Case-based discussions

TB HIV

Dr. Delia Goletti
National Institute for Infectious Diseases L. Spallanzani, Italy
Singapore, September 26-28, 2019
Conflict of interest

In the last year I have been a consultant or I presented talks for:

Diasorin, Janssen, Qiagen, Quidel
Agenda

- TB-HIV in the world
- Immunopathogenesis
- Clinical course of the disease
- TB diagnosis
- TB therapy and TB-HIV therapy
- TB preventive therapy in HIV-LTBI
TB-HIV in 2017

- TB: 10 million
- TB-HIV: 0.9 million
- 1.7 million deaths
- 370,000 deaths estimated to be attributable to HIV–TB coinfection.
Agenda

- TB-HIV in the world
- Immunopathogenesis
- Clinical course of the disease
- TB diagnosis
- TB therapy and TB-HIV therapy
- TB preventive therapy in HIV-LTBI
Immunopathogenesis of TB-HIV

HIV infection is associated to:

- Reduction of apoptosis in *M. tuberculosis*–infected macrophages
- Lower ability of alveolar macrophages to acidify *M. tuberculosis*–infected phagosomes
- Impaired ability of neutrophils to control *M. tuberculosis* growth
- Impaired antigen processing and presentation of *M. tuberculosis*

Innate immunity

- Loss of CD4\(^+\) T cells
  - Selective clonal deletion of *M. tuberculosis*-specific CD4\(^+\) T cells
  - Loss of IFN-\(\gamma^+\)/IL-2\(^+\) CD4\(^+\) T cell precedes the loss of IFN-\(\gamma^+\)/TNF-\(\alpha^+\) CD4\(^+\) T cells
- Impairment of the degranulation and proliferation of CD8 T cells in response to *M. tuberculosis*

Adaptive immunity
Cell-mediated immune response to M. tuberculosis is crucial for granuloma integrity and control of bacillary replication

Esmail at al, Annual Review of Immunology, 2018

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Progression toward active tuberculosis in HIV-uninfected and HIV-infected persons
Agenda

- TB-HIV in the world
- Immunopathogenesis
- Clinical course of the disease
- TB diagnosis
- TB therapy and TB-HIV therapy
- TB preventive therapy in HIV-LTBI
In the absence of ART, is TB occurrence associated to a particular stage of HIV disease?

- Yes, it occurs only at late stages of immune suppression
- Yes, it occurs only at the early stages of HIV disease
- No, it can occur during the all course of the HIV disease
Opportunistic diseases in the course of HIV-infection

- Seroconversion:
  - Acute retroviral syndrome
- Pneumococcal pneumonia
- Candida vaginitis
- ITP
- TBC

- Oral Candida-infection
- Kaposi sarcoma
- Lymphoma
- Dementia
- Oral hairy leukoplakia

- Cachexia
- Toxoplasmosis
- PCP
- HSV
- Candida esophagitis
- Cryptococcosis
- TBC

In absence of ART
Trends in incidence rates of TB according to duration of HIV seroconversion in the pre-ART era and time since initiation of ART.

Before ART initiation

After ART initiation

Lodi et al and Girardi, Thorax, 2014
TB risk is increased in HIV+ patients and depends on CD4 cell counts at the time of ART initiation.


CD4 cell counts at ART initiation

- CD4: <50 µl
- CD4: 50-199 µl
- CD4: 350-499 µl
- CD4: >350 µl

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Does ART reduce HIV-associated TB incidence to background rates?

☐ yes

☐ no
TB rates during long-term ART remained substantially greater than rates in the local HIV-uninfected populations regardless of duration of ART or attainment of CD4 cell counts exceeding 700 cells/mL

Gupta et al, PloS One 2012
ART does not reduce HIV-associated TB incidence to background rates

Tuberculosis incidence by months on ART in the national HIV cohort in England, Wales, and Northern Ireland

Tuberculosis incidence in national HIV cohort compared with that in background HIV-negative population in 2009

Gupta et al, Lancet 2015
Impact of HIV infection on TB localization: pulmonary vs extra-pulmonary TB

HIV-ununfected

infected
Is lung cavitation common in HIV-TB?

