A microscopic image showing several tricholeucocytes, which are white blood cells with a characteristic star-shaped or sunburst appearance of their granules. The cells are stained and appear as light-colored, circular structures with a darker, granular center. The background is a light, slightly textured grey.

**LEUCEMIE A
TRICHOLEUCOCYTES D'UN
SUJET JEUNE TRAITÉ PAR
CLADRIBINE**

F. Ben Moussa, S. Rammeh, M.A. Laâtiri

OBSERVATION (1)

♂ âgé de 37 ans

Décembre 2004 :

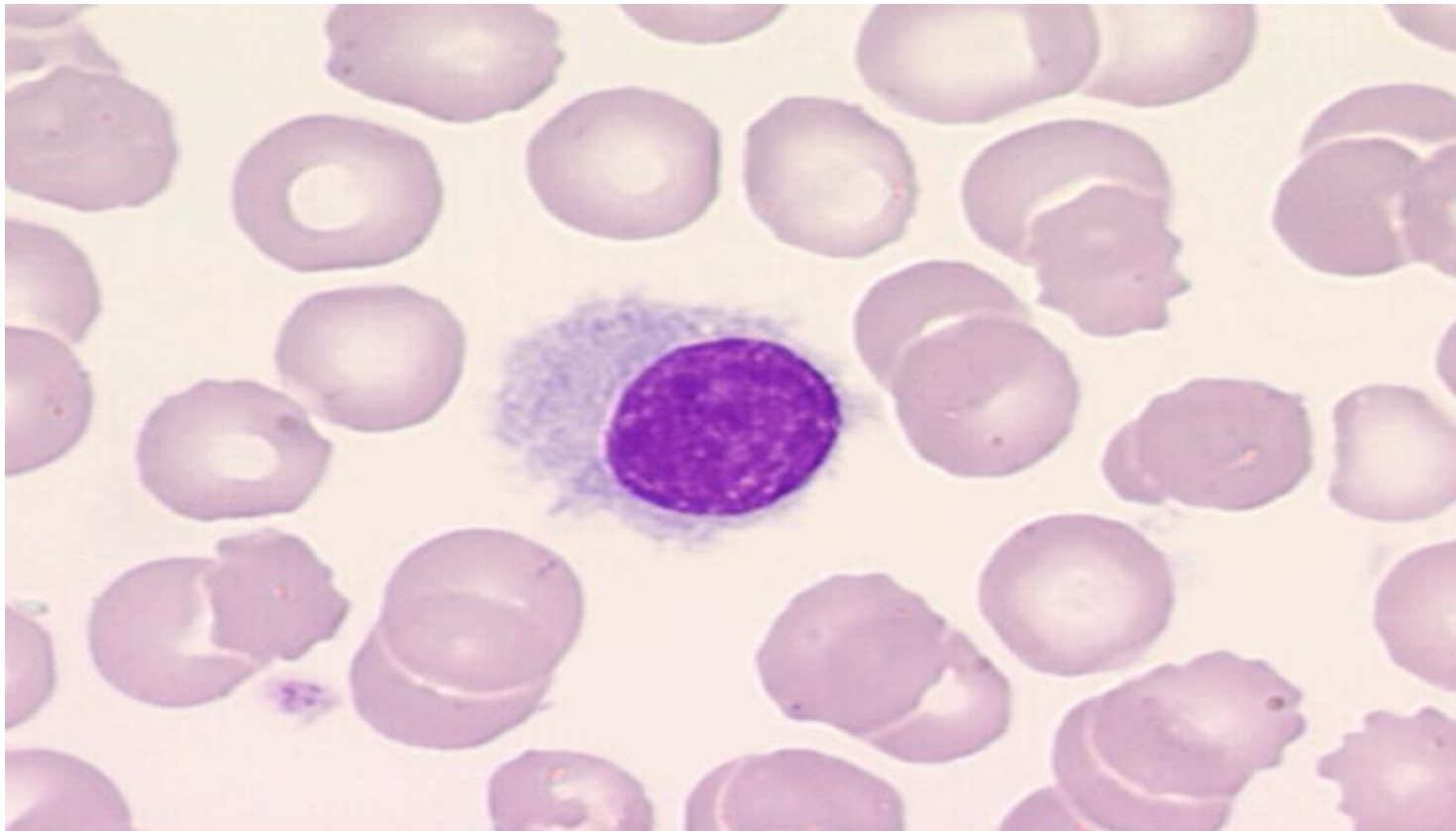
- Fatigue
- Douleur HCG
- SMG 18 cm du RC
- ADP = 0

