Liposomal pegylated Doxorubicin

Reinhard Dummer, Simone Goldinger, Emanuella Guenova,
Lars French, Antonio Cozzio

Department of Dermatology, Zürich, Switzerland

DKG KREBSGESELLSCHAFT
Zertifiziertes Hautkrebszentrum

University Hospital Zurich

Cancer Network zürich

Schwerpunkt Hautkrebs
Dermatologische Klinik
UniverstätsSpital Zürich

Conflict of interest

Related to the presentation

- none

Potential other conflicts

- Honoraria for consultancy from

Amgen, BMS, GSK, MSD, Roche, Millenium, Novartis

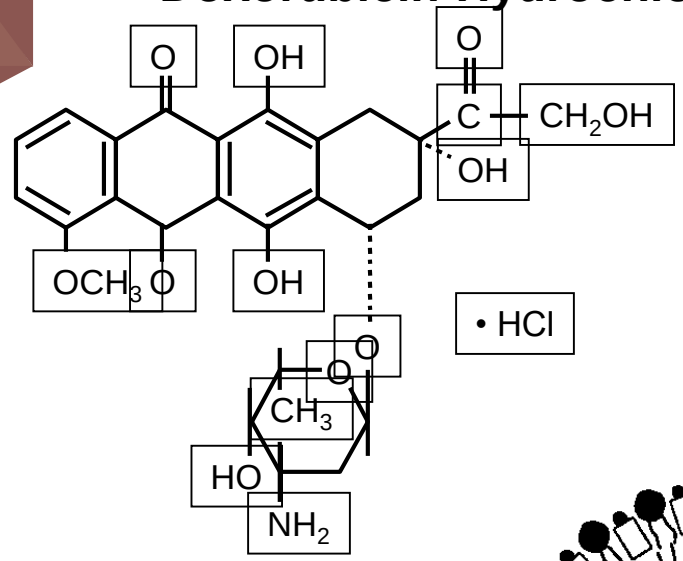
- Research funding to my university from

