

Lipid dysregulation after hematopoietic stem cell transplant

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Received: August 12, 2025.

Accepted: December 17, 2025.

Early view: December 24, 2025.

<https://doi.org/10.3324/haematol.2025.288933>

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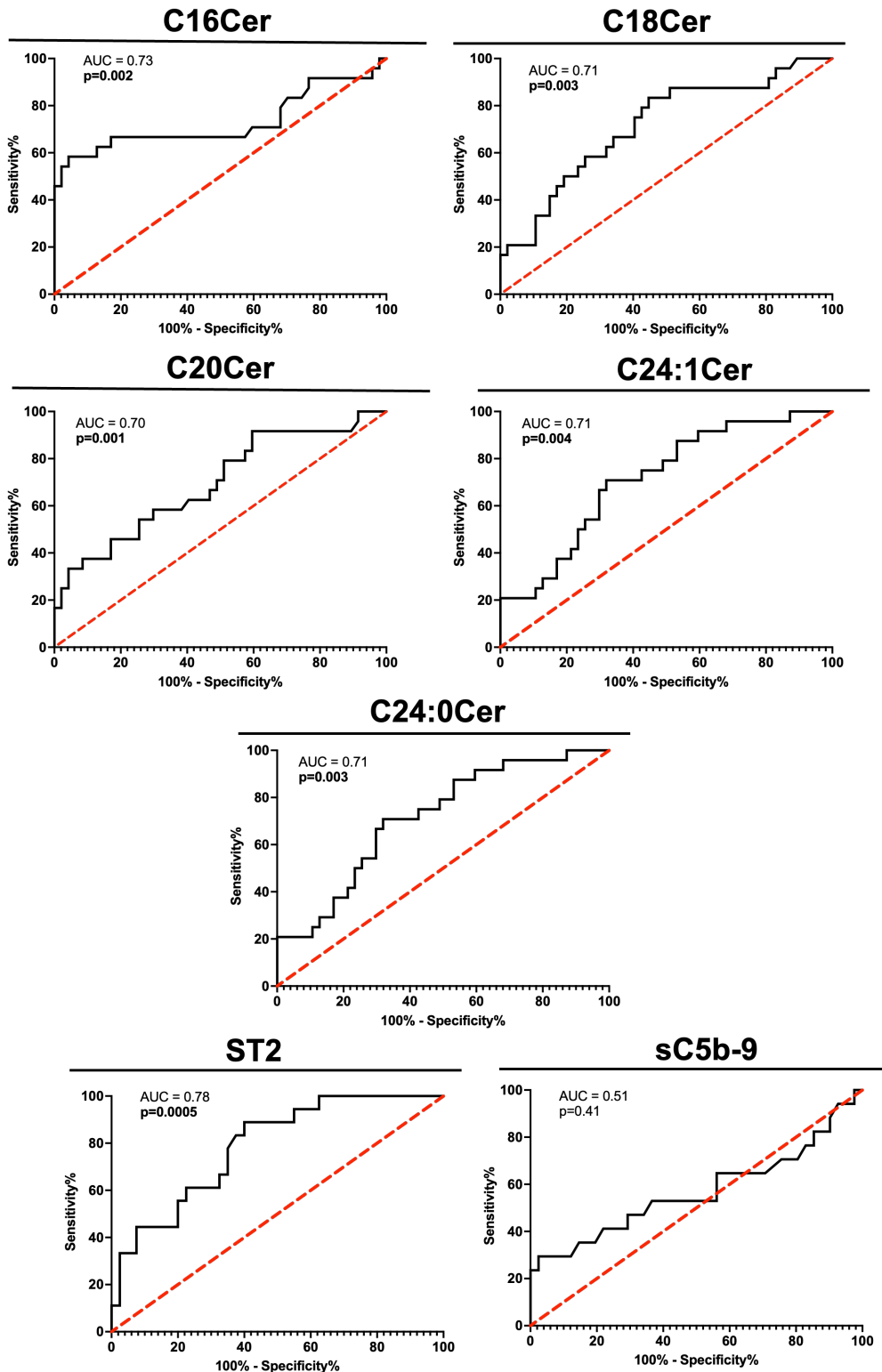
Supplementary Table 1. Baseline concentrations of all ceramide species analyzed in cohort

