

Vztah cytologických charakteristik a cytogenetických změn u nemocných s chronickou lymfatickou leukémií

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A Lapčíková, J Juráňová, R Chytilíková,
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Hemato-onkologická klinika
Fakultní nemocnice Olomouc



EVROPSKÁ UNIE



MINISTERSTVO ŠKOLSTVÍ,
MLÁDEŽE A TĚLOVÝCHOVY



OP Vzdělávání
pro konkurenceschopnost

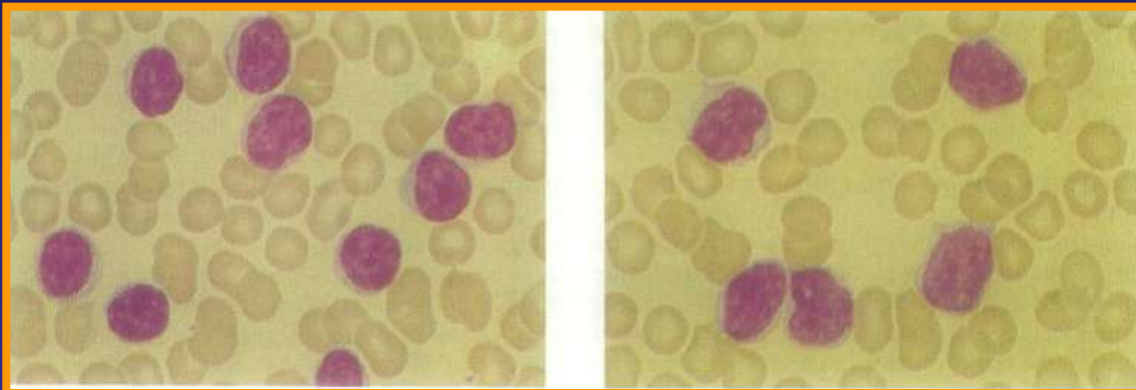


Univerzita P. J. Štefánika
v Olomouci

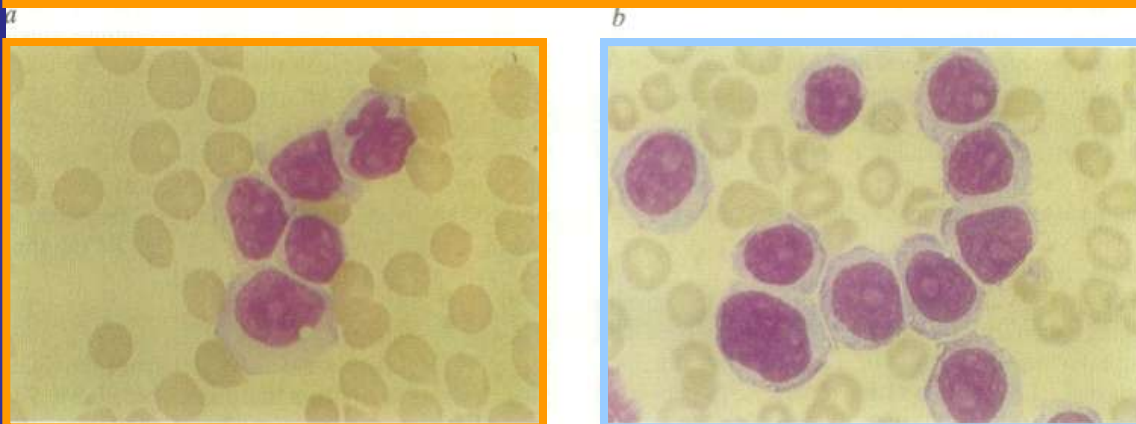
INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

Proposals for the classification of chronic (mature) B and T lymphoid leukaemias

J M BENNETT,* D CATOVSKY,† M-T DANIEL,‡ G FLANDRIN,‡
D A G GALTON,¶ H R GRALNICK,§ C SULTAN,** THE FRENCH-AMERICAN-
BRITISH (FAB) COOPERATIVE GROUP



CLL



CLL / PLL

PLL

Prognostická komplexita u CLL

nádorová buňka

ZAP-70, CD20,
LDT, ...

Sérové markery

s-TK, sCD23, B2M,
VEGF

Klinické stádium
Imunologická odpověď

Morfologie a prognóza?

Genetika

FISH, IgVH

Morfologie a prognóza?

Prognostic relevance of the FAB morphological criteria in chronic lymphocytic leukemia: correlations with IgV_H gene mutational status and other prognostic markers*

J. SCHWARZ¹, D. MIKULENKOVÁ¹, K. ČERMÁKOVÁ¹, V. POLANSKÁ¹, K. MICHALOVÁ¹, I. MARINOV¹, V. CAMPR¹, Š. RANSĐORFOVÁ¹, J. MARKOVÁ¹, L. PAVLIŠTOVÁ², J. BŘEZINOVÁ¹, J. SAJDOVÁ¹, D. ŠPONEROVÁ¹, Z. VOLKOVÁ¹, K. BENEŠOVÁ¹, J. ČERMÁK¹, A. VÍTEK¹, P. CETKOVSKÝ¹

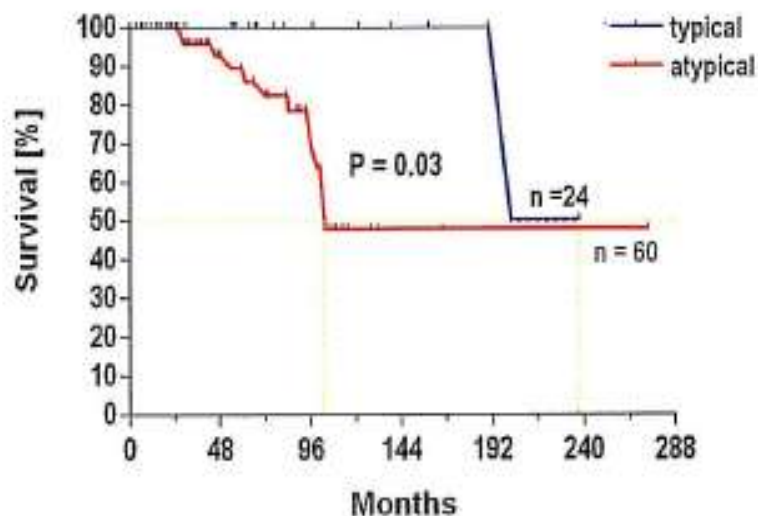


Figure 3. OS according to FAB morphology.

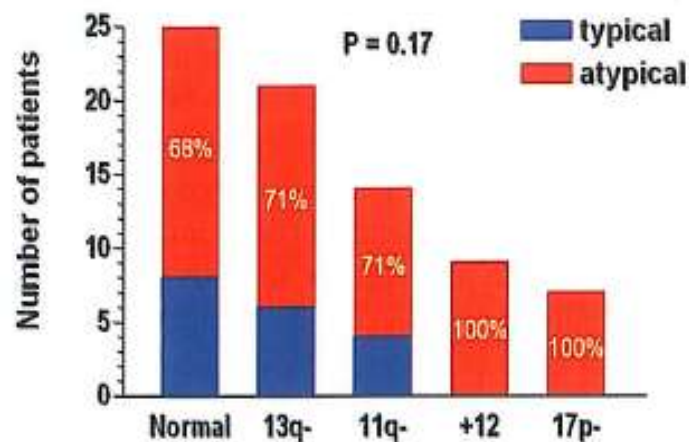


Figure 10. Cytogenetic aberrations and FAB morphology. The group with trisomy 12 and deletion 17 significantly ($p=0.01$) comprises of more atypical FAB cases than the group with normal cytogenetics or deletions of 13q and 11q.

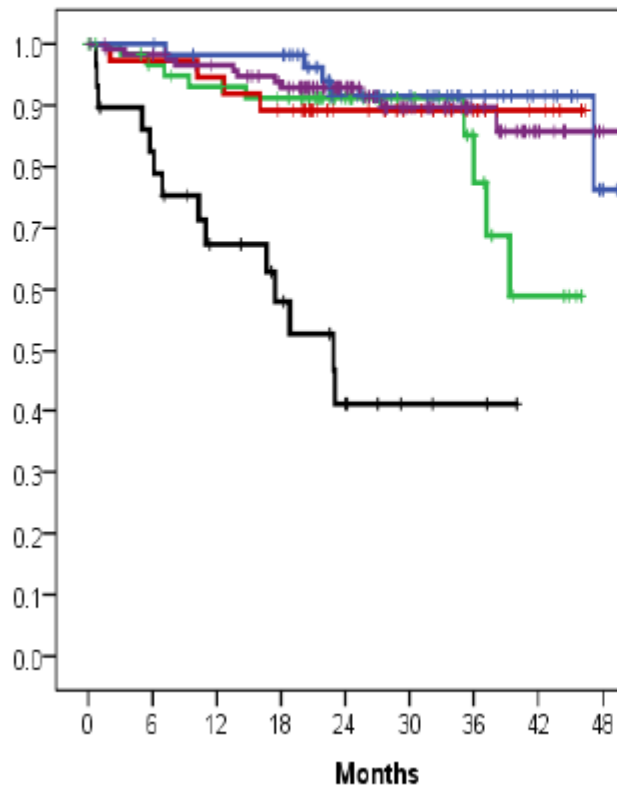
R Bigoni¹, A Cuneo¹, MG Roberti¹, A Bardi¹, GM Rigolin¹, N Piva¹, G Scapoli¹, R Spanedda¹, M Negrini², F Bullrich², ML Veronese², CM Croce² and G Castoldi¹

Antigen	No. of positive cases/Total tested % positive cells (median value, range in parentheses)							
	+12	Abn 13q	Abn 11q	Abn 6q	Other abn	Normal	Failures	Total
CD5/CD19 ⁺	9/9 71% (31-98)	5/5 83% (31-97)	3/3 86.5% (82-93)	2/2 89.5% (89-90)	8/8 71% (36-82)	6/6 52% (30-97)	10/10 80.5% (31-97)	43/43
CD23	5/7 73.5% (45-93)	3/4 90% (35-93)	2/3 78-86	1/2 93%	5/7 72% (40-91)	5/5 71% (50-97)	9/10 83% (70-97)	30/38
CD22	7/8 75% (60-92)	5/5 85% (46-91)	3/3 91% (90-94)	2/2 (88-90)	6/7 68% (48-93)	4/4 71.5% (57-88)	9/10 87% (65-98)	36/39
FMC7	4/7 70% (56-79)	2/4 (32-78)	1/3 57%	0/1	4/5 70% (43-92)	0/5	2/4 (77-91)	13/29 b
bright slg	3/9	3/5	1/3	1/2	3/8	2/6	2/10	15/43 b

