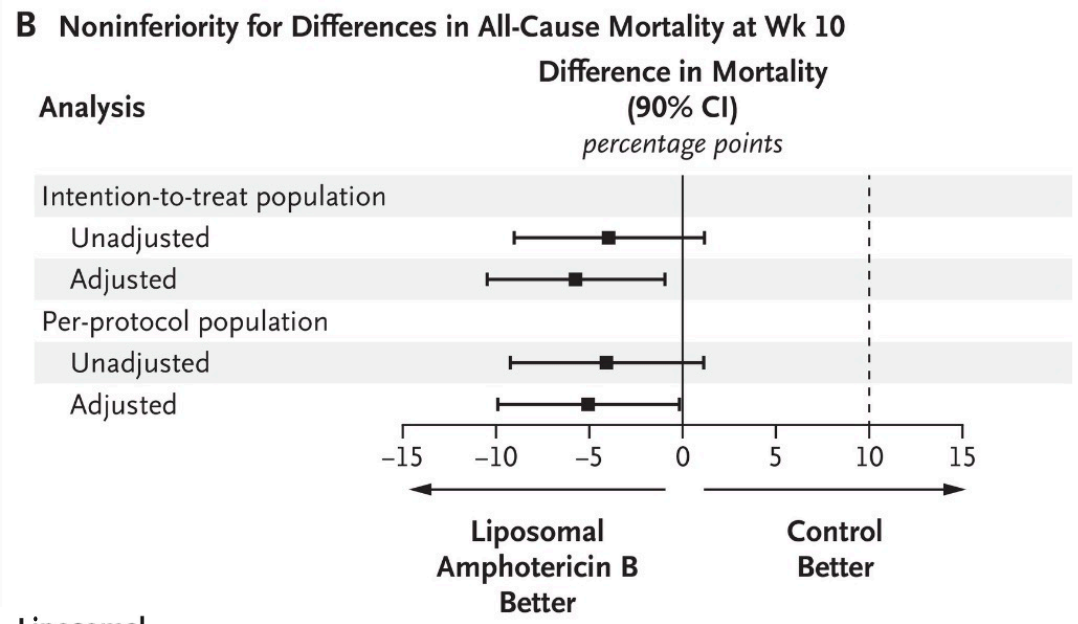


Primary outcome
Death from any cause at 10 weeks
Non-inferiority margin: 10

N Engl J Med 2022; 386:1109-1120

AMBITION-CM: single high dose lipo Ampho B for Crypto M.





Event	Liposomal Amphtericin B (N=420)	Control (N=422)	P Value†
Grade 3 or 4 adverse events — no. of events	382	579	
Any grade 3 or 4 adverse event — no. of participants (%)			
Grade 3 or 4	210 (50.0)	263 (62.3)	<0.001
Grade 3	173 (41.2)	225 (53.3)	<0.001
Grade 4	91 (21.7)	127 (30.1)	0.005

