Forskning, kliniske studier

Andrea Lenartova

Lege, klinisk stipendiat

Bli kvitt KLL ?

Unngå å få KLL?

Sigrid S.Skånland

Anna Parente Ribes

Ludvig A Munthe

Kjetil Taskén

Sigrid S.Skånland

Anna Parente

Anders Østerborg, Stockholm

Ludvig A Munthe

Kjetil Taskén

Carsten U Niemann, København

Richard Rosenquist Brandell, Stockholm

Sigrid S.Skånland

Anna Parente

Anders Østerborg, Stock

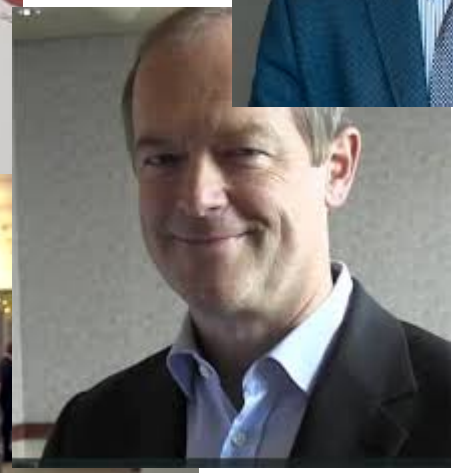
Barbara Eichhorst, Køln

Ludvig A Munthe

Kjetil Taskén

Carsten U Nieman

Paolo Ghia, Italia



Michael Hallek, Køln

Richard Rosenquist Brandell, Stockholm

Sigrid S.Skånland

Anna Parente

Anders Østerborg, Stock

Barbara Eichhorst, Køln

Peter Hillmen,Leeds

Ludvig A Munthe

Kjetil Taskén

Carsten U Nieman

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Michael Hallek, Køln

Richard Rosenquist Brandell, Stockholm

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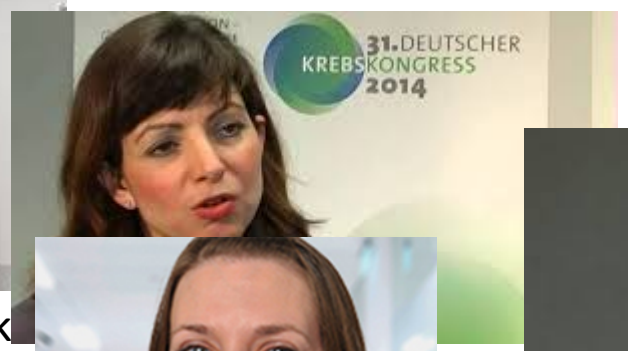


