Immunoglobulins in Peripheral Neuropathy
Clinical Studies for the Treatment of CIDP with Immunoglobulin
Introduction

- Chronic inflammatory demyelinating polyneuropathy, Guillain-Barré syndrome and multifocal motor neuropathy are all forms of peripheral neuropathy.

- If treated early, disease progression may be slowed; however, if treatment is not started until late in the course of the disease, permanent damage may have already occurred.

- The following slides discuss two clinical trials that showed efficacy of intravenous immunoglobulins in chronic inflammatory demyelinating polyneuropathy (CIDP).
Summary of evidence for CIDP

- **Intravenous Immune Globulin CIDP Efficacy (ICE) trial**¹
  - n = 117
  - Primary endpoint met
    - 54%* IVIG treated patients improved ≥1 point on the INCAT scale
  - Secondary endpoints met
    - MRC sum score = +4.7
    - Grip strength (dominant hand) = +16.1

- **Privigen Impact on Mobility and Autonomy (PRIMA) trial**²
  - n = 28
  - Primary endpoint met
    - 60.7% patients showed an improvement in INCAT score
  - Secondary endpoints met
    - MRC sum score = +6.9
    - Grip strength (dominant hand) = +14.1

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*This value for Gamunex decreases to 47.5% if 4 patients with stable, adjusted INCAT score at Week 6 are excluded from the analysis.

CIDP: chronic inflammatory demyelinating polyneuropathy, INCAT: inflammatory neuropathy cause and treatment, IVIG: intravenous immunoglobulin, MRC: Medical Research Council
Evidence for IVIG in CIDP: ICE trial

Intravenous Immune Globulin CIDP Efficacy trial¹

- Designed to assess long-term efficacy of IVIG in CIDP
- Study design:

CIDP: chronic inflammatory demyelinating polyneuropathy
IVIG: intravenous immunoglobulin

Evidence for IVIg in CIDP: ICE trial

ICE trial results\(^1\)

<table>
<thead>
<tr>
<th>Efficacy measurement / endpoint</th>
<th>Result</th>
</tr>
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<tbody>
<tr>
<td>INCAT</td>
<td>54%* (32/59) subjects who were IVIG treated and 21% (12/58) subjects placebo treated improved, p = 0.0002</td>
</tr>
<tr>
<td>MRC sum score</td>
<td>+4.7 (p = 0.004)</td>
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</table>
| Grip strength (kPa)             | Dominant hand = +16.1 (p = 0.007)  
Non-dominant hand = +17.6 (p = 0.001) |
| Safety                          | AEs related to study drug: 55% (62 IVIG subjects)  
SAEs: 9/1096 infusions IVIG group (0.8% per infusion)  
11/575 infusions placebo group (1.9% per infusion)  
Most common AEs: headache, pyrexia and hypertension |

*This value for Gamunex decreases to 47.5% if 4 patients with stable, adjusted INCAT score at Week 6 are excluded from the analysis.

AE: adverse events, CIDP: chronic inflammatory demyelinating polyneuropathy, INCAT: inflammatory neuropathy cause and treatment scale, IVIG: intravenous immunoglobulin, MRC: Medical Research Council, SAE: serious adverse event

Evidence for IVIg in CIDP: PRIMA trial

Privigen Impact on Mobility and Autonomy\(^1\)

- **Primary endpoint:**
  - The percentage of responders (responder rate) at completion visit (Week 25), assessed by adjusted INCAT score

CIDP: chronic inflammatory demyelinating polyneuropathy, INCAT: inflammatory neuropathy cause and treatment scale, IVIG: intravenous immunoglobulin

Evidence for IVIg in CIDP: PRIMA trial

**PRIMA trial results**¹

<table>
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<tr>
<td><strong>INCAT</strong></td>
<td>Total responder rate = 60.7% (76.9% IVIG pre-treated, 46.7% IVIg untreated)</td>
</tr>
<tr>
<td><strong>MRC sum score</strong>&lt;br&gt;(change vs. baseline)</td>
<td>+ 6.9</td>
</tr>
<tr>
<td><strong>Grip strength</strong>&lt;br&gt;(change vs. baseline)</td>
<td>Dominant hand = +14.1&lt;br&gt;Non-dominant hand = +10.4</td>
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<tr>
<td><strong>Safety</strong></td>
<td>AEs: 108/259 infusions (rate per infusion 0.417)&lt;br&gt;AEs possibly related to study drug: 60.7% (17 subjects)&lt;br&gt;SAEs: 4 in 4 subjects&lt;br&gt;Most common AE: headache</td>
</tr>
</tbody>
</table>

MRC sum score and grip strength increased from baseline
AE: adverse events, CIDP: chronic inflammatory demyelinating polyneuropathy, INCAT: inflammatory neuropathy cause and treatment scale, IVIG: intravenous immunoglobulin, MRC: Medical Research Council, SAE: serious adverse event

Responsiveness to IVIg therapy

- Not all patients with CIDP respond to IVIG.
- Factors contributing to lack of responsiveness include:
  - Delay in CIDP diagnosis and treatment:
    - Increases the extent of axonal damage\(^1\)
    - Decreased time between symptom onset and treatment has been shown to correlate with decreased disease activity, disease progression and disability\(^2\)
  - Increase in axonal damage leads to:
    - Decreased compound muscle action potential (CMAP)\(^1\)
    - Muscle atrophy\(^3\)
  - TAG-1 polymorphisms
    - Link found in Japanese population\(^4\)

CIDP: chronic inflammatory demyelinating polyneuropathy, CMAP: compound muscle action potential, IVIG: intravenous immunoglobulin, TAG: transient axonal glycoprotein