

(مقاله مروری)

## بیولوژی، تشخیص و درمان لوسمی مزمن لنفوسیت B

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### چکیده

در دو دهه گذشته پیشرفت قابل ملاحظه‌ای در زمینه شناسایی پاتوفیزیولوژی بیماری **Chronic Lymphocytic Leukemia (CLL)** به دست آمد. پیشرفت ابزارهای تشخیصی موجب شناسایی بیماری در تعداد زیادی از بیماران بدون علامت شد. با بررسی‌های دقیق‌تر CLL بر مبنای تمایل به پیشرفت سریع و یا عدم پیشرفت سریع بیماری به دو گروه با پیش‌آگهی خوب و بد تقسیم شد. CLL قبلاً به عنوان بیماری غیر قابل درمان افراد مسن در نظر گرفته می‌شد. از آنجائی که اکثر بیماران با بیماری CLL و نه به واسطه آن می‌میرند، درمان‌ها بر علامت‌درمانی توسط داروهایی مانند کلرآمبوسیل متمرکز بوده است. این داروها درمان قطعی بیماری نمی‌باشند، حتی در صورتی که زودتر از موعد مناسب به بیماران داده شود دوره زندگی بیمار را کوتاه‌تر نیز می‌کند. در این مقاله سعی شده است ضمن بررسی اپیدمیولوژی و تشخیص بیماری، عوامل موثر در پیش‌آگهی CLL تشریح شود. همچنین در باره درمان‌های مختلف از قبیل شیمی‌درمانی و منوکلونال آنتی‌بادی به اختصار بحث شده است.

واژه‌های کلیدی: لوسمی، لنفوسیت B، پیش‌آگهی

### اپیدمیولوژی و شیوع

[ ]

B-CLL

[ ]

%

[ ]

CLL

CLL

HLA

[ ]

[ ] B-CLL

CLL Dameshek

/

( )

CLL

CD5 B .[ ]

% / CD19

[ ]

[ ]

CLL

Clonal CD5  
Lymphocytosis Of Undetermined Significance  
CLL (CLUS)

(NCI)

(IWCLL) CLL

[ ] (%)

× /L

(13q14 )

CLL

CLL

[ ]

CD23<sup>+</sup> CD5<sup>+</sup> CD19<sup>+</sup>

B

CD79b/CD22

FMC<sup>-</sup>

مشخصات بالینی

[ ]

B

CLL

CD5 CD23

رتبه بندی بالینی

Binet

CLL

B

[ ]

IgM

B

[ ]

Rai

CD79b

CD22

CD21

IgD

(Binet B Rai I/II)

(Rai 0 Binet A)

G0

%

[ ]

(Binet C Rai III/IV)

[ ]

G1

( )

(Survival)

[ ]

B-CLL

CLL

( )

%

Binet

% -

## CLL

## Staging

Binet classification			Rai classification				Median overall survival
Stage	Definition	% of patients	Risk group	Stage	Definition	% of patients	
A	< 3 lymphoid areas	60	Low	0	Lymphocytosis only	30	> 10 yrs
B	> 3 lymphoid areas	30	Intermediate	I	Lymphadenopathy	25	5-7 yrs
				II	Hepato- or splenomegaly ± lymphadenopathy	25	
C	Hemoglobin < 100 g/L or Platelets < 100 x 10 <sup>9</sup> /L	10	High	III	Hemoglobin < 100 g/L	10	1-3 yrs
				IV	Platelets < 100 x 10 <sup>9</sup> /L	10	

× /L

β2

CD23

g/L

P53

VH

% [ ]

[ ]

سایر عوامل دخیل در پیش آگهی:

وضعیت موتاسیون ژن VH

B

CLL

(naive)

Pre-germinal ) .

(

%

.(centers disease

VH

CLL

[ ]

CLL (Survival)

B

CLL

B

(Unmutated)

B

LDH

B

## عوامل پیش آگهی

عوامل پیش آگهی کلاسیک

Stage

( )

VH [ ] Mutated  
CLL Microarray  
% [ ]  
%  
CLL VH  
% [ ]  
% [ ]  
[ ] [ ]  
VH CLL  
[ ]

VH

VH

CLL	CLL	
%	%	VH
M>F	M=F	
CD38+ / CD69+	CD71+ / CD62L+	
		CD38
		ZAP-70
		BCR
%	%	13q14
%	%	11q23
%	%	11q23 17q13
%	%	
VH31-69	VH3-21	VH

