



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Table 1

CMV reactivation adjusted for conditioning, donor serostatus and graft source

	Full Chimerism	Mixed Chimerism
CMV infection	54%	52%
Magnitude Viremia (median) (range)	1600 copies/ml (700, 3600)	1300 copies/ml (600, 3800)
Duration of Viremia	15 days	12 days
Multiple CMV infection	1.8 reactivations	1.6 reactivations
Early with Late CMV infection	22%	20%

donor. None of these groups had an impact on incidence or control of CMV reactivation.

Conclusion: Mixed or full donor engraftment was not associated with incidence or control of CMV infection after SCT. Early chimerism will not be useful in risk stratification or as a predictive indicator for CMV reactivation.

226

Impact of Pathogen-Reduced Psoralen-Treated Platelets on Blood Component Utilization and Safety in Hematology/Oncology Patients in Routine Use

Jessica L. Hanover¹, Marco Amato², Harald Schennach², Manfred Astl², Chih Yu Chen², Jin-Syng Lin¹, Richard J. Benjamin¹, Walter Nussbaumer³.¹ Cerus Corporation, Concord, CA; ² Central Institute for Blood Transfusion and Immunology, Medical University Hospital Innsbruck, Innsbruck, Austria; ³ Department Transfusion Medicine, University Hospital Innsbruck, Innsbruck, Austria

Introduction: In 2013, University Hospital, Innsbruck, Austria introduced pathogen reduction (PR) of all whole-blood buffy-coat and apheresis platelet components (PC) with a psoralen (amotosalen) and UVA light (INTERCEPT™ Blood System) to mitigate bacterial and other infectious risks and replace gamma irradiation for prevention of transfusion-associated graft versus host disease (TA-GVHD). In clinical studies, utilization of psoralen-treated PC did not impact patient risk for hemorrhage, but did affect transfusion frequency and component utilization. We evaluated the influence of psoralen-treated PC on platelet, red cell concentrate (RCC) and plasma use and safety in routine practice in a 1600-bed regional hospital across all patient populations, including hematology/oncology (H/O) patients.

Methods: Comparative effectiveness of conventional versus psoralen-treated PC was analyzed before (control period: April 1, 2011 – December 31, 2012) and after (test period: April 1, 2013 – December 31, 2014) PR implementation. Patient demographics, component characteristics and transfusion-related adverse events (AE) were extracted from blood bank electronic medical records. Patients were transfused with PC based on clinicians' assessment of clinical condition and peripheral blood platelet count of <20,000/uL in non-bleeding patients. Changes in component utilization were investigated in all patients; here we focus on the H/O patient subset.

Results: For both periods, similar numbers of all patients were transfused (control = 1797; test = 1694) with comparable numbers of PC (control = 8611; test = 7705). H/O patients accounted for 522 (control = 29.0%) and 452 (test = 26.7%) of patients transfused, and received the largest proportion of PC during both periods (control = 5126, 59.5%; test = 4070, 52.8%). H/O patients had fewer days of PC support in the test period (control = 14.7, test = 12.3; $P = .03$) with similar mean per-patient PC usage (control = 9.8, test = 9.0 PC/patient; $P = .41$). In H/O patients, PC age at transfusion was higher (control = 3.5 days, test = 3.8 days; $P < .01$), as unlike conven-

tional PC, psoralen-treated PC did not require bacterial reculture at day 4 for use out to 7 days. No increases in PC, plasma and RCC utilization, or AE, were observed in the H/O group post-PR introduction. H/O patients (control = 4.2%, test = 4.4%; $P = .88$) were more likely to experience an AE than the total population (control = 1.3%, test = 1.4%; $p = 1.00$). No cases of TRALI, TA-GVHD, transfusion-related sepsis, transfusion-transmitted viral infections, or any deaths were attributed to PC transfusion.

Conclusions: In routine use of PR psoralen-treated PC, blood component utilization and safety were not impacted in H/O patients, compared to prior conventional PC use. RCC use per patient was comparable, suggestive of no increase in significant bleeding.

227

Impact of Pretransplant Respiratory Virus Detection through Universal Screening in Children Undergoing Hematopoietic Cell Transplantation (HCT)

Yae-Jean Kim^{1,2}, Alpna Waghmare¹, Jane M. Kuypers³, Keith R. Jerome³, Steven A. Pergam⁴, Hu Xie¹, Wendy M. Leisenring¹, Chikara Ogimi⁵, Michael J. Boeckh^{4,6,7}, Janet A. Englund^{5,8}.¹ Fred Hutchinson Cancer Research Center, Seattle, WA; ² Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University, Seoul, Republic of Korea; ³ Laboratory Medicine, University of Washington, Seattle, WA; ⁴ Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, WA; ⁵ Seattle Children's Hospital, Seattle, WA; ⁶ Medicine, University of Washington, Seattle, WA; ⁷ School of Medicine, University of Washington, Seattle, WA; ⁸ Pediatrics, University of Washington, Seattle, WA

Background: Pretransplant respiratory virus infection among patients undergoing HCT has been previously shown to have a negative impact on transplant outcomes in HCT recipients of all ages (Clin Inf Dis 61:192, 2015). We examined the impact of pretransplant detection of 11 respiratory viruses in a pediatric HCT population.

