Clinical Safety and Efficacy of Narsoplimab in Pediatric and Adult Patients with Transplant-Associated Thrombotic Microangiopathy: A Real-World Experience

M. CASTELLI [1], M.C. MICÒ [1], A. GRASSI [1], M.C FINAZZI [1], A. ALGAROTTI [1], B. RAMBALDI [1],C. MELI [1], G. RIZZUTO [1], C. PAVONI [1], F. VENDEMINI [2], M. VERNA [2], S. BONANOMI [2], A. BALDUZZI [3], A. BIONDI [3], A. RAMBALDI [4], G. GOTTI [2]

1 Department of Oncology and Hematology, Azienda Socio Sanitaria Territoriale Papa Giovanni XXIII, Bergamo, Italy. 2 Pediatrics, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy. 3 School of Medicine and Surgery, University of Milano-Bicocca ,Italy . 4 Department of Oncology and Hematology, University of Milan and Azienda Socio Sanitaria Territoriale Papa Giovanni XXIII, Bergamo, Italy

INTRODUCTION

Transplant - associated thrombotic microangiopathy (TA-TMA) is a life-threatening complication, with no approved therapy. **Complement inhibition** is increasingly recognized as an effective treatment option in this context. **Narsoplimab (OMS721)** is a fully human IgG4 monoclonal antibody that binds MASP-2, the effector enzyme of the lectin pathway of the complement system[1]. A recent pivotal trial demonstrated the safety and efficacy of narsoplimab in patients with TA-TMA [2].

AIM

We report the results of a real-world experience with narsoplimab in a series of **pediatric and adult patients** with TA-TMA.

METHOD

The diagnosis of TA-TMA was based on the presence of these criteria [3]:

- Anemia,
- Thrombocytopenia,
- Elevated lactate dehydrogenase (LDH),
- Decreased serum haptoglobin,
- Schistocytes in the peripheral blood smear,
- Hypertension,
- Proteinuria.

Narsoplimab was **administered** intravenously at the dose **of 4 mg/kg twice weekly** for at least 8 doses. **Response criteria** were defined as improvement in both laboratory TMA markers and any clinical benefit [2].

RESULTS

Fifteen patients (11 adults and 4 pediatrics), were treated under a compassionate use program between January 2018 and April 2023 (Table 1).

Fourteen patients (93%) were defined as **high-risk TA-TMA** for the presence of 1 or more of these features[3]:

- LDH > 2 times the ULN,
- Random urine protein-to-creatinine ratio (rUPCR) ≥ 1 mg/mg,
- Multiorgan dysfunction,
- Concurrent acute GvHD ≥ grade 2,
- Infection.

Fourteen patients (93%) were **transfusion dependent** at baseline. Twelve patients (80%) were on **calcineurin inhibitors** at TA-TMA onset.

Patients received a median of 11 (range, 8-34) doses of narsoplimab. All infusions were well-tolerated with **no narsoplimab-related adverse events**.

Eleven patients responded to treatment (73%), based on the achievement of transfusion independence (10 patients) as well as clinical and laboratory improvement, which occurred in all responders. The median time to response was 50 days (range, 9 - 105).

100-day survival was 80% in the study population and 100% for responders (Figure 1 and 2).

Three of the four patients who failed to respond, eventually died with laboratory and clinical evidence of persisting TA-TMA.

Variable	Overall (N=15)
Age (years), median (range)	61 (6 – 71)
Male, No (%)	6 (40%)
Diseases, No. (%)	
Myeloid Malignancies	9 (60%)
Lymphoid Malignancies	5 (33%)
Other	1 (7%)
Cell source, No. (%)	
Bone marrow	4 (27%)
Peripheral blood	10 (67%)
Cord blood	1 (7%)
Matched donor, No. (%)	6 (40%)
Matched related	2
Matched unrelated	4
Mismatched donor, No. (%)	9 (60%)
Mismatched related	3
Mismatched unrelated	6
Conditioning regimen, No (%)	
MAC	8 (55%)
RIC	7 (45%)
Disease status at transplant, No (%)	
Active disease	7 (45%)
CR1	4 (22%)
CR2 or more	4 (22%)
Baseline platelet count, x10^9/L, No (%)	
≤ 20, No. (%)	9 (60%)
> 20, No. (%)	6 (40%)
Baseline hemoglobin, g/dL (range)	9.1 (7.7 - 12.3)
Baseline LDH, U/L (range)	497 (237 - 1201)
Kidney dysfunction (rUPCR ≥1 mg/g) (N=14)	8 (57%)
Neurological symptoms, No (%)	4 (27%)

Table 1. Demographic and transplant's characteristics of study population

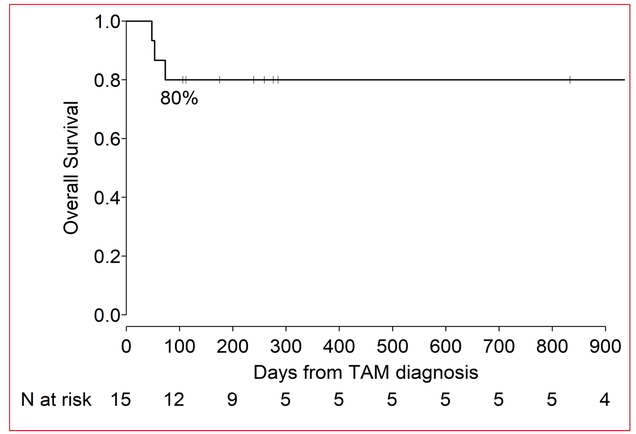

Figure 1. 100-day Overall Survival after TA-TMA diagnosis

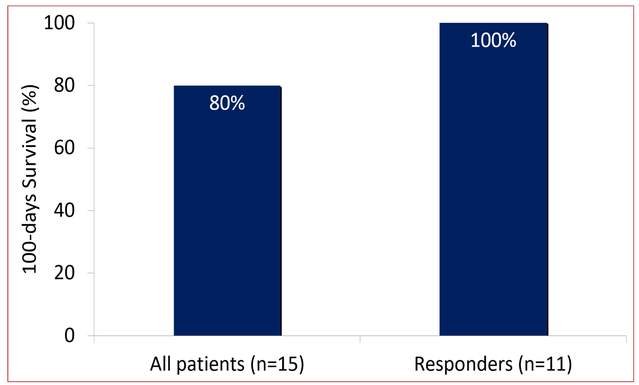

Figure 2. 100-day Overall Survival in responder patients

CONCLUSIONS

In this study of high-risk TA-TMA patients, the inhibition of the lectin pathway of complement activation with narsoplimab proved to be not only an **effective** but also a remarkably **safe** treatment option with no evidence of an increased risk of infectious complications in both children and adults.

REFERENCES

[1] Gavriilaki E. et al. Exp Hematol Oncol. 2021 Dec 19;10(1):57.
[2] Khaled SK, et al. J Clin Oncol. 2022 Aug;1;40(22):2447-2457
[3] Schoettler ML, et al. Transplant Cell Ther. 2023 Mar;29(3):151-163.

CONTACT INFORMATION

Marta Castelli
University of Milan (Italy)
Email: marta.castelli@unimi.it.