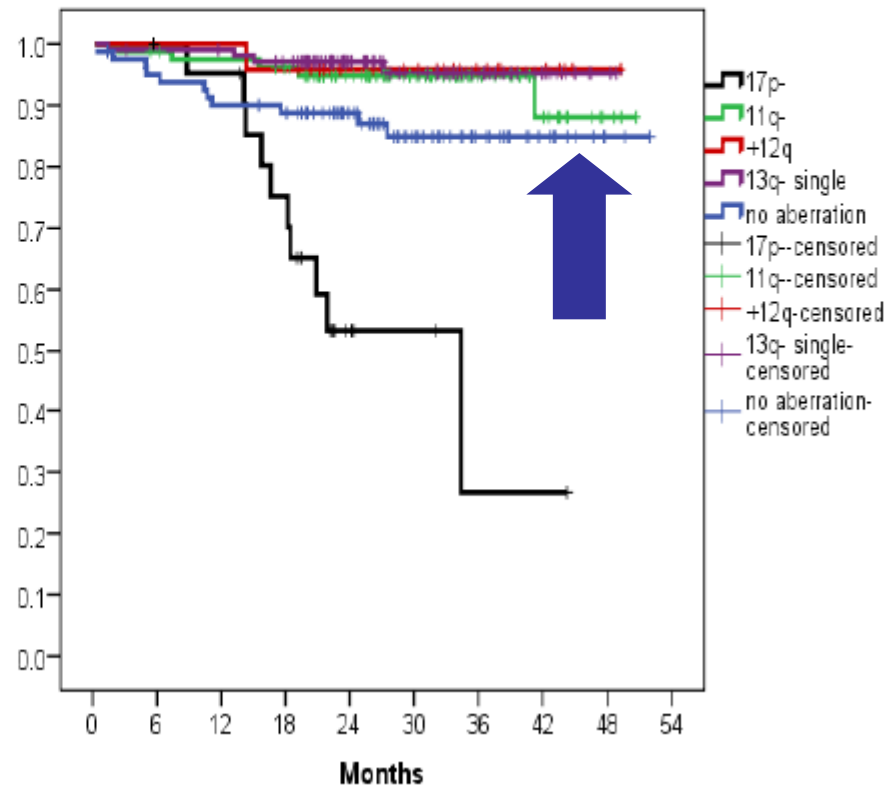
Cytogenetika : prognóza

CLL8 Genetic Analyses: OS

FC



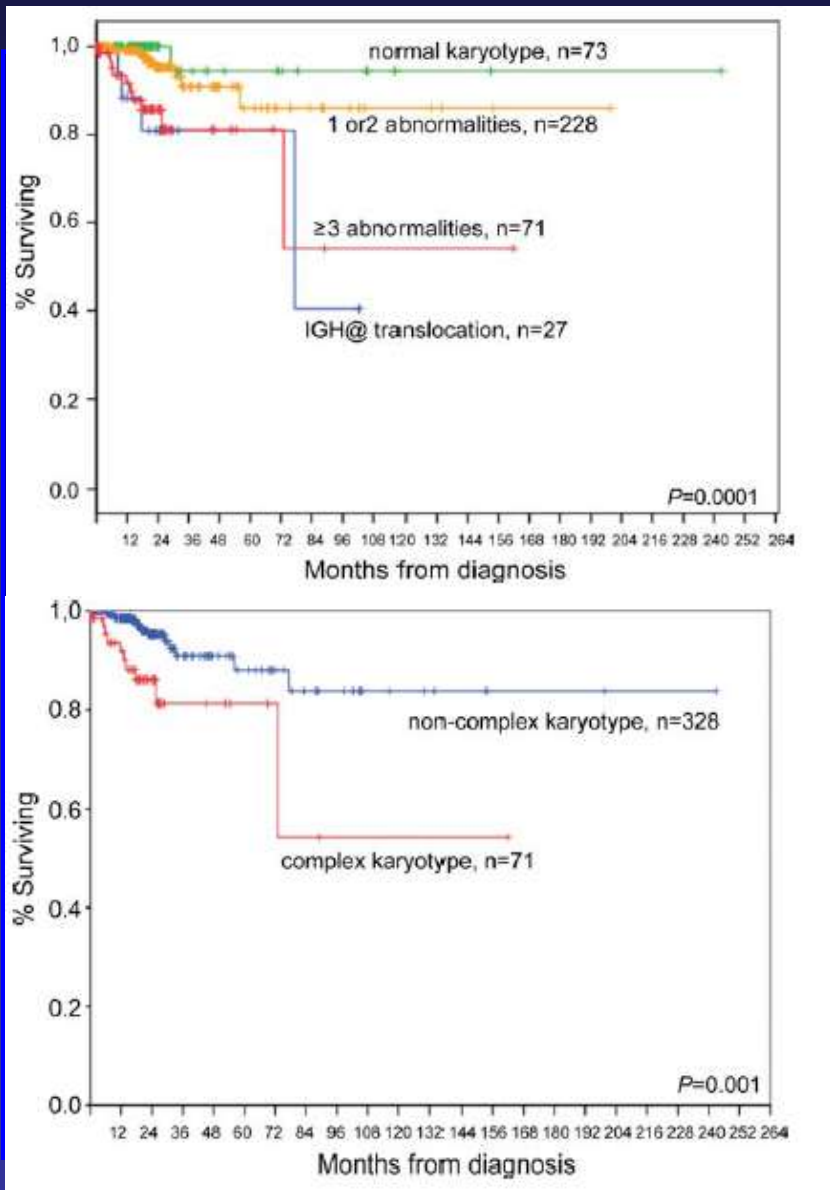
FCR



Hallek M, et al. *Blood*. 2008;112: Abstract 325.

CLL s „normální“ genetikou

Přídavné genetické změny!



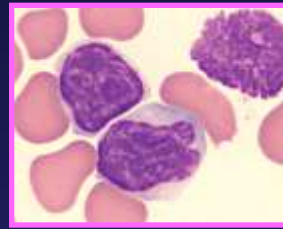
- V_H3-21: přídavné genetické změny v době dg. u 7/17 (41 %) nemocných
- inv (9), del 14q, dup c-myc, IgH rearr., der(18) t(X;18) ...
- výběr sond?
- mapování genomu?
- mapování mutací genů?

Jaký je význam morfologie
u nemocných s CLL
v roce 2010?

