Casi Clinici: Leucemia linfatica cronica

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CAGLIARI

10 Luglio 2023

T Hotel

Disclosures of Brunella Mola

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
No dislosures to declare							

Marzo 2018

Hb	WBC	Ne	Ly	PLT
13,8 g/dl	15 600/mmc	5100/mmc	9500/mmc	160 000/mmc

70 anni

Non LN

Non epatosplenomegalia

APR:

- Ipertensione arteriosa sistemica
- Dislipidemia
- Ex fumatore

Marzo 2018

Immunofenotipo SVP → linfociti B monoclonali per la catena leggera lambda (bassa intensità), CD20+ Dim, CD5+, CD 200+, CD23+, CD10-,

LLC stadio A Binet/ 0 Rai → W&W

Classical immunophenotype of lower grade lymphoproliferative disorders

	CD5	CD19	CD20	CD23	CD10	CD25	CD103	CD200	sIg
CLL	+	+	Dim	+	–	+/–	–	+	Dim
MCL	+	+	Bright	–/Dim	–	+/–	–	–	Bright
FL	–	+	+	+/–	+	–	–	–	+
MZL	–/+	+	Bright	–/+	–	+/–	–	–	+/Bright
HCL	–	Bright	Bright	–	–	+	+	+	+
HCL variant	–	Bright	Bright	–	–	–	+	–	+
WM/LPL	–/+	+	+	+/–	–/+	+/–	–	+	+/Variable
B-PLL	–	+	Bright	–/+	–	–	–	–/+	Bright

The order of descriptors reflects the predominant expression pattern (ie, +/– implies that most cases express the antigen). "Bright" and "Dim" refer to expression levels relative to that of normal B lymphocytes.

CD: cluster of differentiation; sIg: surface immunoglobulin; CLL: chronic lymphocytic leukemia; MCL: mantle cell lymphoma; FL: follicular lymphoma; MZL: marginal zone lymphoma; HCL: hairy cell leukemia; WM: Waldenström macroglobulinemia; LPL: lymphoplasmacytic lymphoma; B-PLL: B cell prolymphocytic leukemia.

Gennaio 2022

Hb	WBC	Ne	Ly	PLT
11,7 g/dl	105 500/mmc	1800/mmc	92 030/mmc	82 000/mmc

- Milza 16 cm
- LN 3 cm in sede periaortica paracavale e peri iliaca bilaterale

Stadio Binet C, Rai IV → Indicazione a terapia

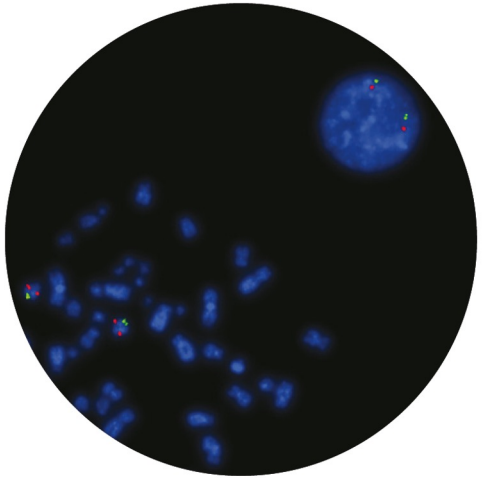
Table 1. Staging systems for CLL

Stage		Definition
Binet system		
Binet A		Hb ≥100 g/l (6.21 mmol/l), platelets ≥100 × 10^9/l <3 involved lymphoid sites[a]
Binet B		Hb ≥100 g/l (6.21 mmol/l), platelets ≥100 × 10^9/l ≥3 involved lymphoid sites[a]
Binet C		Hb <100 g/l (6.21 mmol/l), platelets <100 × 10^9/l
Rai system		
Low-risk	Rai 0	Lymphocytosis >5 × 10^9/l
Intermediate-risk	Rai I	Lymphocytosis and lymphadenopathy
	Rai II	Lymphocytosis and hepatomegaly and/or splenomegaly with/without lymphadenopathy
High-risk	Rai III	Lymphocytosis and Hb <110 g/l (6.83 mmol/l) with/without lymphadenopathy/organomegaly
	Rai IV	Lymphocytosis and platelets <100 × 10^9/l with/without lymphadenopathy/organomegaly

B. Eichhorst, Chronic lymphocytic leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up, 2020

Profilo di rischio

- IGVH: Mutato
- FISH: del 13q14 → Prognosticamente favorevole
- TP53: Mutato
- NOTCH-1: Negativo



