Tuberculose

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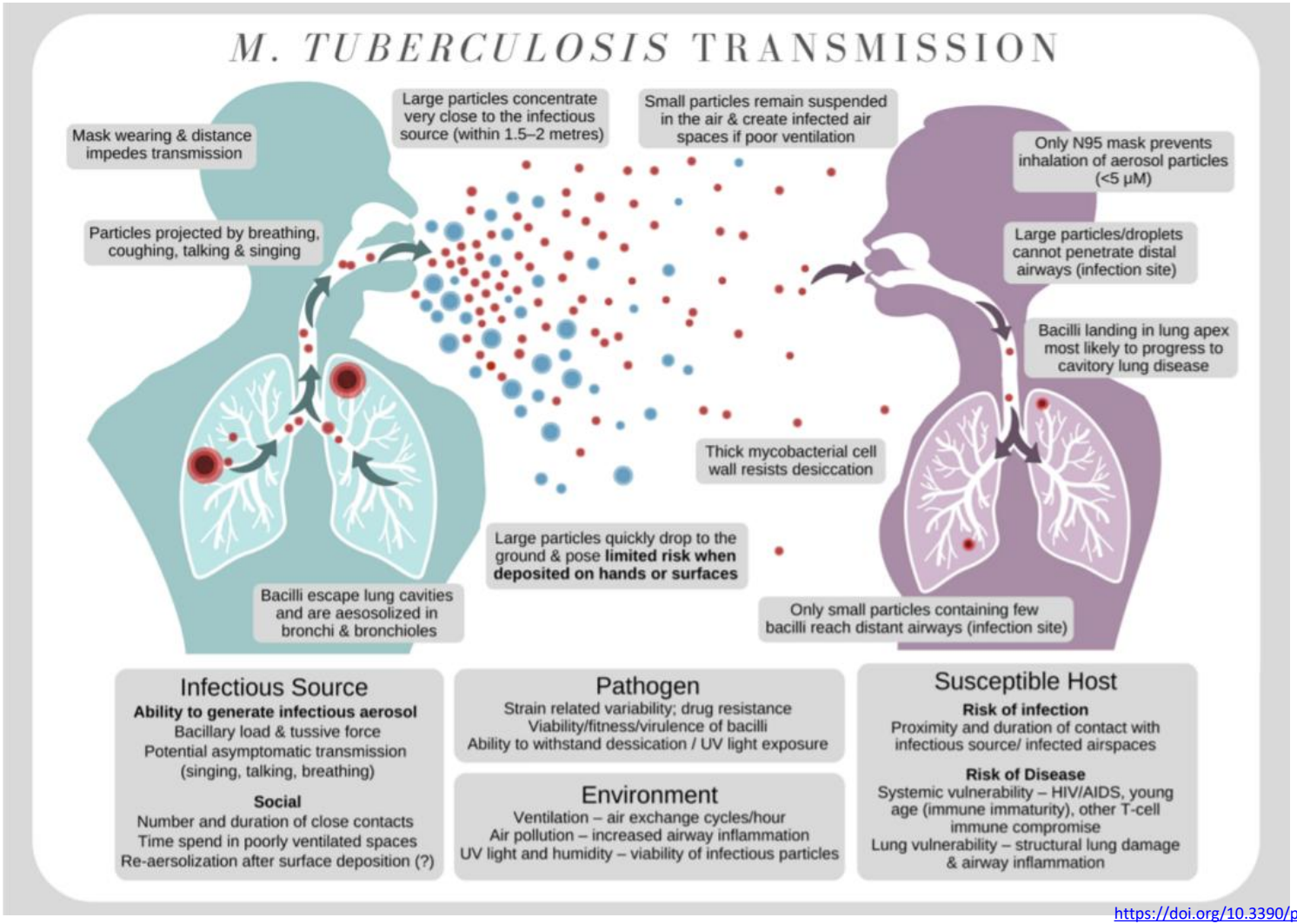

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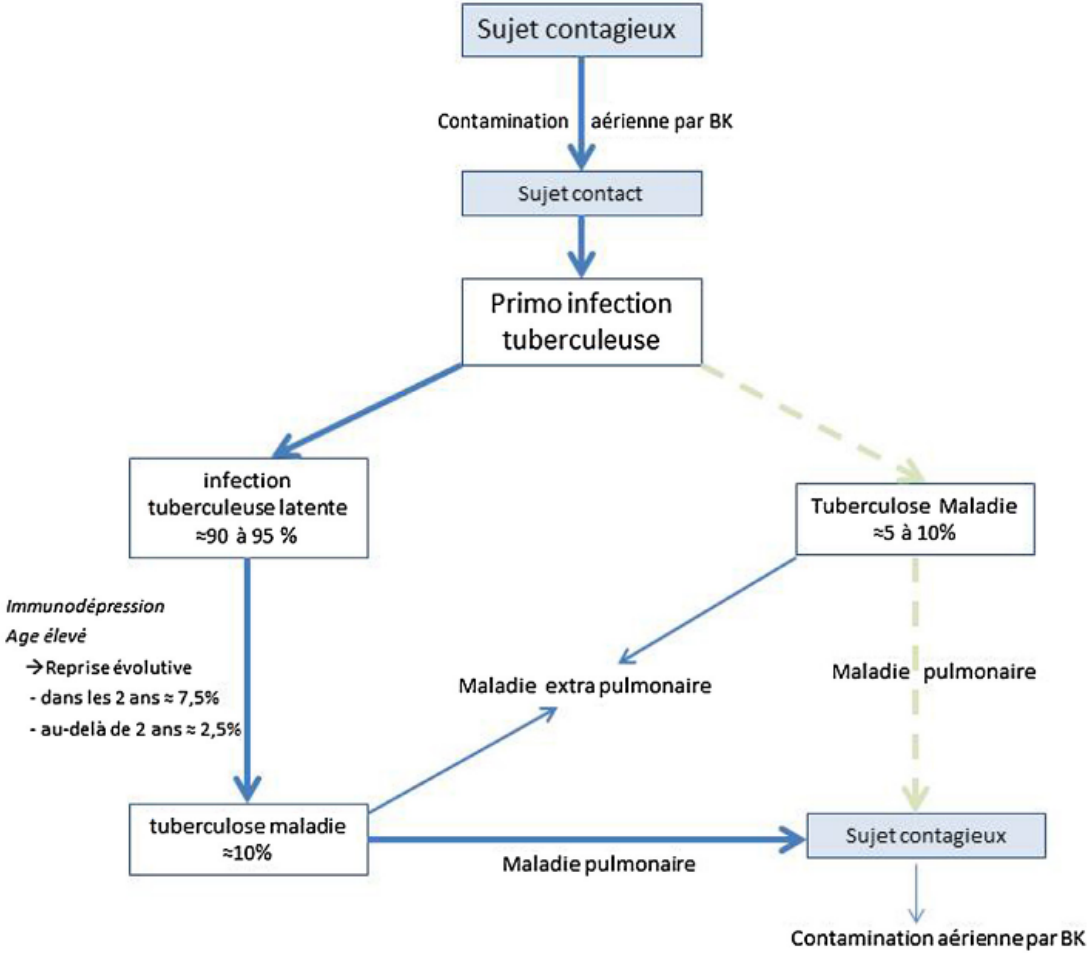
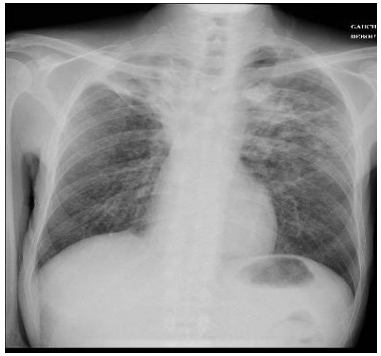
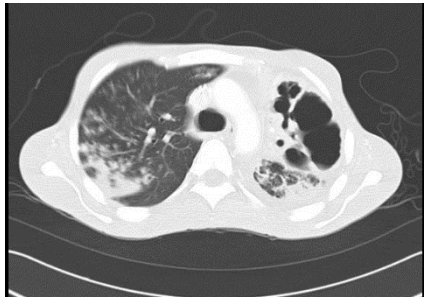






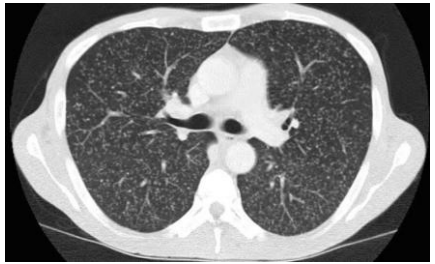
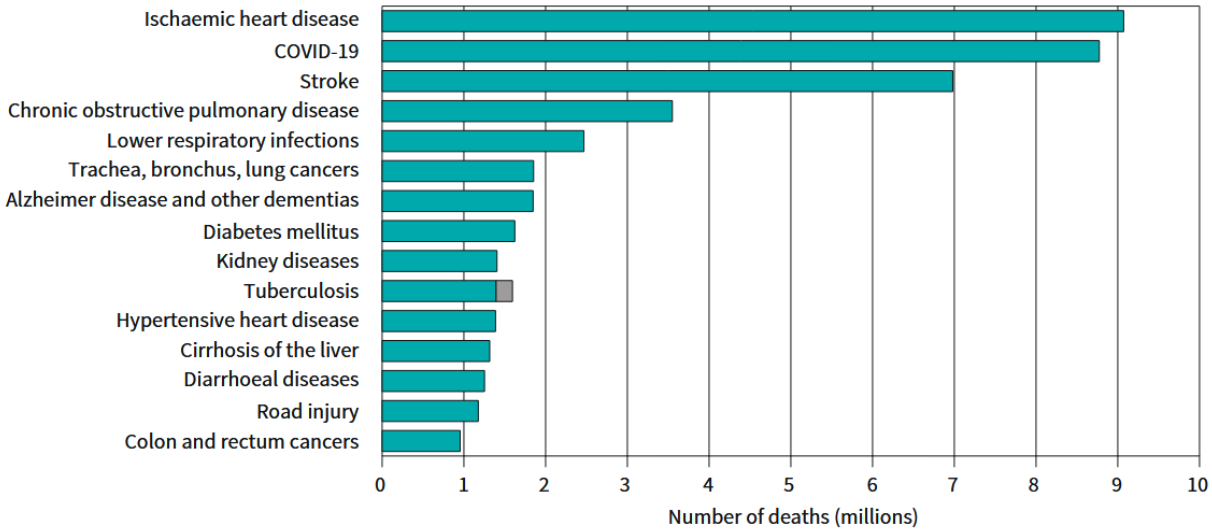


Fig. 1. Histoire naturelle de la tuberculose. BK : bacille de Koch.

FIG. 12

Top 15 causes of death worldwide in 2021[a,b]

Deaths from TB among people with HIV are shown in grey.



Cas clinique

Patiente de 18 ans, originaire de Centre-Afrique, prise en charge aux urgences prise en charge le 22/11/2018 aux urgences pour céphalées fébriles et vomissements apparus depuis quelques jours.

Statut d'édition : Complet

ANALYSES	RESULTATS	Unités	Valeurs de Références	Valeurs Précédentes	Val.
HEMATOLOGIE					
CYTOLOGIE SANGUINE					
NFP					
Globules blancs *Analyseur XN-10 , Sysmex*	5.00	x10^9/l	4.00-11.00		VALAR
Globules rouges *Analyseur XN-10 , Sysmex*	4.36	x10^12/l	3.90-5.20		VALAR
Hémoglobine *Analyseur XN-10 , Sysmex*	12.0	g/dl	11.5-15.0		VALAR
Hématocrite *Analyseur XN-10 , Sysmex*	35.5	%	34.0-43.0		VALAR
VGM *Analyseur XN-10 , Sysmex*	81.4	fl	78.0-102.0		VALAR
TCMH *Analyseur XN-10 , Sysmex*	27.5	pg	26.0-32.0		VALAR
CCMH *Analyseur XN-10 , Sysmex*	33.8	g/dl	32.0-36.0		VALAR
IDR *Analyseur XN-10 , Sysmex*	13.5	%	11.0-16.0		
Plaquettes *Analyseur XN-10 , Sysmex*	236	x10^9/l	185-445		VALAR
VPM *Analyseur XN-10 , Sysmex*	10.4	fl	7.5-11.0		
Polynucléaires neutrophiles	4.31	*x10^9/l*	*1.80-7.50*		VALAR
Polynucléaires éosinophiles	0.00	*x10^9/l*	*0.00-0.50*		VALAR
Polynucléaires basophiles	0.02	*x10^9/l*	*0.00-0.09*		VALAR
Lymphocytes	↓ **0.49**	*x10^9/l*	*1.20-4.00*		VALAR
Monocytes	↓ **0.18**	*x10^9/l*	*0.20-0.70*		VALAR
Polynucléaires neutrophiles	86.20	%			
Polynucléaires éosinophiles	0.00	%			
Polynucléaires basophiles	0.40	%			
Lymphocytes	9.80	%			
Monocytes	3.60	%			
HEMOSTASE					

BIOCHIMIE

IONS ET SUBSTRATS

Sodium *potentiométrie indirecte*	↑ **130**	mmol/l	136-145	VALAR
Potassium *potentiométrie indirecte*	4.4	mmol/l	3.4-4.5	VALAR
Chlore *potentiométrie indirecte*	↑ **95**	mmol/l	98-107	VALAR
Bicarbonates *méthode enzymatique, PEP carboxylase*	22	mmol/l	22-29	VALAR
Urée *méthode enzymatique, uréase/GLDH*	3.1	mmol/l	2.9-7.5	VALAR
Créatinine *méthode enzymatique PAP, standard IDMS*	60	µmol/l	44-80	VALAR
Estimation du débit de filtration glomérulaire par l'équation CKD-EPI	127	ml/min/1.73 m2		

Si patient Afro-américain, résultat à multiplier par 1.159

Classification des stades d'évolution de la maladie rénale chronique

Stade	DFG (mL/min/1,73m2)	Définition
1	>ou= 90	Maladie rénale chronique *avec DFG normal ou augmenté
2	Entre 60 et 89	Maladie rénale chronique *avec DFG légèrement diminué
3A	Entre 45 et 59	Insuffisance rénale chronique modérée
3B	Entre 30 et 44	Insuffisance rénale chronique modérée
4	Entre 15 et 29	Insuffisance rénale chronique sévère
5	< 15	Insuffisance rénale chronique terminale

*Avec marqueurs d'atteinte rénale : albuminurie, hématurie, leucocyturie, ou anomalies morphologiques ou histologiques, ou marqueurs de dysfonction tubulaire, persistant plus de 3 mois (et à deux ou trois examens consécutifs)

Glucose *méthode enzymatique, hexokinase/G6PDH*	↑ **6.5**	mmol/l	4.1-5.9	VALAR
Protéines *biuret*	70	g/l	64-83	VALAR

PROTEINES SPECIFIQUES

Protéine C réactive *immunoturbidimétrie*	↑ **21.5**	mg/l	<5.0	MV
Procalcitonine *immunodosage en phase homogène (technologie TRACE)*	0.16	µg/l	<0.50	VALAR

Cas clinique

- PL:
  - Protéinorachie 1,06 g/L
  - Glycorachie 2,68 mmol/L
  - Hématies : 26/mm^3
  - Leucocytes : 87/mm^3
    - Polynucléaires neutrophiles : 34 %
    - Lymphocytes : 64 %
    - Monocytes : 2 %
  - Lactates dans le LCS : 3,3 mmol/L
- TDM cérébrale normale

Cas clinique

Microbiologie LCS:

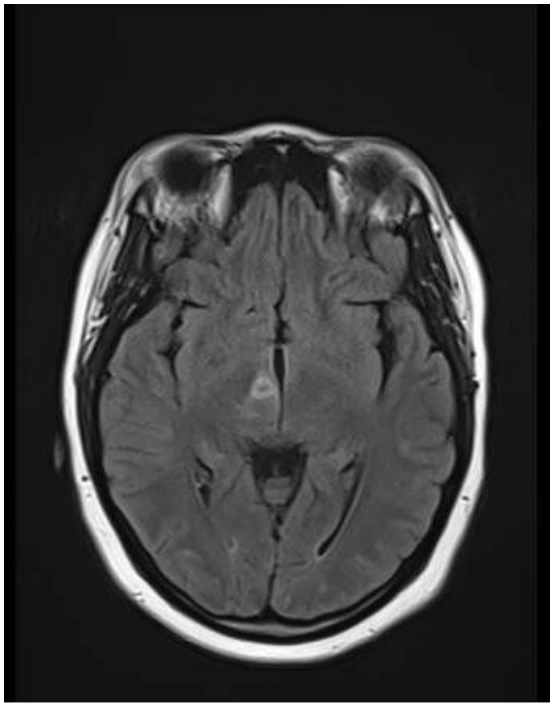
- Examen direct négatif
- Antigène pneumocoque négatif
- PCR HSV négative
- PCR entérovirus négative

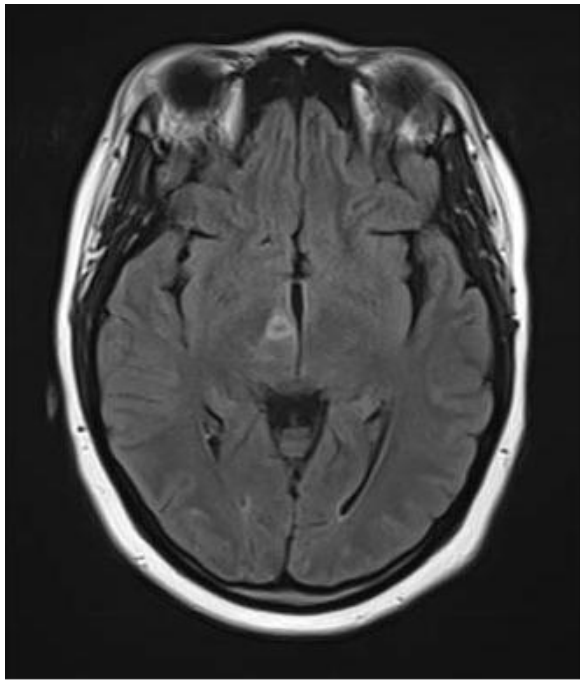
Cas clinique

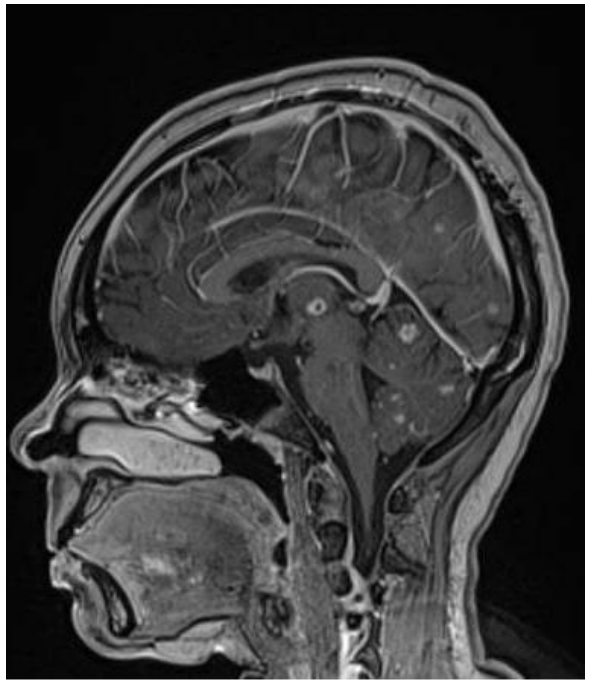
- Réalisation d'une seconde PL 48 heures après devant une dégradation neurologique avec apparition d'une atteinte des paires crâniennes:
  - Protéinorachie 1,1 g/L
  - Glycorachie 1,11 mmol/L
  - GR: 26/mm^3
  - GB: 87/mm^3
    - PNN 34 %
    - Lymphocytes 64 %
    - Monocytes 2 %

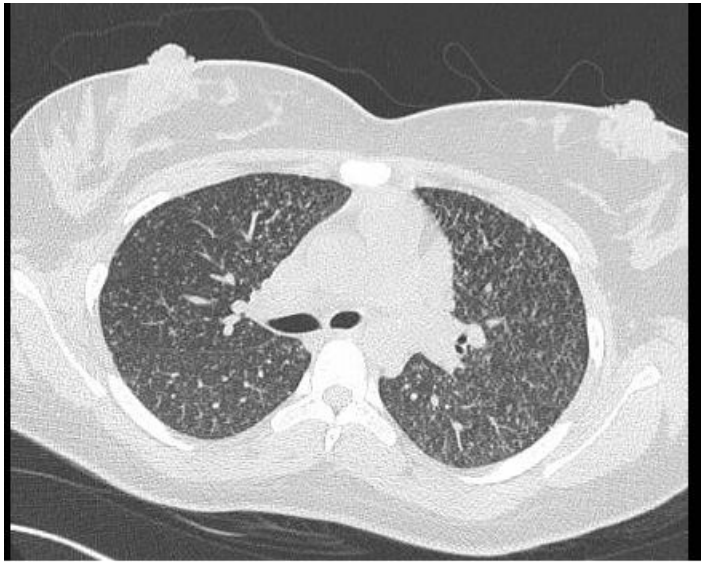
Cas clinique

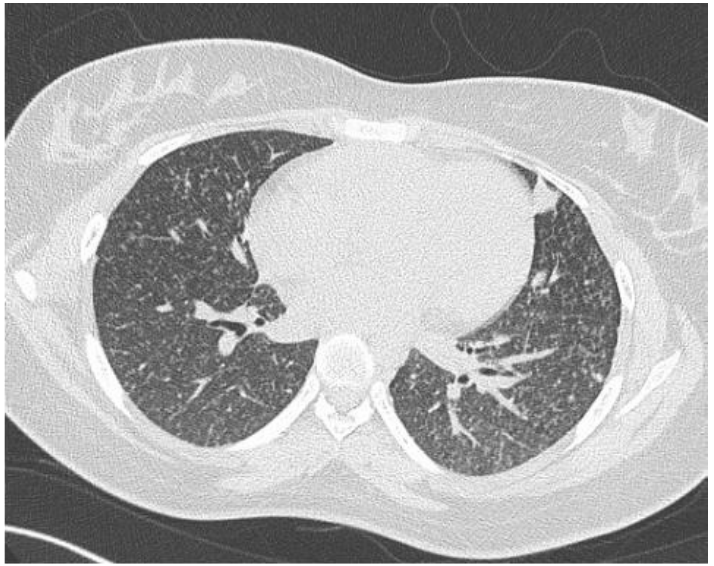
- Quantiféron:
  - Mitogène : 1,65
  - peptides de protéines de *Mycobacterium* du complexe *tuberculosis* : > 10
- Sérologie toxoplasmose négative











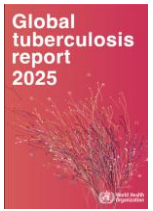
Cas clinique

- PCR BK Cepheid positive dans le LCR à 26 cycles
  - Souche sensible à la rifampicine
- Cultures positives à *Mycobacterium tuberculosis* sensible à la rifampicine
- PCR BK négative dans les crachats

DONNÉES ÉPIDEMIOLOGIQUES

Quelques faits marquants

- Environ ¼ de la population mondiale a été infecté par la tuberculose.
- 5 (-10%) d'entre eux feront une tuberculose maladie dans leur vie, risque accru dans les 2 ans
- En l'absence de traitement à 5 ans, 50% des patients avec une tuberculose pulmonaire BAAR+ décédent. Avec un traitement recommandé 85% guerison
- En l'absence de traitement, une personne ayant une tuberculose pulmonaire active contagieuse peut infecter en moyenne 10 à 15 autres personnes/ an
- 3ème cause infectieuse de mortalité dans le monde en 2021 (après COVID et Infections respiratoires

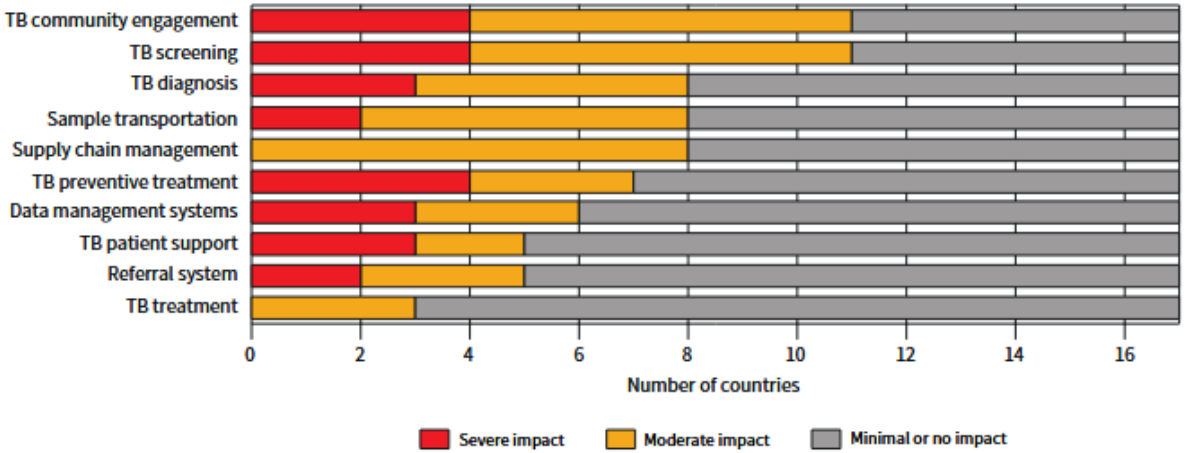


https://iris.who.int/server/api/core/bitstreams/e97dd6f4-b567-4396-8680-717bac6869a9/content

https://www.has-sante.fr/upload/docs/application/pdf/2023-09/evaluation_des_strategies_de_depistage_et_de_reperage_precoce_de_la_tuberculose_pulmonaire_-_note_de_2023-09-07_09-30-39_346.pdf

FIG. 30

Reported impacts on TB services and associated support systems in 2025, for 17 countries[a] that reported receiving Global Fund grants and bilateral funding from USAID in 2024

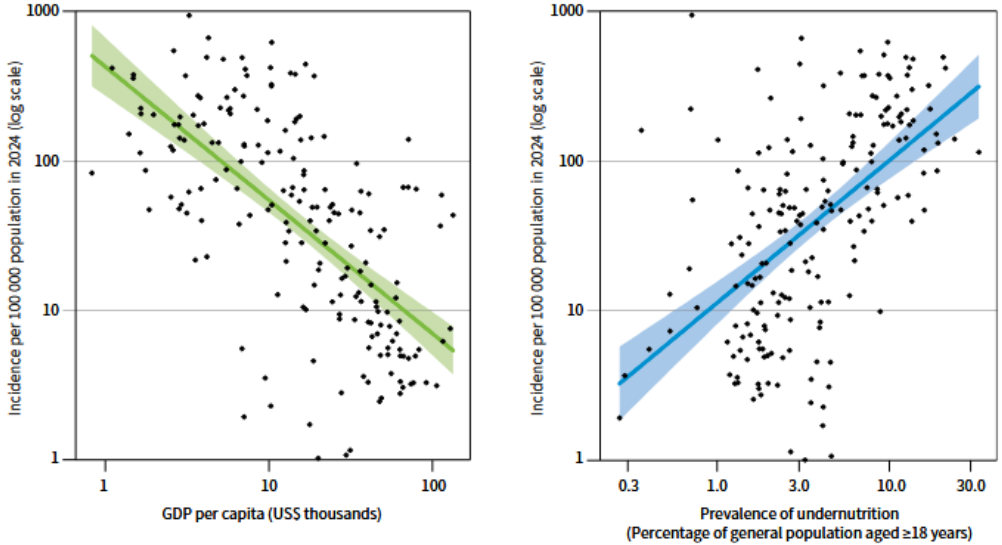


[a] As of August 2025, information was not available for four of the 21 countries shown in Fig. 29. Information was obtained from WHO country offices between April and August 2025.