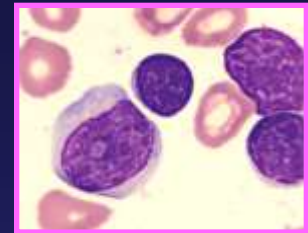
buněčné atypie



TYPICKÁ CLL



ATYPICKÁ CLL



CLL/PLL

cytogenetické změny

STABILNÍ GENOM



NESTABILNÍ GENOM

abnormity fenotypu

TYPICKÝ FENOTYP

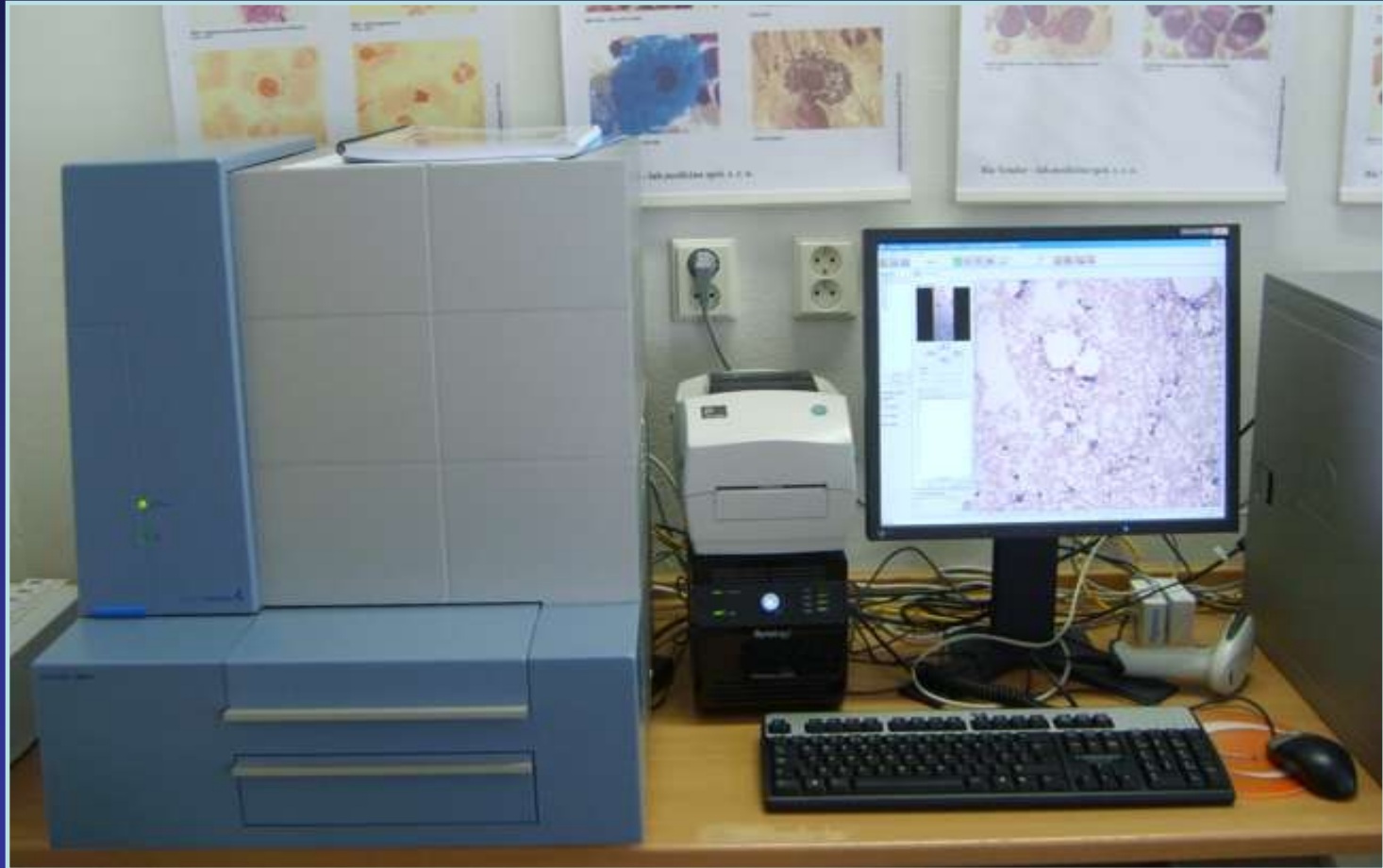


ATYPICKÝ FENOTYP

Nové technologie

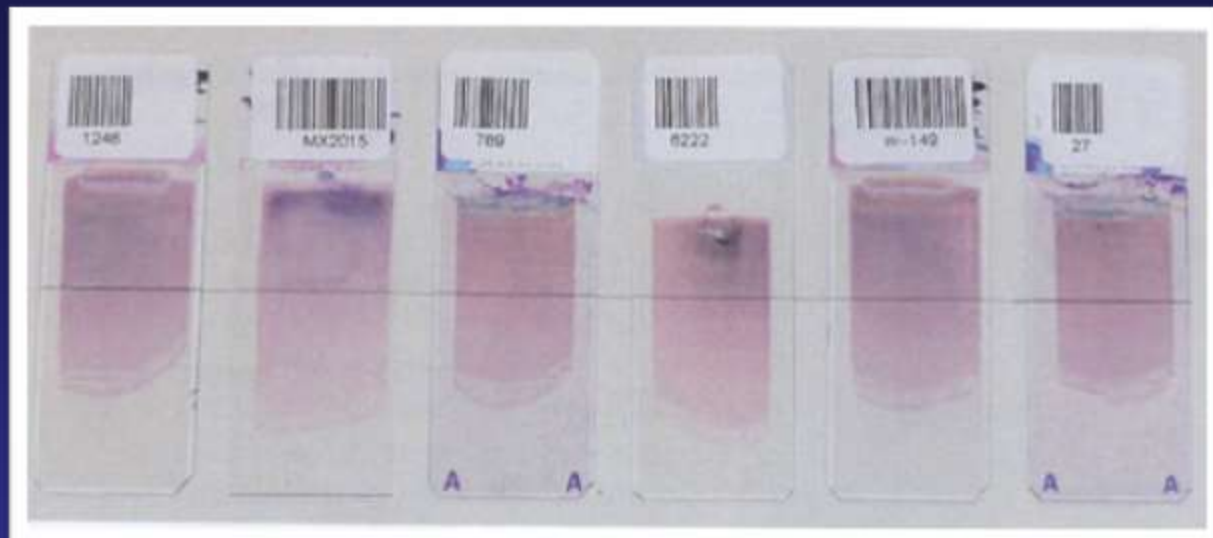
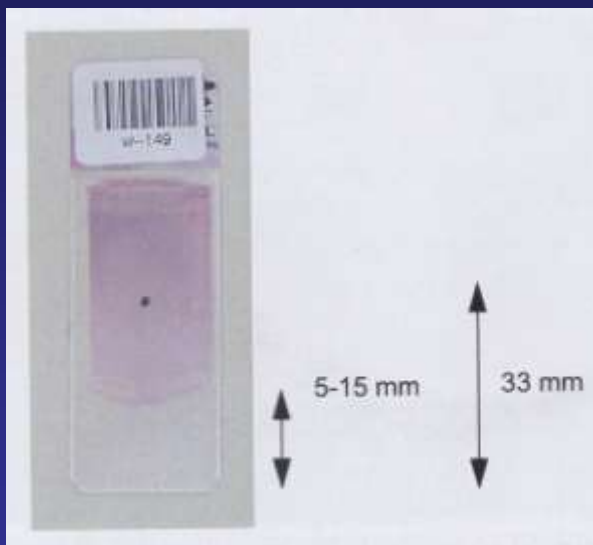
- DM 96 a Expert viewer firmy Sysmex
- Dot Slide firmy Olympus
- Nikon Coolscope
- Možnost kombinace s telekomunikačními systémy (on-line konzultace a telekonference)

Cella Vision DM 96

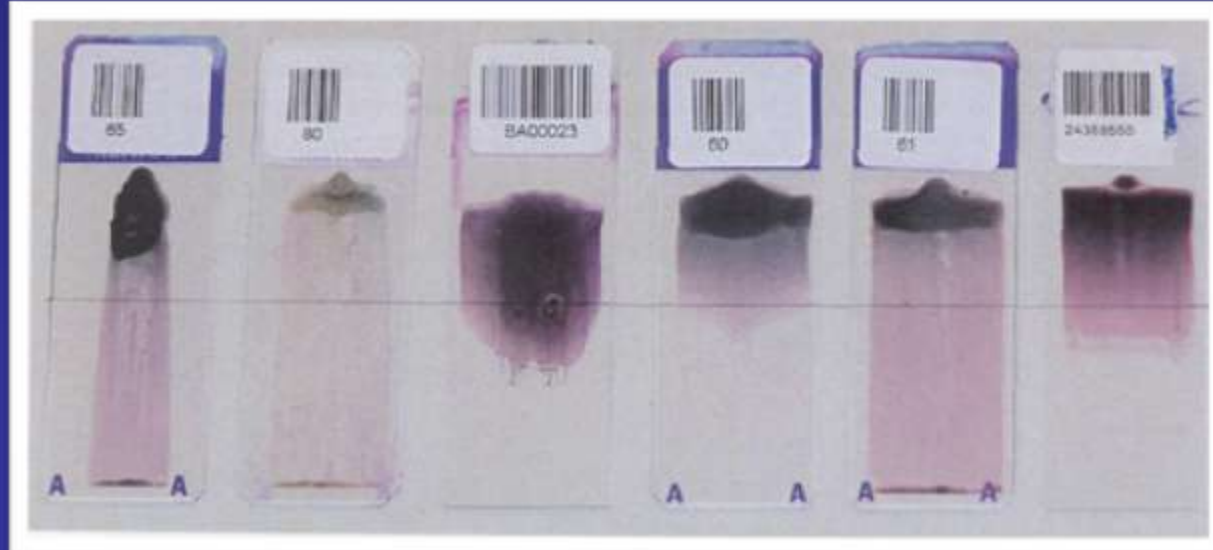


Příprava nátěru periferní krve pro CellaVision DM 96

přijatelné nátěry

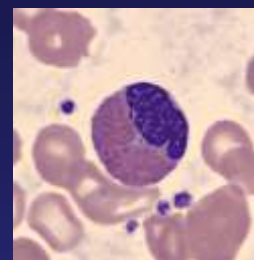
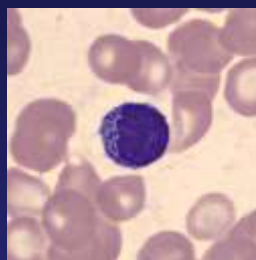
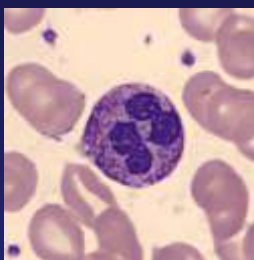


nepřijatelné nátěry

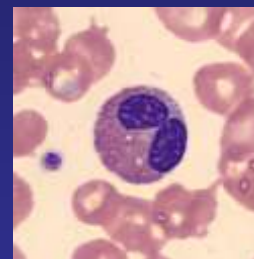
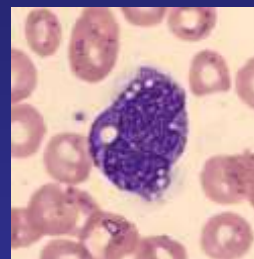
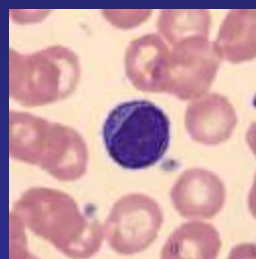


Barvení krevního nátěru pro CellaVision DM 96

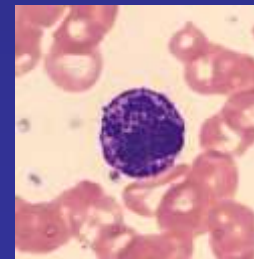
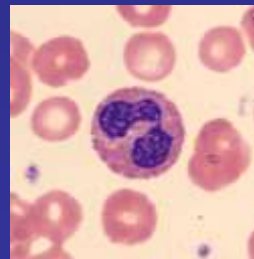
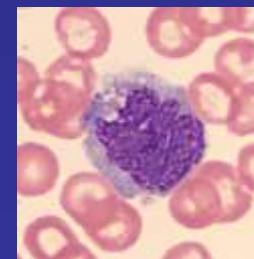
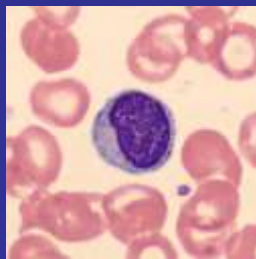
1. barvení



