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New Recurrent Balanced Translocations in Acute Myeloid Leukemia and Myelodysplastic Syndromes: Cancer and Leukemia Group B (CALGB) 8461

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Abstract

Acquired chromosome abnormalities in patients with acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) are among the most valuable determinants of diagnosis and prognosis. In search of new recurrent balanced translocations we reviewed the Cancer and Leukemia Group B (CALGB) cytogenetics database containing pretreatment and relapse karyotypes of 4,701 adults with AML and 565 with MDS who were treated on CALGB trials. We identified all cases with balanced structural rearrangements occurring as a sole abnormality or in addition to one other abnormality, excluded abnormalities known to be recurrent, and then reviewed the literature to determine whether any of what we considered unique, previously unknown abnormalities had been reported. As a result, we identified seven new recurrent balanced translocations in AML or MDS: t(7;11)(q22;p15.5), t(10;11)(q23;p15), t(2;12)(p13;p13), t(12;17)(p13;q12), t(2;3)(p21;p21), t(5;21)(q31;q22) and t(8;14)(q24.1;q32.2), and, additionally, t(10;12)(p11;q15), a new translocation in AML previously reported in a case of acute lymphoblastic leukemia. Herein we report hematologic and clinical characteristics, and treatment outcomes of patients with these newly recognized recurrent translocations. We also report 52 unique balanced translocations, together with the clinical data of patients harboring them, that to our knowledge have not been previously published. We hope that once the awareness of their existence is increased, some of these translocations may become recognized as novel recurring abnormalities. Identification of additional cases with both the new recurrent and the unique balanced translocations will enable determination of their prognostic significance and help to provide insights into the mechanisms of disease pathogenesis in patients with these rare abnormalities.

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Introduction

Pretreatment cytogenetic findings are among the most important diagnostic and prognostic factors in acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) (Mrózek et al., 2001, 2004; Haase et al., 2007; Johansson and Harrison, 2009; Olney and Le Beau, 2009; Vardiman et al., 2009; Grimwade and Mrózek, 2011). Non-random chromosome abnormalities are independent predictors of the probability of achievement of complete remission (CR), disease-free survival (DFS), and overall survival (OS) (Grimwade et al., 1998, 2010; Byrd et al., 2002; Mrózek et al., 2004), and are used to select treatment (Döhner et al., 2010). Recurrent balanced structural rearrangements detected in AML and MDS, particularly if they occur as a sole abnormality in at least some cases and are rarely or never present in other types of hematologic and non-hematologic malignancies, are considered to be the most important, primary chromosome abnormalities, which are assumed to play an essential role in leukemogenesis.

It is well established that AML and MDS are very heterogeneous cytogenetically with over 300 structural and numerical chromosome abnormalities recognized as recurrent to date (Mrózek et al., 2001; Mitelman et al., 2007, 2012). The incidence of specific aberrations varies considerably, with some being relatively frequent, such as t(15;17)(q22;q21), t(8;21)(q22;q22), inv(16)(p13.1q22), or t(9;11)(p22;q23), while others are very rare, reported in only a few patients worldwide (Mitelman et al., 2012). This makes correlations of such rare aberrations with a patient's pretreatment characteristics and clinical outcome difficult, and therefore publication of data on each patient carrying one of these abnormalities is a valuable resource. Furthermore, a substantial proportion of patients harbor aberrations that are not yet recognized as recurrent. Johansson and Harrison (2009) estimate that non-recurring aberrations constitute 85% of balanced chromosome translocations detected in AML patients. However, it is possible that at least some of such unique abnormalities may become recognized as recurrent once the awareness of their existence is increased. This is important because the ascertainment of breakpoints in many leukemia-associated balanced translocations and inversions has led to the detection of genes whose disruption and/or deregulation contributes to leukemogenesis (Mitelman et al., 2007).

In this study we report cytogenetic and clinical data for seven new recurrent balanced translocations in AML or MDS, and another translocation that occurred in single cases of AML and acute lymphoblastic leukemia (ALL). We also describe 51 patients with 52 “unique” balanced chromosome aberrations that to the best of our knowledge have not been previously reported.

Patients and Methods

To identify new balanced aberrations we reviewed the cytogenetics database created as a result of the ongoing prospective cytogenetics companion trial 8461 conducted by Cancer and Leukemia Group B (CALGB, now part of the Alliance for Clinical Trials in Oncology cooperative group) since 1984 (Byrd et al., 2002). The database contained pretreatment and relapse karyotypes of 4,701 adults diagnosed with AML and 565 diagnosed with MDS enrolled on CALGB 8461. The patients had a primary diagnosis of AML or MDS. We used ≥20% as the requisite blast percentage for diagnosis of AML as defined by the World Health Organization (WHO) criteria (Vardiman et al., 2009). Since many patients were diagnosed before the publication of the WHO classification, we provide information on their diagnoses according to the French-American-British (FAB) Cooperative Group classification (Bennett et al., 1985). All patients were enrolled on CALGB treatment studies and provided written Institutional Review Board-approved, protocol-specific informed consent for participation in these studies in accordance with federal and institutional guidelines.

Cytogenetic analyses of marrow and/or blood were performed in CALGB institutional cytogenetic laboratories between 1985 and 2009. The G- or, rarely, Q-banded karyotypes were interpreted according to the International System for Human Cytogenetic Nomenclature ISCN 2009 (Shaffer et al., 2009) and the results were centrally reviewed (Mrózek et al., 2008). During initial screening, balanced structural rearrangements occurring as a sole abnormality or in addition to one other abnormality in at least one clone were identified. Cases with known recurrent balanced translocations (Mrózek et al., 2001; Mitelman et al., 2012; http://AtlasGeneticsOncology.org) were eliminated leaving a list of rare and apparently unique balanced aberrations. We then compared this list to all cases within the database (including those with a complex karyotype) to identify additional patients with these rearrangements.

Overall, 80 patients with apparently unique abnormalities were identified. Next, we performed a search for published cases with abnormalities identical or similar to the ones we identified using the Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer (Mitelman et al., 2012) and the Atlas of Genetics and Cytogenetics in Oncology and Haematology (http://AtlasGeneticsOncology.org). Once identified, the literature cases were reviewed with attention to clinical presentation, patient and disease characteristics, and treatment outcome. If the abnormality was reported as recurrent by the authors within the published report, it was not included in this study. Once an abnormality identical or virtually identical to the one identified by us was found, the translocation was classified as a new recurrent one.

For CALGB patients we report on, the following definitions of clinical endpoints are used. CR required an absolute neutrophil count $\geq 1.5 \times 10^9$/l, platelet count $>100 \times 10^9$/l, no leukemic blasts in the blood, bone marrow cellularity greater than 20% with maturation of all cell lines, no Auer rods, less than 5% bone marrow blast cells, and no evidence of extramedullary leukemia, all of which had to persist for at least four weeks (Cheson et al., 1990). Relapse was defined by ≥5% bone marrow blasts, circulating leukemic blasts, or the development of extramedullary leukemia. DFS was measured from the date of CR until the date of relapse or death; patients alive and relapse-free at last follow-up were censored. OS was measured from the date of study entry until the date of death (from any cause), and patients alive at last follow-up were censored.

Results and Discussion

New Recurrent Balanced Translocations

We identified seven new recurrent balanced translocations in AML or MDS, and one we found in AML that was present in a single case of ALL in the literature. Cytogenetic data, pretreatment characteristics, treatment received, and clinical outcome of each patient with one of these translocations are summarized below and presented in Table 1.

Translocations involving band 11p15—Band 11p15 is rearranged in several recurrent, albeit rare, translocations and inversions detected predominantly in myeloid neoplasia, i.e., AML, MDS, and chronic myelogenous leukemia (CML). Approximately one-third of these chromosome rearrangements involve the *NUP98* gene, mapped to 11p15.5, which is fused with a number of partner genes located at the breakpoints in chromosomes participating in these balanced aberrations (Nebral et al., 2005; Romana et al., 2006; Gough et al., 2011; Mitelman et al., 2012). We report two new recurrent translocations involving band 11p15.

t(7;11)(q22;p15.5) [n=4]: The first new recurrent translocation, t(7;11)(q22;p15.5), was detected in an 87-year-old male diagnosed with refractory anemia with ring sideroblasts (RARS) where the t(7;11) was the sole chromosome aberration (case 1 in Table 1). The patient had no history of chemotherapy or radiation exposure and had received epoetin alfa for one year prior to enrolling on CALGB 10105 (Gupta et al., 2006). He was treated with the oral VEGF receptor tyrosine kinase inhibitor vatalanib for two months. He then declined further therapy in favor of transfusion support only. At the time of last follow-up, his OS was 52.8 months.

Our review of the literature identified three cases with t(7;11)(q22;p15), all occurring in AML patients. A 47-year-old male was diagnosed with FAB AML-M6, where t(7;11)(q22;p15) was part of a complex karyotype. Notably, at diagnosis he had severe anemia with a hemoglobin level of 17 g/l. He received cytarabine and daunorubicin chemotherapy and required a second induction because of persistent disease, but did achieve a CR. He refused additional chemotherapy and had a DFS of 14 months at last follow-up (Kirsch et al., 1985). The second case, reported in a study screening for the presence of *NUP98* rearrangements by fluorescence in situ hybridization (FISH), was a 65-year-old male with AML who had t(7;11)(q22;p15) as the sole abnormality. Additional clinical details were not reported (Nebral et al., 2005). In the third case, t(7;11)(q22;p15) was the sole cytogenetic abnormality in a 5-year-old female diagnosed with AML-M7. She did not achieve a CR following cytarabine and daunorubicin-based chemotherapy and died of progressive disease (Ribeiro et al., 1993). Including our case, three of the four patients with t(7;11)(q22;p15) had this translocation as a sole chromosome abnormality at diagnosis.

t(10;11)(q23;p15) [n=4]: The second new recurrent translocation involving 11p15, t(10;11)(q23;p15), was detected in a 52-year-old female diagnosed with AML-M4 who presented with a white blood cell count (WBC) of 76.5 $\times 10^9$/l, splenomegaly, and salmonella enteritis septicemia (case 2 in Table 1). She achieved a CR following a single course of induction chemotherapy with cytarabine and daunorubicin, and received two cycles of high-dose cytarabine consolidation followed by two cycles of cytarabine and daunorubicin maintenance on CALGB 8525 (Mayer et al., 1994). Approximately seven months after her initial diagnosis, at the end of the second cycle of maintenance, she developed central nervous system relapse with a cerebellar mass and leukemic blasts in the cerebral spinal fluid. A bone marrow aspirate and biopsy confirmed marrow relapse. She was treated with intrathecal chemotherapy and cranial radiation; however, she died approximately three weeks later due to progressive disease. Her DFS was 8.1 months; her OS was 9.2 months.

There are three reported cases in the literature with t(10;11)(q23;p15), all of whom were diagnosed with AML. The first patient, a 59-year-old male, was diagnosed with AML-M2 and achieved a CR after receiving what was reported as “standard chemotherapy” (Jankovic et al., 2008). Five years later, he relapsed; cytogenetic analysis was not performed at this time, nor was it performed at diagnosis. The patient received two cycles of chemotherapy with mitoxantrone, cytarabine, and etoposide and achieved a second CR that lasted 8 years. He then presented, at age 73, with pancytopenia and relapse. Cytogenetic and FISH analyses revealed a karyotype of 45,X,–Y,t(10;11)(q23;p15) with a *NUP98/HHEX* fusion gene. The patient received fludarabine, cytarabine, and filgrastim chemotherapy followed by intermediate-dose cytarabine and daunorubicin and autologous stem cell transplantation (SCT). He remained in CR at last follow-up eight years later (personal communication, Christina Mecucci, February 2012). As cytogenetic findings at diagnosis and at the time of first relapse are not available, it is unknown whether the t(10;11) was an original, persistent abnormality, or was acquired during the course of the disease.

The second patient was a 39-year-old male with a history of Hodgkin lymphoma who developed therapy-related AML (t-AML) 16 years after completing chemotherapy and radiation for his primary malignancy. He had a complex karyotype containing t(10;11)(q23;p15) in all abnormal clones. The patient achieved a CR after one cycle of high-dose cytarabine and received one cycle of consolidation; he relapsed four months later. His DFS and OS were five and six months, respectively (Larson et al., 1988). The last case was a 4-year-old female diagnosed with t-AML-M2 and had a karyotype of 46,XX,t(10;11)(q22-24;p15)/46,idem,add(6)(p25), 14 months after her diagnosis of ALL (Pui et al., 1995). She received induction chemotherapy with cytarabine, daunorubicin, and etoposide followed by allogeneic sibling SCT. She relapsed 45 days after SCT and died of progressive disease, with an OS of 5.5 months (personal communication, Susana Raimondi, February 2012).

