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**GENOTYPING OF HUMAN CYTOMEGALOVIRUS (HCMV) GLYCOPROTEIN B (gB) IN HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS WITH ACTIVE HCMV INFECTION: IMPACT OF gB GENOTYPES ON THE PATIENT’S OUTCOME**


Based on sequence variation in the UL55 gene that encodes glycoprotein B (gB), human cytomegalovirus (HCMV) can be classified into four gB genotypes. There is little information about the CMV gB genotype and clinical outcome in patients who underwent an allogeneic hematopoietic stem cell transplant (HSCT) in Brazil.

**Objectives:** The goal of this study was to determine the distribution of gB genotypes in allogeneic HSCT patients with CMV infection and the effect of gB type on clinical outcome including CMV disease.

**Study design:** The diagnosis of HCMV infection after allogeneic HSCT was detected by Antigenemia (AGM) and Nested-PCR (N-PCR). All patients with CMV infection received ganciclovir preemptive treatment. Positive samples from patients with active HCMV infection were submitted to genotyping using the N-PCR to amplify a region of UL55, followed by restriction analysis based on Hinf I and Rsa I digestion and subsequent sequencing aligned with known CMV variants in GenBank.

**Results:** Were evaluated 55 allogeneic HSCT recipients, 41/55 patients (74,5%) presented active HCMV infection detected by AGM and Nested-PCR. All patients with active HCMV infection received ganciclovir preemptive treatment. Positive samples from patients with active HCMV infection were submitted to genotyping using the N-PCR to amplify a region of UL55, followed by restriction analysis based on Hinf I and Rsa I digestion and subsequent sequencing aligned with known CMV variants in GenBank.

**Conclusions:** In this study the most prevalent genotype in patients with HCMV active infection was gB type 1 and moreover, the mixture of HCMV gB genotypes was associated with gastrointestinal disease, and these two patients had infection with a mixture of HCMV gB genotypes.

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**RELAPSE AFTER ALLOGENEIC STEM CELL TRANSPLANTATION (SCT): RETRANSLANTATION DOES NOT IMPROVE OUTCOME IN COMPARISON TO SUPPORTIVE CARE AND CHEMOTHERAPY**

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Relapse post allogeneic SCT is a life threatening event and we report here our treatment strategies.

Between 12/1994 and 6/2010 449 pts. (median age: 42 years, 16 – 70) underwent allogeneic SCT from an unrelated (n = 263) or a matched related (n = 186) donor for treatment of acute myeloblastic leukemia, AML (n = 277) or acute lymphocytic leukemia, ALL (n = 172). 240 pts. were transplanted in CR1, 209 pts. beyond CR1, 241 pts. were male, 208 pts. were female. Post allogeneic SCT 193/449 pts. (43 %) are alive in complete remission (CR), 142/449 pts. (32 %) relapsed and 114/449 pts. (25 %) died due to non relapse mortality (NRM). In the 142 relapsed patients the median duration of remission post allogeneic SCT was short (5 months, 1 – 135) and the median age of the patients at relapse was 43 years (17 – 68). Our treatment strategies for relapse were as follows: Firstly stop of immunosuppression. Thereafter, in fit patients reinduction chemotherapy with preparative regimen of a median time of 32 days after the transplant. The distribution of HCMV gB genotypes in 30/41 patients with HCMV infection detected by AGM and Nested-PCR was as follow: gB1, 10/30 (33,3%); gB3, 2/30 (6,7%); gB4, 2/30 (6,7%) and two patients (6,7 %) had mixed infection with gB1+gB3 and gB2+gB3. The sequencing confirmed the four CMV gB genotypes. HCMV disease developed in 2 patients, characterized for gastrointestinal disease, and these two patients had infection with a mixture of HCMV gB genotypes.

**Conclusions:** in this study the most prevalent genotype in patients with HCMV active infection was gB type 1 and moreover, the mixture of HCMV gB genotypes was associated with gastrointestinal disease. It suggests that gB genotypes may have influence on the patient’s outcome in a Brazilian population.

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**THE TIMING OF ALEMTUZUMAB SIGNIFICANTLY IMPACTS MIXED CHIMERISM AND ACUTE GRAFT VERSUS HOST DISEASE**


Reduced-intensity conditioning (RIC) regimens that contain alemtuzumab are often associated with a high incidence of mixed chimerism and a low incidence of acute graft versus host disease (GVHD). Both observations may be due to alemtuzumab-mediated depletion of graft lymphocytes. To determine if the timing of alemtuzumab administration influences the risk of acute GVHD and acute and chronic GVHD, we compared the outcomes of 102 patients with non-malignant diseases who underwent RIC-HCT using fludarabine and melphalan at our institution with 2 different alemtuzumab schedules. Forty-nine patients received a proximal alemtuzumab schedule, consisting of a median dose of 1mg/kg alemtuzumab divided over 4-5 consecutive days between days +12 to +4. Fifty-two patients received a distal alemtuzumab schedule, consisting of a median dose of 2.6mg/kg alemtuzumab divided over 3-4 consecutive days between days -23 to -10. All patients engrafted at a median of 11.5 days with the exception of 1 patient in each group who died at day +17 and +15. Excluding these 2 patients, the overall incidence of acute rejection and/or mixed chimerism in the proximal group (2 patients with acute rejection) was 35/48 patients (73%) versus 20/51 patients (39%) in the distal group (no acute rejection) (p = 0.01). Acute GVHD prophylaxis was rarely weaned in the majority of patients with mixed chimerism. Six patients in the proximal group and 4 patients in the distal group received hematopoietic cell boost (p = 0.16), and donor lymphocyte infusions (DLI) were administered to 18 patients in the proximal group and 5 patients in the distal group (p = 0.002). Prior to these interventions, acute GVHD grades II-IV developed in only 1 patient in the proximal group (2%), and 9 patients in the distal group (17%) (p = 0.05). Following these interventions, acute GVHD grades II-IV occurred in 7 patients in the proximal group and 6 patients in the distal group, making the total overall incidence of acute GVHD grades II-IV 16% in the proximal group versus 29% in the distal group (p = 0.1). Ultimately, 4 patients in the proximal group and 1 patient in the distal group required a second transplant. We conclude that the timing of alemtuzumab significantly influences the incidences of both mixed chimerism and acute GVHD. Further studies to optimize the doses given of alemtuzumab are warranted.