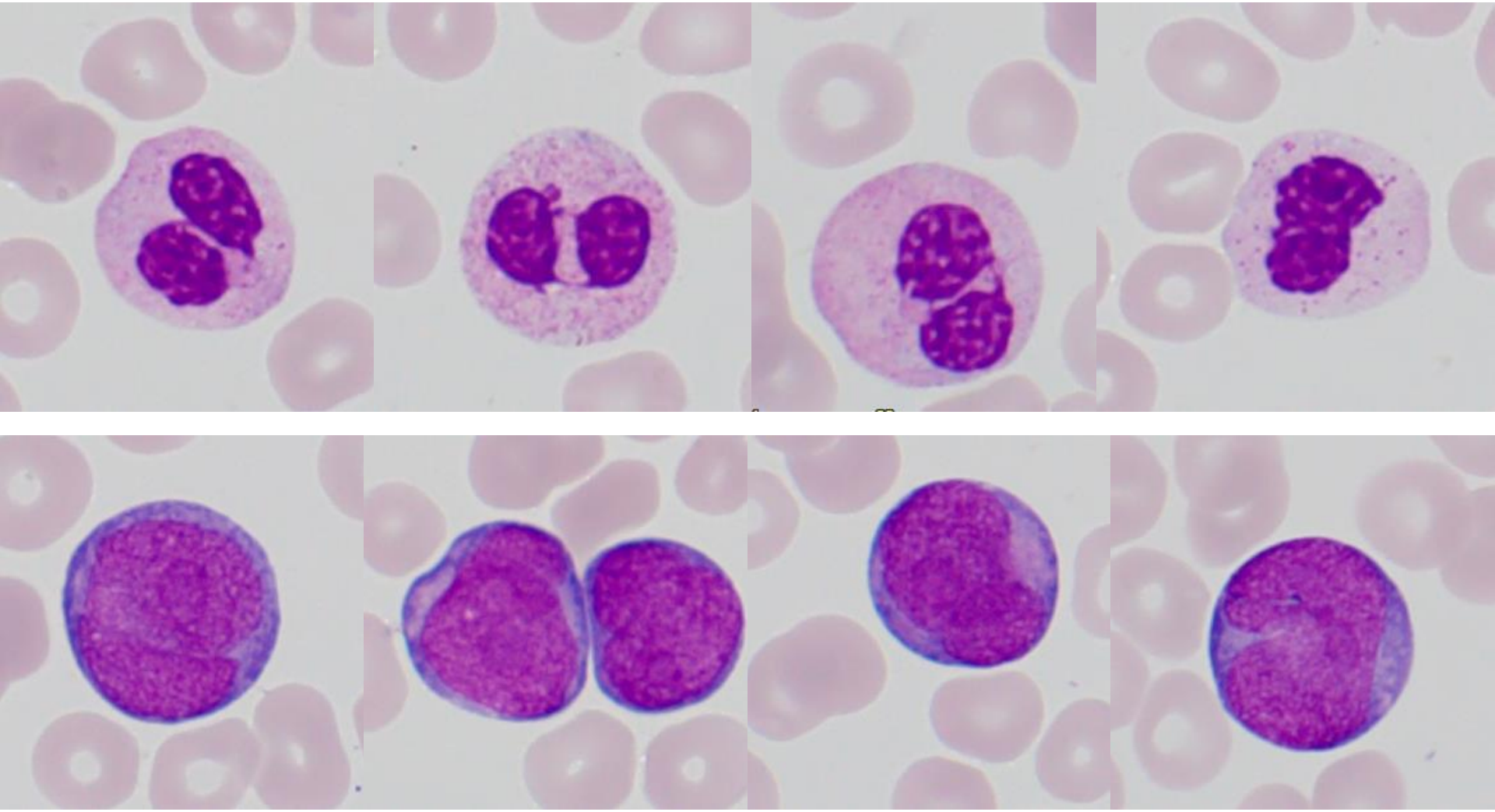
M. V, 77 ans

Bénédicte Ribourtout
CHU d'Angers
17/10/2017

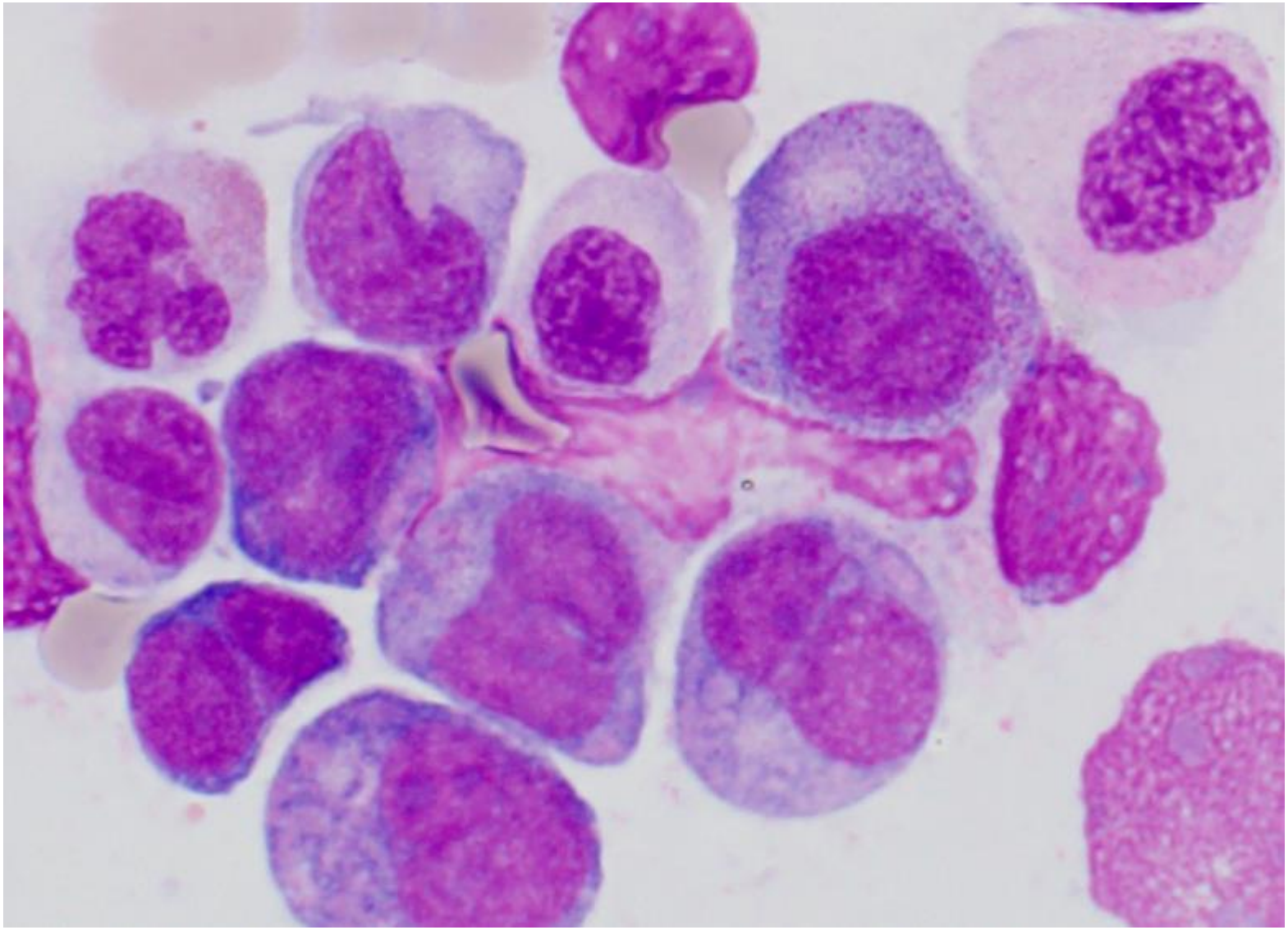
Présentation

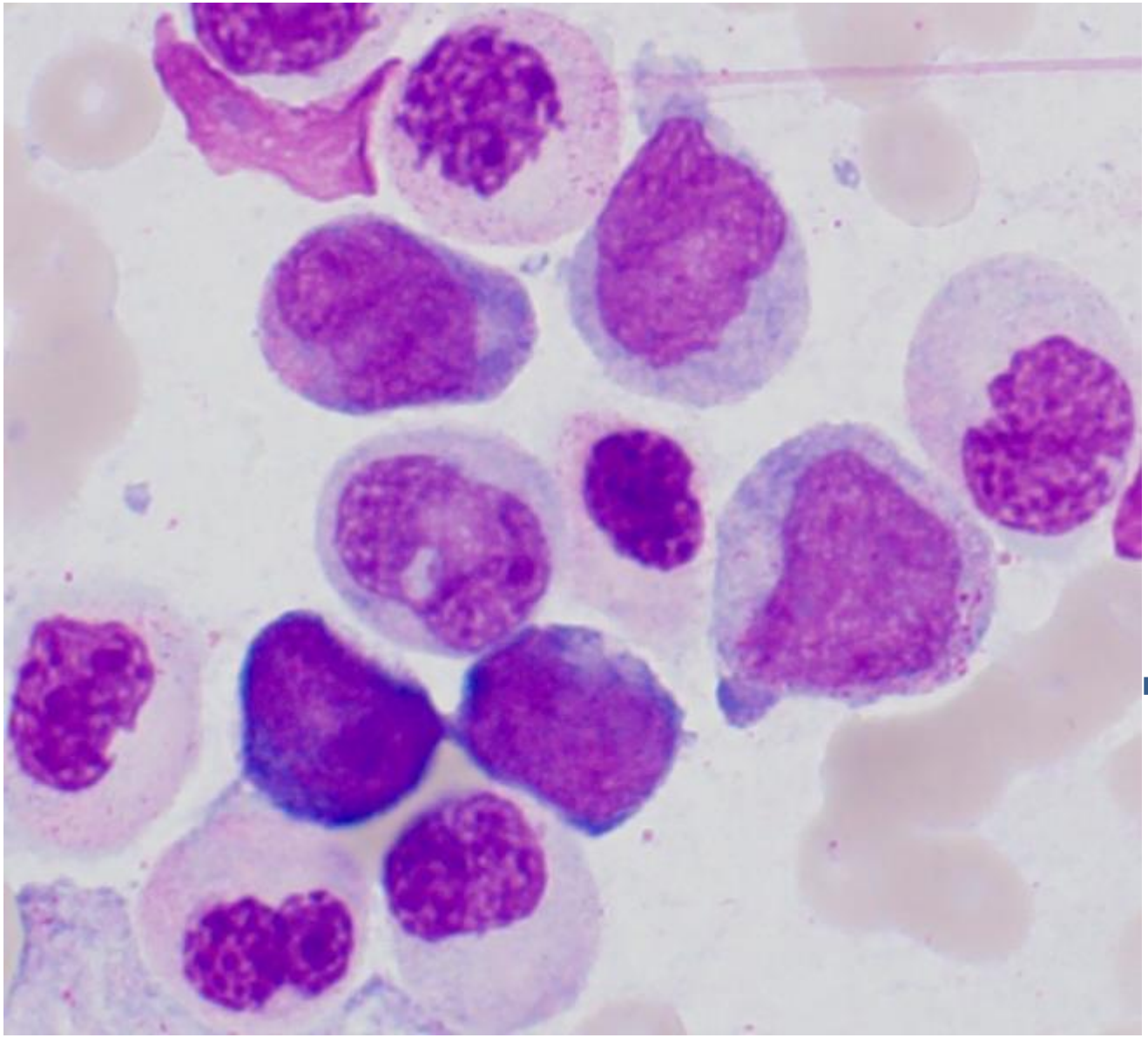
- Homme de 77ans
- AEG, perte de 6 kg
- Examen clinique : pas de sd tumoral (pas de splénomégalie)
- ATCD :
  - pas d'ATCD de néoplasie
  - thrombose veineuse superficielle du membre inférieur gauche sans contexte particulier 2013
- Hémogramme du 11/08/2016 : GB 35,4 G/L, Hb 9,7 g/dL, VGM 94.8 fL, plaquettes 10 G/L, PNN 11,04 G/L, monocytes 2,62 G/L, blastes 36,6%

Frottis sanguin



Myélogramme





- 39% de blastes
- Dysgranulopoïèse majeure (aspect pseudo-Pelger, condensation anormale de la chromatine
- De rares blastes présentaient un corps d'Auer