Our patient did not have a history of chemotherapy or radiation exposure and presented with de novo AML, while two of the three cases with t(10;11)(q23;p15) from the literature had t-AML (Larson et al., 1988; Pui et al., 1995). Without additional clinical information it is not possible to determine whether the third reported patient (Jankovic et al., 2008) may have had t-AML, although the five and eight years elapsed between his first and second relapse, respectively, might suggest this possibility.

Translocations involving band 12p13—Band 12p13 is a chromosomal locus that is involved in the most common, cryptic translocation in pediatric B lineage ALL, t(12;21)(p13;q22), but also is involved in several rare, but recurrent balanced translocations in AML and MDS (Mitelman et al., 2012). We have identified two new recurrent translocations involving band 12p13 in patients with AML. Given its occurrence in myeloid and lymphoid malignancies, this locus may be involved in both ALL and AML pathogenesis.

t(2;12)(p13;p13) [n=3]: We report two male patients with AML who acquired the t(2;12)(p13;p13) at the time of relapse. The first patient (case 3 in Table 1) was a 76-year-old male with a history of prostate cancer and radiation therapy who presented with left flank pain and hematuria, and was found to have a WBC of 18.3 × 10^9/l with circulating myeloid blasts. He was diagnosed with AML-M4, had a pretreatment karyotype of 45,XY,der(7)t(7;17)(p11.2;q11.2),–17, and received induction chemotherapy with cytarabine, daunorubicin, and etoposide on CALGB 9720 (Baer et al., 2011). He achieved a complete morphologic and cytogenetic remission, and received one cycle of consolidation with cytarabine, daunorubicin, and etoposide followed by observation. Approximately two months after his last cycle of chemotherapy, he developed progressive leukocytosis; bone marrow aspirate and biopsy confirmed relapse. His karyotype at this time was 46,XY,t(3;20)(q21;q13.3)/46,XY,t(2;12)(p13;p13). The patient received salvage chemotherapy with etoposide, cytarabine, and mitoxantrone. He developed sepsis and multi-organ system failure during this treatment and died of progressive disease. His OS was 6.3 months.

Our second patient (case 4 in Table 1) was a 41-year-old man diagnosed with AML-M2 with t(5;13)(q15;q14) and a marker chromosome, after presenting with night sweats, bilateral lower extremity edema, weight loss, and a WBC of 68.0 × 10^9/l. He received induction chemotherapy with cytarabine, daunorubicin, and etoposide on CALGB 9621 (Kolitz et al., 2004), and a day 14 bone marrow biopsy was negative for morphologic evidence of disease. However, he continued to have cytogenetic evidence of disease and on day 54 of induction, a repeat bone marrow biopsy revealed morphologic relapse. At this time, a second clone that contained the t(2;12)(p13;p13) in addition to t(5;13)(q15;q14) and a marker chromosome was acquired. The patient received additional therapy with lintuzumab in combination with mitoxantrone and cytarabine without a response. His OS was 4.3 months. To our knowledge, the t(5;13)(q15;q14), detected both at diagnosis and relapse, has not been previously reported in AML and is included among the unique balanced translocations listed in Table 2 (case no. 27).

In the literature, we identified a patient with t(2;12)(p13;p13), which was also detected at relapse. A 50-year-old male presented with fatigue, lymphadenopathy, anemia, and leukocytosis. His diagnosis was reported by the authors as an overlap between AML, MDS, and a myeloproliferative disorder, with a normal karyotype (Hagiwara et al., 1998). He was treated with cytarabine, daunorubicin, 6-mercaptopurine and prednisone, and after achieving a CR, received four courses of unspecified postremission chemotherapy. Approximately one year later, he developed bilateral inguinal adenopathy, and had 80% blasts in the bone marrow. At this time, his karyotype was 46,Y,t(X;13)(q28;q14),t(2;12)(p13;p13). No additional clinical information was provided about the patient.

In both patients we reported and the one described by Hagiwara et al. (1998), t(2;12)(p13;p13) was acquired at the time of relapse suggesting that it may play a role in disease progression rather than being a leukemia initiating event. Notably, neither of our patients responded to cytarabine and mitoxantrone based chemotherapy and both died shortly after relapse.

t(12;17)(p13;q12) [n=2]: We report a 21-year-old female with a history of juvenile rheumatoid arthritis (JRA) who presented with fever, splenomegaly, and a WBC of 32 × 10^9/l with circulating myeloid blasts (case 5 in Table 1). She had been receiving treatment with hydroxychloroquine for her diagnosis of JRA prior to presentation. She was diagnosed with AML-M2, and a t(12;17)(p13;q12) was detected in both abnormal clones, one of which had t(12;17) as a sole chromosome abnormality, whereas the other contained +13 in addition to t(12;17). The patient underwent two inductions with cytarabine and daunorubicin on CALGB 9222 (Moore et al., 2005), but had residual disease after the second induction and went on to receive salvage chemotherapy. It is unknown what her further treatment was; however, her OS was 37.4 months and she is reported to have died from biphenotypic leukemia.

We identified a single patient with an identical t(12;17)(p13;q12), occurring as a sole chromosome aberration, in the literature. This was a 20-year-old male who presented with t-AML 11 years after treatment for ALL with a WBC of 38.7 × 10^9/l. He received combination chemotherapy of unknown type but did not achieve a CR. His OS was <2 months (UKCCG 2002).

A translocation very similar to that found in our case 5, which results in the *TAF15-ZNF384* fusion gene but was variously described as t(12;17)(p13;q11) (Martini et al., 2002) or t(12;17)(p13;q12) (Nyquist et al., 2011), has been reported as a recurrent abnormality in ALL. However, one of the five patients included in a study that cloned the *TAF15-ZNF384* fusion gene created as a result of t(12;17) was diagnosed with AML (Martini et al., 2002). Clinical data of this patient were reported by La Starza et al. (2005). He was a 29-year-old male who presented with a WBC of 65.6 × 10^9/l, and was diagnosed with AML-M1; his karyotype was 46,XY,t(12;17)(p12;q11)/46,idem,i(8)(q10),inc. He received "standard chemotherapy" and subsequently relapsed and died eight months after diagnosis. Another patient with AML harboring t(12;17)(p13;q11) was a 23-year-old female diagnosed with AML-M2, but no information was provided regarding her clinical course (Weinkauff et al., 1999). While it is at present uncertain whether t(12;17)(p13;q12) and t(12;17)(p13;q11) are in fact the same translocation, interestingly, all four patients with AML and t(12;17) were young adults in their twenties, and the outcome of the three patients with data available was poor.

Other translocations

t(2;3)(p21;p21) [n=2]: Reciprocal translocations between 2p and 3p are very rare in AML; to date, only two patients with t(2;3) were reported, but breakpoints in these translocations were different (Wang et al., 2010). We identified a 21-year-old male who presented for evaluation of a persistent tooth infection, as well as leg and groin cellulitis, and was diagnosed with AML-M2 with a karyotype of 47,XY,+9/47,idem,t(2;3)(p21;p21) (case 6 in Table 1). He achieved a CR following cytarabine and daunorubicin induction chemotherapy and completed consolidation with high-dose cytarabine followed by mitoxantrone and diaziquone on CALGB 9222 (Moore et al., 2005). At last follow-up, he was disease-free, with DFS and OS of 151.8 months and 153 months, respectively.

The second AML patient, reported by Wang et al., (2010), was also male; the t(2;3)(p21;p21) was detected at the time of relapse together with del(3)(q21q26) and t(7;11)(p21;p14). His pretreatment karyotype was normal and he was found to harbor an internal tandem duplication of *FLT3* (*FLT3*-ITD) and an *NPM1* mutation. At the time of relapse he was still *FLT3*-ITD-positive, whereas *NPM1* mutational status was not evaluated. No additional clinical information was provided.

t(5;21)(q31;q22) [n=4]: We identified a 51-year-old female with Turner syndrome who presented with mild pancytopenia and was diagnosed with AML-M4 with t(5;21)(q31;q22) detected as a sole acquired abnormality (case 7 in Table 1). At diagnosis, the marrow was described as having abundant dyspoiesis within the myeloid cells. The patient required two cycles of induction chemotherapy with cytarabine, daunorubicin, and etoposide on CALGB 19808 (Kolitz et al., 2010), and achieved a CR on day 75 of induction. Following this, she received high-dose cytarabine and etoposide for stem cell mobilization followed by myeloablative treatment with busulfan and etoposide and autologous SCT; however, she relapsed 6.6 months later and eventually died of progressive disease. Her OS was 11 months.

In the literature, t(5;21)(q31;q22) was reported in a patient with AML as part of a complex pretreatment karyotype that in addition to t(5;21)(q31;q22) included −7. The patient was a 37-year-old male diagnosed with AML-M2, which was refractory to chemotherapy. The regimen used for induction was not reported and he died three months following his diagnosis (Streubel et al., 1998).

t(8;14)(q24;q32) [n=5]: Our first patient (case 8 in Table 1) was a 35-year-old male diagnosed with AML-M4, who presented with a WBC of 123.2 $\times 10^9$/l, 80% myeloid blasts in blood, and t(8;14)(q24.1;q32.2) as a sole chromosome abnormality. He underwent induction chemotherapy with cytarabine, daunorubicin and etoposide with the multidrug resistance protein inhibitor valspodar on CALGB 19808 (Kolitz et al., 2010) and achieved a CR. His consolidation consisted of an autologous SCT with busulfan and etoposide conditioning after high-dose cytarabine and etoposide for stem cell mobilization. His DFS was 9.8 months and at the time of relapse a clone with t(8;14) as a sole abnormality was present. He underwent allogeneic SCT, but died of a cardiopulmonary arrest approximately two months after the procedure. His OS was 17.3 months.

In the second patient (case 9 in Table 1), t(8;14)(q24.1;q32) was found at the time of relapse. This occurred in a 57-year-old female who presented with AML-M2 and a normal karyotype. She required two cycles of induction with cytarabine, daunorubicin, and etoposide chemotherapy on CALGB 10503 (Blum et al., 2010) to achieve a CR, however, declined further treatment on protocol and received consolidation with high-dose cytarabine only. Her DFS was 9.1 months, and at the time of relapse her karyotype contained two reciprocal translocations, t(8;12)(q22;p11.2) and t(8;14)(q24.1;q32). She received salvage chemotherapy, including high-dose cytarabine; however, she died of progressive disease. Her OS was 15.4 months. In both of these cases, the morphology and flow cytometry were consistent with AML, not Burkitt lymphoma.

To our knowledge, three patients with AML and t(8;14)(q24;q32) have been previously reported. A 65-year-old male diagnosed with AML-M2 harbored t(8;14) as part of a complex karyotype (Solé et al., 1992); no additional information was provided. A second patient, diagnosed with AML-M0, also presented with t(8;14)(q24;q32) in the context of a complex karyotype; he did not achieve a CR and died on day 15 with an aplastic bone marrow (Lee et al., 1987). A third patient, a 59-year-old female also diagnosed with AML-M0, had t(8;14)(q24.1;q32) and del(7)(q32q34) as the only chromosome abnormalities. The presence of del(7q) as a secondary abnormality known to be recurrent in AML, and the results of flow cytometry analysis, supported a myeloid origin of the leukemic cells (Hoppman-Chaney et al., 2010). FISH demonstrated that while t(8;14) in this patient had led to creation of a *MYC*/*IGH* fusion, this fusion was atypical without the *IGH* gene disruption well-known to the *MYC*/*IGH* fusion characteristic of Burkitt lymphoma with t(8;14)(q24.1;q32) (Boerma et al., 2009). This finding, coupled with a lack of increase in *MYC* expression demonstrated by real-time polymerase chain reaction analysis (Hoppman-Chaney et al., 2010), suggests the rare t(8;14) occurring in AML may differ molecularly from t(8;14) associated with Burkitt lymphoma.

t(10;12)(p11;q15), a translocation previously described in ALL [n=2]: In several instances, the same primary cytogenetic abnormality has been found to occur both in patients diagnosed with AML and those diagnosed with ALL. Examples include t(10;11)(p13;q21), resulting in an *MLLT10*/*PICALM* gene fusion, t(9;22)(q34;q11.2)/*BCR*/*ABL1* or certain translocations involving the *MLL* gene, such as t(1;11)(p32;q23) or t(11;19)(q23;p13.3) (Mitelman et al., 2012; http://AtlasGeneticsOncology.org). Therefore, below we report a translocation detected in an AML patient that has thus far only been reported in a patient with ALL.

