Published in final edited form as:

Leuk Res. 2013 May ; 37(5): 552–555. doi:10.1016/j.leukres.2013.01.003.

Chromosome 5q deletion is extremely rare in patients with myelofibrosis

Koichi Takahashi^{1,4}, Jorge Cortes², Sherry Pierce², Lynne Abruzzo³, Hagop Kantarjian², and Srdan Verstovsek²

¹Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX

²Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX

³Department of Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX

⁴Department of Hematology and Oncology, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Abstract

Chromosome 5q deletion can be found in rare cases of myelofibrosis (MF) but the incidence, clinical significance and response to therapies are not well studied. We retrospectively reviewed charts of 939 patients with MF and identified 8 patients [0.8%] who carried 5q deletion. Of the 8, seven had complex cytogenetic abnormalities and one had additional clone with different cytogenetic abnormality. All 8 had significant three-lineage pancytopenia. Three patients took lenalidomide and one (patient with 5q-clone) achieved long-lasting hematologic response. Two patients responded to JAK2 inhibitor therapy. MF patients with 5q deletion often have complex karyotype and poor outcome.

Keywords

myelofibrosis; 5q deletion; lenalidomide

INTRODUCTION

Myelofibrosis (MF) is myeloproliferative neoplasm (MPN) characterized by cytopenia, extramedullary hematopoiesis with enlarged spleen and/or liver, megakaryocytic hyperplasia, reactive bone marrow fibrosis and various systemic symptoms. MF can present

© 2013 Published by Elsevier Ltd.

Corresponding Author: Srdan Verstovsek, M.D., Ph.D., Department of Leukemia, The University of Texas, MD Anderson Cancer Center, 1515 Holcombe Blvd. Unit 418, Houston, TX 77030, Phone: 713-745-3429, Fax: 713-794-4297, sverstov@mdanderson.org.

Conflict of Interest: Authors have no conflict of interest to disclose.

Author Contributions: KT designed the study, collected and analyzed the data, and wrote the manuscript, JC treated the patients, reviewed and approved the manuscript, SP collected the data. LA performed cytogenetic analysis, reviewed and approved the manuscript, and SV designed the study, treated the patients, analyzed the data and wrote and approved the manuscript.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

in a form of either primary myelofibrosis (PMF) or secondary MF developed after polycythemia vera (PV) or essential thrombocythosis (ET) (post-PV MF and post-ET MF, respectively). Natural history of MF is heterogeneous and significant inter-patient variability is observed in their survival. In order to better predict the disease course, several prognostic models have been developed for PMF such as International Prognostic Scoring System (IPSS) or dynamic IPSS (DIPSS).[1, 2] Cytogenetic abnormalities have also been recognized to be important factor to predict prognosis and refined version of DIPSS incorporates cytogenetic abnormalities, among other clinical factors (called DIPSS-plus).[3–5]

Chromosome 5q deletion is known to be associated with various myeloid malignancies. Its clinical significance is best studied in myelodysplastic syndromes (MDS) where impressive response has been observed to lenalidomide therapy.[6] Pathophysiologic mechanism of MDS with 5q deletion has been studied and several responsible genes that are located within the commonly deleted region (CDR) of 5q31 and 5q32 have been identified, such as *RPS14*, *SPARC*, *CTNNA1*, and *EGR-1*. [7–11] Upregulation of *SPARC* was observed in lenalidomide treated erythroblasts and its role in the response to lenalidomide therapy is being speculated. [12]

In contrast to MDS, 5q deletion is rare in MF. Limited number of reports described its incidence, patients' clinical features and their outcome. Herein, we report the incidence and clinical characteristics of patients with MF, primary or secondary, with 5q deletion seen at MD Anderson Cancer Center (MDACC) during the last decade.

