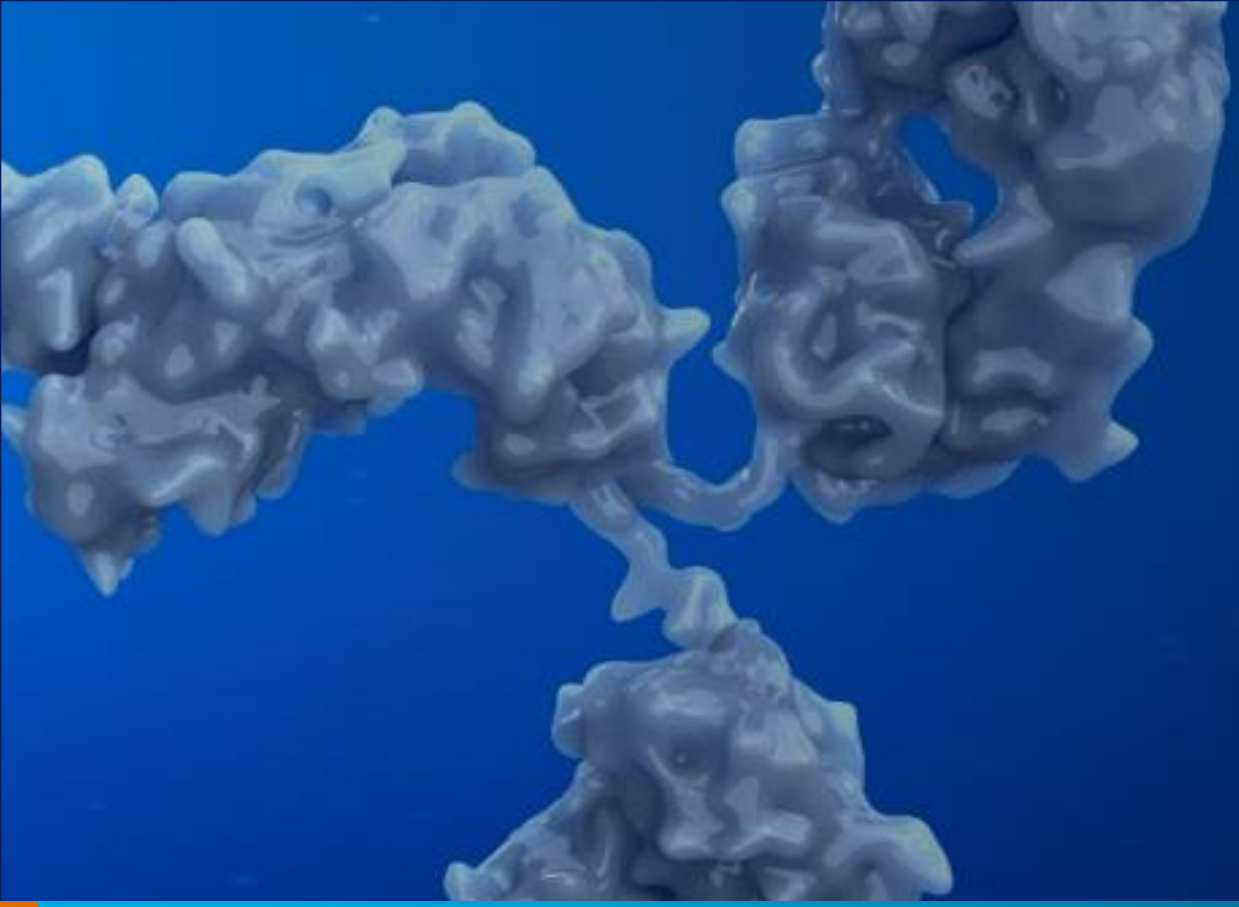

OMEROS®

Narsoplimab (OMS721)

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Center for Medicare & Medicaid Services
ICD-10 Coordination and Maintenance Committee Meeting
September 8, 2020

