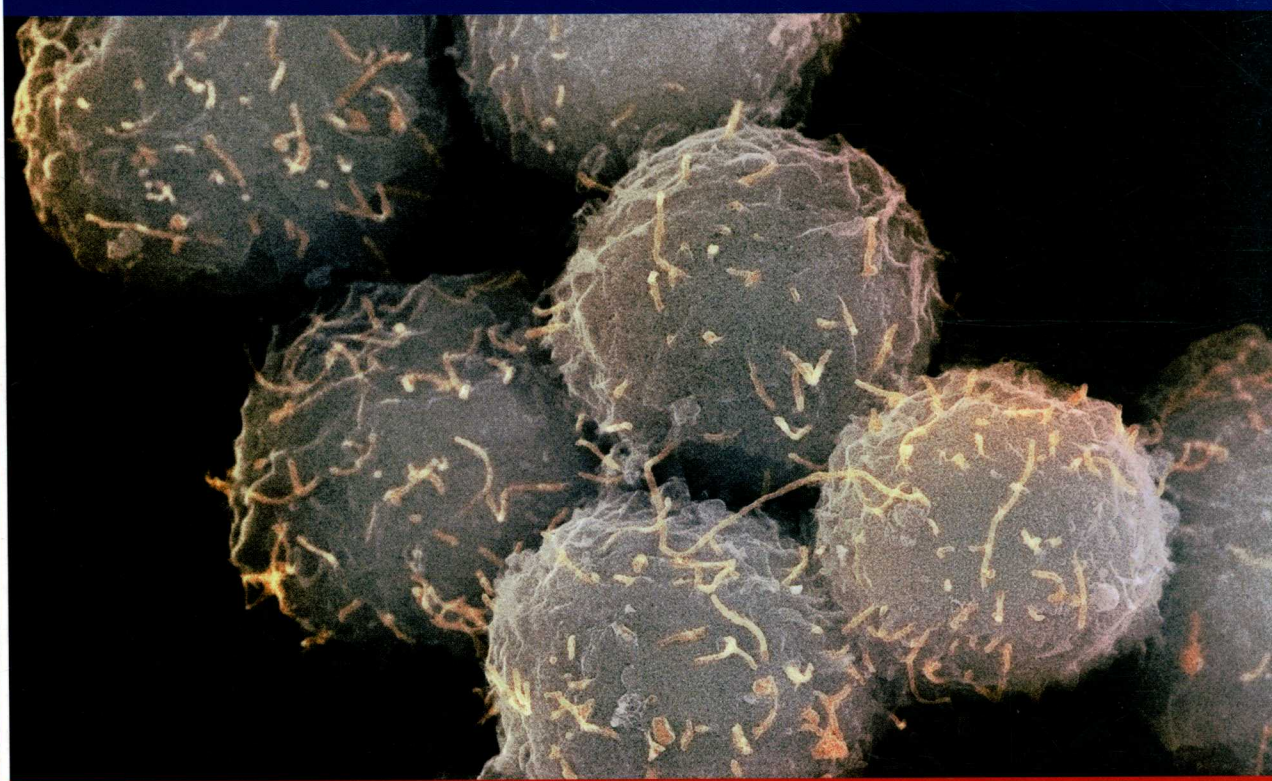
VOLUME ONE

THOMAS' HEMATOPOIETIC CELL TRANSPLANTATION



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Thomas' Hematopoietic Cell Transplantation

Stem Cell Transplantation

VOLUME I

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Preface to the First Edition

The widespread application of bone marrow transplantation (BMT) to the treatment of a steadily increasing number of life-threatening hematological, oncological, hereditary, and immunological disorders is the culmination of more than four decades of research by many investigators. Early attempts in the 1950s to transplant living cells from one individual to another were carried out in the face of considerable skepticism. It was generally accepted as axiomatic that the immunological barrier to "foreign tissue" could never be overcome.

The horrors of Nagasaki and Hiroshima spurred interest in studies of the lethal effects of irradiation. It was discovered that mice given total body irradiation in doses lethal to the marrow could be protected from death by shielding the spleen or by an infusion of marrow, and that the marrow of such animals contained living cells of donor origin. These observations suggested that patients with leukemia might be given a lethal exposure of total body irradiation, which would destroy the malignant cells along with remaining normal marrow. The exposure would also destroy the immune system, making it possible to protect against lethality by a transplant of normal marrow cells.

The theory was correct, but results were disappointing. Because the procedure was both unproved and dangerous, only those patients who had no other options were considered. Except for a few patients with an identical twin donor, there were no survivors beyond a few months. Understanding of the human leukocyte antigen (HLA) system was not yet available, and little was known about the complication we now call graft-versus-host disease (GVHD). Thus, after a brief period of enthusiasm, most investigators abandoned this seemingly hopeless pursuit. Fortunately, work in animal models continued. Studies in inbred rodents defined the genetics of the major histocompatibility system and the fundamental rules of transplantation biology. Immunosuppressive drugs were developed to limit the severity of the immune reactions between donor and host. Demonstration of successful marrow transplants in the canine model using littermates matched for the major histocompatibility complex set the stage for successful transplantation of marrow between human siblings. Thus, it is clear that a long series of experimental studies in animals ultimately made human marrow transplantation possible.

By the late 1960s, much was known about the HLA system, more effective antibiotics were available, and platelet transfusions were becoming routine. Thus began the modern era of human BMT. The past 25 years have witnessed an almost exponential growth in the number of transplants being performed and the number of diseases being considered for BMT. Initially, most grafts employed marrow from an HLA-identical sibling. Autologous marrow, long known to be effective in animal systems, is now being used with increasing frequency following intensive cancer chemotherapy. Hematopoietic progenitor cells from the peripheral blood are now being used for BMT, either alone or to supplement marrow. As a result of increasing national and international cooperation, large panels of volunteer marrow donors of known HLA type are becoming available to patients whose own marrow cannot be used or who do not have a family donor.

