III. 学会等発表実績

様式第１９

学　会　等　発　表　実　績

委託業務題目「本邦における造血細胞移植一元化登録研究システム及び研究データ質管理システムの確立」

機関名　一般社団法人　日本造血細胞移植データセンター

１．学会等における口頭・ポスター発表

発表した成果（発表題目、口頭・ポスター発表の別）	発表者氏名	発表した場所（学会等名）	発表した時期	国内・外の別
Influence of graft-versus-host disease on late relapse after allogeneic hematopoietic cell transplantation for hematological malignancies: a nationwide retrospective study from the late complications and quality-of-life working group of JSHCT.(oral presentation)	Yamashita T, Kuwabara H, Ohashi K, Uchida N, Fukuda T, Miyamura K, Mori S, Kato K, Tanaka J, Adachi S and Atsuta Y.	The 40th annual meeting of the European Group for Blood and Marrow Transplantation	Apr. 2014.	国外
Improved, Improved explants method to isolate umbilical cord-derived mesenchymal stem cells and their immunosuppressive properties (poster)	Yuka Mori, Tokiko Nagamura-Inoue, Jun Ohshimo, Takahisa Shimazu, Haiping He, Astuko Takahashi, Hajime Tsunoda, and Arinobu Tojo	ISCT Annual Meeting Accommodation	Apr. 2014.	国外
臍帯血・臍帯由来間葉系幹細胞のセミパブリックバンク樹立について（口演）	長村（井上）登紀子, 何　海萍, 森　有加, 高橋　敦子, 山本由紀,島津貴久, 中井未来, 東條　有伸	第 62 回日本輸血・細胞治療学会	2014年5月	国内
Impact of GVHD on outcome after allogeneic hematopoetic stem cell transplantation for CMML. （口演）	Itonaga H,Iwanaga M,Aoki K,Aoki J,Ishiyama K,Kobayashi T,Sakura T,Fukuda T,Yujiri T,Hirokawa M,Morishima Y,Nagamura-Inoue T,Atsuta Y,Ishikawa T,Miyazaki Y.	第 76 回日本血液学会学術集会	2014年10月	国内
A new risk score for overall survival after allogeneic HSCT in Japan. （口演）	Fuji S,Nakamura F,Yokoyama H,Kanamori H,Kobayashi N,Atsuta Y,Fukuda	第 76 回日本血液学会学術集会	2014年10月	国内

	T.			
An allele mismatch has similar adverse impact in related HSCT compared with an antigen mismatch. （口演）	Fuji S,Kanda J,Miyamura K,Kudo K,Hidaka m,Adachi S,Ichinohe T,Atsuta Y,Kanda Y.	第 76 回日本血液学会学術集会	2014年10月	国内
UBMT or immediate UCBT for patients with high-risk AML in first complete remission. （口演）	Yanada M,Kanda J,Othtake S,Fukuda T,Miyawaki S,Miyamura K,Morishima Y,Kobayashi Y,Atsuta Y,Miyazaki Y,Kimura F,Ohnishi K,Takami A,Naoe T,Kanda Y.	第 76 回日本血液学会学術集会	2014年10月	国内
Allogeneic hematopoietic stem cell transplantation for infants with acute lymphoblastic leukemia. （口演）	Kato M,Hasegawa D,Koh K,Inagaki J,Kato K,Goto H,Takita J,Yabe H,Sawada A,Atsuta Y,Kato K.	第 76 回日本血液学会学術集会	2014年10月	国内
Phaese 2 study of empirical loe dose L-AMB in patients with refractory febrile neutropenia. （口演）	Miyao K,Sawa M,Atsuta Y, Suzuki R,Inagaki Y,Sakemura R,Sakai T,Kato T,Sahashi S,Tsusita N,Ozawa Y,Tsuzuki M,Kohno A,Adachi T,Watanabe K,Ohbayashi K,Emi N.	第 76 回日本血液学会学術集会	2014年10月	国内
Impact of MRD and TKI on allogeneic hematopoietic cell transplantation for Ph+ALL.（口演）	Nishiwaki S, Imai K,Mizuta S, Ohashi K, Kanamori H, Fukuda T,Mori S, Nagamura-Inou T,Suzuki R, Atsuta Y,Tanaka J.	第 76 回日本血液学会学術集会	2014年10月	国内
Reduced-intensity condituioning of allogeneic transplantation for nodal peripheral tT-cell lymphomas. （口演）	Aoki K, Suzuki R,Chihara D, Suzuki T,Sung-Won Kim,Fukuda T, Uchida N, Tsudo M,Matsuoka K,Ago H, Nagamura-Inoue T,Morishima	第 76 回日本血液学会学術集会	2014年10月	国内