Køln

Jennifer Woyach, Ohio

men,Leeds

Ludvig A Munthe

Kjetil Taskén

Carsten U Nieman

Paolo Ghia, Italia

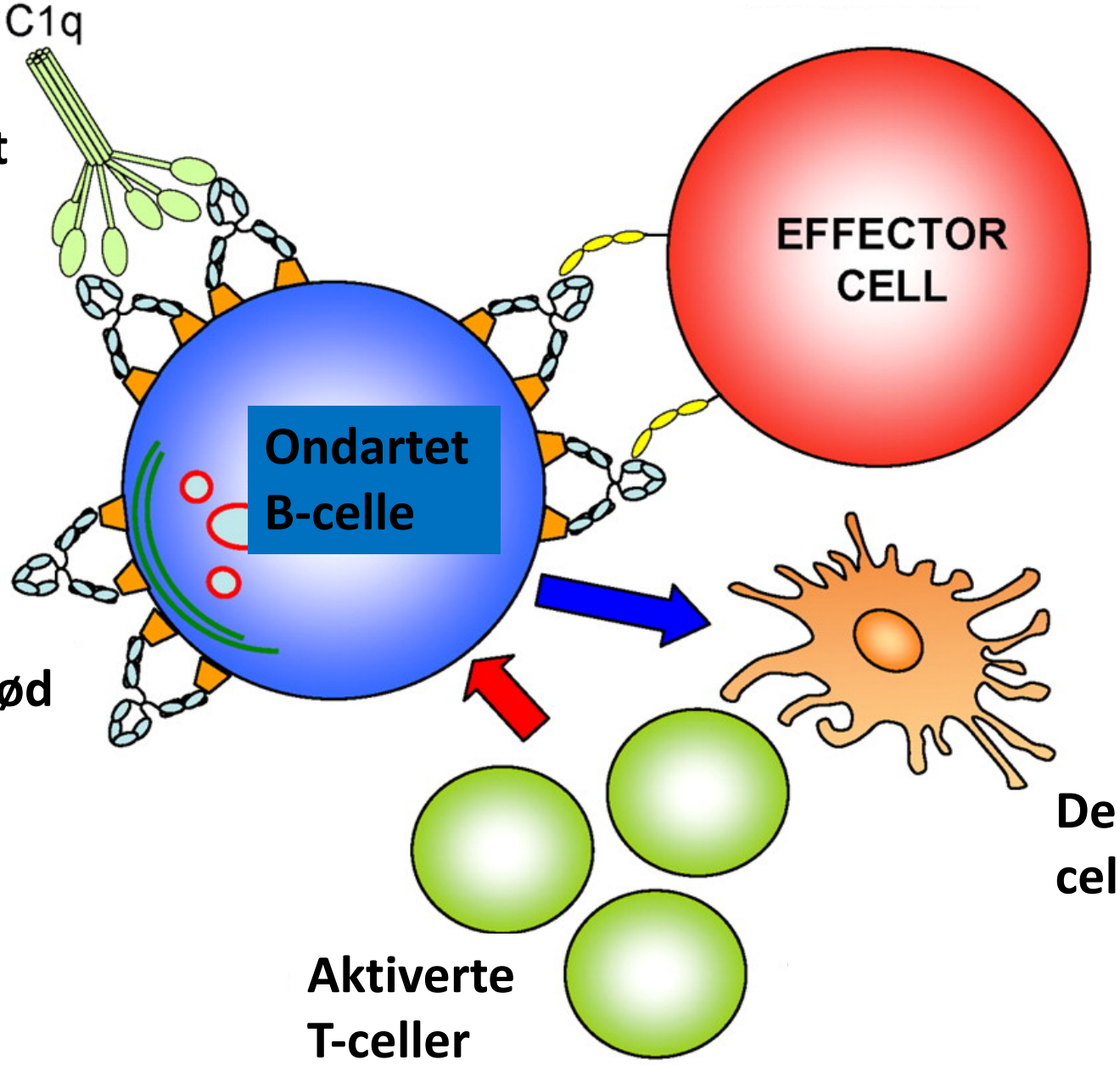
Michae

William Wierda , Texas

Richard Rosenquist Brandell, Stockholm

Antistoff derivert celledrap

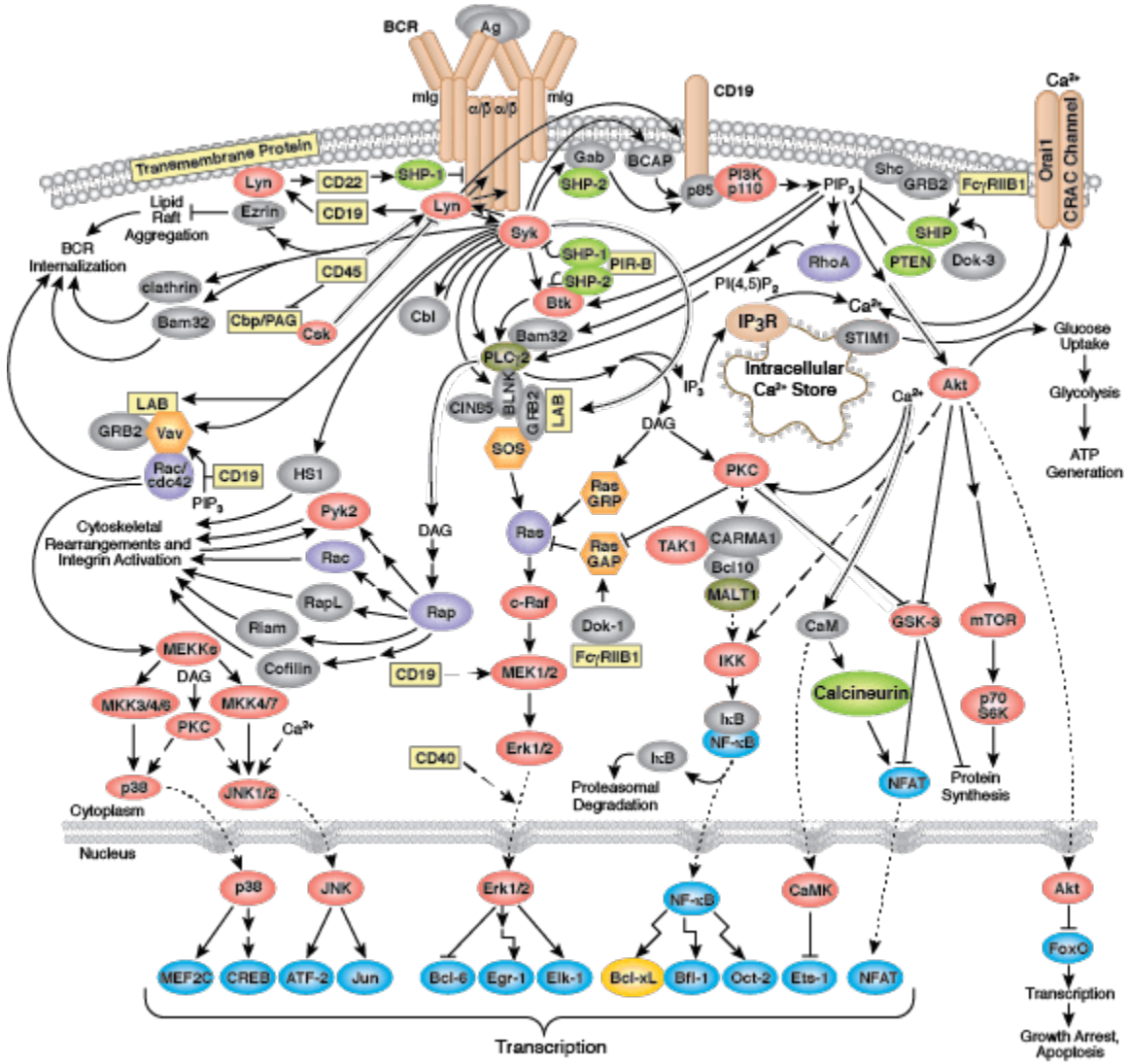
Komplement derivert celledrap

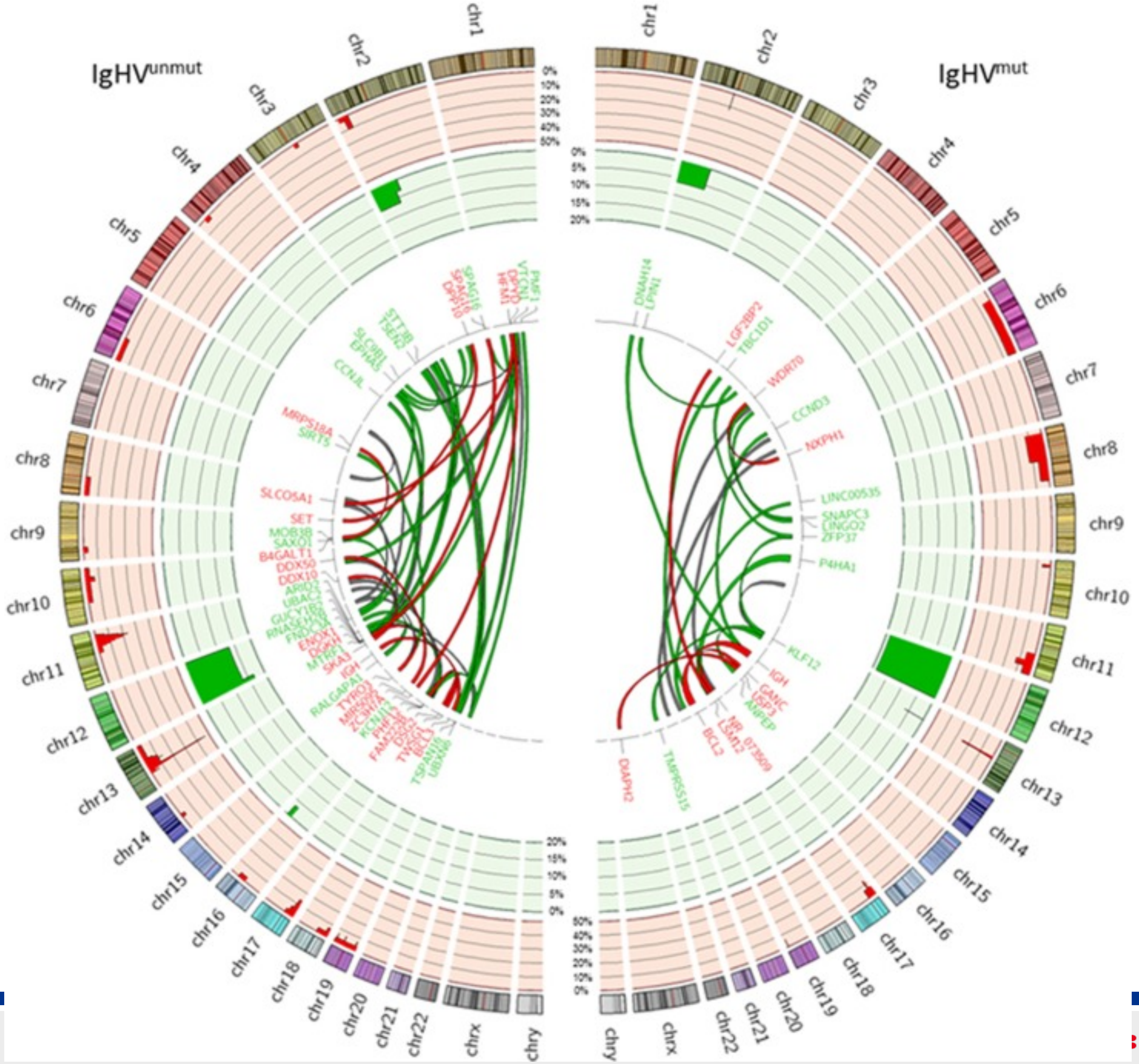


Programert celledød

Dendritisk celle

Aktiverte T-celler


BCR
Ag
mIg
α/β α/β
mIg
CD19
Ca2+
Orai1
CRAC Channel
Transmembrane Protein
