Tacrolimus Time in Therapeutic Range after Hematopoietic Stem Cell Transplant

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Introduction

- Tacrolimus is used with other immunosuppressive agents to prevent graft versus host disease (GVHD) in patients receiving allogeneic hematopoietic stem cell transplant (HSCT).
- Tacrolimus trough levels are monitored due to its narrow therapeutic index:
  - Subtherapeutic levels increase the risk of developing GVHD
  - Supratherapeutic levels increase the risk of toxicity (acute kidney injury [AKI] and posterior reversible encephalopathy syndrome [PRES])
- The optimal tacrolimus therapeutic range after allogeneic HSCT is not well defined in literature.

Objectives

- **1º Objective:** GVHD incidence within 6 months following HSCT
- **2º Objectives:** time to GVHD, average tacrolimus levels, time within specified tacrolimus trough level ranges as defined below:
  - Tacrolimus goal 8-13 ng/mL months 1-3
  - Tacrolimus goal 5-8 ng/mL months 4-6
- **Safety Objectives:** incidence of AKI, PRES, all-cause mortality, tacrolimus discontinuation within 6 months

Methods

- Single-center, retrospective chart review conducted April 2018 to April 2023

Inclusion Criteria	Exclusion Criteria
• Age 18-89 years old • HSCT patients receiving tacrolimus for GVHD prevention	• Syngeneic HSCT • CD34 selected graft • Prior allogeneic HSCT

Results

Table 1. Demographics	GVHD, n=121	No GVHD, n=37	P-value
Age in years, mean (SD)	53.8 (13.8)	59.6 (13.4)	0.025
Male Sex, no. (%)	73 (60.3)	23 (62.2)	0.842
Diagnosis, no. (%)			0.404
AML	58 (47.9)	19 (51.4)	
MDS	30 (24.8)	6 (16.2)	
Other*	33 (27.3)	12 (32.4)	
Donor, no. (%)			0.401
Matched Unrelated	43 (35.5)	15 (40.5)	
Matched Related	26 (21.5)	7 (18.9)	
Other**	52 (43)	15 (40.5)	
Immunosuppression, no. (%)			0.077
Cy/Tacrolimus/MMF	46 (38)	21 (56.8)	
Tacrolimus/MTX	50 (41.3)	13 (35.1)	
Tacrolimus/MMF	25 (20.7)	3 (8.1)	

Table 2. GVHD Characteristics	GVHD n=121
Time to GVHD in days from HSCT, median (IQR)	37 (23-57)
Type of GVHD, no. (%)	
Skin	79 (65.3)
Upper Gastrointestinal	72 (59.5)
Other***	64 (52.9)

Results

Figure 1. Mean Tacrolimus Time in Therapeutic Range (TTTR) 6 Months Following HSCT, N=158

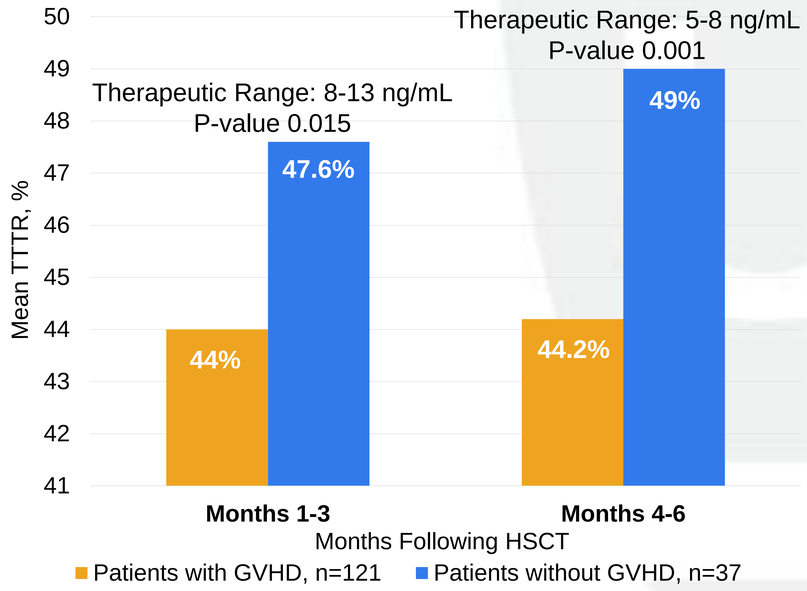
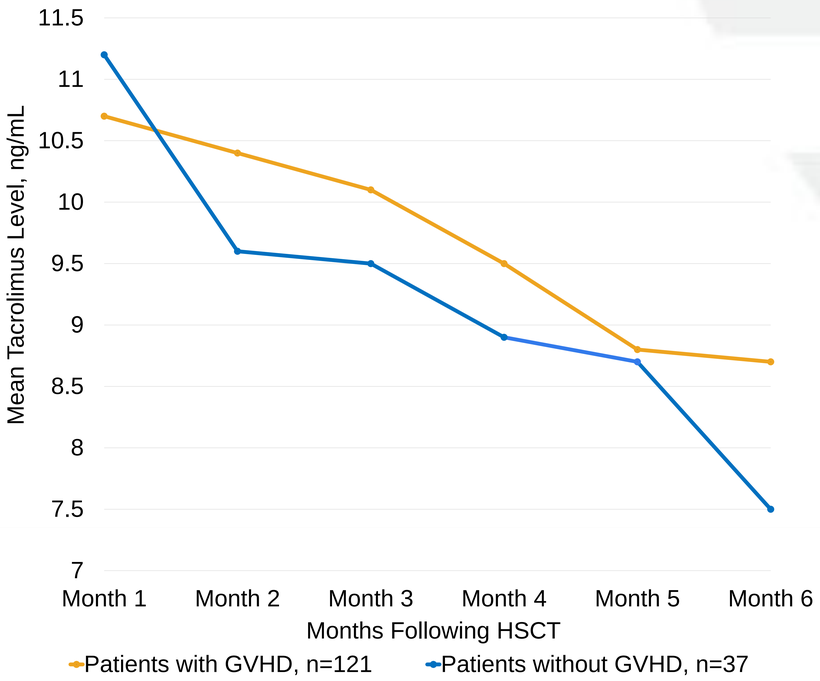