	Y,Sakamaki H, Atsuta Y, Suzumiya J.			
Comparison of unrelated bone marrow and umbilical cord blood transplants in young adult leukemia. （口演）	Terakura S, Atsuta Y, Tsukada N, Kobayashi T, Tanaka M, Kanda J, Ohashi K,F Takahiro,U Naoyuki,T Satoshi, Nagamura-Inoue T,Morishima Y, Miyamura K.	第 76 回日本血液学会学術集会	2014年10月	国内
医学統計：生存解析を実施する際に知っておきたい pitfall（口演）	熱田由子	第 76 回日本血液学会学術集会、Morning Discussion3	2014年10月	国内
Impact of Race on Graft-Versus-Host Disease Rates after HLA-Matched Sibling Bone Marrow or Preipheral Blood Hematopoietic Cell Transplantion:Comparison of North American Caucasian Versus Japanese Populations. (oral presentation)	Junya Kanda, Yachiyo Kuwatsuka, Ruta Brazauskas, Zhen-Huan Hu, Koji Nagafuji, Takahiro Fukuda, Hisashi Sakamaki, Carmen Sales-Bonfim, Jignesh Dalal, Theresa Hahn, Marcelo Pasquini, Yoshiko Atsuta, Wael Saber, on behalf of the CIBMTR International Studies Working Committee and the JSHCT Source and GVHD working group.	BMT Tandem Meeting. Oral Abstracts-Session A.	2015年2月	国外
EZR(ersy R)による造血幹細胞移植データ解析（口演）	神田善伸	第 37 回日本造血細胞移植学会総会	2015年3月	国内
我が国における POEMS 症候群に対する造血幹移植の有効性・長期予後の検討～一元化データを用いた解析（口演）	堺田恵美子、川尻千華、大和田千桂子、宮本敏浩、東 太一、田口 淳、森 毅彦、長谷川雄一、近藤忠一、湯尻俊昭、吉満 誠、通堂 満、岩崎年宏、重松明男、鈴木律朗、熱田由子、廣川 誠、坂巻 壽、中世古知昭	第 37 回日本造血細胞移植学会総会	2015年3月	国内