Method: Patients transplanted from 3/2010 to 3/2016 were retrospectively studied through day 100 post-HCT. All pediatric patients were universally screened for respiratory viruses prior to HCT using RT-PCR. Respiratory virus test results <90 days before HCT were included. Viruses were categorized into three groups: adenoviruses, respiratory syncytial virus, influenza viruses, human metapneumovirus, and parainfluenza viruses type 1–4 (group 1); human rhinoviruses (group 2); and human coronaviruses (group 3). HCT was delayed whenever possible if any respiratory virus was detected pre-HCT. Transplant outcomes included “days alive and out of hospital by day 100” post-HCT (analyzed by univariable and multivariate linear regression models) and overall mortality (estimated and analyzed by Kaplan-Meier curves and Cox models).

Results: Of 218 pediatric HCT recipients, respiratory viruses were detected prior to HCT in 81 patients (37%). Group 2 viruses were most commonly detected (24%), followed by group 1 (11%) and group 3 (2%). Median day of last positive virus test result prior to transplant was –16 (IQR –27 to –11). Death occurred in 3% (6/218) of all patients by day 100 (only in allograft recipients). No significant difference in overall mortality was seen between children with and without pretransplant respiratory virus detection in all patients and in the allogeneic HCT subset.

In a multivariable linear regression analysis in allogeneic HCT recipients, patients with group 1 and group 2 viruses had significantly fewer days alive and out of hospital compared to

those without a pretransplant virus (mean difference: group 1, -12.7 , 95% CI -21.9 to -3.5 , $P = .007$; group 2, -7.4 , 95% CI -14.0 to -0.9 , $P = .026$; group 3, -9.6 , 95% CI, -31.3 to 12.1 , $P = .386$) after adjusting for recipients' age < 5 years at transplant (mean difference vs. ≥ 5 years: -7.3 , 95% CI, -13.6 to -1.1 , $P = .021$) and cord blood as a stem cell source (mean difference vs. non-cord recipients: -12.0 , 95% CI -18.6 to -5.4 , $P < .001$).

Conclusion: In pediatric HCT recipients, pretransplant detection of respiratory viruses, including human rhinoviruses, is associated with increased hospitalization within the first 100 days. More data are needed to define the reasons for prolonged hospitalization in children with pretransplant respiratory virus detection.

228

Incidence, Severity, Day 100 Treatment Efficacy and Therapy Toxicity of Cytomegalovirus (CMV) Infections with Early Pre-Emptive Therapy in Adult Cord Blood (CB) Transplant Recipients

Carmen Lau¹, **Valkal Bhatt**², **Parastoo Dahi**³, **Sean M. Devlin**⁴, **Yeon Yoo**³, **Nelly G. Adel**⁵, **Chris Mazis**⁶, **Miguel-Angel Perales**³, **Sergio A. Giralt**³, **Guenther Koehne**³, **Doris M. Ponce**³, **Genovefa A. Papanicolaou**⁷, **Juliet N. Barker**³.

¹ Bone Marrow Transplant, Memorial Sloan Kettering Cancer Center, New York, NY; ² Department of Pharmacy, Memorial Sloan Kettering Cancer Center, New York, NY; ³ Department of Medicine, Adult Bone Marrow Transplant Service, Memorial Sloan Kettering Cancer Center, New York, NY; ⁴ Department of Biostatistics and Epidemiology, Memorial Sloan Kettering Cancer Center, New York, NY; ⁵ Department of Pharmacy, Memorial Sloan-Kettering Cancer Center, New York, NY; ⁶ Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; ⁷ Memorial Sloan Kettering Cancer Center, New York, NY

Introduction: CMV infection can increase mortality after CBT. We are investigating: 1) the efficacy of pre-transplant ganciclovir (GAN) prophylaxis, 2) the efficacy of early pre-emptive therapy & 3) the toxicities of anti-viral therapy. Our aim is to rapidly eradicate viremia & prevent disease without prohibitive toxicity.

