Awareness Improvement Mobilization

ЛЕЧЕНИЕ ТУБЕРКУЛЕЗА

Tuberculosis Treatment

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Kaliningrad 30 October 2015

EATG European AIDS Treatment Group

Awareness, Improvement, Mobilization (AIM):
Углубление знаний по лечению ВИЧ и сопутствующих инфекций
(гепатит С и туберкулез)

ITPCru
Международная коалиция по готовности к лечению
Восточная Европа и Центральная Азия

ЛЕЧЕНИЕ ТБ

TB treatment (1/2)

ЛЕЧЕНИЕ ТБ

TB treatment (2/2)

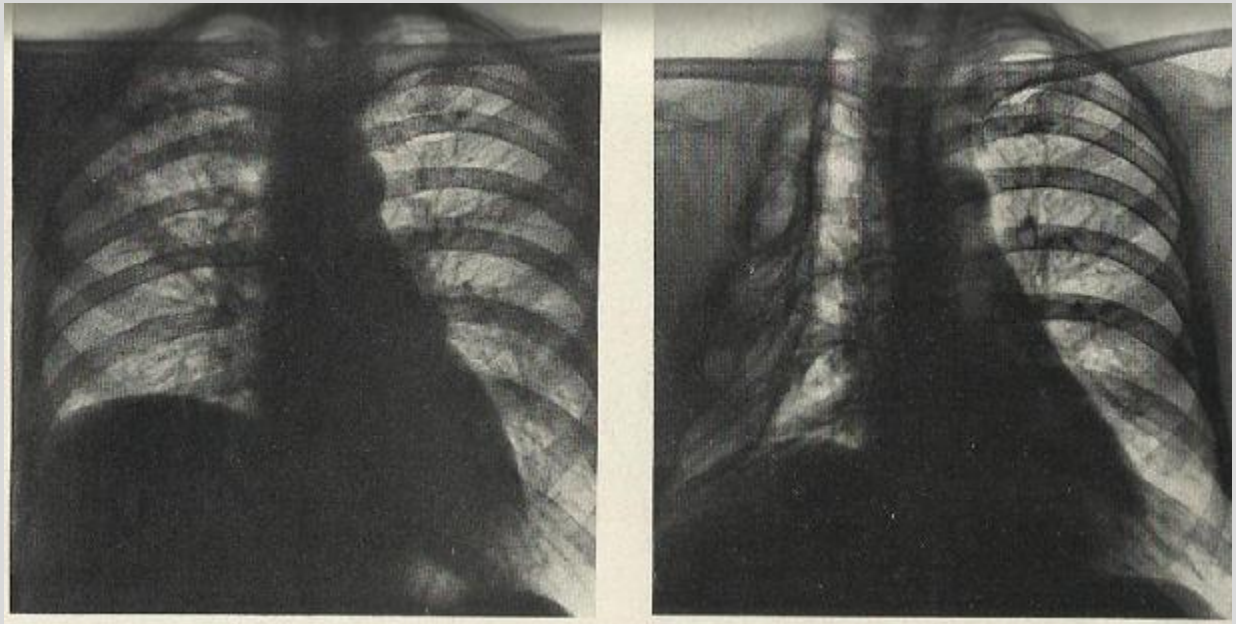


Abb. 258. Aufn.-Nr. 1320. ♂, 30 Jahre. Tuberkulose im rechten Ober- und Mittelgeschoß mit kleiner Kaverne und geringer Streuung links.

Abb. 259. Dieselbe Fall. Voller Erfolg nach einzeitiger Plastik 1—8.