小児および成人における移植後非感染性肺合併症に関する研究-二次調査解析結果報告（20-18：GVHD以外の合併症WG）（口演）	鬼塚真仁、小川啓恭、福田隆浩、日高道弘、金森平和、岡田恵子、井上雅美、加藤剛二、森島泰雄、坂巻　壽、鈴木律朗、熱田由子、日野雅之、藤井伸治、仲宗根秀樹	第37回日本造血細胞移植学会総会	2015年3月	国内
TRUMPデータを用いた、肝臓急性移植片対宿主病発症リスク因子の解析（口演）	新井康之、諫田淳也、仲宗根秀樹、近藤忠一、内田直之、福田隆浩、大橋一輝、小川啓恭、長村登紀子、森島泰雄、廣川　誠、熱田由子、村田　誠	第37回日本造血細胞移植学会総会	2015年3月	国内
40-55歳に対するリン酸フルダラビンとメルファランを前処置とした非血縁間骨髄移植の有効性（口演）	渡邊慶介、澤　正史、河野彰夫、飯田浩充、内田俊樹、大西　康、大橋春彦、熱田由子、鈴木律朗、寺倉精太郎、西田徹也、村田誠、宮村耕一、森下剛久	第37回日本造血細胞移植学会総会	2015年3月	国内
成人急性リンパ性白血病に対する同種造血幹細胞移植における全身放射線照射とbusulfan/cyclophosphamideによる骨髄破壊的前処置の比較：成人急性リンパ性白血病Working Groupによる後方視的解析（口演）	三橋健次郎、賀古真一、重松明男、熱田由子、大橋一輝、福田隆浩、金森平和、高橋聡、衛藤徹也、長村登紀子、森島泰雄、田中淳司	第37回日本造血細胞移植学会総会	2015年3月	国内
成人AMLに対する同種造血幹細胞移植における細胞遺伝学的リスク層別化システムの開発：成人AML WGによる二次調査研究（口演）	山下卓也、内田直之、福田隆浩、岩戸康治、大橋一輝、衛藤徹也、小川啓恭、長村登紀子、森島泰雄、一戸辰夫、熱田由子、高見昭良	第37回日本造血細胞移植学会総会	2015年3月	国内
白血病HLA適合血縁者間移植においてGVHDの発症は移植後白血病再発に影響を与えるか（口演）	森島泰雄、森島聡子、村田　誠、松尾恵太郎、諫田淳也、大橋一輝、福田隆浩、金森平和、石川　淳、熱田由子、一戸辰夫、	第37回日本造血細胞移植学会総会	2015年3月	国内
「本邦における非血縁者間末梢血幹細胞移植の移植成績に関する観察研究」中間解析（口演）	田中　喬、小澤幸泰、澤　正史、城　友泰、金森平和、大橋一輝、谷本光音、栗山幸大、直川匡晴、奥村廣和、千葉　滋、福田隆浩、	第37回日本造血細胞移植学会総会	2015年3月	国内

	倉橋信悟、宮尾康太郎、上田恭典、岡本真一郎、熱田由子、日野雅之、田中淳司、宮村耕一			
ホモ接合型 HLA ハプロタイプを持つ患者の血縁者間造血幹細胞移植における HVG 方向のみ HLA 不適合の影響：JSHCT　HLA ワーキンググループによる後方視的解析（口演）	諫田淳也、池亀和博、藤　重夫、福田隆浩、黒川峰夫、小川啓恭、大橋一輝、金森平和、石川　淳、井上雅美、一戸辰夫、熱田由子、神田善伸	第 37 回日本造血細胞移植学会総会	2015年3月	国内
レシピエント HLA-C グループの違いによって異なってライセシングされた NK 細胞は、同種造血細胞移植後の AML,ALL 患者の予後に影響を及ぼしている(TRUMP 登録の解析)(口演)	有馬靖佳、中村文明、田中淳司、屋部登志雄、土岐典子、福田隆浩、宮村耕一、岩戸康治、衛藤徹也、熱田由子、森島泰雄、神田善伸	第 37 回日本造血細胞移植学会総会	2015年3月	国内
わが国における遺伝性疾患に対する同種造血細胞移植の成績：JSHCT 遺伝性疾患ワーキンググループによる後方視的解析（口演）	矢部普正、森尾友宏、今井耕輔、加藤剛二、高田英俊、梶原道子、井上雅美、高橋義行、河　敬世、加藤俊一、熱田由子、矢部はるみ	第 37 回日本造血細胞移植学会総会	2015年3月	国内
造血細胞移植後長期生存者におけるスクリーニング・予防医療の国際ガイドラインに従った検査項目の医療現場における実施可能性 -JSHCT 国際委員会調査委-（口演）	熱田由子、高橋　聡、諫田淳也、飯田美奈子、高見昭良、小島勢二、岡本真一郎	第 37 回日本造血細胞移植学会総会	2015年3月	国内
長期フォローアップ外来の設置が同種造血細胞移植後長期生存者の晩期合併症管理に与えた影響（口演）	瀬戸愛花、武田みずほ、佐藤貴彦、加藤実穂、加賀谷裕介、中島麻梨絵、川島直実、渡壁恭子、福島庸晃、倉橋信悟、小澤幸泰、熱田由子、宮村耕一	第 37 回日本造血細胞移植学会総会	2015年3月	国内
骨髄破壊的前処置を用いた血液悪性疾患に対する複数臍帯血移植（C-SHOT0507）と単一臍帯血移植（ＴＲＵＭＰデータ）の国内比較：matched control analysis.（口演）	和気　敦、甲斐俊朗、岡田昌也、加藤剛二、小林直樹、青墳信之、石川　淳、高橋　聡、衛藤徹也、谷口修一、熱田由子、加藤俊一	第 37 回日本造血細胞移植学会総会	2015年3月	国内
ＡＴＬに対する同種造血幹細胞移植における各種リスクスコアの有用性の検討　ＪＳＨＣＴ　ＡＴＬワーキン	吉満　誠、田野崎隆二、加藤光次、石田高司、雀　日承、福田隆浩、高塚祥芝、衛藤徹	第 37 回日本造血細胞移植学会総会	2015年3月	国内