NFS :

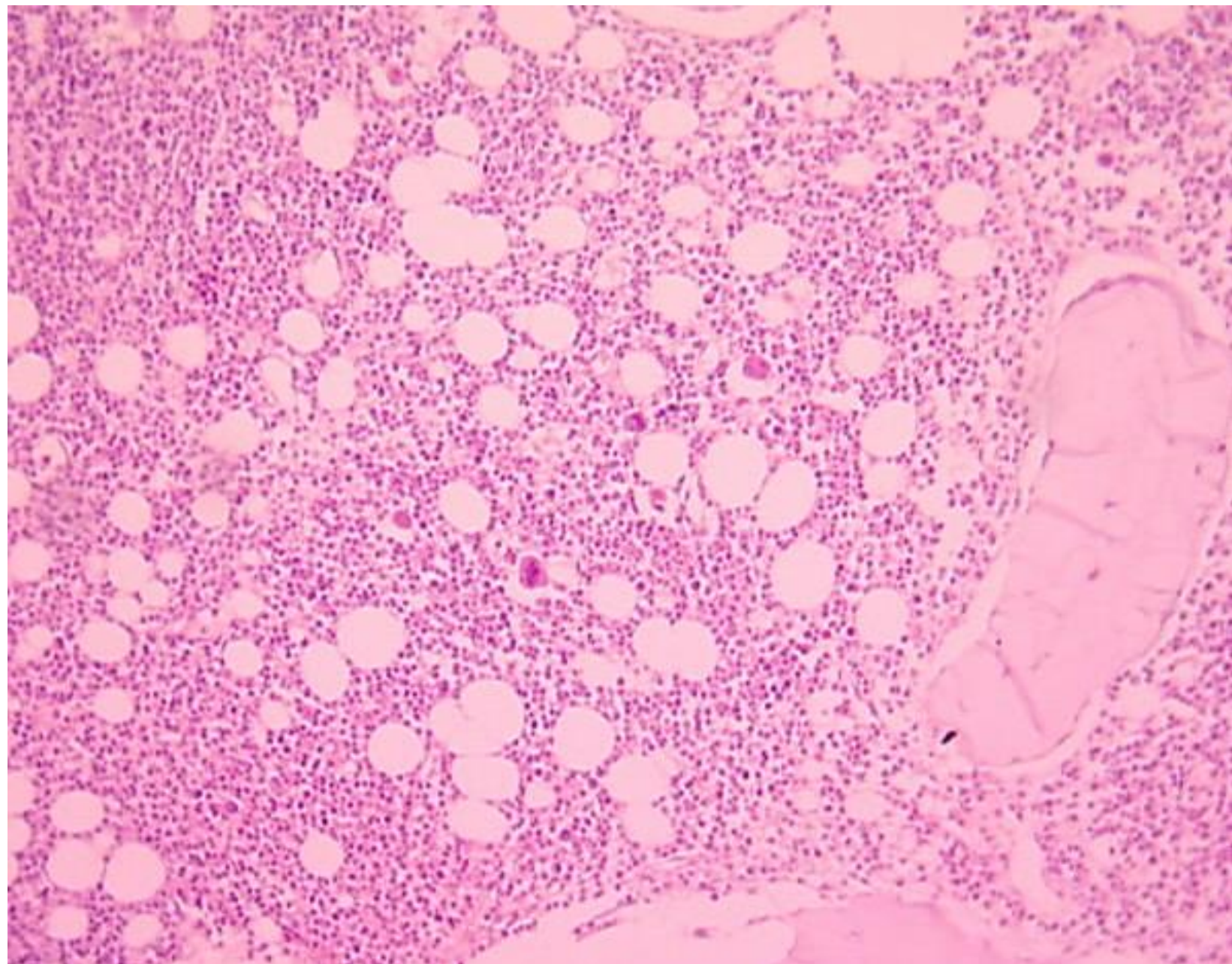
GB	=	47,7.10 ⁹ /l	(69% aspect tricho)
Hb	=	12,1 g/dl	
Pq	=	124.10 ⁹ /l	

