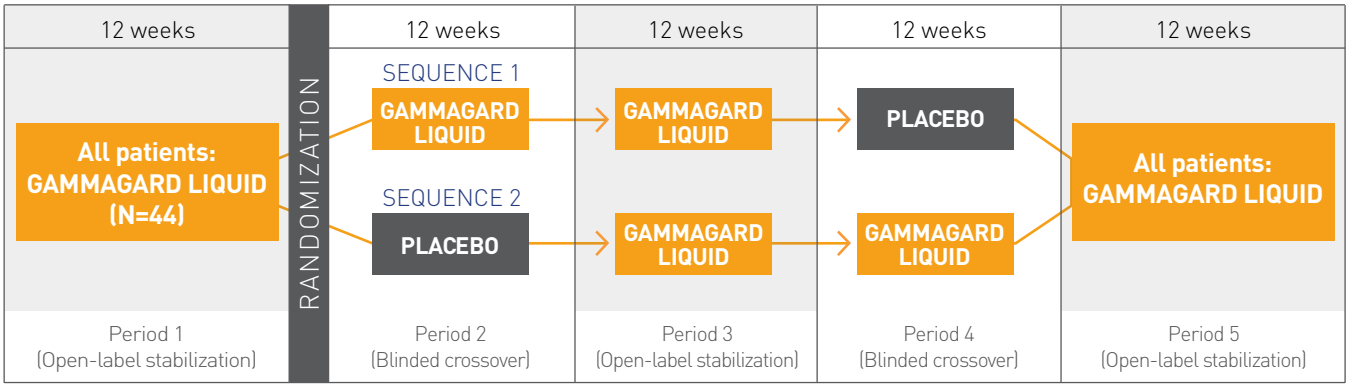

## The largest controlled multifocal motor neuropathy (MMN) clinical trial to date

The efficacy and safety of GAMMAGARD LIQUID® [Immune Globulin Infusion (Human)] 10% were evaluated in 44 adult patients with MMN over the course of 60 weeks, as shown below.[1,2]

### Study design: Hahn et al. 2013




- Patients were randomized 1:1 to either double-blind treatment of IVIG (GAMMAGARD LIQUID) followed by placebo for 12 weeks each or the reverse. Open-label IVIG was administered for 12 weeks at the beginning and end of the study for clinical stabilization, and between double-blinded periods to prevent a carryover effect[2]
- The co-primary efficacy endpoints were maximal grip strength in the more affected hand measured with a DynEx digital dynamometer and disability as determined by the upper limb portion of Guy's Neurologic Disability Score (GNDS).[2] Secondary efficacy outcomes included requirement for accelerated switch and time required for the 9-hole peg board test with the dominant and non-dominant hand[2]

## INDICATION

GAMMAGARD LIQUID is indicated as a maintenance therapy to improve muscle strength and disability in adult patients with Multifocal Motor Neuropathy (MMN). GAMMAGARD LIQUID for MMN is for intravenous use only.

## IMPORTANT SAFETY INFORMATION

**WARNING: THROMBOSIS, RENAL DYSFUNCTION, and ACUTE RENAL FAILURE**

- **Thrombosis may occur with immune globulin (IG) products, including GAMMAGARD LIQUID. Risk factors may include advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling vascular catheters, hyperviscosity, and cardiovascular risk factors. Thrombosis may occur in the absence of known risk factors.**
- **Renal dysfunction, acute renal failure, osmotic nephrosis, and death may occur in predisposed patients with immune globulin intravenous (IGIV) products. Patients predisposed to renal dysfunction include those with any degree of pre-existing renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs. Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. GAMMAGARD LIQUID does not contain sucrose.**
- **For patients at risk of thrombosis, administer GAMMAGARD LIQUID at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk of hyperviscosity.**

### Contraindications

- History of anaphylactic or severe systemic hypersensitivity reactions to human IG
- IgA-deficient patients with antibodies to IgA and a history of hypersensitivity to human IG. Anaphylaxis has been reported with intravenous (IV) use of GAMMAGARD LIQUID.

