Real-life: l'approccio diagnostico-terapeutico al paziente ottuagenario nei linfomi non Hodgkin

Dr Piero Maria Stefani

DISCLOSURE

- TAKEDA
- ROCHE
- PFIZER

CASO CLINICO

♂ 1932

- BMI 21
- K prostata radiotrattato, ipertrofia prostatica
- epatopatia HBV correlata misconosciuta HBV-DNA negativo
- cardiopatia ipertensiva in compenso, ECG: RS, EAS, extrasistolia sopraventricolare isolata.
- Ecocardiogramma: FE Vsx 62,6 %. Ventricolo sinistro ipertrofico, di normali dimensioni e funzione sistolica complessiva. Lieve-media dilatazione atriale sinistra. Alterato rilasciamento diastolico. Lieve rigurgito valvolare mitralico.
- Vasculopatia carotidea non critica.

Terapia domiciliare: VALSARTAN/HCT 80/12,5 mg 1 c; ASA 100 mg 1 c; TAMSULOSINA 0,4 mg 1 c

Aprile 2017. Comparsa improvvisa di tumefazione sottomandibolare destra compatibile con adenopatia: valutazione Ematologica prioritaria B

CASO CLINICO

- Biopsia Neoformazione sottomandibolare dx e ghiandola sottomandibolare: localizzazione di linfoma B diffuso a grandi cellule di tipo ABC.
- Biopsia osteomidollare: cellularità 10%. Midollo emopoietico con lieve ritardo maturativo della serie mieloide. Non evidente localizzazione di processo linfoproliferativo.

- PET: più aree di iperaccumulo dell'indicatore di verosimile pertinenza linfonodale in laterocervicale destra, giugulare, sottomandibolare e sovraclaveare dello stesso lato, di cui quella di maggiori dimensioni (24 mm in assiale) presenta SUV max 23,72 e quella più captante SUV max di 27,87, ipercaptanti con gradiente variabile da modesto a discreto, alcune aree anch'esse probabilmente di pertinenza linfonodale di dimensioni massime di circa 10 mm in sede ilare e parailare polmonare bilateralmente.

- Nella norma emocromo, funzione epatorenale, albumina, protidogramma, β2-microglobulina e LDH

Valutazione geriatrica multidimensionale

MISURA	FIT	UNFIT	FRAIL
ADL	6	5*	≤4*
IADL	8	7- 6*	≤5*
CIRS	0 score = 3-4 < 5 score = 2	0 score = 3-4 5-8 score = 2	1 score = 3-4 > 8 score = 2
ETÀ		**≥ 80 fit**	**≥ 80 unfit**

* n. di funzioni residue

CASO CLINICO

Linfoma non Hodgkin B diffuso a grandi cellule fenotipo ABC stadio II A R-IPI= 1, CNS-IPI= 1

VGM:

- **ADL 6/6**
- **IADL 8/8**
- **CIRS-G=3**
- **0 SCORE >3**
- **0 SCORE >2**

= UNFIT SOLO PER ETA' ➡ 80ENNE FIT

- **6RCOMP21 (+ G-CSF, EPO)**
- **TOSSICITA': neuropatia lieve e stipsi da VCR con conseguente riduzione di dose, HBV-DNA sempre non quantificabile , intercorrente TVP su PICC, stabilmente nella norma i regimi pressori e i livelli glicemici (Hb glicata)**
- **PET dopo IV ciclo: non adenopatie laterocervicali sovraclaveari e mediastiniche, aree focali di iperaccumulo polmonare a significato flogistico**
- **PET dopo il VI (10/2017) : CR metabolica e tuttora in CR a ottobre 2019**

epidemiologia

- aumento dell'incidenza di linfomi compreso tra l'8% e il 10% annuo in Europa e negli Stati Uniti, in particolare per i pazienti di età superiore ai 65 anni.
- Incidenza di linfoma negli ultimi 25 anni in aumento di oltre il 50% e anche oltre nei pazienti con più di 60 anni.
- Istologia. Linfoma B diffuso a grandi cellule (DLBCL), Linfoma periferico a cellule T, Linfoma linfocitico/infoplasmocitario, Linfoma a grandi cellule anaplastiche, Linfoma linfoblastico, Linfoma di Burkitt.
- Il fenotipo ABC è prevalente nei pazienti con più di 80 anni rispetto ai pazienti di età compresa tra 50 e 60 anni.
- Caratteristica l'espressione di BCL2 o complessità citogenetica, come le traslocazioni IRF4, 1q21, 18q21, 7p22 e 7q21, 3q27, mutazioni di BCL6, CD79B, KMT2D e MYD88.
- L'età media dei pazienti MYC-IG riarrangiati è quasi un decennio più vecchia dei pazienti MYC-non-IG riarrangiati.

Copie-Bergman C. Blood. 2015;126(22): 2466-74
Carson KR,. J Geriatr Oncol 2015; 6: 211–218
Dubois S. Clin Cancer Res 2016;22(12): 2919-28
Eyre TA. Br J Haematol 2016; 173: 487–491.119.

Outcome of frail elderly patients with diffuse large B-cell lymphoma prospectively identified by Comprehensive Geriatric Assessment: results from a study of the Fondazione Italiana Linfomi

Francesco Merli[1], Stefano Luminari[2], Giuseppe Rossi[3], Caterina Mammi[1], Luigi Marcheselli[2], Angela Ferrari[1], Michele Spina[4], Alessandra Tucci[3], Caterina Stelitano[5], Isabella Capodanno[1], Alberto Fragasso[6], Luca Baldini[7], Chiara Bottelli[3], Elisa Montechiarello[5], Stefano Fogazzi[3], Cinzia Lamorgese[3], Lara Cavalli[3] & Massimo Federico[2]; for the Fondazione Italiana Linfomi

Leukemia & Lymphoma, January 2014; 55(1): 38–43

Table I. Patient characteristics and comparison with fit elderly patients.

		Frail ($n=94$)		Fit ($n=224$)		
Variable†	Status	*n*	%	*n*	%	*p*-Value
Age, median (range)		78 (65–93)		72 (65–80)		<0.001
Gender	F	62	66	120	54	0.047
	M	32	34	104	46	
AA stage	II	36	38	70	31	0.242
	III–IV	58	62	154	69	
Symptoms	A	75	80	135	60	0.001
	B	19	20	89	40	
aaIPI	0	16	18	34	16	0.339
	1	26	29	80	37	
	2	34	38	81	38	
	3	13	15	19	9	
ADL	6	55	68	224	100	*
	<6	26	32	—	—	
IADL	8	20	40	176	79	<0.001
	<8	30	60	48	21	
GS	No	57	75	224	100	*
	Yes	19	25	—	—	
CIRS-G	Grade 1–2	17	19	195	87	*
	Grade 3<3	7	8	29	13	
	Grade 3≥3	48	53	—		
	Grade 4≥1	18	20	—		

Table III. Treatment of frail patients.

Therapy	R+	R−	Total (%)
Polychemotherapy with anthracyclines*	31	36	67 (71%)
Polychemotherapy without anthracyclines†	5	1	6 (6%)
Mono-chemotherapy, radiotherapy, palliation	1	20	21 (22%)
Total (%)	37 (39%)	57 (61%)	94

R, rituximab; CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone; CEOP, cyclophosphamide, epirubicin, vinblastine, prednisone; CNOP, cyclophosphamide, mitoxantrone, vincristine, prednisone; P-VEBEC, prednisone, vinblastine, epirubicin, bleomycin, etoposide, cyclophosphamide; CVP, cyclophosphamide, vincristine, prednisone.
*Includes CHOP, mini-CEOP, CNOP, P-VEBEC.
†Includes CVP.

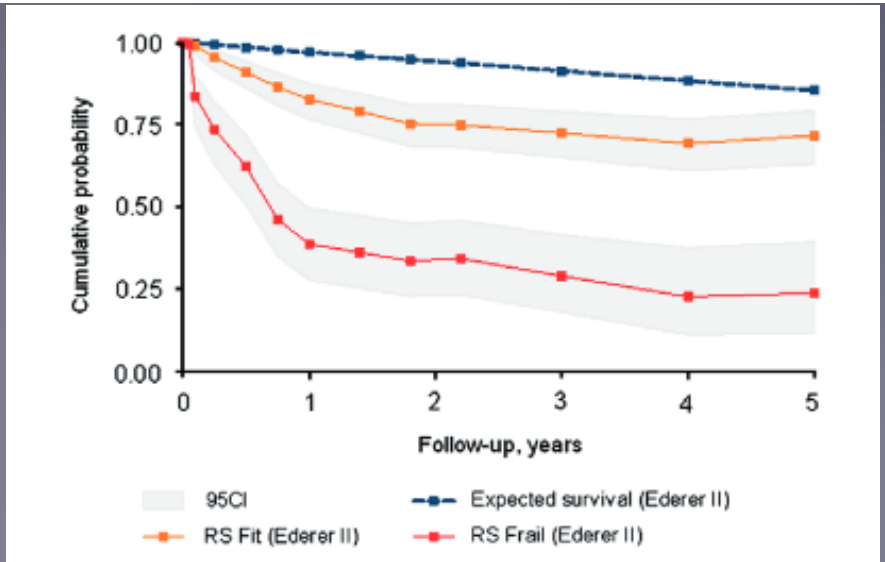

Figure 2. Relative survival (RS) for frail and fit patients and for a matched population of healthy subjects.

Valutazione geriatrica multidimensionale

MISURA	FIT	UNFIT	FRAIL
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Nonpegylated liposomal doxorubicin combination regimen in patients with diffuse large B-cell lymphoma and cardiac comorbidity. Results of the HEART01 phase II trial conducted by the Fondazione Italiana Linfomi

Hematological Oncology. 2017;1–8.