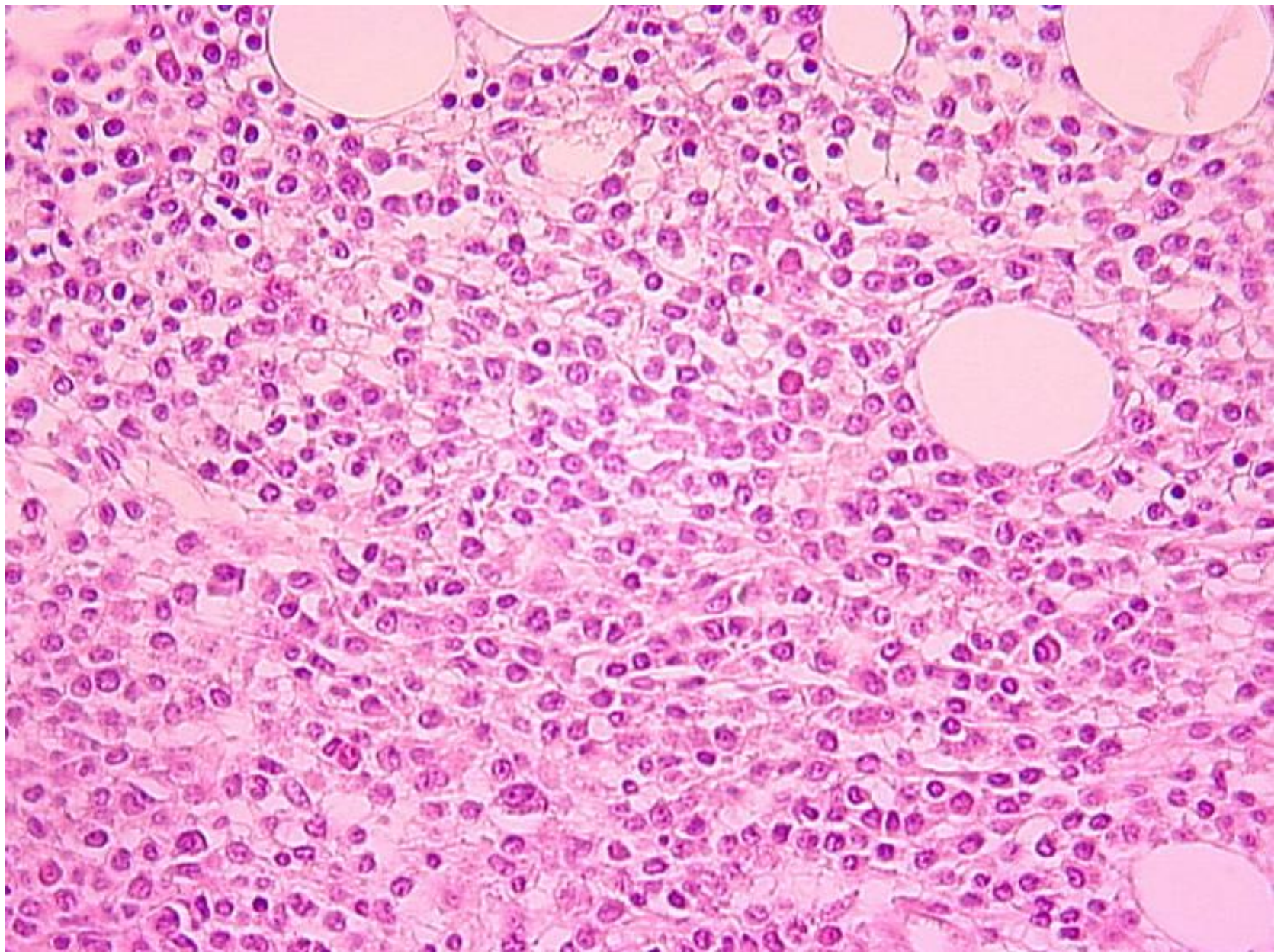
OBSERVATION (2)

