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# POSTER ABSTRACTS

## 721.ALLOGENEIC TRANSPLANTATION: CONDITIONING REGIMENS, ENGRAFTMENT AND ACUTE TOXICITIES

### Effect of Early Cytomegalovirus Reactivation on Relapse in Adult Patients with Myelodysplastic Syndromes after Allogeneic Hematopoietic Stem Cell Transplantation: A Registry Study from the Japan Society for Transplantation and Cellular Therapy (JSTCT)

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**Background**

Cytomegalovirus reactivation (CMVR) is a well-known complication contributing to morbidity and mortality in patients undergoing allogeneic hematopoietic stem cell transplantation (HSCT). Previous studies have demonstrated that CMVR is associated with poor clinical outcomes following HSCT. However, some studies have shown that CMVR following HSCT may have a recurrence-suppressing effect on hematological diseases, including acute myeloid leukemia and acute lymphoblastic leukemia. Conversely, data on the relevance between CMVR and relapse in patients with myelodysplastic syndromes (MDS) following HSCT remain limited and inconclusive. This nationwide retrospective study aimed to examine the association between CMVR and MDS relapse following HSCT.

**Methods**

This study was conducted by the Adult Myelodysplastic Syndromes Working Group of the Japan Society for Transplantation and Cellular Therapy (JSTCT). Clinical data were collected by the JSTCT and the Japanese Data Center for Hematopoietic Cell Transplantation employing the Transplant Registry Unified Management Program (TRUMP). Overall, 1,082 patients aged ≥16 years who were diagnosed with de novo MDS, underwent initial allogeneic HSCT between 2010 and 2018, and survived until 100 days post-transplant without disease relapse were examined. Patients who received cord blood transplantation, in vivo T-cell depletion, and prophylactic anti-CMV treatment were excluded. CMVR was defined as the initiation of CMV preemptive or definitive therapy within 100 days post-transplant. Patients underwent pp65 antigenemia monitoring commencing at the time of neutrophil engraftment after HSCT. Preemptive therapy was typically instituted upon the detection of a minimum of 2 CMV pp65 antigen-positive cells per 50,000 white blood cells. In analysis, CMVR and acute/chronic graft-versus-host disease (GVHD) were evaluated as time dependent covariates. This retrospective study was approved by the Data Management Committee of the JSTCT and the ethics committee of the Ehime University School of Medicine.

**Results**

Of the 1,082 patients, 622 (57.5%) experienced CMVR. The median time from HSCT to the onset of CMVR was 46 (range, 4-97) days. In contrast, reactivation beyond 100 days after HSCT was observed in 20 patients (1.8%). End-organ disease due to CMV infection was detected in 79 (7.3%) patients with a median of 61 (range, 19-385) days. CMV infections included enteritis (n = 65), retinitis (n = 5), pneumonitis (n = 4), hepatitis (n = 3), and others (n = 3). Of the whole cohort, the 5-year cumulative incidence of relapse (CIR), non-relapse mortality (NRM), disease-free survival, and overall survival (OS) were 15.6%, 26.7%, 57.7%, and 60.5%, respectively. The OS of patients with CMVR was significantly lower than that of patients without CMVR (P = 0.047). A total of 423 patients died at the time of analysis, and no difference in the cause of death was found between patients with and without CMVR. Then, the effect of CMVR on relapse after HSCT was analyzed by patient, disease, and transplant characteristics. Interestingly, in patients with <5% bone marrow blast count at the time of HSCT, CMVR was significantly associated with a lower CIR (5-year CIR, 7.6% vs. 16.4%; P = 0.002). On the contrary, no difference in the CIR was found between patients with and without CMVR in the group with ≥5% bone marrow blast count (5-year CIR, 19.4% vs. 18.0%; P = 0.72). Moreover, the OS of patients with CMVR was significantly lower than that of patients without CMVR in the group with ≥5% bone marrow blast count (P = 0.009). However, the OS of patients with <5% bone marrow blast count was similar between with and without CMVR (P = 0.82). In the multivariate analysis, CMVR was significantly associated with a lower CIR in the group with <5% bone marrow blast count (hazard ratio [HR], 0.40; 95% confidence interval [CI], 0.23-0.70; P = 0.001). Furthermore, in the analysis excluding patients with grade II-IV acute GVHD, CMVR was similarly associated with a lower CIR in the group with <5% bone marrow blast count (HR, 0.38; 95% CI, 0.18-0.80; P = 0.011).

