



EUROPEAN
HEMATOLOGY
ASSOCIATION

The central graphic features a wireframe globe with a blue grid, surrounded by a network of glowing blue nodes and lines. Scattered around the globe are several colorful, faceted geometric shapes in shades of red, orange, yellow, green, and blue. The text 'EHA 2021 VIRTUAL' is prominently displayed in the center.

EHA 2021 VIRTUAL

| **Connecting Hematology - For Clinical and Research Excellence**

NARSOPLIMAB (OMS721) TREATMENT CONTRIBUTES TO IMPROVEMENTS IN ORGAN FUNCTION IN ADULT PATIENTS WITH HIGH-RISK TRANSPLANT-ASSOCIATED THROMBOTIC MICROANGIOPATHY

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June 11, 2021

Stem cell transplantation – Clinical

DISCLOSURES

MAP: Advisory board – MolMed, NexImmune; DSMB – Cidara Therapeutics, Servier, Medigene; Honoraria – Abbvie, Astellas, Bellicum, Celgene, Bristol-Myers Squibb, Incyte, Kite/Gilead, Merck, Miltenyi Biotec, Novartis, Nektar Therapeutics, Omeros, Takeda; Research support – Incyte, Kite/Gilead, Miltenyi Biotec, and Novartis; Volunteer – Board of Directors of Be The Match (National Marrow Donor Program, NMDP), CIBMTR Cellular Immunotherapy Data Resource (CIDR) Executive Committee

MSC: Advisory board – Jazz, Omeros; Speakers bureau – Jazz, Amgen, Sanofi, Servier

RFD: Advisory board – Astellas, Basilea, Gentium, Genzyme, Gilead Sciences, Incyte, Jazz Pharmaceuticals, MSD, Omeros, Pfizer, Sanofi-Oncology, Therakos; Research support – Celgene, Genzyme, Janssen, MSD, Novartis, Omeros, Pierre-Fabre, Roche-Diagnostics, Sanofi-Oncology; Speaker bureau – Amgen, Astellas, Bristol Myers-Squibb, Celgene, Gentium, Genzyme, Gilead Sciences, Incyte, Jazz Pharmaceuticals, MSD, Novartis, Pierre-Fabre, Omeros, Pfizer, Sanofi-Oncology, Therakos

SG: Advisory board – Omeros; Research support – Amgen, Celgene, CSL Behring, Janssen, Pfizer, Quintiles, Sanofi

VTVH: Advisory board – Alexion, Janssen, Omeros; Consultant – Omeros; Research funding – Jazz; Travel support – Alexion

JL: Advisory board – Omeros; Research grant – Alexion, Jazz Pharma, Omeros

NL: Advisory board – AbbVie, Aduro, Lilly, Takeda

OP: Advisory board – Jazz, Gilead, MSD, Omeros, Shionogi, SOBI; Honoraria or travel support – Astellas, Gilead, Jazz, MSD, Neovii Biotech, Novartis, Pfizer, Therakos; Research support – Gilead, Incyte, Jazz, Neovii Biotech, Takeda

AR: Advisory board – Amgen, Astellas, Celgene, Gilead, Italfarmaco, Jazz, Novartis, Omeros, Pfizer, Roche, Sanofi Aventis; Consultant – Omeros; Lecturer – Pfizer; Symposia – Amgen, Celgene, Novartis, Roche; Travel support – Amgen, Celgene, Gilead, Italfarmaco, Novartis, Roche

MS: Ad-hoc advisory board – Kite, A Gilead Company; Consultant – Angiocrine Bioscience, Inc., Omeros, McKinsey & Company; Research support – Angiocrine Bioscience, Inc.; One-time speaking commitment: i3Health (CME)