We identified a 24-year-old male who presented with fevers, night sweats and weight loss, and was diagnosed with AML-M1 with extramedullary involvement of the pleura and pleural effusions (case 10 in Table 1). He had a t(10;12)(p11;q15) accompanied by +4 in all abnormal cells. He required two cycles of induction with cytarabine and daunorubicin chemotherapy on CALGB 8525 (Mayer et al., 1994) to achieve a CR. He was then removed from study because of non-medical (insurance) issues. He received two cycles of cytarabine and daunorubicin consolidation, but relapsed eight months after completing this therapy. Following salvage chemotherapy, he underwent an allogeneic SCT and his OS at the time of last follow-up was 27.4 months.

To our knowledge, the only published case of t(10;12)(p11;q15) was included in a series of pediatric patients with early T-cell precursor ALL (Coustan-Smith et al., 2009). The patient was a 14-year-old female with ALL-L1 who had the following karyotype: 47,XX,+4,t(10;12)(p11.2;q15)/47,idem,del(5)(q22q35). No other clinical features or outcome were reported. While there are few similarities identified between these two patients with t(10;12), each karyotype contained a secondary +4. Trisomy 4 can occur as a sole abnormality or together with double minutes, but it is rarely seen as an aberration secondary to recurring balanced abnormalities in AML other than t(8;21)(q22;q22) (Mitelman et al., 2012). However, our review of the CALGB cytogenetics database and the literature (Carlson et al., 2000; Nakamura et al., 2003; Mulaw et al., 2012) revealed that +4 is a recurrent aberration secondary to t(10;11)(p13;q14-21), a translocation which can occur in patients diagnosed with either AML or ALL (Mitelman et al., 2012).

Unique Balanced Translocations

After our initial evaluation there remained 52 balanced translocations detected in 51 patients that to our knowledge have not been previously reported by others (cases 11-61 in Table 2).

Of these, the translocation was a sole aberration in at least one clone in 36 patients, whereas in 10 patients there was one additional structural, and in five patients one additional numerical abnormality present. In four patients listed in Table 2 (and one in Table 1), the constitutional nature of balanced translocations could not be excluded. While we believe these translocations (detected in patients no. 11, 45, 48, and 55 in Table 2 and patient no. 2 in Table 1) should be reported in our study because they could still represent acquired, leukemia-related abnormalities, we have clearly indicated their uncertain status in both Tables.

We reviewed the breakpoints in each of the 52 translocations listed in Table 2 and identified 19 breakpoints as recurrent among our cases. We arranged the patients in Table 2 according to 12 shared common breakpoints. Of note, each patient is listed only once even though some translocations contained two recurrent breakpoints. Therefore, some patients harboring abnormalities with recurrent breakpoints are not grouped together in the Table. These additional recurrent breakpoints are: 3q25 (cases no. 28 and 47), 4p16 (12 and 48), 5p13 (19 and 49), 12p11.2 (22 and 51), 12q12 (13 and 56), 12q24.1 (18 and 50), and 21q22 (14 and 49). With only one case to evaluate for each translocation it was not possible to ascertain whether a particular outcome or clinical feature is associated with a specific translocation. This comprehensive list is presented so that it may become feasible to make clinical associations once additional patients with these translocations are identified in the future.

Conclusion

Non-random chromosome abnormalities remain an important consideration in the management of patients with newly diagnosed AML, continuing to provide prognostic information and guide treatment decisions. To continue to expand cytogenetic classification and possibly identify novel genes that might serve as the target of therapeutic intervention, recognition of new, recurrent abnormalities is important. We have identified seven previously unrecognized as recurrent balanced translocations in myeloid diseases and 52 unique abnormalities. Given the small number of cases with these abnormalities, it is not currently possible to determine their prognostic significance. However, we provide data on disease characteristics and clinical outcomes, which, when considered with data from other studies, should allow us to learn more about the biologic and clinical significance of these chromosome abnormalities.

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Appendix

The following CALGB/Alliance institutions participated in this study. For each of these institutions the current or last principal investigator, and cytogeneticists who analyzed the cases are listed.

Duke University Medical Center, Durham, NC: Jeffrey Crawford and Sandra H. Bigner (grant no. U10CA047577); North Shore University Hospital, Manhasset, NY: Daniel R. Budman and Prasad R. K. Koduru (grant no. U10CA035279); The Ohio State University Medical Center, Columbus, OH: Clara D. Bloomfield and Nyla A. Heerema (grant no.

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* Deceased.

References

Anastasi J, Feng J, Dickstein JI, Le Beau MM, Rubin CM, Larson RA, Rowley JD, Vardiman JW. Lineage involvement by BCR/ABL in Ph+ lymphoblastic leukemias: Chronic myelogenous leukemia presenting in lymphoid blast vs Ph+ acute lymphoblastic leukemia. Leukemia. 1996; 10:795–802. [PubMed: 8656674]

Atlas of Genetics and Cytogenetics in Oncology and Haematology. URL http://AtlasGeneticsOncology.org

Baer MR, George SL, Sanford BL, Mrózek K, Kolitz JE, Moore JO, Stone RM, Powell BL, Caligiuri MA, Bloomfield CD, Larson RA. Escalation of daunorubicin and addition of etoposide in the ADE regimen in acute myeloid leukemia patients aged 60 years and older: Cancer and Leukemia Group B Study 9720. Leukemia. 2011; 25:800–807. [PubMed: 21321569]

Bao L, Wang X, Ryder J, Ji M, Chen Y, Chen H, Sun H, Yang Y, Du X, Kerzic P, Gross SA, Yao L, Lv L, Fu H, Lin G, Irons RD. Prospective study of 174 de novo acute myelogenous leukemias according to the WHO classification: Subtypes, cytogenetic features and FLT3 mutations. Eur J Haematol. 2006; 77:35–45. [PubMed: 16573742]

Behm FG, Raimondi SC, Schell MJ, Look AT, Rivera GK, Pui CH. Lack of CD45 antigen on blast cells in childhood acute lymphoblastic leukemia is associated with chromosomal hyperdiploidy and other favorable prognostic features. Blood. 1992; 79:1011–1016. [PubMed: 1531305]

Bennett JM, Catovsky D, Daniel MT, Flandrin G, Galton DA, Gralnick HR, Sultan C. Proposed revised criteria for the classification of acute myeloid leukemia. A report of the French-American-British Cooperative Group. Ann Intern Med. 1985; 103:620–625. [PubMed: 3862359]

Blum W, Donohue K, Marcucci G, DeAngelo DJ, Uy GL, Powell BL, Stock W, Baer M, Kolitz JE, Wetzler M, Hoke E, Moser BK, Larson RA. Challenges for conducting clinical trials evaluating maintenance chemotherapy in acute myeloid leukemia (AML): A Cancer and Leukemia Group B (CALGB) study. Blood. 2010; 116:898–899.

Boerma EG, Siebert R, Kluin PM, Baudis M. Translocations involving 8q24 in Burkitt lymphoma and other malignant lymphomas: A historical review of cytogenetics in the light of todays knowledge. Leukemia. 2009; 23:225–234. [PubMed: 18923440]

Byrd JC, Mrózek K, Dodge RK, Carroll AJ, Edwards CG, Arthur DC, Pettenati MJ, Patil SR, Rao KW, Watson MS, Koduru PRK, Moore JO, Stone RM, Mayer RJ, Feldman EJ, Davey FR, Schiffer CA, Larson RA, Bloomfield CD. Pretreatment cytogenetic abnormalities are predictive of induction success, cumulative incidence of relapse, and overall survival in adult patients with de novo acute myeloid leukemia: Results from Cancer and Leukemia Group B (CALGB 8461). Blood. 2002; 100:4325–4336. [PubMed: 12393746]

Carlson KM, Vignon C, Bohlander S, Martinez-Climent JA, Le Beau MM, Rowley JD. Identification and molecular characterization of *CALM*/*AF10* fusion products in T cell acute lymphoblastic leukemia and acute myeloid leukemia. Leukemia. 2000; 14:100–104. [PubMed: 10637483]

Cassileth PA, Harrington DP, Appelbaum FR, Lazarus HM, Rowe JM, Paietta E, Willman C, Hurd DD, Bennett JM, Blume KG, Head DR, Wiernik PH. Chemotherapy compared with autologous or allogeneic bone marrow transplantation in the management of acute myeloid leukemia in first remission. N Engl J Med. 1998; 339:1649–1656. [PubMed: 9834301]

Cauwelier B, Dastugue N, Cools J, Poppe B, Herens C, De Paepe A, Hagemeijer A, Speleman F. Molecular cytogenetic study of 126 unselected T-ALL cases reveals high incidence of *TCRβ* locus rearrangements and putative new T-cell oncogenes. Leukemia. 2006; 20:1238–1244. [PubMed: 16673021]

Cheson BD, Cassileth PA, Head DR, Schiffer CA, Bennett JM, Bloomfield CD, Brunning R, Gale RP, Grever MR, Keating MJ, Sawitsky A, Stass S, Weinstein H, Woods WG. Report of the National Cancer Institute-sponsored workshop on definitions of diagnosis and response in acute myeloid leukemia. J Clin Oncol. 1990; 8:813–819. [PubMed: 2185339]

Coustan-Smith E, Mullighan CG, Onciu M, Behm FG, Raimondi SC, Pei D, Cheng C, Su X, Rubnitz JE, Basso G, Biondi A, Pui C-H, Downing JR, Campana D. Early T-cell precursor leukaemia: A subtype of very high-risk acute lymphoblastic leukaemia. Lancet Oncol. 2009; 10:147–156. [PubMed: 19147408]

Cox MC, Panetta P, Lo-Coco F, Del Poeta G, Venditti A, Maurillo L, Del Principe MI, Mauriello A, Anemona L, Bruno A, Mazzone C, Palombo P, Amadori S. Chromosomal aberration of the 11q23 locus in acute leukemia and frequency of *MLL* gene translocation: Results in 378 adult patients. Am J Clin Pathol. 2004; 122:298–306. [PubMed: 15323147]

Davey FR, Abraham N Jr, Brunetto VL, MacCallum JM, Nelson DA, Ball ED, Griffin JD, Baer MR, Wurster-Hill D, Mayer RJ, Schiffer CA, Bloomfield CD. Morphologic characteristics of erythroleukemia (acute myeloid leukemia; FAB-M6): A CALGB study. Am J Hematol. 1995; 49:29–38. [PubMed: 7741135]

Döhner H, Estey EH, Amadori S, Appelbaum FR, Büchner T, Burnett AK, Dombret H, Fenaux P, Grimwade D, Larson RA, Lo-Coco F, Naoe T, Niederwieser D, Ossenkoppele GJ, Sanz MA, Sierra J, Tallman MS, Löwenberg B, Bloomfield CD. Diagnosis and management of acute myeloid leukemia in adults: Recommendations from an international expert panel, on behalf of the European LeukemiaNet.; European LeukemiaNet. Blood. 2010; 115:453–474. [PubMed: 19880497]

Farag SS, Archer KJ, Mrózek K, Ruppert AS, Carroll AJ, Vardiman JW, Pettenati MJ, Baer MR, Qumsiyeh MB, Koduru PR, Ning Y, Mayer RJ, Stone RM, Larson RA, Bloomfield CD. Pretreatment cytogenetics add to other prognostic factors predicting complete remission and long-term outcome in patients 60 years of age or older with acute myeloid leukemia: Results from Cancer and Leukemia Group B 8461. Blood. 2006; 108:63–73. [PubMed: 16522815]

Gough SM, Slape CI, Aplan PD. *NUP98* gene fusions and hematopoietic malignancies: Common themes and new biological insights. Blood. 2011; 118:6247–6257. [PubMed: 21948299]

Grimwade D, Walker H, Oliver F, Wheatley K, Harrison C, Harrison G, Rees J, Hann I, Stevens R, Burnett A, Goldstone A. The importance of diagnostic cytogenetics on outcome in AML: Analysis of 1,612 patients entered into the MRC AML 10 trial. Blood. 1998; 92:2322–2333. [PubMed: 9746770]

Grimwade D, Hills RK, Moorman AV, Walker H, Chatters S, Goldstone AH, Wheatley K, Harrison CJ, Burnett AK. on behalf of the National Cancer Research Institute Adult Leukaemia Working Group. Refinement of cytogenetic classification in acute myeloid leukemia: Determination of prognostic significance of rare recurring chromosomal abnormalities among 5876 younger adult patients treated in the United Kingdom Medical Research Council trials. Blood. 2010; 116:354–365. [PubMed: 20385793]

Grimwade D, Mrózek K. Diagnostic and prognostic value of cytogenetics in acute myeloid leukemia. Hematol Oncol Clin North Am. 2011; 25:1135–1161. [PubMed: 22093581]

Gupta P, Sanford BL, Yu D, Vij R, Hurd DD, Odenike O, Bloomfield CD, Hasserjian RP, Larson RA. A phase II study of an oral VEGF receptor tyrosine kinase inhibitor (PTK787/ZK22584) in patients with myelodysplastic syndrome (MDS): A Cancer and Leukemia Group B study 10105. Blood. 2006; 108:753a.