Euroguidelines

N Engl J Med 2022; 386:1109-1120

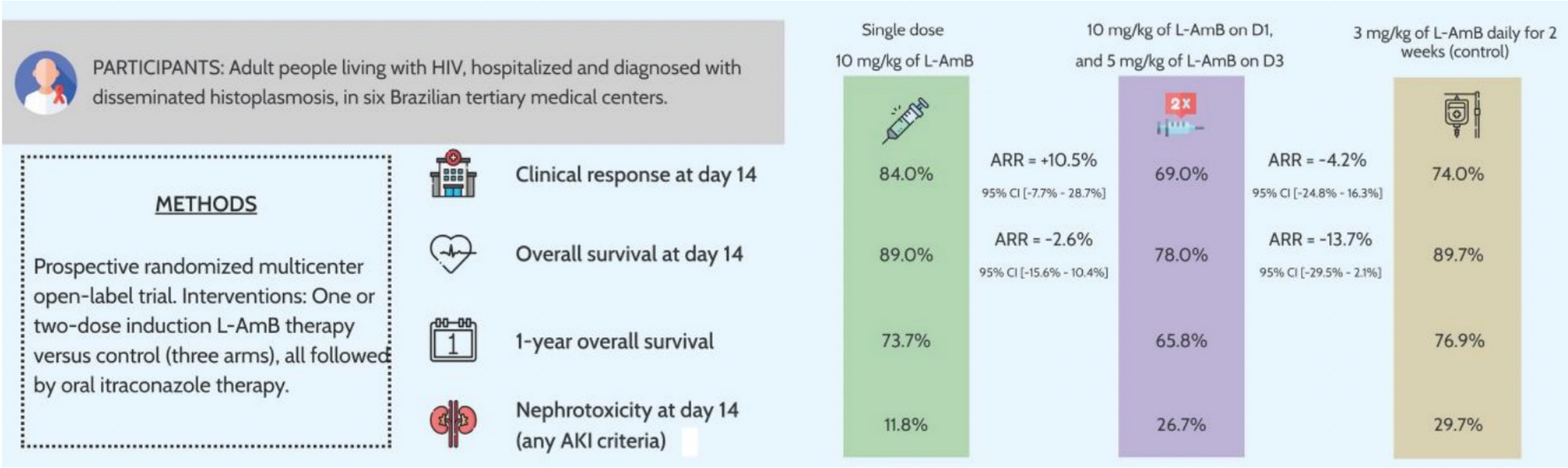
Clinical Infectious Diseases

MAJOR ARTICLE

Early Antiretroviral Therapy Not Associated With Higher Cryptococcal Meningitis Mortality in People With Human Immunodeficiency Virus in High-Income Countries: An International Collaborative Cohort Study

Suzanne M. Ingle,[1,a] Jose M. Miro,[2,3,a] Margaret T. May,[1] Lauren E. Cain,[4,5] Christine Schwimmer,[6] Robert Zangerle,[7] Helen Sambatakou,[8] Charles Cazanave,[9] Peter Reiss,[10] Vanessa Brandes,[11] Heiner C. Bucher,[12] Caroline Sabin,[13] Francesc Vidal,[14,15] Niels Obel,[16] Amanda Mocroft,[17] Linda Wittkop,[18] Antonella d'Arminio Monforte,[19] Carlo Torti,[20] Cristina Mussini,[21] Hansjakob Furrer,[22] Deborah Konopnicki,[23] Ramon Teira,[24] Michael S. Saag,[25] Heidi M. Crane,[26] Richard D. Moore,[27] Jeffrey M. Jacobson,[28] W. Chris Mathews,[29] Elvin Geng,[30] Joseph J. Eron,[31] Keri N. Althoff,[32] Abigail Kroch,[33] Raynell Lang,[32] M. John Gill,[34] and Jonathan A. C. Sterne,[1] on behalf of ART-CC, COHERE in EuroCoord, CNICS, and NA-ACCORD

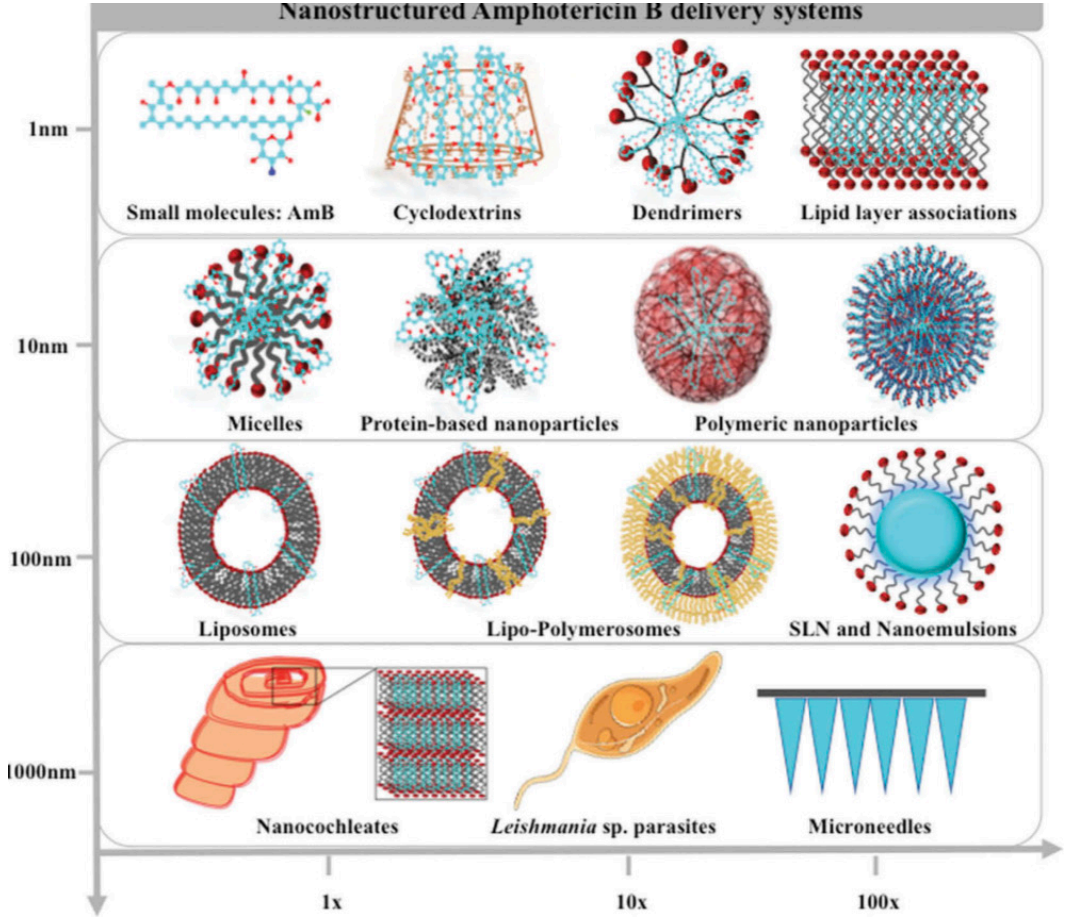
Can sdLipAmpB used to treat HIV-histo?