Stefano Luminari[1,2] | Elda Viel[3] | Andrés José Maria Ferreri[4] | Francesco Zaja[5] |

Variable	N	%	Missing N (%)
Age			
Median	76		
Range	53-90		-
>60	47	94	
Sex, M	35	70	-
Stage			
I-II	19	38	-
III-IV	31	62	
PS > 1	7	14	-
LDH > UNL	23	51	5 (10)
ENS > 1	5	10	-
Bulky[a]	5	10	1 (2)
IPI			
0-1	11	24	
2	16	26	5 (10)
3-5	18	40	
Cardiac disorders			
Ischemic cardiopathy	21	35	
Atrial fibrillation	9	15	
Left ventricular hypertrophy	8	13	
LVEF <50%	7	12	
Ventricular arrhythmia	5	8	-
Moderate/severe mitral valve disease	3	5	
Moderate aortic valve disease	3	5	
Pulmonary hypertension	2	3	
Uncontrolled hypertension	2	3	
Altered ECG	27	59	4 (8)
LVEF			
Median	60	-	3 (6)

Response	N	% (95CI)
CR	28	56 (41-70)
PR	8	16 (4-29)
ORR	36	72 (58-84)
SD/PD	10	20 (10-34)
NA/EW	4	8 (2-19)
3-yr survival	# events	% (95CI
OS	22	50 (34-65)
PFS	30	38 (24-51)
FFS	36	27 (15-40)

	Population (N = 50)	
Cardiac disorder	**Grades 1-2, n (%)**	**Grades 3-4, n (%)**
Heart failure	1(2)	1(2)
LVEF drop ≥20%	2(4)[a]	3(6)
Increased troponin	2(4)	-
Angina	-	1(2)
Atrial fibrillation	-	1(2)
Tot	**5(10)**	**6(12)**

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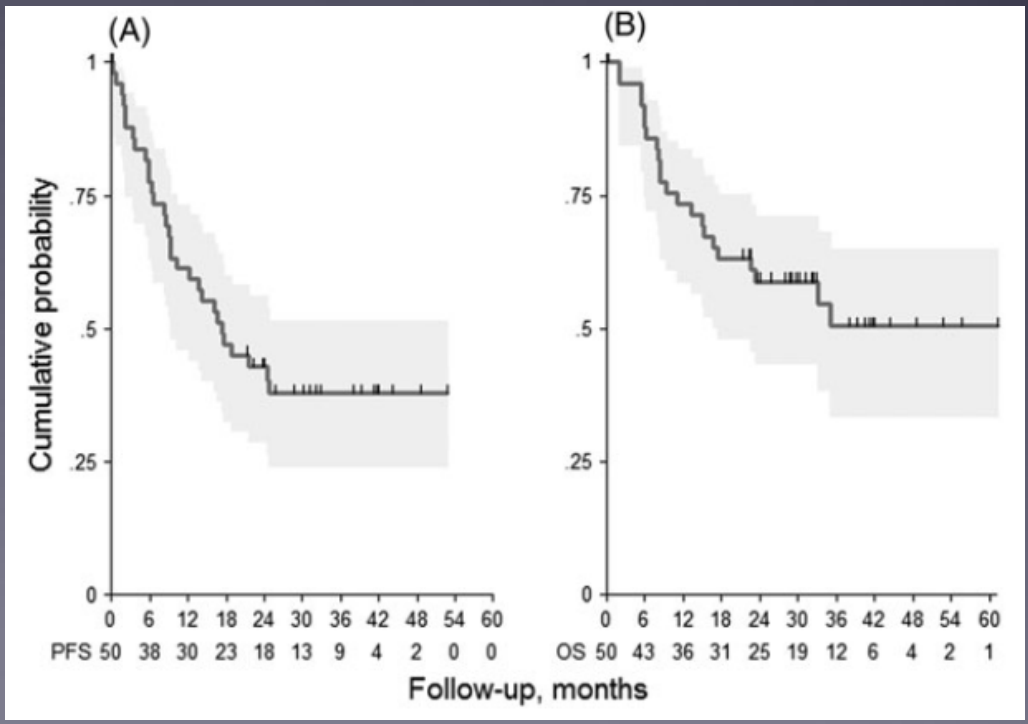
Adverse event	Population (N = 50)	
	Any grade (%)	Grades 3–4 (%)
Blood and lymphatic system disorders		
Neutropenia	78	64
Anemia	88	46
Thrombocytopenia	58	8
Febrile neutropenia	2	2
Gastrointestinal disorders		
Constipation	6	-
Nausea	6	2
Diarrhea	2	-
Abdominal pain	2	-
Vomiting	4	-
Stomatitis	4	-
Infections	22	6
General disorders		
Pyrexia	4	-
Asthenia	10	2
Nervous system disorders		
Paresthesia	18	0



A, Progression free survival (PFS); B, overall survival (OS)

Attenuated immunochemotherapy regimen (R-miniCHOP) in elderly patients older than 80 years with diffuse large B-cell lymphoma: a multicentre, single-arm, phase 2 trial

Lancet Oncol 2011; 12: 460–68

Frédéric Peyrade, Fabrice Jardin, Catherine Thieblemont, Antoine Thyss, Jean-François Emile, Sylvie Castaigne, Bertrand Coiffier, Corinne Haioun,

	Patients (n=149)
Men	51 (34%)
Age (years)	83 (80–95)
Performance status	
0	27 (18%)
1	72 (48%)
2	50 (34%)
Ann Arbor stage	
I	13 (9%)
II	24 (16%)
III	35 (23%)
IV	77 (52%)
Tumour mass ≥10 cm	30 (20%)
>1 extranodal sites	55 (37%)
LDH concentration >618 U/L	102 (68%)
B symptoms*	49 (33%)
β2-microglobulin ≥3 mg/L	82/112 (73%)
Serum albumin <35 g/L	69/137 (50%)
IPI	
0–1	13 (9%)
2	31 (21%)
3	46 (31%)
4–5	59 (40%)
Age-adjusted IPI	
0	15 (10%)
1	36 (24%)
2	66 (44%)
3	32 (21%)
IADL scale†	
Without limitation (score 4)	63 (47%)
With limitation (score <4)	72 (53%)

R-miniCHOP: R 375 mg/m²,
Doxorubicina 25 mg/m²,
CTX 400 mg/m²,
VCR 1 mg,
Prednisone 40 mg/m² d1-5

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	Hazard ratio (95% CI)	p value
Age-adjusted IPI 2–3	1·4 (0·6–3·5)	0·46
Number of extranodal sites >1	1·2 (0·6–2·4)	0·59
Serum albumin ≤35g/L	3·2 (1·4–7·1)	0·0053
β2-microglobulin ≥3mg/L	0·9 (0·4–1·9)	0·75
Tumour mass >10 cm	1·4 (0·6–2·9)	0·43
IADL score <4	1·9 (1·0–3·9)	0·064

IPI=international prognostic index. IADL=instrumental activities of daily living.

Table 3: **Multivariate analyses of prognostic factors for overall survival**

	Patients (n=149)
Complete response	59 (40%)
Unconfirmed complete response	34 (23%)
Partial response	16 (11%)
Stable disease	2 (1%)
Progression during treatment	8 (5%)
Death	27 (18%)
Not assessed	3 (2%)

Table 5: **Response at end of treatment**

	No toxicity	Grade 1–2	Grade 3	Grade 4	Grade 5
Infection without neutropenia	113 (76%)	22 (15%)	12 (8%)	0 (0%)	2 (1%)
Febrile neutropenia	138 (93%)	1 (1%)	7 (5%)	0 (0%)	3 (2%)
Constitutional symptoms	69 (46%)	68 (46%)	7 (5%)	2 (1%)	3 (2%)
Neurological toxicity	109 (73%)	30 (20%)	7 (5%)	3 (2%)	0 (0%)
Pulmonary toxicity	118 (79%)	25 (17%)	4 (3%)	1 (0%)	1 (1%)
Renal toxicity	137 (92%)	8 (5%)	2 (1%)	1 (0%)	1 (1%)
Cardiac arrhythmia	134 (90%)	11 (7%)	2 (1%)	2 (1%)	0 (0%)
Cardiac (other)	133 (89%)	13 (9%)	2 (1%)	0 (0%)	1 (1%)
Vascular toxicity	137 (92%)	8 (5%)	3 (2%)	1 (1%)	0 (0%)
Mucositis	138 (93%)	11 (7%)	0 (0%)	0 (0%)	0 (0%)
Creatinine	117 (79%)	31 (21%)	0 (0%)	1 (1%)	0 (0%)
Transaminases	128 (86%)	20 (13%)	0 (0%)	1 (1%)	0 (0%)

Data are number (%). Percentages do not add up to 100% in some cases because of rounding.

Table 6: **Incidence of non-haematological toxicity by grade**

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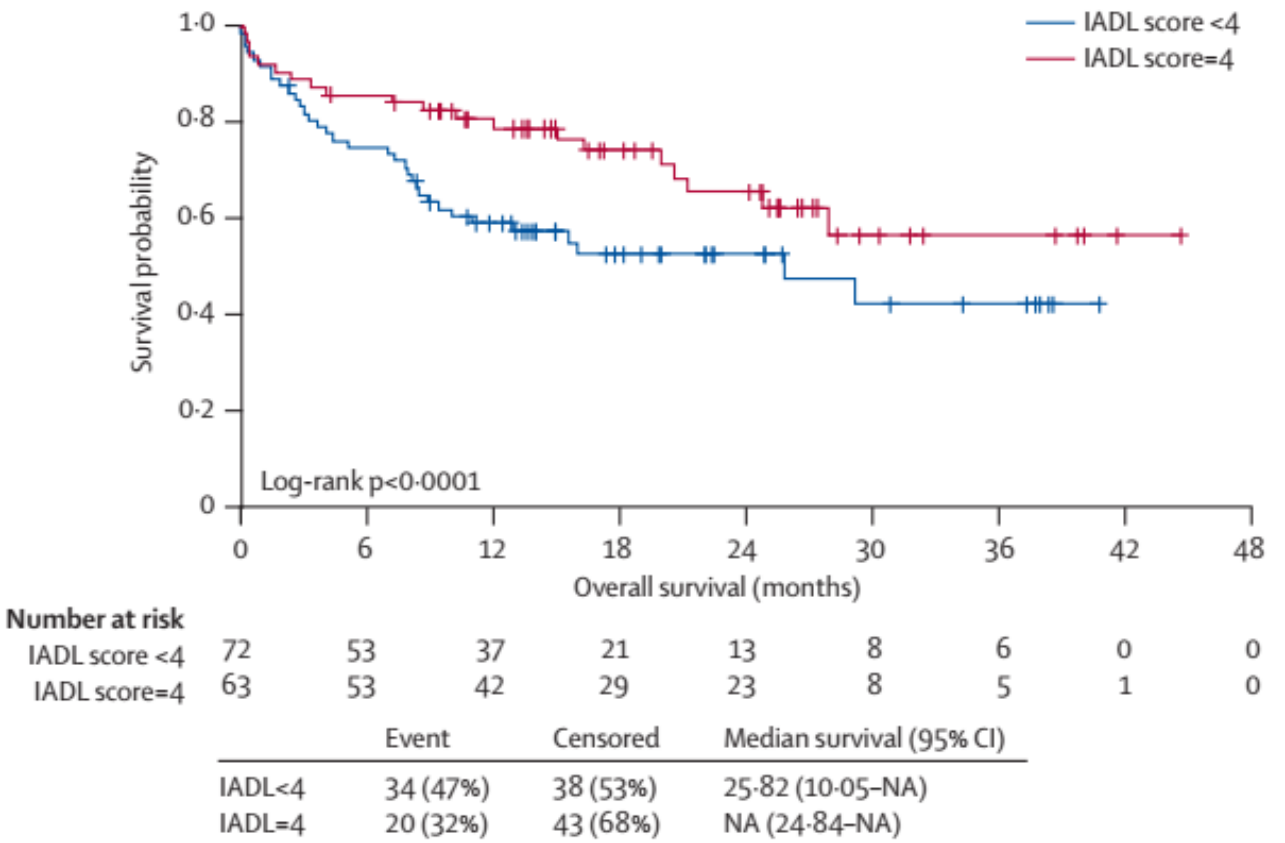