FIG. 36

Relationship between two SDG-related indicators[a,b] and the TB incidence rate

Each dot represents a country or area.



Facteurs de risque d'évolution vers la TB maladie

	Annual risk of tuberculosis for the first 2–3 years after a positive TST or IGRA*	Reference
Very high risk		
People with HIV†	1·7–2·7%	Gupta et al[25] Campbell et al[24]
Child or adolescent (<18 years) tuberculosis contact	2·9–14·6%	Gupta et al[25] Martinez et al[23]
Adult (≥18 years) tuberculosis contact	0·8%–3·7%	Gupta et al[25] Campbell et al[24]
Silicosis	3·7%	Campbell et al[24]
High risk		
Stage 4 or 5 chronic kidney disease with or without dialysis	0·3–1·2%	Campbell et al[24]
Transplant recipients (solid organ or haematopoietic)	0·1–0·7%	Campbell et al[24]
Fibronodular disease	0·2–0·6%	From incidence rates in three longitudinal studies; Grzybowski et al[25,26] Nolan and Elarth[27]
Receiving immunosuppressing drugs (eg, tumour necrosis factor α inhibitors or steroids)‡	0·5%	Campbell et al[24]
Cancer (lung cancer, sarcoma, leukaemia, lymphoma, or gastrointestinal cancer)	0·1–0·4%	Estimated from hazard ratio in a population-based study; Kumar et al[28]
Moderate risk		
Granuloma on chest x-ray	0·1%	From incidence rates in two longitudinal studies; Grzybowski et al[25] Horwitz and colleagues[29]
Diabetes	0·1–0·2%	Estimated from pooled relative risk in observational studies; Jeon and Murray[30]
Undernutrition	0·1%	Estimated from pooled relative risk in observational studies; Franco et al[31]
Heavy alcohol use (≥3 drinks per day)	0·1–0·2%	Estimated from pooled relative risk in observational studies; Lönnroth et al[32]
Heavy tobacco cigarette smoker (≥1 pack per day)	0·1%	Estimated from pooled odds ratios and relative risks in two meta-analyses of observational studies; Lin et al[33] Bates et al[34]
Low risk		
General, adult population with no known risk factor	0·03%	Campbell et al[24]
People with a positive two-step TST booster and no known risk factor	0·02%	Extrapolated from a longitudinal study and a randomised trial; Comstock et al[35] Ferebree SH[36]

Trajman et al. Lancet 2025

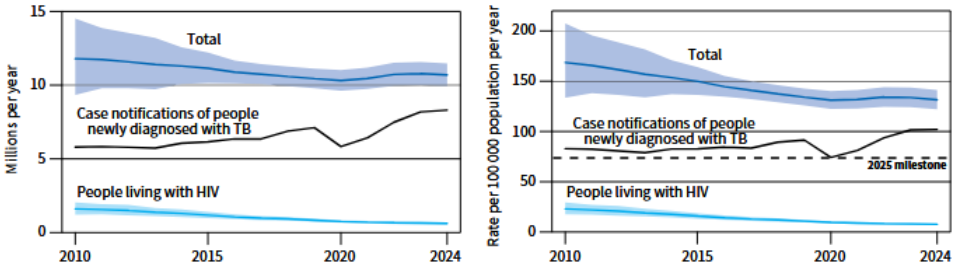
Quelques faits marquants

- Evolution et Impact de la pandémie COVID-19

FIG. 1

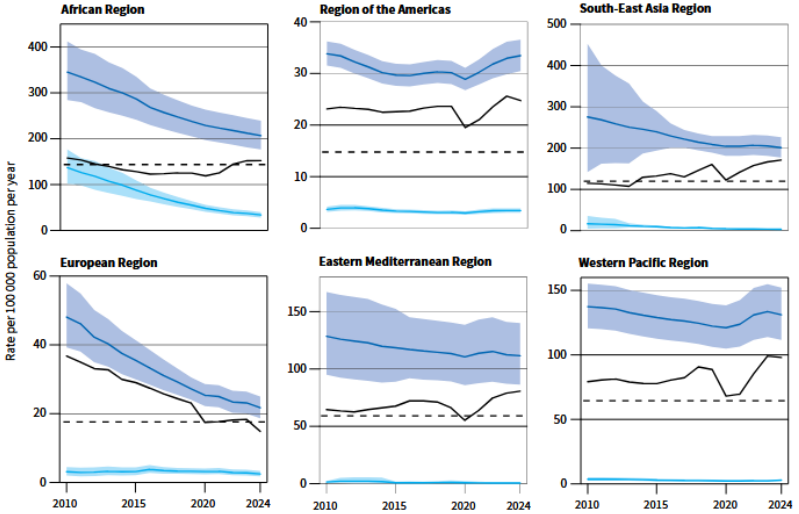
Global trends in the estimated number of incident TB cases (left) and the incidence rate (right), 2010–2024

The horizontal dashed line shows the 2025 milestone of the End TB Strategy, which is a 50% reduction in the TB incidence rate between 2015 and 2025. Shaded areas represent 95% uncertainty intervals.



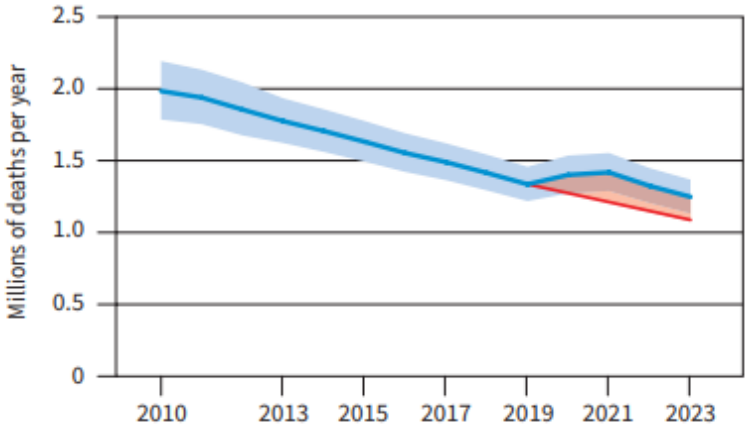
Trends in estimated TB incidence rates by WHO region, 2010–2024

The overall TB incidence rate is shown in **blue** and the incidence rate among people living with HIV is shown in **light blue**. The **black** solid lines show case notifications of people newly diagnosed with TB, for comparison with estimates of the overall incidence rate. Shaded areas represent 95% uncertainty intervals. The horizontal dashed line shows the 2025 milestone of the End TB Strategy, which is a 50% reduction in the TB incidence rate between 2015 and 2025. Indonesia is included in the WHO Western Pacific Region for the whole time series.



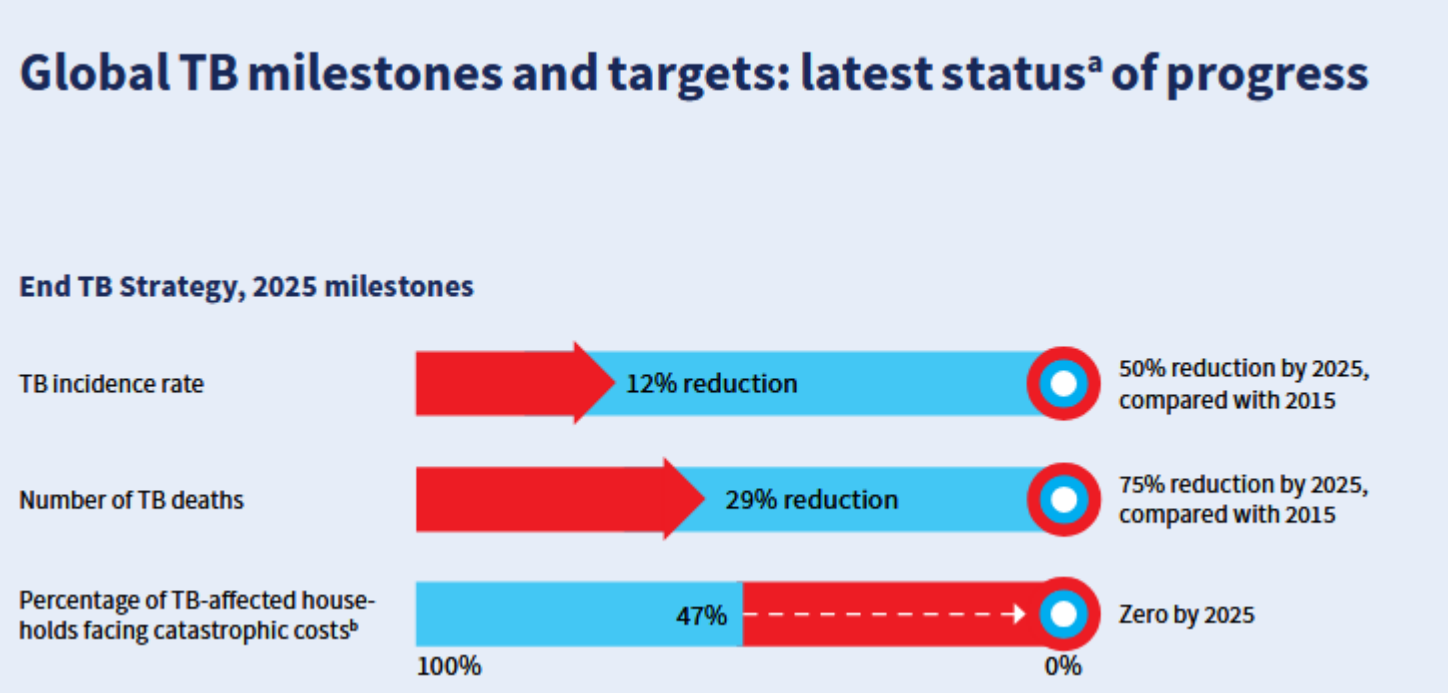
Estimated number of excess TB deaths during the COVID-19 pandemic and its aftermath, 2020–2023

The **blue** shaded area represents the 95% uncertainty interval of the actual number of deaths estimated to have been caused by TB; the **red** line shows the estimated number of deaths that would have been caused by TB in the absence of the COVID-19 pandemic; the **red** shaded area shows the excess number of deaths caused by TB due to disruptions associated with the COVID-19 pandemic.

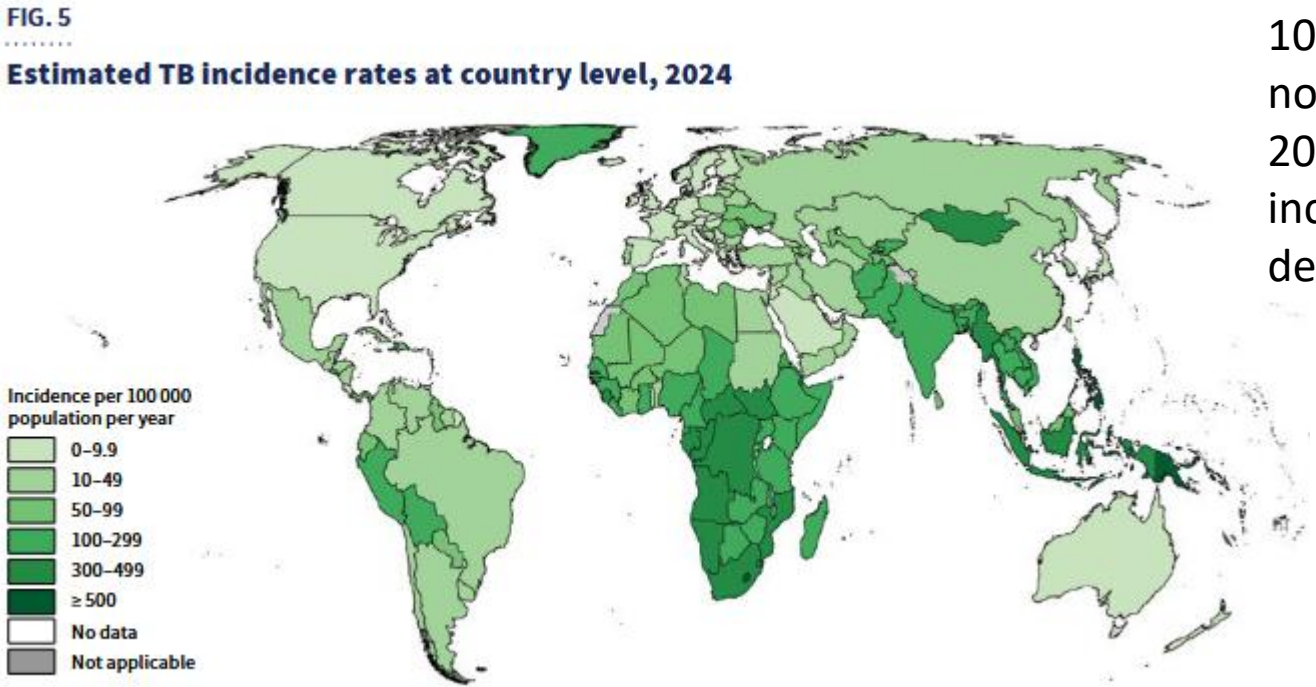


≈2020-2022: 1 million de morts en excès

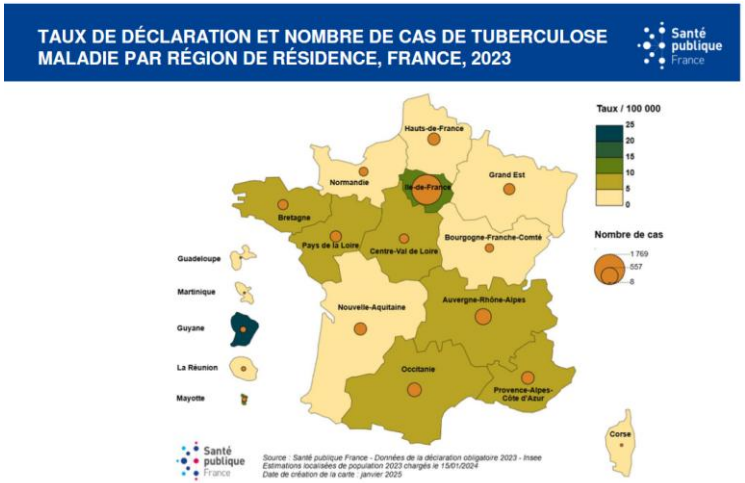
Où en sommes nous de la lutte contre la TB ?

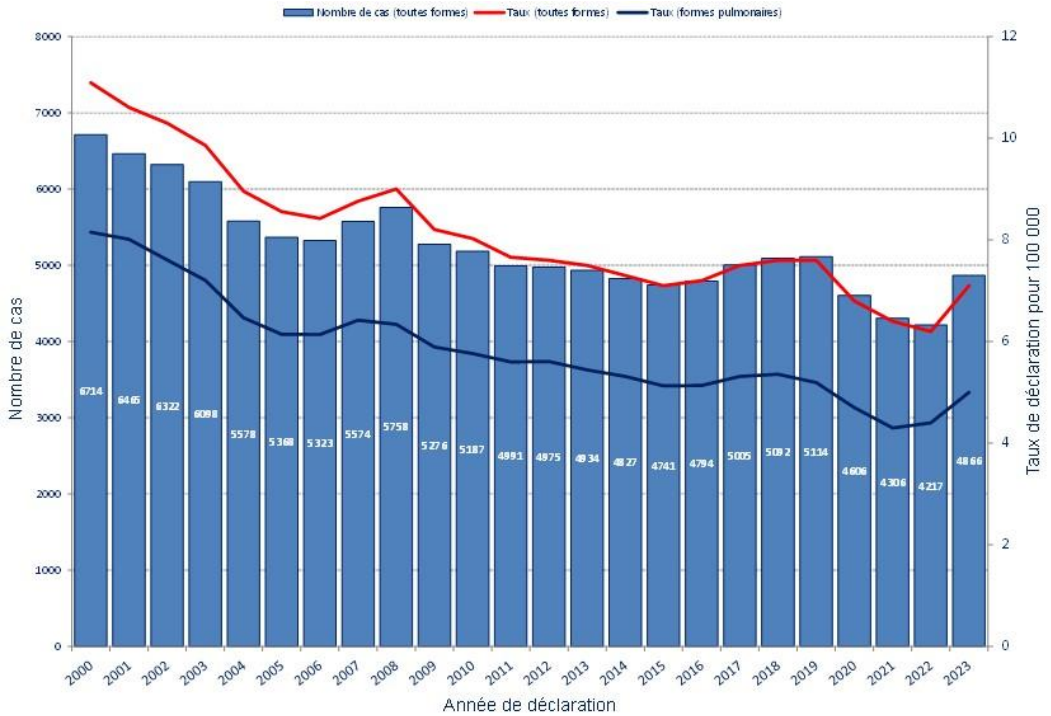


Quelques faits marquants



10,7 Millions de nouveaux cas en 2024 soit une incidence globale de 131/100000

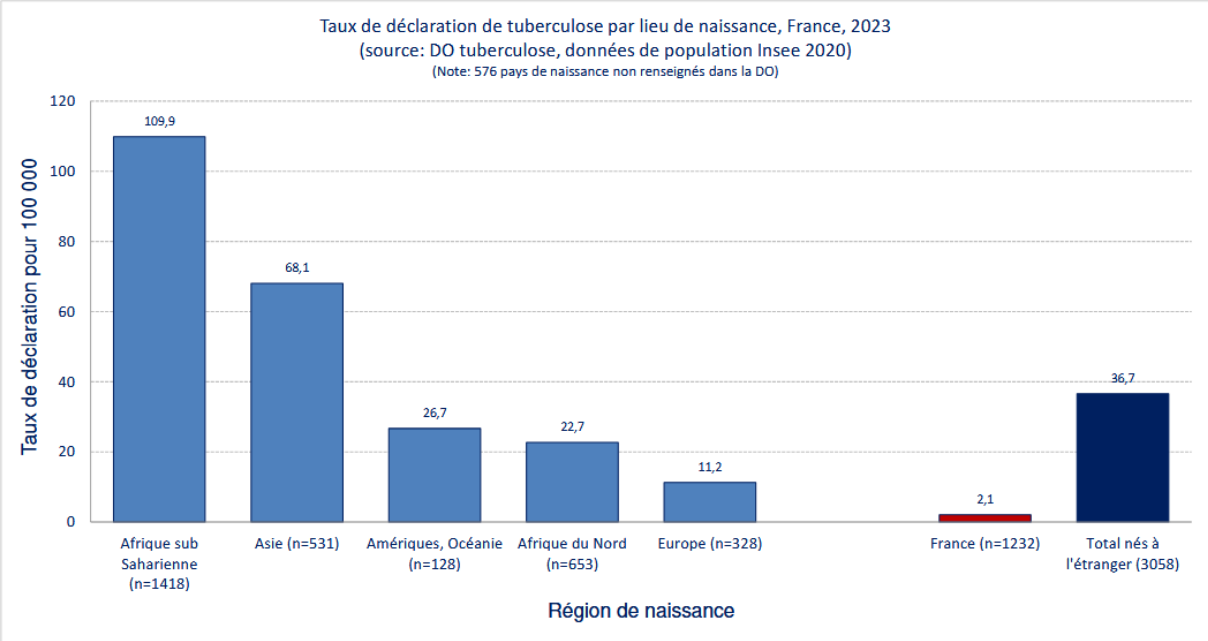




https://www.santepubliquefrance.fr/maladies-et-traumatismes/maladies-et-infections-respiratoires/tuberculose/donnees

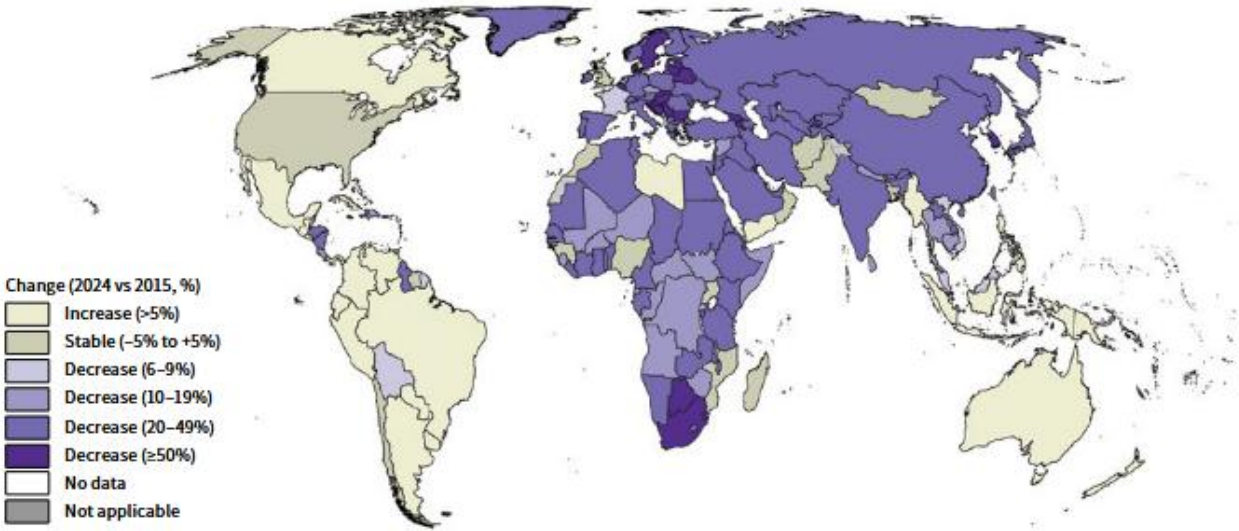
TAUX DE DÉCLARATION DE TUBERCULOSE MALADIE PAR RÉGION DE NAISSANCE, FRANCE, 2023

Santé publique France

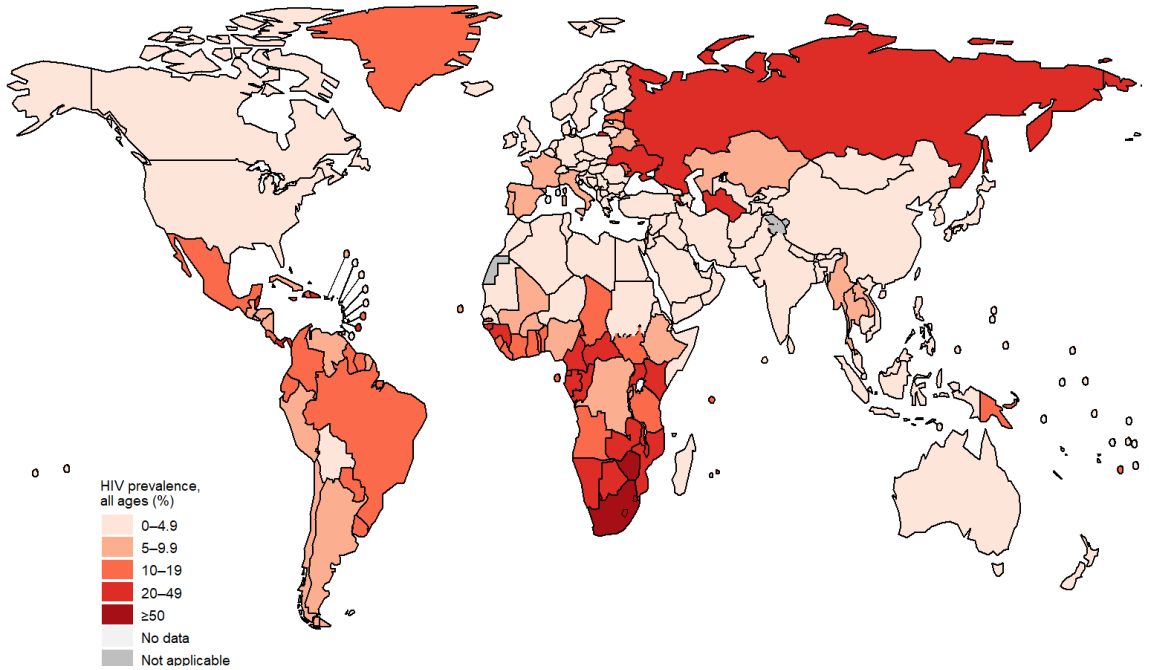


Change (%) in the estimated TB incidence rate (new cases per 100 000 population per year) at country level, 2024 compared with 2015

The first milestone of the End TB Strategy was a 20% reduction by 2020, compared with 2015; the second milestone is a 50% reduction by 2025, compared with 2015. The last two categories (decrease 20–49%, and decrease ≥50%) distinguish the countries that have made the most progress towards the second milestone of the End TB Strategy.



