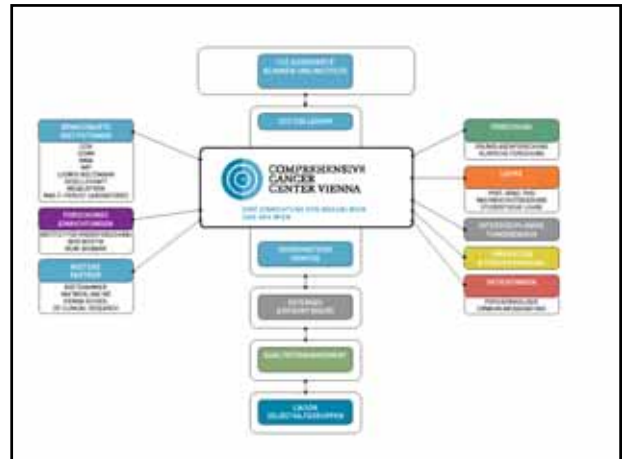


MEDIZINISCHE UNIVERSITÄT WIEN

Klinische Studien: Lymphome

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www.haematologie-wien.at

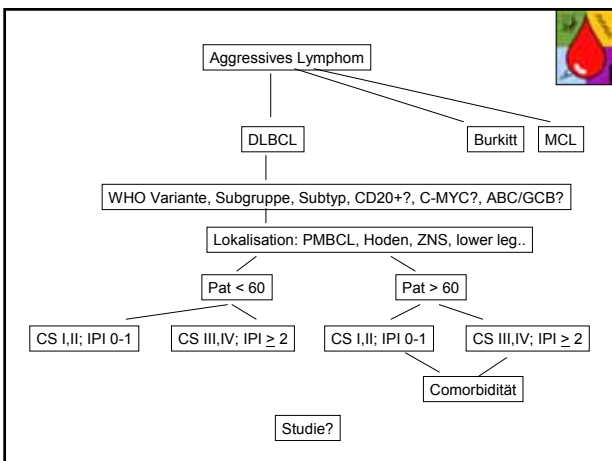


Von der molekularen Pathologie...zur zielgerichteten Therapie

- Zelluläre Therapie (Microenvironment)
- Antikörper
- Signaltransduktionsinhibitoren
- Transkriptionsinhibitoren

Aggressive Lymphome

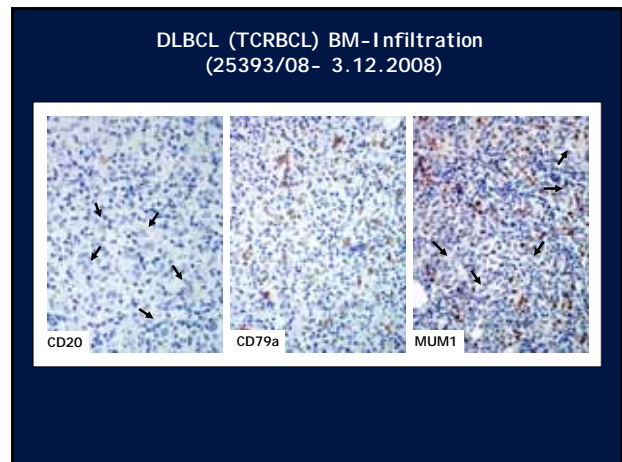
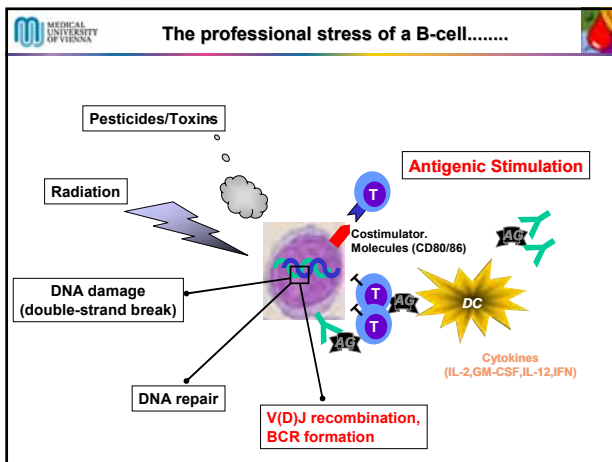
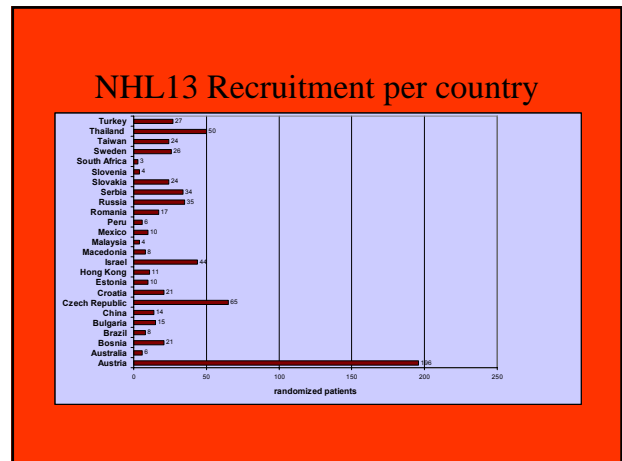
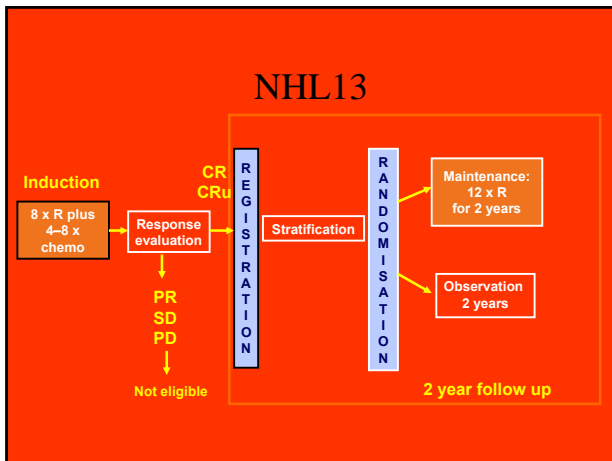
DLBCL
 Burkitt
 Mantelzell-Lymphom