BMS, Celgene, GSK, MSD, Roche, Novartis

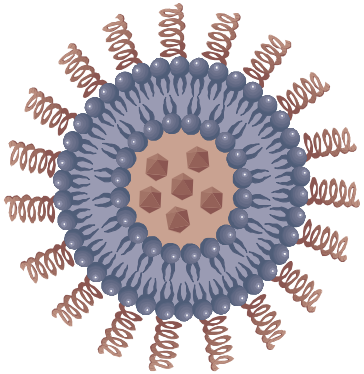
University Hospital Zurich

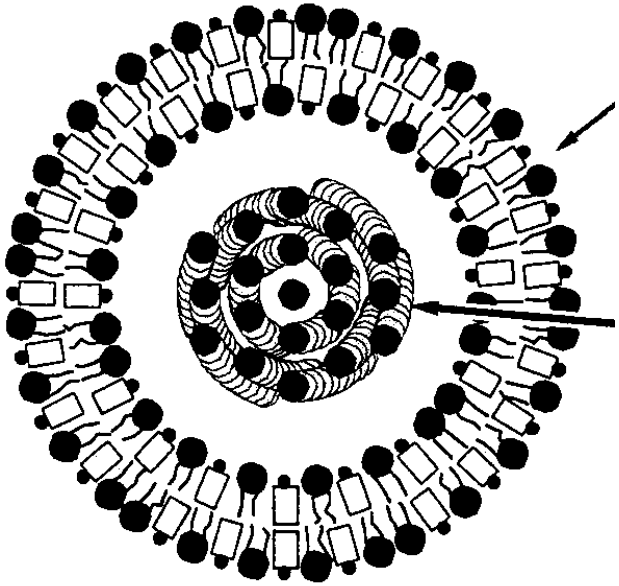
Liposomal pegylated Doxorubicin

Doxorubicin-Hydrochlorid



pegylated Liposom



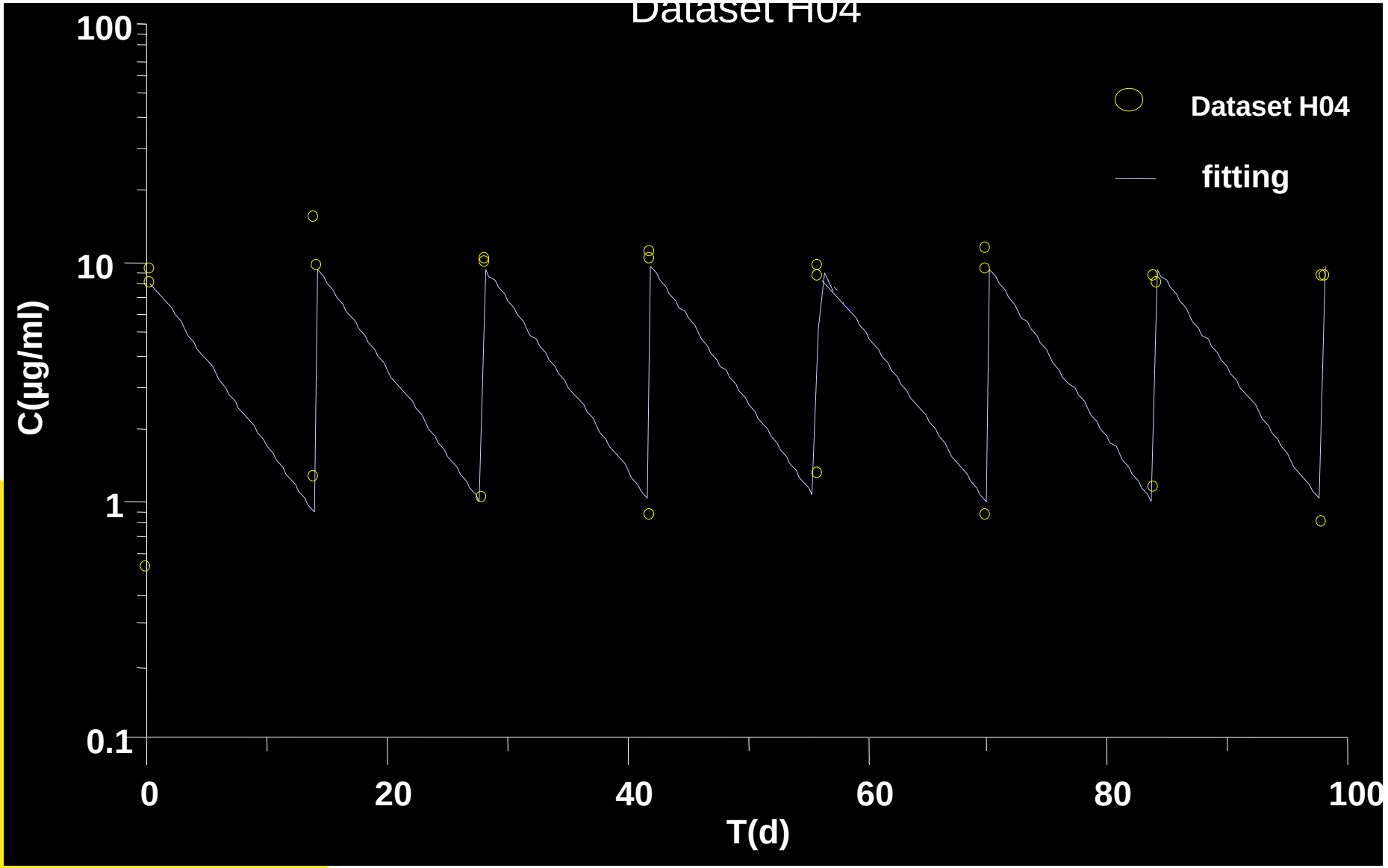


Doxorubicin is encapsulated in a Citrat-complex

University Hospital Zurich

PK of multiple doses of Caelyx –

20 mg/m² every 14 days



EORTC
European Organisation for Research and Treatment of Cancer

EORTC Cutaneous Lymphoma Task Force

Phase II clinical trial with Caelyx mono-chemotherapy in patients with advanced Mycosis fungoides stage IIb, IVa and IVb with or without previous chemotherapy

EORTC protocol 21012

Prospective International Multicenter Phase II Trial of Intravenous Pegylated Liposomal Doxorubicin Monochemotherapy in Patients With Stage IIB, IVA, or IVB Advanced Mycosis Fungoides: Final Results From EORTC 21012

Published Ahead of Print on October 8, 2012

Reinhard Dummer, Pietro Quaglino, Jürgen C. Becker, Baktiar Hasan, Matthias Karrasch, Sean Whittaker, Stephen Morris, Michael Weichenthal, Rudolf Stadler, Martine Bagot, Antonio Cozzio, Maria G. Bernengo, and Robert Knobler

See accompanying article doi: 10.1200/JCO.2012.44.5650

JOURNAL OF CLINICAL ONCOLOGY

Study design and Endpoints

Treatment plan:

Caelyx iv 1hour 20 mg/m2 on day 1 and 15, every 28 days.

