MDR-TB Treatment Regimens, Outcomes, and Cost in Haiti

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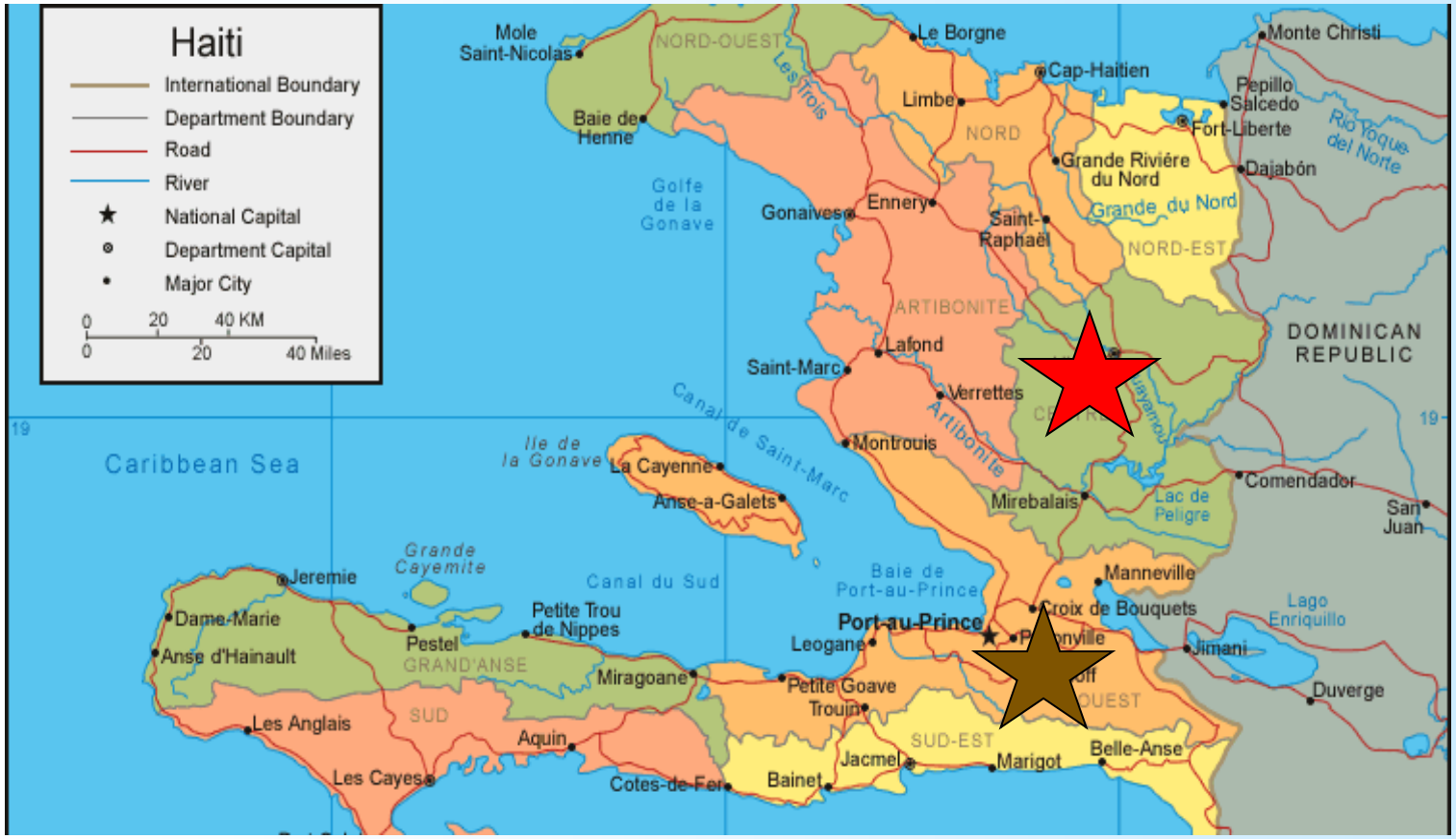
Two MDR-TB sites in Haiti