Clin Infect Dis 2023 May 26;ciad313

IID INSTITUTE OF INFECTIOUS DISEASES

Nanostructured Ampho B delivery systems



Expert Opinion on Drug Delivery Aug 2019;16(10)

Oral LNC Ampho B for HIV/CM: Proof of concept

Oral Lipid Nanocrystal Amphotericin B for Cryptococcal Meningitis: A Randomized Clinical Trial

Boulware et al., 2023 | *Clinical Infectious Diseases*

IDSA Infectious Diseases Society of America

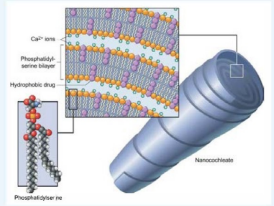
BACKGROUND: We conducted a randomized clinical trial to evaluate the antifungal efficacy of oral lipid nanocrystal (LNC) amphotericin (MAT2203) with flucytosine (5FC) in the treatment of cryptococcal meningitis.

PARTICIPANTS: We recruited adults with HIV diagnosed with cryptococcal meningitis from three hospitals in Uganda.

METHODS

Study participants had a positive CSF CrAg, Glasgow Coma Scale score = 15, and had to be able to tolerate oral medication. Participants were randomized to either the IV amphotericin control arm or to an interventional arm.

	ARM 1: 7 doses of IV Amphotericin + 5FC	ARM 2: 2 doses of IV Amphotericin + MAT2203 + 5FC	ARM 3: Oral MAT2203 + 5FC
	N=41	N=40	N=40
18-week Survival	85%	90%	85%
2-week CSF Sterility	67.6%	62.2%	63.6%
Grade 3-4 Hgb AEs	43.9%	20%	22.5%
Grade 3-4 K+ AEs	17%	5.1%	5%



