

Targeted therapy in malignant lymphoma: clinical implications and perspectives

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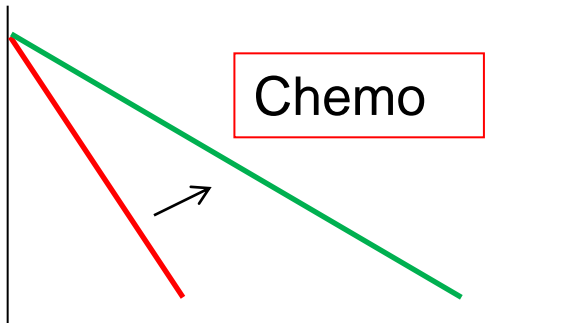
Oncology Institute of Southern Switzerland

Bellinzona



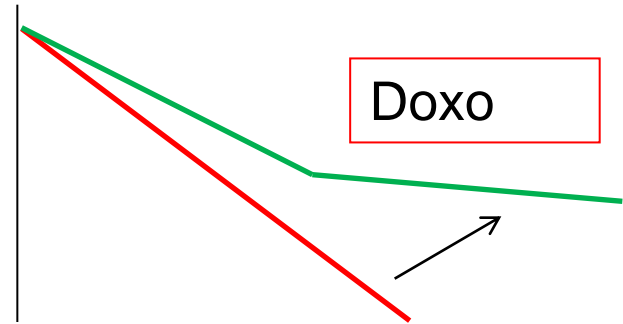
Improvement in lymphoma treatment: DLBCL

1st phase



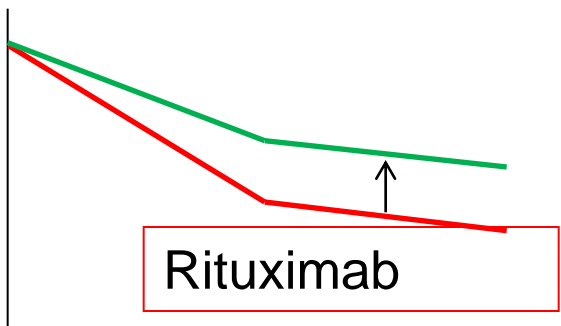
Survival improvement

2nd phase



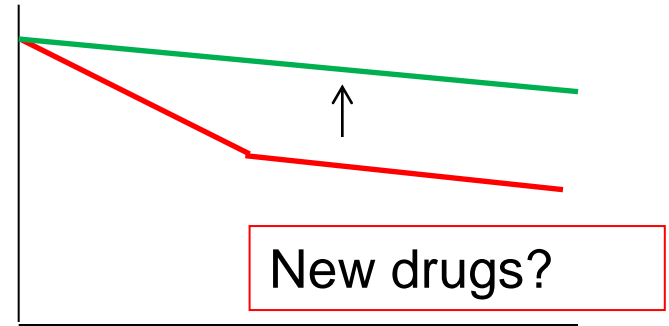
Some are cured

3rd phase



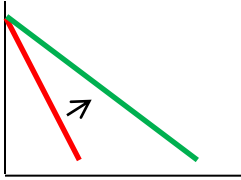
More are cured

4th phase



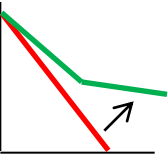
All are cured, no side effects

Can targeted drugs move us along these steps?