Strategies to improve outcome in aggressive NHL in the R-CHOP era

Aggressive NHL

- Increase remission rate
 - Overcome primary resistance
 - Dose/density
 - Add novel substances
- Decrease relapse rate
 - Maintain remission
 - Rituximab
 - Novel substances

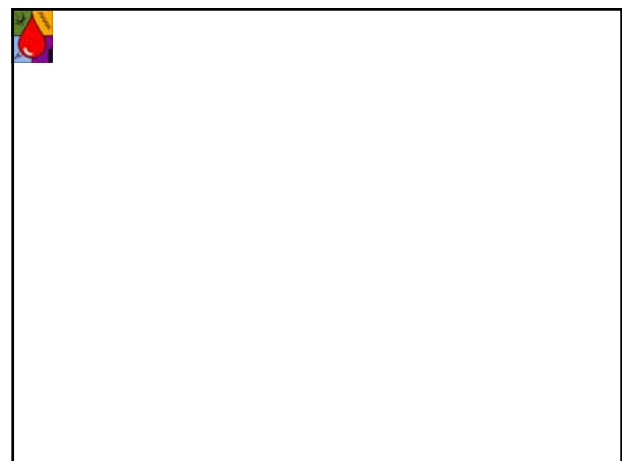


Lenalidomide and DLBCL

Objective Response of Patients Receiving Lenalidomide Therapy by Histology Type (N = 49)

Histology	No. of Patients	CR	CRu	PR	SD	PD	ORR (%)
Aggressive NHL	49	2	4	11	11	21	35
Diffuse large B-cell lymphoma	26	1	2	2	7	14	19
Follicular center lymphoma, grade 3	5	0	1	2	0	2	60
Mantle-cell lymphoma	15	1	1	6	2	5	53
Transformed low-grade lymphoma	3	0	0	1	2	0	33

Wiernik, P. H. et al. J Clin Oncol; 26:4952-4957 2008



Mantelzell Lymphom



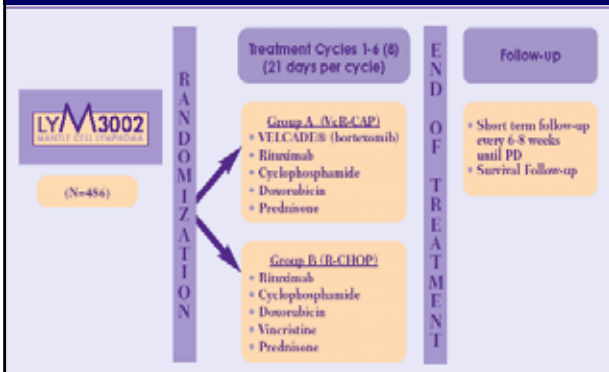
A randomized, open-label, multicentre Phase 3 study of R-CHOP or VcR-CAP (Velcade, Rituximab, Cyclophosphamide, Doxorubicin, and Prednisone)

in patients with newly diagnosed mantle cell lymphoma, who are not eligible for a bone marrow transplant