Duration of 1 cycle = 28 days. Max 6 cycles.

Primary endpoint

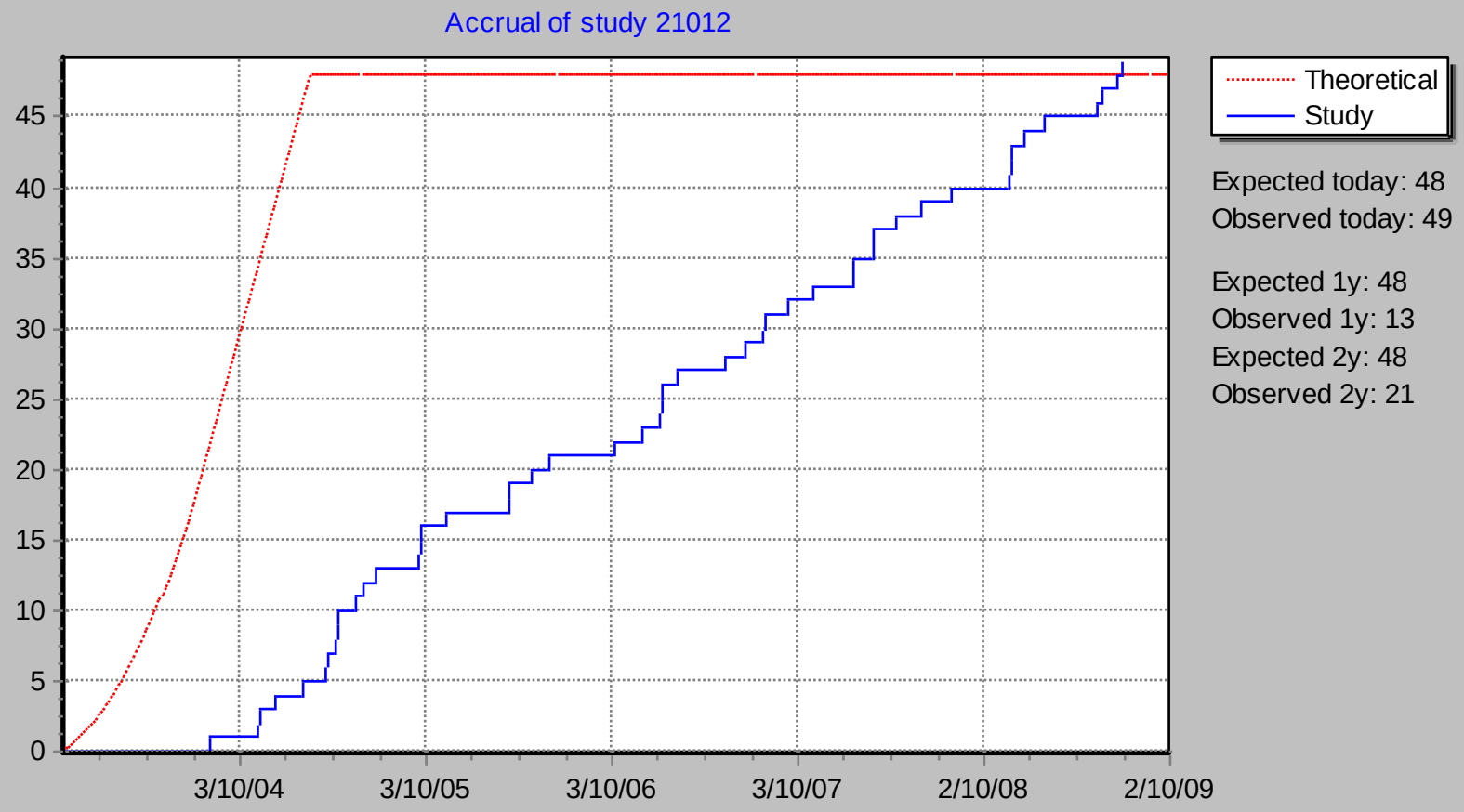
Response rate (proportion of patients who achieve a complete clinical response (CCR) or partial response (PR)