***Please see additional Important Safety Information throughout and click for Full Prescribing Information.***

Statistically significant improvement in functioning in primary endpoints vs placebo:

# Significantly improved grip strength and reduced disability[1]

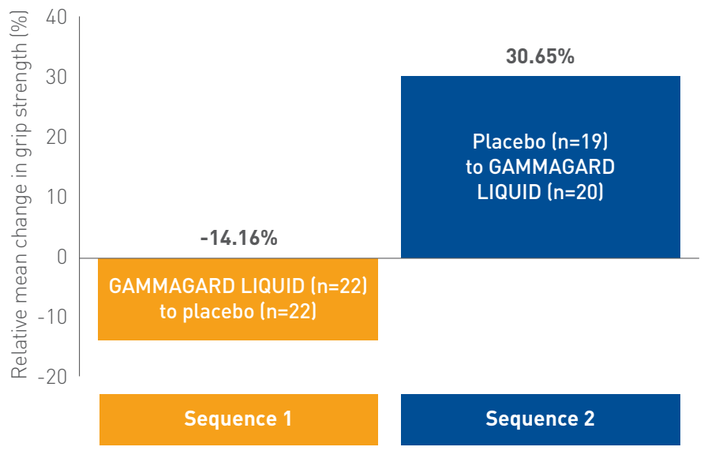
## Improved grip strength*

The difference in relative change in mean grip strength for GAMMAGARD LIQUID and placebo of 22.30% (95% CI, 9.92-34.67) was statistically significant (*P*<0.001).*[1]

**SEQUENCE 1:** GAMMAGARD LIQUID to placebo: Placebo –30.52% (SD 29.68); GAMMAGARD LIQUID –16.36% (SD 32.84).[1] Relative mean change calculated by subtracting the GAMMAGARD LIQUID value from the placebo value.[1]

**SEQUENCE 2:** Placebo to GAMMAGARD LIQUID: GAMMAGARD LIQUID +1.46% (SD 10.72); placebo –29.19% (SD 39.95).[1] Relative mean change calculated by subtracting the placebo value from the GAMMAGARD LIQUID value.[1]

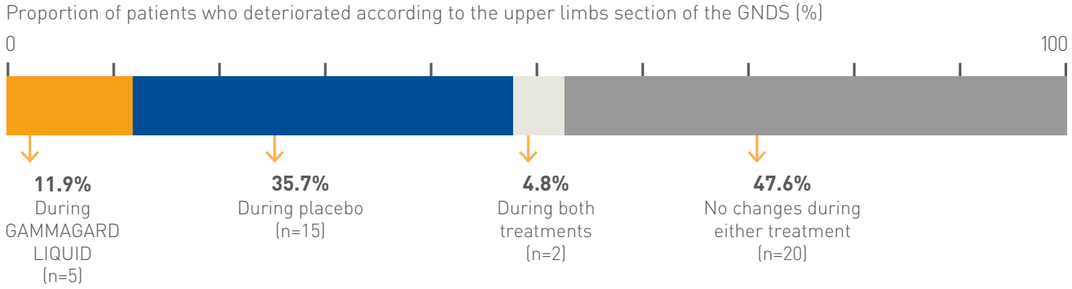
*Measured in the more affected hand following treatment (ITT; N=41).




## Reduced disability

Three times more patients receiving placebo had worsening disability than GAMMAGARD LIQUID (*P*=0.021).[1,2]

As determined by GNDS scores that include tasks of daily living, including tying shoestrings, zipping and buttoning clothing, and washing hair.[3]




ITT; N=42
CI, confidence interval; GNDS, Guy's Neurologic Disability Score; ITT, intent to treat; MMN, multifocal motor neuropathy; SD, standard deviation.

## IMPORTANT SAFETY INFORMATION (continued)

### Warnings and Precautions

**Hypersensitivity:** Severe hypersensitivity reactions may occur, even in patients who have tolerated previous treatment with human IG. If a hypersensitivity reaction occurs, discontinue infusion immediately and institute appropriate treatment. IgA-deficient patients with antibodies to IgA are at greater risk of developing potentially severe hypersensitivity reactions, including anaphylaxis.