Number at risk

IADL score <4	72	53	37	21	13	8	6	0	0
IADL score=4	63	53	42	29	23	8	5	1	0

	Event	Censored	Median survival (95% CI)
IADL<4	34 (47%)	38 (53%)	25·82 (10·05–NA)
IADL=4	20 (32%)	43 (68%)	NA (24·84–NA)

Interpretation R-miniCHOP offers a good compromise between efficacy and safety in patients aged over 80 years old. R-miniCHOP should be considered as the new standard treatment in this subgroup of patients.

Combination of ofatumumab and reduced-dose CHOP for diffuse large B-cell lymphomas in patients aged 80 years or older: an open-label, multicentre, single-arm, phase 2 trial from the LYSA group

Lancet Haematol 2017; 4: e46–55

Frédéric Peyrade, Serge Bologna, Vincent Delwail, Jean François Emile, Laurent Pascal, Christophe Fermé, Jean-Marc Schiano, Bertrand Coiffier,

	Patients (n=120)
Age (years)	83 (80–95)
Performance status (ECOG)	
0–1	85 (71%)
2	23 (19%)
3–4	12 (10%)
Ann Arbor stage	
I	16 (13%)
II	12 (10%)
III	24 (20%)
IV	68 (57%)
≥2 extranodal sites	44 (37%)
B symptoms	23 (19%)
>10 cm tumour mass	11 (9%)
LDH above upper limit	69 (58%)
>35 g/L albumin concentration	67 (56%)
IPI score	
0	0
1	15 (13%)
2	23 (19%)
3	40 (33%)
4	31 (26%)
5	11 (9%)
Age-adjusted IPI score	
0	17 (14%)
1	35 (29%)
2	43 (36%)
3	25 (21%)

Histology	
GCB	26 (22%)
Non-GCB	41 (34%)
Unclassifiable	15 (13%)
Others lymphomas	11 (9%)
Unavailable	27 (23%)
Charlson comorbidity score in classes (n=113)	
Low	49 (41%)
Intermediate	35 (29%)
High	29 (24%)
IADL scale (n=118)	
<4	64 (53%)
4	54 (45%)
Buzby index (NRI; n=110)	
No or mild undernutrition	71 (59%)
Moderate undernutrition	27 (23%)
Severe undernutrition	12 (10%)

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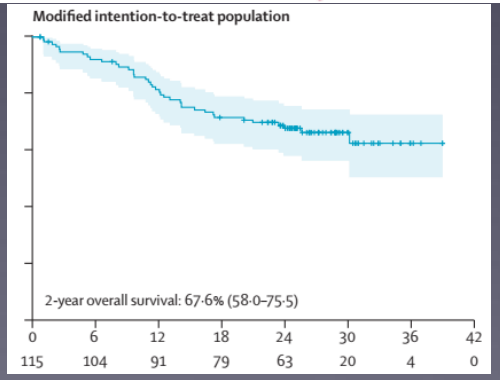
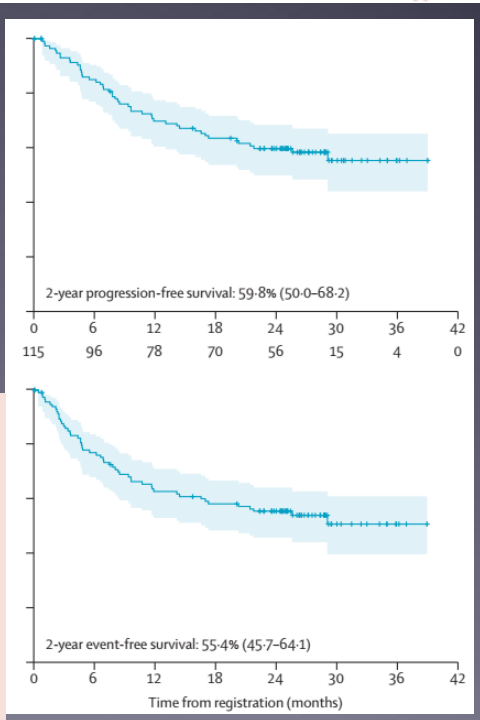
	2-year overall survival	Hazard ratio (95% CI)	Log-rank p value
Age-adjusted IPI 0–1 *vs* 2–3	82% *vs* 56%	3·1 (1·5–6·5)	0·0001
Serum albumin <35g/L *vs* >35g/L	69% *vs* 70%	1·1 (0·5–2·2)	0·8
IADL score <4 *vs* 4	62% *vs* 77 %	1·8 (0·9–3·5)	0·09
Severe undernutrition *vs* no undernutrition	70% *vs* 72%	0·9 (0·3–3·1)	0·99
GCB *vs* non-GCB	76% *vs* 55%	1·9 (0·7–4·9)	0·15
Charlson comorbidity index			
High *vs* low	60% *vs* 77%	1·7 (0·71–3·8)	0·3
Intermediate *vs* low	62% *vs* 77%	1·8 (0·8–3·8)	0·3

IPI=International Prognostic Index. IADL=instrumental activities of daily living. GCB=germinal centre B.

Table 4: **Univariate analysis of prognostic factors for overall survival**





	Pre-phase (n=120), grade 3–4	Treatment period (n=115), grade 3–4
Febrile neutropenia	0	7 (6%)
Neutropenia	0	24 (21%)
Thrombocytopenia	0	2 (2%)
Infections and infestations	4 (3%)	9 (8%)
Cardiac arrhythmia	0	3 (3%)
Cardiac (other*)	0	4 (3%)
Pulmonary toxicity	0	7 (6%)
Neurological toxicity	0	6 (5%)
Vascular toxicity	1 (1%)	5 (4%)
Asthenia	1 (1%)	4 (3%)
Gastrointestinal disorders	0	4 (3%)
Depression confusion	0	3 (3%)
Infusion-related reaction	0	2 (2%)

Interpretation Our result suggest that, in patients older than 80 years with DLBCL, ofatumumab and pre-phase treatment seem to improve overall survival compared with the previously reported data. The combination of pre-phase treatment, a monoclonal antibody against CD20, and miniCHOP can be considered a new treatment platform for use in randomised clinical trial design for DLBCL treatment in patients older than 80 years.

Gemcitabine-oxaliplatin plus rituximab (R-GemOx) as first-line treatment in elderly patients with diffuse large B-cell lymphoma: a single-arm, open-label, phase 2 trial

Qiu-Dan Shen, Hua-Yuan Zhu*, Li Wang, Lei Fan, Jin-Hua Liang, Lei Cao, Wei Wu, Yi Xia, Jian-Yong Li, Wei Xu*

Lancet Haematol 2018

	Age 60–69 years (n=14)	Age ≥70 years (n=46)
Men	8 (57%)	30 (65%)
Women	6 (43%)	16 (35%)
Ann Arbor stage		
I	3 (21%)	13 (28%)
II	2 (14%)	6 (13%)
III	7 (50%)	15 (33%)
IV	2 (14%)	12 (26%)
≥2 extranodal sites	4 (29%)	6 (13%)
Bulky disease ≥7·5 cm	0	6 (13%)
B symptoms	4 (28%)	14 (30%)
ECOG performance status score ≥2	14 (100%)	13 (28%)
Lactate dehydrogenase >ULN	4 (29%)	16 (35%)
β2-microglobulin >2·53 mg/L	8 (57%)	29* (64%)
Serum albumin <35 g/L	2 (14%)	16 (35%)
Bone marrow involvement	1 (7%)	3 (7%)
IPI score		
0–1	2 (14%)	17 (37%)
2	8 (57%)	8 (17%)
3	1 (7%)	8 (17%)
4–5	3 (21%)	13 (28%)
NCCN-IPI		
0–1	0	0
2–3	9 (64%)	19 (41%)
4–5	3 (21%)	16 (35%)
≥6	2 (14%)	11 (24%)
CCI		
3–4	9 (64%)	30 (65%)
≥5	5 (36%)	16 (35%)
Cell-of-origin subtype		
Germinal centre B-like	6 (43%)	13 (38%)
Non-germinal centre B-like	8 (57%)	33 (72%)

	Complete response	Partial response	Stable disease	Progressive disease	Overall response	p value
All patients	28 (47%)	17 (28%)	10 (17%)	5 (8%)	45 (75%)	--
Sex						
Men	18 (47%)	11 (29%)	6 (16%)	3 (8%)	29 (76%)	0·76
Women	10 (46%)	6 (27%)	4 (18%)	2 (9%)	16 (73%)	--
Age						
60–69 years	7 (50%)	4 (29%)	2 (14%)	1 (7%)	11 (79%)	0·66
70–79 years	12 (40%)	9 (30%)	6 (20%)	3 (10%)	21 (70%)	--
≥80 years	9 (56%)	4 (25%)	2 (13%)	1 (6%)	13 (81%)	--
IPI score						
0–2	20 (57%)	10 (29%)	4 (11%)	1 (3%)	30 (86%)	0·023
3–5	8 (32%)	7 (28%)	6 (24%)	4 (16%)	15 (60%)	--
NCCN-IPI score						
2–3	18 (64%)	6 (21%)	4 (14%)	0 (0%)	24 (86%)	0·089
4–5	7 (37%)	7 (37%)	3 (16%)	2 (11%)	14 (74%)	--
≥6	3 (23%)	4 (31%)	3 (23%)	3 (23%)	7 (54%)	--
Subtype						
Germinal centre B-like	11 (58%)	5 (26%)	2 (11%)	1 (5%)	16 (84%)	0·63
Non-germinal centre B-like	17 (41%)	12 (29%)	8 (20%)	4 (10%)	29 (71%)	--