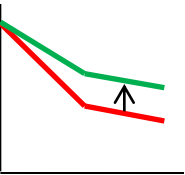
1st phase

MCL



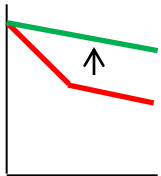
2nd phase

FL



3rd phase

PTCL

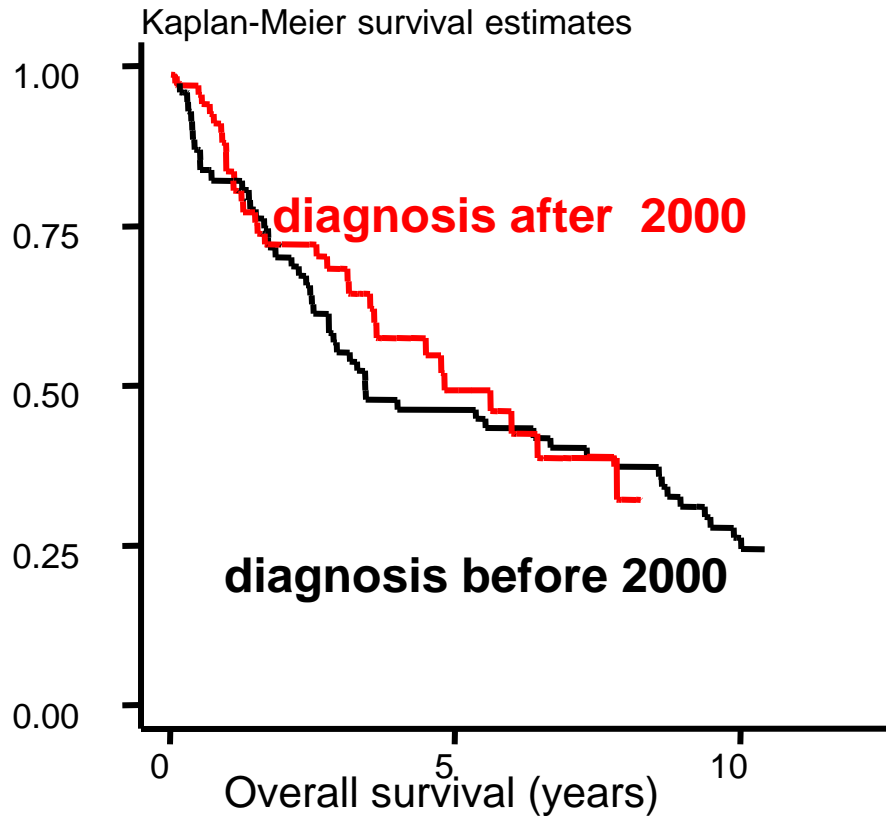


4th phase

HL

Improvement in MCL

Survival



Median OS 4y > 5y

We want:
improve survival

We need:
more active treatment

A. Conconi, IOSI-Novara database

Promising targeted drugs

Phase I-II data (caution!)	RR in relapse
Bortezomib	30%
Everolimus / Temsirolimus	20%
Lenalidomide	50%
Ibrutinib (PCI 32765)	60%
CAL 101	50%