Currently, thousands of transplants are being performed each year world-wide. With the demonstration that marrow could be transplanted and that the cure rate would be substantial, the logical step was taken to treat patients early during the course of their respective disease (i.e. in leukemia when the burden of malignant cells was relatively low and when the patient was in excellent clinical condition). With improved patient selection, development of improved tissue typing methods, availability of potent antimicrobial agents, advances in supportive care, and improved prevention of GVHD, the results of BMT have continued to improve.

Marrow transplantation is now being applied to a long list of diseases with a wide range of results depending on the disease, the type of transplant, and the stage of the disease. For some of the diseases, BMT has already proven to be the most effective therapy (e.g., some leukemias and severe aplastic anemia), whereas for others it is the only available curative treatment (e.g., thalassemia). In very rare genetic disorders, one successful BMT may establish the success of the treatment. For other more common disorders, controlled trials are necessary to define the proper role of allogeneic or autologous BMT, or therapy not involving BMT.

Only through rigorous study and long-term follow-up can novel approaches be confirmed as effective (or ineffective). For those working in the field of marrow transplantation, a source of intellectual satisfaction has been the interdisciplinary nature of the studies. A view of the wide-ranging disciplines involved can be gleaned by reading the chapter titles for this book. A successful BMT program is always a team effort. There must be cooperation between blood banks, referring physicians, radiation oncologists, immunologists, and physicians from many subspecialties. A dedicated support staff of technicians, data managers, and, above all, nurses, is crucial. The nursing team in particular is responsible for the day-to-day care of patients. Nurses not only provide the bedside management of complex protocol studies, but also bear the burden of emotional support through the difficult hospital period. They are the most readily available source of information for the patients and families day and night. Without a strong nursing team, the entire BMT program is jeopardized.

Most important are the patients who come to the transplant center with the courage to accept days, weeks, and sometimes months of discomfort in the hope of surviving a fatal disease. We must ensure that we acknowledge and respect the dignity and individuality of each patient, that we provide adequate information for informed decision making and then include patients and families in the decision process. The greatest reward for clinical investigators is to see patients reintegrated into their personal, social, and professional lives, free of their disease and its complications.

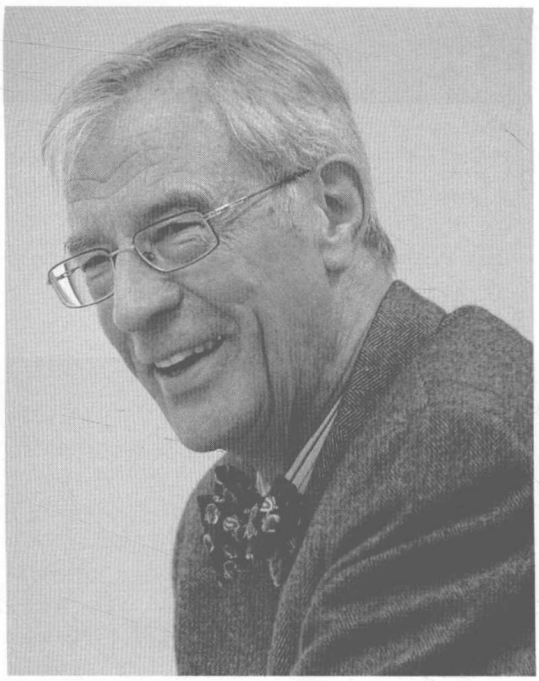
Stephen J. Forman
Karl G. Blume
E. Donnall Thomas
Summer, 1993

time, there was little understanding of the principles of human histocompatibility and so attempts to expand these studies to patients without identical twins were uniformly unsuccessful. These failures were the stimulus for a long series of experiments conducted by Don in the canine model, showing that it was possible to expose dogs to supralethal doses of irradiation and rescue them by reinfusing their own marrow, that the marrow could be cryopreserved, and that large doses of peripheral blood could substitute for marrow. However attempts at allogeneic transplantation in this outbred species continued to fail because of graft-versus-host disease or graft rejection.

In 1963, Don moved to Seattle and the University of Washington to become the first head of the Division of Oncology. There he developed techniques for rudimentary histocompatibility typing in the dog and, by the mid-1960s, showed that by selecting matched donors and using methotrexate posttransplant, it was possible to successfully transplant marrow between matched littermates in almost every case. At the same time, based on the work of Dausset, Payne, Amos, and others, understanding of human histocompatibility dramatically increased and so, in the late 1960s, Don made the decision to return to the subject of allogeneic transplantation in humans. He began to assemble a team of physicians, nurses, and support personnel (many of whom are still part of the current Seattle Transplant Program) and obtained a program project grant from the National Cancer Institute. In November 1968, Dr. Robert Good and his colleagues carried out the first marrow transplant from a matched sibling for an infant with immunodeficiency, and in March 1969, Don performed the first matched sibling donor transplant for a patient with leukemia.

The Seattle Transplant Program was originally housed at the Seattle Public Health Hospital, but in 1972, when the hospital was faced with closure by the federal government, the Program moved to Providence Hospital. In 1975, Don and his team moved to the newly created Fred Hutchinson Cancer Research Center, a move that provided Don with increased space, resources, and scientific collaborations. That same year, he and his colleagues published their classic *New England Journal of Medicine* paper summarizing the field of allogeneic transplantation and particularly the early Seattle experience. These results demonstrated not only the feasibility of the procedure but also that there was a plateau on the survival curves following transplantation, suggesting that some of these patients were cured with this novel technique. Don continued to lead the Clinical Research Division of the Center and its transplant program until his partial retirement in 1989. He continued writing manuscripts, delivering lectures, and participating in research discussions at the Center.