ググループによる後方視的解析（口演）	也、内田直之、森内幸美、長村登紀子、森慎一郎、坂巻　壽、熱田由子、宇都宮　與			
慢性ＧＶＨＤ患者における医師の治療指標標的臓器と患者自身の評価による苦痛ハイスコア臓器一致度の検討（ポスター）	武田みずほ、熱田由子、川島直実、瀬戸愛花、倉橋信悟、福島庸晃、渡壁恭子、加賀谷裕介、加藤実穂、中島麻梨絵、佐藤貴彦、小澤幸泰、宮村耕一、上田美寿代、高坂久美子	第37回日本造血細胞移植学会総会	2015年3月	国内
小児領域における移植後リンパ増殖性疾患の後方視的検討(一元化データを用いた検討）（ポスター）	上山潤一、小林良二、井上雅美、菊田　敦、後藤裕明、坂巻　壽、澤田明久、加藤剛二、大隅朋生、古賀友紀、三井哲夫、角南勝介、深野怜司、関水匡大、大木健太郎、森　健、森　鉄也、田中文子、鈴木律朗、熱田由子	第37回日本造血細胞移植学会総会	2015年3月	国内

２．学会誌・雑誌等における論文掲載

掲載した論文（発表題目）	発表者氏名	発表した場所（学会誌・雑誌等名）	発表した時期	国内・外の別
Age influences post-GVHD non-relapse mortality in adults with acute GVHD of varying severity following allogeneic hematopoietic cell transplantation.	Nakane T, Fukuda T, Kanda J, Taniguchi S, Eto T, Ohashi K, Nakamae H, Kurokawa M, Mori T, Morishima Y, Nagamura-Inoue T, Sakamaki H, Atsuta Y, Murata M.	Leuk Lymphoma.	2015	国外
Impact of HLA Mismatch Direction on the Outcome of Unrelated Bone Marrow Transplantation: A Retrospective Analysis from the Japan Society for Hematopoietic Cell Transplantation.	Kanda J, Ichinohe T, Fuji S, Maeda Y, Ohashi K, Fukuda T, Miyamura K, Iwato K, Eto T, Nakamae H, Kobayashi N, Mori T, Mori SI, Morishima Y, Atsuta Y, Kanda Y; HLA Working Group of the Japan Society for Hematopoietic Cell Transplantation.	Biol Blood Marrow Transplant.	2015	国外
Increasing Incidence of Chronic Graft-versus-Host Disease in Allogeneic Transplantation - A	Arai S, Arora M, Wang T, Spellman SR, He W, Couriel DR, Urbano-Ispizua A, Cutler	Biol Blood Marrow Transplant.	2015	国外