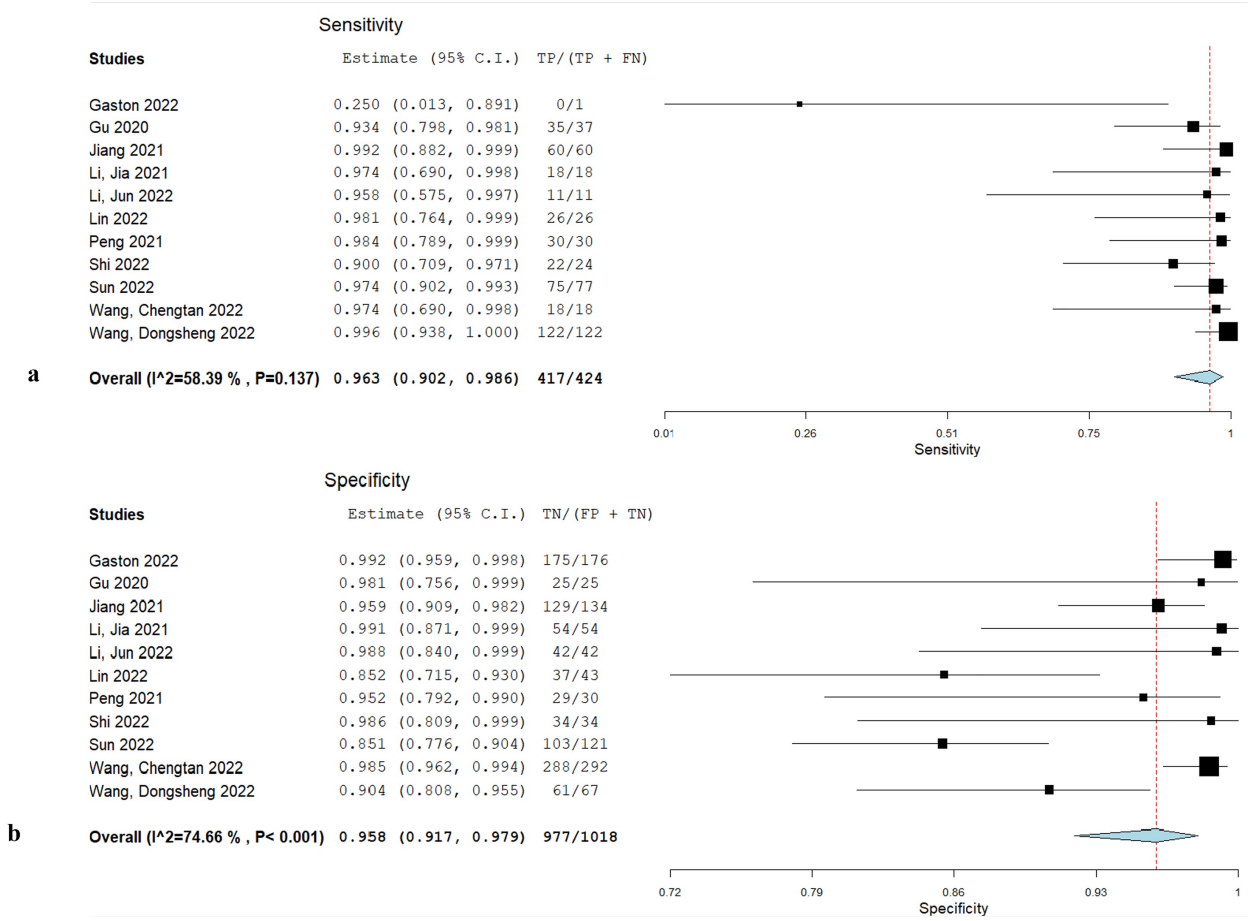
Clinical antifungal activity did not differ between oral LNC-amphotericin and IV amphotericin

CONCLUSION: Oral LNC-amphotericin B with 5FC demonstrated similar antifungal activity, similar survival, and less toxicity than IV amphotericin and 5FC. Oral LNC-amphotericin B appears to be a promising antifungal candidate to be moved forward in future clinical trials for the treatment of severe fungal infections.

Clinical Infectious Diseases https://doi.org/10.1093/cid/ciad440

Clin Infect Dis 2023 Aug 22

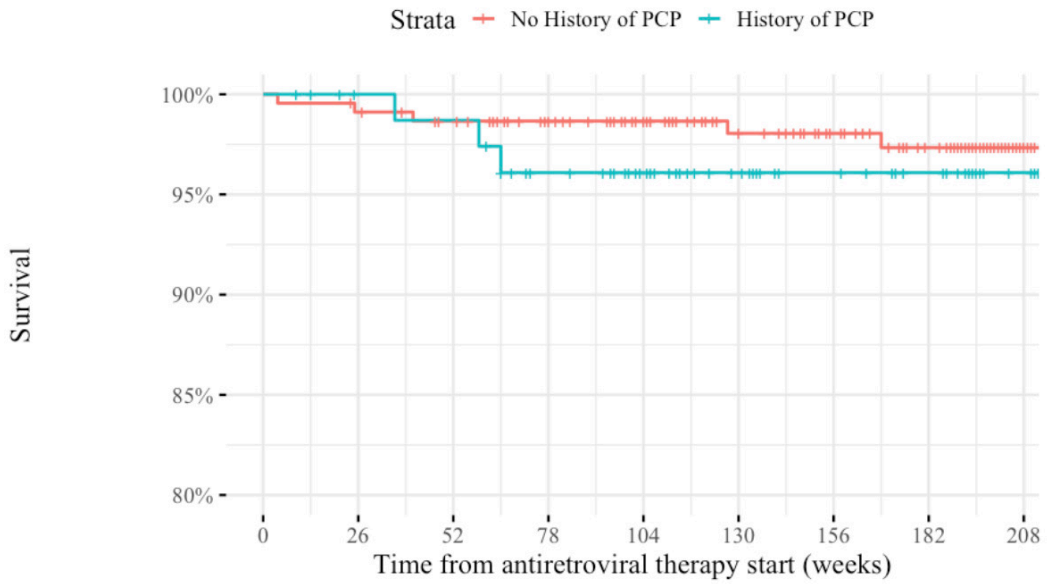
MNGS promising option for PJP diagnosis: BAL and Blood

