gamifant®
emapalumab-lzsg

Gamifant® (emapalumab-lzsg) Clinical Overview

INDICATIONS

Gamifant (emapalumab-lzsg) is an interferon gamma (IFNγ)-neutralizing antibody indicated for the treatment of adult and pediatric (newborn and older) patients with:

- Primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent, or progressive disease or intolerance with conventional HLH therapy.
- HLH/macrophage activation syndrome (MAS) in known or suspected Still's disease, including systemic Juvenile Idiopathic Arthritis (sJIA), with an inadequate response or intolerance to glucocorticoids, or with recurrent MAS.

IMPORTANT SAFETY INFORMATION

Infections

Gamifant may increase the risk of fatal and serious infections with pathogens including mycobacteria, herpes zoster virus, and histoplasma capsulatum. Do not administer Gamifant in patients with these infections until appropriate treatment has been initiated.

In patients with primary HLH receiving Gamifant in clinical trials, serious infections such as sepsis, pneumonia, bacteremia, disseminated histoplasmosis, necrotizing fasciitis, viral infections, and perforated appendicitis were observed in 32% of patients.

In patients with HLH/MAS in Still's disease receiving Gamifant in clinical trials, serious infections such as pneumonia, cytomegalovirus infection, cytomegalovirus infection reactivation, and sepsis were observed in 13% of patients.

Please see additional Important Safety Information on page 12.
Click here for full Prescribing Information for Gamifant.

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The Only FDA-Approved, IFNγ-neutralizing Antibody for Patients With Primary HLH or HLH/MAS in Still's Disease[1-3]

Overview of Gamifant® (emapalumab-lzsg)

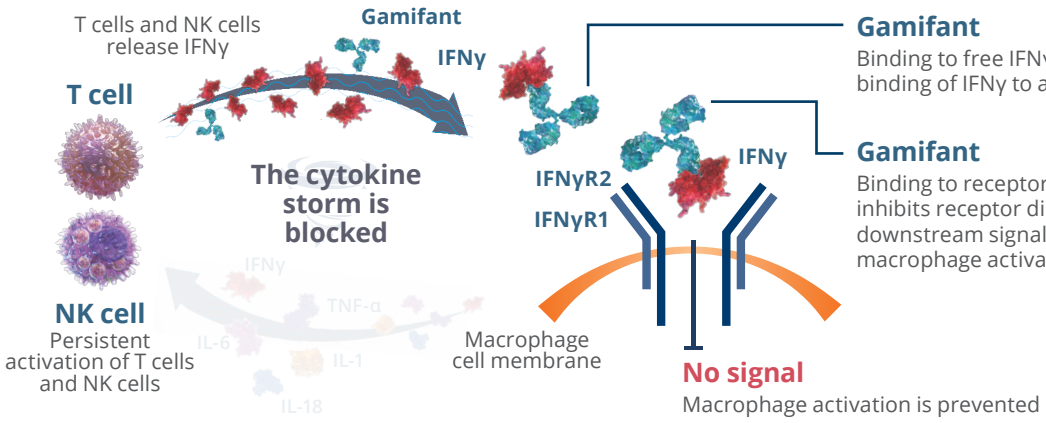
- Gamifant is indicated for the treatment of[1]:
  - adult and pediatric (newborn and older) patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent or progressive disease or intolerance with conventional HLH therapy (approved November 20, 2018)[2]
  - adult and pediatric (newborn and older) patients with HLH/macrophage activation syndrome (MAS) in known or suspected Still's disease, including systemic Juvenile Idiopathic Arthritis (sJIA), with an inadequate response or intolerance to glucocorticoids, or with recurrent MAS (approved June 27, 2025)[3]
- Gamifant is a monoclonal antibody specifically designed to help control IFNγ-driven hyperinflammation. Gamifant provides a targeted approach to controlling the hyperinflammatory surge, minimizing off-target effects.[1,4]