Secondary endpoints

1) Duration of response
2) Time to progression (TTP)
3) Toxicity

University Hospital Zurich

1st protocol draft: July 2010
Accrual: start on 03/10/2004, closed for recuitment on 03/07/2009



University Hospital Zurich

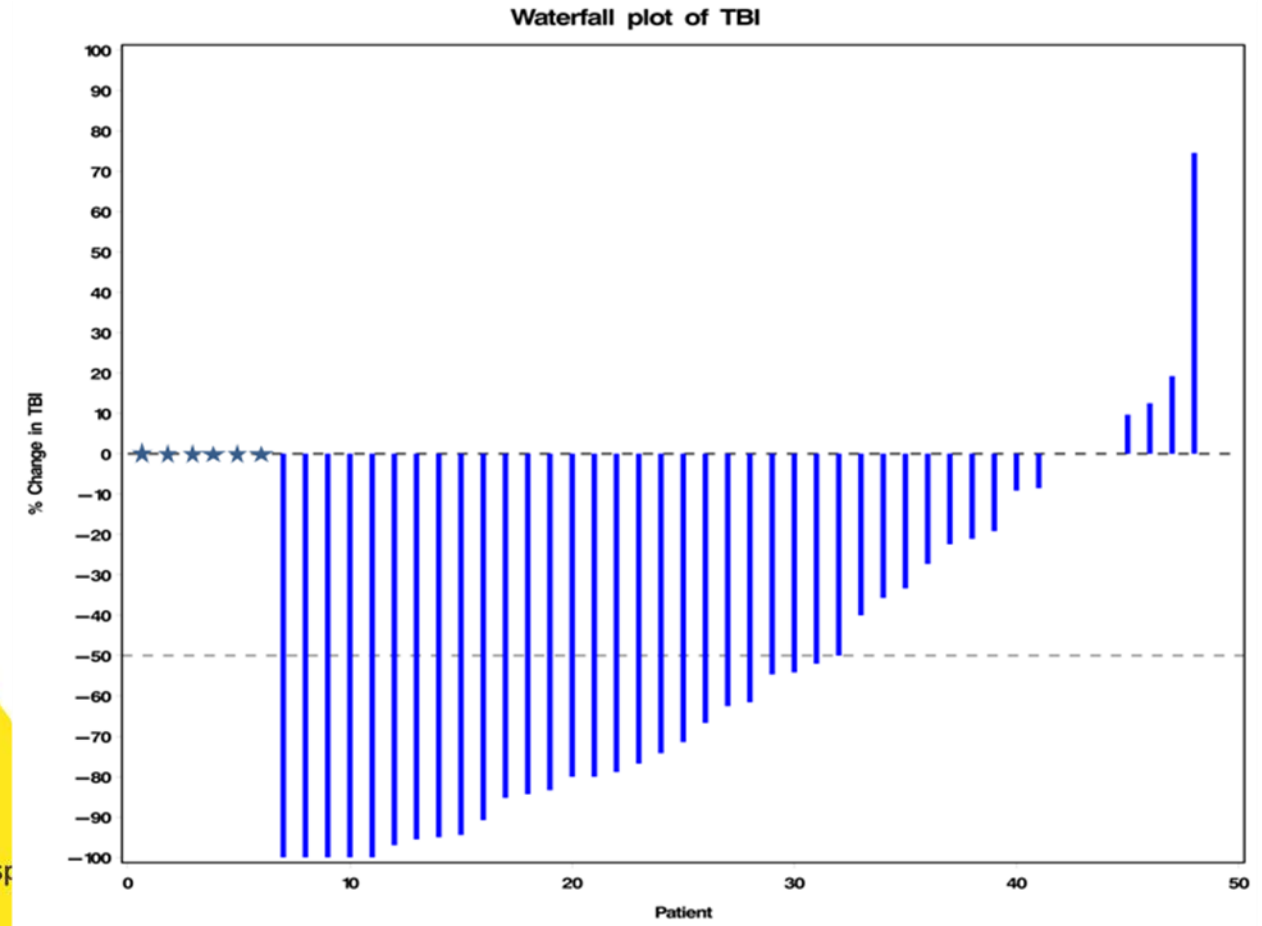
Dose intensity

	Treatment (N=49)
Number of cycles Received	
Median	**5.0**
Range	**1.0 - 6.0**
N obs	**49**
Caelyx relative dose intensity(category)	
<=50%	**4 (8.2)**
50-70%	**2 (4.1)**
70-90%	**17 (34.7)**
90-110%	**26 (53.1)**
Treatment duration (weeks)	
Median	**20.0**
Range	**4.0 - 32.1**
N obs	**49**

Grade 3/4 toxicity during Treatment

	Treatment
	(N=49)
	N (%)
Allergy/Hypersensitivity(Grade)	
4	**1 (2.0)**
Other cardiology(Grade)	
3	**1 (2.0)**
Other constitutional Symptoms(Grade)	
3 (weight gain)	**1 (2.0)**
4(Deterioration of general condition)	**1 (2.0)**
