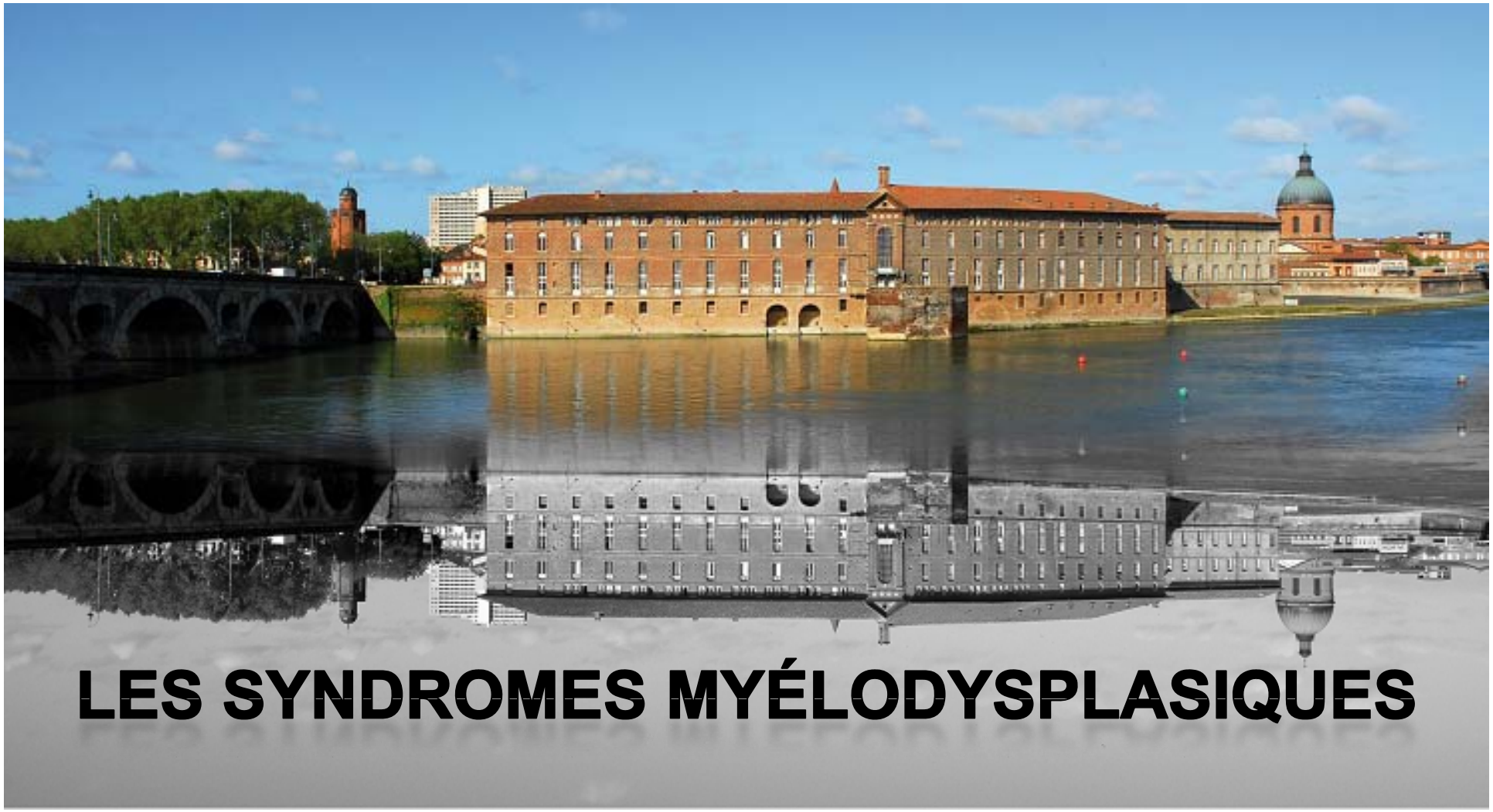


LES SYNDROMES MYÉLODYSPLASIQUES

Pr Odile BEYNE-RAUZY

Médecine Interne

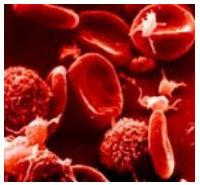
Hôpitaux de Toulouse

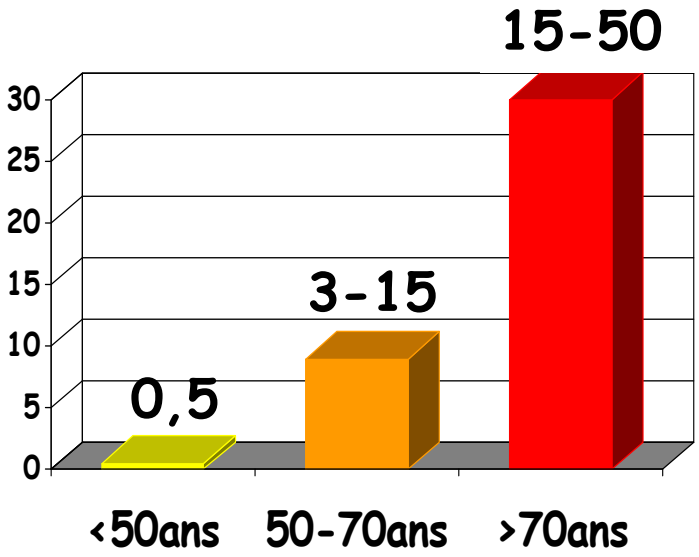
Université Paul Sabatier TOULOUSE III

CRCT centre de recherches en cancérologie de Toulouse

Groupe Francophone des Myélodysplasies

SMD = Sujet âgé





Diagnostic
70 ans

Pas de guérison

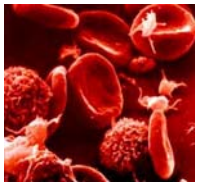
Maladie chronique

70/100 000 hab > 80 ans
vs 5/100 000

10% de la population française aura plus de 75 ans en 2020…

Rollison 2006 ASH, Sekeres 2009 J Natl Inst

Prise en charge globale : multidisciplinaire



Patient

Biologiste

FRAGILITE ET COMORBIDITES

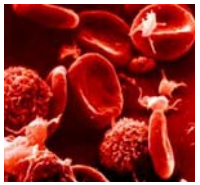
AGRESSIVITE DE LA MALADIE

Hématologue

Gériatre

CHOIX THERAPEUTIQUE

Réseau ville-hôpital



Hôpital

Gériatre

Hématologue

Biologiste

Patient

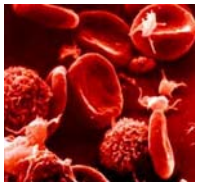
Ville

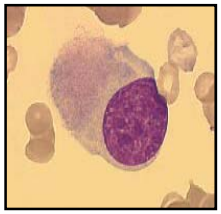
Généraliste

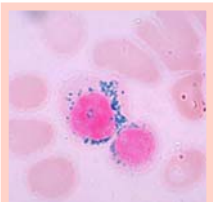
IDE

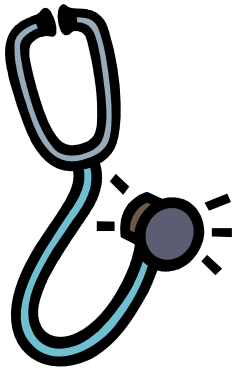
Biologiste

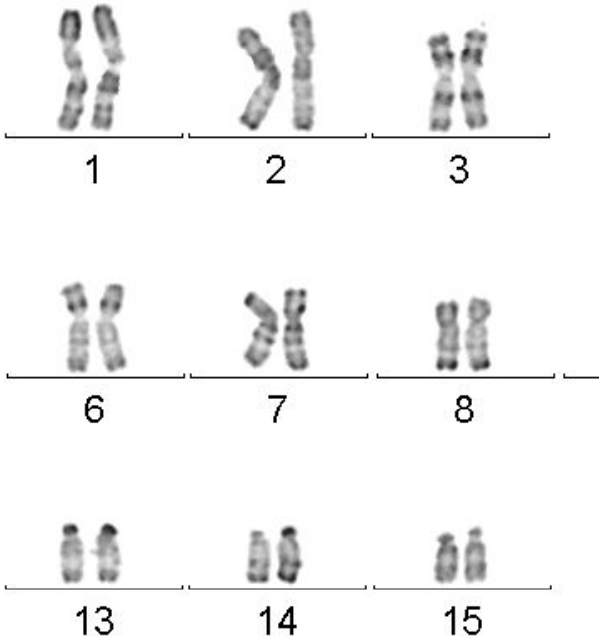
Diagnostic

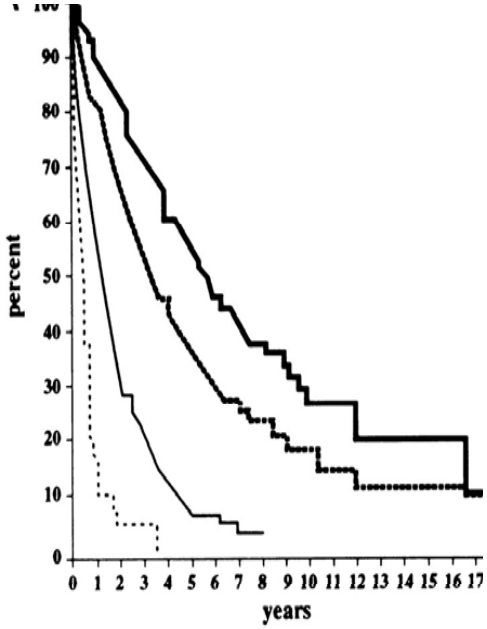






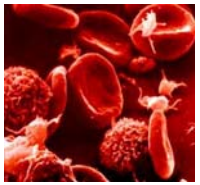




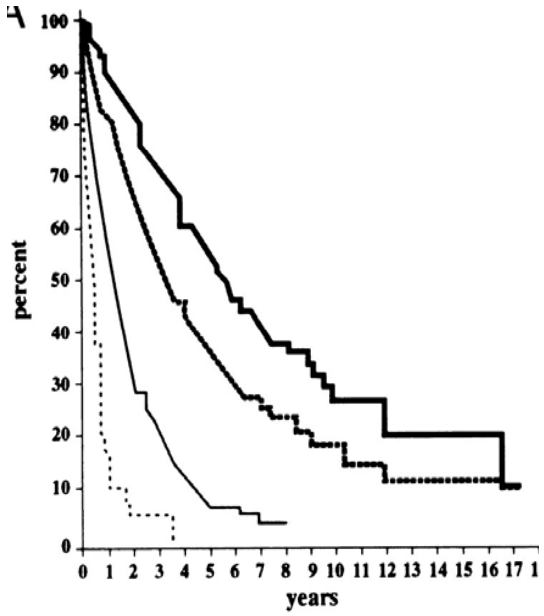


Projet de soin

SMD low risk (faible risque) et high risk (haut risque)