Appropriately, Don received almost every possible award for his work, including the American Society of Hematology's Henry M. Stratton Award, the General Motor's Kettering Prize, the American Society of Oncology's Karnofsky Award, the Presidential Medal of Science, and, of course, the 1990 Nobel Prize in Medicine which he shared with Joseph Murray. With each award, Don always emphasized how much of his work was a team effort. He invariably mentioned the contributions of Rainer Storb, Dean Buckner, Reg Clift, Paul Neiman, Alex Fefer, and Bob Epstein, who helped form the original Seattle Transplant Team, and of Ted Graham, who moved with Don from Cooperstown to help in the animal research. Don never failed to credit the nursing and support staff who played such a critical role in these efforts and, like Karl, always acknowledged the patients and their families who were true partners in his work.



KARL G. BLUME, M.D.
April 10, 1937–January 9, 2013

Karl G. Blume was born in Germany on April 10, 1937; he received his medical education under the mentorship of Professor Georg W. Löhr at the University of Freiburg and graduated in 1963. After graduation he undertook his residency at Marburg and then held two fellowships: one at Freiburg and the other at City of Hope in 1970 and 1971, respectively. His early work was in red cell biochemistry, and he pursued his postdoctoral fellowship under Dr. Ernest Beutler.

In 1975, after discussions with Dr. E. Donnall Thomas in Seattle and with his encouragement, Dr. Beutler decided to develop an allogeneic bone marrow transplantation (BMT) program at City of Hope and recruited Karl to return to City of Hope to establish the program. The program at City of Hope was, in many ways, derived from work and discussions that Karl had with colleagues at the Fred Hutchinson Cancer Research Center and resulted in lifelong friends from those early days of the development of transplantation to treat diseases of bone marrow and immune system origin. The first transplantation at City of Hope was performed on May 18, 1976.

Karl's clinical and research work focused on the problems that confront patients undergoing transplantation, namely, prevention of relapse, understanding the process of immune reconstitution, the treatment and prevention of graft-versus-host disease and cytomegalovirus infection management, and, among his early insights, issues related to patients' quality of life after transplantation and their long-term health. In 1981, Karl was the principal investigator for City of Hope's National Cancer Institute's first approved program project grant in transplantation, which contained projects that focused on those problems, and he organized a talented group of young laboratory and clinical scientists to work together in understanding and solving these challenges. He published the first results from City of Hope on the transplants for acute leukemia in the *New England Journal of Medicine* in 1981, showing the impact of remission status on outcome.

Based on his success at City of Hope, in 1987 Karl was recruited by Stanley Schrier and Ron Levy to begin a new transplant program

at Stanford University. Thus, he again developed from scratch his second successful transplantation program, mentoring numerous young physicians and inspiring colleagues and staff to work with him in a common quest to cure patients with hematologic malignancy and return them to their normal lives. Just as he had done at City of Hope, he developed and led another successful program project grant application. He also established the Division of Blood and Marrow Transplantation at Stanford University, taking a personal interest in the lives of each of his patients, incorporating all aspects of the care team into their treatment, including nursing, social work, dietary, and physical therapy, and confirming again a model for patient care and research in use at transplant programs around the country. During that time, he trained both Rob Negrin and Nelson Chao, who went on to direct transplantation programs at Stanford University and at Duke University, respectively. Therefore, Karl was responsible for at least three of the major BMT programs in the United States, not to mention the numerous fellows he trained and mentored at City of Hope and Stanford University.

In 2000, Karl attained emeritus status at Stanford University and stepped down from the role of chief of the BMT division to develop the Stanford Cancer Institute. He continued to serve Stanford University as associate director of research in the Department of Medicine. In 2003, he directed his energies toward developing and achieving the coveted National Cancer Institute-designated cancer center status for the Stanford Cancer Institute, a first for the university.

Karl was also a driving force in 1994 in the founding of the American Society of Blood and Marrow Transplantation, now an international organization for physicians and researchers committed to serving patients with a variety of blood diseases. He was also a leader in the American Society of Hematology and, for many years, was in charge of the organization's Career Development Program. Early on, he recognized that our responsibilities were not only to our patients now but also to those who come to us in the future. He became the first honorary member of ASBMT and, with Richard O'Reilly, was the first coeditor of *The Biology of Blood and Marrow Transplantation*, the major journal in the field. Karl worked tirelessly to make it the central journal in the field, and when there were questions about the cost of the first issues, he made a personal financial donation to ensure the journal's successful launch.

Karl won many honors, both in the United States and Germany, but his major legacy is the impact he had on the thousands of patients he treated and the others he inspired to follow in his footsteps. All of us who knew and loved him knew that his highest priorities remained the quality of life of his patients and their families and the well-being of his transplantation team and those of his colleagues around the country and world. He held us all to high standards of excellence, but he maintained it with wonderful warmth, humor, and sensitivity over the decades and across continents. All of us who worked with him benefited from his respect and could always count on him to extend a helping hand and open ears, as he wanted nothing more than to help, to give of himself, and to be a force for good in this world.

In addition to his interest in music, sports – especially Stanford athletics – and the politics of the world and its impact on all of us, he was an exemplary family man. His children, Philipp and Caroline, could always rely on him for advice, affection, and guidance. In his last years, the lives and activities of his grandchildren, Adrian, Katie, Laura, Kevin, and David, were his focus and, of course, they adored him. Vera, his wife of 45 years, was his partner in his life and his work, as Dottie was to Don, and, at difficult times, always his source of strength and calm.

