Place du mot complexe dans les CR de Cytogénétique Hématologique

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The complex karyotype in hematological malignancies: a comprehensive overview by the Francophone Group of Hematological Cytogenetics (GFCH).

Nguyen-Khac F, Bidet A, Daudignon A, Lafage-Pochitaloff M, Ameye G, Bilhou-Nabéra C, Chapiro E, Collonge-Rame MA, Cuccuini W, Douet-Guilbert N, Eclache V, Luquet I, Michaux L, Nadal N, Penther D, Quilichini B, Terre C, Lefebvre C, Troadec MB, Véronèse L.

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The complexity of a karyotype is related to its negative prognostic impact.
Therefore, the prognostic risk of complexity has to be determined for each malignancy.

Table 1. CKs with a prognostic impact*.

Hematological malignancies	Definition of a CK	Frequency	Prognostic impact	Prognostic scoring system (PSS)	References
MDS	***de novo* MDS and t-MDS** CK with CAs = 3 CK with CAs > 3	***de novo* MDS** CK with CAs = 3 2% CK with CAs > 3 3–7% **t-MDS** CK with CAs = 3 6% CK with CAs > 3 31%	OS, time to progression to AML	**IPSS** CAs > = 3: Poor **IPSS-R$** CAs = 3: Poor CAs > 3: Very Poor	Greenberg 1997 [163] Mauritzon 2002 [164] Kantarjian, 2008 [165] Schanz 2012 [8] Greenberg 2012 [5] Kuendgen 2021 [10]
Adult AML	After exclusion of WHO-designated recurring CAs§ **ELN** 3 or more CAs **MRC** 4 or more CAs	**All AML** 10–12% **AML > 60y** 23% **secondary AML/t-AML** up to 25%	OS, EFS	**ELN** CAs > = 3: Adverse	Byrd 2002 [28] Schoch 2004 [32] Schoch 2005 [36] Grimwade 2010 [27] Döhner 2017 [26] Bager 2018 [47] Daneshbod 2019 [31]
MPN and MDS/MPN	3 or more CAs	**CML** 1% **PMF** 7.5% **PV, ET** 3–8% **CMML** 5–8%	**CML** Blast crisis **PMF, PV, ET, CMML** OS, time to progression to AML	**PMF** **IPSS, DIPSS, MIPSS70 + v2** CAs > = 3: Unfavorable **CMML** **CPSS, CPSS-Mol** CAs > = 3: High risk classification	Bacher 2009 [62] Hussein 2010 [66] Gangat 2011 [64] Such 2011 [73] Wang 2014 [72] Guglielmelli 2018 [65] Hochhaus 2020a [57]
Adult T-ALL	5 or more CAs Excluding cases with a recurrent translocation	7–13%	EFS		Moorman 2007 [80] Marks 2009 [83] Lafage-Pochitaloff 2014 [84]
CLL	3 CAs = low-CK 4 CAs = intermediate-CK 5 or more CAs = high-CK Excluding +12, +19, +other CAs	CK: 11–19% HCK: 4–8%	TTFT, PFS, OS		Puiggros 2017 [104] Rigolin 2017 [105] Baliakas 2019 [101]
MCL	4 or more CAs, including the t(11;14)	19–59%	TTFT, OS		Sarkozy 2014 [124] Greenwell 2018 [125] Obr 2018 [126]

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MDS

Table 1. CKs with a prognostic impact*.

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MDS

Tableau 3. IPSS « classique »

	0	0,5	1	1,5	2
Pourcentage de blastes médullaires	< 5	05-10	-	11-20	21-30
Caryotype	**Favorable :** normal, perte isolée de l'Y, del(5q) ou del(20q) isolée	**Intermédiaire :** autres anomalies	**Défavorable :** complexe (3 anomalies ou plus), anomalies du chromosome 7		
Cytopénies*	0 ou 1	2 ou 3			