Methods: Adult CMV seropositive CB recipients were transplanted 2013-2016 with Cy 50/ Flu 150/ Thio 5-10/ TBI 400 cGy conditioning + CSA/ MMF + GAN prophylaxis (5 mg/kg IV daily) days -7 to -2 . Viremia was monitored by Roche qPCR (lower limit 137 IU/ml) twice weekly from \leq day +14. Treatment was usually initiated at 1st-2nd qPCR positivity. Maintenance vs induction Foscarnet (FOS), GAN or valganciclovir (VALGAN) dosing was based on viremia level & assessment of severe infection vs toxicity risks. Response was 3 consecutive negative qPCR & no disease.

Results: 42 pts [median 51 years (range 23-66), 33 acute leukemias, 6 MDS/ MPD, 3 lymphomas] received double unit grafts [median HLA-match 5/8 (range 2-7/8) & inf. CD34+ cell dose 1.3 (range .2-3.2) $\times 10^5$ /kg/unit]. 98% engrafted & 86% (26 gr. II, 7 gr. III, 3 gr. IV) developed grades II-IV aGVHD by day 100 (median onset 29 days, range 19-35). By day 100, 35 pts reactivated CMV [median onset 33 days (range 5-74) & viral load at 1st detection < 137 IU/ml (range < 137 -245)] for an 83% (95%CI 67-92) day 100 cumulative incidence. Median peak viremia was 293 IU/ml (range < 137 -146,304). Of 31 pts with both CMV & aGVHD, 15 developed viremia before & 16 after aGVHD onset. Median detection to therapy time was 3 days (range 0-39). Treatment dosing & responses are shown

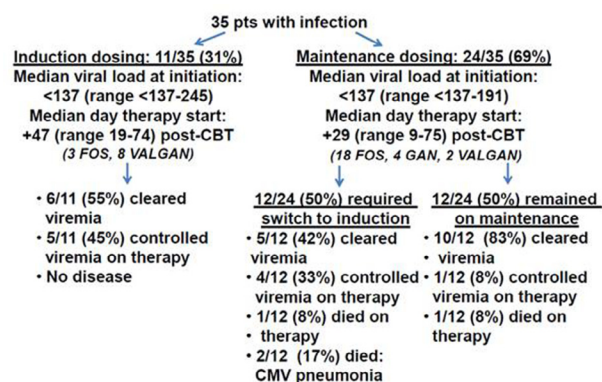


Figure 1. CMV infections & treatment efficacy in the 1st 100 days post-CBT.

Table 1

Toxicities of CMV therapy within the first 100 days post-CBT

Foscarnet (n = 25)*	Value
Nephrotoxicity requiring dose reduction or therapy change	N = 8 pts (32%, 3 induction, 5 maintenance) Median: 1.7 fold (range 1.2-3.4) creatinine increase over baseline
Ganciclovir/ valganciclovir (n = 31)*	Value
G-CSF treatment (ANC < 2) Number of doses	N = 19 pts (61%) Median: 4 (range 1-13)

* 21 pts received both (started with one & switched to the other)

(Figure 1). Pts who received induction (n = 11) started therapy later usually with VALGAN. By day 100, only half cleared but none developed disease. Pts commenced on maintenance (n = 24) received therapy earlier (mostly FOS). 10 cleared viremia whereas half required dose intensification (10 lack of viremia response & 2 CMV pneumonia). The 2 pneumonia pts developed disease 26 & 12 days post-therapy initiation (peak viremia 1330 & 613 IU/ml, respectively), & both died (2/4 study deaths by day 100). 4 pts received only FOS, 10 only GAN/ VALGAN, & 21 had courses of each. Switches were due to toxicity, inadequate response or convenience (VALGAN). One-third of FOS pts & over half of GAN/ VALGAN pts had significant toxicities (Table 1).

Conclusion: CMV infection is frequent in seropositive CBT recipients & pre-CBT GAN prophylaxis is not effective. Early monitoring with early pre-emptive therapy is effective in most pts. The development of lethal CMV pneumonia in 2 pts on maintenance suggests escalation to induction may be appropriate if rapid viremia eradication is not achieved. However, FOS/ GAN/ VALGAN toxicities are significant. The optimal dosing to enhance efficacy but mitigate toxicity, how to predict pts at greatest disease risk, appropriate therapy duration, & how to predict recurrence are not known.

229

Maribavir Versus Valganciclovir for Pre-Emptive Treatment of Cytomegalovirus Viremia: A Randomized, Dose-Ranging, Phase 2 Study Among Hematopoietic Stem Cell Transplant and Solid Organ Transplant Recipients

Johan A. Maertens¹, **Catherine Cordonnier**², **Peter Jaksch**³, **Xavier Poiré**⁴, **Jingyang J. Wu**⁵, **Anna Wijatyk**⁵, **Faouzi Saliba**⁶, **Oliver Witzke**⁷, **Stephen Villano**⁸.

¹ Universitaire Ziekenhuizen, Leuven, Belgium; ² Henri Mondor Hospital and University Paris-Est-Créteil, Créteil, France;