- yes
- no
Pulmonary TB characteristics in HIV-infected patients

AFB negative sputum

Cavitation

HIV-infected patients with culture-confirmed pulmonary TB

Chamie et al, Int J Tuberc Lung Dis. 2010
IRIS
TB immune reconstitution inflammatory syndrome (IRIS)

- TB-IRIS can occur in approximately 18% of HIV–TB coinfected people upon ART initiation.

- Transient worsening or appearance of new symptoms, signs or radiographic manifestations of TB after initiation of ART. Risk factors:
  - High HIV load
  - Low CD4+ T cell count (below 100/µl)
  - ART initiation soon after TB diagnosis

- To exclude:
  - Drug resistance
  - No adherence to therapy
  - Concurrent pathologies; i.e. lymphoma
Pathogenesis of IRIS and immune responses

- Dysregulated recovery of specific immune response (to ESAT-6, α-crystallins 1 and 2, and PPD) resulting in granulomatous and necrotizing inflammation directed at mycobacterial antigens released by dead or dying organisms.
- Pro- and anti-inflammatory cytokines and chemokines of both innate and adaptive origins are involved.
- IL-6 has been described as a major pathological indicator of TB-IRIS. Increased serum concentrations of IL-6 before ART are associated with development of TB-IRIS (Narendran, Plos One 2013) and early mortality (Ravimohan, Lancet ID, 2015).
- Microarray profiling revealed that TLR signaling and inflammasome activation are critical in mediating TB-IRIS pathogenesis (Lai, Nat Com 2015).
Paradoxical TB-associated IRIS and ART-associated TB

Paradoxical IRIS

ART-associated TB
(unmasking TB-associated IRIS)
IRIS: organs’ involvement

Respiratory system
- Expansion of pulmonary infiltrates

Lymph nodes
- Nodes enlargement

Abdominal organs:
- Abdominal nodes enlargement
- Liver function derangement (cholestatic pattern)

Central nervous system
- Tuberculosis-meningitis-associated IRIS (TBMIRIS)
Agenda

- TB-HIV in the world
- Immunopathogenesis
- Clinical course of the disease
- TB diagnosis
- TB therapy and TB-HIV therapy
- TB preventive therapy
TB diagnosis in HIV-infected persons

- Microbiology
- Radiology
- TST
- IGRA
- Experimental tests
# Technologies for TB diagnosis

## TABLE 1. Technologies reviewed by WHO for TB case detection

<table>
<thead>
<tr>
<th>Year</th>
<th>Method</th>
<th>Technology reviewed by WHO</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>Culture (growth-based)</td>
<td>Commercial liquid culture and rapid speciation strip tests</td>
</tr>
<tr>
<td>2010</td>
<td>Microscopy</td>
<td>LED microscopy</td>
</tr>
<tr>
<td>2010</td>
<td>NAAT</td>
<td>Xpert MTB/RIF</td>
</tr>
<tr>
<td>2016</td>
<td>Antigen detection test</td>
<td>Urine LAM rapid test</td>
</tr>
<tr>
<td>2016</td>
<td>NAAT</td>
<td>Loop-mediated amplification test (LAMP)</td>
</tr>
</tbody>
</table>