Ulrici H: Klinik der Lungentuberkulose Berlin: Springer 3rd ed. 1944

СОВРЕМЕННЫЕ ПРЕПАРАТЫ ЛЕЧЕНИЯ

Modern drug treatment of TB (1/3)

1943: **стрептомицин** streptomycin (STM, S)
1949: **Пара-аминосалициловая кислота,** *ПАСК* PAS (para-aminosalicylic acid)
1952: **изониазид** *isoniazid* (INH, H)
1954: **пиразинамид** *pyrazinamide* (PZA, Z)
1955: **циклосерин** cycloserine
1956: **этионамид** ethionamide (1963 clinical standard)
1957: **канамицин** kanamycin (KM)

СОВРЕМЕННЫЕ ПРЕПАРАТЫ ЛЕЧЕНИЯ

Modern drug treatment of TB (2/3)

1959: **рифамицин B→ рифампицин** (1963)
rifamycin B --> rifampicin (1963) (RMP, R)
1962: **этамбутол** ethambutol (EMB, E)
1965: **Рифапентин** rifapentine
1987: **левофлоксацин** levofloxacin
1989: **моксифлоксацин** moxifloxacin (MXF)
1999: **гатифлоксацин** gatifloxacin
2012: **бедаквилин** bedaquiline

- Herzog H Respiration 1998;65:5-15;
  Leão SC; Portaels F in: Palomino JC; Leão SC; Ritacco V: Tuberculosis 2007, 25-51

СОВРЕМЕННЫЕ ПРЕПАРАТЫ ЛЕЧЕНИЯ

Modern drug treatment of TB (2/3)

1954-1957: Эдингбурский метод: Стрептомицин + ПАСК + изониазид

Edinburgh method: streptomycin + PAS + isoniazid

100% излечение ТБ - разумная цель

cure for tuberculosis is a reasonable objective

Сер Джон Крофтон

Sir John Crofton (1912-2009)

http://www.who.int/bulletin/volumes/87/12/09-051209/en/index.html

СТАНДАРТЫ ЛЕЧЕНИЯ ЛЕГОЧНОГО и ВОСПРИИМЧИВОГО К ПРЕПАРАТАМ ТБ

Standard treatment for pulmonary, drug susceptible TB (DS-TB)

начальная стадия: 2 месяца изониазид + рифампицин + пиразинамид + этамбутол

2 months initial phase: isoniazid + rifampicin + pyrazinamide + ethambutol (2HRZE)

и после followed by

4 месяца закрепительная стадия: изониазид + рифампицин (4HR)

4 months consolidation phase: isoniazid + rifampicin (4HR)

ЛЕЧЕНИЕ С КОИНФЕКЦИЕЙ ВИЧ

Treatment in HIV-coinfected (1/2)

Одинаковая схема Same regimen

Начать прием АРВ (2 НИОТа, 1 ННИОТ) Start ART (2 NRTI, 1 NNRTI)

Котримоксазол co-trimoxazole

ЛЕЧЕНИЕ С КОИНФЕКЦИЕЙ ВИЧ

Treatment in HIV-coinfected (2/2)

Более высокая смертность Higher mortality

Воспалительный синдром восстановления иммунитета

Immune reconstitution inflammatory syndrome (IRIS)

Риск приобретения лекарственно-устойчивого ТБ Risk of drug-resistant TB

ЛЕЧЕНИЕ ЛЕКАРСТВЕННО-УСТОЙЧИВОГО ТБ (МЛУ ТБ)

