Ⅲ. 学会等発表実績

学 会 等 発 表 実 績

委託業務題目「小児骨髄系腫瘍に対する標準的治療法の確立に関する研究」
機関名　国立大学法人京都大学

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
Pediatric AML with FLT3-ITD/WT allelic ratio, NUP98-NSD1 chimera, NPM1, and WT1 mutations - JPLSG AML05 study.	Shimada A, Yamashita Y, Tomizawa D, Tawa A, Watanabe T, Yokozawa T, Yamada M, Kudo K, Taga T, Iwamoto S, Terui K, Moritake H, Kinoshita A, Takahashi H, Nakayama H, Koh K, Goto H, Kosaka Y, Saito AM, Fujimoto J, Horibe K, Hara Y, Oki K, Hayashi Y, Adachi S	25th Annual Meeting of the I-BFM Study Group Prague, April 27, 2014	April 27, 2014	国外
Hematopoietic stem cell transplantation for children with relapsed AML in Japan. (oral)（口演）	Nakayama H, Kudo K, Shimada A, Yabe H, Horibe K, Miyamura T, Moritake H, Tomizawa D, Taga T, Adachi S.	25th Annual Meeting of I-BFM Study Group, Prague	April 27, 2014	国外
Outcome of children with relapsed acute myeloid leukemia following initial therapy by Japanese AML99 protocol. (poster)	Nakayama H, Kudo K, Shimada A, Yabe H, Horibe K, Miyamura T, Moritake H, Tomizawa D, Taga T, Adachi S.	9th Biennial Childhood Leukemia Symposium, Prague	2014年4月28日	国外
Risk-oriented therapy for myeloid leukemia of Down syndrome: a nationwide prospective study by the Japanese Pediatric Leukemia / Lymphoma Study Group (JPLSG).（ポスター）	Taga T, Watanabe T, Kudo K, Tomizawa D, Terui K, Moritake H, Kinoshita A, Iwamoto S, Nakayama H, Takahashi H, Shimada A, Taki T, Toki T, Ito E, Goto H, Koh K, Saito AM, Horibe K, Nakahata T, Tawa A, Adachi S.	56th Annual meeting of American Society of Hematology (San Francisco)	December 6-9, 2014	国外
Poor prognosis of FAB-M4 and M5 patients in pediatric acute myeloid leukemia with FLT3-ITD（ポスター）	Hara H, Shiba N, Ohki K, Myoung-ja Park, Shimada S, Tomizawa D, Taga T, M. Saito A, Fujimoto J, Arakawa H, Tawa T, Horibe K, Adachi S, Hayashi H.	56th Annual meeting of American Society of Hematology (San Francisco)	December 6-9, 2014	国外
Pediatric Acute Megakaryoblastic Leukemia without Down Syndrome: A Retrospective Study By the International Berlin-Frankfurt-Munster Study Group (I-BFMSG)（ポスター）	Inaba H, Yinmei Zhou, Oussama Abla, Adachi S, Anne Auvrignon, H. Berna Beverloo, Eveline de Bont, Tai-Tsung Chang, Ursula Creutzig, Michael Dworzak, Sarah Elitzur, Alcira Fynn, Erik Forestier, Henrik Hasle, Der-Cherng Liang, Vincent Lee, Franco Locatelli, Riccardo Masetti, Barbara De Moerloose, Dirk Reinhardt, Laura Rodriguez, Shuhong Shen, Taga T, Tomizawa D, Allen E.J. Yeoh, Martin Zimmermann, and Susana C. Raimondi.	56th Annual meeting of American Society of Hematology (San Francisco)	December 6-9, 2014	国外

High event-free survival rate with minimum-dose-anthracycline treatment in childhood acute promyelocytic leukemia: A nationwide prospective study by the Japanese Pediatric Leukemia / Lymphoma Study Group (JPLSG). (ポスター)	Takahashi H, Watanabe T, Kinoshita A, Yuza Y, Moritake H, Terui K, Iwamoto S, Nakayama H, Shimada A, Kudo K, Taki T, Yabe M, Matsushita H, Yamashita Y, Koike K, Ogawa A, Kosaka Y, Tomizawa D, Taga T, Moriya Saito A, Horibe K, Nakahata T, Miyachi H, Tawa A, Adachi S.	56th Annual Meeting of the American Society of Hematology (San Francisco)	December 6-9, 2014	国外
Outcome of adolescent and young adults with acute myeloid leukemia treated with pediatric protocols: a report from the 3 Japanese cooperative studies. (口演)	Tomizawa D, Watanabe T, Hanada R, Horibe K, Horikoshi Y, Iwamoto S, Kinoshita A, Moritake H, Nakayama H, Shimada A, Taga T, Takahashi H, Tawa A, Terui K, Hori H, Kawano Y, Kikuta A, Manabe A, Adachi S.	56th Annual meeting of American Society of Hematology (San Francisco)	December 6-9, 2014	国外
Poor prognosis associated with FAB subtypes M4 and M5 in Japanese pediatric acute myeloid leukemia patients with FLT3-ITD. (ポスター)	Hara Y, Shiba N, Ohki K, Park M-J, Shimada A, Tomizawa D, Saito AM, Fujimoto J, Taki T, Kinoshita A, Taga T, Arakawa H, Tawa A, Horibe K, Adachi S, Hayashi Y.	56th Annual meeting of American Society of Hematology (San Francisco)	December 6-9, 2014	国外
The prognostic impact of high MEL1 gene expression in pediatric acute myeloid leukemia (ポスター)	Shiba N, Ohkil K, Hara Y, Yamato G, Myoung-ja Park, Ichikawa H, Kobayashi T, Tomizawa D, Sotomatsu M, Arakawa H, Horibe K, Taga T, Adachi S, Tawa A, Hayashi Y.	56th Annual meeting of American Society of Hematology (San Francisco)	December 6-9, 2014	国外
Clinical features of Patients with ASXL1 and ASXL2 mutations in pediatric acute myeloid leukemia (ポスター)	Yamato G, Shiba N, Yoshida K, Ohkil K, Myoung-ja Park, Hara Y, Tomizawa D, Sotomatu M, Taga T, Adachi S, Tawa A, Horibe K, Arakawa H, Ogawa S, Hayashi Y.	56th Annual meeting of American Society of Hematology (San Francisco)	December 6-9, 2014	国外
The Prognostic Relevance of the 2008 WHO Classification of Myeloid Neoplasms in Childhood Acute Myeloid Leukemia. (ポスター)	Kinoshita A, Miyachi H, Matsushita H, Yabe M, Taki T, Watanabe T, Saito AM, Tomizawa D, Taga T, Takahashi H, Matsuo H, Kodama K, Ohki K, Hayashi Y, Tawa A, Horibe K, Adachi S.	ミラノ (19th Congress of European Hematology Association)	2014年6月12日-15日	国外
Secondary cancers after cancer diagnosis in childhood: a hospital-based retrospective cohort study in Japan. ポスター	Ishida Y, Qiu D, Maeda M, Fujimoto J, Kigasawa H, Kobayashi R, Sato M, Okamura J, Yoshinaga S, Rikiishi K, Shichino H, Kiyotani C, Kudo K, Asami K, Iwamoto S, Kawaguchi H, Inada H, Adachi S, Manabe A, Kuroda T.	The 49th Congress of the International Society of Paediatric Oncology (SIOP) (Toronto)	2014年10月	国外
Current status of cancer survivorship research in Japan (focused on the secondary cancers)シンポジウム講演 (口演)	Ishida Y.	Society of International Pediatric Oncology (SIOP) Asia Congress (Seoul)	2014年4月	国外

