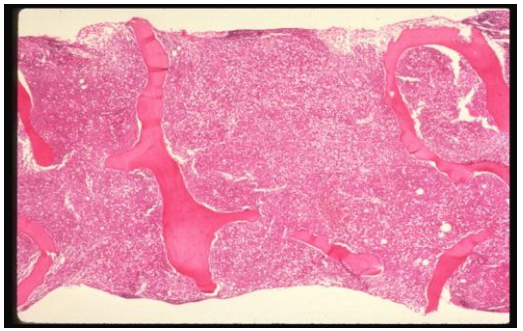
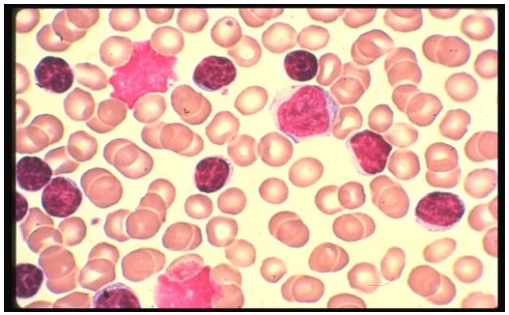
Introduction to Chronic Lymphocytic Leukaemia (CLL)

Chronic Lymphocytic Leukaemia

- Commonest leukaemia in western world
- Heterogeneous natural history
- Progression associated with increased tumour bulk and genetic complexity





Epidemiology of CLL

- One of the most common B-cell malignancies in the Western world[1]
  - Annual CLL incidence 4.3 new cases per 100,000 population[1,2]
- Median overall survival = 7 years[1]
  - But many patients live for >10 years[1]
  - More patients living with CLL than diagnosed each year
- Incidence varies considerably by gender, race and geography:[2]
  - Affects x2 more males than females
  - Higher rate among Caucasians than black people
  - Significantly lower rate in people of Asian descent
- Highest familial incidence of all B-cell malignancies[1]
  - 10% of patients with family history of disease[1]

1. Catovsky, D., Montserrat, E. (2011). In: Hoffbrand, A., Catovsky, D., *et al.*, eds. Postgraduate Haematology. Oxford: Wiley-Blackwell; p530-57.
2. SEER. (2013). Available from: http://seer.cancer.gov/statfacts/html/clyl.html (Accessed: 25 Sept 2013).

Incidence of CLL by Region

US
Estimated 9,700 men and 5,900 women diagnosed with CLL, and 4,500 deaths from the disease in 2013[1]

Asia
Incidence markedly lower in China and Japan, but rising due to influence of Westernised lifestyle and environment[2]

Europe
Incidence rate of 5.87 and 4.01 new cases per 100,000 population per year in men and women, respectively[3]

Africa
Incidence appears lower than US and Western Europe, but higher than Asia. Evidence of increased frequency among younger African population[4]

Latin America
Definitive epidemiological data lacking but incidence among Hispanics lower than Caucasians (according to US data). [1]

1. SEER. (2013). Available from: http://seer.cancer.gov/statfacts/html/clyl.html (Accessed: 25 Sept 2013).
2. Shang-Ju, W (2010). Blood 116(22) 4430-5.
3. Sant, M., Allemani, C.*, et al.* (2010). *Blood*. **116**(**19**): 3724-34.
4. Fleming, AF (1985). Leukemia Research, 9 (6) 735-740.

Diagnosis of CLL – WBC count

- Full blood count and differential white blood cell (WBC) count are required to confirm lymphocytosis
  - IWCLL diagnostic guidelines require: ≥5.0 x 10^9/L (≥5000 cells/μl) in the peripheral blood[1]
  - ESMO diagnostic criteria additionally require: lymphocytosis present for >3 months[2]

Lymphocytosis

The absolute lymphocyte count (ALC) is calculated by multiplying total WBC by the % of lymphocytes on the white blood cell differential count:

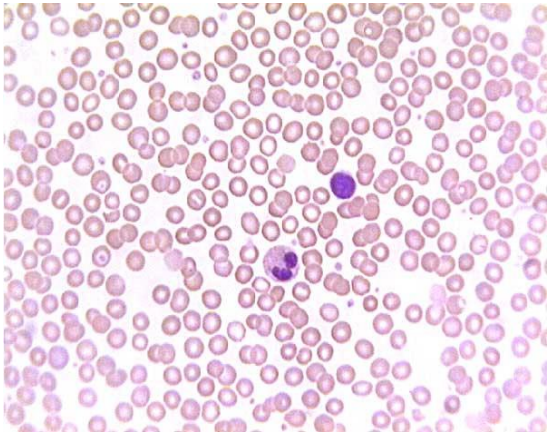
$$ALC = WBC \times \%\ lymphocytes \div 100$$

Lymphocytosis is defined as ALC >4.0 x 10^9/L. About 1.3% of people over 50 years have ALC >4.0 x 10^9/L and over half of these will have an abnormal immunophenotype.

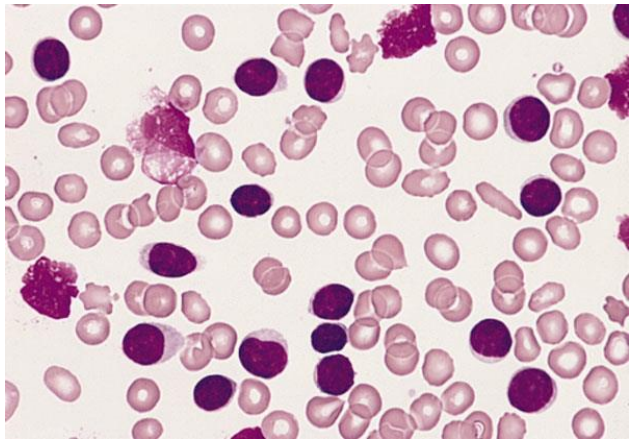
1. Hallek, M., Cheson, B.D., *et al.* (2008). *Blood*. **111**(**12**): 5446-56.
2. Eichhorst, B., Dreyling, M., *et al.* (2011). *Ann Oncol*. **22 Suppl 6**: vi50-4.

Diagnosis of CLL – Blood Smear

- Blood smear required to assess malignant cell morphology[1,2]
- Malignant B-cells in CLL have characteristic appearance:[1,2]
  - Small, round lymphocytes that appear mature
  - Narrow border of cytoplasm
  - Dense nucleus with no discernable nucleoli and partially aggregated chromatin



In this normal blood smear, there are fewer white cells present, including a lymphocyte and a neutrophil – both of which appear normal



The right blood smear from a CLL patient contains an increased number of mature-looking small lymphocytes and no other white blood cell types

1. Eichhorst, B., Dreyling, M., *et al.* (2011). *Ann Oncol*. **22 Suppl 6**: vi50-4.
2. Hallek, M., Cheson, B.D., *et al.* (2008). *Blood*. **111**(**12**): 5446-56.