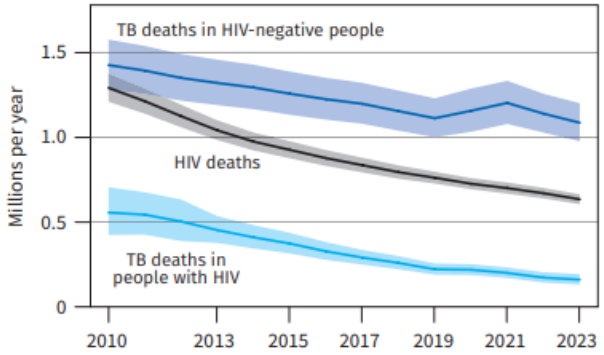
Poids de la co-infection VIH



Mortalité de la Tuberculose

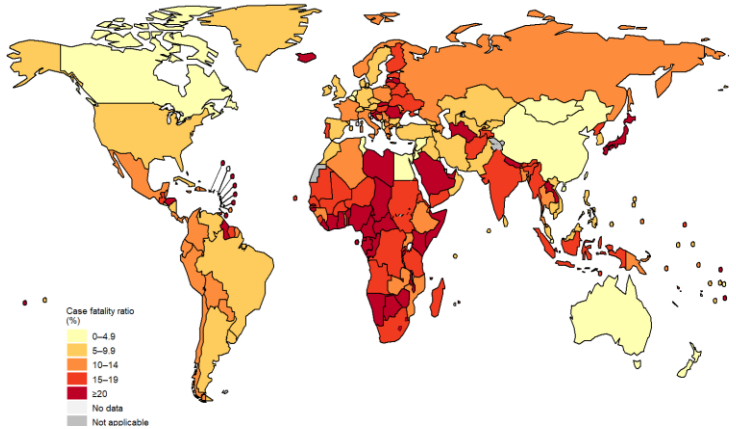
Global trends in the estimated number of deaths caused by TB and HIV (in millions), 2010–2023[a,b]

Shaded areas represent 95% uncertainty intervals.



[a] For HIV/AIDS, the latest estimates of the number of deaths in 2023 that have been published by UNAIDS are available at http://www.aids.org/en/ (accessed 12 July 2024). For TB, the estimates for 2023 are those published in this report.

[b] Deaths from TB among people with HIV are officially classified as deaths caused by HIV/AIDS in the International Classification of Diseases.



≈ 1.30 million décès (95% UI: 1.18–1.43 million)

Résistance aux anti-tuberculeux

Extensively drug-resistant TB (XDR-TB): TB disease caused by a strain of *M. tuberculosis* complex that is resistant to rifampicin (and may also be resistant to isoniazid), and that is also resistant to at least one fluoroquinolone (levofloxacin or moxifloxacin) and to at least one other "Group A" drug (bedaquiline or linezolid).

MDR/RR-TB: refers to either multidrug-resistant TB (MDR-TB) or rifampicin-resistant TB (RR-TB).

Multidrug-resistant TB (MDR-TB): TB disease caused by a strain of *M. tuberculosis* complex that is resistant to rifampicin and isoniazid.

Pre-extensively drug-resistant TB (pre-XDR-TB): TB disease caused by a strain of *M. tuberculosis* complex that is resistant to rifampicin (and may also be resistant to isoniazid), and that is also resistant to at least one fluoroquinolone (either levofloxacin or moxifloxacin).

Rifampicin-resistant TB (RR-TB): TB disease caused by a strain of *M. tuberculosis* complex that is resistant to rifampicin. These strains may be susceptible or resistant to isoniazid (i.e. multidrug-resistant TB [MDR-TB]), or resistant to other first-line or second-line TB medicines.

Rifampicin-susceptible, isoniazid-resistant TB (Hr-TB): TB disease caused by a strain of *M. tuberculosis* complex that is resistant to isoniazid but susceptible to rifampicin.

Avant 2022

Tuberculose ultra-résistante:

- Résistance aux FQ
- ET Résistance à un agent injectable: capréomycine, kanamycine, amikacine

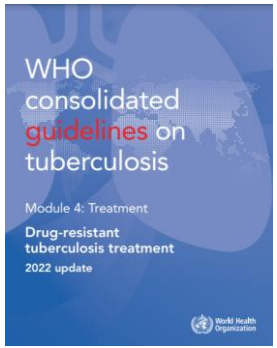
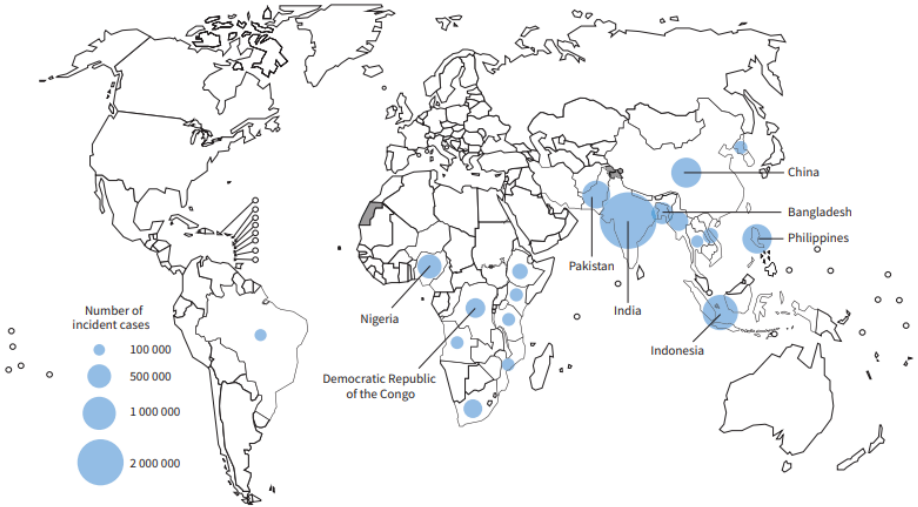


Table 3.1. Grouping of medicines recommended for use in longer MDR-TB regimens[a]

Groups and steps	Medicine	Abbreviation
Group A: Include all three medicines	Levofloxacin *or* moxifloxacin	Lfx Mfx
	Bedaquiline[b,c]	Bdq
	Linezolid[d]	Lzd
Group B: Add one or both medicines	Clofazimine	Cfz
	Cycloserine *or* terizidone	Cs Trd
Group C: Add to complete the regimen and when medicines from Groups A and B cannot be used	Ethambutol	E
	Delamanid[e]	Dlm
	Pyrazinamide[f]	Z
	Imipenem–cilastatin *or* meropenem[g]	Ipm–Cln Mpm
	Amikacin (*or* streptomycin)[h]	Am (S)
	Ethionamide *or* prothionamide[i]	Eto Pto
	P-aminosalicylic acid[i]	PAS

Estimated number of incident TB cases in 2023, for countries with at least 100 000 incident cases[a]



[a] The labels show the eight countries that accounted for about two thirds of the global number of people estimated to have developed TB in 2023.

- Seules 2/5 personnes avec une tuberculose pharmacorésistante environ ont eu accès au traitement en 2022.
- En 2022, 3.3% (95% UI: 2.6–4.0%) des nouveaux cas de TB ont une MDR/RR-TB et 17% (95% UI: 11–23%) parmi ceux pré-traités

Estimated number of people who developed MDR/RR-TB (incident cases) in 2023, for countries with at least 1000 incident cases[a]

[a] The labels show the five countries that accounted for more than half of the global number of people estimated to have developed MDR/RR-TB in 2023.

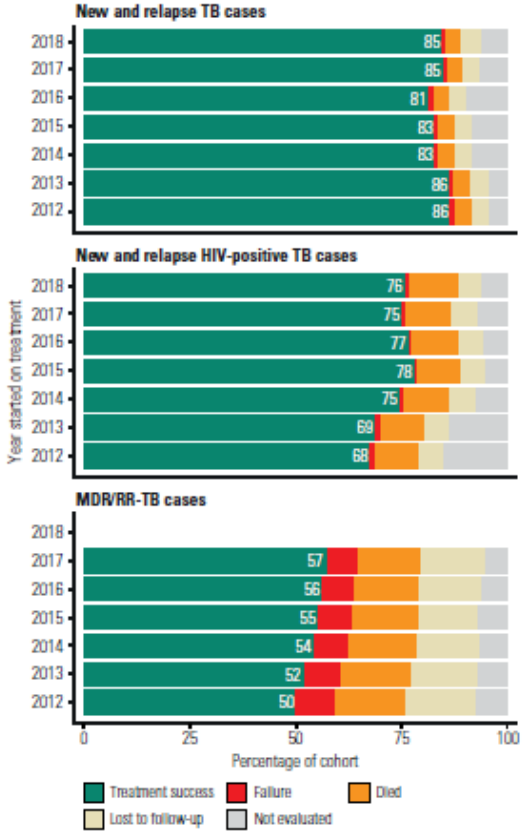
≈400 000 personnes (95% UI: 360 000– 440 000) ont developpé un MDR/RR-TB en 2023

Résistance aux anti-tuberculeux

Impact majeur sur la mortalité liée à la tuberculose

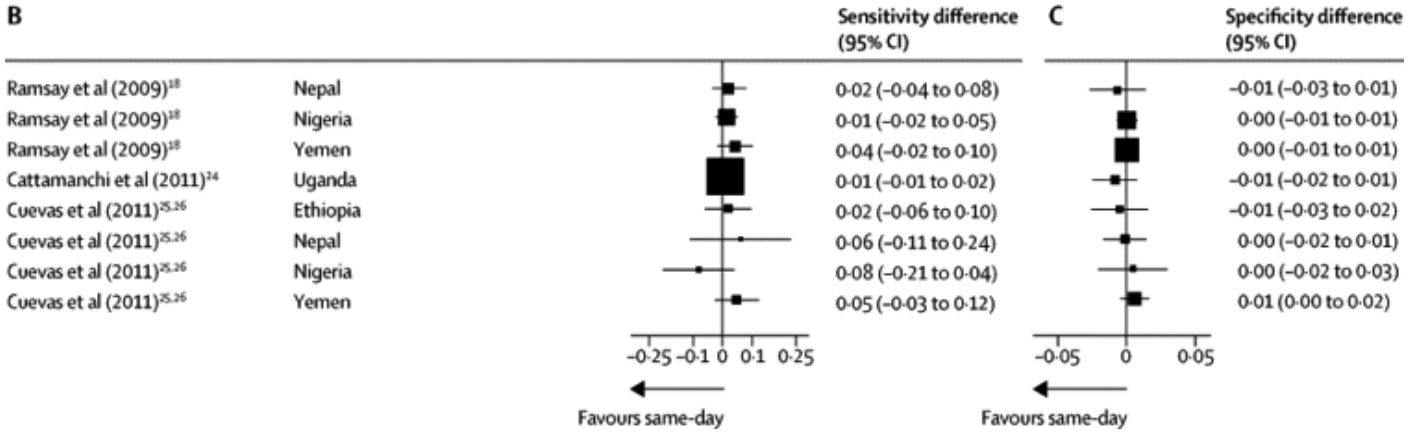
FIG. 5.30

Treatment outcomes for new and relapse TB cases, new and relapse HIV-positive TB cases, and MDR/RR-TB cases, globally[a], 2012–2018



PERFORMANCES DES TESTS DIAGNOSTIQUES

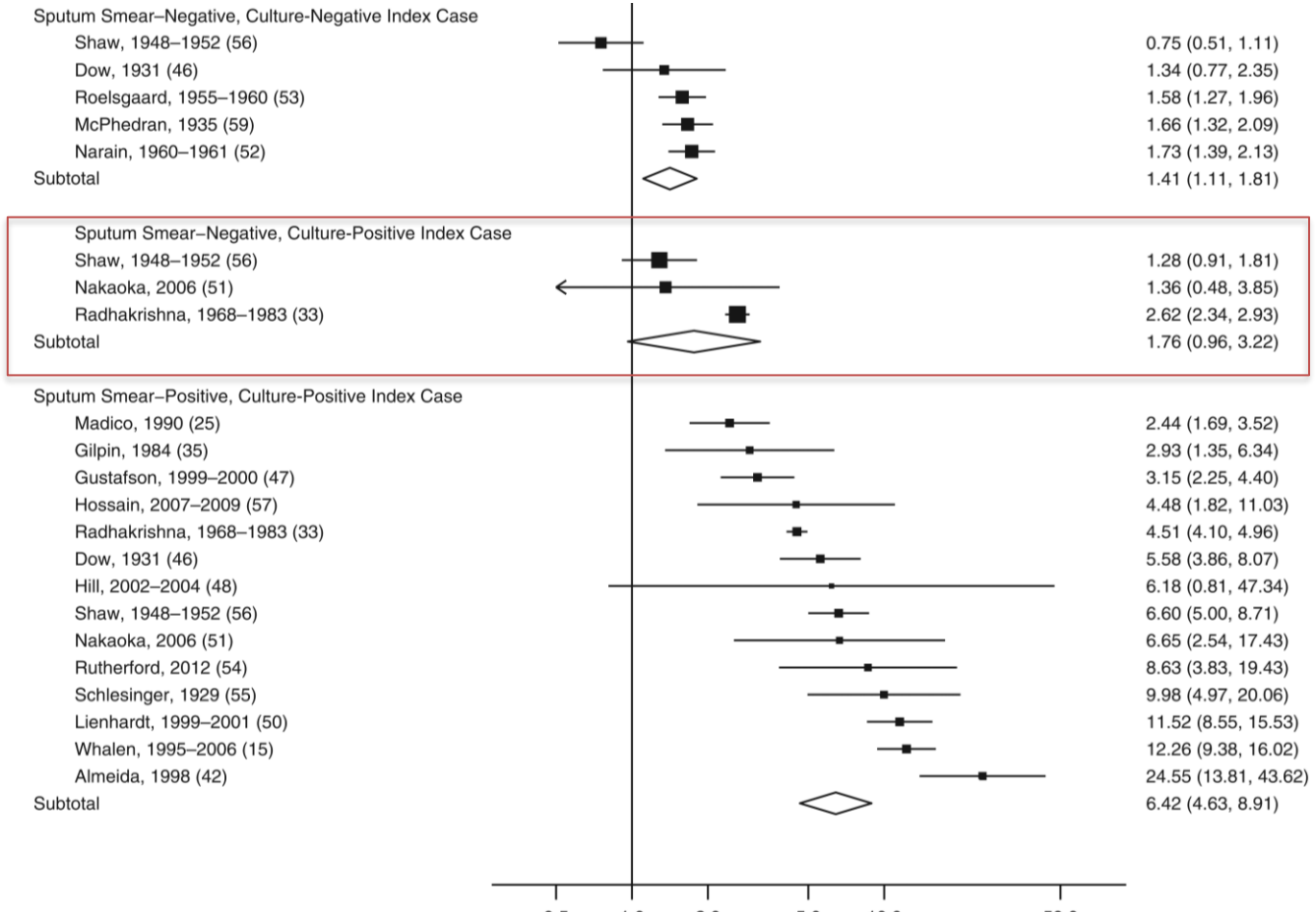
A propos des crachats



Davis et al. Lancet Infectious Diseases 2013

Sensibilité de l'examen des crachats 2 crachats le même jour versus 1 crachat deux jours de suite

Crachats et risque de transmission (Martinez et al. American journal of epidemiology 2017)



Adénosine déaminase

	TB neuro-méningée	Péricardite	Tuberculose péritonéale	Pleurésie
Sensibilité	89 %	95 %	82 %	93 %
Spécificité	91 %	84 %	79 %	87,3 %
VPP	89 %	72 %	86 %	21 %
VPN	88 %	98 %	74 %	99 %

Concentration élevée en faveur dune tuberculose

Pormohammad et al. J Infection 2017
Pandie et al. BMC medicine 2014
Young-Lee Journal of Infection 2015
Blakiston JCM 2018

PCR Gene Xpert

	Neuro-méningée	Péricardite	Tuberculose péritonéale	Pleurésie	Génito-urinaire	GGS	Os
Se	71 %	66 %	59 %	51 %	83 %	87 %	92 %
Spé	98 %	96 %	98 %	99 %	99 %	79-86%	82 %

La prévalence de la maladie affecte la sensibilité et la spécificité.
En zone de faible prévalence, réduction de la sensibilité…

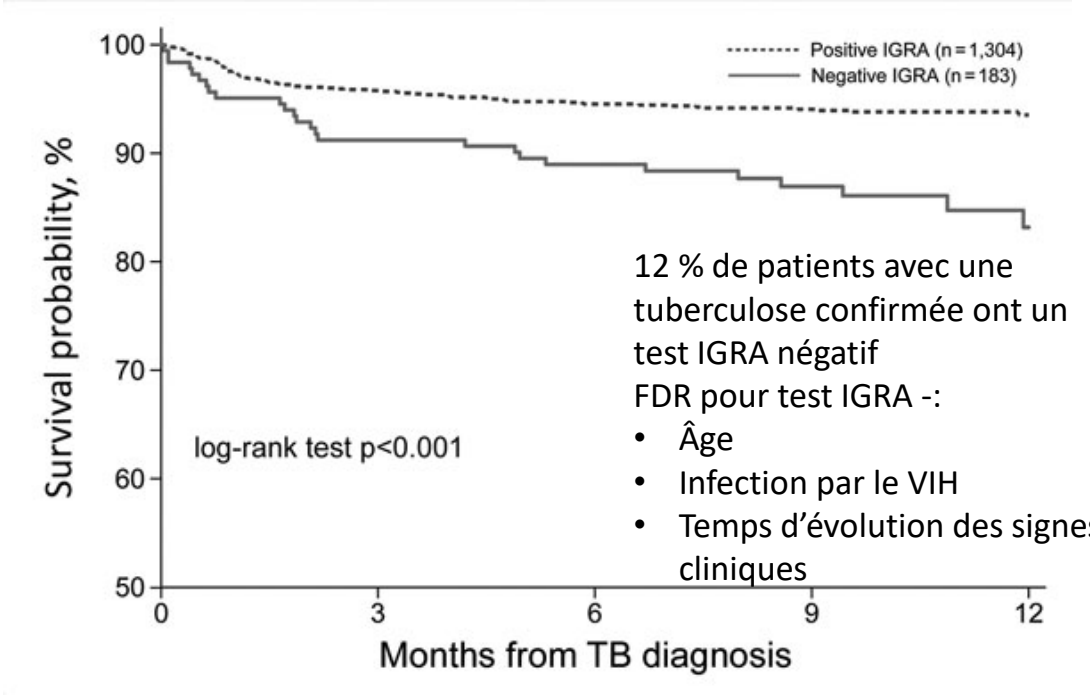
Méta-analyse Cochrane Juillet 2018

Test IGRA:
diagnostic de tuberculose maladie

Sensibilité	88 %
Spécificité	60 %
VPP	81 %
VPN	70 %

Du et al. Scientific reports 2018

Test IGRA: trop souvent négatif en cas de tuberculose maladie



12 % de patients avec une tuberculose confirmée ont un test IGRA négatif
FDR pour test IGRA -:

- Âge
- Infection par le VIH
- Temps d'évolution des signes cliniques

N'Guyen Emerging Infectious Diseases 2018

Surveillance

Surveillance minimale du traitement d'une tuberculose pulmonaire.

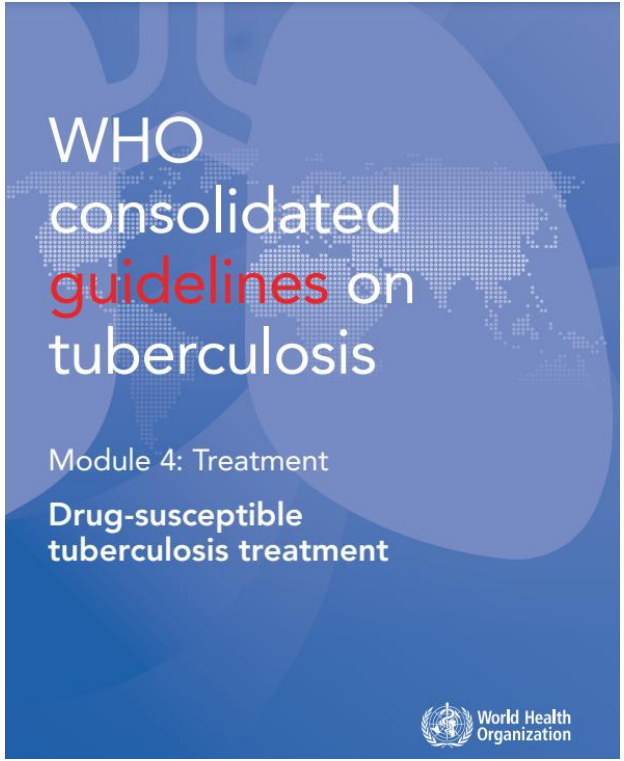
	Initial	J 10-15	J 30	M2	M4	M6	M9	M12-18
Consultation	∴	∴	∴	∴	∴	∴	∴	∴
Bactériologie	∴	❖		∴		∴ si expectoration		
Radio thorax	∴	∴	∴	∴ si expectoration	∴	∴	∴	∴
Transaminases	∴	∴	∴	∴				
Uricémie	∴			si anomalie				
Créatinémie	∴							

❖ L'examen bactériologique précoce entre le 10e et 15e jour de traitement est indiqué chez les malades hospitalisés en isolement afin de vérifier la négativation de l'examen micoscopique.