Frottis sanguin :



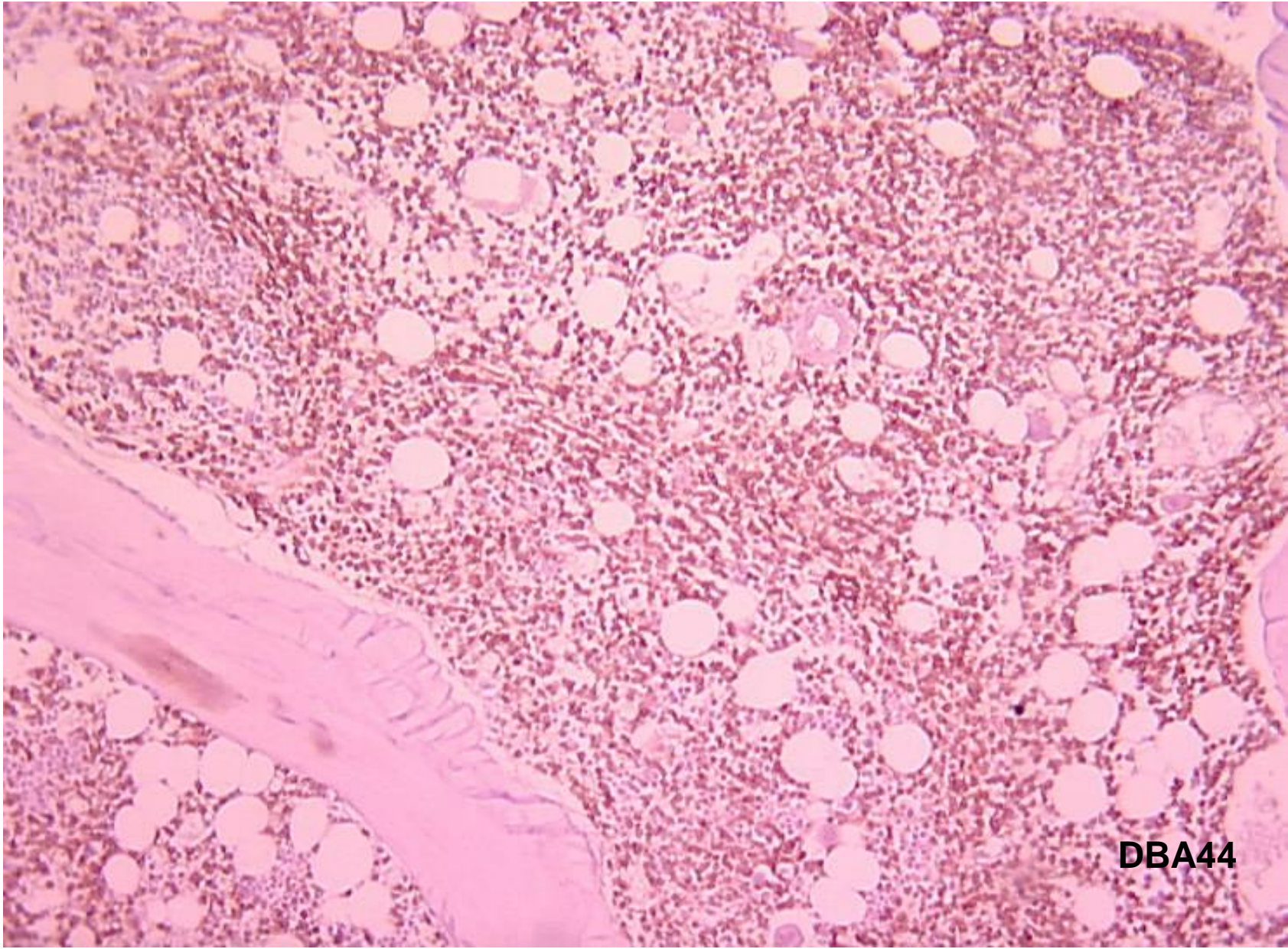
BOM →







CD20



DBA44

OBSERVATION (3)