Spectrum of CLL

- Monoclonal B lymphocytosis
- Stage A CLL
- Progressive CLL
- Refractory CLL

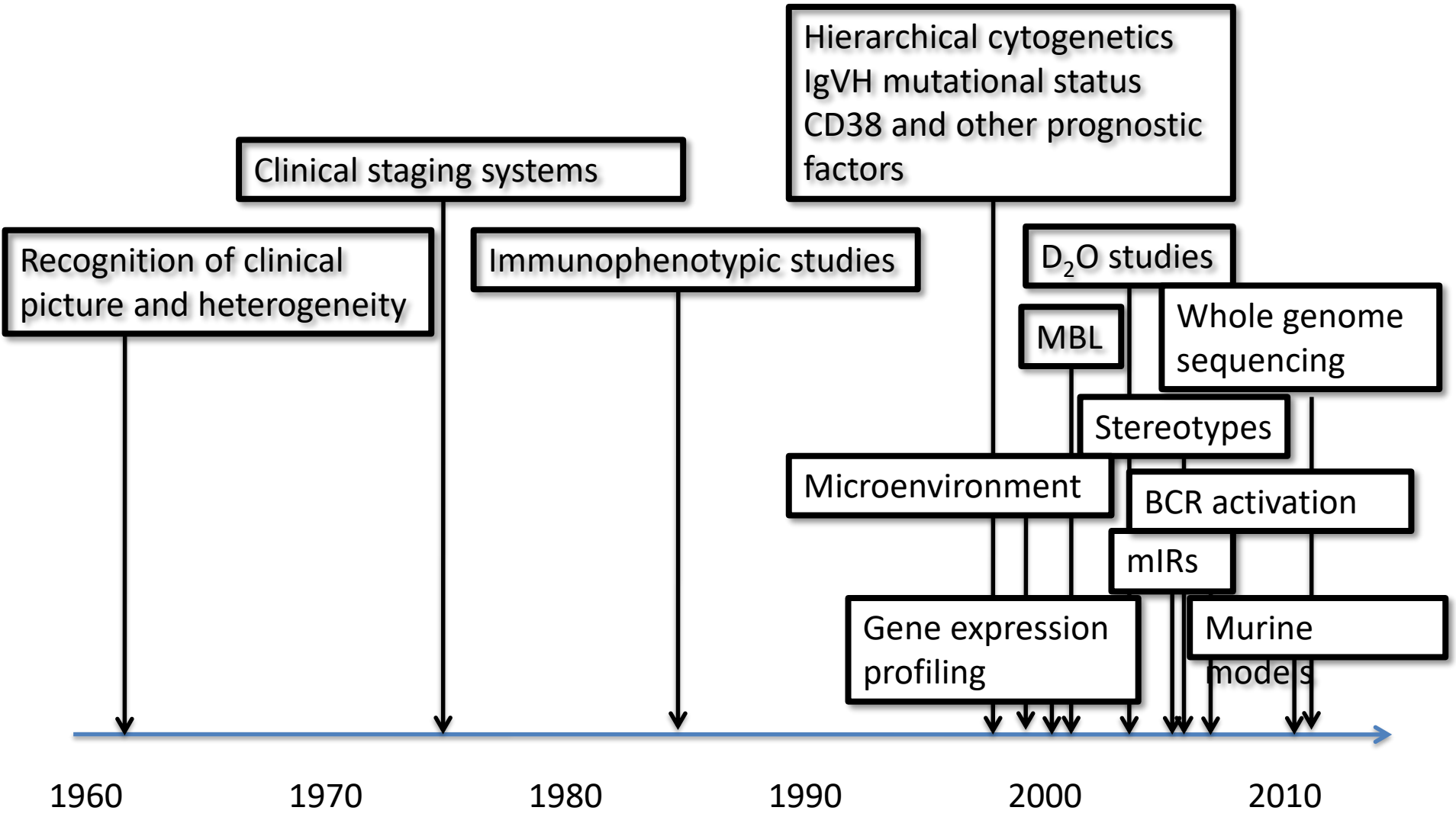
- Richter transformation

Unmutated IgVH

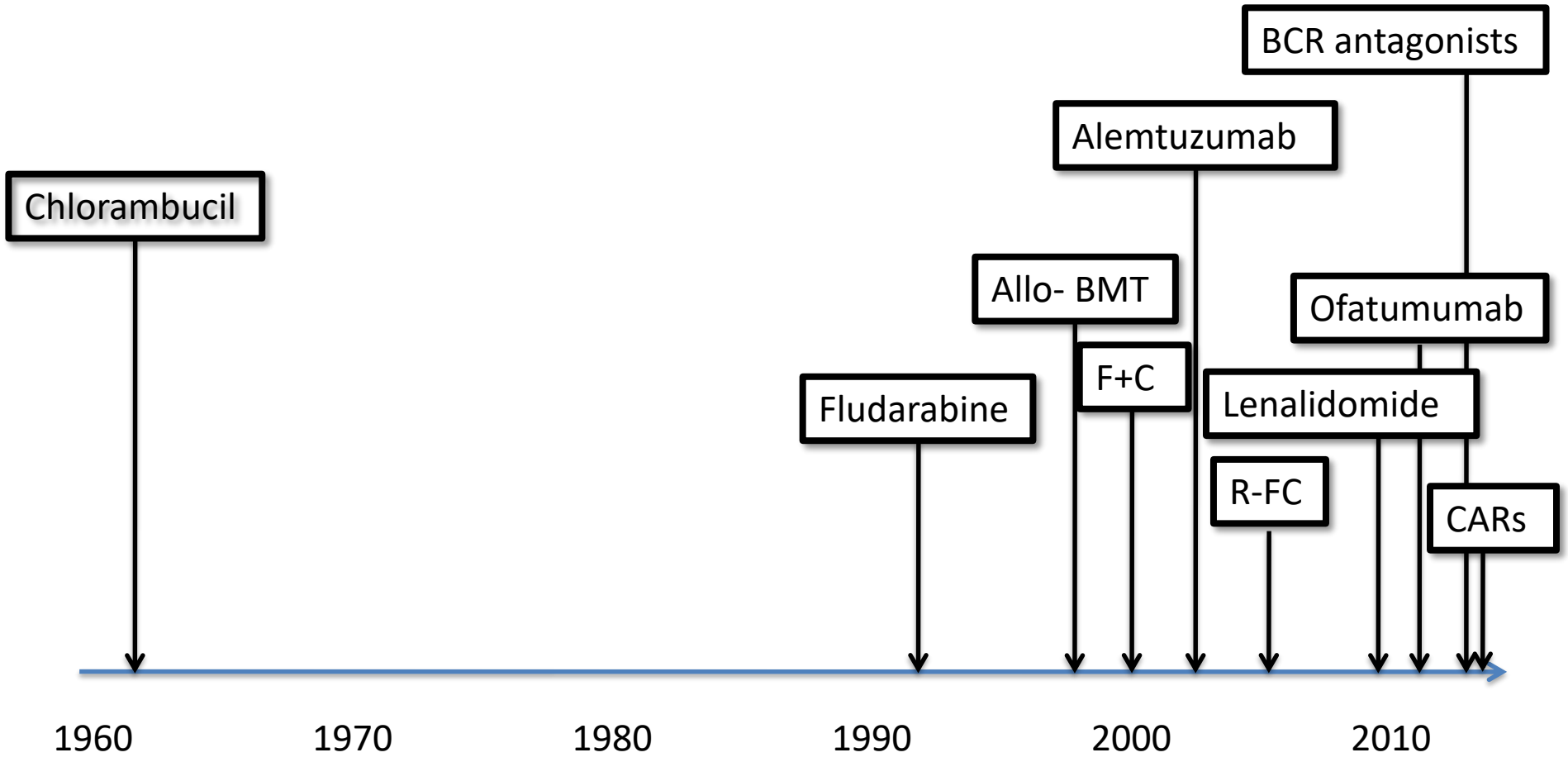
Mutated IgVH
Zap 70+
11q23

P53

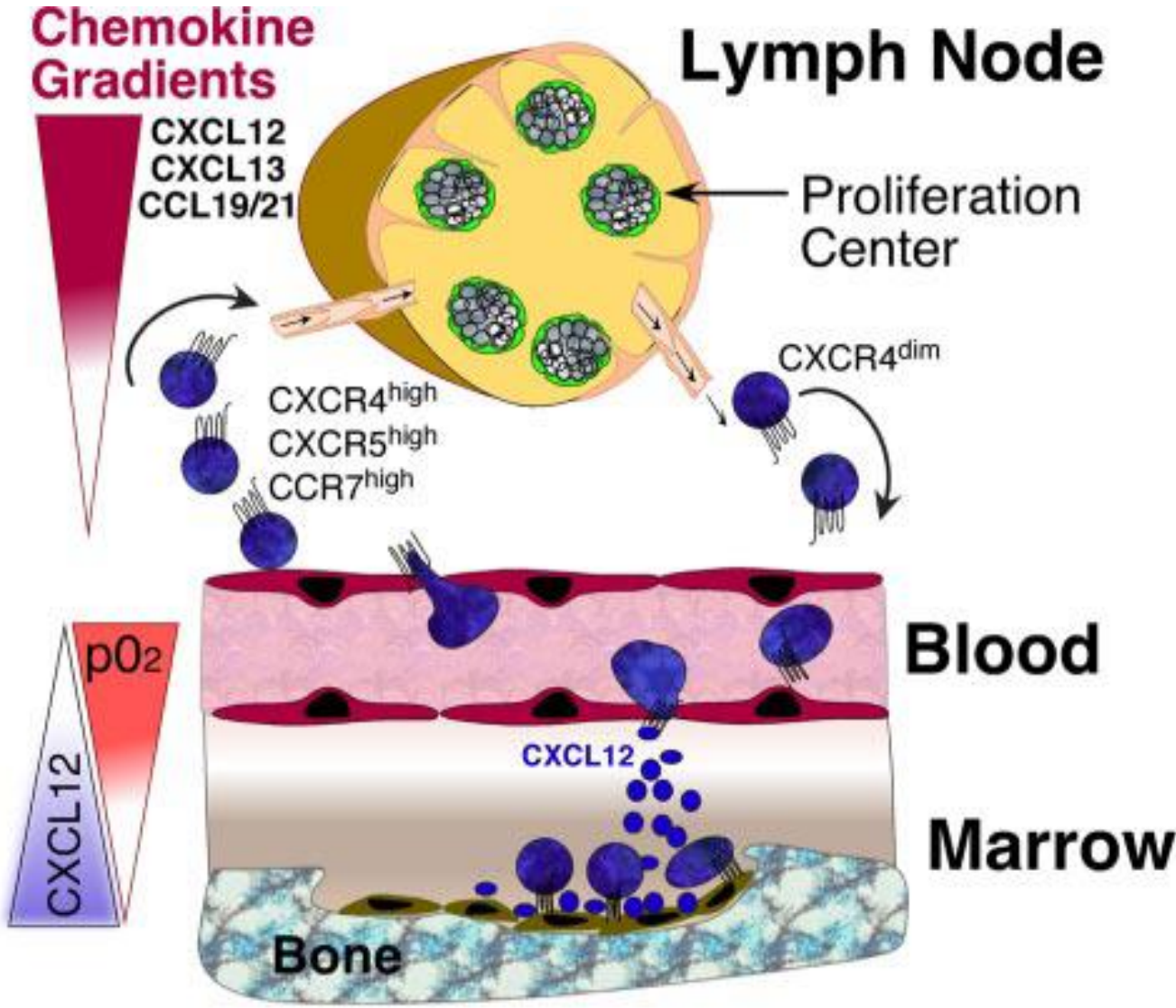
Perspective: Biology



Perspective: Therapy



How and why our cancer started?