Zentren: AKH Wien/Onkologie (Drach)
Salzburg/Onkologie (Greil)
Innsbruck /Hämatologie (Willenbacher)

LYM 3002: VcR-CAP vs. R-CHOP in newly diagnosed MCL

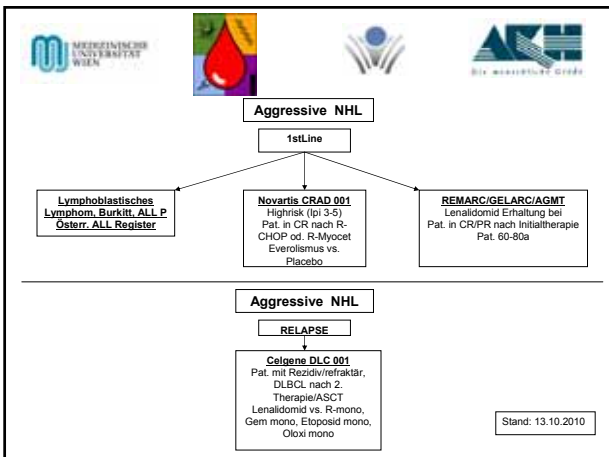
Treatment Schedule



CC-5013-MCL-001 EMERGE

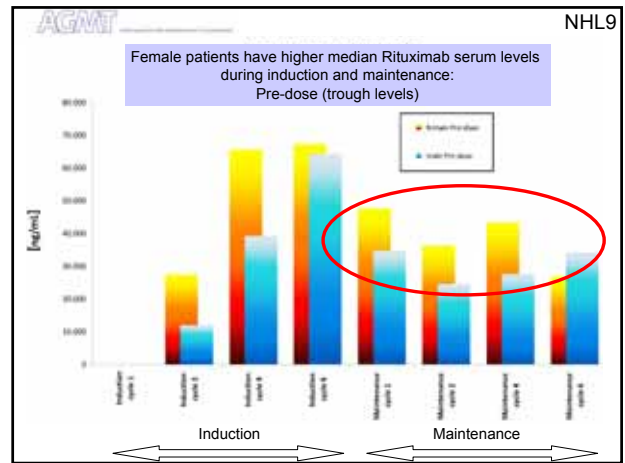
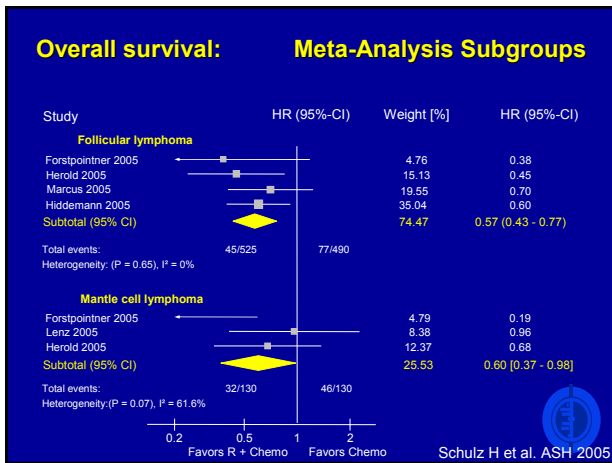
A phase II, multi-center, single-arm, open-label study to determine the efficacy and safety of single-agent lenalidomide in patients with mantle cell lymphoma who have relapsed or progressed after treatment with bortezomib or are refractory to bortezomib

Zentren: AKH Wien/Onkologie (Drach)
Innsbruck/Hämatologie (Willenbacher)



Folikuläres Lymphom (Indolente Lymphome)