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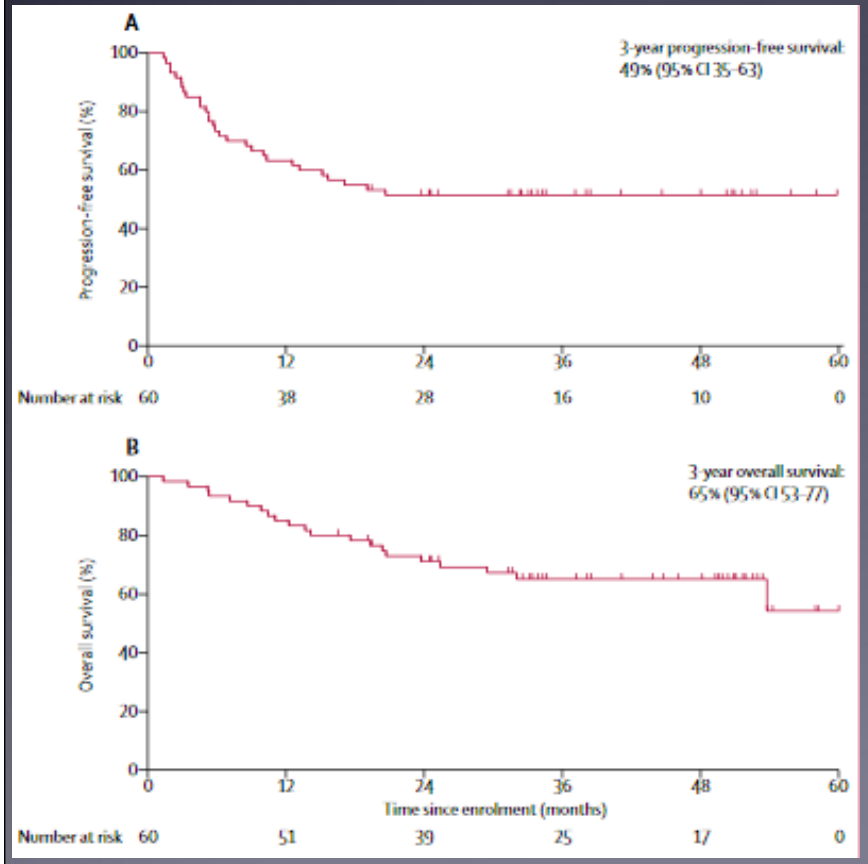
Qiu-Dan Shen*, Hua-Yuan Zhu*, Li Wang, Lei Fan, Jin-Hua Liang, Lei Cao, Wei Wu, Yi Xia, Jian-Yong Li, Wei Xu

Lancet Haematol 2018



	Progression-free survival				Overall survival			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	Log-rank p value	Hazard ratio (95% CI)	Log-rank p value	Hazard ratio (95% CI)	Log-rank p value	Hazard ratio (95% CI)	Log-rank p value
CCI ≥5	1·4 (0·7–3·0)	0·34	..	..	1·5 (0·6–3·6)	0·36	..	..
ECOG performance status score ≥2	1·2 (0·6–2·5)	0·59	..	..	1·7 (0·7–3·9)	0·26	..	..
Men	0·8 (0·4–1·7)	0·55	..	..	1·7 (0·7–4·0)	0·22	..	..
Bulky disease ≥7·5 cm	4·1 (1·5–10·9)	0·0050	3·0 (1·0–9·0)	0·044	2·4 (0·7–8·1)	0·18	..	..
≥2 extranodal sites	2·4 (1·2–5·0)	0·018	1·1 (0·4–2·9)	0·30	2·1 (0·9–5·1)	0·10	..	..
Serum albumin <35 g/L	2·2 (1·1–4·5)	0·034	0·7 (0·3–1·8)	0·46	2·6 (1·9–6·1)	0·033	1·1 (0·4–2·9)	0·80
Non-germinal centre B-like subtype	2·1 (0·9–5·2)	0·10	..	..	5·1 (1·2–22·3)	0·027	3·7 (0·8–17·0)	0·10
Lactate dehydrogenase >ULN	2·7 (1·3–5·6)	0·0060	0·7 (0·2–2·3)	0·59	2·9 (1·2–6·9)	0·015	1·0 (0·3–3·2)	0·99
β2-microglobulin >2·53 mg/L	5·2 (1·8–15·0)	0·0020	5·1 (1·7–15·0)	0·0030	7·1 (1·6–30·7)	0·0090	4·2 (0·9–18·8)	0·076
Ann Arbor stage III–IV	1·9 (0·9–4·2)	0·10	..	..	3·7 (1·2–11·1)	0·0096	1·3 (0·4–4·7)	0·64
NCCN-IPI score >4	1·8 (1·2–2·7)	0·0040	..	..	2·7 (1·4–4·9)	0·0020	..	..
IPI score 3–5	3·7 (1·7–7·7)	0·0010	2·6 (1·1–5·8)	0·024	4·9 (1·8–12·7)	0·0010	4·4 (1·6–11·9)	0·0040

	Grade 1–2	Grade 3	Grade 4
Neutropenia	11 (18%)	7 (12%)	2 (3%)
Thrombocytopenia	13 (22%)	3 (5%)	2 (3%)
Anaemia	18 (30%)	4 (7%)	0
Febrile neutropenia	2 (3%)	2 (3%)	1 (2%)
Nausea	8 (13%)	5 (8%)	0
Vomiting	9 (15%)	3 (5%)	0
Diarrhoea	2 (3%)	1 (2%)	0
Mucositis	2 (3%)	0	0
Neurological toxicity	1 (2%)	1 (2%)	0
Atrial fibrillation	1 (2%)	0	0
Heart failure	1 (2%)	1 (2%)	0
Creatinine elevation	0	1 (2%)	0
Elevation of aminotransferases	5 (8%)	0	0

Interpretations The R-GemOx regimen shows high efficacy and safety as a front-line treatment in an elderly patient subpopulation and might be a therapeutic option for management of diffuse large B-cell lymphoma in elderly patients.

Charlson comorbidity index

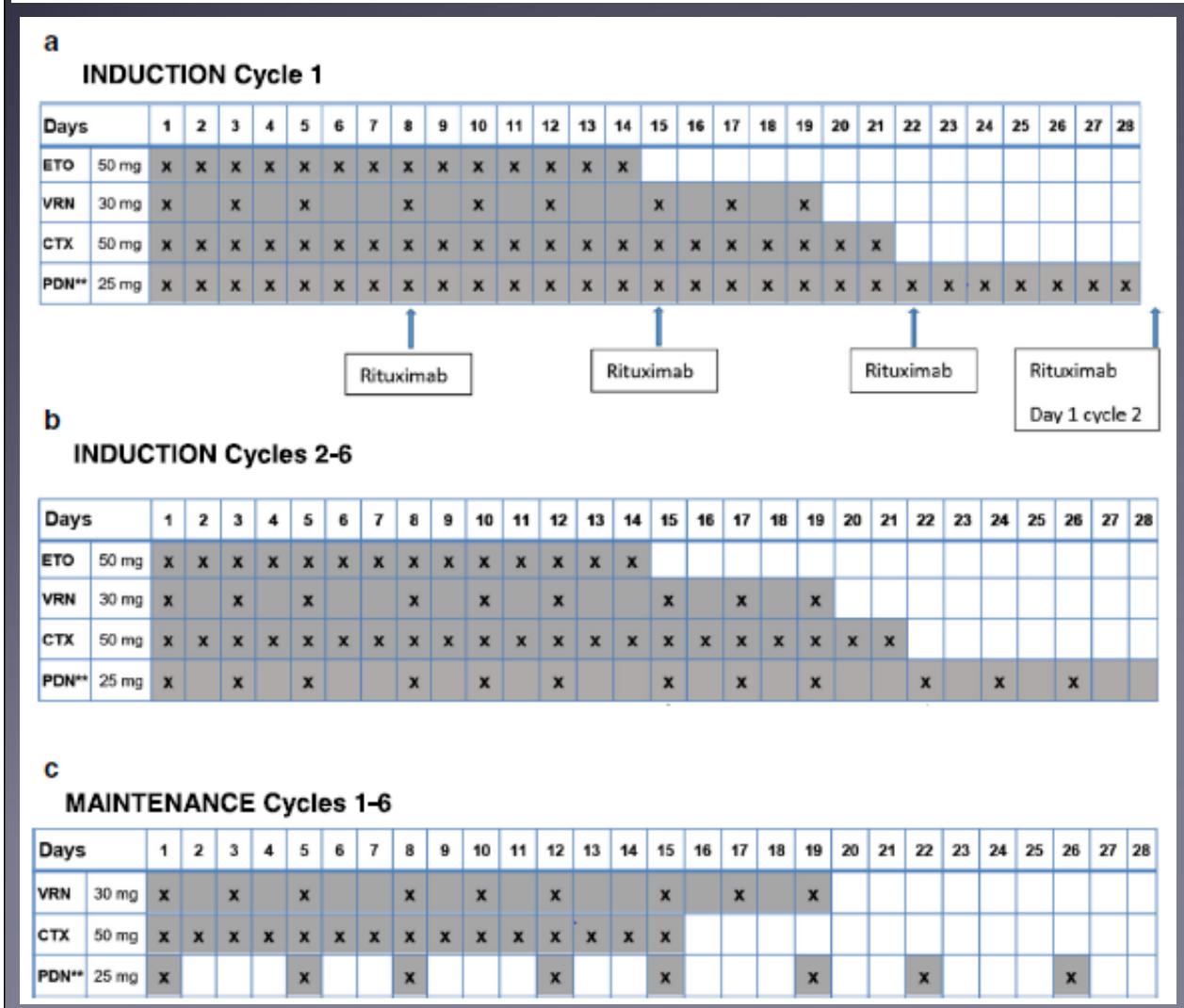
Comorbidities	Assigned weights for comorbidities
Myocardial infarction	1
Congestive heart failure	1
Peripheral vascular disease	1
Cerebrovascular disease	1
Dementia	1
Chronic obstructive pulmonary disease (COPD)	1
Connective tissue disease	1
Ulcer disease	1
Mild liver disease	1
Diabetes mellitus without end-organ damage	1
Hemiplegia	2
Moderate to severe chronic kidney disease	2
Diabetes with end-organ damage	2
Solid tumor	2
Leukemia	2
Lymphoma	2
Moderate to severe liver disease	3
Metastatic solid tumor	6
Acquired immunodeficiency syndrome (AIDS)	6

Add 1 point per decade to ages over 40 years.