Gamifant pivotal clinical trials

- The efficacy of Gamifant in primary HLH was evaluated in a multicenter, open-label, single-arm trial in pediatric patients with suspected or confirmed primary HLH who were either treatment-naïve (n=7) or treatment experienced (n=27) with refractory, recurrent, or progressive disease or were intolerant of conventional HLH therapy.[1,5]
- Data evaluating the efficacy and safety of Gamifant in HLH/MAS in Still's disease were pooled across 2 open-label, single-arm, multicenter studies with 39 patients who had HLH/MAS in Still's disease, including sJIA, with an inadequate response to high-dose glucocorticoid treatment.[1]

Gamifant targets IFNγ, an upstream mediator of hyperinflammation

Mechanism of Action[1,6-8]



Gamifant binds to free and receptor-bound forms of IFNγ.[1,6]

This neutralizes IFNγ activity and prevents intracellular signaling.[1,6,7]

Hyperactivation of macrophages by excess IFNγ is prevented.[1,9]

Hyperinflammation is subdued.[1,10]

FDA=US Food and Drug Administration; IFNγ=interferon gamma; IL-18=interleukin-18; NK=natural killer.

IMPORTANT SAFETY INFORMATION (continued)

Infections (continued)

Evaluate patients for tuberculosis risk factors and test for latent infection prior to initiating Gamifant. Administer tuberculosis prophylaxis to patients at risk for tuberculosis or known to have a positive purified protein derivative (PPD) test result.

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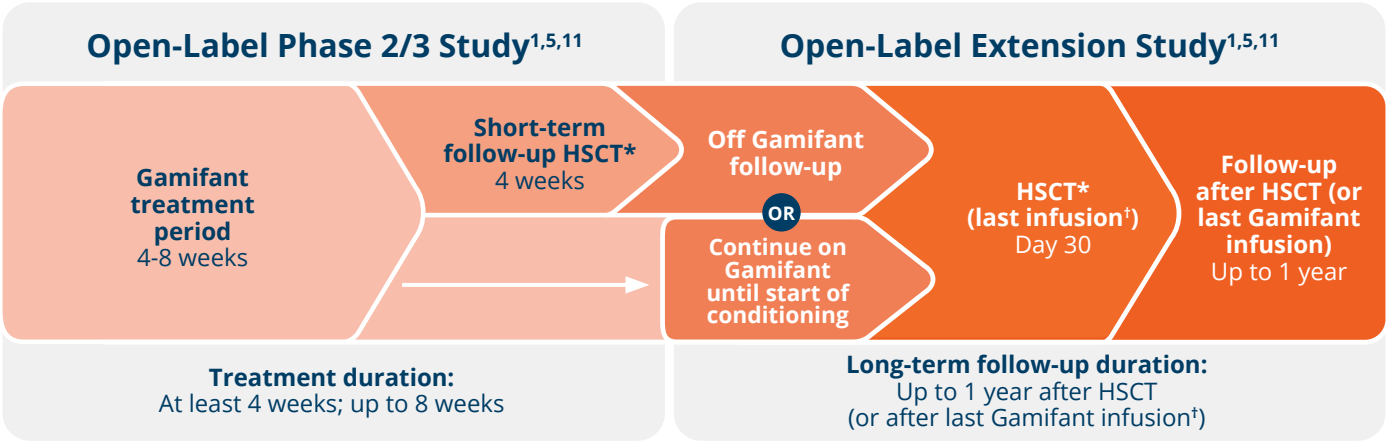
Pivotal Clinical Trial of Gamifant® (emapalumab-lzsg) in Primary HLH