Haase D, Germing U, Schanz J, Pfeilstöcker M, Nösslinger T, Hildebrandt B, Kundgen A, Lübbert M, Kunzmann R, Giagounidis AA, Aul C, Trümper L, Krieger O, Stauder R, Müller TH, Wimazal F, Valent P, Fonatsch C, Steidl C. New insights into the prognostic impact of the karyotype in MDS and correlation with subtypes: Evidence from a core dataset of 2124 patients. Blood. 2007; 110:4385–4395. [PubMed: 17726160]

Hagiwara S, Yuo A, Miwa A, Takezako N, Hirano N, Togawa A. A rare atypical myeloproliferative-disorder-like hemopathy with marked dysplasia, peripheral dominant myeloblast proliferation and extramedullary hematopoiesis was converted into typical acute myeloid leukemia with an interval of complete hematological remission. Int J Hematol. 1998; 67:411–416. [PubMed: 9695415]

Hashii Y, Kim JY, Sawada A, Tokimasa S, Hiroyuki F, Ohta H, Makiko K, Takihara Y, Ozono K, Hara J. A novel partner gene CIP29 containing a SAP domain with MLL identified in infantile myelomonocytic leukemia. Leukemia. 2004; 18:1546–1548. [PubMed: 15284855]

Heerema NA, Sather HN, Sensel MG, La MK, Hutchinson RJ, Nachman JB, Reaman GH, Lange BJ, Steinherz PG, Bostrom BC, Gaynon PS, Uckun FM. Abnormalities of chromosome bands 15q13-15 in childhood acute lymphoblastic leukemia. Cancer. 2002; 94:1102–1110. [PubMed: 11920481]

Hoppman-Chaney NL, Cherry D, Holladay C, Yuhas J, Wang R, Velagaleti G. Identification of a patient with 7q32 deletion-associated acute myeloid leukemia and an incidental t(8;14). Cancer Genet Cytogenet. 2010; 197:179–184. [PubMed: 20193852]

Hu N, Bian ML, Le Beau MM, Rowley JD. Cytogenetic analysis of 51 patients with chronic myeloid leukemia. Chin Med J (Engl). 1990; 103:831–839. [PubMed: 2125257]

Jankovic D, Gorello P, Liu T, Ehret S, La Starza R, Desjobert C, Baty F, Brutsche M, Jayaraman P-S, Santoro A, Mecucci C, Schwaller J. Leukemogenic mechanisms and targets of a NUP98/HHEX fusion in acute myeloid leukemia. Blood. 2008; 111:5672–5682. [PubMed: 18388181]

Johansson, B.; Harrison, CJ. Acute myeloid leukemia. In: Heim, S.; Mitelman, F., editors. Cancer Cytogenetics. 3rd. Hoboken, New Jersey: John Wiley & Sons, Inc.; 2009. p. 45-139.

Karst C, Gross M, Haase D, Wedding U, Höffken K, Liehr T, Mkrtchyan H. Novel cryptic chromosomal rearrangements detected in acute lymphoblastic leukemia detected by application of new multicolor fluorescent in situ hybridization approaches. Int J Oncol. 2006; 28:891–897. [PubMed: 16525638]

Kerndrup GB, Kjeldsen E. Acute leukemia cytogenetics: An evaluation of combining G-band karyotyping with multi-color spectral karyotyping. Cancer Genet Cytogenet. 2001; 124:7–11. [PubMed: 11165315]

Kirsch IR, Brown JA, Lawrence J, Korsmeyer SJ, Morton CC. Translocations that highlight chromosomal regions of differentiated activity. Cancer Genet Cytogenet. 1985; 18:159–171. [PubMed: 3863696]

Kiuru-Kuhlefelt S, Kristo P, Ruutu T, Knuutila S, Kere J. Evidence for two molecular steps in the pathogenesis of myeloid disorders associated with deletion of chromosome 7 long arm. Leukemia. 1997; 11:2097–2104. [PubMed: 9447826]

Kolitz JE, George SL, Dodge RK, Hurd DD, Powell BL, Allen SL, Velez-Garcia E, Moore JO, Shea TC, Hoke E, Caligiuri MA, Vardiman JW, Bloomfield CD, Larson RA. Dose escalation studies of cytarabine, daunorubicin, and etoposide with and without multidrug resistance modulation with PSC-833 in untreated adults with acute myeloid leukemia younger than 60 years: Final induction results of Cancer and Leukemia Group B study 9621. J Clin Oncol. 2004; 22:4290–4301. [PubMed: 15514371]

Kolitz JE, George SL, Marcucci G, Vij R, Powell BL, Allen SL, DeAngelo DJ, Shea TC, Stock W, Baer MR, Hars V, Maharry K, Hoke E, Vardiman JW, Bloomfield CD, Larson RA. P-glycoprotein inhibition using valspodar (PSC-833) does not improve outcomes for patients younger than age 60 years with newly diagnosed acute myeloid leukemia: Cancer and Leukemia Group B study 19808. Blood. 2010; 116:1413–1421. [PubMed: 20522709]

Kristensen TD, Wesenberg F, Jonsson OG, Carlsen NT, Forestier E, Kirchhoff M, Lundsteen C, Schmiegelow K. High-resolution comparative genomic hybridisation yields a high detection rate of chromosomal aberrations in childhood acute lymphoblastic leukaemia. Eur J Haematol. 2003; 70:363–372. [PubMed: 12756018]

Laï J-L, Estienne MH, Fenaux P, Lepelley P, Huart JJ, Bauters F, Deminatti M. Translocation t(10;17)(p13;q12) in two cases of acute nonlymphocytic leukemia with phagocytic activity of blasts. A new cytogenetic entity? Cancer Genet Cytogenet. 1989; 39:45–53. [PubMed: 2731147]

Lai J-L, Preudhomme C, Zandecki M, Flactif M, Vanrumbeke M, Lepelley P, Wattel E, Fenaux P. Myelodysplastic syndromes and acute myeloid leukemia with 17p deletion. An entity characterized by specific dysgranulopoïesis and a high incidence of P53 mutations. Leukemia. 1995; 9:370–381. [PubMed: 7885035]

Larson RA, Wernli M, Le Beau MM, Daly KM, Pape LH, Rowley JD, Vardiman JW. Short remission durations in therapy-related leukemia despite cytogenetic complete responses to high-dose cytarabine. Blood. 1988; 72:1333–1339. [PubMed: 3167210]

La Starza R, Aventin A, Crescenzi B, Gorello P, Specchia G, Cuneo A, Angioni A, Bilhou-Nabera C, Boqué C, Foà R, Uyttebroeck A, Talmant P, Cimino G, Martelli MF, Marynen P, Mecucci C, Hagemeijer A. *CIZ* gene rearrangements in acute leukemia: Report of a diagnostic FISH assay and clinical features of nine patients. Leukemia. 2005; 19:1696–1699. [PubMed: 15990865]

Lee EJ, Pollak A, Leavitt RD, Testa JR, Schiffer CA. Minimally differentiated acute nonlymphocytic leukemia: A distinct entity. Blood. 1987; 70:1400–1406. [PubMed: 3663939]

Marcucci G, Moser B, Blum W, Stock W, Wetzler M, Kolitz JE, Thakuri M, Carter T, Stuart RK, Larson RA. A phase III randomized trial of intensive induction and consolidation chemotherapy oblimersen, a proapoptotic Bcl-2 antisense oligonucleotide in untreated acute myeloid leukemia patients 60 years old. J Clin Oncol. 2007; 25:360s.

Martini A, La Starza R, Janssen H, Bilhou-Nabera C, Corveleyn A, Somers R, Aventin A, Foà R, Hagemeijer A, Mecucci C, Marynen P. Recurrent rearrangement of the Ewing's sarcoma gene, *EWSR1*, or its homologue, *TAF15*, with the transcription factor *CIZ*/*NMP4* in acute leukemia. Cancer Res. 2002; 62:5408–5412. [PubMed: 12359745]

Mashal R, Shtalrid M, Talpaz M, Kantarjian H, Smith L, Beran M, Cork A, Trujillo J, Gutterman J, Deisseroth A. Rearrangement and expression of p53 in the chronic phase and blast crisis of chronic myelogenous leukemia. Blood. 1990; 75:180–189. [PubMed: 1967214]

Mayer RJ, Schiffer CA, Peterson BA, Budman DR, Silver RT, Rai KR, Cornwell GG, Ellison RR, Maguire M, Berg DT, Davis RB, Mcintyre OR, Frei E. Intensive postremission therapy in adults with acute nonlymphocytic leukemia using various dose schedules of ara-C: A progress report from the CALGB. Semin Oncol. 1987; 14(Suppl 1):25–31. [PubMed: 3296206]

Mayer RJ, Davis RB, Schiffer CA, Berg DT, Powell BL, Schulman P, Omura GA, Moore JO, McIntyre OR, Frei E 3rd. Intensive postremission chemotherapy in adults with acute myeloid leukemia. N Engl J Med. 1994; 331:896–903. [PubMed: 8078551]

Milton JM, Garson OM, Paton CM, Hurley TF. A complicated but nonrandom karyotype in preleukemia. Cancer Genet Cytogenet. 1984; 13:37–41. [PubMed: 6467181]

Mitelman F, Johansson B, Mertens F. The impact of translocations and gene fusions on cancer causation. Nat Rev Cancer. 2007; 7:233–245. [PubMed: 17361217]

Mitelman, F.; Johansson, B.; Mertens, F., editors. Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer. 2012. Available at: http://cgap.nci.nih.gov/Chromosomes/Mitelman

Moore JO, Dodge RK, Amrein PC, Kolitz J, Lee EJ, Powell B, Godfrey S, Robert F, Schiffer CA. Granulocyte-colony stimulating factor (filgrastim) accelerates granulocyte recovery after intensive postremission chemotherapy for acute myeloid leukemia with aziridinyl benzoquinone and mitoxantrone: Cancer and Leukemia Group B Study 9022. Blood. 1997; 89:780–788. [PubMed: 9028308]

Moore JO, George SL, Dodge RK, Amrein PC, Powell BL, Kolitz JE, Baer MR, Davey FR, Bloomfield CD, Larson RA, Schiffer CA. Sequential multiagent chemotherapy is not superior to high-dose cytarabine alone as postremission intensification therapy for acute myeloid leukemia in adults under 60 years of age: Cancer and Leukemia Group B study 9222. Blood. 2005; 105:3420–3427. [PubMed: 15572587]

Mrózek K, Heinonen K, Bloomfield CD. Clinical importance of cytogenetics in acute myeloid leukaemia. Best Pract Res Clin Haematol. 2001; 14:19–47. [PubMed: 11355922]

Mrózek K, Heinonen K, Theil KS, Bloomfield CD. Spectral karyotyping in patients with acute myeloid leukemia and a complex karyotype shows hidden aberrations, including recurrent overrepresentation of 21q, 11q, and 22q. Genes Chromosomes Cancer. 2002; 34:137–153. [PubMed: 11979548]

Mrózek K, Heerema NA, Bloomfield CD. Cytogenetics in acute leukemia. Blood Rev. 2004; 18:115–136. [PubMed: 15010150]

Mrózek K, Carroll AJ, Maharry K, Rao KW, Patil SR, Pettenati MJ, Watson MS, Arthur DC, Tantravahi R, Heerema NA, Koduru PRK, Block AW, Qumsiyeh MB, Edwards CG, Sterling LJ, Holland KB, Bloomfield CD. Central review of cytogenetics is necessary for cooperative group correlative and clinical studies of adult acute leukemia: The Cancer and Leukemia Group B experience. Int J Oncol. 2008; 33:239–244. [PubMed: 18636143]

Mulaw MA, Krause AJ, Deshpande AJ, Krause LF, Rouhi A, La Starza R, Borkhardt A, Buske C, Mecucci C, Ludwig W-D, Lottaz C, Bohlander SK. *CALM*/*AF10*-positive leukemias show upregulation of genes involved in chromatin assembly and DNA repair processes and of genes adjacent to the breakpoint at 10p12. Leukemia. 2012; 26:1012–1019. [PubMed: 22064352]

Nagasaka M, Maeda S, Maeda H, Chen HL, Kita K, Mabuchi O, Misu H, Matsuo T, Sugiyama T. Four cases of t(4;11) acute leukemia and its myelomonocytic nature in infants. Blood. 1983; 61:1174–1181. [PubMed: 6340755]