**Conclusion**

This study presents that CMVR may have different effects on MDS relapse depending on the bone marrow blast count at the time of HSCT. Although more studies are needed to understand the underlying mechanisms of this association, these findings may serve as a basis for devising effective CMV prophylaxis after HSCT.

**Disclosures Matsuda:** *SymBio:* Honoraria; *Ono Pharmaceutical:* Honoraria; *Sanofi:* Honoraria; *Kyowa Kirin:* Honoraria; *AbbVie:* Honoraria. **Doki:** *Novartis Pharma K.K.:* Honoraria; *Janssen Pharmaceutical K.K.:* Honoraria. **Kanda:** *AbbVie:* Research Funding, Speakers Bureau; *CSL Behring:* Speakers Bureau; *Japan Blood Products Organization:* Research Funding, Speakers Bureau; *Otsuka Pharmaceutical:* Research Funding, Speakers Bureau; *AstraZeneca:* Speakers Bureau; *Human Life CORD:* Speakers Bureau; *Sumitomo Pharma:* Research Funding, Speakers Bureau; *Amgen:* Speakers Bureau; *Takeda Pharmaceutical:* Research Funding, Speakers Bureau; *Meiji Seika Pharma:* Speakers Bureau; *Asahi Kasei Pharma:* Research Funding, Speakers Bureau; *Daiichi Sankyo:* Research Funding, Speakers Bureau; *Saitama Hokeni Kyokai:* Speakers Bureau; *MSD:* Speakers Bureau; *Kyowa Kirin:* Research Funding, Speakers Bureau; *Janssen Pharmaceutical:* Speakers Bureau; *Sanofi:* Speakers Bureau; *Pfizer:* Speakers Bureau; *Chugai Pharmaceutical:* Research Funding, Speakers Bureau; *Novartis:* Speakers Bureau; *Bristol Myers Squibb:* Speakers Bureau; *Towa Pharma:* Speakers Bureau; *Precision:* Speakers Bureau; *FUJIFILM Wako Pure Chemical:* Speakers Bureau; *Alexion Pharma:* Speakers Bureau; *Wakunaga Pharmaceutical:* Speakers Bureau; *Eisai:* Research Funding, Speakers Bureau; *Nippon Shinyaku:* Speakers Bureau; *Shionogi Pharma:* Research Funding; *Taiho Pharmaceutical:* Research Funding; *Nippon Kayaku:* Research Funding; *JCR Pharmaceuticals:* Research Funding. **Kanda:** *Amgen:* Ended employment in the past 24 months, Honoraria; *Janssen Pharmaceutical K.K.:* Honoraria; *Novartis Pharma K.K.:* Honoraria; *Sanofi K.K.:* Honoraria; *AbbVie Pharma:* Honoraria; *Megakaryon Co.:* Honoraria; *Eisai Co.:* Research Funding. **Nakamae:** *Parexel International Inc:* Research Funding; *CMIC Company:* Research Funding; *Novartis:* Research Funding; *Takeda Pharmaceutical Company:* Honoraria; *Alexion Pharma:* Research Funding; *Meiji Seika Pharma:* Research Funding; *DAIICHI SANKYO COMPANY:* Honoraria; *Janssen Pharmaceutical K.K.:* Honoraria; *Nihon Shinyaku:* Honoraria; *Sumitomo Dainippon Pharma:* Honoraria; *Bristol-Myers Squibb:* Research Funding; *Amgen:* Honoraria; *Otsuka:* Honoraria; *Abbvie:* Honoraria; *Astellas:* Honoraria. **Ichinohe:** *Chugai:* Honoraria, Research Funding; *Kyowa Kirin:* Research Funding; *Nippon Kayaku Co.:* Honoraria; *Novartis:* Honoraria; *Ono Pharmaceutical Co.:* Honoraria; *AsahiKasei Pharma Co.:* Honoraria, Research Funding; *Abbvie Co.:* Honoraria, Research Funding; *Nippon Shinyaku Co.:* Honoraria, Research Funding; *Repertoite Genesis Inc.:* Research Funding; *Takeda Pharmaceutical Co.:* Honoraria; *Wakunaga Pharmaceutical Co., Ltd.:* Research Funding; *Sumitomo Pharma Co:* Honoraria, Research Funding. **Atsuta:** *Meiji Seika Pharma Co, Ltd.:* Honoraria; *Novartis Pharma KK:* Speakers Bureau; *JCR Pharmaceuticals Co., Ltd.:* Consultancy; *Otsuka Pharmaceutical Co., Ltd:* Speakers Bureau; *CHUGAI PHARMACEUTICAL CO., LTD.:* Speakers Bureau.