The metronomic all-oral DEVEC is an effective schedule in elderly patients with diffuse large b-cell lymphoma

Investigational New Drugs (2019) 37:548–558

M. Christina Cox[1,2] · Sabrina Pelliccia[2] · Luigi Marcheselli[3] · Roberta Battistini[4] · Annalisa Arcari[5] · Paola Anticoli Borza[6] · Caterina Patti[7] · Ivana Casaroli[8] · Francesca di Landro[9] · Arianna Di Napoli[10] · Francesca Fabbri[11] · Matteo Caridi[10] · Agostino Tafuri[2,10] · Guido Bocci[12] · Gerardo Musuraca[11]



51 pazienti:

1) treatment-naïve frail ≥65y, o unfit e ≥85y;
2) R/R ≥55y.

Caregiver obbligatorio.

Profilassi antitrombotica per cicli VP16.

Tossicità gastrointestinale da VRN orale.

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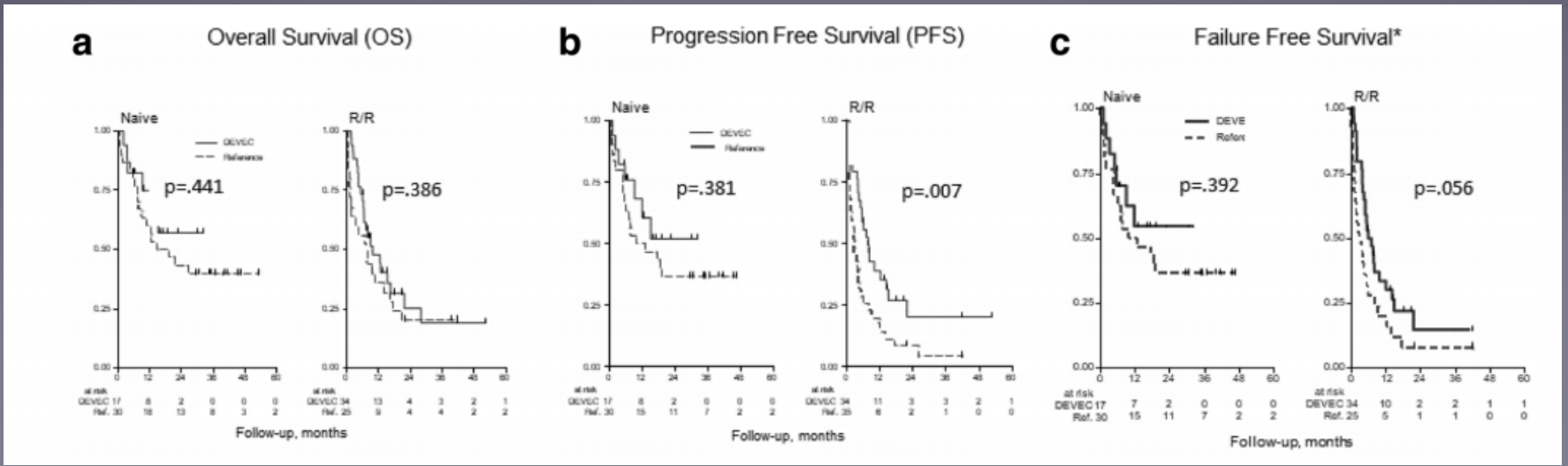
Factor	Naïve [*n*=47]			R/R [*n*=69]		
	DEVEC *n*=17	Reference *n*=30	*p*-value	DEVEC *n*=34	Reference *n*=35	*p*-value*
	n (%)	**n (%)**		**n (%)**	**n (%)**	
Median Age (range)	**85 (77-93)**	**83 (80-92)**	**0.498**	**78 (57-91)**	**72 (65-86)**	**0.002**
Gender Female	**5 (39)**	**14 (47)**	**0.743**	**13 (45)**	**19 (54)**	**0.616**
PS-Ecog >1	**13 (76)**	**9 (30)**	**0.003**	**14(41%)**	**NA**	**-**
Stage III-IV	**14 (82)**	**17 (57)**	**0.111**	**29 (85)**	**28 (80)**	**0.752**
IPI 4-5	**9 (60)**	**9 (30)**	**0.105**	**15 (44)**	**20 (60)**	**0.135**
[a]Frail (CGA)	**15 (88)**	**NA***		**17 (50)**	**0**	**<.001**
[b]CHT lines ≥2				**22 (65)**	**0**	**<.001**
[c]Refractory	**-**	**-**		**21 (62)**	**15 (43)**	**0.04**



OVERVIEW

Ref	Median Age	N	FU (m)	ORR/CR %	OS/PFS %	TRM%
Peyrade 2011 R miniCHOP	> 80	149	20	76/63	59/47 2 yrs	8
Park 2016 R Benda	80 (65/89)	24	29	78/52	10,2/5,7 m	0
Peyrade 2018 O miniCHOP	> 80	120	26,8	81/56	64/55,4 2 yrs	0
Shen 2018 R GemOx	> 80 (27%)	60	45	75/47	65/49 3 yrs	0
Storti 2018 R Benda	> 70 frail	45	33	62/53	51/38 2 yrs	4
Cox 2019 DeVEC	85 83	17 TN 34 RR	24 36	82/65 71/38	67/61 1 yrs 48/39	1,9

I linfomi primitivi cerebrali

- Il 20% di tutti i pazienti PCNSL ha > 80 anni,
- L'incidenza del PCNSL è aumentata da 0.1 per 100.000 negli anni '70 a 0.4 per 100.000 negli anni '80, e nei pazienti anziani di età compresa tra i 70 e i 79 anni è di 4,32 rispetto allo 0,08 del terzo decennio di vita.
- La sopravvivenza globale mediana (OS) di tutti i pazienti negli ultimi 40 anni è passata da 12,5 a 25 mesi, ma limitatamente ai pazienti di età inferiore ai 70 anni.
- Nella popolazione anziana (> 70 anni) è rimasta nell'intervallo di 6-7 mesi.
- Molti studi clinici escludono i pazienti di età superiore ai 70 anni (MATRIX).
- La frazione di pazienti che non vengono trattati con chemioterapia incrementa da 14% a 23% e al 44% nei gruppi di età di 61-70, 71-80 e >80 anni, rispettivamente.

Primary CNS Lymphoma in the Elderly: The Challenge.
T Siegal. Acta Haematol 2019;141:138–145.

I linfomi primitivi cerebrali

- CRR: 30%-69%
- regimi meno tossici da HD-MTX o l'MTX-procarbazina-vincristina (MPV) con o senza consolidamento con AraC (3-4 gr/mq/die d1-2) sono ugualmente efficaci anche oltre i 70 aa. ma con incremento di tossicità.
- TRM 14,4%.
- Nessuna evidenza sul ruolo del mantenimento (temozolamide, procarbazina, rituximab , lenalidomide). IBRUTINIB 560 mg?
- OS compresa tra 7,9 e 36 mesi, più lunga della PFS, relativamente breve, per effetto della terapia di salvataggio (WBRT) nonostante l'impatto negativo sulla qualità della vita.

Jahnke K. Ann Oncol. 2005 Mar;16(3):445–9
Siegal T. Acta Haematol 2019;141:138–145;
Kasenda B. Ann Oncol. 2015 Jul;26(7):1305–13;
Houillier C. J Neurooncol. 2017 Jun;133(2):315–20

Outcomes of the oldest patients with primary CNS lymphoma treated at Memorial Sloan-Kettering Cancer Center

Neuro-Oncology 14(10):1304–1311, 2012.

Mary R. Welch, Antonio Omuro, and Lisa M. DeAngelis

- 24 pazienti, età media 82 (range 80-90 anni).
- 13 (65%) VFG ≥50 mL/min, 7 (35%) tra 28 e 45 mL/min.
- MTX 2-3,5 g/mq ogni 2 settimane in 2 ore seguita 24 ore dopo rescue folinico per 5 cicli seguiti da HDAraC.
- In associazione a Vincristina 1-1,4 mg/mq d1 di ogni ciclo e procarbazina d1-7 100 mg/mq/die.

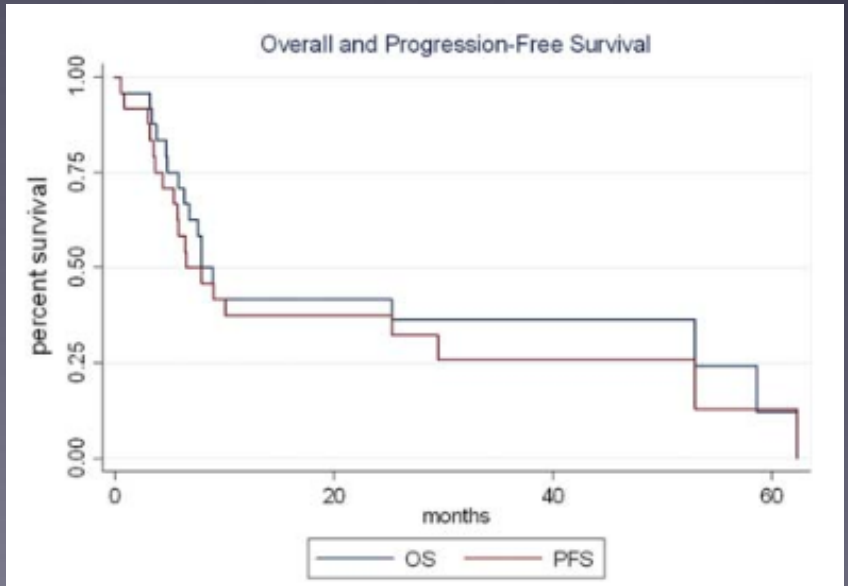


Fig. 1. Overall and progression-free survival in oldest PCNSL patients.

stadiazione ed inquadramento generale

Lymphoma	Geriatric assessment
Clinical examination (performance status, lymphoma clinical extension)	Physiological status
LDH levels, biochemical assessment	- Renal function - Cardiac function - Nutrition: albumin level, weight loss, body mass index (BMI), risk of infection
HBV, HCV, HIV serology	Global health status, "comprehensive geriatric assessment" (CGA)
Bone marrow assessment[a]	Assessment of comorbidities including classification according to severity grades
	Listing of medications
CT scan of the body (extension)	Evaluation of geriatric factors = dependencies with the ADL (Activities in Daily Living) and IADL (Instrumental Activities in Daily Living) questionnaires
18FDG/PET[b]	Mood evaluation with the GDS15 (Geriatric Depression scale) auto-questionnaire
	Geriatric syndromes (including vision and hearing problems, bladder problems, dizziness, falls, delirium (a kind of temporary confusion) and dementia mainly)
	Evaluation of life expectancy

Thieblemont C. Management of aggressive lymphoma in very elderly patients. Hematological Oncology. 2017;35(S1):49–53.