Nakamura F, Maki K, Arai Y, Nakamura Y, Mitani K. Monocytic leukemia with CALM/AF10 rearrangement showing mediastinal emphysema. Am J Hematol. 2003; 72:138–142. [PubMed: 12555219]

Nebral K, König M, Schmidt HH, Lutz D, Sperr WR, Kalwak K, Brugger S, Dworzak MN, Haas OA, Strehl S. Screening for *NUP98* rearrangements in hematopoietic malignancies by fluorescence *in situ* hybridization. Haematologica. 2005; 90:746–752. [PubMed: 15951287]

Nyquist KB, Thorsen J, Zeller B, Haaland A, Trøen G, Heim S, Micci F. Identification of the *TAF15-ZNF384* fusion gene in two new cases of acute lymphoblastic leukemia with a t(12;17)(p13;q12). Cancer Genet. 2011; 204:147–152. [PubMed: 21504714]

Offit K, Burns JP, Cunningham I, Jhanwar SC, Black P, Kernan NA, O'Reilly RJ, Chaganti RSK. Cytogenetic analysis of chimerism and leukemia relapse in chronic myelogenous leukemia patients after T cell-depleted bone marrow transplantation. Blood. 1990; 75:1346–1355. [PubMed: 2310831]

Oh SH, Park TS, Cho SY, Kim MJ, Huh J, Kim B, Song SA, Lee JY, Jun KR, Shin JH, Kim HR, Lee JN. Acute myeloid leukemia associated with t(10;17)(p13-15;q12-21) and phagocytic activity by leukemic blasts: A clinical study and review of the literature. Cancer Genet Cytogenet. 2010; 202:43–46. [PubMed: 20804920]

Olney, HJ.; Le Beau, MM. Myelodysplastic syndromes. In: Heim, S.; Mitelman, F., editors. Cancer Cytogenetics. 3rd. Hoboken, New Jersey: John Wiley & Sons, Inc.; 2009. p. 141-178.

Olney HJ, Mitelman F, Johansson B, Mrózek K, Berger R, Rowley JD. Unique balanced chromosome abnormalities in treatment-related myelodysplastic syndromes and acute myeloid leukemia: Report from an International Workshop. Genes Chromosomes Cancer. 2002; 33:413–423. [PubMed: 11921275]

Olopade OI, Thangavelu M, Larson RA, Mick R, Kowal-Vern A, Schumacher HR, Le Beau MM, Vardiman JW, Rowley JD. Clinical, morphologic, and cytogenetic characteristics of 26 patients with acute erythroblastic leukemia. Blood. 1992; 80:2873–2882. [PubMed: 1450412]

Petersdorf S, Kopecky K, Stuart RK, Larson RA, Nevill TJ, Stenke L, Slovak ML, Tallman MS, William CL, Erba H, Appelbaum FR. Preliminary results of Southwest Oncology Group S0106: An international intergroup phase 3 randomized trial comparing the addition of gemtuzumab ozogamicin to standard induction therapy followed by a second randomization to post-consolidation gemtuzumab ozogamicin versus no additional therapy for previously untreated acute myeloid leukemia. Blood. 2009; 114:326–327.

Poitras JL, Costa D, Kluk MJ, Amrein PC, Stone RM, Lee C, Dal Cin P, Morton CC. Genomic alterations in myeloid neoplasms with novel, apparently balanced translocations. Cancer Genet. 2011; 204:68–76. [PubMed: 21504705]

Powell BL, Moser BK, Stock W, Gallagher RE, Willman CL, Stone RM, Rowe JM, Coutre SE, Feusner JH, Gregory J, Couban S, Appelbaum FR, Tallman MS, Larson RA. Adding mercaptopurine and methotrexate to alternate week ATRA maintenance therapy does not improve the outcome for adults with acute promyelocytic leukemia (APL) in first remission: Results from North American Leukemia Intergroup trial C9710. Blood. 2011; 118:118–119.

Pui C-H, Relling MV, Behm FG, Hancock ML, Boyett JM, Raimondi SC, Krance RA, Mahmoud HH, Ribeiro RC, Sandlund JT, Head DR, Evans WE, Crist WM, Rivera GK. L-asparaginase may potentiate the leukemogenic effect of the epipodophyllotoxins. Leukemia. 1995; 9:1680–1684. [PubMed: 7564509]

Raimondi SC, Peiper SC, Kitchingman GR, Behm FG, Williams DL, Hancock ML, Mirro J Jr. Childhood acute lymphoblastic leukemia with chromosomal breakpoints at 11q23. Blood. 1989; 73:1627–34. [PubMed: 2496771]

Raimondi SC, Roberson PK, Pui C-H, Behm FG, Rivera GK. Hyperdiploid (47-50) acute lymphoblastic leukemia in children. Blood. 1992; 79:3245–3252. [PubMed: 1596566]

Raimondi SC, Chang MN, Ravindranath Y, Behm FG, Gresik MV, Steuber CP, Weinstein HJ, Carroll AJ. Chromosomal abnormalities in 478 children with acute myeloid leukemia: Clinical characteristics and treatment outcome in a cooperative pediatric oncology group study-POG 8821. Blood. 1999; 94:3707–3716. [PubMed: 10572083]

Riesch M, Niggli FK, Leibundgut K, Caflisch U, Betts DR. Loss of X chromosome in childhood acute lymphoblastic leukemia. Cancer Genet Cytogenet. 2001; 125:27–29. [PubMed: 11297764]

Ribeiro RC, Oliveira MS, Fairclough D, Hurwitz C, Mirro J, Behm FG, Head D, Silva ML, Raimondi SC, Crist WM, Krance R. Acute megakaryoblastic leukemia in children and adolescents: A retrospective analysis of 24 cases. Leuk Lymphoma. 1993; 10:299–306. [PubMed: 8220128]

Romana SP, Radford-Weiss I, Ben Abdelali R, Schluth C, Petit A, Dastugue N, Talmant P, Bilhou-Nabera C, Mugneret F, Lafage-Pochitaloff M, Mozziconacci M-J, Andrieu J, Lai J-L, Terre C, Rack K, Cornillet-Lefebvre P, Luquet I, Nadal N, Nguyen-Khac F, Perot C, Van den Akker J, Fert-Ferrer S, Cabrol C, Charrin C, Tigaud I, Poirel H, Vekemans M, Bernard OA, Berger R. *NUP98* rearrangements in hematopoietic malignancies: A study of the Groupe Francophone de Cytogénétique Hématologique. Leukemia. 2006; 20:696–706. [PubMed: 16467868]

Schiffer CA, Davis RB, Schulman P, Cooper B, Coyle T, Lee EJ, Del Duca V. Intensive postremission therapy of acute myeloid leukemia with cytoxan/etoposide and diaziquone/mitoxantrone. Blood. 1991; 78(Suppl 1):461a.

Schoch C, Schnittger S, Klaus M, Kern W, Hiddemann W, Haferlach T. AML with 11q23/*MLL* abnormalities as defined by the WHO classification: Incidence, partner chromosomes, FAB subtype, age distribution, and prognostic impact in an unselected series of 1897 cytogenetically analyzed AML cases. Blood. 2003; 102:2395–2402. [PubMed: 12805060]

Sessarego M, Panarello C, Coviello DA, Boccaccio P, Ajmar F. Karyotype evolution in CML: High frequency of translocations other than the Ph. Cancer Genet Cytogenet. 1987; 25:73–80. [PubMed: 3467834]

Shaffer, LG.; Slovak, ML.; Campbell, LJ., editors. ISCN 2009: An International System for Human Cytogenetic Nomenclature. Basel: S. Karger; 2009.

Shah NK, Wagner J, Santos G, Griffin CA. Karyotype at relapse following allogeneic bone marrow transplantation for chronic myelogenous leukemia. Cancer Genet Cytogenet. 1992; 61:183–192. [PubMed: 1638501]

Shearer BM, Sukov WR, Flynn HC, Knudson RA, Ketterling RP. Development of a dual-color, double fusion FISH assay to detect *RPN1/EVI1* gene fusion associated with inv(3), t(3;3), and ins(3;3) in patients with myelodysplasia and acute myeloid leukemia. Am J Hematol. 2010; 85:569–574. [PubMed: 20556821]

Sierra M, Hernández JM, García JL, Gutiérrez NC, Pérez JJ, Vidriales MB, Ramos F, Hernández JM, Romero M, González MB, Galende J, San Miguel JF. Hematological, immunophenotypic, and cytogenetic characteristics of acute myeloblastic leukemia with trisomy 11. Cancer Genet Cytogenet. 2005; 160:68–72. [PubMed: 15949573]

Solé F, Caballín MR, Coll MD, Woessner S, Besses C, Sans-Sabrafen J, Egozcue J. Cytogenetic studies in acute nonlymphocytic leukemia. Cancer Genet Cytogenet. 1992; 60:117–124. [PubMed: 1606554]

Steudel C, Wermke M, Schaich M, Schäkel U, Illmer T, Ehninger G, Thiede C. Comparative analysis of *MLL* partial tandem duplication and *FLT3* internal tandem duplication mutations in 956 adult patients with acute myeloid leukemia. Genes Chromosomes Cancer. 2003; 37:237–251. [PubMed: 12759922]

Streubel B, Sauerland C, Heil G, Freund M, Bartels H, Lengfelder E, Wandt H, Ludwig WD, Nowotny H, Baldus M, Grothaus-Pinke B, Büchner T, Fonatsch C. Correlation of cytogenetic, molecular cytogenetic, and clinical findings in 59 patients with ANLL or MDS and abnormalities of the short arm of chromosome 12. Br J Haematol. 1998; 100:521–533. [PubMed: 9504635]

Sun J, Yin CC, Cui W, Chen SS, Medeiros LJ, Lu G. Chromosome 20q deletion: A recurrent cytogenetic abnormality in patients with chronic myelogenous leukemia in remission. Am J Clin Pathol. 2011; 135:391–397. [PubMed: 21350093]

Swansbury GJ, Slater R, Bain BJ, Moorman AV, Secker-Walker LM. Hematological malignancies with t(9;11)(p21-22;q23) – a laboratory and clinical study of 125 cases. Leukemia. 1998; 12:792–800. [PubMed: 9593283]

Szatrowski TP, Dodge RK, Reynolds C, Westbrook CA, Frankel SR, Sklar J, Stewart CC, Hurd DD, Kolitz JE, Velez-Garcia E, Stone RM, Bloomfield CD, Schiffer CA, Larson RA. Lineage specific treatment of adult patients with acute lymphoblastic leukemia in first remission with anti-B4-blocked ricin or high-dose cytarabine: Cancer and Leukemia Group B Study 9311. Cancer. 2003; 97:1471–1480. [PubMed: 12627512]

Taviaux S, Brunel V, Dupont M, Fernandez F, Ferraz C, Carbuccia N, Sainty D, Demaille J, Birg F, Lafage-Pochitaloff M. Simple variant t(8;21) acute myeloid leukemias harbor insertions of the *AML1* or *ETO* genes. Genes Chromosomes Cancer. 1999; 24:165–171. [PubMed: 9885986]

United Kingdom Cancer Cytogenetics Group (UKCCG). Translocations involving 12p in acute myeloid leukemia: Association with prior myelodysplasia and exposure to mutagenic agents. Genes Chromosomes Cancer. 1992; 5:252–254. [PubMed: 1384679]

Vardiman JW, Thiele J, Arber DA, Brunning RD, Borowitz MJ, Porwit A, Harris NL, Le Beau MM, Hellström-Lindberg E, Tefferi A, Bloomfield CD. The 2008 revision of the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia: Rationale and important changes. Blood. 2009; 114:937–951. [PubMed: 19357394]

Wang ES, Sait SNJ, Gold D, Mashtare T, Starostik P, Ford LA, Wetzler M, Nowak NJ, Deeb G. Genomic, immunophenotypic, and *NPM1/FLT3* mutational studies on 17 patients with normal karyotype acute myeloid leukemia (AML) followed by aberrant karyotype AML at relapse. Cancer Genet Cytogenet. 2010; 202:101–107. [PubMed: 20875872]

Weinkauff R, Estey EH, Starostik P, Hayes K, Huh Y, Hirsch-Ginsberg C, Andreef M, Keating M, Kantarjian HM, Freireich EJ, Albitar M. Use of peripheral blood blasts vs bone marrow blasts for diagnosis of acute leukemia. Am J Clin Pathol. 1999; 111:733–740. [PubMed: 10361507]