METHODS

We retrospectively reviewed charts, based on the IRB approved protocol, of 939 consecutive patients with MF who were referred to MDACC between 2000 and 2010. Diagnosis of MF was based on the World Health Organization and included both primary MF and post-PV/post-ET MF.[13] Laboratory data that was obtained at the time of referral to MDACC was reviewed. Cytogenetic analyses were conducted in the Clinical Cytogenetics Laboratory at MDACC by a dedicated cytogeneticist (LA). Cytogenetic analyses were conducted on unstimulated bone marrow cells after culture (24–72 hours), and G-banding analysis was performed according to standard techniques. The ISCN 2005 criteria were used for identification of abnormal clones.[14] When possible, at least 20 metaphases were analyzed for each case. Karyotypes were defined as complex when they included three or more chromosomal abnormalities. For mutation analyses, genomic DNA from bone marrow samples was isolated using the Autopure extractor (QIAGEN/Gentra, Valencia, CA). Detection of JAK2 V617F and MPL W515L point mutations were performed as previously reported.[15, 16] Overall survival (OS) was defined as the time interval between initial diagnosis date and date of death, or date of last follow up, whichever occurred first. Survival difference was compared between 2 groups by log-rank test. All statistical analyses were conducted by IBM SPSS Statistics version19 (IBM, Armonk, NY).

RESULTS

Among 939 patients with MF seen at MDACC between 2000 and 2010, 8 patients (0.8%) carried 5q deletion abnormality. Clinical characteristics of each patient are summarized in Table 1. Median age at time of diagnosis was 53 (range, 34–76) and there was no dominance by sex. Five patients had PMF, two had post-ET MF, and one had post-PV MF. Median white blood cell count (WBC), hemoglobin (Hb) and platelet count (Plt) at time of referral to MD Anderson were 2.9 ($\times 10^3/\mu\text{L}$) (range, 1.3–14.1), 9.6 (g/dL) (range, 6.4–11.9), and 46 ($\times 10^3/\mu\text{L}$) (range, 9–267), respectively. At the time of referral, one patient was taking hydroxyurea and the other patient was receiving erythropoietin injection; rests of the patients were not taking any treatment for MF. Median bone marrow cellularity was 80 % (range; 20–100) and median initial bone marrow blast cell counts was 1.5 % (range; 0–12). Two patients had bone marrow fibrosis grade evaluated according to the current European consensus and both had MF-2 grade.[17] Fibrosis grading was evaluated by 4-score grading system (1+ to 4+) in six patients and three had 4+, two had 3+ and one had 2+ score. DIPSS-Plus was calculated in five patients with PMF; two patients were high risk and other three were intermediate-2 risk. In seven patients, 5q deletion was associated with other complex cytogenetic abnormalities, while one patient had additional clone with different cytogenetic abnormality (i.e. none of the patient had 5q deletion as a sole abnormality). Deletion of 5q13q33 was the most commonly deleted region (N=5), one patient had 5q22q31 and the other patient had 5q22q35 deletion. Three patients had co-abnormalities of 7q deletion or monosomy 7; other three patients had 20q deletion. After median follow up of 70 months, six patients have died, with median overall survival (OS) of 46 months (range, 6–468), while median OS of non-del 5q counterpart was 72 months (range, 1–395) ($P = 0.37$). Among patients that died, two transformed to acute myeloid leukemia (AML). Three patients took lenalidomide during their course of treatment (patients 1, 4, and 7). Response to lenalidomide (10mg daily) was observed in one patient only (patient 4), with a symptomatic improvement (manifested by improvement of fatigue and weight gain) as well as hematologic response (normalization of the blood cell count). Interestingly, bone marrow biopsy taken 5 months from the start of the therapy showed improvement in fibrosis (from 4+ to MF-1). The response is ongoing for 3 years and patient is still taking lenalidomide 5mg oral daily at present, although she did not achieve cytogenetic response and 5q deletion abnormality has been persistently detected in serial bone marrow analyses. One patient underwent stem cell transplant and achieved complete remission but died approximately 1 year after the transplant from unknown cause. Two patients (patients 7 and 8) received JAK2 inhibitor therapy and both experienced good response. Patient 7 received CEP-701 and had both clinical and hematologic response for more than 2 years, when she died from infectious complication. Response to the CEP-701 in patient 7 is detailed elsewhere.[18] Patient 8 was treated with ruxolitinib and had improvement in her splenomegaly and experiencing better quality of life, which is now ongoing for 4 years.[19, 20] Both patients treated by JAK2 inhibitor had persistent chromosomal abnormalities with 5q deletion.