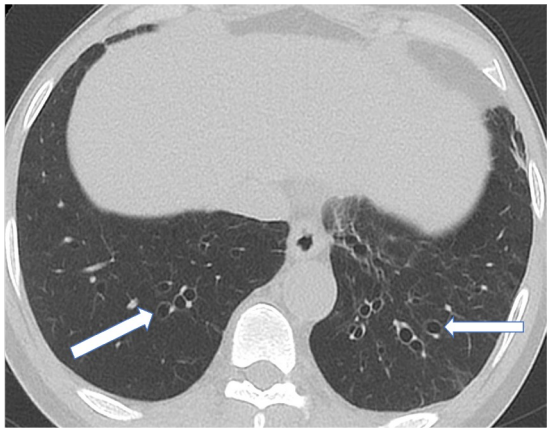


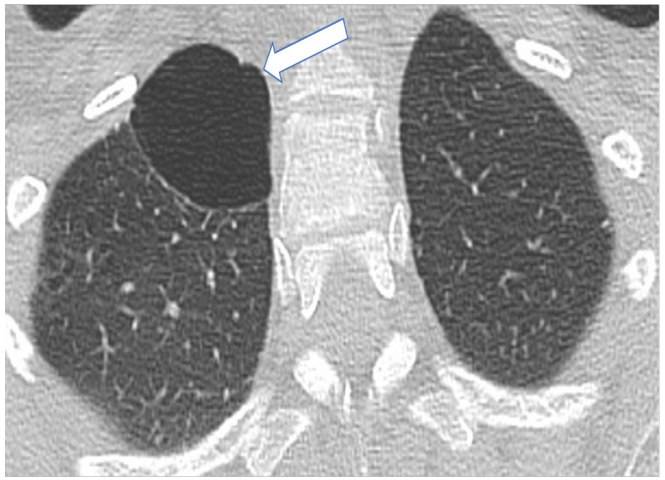
Open Forum Infect Dis 2023 Aug 18

PCP in ART era: Long term outcomes

- Lower lung capacity/diffusion impairment



