Predictive Value of ST2, REG3a, and MAGIC Algorithm in Haploidentical Transplantation With Post-Transplant Cyclophosphamide Outcomes

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Context and Background

Recent studies have described protein biomarkers in peripheral blood associated to allogeneic-stem-cell transplantation (allo-SCT) outcomes, as Suppressor of Tumorigenicity-2 (ST2) and Regenerating islet-derived 3α (REG3α) .

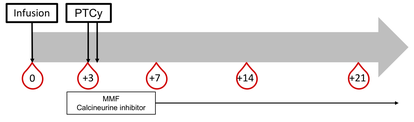
To date, two studies have focused on haploidentical allo-SCT with post-transplant cyclophosphamide (haplo-SCT-PTCy). These works evaluate ST2 and REG3α at days +15 and +30, although they agree in their association with higher rates of transplant related mortality (TRM), they showed discordant results regarding graft-versus-host disease (GVHD) and do not include the analysis of the MAGIC algorithm.

The objective is to analyze ST2, REG3a and MAGIC algorithm early weekly after haplo-SCT-PTCy and its association with transplant outcomes.

Methods

Prospective study with 151 consecutive patients who underwent haplo-SCT-PTCy at University Hospital of Salamanca (2012-2020).

Serial serum samples were collected on days 0, +3, +7, +14 and +21 in 81 patients. ST2 and REG3a serum concentration was stablished by Luminex XMap. Median luminescence levels between groups were compared using Wilcoxon-Mann-Whitney test. Cut-off points for each cytokine were estimated using Cutoff-Finder application in R. MAGIC algorithm was determined from the ST2 and REG3α values. Log-rank was used to compare survival curves. Multivariable analyses were carried out with Cox regression, including the most significant clinical variables.



Results

Patient characteristics' are shown in table 1.

Recipient median age of 50 years, 73% of transplants were performed with reduced intensity conditioning. Median follow up of 35 months.

Characteristics	n (%)
Recipient / donor age; median (range)	50 (16-73) / 39 (14-75)
Recipient / donor male sex	85 (56) / 85 (56)
Male receptor / Female donor	37 (24)
Hematological disease	
AML / MDS	63 (42) / 19 (13)
HL / NHL	22 (15) / 24 (16)
ALL	9 (6)
CMML	5 (3)
Others	4 (5)
Previous treatments ≥2	93 (61)
Previous autologous / allogenic transplantation	35 (23) / 13 (8)
Disease risk index ≥ high and very high	27 (18)
Sorror, n (%) ≥3	44 (29)
Conditioning	
Myeloablative	
Flu (150mg/m^2) + Bu (9,6mg/Kg) + Thio (10mg/Kg)	35 (23)
Flu(150mg/m2)+Bu (9,6 mg/kg) + Cy(29mg/kg)	29 (19)
	6 (4)
Reduced intensity	
Flu (150 mg/m^2) + Bu (3,2 o 6,4mg/Kg) + Cy	112 (73)
(29mg/Kg)	99 (65)
Flu (150 mg/m^2) + TBI (2Gy) + Cy (29 mg/kg)	5 (3)
Flu(150mg/m2)+Bu(6,4mg/kg)+Thio(10mg/kg)	8 (5)
Sequential	5 (4)
GVHD prophylaxis	
Tacro + MMF + Cy	148 (98)
CsA + MMF + Cy	3 (2)
CD34+x10^8 infused dose, median (range)	6,26 (2.59-9,34)
Graft source: Peripheral blood	148 (98)
Median follow up months, n (range)	35 (9-87)
OS 2 years	66%
PFS 2 years	60%
NRM day 100 / 1 year	14% / 24%
Cumulative incidence of aGVHD II-IV day 180	57%
Cumulative incidence of aGVHD III-IV day 180	13%
GRFS (Graft versus host-free relapse-free survival) 2 years	49%

Table 1. Patients characteristics'

Higher levels of ST2 were associated with higher NRM 1-year (0, +7, +14), lower OS 2-years (+7, +14) and GRFS 2-years (+14, +21). Higher levels of REG3α were associated with higher NRM 1-year (0, 7, 14, 21), lower OS 2-years (0, +7, +14, +21) and lower GRFS-2y (+14).

Similarly, the analysis of MAGIC algorithm in univariate analysis, distinguished two statistically significant risk groups for OS (0, +14), NRM 1-year (0, +14) and GRFS (+14) Figure 1.

On multivariate analysis, OS was independently associated with HCT-CI ≥3, ST2 (0, +7, 14, +21), REG3α (0, +14, +21) and MAGIC (0, +14), NRM with ST2 (0, +14), REG3α (14) and HCT-CI ≥3. ST2 (+7, +14, +21) REG3α (+14), MAGIC (+14) and HCT-CI ≥3 were the only variables associated to GRFS. Table 2.

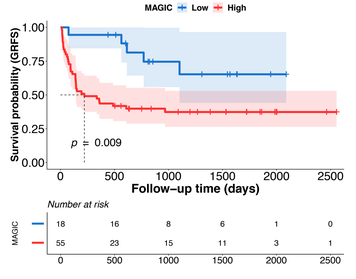


Figure 1. GRFS according to MAGIC on day 14

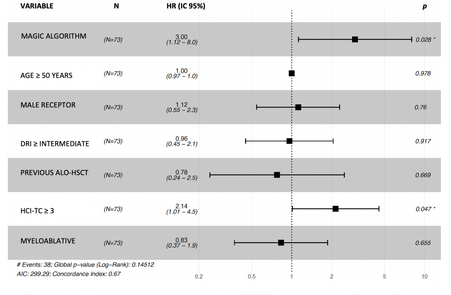


Table 2. Multivariate analysis for GRFS at day 14. Forest Plot

Conclusions

These results confirm the prognostic role of ST2, REG3α and MAGIC algorithm in haplo-SCT outcomes in the largest single-center cohort to date of a homogeneous series of haplo-SCT. We also demonstrate, for the first time, the MAGIC algorithm prognostic impact in haplo-SCT on day +14.

Standardization in prospective and larger series is required before its incorporation into the clinical practice.

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