Recurrent CDC25C mutations drive malignant transformation in FPD/AML(ポスター)	Yoshimi A, Toya T, Kawazu M, Ueno T, Tsukamoto A, Iizukal H, Nakagawa M, Nannya Y, Arai S, Ichikawa M, Harada H, Usuki K, Hayashi Y, Ito E, Kirito K, Nakajima H, Mano H, Kurokawa M.	AACR Annual Meeting 2014	2014年4月5～9日	国外
A patient of juvenile myelomonocytic leukemia with an NRAS mutation who developed acute lymphoblastic leukemia.ポスター	Kudo K, Matsuoka A, Muramatsu H, Okuno Y, Ogura T, Tomii T, Kitazawa H, Ito R, Horikoshi Y, Xinan Wang, Ito M, Kojima S.	9th Biennial Childhood Leukemia Symposium, : Plague, Czech Republik	April 28-29, 2014	国外
Recent employment trend of Childhood Cancer Survivors in Japan: A Cross-Sectional Survey. ポスター	Ishida Y, Hayashi M, Inoue F, Ozawa M.	The 49th Congress of the International Society of Paediatric Oncology (SIOP) (Toronto)	2014年10月	国外
A Support System for Childhood Cancer Survivors with Job-Hunting Difficulty. (ポスター)	Hayashi M, Inoue F, Ishida Y, Ozawa M.	The 49th Congress of the International Society of Paediatric Oncology (SIOP) (Toronto)	2014年10月	国外
第一寛解期の中間リスク群小児急性骨髄性白血病に対する造血幹細胞移植の意義を検証する臨床決断分析（口演）	長谷川大一郎，工藤寿子，田渕健，熱田由子，井上雅美，澤田明久，康勝好，加藤剛二，稲垣二郎，石田宏之，富澤大輔，足立壮一	第36回日本造血細胞移植学会、沖縄コンベンションセンター	平成26年3月7日-9日	国内
小児急性骨髄性白血病におけるGATA2変異の解析(口演)	原 勇介，柴 徳生，大木 健太郎，朴 明子，足立 壮一，多賀 崇，荒川 浩一，多和 昭雄，堀部 敬三，林 泰秀	第117回日本小児科学会学術集会	平成26年4月11-13日	国内
小児急性骨髄性白血病における分子生物学的背景を用いた新たな治療層別化への試み(口演)	柴 徳生，吉田 健一，大木 健太郎，金澤 崇，足立 壮二，多和 昭雄，伊藤 悦朗，荒川 浩一，小川 誠司，林 泰秀，JPLSG AML委員会	第117回日本小児科学会学術集会	平成26年4月11-13日	国内
小児急性骨髄性白血病における寛解導入療法終了後非寛解例の分子生物学的異常の同定と臨床像の検討(ポスター)	原 勇介，大木 健太郎，柴 徳生，朴 明子，富澤 大輔，多賀 崇，足立 壮一，荒川 浩一，多和 昭雄，林 泰秀	第73回日本癌学会学術総会	平成26年9月25-27日	国内
Accelerated and blast phase of pediatric chronic myeloid leukemia.:Report from JPLSG CML-11 study (ポスター)	Watanabe A. Tanizawa A, Tono C, Shima H, Muramatsu H, Kurosawa H, . Ito M, Yuza Y, Hotta N, Okada M, . Hosoi H, Saito A, Adachi S, Horibe K, Mizutani S, Shimada H.	第76回日本血液学会、大阪国際会議場	平成26年10月31日-11月2日	国内
CSF3R and CALR mutations and cytogenetic findings in pediatric myeloid malignancies. （口演）	Sano H, Ohki K, Park M-J, Shiba N, Hara Y, Sotomatsu M, Tomizawa D, Taga T, Kiyokawa N, Tawa A, Horibe K, Adachi S, Hayashi Y.	第76回日本血液学会、大阪国際会議場	平成26年10月31日-11月2日	国内

Genetic analyses of patients who did not achieve complete remission after induction therapy. (口演)	Hara Y, Ohki K, Shiba N, Shimada A, Tomizawa D, Taga T, Adachi S, Arakawa H, Tawa A, Hayashi Y.	第76回日本血液学会、大阪国際会議場	平成26年10月31日-11月2日	国内
Pediatric AML with FLT3-ITD/WT, NUP98-NSD1, NPM1, and WT1 mutations affected the clinical outcome. (口演)	Shimada A, Yamashita Y, Tomizawa D, Shiba N, Tawa A, Watanabe T, Yokozawa T, Kudo K, Taga T, Iwamoto S, Terui K, Moritake H, Kinoshita A, Takahashi H, Nakayama H, Koh K, Goto H, Kosaka Y, Saito A, Fujimoto J, Horibe K, Hara Y, Oki K, Hayashi Y, Adachi S.	第76回日本血液学会、大阪国際会議場	平成26年10月31日-11月2日	国内
The prognostic impact of high EVI1-related genes expression in pediatric acute myeloid leukemia. (口演)	Shiba N, Hara Y, Ohki K, Yamato G, Park M-J, Kobayashi T, Ichikawa H, Tomizawa D, Taki T, Shimada A, Sotomatsu M, Arakawa H, Horibe K, Adachi S, Tawa A, Hayashi Y.	第76回日本血液学会、大阪国際会議場	平成26年10月31日-11月2日	国内
Incidence and clinical impact of FLT3 mutation in childhood acute promyelocytic leukemia; JPLSG AML-P05 study (口頭)	Yamashita Y, Takahashi H, Shimada A, Yamada M, Kinoshita A, Yuza Y, Moritake H, Terui K, Tomizawa D, Taga T, Horibe K, Adachi S.	第56回日本小児血液・がん学会、岡山コンベンションセンター	平成26年11月28日-30日	国内
小児がん診断後の二次がん発症に関する疫学研究-15病院における後ろ向きコホート	石田也寸志、邱冬梅、前田美穂、藤本純一郎、気賀沢寿人、小林良二、佐藤真穂、岡村純、吉永信治、力石健、七野浩之、清谷知賀子、工藤寿子、浅見恵子、堀浩樹、川口浩史、稲田浩子、足立壮一、真部淳、黒田達夫	第56回日本小児血液・がん学会、岡山コンベンションセンター	平成26年11月28日-30日	国内
Chemotherapy is effective for pediatric RAEB/RAEB-T: Results from the JPLSG AML05 and JSPHO MDS studies. (口演)	Shimada S, Kinoshita A, Manabe A, Yabe M, Miyachi H, Matsushita H, Taki T, Inoue M, Hasegawa D, Hama A, Hasegawa D, Horibe K, Itou M, Tawa A, Kojima S, Adachi S.	第56回日本小児血液・がん学会学術集会	2014年11月30日	国内
小児急性骨髄性白血病におけるASXL1、ASXL2遺伝子変異と臨床像. (口演)	大和玄幸，柴徳生，吉田健一，大木健太郎，朴明子，原勇介，外松学，富澤大輔，足立壮一，多和昭雄，堀部敬三，荒川浩一，小川誠司，林泰秀	第56回日本小児血液・がん学会学術集会（岡山）	平成26年11月29日-12月1日	国内
小児AMLにおけるIKZF1欠失の頻度と予後解析: JPLSG AML-05. (口演)	大木健太郎，朴明子，原勇介，柴徳生，外松学，富澤大輔，多賀崇，齋藤明子，藤本純一郎，多和昭雄，堀部敬三，足立壮一，林泰秀	第56回日本小児血液・がん学会学術集会（岡山）	平成26年11月29日-12月1日	国内
小児急性骨髄性白血病における寛解導入療法非寛解例の遺伝子解析による予後不良因子の同定（口演）	原勇介，大木健太郎，柴徳生，朴明子，富澤大輔，多賀崇，足立壮一，多和昭雄，林泰秀	第56回日本小児血液・がん学会学術集会（岡山）	平成26年11月29日-12月1日	国内