Burger et al. Blood, 2013 121: 1501-1509

Sterotyped BCRs in CLL

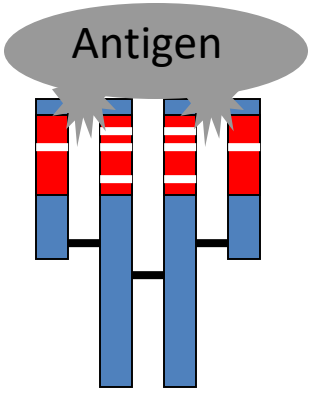
Set	N	IGHV gene†	IGHD gene‡ (reading frame)	IGHJ gene§	Average Intra-subset homology‖	IGKV/IGLV gene (no. cases with indicated gene/total no. cases with available data)
Confirmed subsets						
1*	20	*IGHV1-18* (4), *IGHV1-2* (4), *IGHV1-3* (8), *IGHV5-a* (3)	*IGHD6-19* (3)	*IGHJ4*	71.2	*IGKV1-39*/*IGKV1D-39* (15/15)
2*	18	*IGHV3-21* (16), *IGHV3-11* (1), *IGHV3-48* (1)	ND	*IGHJ6*	85.2	*IGLV3-21* (15/17)
3*	12	*IGHV1-69* (9), *IGHV1-2* (1), *IGHV1-8* (1), *IGHV4-34* (1)	*IGHD2-2* (3)	*IGHJ6*	82.2	*IGKV1-39*/*IGKV1D-39* (3/9), *IGKV3-11* (3/9)
4*	13	*IGHV4-34*	*IGHD5-5* (1)/*D4-17* (3)	*IGHJ6*	75.4	*IGKV2-30* (11/11)
5*	10	*IGHV1-69*	*IGHD3-10* (3)	*IGHJ6*	78.3	*IGKV1-33*/*IGKV1D-33* (2/7), *IGLV3-21* (2/7)
6*	8	*IGHV1-69*	*IGHD3-16* (2)	*IGHJ3*	92.3	*IGKV3-20* (6/8)

blood

Prepublished online March 13, 2012;
doi:10.1182/blood-2011-11-393694

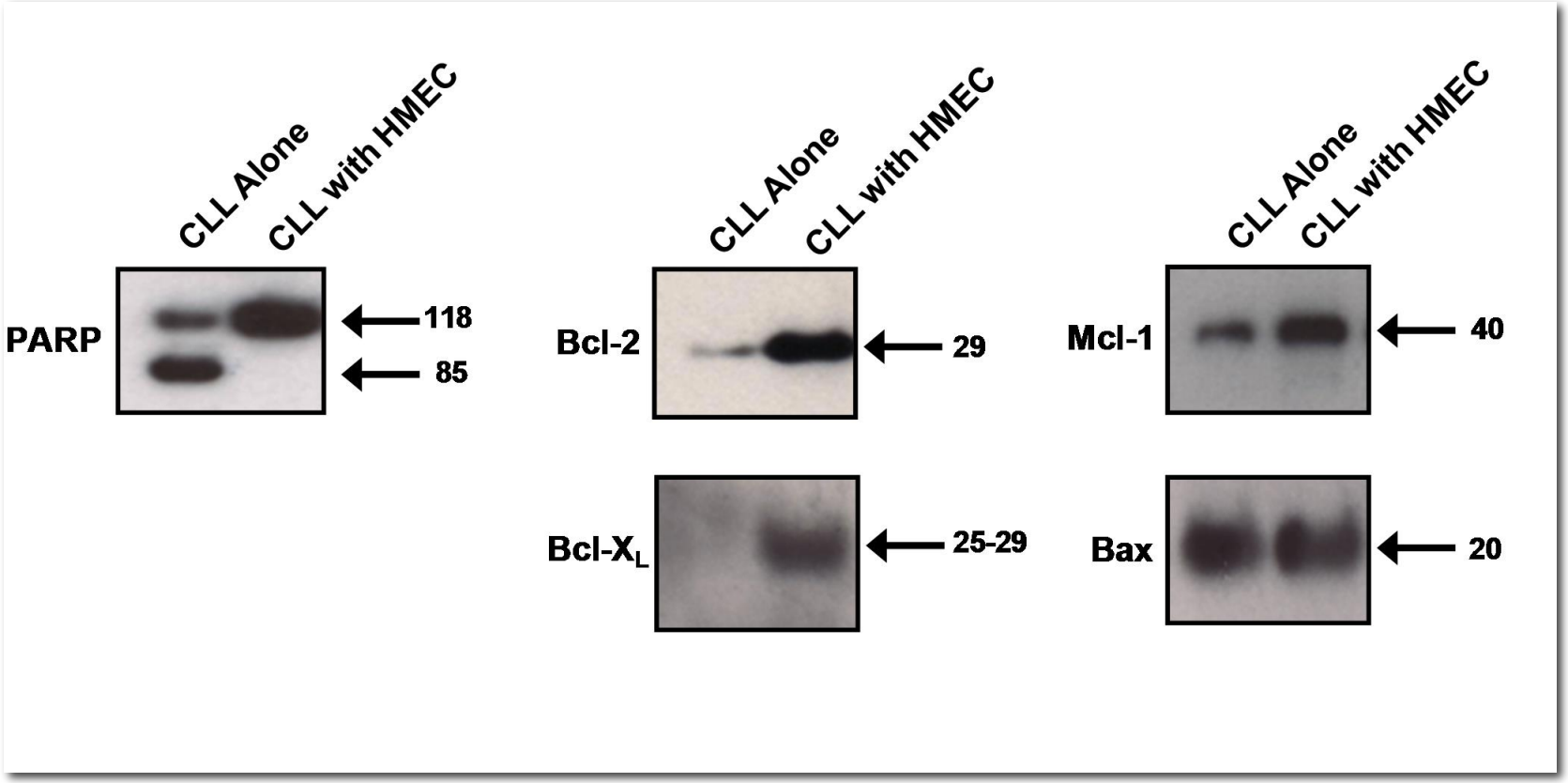
Stereotyped B-cell receptors in one third of chronic lymphocytic leukemia: towards a molecular classification with implications for targeted therapeutic interventions

Andreas Agathangelidis, Nikos Darzentas, Anastasia Hadzidimitriou, Xavier Brochet, Fiona Murray, Xiao-Jie Yan, Zadie Davis, Ellen J. van Gastel-Mol, Cristina Tresoldi, Charles C. Chu, Nicola Cahill, Veronique Giudicelli, Boris Tichy, Lone Bredo Pedersen, Letizia Foroni, Lisa Bonello, Agnieszka Janus, Karin Smedby, Achilles Anagnostopoulos, Helene Merle-Beral, Nikolaos Laoutaris, Gunnar Juliusson, Paola Francia di Celle, Sarka Pospisilova, Jesper Jurlander, Christian Geisler, Athanasios Tsaftaris, Marie-Paule Lefranc, Anton W. Langerak, David Graham Oscier, Nicholas Chiorazzi, Chrysoula Belessi, Frederic Davi, Richard Rosenquist, Paolo Ghia and Kostas Stamatopoulos