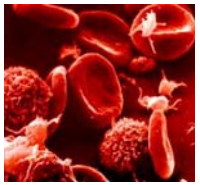


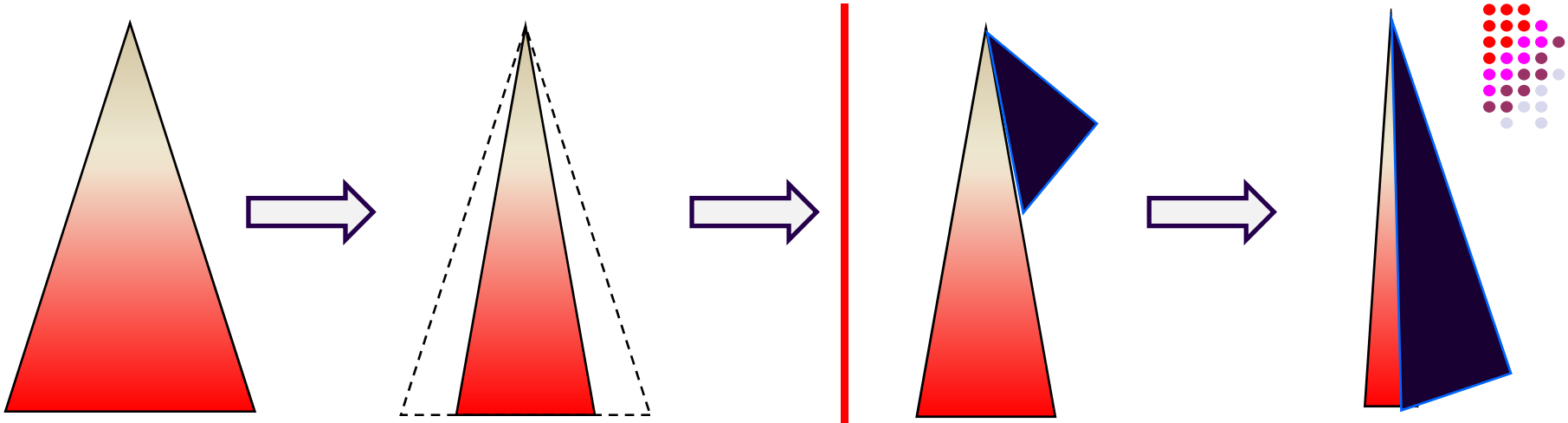
	Score IPSS	Médiane de survie (année)
LOW	Low = 0	5,7
	Int-1 = 0,5-1	3,5
HIGH	Int-2 = 1,5-2	1,2
	High > 2	0,4



Greenberg 1997 Blood

Histoire naturelle





Hématopoïèse normale

Faible risque

Hématopoïèse clonale

Excès de mort cellulaire

Haut risque

Clone leucémique

Prolifération

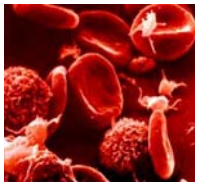
Instabilité chromosomique

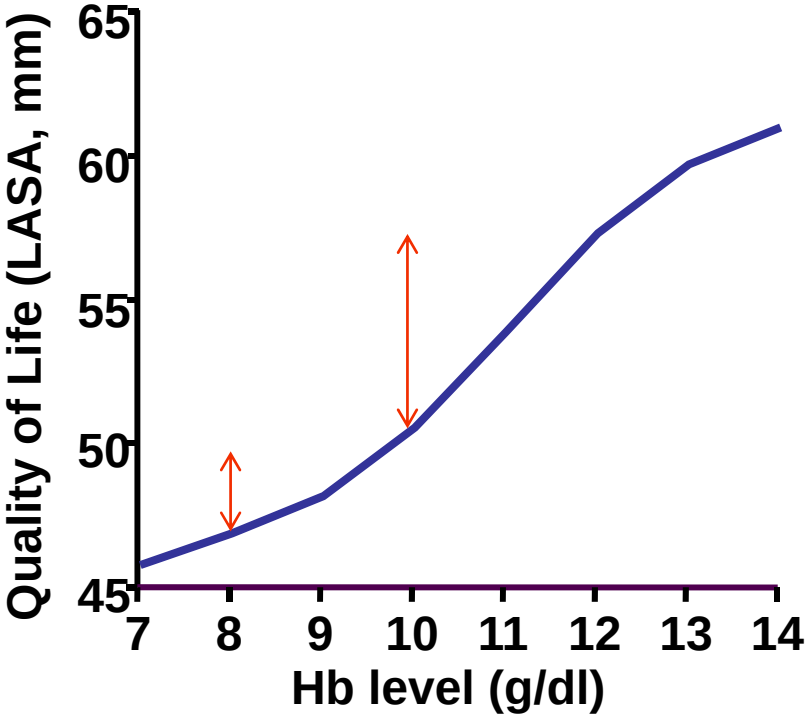
LAM

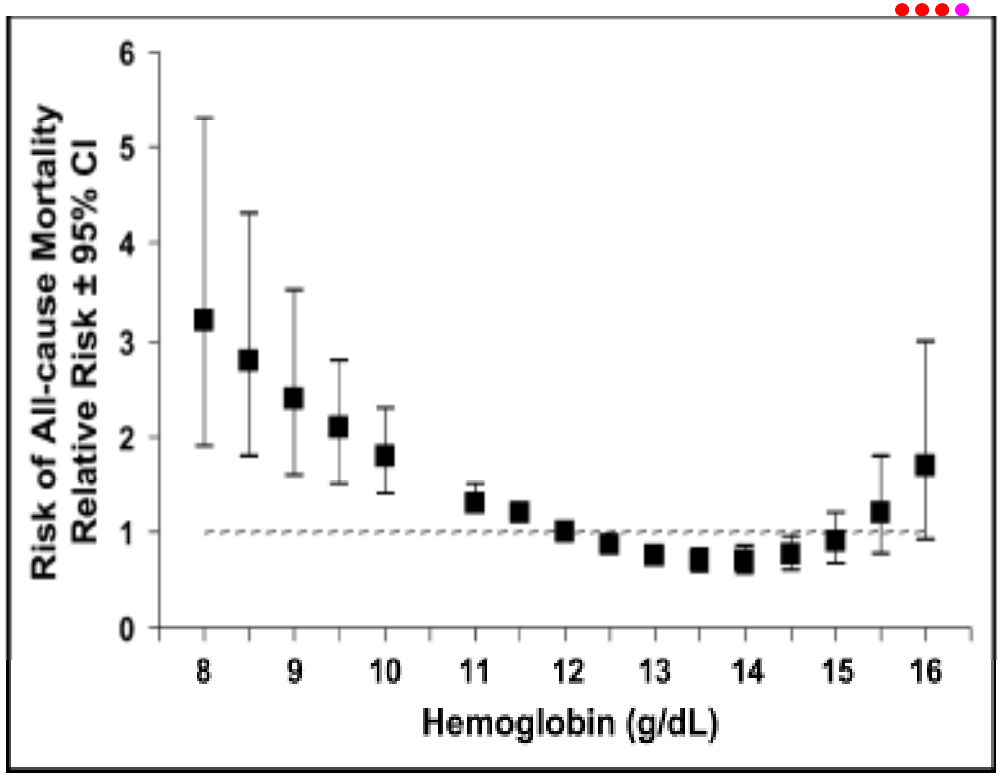
Facteurs de croissance
Stimuler moelle normale

Hypométhylants
Contrôler le clone leucémique

Pouvoir de l'anémie





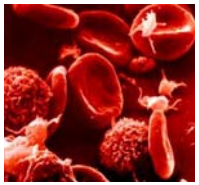


Qualité de vie

Morbi-mortalité
Dépendance

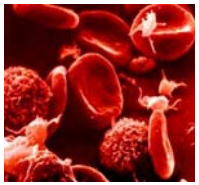
Izaks 1999 JAMA, Crawford Cancer 2002, Penninx, Chaves 2004 J Am Geriat Soc, Steensma 2007 Mayo Clin Proc

Madame O. née en 1930, 80 ans



- Antécédents :
  - Appendicectomie en 1940
  - Thyroïdectomie en 1976
  - Cholecystectomie en 1977
- Profession : ménages
- A domicile seule, 2 enfants
- Tt Tardyféron 1cp/j
- Syndrome anémique sévère

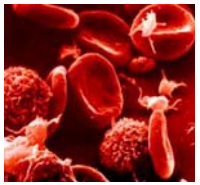
Madame O. née en 1930, 80 ans



- Hémogramme en 09/2009 :
  - Hb 7,3 g/dl VGM 102μ^3
  - Plaquettes 474 G/L
  - GB 6,7 PNN 4,3 Mono 0,8 Lympho 1,4
  - Reticulocytes 35 G/L

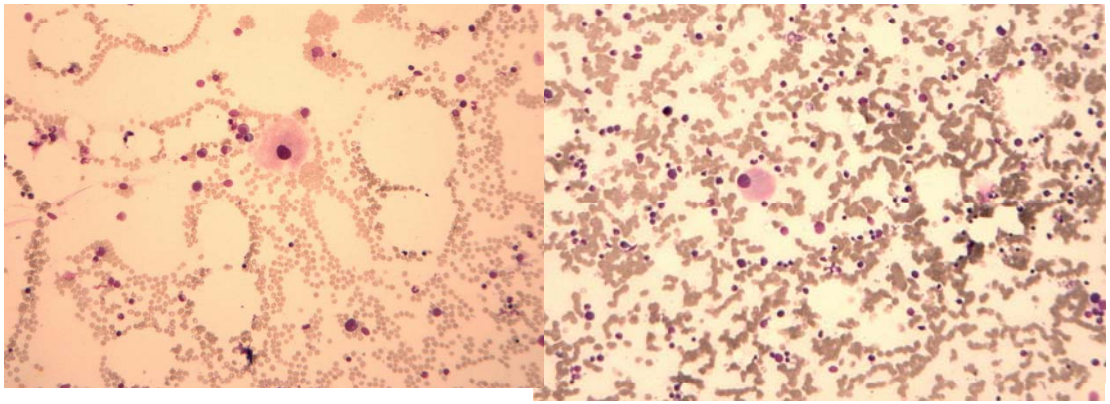
  - Vitamines B9, B12 normales, TSH normale