	TA-TMA	No TA-TMA	p-value
C16Cer (nmol/L)	248.56 (94.33-2289)	152 (93.95-252.65)	0.001
C16-OHCer (nmol/L)	12.65 (9.94-176)	13.01 (9.94-19.69)	0.15
C16 DHCer (nmol/L)	25.67 (11.12-647.5)	24.47 (9.82-79.89)	0.76
C18Cer (nmol)	120.25 (56.23-1241.5)	80.81 (34.66-242.09)	0.003
C18 DHCer (nmol/L)	14.36 (9.52-298.5)	13.92 (9.52-46.87)	0.30
C20Cer (nmol/L)	111.46 (52.74-1598)	86.1 (33.7-235.05)	0.009
C22Cer (nmol/L)	607.56 (237.01-5466.5)	416.89 (190.67-1329.53)	0.008
C24:1Cer (nmol/L)	657.22 (326.8-4359)	485.87 (206.33-878.46)	0.003
C24Cer (nmol/L)	1527.94 (646.04-9745.5)	1312.24 (503.46-2825.71)	0.13
C24 DHCer (nmol/L)	82.19 (14.43-1535)	85.5 (15.96-630.39)	0.91
C24-OHCer (nmol/L)	34.49 (11.72-201.5)	29.9 (7.81-88.81)	0.44
C26:1Cer (nmol/L)	13.03 (9.77-41.5)	12.58 (9.92-18.65)	0.02
C26:0Cer (nmol/L)	18.6 (10.77-73.5)	14.32 (9.74-22.88)	0.01
Sphingosine (nmol/L)	26.72 (9.69-52.44)	21.04 (14.36-86.17)	0.12

Supplementary Table 2. Day 14 concentrations of all ceramide species analyzed in cohort