NN: Employee – Omeros

SW: Employee – Omeros

Support: This study was sponsored by Omeros Corporation, Seattle, WA

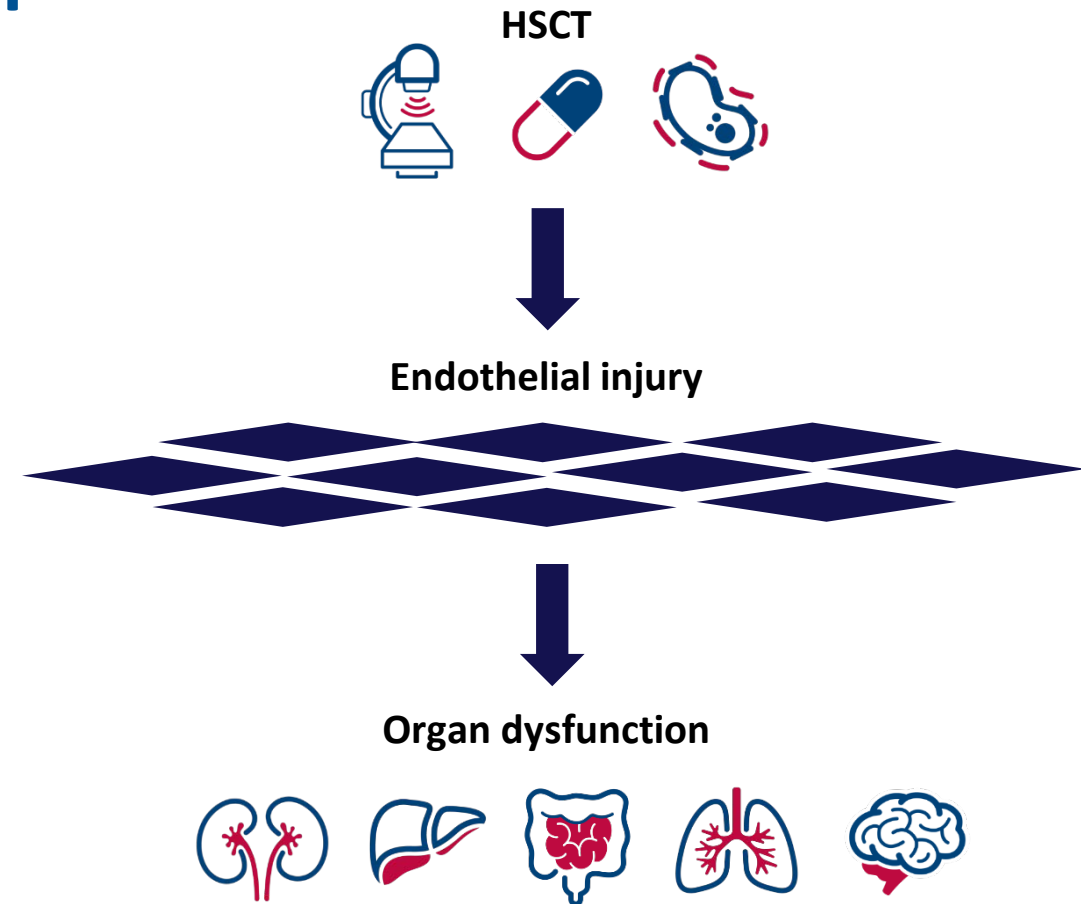
Acknowledgements: Medical writing support was provided by Charlotte A. Osborne, PhD, CMPP of Omeros Corporation, Seattle, WA

Narsoplimab is an investigational agent and has not been approved by any regulatory agency.