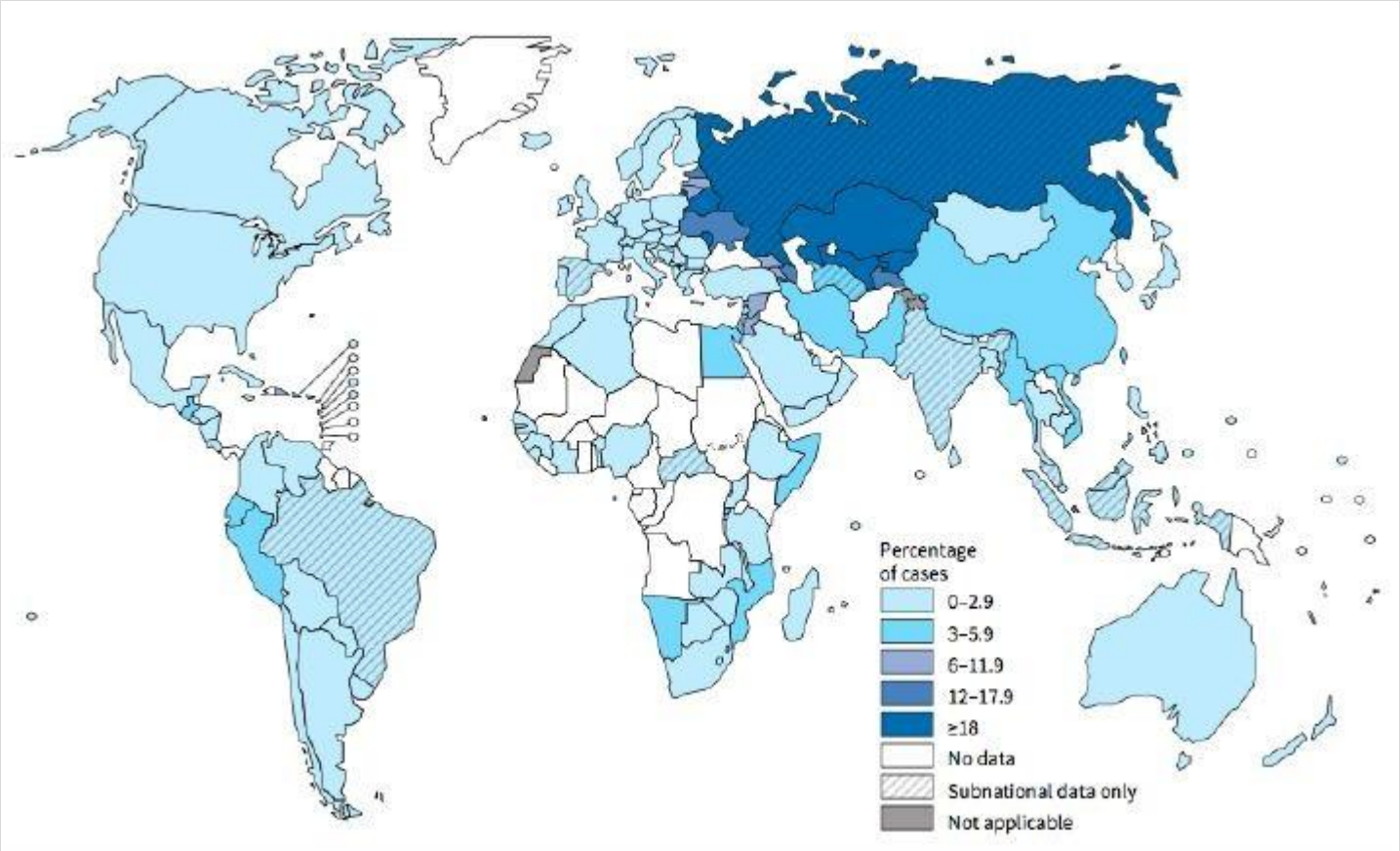
Treatment of Drug-resistant TB (MDR) (1/5)

Значение лекарственно-устойчивого ТБ: устойчивость к изониазиду и рифампицину и, потенциально, другим противотуберкулезным препаратам первой линии

Definition of multidrug-resistant tuberculosis (MDR-TB): Resistance against isoniazide and rifampicin and possibly other first-line anti-tuberculotic agents