Hand-foot skin reaction(Grade)	
3	**1 (2.0)**
Other dermatology(Grade)	
3	**3 (6.1)**
Stomatitis(Grade)	
3	**1 (2.0)**
Other Gastro Intestinal(Grade)	
3	**2 (4.1)**
Other Infection(Grade)	
3 (cellulitis staphylococcal)	**1 (2.0)**
4 (infection from skin lesions)	**1 (2.0)**
Other Pulmonary(Grade)	
4 (pulmonary embolism)	**1 (2.0)**
All other toxicity(Grade)	
3 (confusion, middle ear inflammation)	**2 (4.1)**
4 (Suspected Cardiac Ischemia)	**1 (2.0)**

Waterfall Plot of the Percentage Change in Tumor Burden Index (TBI)



University Hosp
Zurich

Best Overall Response

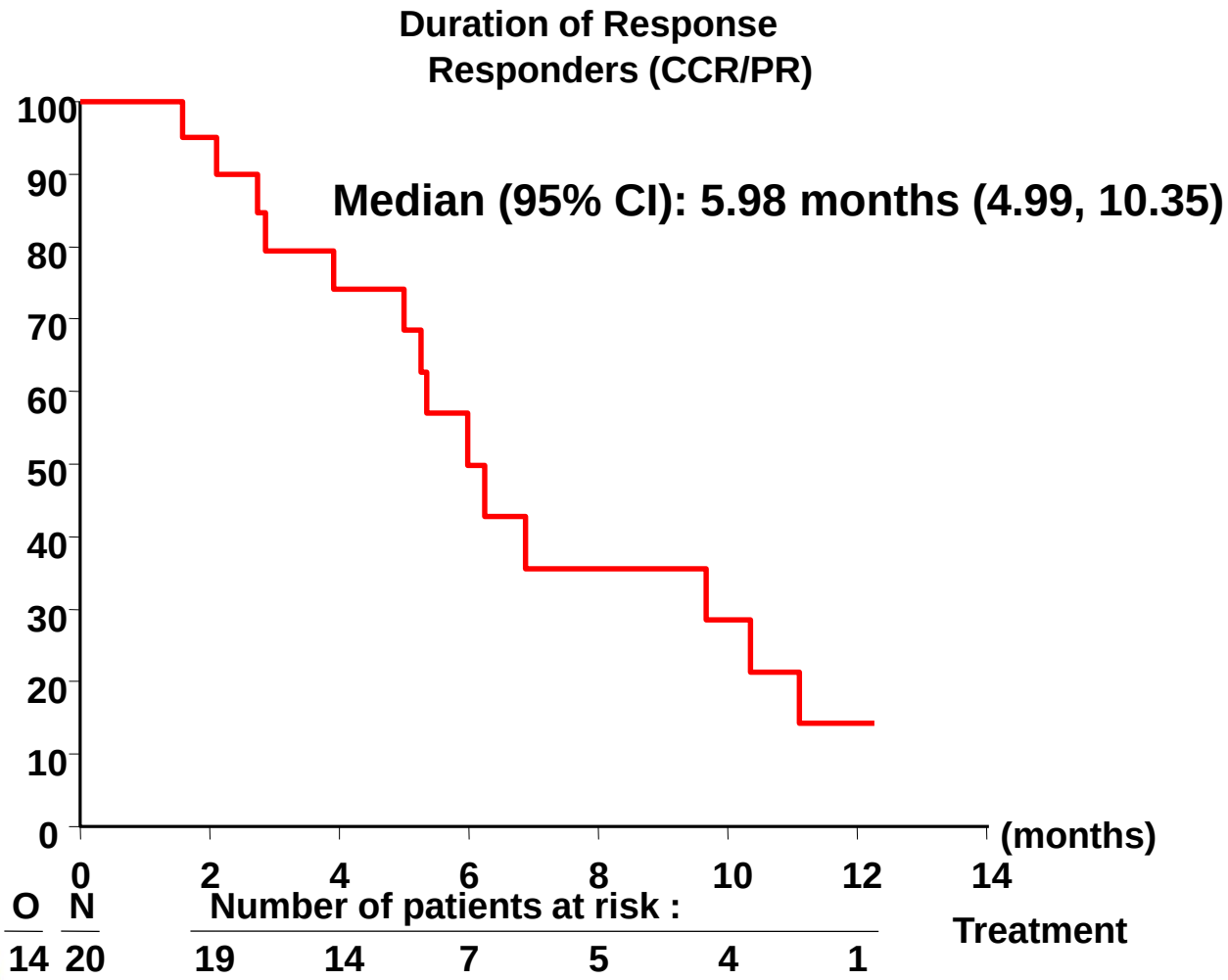
	Treatment
	(N=49)
	N (%)
Best Overall Response to treatment	
CCR	**3 (6.1)**
PR	**17 (34.7)**
SD	**14 (28.6)**
PD	**5 (10.2)**
Early death-toxicity	**1 (2.0)**
Early death-other	**1 (2.0)**
Not assessable	**8 (16.3)**