Although Don and Karl are most noted for their leadership and pioneering scientific achievements, for those of us who have been fortunate enough to work with them, they are equally admired for the way in which they achieved their success. They were always focused, hardworking, and uncompromising in their laboratories and especially in clinical research. They could both be demanding critics and held others accountable for their actions, yet at the same time, they were always generous with their ideas, loyal to their colleagues, and quick to deflect praise to their coworkers and help younger colleagues who chose this career.

For many of us in the field who had the privilege of knowing and working with both Don and Karl and for the many patients who are alive because of their work and dedication, the sentiment of a Hebrew proverb seems appropriate for each of them: "Say not in grief he is no more, but live in thankfulness that he was."

List of Abbreviations

AA Amyloid A
AA Aplastic anemia
AABB American Association of Blood Banks
aaIPI Age-adjusted International Prognostic Index
AAV Adeno-associated virus
ABC Activated B-cell-like
ABL Abelson leukemia virus
aBMT Autologous bone marrow transplantation
ABMTR Autologous Blood and Marrow Transplant Registry – North America
ABVD Doxorubicin, bleomycin, vinblastine, dacarbazine
ABW Actual body weight
AC Adriamycin (doxorubicin), cyclophosphamide
ACE Adriamycin (doxorubicin), cyclophosphamide, etoposide
ACEI Angiotensin-converting enzyme inhibitor
ACIF Anticomplement immunofluorescence
ACIP Advisory Committee on Immunization Practices
ACOR Association of Online Cancer Resources
ACP Advanced care planning
ACR Albumin-to-urine creatinine ratio
ACS Acute chest syndrome
ACTH Adrenocorticotropic hormone
ACVBP Adriamycin (doxorubicin), cyclophosphamide, vindesine, bleomycin, prednisone
AD Autoimmune disease
ADA Adenosine deaminase
ADCC Antibody-dependent cell-mediated cytotoxicity
ADH Antidiuretic hormone
ADL Activities of daily living
AdV Adenovirus
AEL Acute erythroleukemia
AFP α-Fetoprotein
AGM Aorta–gonad–mesonephros (region)
aGVHD Acute graft-versus-host disease
AH Ancestral haplotype
aHCT Autologous hematopoietic cell transplantation
AHNMD Associated clonal hematologic non-mast-cell lineage disease
AHPCS Autologous hematopoietic progenitor-cell support
aHR Adjusted hazard ratio
AHRQ Agency for Health Care Research and Quality
aHUS Atypical hemolytic uremic syndrome
AIDS Acquired immune deficiency syndrome
AIF Apoptosis-inducing factor
AIHA Autoimmune hemolytic anemia
AIRE Autoimmune regulator
AITD Autoimmune thyroid disease
AITL Angioimmunoblastic T-cell lymphoma
AKI Acute kidney injury
AKIN Acute Kidney Injury Network
aKIR Activating killer immunoglobulin-like receptor
AL Amyloid light-chain
ALA α-Lipoic acid
ALC Absolute lymphocyte count
ALCL Anaplastic large-cell lymphoma
ALDH Aldehyde dehydrogenase
ALG Antilymphocyte globulin
ALK Anaplastic lymphoma kinase
ALL Acute lymphoblastic leukemia
AlloHCT Allogeneic hematopoietic cell transplantation
AlloSCT Allogeneic stem-cell transplantation
ALP Alkaline phosphatase
ALPS Autoimmune lymphoproliferative syndrome
ALT Alanine aminotransferase
AMA Antimitochondrial antibody
AMKL Acute megakaryoblastic leukemia
AML Acute myeloid leukemia
ANC Absolute neutrophil count
ANKL Aggressive natural killer cell leukemia
AOTONJ Antiosteoclastic therapy-associated osteonecrosis of the jaws
AP Accelerated phase
AP-1 Activator protein-1
APACHE Acute Physiology, Age, Chronic Health Evaluation
APBMT Asia Pacific Blood and Marrow Transplantation
APC Antigen-presenting cell
APECED Autoimmune polyendocrinopathy–candidiasis–ectodermal dystrophy
API 4′,6-Diamidino-2-phenylindole
APL Acute promyelocytic leukemia
APMF Acute panmyelosis with myelofibrosis
Ara-C Cytosine arabinoside
ARB Angiotensin receptor blocker
ARDS Acute or adult respiratory distress syndrome
ARF Acute renal failure
ARL AIDS-related lymphoma
ARS Acute radiation syndrome
ARSA Arylsulfatase A
ART Assisted reproductive technology
ASBMT American Society for Blood and Marrow Transplantation
ASCT Autologous stem-cell transplantation
ASO Allele-specific oligonucleotide
ASO-PCR Allele-specific oligonucleotide polymerase chain reaction
AST Aspartate aminotransferase
AT Alkyltransferase
ATG Antithymocyte globulin
ATL Adult T-cell leukemia
ATLL Adult T-cell leukemia/lymphoma
ATM Ataxia Telangiectasia Mutated
ATRA All-*trans*-retinoic acid
AUC Area under the curve
AutoHCT Autologous hematopoietic cell transplantation
AVP Arginine vasopressin
AYA Adolescent and young adult
AZT Zidovudine
BAEP Brainstem auditory evoked potentials
BAFF B-cell-activating factor
BAIAP3 Brain-specific angiogenesis inhibitor 1-associated protein 3
BAL Bronchoalveolar lavage
BC Blast crisis