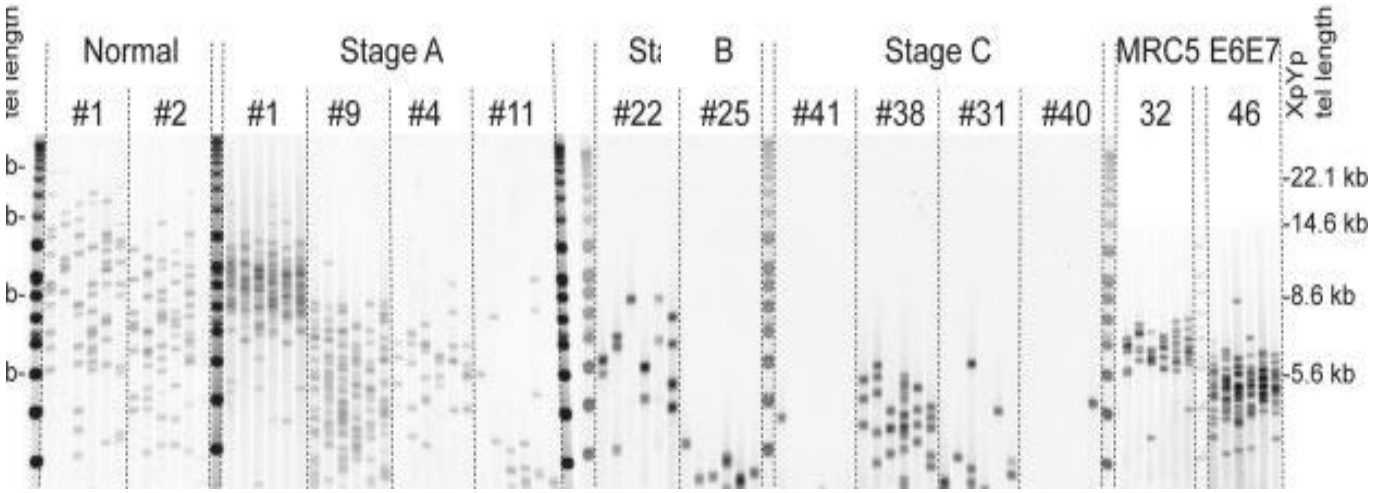
Stamatopoulos 2006

Microvasculature Upregulates BCL2 Family Proteins



CLL cells constitutively express BCL2 family proteins

Role of Telomere Loss

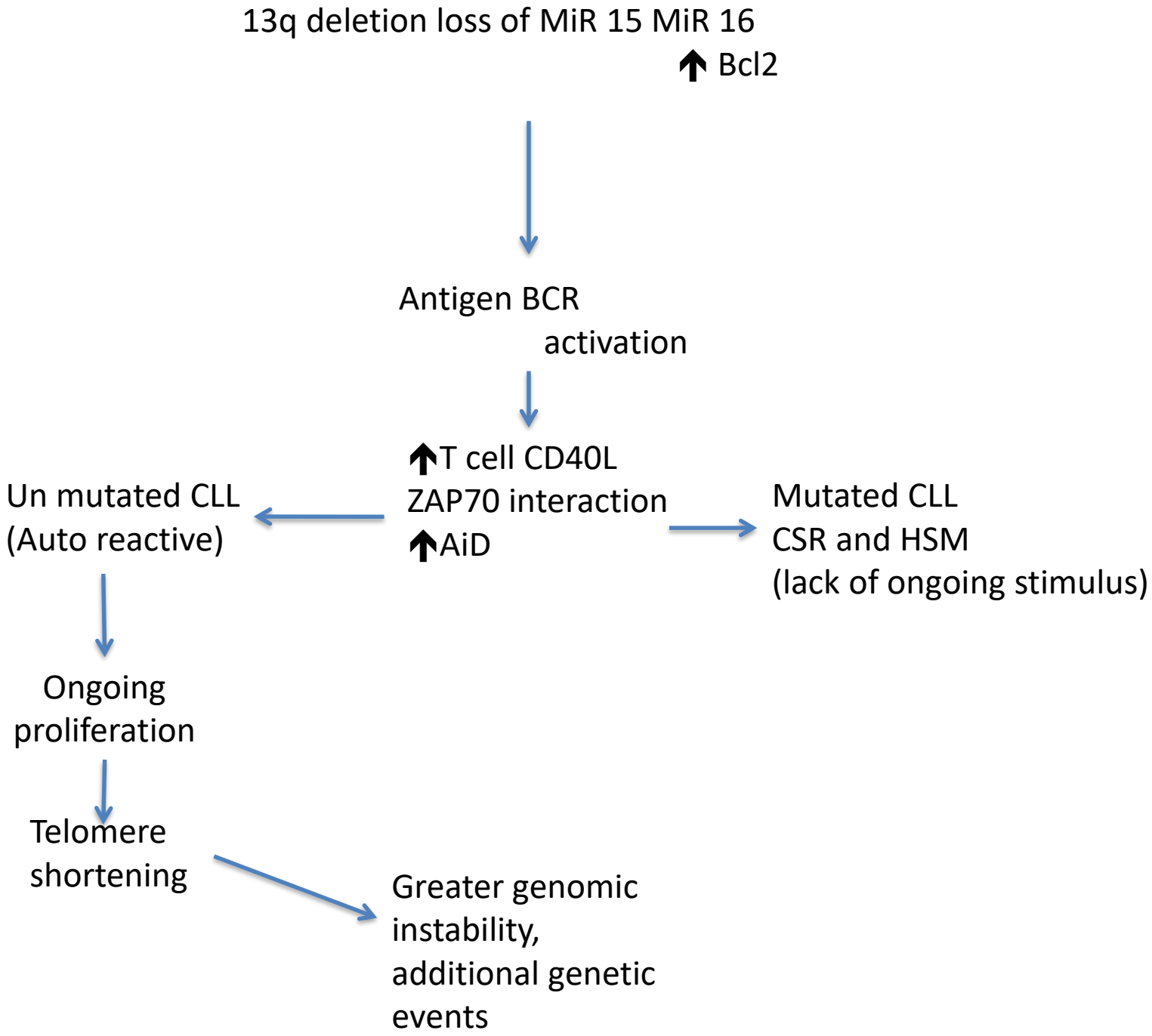


Telomere dysfunction and fusion during the progression of chronic lymphocytic leukemia: evidence for a telomere crisis

Thet Thet Lin,[1] Boitelo T. Letsolo,[1] Rhiannon E. Jones,[1] Jan Rowson,[1] Guy Pratt,[2] Saman Hewamana,[3] Chris Fegan,[3] Chris Pepper,[3] and Duncan M. Baird[1]

[1]Department of Pathology, School of Medicine, Cardiff University, Cardiff, United Kingdom; [2]Department of Haematology, Birmingham Heartlands Hospital, Birmingham, United Kingdom; and [3]Department of Haematology, School of Medicine, Cardiff University, Cardiff, United Kingdom

BLOOD, 16 SEPTEMBER 2010 • VOLUME 116, NUMBER 11


13q deletion loss of MiR 15 MiR 16
↑ Bcl2
Antigen BCR
activation
↑T cell CD40L
ZAP70 interaction
↑AiD
Un mutated CLL
(Auto reactive)
Mutated CLL
CSR and HSM
(lack of ongoing stimulus)
Ongoing
proliferation
Telomere
shortening
Greater genomic
instability,
additional genetic
events

How our Doctors plan our treatment

Considerations before treatment- the 4 Ps

- Progression?
- Peripheral cytopenias
  - Marrow failure
  - Auto immune
- Performance status
- P53

Treatment Criteria in CLL

- Current CLL guidelines recommended treatment only for active, symptomatic disease defined by at least one of following criteria:[1-3]
  - Progressive bone marrow failure (development or worsening of anaemia and/or thrombocytopenia).
  - Massive progressive or symptomatic splenomegaly.
  - Massive lymph nodes or progressive/symptomatic lymphadenopathy.
  - Progressive lymphocytosis with ≥50% increase over 2-month period or LDT <6 months.
  - Autoimmune anaemia and/or thrombocytopenia that responds poorly to standard treatment.
  - Constitutional B symptoms.

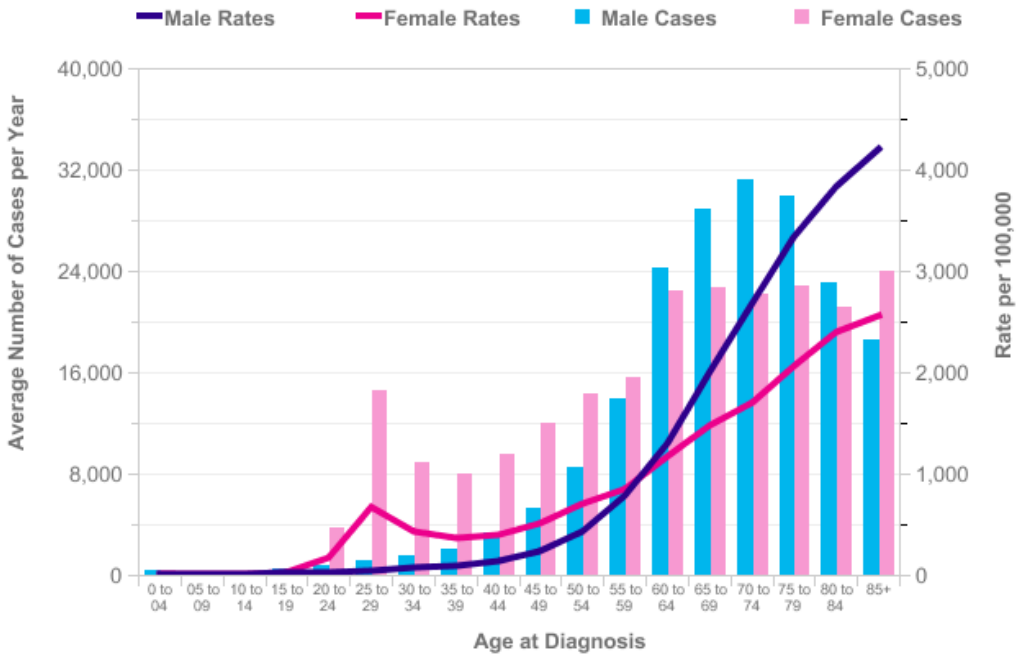
To Treat or Not to Treat?

The decision to initiate treatment in CLL is based on a balance of the benefits of early treatment versus the toxicity profiles of currently available therapies.

1. Eichhorst, B., Dreyling, M., *et al.* (2011). *Ann Oncol.* **22 Suppl 6**: vi50-4.
2. Lobetti-Bodoni, C., Bertoni, F., *et al.* (2013). *Eur J Intern Med.* **24**(**5**): 401-10.
3. Catovsky, D., Montserrat, E. (2011). In: Hoffbrand, A., Catovsky, D., *et al.*, eds. Postgraduate Haematology. Oxford: Wiley-Blackwell; p530-57

CLL is Primarily an Elderly Disease

- CLL is primarily a disease of the elderl
  - Peak incidence between 60-80 years
  - Average age at diagnosis 70 years[1]
  - Only 10% of patients <55 years[2]
  - Very rare below age 40[1]
- Tendency for older patients to presen



http://info.cancerresearchuk.org/cancerstats/faqs/#How

1. Catovsky, D., Montserrat, E. (2011). In: Hoffbrand, A., Catovsky, D., *et al.*, eds. Postgraduate Haematology. Oxford: Wiley-Blackwell; p530-57.
2. Eichhorst, B., Dreyling, M., *et al.* (2011). *Ann Oncol.* **22 Suppl 6**: vi50-4.

Front-Line CLL Therapy – "Go Go"

- "Go go" patients
  - Typically younger, physically fit patients with normal creatinine levels (indicating healthy kidney function) and a low CIRS score [1-3]
  - Treatment aim: prolong survival[1]
  - **First choice therapy: fludarabine + cyclophosphamide + rituximab (FCR) [1-3]**
  - Alternative regimens[1,3]
    - Bendamustine ± rituximab (BR)
  - Del(17p) is associated with low response rates with chemoimmunotherapy
  - Novel agents (ibrutinib) for P53 deleted CLL

1. Cramer, P., Hallek, M. (2011). *Nat Rev Clin Oncol*. **8**(**1**): 38-47.
2. Eichhorst, B., Dreyling, M., *et al.* (2011). *Ann Oncol*. **22 Suppl 6**: vi50-4.
3. NCCN Guidelines. (2015). Available from: http://www.nccn.org/professionals/physician_gls/pdf/nhl.pdf (Accessed: 31 March 2015).