Study design

- A multicenter, open-label, single-arm trial in 27 pediatric patients with primary HLH.[1]
- Patients had a confirmed diagnosis of primary HLH through either fulfillment of 5 of the 8 HLH-2004 criteria, a positive genetic test for mutations associated with primary HLH, or a family history consistent with HLH.[1]
- Patients had refractory, recurrent, or progressive disease or intolerance to conventional therapy.[1]
- Patients received a median of 3 prior therapies before enrollment in the trial.[1]
- Treatment was planned for 8 weeks, but could be shortened to no less than 4 weeks or extended, if needed, for HSCT timing.[5]



- Twenty-seven patients enrolled and 20 patients (74%) completed the study.[1]
- Efficacy was evaluated in 27 patients and safety was evaluated in 34 patients.[1,5]
- Twenty-two patients enrolled in the open-label extension study for up to 1 year after HSCT or after the last Gamifant infusion.[1]

*HSCT may occur in either the 04 or 05 study.[11]
†Last infusion for patients who do not undergo HSCT.[11]

HSCT=hematopoietic stem-cell transplantation.

IMPORTANT SAFETY INFORMATION (continued)

Infections (continued)

Consider prophylaxis for herpes zoster, *Pneumocystis jirovecii*, and fungal infection while receiving Gamifant. Employ surveillance testing during treatment with Gamifant.

Closely monitor patients receiving Gamifant for signs or symptoms of infection, promptly initiate a complete diagnostic workup appropriate for an immunocompromised patient, and initiate appropriate antimicrobial therapy.

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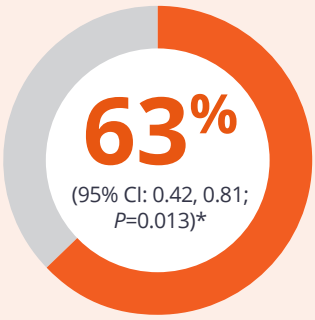
Pivotal Clinical Trial of Gamifant® (emapalumab-lzsg) in Primary HLH (continued)

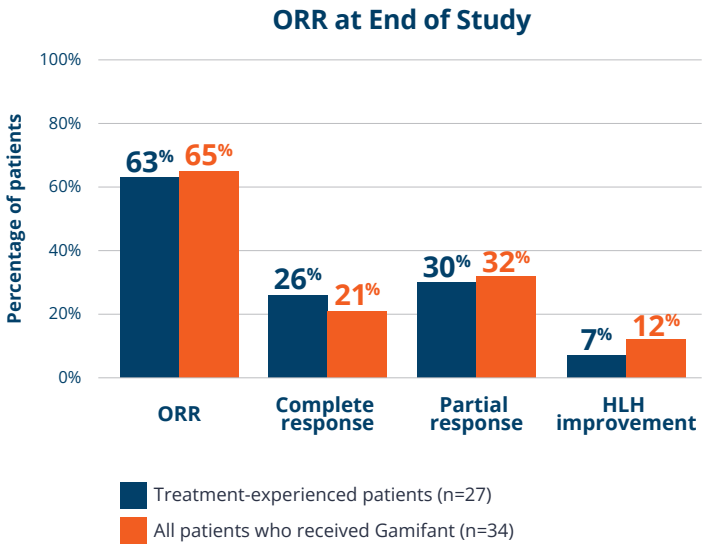
Primary endpoint: overall response rate (ORR)[1]



Gamifant provided a statistically and clinically significant reduction in primary HLH disease activity.

- **63% of treatment-experienced patients (17/27) achieved overall response.†**
- Median time to response was 8 days and responses were generally maintained.[5]
- Median duration of first response, defined as time from achievement of first response to loss of first response, was not reached.[1]

ORR at end of treatment[5,11]



What Is ORR?[1]

ORR is defined as achievement of either a **complete response** or **partial response** or **HLH improvement**, evaluated using an algorithm of objective clinical and laboratory parameters.

Complete response: Normalization of all HLH abnormalities (ie, no fever, no splenomegaly, neutrophils >1x10^9/L, platelets >100x10^9/L, ferritin <2000 µg/L, fibrinogen >1.50 g/L, D-dimer <500 µg/L, normal central nervous system symptoms, and no worsening of soluble CD25 >2-fold from baseline‡).