ESMO Consensus Conference on malignant lymphoma: general perspectives and recommendations for the clinical management of the elderly patient with malignant lymphoma

Annals of Oncology 29: 544–562, 2018

C. Buske[1*], M. Hutchings[2], M. Ladetto[3], V. Goede[4], U. Mey[5], P. Soubeyran[6], M. Spina[7], R. Stauder[8], M. Trněný[9], U. Wedding[10], P. Fields[11] & The ESMO Lymphoma Consensus Conference Panel Members[†]

Levels of evidence

I	Evidence from at least one large randomised, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomised trials without heterogeneity
II	Small randomised trials or large randomised trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case–control studies
V	Studies without control group, case reports, expert opinions

Grades of recommendation

A	Strong evidence for efficacy with a substantial clinical benefit, strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs,. . .), optional
D	Moderate evidence against efficacy or for adverse outcome, generally not recommended
E	Strong evidence against efficacy or for adverse outcome, never recommended

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1. Assessing fitness in elderly patients with malignant lymphoma			
Recommendations:			
1.1 The panel suggests that geriatric assessment should be included in the diagnostic process of clinical trials in order to assess patient fitness	II	B	100% yes (23 voters)
1.2 The panel suggests that a geriatric assessment is included in the diagnostic process to assess patient fitness in routine clinical practise. In cases when geriatric assessment is not possible, geriatric screening (e.g. G-8) can be carried out	II	B	100% yes (23 voters)
2. Assessing quality of life in elderly patients with malignant lymphoma			
Recommendations:			
2.1 Quality of life should be considered as a prognostic indicator of survival	I	A	100% yes (23 voters)
2.2 Quality of life should be included as a major end point in clinical trials in the elderly, either alone (e.g. in the palliative setting) or in combination with a survival end point (as a co-primary or composite end point)	II	B	100% yes (23 voters)
2.3 Other PROs can be considered, including maintenance of functional capacity/dependence, either alone or in combination with survival end points. This type of end point is encouraged in clinical trials but methodological questions remain to be solved. Standardised instruments such as ADL and IADL are available and their use during treatment in clinical practice is encouraged	III	C	100% yes (23 voters)

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7. Diagnostic work-up and treatment of elderly patients with DLBCL

Recommendations:

7.1	For patients treated with curative intent, diagnosis should be carried out in an expert haemato-pathology laboratory with full diagnostic capabilities (immunophenotypic and molecular) and staging should be with PET-CT	V	A
7.2	Cardiac assessment (LVEF) is required for patients treated with curative intent	V	A
7.3	The IPI score should be calculated	I	A
7.4	A CGA is recommended to guide treatment choice	III	A
7.5	The aim of treatment in fully fit patients who are <80 years old should be curative, with a full-dose anthracycline-based regimen preferred. R-CHOP is the recommended first-line treatment choice	I	A
7.6	For fully fit patients who are >80 years old without comorbidities, dose-attenuated R-CHOP may be appropriate	III	B
7.7	For relapsed fit (no organ dysfunction, PS 0–1, no comorbidities), transplant-eligible patients, appropriate salvage treatment with R–DHAP, R-ESHAP, R-ICE or R-GDP is indicated. In the event of an adequate response, ASCT is recommended	II	A
7.8	For transplant-ineligible patients, dose attenuated R-DHAP, R-ESHAP, R-ICE, or less intense regimens such as R-Gem-Ox, are appropriate	III	B
7.9	For transplant-ineligible patients, single-agent chemotherapies such as bendamustine or pixantrone may be considered	I (pixantrone) II (bendamustine)	C

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4. Diagnostic work-up and treatment of elderly patients with FL

Recommendations:

4.1	Elderly patients should be diagnosed based on lymph node histology whenever possible. The aim of staging is to discriminate between patients with limited disease and those with advanced stage disease. Any diagnostics that do not impact on treatment decisions should be avoided, particularly in terminally ill patients	V	A
4.2	Asymptomatic elderly patients should undergo a watch and wait strategy	I	A
4.3	Symptomatic patients with mild symptoms should be offered a chemotherapy-free approach such as rituximab single agent, if possible	III	B
4.4	For patients with high tumour burden tolerating chemotherapy, a rituximab/chemotherapy regimen such as BR is recommended (with bendamustine dose reduction or fewer treatment cycles, if necessary. Be aware of bendamustine-associated infections; consider antibacterial/antiviral prophylaxis)	I	A
4.5	For relapsed patients, rituximab/chemotherapy adjusted to the fitness of the patient is also standard in the elderly. Rituximab maintenance is optional both first line and in relapse.	III	B

Idelalisib should be used with caution in relapsed patients not responding to rituximab/chemotherapy because of its toxicity profile

Idelalisib

Ref.	n.	age	TX	FU m	ORR/CR (%)	OS/PFS	SAE %
Flinn 2014 Ph1/b Ind RR	64	64 (32-91)	Dose finding	n.a.	47/1.6	mDOR 18.4 m mPFS 7.6	Diarrea 35.9 Fatigue 35.9 Nausea 25 Transaminite 20.3
Gopal 2014 Ph2 Ind RR	122	64 (33-87)	300 mg	n.a.	57/6	20 m/11.3 m mDOR 12.5	Diarrea 43 fatigue 30, nausea 30 tosse 29 febbre 28 Transaminite 13 6 morti tossiche
Salles 2017 Ph2 FL RR	72	62 (33-84)	300 mg	24	55.6/13.9	69%/n.r. mPFS 11 m in CR 30 m mDOR 10.8	Diarrea 51.4 Tosse 31.9 febbre 29.2 fatigue 27.8 nausea 27.8 3 morti tossiche
Eyre 2017 UK compassionate	79	64 (29-86)	300 mg	6	57/15	n.r/6 Responders 14	Diarrea 5 Polmonite 4 Transaminite 1 1 morte tossica

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5. Diagnostic work-up and treatment of elderly patients with MCL

5.2 For elderly fit patients, the following chemo-immunotherapeutic regimens are recommended as the preferred first-line treatment options in routine clinical practice:		
1. R-CHOP followed by rituximab maintenance	I	A
2. BR	I	A
3. VR-CAP	I	A
4. R-BAC	V	B
5.3 For vulnerable elderly patients, dose-adapted chemo-immunotherapeutic regimens are considered appropriate. Options include dose-reduced BR, R-CVP or R-CLB	V	B
5.4 For vulnerable patients with severe comorbidities, mild chemo-immunotherapeutic regimens like R-CLB, (dose-reduced) BR or PEP-C are considered appropriate	V	B
5.5 While newer targeted drugs such as ibrutinib and lenalidomide might offer benefits, particularly in vulnerable patients, no data are available from clinical trials for this subset of patients and therefore clear recommendations cannot be given. For relapsed or refractory disease, treatment should be adapted to the age and PS of the patient. Besides non-cross-resistant combination regimens, treatment options include:		
1. Ibrutinib	II	A
2. Lenalidomide ± rituximab	II	B
3. Temsirolimus ± rituximab	II	B
4. Bortezomib	V	B

IBRUTINIB

N	Age in years (range)	Median no. prior regimens (range)	Dose	Response rate	Median duration of response/PFS	Survival	Reference
Ibrutinib							
9	65 (41–82) [entire cohort]	3 (1–10) [entire cohort]	Phase I dose-escalation or fixed dose of 8.3 mg/kg or 560 mg daily	78% ORR 33% CR 44% PR 11% SD	13.6 mo PFS [entire cohort]	Not reported	Advani et al. (10)
111	68 (40–84)	3 (1–6)	560 mg daily	68% ORR 21% CR 47% PR	17.5 mo DOR 13.9 mo PFS	OS 58% (18 mo)	Wang et al. (14)
Bortezomib							
155	67 (30–86)	1 (1–3)	1.3 mg/m^2 d1, 4, 8, 11; 21-d cycle	33% ORR 8% CR/CRu 26% PR 33% SD	9.2 mo DOR	OS 69% (1 y)	Fisher et al. (23)
40	67.5 (45–83)	2 (0–4)	1.5 mg/m^2 d1, 4, 8, 11; 21-d cycle	47% ORR 12.5% CR 35% PR 38% SD	5.3 mo PFS	—	O'Connor et al. (25)
30	67 (48–79)	45% untreated 38% 1 prior 17% 2 prior	1.3 mg/m^2 d1, 4, 8, 11; 21-d cycle	46% ORR 4% CRu 43% PR 43% SD	10 mo DOR	—	Belch et al. (24)
Lenalidomide							
134	67 (43–83)	4 (2–10)	25 mg daily d1–21; 28-d cycles	28% ORR 7.5% CR/CRu 20% PR 29% SD	16.6 mo DOR 4.0 mo PFS	OS 19.0 mo (median)	Goy et al. (26)
57	68 (33–82)	3 (1–13)	25 mg daily d1–21; 28-d cycles	35% ORR 12% CR/CRu 23% PR 44% SD	16.3 mo DOR 8.8 mo PFS	—	Zinzani et al. (33)
26	66 (45–81)	3 (2–7)	25 mg daily d1–21; 28-d cycles; 15 mg maintenance (responders)	31% ORR 8% CR 23% PR 23% SD	22.2 mo DOR 3.9 mo PFS	OS 10.0 mo (median)	Eve et al. (34)
Temsirolimus (175/75-mg dosing arm only)							
54	68 (44–87)	3	175 mg weekly × 3 wks, then 75 mg weekly	22% ORR 2% CR 20% PR	7.1 mo DOR 4.8 mo PFS	OS 11.1 mo (median)	Hess et al. (27)