小児血液疾患領域の臨床試験における逸脱とアウトカム、ポスター（ポスター賞受賞）	西岡絵美子、永井かおり、三和郁子、佐藤則子、生越良枝、染谷こころ、長谷川裕子、鳥居薫、米島麻三子、岡野美江、鶴澤正仁、堀部敬三、足立壮一、石井榮一、角南勝介、真部淳、多和昭雄、多賀崇、高橋浩之、齋藤明子	第6回日本臨床試験学会学術集会総会	平成27年2月20日	国内
小児AMLにおけるG-CSF receptor(CSF3R)遺伝子異常の解析（口演）	佐野 仁志，大木 健太郎，朴 明子，柴 徳生，足立 壮一，堀部 敬三，多和 昭雄，花田 良二，月本 一郎，林 泰秀	第117回日本小児科学会学術集会	平成26年4月11-13日	国内
小児がん親の会におけるピアサポーター養成プログラムの検討 A Trial of the Peer Support Development Program with in Childhood Cancer Parent Group	井上玲子、藤本純一郎、足立壮一、高下裕子、野村一恵、根岸京子	第56回日本小児血液・がん学会学術集会（岡山）	平成26年11月28日-11月30日	国内
入院中の高校生の教育支援状況に関する調査 Research investigation of educational support of hospitalized high school students by questionnaires	川村眞智子、前田美穂、足立壮一	第56回日本小児血液・がん学会学術集会（岡山）	平成26年11月28日-11月30日	国内
当院における思春期・若年性腎(AYA)世代のがんの実態と診療体制についての検討 Management system of adolescents and young adults with cancer :A single center experience	高田亜希子、梅田雄嗣、才田聡、加藤 格、平松英文、渡邉健一郎、平家俊男、足立壮二、荒川芳輝、溝脇尚志、岡本 健、北野俊行、近藤忠一、岡島英明、武藤 学	第56回日本小児血液・がん学会学術集会（岡山）	平成26年11月28日-11月30日	国内
Successful allogeneic hematopoietic stem cell transplantation with reduced intensity conditioning for GATA2 deficiency	才田 聡、梅田雄嗣、森あかね、八角高裕、平松英文、平家俊男、渡邉健一郎、足立壮二	第37回日本造血細胞移植学会総会（神戸市）	平成27年3月5日-7日	国内
11q23転座型小児急性骨髄性白血病に対する造血幹細胞移植治療の検討.（口演）	宮村能子，田渕健，富澤大輔，多賀崇，長谷川大一郎，後藤裕明，沖本由理，加藤剛二，井上雅美，浜本和子，稲垣二郎，河敬世，熱田由子，工藤寿子	第36回日本造血細胞移植学会、沖縄コンベンションセンター	平成26年3月7日-9日	国内
造血器腫瘍のコンパニオン診断の現状と課題（シンポジウム）	宮地勇人	日本検査血液学会	平成26年7月	国内
Clinical outcome of newly diagnosed pediatric acute myeloid leukemia: Single institute experience.	Iwamoto S, Iwasa T, Kihira K, Amano K, Toyoda H, Deguchi T, Hirayama M, Azuma E, Hori H, KomadaY.	第76回日本血液学会、大阪国際会議場	平成26年10月31日-11月2日	国内
APLに対する寛解導入療法中にカテーテル関連静脈血栓症を合併した1例（ポスター）	高橋浩之，羽賀洋一，澤友歌，松岡正樹，小嶋靖子，横須賀とも子，小原明	第56回日本小児血液がん学会総会，岡山	平成26年11月28日-30日	国内
The virological analysis of 3 ciHHV-6 in hematopoietic stem cell transplant patient.（口演）	Miura H, Kawamura Y, Kudo K, Ihira M, Yoshikawa T.	第56回日本小児血液・がん学会、岡山コンベンションセンター	平成26年11月28日-30日	国内

