Low-dose FCR in the treatment of elderly/comorbid patients with CLL/SLL: preliminary results of project Q-lite.

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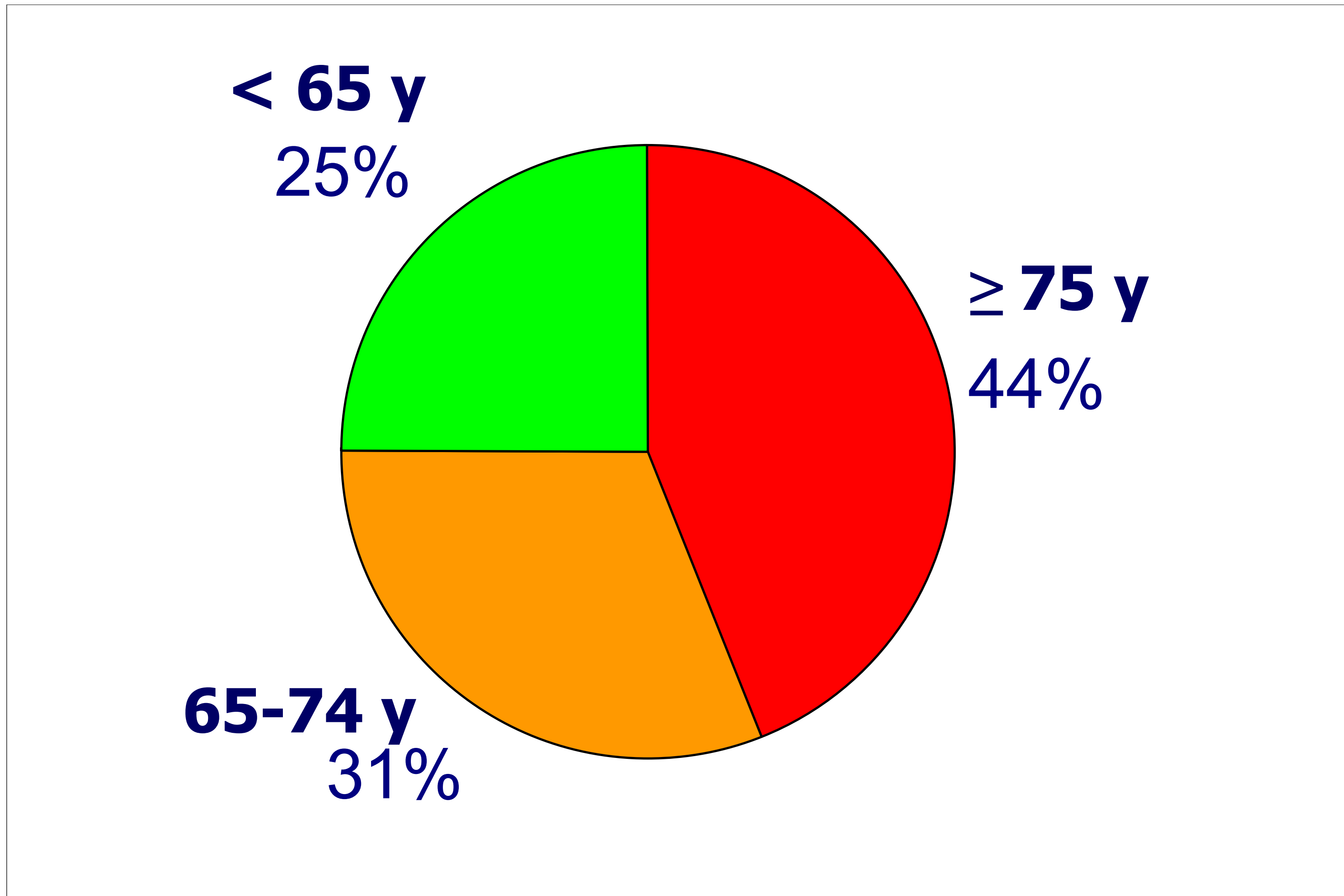
Age of patients with newly diagnosed CLL

