BÜHLMANN Anti-MAG & Anti-Ganglioside Autoantibody ELISAs

Most Sensitive and Efficient Screening and Monitoring of Peripheral Neuropathies
Benefits

1. The only test on the market which is based on human antigen.
2. Best sensitivity as published in comparative studies (Jaskowski T et al., 2007 / Kuijf M et al., 2009), yielding 72% of positives.
3. Reliable standardisation for quantitative testing appreciated by international experts (Willison H J et al., 2011).
4. Most frequently applied anti-MAG autoantibody assay in clinical studies (see “References” on the last page).

Applications

Screening and Differentiation

- Clinically established cut-off value (1'500 BTU) as determined by Kuijf M et al., 2009, supports an efficient and sensitive screening (Joint Task Force of the EFNS and the PNS, 2006 and 2010).
- Excellent differentiation between healthy subjects and patients with a demyelinating neuropathy with immunoglobulin M (IgM) monoclonal gammopathy (IgM-PNP) with an area under the curve of 0.84 (Fig. 2, Kuijf M et al., 2009).
- BÜHLMANN anti-MAG ELISA is the only reliable quantitative tool to differentiate anti-MAG neuropathy into:
  1. typical anti-MAG neuropathy and high titres (>8'000 – 10'000 BTU) of anti-MAG antibodies and
  2. CIDP-like neuropathy, negative Immune fluorescence (IF) results and low BTU titres (< 8'000 BTU); Magy L et al., 2015.

Treatment Follow-up

Monitoring Rituximab treatment is an important tool for patient management. During successful treatment, the measurement of anti-MAG autoantibodies by the BÜHLMANN assay shows significant decrease allowing follow-up of patients in therapy (Fig. 3, Renaud S et al., 2003).
**Benefits**

1. **Combination** of MAG, GM1, GM2, GD1a, GD1b, GQ1b and high agreement with INCAT ELISA.
2. **Best** sensitivity available in the market (78%) as determined by Challah M et al. 2016 (Table 1).
3. **Less** false positive results as compared to other commercial assays.
4. **Less** misdiagnosis than competitors when using GanglioCombi (Table 1).

**Applications**

**Targeted and Sensitive Screening**

Due to high sensitivity (Table 1) and its “unique” combination of relevant neural antigens, the BÜHLMANN GanglioCombi® MAG ELISA is the ideal tool:

- for **screening** acute and chronic autoimmune peripheral neuropathies from one single patient sample (Fig. 4).
- to **confirm** most of the complex pathology patterns of autoimmune neuropathies (Table 2, next page).

**Differentiation**

- Combination of anti-MAG and relevant anti-Ganglioside antibodies onto the BÜHLMANN GanglioCombi® MAG ELISA allows for differentiation of relevant antibodies in pathological samples.
- Confirmation of high prevalence of anti-MAG autoantibodies among neural antibodies in autoimmune neuropathies. 15% of sera that are originally requested for anti-Ganglioside autoantibodies turn out positive for anti-MAG antibodies (Fig. 4).
- Increase of sensitivity and determination by coremeasurement of gangliosides with anti-MAG antibodies, in patients with demyelinating neuropathies and IgM monoclonal antibodies (IgM-PNP). A significant proportion of anti-MAG negative samples from this group show positivity for the relevant anti-ganglioside antibodies offered in the BÜHLMANN kit (Fig. 5).

**Table 1:** Method comparison with clinical samples. ELISA vs. Line Blots

<table>
<thead>
<tr>
<th>Method</th>
<th>BÜHLMANN GanglioCombi ELISA</th>
<th>Dotzen Line Blot</th>
<th>Generic Assays Line Blot</th>
<th>D-tek</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expected positivity</td>
<td>14</td>
<td>12</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Erroneous positivity</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Confirmed diagnosis</td>
<td>17</td>
<td>15</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Misdiagnosis</td>
<td>5</td>
<td>7</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>78%</td>
<td>67%</td>
<td>50%</td>
<td>50%</td>
</tr>
</tbody>
</table>

**Figure 4:** Prevalence of anti-neural autoantibodies

**Figure 5:** Frequency of anti-MAG- and anti-Ganglioside autoantibodies in patients with IgM-PNP
BÜHLMANN Anti-MAG & Anti-Ganglioside Autoantibody ELISAs

Interpretation of Autoimmune Neuropathies

<table>
<thead>
<tr>
<th>Acute Neuropathies (IgG related)</th>
<th>Chronic Neuropathies (IgM related)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>profile</strong></td>
<td><strong>Antibodies ELISA</strong></td>
</tr>
<tr>
<td>&quot;MAG&quot;</td>
<td><strong>Anti-MAG</strong></td>
</tr>
<tr>
<td>GM1</td>
<td><strong>Anti-GM1</strong></td>
</tr>
<tr>
<td>GM2</td>
<td><strong>Anti-MAG</strong></td>
</tr>
<tr>
<td>GD1a</td>
<td><strong>Anti-GM1</strong></td>
</tr>
<tr>
<td>GD1b</td>
<td><strong>Anti-MG1</strong></td>
</tr>
<tr>
<td>GQ1b</td>
<td><strong>Anti-MG1</strong></td>
</tr>
</tbody>
</table>

**Acute Motor Axononal Neuropathy**
- **MAG**
- **Anti-GM1**

**Acute Motor/Sensory Axononal Neuropathy**
- **MAG**
- **Anti-GM1**

**Miller Fisher Syndrome**
- **Anti-GM1**
- **Anti-MG1**

**Neuropathy associated to Cytomegalovirus (CMV)**
- **Anti-MG1**
- **Anti-MG1**

**Multifocal motor neuropathy**
- **Anti-GM1**
- **Anti-MG1**

**Chronic Ataxic Neuropathy**
- **Anti-GM1**
- **Anti-MG1**

**Optalymygosis**
- **Anti-GM1**
- **Anti-MG1**

**Neuropathy associated with IgM monoclonal gammopathy**
- **Anti-GM1**
- **Anti-MG1**

Table 2: Most prevalent pathologies and interpretation of autoimmune neuropathies

<table>
<thead>
<tr>
<th>Acute Neuropathies</th>
<th>Chronic Neuropathies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AMAN</strong></td>
<td><strong>MMN</strong></td>
</tr>
<tr>
<td><strong>AMSAN</strong></td>
<td><strong>CANOMAD</strong></td>
</tr>
<tr>
<td><strong>MFS</strong></td>
<td><strong>MAG Neuropathy</strong></td>
</tr>
<tr>
<td><strong>CMV induced</strong></td>
<td><strong>IgM PNP</strong></td>
</tr>
</tbody>
</table>

**primary immune response**

**secondary immune response**

60 References — BÜHLMANN neural antibody ELISAs in the Literature

anti-MAG Autoantibodies ELISA

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anti-SGPG Autoantibodies ELISA

Table: Most prevalent pathologies and interpretation of autoimmune neuropathies

BÜHLMANN GanglioCombi® ELISA/anti-GM1 Autoantibodies ELISA

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