DISCUSSION

Chromosome 5q deletion is extremely rare in patients with MF; only 0.8% of patients were found to carry the abnormality. We did not find a single patient, among close to a thousand,

with sole abnormality in 5q deletion. Only one patient (patient 4) had a clone with 5q deletion, but with a presence of another clone in the sample, with different cytogenetic abnormality. Seven additional patients had 5q deletion associated with a complex changes. Since our 8 patients with 5q deletion had advance disease features, such as anemia, thrombocytopenia, transfusion dependency and constitutional symptoms, their median overall survival of about 4 years was as expected. This is consistent with reported survival estimate by DIPSS-plus risk assessment tool for patient with MF.[5] Statistically significant difference was not observed in overall survival between patients with 5q deletion and non-5q deleted patients, likely due to very large 95% confidence interval of median survival in 5q deletion group (0–149).

Retrospective case review of 5q deletion-associated MPN was reported by Santana-Davila et al. from Mayo Clinic.[21, 22] According to the report, 23 cases of 5q deletion-associated MPN (of which 14 [61%] were PMF and 1 [4%] was post-ET MF), were significantly more anemic and thrombocytopenic, while survival was not different from non-5q deletion counterpart. Among 14 patients with PMF having 5q deletion, only two patients were found to carry 5q deletion as a sole abnormality. However, median survival of our patients with 5q deletion-associated MF were shorter than that reported by Mayo Clinic (46 vs. 143 months), but in accordance to patients' DIPSS-plus risk score. Both ours and the Mayo clinic's report are very small in patient numbers and the discrepancy in survival could be from sample variance.

Classically, cytogenetic abnormality was not incorporated into prognostic model of PMF due to difficulty in obtaining good sample for cytogenetic analysis, so the information has not been readily available. However, reports from ours and other groups have uncovered the prognostic impact of certain cytogenetic abnormalities in PMF,[4, 23–26] which ultimately led to a recent refinement of DIPSS to DIPSS-plus that incorporated cytogenetic abnormality as a scoring factor.[5] Chromosome 5q deletion or complex cytogenetic abnormalities are considered to be poor prognosis in DIPSS-plus. However, it is still uncertain whether deletion 5q per se portends poor prognosis in MF patients. As manifested in current study, deletion 5q is extremely rare in MF patients. Thereby, previous studies that investigated prognostic impact of cytogenetic result in MF have evaluated deletion 5q/-5 together with other abnormalities such as deletion 7q/-7, making it difficult to evaluate exact prognostic value of deletion 5q by itself.[4, 23, 24, 26] It is very likely that poor prognosis in our cohort was mainly driven by complex cytogenetics rather than deletion 5q itself.

Tefferi et al. reported three cases of 5q deletion-associated MF(of which two patients had 5q deletion as a sole abnormality) who also carried JAK2V617F mutation that experienced impressive response to lenalidomide.[27] One patient, who had 5q13q33 as a sole cytogenetic abnormality, experienced both hematologic and marrow complete remission as well as cytogenetic remission. In addition, the same patient also had reduction in spleen size and elimination of JAK2 V617F clones after lenalidomide therapy. The other two patients also had hematologic response and partial marrow response but did not achieve cytogenetic remission. However, in both patients, spleen size was reduced and JAK2 V617F allele burden decreased. In our separate report, a decrease in JAK2V617F allelic burden was also

seen in small number of MF patients (without 5q deletion) treated with lenalidomide alone long-term.[28]

Response to lenalidomide is most impressive in MDS patients with isolated 5q deletion. In our analysis, none of the patients had 5q deletion as a sole abnormality and seven out of eight patients carried complex karyotype. Indeed, the patient who had good response to lenalidomide (patient 4) was the only patient who did not carry complex karyotype. Therefore, what can be derived from both Mayo Clinic's and MDACC's limited experience so far is that lenalidomide may benefit MF patients with 5q deletion when karyotype shows either isolated 5q deletion or non-complex type. Certainly, the use of lenalidomide should not be restricted only to MF patients with deletion 5q, as previous phase 2 study of lenalidomide in unselected patients with MF showed benefit in patients without 5q deletion. [29] Notably, in our analysis, two patients had long-term clinical and hematologic response to JAK2 inhibitors. Given the high risk nature of 5q deletion and complex karyotype in MF, it is encouraging to know that JAK2 inhibitors has shown efficacy in some cases.

In summary, chromosome 5q deletion was observed in rare cases of MF (0.8%), most of which (7/8) carried complex karyotype with advanced features and poor outcome. However, it is reasonable to consider lenalidomide as a therapy for patients with 5q deletion as a sole abnormality.