Activity	Baseline	Month of Treatment Completed 1	2	3	4	5	6	7	8	End of Treatment Visit
MICROBIOLOGY										
Sputum smears and culture[1]	☐	☐	☐	☐	☐					☐
Drug susceptibility testing[2]	☐			☐						
IMAGING										
Chest radiograph or other imaging[3]	☐		☐							☐
CLINICAL ASSESSMENT										
Weight[4]	☐	☐	☐	☐	☐	☐	☐	☐	☐	
Symptom and adherence review[5]	☐	☐	☐	☐	☐	☐	☐	☐	☐	
Vision assessment[6]	☐	☐	☐	☐	☐	☐	☐	☐	☐	
LABORATORY TESTING										
AST, ALT, bilirubin, alkaline phosphate[7]	☐	☐	☐	☐	☐	☐	☐	☐	☐	
Platelet count[8]	☐	☐	☐	☐	☐	☐	☐	☐	☐	
Creatinine[8]	☐	☐	☐	☐	☐	☐	☐	☐	☐	
HIV[9]	☐									
Hepatitis B and C screen[10]	☐									
Diabetes Screen[11]	☐									

PRISE EN CHARGE THÉRAPEUTIQUE

Prise en charge thérapeutique

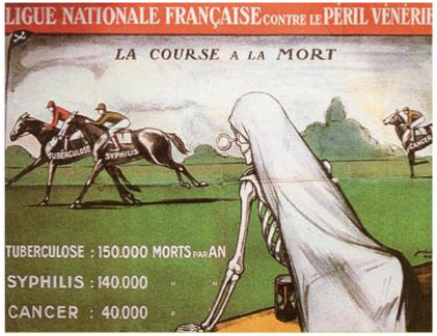


Mise à jour en 2025

Objectifs du traitement :
Réduire la population de bacilles pour réduire la gravité de la maladie et le risque de décès, et de transmission
Eradiquer les bacilles pour réduire le risque de rechute
Réduire le risque de développement de résistance au cours du traitement

Un peu d’histoire

- 1890: identification de *Mycobacterium tuberculosis* par Robert Koch.
- Juillet 1921:
  - Première utilisation du BCG par voie orale
  - Vaccination rapidement déployée chez les nouveaux-nés
- 1944: premier traitement antibiotique disponible

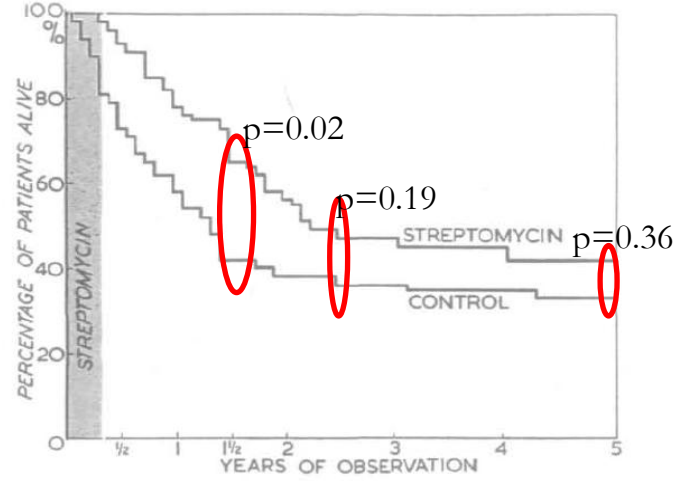


A FIVE-YEAR ASSESSMENT OF PATIENTS IN A CONTROLLED TRIAL OF STREPTOMYCIN IN PULMONARY TUBERCULOSIS[1]

Report to the Tuberculosis Chemotherapy Trials Committee of the Medical Research Council

1954

BY WALLACE FOX, IAN SUTHERLAND, AND THE LATE MARC DANIELS



Percentage survival in streptomycin and control series for a five-year period (55 streptomycin and 52 control patients).

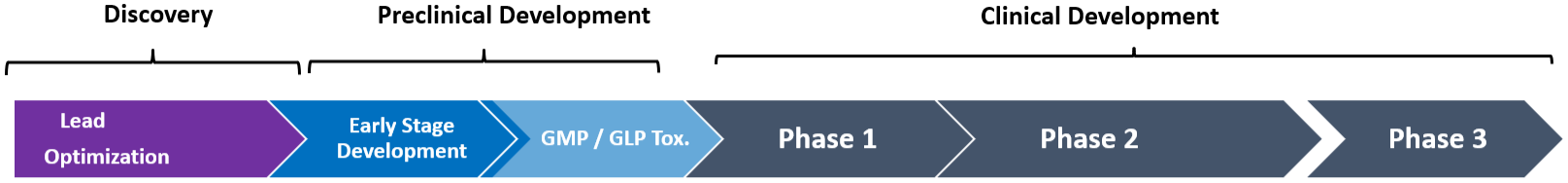
Antituberculeux (abréviations)	**Année de découverte**
Streptomycine (SM)	1944
Acide para-aminosalicylique (PAS ou P)	1945
Thioacétazone (TB1 ou T)	1946
Néomycine	1949
Viomycine (VM ou V)	1951
Isoniazide (INH ou H)	**1952**
Pyrazinamide (PZA ou Z)	**1952**
Thiocarbanilide	1953
D-cyclosérine (CS ou C)	1955
Ethionamide (ETA ou ET)	1956
kanamycine (KM ou K)	1957
Ethambutol (EMB ou E)	**1961**
Capréomycine (CM ou Cm)	1962
Prothionamide	1963
Rifampicine (RMP ou R)	**1967**
Amikacine	1972
Ofloxacine (fluoroquinolone)	1985

Rifapentine 1998
Linezolide 2001
Moxifloxacine 2001
Bédaquiline 2014
Delamanide 2016
Pretomanide 2020

Antibiotiques	Activité sur les bacilles			Proportion de mutants résistants au sein d'une population sensible	Apport dans le traitement
	À multiplication active (caverne) ~10^8 bacilles	À multiplication lente			
		À pH acide (macrophage) ~10^5 bacilles	À pH neutre (foyers caséeux) ~10^5 bacilles		
Isoniazide (INH)	++	+	0	10^{-6}	Antibiotique le plus rapidement bactéricide
Rifampicine (RMP)	++	+	+	10^{-7}	18 mois -> 9 mois
Pyrazinamide (PZA)	0	++	0	> 10^{-5}	9 mois -> 6 mois
Éthambutol (EMB)	±	±	0	10^{-6}	Empêche sélection de RMP-R si résistance primaire à INH

+, ++ : activité bactéricide ; ± : activité bactériostatique ; 0 : pas d'activité.

2025 Global New TB Drug Pipeline[1]



Indazole sulfonamides
Diarylthiazoles
DprE1 Inhibitors
Direct InhA Inhibitors
Mtb energy metabolism
Gyrase Inhibitors
Arylsulfonamides
Inhibitors of MmpL3, Translocase-1, ClpC1, ClpP1P2, PKS13, F-ATP synthase, RNAP
Oxazolidinones
DnaE1 /Nargenicin analogs

TBD10 (MK-3854)
UMN-120/121
FIM-3002*
X20404*
MPL-447*
NTB-3119*
JSF-3285*
CPZEN-45*
MBX-4888A (1810)*
FNDR-20364*

OTB-658
GSK-839*

TBD09 (MK-7762)
TBI-223
TBAJ-587
Macozinone* (PBTZ-169)
TBD11 (CLB-073)*
GSK-286*

Delpazolid
Sutezolid, Tedizolid
Sorfequiline (TBAJ-876)
BTZ-043*
TBA-7371*
Alpibectir (BVL-GSK098)*
Ganfeborole (GSK-656*)
Sanfetrinem
Telacebec* (Q203)
Pyrifazimine (TBI-166)
SQ-109*

Sudapyride (WX-081)
Quabodepistat (OPC-167832*)

Bedaquiline*
Delamanid*
Pretomanid*

*New chemical class. Known chemical classes for any indication are color coded: Rifamycin, oxazolidinone, nitroimidazole, diarylquinoline, benzothiazinone, imidazopyridine amide, beta-lactam. Smaller type indicates candidates requiring additional research/support to advance.

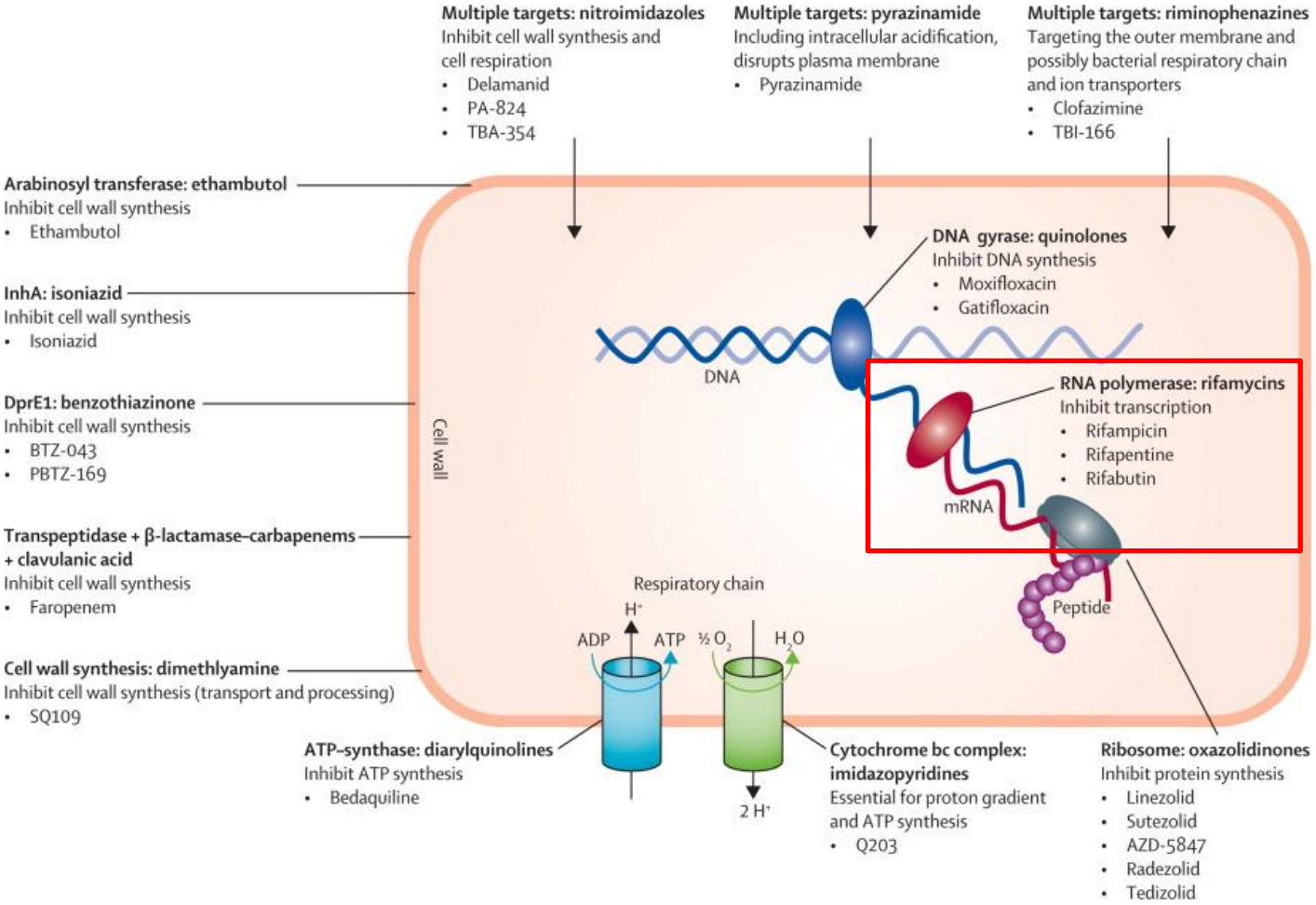
[1] New Molecular Entities not yet approved, being developed for TB or only conditionally approved for TB. Showing most advanced stage reported for each. Details for projects listed can be found at http://www.newtbdrugs.org/pipeline/clinical

Ongoing projects without a lead compound identified: http://www.newtbdrugs.org/pipeline/discovery

WORKING GROUP ON NEW TB DRUGS
www.newtbdrugs.org

Updated: Nov 2025

TUBERCULOSE SENSIBLE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• AZD-5847
• Radezolid
• Tedizolid

Rifampicine

- **Posologie 10-20 mg/kg/j**
- **Bactéricide**, elle est active sur les bacilles des cavernes, du caséum solide et sur les bacilles intra-macrophagiques: activité stérilisante
- La molécule est un **puissant inducteur enzymatique** microsomal, provoquant d'importantes interactions médicamenteuses, en particulier avec les oestroprogestatifs, les anticoagulants oraux,…
- La rifampicine colore les excrétas (larmes, urines, sperme) en rouge orange (prévenir les porteurs de lentilles).
- Elle peut induire des phénomènes immuno-allergiques (thrombopénie, anémie hémolytique, insuffisance rénale aiguë par TNIA), surtout lors des prises discontinues du médicament.
- **Rifabutine (Ansatipine®): 450 à 600 mg/j**

Received: 1 November 2021 | Revised: 4 February 2022 | Accepted: 7 February 2022
DOI: 10.1002/phar.2672

REVIEW OF THERAPEUTICS

PHARMACOTHERAPY accp

Systematic review of drug–drug interactions between rifamycins and anticoagulant and antiplatelet agents and considerations for management

Conan MacDougall[1] | Theora Canonica[2] | Chris Keh[3] | Binh An P. Phan[4] | Janice Louie[5]

Interaction importante avec les AVK
Baisse de l'AUC de NACO

Mais augmentation du risque hémorragique sous NACO
Possibilité d'utiliser la rifabutine

Original Investigation

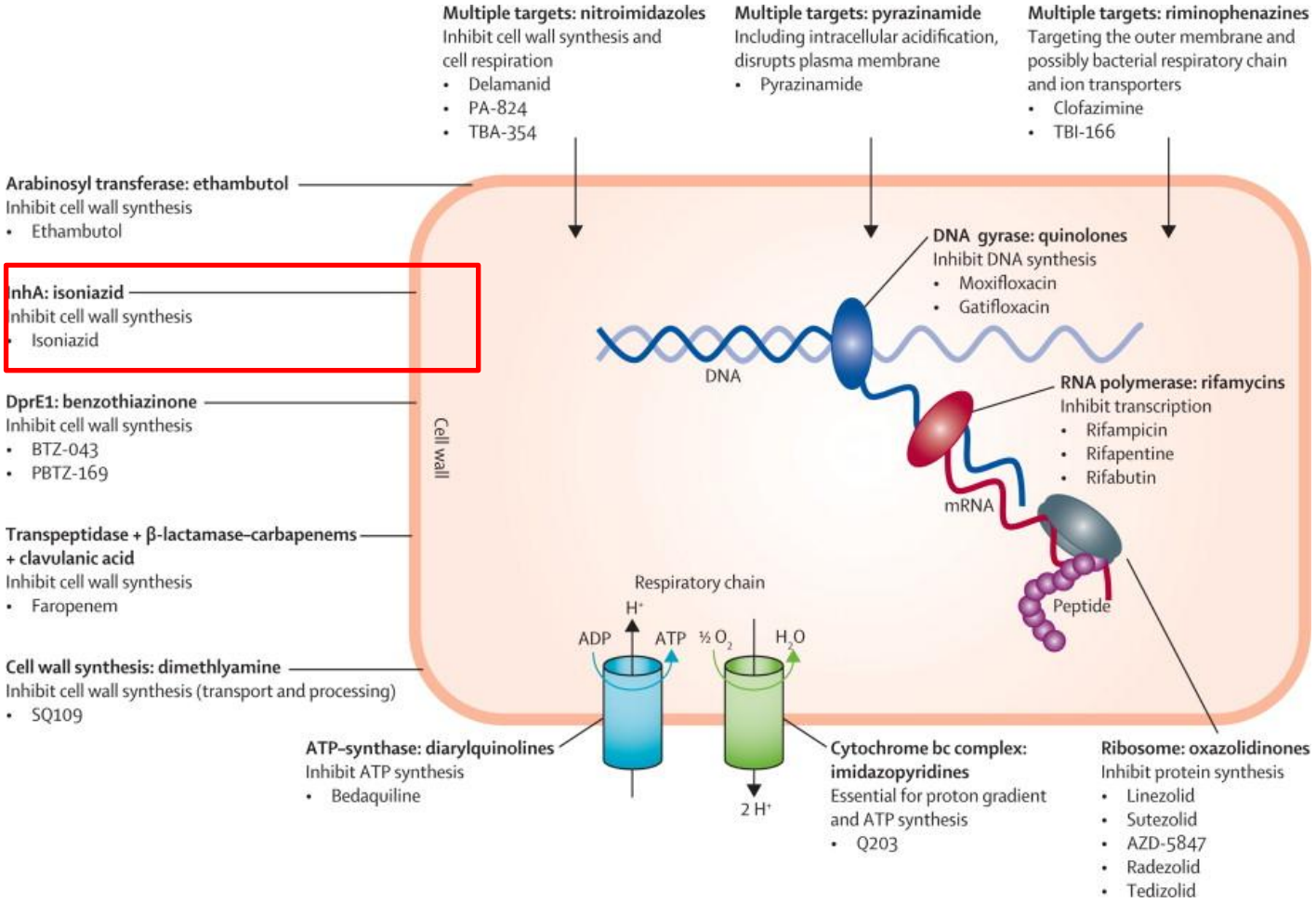
October 3, 2017

Association Between Use of Non–Vitamin K Oral Anticoagulants With and Without Concurrent Medications and Risk of Major Bleeding in Nonvalvular Atrial Fibrillation

Shang-Hung Chang, MD, PhD[1,2,3]; I-Jun Chou, MD[3,4]; Yung-Hsin Yeh, MD[1,3]; et al

Author Affiliations | Article Information

JAMA. 2017;318(13):1250-1259. doi:10.1001/jama.2017.13883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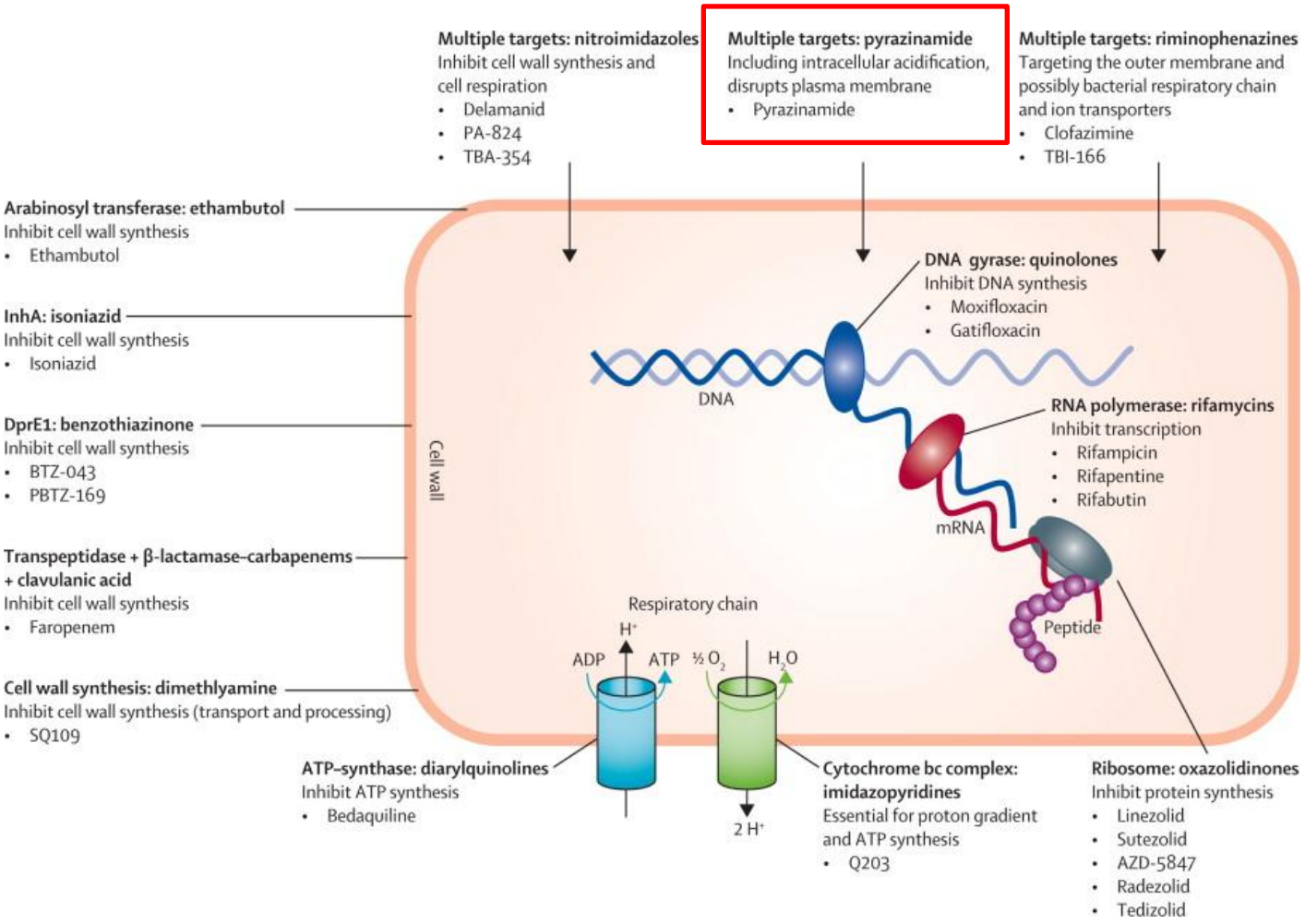
• Tedizolid

Isoniazide

- Puissamment et rapidement **bactéricide**
- Posologie de **3-6 mg/kg/j** (acétyleurs lents-rapides)
- L'isoniazide est actif sur les bacilles des cavernes et à un moindre degré sur les bacilles intramacrophagiques.
- Il n'a pas d'activité sur les bacilles du caséum solide.
- ***Principaux effets secondaires***: nausées, simple élévation des transaminases ou hépatite médicamenteuse dose-dépendante, polynévrites sensitivo-motrices (surtout en cas de carence en vit B6), troubles neuropsychiques, névralgies cervico-brachiales (syndrome épaule-main) et syndromes rhumatoïdes.
- La supplémentation en pyridoxine (vitamine B6) recommandée pour limiter la toxicité neurologique de l'INH chez le patient dénutri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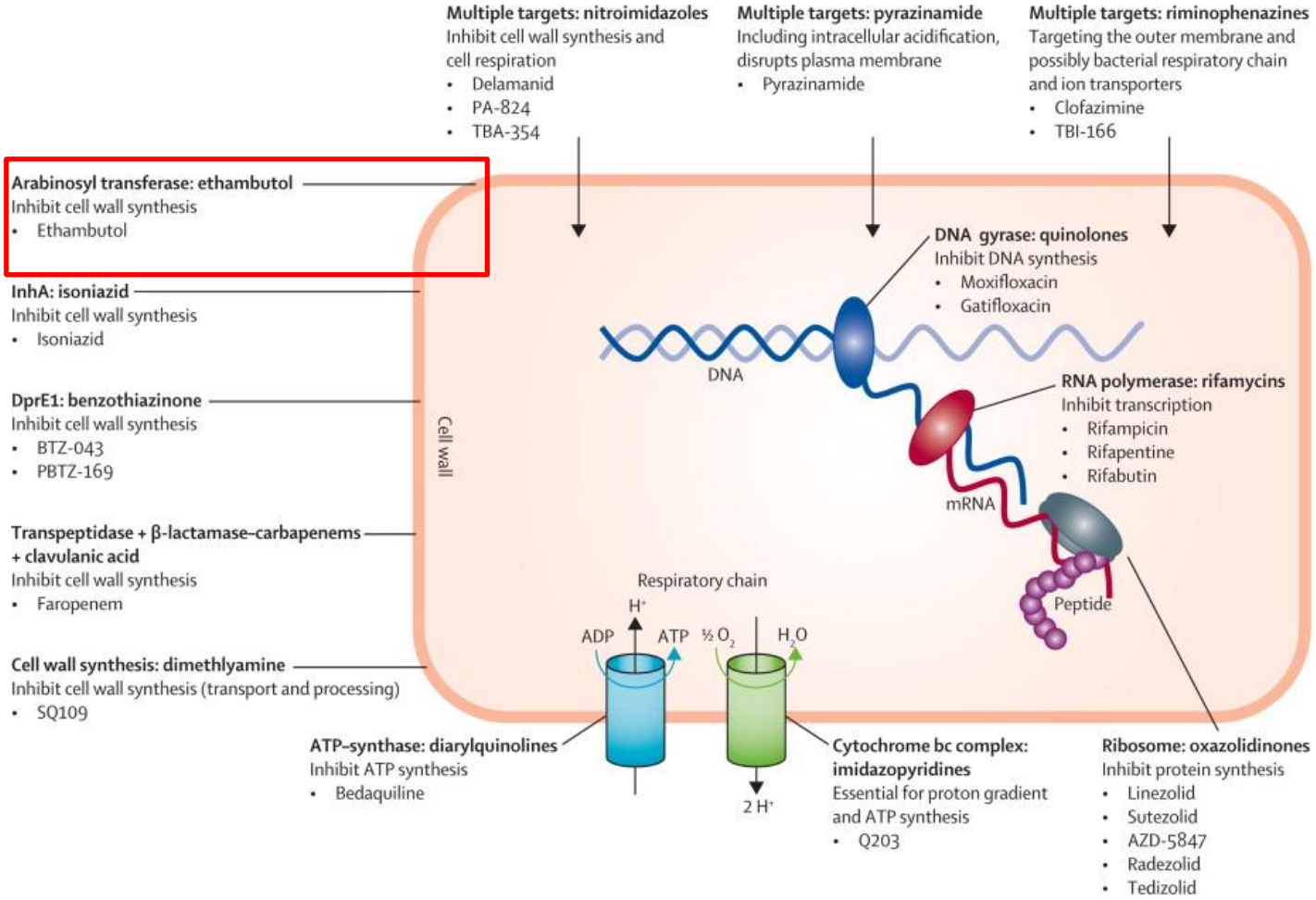
• Tedizolid