## TABLE 2. Technologies reviewed by WHO for drug-susceptibility testing

<table>
<thead>
<tr>
<th>Year</th>
<th>Method</th>
<th>Technology reviewed by WHO</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>Phenotypic</td>
<td>Commercial liquid culture and DST</td>
</tr>
<tr>
<td>2008</td>
<td>Genotypic</td>
<td>Molecular LPAs for first-line anti-TB drug resistance detection</td>
</tr>
<tr>
<td>2010</td>
<td>Phenotypic</td>
<td>Selected noncommercial DST methods (MODS, CRI, NRA)</td>
</tr>
<tr>
<td>2010</td>
<td>Genotypic</td>
<td>Xpert MTB/RIF</td>
</tr>
<tr>
<td>2016</td>
<td>Genotypic</td>
<td>Molecular LPAs for second-line anti-TB drug resistance detection</td>
</tr>
</tbody>
</table>
Comparison of Xpert MTB/RIF with Other Nucleic Acid Technologies for Diagnosing Pulmonary Tuberculosis in a High HIV Prevalence Setting: A Prospective Study

Scott et al, PloS One, 2011

### Table 2. Test performance (including comparison to clinical case definitions) for smear microscopy, MGIT culture, MTBDRplus directly on sputum, LCTB, and Xpert MTB/RIF assays stratified by smear microscopy and HIV status.

<table>
<thead>
<tr>
<th>Test Performance Measure*</th>
<th>Smear Microscopy</th>
<th>MGIT Culture</th>
<th>NAAT Performed Directly on Sputum</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>HIV+</td>
</tr>
<tr>
<td><strong>Comparison to MGIT culture (n=177)</strong></td>
<td></td>
<td></td>
<td>HIV+</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>59 (47–71)</td>
<td>NA</td>
<td>76 (64–85)</td>
</tr>
<tr>
<td>Specificity</td>
<td>100 (96–100)</td>
<td></td>
<td>97 (92–99)</td>
</tr>
<tr>
<td>PPV</td>
<td>100 (91–100)</td>
<td></td>
<td>94 (84–98)</td>
</tr>
<tr>
<td>NPV</td>
<td>80 (72–86)</td>
<td></td>
<td>87 (79–92)</td>
</tr>
<tr>
<td><strong>Comparison to MGIT culture (HIV-positive cohort only, n=124)</strong></td>
<td></td>
<td></td>
<td>HIV+</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>54 (38–69)</td>
<td>NA</td>
<td>70 (54–83)</td>
</tr>
<tr>
<td>Specificity</td>
<td>100 (95–100)</td>
<td></td>
<td>96 (89–99)</td>
</tr>
<tr>
<td>PPV</td>
<td>100 (85–100)</td>
<td></td>
<td>91 (76–98)</td>
</tr>
<tr>
<td>NPV</td>
<td>80 (70–87)</td>
<td></td>
<td>85 (76–92)</td>
</tr>
<tr>
<td><strong>Comparison to MGIT culture (HIV-negative cohort only, n=26)</strong></td>
<td></td>
<td></td>
<td>HIV-</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>66 (32–90)</td>
<td>75 (43–95)</td>
<td>75 (42–94)</td>
</tr>
<tr>
<td>Specificity</td>
<td>100 (70–100)</td>
<td>100 (76–100)</td>
<td>100 (76–100)</td>
</tr>
<tr>
<td>PPV</td>
<td>100 (63–100)</td>
<td>100 (66–100)</td>
<td>100 (69–100)</td>
</tr>
<tr>
<td>NPV</td>
<td>79 (52–93)</td>
<td>82 (56–96)</td>
<td>82 (56–96)</td>
</tr>
</tbody>
</table>

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Diagnostic accuracy of Xpert MTB/RIF for TB detection in different regions with different endemic burden

Li et al, PloS One 2017
Impact of Xpert MTB/RIF specifically among HIV co-infected individuals

Scott et al, Current Opinion in HIV/AIDS, 2017

<table>
<thead>
<tr>
<th>Main study investigations</th>
<th>Main study findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detection of TB</td>
<td>Increased detection, earlier treatment, decreased empiric treatment and more patients completed treatment with fewer LTFU</td>
</tr>
<tr>
<td>Drug-resistant (DR)TB</td>
<td>Presumptive screening enabled rapid diagnosis (2 days with Xpert MTB/RIF, 8 days to confirm with LPA) and reduced treatment time (8 vs. 40 days) with potential to decrease transmission</td>
</tr>
<tr>
<td>Placement (services)</td>
<td>Shortened time to treatment only in TB treatment facilities</td>
</tr>
<tr>
<td>Empiric treatment</td>
<td>Added little to clinical decision</td>
</tr>
<tr>
<td>ART-associated TB</td>
<td>No difference in treatment initiation times, many patients still treated empirically, mortality not reduced</td>
</tr>
<tr>
<td>Mortality</td>
<td>No difference in time to treatment or 2-month mortality</td>
</tr>
</tbody>
</table>