BCC	Basal cell carcinoma
BCMA	B-cell maturation antigen
BCNA	Bicyclic nucleoside analog
BCNU	1,3-Bis(2-chloroethyl)-1-nitrosourea (carmustine)
BCR	B-cell receptor
BCR	Breakpoint cluster region
BD	Bortezomib, dexamethasone
BDP	Beclomethasone 17,21-dipropionate
BEAC	BCNU, etoposide, Ara-C (cytosine arabinoside), cyclophosphamide
BEAM	BCNU, etoposide, Ara-C (cytosine arabinoside), melphalan
BED	Biologically effective dose
BEP	Bleomycin, etoposide, cisplatin
BER	Base excision repair
BFI	Brief Fatigue Inventory
BFM	Berlin–Frankfurt–Münster
BFU-E	Burst-forming units – erythroid
BIW	Twice weekly
BL	Burkitt lymphoma
BLA	Biologics license application
BL-CFC	Blast colony-forming cell
BLS	Bare lymphocyte syndrome
BLyS	B-lymphocyte stimulator
BM	Bone marrow
BMC	Bone marrow cell
BMD	Bone mineral density
BMDW	Bone Marrow Donors Worldwide
BMFS	Bone marrow failure syndromes
BMI	Body mass index
BMSC	Bone marrow stem cell
BMSCT	Blood and Marrow Stem Cell Transplant
BMT CTN	Blood and Marrow Transplant Clinical Trials Network
BMT	Bone marrow transplantation
BMTCN	Blood and Marrow Transplantation Certified Nurse
BMTinfonet	Blood and Marrow Transplant Information Network
BMTSS	Bone Marrow Transplant Survivor Study
BNLI	British National Lymphoma Investigation
BNP	Brain natriuretic peptide
BO	Bronchiolitis obliterans
BOOP	Bronchiolitis obliterans organizing pneumonia
BPDCN	Blastic plasmacytoid dendritic cell neoplasm
BPI	Bactericidal/permeability-increasing
BPI	Brief Pain Inventory
BR	Bendamustine, rituximab
Breg	Regulatory B (cell)
BSE	Bovine spongiform encephalopathy
BSI	Brief symptom inventory
BTK	Bruton's tyrosine kinase
BTLA	B- and T-lymphocyte attenuator
BU	Busulfan
BuMel	Busulfan, melphalan
BUN	Blood urea nitrogen
C1P	Ceramide-1 phosphate
CABSI	Catheter-associated bloodstream infection
CAEBV	Chronic active Epstein–Barr virus
CALGB	Cancer and Acute Leukemia Group B
CALLA	Common acute lymphoblastic leukemia antigen
CAR	Chimeric antigen receptor
CAR	Cocksackie and adenovirus receptor
CAR	CXCL12 adventitial reticular cell
CARES	Cancer Rehabilitation Evaluation System
cART	Combination antiretroviral therapy
CB	Cord blood
CBC	Cord blood cell
CBF	Core binding factor
CBG	Corticosteroid-binding globulin
CBHC	Cord blood hemapoietic cell
CBSC	Cord blood stem cell
CBT	Cognitive–behavioral therapy
CBT	Cord blood transplantation
CBV	Cyclophosphamide, BCNU, etoposide
CC	Complete chimerism
CCG	Children's Cancer Group
CCI	Charlson Comorbidity Index
CCI	Corrected count increment
CCNU	1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea
CCR	Cytologic complete remission
CCSG	Children's Cancer Study Group
CCyR	Complete cytogenetic remission
CDA	Cytidine deaminase
CDAD	*Clostridium difficile*-associated diarrhea
CDAI	Crohn Disease Activity Index
CDC	Centers for Disease Control and Prevention
CDC	Complement-dependent cytotoxicity
CDF	Cumulative distribution function
CDK	Cyclin/cyclin-dependent kinase
CE	Carboplatin, etoposide
CEA	Carcinoembryonic antigen
CEACAM	Carcinoembryonic-antigen-related cell-adhesion molecule
CEC	Carboplatin, etoposide, cyclophosphamide
CEL-NOS	Chronic eosinophilic leukemia-not otherwise specified
CEM	Carboplatin, etoposide, melphalan
CESD	Center for Epidemiologic Studies – Depression
CFAR	Cyclophosphamide, fludarabine, alemtuzumab, rituximab
CFH	Complement factor H
CFU	Colony-forming unit
CFU-B	Colony-forming unit – B-lymphocyte
CFU-BLAST	Colony-forming unit – blast
CFU-E	Colony-forming unit – erythroid
CFU-F	Colony-forming unit – fibrolast
CFU-GEMM	Colony-forming unit – granulocyte/erythroid/macrophage/megakaryocyte
CFU-GM	Colony-forming unit – granulocyte–macrophage
CFU-MEG	Colony-forming unit – megakaryocytic
CFU-Mix	Colony-forming unit – mixed
CFU-S	Colony-forming unit – spleen
CFU-T	Colony-forming unit – T-lymphocyte
CGD	Chronic granulomatous disease
CGH	Comparative genomic hybridization
cGVHD	Chronic graft-versus-host disease
CHD	Coronary heart disease
CHF	Congestive heart failure
CHOEP-14	Doxorubicin, vincristine, etoposide, prednisone
CHOP	Cyclophosphamide, hydroxydaunomycin, vincristine (Oncovin), prednisone
CHR	Complete hematologic response
CHRIs	Child Health Ratings Inventory
CHS	Chediak–Higashi syndrome
CI	Comorbidity index
CI	Confidence interval
CI	Cumulative incidence
CIA	Collagen-induced arthritis
CIBMTR	Center for International Blood and Marrow Transplant Research
CID	Combined immunodeficiency syndrome
CIDP	Chronic inflammatory demyelinating polyneuropathy
CIF	Cumulative incidence function
CIHHV-6	Chromosomal integration of human herpesvirus 6
CIPN	Critical illness polyneuropathy
CJD	Creutzfeldt–Jakob disease
CKD	Chronic kidney disease
CLIA	Clinical Laboratory Approved Amendments
CLL	Chronic lymphoid/lymphocytic leukemia
CLO	Clofarabine