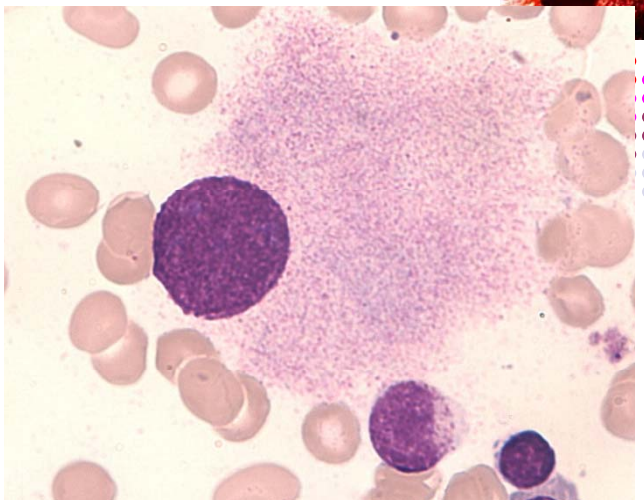
Madame O. née en 1930, 80 ans



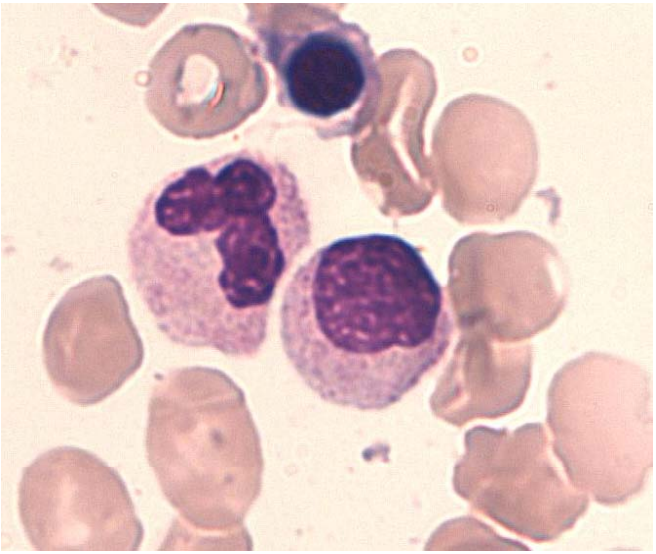
- Médullogramme :
  - Grade 3
  - Mégacaryocytes nombreux et certains sont monolobés
  - Lignée érythroïde 18%
  - Lignée granuleuse 59% avec une dégranulation, des PNN pelgérisés
  - Autres 4% blastes, Perls normal

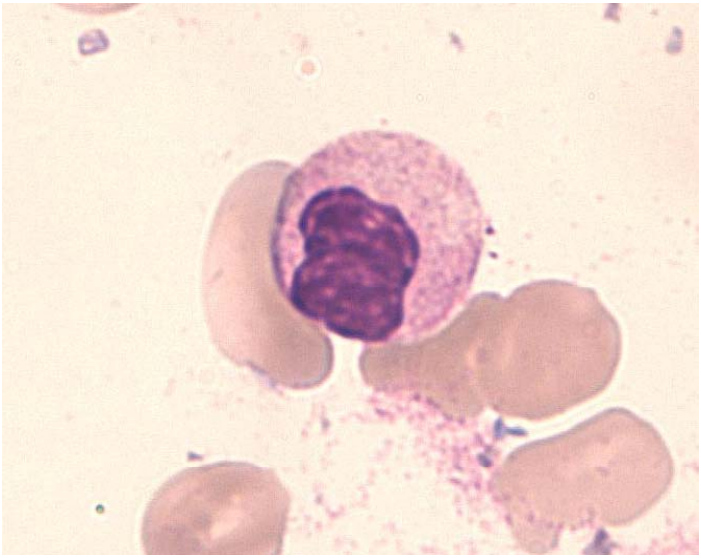
Mégas monolobés type 5q- (petit et fort grossissement)

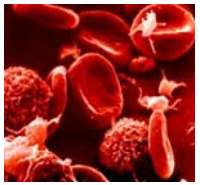


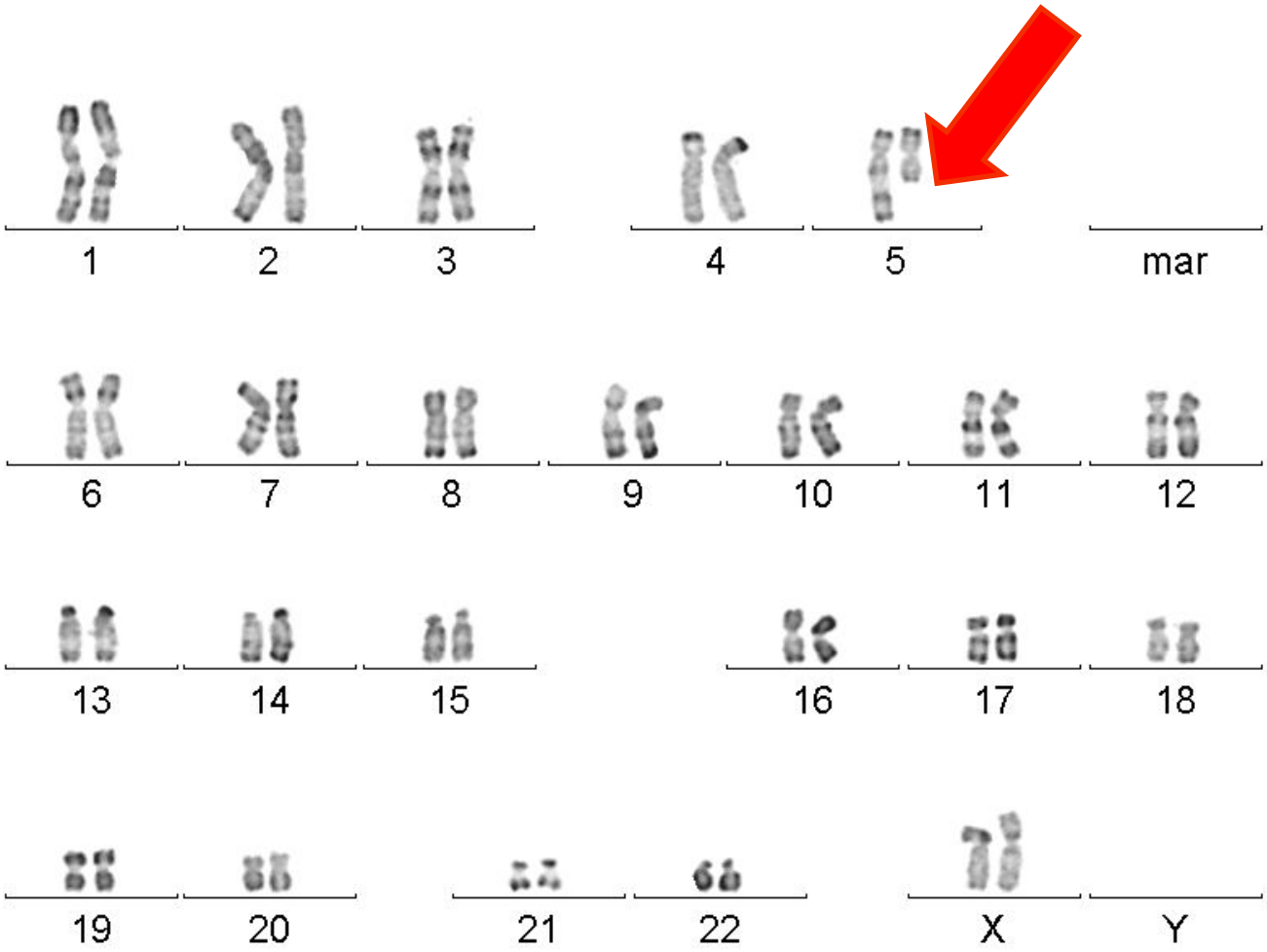


Pelgérisation





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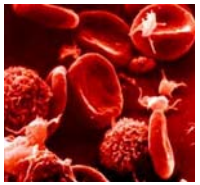
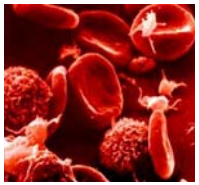
Madame O. née en 1930, 80 ans



- Cytogénétique
  - Caryotype del 5q 100%
- Autres
  - Ferritine 1250µg/l, EPO 900 UI/l

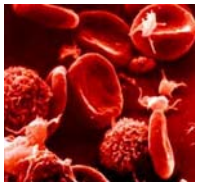
- Diagnostic : syndrome 5q-, IPSS=0

Madame O. née en 1930, 80 ans



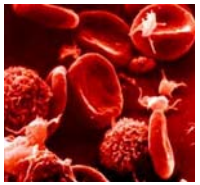
- Epoetin 30000UI et G-CSF 13 1/semaine de juin à septembre 2009 puis double doses mais échec
- Transfusions tous les 15 jours