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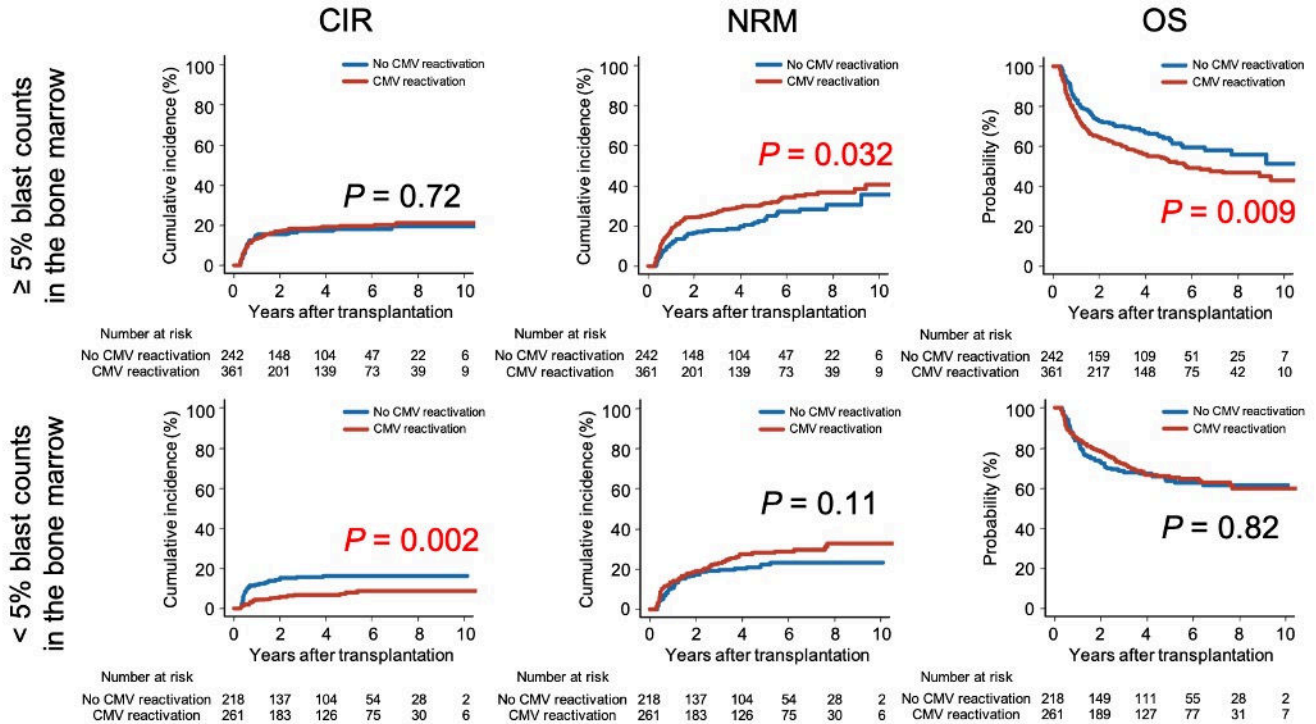