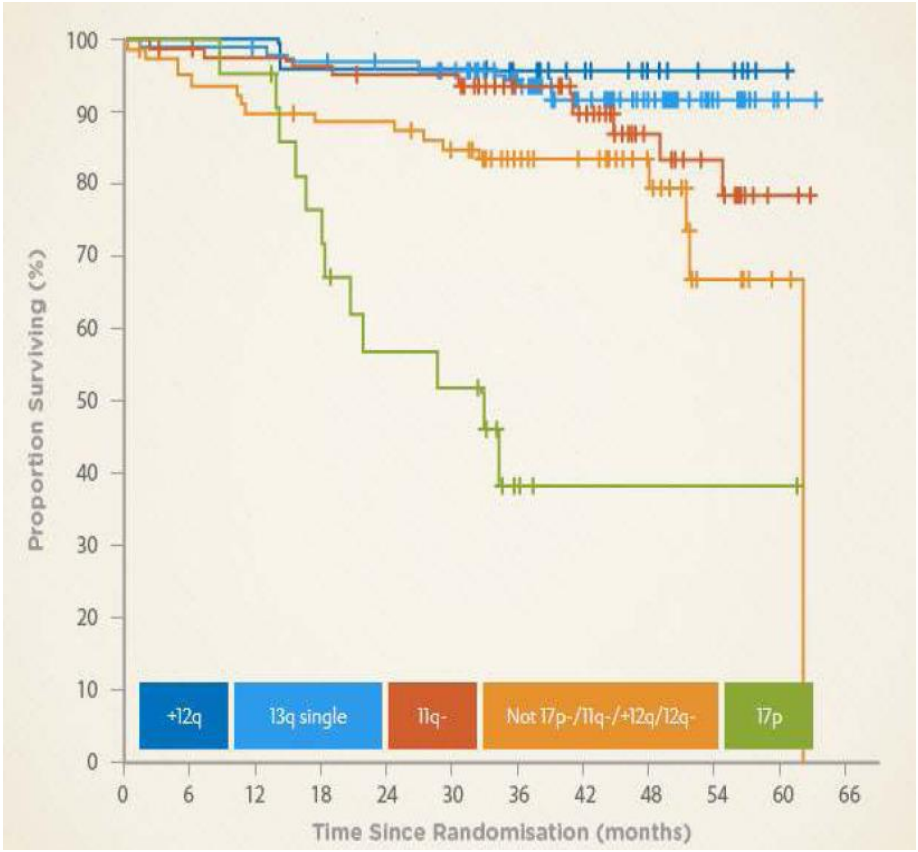
Front-Line CLL Therapy – "Slow Go"

- "Slow go"
  - Elderly patients and those with poor performance status and/or significant comorbidities[1-3]
  - Aim: achieve optimal symptom control[1]
  - **Recommended therapy: obinutuzumab + chlorambucil[3]**
  - Other clinical options[2,3]
    - Ofatumumab + chlorambucil
    - Rituximab + chlorambucil
    - Bendamustine (reduced dose) ± rituximab
    - Chlorambucil

1. Cramer, P., Hallek, M. (2011). *Nat Rev Clin Oncol*. **8**(**1**): 38-47.
2. Eichhorst, B., Dreyling, M.*, et al.* (2011). *Ann Oncol.* **22 Suppl 6**: vi50-4.
3. NCCN Guidelines. (2015). Available from: http://www.nccn.org/professionals/physician_gls/pdf/nhl.pdf (Accessed: 31 March 2015).

The CLL8 trial

- Randomised, multicentre trial of fludarabine + cyclophosphamide (FC) versus FC + rituximab (FCR) in CLL patients
  - Highlights negative impact of del(17p)



	All patients		Del(17p) carriers	
	FC	**FCR**	**FC**	**FCR**
3-year PFS	45%	65%	0%	18%
3-year OS	83%	87%	37%	38%

1. Schnaiter, A., Stilgenbauer, S. (2013). *Hematol Oncol Clin North Am*. **27**(**2**): 289-301.

54th ASH® Annual Meeting and Exposition
Atlanta, GA • December 8-11, 2012
ABSTRACTS, PROGRAM, AND PERSONAL SCHEDULER

3929 Is Chronic Lymphocytic Leukemia Still Incurable?

Program: Oral and Poster Abstracts
Session: 642. CLL - Therapy, excluding Transplantation: Poster III

Monday, December 10, 2012, 6:00 PM-8:00 PM
Hall B1-B2, Level 1, Building B (Georgia World Congress Center)

***Michael J. Keating, MD*[1], *Constantine S Tam*[2], *William G. Wierda, MD, Ph.D.*[1], *Susan O'Brien, M.D.*[3], *Deborah A. Thomas, MD*[4], *Jorge E. Cortes, MD*[5], *Susan Lerner, MS*[6*] *and William Plunkett, PhD*[7]

[1]*Leukemia, MD Anderson Cancer Center, Houston, TX*
[2]*Peter McCallum, Melbourne, Australia*
[3]*The University of Texas MD Anderson Cancer Center, Department of Leukemia, Houston, TX*
[4]*Department of Leukemia, The University of Texas, M. D. Anderson Cancer Center, Houston, TX*
[5]*Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX*
[6]*MD Anderson Cancer Center, Houston, TX*
[7]*The University of Texas M.D. Anderson Cancer Center, Department of Experimental Therapeutics, Houston, TX*

Introduction

Regular Article

CLINICAL TRIALS AND OBSERVATIONS

Eradication of bone marrow minimal residual disease may prompt early treatment discontinuation in CLL

Paolo Strati,[1] Michael J. Keating,[1] Susan M. O'Brien,[1] Jan Burger,[1] Alessandra Ferrajoli,[1] Nitin Jain,[1] Francesco Paolo Tambaro,[2] Zeev Estrov,[1] Jeffrey Jorgensen,[3] Pramoda Challagundla,[3] Stefan H. Faderl,[1] and William G. Wierda[1]

[1]Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX; [2]Dipartimento di Patologia Generale, Seconda Università degli Studi di Napoli, Napoli, Italy; and [3]Department of Hematopathology, The University of Texas MD Anderson Cancer Center, Houston, TX

Key Points

- MRD eradication is a desirable end point in chronic lymphocytic leukemia.
- Early MRD eradication may prompt treatment discontinuation.

The high complete remission rate with first-line combined fludarabine, cyclophosphamide, and rituximab (FCR) begs the question of the value of minimal residual disease (MRD)–negative status as a treatment end point. We report on 237 patients with chronic lymphocytic leukemia who received first-line FCR. MRD was prospectively assessed by 4-color flow cytometry in bone marrow after course 3 and at final response assessment. After course 3 and at final response assessment, 17% and 43% of patients were MRD negative in bone marrow, respectively. A mutated immunoglobulin heavy chain variable gene and trisomy 12 were independently associated with MRD-negative status both after 3 courses of FCR and at final response assessment in multivariable analyses (MVAs).

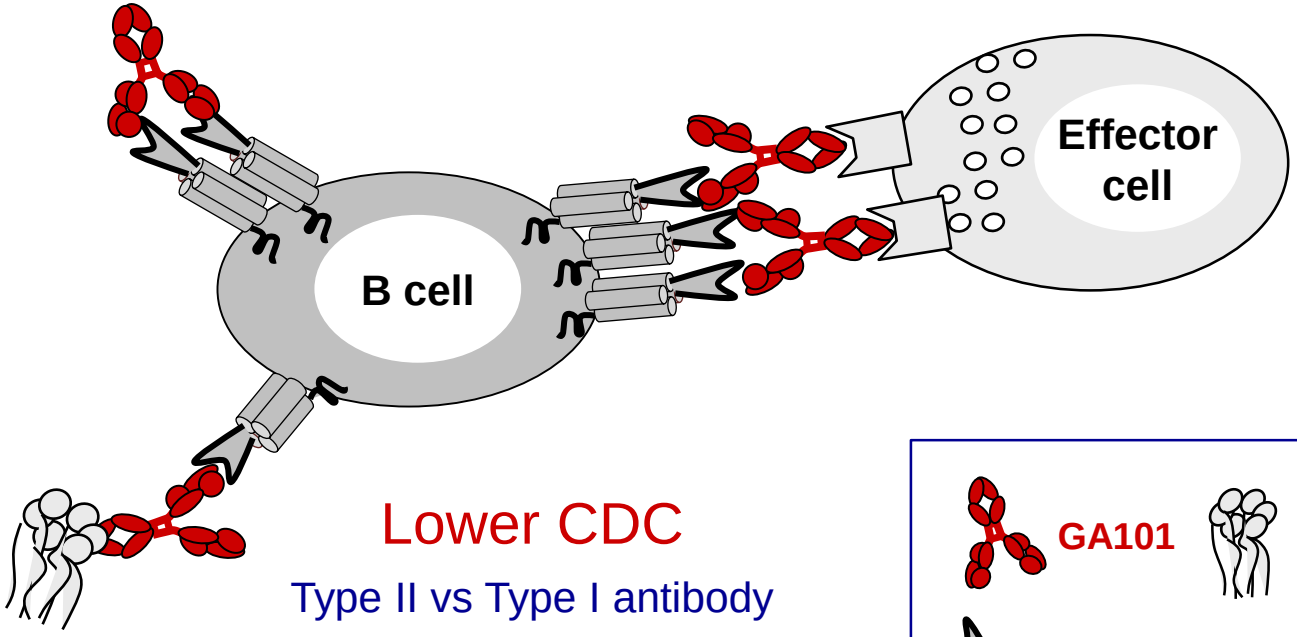
GA101: Mechanisms of action

Increased Direct Cell Death

Type II vs Type I antibody

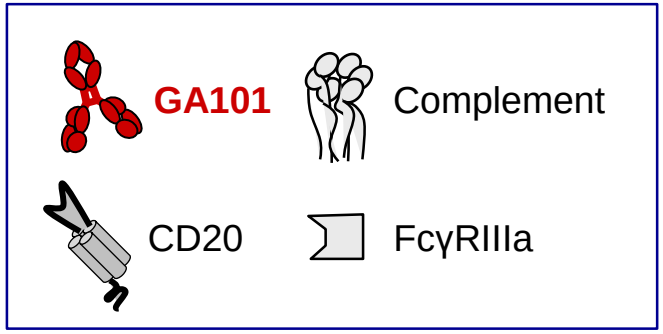
Enhanced ADCC

Glycoengineering for
increased affinity to FcγRIIIa



Lower CDC

Type II vs Type I antibody



ADCC, antibody-dependent cell-mediated cytotoxicity; CDC, complement-dependent cytotoxicity