best overall response (CCR/PR) rate is 40.8%.

90% Confidence Interval is: (31.2%, 100%).

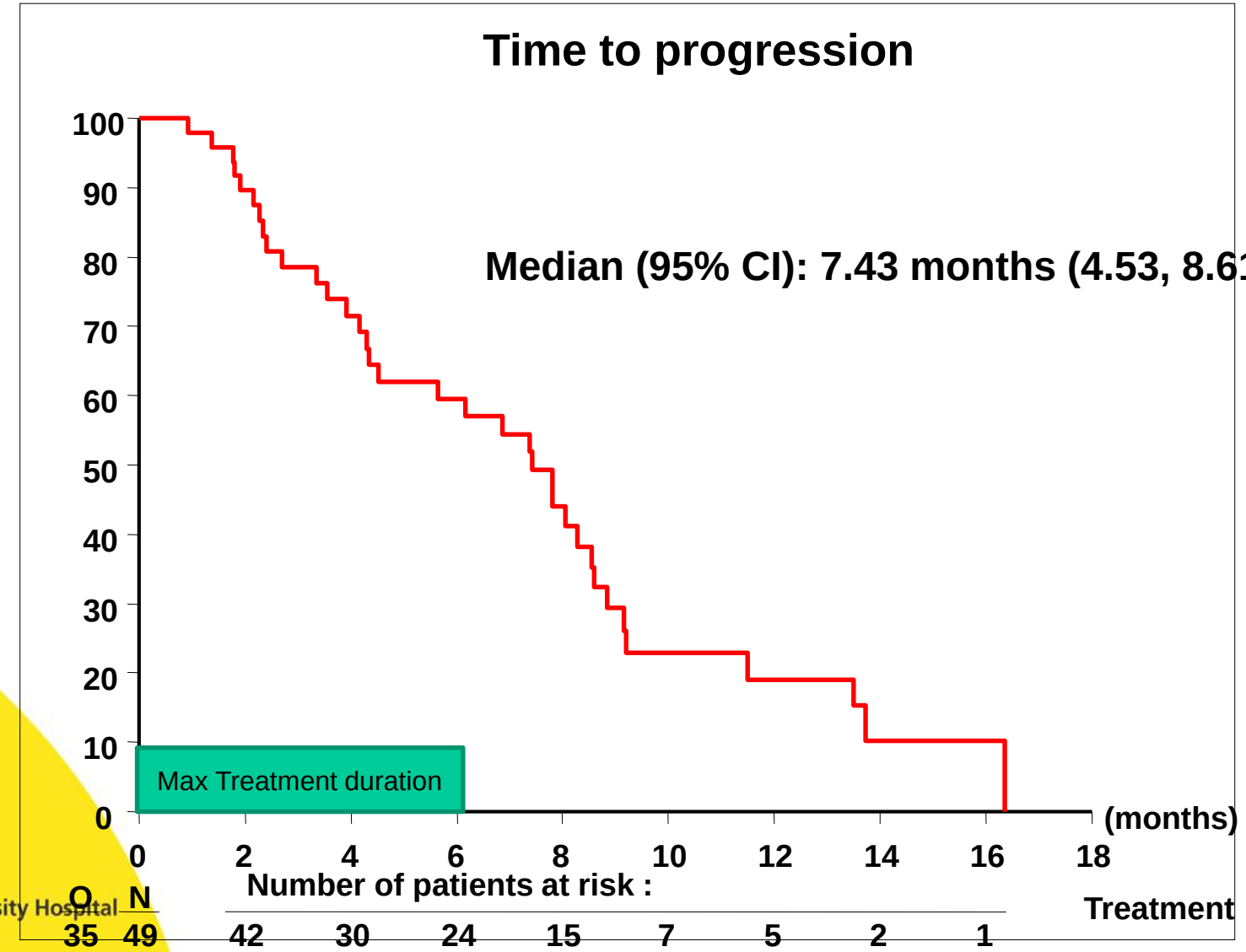
University Hospital Zurich

Duration of Response



University Hospital Zurich

Time To Progression



University Hospital Zurich

Pegylated liposomal doxirubicin: reported trials

	Wollina 2003	DiLorenzo 2005	Pulini 2007	Quereux 2008	EORTC 21012
Patients	34	10	19	25	49
Design	Retrospective multicenter	Retrospective single center	Prospective multicenter	Prospective multicenter	Prospective multicenter controlled
CTCL subtypes and stages	31 MF IB-IVA 1 SS 2PTCL-U 1CD30+ALCL	MF IVB	MF IB-IVB SS PTCL-U	15 MF IIb-IVB 10 SS	31 MF IIB 18 IVA/B
Schedule	20-40 mg/m^2 ev 2-4 wks	20 mg/m^2 ev 4 wks	20 mg/m^2 ev 4 wks	40 mg/m^2 ev 4 wks	20 mg/m^2 ev 2 wks
ORR%	88.2%	30%	84.2%	56%	40.8
CR%	44.1%	0	42.1%	20%	6.1%
PFS (median; mo)	NA	NA	19	5	6.2
OS (median; mo)	17.8	NA	34	43.7	NR
Toxicity gr. III-IV	17.6%	10%	11%	40%	20%

