carcinoma infrequent after allo-HCT, we hypothesized that GI could be observed in oral mucosal cells but not in nasal mucosal cells of long-term HCT survivors.

Methods: We examined epithelial cells from buccal and nasal mucosa of 71 subjects for GI at 15 microsatellite loci spanning 14 human autosomes. The study population included long-term (4–22 yrs, n = 21) and short-term (2–3 months, n = 15) survivors of myeloablative allo-HCT, using GVHD prophylaxis with methotrexate (day 1, 3, 6 and 11) and cyclosporine (for 3–6 months). Controls included long-term (4–12 yrs, n = 14) and short-term (2–3 months, n = 3) survivors of myeloablative auto-HCT, 8 patients treated with intensive chemotherapy without HCT and 5 healthy volunteers. DNA extracted from peripheral blood leukocytes and cells of nasal and buccal mucosa was PCR amplified for a panel of 15 microsatellite markers (ABI-Identifiler). Fragment size analysis was done to identify novel allele peaks (one that was absent in donor and recipient blood pre-transplant but present in recipient mucosa post-transplant) indicative of microsatellite instability (MSI).

Results: MSI was detected in 61% long-term allo-HCT survivors in buccal mucosa, and in 5% long-term allo-HCT survivors in nasal mucosa ($p<0.001$, Fisher exact test). MSI was detected in 12% short-term allo-HCT survivors in buccal mucosa, and in 0% short-term allo-HCT survivors in nasal mucosa ($p = 0.48$). There was no association between MSI and history of clinical oral GVHD. None of the auto-HCT survivors, patients treated with chemotherapy without HCT or healthy volunteers showed MSI in buccal or nasal mucosal cells. No MSI was observed in blood leukocytes of any of the above patients or controls.

Conclusion: GI in long-term allo-HCT suvivors occurs frequently in oral mucosal cells but rarely in nasal mucosal cells. As GI was not observed in the oral mucosa of auto-HCT recipients who received similar transplant conditioning, it cannot be due to cytotoxic therapy, but it should be due to a factor unique to allo-HCT, ie, immunosuppressive drugs given for GVHD prophylaxis or graft vs host oral mucosa reaction (even if clinically silent). The graft-vs-host oral mucosa reaction may be more likely, as the GI was frequently observed late posttransplant (after discontinuation of prophylactic immunossupressive drugs) and rarely early posttransplant.

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HYPOALBUMINEMIA (< 3.0 G/DL) AND POOR KARNOFSKY PERFORMANCE (KPS<80) AT DAY +90 ARE INDEPENDENT PREDICTORS OF WORSE NON-RELAPSE SURVIVAL (NRS) AND OVERALL SURVIVAL (OS) IN ADULT ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION (ALLO-HCT) RECIPIENTS: RESULTS OF A MULTIVARIABLE ANALYSIS

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Acute GVHD (aGVHD) as a predictor of post allo-HCT survival generally relies on criteria with significant inter-observer variability. We study the impact of clinical, laboratory and pharmacologic parameters, during the immediate post-transplant phase [from hematologic engraftment till day 90 (±7)] on NRS and OS. In this analysis, 326 consecutive pts underwent allo-HCT between 09/2000 until 03/2007; 26 pts who died within 90 days from the date of cell infusion and 3 syngeneic allo-HCT recipients were excluded from analysis. A total of 297 (M/F = 170/127) patients, median age 46 (range: 17–69) yrs received an allo-HCT [MRD = 154 (52%), MUD = 109 (37%), MMRD = 3 (1%), MMUD = 31 (10%)] using PBSC = 261 (88%) or BM = 36 (12%) following myeloablative = 99 (33%), RIC = 174 (59%), or NMT = 24 (8%) for various hematologic malignancies stratified by CIBMTR risk [low = 87 (30%); int = 85 (29%); high = 125 (42%)] using various GVHD prophylaxis regimens [MTX-based = 244 (82%); MMF-based = 53 (18%)]. Pre-transplant variables [significant ($p<0.05$) or not-significant (NS) ($p\geq0.05$) in multivariable Cox proportional hazards regression analysis] included: age (≥55 vs. < 55 yrs) [OS: $p = 0.035$, HR = 1.6 (95% CI: 1.0–2.4); NRS: $p = 0.03$, HR = 2.0 (95% CI: 1.1–3.6)], donor-gender [OS: NS; NRS: NS], cell source (BM vs. PB) [OS: NS; NRS: NS], baseline KPS (≤80 vs. >80) [OS: NS; NRS: NS], CIBMTR risk (low vs. int. vs. high) [OS: NS; NRS: NS], regimen (myeloablative vs. RIC/NMT) [OS: NS; NRS: NS], donor/recipient matching-status (MRD, MUD, mismatched (ref)) [OS: p = 0.03, MRD vs. ref: HR = 2.7 (95% CI: 1.2–6.1), MUD vs. ref: HR = 2.7 (95% CI: 1.2- 6.1); NRS: NS], CD34+ dose (< 3×10^6/kg, 3–7.9 $\times 10^6$/kg, ≥8×10^6/kg) [OS: NS; NRS: NS], GVHD prophylaxis (MTX-based vs. MMF-based) [OS: NS; NRS: NS], recipient/donor CMV status [OS: NS; NRS: NS]. Multivariable regression analysis of post-transplant variables at day 90 show that a KPS<80 and hypoalbuminemia <3.0 g/dl are independent predictors of worse NRS and OS. A worsening serum creatinine (≥30%) and additional antimicrobials apart from standard prophylaxis are independent predictors of worse OS; whereas pneumonia (>0 episode by day 90) and cumulative dose of prednisone exceeding 2,650 mg are independent predictors of worse NRS. A KPS <80 and hypoalbuminemia (<3.0 g/dl), at day 90, important predictors of survival that should be considered when prognosticating outcome after allo-HCT.