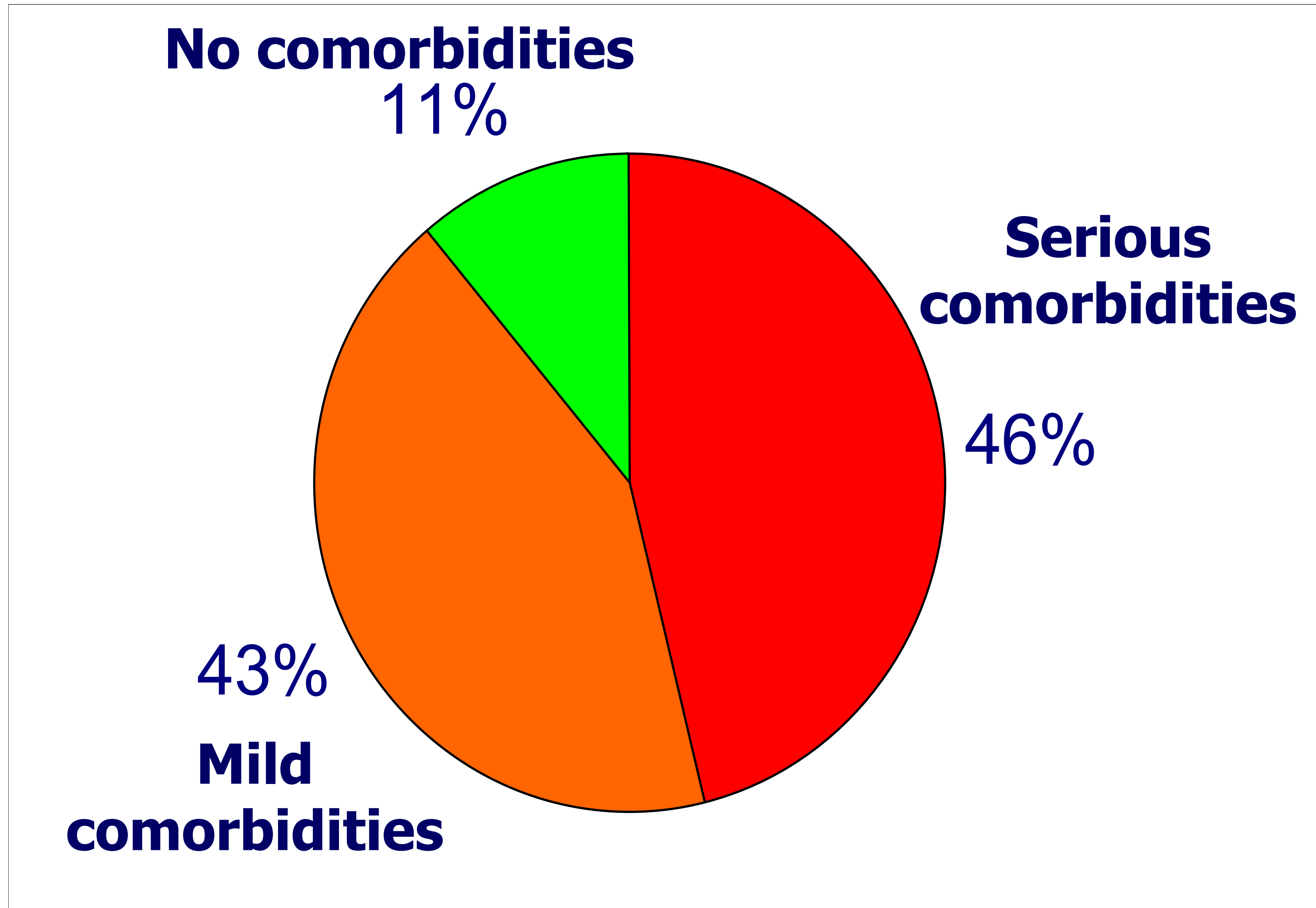


SEER Cancer Statistics, 1975-2002

Age of patients in randomized studies for CLL

Author	Year	Design	Median age
Rai	2001	F vs CLB vs F+CLB	64/62/63
Eichhorst	2006	FC vs F	58/59
Catovsky	2007	FC vs F	64/65
Flinn	2007	FC vs F	61/61
Hillmen	2007	Cam vs CLB	59/60
Knauf	2009	B vs CLB	64/64
Hallek	2009	FCR vs FC	61/61
Robak	2010	FCR vs FC	62/63
Robak	2010	FC vs CC	59/58