Mössner et al. *Blood* 2010;115:4393–4402

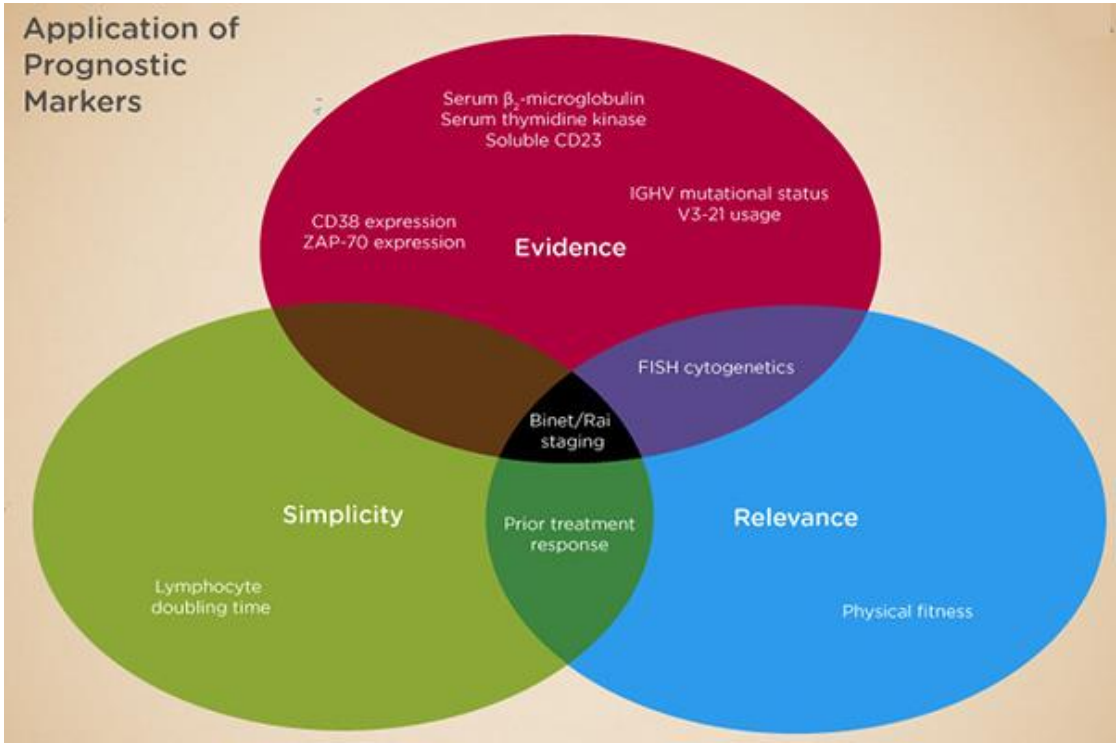
Head-to-Head Comparison of Obinutuzumab (GA101) Plus Chlorambucil (Clb) Versus Rituximab Plus Clb in Patients With Chronic Lymphocytic Leukemia (CLL) and Co-existing Medical Conditions (Comorbidities): Final Stage 2 Results of the CLL11 Trial

Goede V, Fischer K, Busch R, Engelke A, Eichhorst B, Wendtner CM, Chagorova T, De la Serna J, Dilhuydy MS, Opat S, Owen C, Samoylova O, Kreuzer KA, Langerak AW, Ritgen M, Stilgenbauer S, Döhner H, Asikanius E, Humphrey K, Wenger M, Hallek M

DEUTSCHE CLL STUDIENGRUPPE

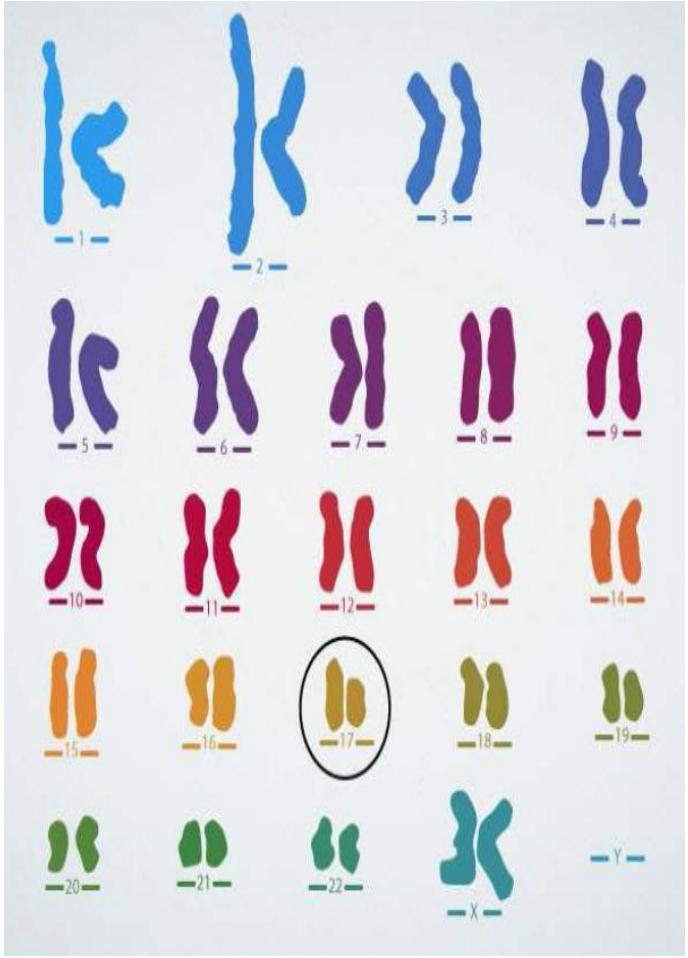
Application of Prognostic Markers

- Illustration of how different prognostic markers in CLL can be used in clinical practice based on their:
  - Simplicity
  - Relevance
  - Strength of supporting evidence



Del(17p)

- Key cytogenetic abnormality in CLL
  - Results in loss of TP53 gene[1]
    - 'Guardian of the genome'
    - Tumour suppressor gene
    - Product p53 is key regulator of cell cycle
- Associated with aggressive, treatment-resistant disease
- Prevalence markedly higher in relapsed/refractory versus untreated CLL[1]
  - 3-10% of newly-diagnosed patients
  - 30-50% with relapsed/refractory disease
- Chemotherapy selects for del(17p) resistant subclones[1-3]
  - Important implications for treatment selection and sequencing



1. Schnaiter, A., Stilgenbauer, S. (2013). *Hematol Oncol Clin North Am*. **27**(**2**): 289-301.
2. Rosenwald, A., Chuang, E.Y., *et al.* (2004).. *Blood*. **104**(**5**): 1428-34.
3. Landau, D.A., Carter, S.L., *et al.* (2013). *Cell*. **152**(**4**): 714-26.

The Hematology Journal (2004) 5, 47–54
© 2004 The European Hematology Association All rights reserved 1466-4680/04 $25.00
www.nature.com/thj

Characterisation of *TP53* abnormalities in chronic lymphocytic leukaemia

Patrick D Thornton[1], Alicja M Gruszka-Westwood[1,2], Rifat A Hamoudi[1,3], Shayne Atkinson[1], Pawel Kaczmarek[1], Ricardo M Morilla[1], Benjamin L Hilditch[1], Roger A'Hern[1], Estella Matutes[1] and Daniel Catovsky*[,1]

[1] *Academic Department of Haematology and Cytogenetics, The Royal Marsden NHS Trust and Institute of Cancer Research, London, UK*

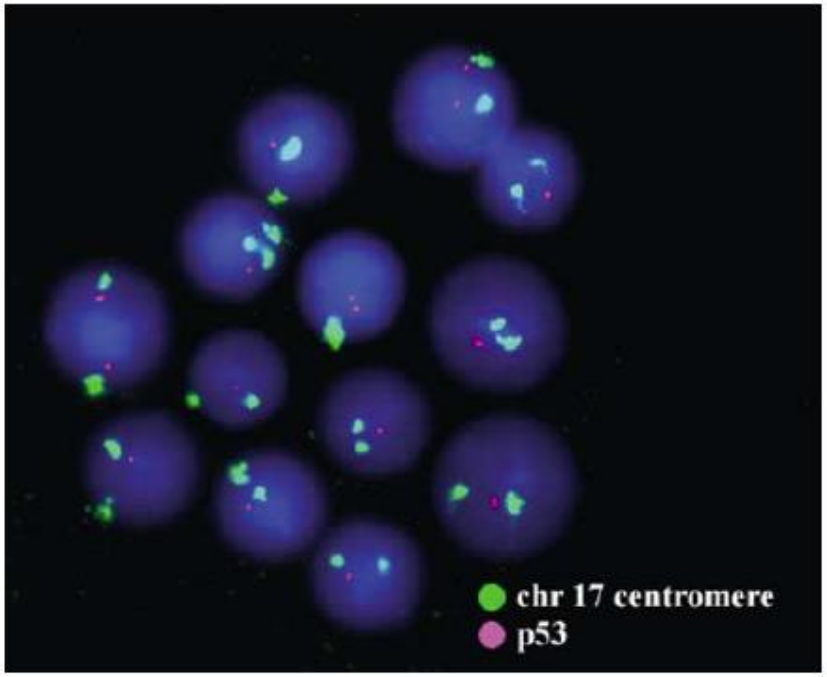
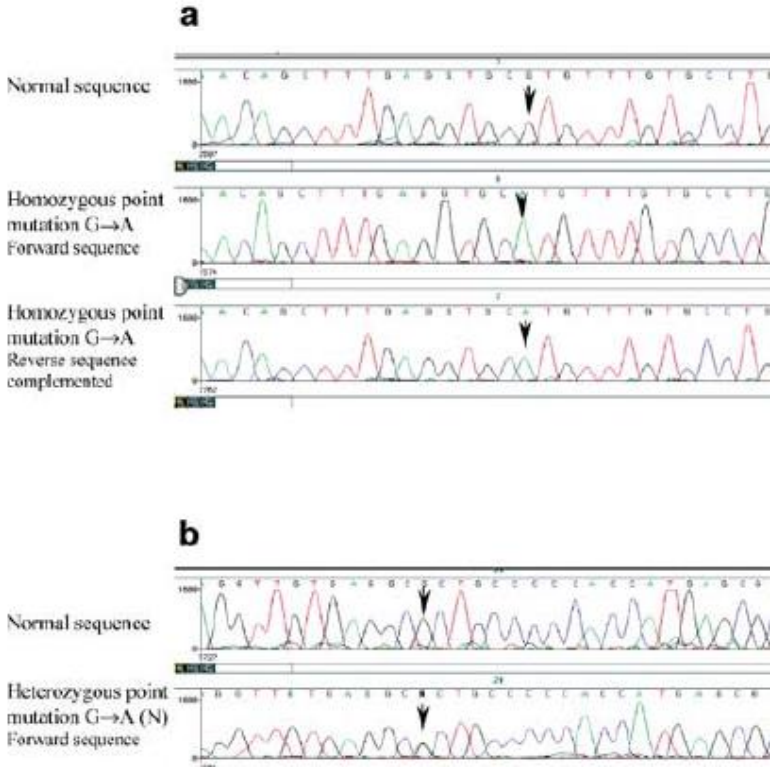