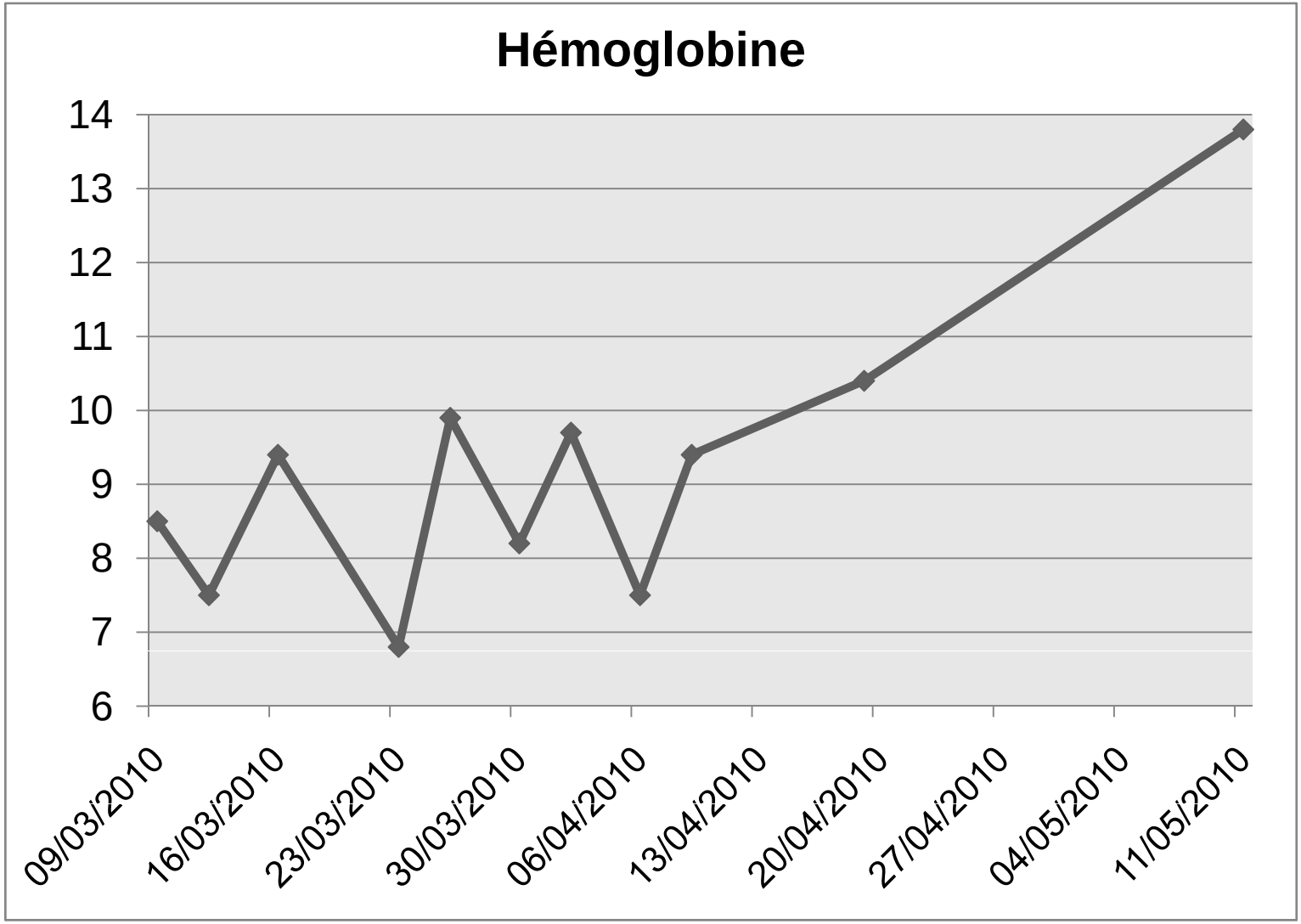
Madame O. née en 1930, 80 ans



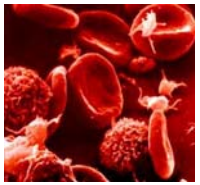
- Mars 2010 : Lenalidomide 5mg/j

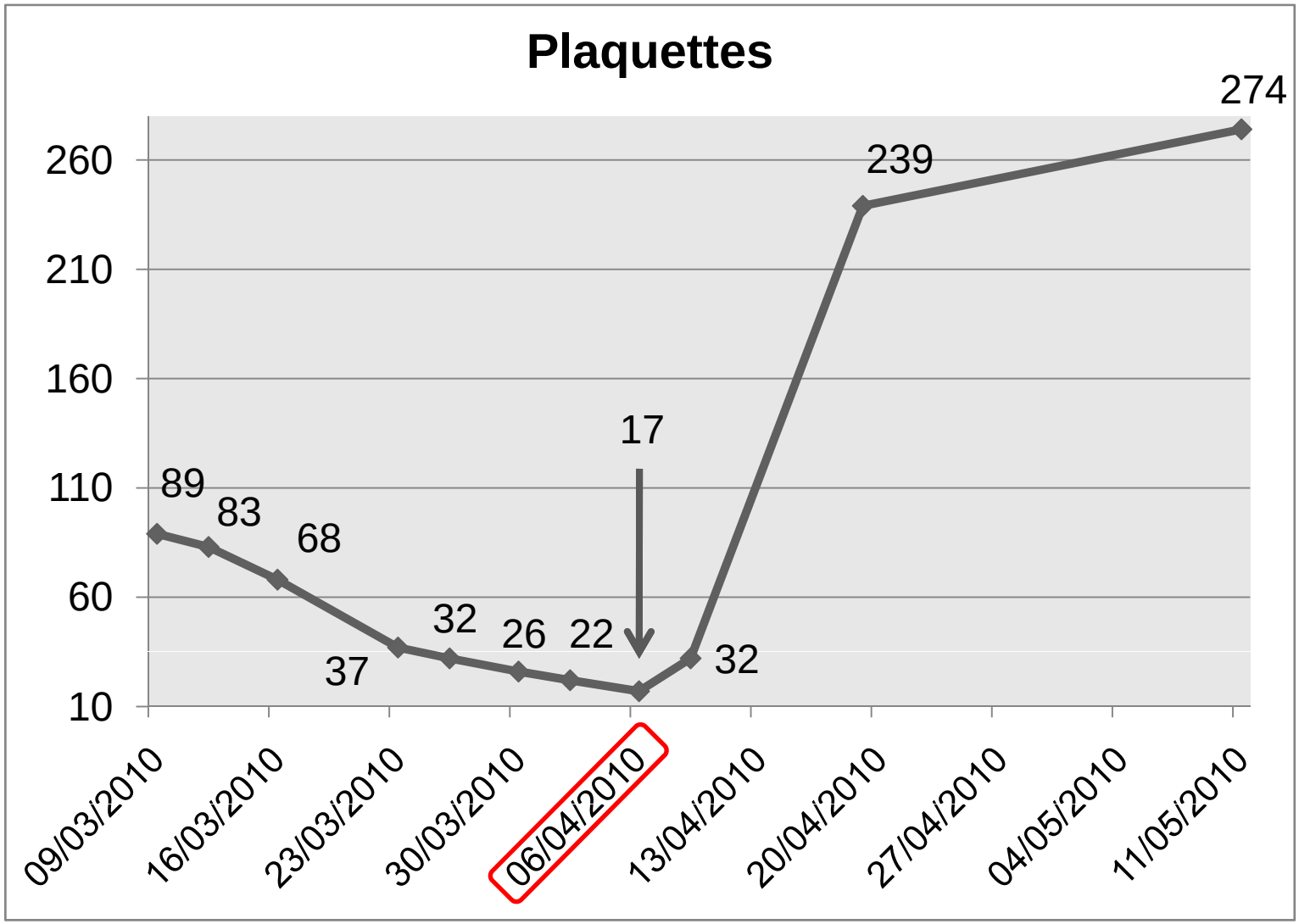
Madame O. née en 1930, 80 ans



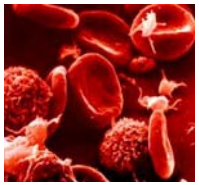


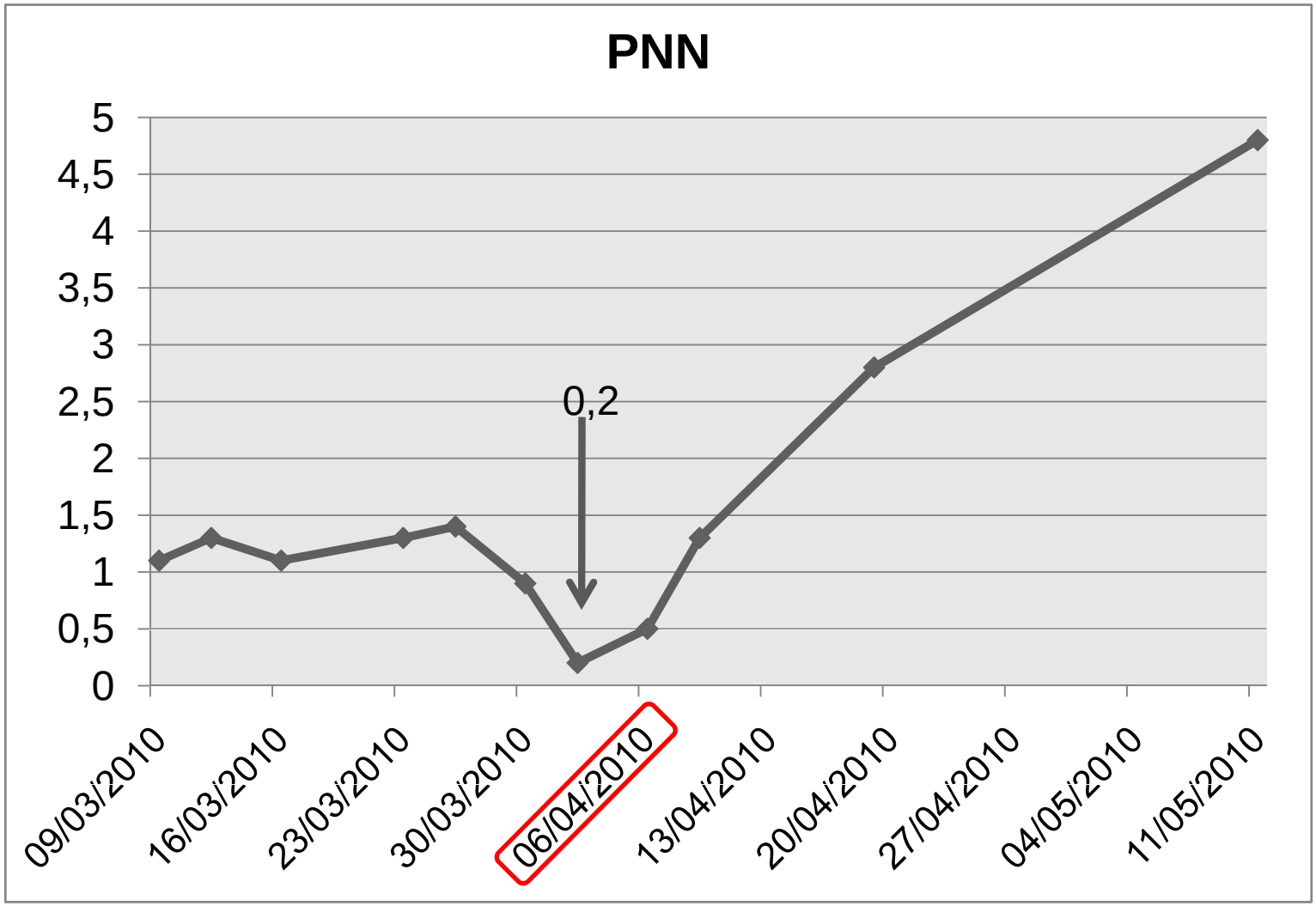
Madame O. née en 1930, 80 ans

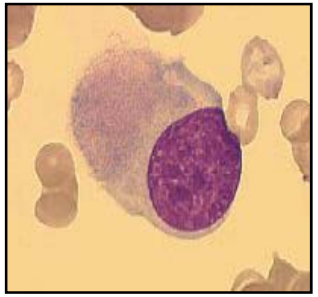




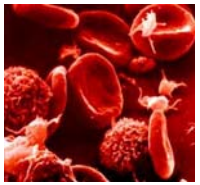
Madame O. née en 1930, 80 ans







Le syndrome 5q^{-}

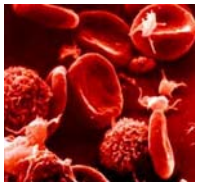


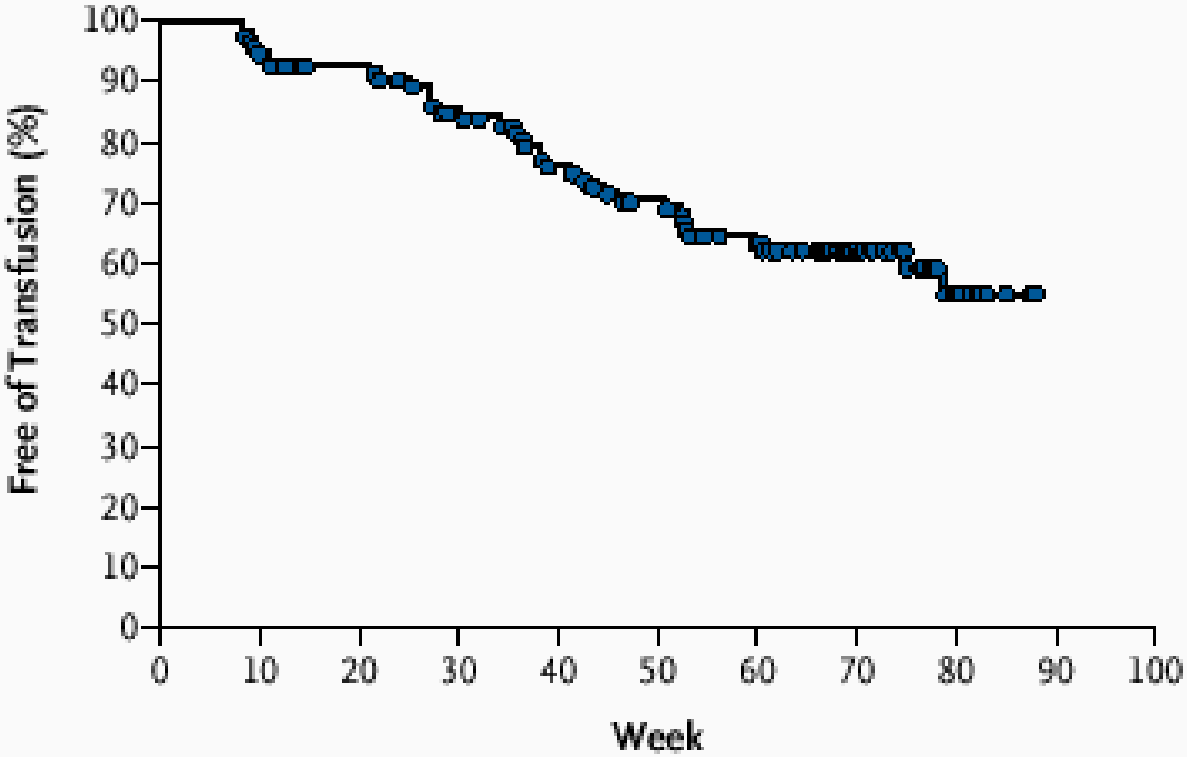
- Femme 3/1, après 60 ans
- Bon pronostic médiane survie 116 mois
- Anémie macrocytaire, neutropénie modérée et taux de plaquettes normal ou thrombocytose
- Morphologie, <5% blastes, cytogénétique
- Pronostic associé au contrôle de la surcharge en fer post-transfusions

Table 2. Erythroid Response to Lenalidomide.

Variable	Continuous Daily Dosing (N=102)*	21-Day Dosing (N=46)*	All Patients (N=148)
Erythroid response — no. (%)			
Transfusion independence	71 (70)	28 (61)	67%
95% CI			59–74
≥50% decrease in no. of transfusions	8 (8)	5 (11)	13 (9)
95% CI			5–15
Total transfusion response	79 (77)	33 (72)	112 (76)
95% CI			68–82
Time to response — wk			
Median	4.7	4.3	4,6s
Range	1–34	1–49	1–49
Hemoglobin — g/dl			
Baseline†			