Comorbidities of patients with newly diagnosed CLL



Thurmes et al., Leuk Lymph 2008

Treatment of elderly patients with CLL - background

* FCR is treatment of choice - but only for younger fit patients [1,2]

* FCR in elderly patients is often too toxic[3,4]

* Fludarabine monotherapy was not beneficial in elderly patients in comparison to chlorambucil (CLL-5)[5]

⇨ Current standard treatment: chlorambucil

1 - Hallek et al., ASH 2009

2 - Robak et al., JCO 2009

3 - Shvidel et al., Leuk Lymphoma 2003

4 - Ferrajoli et al., IWCLL 2005

5 - Eichhorst et al., Blood 2009

Low-dose fludarabine-based protocol in elderly/comorbid CLL patients

Author, year	n	Age	Line	Regimen	ORR/CR (%)	Neutropenia	Other toxicity
Robertson, 1995	80	66	R/R	F	41/10	18 %	19x pneumonia 13xFUO
Bocchia, 1999	30	68	R/R + U	FCE	81/36	43 %	FUO 26 %
Marotta, 2000	20	75	R/R	FC	85/15	20 %	1x infection gr.IV, 1x TLS
Forconi, 2008	14	71	U	FC	100/62	21 %	-
Forconi, 2008	12	71	R/R	FC	84/25	25 %	2x pneumonia

R/R – relapsed/refractory; U – untreated; FCE – FC+ epirubicin

Project Q-lite

Quality of life and physical fitness of elderly/ comorbid patients with CLL/SLL treated with low dose FC/FCR

Indication: CLL patients in need of treatment BUT unfit for full-dose FCR due to age and/or comorbidities

- **post-registration study of safety**
- **1st line and relapsed CLL**
- **evaluation of quality of life (EORTC, Spitzer)**
- **assessment of comorbidities (CIRS)**
- **creatinine clearance (Cockroft-Gault formula)**

Schedule of treatment

Dose reduction of chemotherapy:

fludarabine 50 %, cyclophosphamide 60 % of full dose.

Fludarabine 20 mg/m^2 p.o. (or 12 mg/m^2 i.v.) D1-3

Cyclophosphamide 150 mg/m^2 p.o./i.v. D1-3

± Rituximab 500 mg/m^2 i.v. D1 (375 mg/m^2 in 1st cycle)

Repeated every 28 days, maximum 6 cycles.