Wells RA, Hummel JL, De Koven A, Zipursky A, Kirby M, Dubé I, Kamel-Reid S. A new variant translocation in acute promyelocytic leukaemia: Molecular characterization and clinical correlation. Leukemia. 1996; 10:735–740. [PubMed: 8618456]

Xue Y, Yu F, Xin Y, Lu D, Zou Z, Guo Y, Xie X. t(8;20)(q22;p13): A novel variant translocation of t(8;21) in acute myeloblastic leukaemia. Br J Haematol. 1997; 98:733–735. [PubMed: 9332332]

Yagi T, Morimoto A, Eguchi M, Hibi S, Sako M, Ishii E, Mizutani S, Imashuku S, Ohki M, Ichikawa H. Identification of a gene expression signature associated with pediatric AML prognosis. Blood. 2003; 102:1849–1856. [PubMed: 12738660]

Yamamoto K, Okamura A, Kawano H, Katayama Y, Shimoyama M, Matsui T. A novel t(8;18)(q13;q21) in acute monocytic leukemia evolving from constitutional trisomy 8 mosaicism. Cancer Genet Cytogenet. 2007; 176:144–149. [PubMed: 17656258]

Yasar D, Karadogan I, Alanoglu G, Akkaya B, Luleci G, Salim O, Timuragaoglu A, Toruner GA, Berker-Karauzum S. Array comparative genomic hybridization analysis of adult acute leukemia patients. Cancer Genet Cytogenet. 2010; 197:122–129. [PubMed: 20193845]

Table 1

Cytogenetics, Hematologic and Clinical Characteristics and Treatment Outcome of Patients with New Recurrent Translocations[a]

Study/ Case No.[b]	Age/ Sex	Race	Karyotype	FAB	AML/MDS Type	Hb (g /dL)	Plts ($\times10^9$/L)	WBC ($\times10^9$/L)	PB/BM blasts (%)	Auer rods (+/−)	Organ Involvement	Response[c]	DFS (mo)	OS (mo)	Induction Rx[d]	Post-CR Rx[d]
Translocations involving band 11p15: t(7;11)(q22;p15)																
This study/ Case #1	87/ M	White	46,XY,**t(7;11)(q22;p15.5)**[15]/46,XY[5]	RARS	de novo	9	659	5.1	0/0	-	NR	NR	NA	52.8+	Vatalanib 10105	NA
Kirsch 1985/ Case #1	47/ M	Black	40,XY,−2,add(3)(q?),−5,**t(7;11)(q22;p15)**, add(12)(p?),−14,−15,−16,−17,−18,−18,−19, −21,+4mar[cp50]	M6	de novo	1.7	4	12.5	9/63.6	NR	NR	CR	14+	NR	AD	NR
Nebral 2005/ Case #8	65/ M	NR	46,XY,**t(7;11)(q22;p15)**[2]/46,XY[4]	AMLNOS	NR	NR	NR	NR	NR/NR	NR	NR	NR	NR	NR	NR	NR
Ribeiro 1993/ Case #14	5/ F	NR	46.XX,**t(7;11)(q22;p15)**	M7	de novo	10	26	6.4	26/49	NR	No	R	NA	NR	AD	NA
t(7;11) with an 11p breakpoint specified as 11p14 has been reported in one additional case of AML, 46,XX,i(17)(q10)/46,idem,t(7;11)(q22;p14)/47,XX,+21 (Bao et al., 2006).																
Translocations involving band 11p15: t(10;11)(q23;p15)																
This study/ Case #2	52/ F	White	46,XX,**t(10;11)(q23;p15)**[25]	M4	de novo	8.3	59	76.5	54/33	+	S	CR	8.1	9.2	AD 8525	HIDAC 8525
The constitutional nature of this abnormality could not be excluded.																
Jankovic 2008/ Case #1	73/ M	NR	45,X,−Y,**t(10;11)(q23;p15)**[15]/46,XY[5]	NA	RD	9.1	49	2.35	NR/90	+	NR	CR	96+	252+	FLAG	IDAC/D, AutoSCT
Karyotype detected at the time of 2nd relapse; karyotype at diagnosis is unknown; CR1 duration = 5 years; CR2 duration = 8 years.																
Larson 1988/ Case #2084	39/ M	NR	49,XY,t(1;12)(p36;q11),del(5)(q11q34), +del(5)(q11q34),add(8)(q13),i(8)(q10), add(9)(p22),**t(10;11)(q23;p15)**,inv(18) (q12q21),+21,+mar1[7]/50,idem,+21[2]/ 52,idem, +21,+21,+mar2[2]/48,idem,−22, del(5)(p13p15)[7]/49,idem,+21,−22, del(5)(p13p15)[3]/49,idem,add(16)(p13)[3]/51,idem,+21,+21,add(16)(p13)[2]/ 46,XY[2]	AMLNOS	t-AML	NR	NR	NR	NR/ NR	NR	NR	CR	5	6	HIDAC	HIDAC
Pui 1995/ Case #1B	4/ F	Black	46,XX,**t(10;11)(q22-24;p15)**/46,idem, add(6)(p25)	M2	t-AML	9.9	82	1.5	14/10-18	+	No	R	NA	5.5	ADE	NA
t(10;11) with a 10q breakpoint specified as 10q24 has been reported in one additional case of therapy-related AML, 46,XX,t(10;11)(q24;p15)/47,idem,−12,+2mar (Romana et al., 2006).																
Translocations involving band 12p13: t(2;12)(p13;p13)																
This study/ Case #3	76/ M	White	46,XY,t(3;20)(q21;q13.3)[4]/46,XY, **t(2;12)(p13;p13)**[3]/46,XY[13]	NA	t-AML-RD	8.6	38	33.9	3/84	NR	NR	R	NA	6.3	E/A/ MX	NA
The t(2;12) was acquired at the time of relapse. At diagnosis, the patient had t-AML and the following karyotype: 45,XY,der(7)t(7;17)(p11.2;q11.2),−17[13]/45,XY[7].																
This study/ Case #4	41/ M	White	47,XY,t(5;13)(q15;q14),+mar[9]/47,idem, **t(2;12)(p13;p13)**[11]	NA	de novo-R	9.5	60	16.5	0/26	NR	NR	R	NA	4.3	LI/MX/A	NA
The t(2;12) was acquired at the time of primary resistant disease The karyotype at diagnosis was 47,XY,t(5;13)(q15;q14),+mar[22] (case 27 in Table 2). Patient had primary resistant AML with cytogenetic evolution on day 54 of induction chemotherapy.																
Hagiwara 1998/ Case #1	51/ M	Asian	46,Y,t(X;13)(q28;q14),**t(2;12)(p13;p13)** [13]/46,XY[7]	NA	RD	NR	NR	NR	12/80	NR	LAD	NR	NR	NR	NR	NR
The t(2;12) was acquired at the time of relapse. At diagnosis, the patient had de novo AML and a normal karyotype. A similar translocation has been reported in a patient with AML, 45,X,−X,t(2;12)(p12;p13),del(5)(q?), t(11;14)(?p13;q32),−17,+mar (Lai et al., 1995).																
Translocations involving band 12p13: t(12;17)(p13;q12)																
This study/ Case #5	21/ F	White	46,XX,**t(12;17)(p13;q12)**[9]/ 47,idem,+13[9]/46,XX[2]	M2	de novo	8.5	75	32	54/69	+	S	R	NA	37.4	ADx2 9222	NA
UKCCG 1992/ Case #3	20/ M	NR	46,XY,**t(12;17)(p13;q12)**[12]/46,XY[2]	AML NOS	t-AML	NR	NR	38.7	NR/ NR	NR	NR	R	NA	< 2	NR	NA

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Study/ Case No.[b]	Age/ Sex	Race	Karyotype	FAB	AML/MDS Type	Hb (g /dL)	Plts ($\times 10^9$/L)	WBC ($\times 10^9$/L)	PB/BM blasts (%)	Auer rods (+/−)	Organ Involvement	Response[c]	DFS (mo)	OS (mo)	Induction Rx[d]	Post-CR Rx[d]
Two AML cases with a similar t(12;17)(p13;q11) as the two previous patients have been reported (Weinkauff et al., 1999; Martini et al., 2002; La Starza et al. 2005).																
Other translocations: t(2;3)(p21;p21)																
This study/ Case #6	21/ M	Black	47,XY,+9[16]/47,idem,**t(2;3)(p21;p21)**[9]	M2	de novo	9.3	24	7.6	23/30	+	No	CR	151.8+	153+	AD 9222	HIDAC/MX/AZ 9222
Wang 2010/ Case #04-1272	NR/ M	NR	46,XY,**t(2;3)(p21;p21)**,del(3)(q21q26), t(7;11)(p21;p14)[19]	NA	RD	NR	NR	NR	NR/ NR	NR	NR	NR	NR	NR	NR	NR
The t(2;3) was acquired at the time of relapse. At diagnosis, the patient had de novo AML and a normal karyotype.																
Other translocations: t(5;21)(q31;q22)																
This study/ Case #7	51/ F	White	45,Xc,**t(5;21)(q31;q22)**[10]/45,Xc[10]	M4	de novo	8	145	2.7	6/44	-	No	CR	6.6	11	ADEx2 19808	HIDAC/E, AutoSCT 19808
Streubel 1998/ Case #32	37/ M	NR	45,XY,t(3;12)(q26.2;p12.3), **t(5;21)(q31;q22)**,−7,add(10)(p13-14)	M2	de novo	NR	NR	NR	NR/ NR	NR	NR	R	NA	3	NR	NA
Other translocations: t(8;14)(q24.1;q32.2)																
This study/ Case #8	35/ M	White	46,XY,**t(8;14)(q24.1;q32.2)**[7]/46,XY[21]	M4	de novo	8.2	94	123.2	80/84	+	LAD	CR	9.8	17.3	ADEP 19808	HIDAC/E, AutoSCT 19808
This study/ Case #9	58/ F	White	46,XX,t(8;12)(q22;p11.2), **t(8;14)(q24.1;q32)**[17]/46,XX[8]	NA	RD	13.4	64	2.2	NR/26	NR	NR	R	NA	15.4	FLAG-I/MY	NA
The t(8;14) was acquired at the time of relapse. At diagnosis, the patient had de novo AML and a normal karyotype. This patient is also included in Table 2 (case 22) because she also harbors t(8;12)(q22;p11.2) thus far not previously described.																
Solé 1992 Case #8	65/ M	NR	44,XY,dic(3;7)(q11;q36),−4,del(5)(q22), **t(8;14)(q24;q32)**,−11,+mar	M2	de novo	NR	NR	NR	NR/ NR	NR	NR	NR	NR	NR	NR	NR
Lee 1987 Case #7	NR/ M	NR	45,XY,der(1)t(1;15)(p36;q1?3), **t(8;14)(q24;q32)**,add(13)(q34),del(13) (q12q14),−15/46,idem,add(6)(p25),+mar	M0	de novo	NR	34	98	100/ 99	NR	NR	R	NA	< 1	AD	NA
Hoppman-Chaney 2010 Case #1	59/ F	NR	46,XX,del(7)(q32q34),**t(8;14)(q24.1;q32)** [20]	M0	de novo	7.7	101	91	71/NR	NR	NR	NR	NR	~18	NR	NR
Translocation previously described in ALL: t(10;12)(p11;q15)																
This study/ Case #10	24/ M	White	47,XY,+4,**t(10;12)(p11;q15)**[26]/46,idem, −18[3]/46,XY[2]	M1	de novo	11.9	229	3.7	50/88	+	Pleural fluid	CR	10.9	27.4+	ADx2 8525	AD
Coustan-Smith 2009 Case #6	14/ F	NR	47,XX,+4,**t(10;12)(p11.2;q15)**[3]/ 47,idem,del(5)(q22q35)[3]/46,XX[14]	L1	de novo	NR	NR	2.8	NR/ NR	NR	NR	NR	NR	NR	NR	NR

Abbreviations: x2, two cycles of induction therapy; A, cytarabine; AD, cytarabine, daunorubicin; ADE, cytarabine, daunorubicin, etoposide; ADEP, cytarabine, daunorubicin, etoposide, valspodar; AML NOS, AML not otherwise specified; AutoSCT, autologous stem cell transplantation; AZ, diaziquone; BM, bone marrow; CR, complete remission; D, daunorubicin; DFS, disease-free survival from time of treatment for first diagnosis of recurrent translocation; E, etoposide; F, female; FAB, French-American-British classification; FLAG, fludarabine, cytarabine, filgrastim; Hb, hemoglobin; HIDAC, high-dose cytarabine; I, idarubicin; IDAC; intermediate-dose cytarabine; LAD, lymphadenopathy; LI, lintuzumab (humanized anti-CD33 antibody); M, male; mo, months; MX, mitoxantrone; MY, Mylotarg; NA, not applicable; NR, not reported; OS, overall survival from first diagnosis of AML; PB, peripheral blood; Plts, platelet count; R, primary resistant disease; RD, relapsed AML; Rx, therapy; S, splenomegaly; t-AML, therapy-related AML; WBC, white blood cell count.