卵巣胚細胞腫から発症した急性骨髄性白血病のゲノム解析（ポスター）	犬飼岳史，滝 智彦，根本篤，赤羽 弘資，合井久美子，黒田 格，廣瀬衣子，阿部正子，加賀美恵子，杉田完爾	第56回日本小児血液・がん学会学術集会	2014年11月28日	国内
小児慢性期CML における治療反応性予測因子としての細胞表面マーカー解析 （口演）	嶋 晴子，清河 信敬，谷澤昭彦，黒澤 秀光，渡辺 輝浩，伊藤 正樹，遠野 千佳子，湯坐 有希，村松 秀城，堀田 紀子，岡田 雅彦，嶋田 博之	第56回日本小児血液・がん学会学術集会（岡山）	平成26年11月29日-12月1日	国内
小児慢性期慢性骨髄性白血病に対する多施設共同観察研究（CML-08）平成26年度予備解析：変異解析について （口演）	谷澤 昭彦，黒澤 秀光，渡辺 輝浩，伊藤 正樹，遠野 千佳子，嶋 晴子，湯坐 有希，村松 秀城，堀田 紀子，岡田 雅彦，平位 秀世，嶋田 博之	第56回日本小児血液・がん学会学術集会（岡山）	平成26年11月29日-12月1日	国内
JPLSG CML-08予備解析報告：急性有害事象について （口演）	湯坐 有希，谷澤 昭彦，黒澤 秀光，渡辺 輝浩，伊藤正樹，遠野 千佳子，嶋 晴子，村松 秀城，堀田 紀子，岡田 雅彦，嶋田 博之	第56回日本小児血液・がん学会学術集会（岡山）	平成26年11月29日-12月1日	国内
Impact of imatinib mesylate trough blood level on the clinical outcome of children with chronic myeloid leukemia (JPLSG CML-08 study) （口演）	Muramatsu H, Tanizawa A, Kurosawa H, Watanabe A, Ito M, Tono C, Shima H, Yuza Y, Okada M, Hotta N, Shimada H.	第56回日本小児血液・がん学会学術集会（岡山）	平成26年11月29日-12月1日	国内
A multicenter, prospective observational study for pediatric CML in CP (JPLSG CML-08): preliminary analysis 2014 （口演）	Shimada H, Kurosawa H, Watanabe A, Ito M, Tono C, Shima H, Yuza Y, Muramatsu H, Hotta N, Okada M, Tanizawa A.	第56回日本小児血液・がん学会学術集会（岡山）	平成26年11月29日-12月1日	国内
造血器腫瘍の先進医療を支える臨床検査：コンパニオン診断の現状と展開（シンポジウム） （口演）	宮地勇人	日本臨床検査学会	平成26年11月	国内
CDISC SDTMデータを指標とした収集データ最適化の検討 （ポスター）	永井かおり、齋藤俊樹、西岡絵美子、三和郁子、佐藤則子、生越良枝、染谷こころ、長谷川裕子、鳥居薫、米島麻美子、岡野美江、堀部敬三、齋藤明子	第6回日本臨床試験学会学術集会総会	平成27年2月20日	国内
小児血液がん領域の臨床試験におけるデータ収集 （ポスター）	生越良枝、永井かおり、西岡絵美子、三和郁子、佐藤則子、染谷こころ、長谷川裕子、鳥居薫、米島麻美子、岡野美江、堀部敬三、齋藤明子	第6回日本臨床試験学会学術集会総会	平成27年2月20日	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
Acute Myeloid Leukemia with Myelodysplastic Features in Children. A Report of Japanese Pediatric Leukemia/Lymphoma Study Group.	Kinoshita A, Miyachi H, Matsushita H, Yabe M, Taki T, Watanabe T, Saito AM, Tomizawa D, Taga T, Takahashi H, Matsuo H, Kodama K, Ohki K, Hayashi Y, Tawa A, Horibe K, Adachi S.	Br J Haematol 167:80-86	2014	国外
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Ⅳ. 研究成果の刊行物・別刷

bjh research paper

Acute myeloid leukaemia with myelodysplastic features in children: a report of Japanese Paediatric Leukaemia/ Lymphoma Study Group

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Summary

The clinical characteristics and prognostic relevance of acute myeloid leukaemia (AML) with myelodysplastic features remains to be clarified in children. We prospectively examined 443 newly diagnosed patients in a multicentre clinical trial for paediatric *de novo* AML, and found 'AML with myelodysplasia-related changes' (AML-MRC) according to the 2008 World Health Organization classification in 93 (21·0%), in whom 59 were diagnosed from myelodysplasia-related cytogenetics alone, 28 from multilineage dysplasia alone and six from a combination of both. Compared with 111 patients with 'AML, not otherwise specified' (AML-NOS), patients with 'AML-MRC' presented at a younger age, with a lower white blood cell count, higher incidence of 20–30% bone marrow blasts, unfavourable cytogenetics and a lower frequency of Fms-like tyrosine kinase 3 internal tandem duplication (*FLT3*-ITD), *NPM1* and *CEBPA* mutations. Complete remission rate and 3-year probability of event-free survival were significantly worse in 'AML-MRC' patients (67·7 vs. 85·6%, $P < 0·01$, 37·1% vs. 53·8%, $P = 0·02$, respectively), but 3-year overall survival and relapse-free survival were comparable with 'AML-NOS' patients. By multivariate analysis, *FLT3*-ITD was solely associated with worse overall survival. These results support the distinctive features of the category 'AML-MRC' even in children.

Keywords: paediatric acute myeloid leukaemia, WHO classification, multilineage dysplasia, myelodysplasia.

Acute myeloid leukaemia (AML) is a group of heterogeneous disorders. This heterogeneity was first observed as differences in the morphology of leukaemic cells and the morphological classification, introduced by the French-American-British (FAB) haematologists, has been widely accepted as the cornerstone of AML diagnosis (Bennett *et al*, 1976). With the progress in diagnostic techniques, however, much attention became to be paid to cytogenetic and molecular diversity, which provided deeper insights into the biology of AML. Thus, the World Health Organization (WHO)

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introduced a new classification for AML that incorporated cytogenetics in the system (Harris *et al*, 1999). In 2008, the WHO classification was revised, and recently acquired genetic information and evidence for its clinical impacts was incorporated into an updated classification scheme for AML (Vardiman *et al*, 2009). One of the revisions includes a new category 'AML with myelodysplasia-related changes' (AML-MRC). Patients are assigned to this category for any one of following three reasons: (i) AML arising from previous myelodysplastic syndrome (MDS) or an MDS/myeloproliferative neoplasm, (ii) AML with a specific MDS-related cytogenetic abnormality, and/or (iii) AML with multilineage dysplasia. Although recent studies have validated this system, including the importance of multilineage dysplasia (Weinberg *et al*, 2009), others have suggested that multilineage dysplasia correlates with unfavourable cytogenetics and has no independent impact on prognosis (Miesner *et al*, 2010).

Given that AML with myelodysplastic features has been assumed to be rare in paediatric population, only a few small series have reported the clinical and pathological features of this category of AML in children. This study was undertaken to clarify the clinical features and prognostic significance of this newly defined 'AML-MRC' category in paediatric AML. The evaluation was based on data from children with newly diagnosed AML treated on AML-05 trial conducted by the Japanese Paediatric Leukaemia/Lymphoma Study Group (JPLSG).

Patients and methods

Between November 2006 and December 2010, 485 consecutive patients aged <18 years with suspected AML, excluding acute promyelocytic leukaemia, Down syndrome, secondary AML, myeloid/natural killer cell leukaemia, and myeloid sarcoma were registered in AML-05 (UMIN–CTR, URL: http://www.umin.ac.jp/ctr/index.htm; number UMIN000000511). This study was approved by the institutional review board at each participating institution, and all patients, or the patients' parents/guardians, provided a written informed consent.