ART, antiretroviral therapy; LPA, line probe assay; LTFU, lost to follow up; POC, point of care; TB, tuberculosis.
Imaging tools

Pulmonary TB:
- Chest xRay: 14% of HIV-infected subjects with culture-positive TB have a normal chest xRay
- CT-scan: lymph nodes, mediastin
- HRCT (1 mm slices): interstitial lesions
- 2-deoxy-2-[18F]fluoro-d-glucose positron emission and computed tomography (PET–CT): activity of the lesions (research purposes)

Extra-pulmonary TB:
- NMR (es: bone, CNS)
- CT-scan
- US
Radiological features of HIV+ patients

- Cavitary TB: 580 CD4+ (26%)
- Miliary TB: 152 CD4+ (15%)
- Pleural effusion TB: 105 CD4+ (11%)

From Dr Schininà, INMI
TB-HIV: lung involvement

IRIS

Bronchogenic spread

From dr Schininà, INMI
TB lesions in the column in an HIV-TB coinfected patient

Spondylodiscitis lesions in L3, L5

Caseum
Central nervous system TB in HIV-TB coinfectected patients

Caseum granuloma

TB abscessus

From dr Schininnà, INMI
LTBI

[Images of medical conditions and diagnostic procedures]
Does TST is an accurate test for LTBI in HIV-infected patients?

☐ yes
☐ no
The probability of being TST$^+$ is correlated with CD4$^+$ T cell counts

Elzi et al, CID 2007
Risk assessment of tuberculosis in immunocompromised patients. A TBNET Study

Indeterminate results

Positive results

Sester et al, AJRCCM 2014
IGRA should be used for LTBI diagnosis in HIV-infected subjects (BHIVA 2017)

6.1 Diagnosis of latent TB

- We recommend testing HIV-positive individuals from high- and medium-TB-incidence countries for LTBI, including pregnant women, regardless of their CD4 cell count and receipt of ART, with particular attention to those with newly diagnosed HIV or who have recently been exposed to TB. (GRADE 1B)
- We recommend testing HIV-positive individuals from low-incidence countries for LTBI if they have additional TB risk factors. (GRADE 1C)
- Prior to testing and providing treatment for LTBI, we recommend excluding active TB, by addressing presence of TB symptoms and signs and, where appropriate, conducting investigations (e.g. radiology). (GRADE 1A)
- We suggest that, in the UK setting, IGRA rather than TST should be used when testing HIV-positive individuals for LTBI. (GRADE 2C)
- The IGRA should be repeated if the first result is indeterminate or borderline. (GPP)
- We do not recommend the use of IGRA or TST in the diagnosis, or exclusion, of active TB. (GPP)
IGRA and/or TST should be used for LTBI diagnosis in HIV-infected subjects (ERS/ECDC statement)

**Standard 16 (changed)**

Persons with HIV co-infection who, after careful evaluation, have a positive test (TST and/or IGRAs) for presumed latent infection with *M. tuberculosis* but do not have active tuberculosis should be offered preventive treatment.
# Accuracy of TB-immune tests in published studies

