Management of drug-induced liver injury (TB-DILI) in HIV positive patients treated for TB


### DILI Classification

<table>
<thead>
<tr>
<th>Mild DILI</th>
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<tbody>
<tr>
<td>Clinically well with elevated ALT &lt;200 IU/l and total bilirubin &lt;40umol/l</td>
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<table>
<thead>
<tr>
<th>Moderate DILI</th>
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<tbody>
<tr>
<td>Clinically well and elevated ALT &gt;200 IU/l irrespective of total bilirubin</td>
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<table>
<thead>
<tr>
<th>Severe DILI</th>
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<tbody>
<tr>
<td>Isolated Jaundice (ALT &lt;120 IU/l and total bilirubin &gt;40umol/l)</td>
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<th>Severe DILI</th>
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<tr>
<td>Clinically not well (nausea, vomiting, abdominal pain) meets DILI definition</td>
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### Steps for Management

#### Mild DILI
- **TB confirmed or probable:** Continue TB drugs
- Continue ART
- Repeat ALT and Bilirubin in one week

- **Improved**
- **Stable but elevated for 4 consecutive weeks**
- **Further increase**
- **Meets DILI definition? Re-classify**

- **Stop lab monitoring**
- **Consider other causes**
- Refer for abdominal sonar and further workup

#### Moderate DILI

- **Stop TB treatment, Bactrim and all other hepatotoxic drugs**
- **Stop ART**
  (if the patient has been on a stable ART regimen for >6 months, consider continuing ART)

- **Start Strep (or Kanamycin), EMB, Moxi** (NB: Strep contraindicated if GFR <60)

- **Repeat ALT and Bilirubin** (inpatient: 2-3 days, outpatient: 7 days)

- **Start re-challenge when ALT <100IU/l and Bilirubin normal**

  **Step 1:** Add RIF
  **Step 2:** Check ALT, Bilirubin
  **Step 3:** Add INH
  **Step 4:** Check ALT, Bilirubin
  **Step 5:** ALT, Bilirubin improving/stable, stop Strep and Moxi

  **Final Regimen:** RIF/INH/EMB for 9 months OR refer to table

- **Consider PZA re-challenge (especially if TBM/resistance to other drugs)**

  **Monitor ALT, Bilirubin weekly for 4 weeks after re-challenge**

#### Severe DILI

- **Admit the patient**
- **Consult ID or TB-treatment specialist if available**
- **Assess INR and monitor blood glucose**

- **Stop ART**
  NNRTI-based regimen: Stop NNRTI first and NRTIs 5-7 days later.
  If in liver failure, stop all ART immediately
  PI-based regimen: Stop all ART at once

- **TB treatment regimen for patients with drug-susceptible TB when a first line drug is omitted**

<table>
<thead>
<tr>
<th>Drug omitted</th>
<th>Intensive Phase</th>
<th>Continuation Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH, Moxi, EMB, Strep</td>
<td>RIF, INH/EMB x 2 months</td>
<td>INH, Moxi, EMB x 16 months</td>
</tr>
<tr>
<td>INH</td>
<td>RIF, Moxi, EMB x 12 months</td>
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<tr>
<td>PZA</td>
<td>RIF, INH, EMB x 9 months</td>
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