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6. Diagnostic work-up and treatment of elderly patients with PTCL

Recommendations:

6.1	The final histological diagnosis requires full analysis and integration of the clinical context and expert haematopathological review	IV	A
6.2	Whenever possible, patients should be entered into clinical trials. First-line regimes for elderly patients should be based on a CHOP induction backbone	III	B
6.3	Whenever possible, patients should be entered into clinical trials testing novel agents. However, for elderly relapsed patients considered unsuitable for clinical trials, treatment options include:		
	1. Salvage chemotherapy with gemcitabine or platinum-containing agents	IV	C
	2. Novel agents such as brentuximab vedotin monotherapy for patients with CD30+ T-cell lymphoma	III	B

LINFOMA DI HODGKIN

- Istotipo CM, più spesso stadio avanzato e sintomi B, Epstein-Barr virus (EBV) correlato.
- bassa tolleranza al trattamento a causa di comorbidità preesistenti al di sopra dei 60 anni di età.
- Discordanza di incidenza tra i dati di registro e gli studi clinici: circa 30% nei registri vs meno del 10% di paz > 60 aa nei trials clinici.
- Prognosi migliorata ma in misura inferiore rispetto ai più giovani.
- Stadio I-II favorevole: 2 ABVD+ 20 Gy IF-RT, CR 88% ma PD nel 3%, 5 yrs PFS 79% rispetto 96%.
- Stadio II sfavorevole. TRM inaccettabile dopo BEACOPP anche standard dose
- tossicità polmonare indotta da bleomicina (BLT) per cui vengono raccomandati non più di 2 cicli con bleomicina.

Björkholm . Eur J Haematol. 2018;101:106–114
Böll B. British Journal of Haematology, 2019,184,82–92
Goyal G.Clinical Lymphoma, Myeloma and Leukemia, 2017, 17,812–818

LINFOMA DI HODGKIN

- ChlVPP poco utile. Alternative: PVAG, VEPEMB, Lenalidomide, everolimus, panobinostat, idelalisib, pochi dati su nivolumab e pembrolizumab.
- Brentuximab vedotin- AVD: il sottogruppo di pazienti anziani non ha beneficiato dell'associazione per aumento della tossicità grave, compresa la neutropenia febbrile in più di un terzo dei pazienti (37%).
- Brentuximab vedotin/Bendamustina: ORR/CR 100%/88, ma con tossicità severe nella maggior parte dei pazienti (Friedberg 2017). Il 65% dei pazienti ha subito eventi avversi e due decessi per tossicità. La combinazione di brentuximab vedotin/dacarbazina è meglio tollerata ma con tasso di CR 62% e PFS mediana 17,9 mesi.
- Studio Nordic Lymphoma Group-GHSG (Böll, ASH 2018): protocollo B-CAP (brentuximab vedotin, ciclofosfamide, doxorubicina, prednisone), per pazienti con CIRS-G ≤6 in totale e ≤3 per sistema d'organo) per 6 cicli: 49 pazienti (96% stadio > III), età media 66 aa (range 60-84). Su 48 pazienti valutabili: ORR 98%, CR 21 pazienti, PR 26 pazienti, tasso di risposta metabolica completa del 65%.

Connors N Engl J Med 2018; 378:331-344
Friedberg J.W. Blood 2017 ,130,2829–2837.

Multicenter Phase II Study of Sequential Brentuximab Vedotin and Doxorubicin, Vinblastine, and Dacarbazine Chemotherapy for Older Patients With Untreated Classical Hodgkin Lymphoma

Andrew M. Evens, Ranjana H. Advani, Irene B. Helenowski, Michelle Fanale, Sonali M. Smith, Borko D.

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- HL classico
- > 60 anni
- malattia ≥ stadio II
- PS 0 a 2
- PET/CT+
- malattia bidimensionale misurabile > 1,5 cm,
- frazione di eiezione cardiaca 45%.
- ADL, IADLs, Cumulative Illness Rating Scale (CIRS).
- 2 Bv (1,8 mg/kg una volta ogni 3 settimane), AVD per sei cicli, consolidamento 4 Bv.

Characteristic	No. (N = 48)*	%
Age, years		
60-70	25	52
71-80	15	31
> 80	8	17
Sex		
Female	18	37
Male	30	63
Histology		
Nodular sclerosis	22	46
Mixed cellularity	12	25
Classic, not otherwise specified	12	25
Lymphocyte rich	2	4
ECOG PS		
0	19	40
1	20	41
2	9	19
B symptoms	18	37
Albumin		
Low (< 4.0 g/dL)	22	46
International Prognostic Score		
0-2	20	42
3-7	28	58
Bone marrow		
Involved	11	23
Bulky disease (≥ 10 cm)	5	10
Stage		
II†	9	19
III	18	37
IV	21	44
Median CIRS-G score (range)	7 (0-20)	

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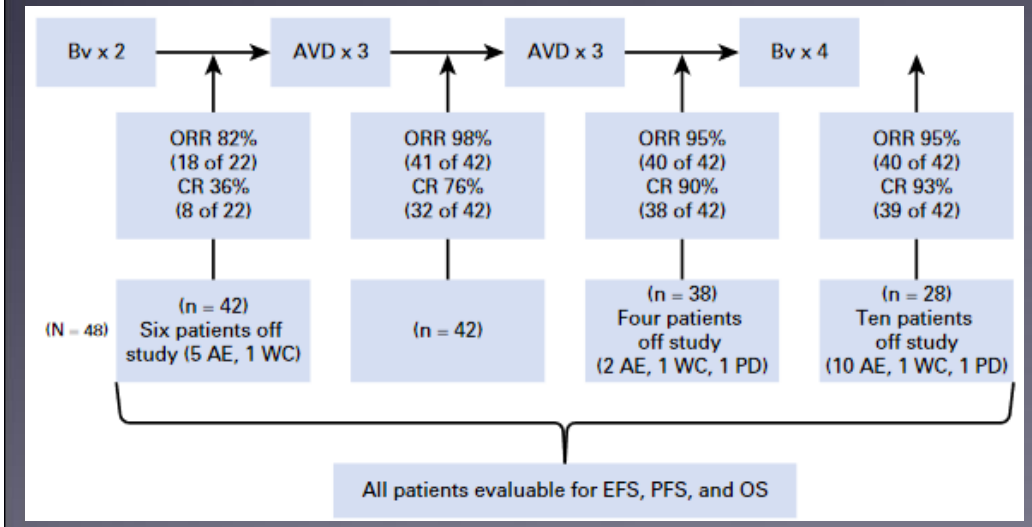

