Long-term immune deficiency after allogeneic stem cell transplantation: B-cell deficiency is associated with late infections

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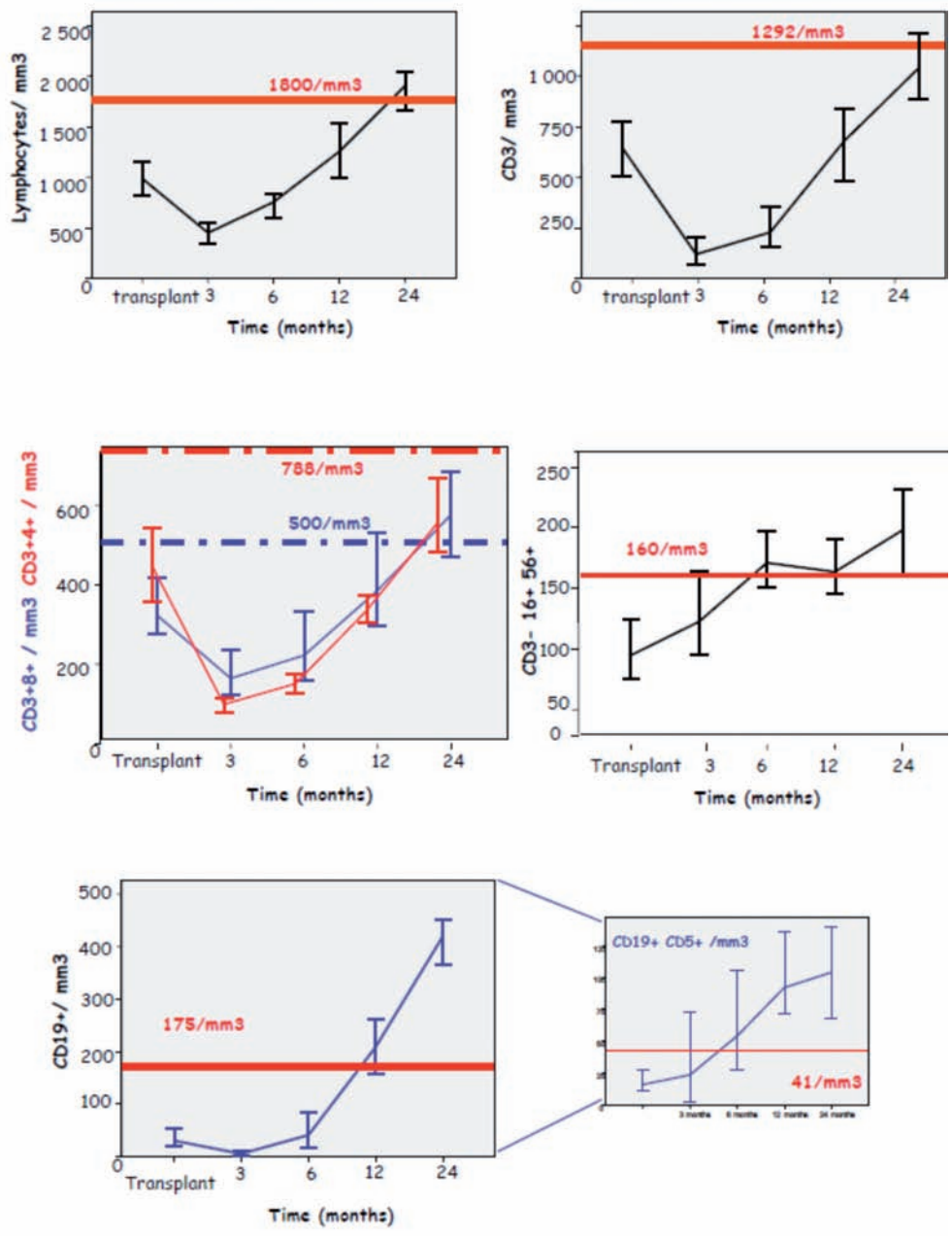
Anti-microbial prophylaxis

Amoxicillin was given at least five years after transplantation, and was continued beyond five years if patients had chronic graft-versus-host disease or received immunosuppressive treatment. Trimethoprim-sulfamethoxazole was withdrawn when immunosuppressive treatment was discontinued and the absolute CD4 count was more than 0.4×10^9/L. Acyclovir was discontinued when immunosuppressive treatment was stopped. Patients were vaccinated according to European recommendations. Briefly, all patients received tetanus toxoid, diphtheria toxoid, and polio combined vaccine within the first year. Patients were vaccinated against Influenza A and B each year before the influenza season. Pneumococcal vaccination was given according to physician's discretion. No prophylactic treatment with immunoglobulins (Ig) was delivered. However, patients with recurrent bacterial infections and with low Ig level (less than 2Gr/L) had Ig treatment substitution