2. barvení

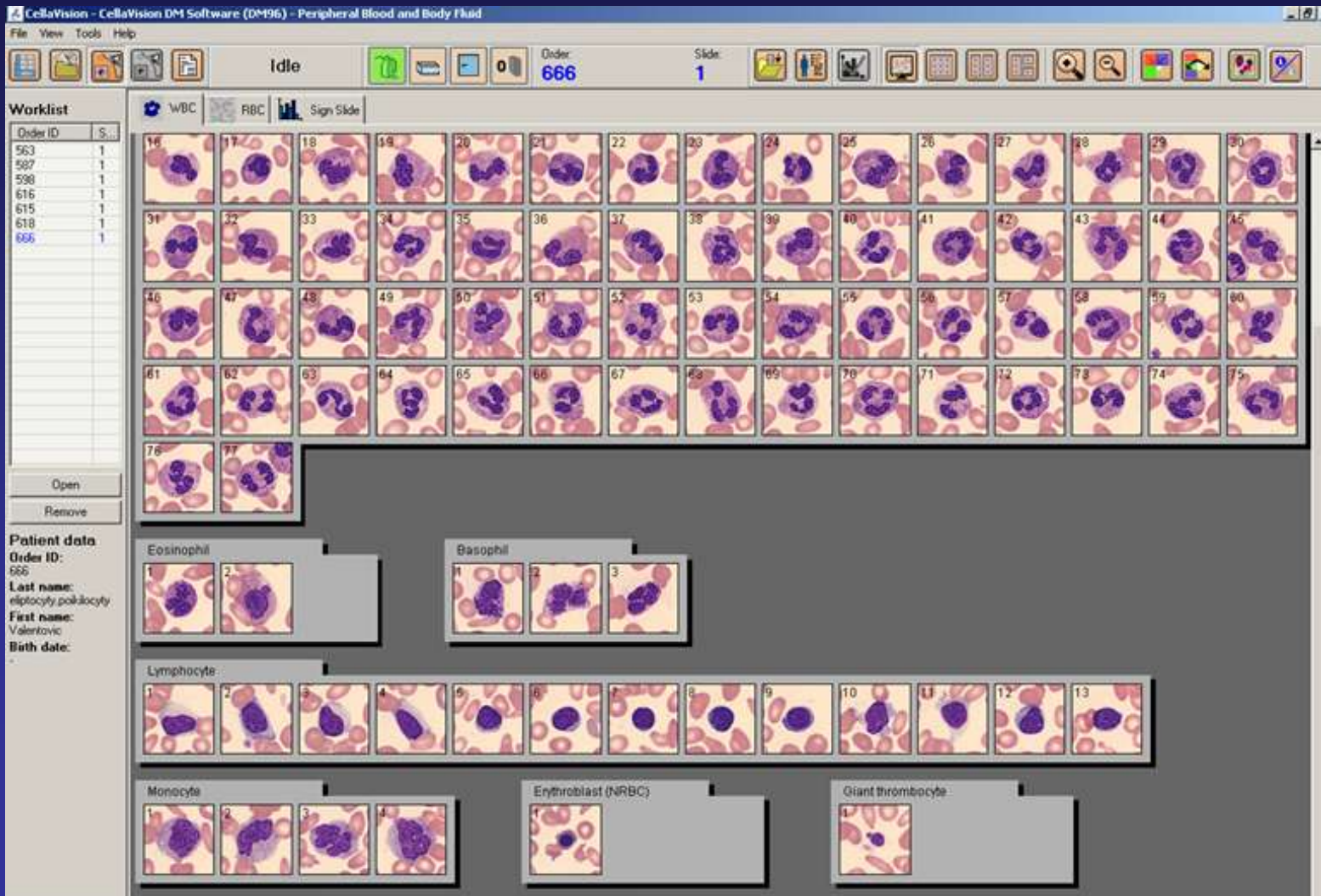


3. barvení



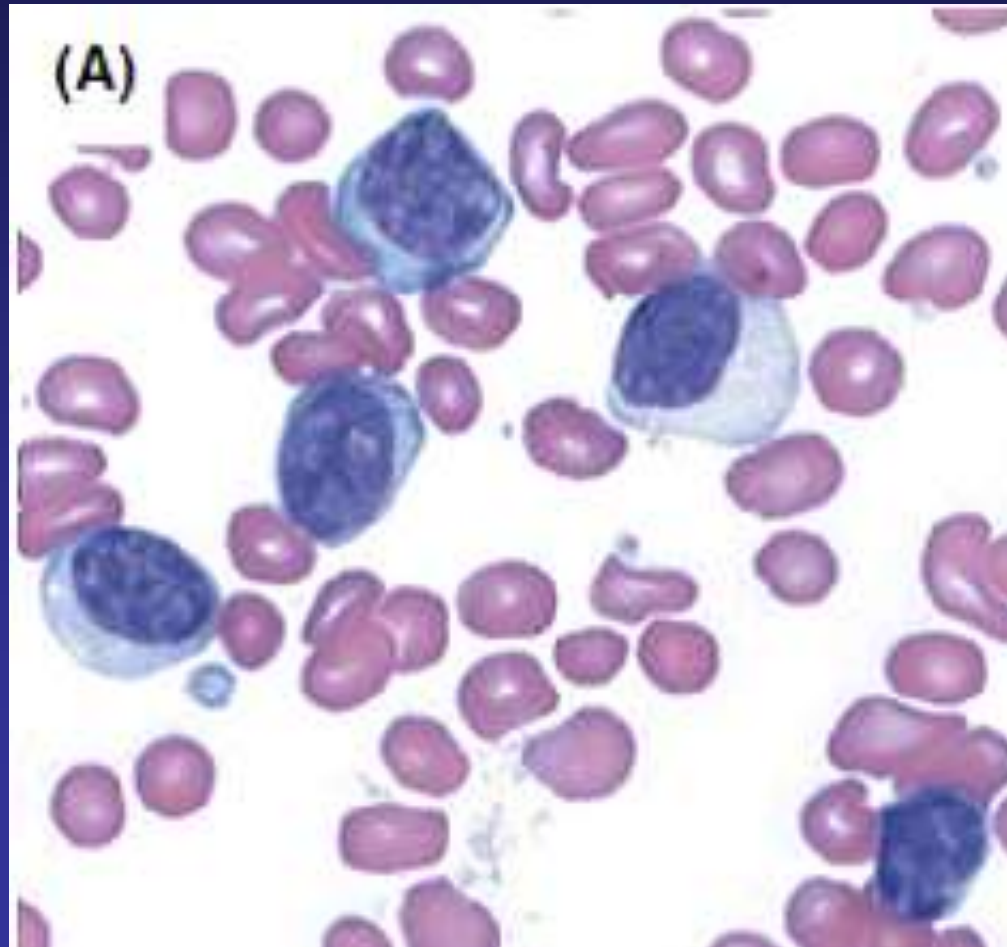
CellaVision DM 96 – periferní krev

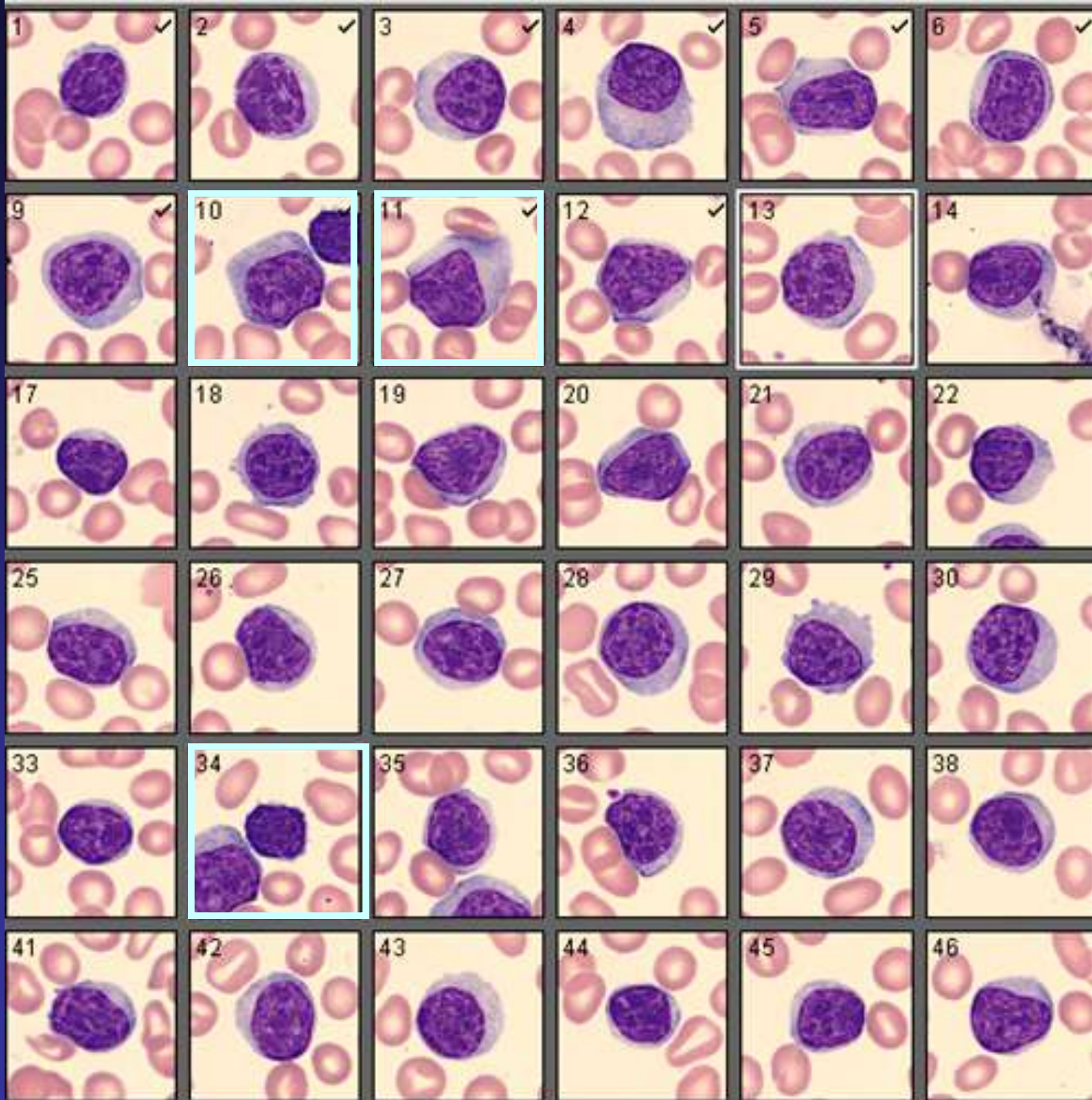
WBC
analýza



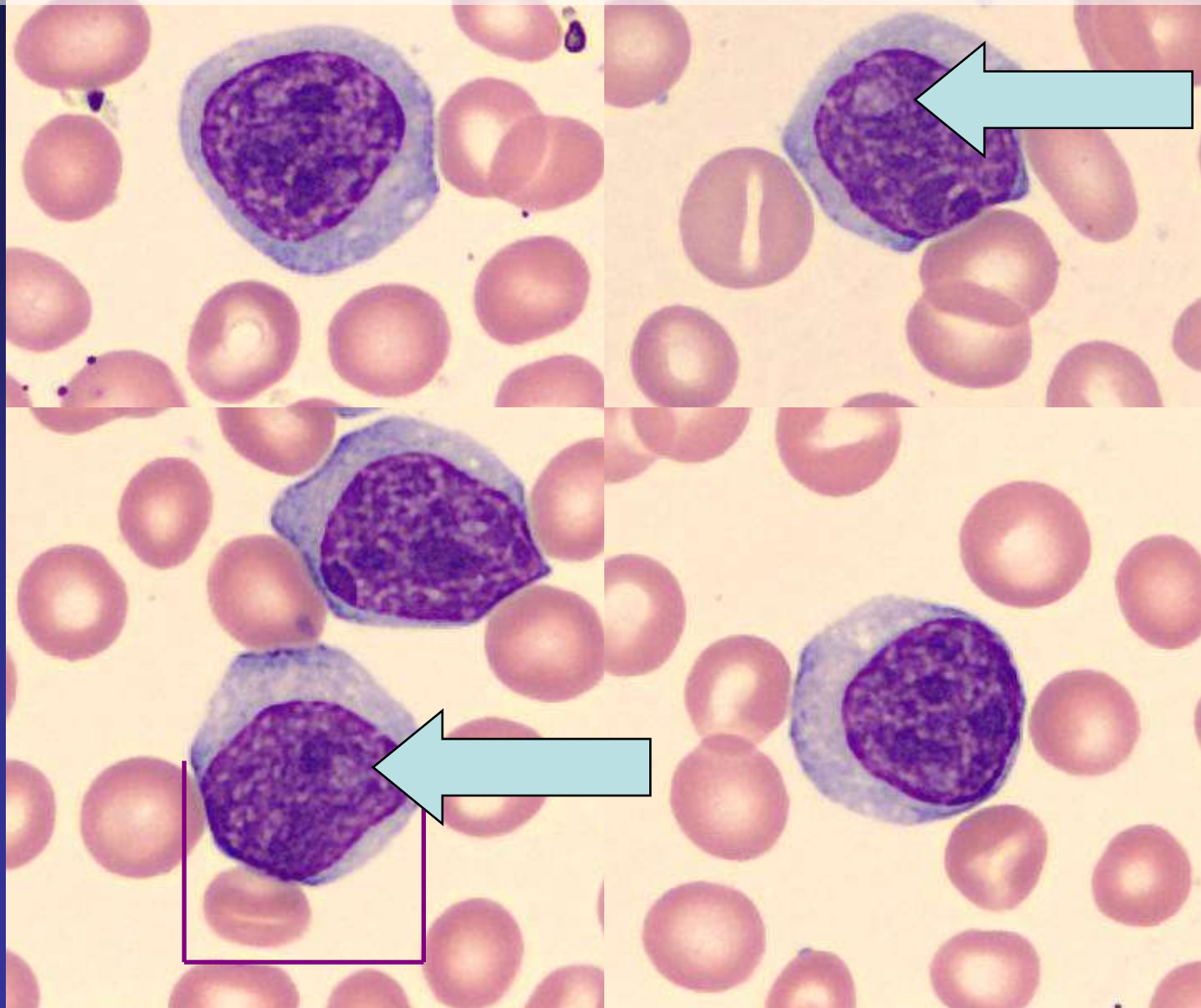
Zkušenosti s využitím metod
virtuální mikroskopie u konkrétních
cytogenetických podskupin