CLP Common lymphoid progenitor
CLR C-type lectin receptor
CMF Cyclophosphamide, methotrexate, fluorouracil
CMI Cellular mediated immunity
CML Chronic myeloid/myelogenous leukemia
CMML Chronic myelomonocytic leukemia
CMN Chronic myeloid neoplasm
CMP Common myeloid progenitor
CMR Complete molecular response
CMV Cytomegalovirus
CMV-Ig Cytomegalovirus antibody-enriched intravenous immunoglobulin
CMV-IP Cytomegalovirus-associated interstitial pneumonia
CNI Calcineurin inhibitor
CNL Chronic neutrophilic leukemia
CNS Central nervous system
COG Children's Oncology Group
ConA Concanavalin A
COP Cryptogenic organizing pneumonia
COPE Coping Orientations to Problems Experienced Scale
COX-2 Cyclooxygenase-2 (inhibitor)
CP Chronic phase
CR Complete remission
CRBSI Catheter-related bloodstream infection
CREG Cross-reactive group
CRM Continual reassessment method
CRS Cytokine release syndrome
CRVT Catheter-related venous thrombosis
CSA Cyclosporine A
CSF Cerebrospinal fluid
CSF Colony-stimulating factor
CSP Cyclosporine
CT Computed tomography
CT Cyclophosphamide, thioTEPA
CTC Cyclophosphamide, thioTEPA, carboplatin
CTC Cytotoxic T cell
CTCL Cutaneous T-cell lymphoma
CTD Cyclophosphamide, thalidomide, dexamethsone
CTL Cytotoxic T-lymphocyte
CTLA Cytotoxic T-lymphocyte antigen
CTLP Cytotoxic T-lymphocyte precursor
CTN Clinical Trials Network
CTX Cyclophosphamide
CTXD Cancer and Treatment Distress
CTZ Chemotactic trigger zone
CVAD Fractionated cyclophosphamide, vincristine, adriamycin, dexamethasone
CVC Central venous catheter
CVD Cardiovascular disease
CVID Common variable immune deficiency
CVRF Cardiovascular risk factor
CVVH Continuous veno-venous hemofiltration
CVVHDF Continuous veno-venous hemodiafiltration
CY Cyclophosphamide
CyBorD Cyclophosphamide, bortezomib, dexamethasone
CYP Cytochrome P
DAD Direct antigen detection
DAF Decay-accelerating factor
DAG Diacylglycerol
DAH Diffuse alveolar hemorrhage
DAMP Damage-associated molecular pattern
DAS Dasatinib
DC Dendritic cell
DCEP Dexamethasone, cyclophosphamide, etoposide, cisplatin
DCK Deoxycytidine kinase
DDR Discoidin domain receptor
DFA Direct fluorescent antibody (test)
DFCI Dana–Farber Cancer Institute
DFS Disease-free survival
DGK Deoxyguanosine kinase
DH Double hit
DHAP Dexamethasone, high-dose cytarabine, cisplatin
DHEA Dehydroepiandrosterone
DHEAS Dehydroepiandrosterone sulfate
DHFR Dihydrofolate reductase
DHPG 9-(1,3-Dihydroxy-2-propoxymethyl)guanine (ganciclovir)
DIC Disseminated intravascular coagulation
DILI Drug-induced liver injury
DIPSS Dynamic International Prognostic Scoring System
DKA Diabetic ketoacidosis
DLA Dog leukocyte antigen
DLBCL Diffuse large B-cell lymphoma
DLCL Diffuse large cell lymphoma
DLCO Diffusion capacity of the lung for carbon monoxide
DLI Donor lymphocyte infusion
DLT Dose-limiting toxicity
DM Diabetes mellitus
DMSO Dimethyl sulfoxide
DN Double negative
DNA Deoxyribonucleic acid
DNAX DNA accessory molecule
DNR Do not resuscitate
DOTA 1,4,7,10-Tetraazacyclododecane-*N*,*N*′,*N*″,*N*‴-tetraacetic acid
DOTMP 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetramethylenephosphonic acid
DPC Days post-coitum
DPTS Delayed pulmonary toxicity syndrome
DR Death receptor
DRG Dorsal root ganglion
DSA Donor-specific antibody
DSB Double-strand break
DSII Disease-Specific Impairment Inventory
DSRCT Desmoplastic small round cell tumor
dsRNA Double-stranded RNA
DST Donor-specific transfusion
DTH Delayed type hypersensitivity
DTI Diffusion-tensor MRI
DTPA Diethylenetriaminepentaacetic acid
DVT Deep venous thrombosis
DXA Dual-energy X-ray absorptiometry
EAE Experimental allergic encephalomyelitis
EAE Experimental autoimmune encephalomyelitis
EATL Enteropathy-associated T-cell lymphoma
EB Embryoid body
EBMT European Group for Blood and Marrow Transplantation
EBMTR European Bone Marrow Transplant Registry
EBNA Epstein–Barr (virus) nuclear antigen
EBV Epstein–Barr virus
EBV-LDP Epstein–Barr virus-associated lymphoproliferative disorder
EC Endothelial cell
EC Epirubicin, cyclophosphamide
ECAT Extracorporal adsorption therapy
ECFC Endothelial colony-forming cells
ECG Electrocardiogram
ECIL European Conference on Infections in Leukaemia
ECM Extracellular matrix
ECP Extracorporeal photopheresis
ED Erectile dysfunction
EDSS Expanded Disability Status Scale
EDTMP Ethylenediaminetetramethylenephosphonic acid
EEG Electroencephalogram
EFS Event-free survival
EGBMT European Group for Blood and Marrow Transplantation
ELISA Enzyme-linked immunosorbent assay