Pyrazinamide

- Posologie de **25 à 30 mg/kg/j**.
- Il est contre-indiqué en cas d'insuffisance hépatocellulaire ou d'insuffisance rénale.
- **Bactéricide**, il est uniquement actif sur les bacilles intramacrophagiques et son activité à ce niveau est forte, détruisant les bacilles quiescents pouvant rester plusieurs années dans les macrophages: stérilisant
- Il évite donc les rechutes et **a permis de raccourcir le traitement antituberculeux à 6 mois+++.**
- Ce médicament a une toxicité hépatique, dose dépendante, moindre que celle de celle de l'isoniazide.
- Il provoque une **hyperuricémie,** (l'absence d'hyperuricémie doit faire douter de la prise du traitement), le plus souvent asymptomatique et ne nécessitant un traitement spécifique qu'en cas de signes cliniques (arthralgies, crises de goutte).
- Photosensibilisation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Inhibit protein synthesis
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• Sutezolid
• AZD-5847
• Radezolid
• Tedizolid

Éthambutol

- Posologie de 20 à 25 mg/kg/j.
- Ce médicament est **bactériostatique** et agit sur les bacilles des cavernes et sur les bacilles intramacrophagiques mais n'a pas d'action sur les bacilles du caséum solide.
- Mais prévient la multirésistance +++
- La principale complication est ophtalmologique, avec névrite optique rétrobulbaire se manifestant initialement par un trouble de la vision des couleurs (dyschromatopsie) puis par une baisse de l'acuité visuelle (surtout pour des doses ≥ 25 mg/kg/j, en cas d' éthylisme chronique, ou chez l'insuffisant rénal).
- Cela impose une consultation d'ophtalmologie avant la mise en route du traitement, puis tous les mois tant que le médicament est poursuivi.

Les schémas recommandés par l'OMS

- Les principes actifs :
  - H: isoniazide,
  - R: rifampicine,
  - Z: isoniazide,
  - E: Ethambutol,
  - P: Rifapentine
  - M : Moxifloxacine
- Les schémas
  - **2 mois : HRZ(E), 4 mois HR**
  - **2 mois : HPMZ, 2 mois HP**
  - **2 mois : HRZ(E), 2 mois HR**
- Préférer la prise quotidienne, et les STR

Comment choisir ?

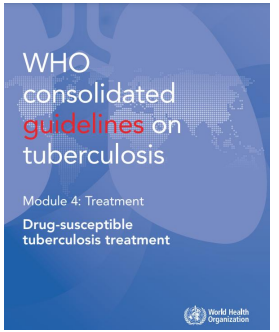


Table 1.2.1. Guide for regimen selection for DS-TB

Regimen	Age				
	0-3 months	3 months-10 years	10-12 years	12-16 years	>16 years
2HRZ(E)/4HR	Ethambutol should be added in settings with a high background prevalence of isoniazid resistance or HIV infection or in CLHIV		Independent of disease severity or HIV status		
2HRZ(E)/2HR		Non-severe TB, > 3 kg, add ethambutol in settings with a high background prevalence of isoniazid resistance or HIV infection or in CALHIV			
2HPMZ/2HPM				Independent of disease severity or HIV status	
Additional factors to be considered if several regimens are possible		Disease severity			
	Patient or family preference				
	Access and cost of regimen component drugs				

CALHIV: children and adolescents living with HIV; CLHIV: children living with HIV; DS-TB: drug-susceptible TB; HIV: human immunodeficiency virus; TB: tuberculosis.

Note: all the regimens envisage daily dosing of all medicines.

Box 2.1. Definition of non-severe pulmonary TB

For the purpose of determining treatment duration for DS-TB, non-severe pulmonary TB is defined as any of the following:

- intrathoracic lymph node TB without airway obstruction;
- pulmonary TB confined to one lobe with no cavities and no miliary pattern; or
- uncomplicated pleural effusion (without pneumothorax or empyema).

Raccourcir la durée de traitement ?

Rifapentine + Moxifloxacine + isoniazide + Pyrazinamide 4 mois non inférieur à SOC 6 mois

Attention Rifapentine + isoniazide + ethambuthol + pyrazinamide inférieur au SOC 6 mois

NEJM 6 May 2021

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.

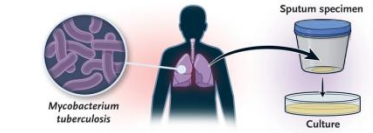
Safety: The percentages of patients who had adverse events of grade 3 or higher or who discontinued the assigned regimen prematurely did not differ significantly between the rifapentine–moxifloxacin group and the control group but were lower in the rifapentine group than in the control group.

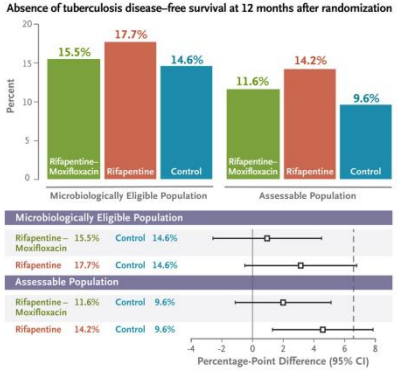
LIMITATIONS AND REMAINING QUESTIONS

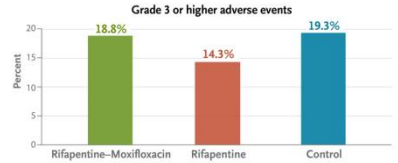
Further study is required to understand the following:

- 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



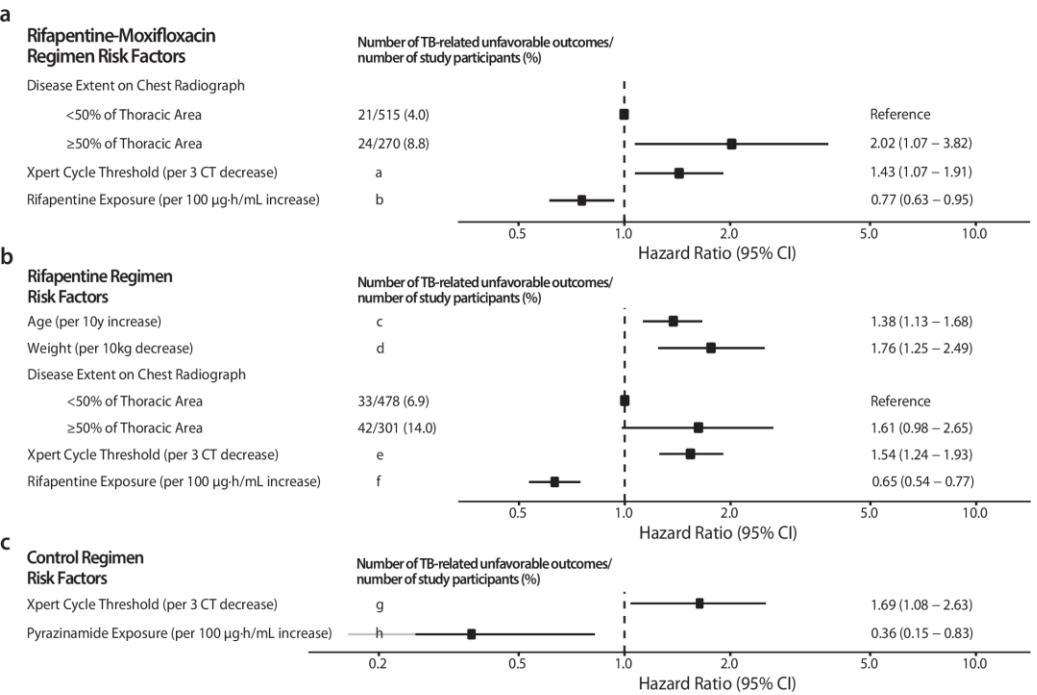


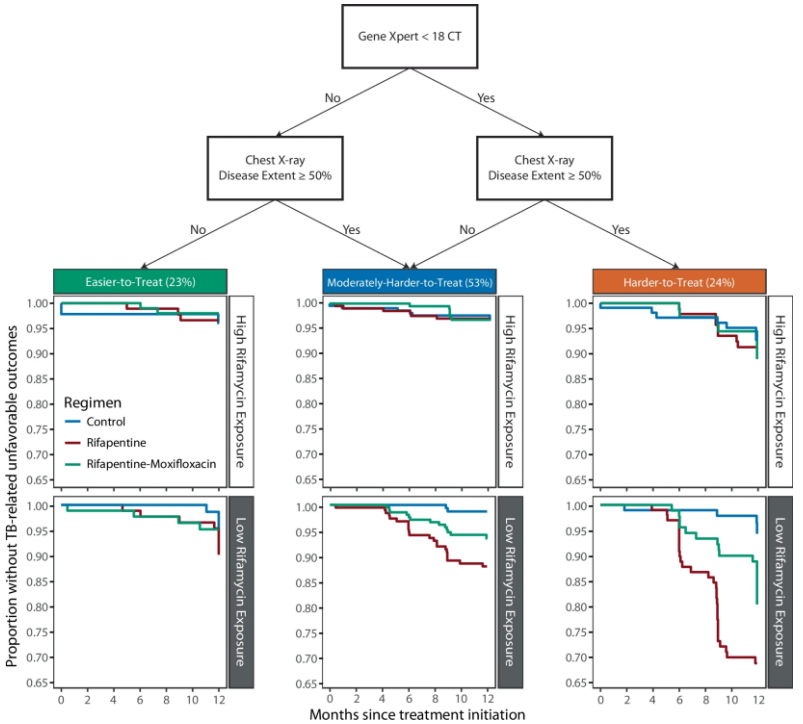


CONCLUSIONS

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.

FDR d'échec du traitement court





Chang et al. Nature Communications 2024

Le traitement court ?

This regimen consisted of **eight weeks of daily isoniazid (H), rifapentine (P), moxifloxacin (M) and pyrazinamide (Z)** , followed by **nine weeks of daily isoniazid, rifapentine, and moxifloxacin** (2HPMZ/2HPM). The dose of rifapentine used was 1200 mg daily.

Rifapentine ½ vie longue (13h vs 2-3 h pour la rifampicine)

Rifapentine non disponible en France!

(Rifapentine is available via the Global Drug Facility in a number of low- and middle-income countries, excluding the WHO Europe region apart from a few exceptions (Republic of Moldova, Uzbekistan, Ukraine and the Russian Federation).

En vrai vie à San Francisco, 11/22 patients ont arrêté prématurément le TTT

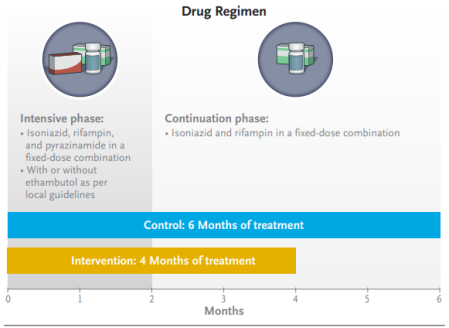
Louie JK, et al., Open Forum Infect Dis. 2024 Mar 26;11(4):ofae178.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 10, 2022 VOL. 386 NO. 10

Shorter Treatment for Nonsevere Tuberculosis in African and Indian Children

A. Turkova, G.H. Wills, E. Wobudeya, C. Chabala, M. Palmer, A. Kinikar, S. Hissar, L. Choo, P. Musoke, V. Mulenga, V. Mave, B. Joseph, K. LeBeau, M.J. Thomason, R.B. Mboizi, M. Kapasa, M.M. van der Zalm, P. Raichur, P.K. Bhavani, H. McIlleron, A.-M. Demers, R. Aarnoutse, J. Love-Koh, J.A. Seddon, S.B. Welch, S.M. Graham, A.C. Hesseling, D.M. Gibb, and A.M. Crook, for the SHINE Trial Team*



TB non sévère

Pas de BAAR à l'ED

Parmi les 1461 enfants éligibles:

144 TB sévères

31 Avec BAAR à l'ED

	No. of Patients	4-Month Treatment	6-Month Treatment	Risk Difference (95% CI)
		no. of participants with event/total no. (%)		*percentage points*
Primary outcome				
Modified intention-to-treat population	1145	16/572 (3)	18/573 (3)	−0.3 (−2.3 to 1.6)
Per-protocol population	1121	14/563 (2)	17/558 (3)	−0.6 (−2.5 to 1.4)
Intention-to-treat population	1204	44/602 (7)	44/602 (7)	0 (−2.9 to 2.9)
Key secondary outcome				
Modified intention-to-treat population	910	10/450 (2)	13/460 (3)	−0.6 (−2.6 to 1.4)
Per-protocol population	895	8/445 (2)	13/450 (3)	−1.1 (−3.1 to 0.9)

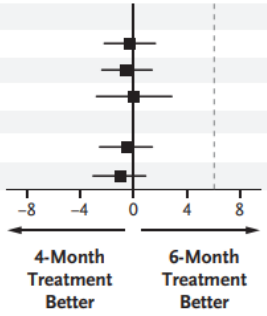
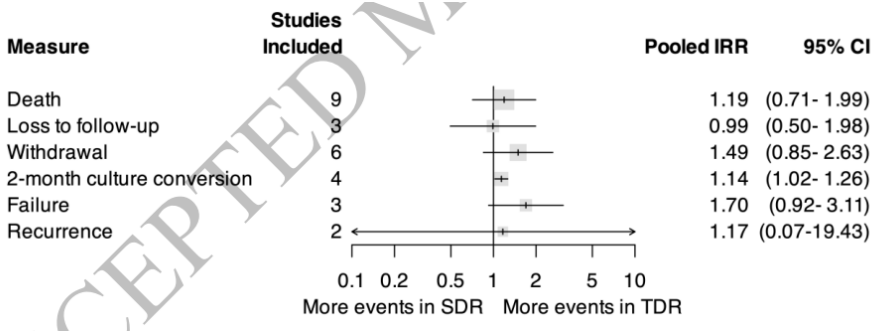


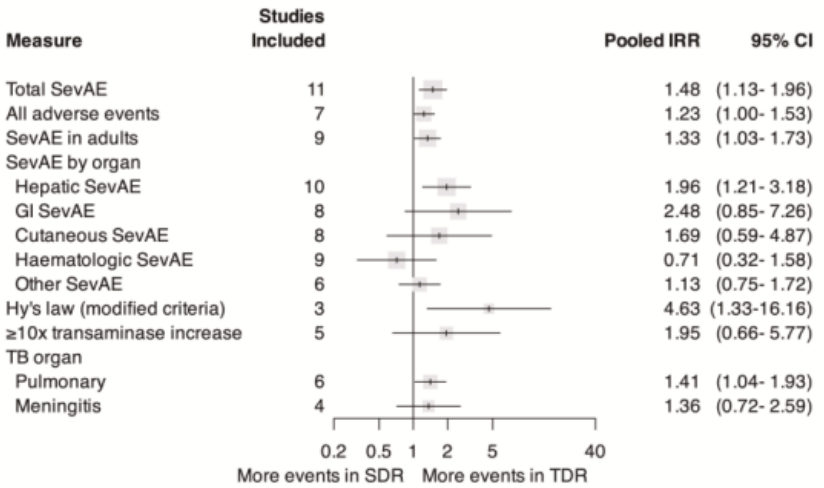
Figure 2. Unadjusted Analysis of the Primary Efficacy and Key Secondary Outcomes in the Trial Populations.

The primary efficacy outcome was unfavorable status by 72 weeks, which was defined as a composite of treatment failure (treatment extension, change, or restart or tuberculosis recurrence), loss to follow-up during treatment, or death, with the exclusion of all the participants who had undergone randomization but did not complete 4 months of treatment (modified intention-to-treat population). The per-protocol population included all the participants in the modified intention-to-treat population except those who had not adhered to the trial regimen. The intention-to-treat population included all the participants who had undergone randomization. Differences have been carried to one decimal place because of the small values. The prespecified margin for noninferiority in the primary efficacy analysis was 6 percentage points (dashed line). The key secondary analysis was unfavorable status at 72 weeks as assessed among the 958 participants who had been independently adjudicated as having tuberculosis at baseline.

Vers une augmentation des doses de Rifampicine?

Des doses de rifampicine > 10 mg/kg pourrait faciliter la négativation des cultures et réduire le risque de résistance





Increasing doses improved sputum culture conversion at week 8 (RR 1.3, 95% CrI 1.1; 1.7 for SCC with 35mg/kg/day).

Dose à 25-35mg/kg???

Gumbo T, et al., Antimicrob Agents Chemother. 2007 Nov;51(11):3781-8.
Arbiv OA, et al., Clin Infect Dis. 2025 Jan 9:ciaf004
Espinosa-Pereiro J,ey al., Clin Infect Dis. 2025 Jan 10:ciaf003

Vers une augmentation des doses de Rifampicine?

ORIGINAL ARTICLE

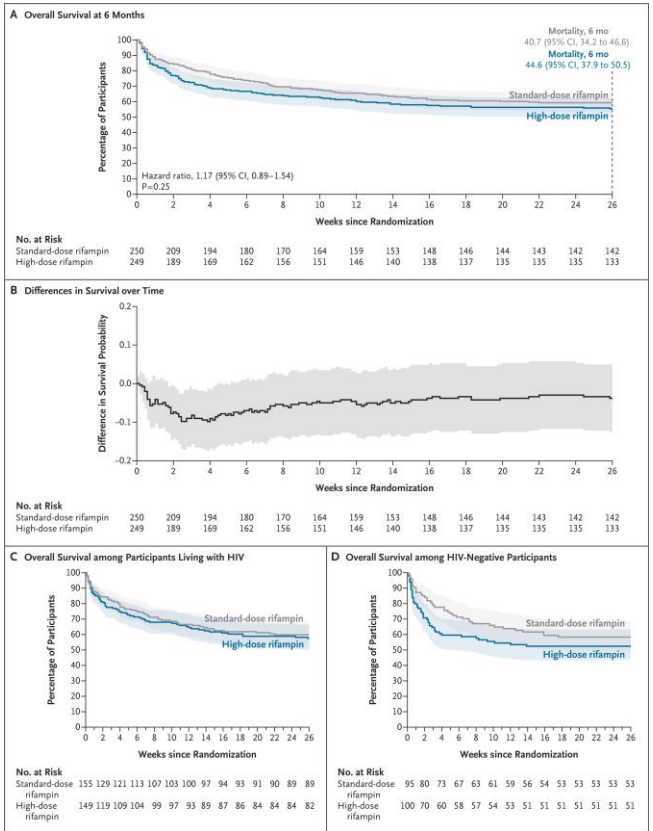
Trial of High-Dose Oral Rifampin in Adults with Tuberculous Meningitis

Authors: David B. Meya, M.B., Ch.B., Ph.D., Fiona V. Cresswell, M.B., Ch.B., Ph.D., Biyue Dai, Ph.D., Nicole Engen, M.S., Kogieleum Naidoo, M.B., Ch.B., Ph.D., Ahmad Rizal Ganiem, Ph.D., Darma Imran, M.D., +28, for the HARVEST Trial Team* Author Info & Affiliations

Published December 17, 2025 | N Engl J Med 2025;393:2434-2446 | DOI: 10.1056/NEJMoa2502866
VOL. 393 NO. 24 | Copyright © 2025

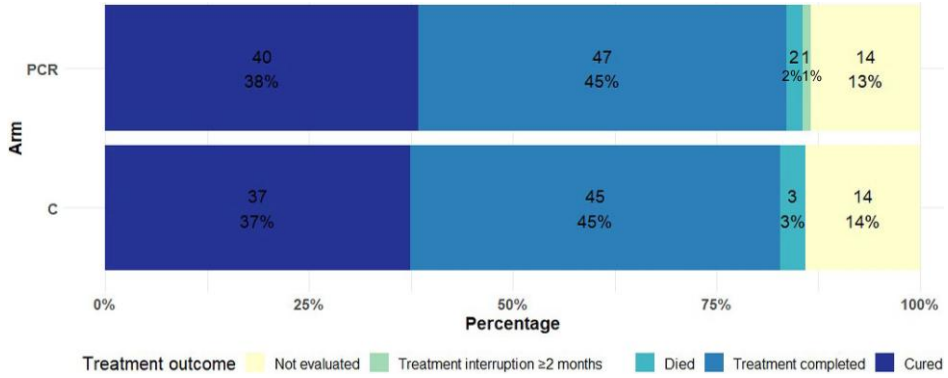
Dose de rifampicine 35 mg/kg/jour

Deux explications avancées :
Baisse des concentrations de corticoïdes du fait de l'interaction médicamenteuse
Plus d'IRIS dans le bras haute dose



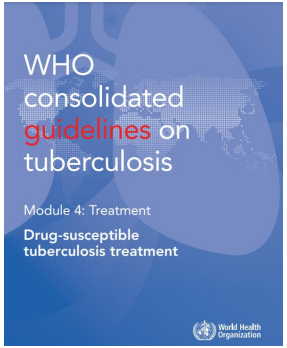
Ethambutol, oui ou non ?