Lyn
CD22
SHP-1
Gab
BCAP
SHP-2
p85
PI3K p110
PIP3
Shc
GRB2
FcγRIIB1
Lipid Raft Aggregation
Ezrin
CD19
Lyn
Syk
SHP
BCR Internalization
clathrin
Bam32
Cbp/PAG
Csk
CD45
SHP-1
PIR-B
SHP-2
Btk
Cbl
RhoA
PTEN
Dok-3
PI(4,5)P2
Ca2+
IP3R
STIM1
Intracellular Ca2+ Store
Glucose Uptake
Glycolysis
ATP Generation
Akt
Bam32
PLC-γ2
IP3
LAB
GRB2
Vav
BLNK
GRB2
LAB
CIN85
SOS
DAG
Rac/ cdc42
CD19
PIP3
HS1
Pyk2
Cytoskeletal Rearrangements and Integrin Activation
Rac
RapL
Rap
Riam
Cofilin
MEKKs
DAG
MKK3/4/6
MKK4/7
PKC
Ca2+
p38
JNK1/2
Cytoplasm
Nucleus
DAG
Ras
Ras GRP
Ras GAP
c-Raf
Dok-1
FcγRIIB1
MEK1/2
CD19
CD40
Erk1/2
PKC
TAK1
CARMA1
Bcl10
MALT1
IKK
IκB
NF-κB
Proteasomal Degradation
CaM
Calcineurin
GSK-3
mTOR
p70 S6K
NFAT
Protein Synthesis
p38
JNK
Erk1/2
NF-κB
CaMK
Akt
FoxO
MEF2C
CREB
ATF-2
Jun
Bcl-6
Egr-1
Elk-1
Bcl-xL
Bfl-1
Oct-2
Ets-1
NFAT
Transcription
Transcription
Growth Arrest, Apoptosis


IgHVunmut
IgHVmut
chr1
chr2
chr3
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chr21
chr22
chrx
chry