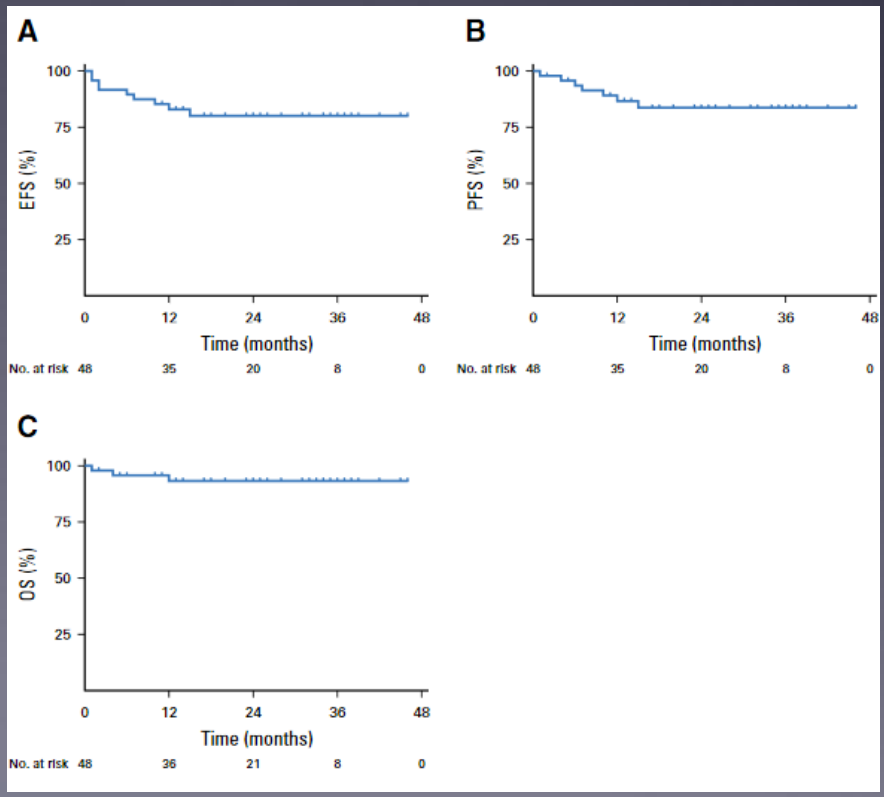

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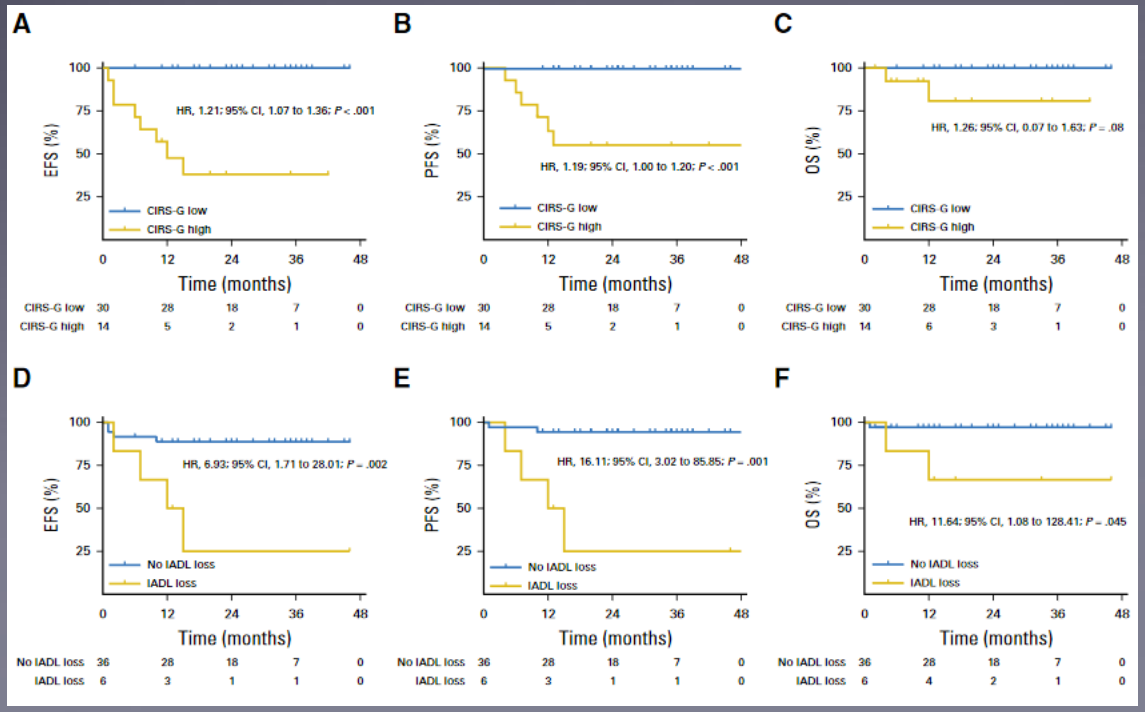
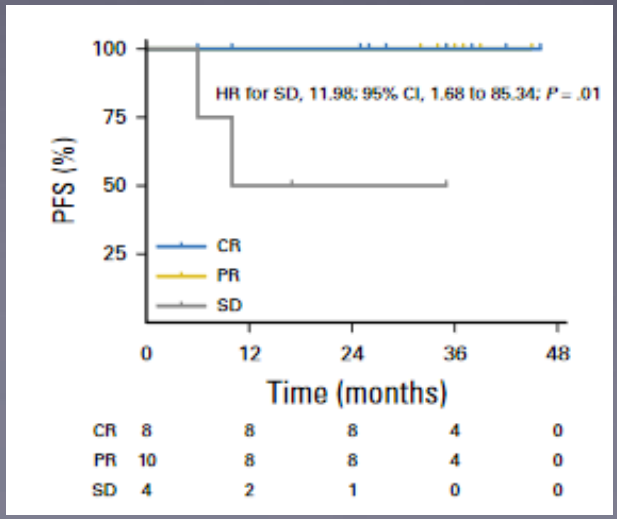
Variable*	Progression-Free Survival SHR†	95% CI	P
Univariable			
Age (continuous variable)‡	1.16	1.04 to 1.26	.005
Female sex	4.97	0.96 to 25.65	.06
Loss of IADLs	14.88	2.68 to 82.52	.002
CIRS-G score (> 10)	1.20	1.06 to 1.38	.005
Mixed cellularity *v* nodular sclerosis histology	0.25	0.06 to 1.1	.07
Multivariable			
Age (continuous variable)	1.15	0.94 to 1.40	.17
Loss of IADLs	13.02	1.0 to 173.53	.05
CIRS-G score (> 10)	1.05	0.84 to 1.30	.68





L'esperienza dell'Ematologia di Treviso: 2014-2019

NHL: 451

Over 80: 49

25 (51%) DLBCL:

10 RCOMP: 1 in corso, 2 refrattari, 7 vivi in CR a 1,2,3,3,4,5,5 anni

4 R-Benda: 2 deceduti refrattari, 2 deceduti per II neoplasia e ESA

7 cure palliative

5 FL, 5 MCL, 7 MZL, 3 T-NHL, 3 WM, 1 L Linfocitico

HD: 117

Over 80:2 (1,7%) di cui

89enne radiotrattato in CR a 4 anni,

83enne 4 MyBVD in CR a 2 anni

Comprehensive geriatric assessment is an essential tool to support treatment decisions in elderly patients with diffuse large B-cell lymphoma: a prospective multicenter evaluation in 173 patients by the Lymphoma Italian Foundation (FIL)

Alessandra Tucci[1], Maurizio Martelli[2], Luigi Rigacci[3], Paola Riccomagno[4], Maria Giuseppina Cabras[5], Flavia Salvi[6], Caterina Stelitano[7], Alberto Fabbri[8], Sergio Storti[9], Stefano Fogazzi[1], Salvatrice Mancuso[10], Maura Brugiatelli[11], Angelo Fama[2], Paolo Paesano[2], Benedetta Puccini[3], Chiara Bottelli[1], Daniela Dalceggio[1], Francesco Bertagna[12], Giuseppe Rossi[1] & Michele Spina[13]; for the Italian Lymphoma Foundation (FIL)

Leukemia & Lymphoma, April 2015; 56(4): 921–926

Table IV. Overall survival time according to patient and treatment characteristics (univariate and multivariate Cox regression analysis).

Variables	Univariate HR (95% CI)	*p*-Value	Multivariate HR (95% CI)	*p*-Value
Age < 80 vs. ≥ 80 years	2.67 (1.61–4.44)	0.0002		
Stage I–II vs. III–IV	1.59 (0.92–2.74)	0.09		
IPI (intermediate-low/low vs. intermediate-high/high)	3.72 (1.80–7.68)	0.0003	4.60 (1.35–15.64)	0.008
CGA	5.61 (2.95–10.64)	0.0001	3.69 (1.09–12.51)	0.03
ADL (≤ 5 vs. 6)	0.3 (0.17–0.51)	0.0001		
IADL (≤ 6 vs. ≥ 7)	0.24 (0.14–0.41)	0.0001		
CIRS-G grade 2 (< 5 vs. ≥ 5)	2.89 (1.04–8.03)	0.04		
CIRS-G grade 3–4 (0 vs. ≥ 1)	2.14 (1.22–3.73)	0.007		
Curative vs. palliative treatment approach	0.27 (0.16–0.46)	0.0001		
Treatment dose (< 70% vs. ≥ 70%)	0.38 (0.17–0.86)	0.02		

IPI, International Prognostic Index; CGA, comprehensive geriatric assessment; ADL, activity of daily living; IADL, instrumental activity of daily living; CIRS-G, Cumulative Illness Rating Score for Geriatrics; HR, hazard ratio; CI, confidence interval.

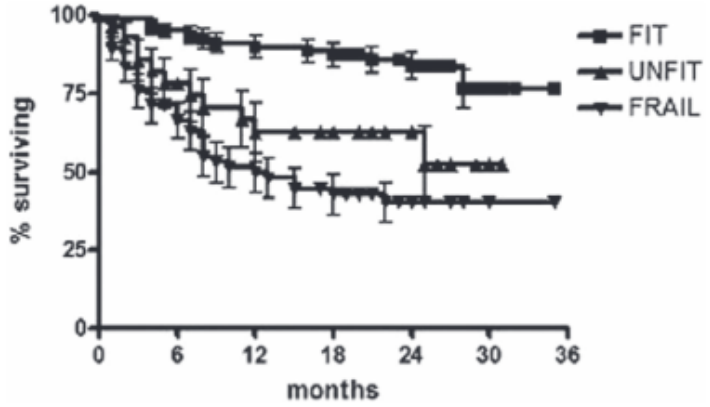


Figure 1. Actuarial overall survival curves of elderly patients with DLBCL classified as "fit," "unfit" and "frail" according to CGA, independent of treatment received.

Il CGA utilizzato è un metodo efficace per identificare pazienti anziani con DLBCL che possono beneficiare di un approccio curativo con immunochemioterapia contenente antraciclina. Suggerisce inoltre la potenziale utilità di identificare diversi gruppi a rischio nella categoria dei pazienti non fit, dimostrando che esiste una proporzione di pazienti unfit che potrebbero ottenere benefici significativi se trattati con intento curativo.

UTILITA' DEL CIRCS: CALCOLATORE ON LINE SUL SITO GIMEMA

CIRS

CIRS

	Points
Cuore	0
Sistema Vascolare	0
Sistema Ematopoietico	0
Apparato Respiratorio	0
Occhi, Orecchie, Naso, Gola e Laringe	0
Apparato Gastrointestinale Superiore	0
Apparato Gastrointestinale Inferiore	0
Fegato	0
Sistema Renale	0
Apparato Genitourinario	0
Apparato Muscolo-scheletrico/tegumentario	0
Sistema Neurologico	0
Sistema Endocrino/metabolico e mammella	0
Malattie Psichiatriche	0
CIRS SCORE Nessun	0

Punteggio CIRS
0→Nessun problema
1→Problema attuale lieve o problema precedente rilevante.
2→Disabilità o morbilità moderata e/o necessità di terapia di prima linea.
3→Patologia grave e/o disabilità costante e rilevante e/o problemi cronici difficili da controllare.
4→Patologia molto grave e/o necessità di trattamento urgente e/o insufficienza di un organo e/o disabilità funzionale grave.

2. Categoria di Rischio	
Risk factors (n)	Risk category
0	Nessun problema
1	Problema Lieve
2	Disabilità moderata
3	Patologia grave
4	Patologia molto grave

Aggiorna Reset Stampa

UTILIZZARE IL CIRS: i limiti dello score 0-1

- LA SITUAZIONE RENALE: il calcolo della VFG, imaging renale.
- IL RISCHIO CARDIOVASCOLARE: BMI, colesterolo, HDL, LDL.
- LA SITUAZIONE METABOLICA: alterata glicemia a digiuno, Hb glicata, danno d'organo correlato
  - nefropatia (proteinuria frazionata)
  - neuropatia
- LA SITUAZIONE NUTRIZIONALE: B12, vitamina D.
- LA SITUAZIONE NEUROPSICOLOGICA.

considerazioni

- La fitness del paziente DEVE essere verificata anche durante la terapia ed al termine, non solo in fase di definizione del programma
- Supporto famigliare (L104): consapevolezza dell'impegno necessario al di fuori dell'ospedale
- Accessibilità a centro hub
- Accessibilità a centro spoke
- Coordinamento hub and spoke: ruolo della REV
- Gestione delle complicanze: differenze tra hub and spoke

Unanswered questions

- Quanto sono effettivamente concretizzabili nella pratica quotidiana i dati di letteratura?
- Sono disponibili risorse strutturali? Ovunque?
- Sono disponibili risorse professionali? Ovunque?
- Sono sostenibili i costi a lungo termine per il paziente e per i famigliari?
- I costi di trattamento ed indotti (es. L104) di un «grande anziano» fit sono sostenibili?
- Quali informazioni devono essere fornite nella somministrazione del consenso informato a paziente e famigliari per un scelta consapevole del percorso terapeutico?