Etude Fast-TB 164 patients
Arrêt précoce de l'Ethambutol) réception de la sensibilité à l'isoniazide évaluée par PCR



Open Forum Infect Dis, Volume 9, Issue 8, August 2022, ofac353, https://doi.org/10.1093/ofid/ofac353

Corticothérapie adjuvante



- Forte recommandation dans le TB neuroménigée :
  - 6 à 8 semaines de Dexaméthasone ou prednisolone
- Recommandation conditionnelle dans la TB péricardique

Corticothérapie adjuvante

The NEW ENGLAND JOURNAL of MEDICINE

CURRENT ISSUE SPECIALTIES TOPICS

ORIGINAL ARTICLE

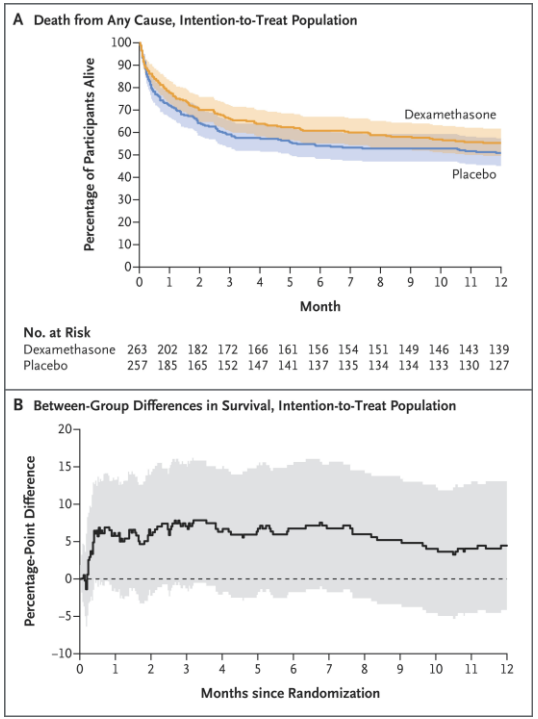
Adjunctive Dexamethasone for Tuberculous Meningitis in HIV-Positive Adults

Authors: 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., +23, for the ACT HIV Investigators* Author Info & Affiliations

Published October 11, 2023 | N Engl J Med 2023;389:1357-1367 | DOI: 10.1056/NEJMoa2216218

VOL. 389 NO. 15 | Copyright © 2023

Essai randomisé
520 patients
Plus de 50 % avec des CD4 < 50
Près de 50 % non traités de leur infection HIV



Corticothérapie adjuvante

The NEW ENGLAND JOURNAL of MEDICINE

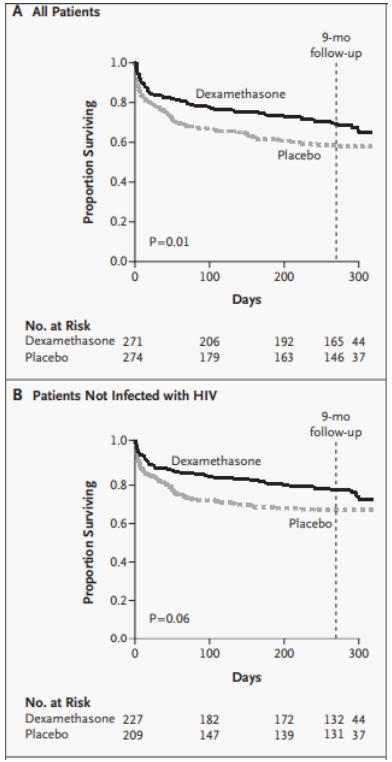
ORIGINAL ARTICLE

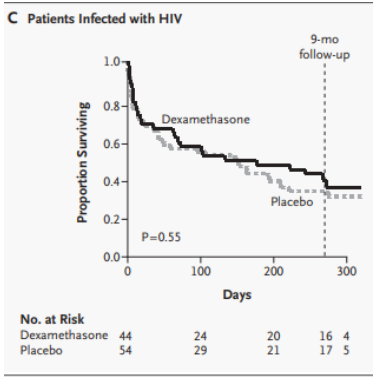
Dexamethasone for the Treatment of Tuberculous Meningitis in Adolescents and Adults

Guy E. Thwaites, M.R.C.P., Nguyen Duc Bang, M.D., Nguyen Huy Dung, M.D., Hoang Thi Quy, M.D., Do Thi Tuong Oanh, M.D., Nguyen Thi Cam Thoa, M.D., Nguyen Quang Hien, M.D., Nguyen Tri Thuc, M.D., Nguyen Ngoc Hai, M.D., Nguyen Thi Ngoc Lan, Ph.D., Nguyen Ngoc Lan, M.D., Nguyen Hong Duc, M.D., Vu Ngoc Tuan, M.D., Cao Huu Hiep, M.D., Tran Thi Hong Chau, M.D., Pham Phuong Mai, M.D., Nguyen Thi Dung, M.D., Kasia Stepniewska, Ph.D., Nicholas J. White, F.R.C.P., Tran Tinh Hien, M.D., and Jeremy J. Farrar, F.R.C.P.

545 Patients
Âgés de plus de 14 ans

2004





Les recommandations françaises (SPLF/SPILF) ?

Situations cliniques		
TB pulmonaire sensible	HRZE (2)/HR (4) HRZE (2)/HR (2) HPMZ (2) / HPM (2)	Extension à 9 mois si culture positive à M2 Arrêt E si PCR S-H Quadithérapie si absence de résultat de Sensibilité Corticothérapie si miliaire hypoxémiante Patient pauci-bacillaire, sans cavernes, immunocompétents, absence de résistance Pb disponibilité rifapentine
TB neuroméningée	HRZE (2) / HR (7 à 10)	2 semaine de traitement IV, rifampicine à 20 mg/kg/j Corticothérapie Discussion anti-TNF
TB osseuse	HRZE (2)/HR (4 à 7)	Possibilité de remplacer Ethambutol par FQ
TB séreuse	HRZE (2)/HR (4)	Corticothérapie discutée uniquement pour péricardite
TB résistance à l'INH	RZEM (2)/RM 4 mois	

Raccourcir encore la durée de traitement encore ?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Treatment Strategy for Rifampin-Susceptible Tuberculosis

Nicholas I. Paton, M.D., Christopher Cousins, M.B., Ch.B., Celina Suresh, B.Sc., Erlina Burhan, M.D., Ka Lip Chew, F.R.C.P.A., Victoria B. Dalay, M.D., Qingshu Lu, Ph.D., Tutik Kusmiati, M.D., Vincent M. Balanag, M.D., Shu Ling Lee, B.Sc., Rovina Ruslami, Ph.D., Yogesh Pokharkar, M.Sc., Irawaty Djaharuddin, M.D., Jani J.R. Sugiri, M.D., Rholine S. Veto, M.D., Christine Sekaggya-Wiltshire, Ph.D., Anchalee Avihingsanon, M.D., Rohit Sarin, M.D., Padmasayee Papineni, F.R.C.P., Andrew J. Nunn, M.Sc., and Angela M. Crook, Ph.D., for the TRUNCATE-TB Trial Team*

20 février 2023

Essai randomisé de non infériorité comparant quadrithérapie standard avec 4 autres stratégies en 8 semaines de traitement
Critère de jugement composite: décès à 96 semaines, traitement toujours en cours, TB active à 96 semaines

Evaluation à 8 semaines:
Si patient symptomatique: poursuite 4 semaines de plus

Si symptomatique à 12 Semaines: switch vers traitement standard

Raccourcir encore la durée de traitement encore ?

B. Rifampicin-linezolid arm

For 8 weeks

DRUG	<40KG	40KG- 54KG	55KG - 70KG	≥71KG
Rifampicin	35mg/kg (rounded to nearest 150mg, maximum 2100mg)*			
Isoniazid	150mg	225mg	300mg	375mg
Pyrazinamide	800mg	1200mg	1600mg	2000mg
Ethambutol	550mg	825mg	1100mg	1375mg
Linezolid	600mg			

C. Rifampicin-clofazimine arm

For 8 weeks

DRUG	<40KG	40KG- 54KG	55KG - 70KG	≥71KG
Rifampicin	35mg/kg (rounded to nearest 150mg, maximum 2100mg)			
Isoniazid	150mg	225mg	300mg	375mg
Pyrazinamide	800mg	1200mg	1600mg	2000mg
Ethambutol	550mg	825mg	1100mg	1375mg
Clofazimine	200mg			

D. Rifapentine-linezolid arm

For 8 weeks

DRUG	<40KG	40KG- 54KG	55KG - 70KG	≥71KG
Isoniazid	5mg/kg rounded to nearest 100mg		300mg	
Pyrazinamide	25mg/kg rounded to nearest 500mg	1000mg	1500mg	2000mg
Rifapentine	1200mg			
Linezolid	600mg			
Levofloxacin	1000mg			

E. Bedaquiline-linezolid arm

For 8 weeks

DRUG	<40KG	40KG- 54KG	55KG - 70KG	≥71KG
Bedaquiline	400 mg once daily for 2 weeks then 200mg three times a week			
Isoniazid	5mg/kg rounded to nearest 100mg		300mg	
Pyrazinamide	25mg/kg rounded to nearest 500mg	1000mg	1500mg	2000mg
Ethambutol	15mg/kg (rounded to nearest 100mg, maximum 1600mg)			
Linezolid	600mg			

Table 2. Primary Efficacy Outcome.*

Outcome	Standard Treatment (N=181)	Strategy with Rifampin–Linezolid (N=184)	Strategy with Rifampin–Linezolid vs. Standard Treatment Adjusted Difference (97.5% CI)†	Strategy with Bedaquiline–Linezolid (N=189)	Strategy with Bedaquiline–Linezolid vs. Standard Treatment Adjusted Difference (97.5% CI)†
Intention-to-treat population‡					
Primary outcome: composite of death, ongoing treatment, or active disease at wk 96 — no. (%)§	7 (3.9)	21 (11.4)	7.4 (1.7 to 13.2)	11 (5.8)	0.8 (−3.4 to 5.1)
Death before wk 96	2 (1.1)	5 (2.7)	—	1 (0.5)	—
Ongoing treatment at wk 96	2 (1.1)	8 (4.3)	—	5 (2.6)	—
Active disease at wk 96¶	1 (0.6)	4 (2.2)	—	3 (1.6)	—
Evaluation by telephone at wk 96 with no evidence of active disease but insufficient evidence of disease clearance when last seen	2 (1.1)	3 (1.6)	—	1 (0.5)	—
No evaluation at wk 96 and insufficient evidence of disease clearance when last seen	0	1 (0.5)	—	1 (0.5)	—
Outcomes classified as unassessable — no. (%)	1 (0.6)	1 (0.5)	—	2 (1.1)	—
Single positive culture at wk 96 but no other evidence of active disease‖	0	1 (0.5)	—	0	—
Death from a cause that was definitively unrelated to tuberculosis**	1 (0.6)	0	—	0	—
No evaluation at wk 96 and sufficient evidence of disease clearance when last seen	0	0	—	2 (1.1)	—
No primary outcome or outcome classified as unassessable — no. (%)	173 (95.6)	162 (88.0)	—	176 (93.1)	—
Assessable population††					
Primary outcome — no./total no. (%)	7/180 (3.9)	21/183 (11.5)	7.5 (1.7 to 13.2)	11/187 (5.9)	0.8 (−3.4 to 5.1)
Per-protocol population‡‡					
Primary outcome — no./total no. (%)	6/177 (3.4)	17/160 (10.6)	6.9 (0.9 to 12.8)	9/176 (5.1)	0.9 (−3.3 to 5.1)

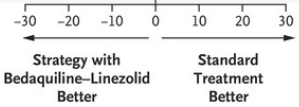
Non-inferiority met

Strategy with Rifampin–Linezolid Better

Standard Treatment Better

B Primary Outcome in Strategy Group with Initial Bedaquiline–Linezolid Regimen vs. Standard-Treatment Group

Subgroup	Strategy with Bedaquiline–Linezolid	Standard Treatment	Difference (95% CI)
	no. of participants with event/total no. (%)		*percentage points*
Sex			
Male	5/116 (4.3)	5/119 (4.2)	0.1 (–4.4 to 4.6)
Female	6/73 (8.2)	2/62 (3.2)	3.6 (–3.9 to 11.2)
Age			
18–34 yr	4/95 (4.2)	5/104 (4.8)	–1.8 (–7.0 to 3.4)
35–65 yr	7/94 (7.4)	2/77 (2.6)	4.8 (–1.1 to 10.7)
Country			
Indonesia or Philippines	6/145 (4.1)	4/139 (2.9)	1.3 (–3.0 to 5.5)
Uganda	4/27 (14.8)	2/28 (7.1)	7.7 (–8.8 to 24.1)
India or Thailand	1/17 (5.9)	1/14 (7.1)	–1.3 (–18.8 to 16.3)
Education			
0–7 yr	3/48 (6.3)	4/49 (8.2)	–2.4 (–12.1 to 7.3)
≥8 yr	8/141 (5.7)	3/132 (2.3)	2.8 (–1.6 to 7.3)
Smoking status			
Never	8/107 (7.5)	2/89 (2.2)	3.7 (–2.2 to 9.5)
Current or former	3/82 (3.7)	5/92 (5.4)	–1.0 (–7.0 to 5.0)
Body-mass index			
<18.5	4/76 (5.3)	5/79 (6.3)	–1.3 (–8.5 to 6.0)
≥18.5	7/113 (6.2)	2/102 (2)	3.3 (–2.0 to 8.6)
Cavitation on chest radiograph			
Absent	5/81 (6.2)	1/87 (1.1)	3.4 (–2.4 to 9.2)
Present	6/108 (5.6)	6/94 (6.4)	–0.6 (–7.0 to 5.9)
Proportion of lung affected on chest radiograph			
≤50%	8/151 (5.3)	3/140 (2.1)	2.8 (–1.0 to 6.6)
>50%	3/38 (7.9)	4/41 (9.8)	–2.2 (–14.4 to 10.1)
WHO smear grade			
Negative	1/50 (2.0)	1/46 (2.2)	0.9 (–16.8 to 18.7)
Scanty or 1+	4/77 (5.2)	0/65	6.4 (–18.7 to 31.6)
2+ or 3+	6/62 (9.7)	5/69 (7.2)	2.0 (–9.8 to 13.8)
Grade on MRC breathlessness scale			
Grade 1	3/112 (2.7)	3/106 (2.8)	1.1 (–3.0 to 5.2)
Grade 2 or higher	8/77 (10.4)	4/75 (5.3)	3.5 (–5.0 to 11.9)
Relapse risk			
Low	1/50 (2.0)	2/47 (4.3)	–0.8 (–7.3 to 5.6)
Intermediate or high	10/139 (7.2)	5/134 (3.7)	2.6 (–2.6 to 7.8)



Dosages des anti-tuberculeux

Clinical Infectious Diseases

IDSA GUIDELINE

Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis

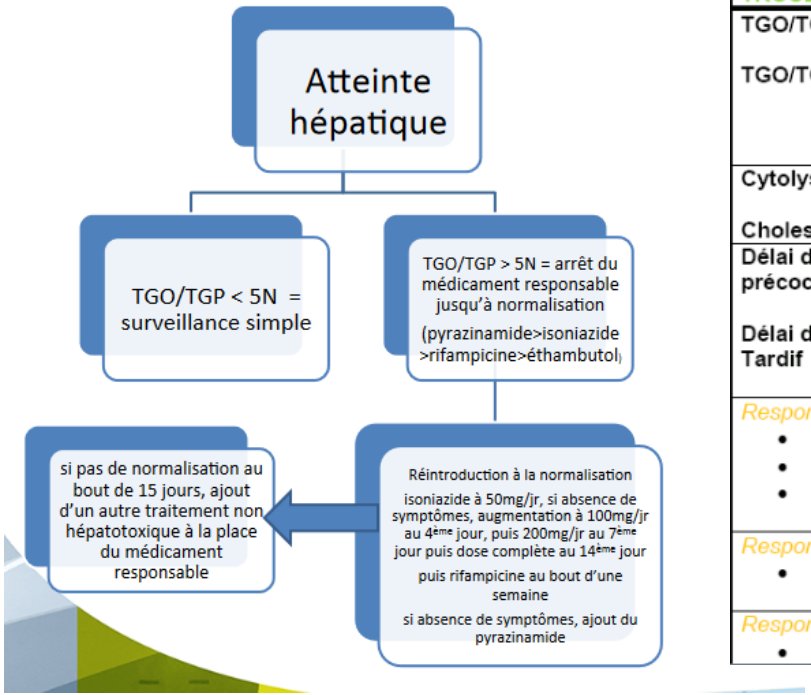
Payam Nahid,[1] Susan E. Dorman,[2] Narges Alipanah,[1] Pennan M. Barry,[3] Jan L. Brozek,[4] Adithya Cattamanchi,[1] Lelia H. Chaisson,[1] Richard E. Chaisson,[2] Charles L. Daley,[5] Malgosia Grzemska,[6] Julie M. Higashi,[7] Christine S. Ho,[8] Philip C. Hopewell,[1] Salmaan A. Keshavjee,[9] Christian Lienhardt,[6] Richard Menzies,[10] Cynthia Merrifield,[1] Masahiro Narita,[12] Rick O'Brien,[13] Charles A. Peloquin,[14] Ann Raftery,[1] Jussi Saukkonen,[15] H. Simon Schaaf,[16] Giovanni Sotgiu,[17] Jeffrey R. Starke,[18] Giovanni Battista Migliori,[11] and Andrew Vernon[8]

Table 9. Conditions or Situations in Which Therapeutic Drug Monitoring May Be Helpful

Poor response to tuberculosis treatment despite adherence and fully drug-susceptible *Mycobacterium tuberculosis* strain
Severe gastrointestinal abnormalities: severe gastroparesis, short bowel syndrome, chronic diarrhea with malabsorption
Drug–drug interactions
Impaired renal clearance: renal insufficiency, peritoneal dialysis, critically ill patients on continuous renal replacement
HIV infection
Diabetes mellitus
Treatment using second-line drugs

Abbreviation: HIV, human immunodeficiency virus.

Toxicité hépatique



TROUBLES HEPATIQUES		
TGO/TGP < 5N **TGO/TGP > 5N**	Atteinte modérée : surveillance Arrêt du traitement jusqu'à normalisation des constantes	! si normalisation trop longue, ajout d'un antituberculeux non hépatotoxique
Cytolyse **Cholestase**	Isoniazide ou pyrazinamide rifampicine	! si réaction d'hypersensibilité associée : rifampicine
Délai d'apparition précoce **Délai d'apparition Tardif**	Isoniazide Pyrazinamide ou rifampicine	
Responsabilité reconnue de l'isoniazide • adaptation des posologies en fonction des concentrations sériques • réintroduction croissante • si cytolyse persistante : arrêt définitif de l'isoniazide		
Responsabilité reconnue de la rifampicine : • arrêt complet de la rifampicine sans réintroduction possible		
Responsabilité reconnue du pyrazinamide : • arrêt du pyrazinamide sans réintroduction possible		

TUBERCULOSE RÉSISTANTE

Table 3.1. Grouping of medicines recommended for use in longer MDR-TB regimens[a]

Groups and steps	Medicine	Abbreviation
Group A: Include all three medicines	Levofloxacin *or* moxifloxacin	Lfx Mfx
	Bedaquiline[b,c]	Bdq
	Linezolid[d]	Lzd
Group B: Add one or both medicines	Clofazimine	Cfz
	Cycloserine *or* terizidone	Cs Trd
Group C: Add to complete the regimen and when medicines from Groups A and B cannot be used	Ethambutol	E
	Delamanid[e]	Dlm
	Pyrazinamide[f]	Z
	Imipenem–cilastatin *or* meropenem[g]	Ipm–Cln Mpm
	Amikacin (*or* streptomycin)[h]	Am (S)
	Ethionamide *or* prothionamide[i]	Eto Pto
	P-aminosalicylic acid[i]	PAS

Tuberculose résistante

Situations	Molécules	durée
Résistance uniquement à l'isoniazide	Rifampicine/ pyrazinamide/ ethambuthol/ lévofloxacine	6 mois
Résistance à la Rifampicine et tuberculose multi-résistante	Bédaquilline Linézolide **Moxifloxacine (si souche sensible)** **Pretomanid** **Bédaquiline (6 mois)** **Lévofloxacine ou Moxifloxacine** **Clofazimine (4 mois)** **Ethionamide** **Ethambuthol** **Isoniazide** **Pyrazinamide**	6 mois Plus de 14 ans Pas d'atteinte du SNC Pas de femmes enceintes 9 mois

Section 1. The 6-month bedaquiline, pretomanid, linezolid and moxifloxacin (BPaLM) regimen for MDR/RR-TB (NEW)

1.1 Recommendation

NEW RECOMMENDATION

No.	Recommendation
1.1	WHO suggests the use of a 6-month treatment regimen composed of bedaquiline, pretomanid, linezolid (600 mg) and moxifloxacin (BPaLM) rather than the 9-month or longer (18-month) regimens in MDR/RR-TB patients. *(Conditional recommendation, very low certainty of evidence)*

Section 2. The 9-month all-oral regimen for MDR/RR-TB (NEW)

2.1 Recommendation

NEW RECOMMENDATION

No.	Recommendation
2.1	WHO suggests the use of the 9-month all-oral regimen rather than longer (18-month) regimens in patients with MDR/RR-TB and in whom resistance to fluoroquinolones has been excluded. *(Conditional recommendation, very low certainty of evidence)*

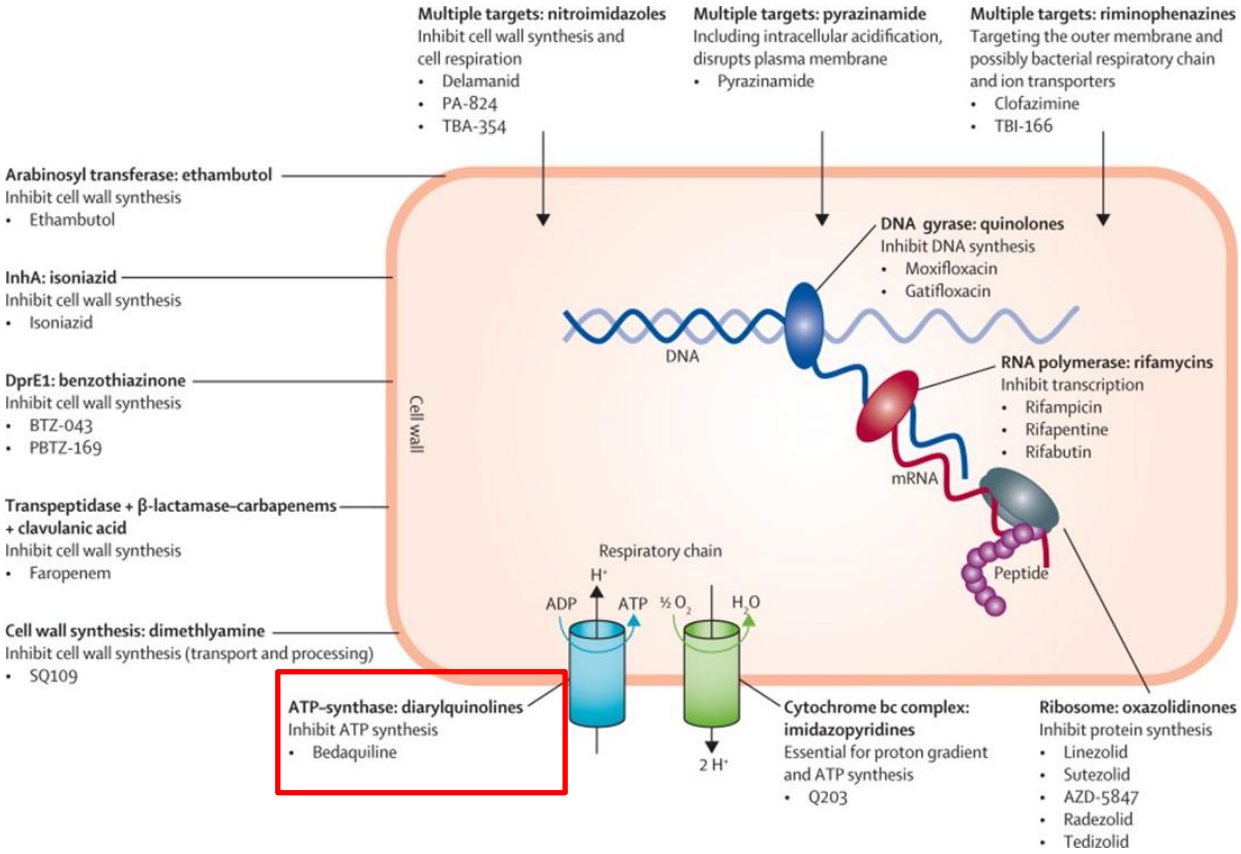
Remarks

1. The 9-month all-oral regimen consists of bedaquiline (used for 6 months), in combination with levofloxacin/moxifloxacin, ethionamide, ethambutol, isoniazid (high-dose), pyrazinamide and clofazimine (for 4 months, with the possibility of extending to 6 months if the patient remains sputum smear positive at the end of 4 months), followed by treatment with levofloxacin/moxifloxacin, clofazimine, ethambutol and pyrazinamide (for 5 months). Ethionamide can be replaced by 2 months of linezolid (600 mg daily).