⇒ Aspect de LAM avec maturation, associée à une dysplasie granulocytaire majeure

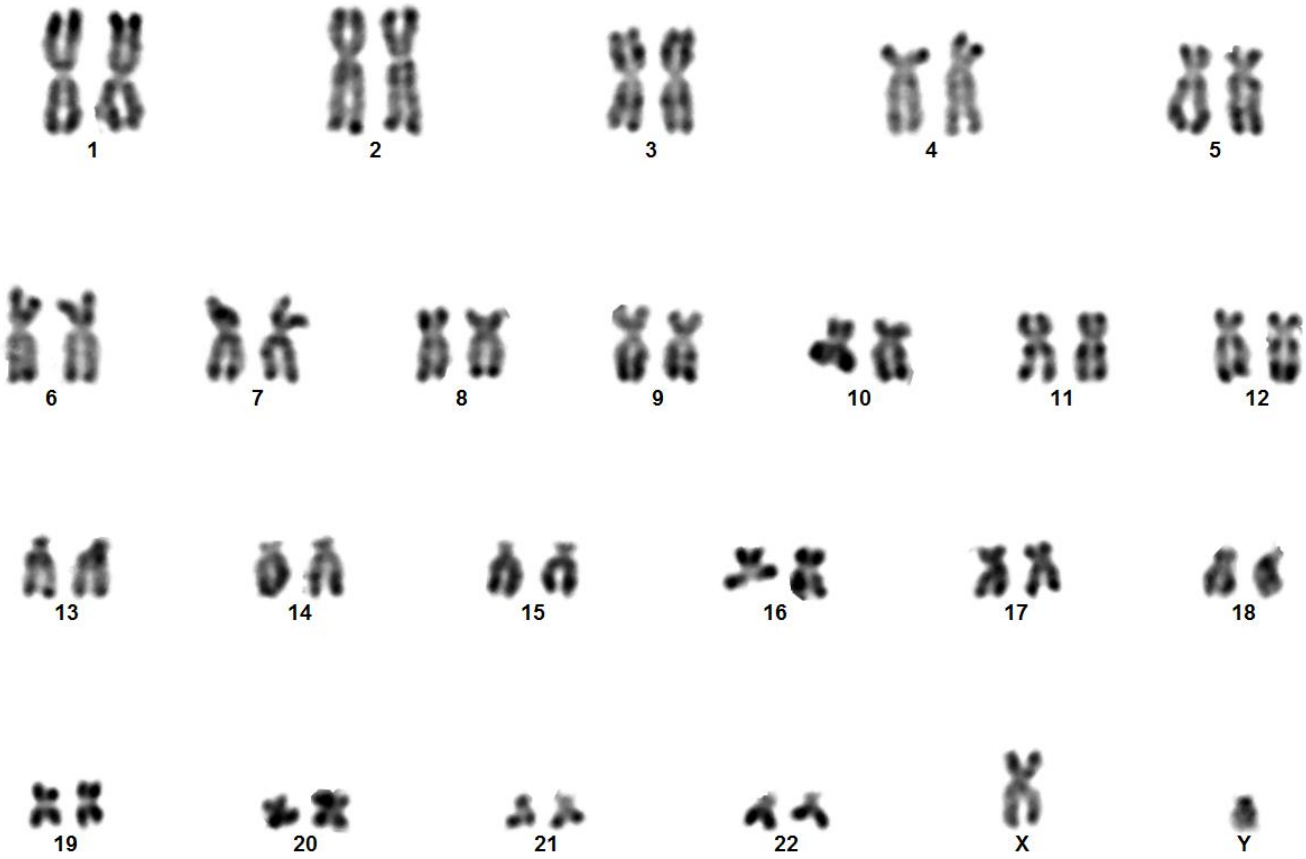
Examens complémentaires

- Immunophénotypage

CD13+ CD33+ CD117+ MPO+ CD2- CD19-

- Caryotype

46,XY[20]



RCP : Décision d'un traitement par Vidaza

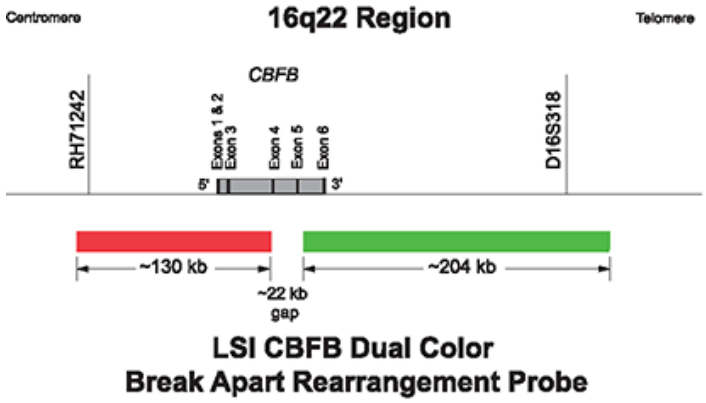
Octobre 2016 : résultats de techniques de haut débit (P. Guardiola)

