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TCT Meeting 2019 | GvHD biomarker algorithms for predicting lethal graft-versus-host disease

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On 23 February 2019 at the 2019 TCT Transplantation and Cellular Therapy Meetings of ASBMT and CIBMTR in Houston, Texas, USA, Professor John E. Levine presented data on behalf of Aaron Etra, both from The Tisch Cancer Institute and Division of Hematology / Medical Oncology, Icahn School of Medicine at Mount Sinai, NY, USA, of a study evaluating the predictive accuracy of different graft-versus-host disease (GvHD) biomarker (BM) combinations. Study endpoint was to determine the best combination of biomarkers at GvHD onset that predict six-month non-relapse mortality (NRM).

To date, the following biomarkers have shown to predict GvHD outcomes:

Organ damage BM:

- **ST2**: soluble receptor for IL-33, secreted by GI tract
- **REG3a**: antimicrobial peptide secreted by Paneth cells
- **AREG**: EGFR ligand required for tissue damage repair

Systemic GvHD BM:

- **TNFR1**: produced by MΦ/activated T cells, promote gut apoptosis
- **IL6** and **TIM3**: promote B and T cell recruitment/activation, inhibit T cell apoptosis

Multiple publications have shown that combinations of these biomarkers predict NRM, but these combinations have never been compared to each other in the same dataset.

Patients and methods:

- N = 522 patients with serum samples at GvHD onset who received transplantation at 19 Mount Sinai Acute GvHD International Consortium (MAGIC) centers from 1 January 2004 to 30 April 2017 were included in this study
- Patients were divided into a training (n = 253; median age: 52 years [range, 1–74]) and a validation (n = 269, median age: 52 years [range, 1–74]) cohort. The training set patients were used to identify the best combinations of biomarkers that predicted NRM. The validation set was used to verify these findings.
- Biomarkers were measured by ELISA

Key findings:

- AREG and IL6 were not predictive of NRM
- All potential combinations of the following were assessed: REG3a, ST2, TNFR1, and TIM3
- In the training cohort, biomarker combinations results showed:
  - Although some novel biomarker combinations were predictive of NRM, no new combination was superior to already published biomarker combinations
- The validation set examined all published combinations
  - Accuracy was similar among all combinations except the combination of TIM3 plus IL6 plus TNFR1 which was inferior

In conclusion, the study authors noted that ST2, REG3a, TNFR1, and TIM3 individually and in combinations were predictors of NRM. Furthermore, no new biomarker combinations were identified that were able to predictor NRM with greater significance compared to published combinations.

Reference

1. Etra A., Levine J.E. *et al*. Comparison of GvHD biomarker algorithms for predicting lethal GvHD and non-relapse mortality. Oral Abstract #67. 2019 TCT Transplantation and Cellular Therapy Meetings of ASBMT and CIBMTR in Houston, Texas, USA. Slides were provided to the GvHD Hub by John E. Levine.