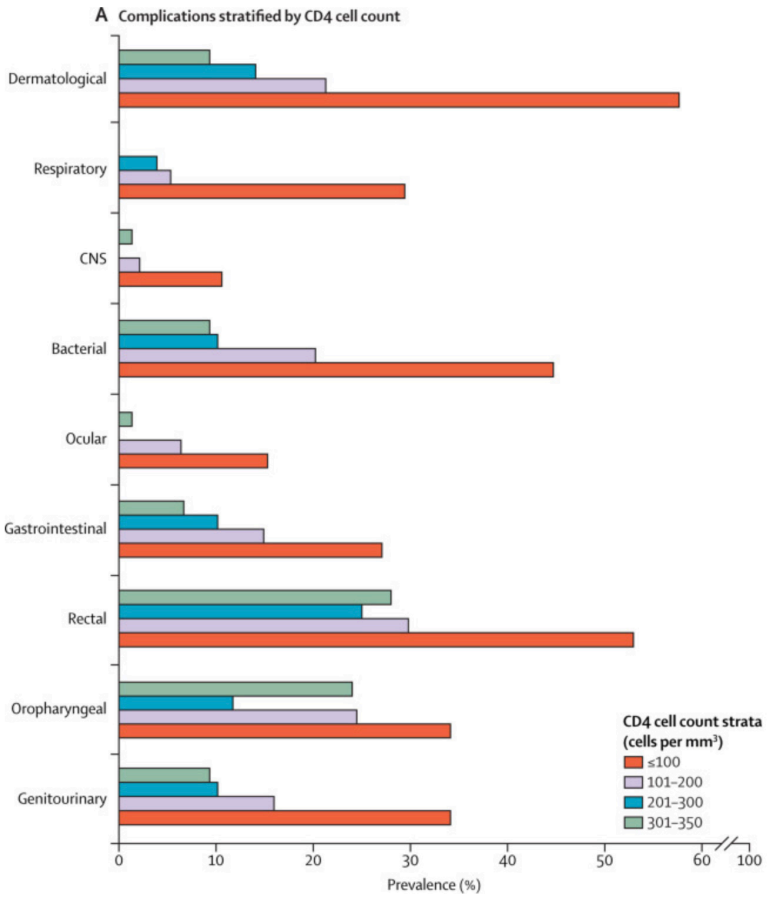


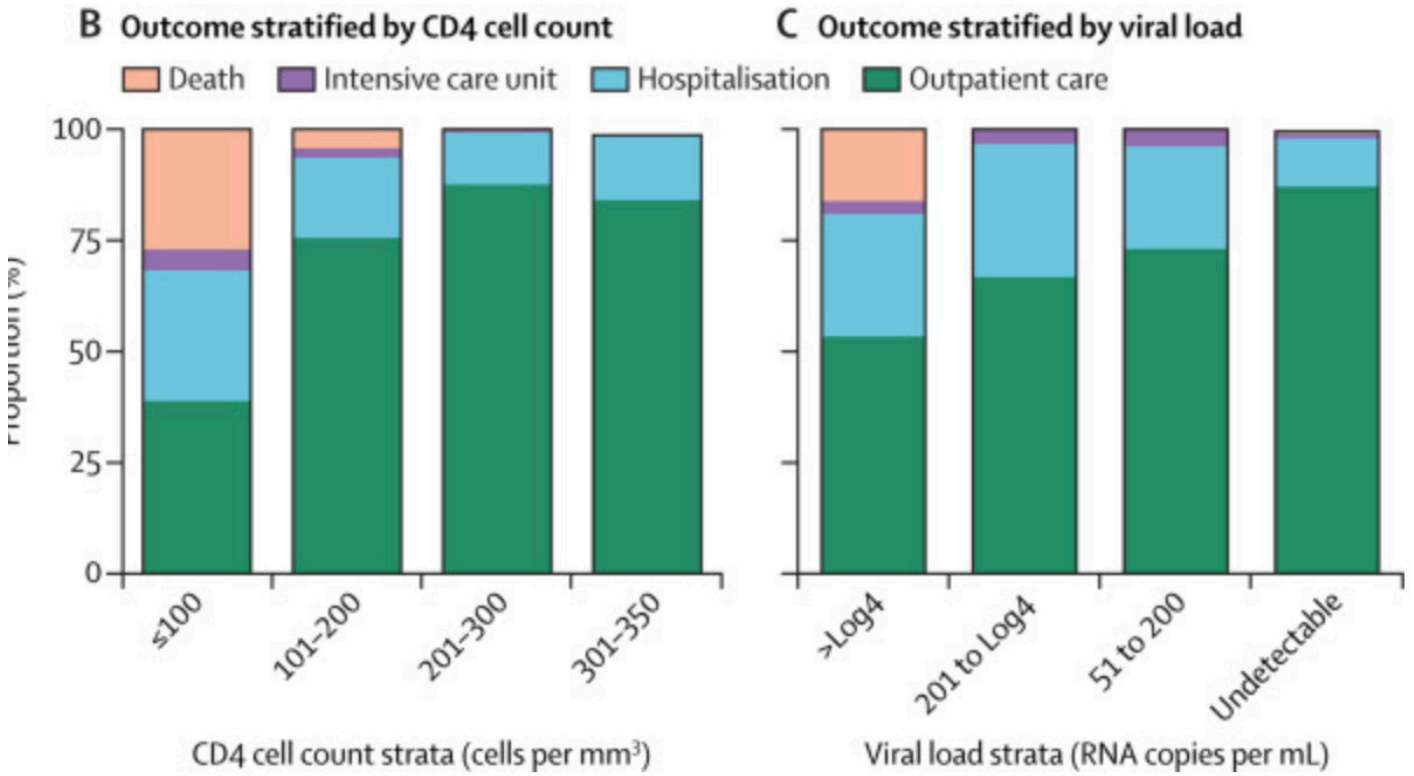


Open Forum Infect Dis 2023 Aug 8

Mpox complications & outcomes stratified by CD4 count:
The emergence of mpox as HIV-OI

