

Primary endpoint: aGvHD; cGvHD.

Secondary endpoints: Neutrophil engraftment; platelet engraftment; non-relapse mortality; relapse; GvHD free relapse-free survival; disease-free survival; overall survival

Eligibility: Undergoing haplo-peripheral hematopoietic stem cell transplantation at 2 U.S. centres (City of Hope Comprehensive Cancer Center and Moffitt Cancer Centre); receiving GvHD prophylaxis for hematologic malignancy between January 2014 and December 2019

TRIAL DESIGN

Retrospective cohort study

SIRO cohort (n = 84)

Drug 1: Sirolimus

(Starting on Day 5)

TAC cohort (n = 339)

Drug 1: Tacrolimus

(Starting on Day 5)

Conditioning regimen: UFlu/TBI 1,200 cGy; Flu/Bu or Flu/MEL 100–140 mg/m2; Flu/MEL 70–140 mg/m2)/TBI 200 cGy; Flu/Cy; For multivariate analysis, Flu/Bu was chosen as the comparator group

Drug 2: PTCy

(50 mg/kg)

Day 3 and 4

Drug 3: MMF

Day 5–35

SIRO cohort

TAC cohort

HCT OUTCOMES

aGvHD and cGvHD

45%

Grade 2–4

(p = 0.60)

47%

Grade 2–4

(p = 0.60)

20%

Grade 3–4

(p = 1.0)

15%

Grade 3–4

(p = 1.0)

47%

cGvHD at 2 years

(p = 0.79)

54%

cGvHD at 2 years

(p = 0.79)

Neutrophil engraftment

94%

At 30 days (p = 0.07)

18 days

p = 0.005

17 days

99%

Platelet engraftment

82%

At 60 days (p = 0.20)

26 days

p = 0.10

27 days

94%

At 2 years

27%

NRM

(p = 0.36)

23%

Relapse

(p = 1.0)

45%

GRFS

(p = 0.04)

57%

DFS

(p = 0.40)

63%

OS

(p = 0.86)

22%

Relapse

(p = 1.0)

50%

GRFS

(p = 0.04)

61%

DFS

(p = 0.40)

64%

OS

(p = 0.86)

MULTIVARIATE ANALYSIS

HR (95% CI)

-10

1

10

SIRO cohort

No difference

TAC cohort

Neutrophil engraftment

0.30 (0.11–0.83; p = 0.02)

GvHD Prophylaxis

0.05 (0.00–0.52; p = 0.01)

Flu/MEL

0.09 (0.01–0.78; p = 0.03)

Flu/MEL/TBI

Platelet engraftment

0.27 (0.10–0.70; p = 0.01)

Flu/MEL/TBI

Grade 2–4 aGvHD (Female vs male)

1.86 (1.15–3.01; p = 0.01)

Donor/Recipient Sex

NRM

1.06 (1–1.05; p = 0.05)

Age ≥60 years

1.85 (1.05–3.33; p = 0.03)

HCT-CI ≥3

3.48 (1.14–10.66; p = 0.03)

Flu/MEL

GRFS

1.01 (1–1.02; p = 0.02)

Age ≥60 years

1.39 (1.11–1.75; p = 0.01)

HCT-CI ≥3

2.39 (1.19–4.81; p = 0.02)

Flu/MEL

DFS

1.03 (1–1.05; p = 0.05)

Age ≥60 years

1.64 (1.20–2.17; p < 0.01)

Disease risk high/very high

1.45 (1.09–1.92; p = 0.01)

HCT-CI ≥3

OS

1.02 (1.01–1.03; p < 0.01)

Age ≥60 years

1.79 (1.28–2.5; p < 0.01)

Disease risk high/very high

This retrospective cohort study demonstrated that sirolimus is a comparable GvHD prophylaxis option to tacrolimus combined with PTCy and MMF.

Abbreviations: aGvHD, acute graft-versus-host disease; allo-HCT, allogenic-hematopoietic cell transplantation; Bu, busulfan; cGvHD, chronic GvHD; CI, confidence interval; Cy, cyclophosphamide; DFS, disease-free survival; Flu, fludarabine; GRFS, GvHD free relapse-free survival; HR, hazard ratio; MEL, melphalan; MMF, mycophenolate mofetil; NRM, non-relapse mortality; OS, overall survival; PTCy, posttransplant cyclophosphamide; TAC, tacrolimus; TBI, total body irradiation; SIRO, sirolimus.

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