- Immuno-Phénotypage (sang périph) « CNTS »:
 - Pop. Lymph. B (CD 19⁺, CD20⁺, CD23⁻, FMC7⁺, CD5⁻)
 - CD103⁺, CD25⁺, (CD11c non fait)
 - Ch. kappa monoclonale

⇒ Leucémie à tricholeucocytes
- TTT : Cladribine 0,1mg/kg J1 à J7

OBSERVATION (4)

- Evolution :
 - toxicité : neutropénie Grade 3
thrombopénie Grade 2
 - disparition de la SMG
 - normalisation NFS (tricho = 0)
- Immuno-Phénotypage (1 mois après ttt) :
tricho = $0,7 \cdot 10^{-2}/l$

OBSERVATION (5)

- 14 mois après : SMG
NFS : GB = $5,2 \cdot 10^9/l$ (10% tricho)
Hb = 15,3
Pq = 110 000
Immuno Phéno (HAO) :
CD103⁺, CD11c⁺, CD25⁺
- TTT : 2ème cure Cladribine
→ RC (SMG = 0, NFS Nle)
- Toxicité : Infection-ORL : Grade 2
Neutropenie : Grade 4
Thrombopenie : Grade 3
- Prophylaxie : Bactrim

COMMENTAIRES (1)

Age jeune

- 53 ans (24-88) *Saven, Blood 1998*
- 55 ans (26-78) *Marotta, Eur J Haematol 2006*
- 56 ans (32-75) *Jehn, Ann Hematol 1999*
- 57 ans (33-77) *Jehn, Leukemia 2004*
- 60 ans (31-86) *Maloisel, Leukemia 2003*

COMMENTAIRES (2)

Hyperleucocytose

- Habituellement : Pancytopenie
- GB : Médiane 3780 (700 – 32000)
Marotta Eur J Hematol 2006
- Hyperleucocytose importante : rare
Shibayama Int J Hematol 1996
Ng MH Int J Hematol 1991

COMMENTAIRES (3)

Evaluation de la réponse

- Critères du NCI (1987):

- * Disparition du syndrome tumoral
- * Hb > 12 g/dl
- * PNN > 1500 / mm³
- * Pq > 100 000 / mm³
- * FS, MO : pas de TCL

COMMENTAIRES (3)

Evaluation de la réponse

- Autres critères:

- * immunohistochimie (BOM)
- * immunophénotypage (sang et moelle)
- * PCR

Matutes

Br J Haematol 1997

Tallman

Clin Cancer Res 1999

Sansville

Am J Clin Pathol 2003

Ravani

Blood 2005

Arons

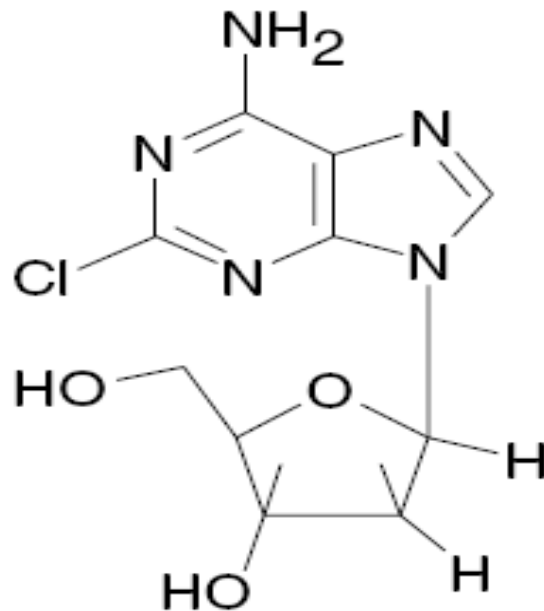
Clin Cancer Res 2006

COMMENTAIRES (3)