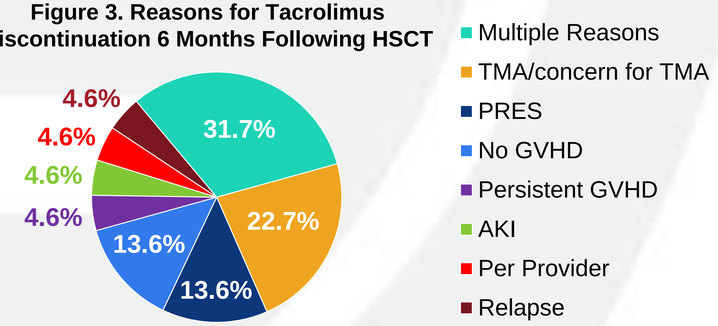
Figure 2. Mean Tacrolimus Levels 6 Months Following HSCT, N=158



Results

Table 3. Safety Outcomes, no. (%)	GVHD, n=121	No GVHD, n=37
AKI Months 1-6	116 (95.9)	35 (94.6)
Months 1-3	110 (90.9)	35 (94.6)
Months 4-6	90 (74.4)	21 (56.8)
PRES Months 1-6	2 (1.7)	2 (5.4)
Months 1-3	2 (1.7)	2 (5.4)
Months 4-6	0	0
Mortality Months 1-6	19 (15.7)	8 (21.6)
Months 1-3	5 (4.1)	6 (16.2)
Months 4-6	14 (11.6)	2 (5.4)
Tacrolimus Discontinuation Months 1-6	16 (13.2)	6 (16.2)
Months 1-3	11 (9.1)	3 (8.1)
Months 4-6	5 (4.1)	3 (8.1)

Figure 3. Reasons for Tacrolimus Discontinuation 6 Months Following HSCT



Discussion

- GVHD occurred in 77% of patients primarily in months 1-2 following HSCT with an overall mean TTTR of 45% in months 1-6 following HSCT
- Patients without GVHD had a significantly higher mean TTTR overall & numerically higher mean tacrolimus level in month 1 followed by lower mean tacrolimus levels thereafter compared to those with GVHD
- Safety outcomes were similar between groups

Conclusions

- Increasing TTTR targeting higher levels earlier such as 8-13 ng/mL in months 1-3, particularly in month 1, and then lower levels later such as 5-8 ng/mL in months 4-6, following HSCT can help to decrease the incidence of GVHD

Disclosure & References

Authors of this presentation have no personal or financial interests to disclose.

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AML= Acute myeloid leukemia, MDS= Myelodysplastic syndrome, TMA= Thrombotic micro-angiography *Other= Non-Hodgkin lymphoma, acute lymphoblastic leukemia, myelofibrosis, chronic myeloid leukemia (not a complete list); **Other= Haploidentical, cord blood, mismatched unrelated; ***Other= Lower gastrointestinal, pulmonary, liver, eyes