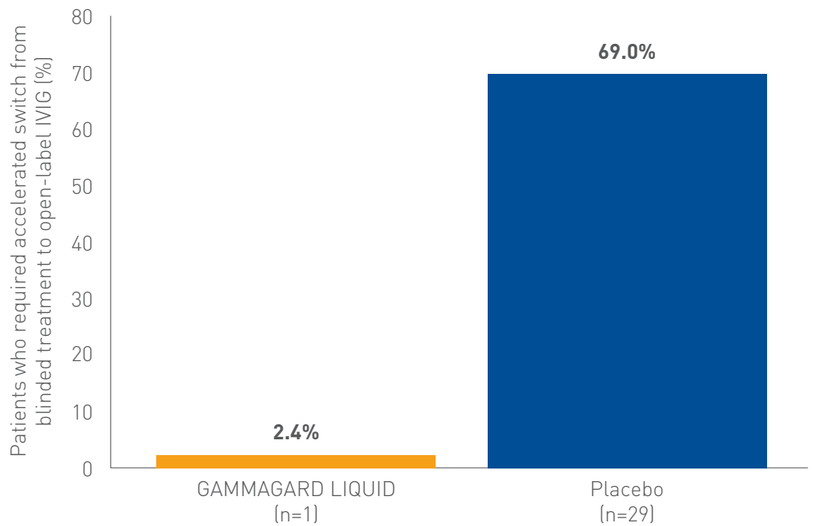
**Renal Dysfunction/Failure:** Acute renal dysfunction/failure, acute tubular necrosis, proximal tubular nephropathy, osmotic nephrosis, and death may occur with IV use of IG products, especially those containing sucrose. Ensure patients are not volume depleted prior to infusion. In patients at risk due to pre-existing renal insufficiency or predisposition to acute renal failure, assess renal function before initiation and throughout treatment, and use the minimum infusion rate practicable for IV administration. If renal function deteriorates, consider discontinuation.

**Hyperproteinemia, increased serum viscosity, and hyponatremia** may occur. It is critical to distinguish true hyponatremia from a pseudohyponatremia because certain treatments may lead to volume depletion, a further increase in serum viscosity, and a predisposition to thromboembolic events.



## Functional deterioration: accelerated switch

Over two-thirds of patients required an accelerated switch from blinded treatment to open-label GAMMAGARD LIQUID vs one patient treated with GAMMAGARD LIQUID (*P*<0.001).[1,2]




## IMPORTANT SAFETY INFORMATION (continued)

### Warnings and Precautions (continued)

**Thrombosis:** May occur following treatment with IG products and in the absence of known risk factors. In patients at risk, administer at the minimum dose and infusion rate practicable. Ensure adequate hydration before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.

**Aseptic Meningitis Syndrome:** Has been reported with use of IG and may occur more frequently in females. Conduct a thorough neurological exam on patients exhibiting signs and symptoms, to rule out other causes of meningitis. Discontinuing IG treatment has resulted in remission within several days without sequelae.

**Hemolysis:** GAMMAGARD LIQUID contains blood group antibodies, which may cause a positive direct antiglobulin reaction and hemolysis. Monitor patients for signs and symptoms of hemolysis and delayed hemolytic anemia and, if present, perform appropriate confirmatory lab testing.

**Transfusion-Related Acute Lung Injury:** Non-cardiogenic pulmonary edema may occur with IV administered IG. Monitor patients for pulmonary adverse reactions. If suspected, perform appropriate tests for presence of anti-neutrophil and anti-HLA antibodies in both product and patient serum. May be managed using oxygen therapy with adequate ventilatory support.

**Transmittable Infectious Agents:** Because GAMMAGARD LIQUID is made from human plasma, it may carry a risk of transmitting infectious agents (e.g., viruses, other pathogens). No confirmed cases of viral transmission or variant Creutzfeldt-Jakob disease (vCJD) have been associated with GAMMAGARD LIQUID.

**Interference with Lab Tests:** False positive serological test results and certain assay readings, with the potential for misleading interpretation, may occur as the result of passively transferred antibodies.