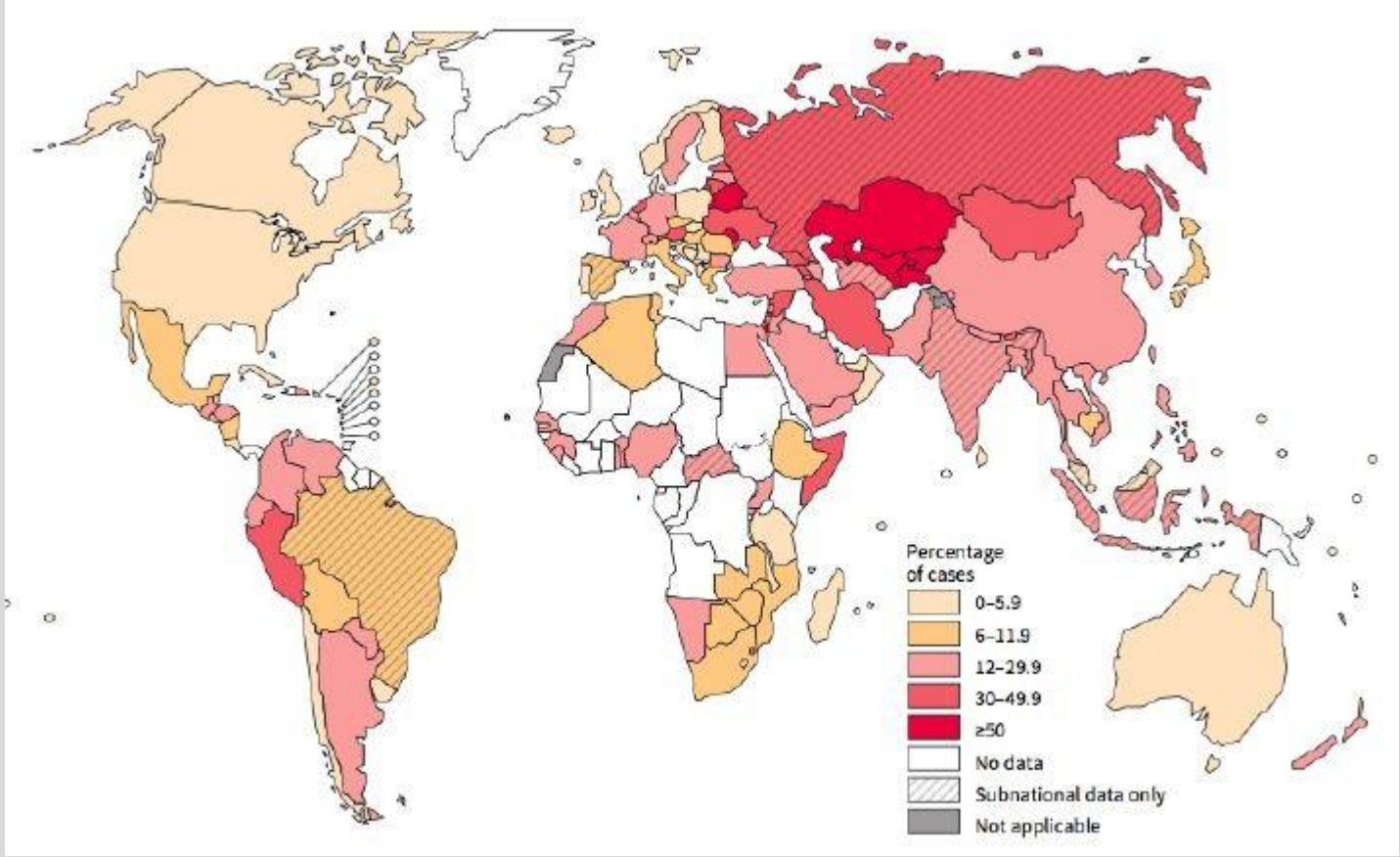
МЛУ ТБ

МЛУ-ТБ среди новых случаев туберкулеза (2/5)



МЛУ ТБ

МЛУ-ТБ среди пролеченных случаев ТБ (3/5)



ЛЕЧЕНИЕ ЛЕКАРСТВЕННО-УСТОЙЧИВОГО ТБ (МЛУ ТБ)

Treatment of Drug-resistant TB (MDR) (4/5)