Trials of combinations including targeted drugs

Bortezomib

Everolimus / Temsirolimus

Lenalidomide

Ibrutinib

+ R-chemo

Bortezomib + Panobinostat

Everolimus as maintenance

Lenalidomide as maintenance

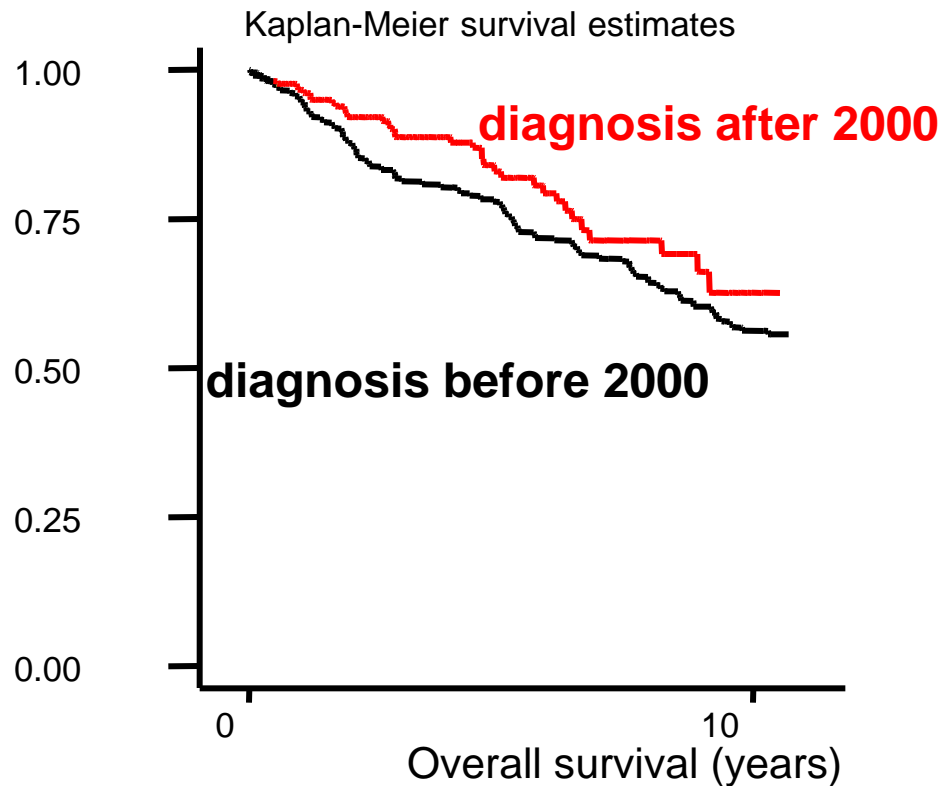
Ibrutinib + Rituximab/Bendamustine

- Tested in 30 R/R CLL/SLL
- Presented at ASH 2011 / EHA 2012
- Feasible, well tolerated
- Efficacy better than historical controls w/o ibrutinib

O` Brian et al., EHA 2012

Improvement in FL

Survival



Median OS 12 y > 13 y

We want:
a plateau

We need:
THE drug which
renders the disease
curable

A. Conconi, IOSI-Novara database

Promising targeted drugs

Phase I-II data (caution!)	RR in relapse
Lenalidomide	50%
Inotuzumab ozogamycin	70%
SAR 3419	50%
Blinatumomab	80%
Ibrutinib (PCI 32765)	60%
CAL 101	60%

Trials of combinations including targeted drugs

Lenalidomide

Ibrutinib

Inotuzumab ozo.

} + R-chemo

Inotuzumab ozogamycin + Temsirolimus

Inotuzumab ozogamycin + Rituximab

Lenalidomide as maintenance

Lenalidomide + Rituximab

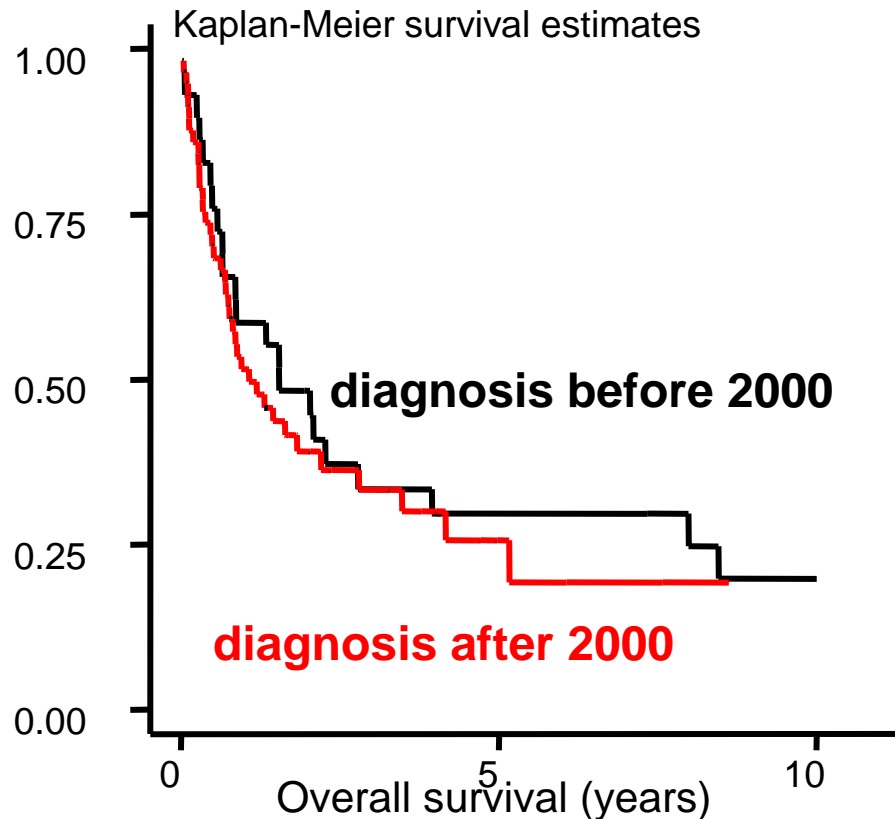
40 treatment naive FL

- 87% Clinical CR
- 87% Molecular CR
- 87% CR persistent at 14 m

Samaniego et al., ASCO 2012

Improvement in PTCL

Survival



Median OS 2 y > same

We want:
improve cure rate

We need:
a drug synergistic with
CHOEP

A. Conconi, IOSI-Novara database

Promising targeted drugs

Phase I-II data (caution!)