ELN European LeukemiaNet
EM Erythema multiforme
EMLA Eutectic Mixture of Local Anesthetic
EN Enteral nutrition
ENKL Extranodal NK/T-cell nasal type leukemia
ENSG European Neuroblastoma Study Group
ENU Ethyl-*N*-nitrosourea
EORTC European Organization for Research and Treatment of Cancer
EPC Endothelial progenitor cell
EPO Erythropoietin
EPOCH Etoposide, prednisone, vincristine (Oncovin), doxorubicin hydrochloride
ER Endoplasmic reticulum
ER Estrogen receptor
ERIC European Research Initiative in chronic lymphocytic leukemia
ERT Enzyme replacement therapy
ESBL Extended-spectrum β-lactamase
ESC Embryonic stem cell
ESFT Ewing sarcoma family of tumors
ET Essential thrombocythemia
ETP Early thymic progenitor
ETS Euthyroid sick syndrome
EWOG European Working Group
EWOG-MDS European Working Group of Myelodysplastic Syndromes in Childhood
FA Fanconi anemia
FAB French–American–British Classification
FACIT-SP Functional Assessment of Chronic Illness Therapy – Spirituality and Wellbeing Scale
FACS Fluorescence-activated cell sorter
FACT Foundation for the Accreditation of Cellular Therapy
FACT Functional Assessment of Chronic Illness Therapies
FACT-BMT Functional Assessment of Cancer Therapy – BMT Module
FAMA Fluorescent-antibody staining of membrane antigen
FasL Fas ligand
FC Facilitator cell
FCH Fibrosing cholestatic hepatitis
FCR Fludarabine, cyclophosphamide, rituximab (RTX)
FDA Food and Drug Administration
FDG [^{18}F]Fluorodeoxyglucose
FDR False discovery rate
FEC Fluorouracil, epirubicin, cyclophosphamide
FEV_1 Forced expiratory ventilation in 1 second
FFP Fresh frozen plasma
FFS Failure-free survival
FHCRC Fred Hutchinson Cancer Research Center
FISH Fluorescence in situ hybridization
FKBP Tacrolimus (FK)-binding protein
FL Follicular lymphoma
FLACC Face, Legs, Activity, Cry, Consolability (pain assessment tool)
FLAIR Fluid attenuated inversion recovery
FLC Free light chain
FLIPI Follicular Lymphoma International Prognostic Index
FLU Fludarabine
FN Febrile neutropenia
FNA Fine-needle aspiration
FNH Focal nodular hyperplasia
FoxP3 Forkhead box P3
FSH Follicle-stimulating hormone
FSI Fatigue Symptom Inventory
FTBI Fractionated total body irradiation
FTBI Full total body irradiation
FTI Farnesyltransferase inhibitor
FTOC Fetal thymic organ culture
5-FU 5-Fluorouracil
FVC Forced vital capacity
GA Glatiramer acetate
GABG German Autologous Bone Marrow Transplant Group
GALT Gut-associated lymphoid tissue
GAP GTPase-activating protein
GBM Glioblastoma multiforme
G-BM G-PBHC and/or G-CSF primed bone marrow
gc Genome copies
GCB Germinal center B-cell-like
G-CSF Granulocyte colony-stimulating factor
GCT Germ-cell tumor
GDP Guanosine diphosphate
GEBDIS German Breast Cancer Dose Intensity Study
GEE Generalized estimating equation
GEL/TAMO Grupo Español de Linfomas/Trasplante Autólogo de Médula Ósea
GEM Gemcitabine
GEM Grid Enabled Measures
GEP Gene expression profiling
GF Graft failure
GFP Green fluorescent protein
GFR Glomerular filtration rate
GGT γ-Glutamyl transferase
GH Growth hormone
GHRH Growth hormone-releasing hormone
GHSG German Hodgkin Study Group
GI Gastrointestinal (tract)
GICAT Gruppo Italiano Collaborativo AIDS e Tumori (Italian Cooperative Group on AIDS and Tumors)
GISL Gruppo Italiano per lo Studio dei Linfomi (Italian Lymphoma Study Group)
GITMO Gruppo Italiano per il Trapianto di Midollo Osseo
GM Galactomannan
GM-CSF Granulocyte–macrophage colony-stimulating factor
GMP Granulocyte macrophage progenitor (cell)
GMP Guanosine monophosphate
GNB Gram-negative bacilli
GnRH Gonadotropin-releasing hormone
gp Glycoprotein
G-PBHC Granulocyte colony-stimulating factor-mobilized peripheral blood hematopoietic cell
GPI Glycosylphosphatidylinositol
GPI-AP Glycosylphosphatidylinositol-anchored protein
GRE Glucocorticoid response element
GSH Glutathione (reduced)
GST Glutathione-*S*-transferase
GTP Good tissue practice
GTP Guanosine triphosphate
GVD Gemcitabine, vinorelbine, liposomal doxorubicin
GVH Graft-versus-host
GVHD Graft-versus-host disease
GVHL Graft-versus-Hodgkin disease (lymphoma)
GVL Graft-versus-leukemia
GVLE Graft-versus-leukemia effect
GVT Graft-versus-tumor
GWAS Genome-wide association study
H&E Hematoxylin and eosin (stain)
HA Hemagglutinins
HAART Highly active antiretroviral therapy
HADS Hospital Anxiety and Depression Scale
HAMA Human antimouse antibody
HA-MRSA Healthcare-associated MRSA
HAV Hepatitis A virus
HBoV Human bocavirus
HBV Hepatitis B virus
HC Hematopoietic cell
HC Hemorrhagic cystitis
HC Histocompatibility complex