MYC translocation in chronic lymphocytic leukaemia is associated with increased prolymphocytes and a poor prognosis



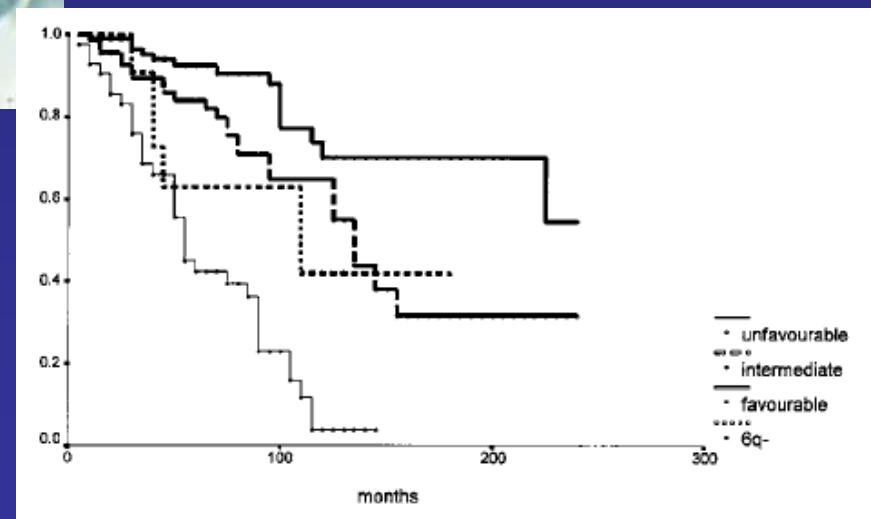
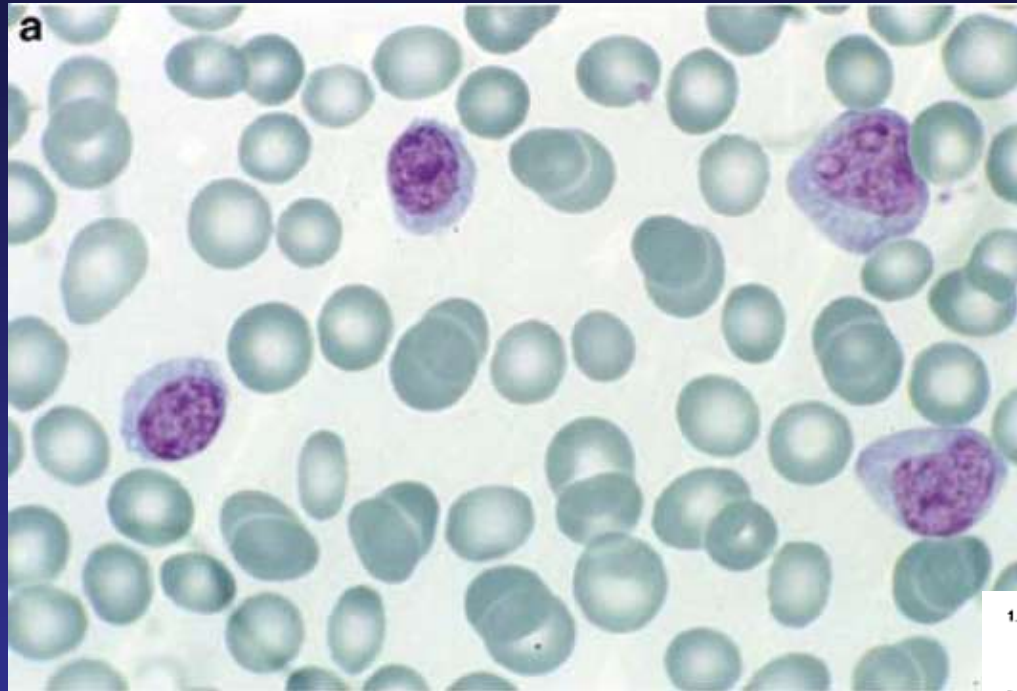


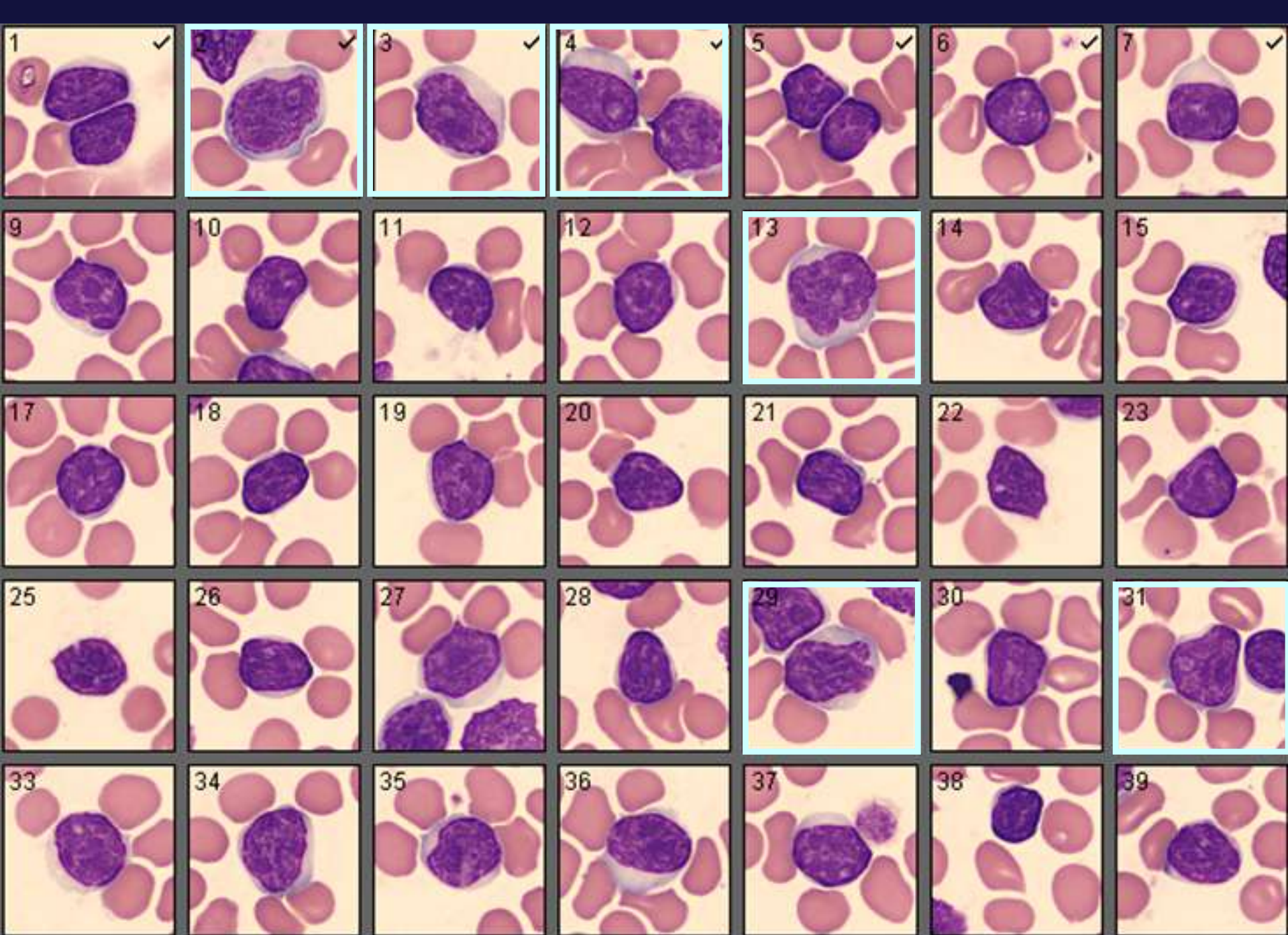
Zmnožení 8q24 (c-myc), delece 11q (ATM)
Typický fenotyp, ZAP-70+ (66 %), IgVH-UM



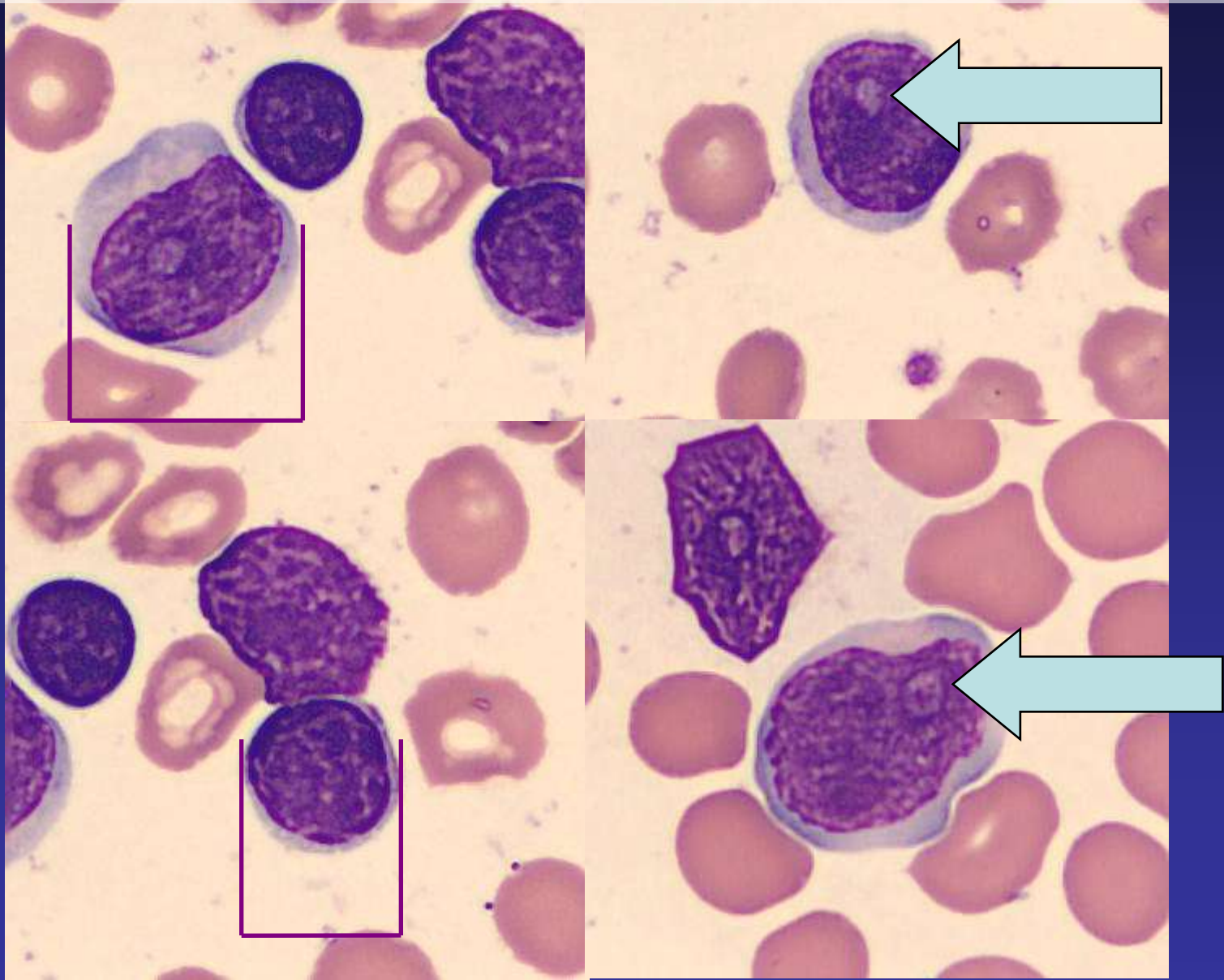
Chronic lymphocytic leukemia with 6q- shows distinct hematological features and intermediate prognosis