Prototyp und häufigster Subtyp eines indolenten NHL

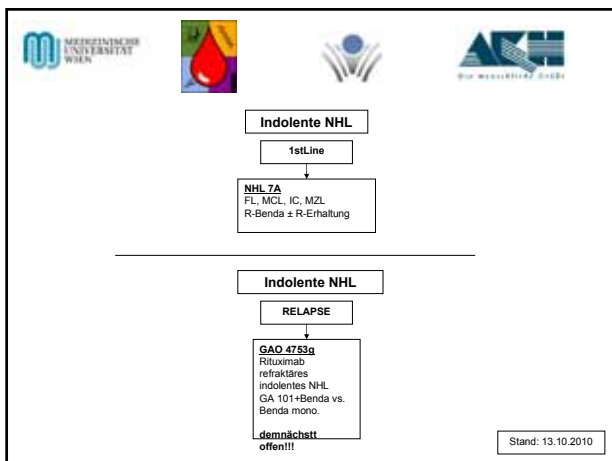


NHL 7-2008/A

Follikuläres Lymphom, Grad I und 2
 Immunozytom, u. kleinzelliges lymphozytisches Lymphom
 Marginalzonen Lymphom, nodales und generalisiertes
 Mantelzell Lymphom

NHL 7-2008/A

Rituximab als Erhaltungstherapie versus Beobachtung.
 Follikuläres Lymphom: 2 bzw. 4 Jahre Erhaltungstherapie.
 Andere Lymphome: 2 Jahre versus Beobachtung.

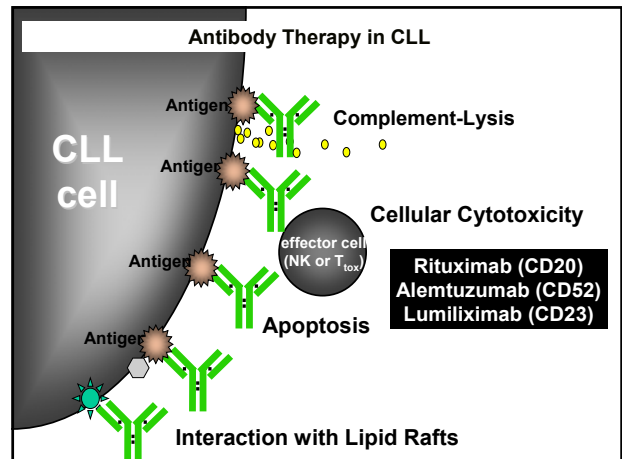


Chronisch lymphatische Leukämie

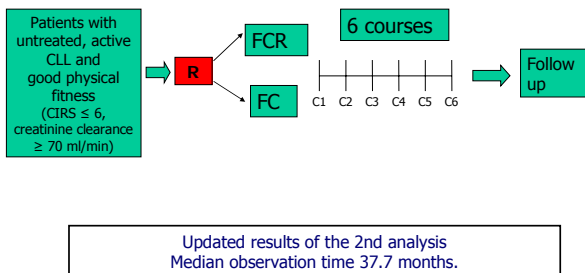
Häufigste Leukämie

Begleiterkrankungen und „maßgeschneiderte“ Therapieentscheidung bei Patienten mit CLL

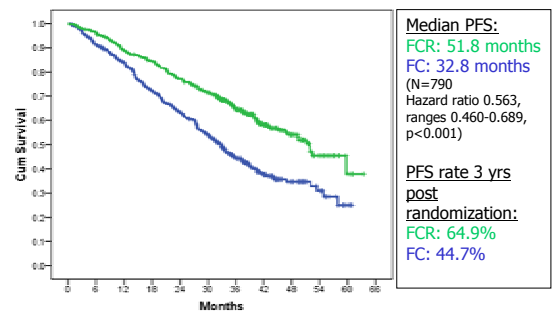
Group 1	Group 2	Group 3
<ul style="list-style-type: none"> independent no comorbidity normal life expectancy 	<ul style="list-style-type: none"> affected 	<ul style="list-style-type: none"> unfit comorbidity reduced life expectancy
„Go go“ Intensive Therapy → Long lasting remissions! Cure?	„Slow go“ Less intensive chemotherapy... effective symptom control.	„No go“ Palliative Therapy
FC-R, FC, FLUCam TX + experimental	FLU, CLB...	growth factors...