References

1. Cervantes F, Dupriez B, Pereira A, Passamonti F, Reilly JT, Morra E, et al. New prognostic scoring system for primary myelofibrosis based on a study of the International Working Group for Myelofibrosis Research and Treatment. *Blood*. 2009; 113:2895–901. [PubMed: 18988864]
2. Passamonti F, Cervantes F, Vannucchi AM, Morra E, Rumi E, Pereira A, et al. A dynamic prognostic model to predict survival in primary myelofibrosis: a study by the IWG-MRT (International Working Group for Myeloproliferative Neoplasms Research and Treatment). *Blood*. 2010; 115:1703–8. [PubMed: 20008785]
3. Reilly JT, Snowden JA, Spearing RL, Fitzgerald PM, Jones N, Watmore A, et al. Cytogenetic abnormalities and their prognostic significance in idiopathic myelofibrosis: a study of 106 cases. *Br J Haematol*. 1997; 98:96–102. [PubMed: 9233570]
4. Tam CS, Abruzzo LV, Lin KI, Cortes J, Lynn A, Keating MJ, et al. The role of cytogenetic abnormalities as a prognostic marker in primary myelofibrosis: applicability at the time of diagnosis and later during disease course. *Blood*. 2009; 113:4171–8. [PubMed: 19131547]
5. Gangat N, Caramazza D, Vaidya R, George G, Begna K, Schwager S, et al. DIPSS plus: a refined Dynamic International Prognostic Scoring System for primary myelofibrosis that incorporates prognostic information from karyotype, platelet count, and transfusion status. *J Clin Oncol*. 2011; 29:392–7. [PubMed: 21149668]
6. List A, Dewald G, Bennett J, Giagounidis A, Raza A, Feldman E, et al. Lenalidomide in the myelodysplastic syndrome with chromosome 5q deletion. *N Engl J Med*. 2006; 355:1456–65. [PubMed: 17021321]
7. Lehmann S, O'Kelly J, Raynaud S, Funk SE, Sage EH, Koeffler HP. Common deleted genes in the 5q- syndrome: thrombocytopenia and reduced erythroid colony formation in SPARC null mice. *Leukemia*. 2007; 21:1931–6. [PubMed: 17625608]
8. Liu TX, Becker MW, Jelinek J, Wu WS, Deng M, Mikhalkovich N, et al. Chromosome 5q deletion and epigenetic suppression of the gene encoding alpha-catenin (CTNNA1) in myeloid cell transformation. *Nat Med*. 2007; 13:78–83. [PubMed: 17159988]
9. Ebert BL, Pretz J, Bosco J, Chang CY, Tamayo P, Galili N, et al. Identification of RPS14 as a 5q-syndrome gene by RNA interference screen. *Nature*. 2008; 451:335–9. [PubMed: 18202658]