- Chlorambucil
- Fludarabin
- Bendamustine
- Ofatumumab
- Rituximab
- Obinutuzumab
- Ibrutinib
- Idelasilib
- Venetoclax
- Duvelisilib

blood Special Report

iwCLL guidelines for diagnosis, indications for treatment, response assessment, and supportive management of CLL

Michael Hallek,[1,2] Bruce D. Cheson,[3] Daniel Catovsky,[4] Federico Caligaris-Cappio,[5] Guillermo Dighiero,[6] Hartmut Döhner,[7] Peter Hillmen,[8] Michael Keating,[9] Emili Montserrat,[10] Nicholas Chiorazzi,[11] Stephan Stilgenbauer,[7] Kanti R. Rai,[11] John C. Byrd,[12] Barbara Eichhorst,[1] Susan O'Brien,[13] Tadeusz Robak,[14] John F. Seymour,[15] and Thomas J. Kipps[16]

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The previous edition of the consensus guidelines of the International Workshop on Chronic Lymphocytic Leukemia (iwCLL), published in 2008, has found broad acceptance by physicians and investigators caring for patients with CLL. Recent advances including the discovery of the genomic landscape of the disease, the development of genetic tests with prognostic relevance, and the detection of minimal residual disease (MRD), coupled with the increased availability of novel targeted agents with impressive