Section 3. Longer regimens for MDR/RR-TB

Recommendations

No.	Recommendation
3.1	In multidrug- or rifampicin-resistant tuberculosis (MDR/RR-TB) patients on longer regimens, all three Group A agents and at least one Group B agent should be included to ensure that treatment starts with at least four TB agents likely to be effective, and that at least three agents are included for the rest of the treatment if bedaquiline is stopped. If only one or two Group A agents are used, both Group B agents are to be included. If the regimen cannot be composed with agents from Groups A and B alone, Group C agents are added to complete it. *(Conditional recommendation, very low certainty of evidence)*


Multiple targets: nitroimidazoles
Inhibit cell wall synthesis and cell respiration
• Delamanid
• PA-824
• TBA-354
Multiple targets: pyrazinamide
Including intracellular acidification, disrupts plasma membrane
• Pyrazinamide
Multiple targets: riminophenazines
Targeting the outer membrane and possibly bacterial respiratory chain and ion transporters
• Clofazimine
• TBI-166
Arabinosyl transferase: ethambutol
Inhibit cell wall synthesis
• Ethambutol
InhA: isoniazid
Inhibit cell wall synthesis
• Isoniazid
DprE1: benzothiazinone
Inhibit cell wall synthesis
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• PBTZ-169
Transpeptidase + β-lactamase–carbapenems + clavulanic acid
Inhibit cell wall synthesis
• Faropenem
Cell wall synthesis: dimethlyamine
Inhibit cell wall synthesis (transport and processing)
• SQ109
Cell wall
DNA gyrase: quinolones
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• Rifapentine
• Rifabutin
mRNA
Peptide
Respiratory chain
H+
ADP
ATP
½ O2
H2O
2 H+
ATP–synthase: diarylquinolines
Inhibit ATP synthesis
• Bedaquiline
Cytochrome bc complex: imidazopyridines
Essential for proton gradient and ATP synthesis
• Q203
Ribosome: oxazolidinones
Inhibit protein synthesis
• Linezolid
• Sutezolid
• AZD-5847
• Radezolid
• Tedizolid

Bédaquilline

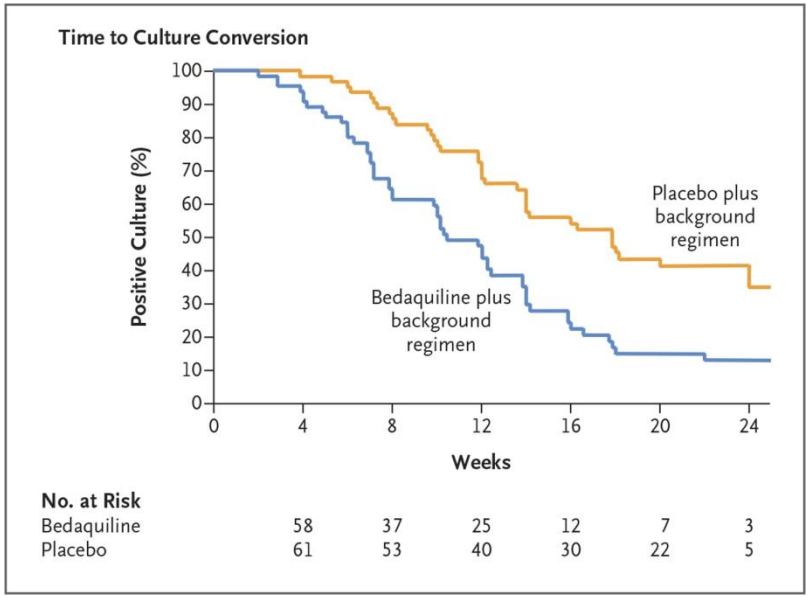
- Premier représentant de la famille des diarylquinolines
- Activité bactéricide sur les bacilles tuberculeux en réplication et dormants. La bedaquiline inhibe spécifiquement l'adénosine 5'-triphosphate (ATP) synthase, une enzyme essentielle à la production d'énergie chez *Mycobacterium tuberculosis*.
- ASMR III
- Posologies: Semaine 1 à 2 : 400 mg (4 comprimés de 100 mg) une fois par jour - Semaine 3 à 24 : 200 mg (2 comprimés de 100 mg) : trois fois par semaine (avec un intervalle d'au moins 48 heures entre chaque prise). La durée de traitement est de 24 semaines.
- pris par voie orale avec de la nourriture, car l'administration avec la nourriture augmente la biodisponibilité orale d'environ deux fois
- Attention à l'allongement du QT

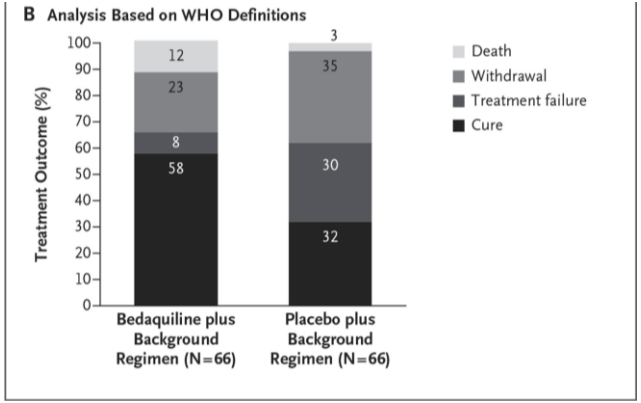
ORIGINAL ARTICLE

Multidrug-Resistant Tuberculosis and Culture Conversion with Bedaquiline

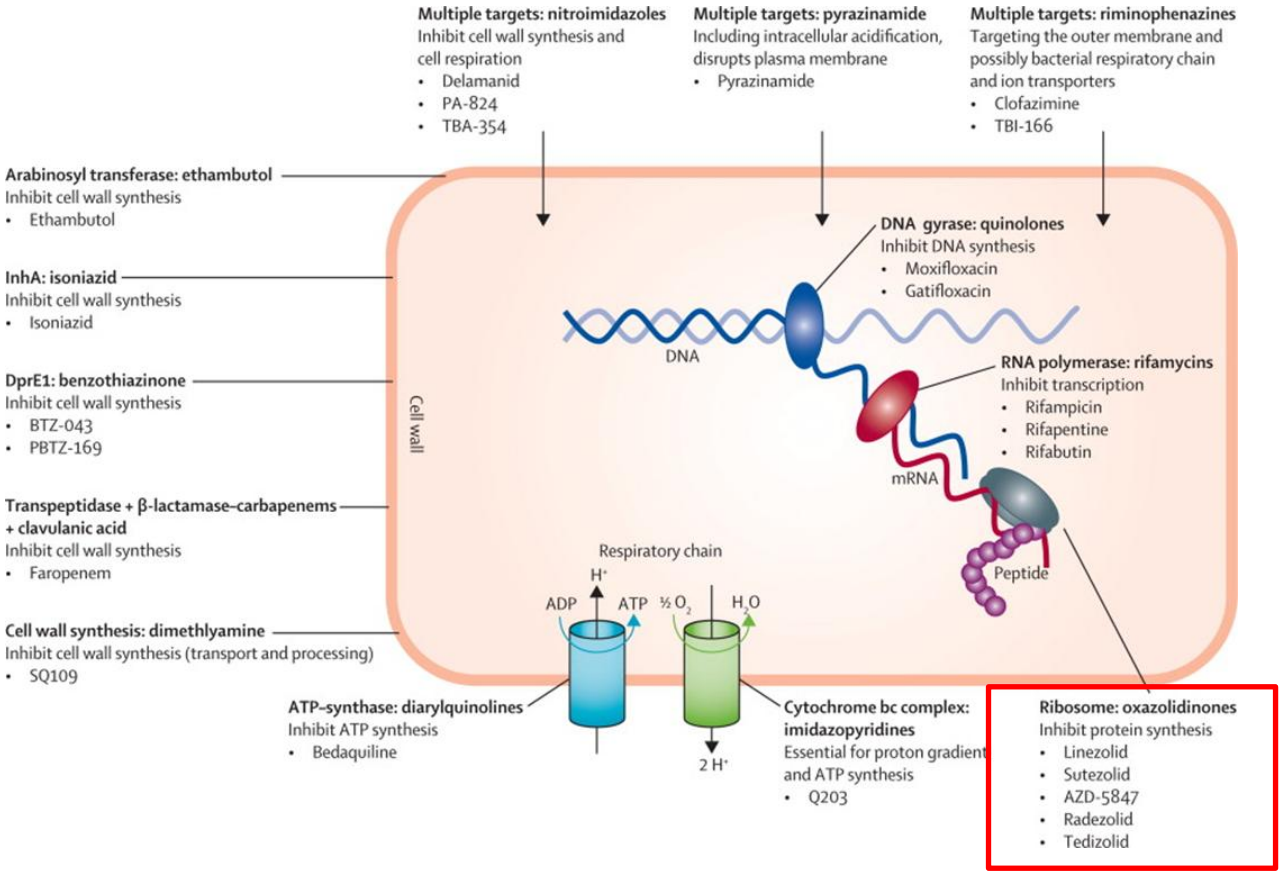
Andreas H. Diacon, M.D., Ph.D., Alexander Pym, M.D., Ph.D., Martin P. Grobusch, M.D., Ph.D., Jorge M. de los Rios, M.D., Eduardo Gotuzzo, M.D., Irina Vasilyeva, M.D., Ph.D., Vaira Leimane, M.D., Koen Andries, D.V.M., Ph.D., Nyasha Bakare, M.D., M.P.H., Tine De Marez, Ph.D., Myriam Haxaire-Theeuwes, D.D.S., Nacer Lounis, Ph.D., et al., for the TMC207-C208 Study Group*

August 21, 2014
N Engl J Med 2014; 371:723-732
DOI: 10.1056/NEJMoa1313865





Mortalité excessive dans le bras bédaquiline
Allongement du Qt contrôle ECG mensuel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Ribosome: oxazolidinones
Inhibit protein synthesis
• Linezolid
• Sutezolid
• AZD-5847
• Radezolid
• Tedizolid

Linézolide

- Oxazolidone
- 600mg dans la tuberculose
- Biodisponibilité proche de 100 %
- Myélotoxicité (thrombopénie, anémie, pancytopénie) possible, apparaissant après 15 jours de traitement et en cas d'antécédent d'anémie, de granulopénie, de thrombopénie ou en cas d'insuffisance rénale
- Syndrome sérotoninergique
- Acidose lactique par cytotoxicité mitochondriale
- Neuropathies optiques ou périphériques lors de traitements prolongés

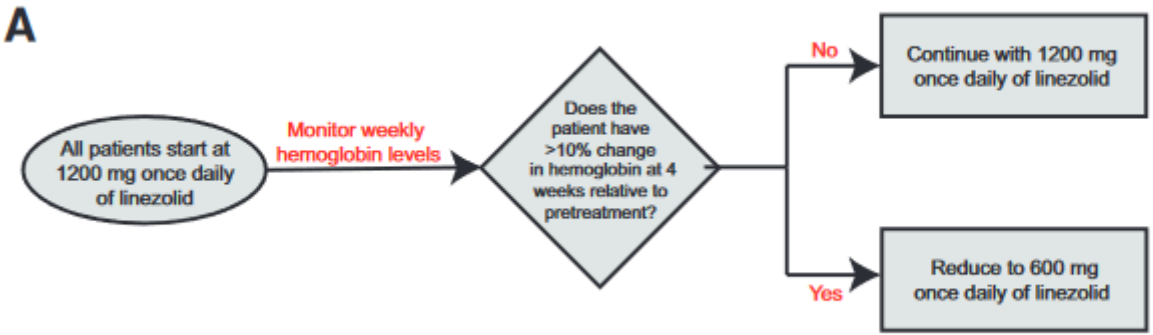
Clinical Infectious Diseases

MAJOR ARTICLE

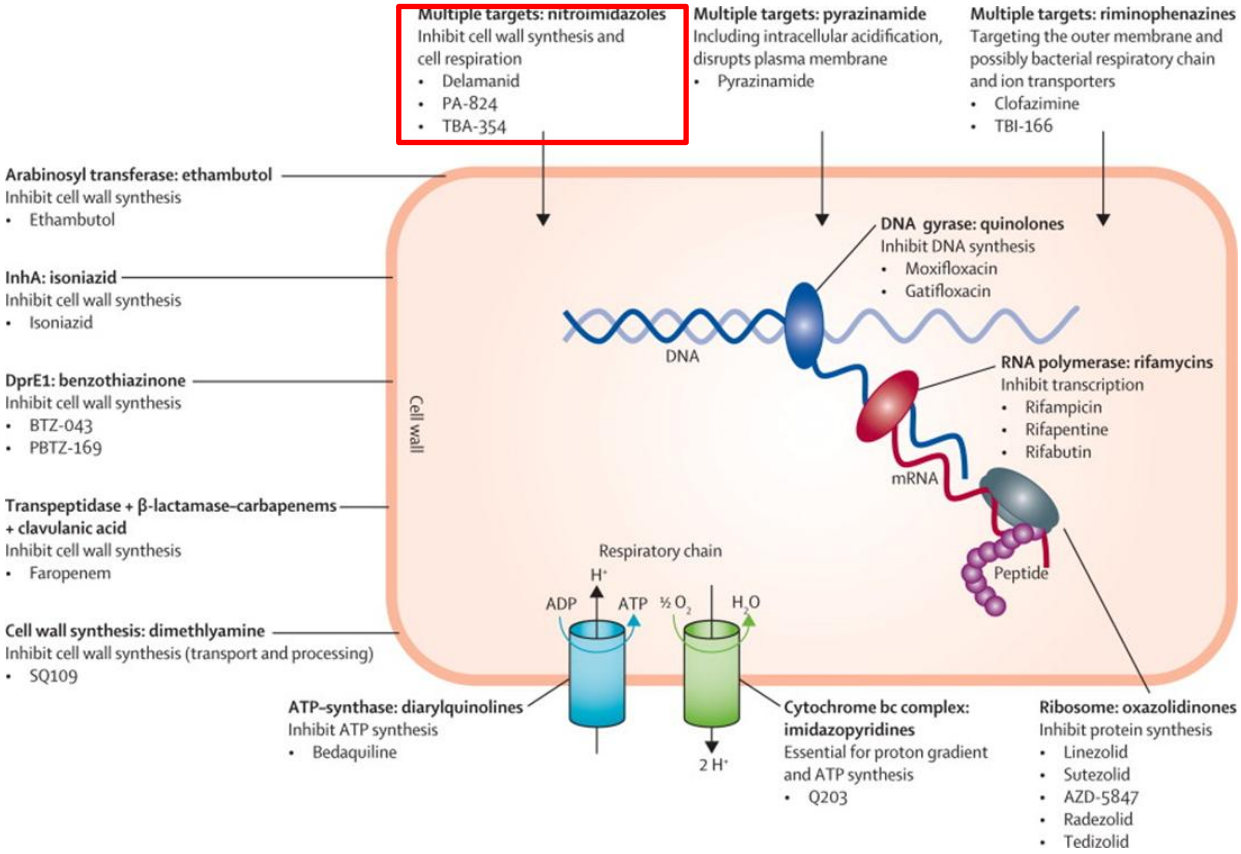
Proposed Linezolid Dosing Strategies to Minimize Adverse Events for Treatment of Extensively Drug-Resistant Tuberculosis

Marjorie Z. Imperial,[1] Jerry R. Nedelman,[2] Francesca Conradie,[3] and R. M. Savic[1]

[1]Department of Bioengineering and Therapeutic Sciences, School of Pharmacy, University of California, San Francisco, California, USA; [2]TB Alliance, New York, New York, USA; and [3]Clinical HIV Research Unit, University of Witwatersrand, Johannesburg, South Africa



L'utilisation de cet algorithme permettrait de réduire de 60 % l'incidence de l'anémie sévère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• Q203
Ribosome: oxazolidinones
Inhibit protein synthesis
• Linezolid
• Sutezolid
• AZD-5847
• Radezolid
• Tedizolid

Delamanide /Prétonamide

- Nitro-imidazolés
- Deux mécanismes d'action:
  - Inhibition de la synthèse de la paroi bactérienne (inhibition de la synthèse de l'acide mycolique)
  - Empoisonnement respiratoire: stress oxydatif?
- Delamanid 100 mg deux fois par jour avec prise alimentaire
- Pretomanide 200 mg par jour en une prise avec prise alimentaire
- Résistance à l'un n'implique pas résistance à l'autre composant

J Antimicrob Chemother 2022; **77**: 880–902
https://doi.org/10.1093/jac/dkab505 Advance Access publication 28 January 2022

Journal of Antimicrobial Chemotherapy

Delamanid or pretomanid? A Solomonic judgement!

Saskia E. Mudde[1]*, Anna M. Upton[2], Anne Lenaerts[3], Hannelore I. Bax[1,4] and Jurriaan E. M. De Steenwinkel[1]

[1]Department of Medical Microbiology and Infectious Diseases, Erasmus University Medical Center, Rotterdam, The Netherlands; [2]Evotec, Princeton, New Jersey, USA; [3]Mycobacteria Research Laboratories, Department of Microbiology, Immunology, and Pathology, Colorado State University, Fort Collins, CO, USA; [4]Department of Internal Medicine, Section of Infectious Diseases, Erasmus University Medical Center, Rotterdam, The Netherlands

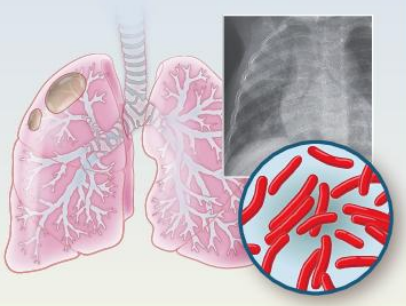
*Corresponding author. E-mail: s.e.mudde@erasmusmc.nl

The NEW ENGLAND JOURNAL of MEDICINE

Treatment of Highly Drug-Resistant Pulmonary TB

NIX-TB, AN OPEN-LABEL, SINGLE-GROUP STUDY

109 Patients
with confirmed tuberculosis



Three-drug regimen (26 wk)

Bedaquiline

Pretomanid
(recently approved)

Linezolid

XDR tuberculosis
N=71
(65%)

Nonresponsive or treatment-intolerant MDR tuberculosis
N=38
(34%)

Clinical resolution at 6 mo after therapy

90% of all patients had favorable outcomes
95% CI, 83–95

89%
95% CI, 79–95

92%
95% CI, 79–98

Linezolid associated with peripheral neuropathy (81%) and myelosuppression (48%)

F. Conradie et al. 10.1056/NEJMoa1901814

ORIGINAL ARTICLE

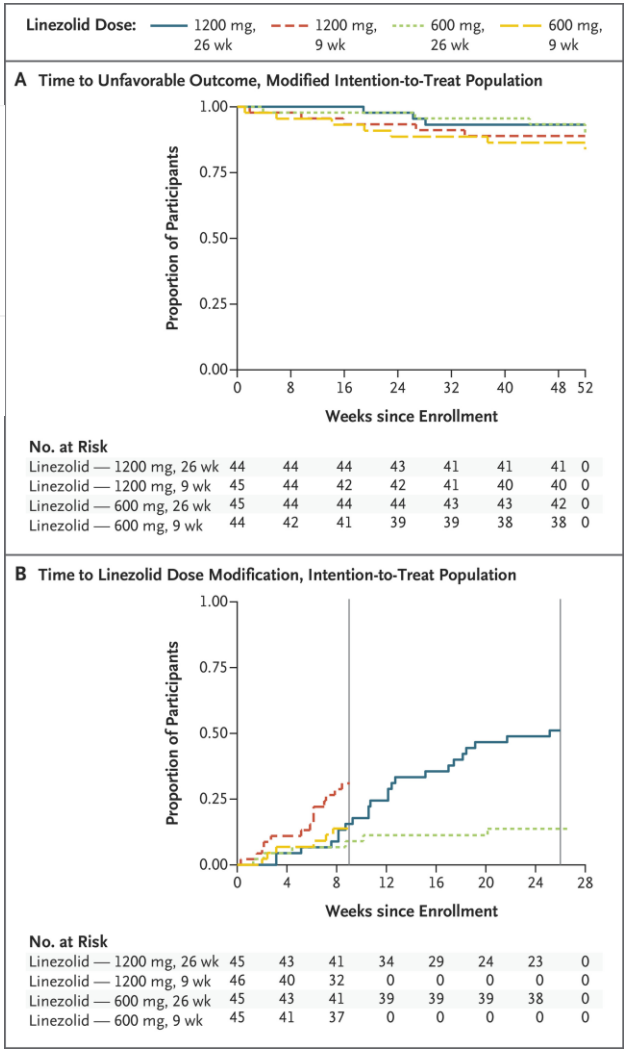
Bedaquiline–Pretomanid–Linezolid Regimens for Drug-Resistant Tuberculosis

Francesca Conradie, M.B., B.Ch., Tatevik R. Bagdasaryan, M.D., Sergey Borisov, M.D., Pauline Howell, M.D., Lali Mikiashvili, M.D., Nosipho Ngubane, M.D., Anastasia Samoilova, M.D., Sergey Skornykova, M.D., Elena Tudor, M.D., Ebrahim Variava, M.D., Petr Yablonskiy, Ph.D., Daniel Everitt, M.D., et al., for the ZeNix Trial Team*

September 1, 2022
N Engl J Med 2022; 387:810-823
DOI: 10.1056/NEJMoa2119430

Réduction de la posologie de linézolide à 600 mg/jour non inférieur pendant 26 semaines à la dose de 1200 mg
Moins de myélosuppression et moins de neuropathie périphérique

20 % de patients VIH
42 % de TB XDR



Effets secondaires et tuberculose multi-résistante

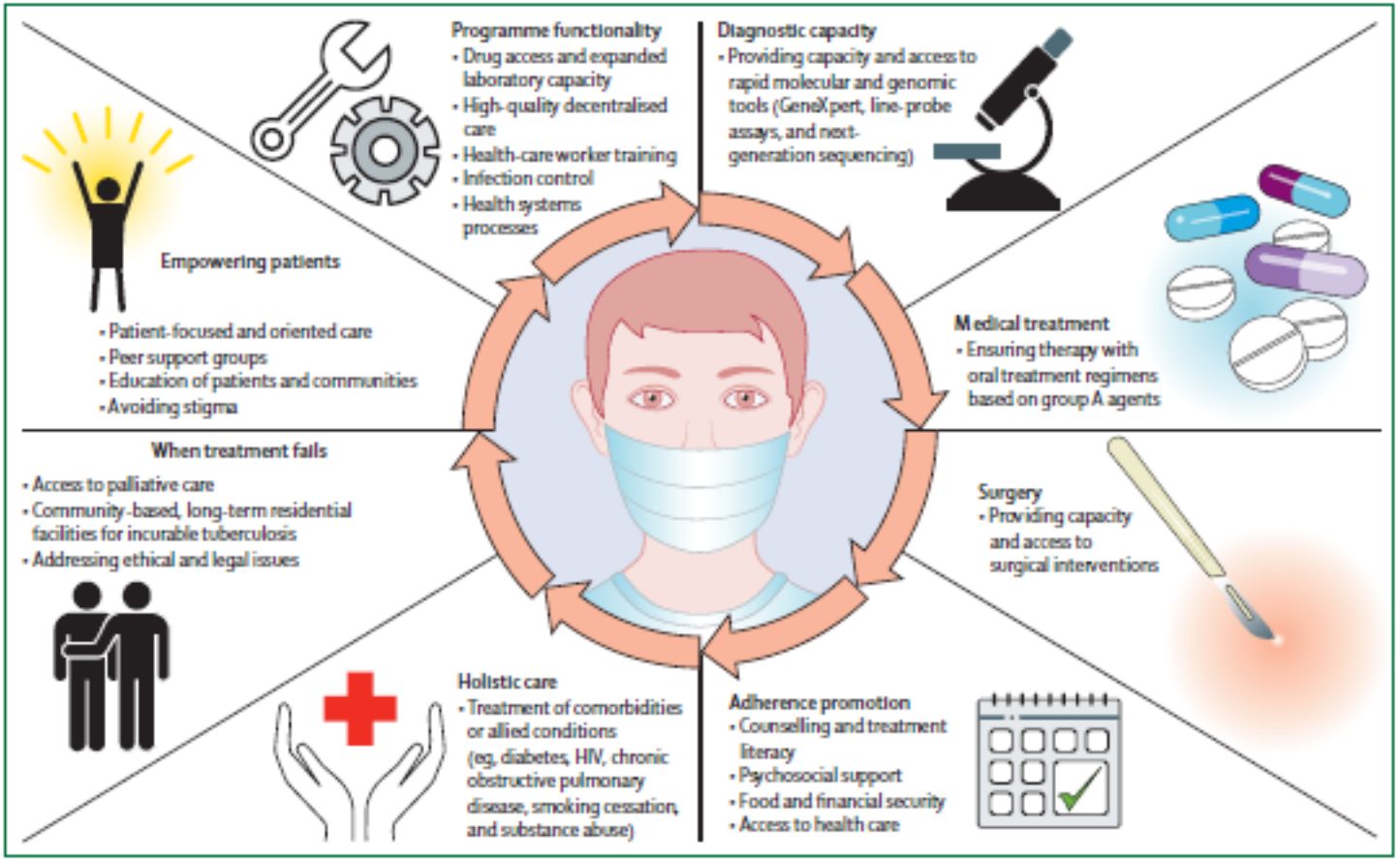
Table 6. Incidence Rate of Clinically Relevant Adverse Events of Special Interest Among Patients During Exposure to a Drug of Interest