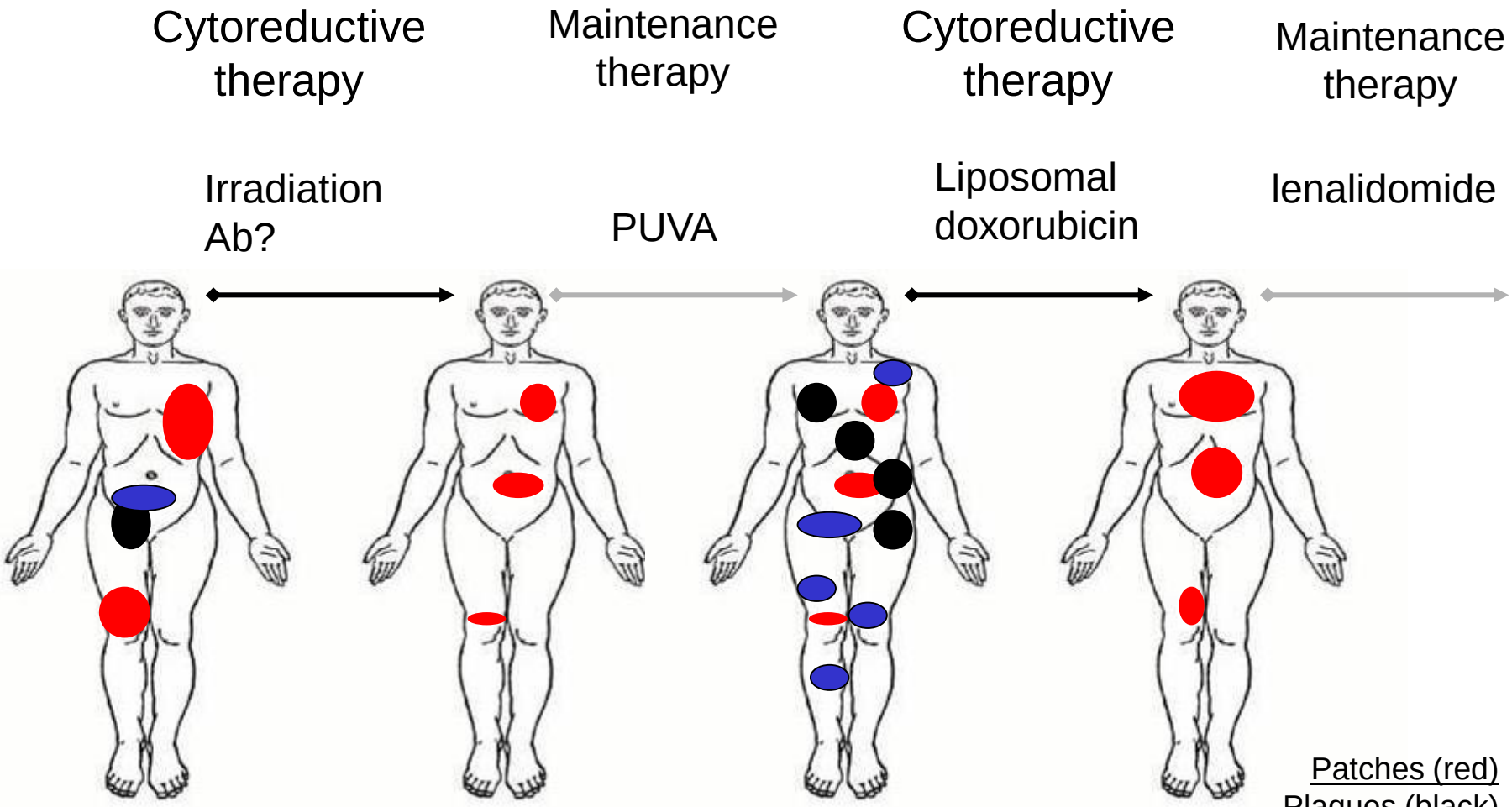
Landmark data for tumor stage MF

- Liposomal encapsulated doxorubicin (Caelyx™) was well tolerated
- 20/49 (40.8%) CCR/PR, excellent effects on skin lesions
- Pretreament with chemo: no worse outcome
- Node involvement, Extensive skin involvement: Lower response rate
- PFS: 7.4 m, Response duration: 6 m.

Maintenance therapy in cutaneous T-cell lymphoma: Who, when, what? ☆

EJC 2007; 43: 2321-2329

R. Dummer[a,*], C. Assaf[b], M. Bagot[c], R. Gniadecki[d], A. Hauschild[e], R. Knobler[f], A. Ranki[g], R. Stadler[h], S. Whittaker[i]



Final results of phase II trial of doxorubicin HCl liposome injection followed by bexarotene in advanced cutaneous T-cell lymphoma

Annals of Oncology 25: 206–210, 2014

D. J. Straus[1], M. Duvic[2], S. M. Horwitz[1], K. Hymes[3], A. Goy[4], F. J. Hernandez-Ilizaliturri[5], T. Feldman[4], B. Wegner[1] & P. L. Myskowski[6]

Response	Week 16: DLI 16 weeks/ 8 cycles ($n = 34$ assessable patients)	Patients receiving Bex ($n = 15$ assessable patients)	Week 32: Bex × 16 weeks ($n = 9$ completed + 6 progressed)
ORR (CCR + PR)	14 (41%)		
CCR	2 (6%)	1	1
PR	12 (35%)	10	6
SD	6 (18%)	4	2
PD	14 (41%)		6
NE	3	5	