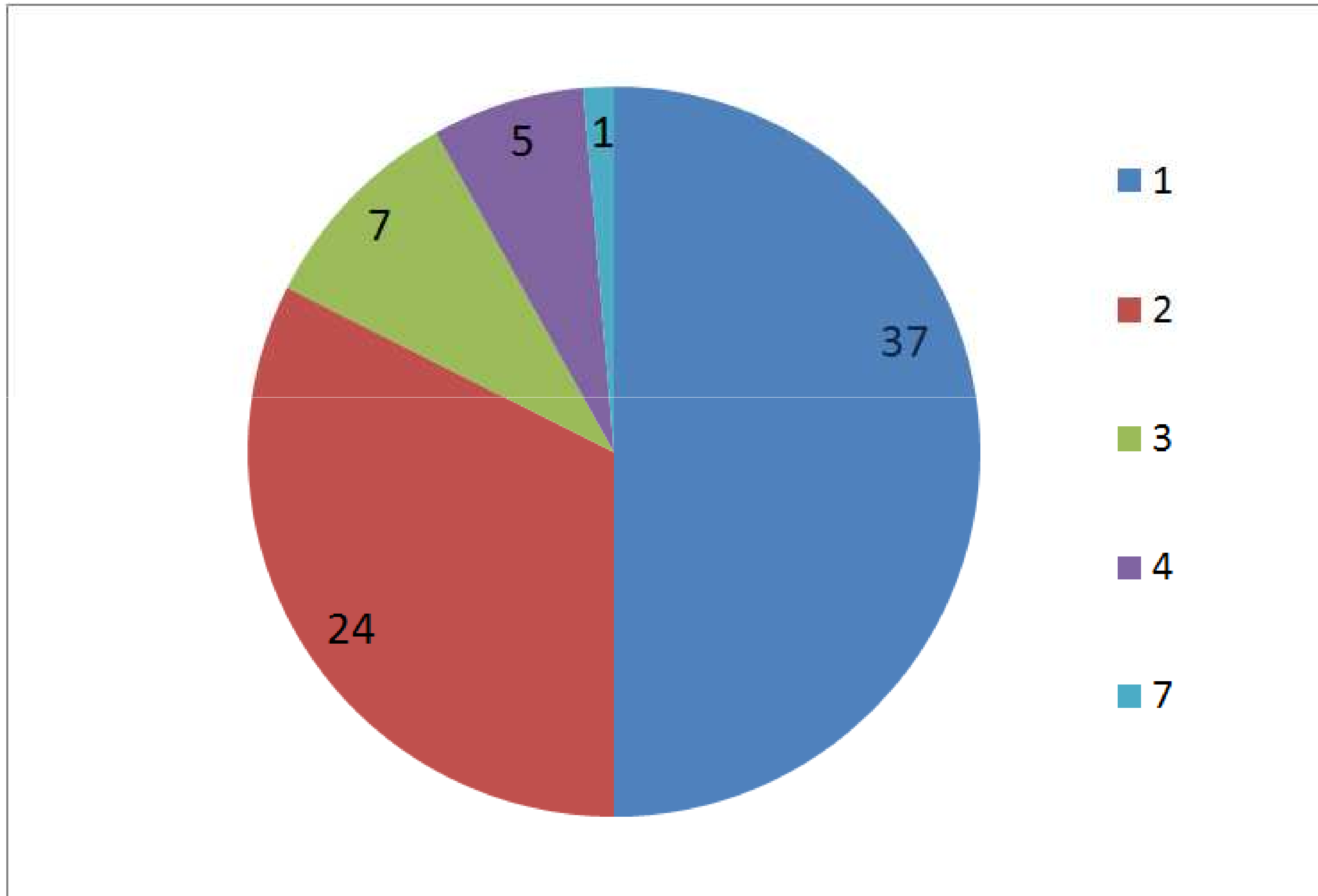
Recommended supportive treatment:

antiemetics, allopurinol, cotrimoxazol, antivirotics.

Patients

- enrollment since 3/2009, 14 sites
- 82 patients enrolled as of 1 Sep 2010
- data available from 74 patients
- 42 males, 32 females (M:F ratio 1.3:1)
- median age 70 years (range 58-83)
- median CIRS 4 (range 0-10)
- CLL n=70, SLL n=4
- FCR n=72, FC n=2

Line of treatment



Prognostic factors

Rai III/IV	57 %
Unmutated IgVH genes	75 %
del 11q	32 %
del 17p	8 %
Bulky lymphadenopathy (≥ 5cm)	39 %

Efficacy (intention to treat)

- 34 patients still on treatment

Overall response	70 %
Complete response (CR+cCR+CRi)	35 %
Stable disease	11 %
Progression	9 %
Not evaluable	11 %

Grade III/IV toxicities

Neutropenia	51 %
Thrombocytopenia	13 %
Anemia	10 %
Infections	13 %
Deaths	4 pts (5 %)

- 2x pneumonia, 1x PE, 1x septic shock

Conclusions

*** Elderly/ comorbid pts: significant part of CLL population**

*** Age/comorbidities: risk factor for toxicity and survival**

*** Low-dose FCR: promising efficacy (ORR/CR 70/35 %)**

*** Toxicity acceptable (serious infections 13%)**

*** Longer follow-up needed for PFS/OS data**

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Thank you for your attention!

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