**Variables influencing the clinical outcomes of BM blast counts <5% group in multivariate analysis**

| Variable | Cumulative incidence of relapse | | | | Non-relapse mortality | | | | Overall survival | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Univariate | | Multivariate | | Univariate | | Multivariate | | Univariate | | Multivariate | |
| | HR (95% CI) | P-value | HR (95% CI) | P-value | HR (95% CI) | P-value | HR (95% CI) | P-value | HR (95% CI) | P-value | HR (95% CI) | P-value |
| CMV reactivation, Yes vs. No | 0.425 (0.244-0.740) | 0.002 | 0.398 (0.227-0.699) | 0.001 | 1.343 (0.931-1.937) | 0.12 | 1.239 (0.822-1.868) | 0.31 | 0.965 (0.711-1.311) | 0.82 | 0.828 (0.587-1.167) | 0.28 |
| Age at HCT, ≥50 vs. <50 years | 1.550 (0.867-2.774) | 0.14 | | | 1.796 (1.199-2.689) | 0.005 | 2.028 (1.281-3.210) | 0.003 | 1.906 (1.353-2.686) | <0.001 | 1.846 (1.248-2.731) | 0.002 |
| CMV serostatus, D+ or R+ vs. D-/R- | 1.220 (0.434-3.427) | 0.71 | | | 0.919 (0.481-1.756) | 0.8 | | | 0.919 (0.481-1.756) | 0.8 | | |
| Unrelated donor vs. related donor | 1.336 (0.717-2.489) | 0.36 | | | 1.369 (0.893-2.100) | 0.15 | | | 1.406 (0.978-2.020) | 0.065 | 1.101 (0.670-1.809) | 0.7 |
| MAC regimen vs. RIC/NMA regimen | 1.391 (0.778-2.487) | 0.27 | | | 0.956 (0.662-1.380) | 0.81 | | | 1.013 (0.738-1.392) | 0.94 | | |
| Source, BM vs. PBSC | 1.638 (0.772-3.474) | 0.2 | | | 0.868 (0.568-1.326) | 0.51 | | | 0.982 (0.676-1.427) | 0.92 | | |
| GVHD prophylaxis, FK-based vs. CsA-based | 1.505 (0.756-2.993) | 0.24 | | | 1.375 (0.875-2.161) | 0.17 | | | 1.416 (0.966-2.077) | 0.075 | 1.225 (0.741-2.026) | 0.43 |
| Anti-thymocyte globulin use, Yes vs. No | 0.865 (0.390-1.918) | 0.72 | | | 1.238 (0.763-2.010) | 0.39 | | | 1.188 (0.781-1.807) | 0.42 | | |
| aGVHD, II-IV vs. Nothing or I | 0.756 (0.429-1.331) | 0.33 | | | 1.717 (1.198-2.462) | 0.003 | 1.570 (1.039-2.372) | 0.032 | 1.458 (1.072-1.984) | 0.016 | 1.463 (1.030-2.079) | 0.034 |
| cGVHD, Yes vs. No | 1.572 (0.890-2.778) | 0.12 | | | 1.547 (1.053-2.273) | 0.026 | 1.375 (0.927-2.039) | 0.11 | 1.428 (1.025-1.989) | 0.035 | 1.360 (0.966-1.916) | 0.078 |
| Chemotherapy before HCT, Yes vs. No | 1.984 (1.162-3.386) | 0.012 | 1.848 (1.071-3.187) | 0.027 | 1.054 (0.712-1.559) | 0.79 | | | 1.348 (0.978-1.859) | 0.068 | 1.130 (0.787-1.622) | 0.51 |
| Azacitidine before HCT, Yes vs. No | 1.975 (1.137-3.433) | 0.016 | 2.273 (1.305-3.960) | 0.004 | 1.167 (0.784-1.736) | 0.45 | | | 1.445 (1.034-2.019) | 0.031 | 1.285 (0.874-1.889) | 0.2 |
| IST before HCT, Yes vs. No | 0.331 (0.120-0.914) | 0.033 | 0.456 (0.160-1.299) | 0.14 | 1.311 (0.853-2.015) | 0.22 | | | 0.925 (0.619-1.381) | 0.7 | | |
| Years of HCT, 2015-2018 vs. 2010-2014 | 1.367 (0.802-2.331) | 0.25 | | | 1.221 (0.848-1.757) | 0.28 | | | 1.261 (0.922-1.724) | 0.15 | | |

**Figure 1**