Working in close collaboration with PLNT, LNSP, MSPP

PIH/ZL Catchment Area

Partners In Health

Zanmi Lasante

Map items:

- ZL Supported Facilty
- Departments

Communes:

- ZL Catchment

Department	Commune	Estimated 2013 Population*
Centre	Belladere	85,677
	Boucan Carre	55,424
	Cerca La Source	55,922
	Hinche	119,562
	Lascahobas	45,377
	Mirebalais	96,700
	Saut d'Eau	38,647
	Savanette	35,810
	Thomonde	61,212
	Total	***594,331***
Lower Artibonite	Petite Riviere	171,436
	Saint-Marc	267,729
	Verrettes	145,404
	Total	***584,569***
Total		**1,178,900**

* l'Institut Haïtien de Statistique et d'Informatique (IHSI) and Ministère de la Santé Publique et de la Population (MSPP)

NORD-OUEST
Bassin Bleu
Borgne
Gros-Morne
Pilate
Limbé
Acul du Nord
NORD
Plaisance
Terre Neuve
Ennery
Marmelade
Dondon
NORD-EST
Gonaïves
Vallières
Saint-Saint Raphaël
L'ARTIBONITE
Estère
Mombin Crochu
Saint Michel de l'Attalaye
Pignon
Desdunes
Dessalines
Grande Saline
Cerca Carvajal
Maïssade
Hôpital Sainte-Thérèse (Hinche)
Hinche
Cerca La Source
Centre de Santé de Cerca-la-Source
Hôpital Saint-Nicolas and SSPE de Saint-Marc
Hôpital Charles Colimon (Petite Rivière)
Verettes
Petite Rivière de l'Artibonite
CENTRE
Centre de Santé de Thomonde
Thomasique
Saint-Marc
Hôpital Dumarsais Estimé (Verettes)
Centre de Santé Saint Michel (Boucan Carré)
Thomonde
Hôpital Bon Sauveur (Cange)
Belladère
La Chapelle
Boucan Carré
Hôpital Notre Dame de la Nativité (Belladère)
Arcahaie
Lascahobas
Saut-d'Eau
Hôpital Universitaire de Mirebalais
Centre de Santé de Lacolline and Clinique Sante Fanm
Cabaret
Mirebalais
Savanette
Thomazeau
Cornillon
Dominican Republic
0 10 20 40 Kilometers
Ganthier
Pétion-Ville