Clinically Relevant[a] Adverse Event of Interest	Drug of Interest	Person-Months of Exposure to Drug of Interest	Patients With at Least 1 Occurrence of a Clinically Relevant AESI,[a] (n/N, %)	Incidence of Clinically Relevant AESI/1000 Person-Months[a] (95% Confidence Interval)
QT prolongation	Bedaquiline or delamanid	19 543	50/2296 (2.2)	2.6 (1.9–3.4)
Hearing loss	Kanamycin, amikacin, capreomycin	4936	182/925 (19.7)	36.9 (31.9–42.6)
Hearing loss or acute renal failure or electrolyte depletion	Kanamycin, amikacin, capreomycin	5864	340/925 (36.8)	72.8 (66.0–80.0)
Peripheral neuropathy or optic neuritis or myelosuppression	Linezolid	23 660	507/1826 (27.8)	22.8 (20.9–24.8)

Safety of treatment regimens containing bedaquiline and delamanid in the endTB cohort Hewison et al. CID Janvier 2022

Table 2.2. Summary of adverse events associated with linezolid and ethionamide

Linezolid adverse events	Ethionamide adverse events
• Myelosuppression (anaemia, decreased level of white blood cells or decreased level of platelets) • Peripheral or optic neuropathy – these conditions may be irreversible, and linezolid should be stopped if they develop • Lactic acidosis – patients who develop recurrent nausea or vomiting, unexplained acidosis or a low bicarbonate level while receiving linezolid should receive immediate medical evaluation, including a lactic acid blood test • Diarrhoea and nausea	• Gastrointestinal upset and anorexia (sometimes intolerable) – symptoms are moderated by food or by taking at bedtime • Hepatotoxicity • Endocrine effects (e.g. gynaecomastia, hair loss, acne, impotence, menstrual irregularity and reversible hypothyroidism) • Neurotoxicity – patients taking ethionamide should take high doses of vitamin B6



Lange et al. Lancet 2019

TUBERCULOSE ET VIH

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

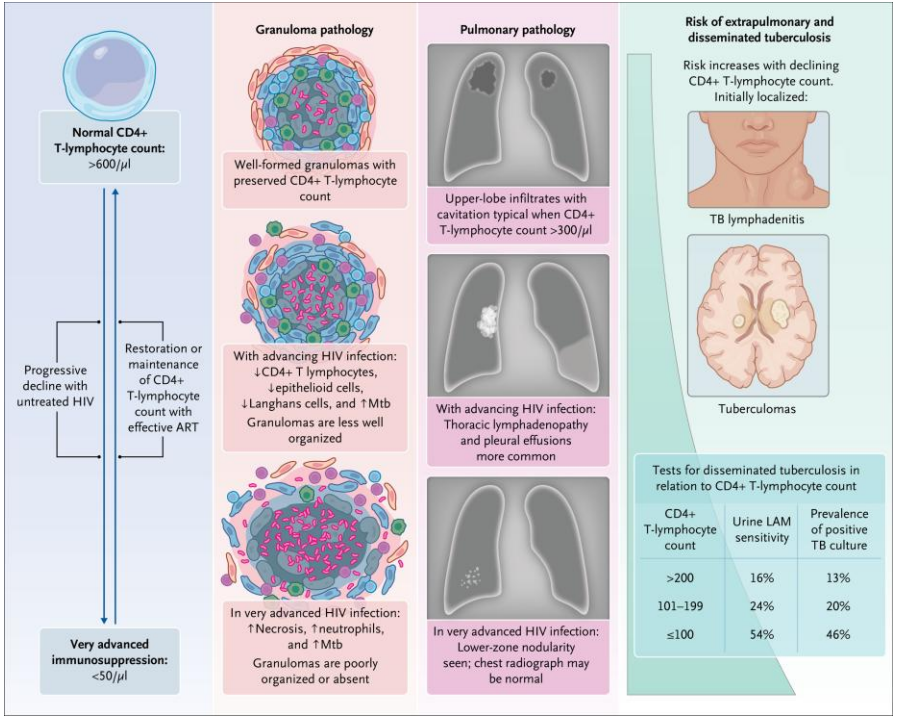
C. Corey Hardin, M.D., Ph.D., *Editor*

HIV-Associated Tuberculosis

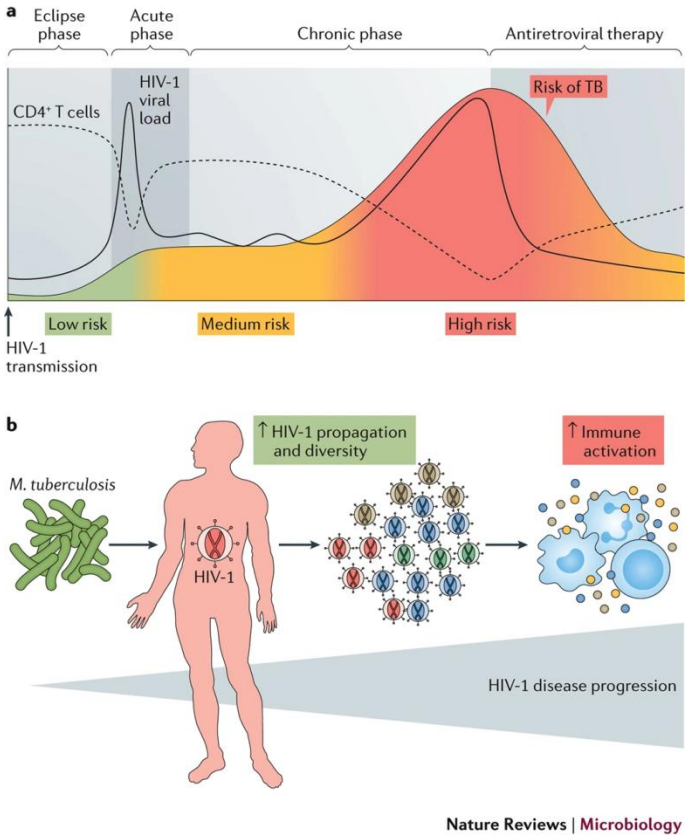
Graeme Meintjes, M.B., ChB., Ph.D., M.P.H., and Gary Maartens, M.B., Ch.B.

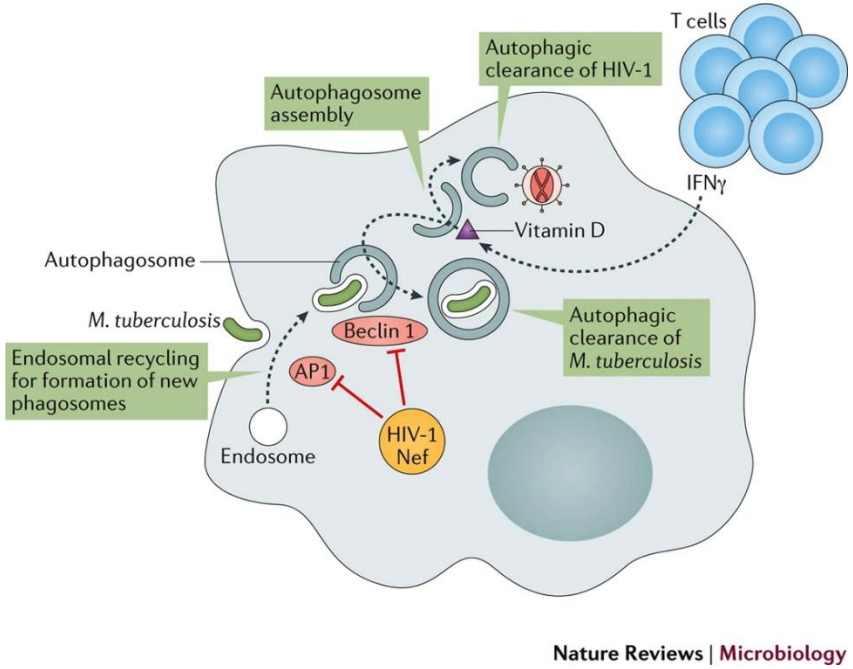
NEJM 2024

Déplétion en CD4: moindre activation des macrophages, réduction de la formation du granulome, augmentation du risque de dissémination
Moindre immunité mémoire au niveau des muqueuses
Augmentation de l'expression de PD-1: altération de la réponse cellulaire spécifique
Altération de la réponse immunitaire innée



Tuberculose et VIH





Bell et al. Nature Reviews Microbiology 2017

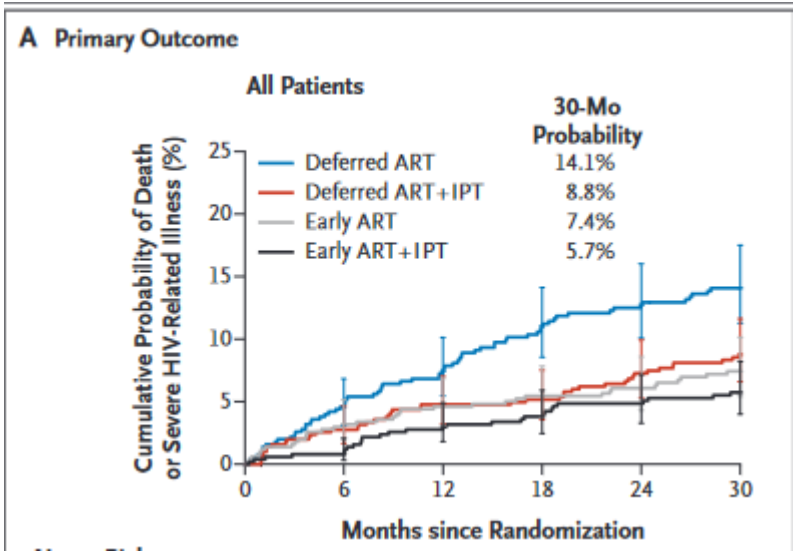
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa

The TEMPRANO ANRS 12136 Study Group*

ABSTRACT



Effet d'un traitement antirétroviral précoce associé à 6 mois d'isoniazide sur la mortalité toute cause, infections bactériennes, cancers classant SIDA ou non

N Engl J Med 2015;373:808-22.
DOI: 10.1056/NEJMoa1507198

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†

Traitement empirique de la tuberculose chez les patients infectés par le VIH avec moins de 100 CD4/mm3 vers traitement guidé

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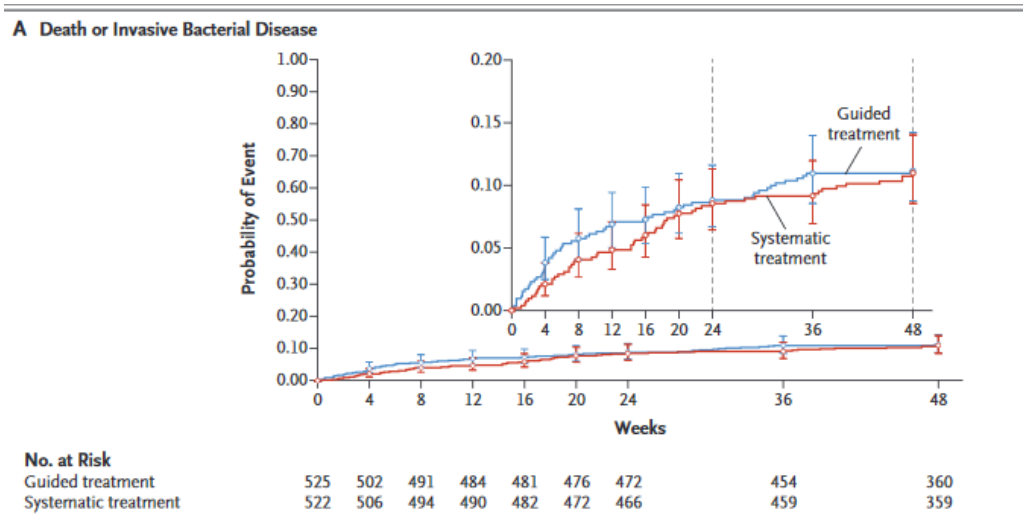

Dépistage basé sur Xpert MTB/RIF test, urinary lipoarabinomannan test, and chest radiography

ORIGINAL ARTICLE

Prednisone for the Prevention of Paradoxical Tuberculosis-Associated IRIS

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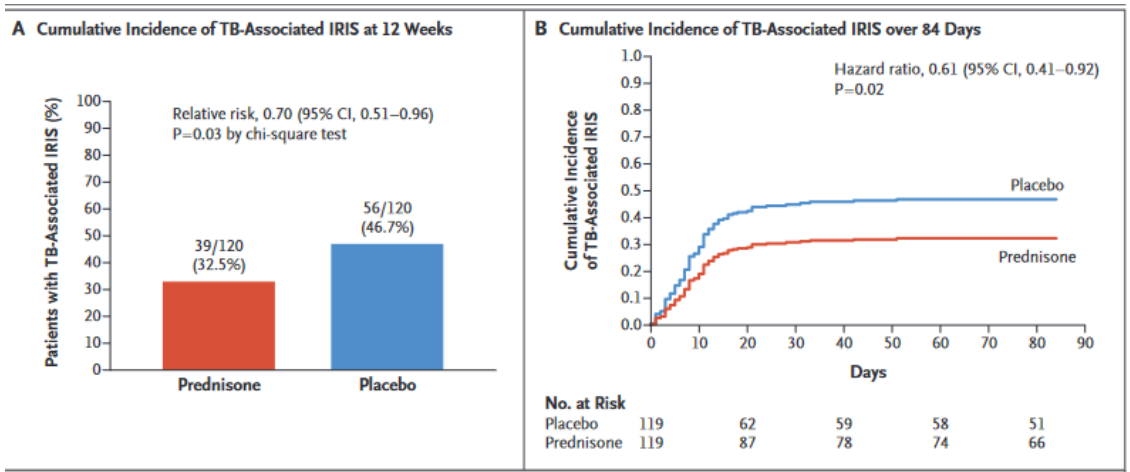

Figure 2. Cumulative Incidence of Paradoxical TB-Associated Immune Reconstitution Inflammatory Syndrome (IRIS).

Panel A shows the cumulative incidence of the primary end point of paradoxical TB-associated IRIS at 12 weeks. If paradoxical TB-associated IRIS had not developed before a patient died, withdrew, or was lost to follow-up, the patient was considered not to have had the syndrome. Panel B shows the cumulative incidence of TB-associated IRIS over 84 days. Diagnosis of TB-associated IRIS was determined according to the International Network for the Study of HIV-associated IRIS criteria.[14] Day 0 is the day ART was initiated.

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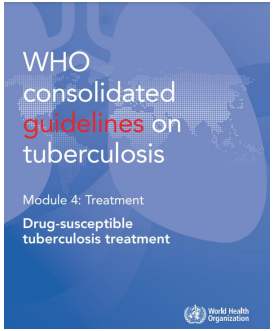


Recommendation 3.1

No.	Recommendation
3.1	It is recommended that TB patients who are living with HIV should receive at least the same duration of daily TB treatment as HIV-negative TB patients (Strong recommendation, high certainty of evidence)

Source of recommendation

Recommendation 3.2

No.	Recommendation
3.2	ART should be started as soon as possible within two weeks of initiating TB treatment, regardless of CD4 cell count, among people living with HIV.[3] Adults and adolescents *(Strong recommendation, low to moderate certainty of evidence);* Children and infants *(Strong recommendation, very low certainty of evidence)*

- https://www.hiv-druginteractions.org/

Recommandations de l'EACS

	Initiation of ART	Comments
General recommendation	As soon as possible within 2 weeks after starting treatment for the opportunistic infection	
TB meningitis	In persons with CD4 < 50 cells/μL, ART should be initiated within the first 2 weeks after initiation of TB treatment, if close monitoring and optimal TB treatment can be ensured ART should be initiated up to 4 weeks after initiation of TB treatment in all other cases.	Corticosteroids are recommended as adjuvant treatment. For further discussion see Diagnosis and Treatment of TB in Persons with HIV Earlier ART start in selected patients could be considered in settings where very close monitoring and optimal treatment are available

TUBERCULOSE LATENTE

Tableau 4 – Modalités de dépistage d'une ITL dans les pays à revenus élevés et à faible incidence de la tuberculose, à partir des données de la littérature (Source : ECDC /OMS).

Groupe cible	Tests	Commentaires
Personnes vaccinées par le BCG	IGRA	L'IDR est affectée par une vaccination antérieure par le BCG alors que les IGRA ne le sont pas
Enfants âgés de moins de 5 ans	IGRA ou IDR	Performances élevées des IGRA chez les enfants âgés de moins de 5 ans
Personnes vivants avec le VIH	IGRA	
Personnes vulnérables*	IGRA	Une seule visite, commodité
Personnes migrantes	IGRA ou IDR	Les IGRA ne nécessitent qu'une seule visite et ne sont pas affectés par une vaccination antérieure par le BCG

*Personnes vulnérables : Sans-abris, détenus, usagers de drogues

Immunodiagnostics	Populations	Pourcentages de progressions si test positif	Pourcentages de progressions si test négatif
IDR à la tuberculine (seuil à 10 ou 15 mm)	Sujets contact	1,25% à 4,8%	0,17% à 0,84%
	Contacts même toit	4% à 13%	0,001%
	Contacts enfants	37% à 67%	0,002%
	Migrants	1,9% à 15,8%	0% à 1,23%
	Immunodéprimés	3,9 à 14,3%	0,59% à 8,57%
	Atteints du VIH	7,61 à 14,3%	0,59 à 0,9%
Tests IGRA	Sujets contact	1,96% à 12,9%	0,56%
	Contacts enfants	2,7% à 12%	0,1% à 0,3%
	Migrants	0,9% à 5,2%	0,17% à 3,3%
	Immunodéprimés	0% à 14,5%	0% à 3,3%
	Atteints du VIH	8,3% à 14,5%	0 à 0,9%

Indications de dépistage ITL (HCSP 2019)

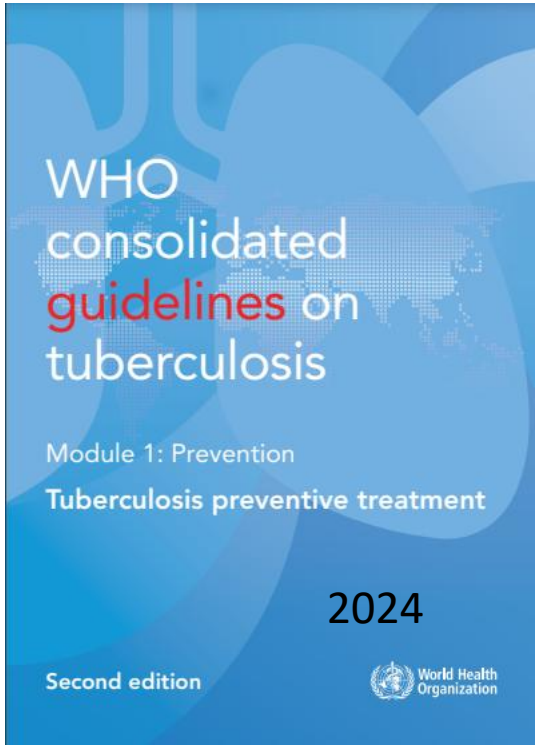
Enfants jusqu'à 18 ans	Vivant au domicile d'un patient Contact de courte durée pour un enfant de moins de 5 ans Contact même de courte durée sur immunodépression
Migrants	Moins de 18 ans Vivant avec des enfants de moins de 18 ans Si immunodépression, si travaille en collectivité d'enfants, ou structures de soins
Professionnels de santé à l'embauche	Pas de suivi
PVVIH	Quelque soit le niveau de CD4
Instauration d'anti-TNF	
Candidats à une transplantation d'organes et de CSH	
Patients dialysés chroniques	

Recos HCSP 2019

Le traitement de première intention des ITL, lorsque la souche de tuberculose est présumée sensible, repose chez l'adulte et chez l'enfant sur l'association des antituberculeux isoniazide et rifampicine pendant 3 mois.

Les alternatives possibles sont isoniazide 6 mois ou rifampicine 4 mois. L'association isoniazide et rifapentine permet une réduction de la durée du traitement, mais la rifapentine n'est pas disponible en France actuellement.

- En cas de contact avec une tuberculose à bacilles résistant à l'INH, le schéma de première intention est une monothérapie par rifampicine pendant 4 mois.
- L'administration d'un traitement antituberculeux préventif chez un sujet contact d'une tuberculose multi-résistante relève d'un avis d'experts comme cela est préconisé par le rapport du HCSP de 2014 sur la tuberculose à bacilles résistant [92]. L'aide du Groupe thérapeutique multidisciplinaire animé par le CNR-MyRMA qui proposera une attitude personnalisée en fonction (a) des résultats de l'enquête autour du cas et (b) des résultats cliniques, biologiques et radiologiques du cas index et du cas contact peut être sollicitée. En tout état de cause, tous les cas d'ITL au contact d'une tuberculose MDR ou XDR doivent faire l'objet d'une attention particulière et d'un suivi clinique au-delà de deux ans.



1.4. TB preventive treatment options

TB preventive treatment with isoniazid or rifamycins

19. The following TB preventive treatment options are recommended regardless of HIV status: 6 or 9 months of daily isoniazid, or a 3-month regimen of weekly rifapentine plus isoniazid, or a 3-month regimen of daily isoniazid plus rifampicin.

20. The following alternative TB preventive treatment options may be used regardless of HIV status: a 1-month regimen of daily rifapentine plus isoniazid or 4 months of daily rifampicin.

(recommendation 17 from the 2020 WHO TPT guidelines has been split into two in the second edition: recommendation 19 for regimens which are strongly recommended and recommendation 20 for alternative regimen options that are conditionally recommended.)

(recommendation withdrawn)

TB preventive treatment with levofloxacin

21. In contacts exposed to multidrug- or rifampicin-resistant tuberculosis, 6 months of daily levofloxacin should be used as TB preventive treatment.

Recommandations de la société Européenne de Rhumatologie

Recommendations			
(1) Screening for latent tuberculosis is recommended in patients prior to starting bDMARDs or tsDMARDs*. Screening should also be considered in patients with increased risk for latent tuberculosis prior to starting csDMARDs, immunosuppressants* and/or glucocorticoids (according to dose and duration).	2b 5*	B D*	9.5 (0.9)
(2) Screening for latent tuberculosis should follow national and/or international guidelines and would typically include a chest X-ray* and Interferon-gamma release assay over tuberculin skin test where available.	2b 5*	B D*	9.5 (0.8)
(3) Choice and timing of latent tuberculosis therapy should be guided by national and/or international guidelines. Special attention should be given to interactions with drugs commonly used to treat AIIRD.	5	D	9.3 (1.4)

On distingue trois grandes catégories :

csDMARD : traitements de fond synthétiques classiques (méthotrexate, léflunomide, sulfasalazine, hydroxychloroquine)

bDMARD : biothérapies ciblées (anti-TNF, anti-IL-6, anti-IL-17, anti-IL-23, anti-CD20, abatacept, bélimumab)

tsDMARD : inhibiteurs de JAK : tofacitinib, baricitinib, upadacitinib ; apremilast

Biothérapies et risque de TB

Mechanism of Action	Biologic	Rheumatologic indications	TB risk	TB screening mandatory
TNF Inhibitors	Infliximab Adalimumab Etanercept Golimumab Certolizumab Pegol	RA, PsA, SpA	High High Medium/High Medium/High Medium/High	Yes
IL-6R Inhibitors	Tocilizumab Sarilumab	RA	Medium	Yes
JAK Inhibitors	Tofacitinib Baricitinib Upadacitinib Filgotinib	RA, PsA, SpA RA RA, PsA, SpA RA	Medium	Yes
CTLA4-Ig	Abatacept	RA, PsA	Low	Yes
IL-12/23 Inhibitor	Ustekinumab	PsA	Low	Yes
IL-23 Inhibitors	Guselkumab Risankizumab	PsA	Low	Yes
IL-17 Inhibitors	Secukinumab Ixekizumab	PsA, SpA	Low	Yes
CD20 Inhibitor	Rituximab	RA	Low	No
PDE4 Inhibitor	Apremilast	PsA	Low	No

*Risk based on mechanism of action and TB IR before the introduction of systematic TB screening.

Andrea Picchianti-Diamanti et al Frontiers Immunology 2025

Merci de votre attention