The central diagnosis was determined by integrating morphological, cytogenetic immunological, molecular and clinical parameters. Bone marrow and peripheral blood smears were sent to a central laboratory, and the morphological review was performed independently by three haematologists. Diagnoses of multilineage dysplasia were made based on the WHO classification criteria (Jaffe *et al*, 2001): cellular dysplasia present in at least 50% of the cells in at least two bone marrow cell lines. For diagnosis of cellular dysplasia in erythroid or myeloid cells, 25 erythroblasts or 10 or more mature neutrophils were respectively evaluated. Diagnosis of dysplastic megakaryocytes was made in cases with dysplastic features in three or more megakaryocytes or at least 50% in six or more cells. When the diagnosis was discordant among the observers, the final diagnosis was made based on agreement after discussion. Flow-cytometric immunophenotyping was determined at the three central laboratories where the same antibody panels were used. Cytogenetic tests were carried out in regional laboratories and reports were reviewed centrally. Diagnosis of AML-MRC from myelodysplasia-related cytogenetic abnormalities was made based on the criteria of the 2008 WHO classification (Swerdlow *et al*, 2008): complex karyotype including three or more unrelated abnormalities, unbalanced abnormalities including -7/del(7q), -5/del(5q), i(17q)/t(17p), -13/del(13q), del(11q), del(12p)/t(12p), del(9q), idic(X)/(q13), balanced abnormalities including t(11;16)(q23;p13.3), t(3;21)(q26.2;q22.1), t(1;3)(p36.3;q21.1), t(2;11)(p21;q23), t(5;12)(q33;p12), t(5;7)(q33;q11.2), t(5;17)(q33;p13), t(5;10)(q33;q21),t(3;5)(q25;q34). Chimeric gene analyses including *RUNX1-RUNX1T1*, *CBFB-MYH11*, *PML-RARA*, *KMT2A-MLLT3*, *KMT2A-MLLT4*, *KMT2A-ELL*, *FUS-ERG*, and *NUP98-HOXA9*, and Fms-like tyrosine kinase 3 internal tandem duplication (*FLT3*-ITD) were examined for all patients at a single laboratory. At the time that all data were submitted to the data centre, a central review of diagnosis was performed individually for each case by multidisciplinary conferencing using electronic mail discussion. Mutation analysis for *CEBPA* and *NPM1* was retrospectively performed by reverse transcription polymerase chain reaction (RT-PCR) and direct sequencing using RNA from diagnostic bone marrow samples.

The therapeutic regimens used in AML-05 trial have been described in detail elsewhere (Tomizawa *et al*, 2013). Definition of complete remission (CR) consisted of <5% blasts in the bone marrow, recovery of neutrophils and platelets and absence of extramedullary disease, which was also evaluated by the same central review system as initial diagnosis. We stratified patients after the second induction course to one of three risk groups; low risk (LR) group for all the core binding factor-AML cases and good initial response after the first induction course, high risk (HR) group for cases presenting with *FLT3*-ITD, unfavourable cytogenetics including -7/del(7q), -5q/del(5q), t(16;21)(p11;q22), or with a poor initial response, and intermediate risk (IR) group for the others. Allogeneic haematopietic stem cell transplantation (HSCT) was indicated for all HR patients after the third or later treatment courses.

Descriptive statistical analyses to assess baseline characteristics and the clinical course of patients were performed using Chi-square tests for categorical variables and Wilcoxon rank-sum tests for continuous variables. Event-free survival (EFS), overall survival (OS) and relapse-free survival (RFS) were defined as previously described (Cheson *et al*, 2003). Probability of 3-year EFS (3-year pEFS), 3-year OS (3-year pOS) and 3-year RFS (3-year pRFS) were estimated using Kaplan–Meier method and log-rank test. Univariate and multivariate Cox hazard models were performed. A two-sided P value <0·05 was considered statistically significant. Follow-up data were actualized as of 1 May, 2012.

Results

Of the 485 patients registered, 42 patients were excluded because of misdiagnosis or refusal by the guardians. Of the 443 eligible patients, multilineage dysplasia was identified in 39 (8·8%) and myelodysplasia-related cytogenetic abnormalities were identified in 65 (14·7%). Five patients with multilineage dysplasia were assigned to the category 'AML with recurrent genetic abnormalities' in the 2008 WHO classification (Swerdlow *et al*, 2008); two with t(8;21)(q22;q22), two with inv(3)(q21q26.2) and one with t(6;9)(p23;q34). As a result, 93 (21%) patients were assigned to the 'AML-MRC' group, while 111 (25%) were assigned to the 'AML, not otherwise specified' (AML-NOS) group. Fifty-nine patients with 'AML-MRC' were diagnosed from myelodysplasia-related cytogenetics alone, 28 from multilineage dysplasia alone, and six from a combination of both. Among the 65 patients with myelodysplasia-related cytogenetics, 47 presented with complex karyotype, six with -7/del(7q), six with -5/del(5q) and complex karyotype, five with del(9q) and one with t(3;5)(q25;q34).

Clinical and cytogenetic characteristics

The clinical, cytogenetic and molecular characteristics of the 'AML-MRC' and 'AML-NOS' patients are shown in Table I. The patients were equally distributed by sex in both of the 'AML-MRC' and 'AML-NOS' group. Compared with the 'AML-NOS' group, the patients with 'AML-MRC' were significantly younger, presented with a significantly lower white blood cell (WBC) count, a higher frequency of refractory anaemia with excess of blasts (RAEB-T) based on FAB classification and unfavourable cytogenetic abnormalities. By gene analyses, the 'AML-MRC' group exhibited a lower frequency of *FLT3*-ITD, *NPM1* and/or *CEBPA* mutations. Most of the patients with *FLT3*-ITD and/or *NPM1* had a normal karyotype and morphological dysplasia.

Table I. Clinical, cytogenetic and molecular characteristics in the AML-MRC and AML-NOS patients.

Characteristics	AML-MRC (%)	AML-NOS (%)	*P*
Number of patients	93	111	
Median age (years)	5·8	8·0	<0·01
Male/Female	48/45	57/54	NS
Median WBC ($\times 10^9$/l)	38·1	75·3	<0·01
FAB subtype			
M0/M1	2/7	8/30	
M2/M4	15/9	18/13	
M5/M6	17/7	19/2	
M7	27 (29·0)	19 (17·1)	0·042
RAEB-T	9 (9·7)	2 (1·8)	0·010
Cytogenetics			
Normal	22 (23·7)	56 (50·5)	<0·01
Complex karyotype	51 (54·8)	0 (0·0)	<0·01
Unfavourable cytogenetics	16 (17·2)	2 (0·2)	<0·01
Others	10 (10·8)	41 (36·9)	
Genetic analysis			
FLT3-ITD	10 (10·8)	27 (24·5)	0·011
NPM1 mutation	3 of 68 (4·4)	10 of 69 (14·5)	0·044
CEBPA mutation	11 of 68 (16·2)	30 of 69 (43·5)	0·013

AML-MRC, acute myeloid leukaemia with myelodysplasia-related changes; AML-NOS, acute myeloid leukaemia, not otherwise specified; WBC, white blood cell count; FAB, French-American-British; RAEB-T, refractory anaemia with excess blasts in transformation; ITD, internal tandem duplication; NS, not significant.

P values were calculated between the 'AML-MRC' and 'AML-NOS' group.

AML-MRC with complex karyotype includes six patients with del (5q) and complex karyotype, and two with t(16;21)(p11;q22) and complex karyotype.

Unfavourable cytogenetics consist of -7/del(7q), -5/del(5q) and t (16;21)(p11;q22).