Multivariable Regression Analysis for OS and NRS† Post-transplant variables at day 90 (±7) post-allo HCT §

	OS	NRS
Hospital stay (≤5 vs. >5 days)*	NS	NS
Days of TPN (>0 vs. 0)*	NS	NS
PRBC transfusion (>0 vs. 0)*	NS	NS
Platelets transfusion (>0 vs. 0)*	NS	NS
Pneumonia episodes (>0 vs. 0)*,¥	NS	p=0.0008; 2.8 (1.5, 5.1)
Episodes of CMV reactivation (>0 vs. 0)*	NS	NS
Cumulative dose of steroids (<2,650mg vs. ≥ 2,650mg)*	NS	p=0.001; 0.4 (0.2, 0.7)
Total days of steroids (<60 vs. ≥60)*	NS	NS
Dose of steroid at day 90 (±7) (<20 vs. ≥20mg/day)	NS	NS
% weight loss (≤10% vs. >10%)**	NS	NS
Acute GVHD (max grade) 0-I vs. II vs. III-IV	NS	NS
KPS at day 90 (±7) (<80 vs. ≥80)	p<0.0001; 4.7 (3.0, 7.4)	p<0.0001; 3.9 (2.0, 7.5)
Total bilirubin at day 90 (±7) (<1.1 vs. ≥1.1mg/dl)	NS	NS
% Creatinine change (≥30 vs. <30)*	p=0.0002; 2.2 (1.5, 3.3)	NS
Albumin at day 90 (±7) < 3.0 g/dl vs. > 3.5 g/dl; 3.0-3.5 g/dl vs. > 3.5 g/dl	p=0.006; 2.5 (1.4, 4.5); 1.5 (0.9, 2.3)	p=0.01; 3.2 (1.4, 7.1); 1.2 (0.6, 2.3)
Additional immunosuppressive therapy (ies) (>0 vs. 0)^	NS	NS
Additional anti-microbial(s) (>0 vs. 0)^^	p=0.002; 2.8 (1.5, 5.3)	NS

†Table entry: p-value (p) for the covariate effect;Hazard ratio (HR) (95% CI).

§The effects of post-transplant variables were adjusted for baseline variables such as age, KPS and patient/donor CMV statuses in this regression, whenever appropriate/necessary. Statistical significance defined as <0.05; NS: not significant ($p\geq0.05$). TPN: total parenteral nutrition.

*from hematopoietic engraftment until day 90 (±7).

**from initiation of conditioning chemotherapy (baseline) until day 90 (±7).

^additional anti-GVHD therapy(ies) apart from standard GVHD prophylaxis and glucocorticoids until day 90 (±7).

^^additional antimicrobials apart from acyclovir, fluconazole or voriconazole (whenever used for primary prohylaxis) and trimethoprin-sulfamethoxazole (or equivalents).

¥development of infiltrates requiring additional/alternative antimicrobials.

12

RAPID IMMUNOSUPPRESSION TAPER FOLLOWING REDUCED INTENSITY HCT FROM RELATED DONOR IS TOLERABLE BUT DOES NOT IMPROVE OUTCOMES OF ADVANCED HEMATOLOGIC MALIGNANCIES

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