RR in relapse

Romidepsin / Belinostat /
Panobinostat / Vorinostat

25%

Alisertib

30%

Everolimus

60%

Denileukin diftitox

50%

Trials of combinations including targeted drugs

Alisertib + Vorinostat

Belinostat + Zevalin

Belinostat + Bortezomib

Denileukin diftitox + chemo

Denileukin diftitox + CHOP

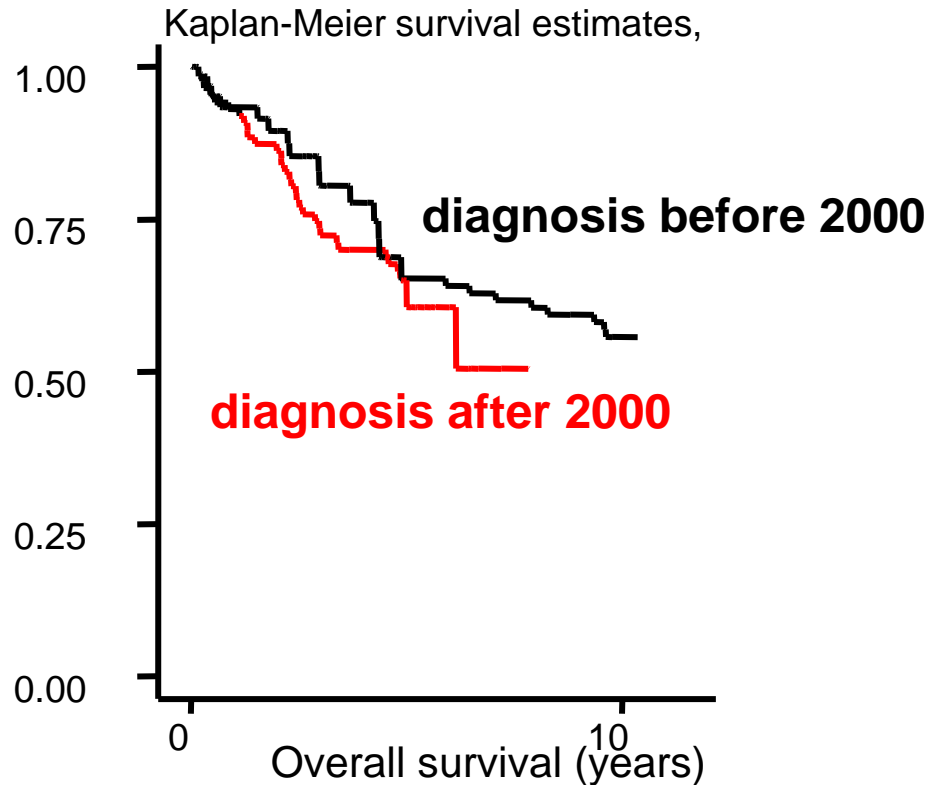
49 aggressive systemic T-cell lymphomas

- RR 65%
- CR 51%
- 20% severe toxicity

Foss et al., ASCO 2010

Improvement in Hodgkin Lymphoma

Survival



Median OS 17 y > same

We want:

less side effects
active treatment for
relapse

We need:

drugs with a better
therapeutic index

A. Conconi, IOSI-Novara database

Promising targeted drugs

Phase I-II data (caution!)

RR in relapse

Brentuximab vedotin

45%

Panobinostat

30%

Everolimus

45%

Lenalidomide

20%

Trials of combinations including targeted drugs

Brentuximab ved.	+ AVD
Brentuximab ved.	after ABVD
Brentuximab ved.	before HDCT
Brentuximab ved.	after HDCT
Panobinostat + ICE	
Panobinostat + Lenalidomide	
Panobinostat + Everolimus	

Panobinostat + Everolimus

- Phase I in 30 Hodgkin (12) or non-Hodgkin (18)
- All patients pretreated (median 3 regimes)
- 50% RR
- Safe and promising

Younes et al., ASH 2011

Conclusions

- Many new classes of targeted therapy
- Many promising drugs
- Next step: how to combine them with existing therapies (phase II)
- Will they bring the necessary improvement? (phase III)