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity for active TB</th>
<th>Specificity for active TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-uninfected</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TST</td>
<td>65</td>
<td>75</td>
</tr>
<tr>
<td>QFT-IT</td>
<td>80</td>
<td>79</td>
</tr>
<tr>
<td>T-SPOT.TB</td>
<td>81</td>
<td>59</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity for active TB</th>
<th>Specificity for active TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-infected</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>N.D.</td>
<td>N.D.</td>
</tr>
<tr>
<td>TST</td>
<td>N.D.</td>
<td>N.D.</td>
</tr>
<tr>
<td>QFT-IT</td>
<td>N.D.</td>
<td>N.D.</td>
</tr>
<tr>
<td>T-SPOT.TB</td>
<td>N.D.</td>
<td>N.D.</td>
</tr>
</tbody>
</table>

- **Sensitivity:**
  - QFT: 61%
  - T SPOT-TB: 65%

- **Specificity:**
  - QFT: 63%
  - T SPOT-TB: 70%
QuantiFERON Plus accuracy in HIV-infected subjects in Zambia

<table>
<thead>
<tr>
<th>Case definition</th>
<th>Smear +ve, within 1 month of treatment</th>
<th>Smear or Xpert +ve within 2 days of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 cell count among PLHIV, cells/μl</td>
<td>212 % (95% CI)</td>
<td>246 % (95% CI)</td>
</tr>
</tbody>
</table>

### Table 4
Comparing the performance of QGIT assay, the TST and QFT-Plus among adult (age ≥ 18 years) pulmonary TB patients

<table>
<thead>
<tr>
<th>Study features</th>
<th>QGIT (n = 112)</th>
<th>TST (n = 92)</th>
<th>QFT-Plus (n = 108)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>74 (66-82)</td>
<td>67 (58-77)</td>
<td>83 (75-90)</td>
</tr>
<tr>
<td>Quantiferon-negative</td>
<td>12 (6-19)</td>
<td>NA</td>
<td>10 (5-17)</td>
</tr>
<tr>
<td>Quantiferon-indeterminate</td>
<td>14 (8-22)</td>
<td>NA</td>
<td>6 (3-13)</td>
</tr>
<tr>
<td>Overall</td>
<td>63 (50-74)</td>
<td>55 (40-70)</td>
<td>85 (75-93)</td>
</tr>
</tbody>
</table>

CD4 counts correlation

QGIT = QuantiFERON®-TB Gold In-Tube assay; TST = tuberculin skin test; QFT-Plus = QuantiFERON®-TB Gold Plus; TB = tuberculosis; +ve = positive; PLHIV = people living with HIV; CI = confidence interval; NA = not applicable.

Telisinghe et al, IJTLD 2017
Agenda

- TB-HIV in the world
- Immunopathogenesis
- Clinical course of the disease
- TB diagnosis
- TB therapy and TB-HIV therapy
- TB preventive therapy in HIV-LTBI
British HIV Association guidelines for the management of TB/HIV co-infection in adults 2017

When to start ART

- We recommend that all individuals with TB should start ART as soon as is practicable, and within 8–12 weeks of the TB diagnosis. (GRADE 1A)
- We recommend that individuals with a CD4 cell count <50 cells/mm³ start ART as soon as is practicable and within 2 weeks. (GRADE 1A)
- We recommend against the early initiation (<2 months) of ART in individuals with CNS TB. (GRADE 1A)
British HIV Association guidelines for the management of TB/HIV co-infection in adults 2017

What ART to start

- We recommend efavirenz (standard dose) in combination with tenofovir (TDF) and emtricitabine as first-line ART. (GRADE 1B)
- We suggest that raltegravir can be used for individuals in whom efavirenz is contraindicated. (GRADE 2B)
- We recommend that rifabutin is used instead of rifampicin where effective ART necessitates the use of ritonavir-boosted protease inhibitors. (GRADE 1C)
- We recommend against the use of fixed-dose combinations containing tenofovir alafenamide (TAF), when co-administered with rifampicin or rifabutin. (GRADE 1D)
- We recommend against the use of nevirapine in ART-naive individuals with TB treated with rifampicin. (GRADE 1B)