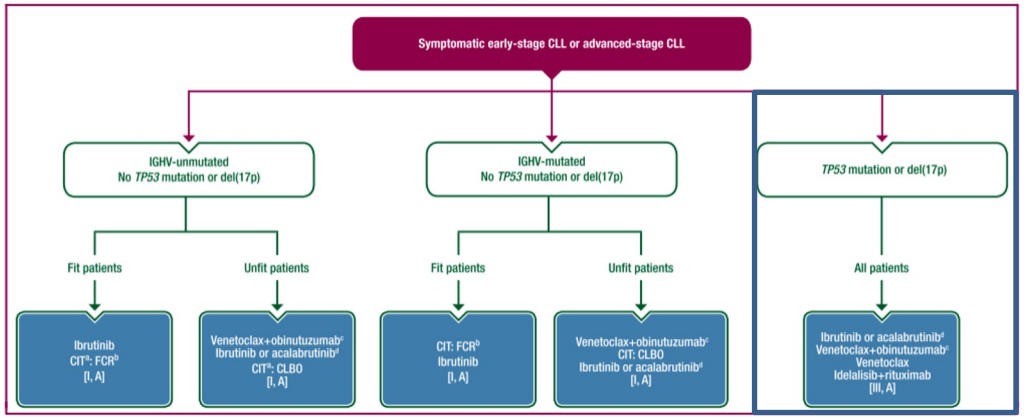
PROGNOSTIC INFORMATION FOR CLL/SLL[a]

Method of Detection	Prognostic Variable	Risk Category
Interphase cytogenetics (FISH)[b]	del(17p)	Unfavorable
	del(11q)	Unfavorable
	+12	Intermediate
	Normal	Intermediate
	del(13q) (as a sole abnormality)	Favorable
DNA sequencing[c]	*TP53*	Wild-type: Favorable Mutated: Unfavorable
	IGHV	>2% mutation: Favorable ≤2% mutation: Unfavorable
CpG-stimulated metaphase karyotype	CK[d] (≥3 unrelated clonal chromosome abnormalities in more than one cell on karyotype)	Unfavorable

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) - Version 3.2023 — June 12, 2023

Opzioni di trattamento

ESMO



NCCN

SUGGESTED TREATMENT REGIMENS[a,b,c,d]
CLL/SLL without del(17p)/*TP53* mutation
(alphabetical by category)

FIRST-LINE THERAPY[e]		
Patients age ≥65 y OR Patients age <65 y with significant comorbidities (creatinine clearance [CrCl] <70 mL/min)	Preferred regimens • Acalabrutinib[f] ± obinutuzumab (category 1) • Ibrutinib[f] (category 1) • Venetoclax[f,g] + obinutuzumab (category 1) • Zanubrutinib[f]	Other recommended regimens • Bendamustine (70 mg/m² in cycle 1 with escalation to 90 mg/m² if tolerated) + anti-CD20 monoclonal antibody[d,h,i] • Chlorambucil + obinutuzumab • Obinutuzumab • High-dose methylprednisolone (HDMP) + rituximab or obinutuzumab (category 2B) • Ibrutinib[f] + obinutuzumab (category 2B) • Chlorambucil (category 3) • Rituximab (category 3)
Patients age <65 y without significant comorbidities	Preferred regimens • Acalabrutinib[f] ± obinutuzumab (category 1) • Ibrutinib[f] (category 1) • Venetoclax[f,g] + obinutuzumab • Zanubrutinib[f]	Other recommended regimens • Bendamustine + anti-CD20 monoclonal antibody[d,h,j] • FCR (fludarabine,[k] cyclophosphamide, rituximab)[j,l] (preferred for patients with IGHV-mutated CLL) • Ibrutinib[f] + rituximab (category 2B) • FR (fludarabine[k] + rituximab)[i,m] (category 3) • HDMP + rituximab or obinutuzumab (category 3)

NCCN Guidelines® Insights: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma, Version 3.2022

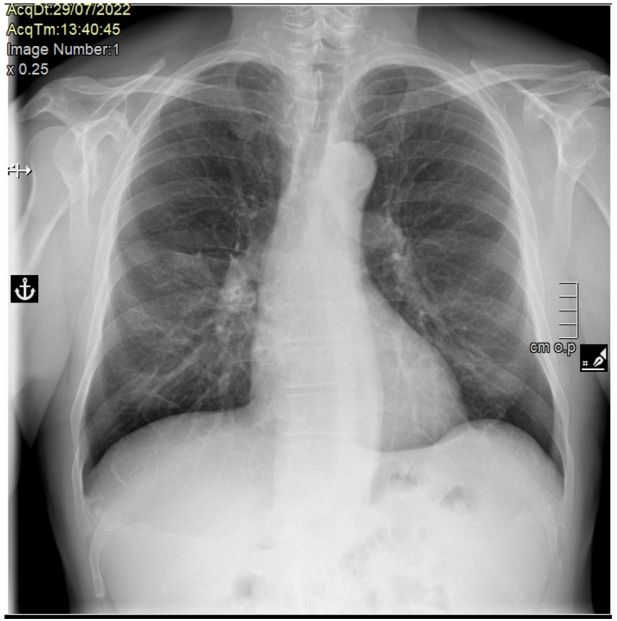
B. Eichhorst, Chronic lymphocytic leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up, 2020