Response to induction therapy

Of the 93 AML-MRC patients, three died of treatment-related mortality (TRM) during induction treatment and 63 achieved a CR at the end of the two induction courses. The CR rate in patients with 'AML-MRC' at the end of the first and second induction course was 67·7% (95% confidence interval [CI], 48·5–77·1%) and 67·7% (95% CI, 48·5–77·1%), respectively. The 'AML-MRC' group showed a similar CR rate at the end of the first induction course compared with the 'AML-NOS' group (67·7% vs. 77·4%, $P = 0·12$), but the CR rate at the end of the second induction course was significantly lower (67·7% vs. 85·6%, $P < 0·01$).

Outcomes and prognostic factors

Twenty-one 'AML-MRC' patients who did not achieve a CR received allogeneic HSCT following salvage chemotherapy, and eight of them were alive. Among the 63 'AML-MRC' patients who achieved a CR, 49 were assigned to the IR group, whereas 12 with unfavourable cytogenetics and/or *FLT3*-ITD and two with poor response for the first induction chemotherapy course were assigned to the HR group and treated with allogeneic HSCT at the first CR. One 'AML-MRC' patient died of TRM during the consolidation chemotherapy and 2 'AML-MRC' patients died of TRM after HSCT. In contrast, of the 93 'AML-NOS' patients who achieved a CR, 75 were assigned to the IR group and 15 with *FLT3*-ITD and three with poor response for the first induction chemotherapy course were assigned to the HR group. Four 'AML-NOS' patients died of TRM during consolidation chemotherapies and one 'AML-NOS' patient died of TRM after HSCT. The 3-year pEFS and 3-year pOS for the 'AML-MRC' patients was 37·1% (95% CI, 26·9–47·3%) and 56·8% (95% CI, 45·2–66·8%), respectively. The median follow-up time of patients in the 'AML-MRC' group was 2·23 years (range, 0·02–5·3). Compared with the 'AML-NOS' patients,

patients with 'AML-MRC' had a significantly worse 3-year pEFS (37·1% vs. 53·8%, $P = 0·02$), but the 3-year pOS (56·8% vs. 68·9%, $P = 0·05$) and 3-year pRFS after achieving a CR were not significantly different (46·9% vs. 62·8%, $P = 0·06$; Fig 1A–C).

By comparison, within the subgroups according to the reason for diagnosis, 3-year pEFS, 3-year pOS and 3-year pRFS was similar between patients with myelodysplasia-related cytogenetics alone and those with morphological dysplasia alone. The six patients with a combination of both were all alive without any events.

By univariate and multivariate analysis for OS and EFS, older age >10 years, sex, higher WBC count >100 × 10^9/l, RAEB-T, unfavourable cytogenetics, multilineage dysplasia, myelodysplasia-related cytogenetics, and the combination of myelodysplasia-related cytogenetics and multilineage dysplasia.multilineage dysplasia were not associated with outcome in the 'AML-MRC' group, but *FLT3*-ITD was solely associated worse OS (Table II). We were not able to apply the univariate and multivariate analysis to *NPM1* mutations and bialleic *CEBPA* mutations due to the small number of cases.

Discussion

We showed here the incidence, clinical characteristics and prognostic relevance of myelodysplastic features in paediatric AML patients who were prospectively diagnosed by the central diagnosis system and treated with the same treatment strategy. To our knowledge, this is the first study to enrol an adequate number of paediatric patients with AML showing myelodysplastic features.

Compared with our previous study of paediatric AML with multilineage dysplasia, which reported a frequency of 2·6% (Adachi *et al*, 2007), the frequency of patients with

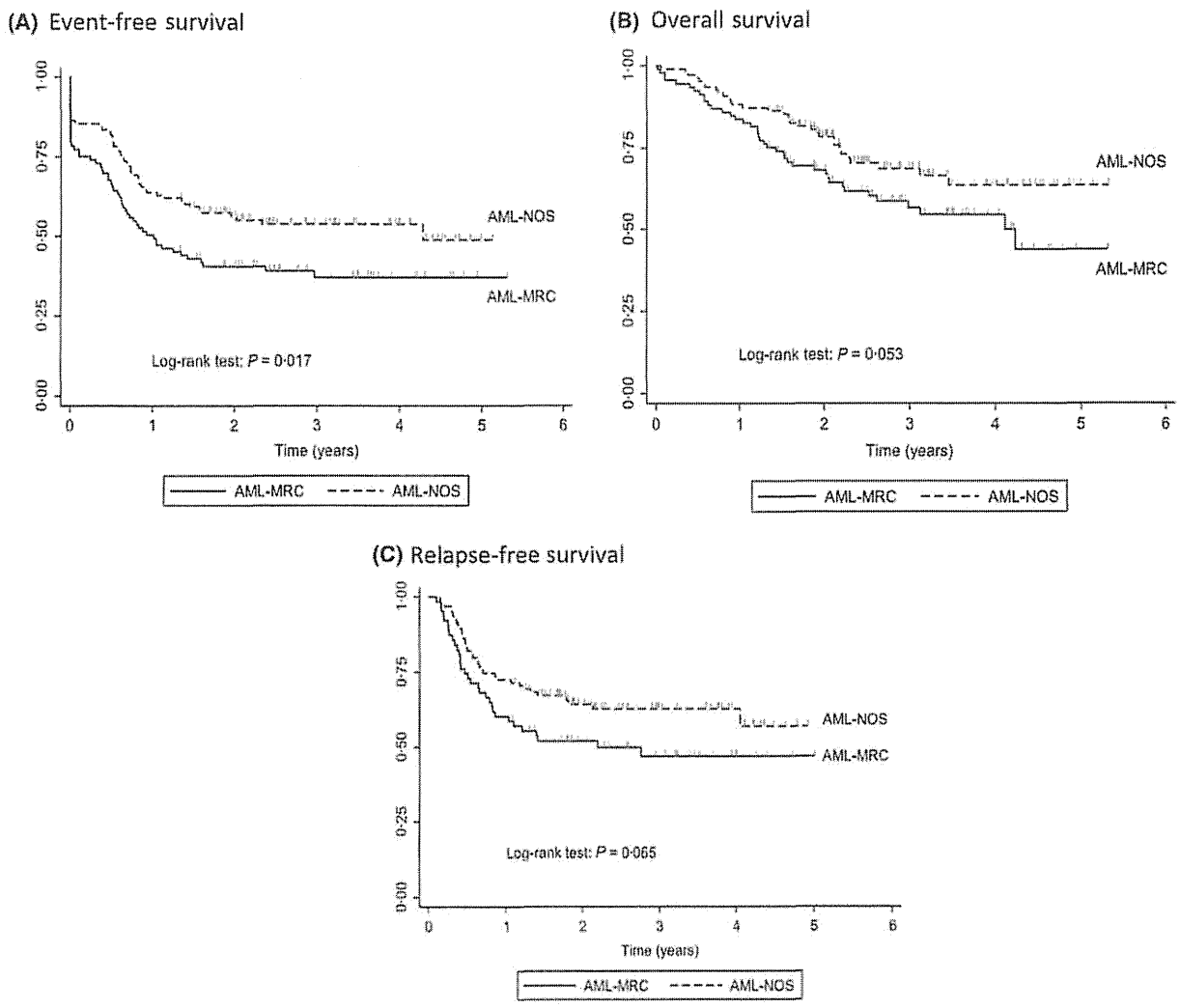

Fig 1. The 3-year probability of (A) event-free survival, (B) overall survival and (C) relapse-free survival for patients with acute myeloid leukaemia with myelodysplasia-related changes (AML-MRC) compared to patients with acute myeloid leukaemia, not otherwise specified (AML-NOS).