Choice of antiretroviral treatment in individuals on established ART

- We recommend that individuals who develop TB on ART with undetectable HIV viral loads do not interrupt their ART. (GRADE 1A)
- We recommend that rifampicin-based TB treatment is used in individuals whose established ART consists of efavirenz (GRADE 1B), nevirapine (GRADE 2C), or raltegravir (GRADE 2C) plus two NRTIs.
- We recommend that rifabutin is used instead of rifampicin where established ART necessitates use of ritonavir. (GRADE 1C)
Length of TB treatment in HIV co-infected patients with drug susceptible pulmonary TB

- In patients with drug-susceptible pulmonary TB who are living with HIV and receiving antiretroviral therapy during TB treatment, a 6-month standard treatment regimen is recommended over an extended treatment for 8 months or more (Conditional recommendation/very low certainty in the evidence).
Improved survival and cure rates with concurrent treatment for MDR-TB/HIV co-infection in South Africa
ART increases CD4-specific Mtb response in LTBI subjects, no in active TB patients
IRIS
Therapy for IRIS

- **Prednisone** is the only drug that has been evaluated by a randomized, double-blind, placebo-controlled trial. Patients with paradoxical TB-IRIS who received prednisone for four weeks had more rapid symptom improvement, reduced need for hospitalization or therapeutic procedures, and better quality of life compared to the placebo arm.

- Recently steroids to prevent TB-IRIS, in high-risk patients (moderate dose of prednisone at the time of ART initiation) led to a 30% reduced risk of developing TB-IRIS compared to those receiving placebo.

- Other nonsteroid inflammatory drugs have shown to be useful.
Agenda

- TB-HIV in the world
- Immunopathogenesis
- Clinical course of the disease
- TB diagnosis
- TB therapy and TB-HIV therapy
- TB preventive therapy in HIV-LTBI
Is any short regimen for preventive therapy recently proposed for the HIV-infected patients?

☐ yes
☐ no
One Month of Rifapentine plus Isoniazid to Prevent HIV-Related Tuberculosis

Swindells et al, NEJM, 2019

| Table 1. Characteristics of the Patients at Baseline. |
|---|---|---|
| Characteristic | 1-Month Group | 9-Month Group | All Patients |
| Continent of residence — no. (%) | | | |
| Africa | 772 (52) | 281 (12) | 1553 (52) |
| Asia | 121 (8) | 214 (8) | 245 (8) |
| South America | 360 (24) | 355 (24) | 715 (24) |
| North America | 243 (16) | 244 (16) | 487 (16) |
| Median age (IQR) — yr | 35 (28–43) | 35 (28–43) | 35 (28–43) |
| Sex — no. (%) | | | |
| Male | 684 (46) | 692 (46) | 1376 (46) |
| Female | 802 (54) | 812 (54) | 1614 (54) |
| Race or ethnic group — no. (%) | | | |
| Black non-Hispanic | 592 (66) | 991 (66) | 1983 (66) |
| White non-Hispanic | 16 (1) | 12 (1) | 28 (1) |
| Asian or Pacific Islander | 122 (8) | 128 (9) | 250 (8) |
| Hispanic | 361 (24) | 369 (25) | 730 (24) |
| Unknown | 5 (1) | 4 (1) | 9 (1) |
| Median body-mass index (IQR) | 22.8 (21–27.1) | 23.5 (20.0–26.9) | 23.5 (20.0–27.1) |
| CD4+ count | | | |
| Median (IQR) — no. of cells/mm³ | 473 (349–634) | 469 (341–614) | 470 (346–635) |
| Patients — no. (%) | | | |
| >250 cells/mm³ | 1299 (87) | 1302 (87) | 2601 (87) |
| 100 to <250 cells/mm³ | 160 (11) | 165 (11) | 325 (11) |
| <100 cells/mm³ | 37 (2) | 37 (2) | 74 (2) |
| Receipt of antiretroviral therapy at entry — no. (%) | | | |
| Efavirenz-based regimen | 650 (43) | 649 (43) | 1299 (43) |
| Nevirapine-based regimen | 97 (6) | 100 (7) | 197 (7) |
| Other | 8 (1) | 6 (1) | 9 (1) |
| None | 746 (50) | 749 (50) | 1495 (50) |
| Viral load in patients receiving antiretroviral therapy | no. total no. (%) | | |
| Undetectable — <40 copies/ml | 569 (76) | 586 (75) | 1155 (77) |
| Detectable — ≥40 copies/ml | 154 (21) | 143 (19) | 297 (20) |
| Unavailable | 27 (4) | 26 (3) | 53 (4) |
| Previous diagnosis of tuberculosis — no. (%) | | | |
| Positive | 311 (21) | 324 (22) | 635 (21) |
| Negative | 1033 (69) | 1021 (68) | 2054 (68) |
| Not done | 152 (10) | 159 (11) | 311 (10) |
| IGRA for tuberculosis — no. (%) | | | |
| Positive | 36 (2) | 37 (2) | 73 (2) |
| Negative | 1 (1) | 2 (1) | 3 (1) |
| Not done | 1459 (98) | 1465 (97) | 2924 (97) |
One Month of Rifapentine plus Isoniazid to Prevent HIV-Related Tuberculosis