Partial response: Normalization of ≥3 HLH abnormalities.

HLH improvement: ≥3 HLH abnormalities improved by at least 50% from baseline.

*_P_ value based on Exact Binomial Test at a one-sided significance level of 2.5% comparing proportion of patients with overall response with the null hypothesis of 40%.[1]
†All patients received dexamethasone as background HLH treatment, with doses of between 5 mg/m^2 and 10 mg/m^2 per day.[1]
‡Soluble CD25 is also referred to as soluble IL-2 receptor.[1]

CD25=cluster of differentiation 25; CI=confidence interval; IL-2=interleukin 2.

IMPORTANT SAFETY INFORMATION (continued)

Increased Risk of Infection With Use of Live Vaccines

Do not administer live or live attenuated vaccines to patients receiving Gamifant and for at least 4 weeks after the last dose of Gamifant. The safety of immunization with live vaccines during or following Gamifant therapy has not been studied.

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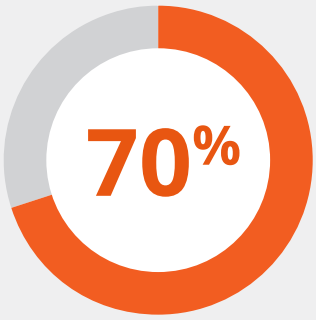
Pivotal Clinical Trial of Gamifant® (emapalumab-lzsg) in Primary HLH (continued)

Key secondary endpoint: HSCT[5]



70% of treatment-experienced patients (19/27) proceeded to HSCT.[1,*]

- Median time to transplant was 83 days for patients who had an inadequate response to initial therapy.[12]
- HSCT is the only cure for primary HLH, but it requires that hyperinflammation be controlled prior to transplant.[5]

Open-label Extension (OLE) Study

- 81% of pivotal study patients were enrolled in the OLE study.[1]
- Patients were monitored for up to 1 year after HSCT or after the last Gamifant infusion.[1]
- The safety and efficacy observed in the OLE was consistent with what was observed in the pivotal trial.[13]

In the pivotal clinical trial, Gamifant was administered for 4 to 8 weeks and nearly half of the patients remained on the starting dose[1,5]

44% of patients remained on the starting dose of 1 mg/kg

30% of patients required a modest dose escalation to 3 mg/kg to 4 mg/kg

26% of patients required a dose escalation to 6 mg/kg to 10 mg/kg

- The median time to dose increase was 27 days, with 22% of patients requiring a dose increase in the first week of treatment.[1]
- All patients received concomitant dexamethasone, which was tapered according to the treating physician's judgment.[1]

*All patients received dexamethasone as background HLH treatment, with doses of between 5 mg/m^2 and 10 mg/m^2 per day.[1]

IMPORTANT SAFETY INFORMATION (continued)

Infusion-Related Reactions

Infusion-related reactions in patients with primary HLH, including drug eruption, pyrexia, rash, erythema, and hyperhidrosis, were reported with Gamifant treatment in 27% of patients. In one-third of these patients, the infusion-related reaction occurred during the first infusion.

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Pivotal Clinical Trial of Gamifant® (emapalumab-lzsg) in Primary HLH (continued)

Dosage and administration of Gamifant in primary HLH[1]

Gamifant is administered by central or peripheral IV infusion over 1 hour twice a week (every 3 to 4 days) until HSCT is performed or unacceptable toxicity. The recommended starting dose is 1 mg/kg.

Dosage may be titrated up if disease response is unsatisfactory as assessed by a healthcare professional.* **After the patient's clinical condition is stabilized, decrease the dose** to the previous level to maintain clinical response. Discontinue Gamifant when a patient no longer requires therapy for the treatment of HLH.