Report from CIBMTR.	CS, Bacigalupo AA, Battiwalla M, Flowers ME, Juckett MB, Lee SJ, Loren AW, Klumpp TR, Prockup SE, Ringdén OT, Savani BN, Socié G, Schultz KR, Spitzer T, Teshima T, Bredeson CN, Jacobsohn DA, Hayashi RJ, Drobyski WR, Frangoul HA, Akpek G, Ho VT, Lewis VA, Gale RP, Koreth J, Chao NJ, Aljurf MD, Cooper BW, Laughlin MJ, Hsu JW, Hematti P, Verdonck LF, Solh MM, Norkin M, Reddy V, Martino R, Gadalla S, Goldberg JD, McCarthy PL, Pérez-Simón JA, Khera N, Lewis ID, Atsuta Y, Olsson RF, Saber W, Waller EK, Blaise D, Pidala JA, Martin PJ, Satwani P, Bornhäuser M, Inamoto Y, Weisdorf DJ, Horowitz MM, Pavletic SZ.			
Allogeneic haematopoietic stem cell transplantation for infant acute lymphoblastic leukaemia with KMT2A (MLL) rearrangements: a retrospective study from the paediatric acute lymphoblastic leukaemia working group of the Japan Society for Haematopoietic Cell Transplantation.	Kato M, Hasegawa D, Koh K, Kato K, Takita J, Inagaki J, Yabe H, Goto H, Adachi S, Hayakawa A, Takeshita Y, Sawada A, Atsuta Y, Kato K.	Br J Haematol.	2015	国外
Allogeneic haematopoietic cell transplantation with reduced-intensity conditioning for elderly patients with advanced myelodysplastic syndromes: a nationwide study.	Aoki K, Ishikawa T, Ishiyama K, Aoki J, Itonaga H, Fukuda T, Kakihana K, Uchida N, Ueda Y, Eto T, Mori T, Kondo T, Iwato K, Morishima Y, Tanaka J, Atsuta Y, Miyazaki Y; Adult MyelodysplasticSyndromes Working Group of the	Br J Haematol.	2015	国外

	Japan Society for Hematopoietic Cell Transplantation (JSHCT).			
Pre-transplant diabetes mellitus is a risk factor for infection-related mortality, after allogeneic hematopoietic stem cell transplantation	Takano K, Fuji S, Uchida N, Ogawa H, Ohashi K, Eto T, Sakamaki H, Morishima Y, Kato K, Suzuki R, Fukuda T.	Bone Marrow Transplant.	2015	国外
Identification of an Interaction between VWF rs7965413 and Platelet Count as a Novel Risk Marker for Metabolic Syndrome: An Extensive Search of Candidate Polymorphisms in a Case-Control Study.	Nakatochi M, Ushida Y, Yasuda Y, Yoshida Y, Kawai S, Kato R, Nakashima T, Iwata M, Kuwatsuka Y, Ando M, Hamajima N, Kondo T, Oda H, Hayashi M, Kato S, Yamaguchi M, Maruyama S, Matsuo S, Honda H.	PLoS One.	2015	国外
Pharmacokinetics for once-daily modified release formulation of tacrolimus hydrate in unrelated hematopoietic stem cell transplantation.	Yano S, Mori S, Saito T, Yokoyama H, Machishima T, Shimada T, Yahagi Y, Sugiyama K, Ogasawara Y, Takahara S, Kasama K, Katsube A, Kamiyama Y, Suzuki K, Inui Y, Usui N, Aiba K, Yamashita T.	Ann Hematol.	2015	国外
Biological significance of HLA locus matching in unrelated donor bone marrow transplantation.	Morishima Y, Kashiwase K, Matsuo K, Azuma F, Morishima S, Onizuka M, Yabe T, Murata M, Doki N, Eto T, Mori T, Miyamura K, Sao H, Ichinohe T, Saji H, Kato S, Atsuta Y, Kawa K, Kodera Y, Sasazuki T.	Blood.	2015	国外
The role of hematopoietic stem cell transplantation for relapsed and refractory Hodgkin lymphoma.	Kako S, Izutsu K, Kato K, Kim SW, Mori T, Fukuda T, Kobayashi N, Taji H, Hashimoto H, Kondo T, Sakamaki H, Morishima Y, Kato K, Suzuki R, Suzumiya J; Adult Lymphoma Working Group of the Japanese Society for Hematopoietic Cell Transplantation.	Br J Haematol.	2015	国外
Comparison of continuous and twice-daily infusions of cyclosporine A for graft-versus-host-disease prophylaxis in pediatric	Umeda K, Adachi S, Tanaka S, Ogawa A, Hatakeyama N, Kudo K, Sakata N, Igarashi S, Ohshima K, Hyakuna N,	Pediatr Blood Cancer.	2015	国外