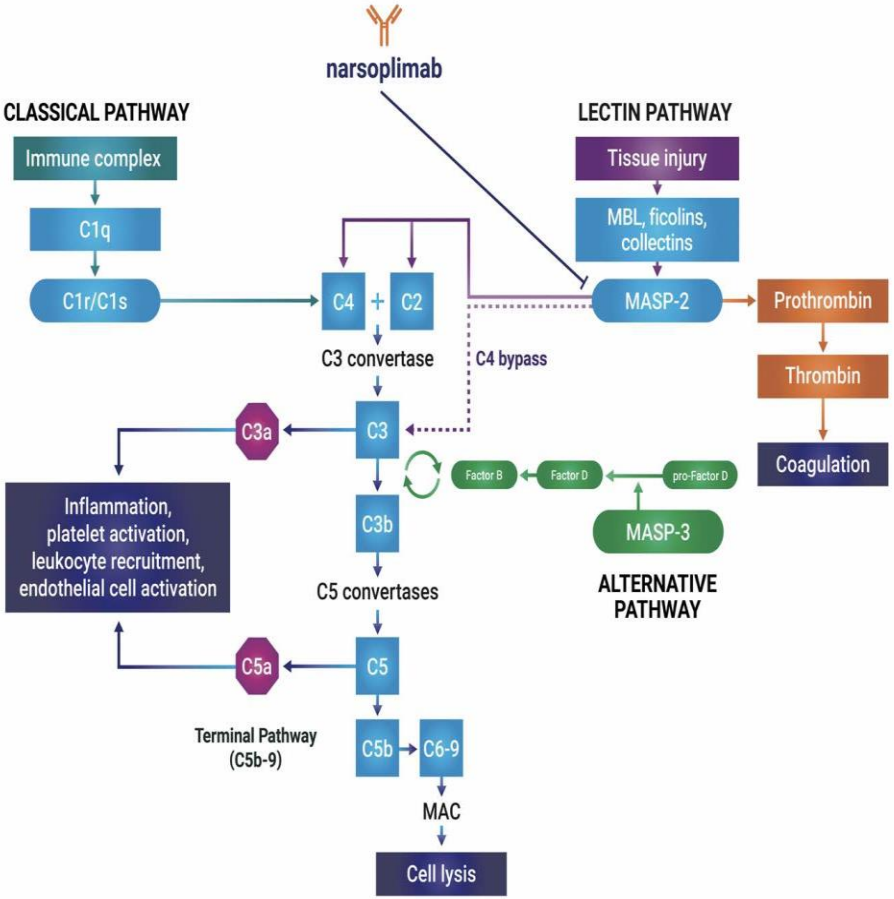
Narsoplimab Product Overview

- What is narsoplimab?
  - A fully human monoclonal antibody with a unique mechanism of action targeting mannan-binding lectin-associated serine protease-2 (MASP-2), the effector enzyme of the lectin pathway of the complement system
  - The inhibition of MASP-2 does not interfere with the antibody-dependent classical complement activation pathway, which is a critical component of the acquired immune response to infection
  - By inhibiting MASP-2 and the lectin pathway, narsoplimab prevents complement-mediated inflammation and endothelial damage while leaving intact the respective functions of the other pathways of innate immunity
- What is the United States regulatory status?
  - Completion of rolling BLA for treatment of HSCT*-TMA** targeted for Q3 2020 with anticipated approval by the FDA later this year or early 2021
  - FDA breakthrough therapy designation
  - FDA orphan drug designation
- Narsoplimab (OMS721) will have a trade name upon FDA approval but does not have any additional identifiers

*HSCT = Hematopoietic Stem Cell Transplant
**TMA = Thrombotic Microangiopathy

Narsoplimab Mechanism of Action

- Narsoplimab binds to mannan-binding lectin-associated serine protease-2 (MASP-2)
- MASP-2 is the effector enzyme of the lectin pathway of complement
- Narsoplimab leaves the classical pathway of complement-mediated immune function fully intact
- Narsoplimab does not directly affect alternative pathway-mediated immune function



Incidence: Severe HSCT-TMA

HSCT-TMA is a serious multisystem and life-threatening complication of HSCT presenting with signs of microangiopathic hemolytic anemia, consumptive thrombocytopenia in the absence of coagulopathy, and microvascular thrombosis with end-organ damage that is associated with highly unfavorable post-HSCT survival.