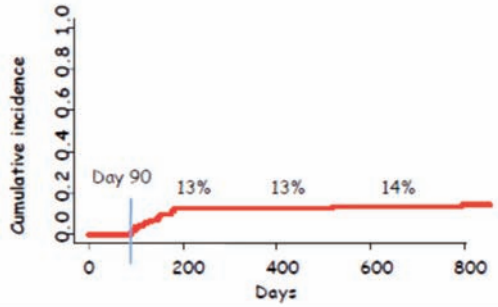
Severe infections: definitions

In brief, these included severe bacterial infections requiring hospitalization including pneumonia, sepsis syndrome, pyelonephritis, meningitis, and ostomyelitis. Bronchitis, sinusitis, and cystitis were excluded. Of note, undocumented pneumonia or sepsis syndromes or septic shock that resolved after antibiotic treatment were considered as bacterial. Viral infections included all documented invasive viral infections requiring hospitalization, namely infections related to herpes simplex virus, adenovirus, respiratory syncytial virus (RSV), human papilloma virus (HPV) in an extensive form, Epstein Barr Virus (EBV), cytomegalovirus (CMV). In addition, we collected less severe, but more common, viral infections such as VZV and viral hepatitis (B or C [HBV or HCV]). We did not include benign, presumably viral, or upper airway infection. Invasive fungal infections include those involving the lung, central nervous system, or septicemia.

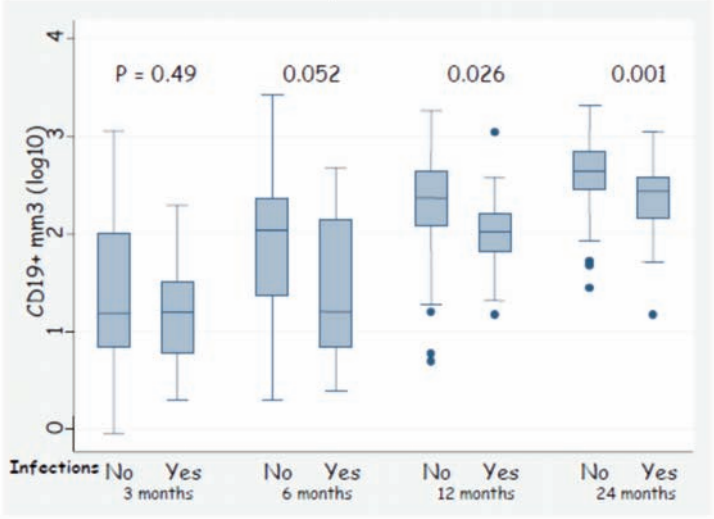


Online Supplementary Figure S1. Reconstitution of immune competent cells after Allogeneic Stem Cell Transplantation (ASCT) assessed by flow cytometry in long term survivors. Median values (±SD) of lymphocytes subsets (total lymphocytes, upper left panel; $CD3^+$ lymphocytes, upper right panel; $CD3^+CD8^+$ and $CD3^+CD4^+$ lymphocytes middle left panel; NK cells, middle right panel; $CD19^+$ lymphocytes, lower left panel; $CD19^+CD5^+$ lymphocytes, lower right panel) are represented at the indicated time (months) following ASCT in the overall population. The y-axis show cells count/mm3. Normal values (healthy controls) are represented by a red line except for $CD3^+CD8^+$ and $CD3^+CD4^+$ lymphocytes panel (blue dot line for $CD3^+CD8^+$ and red dot line for $CD3^+CD4^+$, respectively.

2 A



2 B



Online Supplementary Figure S2. Correlation between infections and B-cell counts (2A) Cumulative incidence of late infections in long-term survivors (2B) B-cell counts according to infections occurrence and presence or absence of chronic GvHD in long-term survivors. Box plots represent $CD19^{+}$ cells in patients with or without infections at the indicated time after ASCT. Lines show the median, limits of the box indicate the 25^{th} and 75^{th} percentiles while errors bars represent the 10^{th} and 90th percentiles.