hematopoietic stem cell transplantation.	Chin M, Goto H, Takahashi Y, Azuma E, Koh K, Sawada A, Kato K, Inoue M, Atsuta Y, Takami A, Murata M; on behalf of the GVHD Working Group of the Japan Society for Hematopoietic Cell Transplantation.			
Impact of conditioning intensity and TBI on acute GVHD after hematopoietic cell transplantation.	Nakasone H, Fukuda T, Kanda J, Mori T, Yano S, Kobayashi T, Miyamura K, Eto T, Kanamori H, Iwato K, Uchida N, Mori S, Nagamura-Inoue T, Ichinohe T, Atsuta Y, Teshima T, Murata M.	Bone Marrow Transplant.	2014	国外
Granulocyte colony-stimulating factor combined regimen in cord blood transplantation for acute myeloid leukemia: a nationwide retrospective analysis in Japan.	Konuma T, Ooi J, Uchida N, Ogawa H, Ohashi K, Kanamori H, Aotsuka N, Onishi Y, Yamaguchi H, Kozai Y, Nagamura-Inoue T, Kato K, Suzuki R, Atsuta Y, Kato S, Asano S, Takahashi S.	Haematologica.	2014	国外
Outcome of allogeneic hematopoietic stem cell transplantation for acute myeloid leukemia patients with central nervous system involvement.	Aoki J, Ishiyama K, Taniguchi S, Fukuda T, Ohashi K, Ogawa H, Kanamori H, Eto T, Iwato K, Sakamaki H, Morishima Y, Nagamura T, Atsuta Y, Takami A.	Biol Blood Marrow Transplant.	2014	国外
Effect of graft sources on allogeneic hematopoietic stem cell transplantation outcome in adults with chronic myeloid leukemia in the era of tyrosine kinase inhibitors: a Japanese Society of Hematopoietic Cell Transplantation retrospective analysis.	Ohashi K, Nagamura-Inoue T, Nagamura F, Tojo A, Miyamura K, Mori T, Kurokawa M, Taniguchi S, Ishikawa J, Morishima Y, Atsuta Y, Sakamaki H.	Int J Hematol.	2014	国外
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厚生労働科学研究委託費

難治性疾患等実用化研究事業
（免疫アレルギー疾患等実用化研究事業　移植医療技術開発研究分野）

本邦における造血細胞移植一元化登録研究システム及び研究データ質管理システムの確立

平成２６年度　委託業務成果報告書

（2/2冊）

業務主任者　熱田　由子

平成２７（２０１５）年　３月

様式第１８

委託業務成果報告書への標記について

委託業務に係る成果報告書の表紙裏に、次の標記を行うものとする。

本報告書は、厚生労働省の難治性疾患等実用化研究事業（免疫アレルギー疾患等実用化研究事業　移植医療技術開発研究分野）による委託業務として、一般社団法人　日本造血細胞移植データセンターが実施した平成２６年度「本邦における造血細胞移植一元化登録研究システム及び研究データ質管理システムの確立」の成果を取りまとめたものです。

Ⅳ．研究成果の刊行物・別刷

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Impact of HLA Mismatch Direction on the Outcome of Unrelated Bone Marrow Transplantation: A Retrospective Analysis from the Japan Society for Hematopoietic Cell Transplantation

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The relative desirability of an unrelated donor with a bidirectional 1-locus mismatch (1MM-Bi), a 1-locus mismatch only in the graft-versus-host direction (1MM-GVH), or a 1-locus mismatch only in the host-versus-graft direction (1MM-HVG) is not yet clear. We analyzed adult patients with leukemia or myelodysplastic syndrome who received a first allogeneic stem cell transplant from an HLA-A, -B, -C, and -DRB1 matched or 1-allele mismatched unrelated donor in Japan. The effects of 1MM-Bi (n = 1020), 1MM-GVH (n = 83), and 1MM-HVG (n = 83) compared with a zero mismatch (0MM) (n = 2570) were analyzed after adjusting for other significant variables. The risk of grades III to IV acute graft-versus-host disease (GVHD) was higher with marginal significance in the 1MM-GVH group than in the 0MM group (hazard ratio, 1.85; $P = .014$). However, there was no significant difference in overall or nonrelapse mortality between the 1MM-GVH and 0MM groups. There was no significant difference in acute GVHD or overall or nonrelapse mortality between the 1MM-HVG and 0MM groups. The risks of acute GVHD and overall mortality were significantly higher in the 1MM-Bi group than in the 0MM group. These findings indicate that unrelated donors with 1MM-GVH and 1MM-HVG are both good candidates for patients without an HLA-matched unrelated donor in a Japanese cohort.