efficacy, prompted an international panel to provide updated evidence- and expert opinion–based recommendations. These recommendations include a revised version of the iwCLL response criteria, an update on the use of MRD status for clinical evaluation, and recommendations regarding the assessment and prophylaxis of viral diseases during management of CLL. (*Blood*. 2018;131(25):2745-2760)

Introduction

In 2008, the International Workshop on Chronic Lymphocytic Leukemia (iwCLL) published consensus guidelines for the design and conduct of clinical trials for patients with CLL that were revised from those previously published by the National Cancer Institute–sponsored Working Group.[1-3] Those guidelines provided definitions intended to standardize the assessment of patients that were adopted by the US Food and Drug Administration and European Medicines Agency for the evaluation of new drugs. Since the publication of those guidelines, there have been major advances in the biology and treatment of patients with CLL, prompting the iwCLL to evaluate and revise the 2008 criteria.

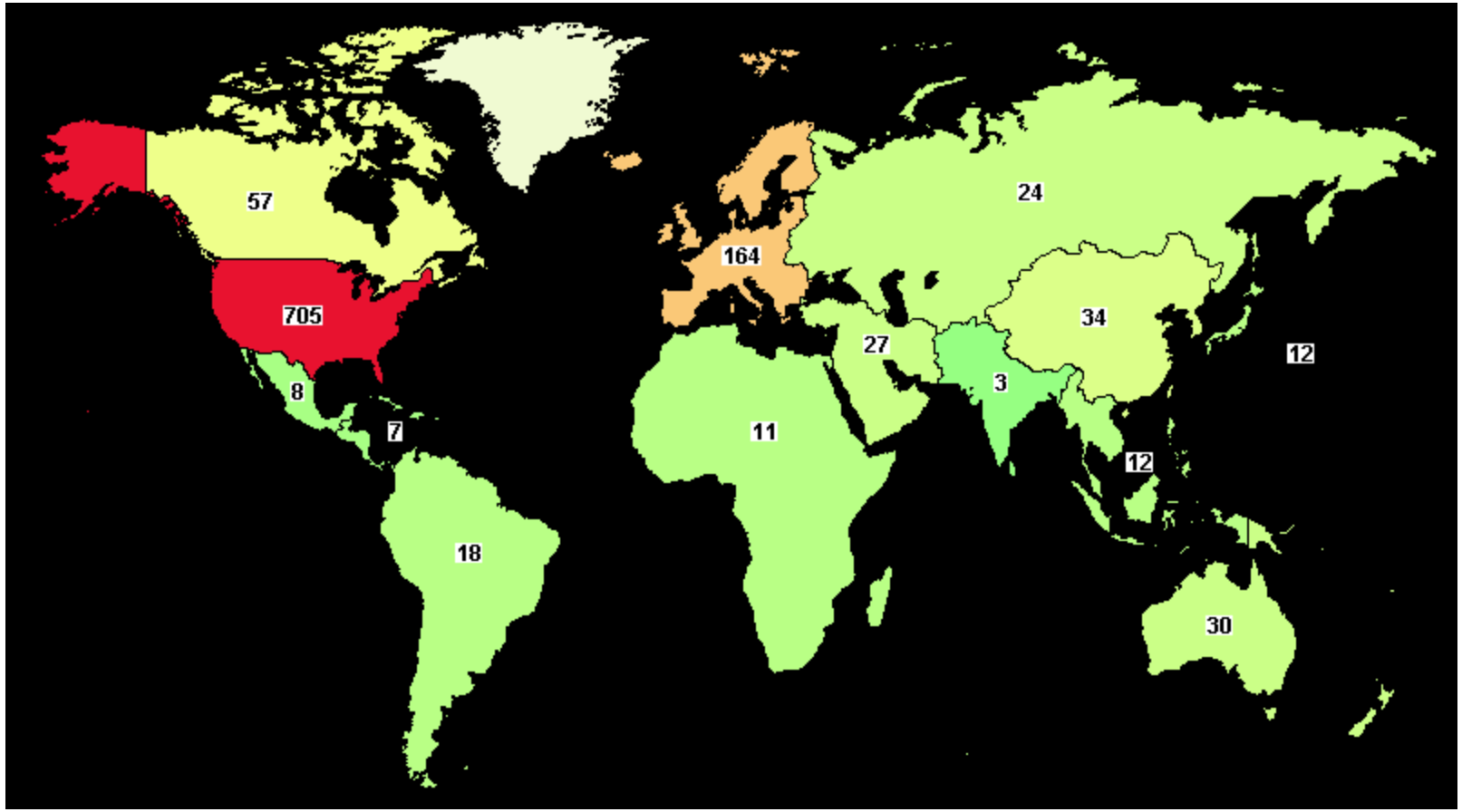
The following major changes or additions were introduced in these updated guidelines.