Table II. Univariate and multivariate analysis of risk factors in the AML-MRC patients.

Variables	Univariate analysis for EFS HR (95% CI)/*P*	Martivariate analysis for EFS HR (95% CI)/*P*	Univariate analysis for OS HR (95% CI)/*P*	Martivariate analysis for OS HR (95% CI)/*P*
Age > 10 years	0·70 (0·31–1·61)/0·40	0·70 (0·26–1·87)/0·48	0·73 (0·30–1·79)/0·49	0·54 (0·20–1·49)/0·24
Female	0·68 (0·40–1·16)/0·16	0·68 (0·36–1·10)/0·10	0·73 (0·39–1·36)/0·32	0·83 (0·43–1·62)/0·59
WBC > 10 × 10^9/l	1·43 (0·65–3·15)/0·38	1·78 (0·75–4·20)/0·19	1·22 (0·48–3·11)/0·68	1·32 (0·47–3·73)/0·60
FLT3-ITD	1·83 (0·86–3·88)/0·12	2·13 (0·89–5·15)/0·09	2·61 (1·14–6·00)/0·02	3·00 (1·15–7·84)/0·03
Unfavourable cytogenetics	1·23 (0·70–2·15)/0·47	1·32 (0·70–2·15)/0·39	1·42 (0·74–2·73)/0·29	1·38 (0·89–3·76)/0·10
MLD	0·61 (0·34–1·11)/0·11	0·17 (0·02–1·24)/0·08	0·63 (0·31–1·28)/0·20	ND
Dysplasia-related cytogenetics	1·22 (0·67–2·24)/0·52	0·23 (0·03–1·86)/0·17	1·15 (0·56–2·35)/0·71	ND
MLD and dysplasia-related cytogenetics	0·20 (0·03–1·43)/0·11	ND	0·04 (0·00–9·39)/0·25	ND

AML-MRC, acute myeloid leukaemia with myelodsyplasia-related changes; WBC, white blood cell count; *FLT*-ITD, *Fms-like tyrosine kinase 3* internal tandem duplication; MLD, multilineage dysplasia; HR, hazard ratio; *P*, *P* value; ND, not determined.

multilineage dysplasia was higher in this study (8·4%). The discrepancy may be explained by the differences between the regional and central diagnosis. Even more surprisingly, the frequency of patients encompassed by the 'AML-MRC' category was as high as 21·0%. In a retrospective study for paediatric AML at a single centre, Davis *et al* (2013) recently reported a concordant result where 'AML-MRC' encompassed 14% of the cases classified using the 2008 WHO classification (Swerdlow *et al*, 2008). Their and our results indicated that AML with myelodysplastic features is not rare in children. In our cohort, two-thirds of the cases with 'AML-MRC' resulted from myelodysplasia-related cytogenetics, whereas the remaining one-third resulted from morphological dysplasia. This is almost consistent with the report from Davis *et al* (2013), although our cohort contained a larger number of cases. In contrast, a majority of the adult patients with 'AML-MRC' presented with multilineage dysplasia with or without myelodysplasia-related cytogenetics (Miesner *et al*, 2010). Of note, the number of cases with a combination of myelodysplasia-related cytogenetics and morphological dysplasia was small in our cohort, suggesting that myelodysplasia-related cytogenetics is not necessarily related to morphological dysplasia in children.

As 'AML with recurrent genetic abnormalities' is accepted as a clinically and cytogenetically distinct category and it takes predominance over 'AML-MRC' in the WHO classification, we carried out further analyses, which excluded the cases with 'AML with recurrent cytogenetic abnormalities' except those cases with a *NPM1* and/or *CEBPA* mutation.

Previous studies among adult patients showed that AML with myelodysplastic features was associated with lower WBC counts, lower bone marrow blast counts and MDS-related cytogenetics (Brito-Babapulle *et al*, 1987; Weinberg *et al*, 2009; Miesner *et al*, 2010). Our patients with 'AML-MRC' also presented with lower WBC counts, had a higher frequency of RAEB-T and unfavourable cytogenetic abnormalities compared with 'AML-NOS'. The median age of our patients with 'AML-MRC' was significantly younger compared with 'AML-NOS'. This may be partly because our cohort excluded patients with 'AML with a previous history of myelodysplastic syndrome or myeloproliferative neoplasms'. Moreover, our cohort included a substantial number of patients with acute megakaryoblastic leukaemia, which is known to be prevalent in infants and associated with complex chromosomal abnormalities (Hama *et al*, 2008).

Acute myeloid leukaemia with myelodysplastic features has been reported to confer a poorer prognosis with a lower rate of achieving CR than other AML types (Goasguen *et al*, 1992; Kuriyama *et al*, 1994; Gahn *et al*, 1996; Miyazaki *et al*, 2003). However, several studies have demonstrated that multilineage dysplasia alone has no independent prognostic relevance, high-risk cytogenetic abnormalities being more significantly associated with prognosis (Haferiach *et al*, 2003; Yanada *et al*, 2005). As in most previous adult studies, the CR rate was worse in our patients with 'AML-MRC'. Moreover, EFS in the 'AML-MRC' group was significantly worse compared with 'AML-NOS'. OS and RFS showed a trend of a poorer outcome, but without statistical significance. A non-significant difference in RFS was thought to indicate that the difference in EFS was not due to relapse, but mainly to failure to achieve CR. On the other hand, a non-significant difference in OS was probably due to the intensive chemotherapies including high-dose cytarabine and HSCT for patients with induction failures and/or high-risk features, which might temper the negative effect of 'AML-MRC' on survival, as previously reported (Taguchi *et al*, 2000). In multivariate analysis, morphological dysplasia or myelodysplasia-related cytogenetics failed to show independent prognostic relevance, but *FLT3*-ITD status solely retained prognostic impact, which agreed with the previous publication in adult patients (Miesner *et al*, 2010). Although it must be taken into account that the observation period is relatively short, our results suggest that myelodysplastic features may not confer significant prognostic impact on 'AML-MRC' patients when achieving a CR after induction chemotherapy, which should be considered in the setting of clinical trials.

Acute myeloid leukaemia patients with myelodysplastic features may exhibit *FLT3*-ITD, *NPM1* and/or *CEBPA* mutations. Wandt *et al* (2008) reported that multilineage dysplasia was prevalent in the *FLT3*-ITD negative patients. We also recognized a lower incidence of *FLT3*-ITD in the 'AML-MRC' group compared with 'AML-NOS'. Of note, *FLT3*-ITD was found almost exclusively in the patients with morphological dysplasia alone. This is probably because most *FLT3*-ITD cases would be expected to have a normal karyotype, even in children (Zwaan *et al*, 2003).