Тест на чувствительность к препаратам перед началом лечения

Drug susceptibility test (DST) before treatment

Минимум 4 препарата с полной или практически полной эффективностью

At least 4 drugs with either certain, or almost certain effectiveness

При возможности, лечение перорально

Treatment with oral agents if possible

ЛЕЧЕНИЕ ЛЕКАРСТВЕННО-УСТОЙЧИВОГО ТБ (МЛУ ТБ)

Treatment of Drug-resistant TB (MDR) (5/5)

ГРУППЫ ПРЕПАРАТОВ ДЛЯ ЛЕЧЕНИЯ МЛУ-ТБ

Groups of drugs to treat MDR-TB

Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis 2014, p 77 (EN)

www.hiv-druginteractions.org

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LATEST ARTICLES

Drug Interactions - Use of electronic databases to detect interactions.

Webcasts - HIV2014, Glasgow

Meeting Report - HIV2014, Glasgow

Drug Interaction – Efavirenz or darunavir/r and pitavastatin

Drug Interaction – Raltegravir and amlodipine

Meeting Report - 54th ICAAC, Washington

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SITE UPDATES

Expansion of the comedications list to over 600 drugs
A major update to the drug interaction database has seen the addition of nearly 90 new comedications...

>>more

Corticosteroids – new comedications and

DRUG INTERACTION CHARTS

Now Includes Cobicistat

Access our comprehensive, user friendly, free, drug interactions charts

CLICK HERE

Providing clinically useful, reliable, up-to-date evidence-based information

To view low bandwidth version click here

INTERACTION CHARTS FOR PHONES AND TABLETS

HIV iChart - NEW VERSION AVAILABLE

A new version of the interaction app for mobile devices is now available. The new app includes tablet support for Android devices and is fully compatible with the latest versions of iOS (iOS7 and above). Note, existing users of the app on **iOS6** should not install the new app.

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www.hiv-druginteractions.org

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Anti-tuberculosis Treatment Selector

Charts reviewed May 2015. Full information available at www.hiv-druginteractions.org and www.hiv-druginteractionslite.org

		ATV/r	DRV/r	FPV/r	IDV/r	LPV/r	SQV/r	EFV	ETV	NVP	RPV	MVC	DTG	EVG/c	RAL	ABC	FTC	3TC	TDF	ZDV
First Line and Second Line Drugs	Amikacin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔[a]	↔[a]	↔[b]	↔
	Capreomycin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑?[a]	↔	↔	↔	↑?[a]	↑?[a]	↑?[b]	↔
	Clofazimine	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	Cycloserine	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	Ethambutol	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	Ethionamide	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	Isoniazid	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	Kanamycin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔[a]	↔[a]	↔[b]	↔
	Moxifloxacin	↑[c]	↔	↔	↔	↔[c]	↔[d]	↔	↔	↔	↔[e]	↔	↔	↔	↔	↔	↔	↔	↔	↔
	Para-aminosalicylic acid	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑?	↔	↔	↔	↔	↔	↑?	↑?	↑?	↔
	Pyrazinamide	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	Rifabutin	↑	↑ ⇑50%	↑	↑	↑	↑	↓38%	⇓37%	↑17%	⇓[*]	f	↔	↑ ⇓	↔	↔	↔	↔	↔	↔
	Rifampicin	⇓72%	⇓	⇓90%	⇓80%	⇓	⇓	⇓26%	⇓	⇓58%	⇓80%	⇓[g]	⇓54%[h]	⇓	⇓40%	⇓	↔	↔	↔	⇓47%
	Rifapentine	⇓	⇓	⇓	⇓	⇓	⇓	⇓	⇓	⇓	⇓	⇓[g]	⇓[i]	⇓	↔	↔	↔	↔	↔	↔
	Streptomycin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔[b]	↔

Colour Legend

- No clinically significant interaction expected.
- These drugs should not be coadministered.
- Potential interaction which may require a dosage adjustment or close monitoring.
- Potential interaction predicted to be of weak intensity (<2 fold ↑AUC or <50% ↓AUC). No *a priori* dosage adjustment is recommended.