- The clinical relevance of the recent discoveries on the genomic alterations found in CLL, including mutations of the *TP53* gene.
- The increasingly important prognostic role of the immunoglobulin variable heavy chain mutational status.
- The current use of clinical staging, novel genetic or biological prognostic markers, and prognostic scores.
- An improved assessment of splenomegaly, hepatomegaly and lymphadenopathy, which was harmonized with the relevant sections of the updated lymphoma response guidelines.
- An updated response assessment for novel targeted drugs (kinase inhibitors, Bcl2 inhibitors) that need to be evaluated during continuous therapy.
- The increasing role of assessing minimal residual disease.
- Updates regarding the baseline assessment and prophylaxis of viral diseases before and under therapy of CLL.

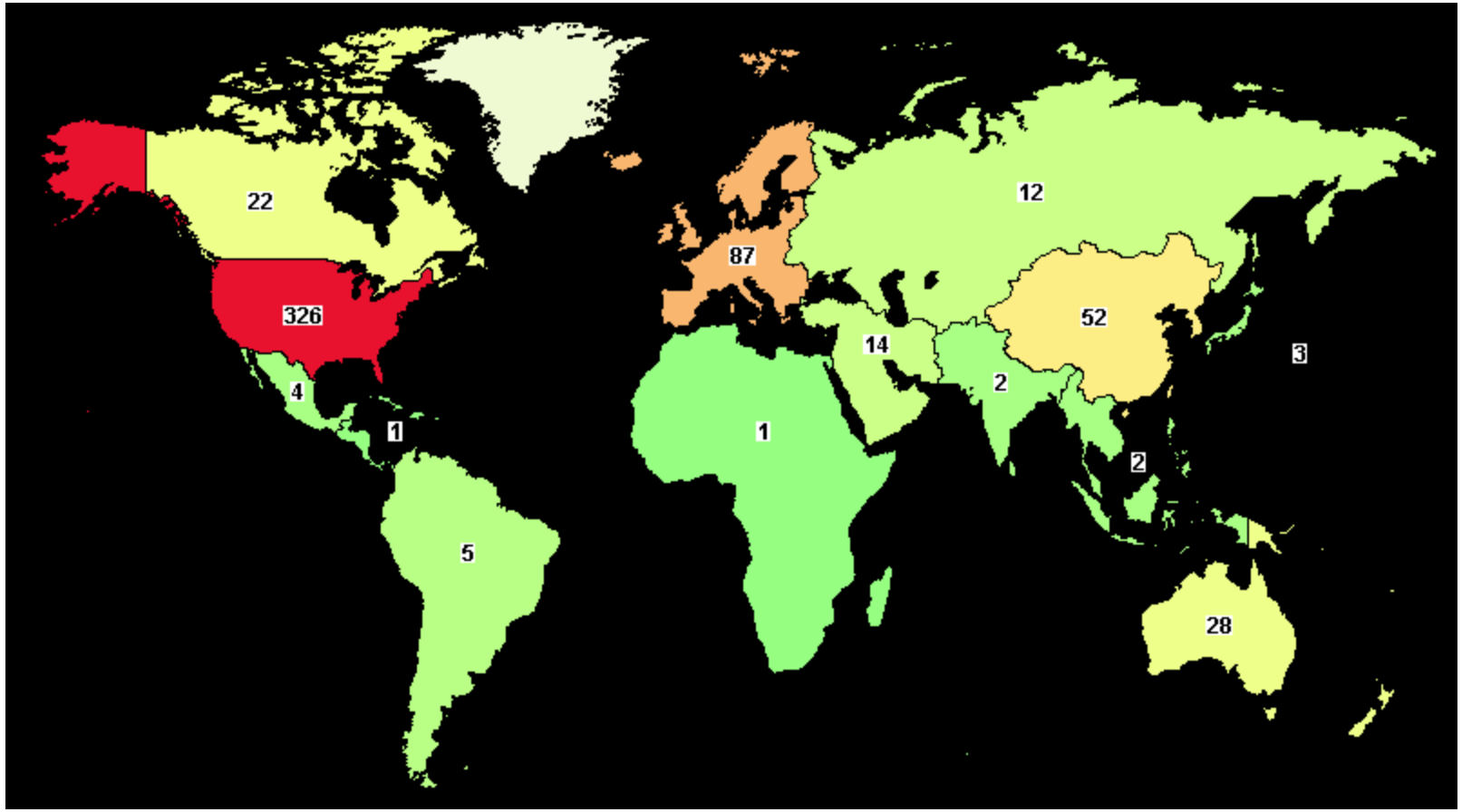
1. Diagnosis of CLL

The World Health Organization classification of hematopoietic neoplasias describes CLL as leukemic, lymphocytic lymphoma, being only distinguishable from small lymphocytic lymphoma (SLL) by its leukemic manifestation.[4] In the World Health Organization classification, CLL, by definition, is always a disease of neoplastic B cells, whereas the entity formerly described as T-CLL is now called T-cell prolymphocytic leukemia.[5]

It is important to verify that the patient has CLL and not some other lymphoproliferative disease that can masquerade as CLL, such as hairy cell leukemia or leukemic manifestations of



Fullførte kliniske studier med KLL pasienter



Planlagte og pågående kliniske studier med KLL pasienter

Helseforskningsloven (hforsknl)
Forskrifter til hforsknl
Merknader til forskrifter til hforsknl

Legemiddelloven (lml)
Forskrift om klinisk utprøving av legemidler til mennesker

Forskrift om befolkningsbaserte helseundersøkelser
Personopplysningsloven (pol)
Personopplysningsforskriften

Overgangsregler om behandling av personopplysninger

Forskningsetikkloven (fel)

Helseregisterloven (hlsregl)
Helsepersonelloven (hlspl)
Pasientrettighetsloven (pasrl)
Menneskerettsloven (mnskrl)
Offentleglova (ofl)

Forvaltningsloven (fvl)