of patients with HSCT-TMA display at least one **high-risk** feature

50%

of HSCT-TMA cases may be **severe**

of severe cases of HSCT-TMA can be **fatal**

Currently HSCT-TMA has no approved treatment

Narsoplimab Registrational Trial

Primary Endpoint	
Population	Complete Response Rate (%)
All treated patients (N=28) (95% CI)	54% (15/28) (34% to 72%)
Patients treated per protocol (≥ 4 weeks of dosing) (n=23)	65% (15/23) (43% to 84%)

Primary endpoints requiring:

1. **Improvement in laboratory markers**
   - Lactate Dehydrogenase (LDH) < 1.5 uL
     AND
   - Platelet count
     - Baseline ≤ 20,000/uL
       - Triple baseline and absolute count > 30,000 and freedom of platelet transfusion
     - Baseline > 20,000/uL
       - Increase by at least 50% and absolute count > 75,000 and freedom from platelet transfusion

AND

2. **Improvement in clinical status (any of the following)**
   - Blood: Transfusion freedom; OR
   - Renal: Reduction of creatinine > 40%; or Normalization of creatinine and reduction of creatine > 20%; OR Discontinuation of renal replacement therapy; OR
   - Pulmonary: Extubation and discontinuation of ventilator support; or Discontinuation of non-invasive mechanical ventilation (continuous positive pressure ventilation); OR
   - Gastrointestinal: Improvement assessed using the gastrointestinal measures in the Mount Sinai Acute GVHD International Consortium (MAGIC); OR
   - Neurological: Limited to stroke, PRES, seizures, weakness

Narsoplimab Registrational Trial

Secondary Endpoint: 100-Day Survival Following HSCT-TMA Diagnosis	
Population	**100-Day Survival**
All treated patients (N=28)	68% (19/28)
Patients treated per protocol (≥ 4 weeks of dosing) (n=23)	83% (19/23)
Treatment responders (n=15)	93% (14/15)

Most narsoplimab-treated patients achieved a complete response with an improvement in laboratory markers (LDH level and Platelet count) and in clinical status including 100-day survival

Safety and Tolerability: Most Common Adverse Events in > 10% of Patients

- Narsoplimab was well tolerated in this very sick population with multiple comorbidities
- The most commonly reported adverse events were nausea, vomiting, diarrhea, hypokalemia, neutropenia and fever
- The observed adverse events are comparable to those typically seen in the post-transplant population
- Six patients died during the trial, all due to causes common in HSCT

Preferred Term, n (%)	(N = 28)
Any Event	26 (92.9)
Vomiting	9 (32.1)
Diarrhoea	8 (28.6)
Hypokalaemia	7 (25)
Nausea	7 (25)
Neutropenia	7 (25)
Pyrexia	7 (25)
Cytomegalovirus Infection	5 (17.9)
Anaemia	4 (14.3)
Back Pain	4 (14.3)
Fatigue	4 (14.3)
Graft Versus Host Disease	3 (10.7)
Haemorrhoids	3 (10.7)
Headache	3 (10.7)
Hypertension	3 (10.7)
Hypoalbuminaemia	3 (10.7)
Lower Respiratory Tract Infection	3 (10.7)
Oedema Peripheral	3 (10.7)
Pruritus	3 (10.7)

Preparation and Administration

- The proposed dosing for narsoplimab in HSCT-TMA is 4mg/kg administered, either peripherally or centrally, by a health care professional via intravenous infusion over 30 minutes in the inpatient or outpatient setting

- Narsoplimab must be diluted for intravenous use
  - An appropriate calculated volume of narsoplimab is diluted in an infusion bag containing 50 mL of D5W or normal saline

- Vials contain no antimicrobial preservatives and are intended for a single use only

- The prepared infusion bag should be kept at room temperature and administered within 4 hours of preparation

- Narsoplimab is administered in the context of patient care according to physician orders

Documentation of Administration

- The administration of narsoplimab should be documented consistent with other intravenous infusions

- The most common sites for documentation in the medical record include:
  - Physician orders
  - Medication administration record
  - Progress notes

Summary

- HSCT-TMA is a complex and life-threatening complication of HSCT
- There are no currently approved treatments for HSCT-TMA
- Narsoplimab is currently pursuing an indication for treatment of HSCT-TMA
- No current ICD-10-PCS appropriately describes the administration of narsoplimab
- Without unique ICD-10-PCS codes, the administration of narsoplimab to HSCT-TMA patients cannot be identified and tracked nor can the disease be fully characterized