Supplemental Materials for

Diffuse Large B Cell Lymphoma in octogenarians aged 85 and older can benefit from treatment with curative intent: a report on 129 patients prospectively registered in the Elderly Project of the Fondazione Italiana Linfomi (FIL)

Supplemental Methods

Starting from the hypothesis that the choice between palliation and full/reduced dose depends on the patient's status at diagnosis, with the aim to limit the selection bias due to the presence of unbalanced confounders, the comparison between PVT and FDT/RDT was performed by inverse probability weight (IPW) analysis on Cox PH regression conducted in overall survival, using stabilized weights with corrected sandwich variance estimation[1]. The stabilized weights were obtained by a first logistic regression to model the probability of treatment (PVT vs FDT/RDT) related to the baseline characteristics (age, sex, bulky disease, B-symptoms, IPI score, Hb level, ADL, IADL, and all comorbidities of CIRS) and by second logistic regression without potential confounders as the marginal probability of treatment.

Supplemental Results

Factors associated with palliative treatment

We conducted a number of logistic regression models to detect factors associated with palliative treatment. The results are shown in the tables 3 and 4.

Specific cause of death

Considering the cumulative incidence function (CIF) for specific cause of death (progression and other causes) we obtain the results shown in supplemental figure 1.
The HR for progression in LO vs EO was 1.49 (95%CI 1.02-2.18, p=0.039) and HR was 2.29 (59%CI 1.26-4.16, p=0.006) for other causes.
The patients in the cohort LO showed a worse specific survival either for progression or other causes.
If we consider the OS for patients treated only with antrhacycline (RCHOP/RCOMP) there is no appreciable difference between EO and LO cohorts: HR = 1.12 (95% CI 0.61-2.03, p=0.721) (supplemental figure 2)

Internal validation model

Since in the model bulky and B-symptoms covariates showed a superimposable effect, it was assumed that the difference in Harrell's C was due to the presence of sGA or EPI.
In the absence of an external validation sample, we performed an internal validation for OS, based on bootstrap methodology, to evaluate the possibile reproducibility of the model.
The results of Harrell's C and slope shinkage after 1000 bootstrap resamples were reported in the supplemental table 5.

The corrected Harrell'C with model including EPI showed a greater value than model including sGA (0.706 vs 0.675) and both showed an acceptable slope shinkage, that excludes an excess of overfitting.

Table S1. Criteria for sGA in patients ≥ 80 years old

	UNFIT	**FRAIL**
ADL	6*	< 6*
	and	*and/or*
IADL	8*	< 8*
	and	*and/or*
CIRS-G	0 score =3-4 *and* <5 score =2	≥1 score =3-4 *and/or* ≥5 score =2

Abbreviations: ADL, activities of daily living; IADL, instrumental ADL; CIRS-G, Cumulative Illness Rating Scale for Geriatrics; sGA, simplified Geriatric Assessment

* Residual functions

Table S2. EPI score and Risk Groups

Factors	**Weight**
FIT	0
UNFIT	3
FRAIL	4
IPI 1	0
IPI 2	1
IPI 3-5	3
Hb < 12 g/dl	1

Low (0-1)
Intermediate (2-5)
High (6-8)

Table S3. Prediction of Palliative treatment, by means of logistic regression (n=370, pall. n=120, 32%): Outcome=1 if Palliative, Outcome = 0 if Full/Reduced. Odds Ratio >1 means that covariate is associate with higher odds for palliative approach

UNFIT/FRAIL (n=370)	**Palliative**	**Univariable**		**Multivariable**	
Covariate	**N (%)**	**OR (95%CI)**	**p-value**	**OR (95%CI)**	**p-value**
Total	120 (32)	-	-	-	-
Age/5 (Continuos, [Age-80)/5])	-	3.25 (2.25-4.69)	<0.001	**2.97 (1.97-4.48)**	<0.001
Gender					
M	39 (23)	1.00			
F	81 (40)	2.29 (1.45-3.61)	<0.001	**2.11 (1.23-3.64)**	0.007
IPI					
1	13 (27)	1.00			
2	24 (28)	1.03 (0.46-2.26)	0.950		
3/5	62 (62)	1.25 (0.61-2.52)	0.541		
ADL					
6	66 (25)	1.00			
<6	54 (51)	3.12 (1.94-4.99)	<0.001		
IADL					
8	37 (18)	1.00			
<8	83 (51)	4.77 (2.98-7.62)	<0.001	**3.44 (2.01-5.86)**	<0.001
Heart (scale 0-4)	-	1.52 (1.23-1.87)	<0.001	**1.54 (1.19-2.00)**	0.001
Hypertension (scale 0-4)	-	1.40 (1.08-1.82)	0.012		
Vascular (scale 0-4)	-	1.08 (0.84-1.38)	0.562		
Respiratory (scale 0-4)	-	1.14 (0.81-1.59)	0.456		
Eye/Ear (scale 0-4)	-	1.14 (0.84-1.55)	0.411		
GI upper (scale 0-4)	-	0.72 (0.48-1.08)	0.117	**0.65 (0.39-1.08)**	0.095
GI lower (scale 0-4)	-	1.27 (0.88-1.82)	0.208		
Liver (scale 0-4)	-	1.01 (0.69-1.48)	0.945		
Kidney (scale 0-4)	-	0.98 (0.68-1.41)	0.912		
Genito-Urinary (scale 0-4)	-	1.05 (0.80-1.37)	0.747		
Muscle (scale 0-4)	-	1.93 (1.46-2.56)	<0.001		
CNS (scale 0-4)	-	1.22 (0.85-1.75)	0.284		
Endocrine (scale 0-4)	-	1.10 (0.85-1.43)	0.460		
Psychology (scale 0-4)	-	2.02 (1.45-2.83)	<0.001	**1.72 (1.16-2.53)**	0.006