Recent studies showed that multilineage dysplasia has no prognostic impact in patients with *NPM1* and/or *CEBPA* mutations (Falini *et al*, 2010; Bacher *et al*, 2012). We were not able to determine whether the *NPM1* and/or *CEBPA* mutations were associated with a good prognosis even in children with AML showing myelodysplastic features because of a low incidence of *NPM1* and/or *CEBPA* mutations in our cohort. AML with myelodysplastic features is a heterogeneous category in the view of molecular alterations (Devillier *et al*, 2012). More information is required regarding these issues.

Comparison within the subgroups in 'AML-MRC' depending on the reasons for diagnosis, the outcomes were similar between the patients with myelodysplasia-related cytogenetics alone and those with morphological dysplasia alone. This suggests that the patients with 'AML-MRC' comprise a group with similar prognostic impact, despite heterogeneity. Although the patients with a combination of myelodysplasia-related cytogenetics and multilineage dysplasia showed an excellent outcome, this may be selection bias because the univariate and murtivariate analysis could not show any prognostic significance of this subtype.

In conclusion, our prospective studies demonstrated that AML with myelodysplastic features are not rare in children. The 'AML-MRC' category was associated with a younger age, lower WBC count, RAEB-T and unfavourable cytogenetics, and exhibited a lower frequency of *FLT3*-ITD, *NPM1* and *CEBPA* mutations. The CR rates and EFS were worse in this category, but OS and RFS were not significantly different compared with 'AML-NOS'. These results support the distinctive features of 'AML-MRC' even in children, but further exploration is necessary because of the heterogeneous nature of this category.

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Authorship

A.K., H.Mi., D.T. and S.A. designed the study and wrote the manuscript. H.Mi., Hir.M. and M.Y. investigated the smears. To.Ta. and Y.H. performed cytogenetically diagnosis. T.W. and A.S. performed statistical analysis. Hid.M., M.K., and K.O. analysed gene mutations. H.T. and Ta.Ta. contributed to the central diagnosis. A.T., and K.H. lead participants in the AML-05 study.

Disclosure of conflicts of interest

The authors have no conflicts of interest to declare.

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EVI1 overexpression is a poor prognostic factor in pediatric patients with *mixed lineage leukemia-AF9* rearranged acute myeloid leukemia

The ecotropic viral integration site-1 gene (*EVI1*) encodes a zinc finger protein that functions as a transcriptional regulator of hematopoietic stem cell self-renewal and long-term multilineage repopulating activity.[1,2] The mixed lineage leukemia gene (*MLL*) rearrangements [i.e. t(11q23)] occur at high frequency in pediatric acute myeloid leukemia (AML) patients with *EVI1* overexpression,[3] and *EVI1* is a transcriptional target of MLL oncoproteins.[4] *EVI1* overexpression has been reported in up to 10% of patients with AML and is associated with an adverse prognosis. However, the prognostic value of *EVI1* overexpression has been studied mostly in adult AML.[5-9] Only two studies have examined *EVI1* overexpression in pediatric AML, but a detailed analysis according to the type of leukemia was not performed because of the small sample size.[3,10]

Recent data from an international consortium, including those from our group, suggest that pediatric *MLL*-rearranged AML can be divided into certain risk groups on the basis of different translocation partners.[11] However, clinical outcome data leading to risk stratification of the *MLL*-rearranged subgroups are still scarce and further investigation is necessary to identify new prognostic factors. Here, we retrospectively examined *EVI1* expression levels and clinical outcomes of pediatric *MLL*-rearranged AML patients treated in the Japanese Pediatric Leukemia/Lymphoma Study Group (JPLSG) AML-05 study.

After excluding patients with acute promyelocytic leukemia, Down syndrome, secondary AML, myeloid/natural killer cell leukemia and myeloid sarcoma, 485 AML patients were enrolled in the AML-05 study. Overall, 42 patients were excluded, mainly because of misdiagnosis. Details of the treatment schedules and risk stratification were described in previous publication.[12] This study was conducted in accordance with the principles set down in the Declaration of Helsinki and was approved by the Ethics Committees of all participating institutions. All patients, or the patients' parents/guardians, provided written informed consent.

RNA obtained from diagnostic bone marrow samples was used to analyze the expression of *EVI1* using a previously established *EVI1* quantitative real-time polymerase chain reaction assay that covers the various *EVI1* splice variants.[7] Event-free survival (EFS) was defined as the time from the diagnosis of AML to the last follow up or the first event (failure to achieve remission, relapse, secondary malignancy, or any cause of death). In this study, most of the events were relapses (n=23) and the rest were deaths with sepsis (n=1) and acute respiratory distress syndrome (n=1). Overall survival (OS) was defined as the time from the diagnosis of AML to any cause of death. All tests were two-tailed and $P<0.05$ was considered statistically significant.

Among 443 eligible AML patients, 69 were diagnosed as *MLL*-rearranged AML and diagnostic samples from 50 patients were analyzed for *EVI1* mRNA expression. No significant differences in the characteristics and clinical outcomes were observed between these 50 patients and the 19 patients who did not have *EVI1* data [EFS ($P=0.20$), OS ($P=0.45$)]. *EVI1* expression levels were dichotomized based on a cut off of 0.1 relative to SKOV3, an ovarian carcinoma cell line over-expressing *EVI1*: values higher than 0.1 were defined as *EVI1*$^+$ and those lower than 0.1 or undetectable

Table 1. Characteristics of patients categorized according to *EVI1* expression status.

	All (n=50)				
	EVI1$^-$ (n=32)		*EVI1*$^+$ (n=18)		*P*
Age (years)					0.03#
median	4.5		6.6		
range	0.1-14.7		0.8-15.1		
Sex, n(%)					0.77*
male	16	(50)	8	(44)	
female	16	(50)	10	(56)	
WBC(x10^9/L)					0.01#
median	48.4		88.7		
range	0.8-459		4.1-322		
Types of *MLL* rearrangement, n(%)					0.96*
MLL-AF6	2	(6)	1	(6)	
MLL-AF9	18	(56)	11	(61)	
MLL-AF10	5	(16)	2	(11)	
MLL-ELL	3	(9)	3	(17)	
MLL-ENL	3	(9)	1	(6)	
MLL-AF17	1	(3)	0	(0)	
FAB, n(%)					<0.0001*
M1	1	(3)	3	(17)	
M2	0	(0)	1	(6)	
M4	2	(6)	6	(33)	
M5	27	(84)	4	(22)	
RAEB-T	0	(0)	3	(17)	
Unclassified	2	(6)	1	(6)	
FLT3-ITD, n(%)	0	(0)	3	(17)	0.04*

*WBC: white blood cell count; FAB: French-American-British. *Fisher's exact test. #Mann-Whitney U test.*