

Report from the p53 Working Group

Presented by Thorsten Zenz

Report from the p53 Working Group

Amsterdam: Kater, Eldering, van Oers

Bournemouth: Oscier, Best

Brno: Pospisilova, Trbusek, Mayer

Liverpool: Lin, Pettitt

Novarra: Rossi, Gaidano

Paris: Cymbalista

Prague: Pekova, Kozak

Sutton: Gonzales, Morgan, Catovsky

Ulm: Zenz, Döhner, Stilgenbauer

Programme p53 Workshop / ERIC (WP7)

- **M. Trbusek: Monoallelic vs. biallelic TP53 inactivation: selection, impact on survival and response to DNA damage**
- **D. Rossi: TP53 disruption in transformation from chronic lymphocytic leukemia to aggressive lymphoma.**
- **D. Gonzales: TP53 mutations in the UKCLL4 trial.**
- **T. Stankovic: p53 defect caused by ATM inactivation: phenotypic and clinical features of ATM mutant tumours and impact on survival in patients treated on CLL4 trial.**
- **T. Zenz: p53 Mutations in CLL: data from the GCLLSG.**
- **A. Pettitt: Cam-Pred (NCRI CLL206) trial of alemtuzumab and high-dose methylprednisolone in 17p- CLL / proposal in relation to a new pan-European collaborative clinical trial for 17p- CLL.**

TP53 mutation in CLL without 17p-

Single center cohorts

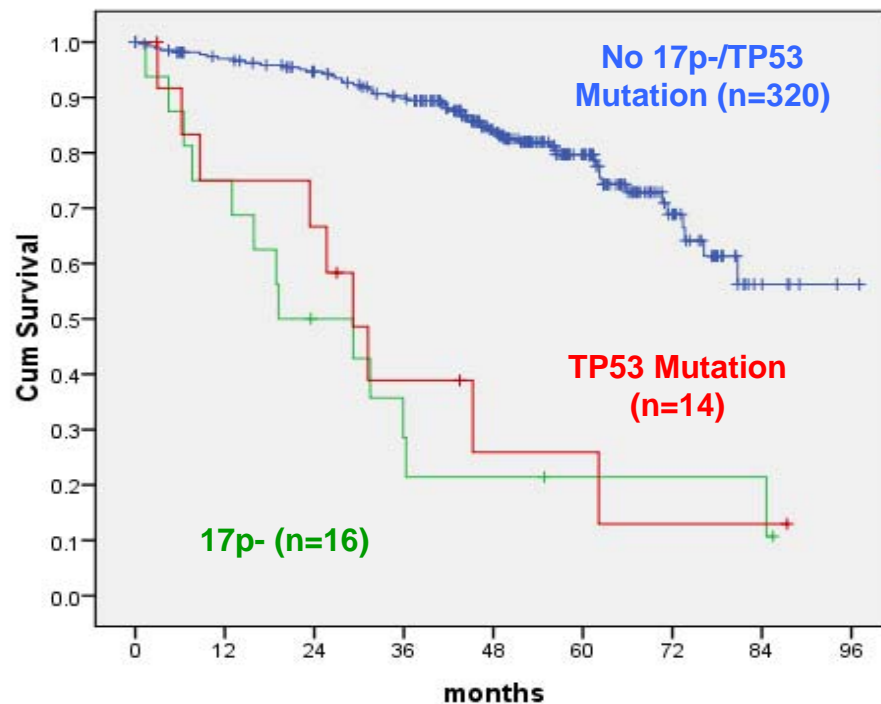
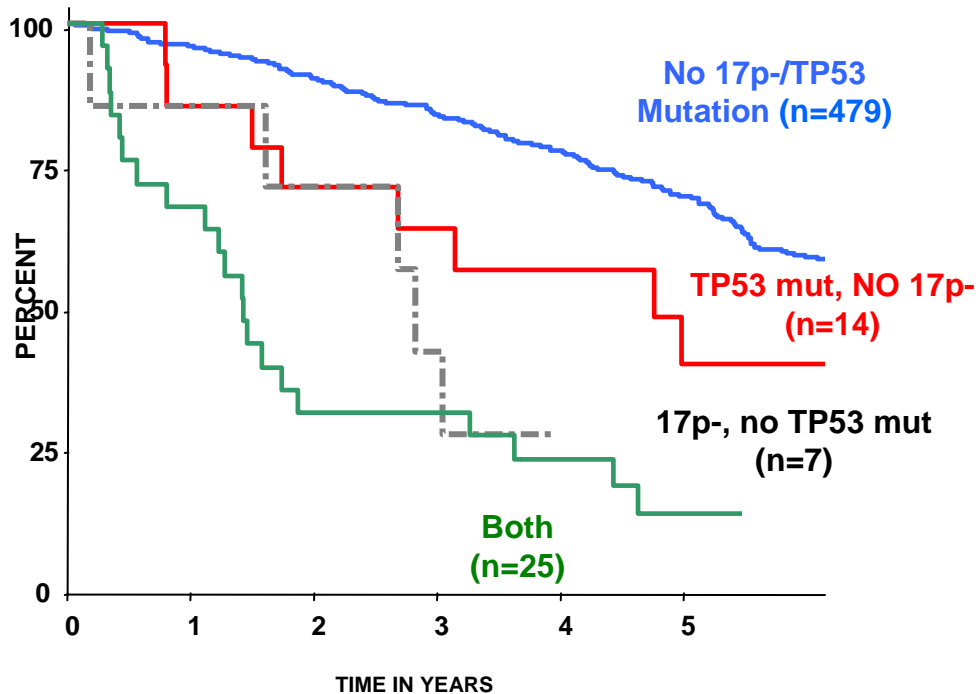
	Zenz et al (OS)		Dicker et al (TTFT)		Rossi et al (OS)	
	Blood '08	p=	Leukemia '09	p=	Clin Cancer Res. ,09	p=
Age	not shown		not shown		HR 5	<0.001
Binet	HR 3.54	<0.001	not shown		HR 3.01	<0.001
VH	HR 1.95	0.08	HR 3.4	<0.001		n.s.
11q-	HR 1.75	0.08	HR 1.1	0.7	not shown	
17p-	HR 11.2	<0.001	HR 1.7	0.15		n.s.
TP53 mutation	HR 3.71	0.02	HR 6.4	<0.001	HR 3.2	0.002