4-HC	4-Hydroperoxycyclophosphamide
HCG	Human chorion gonadotropin
HCoV	Human coronavirus
HCT	Hematopoietic cell transplantation
HCT-CI	HCT-Comorbidity Index
HCV	Hepatitis C virus
HD	Hodgkin disease
HDAC	High-dose Ara-C
HDC	High-dose chemotherapy
HDIT	High-dose immunosuppressive therapy
HDT	High-dose therapy
HEPA	High-efficiency particulate air
HES	Hydroxyethyl starch
HES	Hypereosinophilic syndrome
hESC	Human embryonic stem cell
HEV	Hepatitis E virus
HFTBI	Hyperfractionated total body irradiation
HGF	Hepatocyte growth factor
HGNC	HUGO Genome Nomenclature Committee
HHS	Human and Health Services
HHV	Human herpesvirus
HI	Hemagglutination inhibition
HIB	*Haemophilus influenzae* type B
HIF	Hypoxia-inducible transcription factor
HIV	Human immunodeficiency virus
HL	Hodgkin lymphoma
HLA	Human leukocyte antigen
HLH	Hemophagocytic lymphohistiocytosis
hMPV	Human metapneumovirus
HOVON	Hemato-Oncologie voor Volwassenen Nederland
HPA	Hypothalamic–piuitary–adrenal
HPC	Hematopoietic progenitor cell
HPI	Helicase–primase inhibitor
HPV	Human papillomavirus
HR	Hazard ratio
HR	Homologous recombination
HRCT	High-resolution chest tomography
HRE	Hypoxia-inducible transcription factor response element
HRhV	Human rhinovirus
HRPBC	High-risk primary breast cancer
HRQOL	Health-related quality of life
HRSA	Health Resources and Services Administration
HRT	Hormone replacement therapy
HSC	Hematopoietic stem cell
HSC	Hepatic stellate cell
HSCT	Hematopoietic stem-cell transplantation
HSDD	Hypoactive sexual desire disorder
HSPC	Hematopoietic stem/progenitor cell
HSTCL	Hepatosplenic T-cell lymphoma
HSV	Herpes simplex virus
HSV-TK	Herpes simplex virus thymidine kinase
HT	Histologic transformation
5-HT	5-Hydroxytryptamine (serotonin)
hTERT	Human telomerase reverse transcriptase
HTLV	Human T-cell lymphotropic virus
HTS	High-throughput sequencing
HU	Hydroxyurea
HUS	Hemolytic uremic syndrome
HVEM	Herpes virus entry mediator
HVG	Host-versus-graft (reaction)
IA	Invasive aspergillosis (infection)
IBCSG	International Breast Cancer Study Group
IBDIS	International Breast Cancer Dose Intensity Study
IBMTR	International Bone Marrow Transplant Registry
IBW	Ideal body weight
ICAM	Intracellular adhesion molecule
ICE	Ifosfamide, carboplatin, etoposide
ICOS	Inducible costimulator (protein)
ICOS-L	Inducible costimulator ligand
ICSI	Intracytoplasmic sperm injection
ICU	Intensive care unit
ID	Intermediate dose
iDC	Immature dendritic cells
IDO	Indoleamine 2,3-dioxygenase
IDOX	4-Iodo-4-deoxydoxorubicin
IDSA	Infectious Diseases Society of America
IE	Immediate early (antigen expression)
IEM	Inborn errors of metabolism
IFI	Invasive fungal infection
IFN	Interferon
IFRT	Involved field radiotherapy
Ig	Immunoglobulin
IGCCCG	International Germ Cell Cancer Collaborative Group
IGEV	Ifosfamide, gemcitabine, vinorelbine, prednisone
IGF	Insulin-like growth factor
IGFBP	Insulin-like growth factor binding protein
IgG	Immunoglobulin G
IgH	Immunoglobulin heavy chain
IGRT	Image-guided radiation therapy
IHC	Immunohistochemistry
IHWG in HCT	International Histocompatibility Working Group in Hematopoietic Cell Transplantation
iKIR	Inhibitory killer immunoglobulin-like receptor
IL	Interleukin
IM	Imatinib
IMGT	International ImMunoGenetics
IMID	Immunomodulatory drug
IMPDH	Inosine monophosphate dehydrogenase
IMRT	Intensity-modulated radiation therapy
IMWG	International Myeloma Working Group
IND	Improvised nuclear device
IND	Investigational new drug
iNK-T	Invariant natural killer T (cell)
iNOS	Inducible NO synthase
INR	International normalized ratio
INRG	International Neuroblastoma Risk Group
INRGSS	International Neuroblastoma Risk Group Staging System
INSS	International Neuroblastoma Staging System
INSTI	Integrase strand transfer inhibitor
IORT	Intraoperative radiotherapy
IP	Interstitial pneumonia
IP_3	Inositol-1,4,5-triphosphate
IPD	Invasive pneumococcal disease
IPEX	Immunodysregulation polyendocrinopathy enteropathy X-linked (syndrome)
IPFSG	International Prognostic Factor Study Group
IPI	International Prognostic Index
iPS	Induced pluripotent stem
IPS	Idiopathic pneumonia syndrome
IPS	Interstitial pneumonia syndrome
IPSS	International Prognostic Scoring System
IPV	Inactivated polio vaccine
IRB	Institutional Review Board
IRF	Interferon regulatory factor
IRSG	Intergroup Rhabdomyosarcoma Study Group
IS	Immune synapse
IS	Immunosuppressive
IS	International Scale
ISC	Intestinal stem cell
ISO	Isohemagglutinin
IST	Immunosuppressive therapy
ISW	Immune suppression withdrawal
ITAM	Immunoreceptor tyrosine-binding activation motif
ITCC	Innovative Therapies for Children with Cancer