Safety information

- Infusion-related reactions were reported with Gamifant treatment in 27% of patients. In one-third of these patients, the infusion-related reaction occurred during the first infusion.[1]

The most commonly reported adverse reactions (≥10%) included[1]

- Infection (56%)
- Hypertension (41%)
- Infusion-related reactions (27%)
- Pyrexia (24%)
- Hypokalemia (15%)
- Constipation (15%)
- Rash (12%)
- Abdominal pain (12%)
- Cytomegalovirus infection (12%)
- Diarrhea (12%)
- Lymphocytosis (12%)
- Cough (12%)
- Irritability (12%)
- Tachycardia (12%)
- Tachypnea (12%)

Disseminated histoplasmosis led to drug discontinuation in 1 patient.[1]

- Serious adverse reactions were reported in 53% of patients. The most common serious adverse reactions (≥3%) included infections, gastrointestinal hemorrhage, and multiple organ dysfunction.[1]
- Fatal adverse reactions occurred in 2 (6%) patients and included septic shock and gastrointestinal hemorrhage.[1]
- Additional selected adverse reactions (all grades) reported in <10% of patients treated with Gamifant included vomiting, acute kidney injury, asthenia, bradycardia, dyspnea, gastrointestinal hemorrhage, epistaxis, and peripheral edema.[1]
- 13 of 34 patients (38%) entered the study with ongoing infections or positive microbiological results.[14]

*Day 4: increase to 3 mg/kg. From Day 7 onward: increase to 6 mg/kg. From Day 10 onward: increase to 10 mg/kg (max dose).[1]

IV=intravenous.

IMPORTANT SAFETY INFORMATION (continued)

Infusion-Related Reactions (continued)

Infusion-related reactions in patients with HLH/MAS in Still's disease, including pyrexia, headache, paresthesia, bone pain, pruritic rash, and peripheral coldness, were reported with Gamifant treatment in 13% of patients. Infusion-related reactions were reported as mild in 8% of patients and as moderate in 5% of patients.

Monitor patients for infusion-related reactions, which can be severe. Interrupt the infusion for infusion reactions and institute appropriate medical management before continuing infusion at a slower rate.

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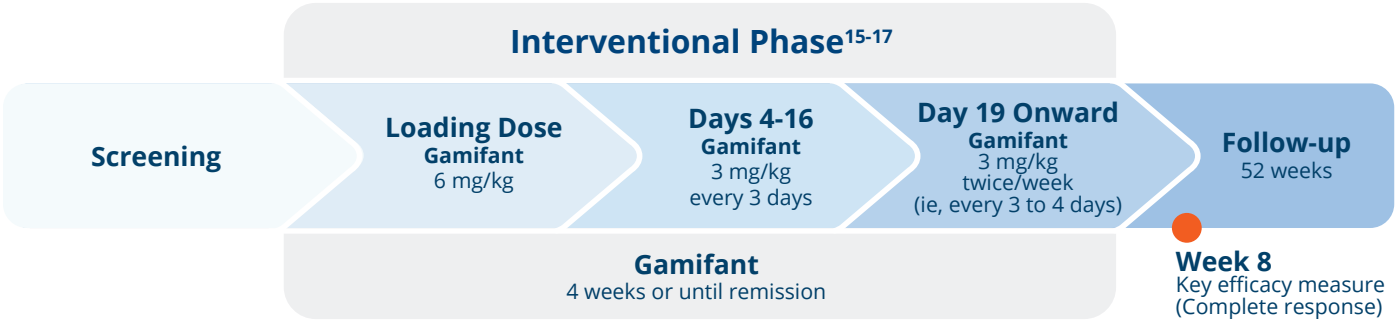
Gamifant® (emapalumab-lzsg) in HLH/MAS in Still's Disease