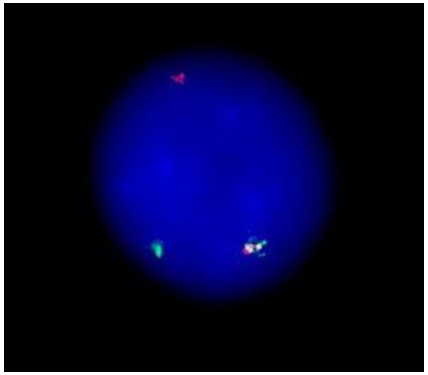
- Mise en évidence d'un transcrit CBFB-MYH11
  - Non retrouvé par la technique de biologie moléculaire utilisée en routine (Primers Biomed 1, van Dongen JJM. Leukemia 1999)

centromère télomère

Exon 1 Exon 4 Exon 35 Exon 43

- Confirmé par FISH interphasique faite a posteriori (sonde CBFB, break apart Abbott 05N44-020) et par biologie moléculaire





Octobre 2016 : résultats de techniques de haut débit (P. Guardiola)

- Mise en évidence d'une mutation JAK2
- Confirmée en BM conventionnelle (leucocytes totaux : quantification : 51,4%)

Discussion

- Cytologie et LAM avec inversion du chromosome 16 ou t(16;16)
- LAM et mutation JAK2

LAM avec inv(16) ou t(16;16) : présentation cytologique

Table 2. Clinical and cytogenetic characteristics and *KIT* mutation status according to *CBFB-MYH11* fusion type in 208 patients with de novo AML and inv(16)/t(16;16)

Characteristic	Non–type A fusion* (n = 26)	Type A fusion (n = 182)	*P*
Age, y			.75
Median	41	41	
Range	22-62	17-74	
Sex, no. of males (%)	14 (54)	113 (62)	.52
Race, no. (%)			.56
White	20 (77)	149 (82)	
Nonwhite	6 (23)	33 (18)	
Hemoglobin, g/dL			.42
Median	8.9	8.8	
Range	6.6-13.0	3.1-14.8	
Platelet count, × 10⁹/L			.33
Median	46	42	
Range	15-208	7-272	
WBC, × 10⁹/L			.007
Median	21.9	33.8	
Range	1.4-87.2	0.4-500.0	
Percentage of blood blasts			.26
Median	43	52	
Range	3-93	0-97	
Percentage of BM blasts			.59
Median	53	58	
Range	22-93	2-89	
FAB (centrally reviewed), no. (%)			.04
M1	3 (14)	2 (1)	
M2	0 (0)	8 (5)	
M4	4 (19)	21 (14)	
M4Eo	14 (67)	121 (78)	
M5	0 (0)	3 (2)	
Cytogenetic characteristics‡			
sole inv(16)/t(16;16), no. (%)	10 (42)	114 (63)	.07
+8, no. (%)	7 (29)	18 (10)	.01
+13, no. (%)	2 (8)	3 (2)	.11
+21, no. (%)	6 (25)	1 (1)	< .001
+22, no. (%)	0 (0)	35 (19)	.02
***KIT*, no. (%)§**			.002
Mutated	0 (0)	48 (27)	
Wild-type	24 (100)	130 (73)	

FAB indicates French-American-British classification; and WBC, white blood count.

*Type E (n = 18), type D (n = 6), type I (n = 2).

‡Patients may have multiple secondary abnormalities and thus can be classified in more than 1 category; 3 patient samples had no mitoses.

Schwind et al, Blood 2013

Original Research

Morphologic and Molecular Characteristics of De Novo AML With *JAK2* V617F Mutation

Juliana E. Hidalgo-López, MD[a]; Rashmi Kanagal-Shamanna, MD[a]; L. Jeffrey Medeiros, MD[a]; Zeev Estrov, MD[b]; C. Cameron Yin, MD, PhD[a]; Srdan Verstovsek, MD, PhD[b]; Sergej Konoplev, MD, PhD[a]; Jeffrey L. Jorgensen, MD, PhD[a]; Mohammad M. Mohammad, MSc[a]; Roberto N. Miranda, MD[a]; Chong Zhao, MD, PhD[a]; John Lee, MD, PhD[a]; Zhuang Zuo, MD, PhD[a]; and Carlos E. Bueso-Ramos, MD, PhD[a]