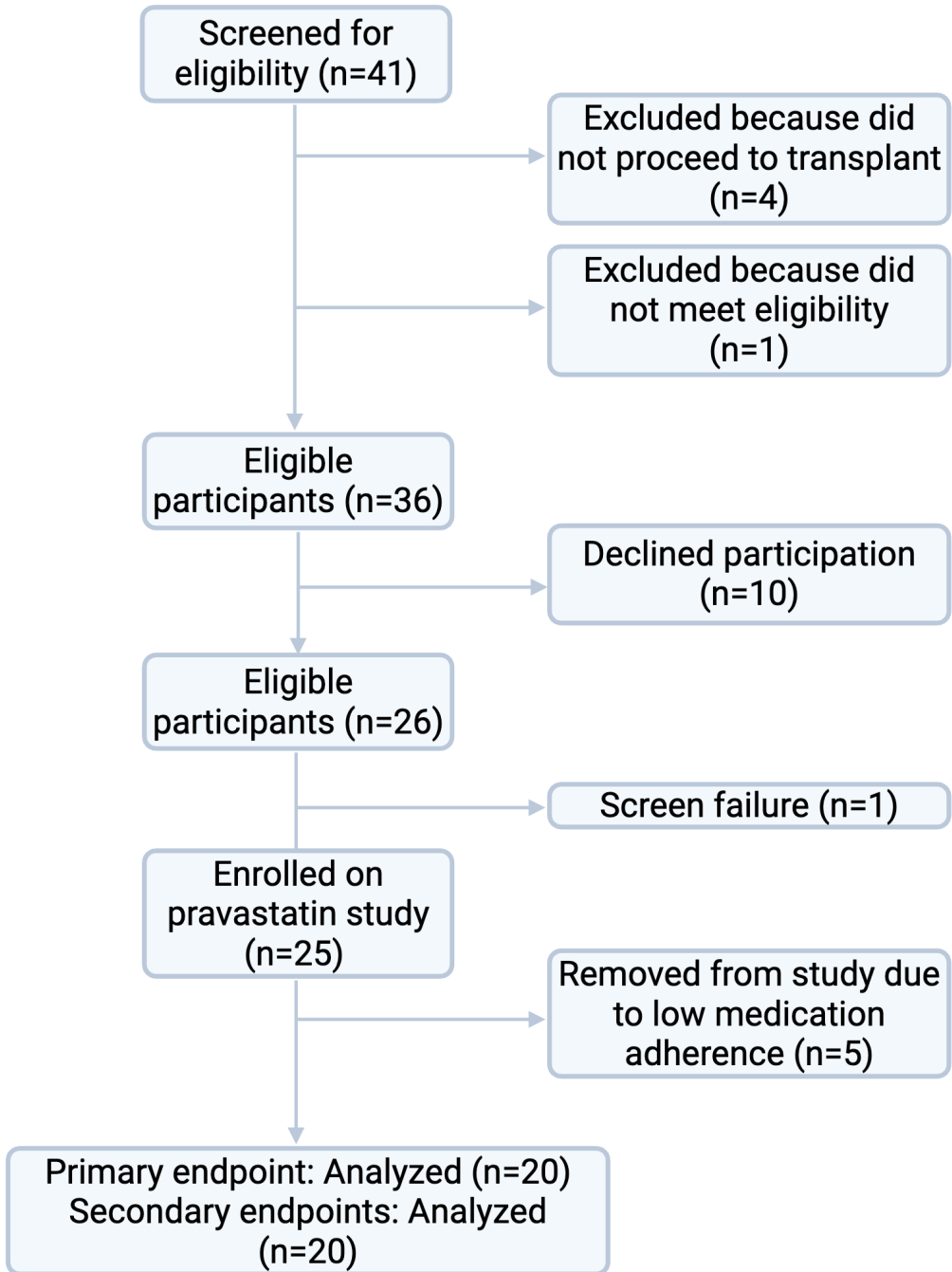
	TA-TMA	No TA-TMA	p-value
C16Cer (nmol/L)	469.4 (226.98-1387.35)	318.05 (142.51-928.93)	0.0007
C16-OHCer (nmol/L)	28.18 (14.09-124.66)	16.98 (9.76-66.67)	<0.0001
C16 DHCer (nmol/L)	44.11 (19.09-477.66)	29.19 (14.46-72.85)	0.06
C18Cer (nmol)	211.49 (136.34-1097.08)	140.85 (35.72-360.74)	0.0008
C18 DHCer (nmol/L)	29.78 (11.28-233.48)	16.3 (9.87-53.04)	0.03
C20Cer (nmol/L)	270.43 (173.72-870.43)	191.91 (62.71-479.87)	0.002
C22Cer (nmol/L)	854.71 (506.03-2517.78)	722.2 (300.24-1645.37)	0.06
C24:1Cer (nmol/L)	1178.22 (551.35-2341.62)	887.57 (333.13-2031.35)	0.009
C24Cer (nmol/L)	1678.37 (1058.81-4420.17)	1612.78 (610.78-3334.26)	0.43
C24 DHCer (nmol/L)	64.62 (33.46-790.48)	73.06 (21.03-216.27)	0.57
C24-OHCer (nmol/L)	61.31 (33.66-138.54)	60.41 (12.17-186.18)	0.53
C26:1Cer (nmol/L)	19.91 (14.8-31.24)	17.25 (10.21-33.16)	0.15
C26:0Cer (nmol/L)	21.55 (12.25-50.92)	19.63 (9.59-42.07)	0.59
Sphingosine (nmol/L)	29.06 (18.37-60.45)	20.54 (14.36-87.51)	0.62

Supplementary Figure 1. ROC analyses of C16Cer, C18Cer, C20Cer, C24:1Cer and C26Cer levels at baseline in plasma from patients with TA-TMA.



Supplementary Figure 1. ROC analyses of baseline C16Cer, C18Cer, C20Cer, C22Cer and C24:1Cer levels in plasma from patients with TA-TMA. Corresponding AUCs are shown in Table 4. Abbreviation: AUC, area under the curve; Cer, ceramide; ROC, receiver operating characteristic; ST2, suppression of tumorigenicity 2; sC5b-9, terminal complement complex