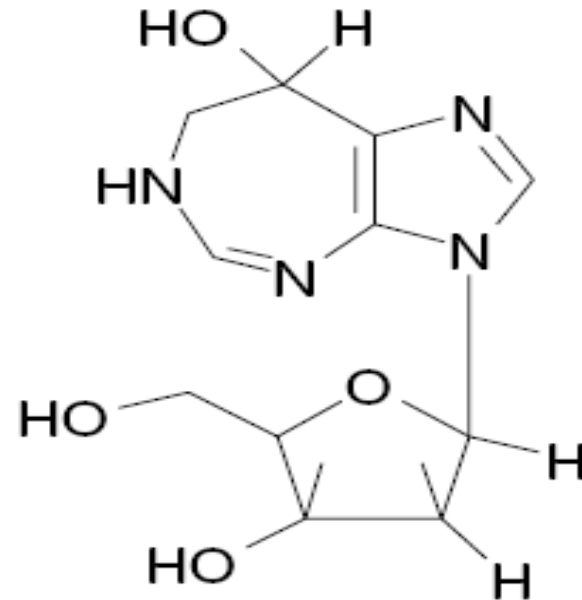
Traitement

- Splenectomie
- Interferon
- Analogues des purines
 - * Désoxycoformycine (DCP) Pentostatine (Nipent®)
 - * 2-Chlorodésoxyadenosine (2-CdA) Cladribine (Leustatine®)

COMMENTAIRES (4)



Cladribine
2-chloro-2'-deoxyadenosine
(2-CdA)



Pentostatin
2'-deoxycorformycin
(DCF)

Figure 1 Chemical structures of purine nucleoside analogues (cladribine and pentostatin) active in hairy cell leukemia.

COMMENTAIRES (4)

PENTOSTATINE

Table 2 Larger clinical studies of pentostatin in hairy cell leukemia

Study	Treatment	Number of patients	CR rate (%)	Duration of CR (median time to relapse)	Rate of relapse at follow-up
Kraut et al. ⁶⁴	2–4 mg/m ² i.v. bi-weekly	23	87	13.5 months	25% relapse at 82 months
Johnston et al. ⁷⁰	4 mg/m ² i.v. weekly × 3 every 8 weeks	28	89	49 months	36% relapse at 49 months
Dearden et al. ⁶⁷	4 mg/m ² i.v. either weekly or bi-weekly	165	82	51.5 months	24% relapse at 71 months
Grever et al. ¹⁵	2–4 mg/m ² i.v. bi-weekly	154	76	67% estimated DFS at 10 years	18.5% relapse at 111 months
Rafel et al. ⁶⁹	4 mg/m ² i.v. bi-weekly	78	72	46 months	19.7% relapse at 29 months
Maloisel et al. ⁷³	4 mg/m ² i.v. bi-weekly	230	79	68.8% estimated DSF at 10 years	NA
Flinn et al. ⁷²	4 mg/m ² i.v. bi-weekly	241	76	67% estimated relapse free survival at 10 years	NA
Ribeiro et al. ⁶⁸	4 mg/m ² i.v. bi-weekly	50	44	No relapse at 21 months for untreated patients; 2/14 previously treated patients relapsed by 47 months	NA
Else et al. ⁷⁴	4 mg/m ² i.v. every 1 or 2 weeks	185	81	15 years	24% at 5 years, 42% at 10 years

Abbreviations: CR, complete response; DFS, disease free survival; NA, not applicable; i.v., intravenously.