[a] Age, karyotype, hematologic and clinical characteristics at the time of diagnosis of AML/MDS with the new recurrent translocation.

[b] Each case from the literature is denoted by the first author's name and year of publication of the study reporting them, followed by the case number.

[c] Response to therapy for AML/MDS with new recurrent translocation (see *footnote d*).

[d] Induction and post-remission therapy refer to initial treatment for patients with de novo AML/MDS or t-AML. For patients with relapsed AML, induction and post-remission therapy refer to treatment given at time of diagnosis of new recurrent translocation. The four- or five-digit number denotes a Cancer and Leukemia Group B study number a given patient was enrolled on as follows: 10105 (Gupta et al., 2006), 8525 (Mayer et al., 1994), 9720 (Baer et al., 2011), 9621 (Kolitz et al., 2004), 9222 (Moore et al., 2005), 10503 (Blum et al., 2010).

Table 2

Cytogenetics, Hematologic and Clinical Characteristics and Treatment Outcome of Patients with Reciprocal Translocations Hitherto Not Reported in AML or MDS[a]

Case no.	Age/Sex	Race	Karyotype	FAB	AML/MDS Type	Hb (g/ dL)	Plts ($\times 10^9$/L)	WBC ($\times 10^9$/L)	PB/BM blasts (%)	Auer rods (+/−)	Organ Involvement	Response[b]	DFS (mo)	OS (mo)	Induction Rx[c]	Post-CR Rx[c]
Common breakpoint: 3p25																
11	56/F	White	46,XX,**t(1;3)(p32;p25)**[37]	M4	de novo	5	153	23.8	50/72	-	No	CR	35.4	66.7+	ADx2 8525	HIDAC 8525
A similar translocation, described as t(1;3)(p32;p26), has been reported in a patient with ALL (Nagasaka et al., 1983). The constitutional nature of this abnormality could not be excluded.																
12	56/M	White	46,XY,**t(3;4)(p25;p16)**[4]/46,XY[18]	M0	de novo	8.1	384	2.9	1/47	-	No	R	NA	1.3	ADE 19808	NA
Common breakpoint: 4q24																
13	39/M	White	46,XY,**t(4;12)(q24;q12)**[16]/46,XY[4]	M4	de novo	11.3	184	3.1	41/22	-	No	CR	37.4	38.8	ADE 10503	AlloSCT
14	27/M	White	46,XY,**t(4;21)(q24;q22)**[2]/46,XY[18]	M1	de novo	9.5	17	114.2	88/90	-	No	DA	NA	1.3	ADEx2 10503	NA
Common breakpoint: 6p21																
15	84/M	White	46,XY,**t(1;6)(p33;p21)**[38]/46,XY[14]	UAL	t-AML	12.5	27	140	84/86	-	H	R	NA	0.6	A/L 8721	NA
16	55/M	White	47,XY,+21[6]/47,idem,**t(6;8)(p21;q24)**[5]/46,XY[9]	M1	de novo	7.9	86	2.8	17/83	-	LAD	R	NA	15.6+	CY/D/V/P/L 9311	NA
A similar translocation, described as t(6;8)(p12;q24), has been reported in accelerated phase CML (Offit et al., 1990).																
Common breakpoint: 8p21																
17	37/F	White	46,XX,**t(1;8)(q32;p21)**,t(11;14) (p15;q24)[16]/46,XX[3]	NA	RD	11.4	99	3.3	7/62	-	H	R	NA	10.3	DEC/VA	NA
The t(1;8) was acquired at the time of relapse. At diagnosis, the patient had de novo AML and a normal karyotype.																
18	60/M	White	47,XY,**t(8;12)(p21;q24.1)**,+10[7]/46,XY[13]	NA	RD	13.8	184	3.2	0/25	NR	NR	NR	NA	46+	AlloSCT	NA
The t(8;12) was acquired at the time of relapse. At diagnosis, the patient had de novo AML and a normal karyotype.																
Common breakpoint: 8q13																
19	75/M	White	47,XY,**t(5;8)(p13;q13)**,+10[15]/46,XY[5]	RA	de novo	10.4	72	2.7	0/2	NA	No	R	NA	9.7	Vatalanib ×2 10105	NA
20	57/F	White	46,XX,**t(8;11;18)(q13;p13;q21.1)**[6]/46,XX[16]	M1	de novo	9.1	28	0.7	8/62	NR	No	CR	11.8	19.5	ADE 10503	B/E, AutoSCT 10503
t(8;11;18)(q13;p13;q21.1) may represent a three-way variant of t(8;18), t(8;11) or t(11;18). The t(8;18)(q13;q21) has been reported in one case of AML-M5b (Yamamoto et al., 2007) and a t(8;11)(q13;p14) with similar, but not identical, breakpoints in one case of AML-M5a with concurrent t(9;11)(p22;q23) (Swansbury et al., 1998). No t(11;18) with similar breakpoints has been published (Mitelman et al., 2012).																
Common breakpoint: 8q22																
21	33/F	White	46,XX,**t(3;17;8)(p21;q25;q22)**[16]/46,XX[4]	M2	de novo	9.6	64	9.2	22/41	+	No	CR	169.7+	170.4+	AD 9222	HIDAC/ CY/E/AZ/MX 9222
t(3;17;8)(p21;q25;q22) may represent a three-way variant of t(8;17), t(3;17) or t(3;8). The t(8;17)(q22;q25) has been reported in one case of pediatric AML (Raimondi et al., 1999) and one case of CML in accelerated phase (Mashal et al., 1990). t(3;17)(p21;q25) has been reported in one case of CML in blastic phase (Sessarego et al 1987) and one case of pediatric ALL (Raimondi et al., 1992). No t(3;8) with similar breakpoints has been published (Mitelman et al., 2012).																
22	58/F	White	46,XX,**t(8;12)(q22;p11.2)**,t(8;14) (q24.1;q32)[17]/46,XX[8]	NA	RD	13.4	64	2.2	NR/26	NR	NR	R	NA	15.4	FLAG-I/MY	NA
The t(8;12) was acquired at the time of relapse. At diagnosis, the patient had de novo AML and a normal karyotype. Similar translocations, described as t(8;12)(q22;p12) (Mrózek et al., 2002) and t(8;12)(q22;p11-12) (Olopade et al., 1992) each being part of complex karyotypes, have been reported in patients with AML-M2 and AML-M6, respectively. This patient is also included in Table 1 (case 9) because she also harbors t(8;14)(q24.1;q32).																
23	28/F	White	46,XX,**t(8;20)(q22;p13)**[12]/46,XX[8]	M4	de novo	11.9	33	11.6	29/56	+	LAD	CR	134.1+	135.5+	ADx2 8221	A 8221
Cases with an identical translocation have been reported; however both were shown to be variants of t(8;21) with *RUNX1/RUNX1T1* gene fusion (Taviaux et al., 1999; Xue et al., 1997).																
Common breakpoint: 11p15																

Case no.	Age/Sex	Race	Karyotype	FAB	AML/MDS Type	Hb (g/ dL)	Plts (×10^9/L)	WBC (×10^9/L)	PB/BM blasts (%)	Auer rods (+/−)	Organ Involvement	Response[b]	DFS (mo)	OS (mo)	Induction Rx[c]	Post-CR Rx[c]
24	44/M	White	46,XY,**t(3;11)(p23;p15)**,del(16)(q22)[40]	M4	de novo	10.1	80	78.6	40/41	NR	No	CR	18.2	40.6	AI 9120	NR
A similar translocation, described as t(3;11)(p24;p15), has been reported in a patient with AML-M5a (Nebral et al., 2005). Karyotypically normal cells were detected in the patient's sample at the time of relapse.																
25	19/M	White	46,XY,**t(3;11)(p11;p15)**[31]	M4	de novo	10	79	108	40/56	+	No	CR	92+	92.9+	AD 9022	HIDAC/CY/E 9022
A similar translocation, described as t(3;11)(p12;p15), has been reported in a patient with T-ALL (Cauwelier et al., 2006). The acquired, non-constitutional nature of the translocation has been confirmed by a cytogenetically normal result of phytohemagglutinin-stimulated blood analysis.																
Common breakpoint: 13q14																
26	32/F	White	47,XX,**t(2;13)(p23;q14)**,+21[4]/46,XX[55]	M2	de novo	8.4	41	8.3	56/52	+	No	CR	13.9	16.1+	AD 8821	CY/E 8821
A similar translocation, described as t(2;13)(p21;q12), has been reported in a patient diagnosed with RAEB (Kiuru-Kuhlefelt et al., 1997), and t(2;13)(p21;q14.11) has been detected in a patient with AML-M6a (Poitras et al., 2011).																
27	41/M	White	47,XY,**t(5;13)(q15;q14)**,+mar[22]	M4	de novo	8.3	29	68	57/31	-	No	R	NA	4.3	ADEP 9621	NA
Karyotypically normal cells were detected in follow-up samples.																
Common breakpoint: 14q32																
28	54/M	White	46,XY,**t(3;14)(q25;q32)**[36]/46,XY[4]	AML NOS	de novo	9.6	282	40.4	92/NR	NR	No	R	NA	11.3	ADx2 8525	NA
A similar translocation, described as t(3;14)(q24;q32), has been reported in one ALL patient (Kristensen et al., 2003).																
29	55/M	White	46,XY,**t(8;14)(q11.2;q32)**[8]/46,XY[12]	M0	de novo	7.8	63	56.2	53/69	-	No	R	NA	4.1	ADE 9621	NA
t(8;14)(q11;q32) is a recurrent translocation in ALL (Mitelman et al., 2012), but hitherto has not been reported in AML. It has been reported as part of a complex karyotype detected in a patient with CML (Hu et al., 1990).																
Common breakpoint: 15q15																
30	33/F	White	46,XX,**t(2;15)(p11;q15) or t(2;15)(p1?3;q22)**[2]/46,XX[17]	M2	de novo	7.7	334	1.5	4/40	-	Skin/ LAD	CR	9	38	ADx2 8821	MX/AZ 8821
A translocation interpreted as t(2;15)(p1?3;q2?2) has been reported in a patient with AML-M4 (Steudel et al., 2003).																
31	55/M	White	46,XY,**t(3;15)(p21;q15)**[4]/45,XY,−20[3]/46,XY[12]	M4	de novo	10.4	59.0	40.1	54/71	+	No	CR	4.4	9.3	AD 8525	IDAC 8525
The t(3;15)(p21;q15) has also been reported to be acquired during blast crisis in a patient with CML (Anastasi et al., 1996) and in a patient with a chronic myeloproliferative disorder (Shearer et al., 2010). Additionally, t(3;15)(p21;q15) was detected in two pediatric patients with ALL, as a sole abnormality in one case and in addition to t(9;22)(q34;q11) in another (Heerema et al., 2002).																
32	59/M	White	46,XY,**t(7;15)(q32;q15)**,del(16) (q13q24)[8]/46,XY[17]	NA	RD	11	216	1.6	1/38	-	NR	R	NA	13.6	A	NA
The t(7;15) was acquired at the time of relapse. At diagnosis, the patient had de novo AML and the following karyotype: 91,XXYY,−3[3]/46,XY[17].																
33	39/M	White	46,XY,**t(11;15)(p15;q15)**[19]/46,XY[1]	M3	NR	10.5	52	7.5	55/89	+	NR	CR	69.7+	70.6+	AD/ATRA 9710	Arsenic, ATRA/D 9710
This patient had a submicroscopic rearrangement, an insertion of *PML* into the *RARA* gene resulting in *PML-RARA* gene fusion, which was confirmed using RT-PCR. Thus, the t(11;15) is likely an aberration secondary to the *PML-RARA* fusion. To our knowledge, there are no reported cases involving *NUP98* as a secondary aberration in APL. There is a reported case of AML-M4 with a similar translocation, t(11;15)(p15;q14) (Milton et al., 1984).																
34	75/M	White	46,XY,**t(15;15)(q15;q26)**[23]/46,XY[4]	M2	t-AML	8.6	135	2.5	4/40	-	No	CR	5.7	20.9+	ADE 9720	ADE 9720
A similar translocation, described as t(15;15)(q14;q26), has been reported in a patient with therapy-related AML (Olney et al., 2002).																
Common breakpoint: 17q11.2																
35	36/F	U	46,XX,**t(10;17)(p13;q11.2)**,add(13) (q34)[18]	M0	de novo	10	32	4.4	34/77	-	No	CR	47.6+	49.9+	ADEx2 10503	A/AlloSCT reduced intensity
Similar translocations, t(10;17)(p13;q12) and t(10;17)(p13;q12-21), have been described in two patients with AML-M0 (Laï et al., 1989), and t(10;17)(p13-15;q12-21) was found in AML-M1 (Oh et al., 2010). Only karyotypically normal cells were detected in a CR sample.																
36	38/M	Black	46,XY,**t(16;17)(q22;q11.2)**[13]/46,XY[7]	M6	de novo	7	54	5.7	50/29	+	No	R	NA	15.4+	ADx2 9022	NA
This case was previously reported as part of a series of patients with AML M6 (Davey et al., 1995).																
Common breakpoint: 17q21																