Goodness of fit test over 5 groups p=0.739

Table S4. Multivariable logistic regression on frailty patients with No Rituximab treatment as outcome

FRAIL (n=120) , No Rituximab	**Multivariable**	
Covariate	**OR (95%CI)**	**p-value**
Age/5 (Continuos, [Age-80)/5])	1.64 (0.98-2.73)	0.058
ADL		
6		
<6	3.23 (1.40-7.42)	0.006
Muscle (scale 0-4)	1.42 (0.95-2.11)	0.089
Kidney (scale 0-4)	2.08 (1.10-3.95)	0.024

Table S5. Harrell's C and slope shinkage after 1000 bootstrap resamples

Model	Original	Training	Test	Optimism	Corrected	Slope shrinkage
Including sGA	**0.689**	0.691	0.680	0.011	**0.675**	**0.912**
Inculding EPI	**0.717**	0.721	0.710	0.011	**0.706**	**0.914**

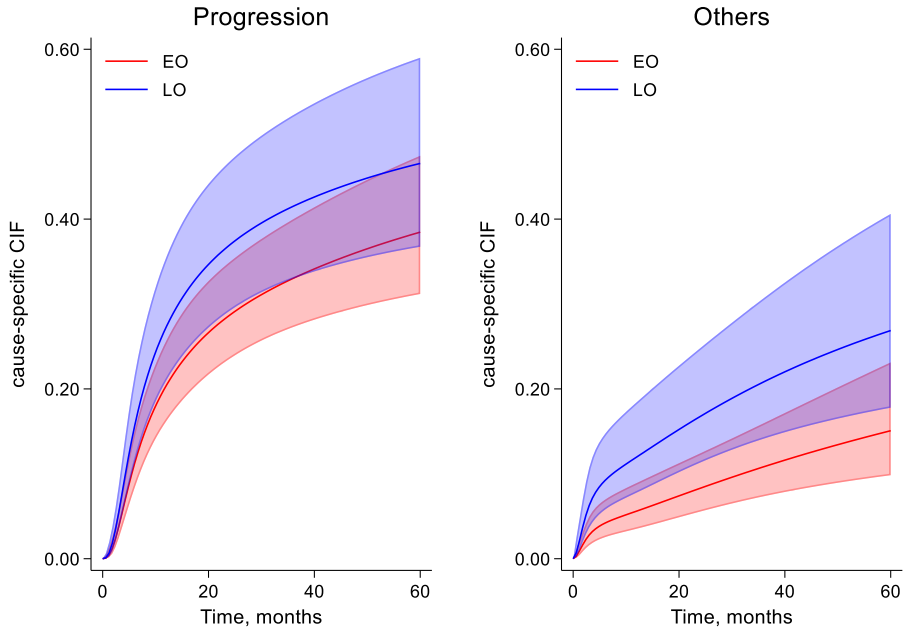

Figure S1. Cumulative incidence function (CIF) for specific cause of death (progression and other causes)

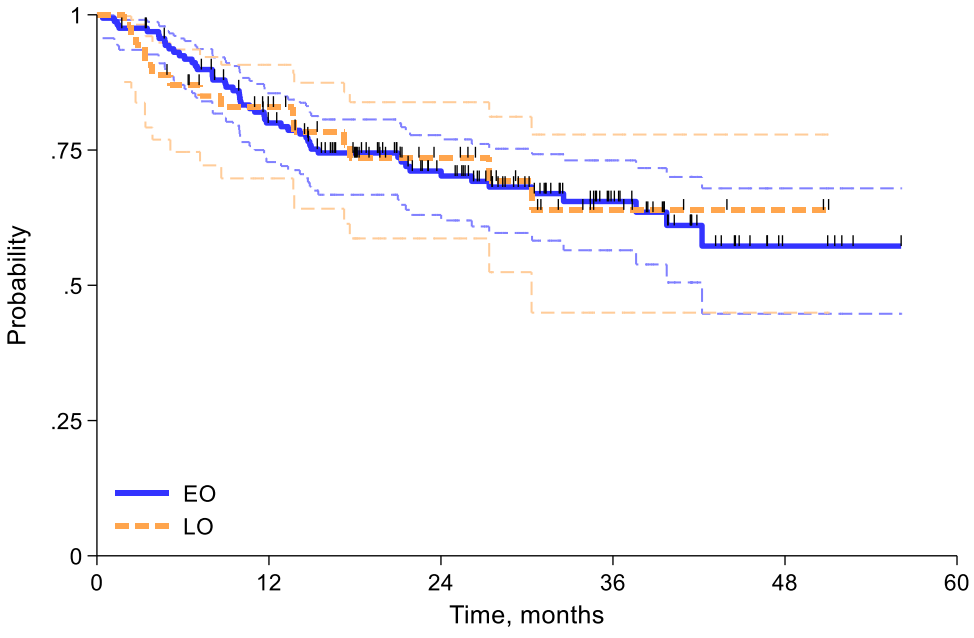

Figure S2. OS for patients treated only with antrhacycline (RCHOP/RCOMP)

Supplemental Reference

1. Shu D, Young JG, Toh S et al. Variance estimation in an inverse probability weighted Cox model. Biometrics. 2020; 77: 1101-17