Median	7.7	8.0	7.8
Range	5.3–10.4	5.6–10.3	5.3–10.4
Response‡			
Median	13.4	13.5	13,4g
Range	9.2–18.6	9.3–16.9	9.2–18.6

List et al. N Engl J Med 2006

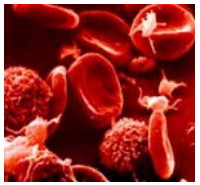




Durée de réponse médiane :
116 semaines soit 2,2 ans

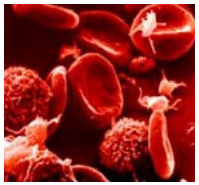
List et al. N Engl J Med 2006

Monsieur M., né en 1929, 78 ans

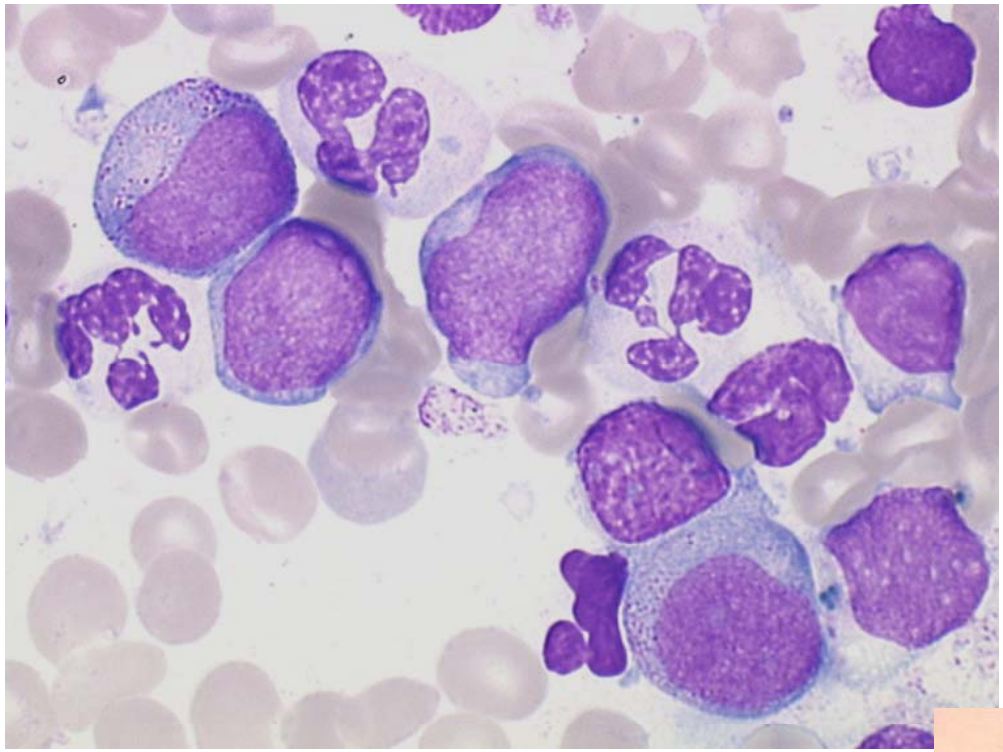


- Agriculteur à la retraite depuis 1989
- Vit à son domicile avec son épouse, 2 enfants à proximité
- Antécédents médicaux : infarctus (1989) et DNID (1995) devenu insulino-requérant, souffle aortique
- Antécédent chirurgical : prostatectomie en 1999 pour adénome (une transfusion de 2 CG),
- Tabac stop en 1977 évalué à 30PA
- Traitement Lipanthyl 1/j, Lexomil ½, Visken 5mg/j, Diafusor patch 5mg, Novonorm 2cp x 3/j et Lévémir 2 injections sous-cutanées /j, Aspégic 100mg arrêté.

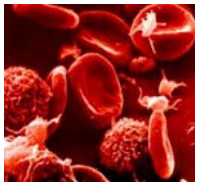
Mr M. 78 ans (né en1929)



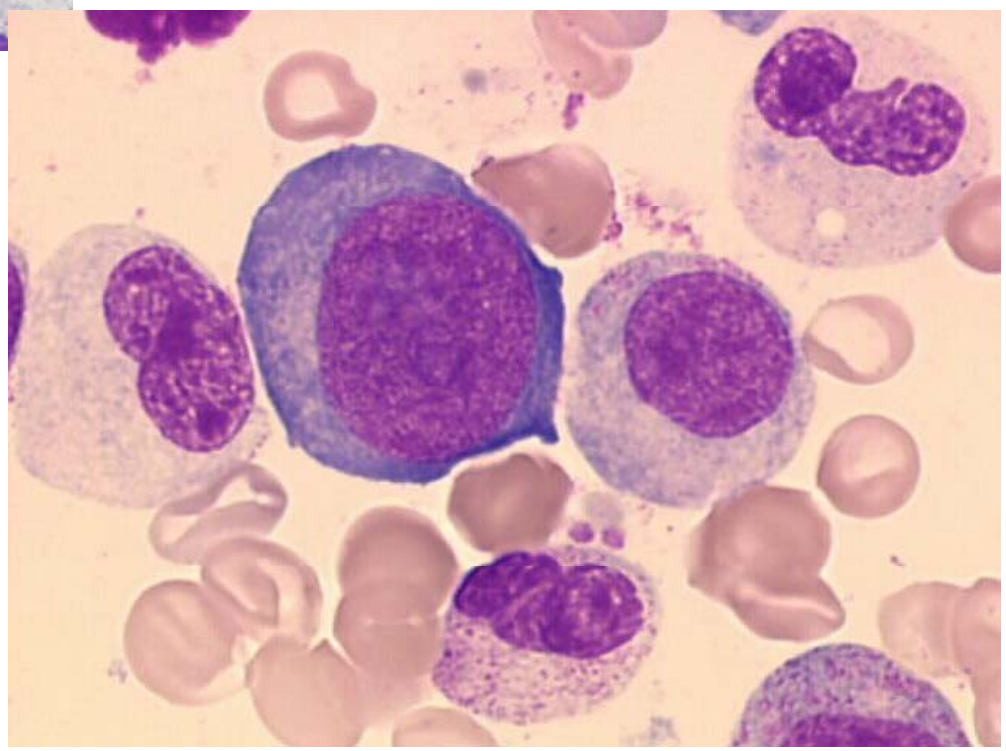
- Asthénie inhabituelle et épistaxis
- Examen clinique normal, poids 65 kg pour 1m60, OMS 1
  - Hb 9,8 g/dl VGM 108
  - GB 2000/mm^3 PNN 400/mm^3, blastes 2%
  - Plaquettes 32000/mm^3
  - Médullogramme grade 3, blastes: 12%
  - Caryotype intermédiaire : translocation rare t(10;12)
- AREB-2, score IPSS 2,5