Case no.	Age/Sex	Race	Karyotype	FAB	AML/MDS Type	Hb (g/ dL)	Plts (×10^9/L)	WBC (×10^9/L)	PB/BM blasts (%)	Auer rods (+/−)	Organ Involvement	Response[b]	DFS (mo)	OS (mo)	Induction Rx[c]	Post-CR Rx[c]
37	48/M	White	46,XY,**t(3;17)(q24;q21)**[25]	M2	de novo	4.9	22	7.5	51/68	-	No	R	NA	16.6+	ADx2 8525	NA
Karyotypically normal cells were detected in follow-up samples.																
38	52/F	White	46,XX,add(7)(q21),**t(7;17)(p21;q21)**[21]	M2	de novo	9.2	101	21.9	8/33	-	H/S	CR	3.7	8.5	ADE 19808	HIDAC/E 19808
A similar translocation, described as t(7;17)(p22;q22), has been reported in a patient with T-ALL (Karst et al., 2006). Only karyotypically normal cells were detected in a CR sample, and there were karyotypically normal cells in the patient's sample at the time of relapse.																
39	63/M	White	46,XY,**t(11;20;17)(q13;q13.1;q21)** [10]/45,idem,-Y[12]/46,XY[3]	M5a	de novo	9	94	50.1	69/99	-	No	CR	2.7	5.2	ADE 9720	ADE 9720
t(11;20;17)(q13;q13.1;q21) may represent a three-way variant of t(11;20), t(20;17) or t(11;17). The t(11;17)(q13;q21) has been reported in a patient with AML-M2 (Yasar et al., 2010) and as a rare variant translocation in AML-M3 (Wells et al., 1996).																
Other breakpoints																
40	18/M	White	46,Y,**t(X;8)(p11.2;q11.2),t(11;13) (q12;q12)**[9]/46,XY[24]	M1	de novo	8.4	70	60.4	92/96	+	Gums	R	NA	3.4	ADx2 8525	NA
41	48/F	White	46,X,**t(X;10;10)(p11.2;p11.2;q13)**, del(12)(p12p13)[14]/46,XX[6]	M0	de novo	12.6	138	21.3	71/84	-	No	CR	10.3	13.6	ADE 10503	HIDAC
This case may represent a variant of a rare recurrent abnormality in AML t(X;10)(p11.2;p11.2) (Mitelman et al., 2012).																
42	55/M	White	46,Y,**t(X;12)(q2?4;q1?5)**[6]	M2	de novo	8.5	38	6.2	33/38	+	No	CR	23.8	78.7+	ADE 19808	HIDAC/E 19808
A similar translocation, described as t(X;12)(q24;q13), has been reported in one AML patient (Kerndrup & Kjeldsen, 2001). Karyotypically normal cells detected in the patient's sample at the time of relapse.																
43	44/F	White	46,XX,**t(1;4)(q42;q21)**[16]/46,XX[4]	M2	NR	10	67	110.8	85/61	+	No	CR	7.4	83.6	ADE 19808	B/E, AutoSCT 19808
A similar translocation, described as t(1;4)(q42;q22), has been reported in one ALL patient (Behm et al., 1992).																
44	57/F	White	47,XX,**t(1;9)(p2?2;p2?4)**,+8[3]/46,XX[1]	M5a	de novo	6.7	47	3.1	27/86	NR	H/S	CR	127.6+	128.6+	AD 8525	LDAC 8525
A similar translocation, described as t(1;9)(p22;p23), has been reported in a patient with CML at the time of relapse following an alloSCT (Shah et al., 1992).																
45	54/M	White	46,XY,**t(1;9;12)(q31;p22;q21)**[32]	M5a	de novo	11.7	28	53.1	88/94	-	LAD; S	CR	12.6	14	AD 9222	HIDAC/CY/E/AZ/MX 9222
The constitutional nature of this abnormality could not be excluded.																
46	53/F	White	46,XX,**t(1;19)(p12;q13.1)**[18]/46,XX[2]	M4	de novo	7.6	64	0.9	27/39	-	No	R	NA	6.5	ADEx2 19808	NA
A similar translocation, described as t(1;19)(p13;q13), has been reported in one patient with ALL-L1 (Riesch et al., 2001).																
47	45/F	White	46,XX,**t(2;3)(q33;q25)**[20]	M1	de novo	10.2	101	12.2	57/60	-	No	R	NA	24.3	ADEx2 9621	NA
The acquired, non-constitutional nature of the translocation has been confirmed by a cytogenetically normal result of phytohemagglutinin-stimulated blood analysis.																
48	66/M	White	46,XY,**t(4;14;8)(p16;q1?1.2;p21)**[37]	M2	de novo	10	80	52.5	26/80	-	No	DA	NA	.5	AD 8221	NA
The constitutional nature of this abnormality could not be excluded.																
49	75/F	White	46,XX,**t(5;21)(p13;q22)**[5]/46,XX[15]	M1	de novo	8.8	26	1.8	0/91	-	No	R	NA	5.5	ADE 9720	NA
50	55/F	White	46,XX,**t(7;12)(p13;q24.1)**[20]	M1	t-AML	9.2	52	46	67/82	+	No	CR	70+	70.9+	ADE 19808	B/E, AutoSCT 19808
A similar translocation, described as t(7;12)(p13;q23), has been reported in AML as part of a complex karyotype (Sierra et al., 2005). Only karyotypically normal cells were detected in a CR sample.																
51	51/M	White	46,XY,**t(7;19;12)(q11.2;q13.2;p11.2)**[18]/46,XY[2]	M1	de novo	8.5	169	18.8	56/80	-	No	CR	29.2+	30.1+	AD/MP 10603	HIDAC/ MP 10603; AlloSCT
52	52/F	White	46,XX,**t(7;22)(p15.3;q13)**[24]/46,XX[6]	M2	de novo	8.8	72	1.5	36/44	-	No	CR	72.2	79.9	AD 9022	HIDAC/CY/E/AZ/MX 9022
53	56/F	His-panic	46,XX,**t(8;14;16)(p11.2;q13;p13.1)**[17]/46,XX[3]	M4	de novo	8.6	32	64.6	56/77	-	No	R	NA	1.4	ADEPx2 9621	NA
This translocation may represent a three-way variant of the known recurrent translocation in AML t(8;16)(p11;p13) (Mitelman et al., 2012).																
54	34/M	White	46,XY,**t(9;10)(p13;p12)**,del(20) (q12q13.3)[17]/46,XY[3]	M5b	de novo	9.8	61	74.1	90/38	-	No	R	NA	4.8	ADE 19808	NA

Case no.	Age/Sex	Race	Karyotype	FAB	AML/MDS Type	Hb (g/ dL)	Plts ($\times 10^9$/L)	WBC ($\times 10^9$/L)	PB/BM blasts (%)	Auer rods (+/−)	Organ Involvement	Response[b]	DFS (mo)	OS (mo)	Induction Rx[c]	Post-CR Rx[c]
55	66/F	White	46,XX,**t(9;13)(q21.1;q33)**[23]	M2	de novo	11.9	33	4.6	14/31	-	No	DA	NA	.5	AD 8525	NA
This case was previously reported as part of a series of older AML patients (Farag et al., 2006). The constitutional nature of this abnormality could not be excluded.																
56	50/F	White	46,XX,**t(11;12)(q23;q12)**[3]/ 47,idem,+21[11]/46,XX[6]	M0	de novo	7.8	141	18.4	55/78	-	No	CR	90+	91+	ADE 19808	HIDAC/E 19808, AlloSCT
A similar translocation, described as t(11;12)(q23;q13), has been reported in two patients with AML-M4 (Hashii et al., 2004; Yagi et al., 2003), and in CML (Sun et al., 2011).																
57	50/F	White	46,XX,**t(11;12)(q24;q24.2)**[3]/46,XX[20]	M1	de novo	8.4	214	30.7	87/81	-	No	CR	67.2+	69.5+	ADEx2 19808	B/E, AutoSCT 19808
A similar translocation, described as t(11;12)(q23;q24), has been reported as a sole abnormality in AML-M0 (Cox et al., 2004) and as part of a complex karyotype in AML-M5a (Schoch et al., 2003). A translocation described as t(11;12)(q23-24;q24) has also been reported in ALL (Raimondi et al., 1989).																
58	68/M	White	46,XY,**t(11;19)(q21;q13)**[22]/45,idem,−17[3]/46,XY[5]	M2	de novo	12.9	368	4.1	45/71	+	No	CR	41.9	45.6	ADx2 8525	IDAC 8525
59	82/M	White	46,XY,**t(13;14)(q12;q24)**[cp14]/47,idem,+4[4]/46,XY[1]	M2	de novo	10.8	85	33.2	74/63	-	S	CR	20.3	34.1	ADx2 10201	HIDAC 10201
60	52/F	White	46,XX,**t(14;20)(q10;q10)**[16]/46,XX[4]	M0	de novo	9.2	130	2.4	63/70	-	No	R	NA	1	ADEPx2 19808	NA
61	65/F	White	46,XX,**t(16;18)(p11.2;q23)**[19]/46,XX[1]	M4	de novo	8.8	149	5.2	2/34	-	No	CR	37.8	40.1	AD 10201	HIDAC 10201

Abbreviations: x2, two cycles of induction therapy; A, cytarabine; AD, cytarabine, daunorubicin; ADE, cytarabine, daunorubicin, etoposide; ADEP, cytarabine, daunorubicin, etoposide, valspodar; AI, cytarabine, idarubicin; AlloSCT, allogeneic stem cell transplantation; AML NOS, AML not otherwise specified; ATRA, all-*trans*-retinoic acid; AutoSCT, autologous stem cell transplantation; AZ, diaziquone; B, busulfan; BM, bone marrow; CY, cytoxan; CR, complete remission; D, daunorubicin; DA, died aplastic; DEC, decitabine; DFS, disease-free survival; E, etoposide; F, female; FAB, French-American-British classification; FLAG, fludarabine, cytarabine, filgrastim; H, hepatomegaly; Hb, hemoglobin; HIDAC, high-dose cytarabine; HSM, hepatosplenomegaly; I, idarubicin; IDAC, intermediate-dose cytarabine; L, l-asparaginase; LAD, lymphadenopathy; LDAC, low-dose cytarabine; M, male; mo, months; MP, midostaurin or placebo; MX, mitoxantrone; MY, mylotarg; NA, not applicable; NR, not reported; OS, overall survival; P, prednisone; PB, peripheral blood; Plts, platelet count; R, primary resistant disease; RD, relapsed AML; S, splenomegaly; t-AML, therapy-related AML; UAL, unclassifiable acute leukemia; V, vincristine; VA, valproic acid; WBC, white blood cell count.

[a] Age, karyotype, hematologic and clinical characteristics are at the time of diagnosis of AML/MDS with the new recurrent translocation.

[b] Response to therapy for AML/MDS with new recurrent translocation (see *footnote c*).

[c] Induction and post-remission therapy refer to initial treatment for patients with de novo AML/MDS or t-AML. For patients with relapsed AML, induction and post-remission therapy refer to treatment given at time of diagnosis of new recurrent translocation. The four- or five-digit number denotes a Cancer and Leukemia Group B [or Southwest Oncology Group (SWOG) in one instance, as indicated] protocol number a given patient was enrolled on as follows: 8525 (Mayer et al., 1994), 19808 (Kolitz et al., 2010), 10503 (Blum et al., 2010), 8721, 9311 (Szatrowski et al., 2003), SWOG 0106 (Petersdorf et al., 2009), 10105 (Gupta et al., 2006), 9222 (Moore et al., 2005), 8221 (Mayer et al., 1987), 9120 (Cassileth et al., 1998), 9022 (Moore et al., 1997), 8821 (Schiffer et al., 1991), 9621 (Kolitz et al., 2004), 9710 (Powell et al., 2011), 9720 (Baer et al., 2011), 10603, 10201 (Marcucci et al., 2007).