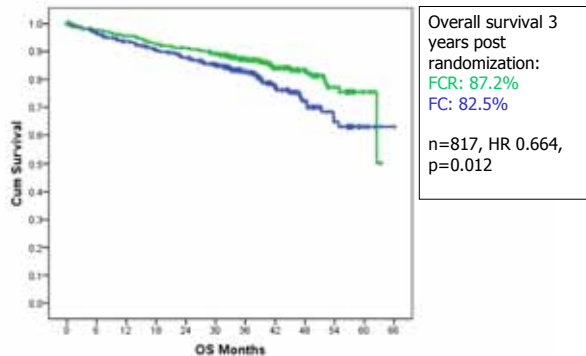
CLL8 Study Design



Progression-free survival



Overall survival



CLL 10 Study of the GLLSG

Phase III Study in first line therapy of B-CLL

Fludarabine
Cyclophosphamid
Rituximab
(FCR)

Fludarabine 25 mg/m² i.v., days 1-3
Cyclophosphamide 250 mg/m², days 1-3,
Rituximab: 375 mg/ m² i.v. on day 0, cycle 1
Rituximab: 500 mg/m² i.v. on day 1, cycle 2-6

Bendamustine
Rituximab
(BR)

Bendamustine 90mg/m² day 1-2
Rituximab 375 mg/m² day 0, cycle 1
Rituximab 500 mg/m² day 1, cycle 2-6

Prephase with Prednisolon 100mg p.o./day for max. 5 days is allowed.

CLL-11

An open-label, multi-center, three arm randomized, phase III study to compare the efficacy and safety of GClb, RClb or Clb alone in previously untreated CLL patients with comorbidities



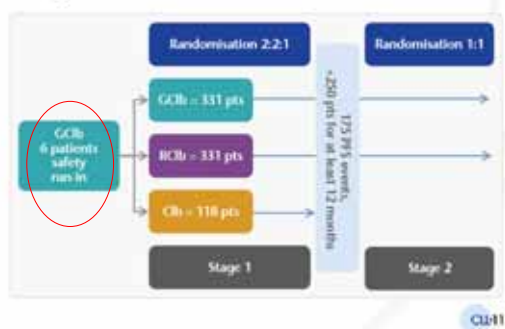
DEUTSCHE STUDIENGRUPPE

CLL-11 Inclusion Criteria

- Total Cumulative Illness Rating Scale (CIRS) score >6 or CrCl <70 mL/min or both
- ANC $\geq 1.5 \times 10^9/L$ and Platelet count $\geq 75 \times 10^9/L$ (unless due to CLL)
- Age 18 years or older
- Life expectancy >6 months
- Able and willing to provide written informed consent and to comply with study protocol procedures

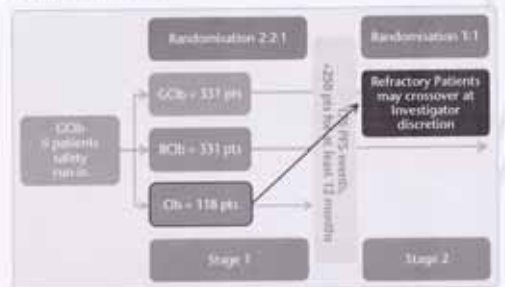
CLL11

CLL1 – Studie der DCLLSG



CLL11

Study Overview:



CLL11

CLL20 Trial for F-refractory or 17p- CLL

Inclusion Criteria

Binet C or A/B

„active disease“ (NCI)

F-refractory disease

OR

17p- (w or w/o prior therapy)