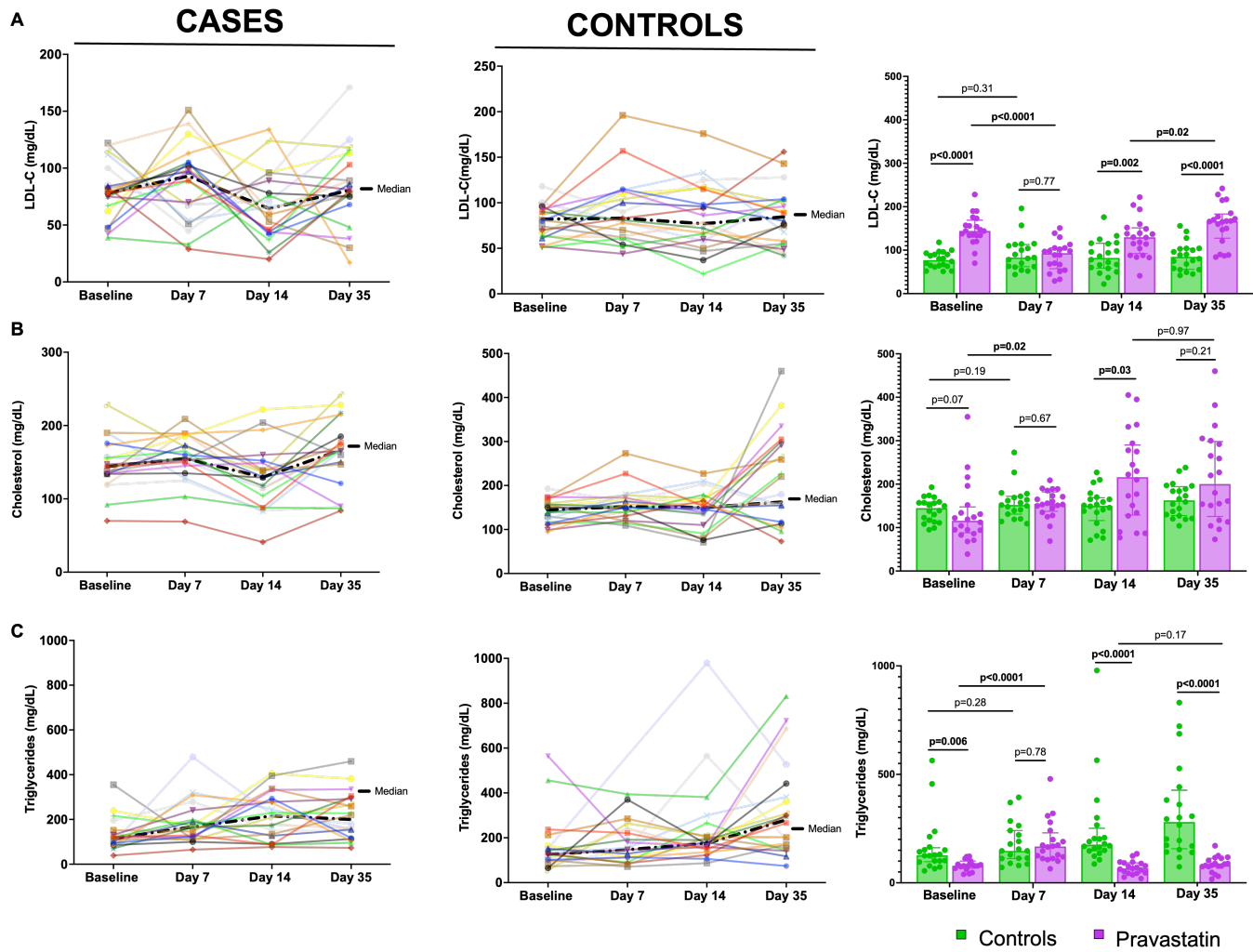
Supplementary Figure 2. CONSORT diagram



Supplementary Table 3. Serious adverse events.