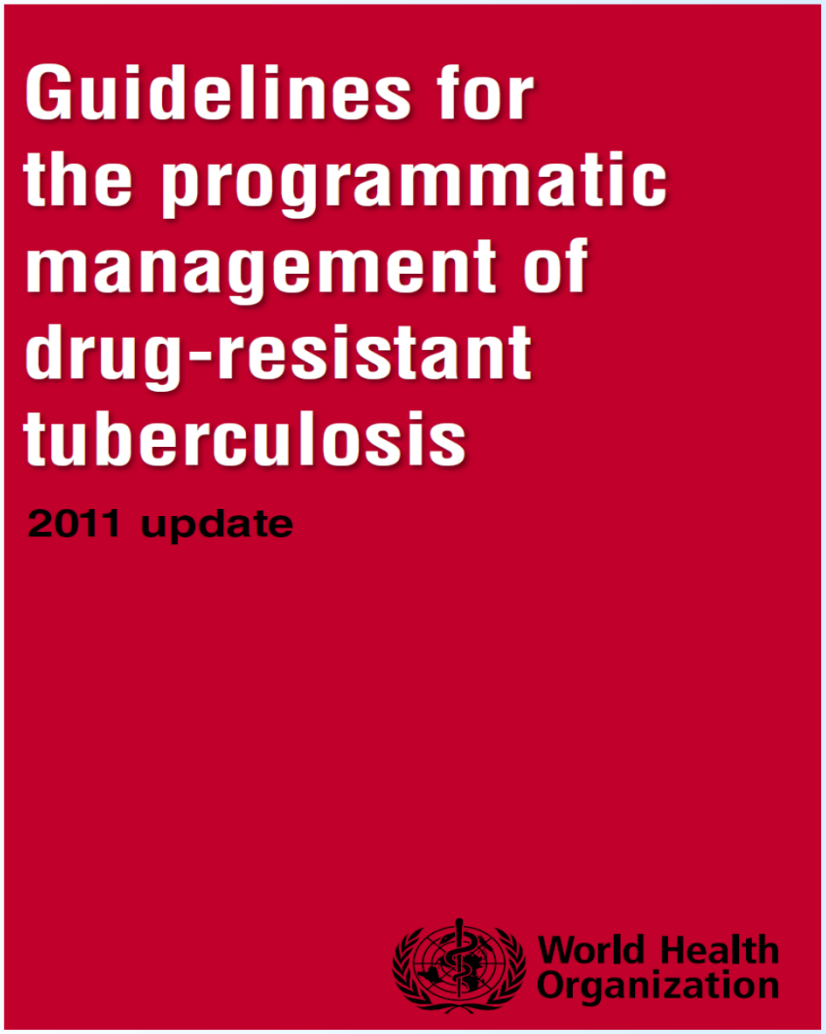
Date:June 2013

Contact: Boston_MEQ@pih.org

Overview of MDR-TB Treatment

- Need at least 4 drugs that are likely to be effective in the intensive phase.
- Do not count PZA or ethambutol, even if sensitive by DST, because DST is not perfect and nearly all patients have already received these medications.
- Always include an injectable agent (kanamycin or capreomycin) and a quinolone.
- Supervision of treatment: Twice-daily DOT is required.
- Monitoring therapy – requires culture capacity.

2011 WHO Guidelines



Empiric MDR-TB Regimen

1. **Injectable agent** – kanamycin or capreomycin
    * Capreomycin preferred for patients with risk factors for renal failure (diabetes), and for those living with HIV
    * If patient develops otoxicity or nephrotoxicity on kanamycin, switch to capreomycin
2. **Fluoroquinolone** – moxifloxacin or levofloxacin
    * Moxifloxacin is preferred for HIV-infected patients and those who present with very severe MDR-TB
    * For patients weighing >50 kg, higher dose levofloxacin (1000mg per day) is preferred
3. **Ethionamide** for all patients
4. **Cycloserine** – avoid if history of seizure disorder or psychiatric disease
5. **PAS** – if contraindication to cycloserine, for severe MDR-TB, or for HIV-infected,
6. **Pyrazinamide** for all patients that did not have side effects in first-line regimen
7. **High dose isoniazid** (because about 20% of patients will be resistant to ethionamide when DST results available)

Individualized MDR-TB Regimen

- Stop high dose isoniazid when second-line DST results available
  - If resistant to ethionamide (due to cross-resistance with isoniazid; nearly 20% of patients) then add PAS
  - If sensitive to ethionamide then continue ethionamide
- If sensitive to ethambutol, add it but do not count it
- If patient is resistant to any of the other second-line medications, their regimen will be developed on an individualized basis.

HIV and MDR-TB Co-infection

- ART for all patients with HIV and MDR-TB, irrespective of CD4 cell count, as early as possible following initiation of MDR-TB treatment.
- Preferably treat with capreomycin, moxifloxacin, ethiomanide, cycloserine, PAS, and pyrazinamide

Duration of treatment and monitoring of therapy

- Intensive phase – continue injectable until 6 consecutive negative cultures (at least 8 months).
- Total treatment duration is 24 months
- Monthly AFB smear and culture (may decrease this frequency for clinically stable patients)