INTRODUCTION

An HLA-identical sibling is the best donor for allogeneic stem cell transplantation because of the low risk of immune complications such as acute graft-versus-host disease (GVHD) and graft rejection. However, for patients without an HLA-identical sibling, an HLA-A, -B, -C, and -DRB1 allele-matched

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unrelated donor is considered the best alternative when an immediate transplant is not necessary [1,2]. Finally, when an HLA-matched unrelated donor is not available, an HLA 1-allele mismatched unrelated donor is an attractive donor source, although the overall survival rate after HLA 1-allele mismatched unrelated transplantation is 5% to 10% lower than that after HLA-matched unrelated transplantation [3-5].

Among 1-allele mismatched unrelated donors, the mismatch is only in the graft-versus-host direction (1MM-GVH) when a mismatched allele of the donor is homozygous. On the other hand, the mismatch is only in the host-versus-graft direction (1MM-HVG) when a mismatched allele of the recipient is homozygous. The effect of the immune reaction caused by an HLA mismatch differs according to whether the mismatch is in the GVH or HVG direction, because a mismatched antigen in the GVH direction can be a major target for donor T cells and can cause GVHD, whereas a mismatched antigen in the HVG direction can be a major target for the remaining recipient T cells and can lead to graft rejection. In related transplantation, the presence of HLA mismatches in the GVH direction is associated with a higher incidence of GVHD, whereas the presence of HLA mismatches in the HVG direction is associated with a higher incidence of rejection [6-8]. Therefore, from a biological perspective, the impact of 1MM-GVH, 1MM-HVG, or bidirectional 1-locus mismatch (1MM-Bi) on the clinical outcome should differ, and questions regarding donor selection priority should arise when several donor candidates with 1MM-Bi, 1MM-GVH, or 1MM-HVG are available for patients without an HLA-matched unrelated donor.

In a recent study by the Center for International Blood and Marrow Transplant Research (CIBMTR), transplantation from an unrelated donor with 1MM-Bi or a donor with 1MM-GVH was significantly associated with higher risks of severe acute GVHD and overall mortality than transplantation from an unrelated donor without a mismatch at the HLA-A, -B, -C, or -DRB1 locus (0MM) [9]. However, transplantation from a donor with 1MM-HVG was not associated with these risks. Therefore, selection of an unrelated donor with 1MM-HVG is recommended when an unrelated donor with 0MM is not available. However, hazard ratios (HRs) of overall and disease-free survival in the 1MM-HVG group as compared with the 0MM group were also high (1MM-HVG HR, 1.37 [$P = .03$] and 0MM HR, 1.38 [$P = .013$]). Although these values were not statistically significant as defined in that study ($P < .01$), these HRs in the 1MM-HVG group were comparable with those in the 1MM-Bi group (1.29 and 1.35, respectively), suggesting the study may have had insufficient power to detect a significant difference between the 1MM-HVG and 0MM groups. Therefore, the effect of the HLA mismatch direction in unrelated bone marrow transplantation (UBMT) needs to be validated in other populations. In the present study, we conducted a retrospective analysis using Japanese national registry data on 3756 patients who underwent HLA-matched or 1-allele mismatched UBMT.

METHODS

Data Collection

Patients who were at least 16 years of age with acute myelogenous leukemia (AML), acute lymphoblastic leukemia (ALL), myelodysplastic syndrome (MDS), or chronic myelogenous leukemia (CML), who received a first BMT from a serologically HLA-A, -B, and -DR matched unrelated donor between 2000 and 2011, and who had full HLA-A, -B, -C, and -DRB1 allele data were included in this study. Data were obtained from the Transplant Registry Unified Management Program (TRUMP) [10], where all UBMTs are registered through the Japan Marrow Donor Program (JMDP). We excluded those who had more than 1-allele mismatch at the HLA-A, -B, -C, or -DRB1 locus; those who lacked data on survival status, survival date, and sex; and those in whom ex vivo or in vivo T cell depletion was used. As a result, 3756 patients were included in this study. The study was approved by the data management committee of TRUMP and by the Institutional Review Board of Saitama Medical Center, Jichi Medical University, where this study was organized.