COMMENTAIRES (4)

CLADRIBINE

Table 1 Larger clinical trials of cladribine in hairy cell leukemia

Study	Treatment	Number of pts	CR rate (%)	Duration of CR (median time to relapse)	Rate of relapse at follow-up
Saven et al. ⁵¹	0.087 or 0.1 mg/kg/d c.i. × 7 days	349	91	96% survival at 48 months	26% at median 29 months
Goodman et al. ⁵⁴	0.1 mg/kg/d c.i. × 7 days	207	95	98	37% at median 44 months
Hoffman et al. ⁵⁶	0.1 mg/kg/d c.i. × 7 days	49	76	RFS 80% at median 55 months follow-up	20% at 55 months
Cheson et al. ⁴⁶	0.1 mg/kg/d c.i. × 7 days	861	50	Median not reached	NA
Robak et al. ⁴⁸	2 h i.v. infusion/5 days or c.i./7 days	41	76	NA	NA
Jehn et al. ³⁰	0.1 mg/kg/d c.i. × 7 days	44	98	DSF 36% at 12 years OS 79% at 12 years	NA
von Rohr et al. ⁴⁹	s.c. bolus injection/5 days	62	76	NA	NA
Luria et al. ⁵⁸	0.15 mg/kg weekly for 6 weeks	25	76	NA	NA
Robak et al. ⁵⁷	0.12 mg/kg/d in 2 h i.v. infusion/5 days	97	77.3	37.4 months	26.7%
Chadha et al. ⁴⁵	0.1 mg/kg/day × 7, c.i.	86	79	RFS 54% at 12 years	
Zinzani et al. ⁵³	0.14 mg/kg/d for 5 d or once a week for 5 cycles	37	81	27% at 122 months	52% at 13 yr
Juliusson et al. ⁶¹	3.4 mg/m ² s.c. qd × 7 days	73	81	NA	NA

Abbreviations: CR, complete response; DFS, disease free survival; OS –overall survival; RFS, relapse free survival; 2-CdA, 2-chlorodeoxyadenosine; NA, not applicable; i.v. –intravenous; s.c., subcutaneous; c.i., continuous infusion; d, day; yr, year.

COMMENTAIRES (4)

Rituximab et Immunotoxines

Table 3 Studies evaluating the efficacy of monoclonal antibodies in the treatment of hairy cell leukemia

Study	Treatment regimen	Patients characteristic	Number of pts	Median age (range)	Response		Median OR duration
					OR	CR	
Lauria et al. ²⁵	RIT – 375 mg/m ² i.v. once a week, × 4	Relapsed	10	55 (41–78)	5 (50%)	1 (10%)	16 + m
Hagberg and Lundholm ⁷⁶	RIT – 375 mg/m ² i.v. once a week, × 4	Relapsed (8 pts) untreated (3 pts)	11	NR	7 (64%)	6 (55%)	14 m (1–34 m)
Niewa et al. ⁸¹	RIT – 375 mg/m ² i.v. once a week, × 4	2-CdA failed	24	53.5 (38–81)	6 (25%)	3 (13%)	NR
Thomson et al. ⁸²	RIT – 375 mg/m ² i.v. once a week, × 8	Refractory/relapsed	15	(35–71)	12 (80%)	8 (53%)	8 > 45 m
Kreitman et al. ²⁶	BL22 – 0.2–4 mg i.v. every other day × 3 for 16 cycles	Refractory	16	54	13 (81%)	11 (69%)	4 > 14 m
Kreitman et al. ⁸⁴	LMB-2 – 30, 40 and 63 µg/kg i.v. every other day for 3 doses repeated monthly	Refractory	4	59 (47–66)	4 (100%)	1 (25%)	CR 20 m

Abbreviations: HCL, hairy cell leukemia; RIT, rituximab; BL-22, RFB4 (dsFv)-PE-38 anti-CD22 MoAb; LMB2, Tac (Fv) PE-38 anti-CD25 MoAb; OR, overall response; CR, complete response; MR, minor response; NR, not reported; 2-CdA, cladribine; yrs, years; m, month; pts, patients.