Swinde's et al, NEJM, 2019
### Recommended drugs for LTBI treatment

**Table 2** Recommended dosages of drugs for the treatment of LTBI

<table>
<thead>
<tr>
<th>Drug regimen</th>
<th>Dose per kg body weight</th>
<th>Maximum dose</th>
</tr>
</thead>
</table>
| Isoniazid alone, daily for 6 or 9 months          | Adults: 5 mg  
Children: 10 mg (range: 7-15 mg) | 300 mg       |
| Daily rifampicin alone for 3-4 months             | Adults: 10 mg  
Children: 15 mg (range: 10-20 mg) | 600 mg       |
| Daily isoniazid plus rifampicin for 3-4 months    | Isoniazid:  
Adults: 5 mg  
Children: 10 mg (range: 7-15 mg)  
Rifampicin:  
Adults: 10 mg  
Children: 15 mg (range: 10-20 mg) | Isoniazid: 300 mg  
Rifampicin: 600 mg |
| Weekly rifapentine plus isoniazid for 3 months (12 doses) | Individuals aged ≤12 years: Isoniazid: 15 mg  
Individuals aged 2-11 years: Isoniazid: 25 mg  
Rifapentine:  
10.0-14.0 kg = 300 mg  
14.1-25.0 kg = 450 mg  
25.1-32.0 kg = 600 mg  
32.1-50.0 kg = 750 mg  
>50 kg = 900 mg | Isoniazid: 900 mg  
Rifapentine: 900 mg |
Adults, adolescents living with HIV

Adults and adolescents living with HIV, with unknown or a positive tuberculin skin test (TST) and are unlikely to have active TB should receive preventive treatment of TB as part of a comprehensive package of HIV care.

Treatment should be given to these individuals irrespective of the degree of immunosuppression and also to those on antiretroviral treatment (ART), those who have previously been treated for TB and pregnant women. *(Strong recommendation, high-quality evidence. Existing recommendation)*
Gaps in the implementation of preventive treatment for PLHIV
Preventive therapy coverage in HIV-infected patients

Preventive therapy started in 36% of the eligible HIV-infected subjects in the 59 countries that reported it.

For seven countries, data are for people currently enrolled in HIV care: Congo, Ecuador, Grenada, Kenya, Mozambique, Nepal and Ukraine.
Conclusions

- HIV-epidemiology: high burden
- Immunopathogenesis: still difficult to completely understand
- Clinical diagnosis: different features in HIV. Think about!
- Diagnosis: difficult. Several steps are involved for both active TB and LTBI
- Therapy: TB treatment and ART are needed. IRIS: be careful!
- IPT in HIV-infected: extremely important
Thank you!

Grazie!
Thank you

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