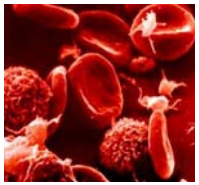
Dégranulation granuleux + blastes



Dégranulation granuleux

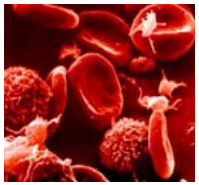


Mr M. 78 ans (né en1929)



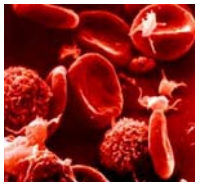
- Traitement de support : transfusions 2CG le 1/08/2007 , 5UP 6/09/2007

- Cycle 1 : 75mg/m²/j pendant 7 jours (J1 25/09/2007)
- J15 épisode fébrile avec signes respiratoires évolution favorable sous bi-antibiothérapie pendant 10 jours



- Episode rhinopharyngé sans fièvre début 12/07 (avant C4) et 02/08 (avant C6) évolution favorable sous antibiotiques
- Intercycle C6-C7 (mars 2008) : cellulite de la main suite à une plaie
  - Chirurgie
  - TAZO-VANCO-FLAGYL relai RIFADINE-TAVANIC
  - Confusion 28 mars

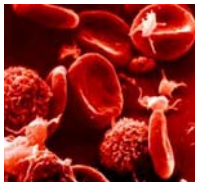
Mr M. 78 ans

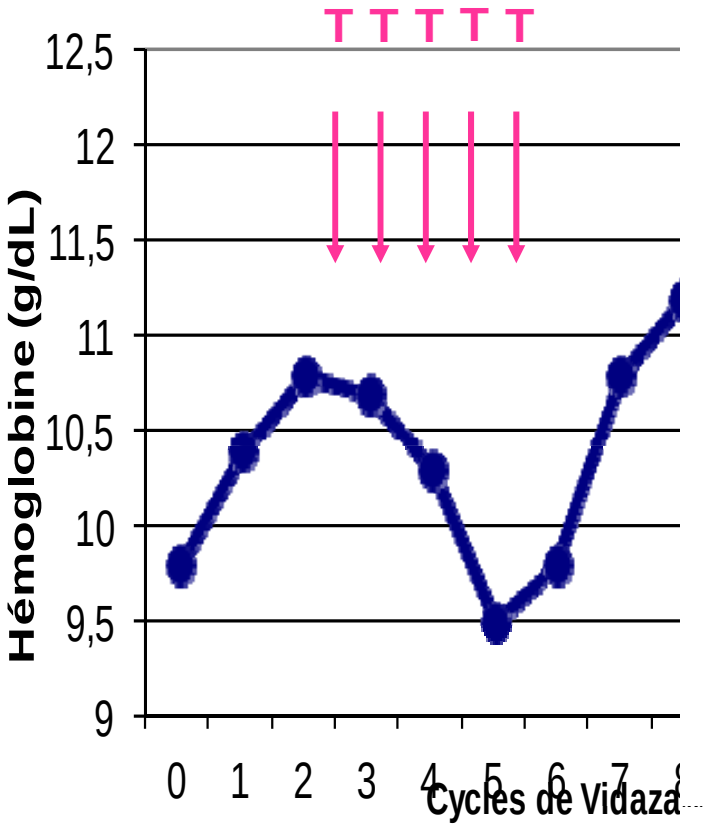


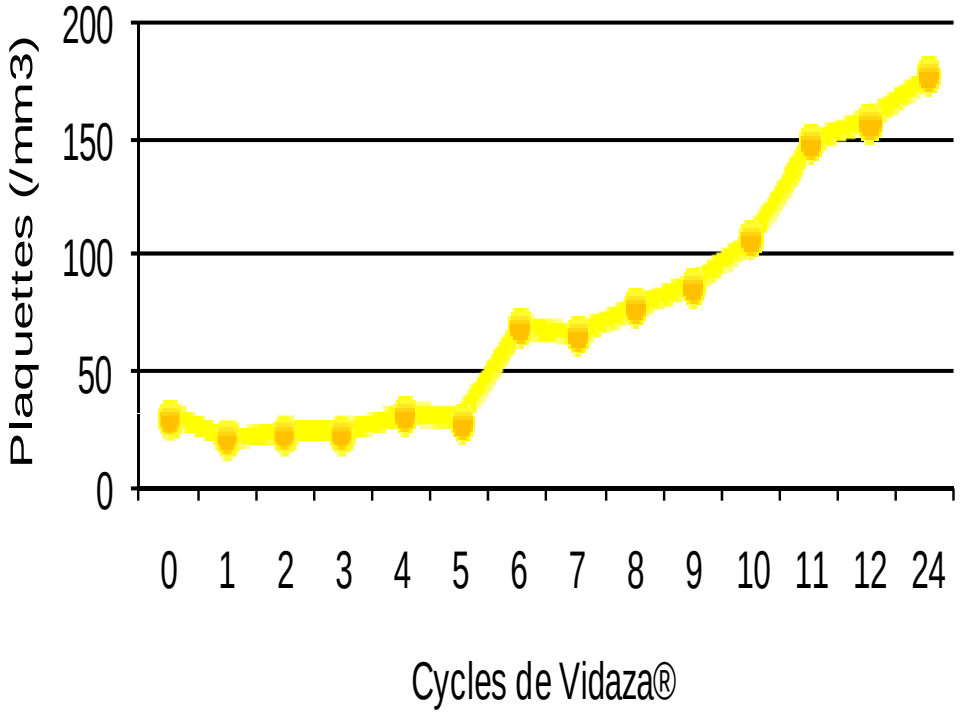
- Evaluation post C6 (04/04/2008)
- Hémogramme
  - Hb 10,9 g/dl
  - PNN 230/mm^3
  - Plaquettes 48000/mm^3