### Adverse Reactions

The serious adverse reactions in the clinical study for MMN were pulmonary embolism and blurred vision. The most common adverse reactions observed in ≥5% of subjects were headache, chest discomfort, muscle spasms, muscular weakness, nausea, oropharyngeal pain, and pain in extremity.

***Please see additional Important Safety Information throughout and click for Full Prescribing Information, including Boxed Warning regarding Thrombosis, Renal Dysfunction and Acute Renal Failure.***

# Safety profile and infusion experience[1,2]

GAMMAGARD LIQUID
[Immune Globulin Infusion (Human)] 10%

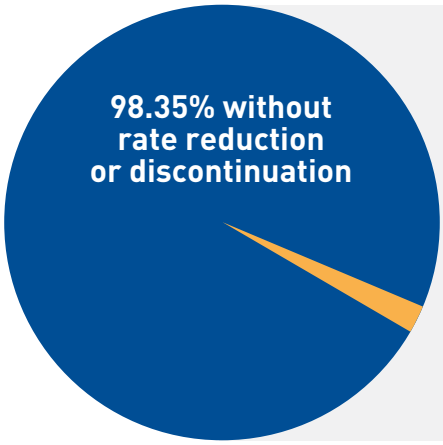
## Adverse reactions (ARs) occurring in ≥5% of patients*[1]

| | GAMMAGARD LIQUID | | Placebo | |
|---|---|---|---|---|
| AR | By infusion (N=983) N (%) | By subject (N=44) N (%) | By infusion (N=129) N (%) | By subject (N=43) N (%) |
| Headache | 28 (2.85%) | 14 (31.82%) | 3 (2.33%) | 2 (4.65%) |
| Nausea | 28 (2.85%) | 3 (6.82%) | 2 (1.55%) | 1 (2.33%) |
| Muscular weakness | 4 (0.41%) | 3 (6.82%) | 1 (0.78%) | 1 (2.33%) |
| Pain in extremity | 4 (0.41%) | 3 (6.82%) | 1 (0.78%) | 1 (2.33%) |
| Oropharyngeal pain | 4 (0.41%) | 3 (6.82%) | 0 (0.00%) | 0 (0.00%) |
| Chest discomfort | 3 (0.31%) | 3 (6.82%) | 0 (0.00%) | 0 (0.00%) |
| Muscle spasms | 3 (0.31%) | 3 (6.82%) | 0 (0.00%) | 0 (0.00%) |

*Defined as adverse events occurring during or within 72 hours of infusion or any causally related event occurring within the study period.[1]

- 72% (n=126/176) of non-serious ARs were considered mild, 21% (n=37/176) moderate and 7% (n=13/176) severe†[1]
- Two serious ARs occurred, pulmonary embolism and blurred vision, both of which were judged to be treatment related[1]

†**Mild:** transient discomfort that resolves spontaneously or with minimal intervention. **Moderate:** limited impairment of function that resolves spontaneously or with minimal intervention and no sequelae. **Severe:** marked impairment of function that can lead to temporary inability to resume normal life pattern; requires prolonged intervention or results in sequelae.[1]




## GAMMAGARD LIQUID INFUSION EXPERIENCES[2]

- **98.35%** of infusions with GAMMAGARD LIQUID were completed without the need for rate reduction or discontinuation for any reason
- **1.65%** of infusions required a reduction in rate or discontinuation for any reason‡

‡0.78% (n=1/129) of infusions with placebo required a reduction in rate or discontinuation for any reason.[2]

## IMPORTANT SAFETY INFORMATION (continued)

### Drug Interactions

Passive transfer of antibodies may transiently interfere with immune responses to live attenuated virus vaccines (e.g., measles, mumps, rubella, and varicella).

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**References: 1.** GAMMAGARD LIQUID. Prescribing information. Baxalta US Inc. **2.** Hahn AF, Beydoun SR, Lawson V; IVIG in MMN Study Team. A controlled trial of intravenous immunoglobulin in multifocal motor neuropathy. *J Peripher Nerv Syst.* 2013;18(4):321-330. **3.** Sharrack B, Hughes RA. The Guy's Neurological Disability Scale (GNDS): a new disability measure for multiple sclerosis. *Mult Scler.* 1999;5(4):223-233.


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