Figure 1 Hemizygous p53 deletion by FISH analysis.

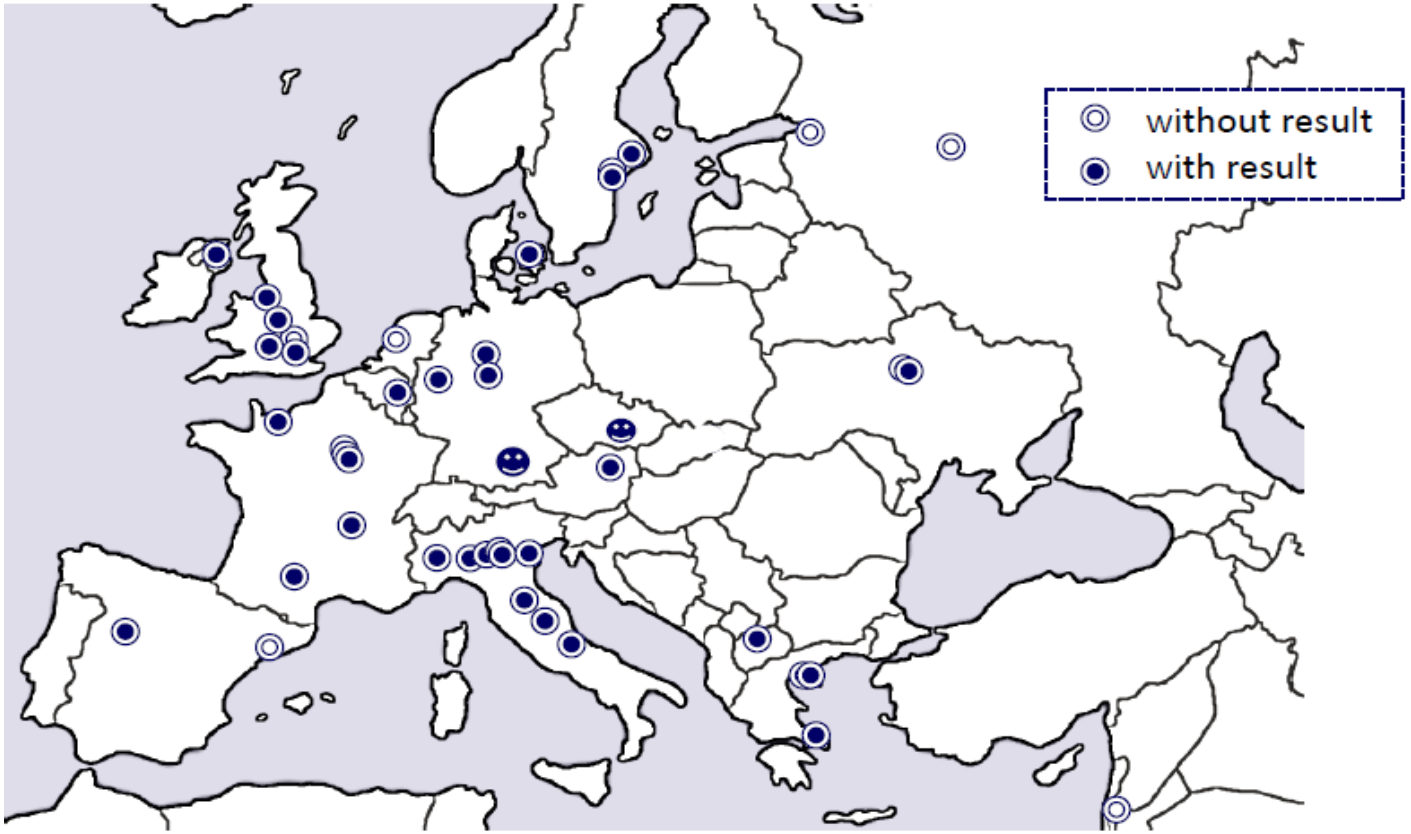


Participating Labs

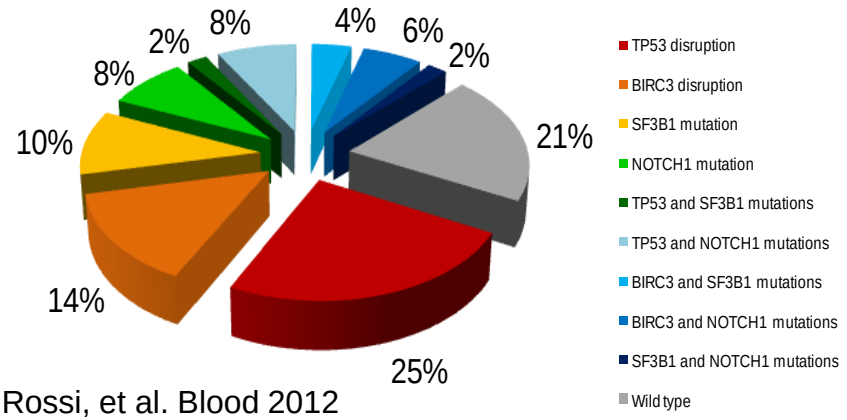
- 49 centers participated in the study and asked for samples

european research initiative on CLL
TP53 Certified Center

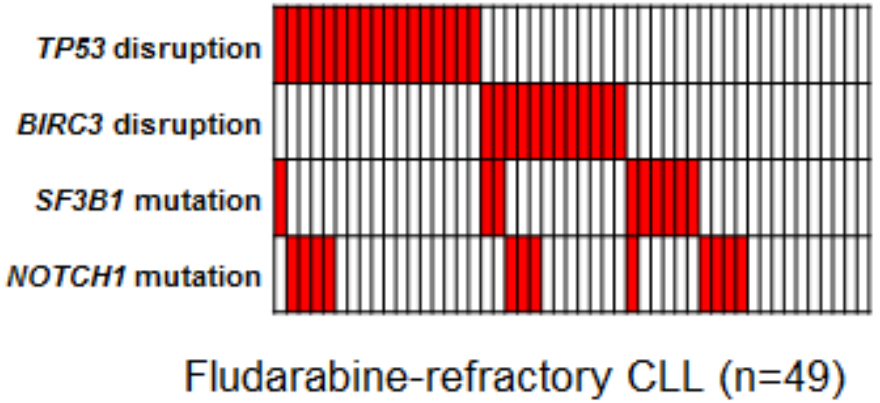
Belfast: ERIC TP53 Network Reference Centre

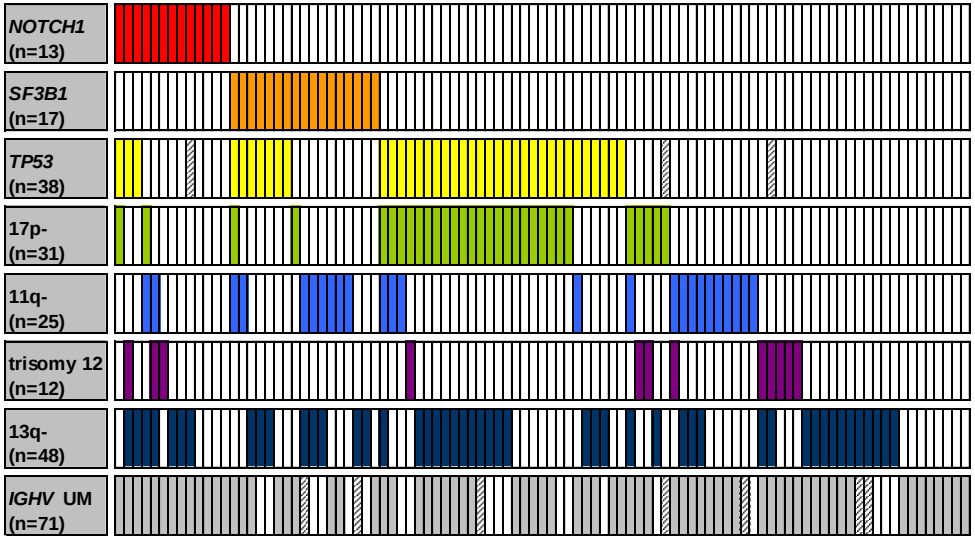


Molecular basis of fludarabine-refractory CLL



Rossi, et al. Blood 2012





CLL2H
Alemtuzumab treatment in Fludarabine-refractory CLL (n=97)

Stilgenbauer et al ASH

Treatment of Relapsed CLL

- CLL remains incurable
  - All patients will eventually relapse (unless die of other causes in remission)
- Most relapse within 2 years with 2nd exposure to chemotherapy
- Consider new therapeutic strategies or clinical trial
- Most patients ineligible for allogenic stem cell transplant due to age or comorbidities[1]

1. Gribben, J.G., O'Brien, S. (2011). *J Clin Oncol*. **29**(**5**): 544-50.
2. Eichhorst, B., Dreyling, M.*, et al.* (2011). *Ann Oncol*. **22 Suppl 6**: vi50-4.
3. Ghielmini, M., Vitolo, U.*, et al.* (2013). *Ann Oncol*. **24**(**3**): 561-76.

