Maintenance
Immunosuppression in Patients
with Autoimmune Hepatitis (AIH)

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AASLD Practice Guidelines: Remission Criteria in AIH

- Disappearance of symptoms
- Normal serum bilirubin and gamma globulin levels
- Serum aminotransferase level normal or less than twice normal
- Normal hepatic tissue or minimal inflammation and no interface hepatitis

Pathogenesis of AIH

- Cell mediated cytotoxicity associated with liver infiltrating cytotoxic T-cells
- Immunosuppression does not treat the underlying predisposition or causative factors
- Therapy suppresses the cascade of immune activation
- Withdrawal of therapy = relapse

Natural History of Untreated Autoimmune Hepatitis

Percentage of Patients in Remission after Treatment Withdrawal

% Remaining in Remission

## Frequency of Relapse

<table>
<thead>
<tr>
<th>Author</th>
<th>Duration to Relapse</th>
<th>Percent Relapse after Withdrawal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Czaja et al. (1980)</td>
<td>At 6 months</td>
<td>49%</td>
</tr>
<tr>
<td></td>
<td>After 3 re-treatments</td>
<td>86%</td>
</tr>
<tr>
<td>Hegarty et al. (1983)</td>
<td>median = 9 weeks</td>
<td>87%</td>
</tr>
<tr>
<td>Czaja et al. (1987)</td>
<td>mean = 5 ± 1 month</td>
<td>64%</td>
</tr>
<tr>
<td>Kanzler et al. (2001)</td>
<td>mean = 15 months</td>
<td>75%</td>
</tr>
<tr>
<td>Montano-Loza et al. (2007)</td>
<td>mean = 10 ± 2 months</td>
<td>77%</td>
</tr>
</tbody>
</table>
Consequences of Relapse After Drug Withdrawal

• Progression to cirrhosis: 40%
• Development of esophageal varices: 25%
• Death from hepatic failure: 15%

Consequences of Treatment Withdrawal in Type 1 AIH

Consequences of Retreatment

• Repeated exposure to HIGH DOSE corticosteroids
  – Major drug related side effects: 59% in patients who relapsed

• Increased risk of subsequent relapse
  – 86% relapse rate after three retreatments

We Cannot Predict Who Will Relapse

- Histological
  - Relapse occurred in 20% of patients even with normal hepatic architecture

- Clinical
  - Relapse occurred in 60%, 75%, and 74% respectively of patients who had normal serum AST, gamma globulin, and IgG levels

## Maintenance Therapy = Continued Remission

<table>
<thead>
<tr>
<th>Author</th>
<th>Treatment</th>
<th>Continued Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stellon et al. (1988)</td>
<td>AZA alone</td>
<td>88%</td>
</tr>
<tr>
<td>Johnson et al. (1995)</td>
<td>AZA alone</td>
<td>83%</td>
</tr>
<tr>
<td>Kanzler et al. (2001)</td>
<td>Corticosteroids alone/±AZA/±Cyclophosphamide</td>
<td>67%</td>
</tr>
</tbody>
</table>
# Cost of Maintenance

## Immunosuppression for One Year

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisone</td>
<td>10 mg/day</td>
<td>$120.24</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>50 mg/day</td>
<td>$433.68</td>
</tr>
</tbody>
</table>
Cost of One Percutaneous Liver Biopsy

- Radiology & Professional Fees = $2,084.00
- Pathology Fee = $222.65
- Liver Biopsy Kit Fee = $44.00
- Major & Minor Complications = $$$$$$

$2,350.65 +++
Cost Analysis

Maintenance Immunosuppression x 1 year

One Liver Biopsy
We Must Maintain Immunosuppression

• High frequency of relapse after treatment withdrawal
• Grave consequences of relapse
• To avoid frequent use of high dose steroids
• We cannot predict those who will relapse
• Maintenance therapy keeps patients in remission
• Cost effectiveness