WHO PS 0-2

Exclusion Criteria

> 5 different regimens

major organ dysfunction

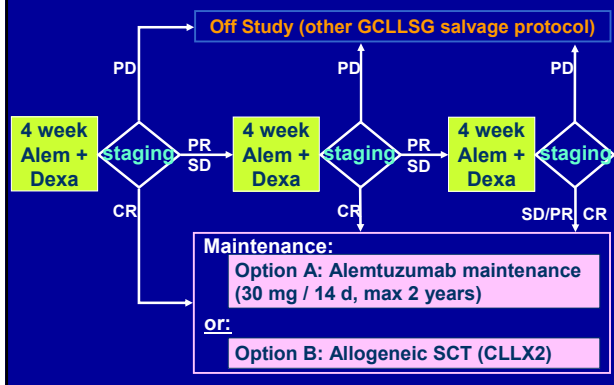
active infection

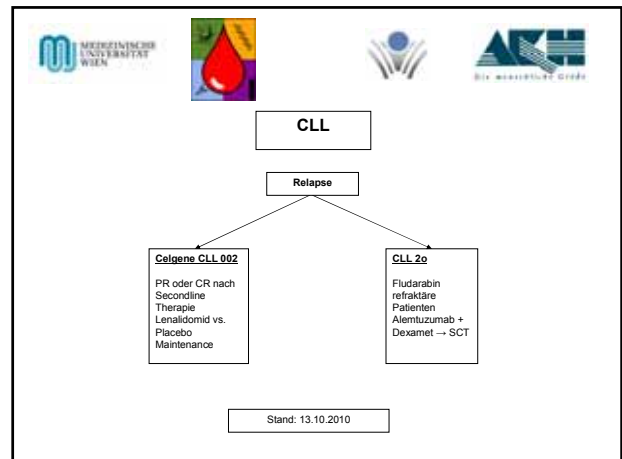
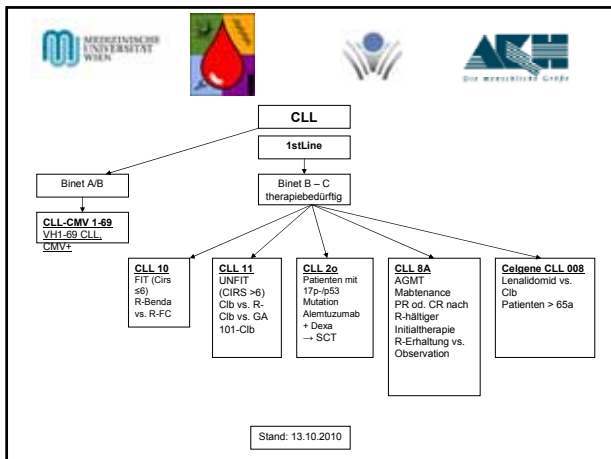
B-PLL or Richter

auto or allo SCT < 6 mo

Stilgenbauer S et al. ASH 2009

CLL20 Trial for F-refractory or 17p- CLL





Morbus Hodgkin

HD 18

Einschlusskriterien:
 Erstdiagnose, unbehandelt, histologisch gesichert.
 18 – 60 Jahre
 Stadium IIB mit gr. Mediastinaltumor oder Extranodalbefall, III, IV.

HD 18

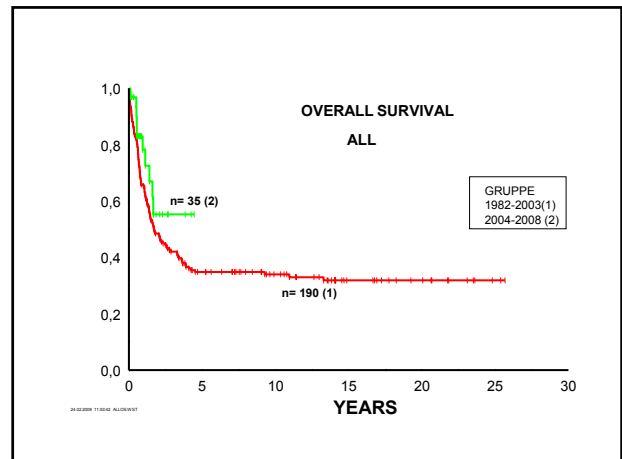
EXPERIMENTELLE ARME: Für PET-2 positive Patienten: 8x BEACOPPesk + Rituximab + 30Gy Rest-RT (bei PET-8 positiver PR) (Arm B)
 Für PET-2 negative Patienten: 4x BEACOPPesk + 30 Gy Rest-RT (bei PET-4-positiver PR) (Arm D)

STANDARDARM Für PET-2 positive Patienten: 8x BEACOPPesk + 30Gy Rest-RT (bei PET-8-positiver PR) (Arm A)
 Für PET-2 negative Patienten: 8x BEACOPPesk + 30Gy Rest-RT (bei PET-8-positiver PR) (Arm C)

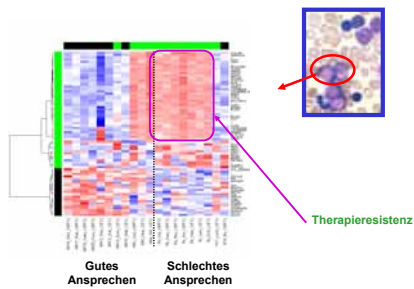
Akute lymphatische Leukämie & Lymphoblastische Lymphome

ALL
 Burkitt
 Lymphoblastische Lymphome

B lymphoblastic leukaemia/lymphoma not otherwise specified



Vorhersage der Medikamentenwirkung bereits nach dem 1. Therapiezyklus: Auf dem Weg zu maßgeschneiderten Leukämitherapien



