Realization of the program

**Diagnostics and**

Treatment of MDR TB in Orel Oblast

Russian Federation

November 2002-October 2006
Date of the initiation of the program: November 2002

Participants:

- Ministry of health of RF
- Health Care department of the Administration of Orel Oblast
- UIN Ministry of Justice of RF
- Orel Oblast TB Dispensary
- Central SRI of TB RAMS
- SRI of phtisiopulmonology MMA n.a. IM Sechenov
- World Health Organization
- Centers for Disease Control and Prevention (USA)
- US Agency for International Development
Goal of the Study

To evaluate the preliminary results of the program of diagnostics and treatment of MDR TB in Orel Oblast.

Materials of the Study:

200 MDR TB patients, registered for treatment within the period of November 2002 till December 2005.

- 56 – newly detected
- 144– previously treated
Methods:

• Sputum smear microscopy with Ziehl-Neelsen staining.
• Cultures were done on two nutrient medias: L-J and FINN II.
• Drug Resistance was detected with the absolute concentrations indirect method on solid L-J media to H, R, E, S, K, Cap, Ofl, Cic, Pro, PASK.
Chemotherapy regimen

Intensive phase of treatment – not less than 6 months
- Capreomycin / Kanamycin
- Ofloxacin
- Protonamide
- Pyrazinamide
- Cycloserine
- [Ethambutol]
- [PASK]

Continuation phase from 12 to 18 months
- Ofloxacin
- Protonamide
- Cycloserine
- [Ethambutol]
- [PASK]
Monitoring of Side Effects of the Chemotherapy

At baseline and then not less than monthly during treatment

- General blood and urine test
- Bilirubin, transaminase, acid urea, glucose, creatinine of blood serum, electrolytes ($K^+$, $Na^+$, $Mg^{2+}$, $Ca^{2+}$)
- Thyroid gland hormones
- Stool test for disbacteriosis
- EEG, ECG, audiogram
- Consultations: psychiatrist, ophthalmologist and otorhinolaryngologist
AGE AND GENDER DISTRIBUTION OF THE ENROLLED PATIENTS,

200 PATIENTS

**Female**: 35 (17.5%), **Male**: 165 (82.5%)

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>15–24</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>25–34</td>
<td></td>
<td>14</td>
</tr>
<tr>
<td>35–44</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>45–54</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>55–64</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>65 years and older</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>
DRUG RESISTANCE OF MBT IN THE ENROLLED PATIENTS (%)

72%

28%

primary MDR

acquired MDR

In combination with DR to all the 1st line drugs— in 29 out of 56 patients

In combination with all the 1st line drugs – in 95 out of 144 patients
DIAGNOSTICS AND TREATMENT OF MDR TB  
IN OREL OBLAST RUSSIAN FEDERATION

STATUS OF THE ENROLLED PATIENTS BY 01.10.2006  
(abs number, 200 patients)

- **94; 47%** completed treatment
- **24; 12%** treatment interrupted on medical reasons
- **6; 3%** defaulted
- **2; 1%** died
- **26; 13%** transferred out
- **26; 13%** intensive phase
- **18; 9%** continuation phase
- **4; 2%** failure

(abs number, 200 patients)
Location of Treatment

30 patients, registered within the period of 11.02-12.05 (by 01.10.2006)

- Orel Oblast TB Dispensary
  - In-patient facility – 4 patients
  - Day-patient facility – 4 patients
  - Home treatment – 3 patients
- TB Hospital at SIZO # 1 Orel – 2 patients
- Orel Oblast Psychiatric hospital – 1
- TB cabinets at Central rayon hospitals– 8
- FOP – 8
DURATION OF THE INTENSIVE PHASE

137 patients who have completed it

- 5 мес.: 3 cases
- 6 мес.: 45 cases
- 7 мес.: 35 cases
- 8 мес.: 27 cases
- 9 мес.: 13 cases
- 10 мес.: 5 cases
- 11 мес.: 7 cases
- 12 мес.: 2 cases
Duration of treatment in patients with completed treatment
(by 01.10.06)

n=94
SIDE EFFECTS
(in 200 patients, who were on treatment for more than 1 month.)