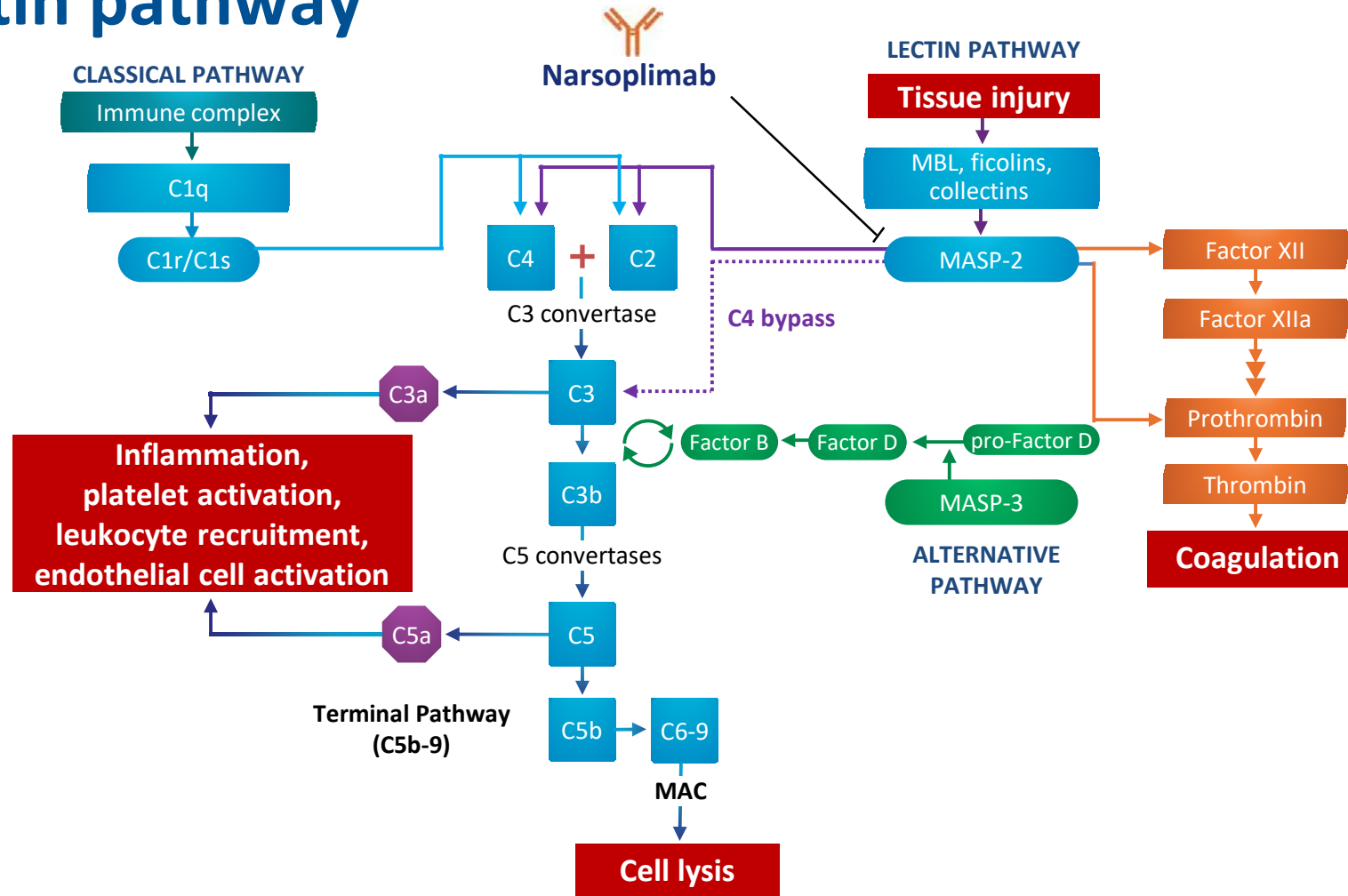


HSCT-TMA is initiated by endothelial injury associated with transplantation

- Endothelial injury activates the lectin pathway of the complement system
- Complement activation leads to inflammation and thrombus formation that result in organ dysfunction and failure
- HSCT-TMA has been reported to occur in up to 39% of patients undergoing allogeneic HSCT but remains under-recognized



Narsoplimab inhibits MASP-2, the effector enzyme of the lectin pathway



Narsoplimab was investigated in an open-label pivotal trial for HSCT-TMA

- Primary endpoints:
 - Efficacy (improvement in laboratory markers AND clinical status)
 - Safety and tolerability
- Secondary endpoints:
 - Survival (100-day and overall)
 - Change from baseline in laboratory markers

Organ	Criteria for Improvement in Clinical Status (Any of the following)
Blood	Transfusion freedom
Kidney	Reduction of creatinine > 40% or Normalization of creatinine and reduction of creatinine > 20%
	or Discontinuation of renal replacement therapy
	Extubation and discontinuation of ventilator support or Discontinuation of non-invasive mechanical ventilation (continuous positive pressure ventilation)
Gastrointestinal (Tissue diagnosis)	Improvement assessed using the gastrointestinal measures in the MAGIC criteria
Neurologic	Limited to stroke, PRES, seizures, weakness



The study population was high-risk and had multiple risk factors for poor outcomes

Demographics	N = 28
Median age (years)	48 (range 22–68)
Male gender, n (%)	20 (71.4)
Malignant underlying disease, n (%)	27 (96.4)
Risk factors for poor outcomes related to HSCT itself and HSCT-TMA:	
Presence of GVHD, n (%)	19 (67.9)
Significant infection, n (%)	24 (85.7)
Kidney dysfunction, n (%)	21 (75.0)
Neurologic dysfunction, n (%)	16 (57.1)
Pulmonary dysfunction, n (%)	5 (17.9)
Multiple organ TMA involvement, n (%)	14 (50.0)