**Cytopénies définies par : polynucléaires neutrophiles < 1 800/mm³, plaquettes < 100 000/mm³, hémoglobine < 10 g/dL.*

Greenberg P., Blood, 1997

Tableau 4. IPSS révisé

A) Classification cytogénétique de l'IPSS-R

	Proportion de patients (%)	Caryotype	Survie médiane (années)	Délai jusqu'à 25 % de LAM (années)
Très favorable	4 %	-Y, del(11q)	5,4	NA
Favorable	72 %	Normal, del(5q), del(12p), del(20q), double avec del(5q)	4,8	9,7
Intermédiaire	13 %	Del(7q), +8, +19, i(17q), autre anomalie simple ou double	2,7	2,5
Défavorable	4 %	-7, inv(3)/t(3q)/del(3q), double avec -7/del(7q) ; complexe avec 3 anomalies	1,5	1,7
Très défavorable	7 %	Complexe > 3 anomalies	0,7	0,7

B) IPSS -R

Variable pronostique	0	0.5	1	1.5	2	3	4
Cytogénétique	Très favorable		Favorable		Intermédiaire	Défavorable	Très défavorable
Blastes médullaires	≤ 2 %		3-4 %	5-10 %	5-10 %	> 10 %	
Hémoglobine (g/dL)	≥ 10		8- < 10	< 8			
Plaquettes (G/L)	≥ 100	50- < 100	< 50				
Neutrophiles (G/L)	≥ 0,8	< 0,8					

Greenberg P., Blood, 2012

→ Caryotype complexe à x anomalies. Score cytogénétique IPSS-R = y

LAM

Adult AML	After exclusion of WHO-designated recurring CAs§ **ELN** 3 or more CAs **MRC** 4 or more CAs	**All AML** 10–12% **AML > 60y** 23% **secondary AML/t-AML** up to 25%	OS, EFS	**ELN** CAs > = 3: Adverse	Byrd 2002 [28] Schoch 2004 [32] Schoch 2005 [36] Grimwade 2010 [27] Döhner 2017 [26] Bager 2018 [47] Daneshbod 2019 [31]

§ t(8;21), inv(16) and t(16;16), t(9;11), t(v;11)(v;q23.3), t(6;9), inv(3) and t(3;3), t(9;22).

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Complex Karyotype (CK) 3 or more unrelated abnormalities in the absence of recurring abnormalities such as : t(8;21), inv(16), t(16;16), t(v;11)(v;q23,3), t(6;9), inv(3), t(3;3) or t(9;22). Also exclude hyperdiploid with 3 or more trisomies or polysomies without structural abnormalities. Poor prognosis is still debated in pediatric cases

Bidet et al., Cur Res Trans Med 2023

LAM

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Nguyen-Khac et al., Leukemia 2022

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Bidet et al., Cur Res Trans Med 2023

→ Ne pas employer le mot complexe. Présence d'une anomalie x / Caryotype hyperdiploïde...
+ Pronostic

LLC

TABLE 1 Guidelines for counting aberrations in karyotypes

In all hematologic malignancies:
1. Count one (1) aberration[a] for each item between commas, in all clones and subclones[b]
2. Count a single change only once if it is present in several subclones[c]
3. Count each numerical change (including -Y, -X, +15)[d], balanced translocation, simple structural change and each complex structural change[e] as one (1) aberration
4. Count each chromosome marker as one (1) aberration[a]
5. Count one (1) aberration for tetraploidy (92 chromosomes) or near-tetraploidy (81-103 chromosomes)[f]
6. Do not count constitutional aberrations[g]
In CLL, additionally:
7. Distinguish between a CK with three (3) to four (4) abnormalities and a high CK with five (5) or more abnormalities
8. -Y, -X and +15 have to be flagged up in the cytogenetics report[d]
9. Count one (1) aberration for FISH abnormalities [del(13)(q), +12, del (11)(q) and del(17)(p)] only if they are observed in the karyotype[h]
10. CKs with +12,+19 have to be classified separately

GFCH
Groupe Francophone de Cytogénétique Hématologique

Jondreville et al, Am J Hematol 2020

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Jondreville et al, Am J Hematol 2020

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→ Ne pas employer le mot complexe. Caryotype présentant l'association trisomie 12 + trisomie 19 + anomalie x… + Pronostic (Différence entre autre tri ou anomalie de structure ?)