A Cuneo¹, GM Rigolin¹, R Bigoni¹, C De Angeli¹, A Veronese^{2,3,4}, F Cavazzini¹, A Bardi¹, MG Roberti¹, E Tammiso¹, P Agostini¹, M Ciccone¹, M Della Porta¹, A Tieghi¹, L Cavazzini⁵, M Negrini^{2,3,4} and G Castoldi¹



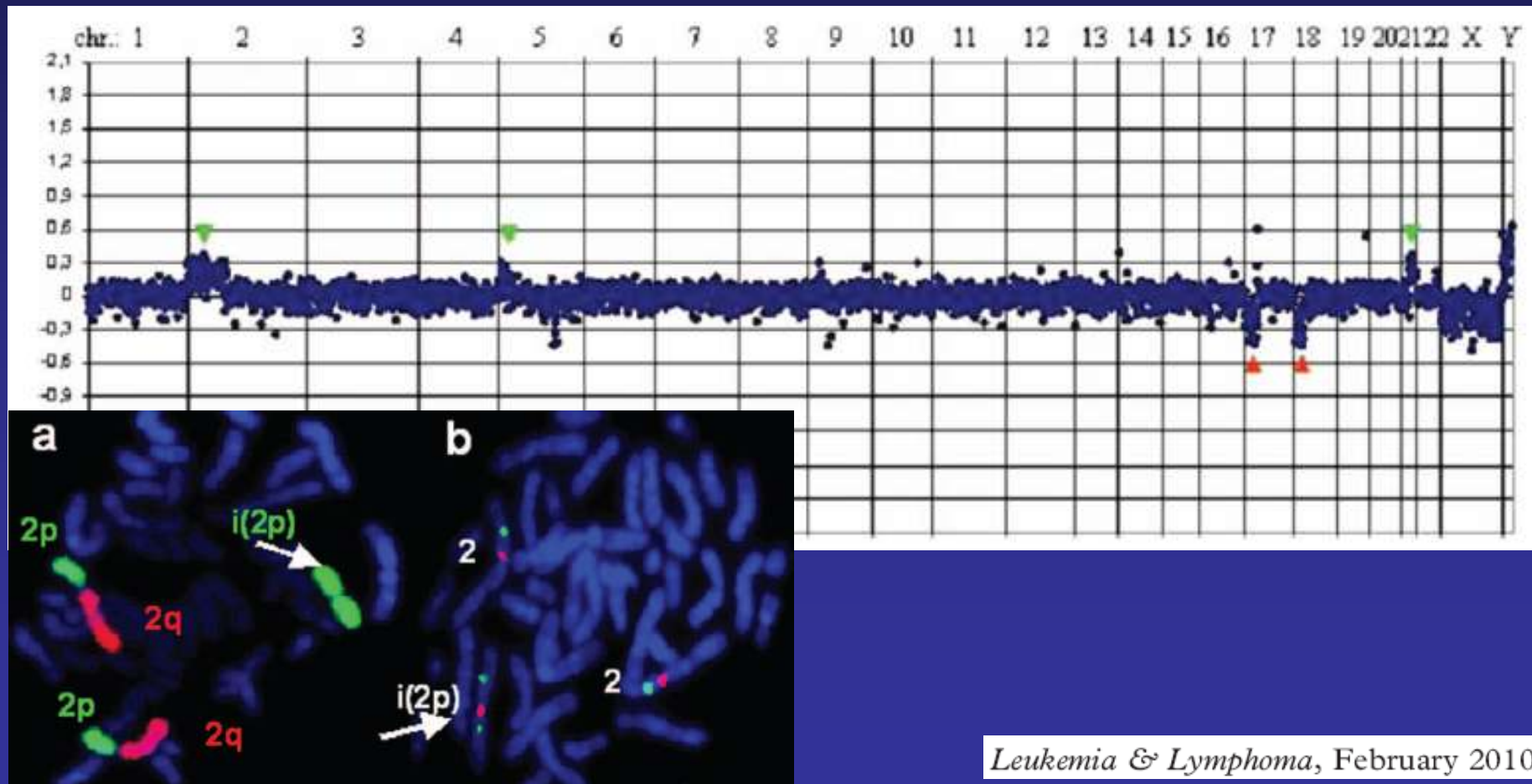


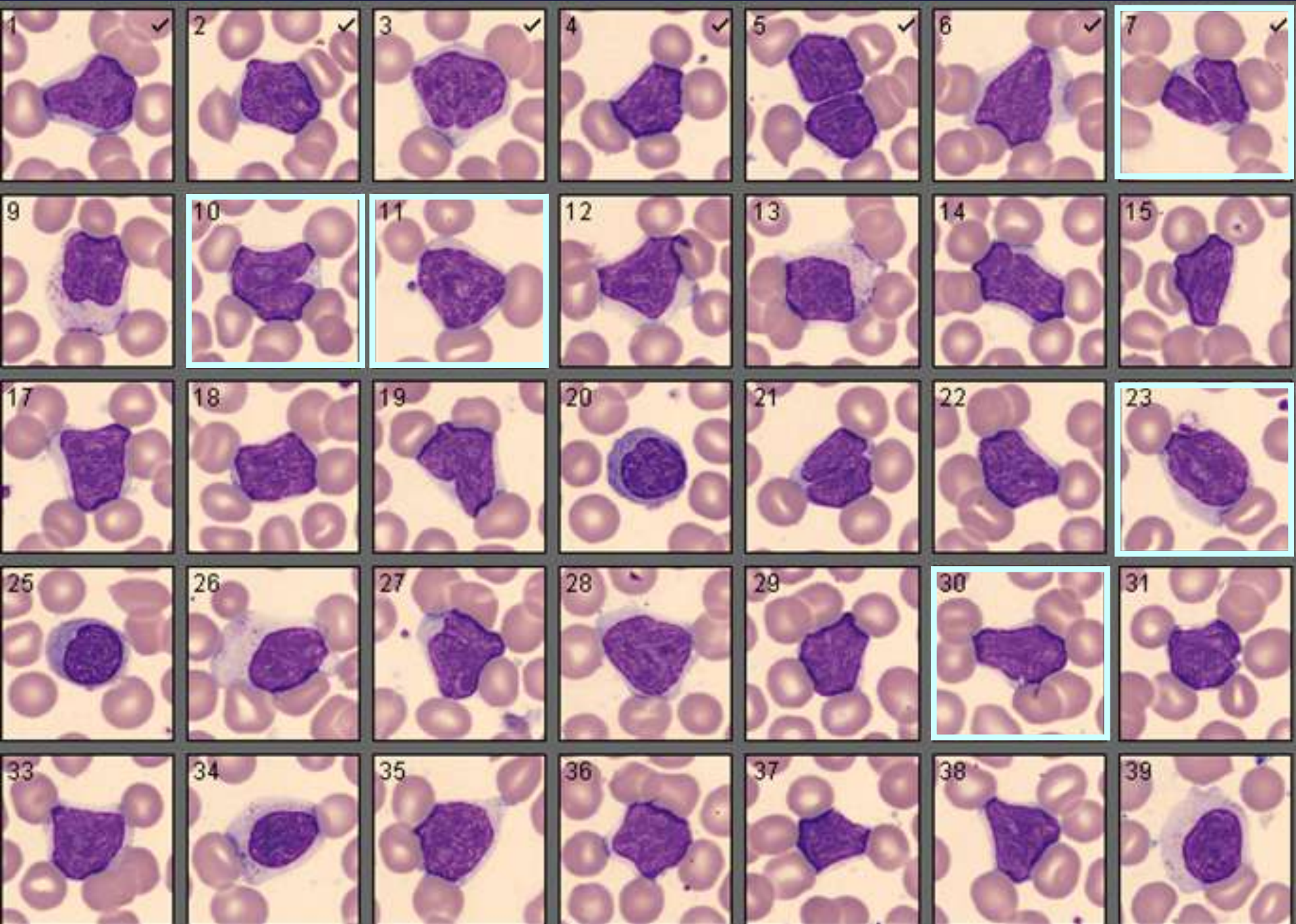
Delece 6q21-q27, delece 13q14
Typický fenotyp, ZAP-70+ (46 %), IgVH-UM