10. Boultonwood J, Fidler C, Strickson AJ, Watkins F, Gama S, Kearney L, et al. Narrowing and genomic annotation of the commonly deleted region of the 5q- syndrome. *Blood*. 2002; 99:4638–41. [PubMed: 12036901]
11. Joslin JM, Fernald AA, Tennant TR, Davis EM, Kogan SC, Anastasi J, et al. Haploinsufficiency of EGR1, a candidate gene in the del(5q), leads to the development of myeloid disorders. *Blood*. 2007; 110:719–26. [PubMed: 17420284]
12. Pellagatti A, Jadersten M, Forsblom AM, Cattani H, Christensson B, Emanuelsson EK, et al. Lenalidomide inhibits the malignant clone and up-regulates the SPARC gene mapping to the commonly deleted region in 5q- syndrome patients. *Proc Natl Acad Sci U S A*. 2007; 104:11406–11. [PubMed: 17576924]
13. Vardiman JW, Harris NL, Brunning RD. The World Health Organization (WHO) classification of the myeloid neoplasms. *Blood*. 2002; 100:2292–302. [PubMed: 12239137]
14. Shaffer, L.; Tommerup, N. *ISCN 2005: an international system for human cytogenetic nomenclature*. Basel: S. Karger; 2005.
15. McClure R, Mai M, Lasho T. Validation of two clinically useful assays for evaluation of JAK2 V617F mutation in chronic myeloproliferative disorders. *Leukemia*. 2006; 20:168–71. [PubMed: 16270039]
16. Pardanani AD, Levine RL, Lasho T, Pikman Y, Mesa RA, Wadleigh M, et al. MPL515 mutations in myeloproliferative and other myeloid disorders: a study of 1182 patients. *Blood*. 2006; 108:3472–6. [PubMed: 16868251]
17. Thiele J, Kvasnicka HM, Facchetti F, Franco V, van der Walt J, Orazi A. European consensus on grading bone marrow fibrosis and assessment of cellularity. *Haematologica*. 2005; 90:1128–32. [PubMed: 16079113]
18. Santos FP, Kantarjian HM, Jain N, Manshouri T, Thomas DA, Garcia-Manero G, et al. Phase 2 study of CEP-701, an orally available JAK2 inhibitor, in patients with primary or post-polycythemia vera/essential thrombocythemia myelofibrosis. *Blood*. 2010; 115:1131–6. [PubMed: 20008298]
19. Verstovsek S, Mesa RA, Gotlib J, Levy RS, Gupta V, DiPersio JF, et al. A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis. *N Engl J Med*. 2012; 366:799–807. [PubMed: 22375971]
20. Verstovsek S, Kantarjian H, Mesa RA, Pardanani AD, Cortes-Franco J, Thomas DA, et al. Safety and efficacy of INCB018424, a JAK1 and JAK2 inhibitor, in myelofibrosis. *N Engl J Med*. 2010; 363:1117–27. [PubMed: 20843246]
21. Santana-Davila R, Tefferi A, Holtan SG, Ketterling RP, Dewald GW, Knudson RA, et al. Primary myelofibrosis is the most frequent myeloproliferative neoplasm associated with del(5q): clinicopathologic comparison of del(5q)-positive and -negative cases. *Leuk Res*. 2008; 32:1927–30. [PubMed: 18538839]
22. Santana-Davila R, Holtan SG, Dewald GW, Ketterling RP, Knudson RA, Hanson CA, et al. Chromosome 5q deletion: specific diagnoses and cytogenetic details among 358 consecutive cases from a single institution. *Leuk Res*. 2008; 32:407–11. [PubMed: 17707907]
23. Hussein K, Pardanani AD, Van Dyke DL, Hanson CA, Tefferi A. International Prognostic Scoring System-independent cytogenetic risk categorization in primary myelofibrosis. *Blood*. 2010; 115:496–9. [PubMed: 19901264]
24. Hidaka T, Shide K, Shimoda H, Kameda T, Toyama K, Katayose K, et al. The impact of cytogenetic abnormalities on the prognosis of primary myelofibrosis: a prospective survey of 202 cases in Japan. *Eur J Haematol*. 2009; 83:328–33. [PubMed: 19549278]
25. Dingli D, Schwager SM, Mesa RA, Li CY, Dewald GW, Tefferi A. Presence of unfavorable cytogenetic abnormalities is the strongest predictor of poor survival in secondary myelofibrosis. *Cancer*. 2006; 106:1985–9. [PubMed: 16568439]
26. Caramazza D, Begna KH, Gangat N, Vaidya R, Siragusa S, Van Dyke DL, et al. Refined cytogenetic-risk categorization for overall and leukemia-free survival in primary myelofibrosis: a single center study of 433 patients. *Leukemia*. 2011; 25:82–8. [PubMed: 20944670]

27. Tefferi A, Lasho TL, Mesa RA, Pardanani A, Ketterling RP, Hanson CA. Lenalidomide therapy in del(5)(q31)-associated myelofibrosis: cytogenetic and JAK2V617F molecular remissions. *Leukemia*. 2007; 21:1827–8. [PubMed: 17460705]
28. Quintas-Cardama A, Kantarjian HM, Manshouri T, Thomas D, Cortes J, Ravandi F, et al. Lenalidomide plus prednisone results in durable clinical, histopathologic, and molecular responses in patients with myelofibrosis. *J Clin Oncol*. 2009; 27:4760–6. [PubMed: 19720904]
29. Tefferi A, Cortes J, Verstovsek S, Mesa RA, Thomas D, Lasho TL, et al. Lenalidomide therapy in myelofibrosis with myeloid metaplasia. *Blood*. 2006; 108:1158–64. [PubMed: 16609064]