Histocompatibility

Histocompatibility data for serological and genetic typing for the HLA-A, -B, -C, and -DR loci were obtained from the TRUMP database, which includes HLA allele data determined retrospectively by the JMDP using frozen samples [11,12]. The extent of HLA testing was exons 2 and 3 for HLA class I and exon 2 for HLA class II. Exon 4 and exon 3 were additionally analyzed for classes I and II, respectively, if required. An HLA mismatch in the GVH direction was defined as when the recipient's antigens or alleles were not shared by the donor, and a mismatch in the HVG direction was defined as when the donor's antigens or alleles were not shared by the recipient.

Endpoints

The primary endpoint of the study was overall survival. Other endpoints assessed were relapse, nonrelapse mortality, neutrophil engraftment, acute GVHD, and chronic GVHD. Neutrophil recovery was considered to have occurred when the absolute neutrophil count exceeded 0.5×10^9 cells/L for 3 consecutive days after transplantation. The physicians who performed transplantation at each center diagnosed and graded acute and chronic GVHD according to the traditional criteria [13,14]. The incidence of chronic GVHD was evaluated in patients who survived without relapse for more than 100 days.

Statistical Analysis

The probability of overall survival was estimated according to the Kaplan-Meier method, and groups were compared using the log-rank test. The probabilities of relapse, nonrelapse mortality, neutrophil engraftment, and acute and chronic GVHD were estimated on the basis of cumulative incidence curves [15]. Competing events were death without relapse for relapse, relapse for nonrelapse mortality, death without engraftment for neutrophil engraftment, and death or relapse without GVHD for acute and chronic GVHD. The groups were compared using Gray's test [16]. The Cox proportional hazards model was used to evaluate the effect of confounding variables on overall survival, whereas Fine and Gray's proportional hazards model was used for the other endpoints [17]. Based on the report by the CIBMTR, we classified the conditioning regimens as myeloablative if total body irradiation > 8 Gy, oral busulfan ≥ 9 mg/kg, intravenous busulfan ≥ 7.2 mg/kg, or melphalan > 140 mg/m^2 was used in the conditioning regimen; otherwise, we classified the conditioning regimen as reduced intensity [18]. For patients with insufficient data regarding the doses of the agents used in the conditioning regimen, we used the information on conditioning intensity (myeloablative or reduced intensity) reported by the treating clinicians. We defined AML and ALL in the first or second remission, CML in the first or second chronic phase or accelerated phase, and MDS with refractory anemia or refractory anemia with ringed sideroblasts as standard-risk diseases and other conditions as high risk.

The following possible confounding variables were considered: the recipient's age group (16 to 49 years or ≥50 years), the recipient's sex, sex mismatch between the recipient and donor (match, male [donor]/female [recipient] or female [donor]/male [recipient]), disease (AML, ALL, CML, or MDS), disease status before transplantation (standard or high risk), type of GVHD prophylaxis (cyclosporine based, tacrolimus based, or other/missing), type of conditioning regimen (myeloablative, reduced intensity, or missing), and year of transplantation (2000-2005 or 2006-2011). Factors other than HLA matching were selected in a stepwise manner from the model with a variable retention criterion of $P < .05$. We then added HLA matching to the final model. For multiple comparisons, a value of $P < .01$ was used to determine statistical significance.

All statistical analyses were performed with Stata version 13 (Stata Corp., College Station, TX) and EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan) [19]. EZR is a graphical user interface for R (The R Foundation for Statistical Computing, version 2.13.0, Vienna, Austria). More precisely, it is a modified version of R commander (version 2.0-1) designed to add statistical functions that are frequently used in biostatistics.

RESULTS

Patient Characteristics

Table 1 shows patient and transplant characteristics. The median age of recipients at transplantation was 43 years (range, 16 to 77). The diagnosis for transplant was