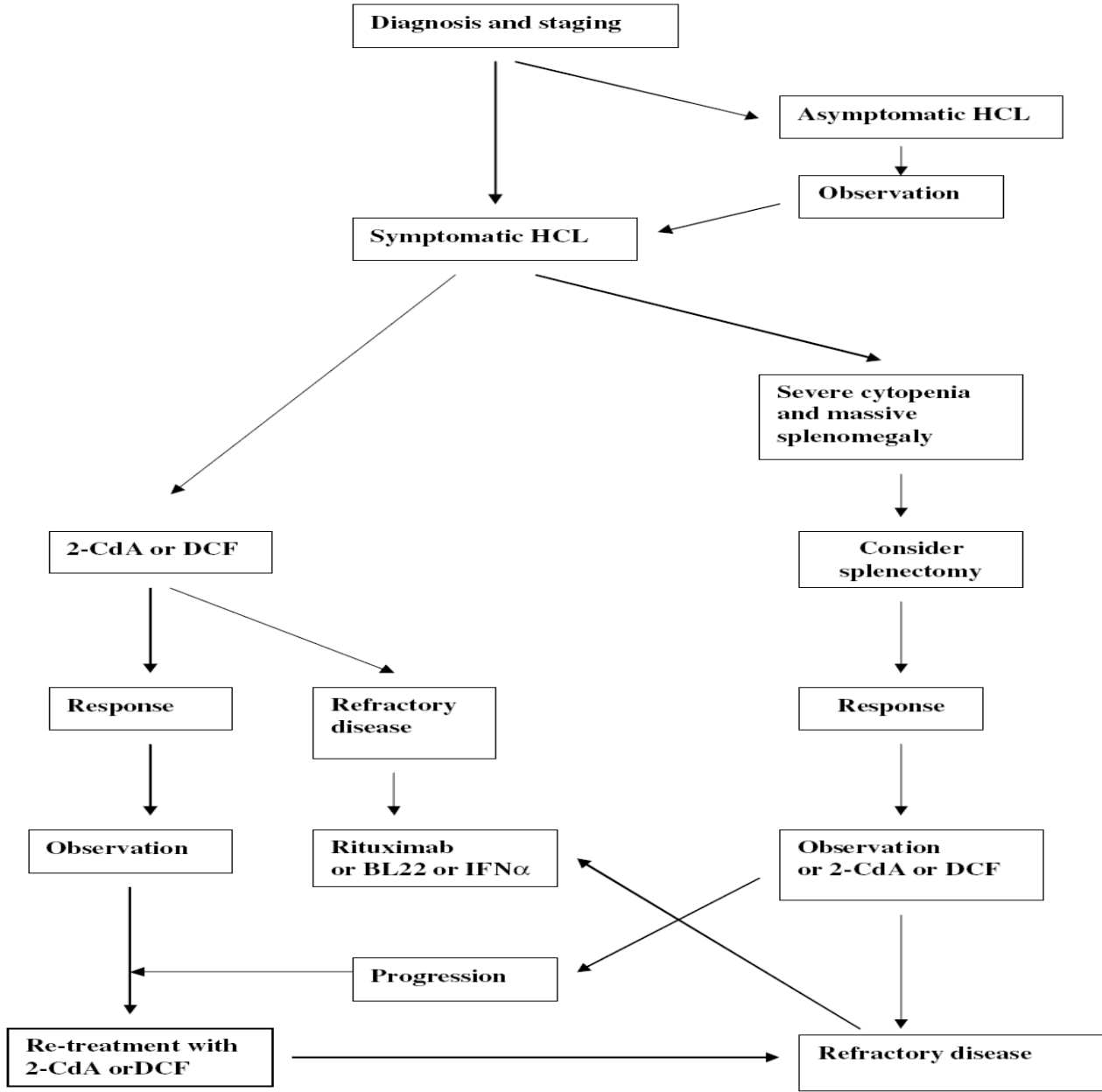


Figure 2 Proposed treatment algorithm for hairy cell leukemia (HCL). *Abbreviations:* 2-CdA, cladribine; DCF, pentostatin; IFN- α , interferon- α ; BL22, anti-CD22 immunotoxin.

MERCI