Abstract

Background: *JAK2* V617F mutation (mut) in acute myeloid leukemia (AML) is rare. We describe the clinicopathologic findings of a single-institution series of 11 de novo AML cases with *JAK2* V617. **Methods:** We identified cases of de novo AML with *JAK2* V617F over a 10-year period. We reviewed diagnostic peripheral blood and bone marrow (BM) morphologic, cytogenetic, and molecular studies, including next-generation sequencing. The control group consisted of 12 patients with *JAK2* wild-type (wt) AML matched for age, sex, and diagnosis. **Results:** We identified 11 patients (0.5%) with *JAK2* V617F, with a median age at diagnosis of 72.5 years (range, 36–90 years). Ten neoplasms were classified as AML with myelodysplasia-related changes and 1 as AML with t(8;21)(q22;q22). All *JAK2*mut AML cases showed at least bilineage dysplasia, 7 of 11 showed fibrosis, 8 of 11 had an abnormal karyotype, and 5 had deletions or monosomy of chromosomes 5 and 7. Using the European LeukemiaNet (ELN) classification, 9 patients (82%) with *JAK2*mut AML were intermediate-2 and adverse risk. Cases of *JAK2*mut AML did not have mutations in other activating signaling pathways (P=.013); 7 (64%) showed additional mutations in at least one gene involving DNA methylation and/or epigenetic modification. Patients with *JAK2*mut AML had a significantly higher median BM granulocyte percentage (12% vs 3.5%; P=.006) and a higher frequency of ELN intermediate-2 and adverse risk cytogenetics (P=.04) compared with those with *JAK2*wt AML. *JAK2*mut AML showed higher circulating blasts, but this difference was not significant (17% vs 5.5%; P=not significant). No difference was seen in the median overall survival rate of patients with *JAK2*mut AML versus those with *JAK2*wt AML (14 vs 13.5 months, respectively). **Conclusions:** De novo *JAK2*mut AML is rare and frequently found in patients with dysplasia, BM fibrosis, and abnormal karyotype with intermediate- or high-risk features; gene mutations in DNA methylation and epigenetic-modifying pathways; and absence of gene mutations in activating signaling pathways.

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Cas de LAM *de novo* avec mutation JAK2 V617F

Table 1. Review of Cases of De Novo AML and *JAK2* Mutation Reported in the Literature

Characteristics	Lee et al,[10] 2006	Jelinek et al,[15] 2005	Döhner et al,[14] 2006	Steensma et al,[13] 2006	Veiga et al,[11] 2007	Swaminathan et al,[12] 2010	Balatzenko et al,[16] 2015	Eghtedar et al,[37] 2012
Pts with de novo *JAK2* mutant AML, n (%)	3 (2.7)	2 (5.1)	4 (2.4)	3 (1.8)	8 (2.3)	6 (2.3)	3 (0.8%)	10 (26.0%)
Age at diagnosis, y	32–67	51–52	ND	ND	44–82	15–65	42–73	45–88
Dysplasia	ND	1	ND	ND	ND	ND	ND	ND
FAB/WHO diagnosis	2 pts t(8:21) & 1 pt without maturation	2 pts M7	4 pts t(8:21)	1 pt M6 1 pt M7 1 pt M2	4 pts M2 2 pts M1 1 pt t(8:21) 1 pt inv(16)	4 pts t(8:21) 2 pts M4	3 pts M0	ND
Fibrosis	ND	ND	ND	ND	ND	ND	ND	ND
Complex karyotype	0	1	ND	ND	0	0	ND	ND
Splenomegaly	ND	1	ND	ND	ND	ND	ND	ND

Abbreviations: AML, acute myeloid leukemia, FAB, French-American-British; ND, no data; pts, patients.

Hidalgo-Lopez et al*, J Natl Compr Canc Netw* 2017

Cohorte de Hidalgo-Lopez *et al*

- 11 cas de LAM avec mutation JAK2 V617F
- Dysplasie multilignée et/ou caryotype avec anomalies liées aux SMD (-/del5q ou 7 : 45% des patients ; 1/3 : caryotype complexe)

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Evolution

- Echec de traitement par Vidaza (myélogramme du 06/01/2017 : 40% de myéloblastes)
- Décision d'une prise en charge palliative en janvier 2017
- Décès en mars 2017