Laboratory Monitoring for Toxicity

- Baseline - potassium, creatinine, SGOT/SGPT/bilirubin, complete blood count, HIV test, pregnancy test for women of reproductive age
- SGOT/SGPT monthly X 3 months; if HIV+ then monthly throughout treatment
- Potassium and creatinine weekly for first month, then monthly while on injectable agent (2 weeks for diabetics, age>50, and HIV+); for HIV+ also monthly while on maintenance
- Complete blood count every 3 months; for HIV+ monthly throughout treatment
- TSH every 3-6 months

Side effects at PIH (n=111 patients)

SE/Year	Number/111 pts	%
Gastric problem	19	17%
Psychosis/nervous breakdown	23	21%
Peripheral neuropathy	24	22%
Ototoxicity	21	19%
Hypothyroidism	9	8%
Vestibulo/cochlear problem	5	5%
Hyperactivity	5	5%

PIH MDR-TB outcomes

- 158 patients started on treatment since 2008
  - 78 (49%) women; 25 (16%) HIV+
- 12 (8%) died
- 13 (8%) lost to follow up
- **133 (84%) in care or completed treatment**
  - **31 (23%) inpatient**
  - **26 (20%) outpatient**
  - **76 (57%) completed treatment**

Side Effects at GHESKIO (n=76)

- Ototoxicity 22%
- Psychiatric toxicity (depression or psychosis) 20%
- Peripheral neuropathy 17%
- Severe nausea, vomiting, or diarrhea 17%
- Arthritis 12%
- Anemia 12%
- Hypokalemia 9%
- Hypothyroidism (TSH> 10) 8% *(TSH was not routinely checked)*
- Renal toxicity 4%
- Hepatitis 1%

GHESKIO MDR-TB outcomes

- 141 patients started on treatment since program started in 2008 (most since earthquake)
  - 72 (51%) women; 30 (21%) HIV+
- 17 (12%) died
- 6 (4%) lost to follow up
- **118 (84%) in care or completed treatment**
  - **32 (27%) inpatient**
  - **46 (39%) outpatient**
  - **40 (34%) completed treatment**
- Outcomes are poorer in HIV+ patients (17 [57%] on treatment, 4 [13%] cured, 7 [23%] died, 2 [7%] abandoned)

Community-based MDR-TB care

- Inpatient care: ~3 months (if patient is clinically stable and adherent to medications)
- Outpatient: 21 months
  - DOTS
    - Close supervision of fieldworkers (GPS, daily phone calls, surprise visits)
  - Close monitoring for clinical response and toxicity
  - Strong partnership with patient and family members
  - Social support (transportation, phone cards, meetings, food rations, and a monetary prize upon completion of treatment)

Cost of Outpatient Medical Care (21 Months) w/out MDR-TB drugs

- Ancillary Drugs: $ 11/month; $231 total for 21 months
- Lab Testing and Radiology:
  - TB diagnostics (smear, GeneXpert, ID, culture and DST: $194
  - Monitoring for toxicity: ~$450
  - CXR every 6 months: $100
  - AFB/culture every month: $1134
  - Total laboratory: ~$1878
- Outpatient Medical Care
  - Transportation to clinic: $5/visit for about 36 visits - $180
  - Clinic-based labor with overhead (MD, nurse, social worker, etc): $40/month; $840 total
  - Total outpatient medical care: $1020
- Supervision of Medications
  - Auxiliary nurse ($100/month X ~5 months outpatient) or CHW ($50/month X 16 months outpatient) for DOT (2X daily DOT): $50/month = $1300 total
  - Transport for CHW: $130/month; $2730 total
  - Total medication supervision: $4,030
- Social Support
  - Phone cards: $11 per month; $231 total
  - Nutrition supplement: $50/month; $1050 total for 21 months
  - Total: $1281
  - End-of-treatment prize: $200
  - *TOTAL FOR 21 MONTHS OF TREATMENT:* ***$8640***

Needs for Scale-up of MDRTB Treatment

- Training:
  - Laboratory personnel
  - Health care workers (MDs, RNs, RN aides, fieldworkers)
- Legal/logistical aspects of care
- Scale-up MDR-TB treatment with guidance of PNLT
- Funding for drugs, medical care, and social support