Table 1

Clinical Summary of 8 cases with MF having 5q deletion

Pt	Age/Sex	Dx	Cytogenetic	Time from Dx to relapse (month)	DIPSS Plus	WBC	Hb	Plt	BM BL	BM FG, [†]	JAK2/MPL	Status	Brief comment of the case
1	61M	PMF	46,XY,del(5)(q13q33),t(6;9)(q21;q22)[17];47,XY,del(7)(q22b34),+8,-18,del(20)(q11.2q13.3),+21,add(21)(1)	99	High	2.9	7	57	1	MF-2	-/-	Dead	Refractory to multiple lines of treatment including, erythropoietin, thalidomide, danazole, 5-azacitidine, and lenalidomide
2	50M	PMF	46,XY,del(1)(p34),del(5)(q13q33) [inv(7)(p13p22),del(20)(q11.2)(10);der(7)inv(7)(p13p22add7)(q36),del20q11.2[7]	2	Int-2	1.5	10.6	25	2	2+	UK/UK	Dead	No response to Thalidomide. Underwent successful SCT but died after a year from unknown cause.
3	52F	PMF	45-50,XY,-2,del(2)(p14),-3,del(3)(p13),add(4)(q35),del(5)(q22q31),-6,-7,del(11)(p11.2),-13,-17,+4,-7mar,ring[cp10]	7	High	2.9	8.8	9	1	3+	UK/UK	Dead	Transformed to AML 1 year after diagnosis. Did not receive treatment for leukemia and died.
4	54F	Post-ET MF	46,XX,t(1;12)(q32;q15)[10];46,ide m,del(5)(q13q33[2]	78	NA	5.1	10.9	159	0	3+	-/+	Alive	No response to Thalidomide, then acquired 5q deletion. Started on Lenalidomide and having good clinical and hematological response.
5	48M	PMF	46,XY (6)/39-44,XY,del(5)(q13q33),-13,der(13;15)(q10q10),-15,-16,-17,-17,-18,+1-5mar[cp14]	0	Int-2	1.3	10.3	35	3	4+	UK/UK	Dead	Did not tolerate peg-interferon, transformed to AML 1 year after diagnosis Did not receive further therapy due to poor performance status.
6	76M	Post-ET MF	46,XY,del(5)(q13q33),-9,add(17)(p13),der(17;18)(q10;q10),-21[+44,-mar[4];44-45,+1,-2mar[cp21];46,XY[14]	43	NA	14.1	8.6	287	12	MF-2	+/UK	Dead	Started on Hydroxyurea Enrolled in Ponalkdomide trial but stopped after 3 months because of unrelated complication
7	34F	Post-PV MF	46,XX,del(6)(q21q33[7];46,X,del (8)(q22q28)[6];46,XX,add(3)(q27),del(3)(q21q26.2),del(5)(q31q35),del(6)(p21.1p23),add(20)(q13.2)[2];46,XX,del(2)(p11.2p25)[1];46, XY[4]	453	NA	1.4	6.4	16	2	4+	+/UK	Dead	Progressed after Cloramibucil, hydroxyurea and thalidomide. Experienced dramatic improvement of anemia, neutropenia, thrombocytopenia after enrolled in CEP-701 trial. Splenomegaly improved. Died with sepsis.
8	50F	PMF	del(5)(q22q35)[45-46,XX[cp2]66,XXX,-1,-2,+3,-5,+6,-7,+8,+9,-10,-11,+12,-17,-18,-20,-21,+2[11];46,XX[17]	46	Int-2	5.4	11.9	168	1	4+	+/UK	Alive	Excellent response to INCB48424 with improvement of cytopenia and splenomegaly.

* Months from original diagnosis til cytogenetic analysis at our institution.

[†] Bone marrow fibrosis grade is based on European Consensus[17] in 2 patients and rest were graded with 4 grading system(1+–4+).

Pt = Patient; Dx = Diganosis; WBC = White Blood Cell count; Hb = Hemoglobin; Plt = Platelet; BM BL = Bone Marrow Blast; JAK2 = JAK2 V617F mutation; MPL = MPL 515 mutation; SCT = Stem Cell Transplant; Trans = Transformation to AML; M = Male; F = Female; PMF = Primary Myelofibrosis; ET = Essential Thrombocytosis; PV = Polycythemia Vera; NA = Not Applicable; UK = Unknown