Study design

- 2 open-label, single-arm, multicenter studies in patients with HLH/MAS in Still's disease, including sJIA, with an inadequate response to high-dose glucocorticoid treatment.[1]
- The pooled analysis included all 39 patients from Study NI-0501-06 and Study NI-0501-14, and 37 patients completed the studies.[1]
- Patients had confirmed or suspected diagnosis of Still's disease, including sJIA or AOSD.[1]
- Patients had a diagnosis of active MAS with[1]:
  - Ferritin >684 ng/mL; and
  - Any 2 of 4 laboratory criteria: platelet count ≤181 × 10^9/L; AST >48 U/L; triglycerides >156 mg/dL; fibrinogen levels ≤360 mg/dL
- Patients had an inadequate response to high-dose IV glucocorticoids.[15]
- The interventional phase involved treatment with Gamifant for 4 weeks or until remission.[15] Patients were evaluated at Week 8 after the initial loading dose of Gamifant.[16]



IMPORTANT SAFETY INFORMATION (continued)

Adverse Reactions

Primary HLH

Serious adverse reactions were reported in 53% of patients. The most common serious adverse reactions (≥3%) included infections, gastrointestinal hemorrhage, and multiple organ dysfunction. Fatal adverse reactions occurred in 2 (6%) of patients and included septic shock and gastrointestinal hemorrhage.

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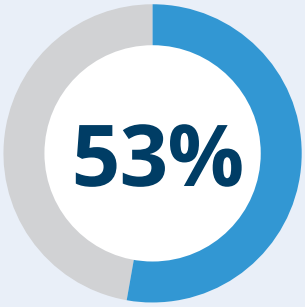
Gamifant® (emapalumab-lzsg) in HLH/MAS in Still's Disease (continued)

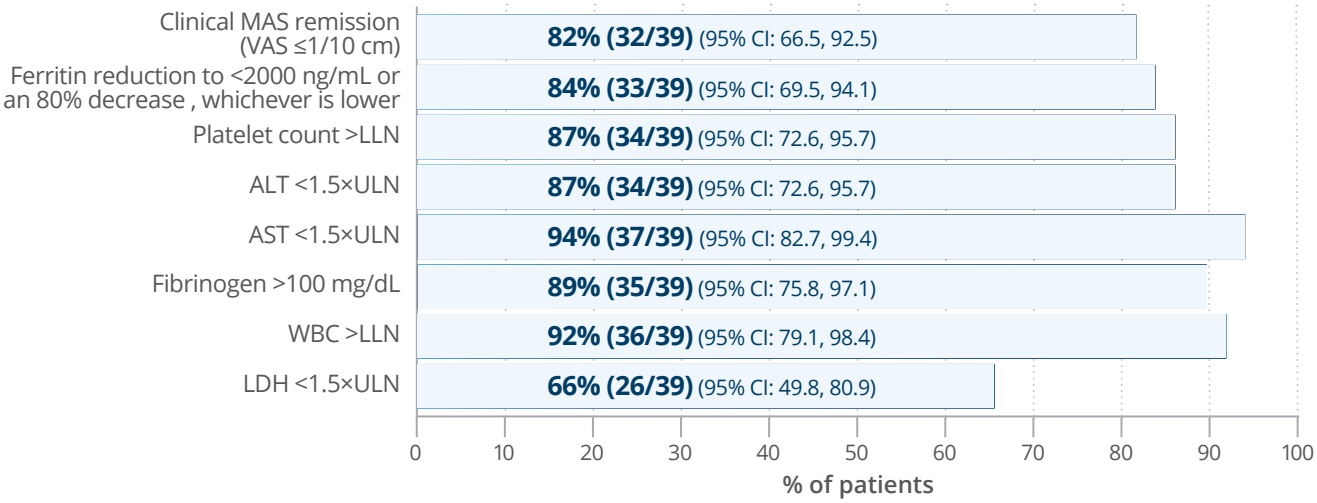
Key efficacy measure[1]:

Complete Response (CR) at Week 8



of patients (21/39) achieved CR at Week 8 (95% CI: 37.2, 69.9).