. % . CLL VH  
 ZAP-70 . VH  
 VH1-69 VH4-34 VH3-07 VH3-21  
 . [ ] % .  
 :CD38 . VH1-69 CLL  
 . CD38 . VH3-21  
 CD38 VH3-21  
 CD38 . cADP-Ribos VH1-69 [ ]  
 CD38 . Ca<sup>2+</sup>  
 B T J D VH  
 B CD38 [ ] NK CD3  
 . CLL [ ] VH1-69 VH1-69  
 CD38  
 % [ ] VH CLL  
 CD38 J D  
 CD38 [ ]  
 . [ ] [ ] VH3-21 Ig  
 . CLL  
 [ ]  
**اختلالات کرموزومی** Zeta - associated protein-70 (ZAP-70)  
 S IgVH  
 CLL  
 [ ] ZAP-70 .  
 % - TCR T ζ  
 [ ] T . T  
 Fluorescence In situ ZAP-70 B . NK  
 % Hybridization (FISH) ZAP-70 mRNA .  
 [ ] [ ] CLL  
 [ ] [ ] ZAP-70  
 ) 11q ( % ) 13q : CLL ZAP-70 .  
 . ( % ) ( % [ - ]

17P %

CLL 17p (q6) (%)

VH 11q

( ) 17p

13q

[ ] ( )

VH 12q 11q 17p

Bechter [ ] 13q

[ ]

Verstovek [ ] P53 17p<sub>13</sub>

CLL %

(Richter's transformation)

CLL [ ] [ ]

[ ]

Tckirkov [ ] [ ]

mRNA تلو مرها

Human Telomerase Reverse Transcriptase (hTERT) (6-12Kbp) TTAGGG

hTERT

[ ] VH

**اختلالات ایمنولوژیک ناشی از بیماری CLL**

۱. هیپوگاما گلوبولینمی

CLL

3'

%) [ ] T

(

DNA [ ]

% [ ]

Telomeric Repeat Binding Factor I TRAF I

TRAF II

[ ]

درمان B-CLL

[ ] %

CLL

IVIg

[ ]

۲. خود ایمنی

CLL

[ ]

(AIHA)

[ ]

% -

[ ]

T  
[ - ]  
AIHA

(a .

(c

(b

( CD20

(e

(d

[ ]

( anti CD52)

(f

[ ]

(g

ترانس فرمیشن ریشتتر

CLL %

% -

CLL

Pro lymphocytic Leukemia (PLL)

Objective)

NCI

(response

Richter Syndrome

(% )

- ]

(RS)

[

[ ] CLL

% - %

OR

[ ]

-

% -

T

[ ]

%

OR

CLL

anti CD52

[ ]

% -

CR

EBV

RS

[ ]

OR

( )

[ ]

% % CR %

II

[ ]

[ ]

anti CD52

CLL

Alemtuzumab

(anti CD20)

Rituximab

(antiCD52)

### نقش سلول های T در CLL

[ ] CLL

[ ] ( / - ) T

II

CLL

T

antiCD20 (Chimeric )

T

IL-4 IFN- $\gamma$

CLL

CD8<sup>+</sup> CD4<sup>+</sup>

[ ]

IL-4

CD4 T

CR

M.D

[ ]

CLL

T

[ ]

[ ]

mRNA

( )

%

CD52

CLL22

CLL17

T

T B

[ ]

CD40

[ ]

RNA

CLL22

(anti CD52)

T

[ ]

CD52

antiCD52

(CD4 T )

(ADCC)

[ ]

OR

anti CD52

[ ]

TNF-a IL-13 IL-8 IFN- $\gamma$  IL-4

[ ]

% -

IL-4 [ ]

%

[ ] in vivo

T

%

OR

CLL



TCLI	ZAP-70			
miR-181 miR-29			[ ] (Pseudo-Follicles)	
CLL	RNA	Ki-67	Bcl-2	B
	[ ]	CD4 <sup>+</sup>	T	
				CD154+ (CD40L)

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[ ]

**MicroRNA**

RNA (Micro RNA) RNA

(nt 24-19)

RNA

Micro RNA (Pre mi RNA)

nt 100-70 RNA

Pre mic RNA

Dicer

Micro

mRNA 3' RNA

mRNA

Micro RNA

CD5<sup>+</sup> B miR- 16-1 miR-15a

13q14.3

CLL Micro RNA

CLL

Micro RNA

miR16-1 miR-15a

13q14.3

Bcl-2 Micro RNA

IgVH CLL

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