Relapsed CLL – Novel Agents

- Phosphatidylinositol 3-kinase (PI3K) inhibitors
- Bruton's tyrosine kinase (BTK) inhibitors
  - Ibrutinib: first-in-class BTK inhibitor
  - As of late 2013, additional BTK inhibitors in clinical development (phase 1)
- BCL-2 inhibitors
  - ABT-199: BCL-2-specific inhibitor engineered with lower activity against BCL-xL[5]
    - Promising Phase I activity in B-cell malignancies

1. Ferrajoli, A., Lee, B.N., *et al*. (2008). *Blood*, 111: 5291–5297.
2. Chanan-Khan, A., Miller, K.C., *et al*. (2006). *J Clin Oncol*, 24: 5343–5349.
3. Sher, T. Miller, K.C., *et al*. (2010). *Leuk Lymphoma*, 51: 85–88.
4. Davids, M.S., Letai, A. (2013). Cancer Cell. 23(2): 139-41.
5. Ujjani, C., Cheson, B.D. (2013). *Expert Rev Hematol*, 6(2): 191–203.

Abstract #234

: Updated Efficacy and Safety From the Phase 3 RESONATE-2 Study: Ibrutinib as First-Line Treatment Option in Patients 65 Years and Older with Chronic Lymphocytic Leukemia/Small Lymphocytic Leukemia

- Oral presentation: Saturday, December 3, 2016, 5:15 PM PT

Updated results from the pivotal Phase 3 RESONATE-2 trial (PCYC-1115) showed that IMBRUVICA continued to be efficacious as first-line therapy in CLL/SLL at a median 29 months of follow-up. IMBRUVICA reduced the risk of progression or death by 88% compared with chlorambucil, a commonly used chemotherapy agent. At 24 months, PFS was 89% for patients taking IMBRUVICA and 34% for chlorambucil (HR= 0.121; 95% CI (0.074-0.198); p<0.0001). Of note, in the high-risk del11q subgroup ibrutinib was associated with a 99% reduction in risk of progression or death compared to chlorambucil (HR= 0.014; 95% CI (0.002-0.108); p<0.0001) and 82% reduction for those without del11q (HR=0.180, 95% CI (0.106-0.303), p<0.0001). With longer follow-up, investigator-assessed ORR was 92% with ibrutinib and 36% with chlorambucil; in the ibrutinib arm, CR or CR with incomplete bone marrow recovery (Cri) improved from 11% at 18.4 months to 18%. In ibrutinib-treated patients, ORR was 100% for patients with del11q and 90% for those without the genetic alteration.[6]

‡

A Phase 2 Study of the Selective Phosphatidylinositol 3-kinase Delta (PI3Kδ) Inhibitor Idelalisib (GS-1101) in Combination with Rituximab in Treatment-naïve Patients ≥65 Years with Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL)

SM O'Brien,[1] N Lamanna,[2] TJ Kipps,[3] I Flinn,[4] AD Zelenetz,[4] JA Burger,[1] L Holes,[6] DM Johnson,[6] J Gu,[6] RD Dansey,[6] RL Dubowy,[6] and SE Coutre[7]

[1]University of Texas M. D. Anderson Cancer Center, Houston, TX, USA; [2]Columbia University Medical Center, New York, NY, USA; [3]University of California, San Diego Moores Cancer Center, La Jolla, CA, USA; [4]Sarah Cannon Research Institute, Nashville, TN, USA; [5]Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [6]Gilead Sciences, Seattle, WA; [7]Stanford Cancer Center, Stanford, CA, USA

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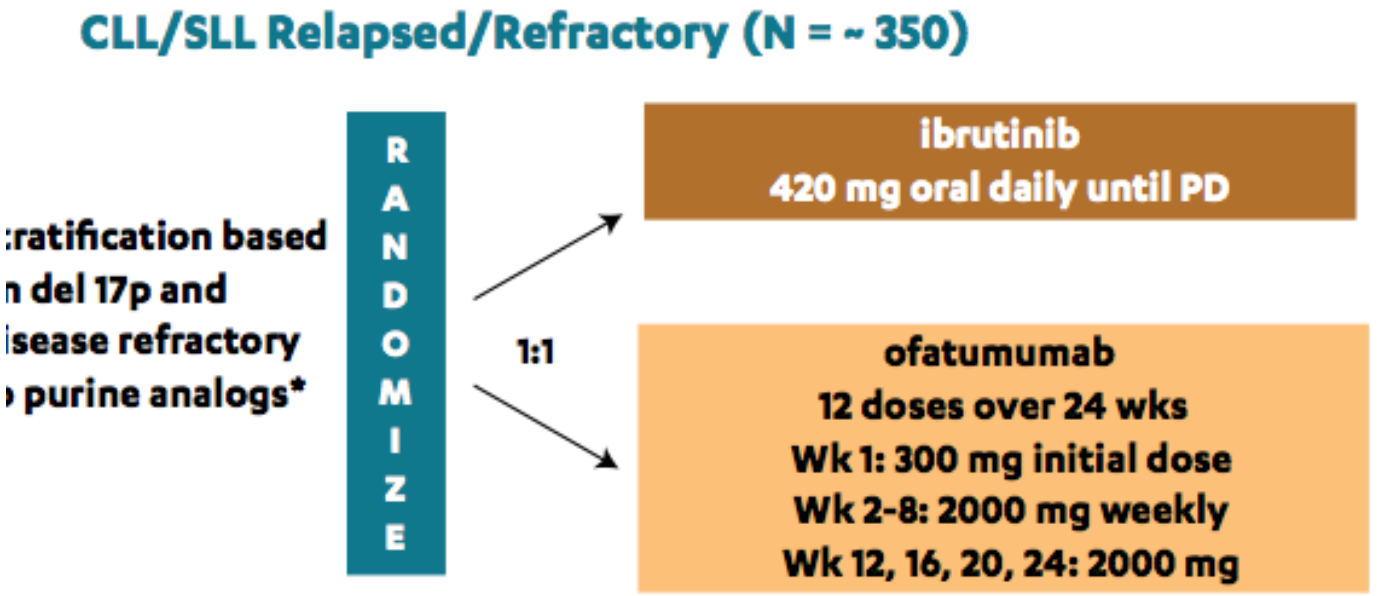
Phase 3 Study relapsed CLL

Idelalisib and Rituximab in Relapsed Chronic Lymphocytic Leukemia

Furman RR et al. N Engl J Med 2014;370:997-1007.

ure 2. PCYC-1112-CA (RESONATE™) Study Design



New Considerations before treatment- the 3 Cs

- Chromosomes?
- Chemotherapy (or not)
- Clinical Trial

Bring Clinical Trails to Ireland

- Relationships with Pharma
- Performance and publication of previous trials
- Good recruitment
- Support for clinical trials units
- Cancer trials Ireland
- Irish Blood Cancer Network

Venice -1

M15-550 Study March 2017 update! AKA VENICE 1

Open-Label, Single Arm, Phase 3b, Multi-Center Study Evaluating the Efficacy of Venetoclax (ABT-199) in Relapsed/Refractory Subjects with Chronic Lymphocytic Leukemia (CLL) Including Those with the 17p Deletion or TP53 Mutation OR Those Who Have Received Prior Treatment with a B-Cell Receptor Inhibitor

ear Investigators and study teams,

don't know about you, but I am in shock that I need to be getting into Easter mode! This year is flying by at a rate of knots and as the sunny weather tentatively peeps its head around the corner I am writing to give you a study pdate on what happened in the UK and Ireland in March. Thank you all so much for your hard work in identifying patients, setting up your sites and in data entry. In particular I would like to acknowledge the following 2 Investigators nd teams.

Dr. Patrick Thornton **and team at Beaumont hospital, Dublin who enrolled their second patient**

Dr. Francesco Forconi **and team in Southampton who screened their 3rd patient.**

hat's 6 enrolled and 1 in screening .

PI	Date opened	In screening	Enrolled	CRA
Dr. Marian Macheta	15 Nov 16	0	0	Elena Townson
Dr. Abraham Jacob	5 Dec 16	0	1	Lucinda Driscoll
Dr. Francesco Forconi	6 Dec 16	1	2	Elena Townson
Prof Elisabeth Vandenberghe	7 Dec 16	0	1	Christine Murphy
Dr. Patrick Thornton	27 Jan 17	0	2	Christine Murphy

CLL 13

DEUTSCHE
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Suche
DCLLSG
Home
Aktuelles
Über uns
CLL Information
Studien
Patienten
Publikationen
Deutsch
CLL13 Trial
Title
A phase 3 multicenter, randomized, prospective, open-label trial of standard chemoimmunotherapy (FCR/BR) versus rituximab plus venetoclax (RVe) versus obinutuzumab (GA101) plus venetoclax (GVe) versus obinutuzumab plus ibrutinib plus venetoclax (GIVe) in fit patients with previously untreated chronic lymphocytic leukemia (CLL) without del(17p) or TP53 mutation