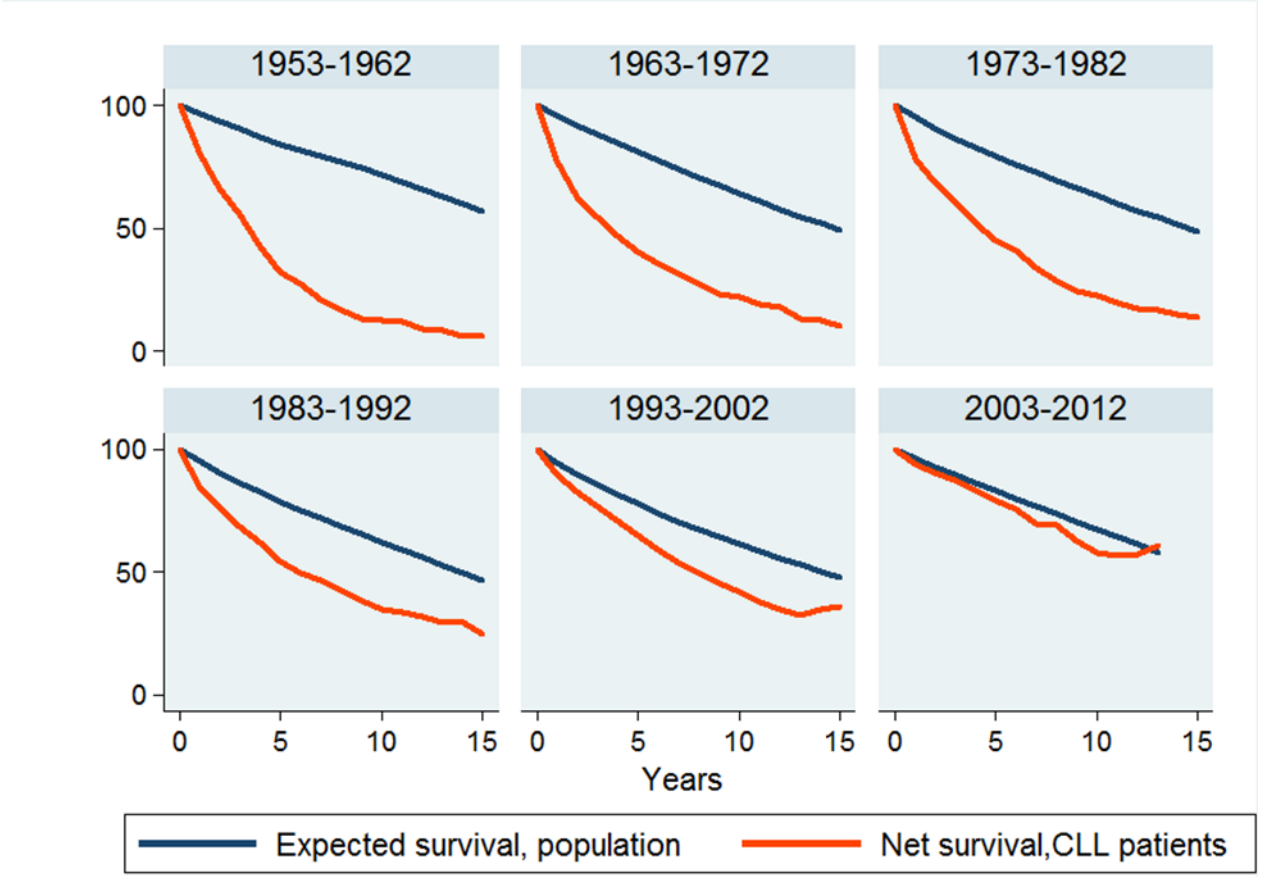
KLL studier på AHUS -

1) Relaps pasienter: VISION ibrutinib + venetoclax hos pasienten som har resisdiv. Multisenter studie. 6 pasienter inkludert på AHUS og 1 i Trondheim. Inklusjon har stoppet.

2) Under pågående behandling med Ibrutinib -start og stopp studie . Trondheim og Ahus. Starter inklusjon ila høsten. REK godkjenning er i orden.

3)"Alle" - Acalabrutinib, A Phase 3b, Multicenter, Open-Label, Single-Arm Study of Acalabrutinib (ACP-196) in Subjects with Chronic Lymphocytic Leukemia . Oppstart til høsten. Venter på REK og SLV godkjenning I Norge.


OSLO CANCER CLUSTER


1953-1962
1963-1972
1973-1982
1983-1992
1993-2002
2003-2012
100
50
0
0
5
10
15
Years
Expected survival, population
Net survival,CLL patients

Bli kvitt KLL ?

Unngå å få KLL?

- Hva fungerer hos MEG?