ЛЕЧЕНИЕ ЛЕКАРСТВЕННО-УСТОЙЧИВОГО ТБ (МЛУ ТБ)

Тест на чувствительность к препаратам перед началом лечения

Drug susceptibility test (DST) before treatment

Минимум 4 препарата с полной или практически полной эффективностью

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При возможности, лечение перорально

Treatment with oral agents if possible

ЛЕЧЕНИЕ ЛЕКАРСТВЕННО-УСТОЙЧИВОГО ТБ (МЛУ ТБ)

8Km6-Lfx7-Eto7-Cs7-Z7/12Lfx7-Eto7-Cs7-Z7 = 8 мес.:

Kanamycin (Km) = injection
Levofloxacin (Lfx)
Ethionamide (Eto)
Cycloserine (Cs)
Pyrazinamide (Z)

STEP 1	**Choose an injectable (Group 2)**	**Kanamycin** **Amikacin** **Capreomycin**
	Choose a drug based on DST and treatment history. Streptomycin is generally not used because of high rates of resistance in patients with MDR-TB.	
STEP 2	**Choose a higher generation fluoroquinolone (Group 3)**	**Levofloxacin** **Moxifloxacin**
	Use a later generation fluoroquinolone. If levofloxacin (or ofloxacin) resistance is documented, use moxifloxacin. Avoid moxifloxacin if possible when using bedaquiline (see Annex 4).	
STEP 3	**Add Group 4 drugs**	**Cycloserine/terizidone** **Para-aminosalicylic acid (PAS)** **Ethionamide/prothionamide**
	Add two or more Group 4 drugs until there are at least four second-line anti-TB drugs likely to be effective. Ethionamide/prothionamide is considered the most effective Group 4 drug. Consider treatment history, side-effect profile, and cost. DST is not considered reliable for the drugs in this group.	

STEP 4	**Add Group 1 drugs**	**Pyrazinamide** **Ethambutol**

Pyrazinamide is routinely added in most regimens; ethambutol can be added if the criteria for an effective drug are met (see Section 5.7.1 for definition of "effective drug"). If isoniazid is unknown or pending it can be added to the regimen until DST results become available, see Section 5.8.

STEP 5	**Add Group 5 drugs**	**Bedaquiline** **Linezolid** **Clofazimine** **Amoxicillin/clavulanate** **Imipenem/cilastatin plus clavulanate** **Meropenem plus clavulanate** **High-dose isoniazid** **Clarithromycin** **Thioacetazone**

Awareness Improvement Mobilization

Благодарю за внимание!

Thank you for your attention!

XDR-TB: Countries reporting at least one case

Global AIDS Report 2013

Extensive Drug-resistant TB (XDR-TB)

- Definition *(WHO 2013)*

- MDR-TB, and additional resistance to
- one of the second line injectables, Am, Km, Cp
- one of the fluroquinolones

- Risk factors

- HIV infection
- Incorrect TB treatment *(Lancet Infect Dis 2013;13:529)*
- Intermittent treatment, prescription errors, poor compliance and substandard quality of drugs
- Two or more previous courses of ATT *(PLOS One 2008;3:e2957)*
- Bilateral/cavitary lesions in MDR-TB *(AM J Resp Crit Care Med 2010;182:426)*

XDR-TB

Rules for constructing regimen:

- Empiric regimen (until DST available)

- May use > 4 drugs in the intensive phase *(Clin Epidemiol 2014;6:111)*
- Existing MDR-TB regimen+ Inj (Am) + not used Group 4 + 2 group 5 (Cfx, Amx/Clv, Lzd)
- Cfx has better culture conversion rates *(J Antimicrob Chemother Jun 2014 epub)*

- Individualise according to DST
- High dose INH (if inhA resistance) *(Int J Tuberc Lung Dis 2008;12:129)*
- Duration: 18 mo′ s post culture conversion