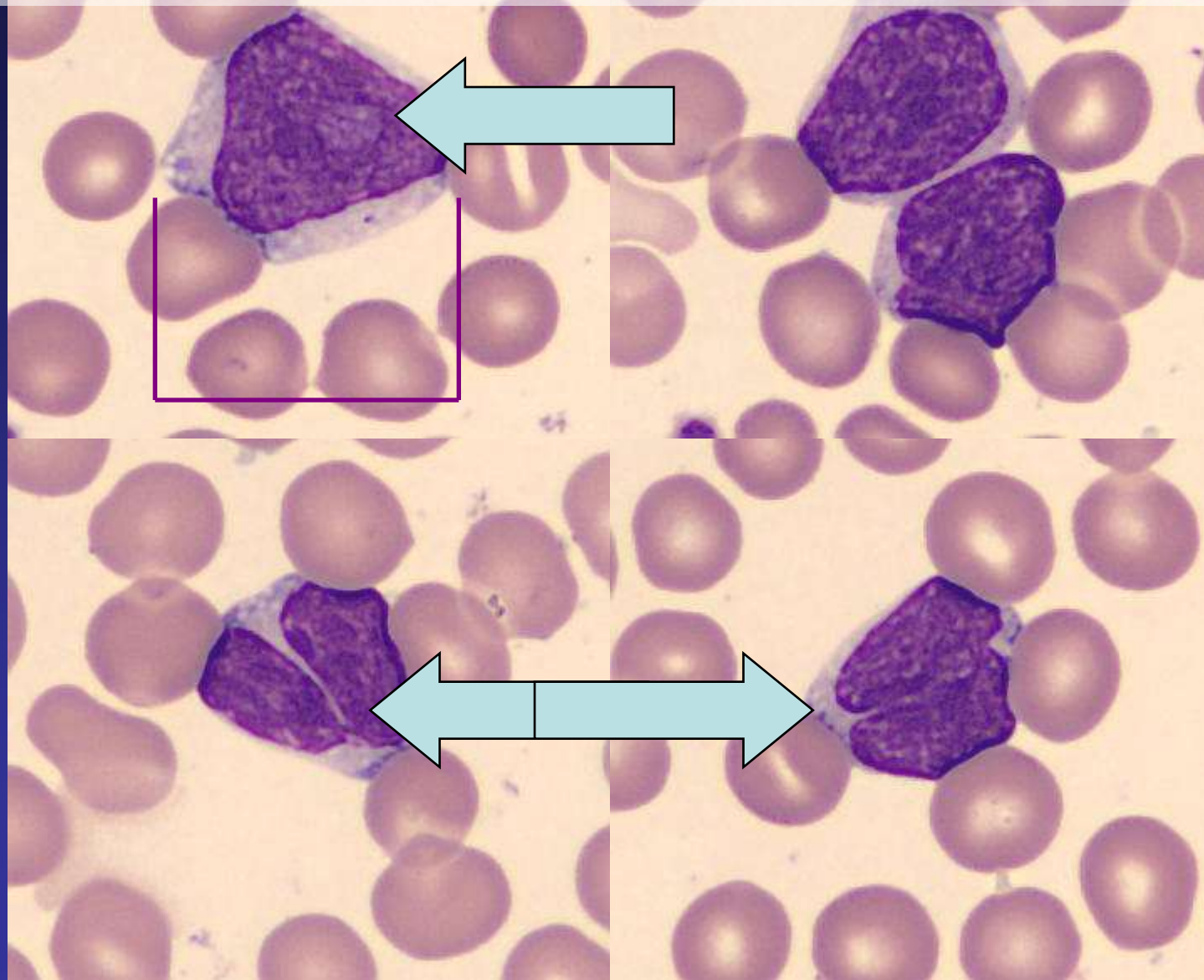
Gain of chromosome 2p in chronic lymphocytic leukemia: significant heterogeneity and a new recurrent dicentric rearrangement

MARIE JAROSOVA¹, HELENA URBANKOVA¹, RADEK PLACHY¹, TOMAS PAPAŽIK¹,
MILENA HOLZEROVA¹, JANA BALCARKOVA¹, ZUZANA PIKALOVA¹,
VLADIMIR DIVOKY^{1,2}, & KAREL INDRAK¹



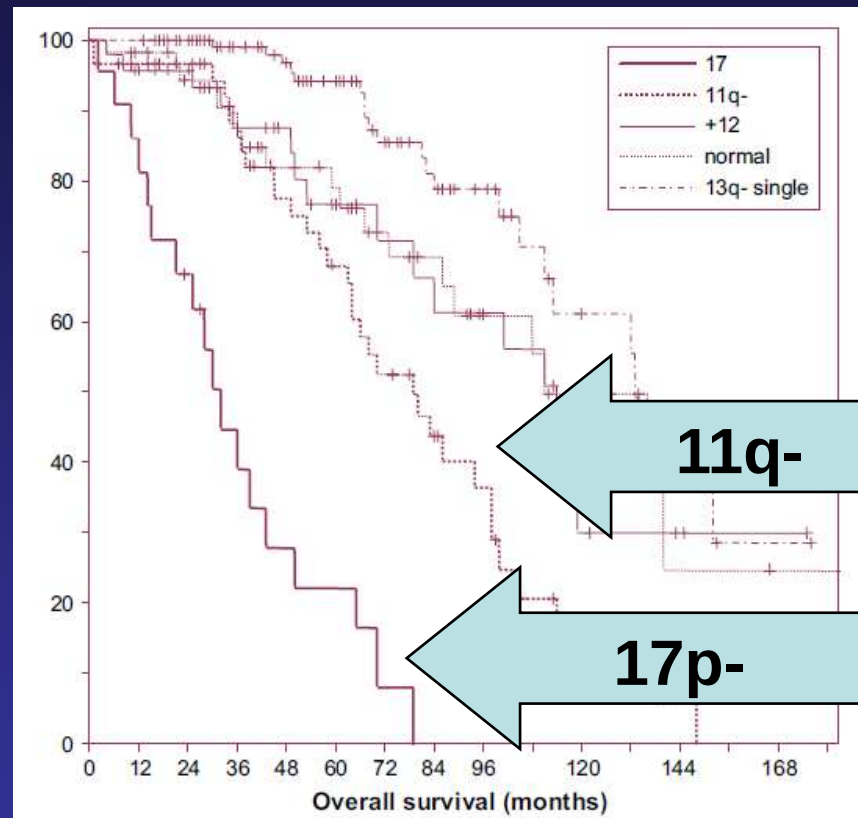


zmnožení oblasti 2p, (4 kopie genu REL, N-MYC, ALK).
Typický fenotyp, ZAP-70+ (46 %), IgVH-UM

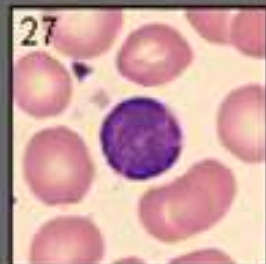
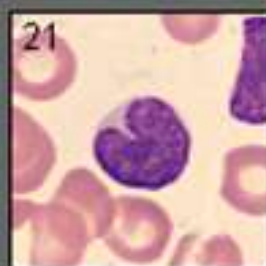
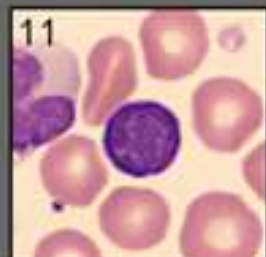
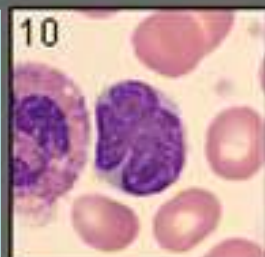


Deletions at 11q identify a subset of patients with typical CLL who show consistent disease progression and reduced survival

JR Neilson¹, R Auer¹, D White², N Bienz¹, JJ Waters¹, JA Whittaker², DW Milligan¹ and CD Fegan¹



Best Practice & Research Clinical Haematology
Vol. 20, No. 3, pp. 439–453, 2007



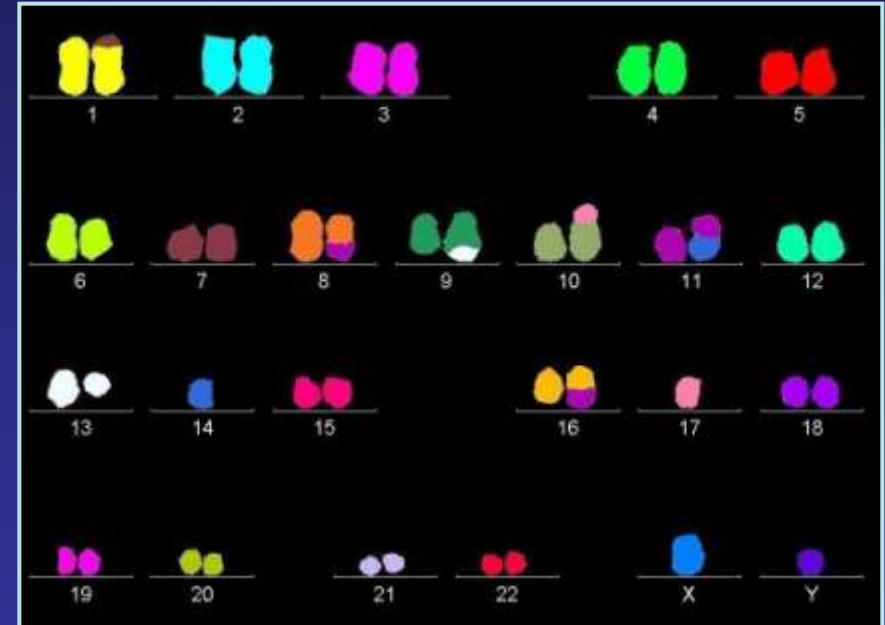
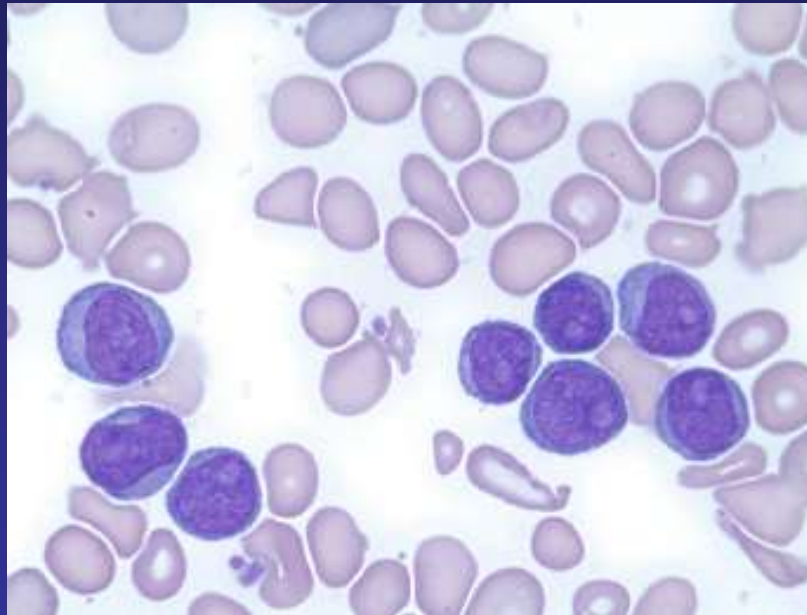
Delece 11q (ATM)