Individual components of the composite endpoint at Week 8[1]



What is CR?[1]

CR: a composite endpoint consisting of clinical resolution of HLH/MAS signs and symptoms as determined by clinician's assessment and normalization of 7 laboratory parameters:

- A VAS of ≤1 cm (range 0 to 10 cm)
  AND
  1. WBC >LLN
  2. Platelet count >LLN
  3. LDH <1.5×ULN
  4. ALT <1.5×ULN
  5. AST <1.5×ULN
  6. Fibrinogen >100 mg/dL
  7. Ferritin levels decreased by at least 80% from values at screening or baseline (whichever was higher) or <2000 ng/mL, whichever was lower

ALT=alanine aminotransferase; AST=aspartate aminotransferase; LDH=lactate dehydrogenase; LLN=lower limit of normal; ULN=upper limit of normal; VAS=visual analog scale; WBC=white blood cell.

IMPORTANT SAFETY INFORMATION (continued)

Adverse Reactions (continued)

Primary HLH (continued)

The most common adverse reactions were (≥10%) for Gamifant included infection (56%), hypertension (41%), infusion-related reactions (27%), pyrexia (24%), hypokalemia (15%), constipation (15%), rash (12%), abdominal pain (12%), CMV infection (12%), diarrhea (12%), lymphocytosis (12%), cough (12%), irritability (12%), tachycardia (12%), and tachypnea (12%).

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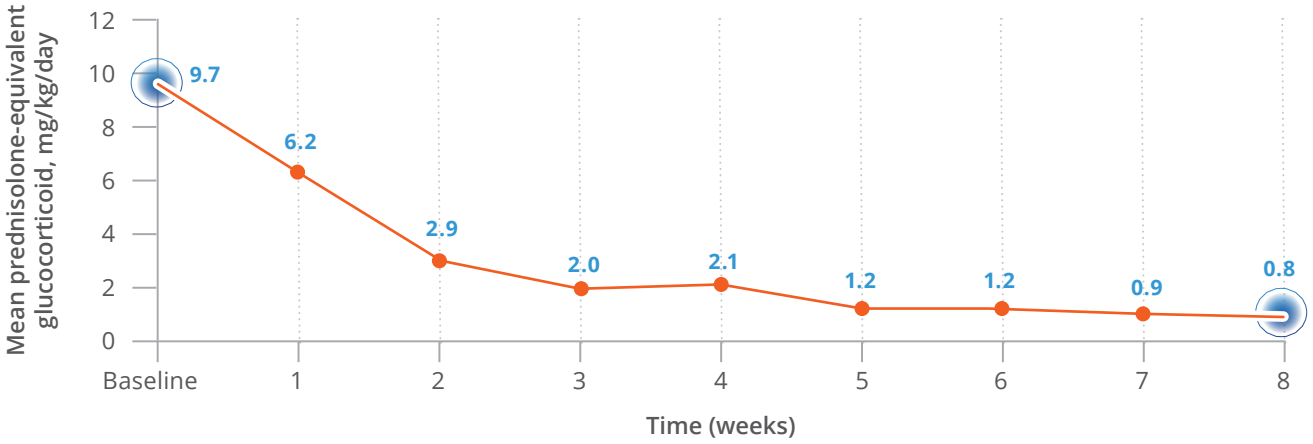
Efficacy of Gamifant® (emapalumab-lzsg) in HLH/MAS (continued)

Exploratory endpoint

Change in mean prednisolone-equivalent glucocorticoid dose*: Mean dose was 9.7 mg/kg/day at baseline and 0.8 mg/kg/day at Week 8.[18]



*Assessment of changes in glucocorticoid use was not statistically powered to evaluate treatment effect. These data are descriptive in nature and are observational only. No formal conclusion can be drawn.