Prospective trial data: OS

UKCLL4

Courtesy of D. Gonzales

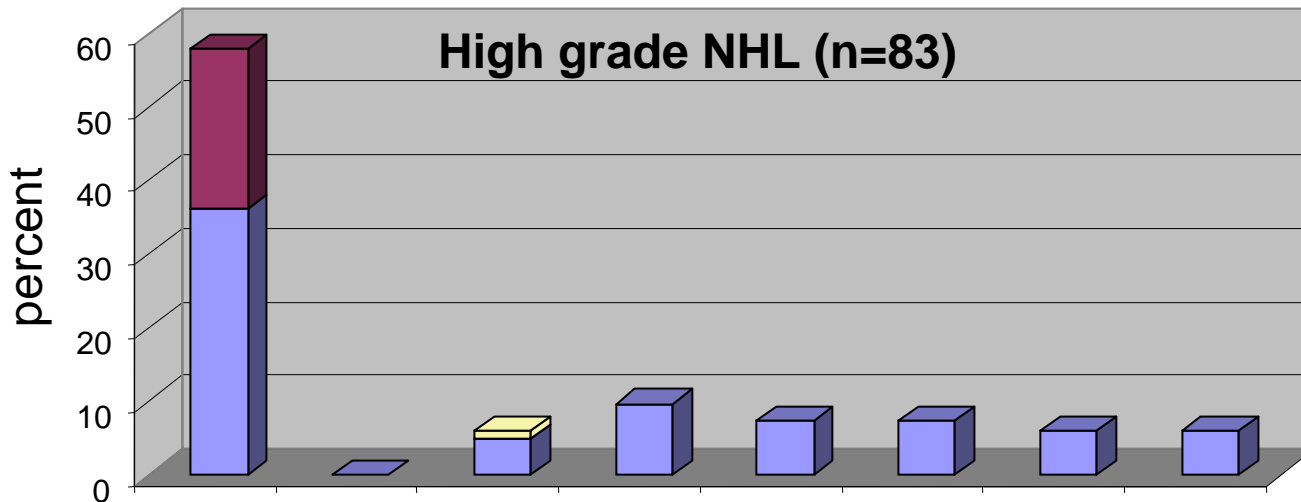
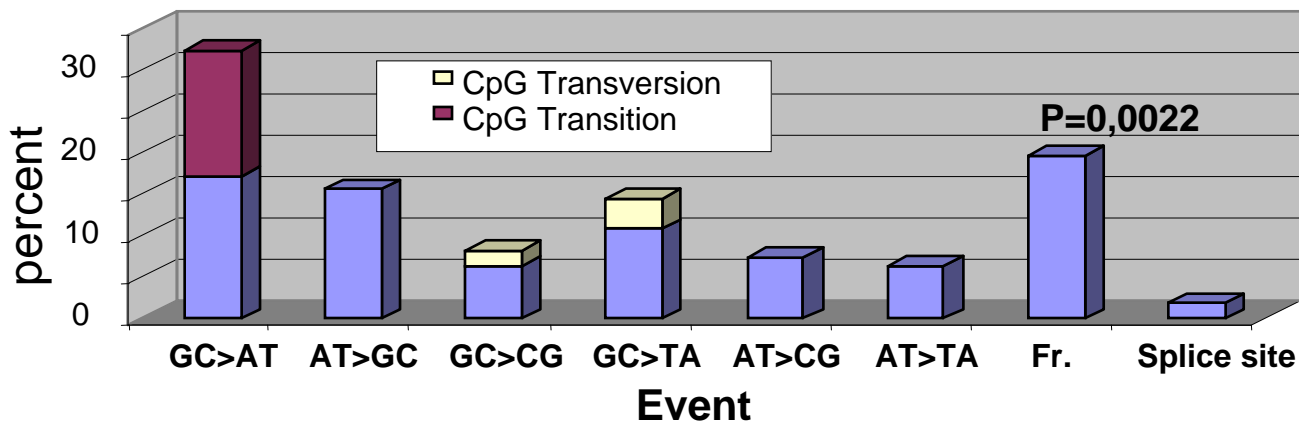
CLL4 GCLLSG



Also: Grever et al JCO ,07

TP53 Mutation Profile

CLL (n=268)



University of Ulm, Ulm, Germany, University Hospital Brno, Czech Republic, Biostatistic:
DKFZ, Heidelberg, Germany, Roche Molecular Systems, Pleasanton, CA, USA,
Royal Bournemouth Hospital, Bournemouth, UK, University of Liverpool, UK

Questions to be answered within ERIC

- **Intronic mutations (Brno, Sutton, Ulm,..)**
- **Method of detection (Brno, Sutton, Ulm, ...)**
- **Integration into current work-up (all)**
- **Surrogate assays (p53/p21, miR-34a, MLPA, Nutlin assay) (Amsterdam, Bournemouth, Brno, Liverpool, Ulm)**

Short term goals

- Establish a comprehensive map of TP53 mutations in CLL
- Define the diagnostic and therapeutic approach to CLL with TP53 mutation
- Search for approaches for functional p53 testing (miRs, p53 targets, surrogates)