- 119; 59% no side effects
- 59; 30% correction of side effects without any changes in the regimen
- 22; 11% dose decrease, temporal discontinuation of the drug
- 13; 7% discontinuation of the drug

- 106; 52%
The accompany diseases in all 200 patients (75%)

- Alcoholism – 68%
- Diabetes – 10%
- Cardiovascular diseases – 11%
- Drug addiction – 5%
- Diseases of urinary system – 7.5%
- Disturbance of nervous system – 9%
- Gastrointestinal disturbances – 17%
# Rate of side effects in all the 200 patients (1)

390 side effects

<table>
<thead>
<tr>
<th>SIDE EFFECTS</th>
<th>Abs. number</th>
<th>%</th>
<th>DRUG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hearing deterioration</td>
<td>63</td>
<td>31,5</td>
<td>K; Cap</td>
</tr>
<tr>
<td>Vestibular disturbances</td>
<td>3</td>
<td>1,5</td>
<td>K; Cap</td>
</tr>
<tr>
<td>Nephrotoxicity</td>
<td>15</td>
<td>7,5</td>
<td>K; Cap; Ofl</td>
</tr>
<tr>
<td>Laboratory hepatotoxicity</td>
<td>15</td>
<td>7,5</td>
<td>Ofl: Prot</td>
</tr>
<tr>
<td>Toxic hepatitis</td>
<td>3</td>
<td>1,5</td>
<td>Ofl</td>
</tr>
<tr>
<td><strong>Dyspeptic disorders, diarrhea</strong></td>
<td>50</td>
<td>25,0</td>
<td>Prot; Ofl</td>
</tr>
<tr>
<td>Sic reactions</td>
<td>11</td>
<td>5,5</td>
<td>K; Cap</td>
</tr>
<tr>
<td>Stomach bleeding</td>
<td>1</td>
<td>0,5</td>
<td>Ofl</td>
</tr>
<tr>
<td>EEG changes</td>
<td>29</td>
<td>14,5</td>
<td>Cs</td>
</tr>
<tr>
<td><strong>EEG changes and clinical symptoms</strong></td>
<td>55</td>
<td>27,5</td>
<td>Cs, Ofl</td>
</tr>
</tbody>
</table>
## Rate of side effects in all the 200 patients (2)

390 side effects

<table>
<thead>
<tr>
<th>SIDE EFFECTS</th>
<th>Abs. number</th>
<th>%</th>
<th>DRUG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthralgia</td>
<td>42</td>
<td>21,0</td>
<td>Z; Prot; Ofl</td>
</tr>
<tr>
<td>Anemia</td>
<td>10</td>
<td>5,0</td>
<td>Ofl; Cap; Cs</td>
</tr>
<tr>
<td>Leucopenia</td>
<td>1</td>
<td>0,5</td>
<td>Prot</td>
</tr>
<tr>
<td>Laboratory hypothyroidism</td>
<td>29</td>
<td>14,5</td>
<td>Prot</td>
</tr>
<tr>
<td>Eosinophilia</td>
<td>11</td>
<td>5,5</td>
<td>Cap; K; Ofl</td>
</tr>
<tr>
<td>Hypomagnesemia</td>
<td>14</td>
<td>7,0</td>
<td>Cap; Ofl</td>
</tr>
<tr>
<td>Hyperleucocytosis</td>
<td>2</td>
<td>1,0</td>
<td>Ofl</td>
</tr>
<tr>
<td>Exacerbation of the chronic gastritis</td>
<td>3</td>
<td>1,5</td>
<td>Ofl</td>
</tr>
<tr>
<td>Cardiovascular disturbances</td>
<td>14</td>
<td>7,0</td>
<td>Ofl</td>
</tr>
<tr>
<td>Disbacteriosis</td>
<td>17</td>
<td>8,5</td>
<td>Ofl</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>1</td>
<td>0,5</td>
<td>Ofl</td>
</tr>
<tr>
<td>Candidosis</td>
<td>1</td>
<td>0,5</td>
<td>Ofl</td>
</tr>
</tbody>
</table>
TIME SPAN OF THE DEVELOPMENT OF SIDE EFFECTS OF CHEMOTHERAPY

- Green bars: correction without changes in the regimen
- Light grey bars: dose modification
- Red bars: discontinuation of the drug

The diagram shows the distribution of time spans in months for the development of side effects of chemotherapy. The x-axis represents the months (1-18), and the y-axis represents the frequency of side effects. The legend is located at the bottom of the diagram.
Culture conversion in MDR TB patients under the DOTS+ program

<table>
<thead>
<tr>
<th>Month</th>
<th>1 month</th>
<th>2 month</th>
<th>3 month</th>
<th>4 month</th>
<th>5 month</th>
<th>6 month</th>
<th>7 month</th>
<th>8 month</th>
<th>9 month</th>
<th>11 month</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>25.3%</td>
<td>18.9%</td>
<td>10.0%</td>
<td>4.2%</td>
<td>3.2%</td>
<td>1.6%</td>
<td>2.1%</td>
<td>1.6%</td>
<td>0.5%</td>
<td>1.0%</td>
<td>68.9%</td>
</tr>
</tbody>
</table>

C+ 31.1%
Results:

- Culture conversion in MDR TB Patients was achieved in 68.9% of patients, enrolled into the program.
- Side effects of the treatment with second line drugs are not the serious obstacle for the adequate TB treatment.
- Experience of the DOTS + project in Orel Oblast proves possibility of the effective treatment of MDR TB in oblast level TB service facilities.