Leukämien und Lymphome 2010

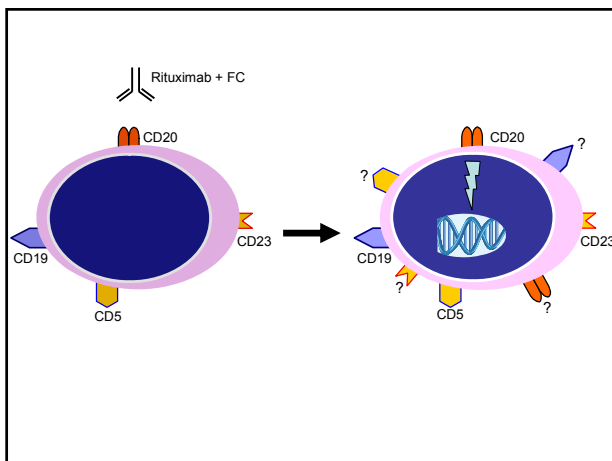
nature
DNA sequencing of a cytogenetically normal acute myeloid leukaemia genome
T.J. Ley et al. *Nature* 456, 66-72 (2008) doi:10.1038/nature07485

- 2007:
 - Entschlüsselung des gesamten Genoms einer Leukämie
 - Dauer: 3 Monate, 20 Geräte
 - Kosten 1 Million \$

↓

- 2010
 - Dauer: 1 Woche, 6 Geräte
 - Kosten 100.000 \$

Plan des NIH: 2012: 10.000 \$ - möglich für alle Patienten



FC/FCR (add. CLL-8)

Therapy/response assessment after 3 months (at planned interim staging)

FC 6M
RFC 6Mo

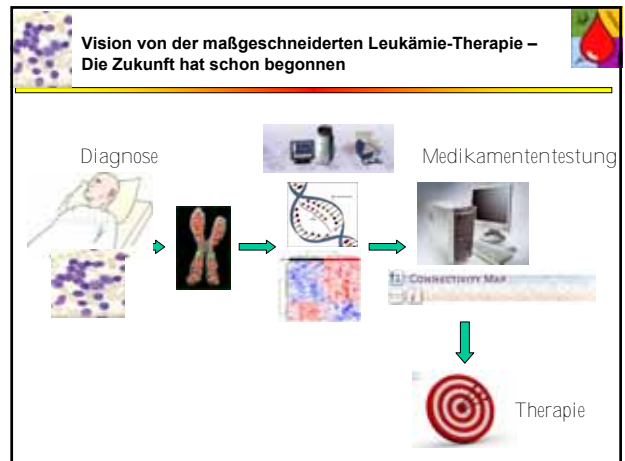
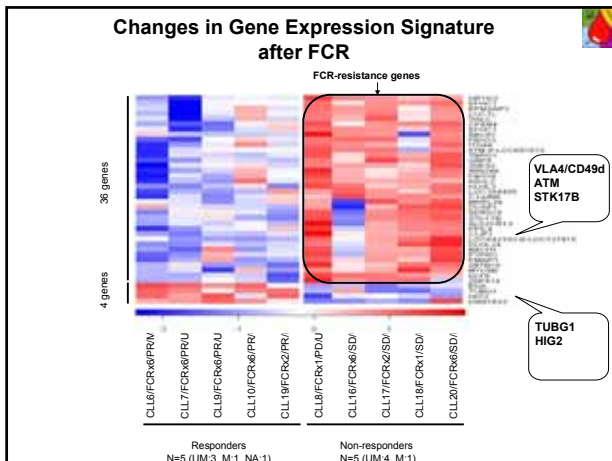
Prether Interim Staging (IS) (after C3-4Mo) Final Re-staging (FRS) (9 Mo after Therapy)

C1 C2 C3 C4 C5 C6 IMo

Study Duration: Recruitment phase (38 M= +/- 3Y), Therapy and Follow up (62 M= +/- 5Y)

Therapy: FC: F: 25 mg/m² iv day 1-3 (C1-C6) max 6 courses
C: 250 mg/m² iv day 1-3 (C1-C6) max 6 courses

RFC: R: 375 mg/m² iv day 1 (C1) 500 mg/m² iv day 1 (C2-C6)
F: 25 mg/m² iv day 1-3 (C1-C6) max 6 courses
C: 250 mg/m² iv day 1-3 (C1-C6) max 6 courses



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