Euroguidelines

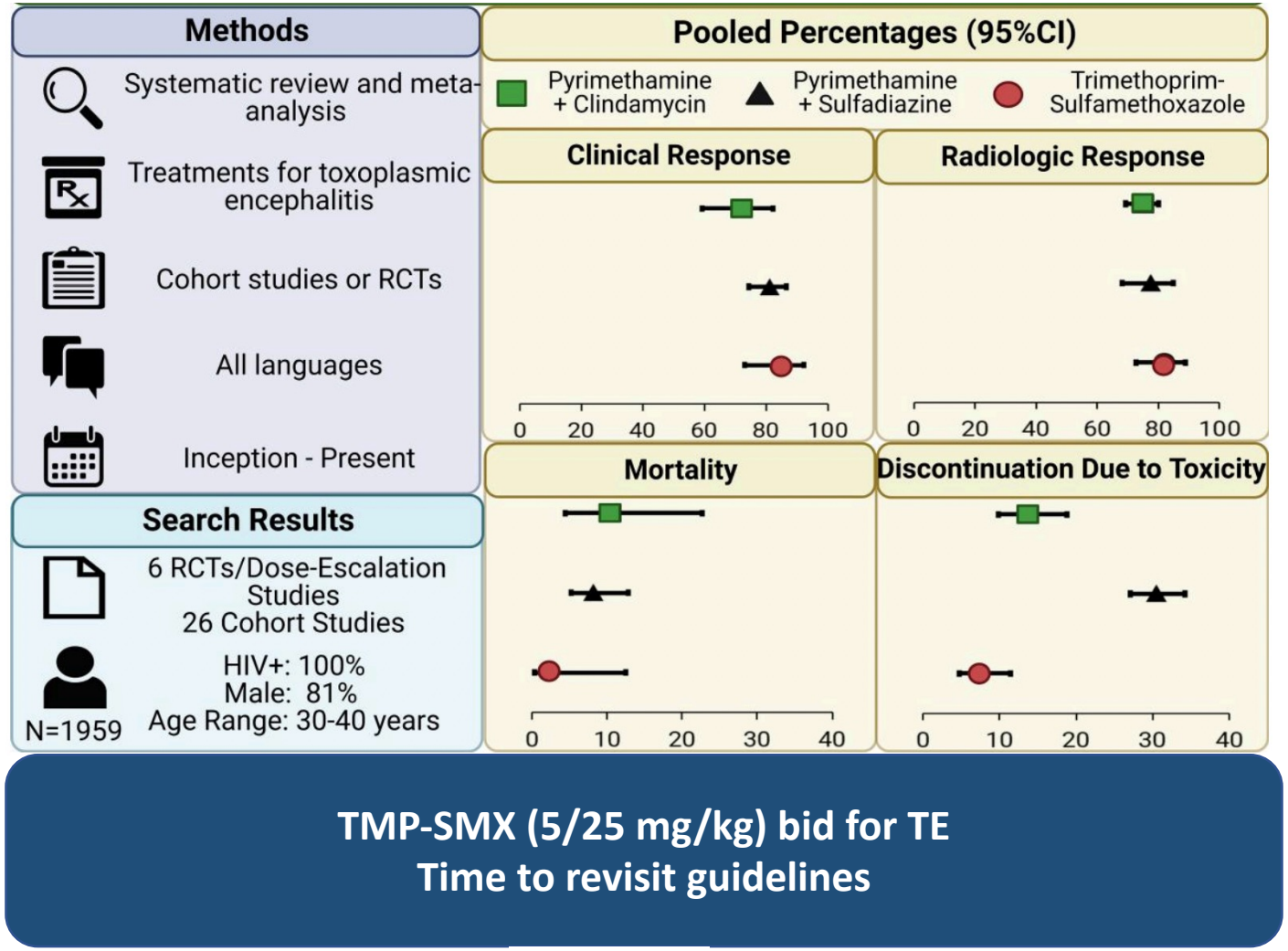




Lancet Mar 2023;401:939-949

Treating TE in PWH

Euroguidelines

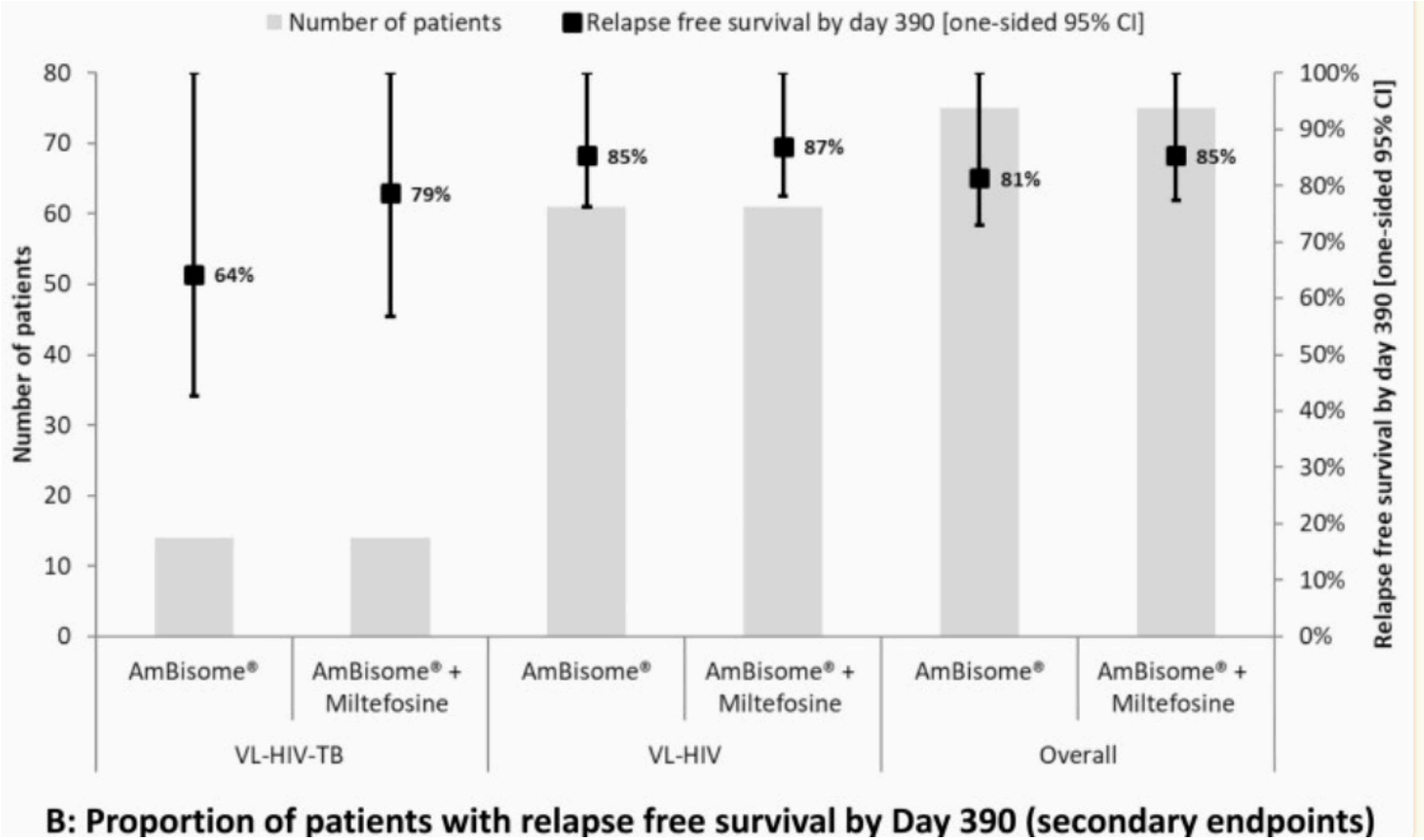


TMP-SMX (5/25 mg/kg) bid for TE
Time to revisit guidelines

Clin Infect Dis 2023 Feb 8;76(3):e1302-e1319

HIV and visceral leishmaniasis

Euroguidelines



B: Proportion of patients with relapse free survival by Day 390 (secondary endpoints)

Clin Infect Dis 2022 Oct 15; 75(8): 1423–1432

Summary

- OI's: here to stay, continue to demand our attention in foreseeable future

- Important advances in
  - Screening and diagnosis with POC rapid tests
  - Shortening duration of treatment with better safety

- Access to novel tools critical for scale-up

- Strategies for preventing late presentation urgently needed

Thank you