IMPORTANT SAFETY INFORMATION (continued)

Adverse Reactions (continued)

HLH/MAS

Serious adverse reactions were reported in 12 patients (31%), with the most common serious adverse reaction being pneumonia (5%). Fatal adverse reactions occurred in two patients (5%) and included multiple organ dysfunction and circulatory shock.

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Gamifant® (emapalumab-lzsg) in HLH/MAS in Still's Disease (continued)

In the pivotal clinical trials, Gamifant was administered for 4 weeks or until remission

- The median cumulative Gamifant dose was 33.0 mg/kg (12.0-175.0) with a median duration of exposure of 29.0 days for the NI-0501-06/NI-0501-14 pooled data.[19]

Dosage and administration of Gamifant in HLH/MAS in Still's disease

Gamifant is administered by central or peripheral intravenous infusion. The recommended initial dose of Gamifant is 6 mg/kg. Following this dose, Gamifant should be administered as follows[1,*]:

✚ Continue administering Gamifant twice per week until HLH/MAS remission is achieved based on healthcare provider assessment.

*For patients with unsatisfactory improvement in their clinical condition as assessed by a healthcare provider, Gamifant may be increased to a maximum cumulative dose of 10 mg/kg over 3 days AND administered every 2 days or once daily. After the patient's clinical condition has improved, consider decreasing the dose to the previous level and assess whether clinical response is maintained. If the clinical condition is not stabilized while receiving the maximum dosage, consider discontinuing Gamifant.[1]

IMPORTANT SAFETY INFORMATION (continued)

Adverse Reactions (continued)

HLH/MAS (continued)

The most common adverse reactions (≥10%) for Gamifant included viral infection (44%), rash (21%), anemia (18%), leukopenia (15%), thrombosis (15%), bacterial infections (13%), headache (13%), hyperglycemia (13%), infusion-related reactions (13%), abdominal pain (10%), hypertension (10%), pyrexia (10%), and thrombocytopenia (10%).

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Gamifant® (emapalumab-lzsg) in HLH/MAS in Still's Disease (continued)

Safety information

In patients with HLH/MAS in Still's disease, Gamifant demonstrated a safety profile consistent with the safety profile that had been previously established.[3] Serious adverse reactions were reported in 31% (12/39) of patients.[1] Fatal adverse reactions occurred in 5% (2/39) of adult patients and included circulatory shock and multiple organ dysfunction.[1] 3% (1/39) of patients discontinued treatment due to an event of pneumonia.[1]

Adverse reactions[1]	Gamifant % (N=39)
Viral infection **Cytomegalovirus (CMV) infection or reactivation**	44 36
Rash	21
Anemia	18
Leukopenia	15
Thrombosis	15
Bacterial infection	13
Headache	13
Hyperglycemia	13
Infusion-related reactions	13
Abdominal pain	10
Hypertension	10
Pyrexia	10
Thrombocytopenia	10

- The most common adverse reactions (≥20%) were viral infections, including CMV infection or reactivation, and rash.[1]

IMPORTANT SAFETY INFORMATION

Infections

Gamifant may increase the risk of fatal and serious infections with pathogens including mycobacteria, herpes zoster virus, and histoplasma capsulatum. Do not administer Gamifant in patients with these infections until appropriate treatment has been initiated.

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Indications and Important Safety Information

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Infusion-related reactions in patients with HLH/MAS in Still's disease, including pyrexia, headache, paresthesia, bone pain, pruritic rash, and peripheral coldness, were reported with Gamifant treatment in 13% of patients. Infusion-related reactions were reported as mild in 8% of patients and as moderate in 5% of patients.

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Adverse Reactions

Primary HLH

Serious adverse reactions were reported in 53% of patients. The most common serious adverse reactions (≥3%) included infections, gastrointestinal hemorrhage, and multiple organ dysfunction. Fatal adverse reactions occurred in 2 (6%) of patients and included septic shock and gastrointestinal hemorrhage.

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For statutory pricing disclosures, please click here for more information.

References:

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