Atypický fenotyp, CD38+, ZAP-70+ (59 %), IgVH UM



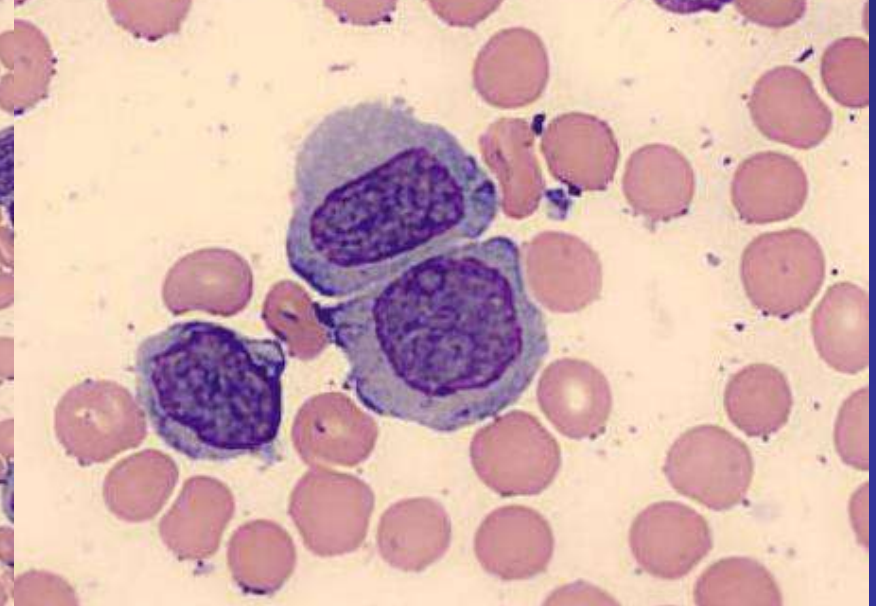
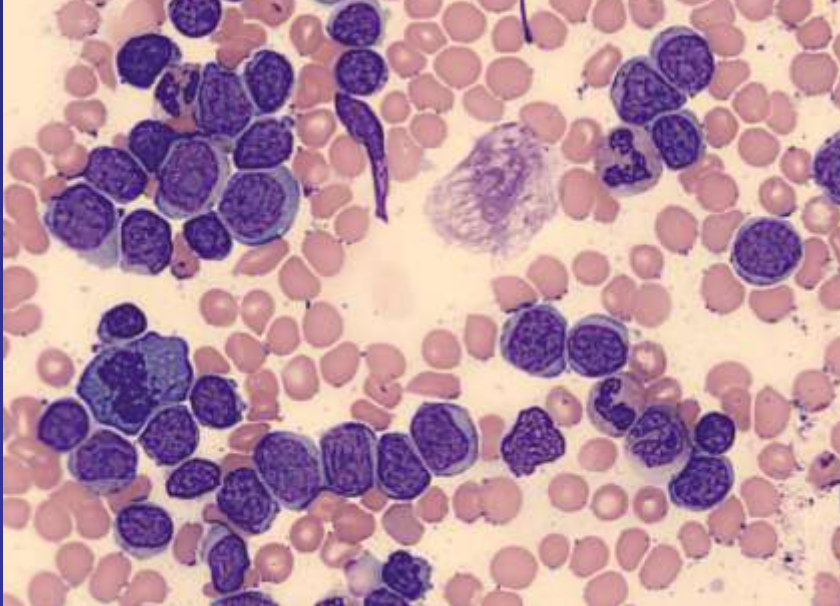
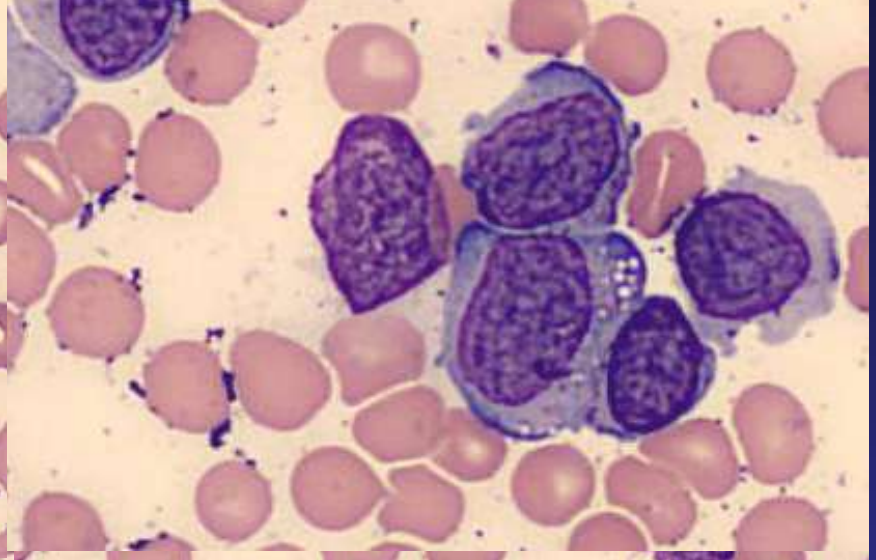
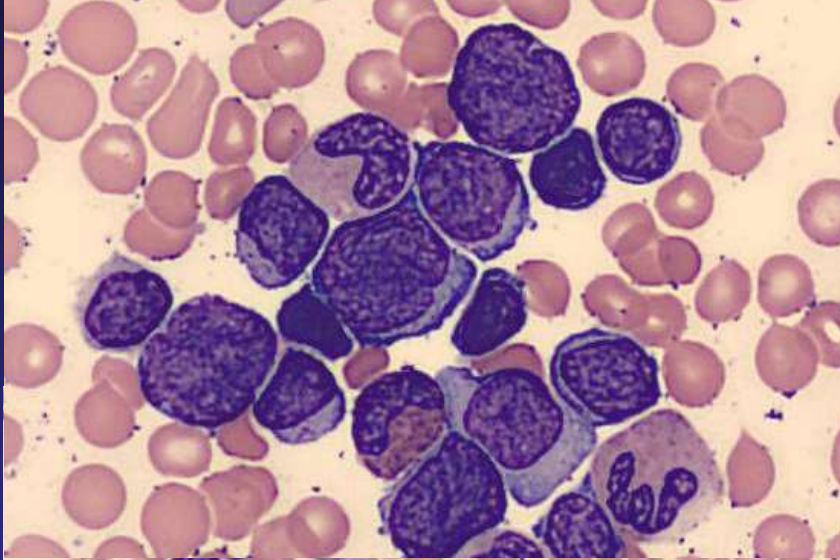
Complex karyotype including chromosomal translocation (8;14) (q24;q32) in one case with B-cell prolymphocytic leukemia

Ricardo H. Crisostomo, Jose A. Fernandez *, William Caceres



44,XY,der(1)t(1;7)(p?36;q),del(7q),der(8)t(8;11)(p?;?q),i(8)(q10),der(9)t(9;13)(q?33;q?14),dic(10;17)(p?13;p11),?dic(11;14)(p11;p11),der(16)t(11;16)(?q;q?12)

Komplexní změny karyotypu amplifikace c-myc, delece 17p



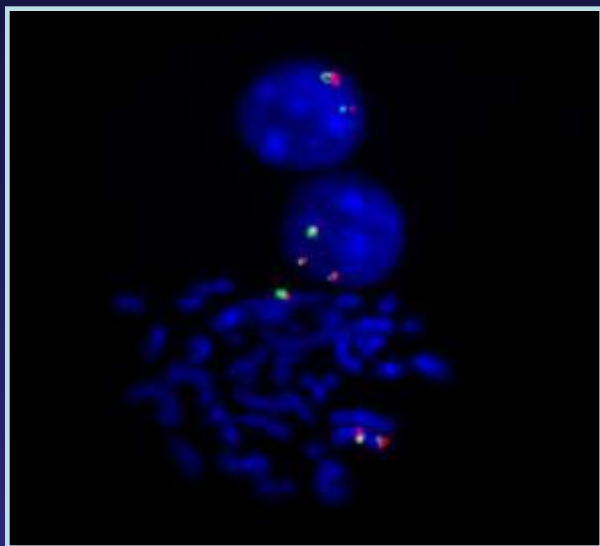
Závěr I

- morfologie buněk CLL může přinést **přídavnou prognostickou** informaci
- atypická CLL je často spojena s výskytem **nepříznivých** genetických změn a aberantním fenotypem
- přítomnost prolymfocytů je spojena s vyšší proliferací CLL

Závěr II

- metody virtuální mikroskopie (VM) umožňují maximální **standardizaci** morfologického hodnocení
- standardní barvení – výběr konkrétních populací – archivace – sdílení obrazů
- VM může přispět k **hodnocení prognózy** nemocného s CLL v co nejširším kontextu ostatních vyšetřovacích metod

Poděkování

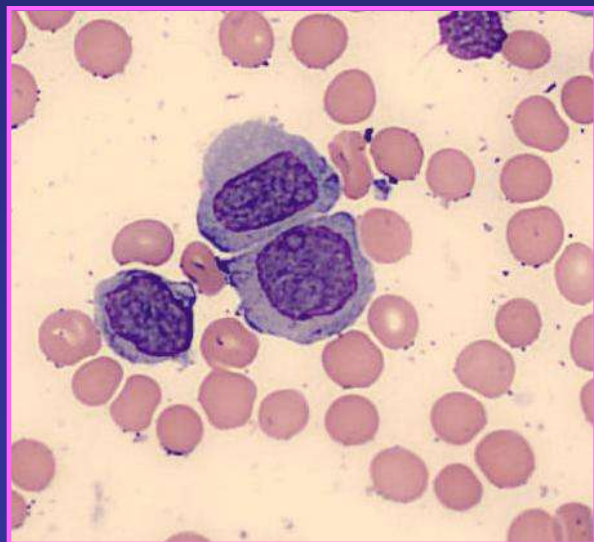


Cytogenetická laboratoř

M. Jarošová

M. Holzerová

R. Chytilíková



Morfologická laboratoř

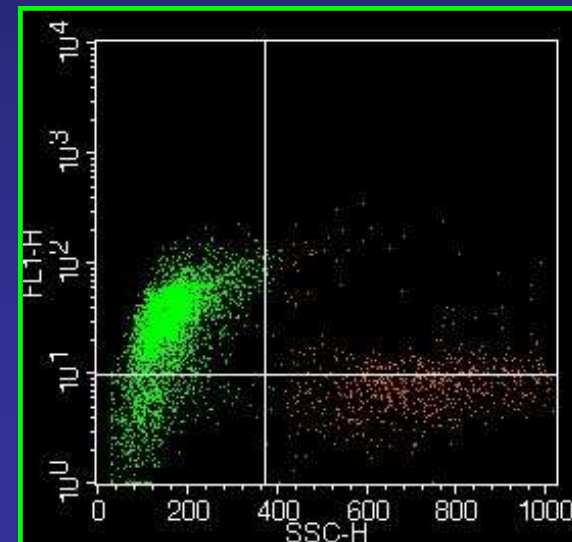
A. Lapčíková

J. Juráňová

Průtoková cytometrie

Z. Pikalová

M. Novák



Podpořeno granty: MSM 6198959205 a ESF CZ.1.07/2.2.00/07.0294.