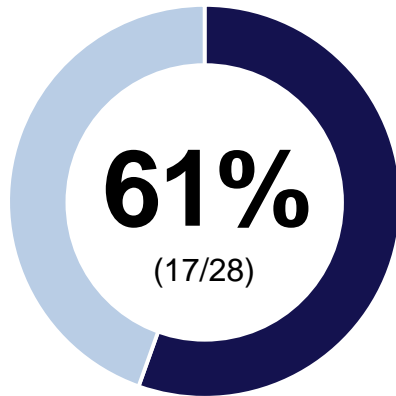
This heterogeneous population was highly reflective of “real-world” practice



Kidney dysfunction defined as doubling of serum creatinine from pre-transplant.
GVHD, graft versus host disease; HSCT, hematopoietic stem cell transplantation; HSCT-TMA hematopoietic stem cell transplantation-associated thrombotic microangiopathy; TMA, thrombotic microangiopathy.

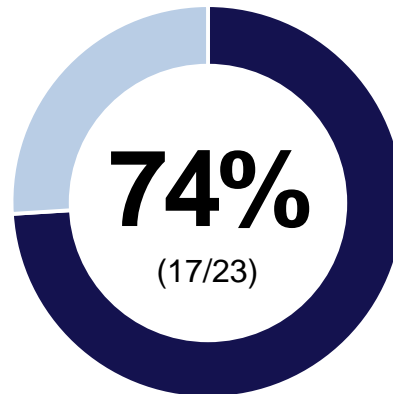
Most patients responded to narsoplimab

All treated patients (N=28)
(95% CI)



(40.6% to 78.5%)
 $P < 0.0001^*$

Patients treated per protocol (≥ 4 weeks of dosing) (n=23)
(95% CI)



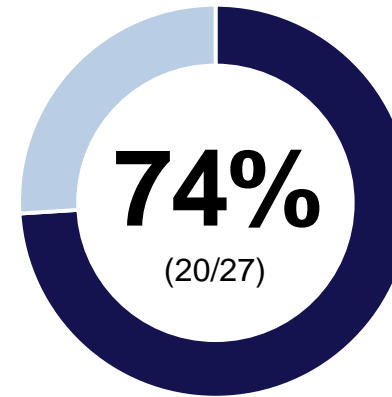
(51.6% to 89.8%)
 $P < 0.0001^*$

- Patients received a range of 2–8 scheduled doses (mean 6.3 doses)
- Median duration of treatment was 8 weeks

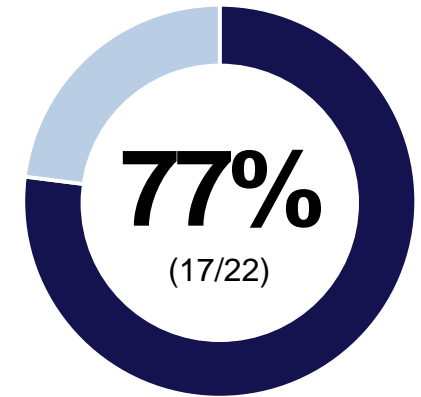
Patients treated with narsoplimab experienced improvement in organ function

Organ	Criteria for Improvement in Organ Function (Any of the following)
Kidney	Reduction of creatinine > 40% or Normalization of creatinine and reduction of creatinine > 20% or Discontinuation of renal replacement therapy
Pulmonary	Extubation and discontinuation of ventilator support or Discontinuation of non-invasive mechanical ventilation (continuous positive pressure ventilation)
Gastrointestinal (Tissue diagnosis)	Improvement assessed using the gastrointestinal measures in the MAGIC criteria
Neurologic	Limited to stroke, PRES, seizures, weakness

Improvement in any organ function:



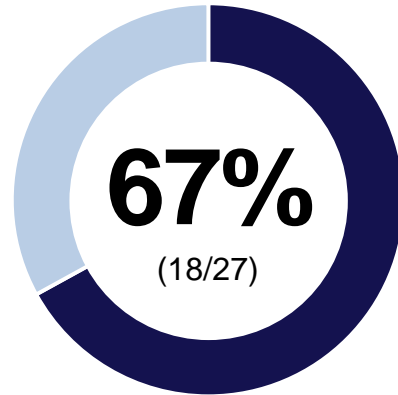
All treated patients



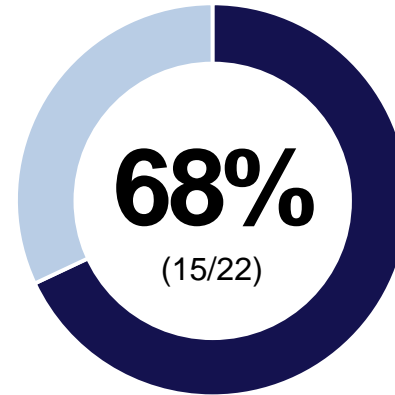
Patients treated per protocol



Improvement in kidney function with narsoplimab



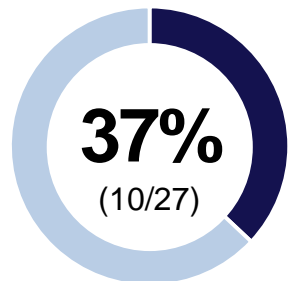
All treated patients



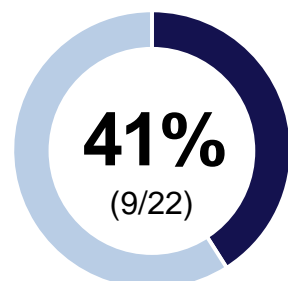
Patients treated per protocol



Reduction of creatinine >40%:

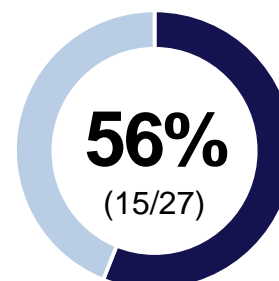


All treated patients

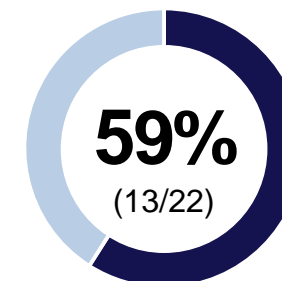


Patients treated per protocol

Creatinine <ULN and reduction of creatinine >20%:

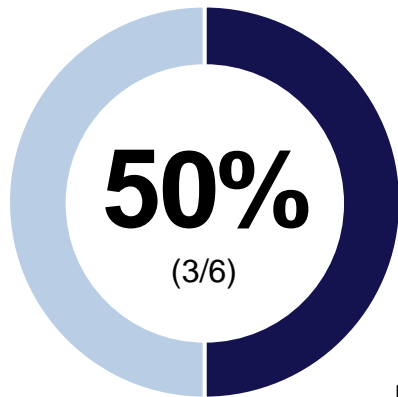


All treated patients

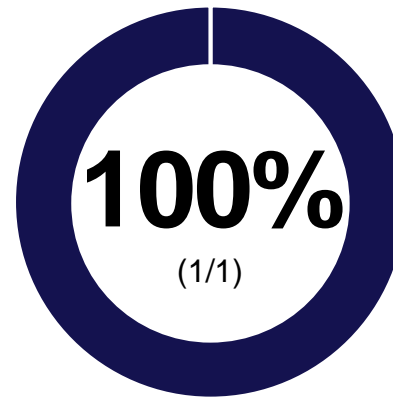
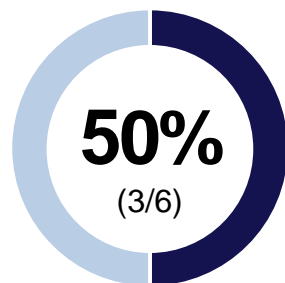


Patients treated per protocol

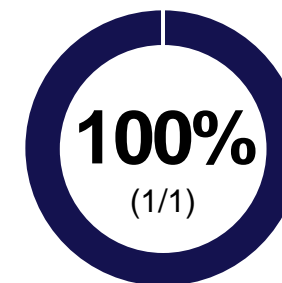
Improvement in neurologic and GI function with narsoplimab



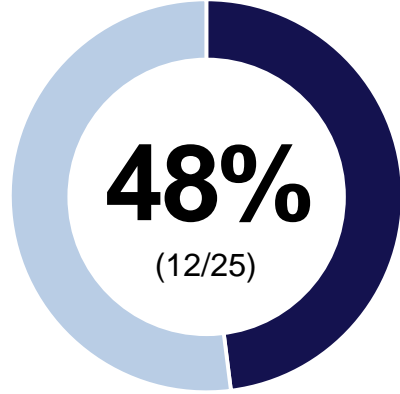
Improvement in reversible neurologic conditions:



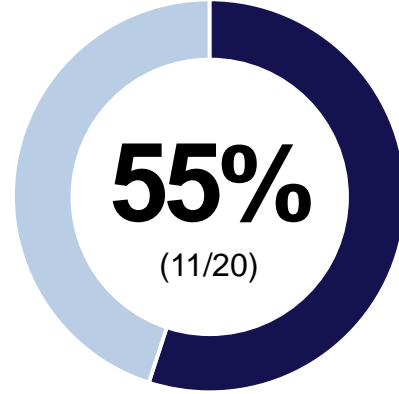
Improvement in >1 grade in MAGIC GI criteria:



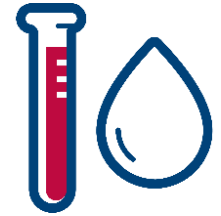
Freedom from transfusion with narsoplimab



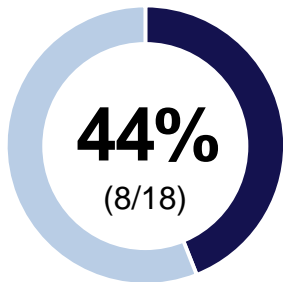
All treated patients



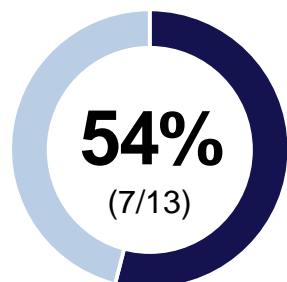
Patients treated per protocol



Freedom from platelet transfusion:

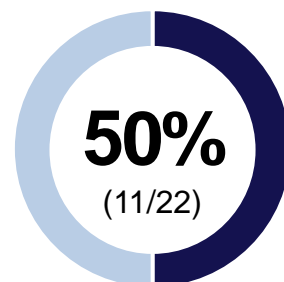


All treated patients

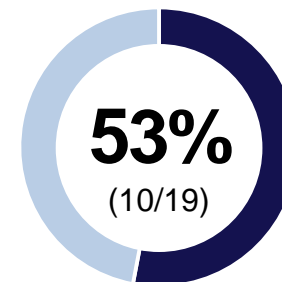


Patients treated per protocol

Freedom from red blood cell transfusion:



All treated patients



Patients treated per protocol

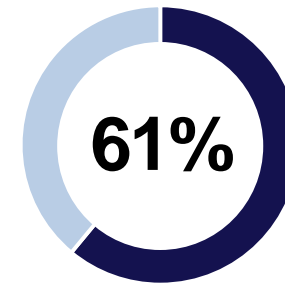
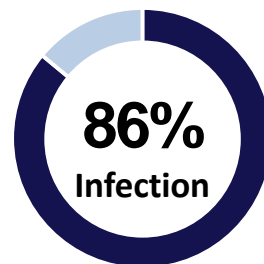
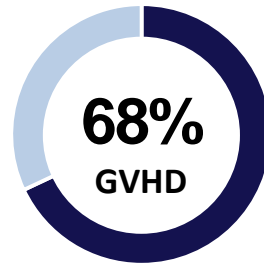
Narsoplimab was well tolerated in this very sick population with multiple comorbidities

- The observed adverse events are comparable to those typically seen in the post-transplant population
- Six patients died during the core study period due to causes common in HSCT:
 - 1 of septic shock, 2 of progressive AML, 2 of neutropenic sepsis, and 1 of GVHD and TMA

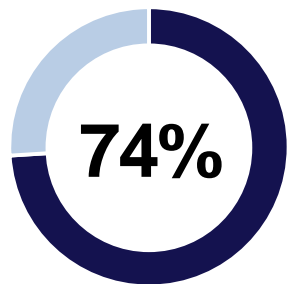
Adverse Events, n (%)	(N = 28)
Any Event	27 (96.4)
Pyrexia	10 (35.7)
Diarrhea	9 (32.1)
Vomiting	9 (32.1)
Nausea	7 (25.0)
Neutropenia	7 (25.0)
Fatigue	6 (21.4)
Hypokalemia	6 (21.4)
Back pain	5 (17.9)

Narsoplimab resulted in clinically meaningful improvements in patients with HSCT-TMA

At baseline, patients were at high risk for poor outcomes



of all treated patients responded to narsoplimab



achieved a significant improvement in any organ function

In this study, narsoplimab was safe and well tolerated



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