- Médullogramme grade 2, 12% blastes

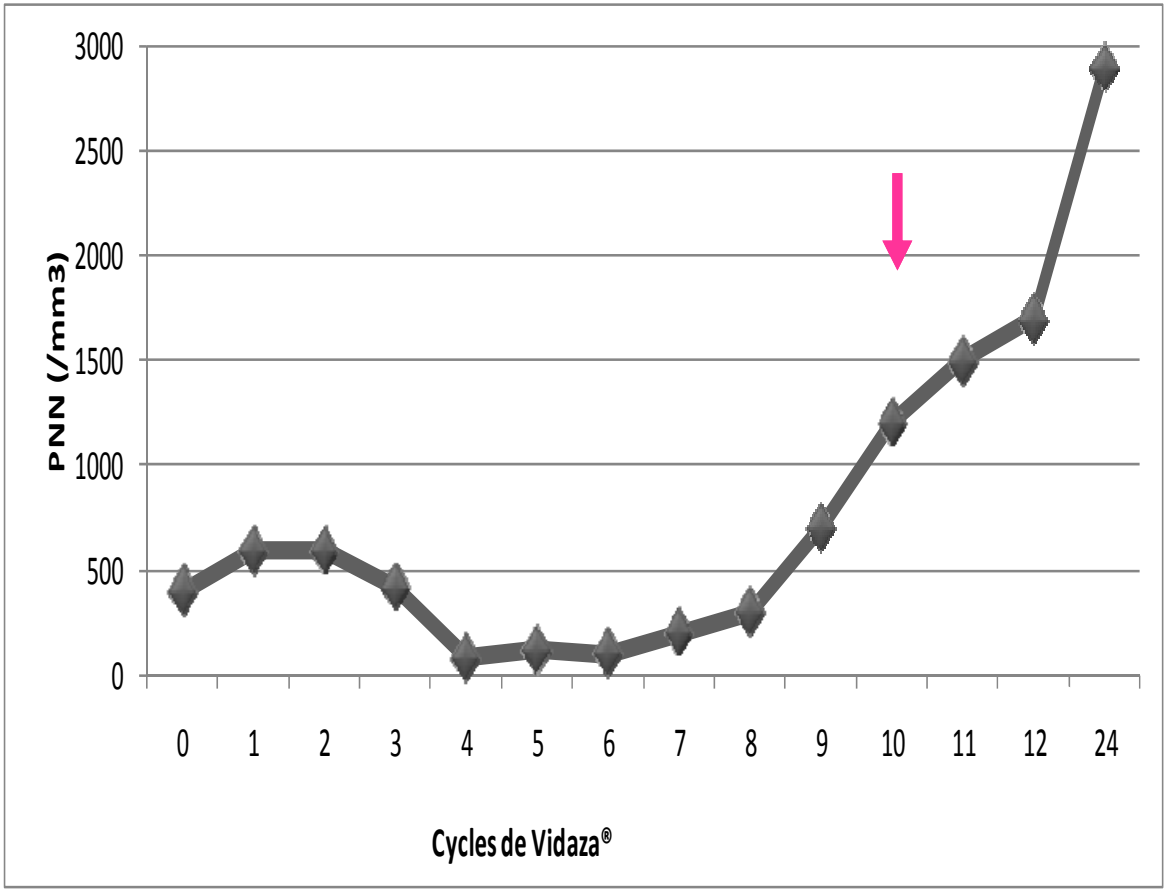
Monsieur M., né en 1929, 78 ans



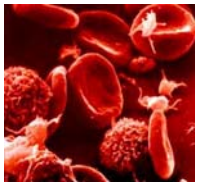




Monsieur M., 78 ans

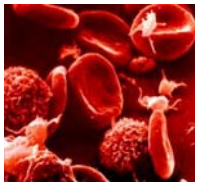


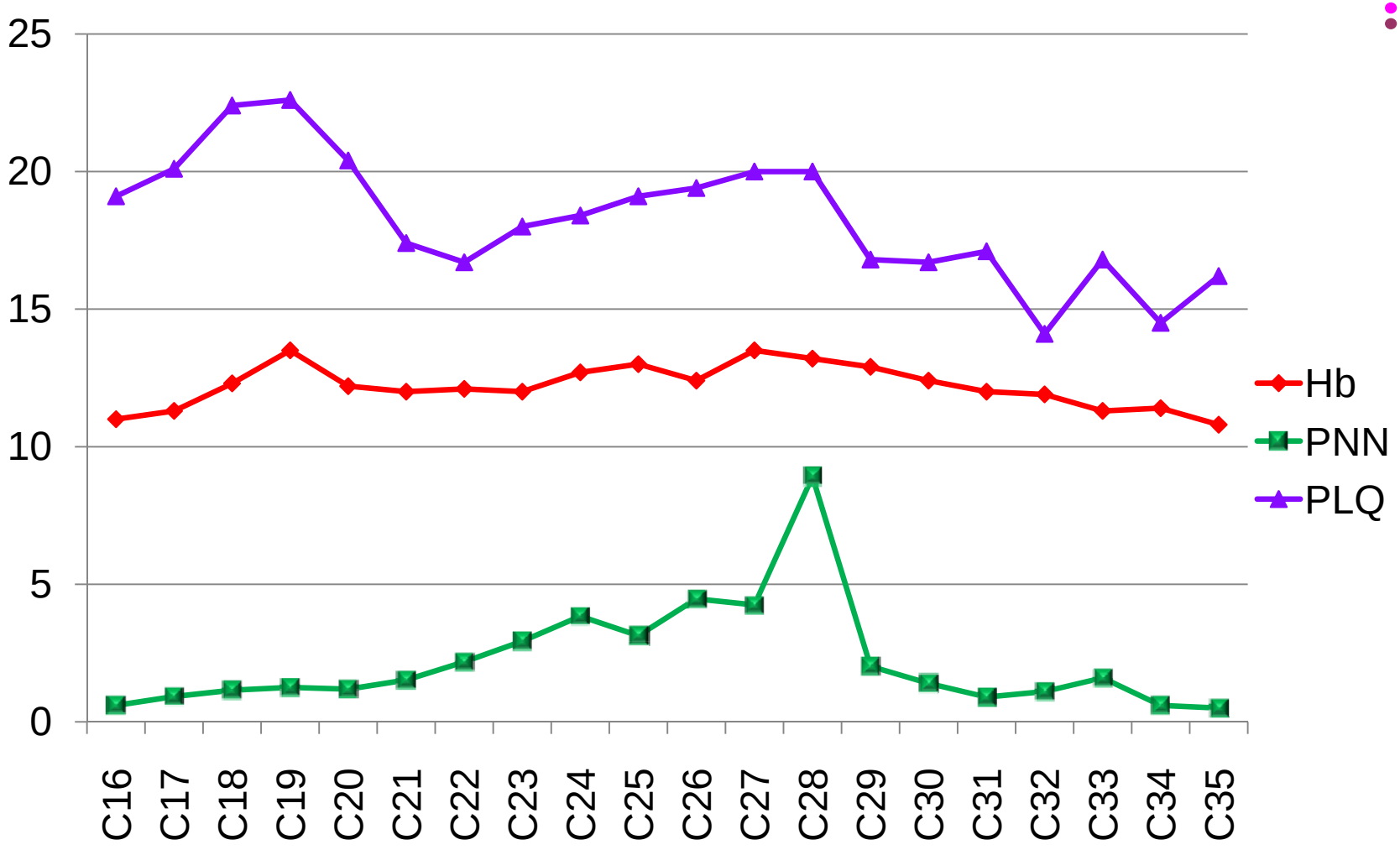
Mr M. 79 ans



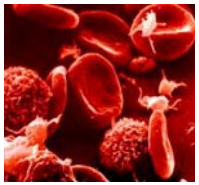
- Janvier 2009 :
  - Passage en AC/FA
  - Introduction de la Coumadine et Cordarone

Monsieur M. 81 ans



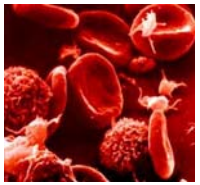


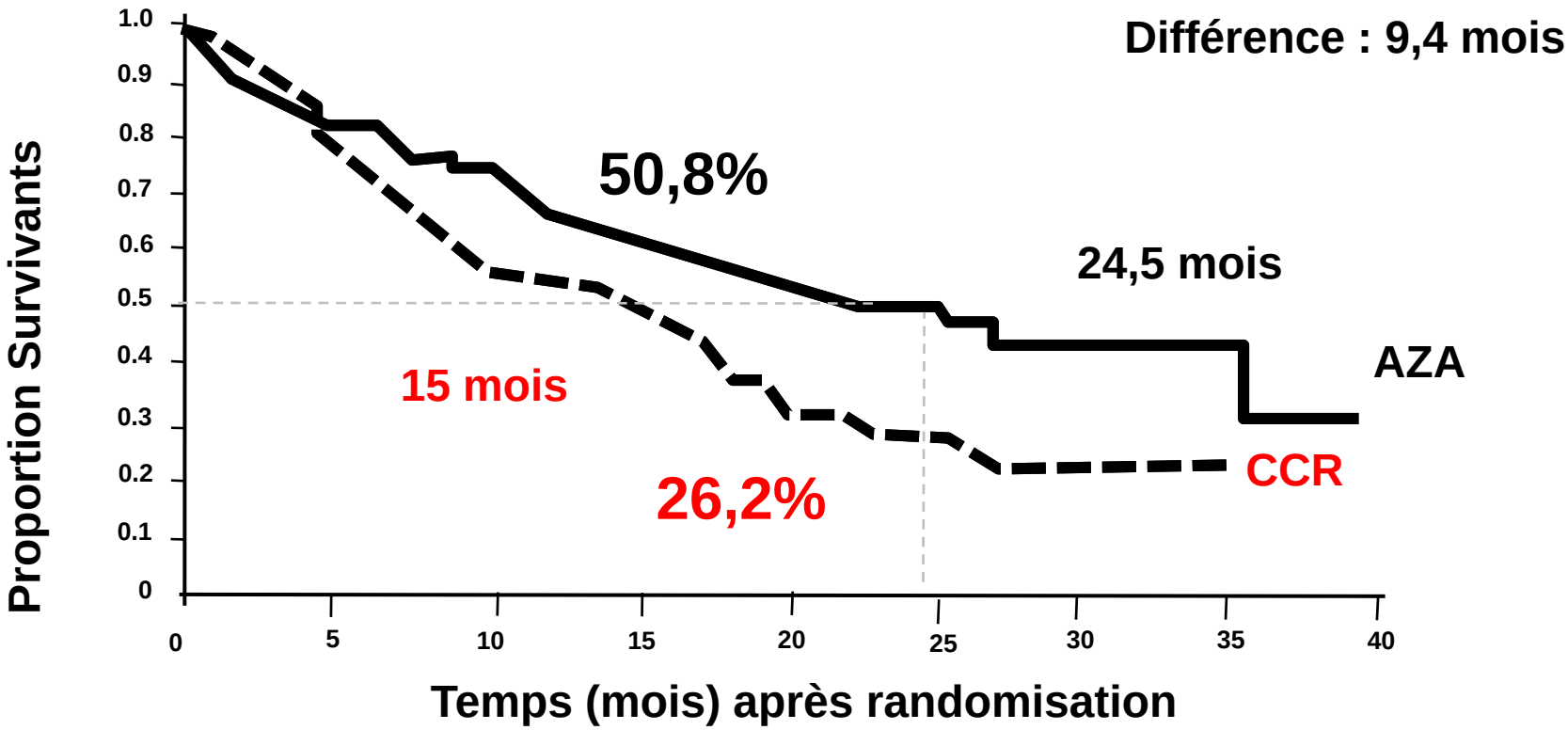
Mr M. 81 ans



- Evaluation post C33 (09/08/2010)
- Hémogramme
  - Hb 11,4 g/dl
  - PNN 600/mm^3
  - Plaquettes 145000/mm^3
- Médullogramme grade 3, 4% de blastes
- Traité à domicile via HAD jusqu'à C44

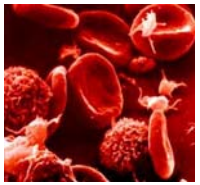
Azacitidine *versus* CCR (AZA-001 Trial)