SAE Term	# of Patients	Resolved?	Relationship to Pravastatin	Subject IDs	Number of Participants with Grade 1	Number of Participants with Grade 2	Number of Participants with Grade 3	Number of Participants with Grade 4	Number of Participants with Grade 5
Respiratory Failure	2	Yes	Unrelated	PRAV - 01, 06	N/A	N/A	N/A	2	N/A
Respiratory Failure	1	No (ongoing at end of study participation)	Unrelated	PRAV - 23	N/A	N/A	N/A	1	N/A
Somnolence	1	Yes	Unrelated	PRAV - 01	N/A	N/A	N/A	1	N/A
Cerebrospinal Fluid Leak	1	No (ongoing at end of study participation)	Unrelated	PRAV - 01	N/A	N/A	1	N/A	N/A
Hypertension	2	Yes	Unrelated	PRAV - 02, 22	N/A	N/A	1	1	N/A
Seizure	1	Yes	Unlikely	PRAV - 04	N/A	N/A	1	N/A	N/A
Ventricular Arrhythmia	1	Yes	Unrelated	PRAV - 07	N/A	N/A	1	N/A	N/A
Encephalopathy	1	Yes	Unrelated	PRAV - 07	N/A	N/A	1	N/A	N/A
Delirium	1	Yes	Unrelated	PRAV - 07	N/A	N/A	1	N/A	N/A
Leukocytosis	1	Yes	Unrelated	PRAV - 08	1	N/A	N/A	N/A	N/A
Maculo-papular Rash	1	Yes	Unrelated	PRAV - 08	N/A	1	N/A	N/A	N/A
Hypotension	1	Yes	Unrelated	PRAV - 12	N/A	N/A	1	N/A	N/A
Septic Shock	2	Yes	Unrelated	PRAV - 14, 18	N/A	N/A	N/A	2	N/A
Hypoxia	1	Yes	Unrelated	PRAV - 14	N/A	N/A	N/A	1	N/A
Diarrhea	1	Yes	Unrelated	PRAV - 16	N/A	N/A	1	N/A	N/A
Neck Pain	1	Yes	Unrelated	PRAV - 16	N/A	N/A	1	N/A	N/A
Breast Mass	1	Recovered with sequelae	Unrelated	PRAV - 16	1	N/A	N/A	N/A	N/A
Upper Respiratory Infection	1	Yes	Unrelated	PRAV - 17	N/A	N/A	1	N/A	N/A
Cytokine Release Syndrome	1	Yes	Unrelated	PRAV - 18	N/A	N/A	N/A	1	N/A
Anaphylaxis	1	Yes	Unrelated	PRAV - 18	N/A	N/A	N/A	1	N/A
Worsening Hypoxia	1	Recovered with sequelae (ongoing hypoxia AE after resolution of SAE (transfer from ICU back to BMT) - hypoxia eventually resolved)	Unrelated	PRAV - 19	N/A	N/A	N/A	1	N/A
Acute Kidney Injury	1	Yes	Unrelated	PRAV - 22	N/A	N/A	1	N/A	N/A
Acute Kidney Injury	1	No (ongoing at end of study participation)	Unrelated	PRAV - 23	N/A	N/A	N/A	1	N/A
Worsening Acute Kidney Injury	1	Yes	Unrelated	PRAV - 22	N/A	N/A	1	N/A	N/A
Sinusoidal Obstructive Syndrome	1	Yes	Unrelated	PRAV - 23	N/A	N/A	N/A	1	N/A
Gastrointestinal Graft Versus Host Disease	1	Yes	Unrelated	PRAV - 25	N/A	N/A	1	N/A	N/A
Facial Pain	1	Yes	Unrelated	PRAV - 26	N/A	1	N/A	N/A	N/A
Pruritus	1	Yes	Unrelated	PRAV - 26	N/A	N/A	1	N/A	N/A
Flushing	1	Yes	Unrelated	PRAV - 26	N/A	1	N/A	N/A	N/A
Suicidal Ideation	1	Yes	Unrelated	PRAV - 26	N/A	N/A	N/A	1	N/A

Supplementary Figure 3. Additional lipid dynamics in pravastatin treated patients and controls.



Supplementary Figure 3. LDL-C, cholesterol and triglyceride changes are shown for cases (purple) and controls (green) at baseline (pre-conditioning), days 7, 14 and 35 after HSCT. Each colored line on the graphs represents changes in LDL-C, total cholesterol and triglycerides at each timepoint. The black-dashed line represents the median HDL-C concentration at each timepoint. (A) LDL-C, (B) cholesterol and (C) triglyceride changes over time are represented. Each colored symbol represents a single patient and their respective changes in HDL-C over time. Bar graphs for each lipid exhibiting comparisons of the concentrations of LCL-C, cholesterol and triglycerides at baseline, days 7, 14 and 35 are shown. LDL-C: low-density lipoprotein cholesterol