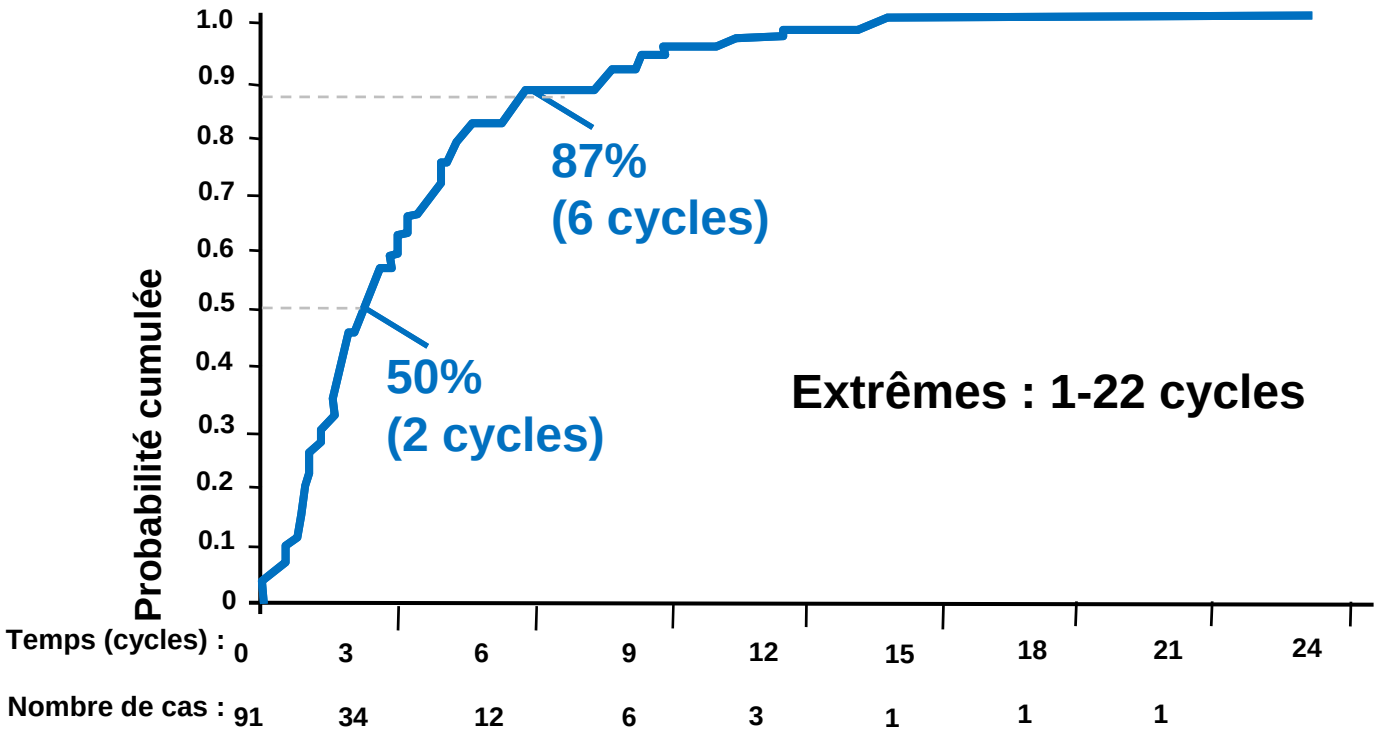




Fenaux 2009 Lancet Oncology

AZA-001 Trial





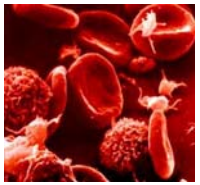
Délai de réponse varie de 2 à > 6 cycles

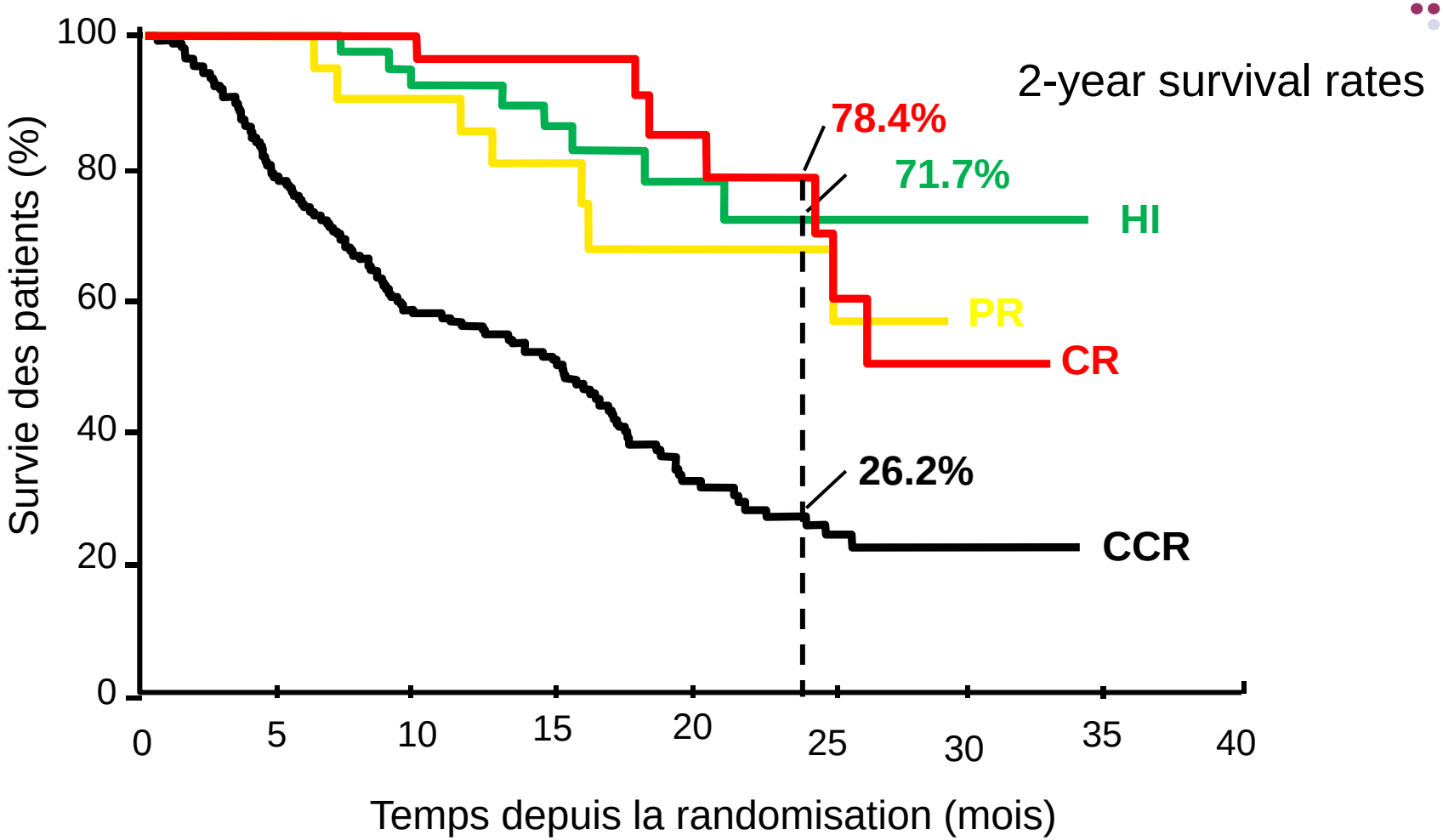
Délai médian de RP/HI à RC = 3,2 mois

Délai médian indépendance transfusionnelle = 1,6 mois

Silverman 2009 Blood

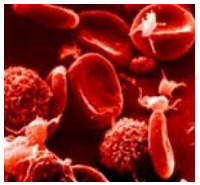
Survie globle selon la réponse au traitement





List 2008 ASCO

Azacitidine *versus* CCR
(AZA-001 Trial)

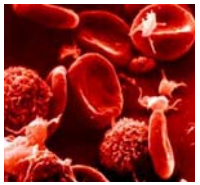


- Bénéfice confirmé >75ans
- Survie 55% à 2 ans *versus* 15%

Source ASH 2008 Abs 3629 – Po III-711 – J SEYMOUR et al.

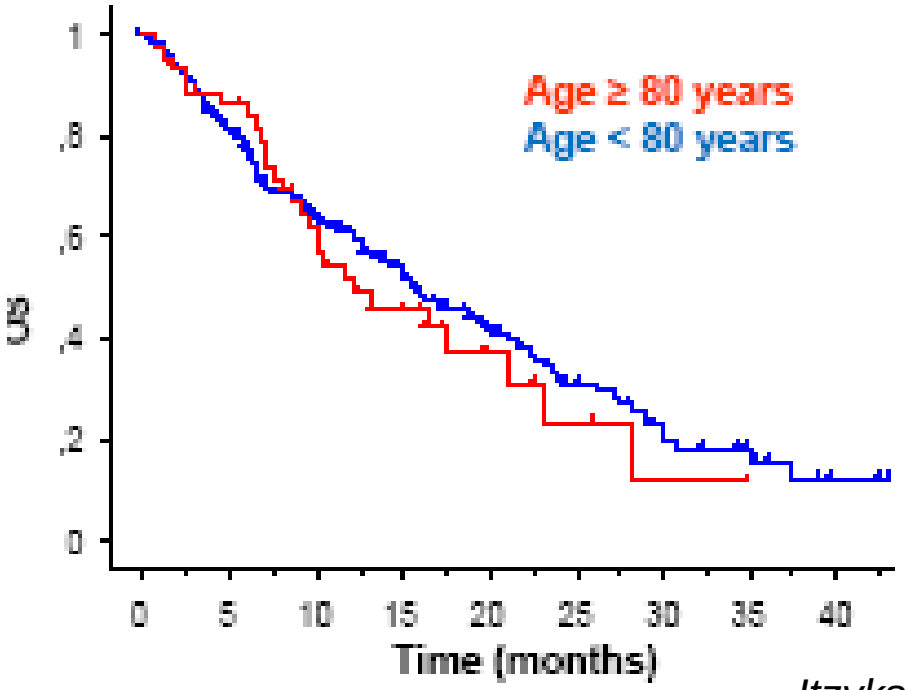
Abs 3636 – Po III-718 – P FENAUX et al.

Tolerance and efficacy > 80 yrs



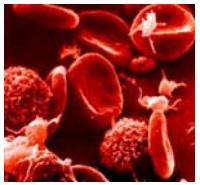
	< 80 yrs	> 80 yrs	p
Dose reduction	33%	49%	0.04
Interruption	29%	29%	ns
Febrile neutropenia	39%	27%	ns
Bleeding	13%	18%	0.04

French ATU
45 patients
Median age 83 yrs
2-yrs survival 23%



Itzykson ASH 2009

AMM janvier 2009



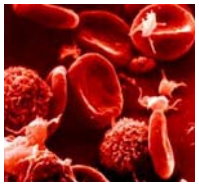
- « Vidaza® est indiqué dans le traitement des patients adultes non éligibles pour une transplantation de cellules souches hématopoïétiques et présentant :

- un syndrome myélodysplasique (SMD) de risque intermédiaire-2 ou élevé selon l'index pronostique international (International Prognostic Scoring System, IPSS),

- une leucémie myélomonocytaire chronique (LMMC) avec 10-29 % de blastes médullaires sans syndrome myéloprolifératif,

- une leucémie aiguë myéloblastique (LAM) avec 20-30% de blastes et dysplasie de lignées multiples, selon la classification de l'Organisation Mondiale de la Santé (OMS).»

Révolutions thérapeutiques



- L'EPO améliore
  - La qualité de vie
  - **La survie**

Park Blood 2008

Jadersten JCO 2008

- Le Lenalidomide
  - 1e thérapeutique ciblée

List NEJM 2005

- L'AZA améliore
  - La qualité de vie
  - Les cytopénies
  - **La survie**

Fenaux Lancet Oncol 2009