Luglio – Ottobre 2022

Hb	WBC	Ne	Ly	PLT
10,9 g/dl	129 200/mmc	2770/mmc	89 990/mmc	68 000/mmc

- Febbre (T max 39,4°C), tosse

  Rx → torace flogosi polmonare



- Episodi ricorrenti di IVU

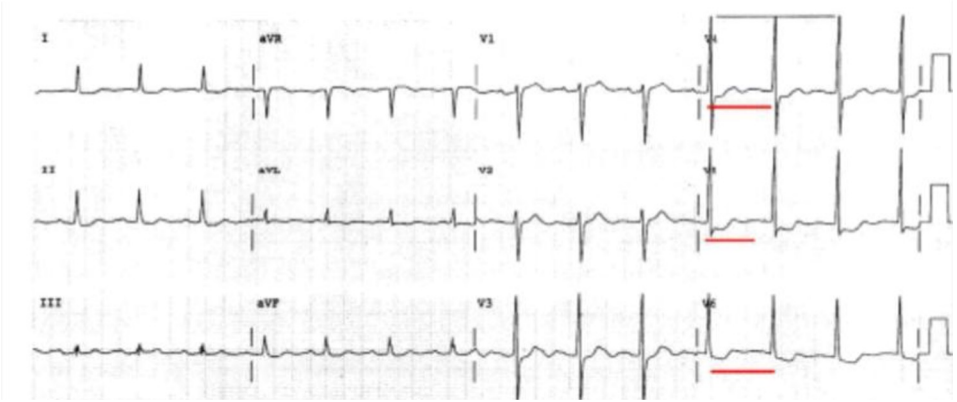
Dicembre 2022

Hb	WBC	Ne	Ly	PLT
10,7 g/dl	134 000/mmc	1880/mmc	112 000/mmc	69 000/mmc

Rivalutazione cardiologica pre-terapia→ riscontro di dispnea e dolore toracico da sforzo.

Dicembre 2022

Test da sforzo→ riscontro di sottoslivellamento in sede anteriore



→ Coronarografia controindicata per piastrinopenia

→Controindicazione a Ibrutinib

Table 2. Phase III Randomized Studies of Small Molecule Inhibitor Therapy for Relapsed/Refractory CLL/SLL

Trial	Regimen	Patients n	Patient Characteristics	Median Follow-Up	ORR	PFS	OS
ASCEND[21]	**Acalabrutinib**	155 [del(17p), n=28; mutated *TP53*, n=39]	Median age, 67–68 y with ECOG PS ≤2 and adequate hematologic, hepatic, and renal function	36 mo	83%	Median: NR 36-mo: 63% (HR, 0.29; *P*<.0001)	36-mo: 80%
	Investigator's choice (IdR or BR)	155 (IdR, n=119; BR, n=36); [del (17p), n=21; mutated *TP53*, n=34]		36 mo	85%	Median: 17 mo 36-mo: 21%	36-mo: 73%
RESONATE[22]	**Ibrutinib**	195 [del(17p), n=63; mutated *TP53*, n=79]	Median age, 67 y	74 mo	91% (11% CR)	Median: 44 mo 60-mo: 40%	Median: 68 mo
	Ofatumumab	196 [del(17p), n=64; mutated *TP53*, n=68]		74 mo		Median: 8 mo 60-mo: 3%	Median: 65 mo
ELEVATE-RR[27]	**Acalabrutinib**	268	Age ≥18 y; ECOG PS ≤2 and the presence of del(17p) and/or del(11q)	41 mo	81% (3% CR)	Median: 38 mo (for both treatment arms)	Median: NR (in either arm)
	Ibrutinib	265		41 mo	77% (4% CR)		
ALPINE[31]	**Zanubrutinib**	207 [del(17p) and/or mutated *TP53*, n=41]	Median age, 67 y; ECOG PS ≥1; relapsed/refractory disease ≥1 prior systemic therapy	15 mo	78%	12-mo: 95% (HR, 0.40; *P*=.0007)	12-mo: 97%
	Ibrutinib	208 [del(17p) and/or mutated *TP53*, n=38		15 mo	63% (1% CR)	12-mo: 84%	12-mo: 93%
MURANO[25]	**Venetoclax + rituximab**	194 [del(17p), n=46; mutated *TP53*, n=48]	Age ≥18 y; ECOG PS 0–1; relapsed/refractory disease requiring therapy and adequate bone marrow, liver, and kidney function	59 mo	92% (8% CR)	Median: 54 mo (HR, 0.19; *P*<.0001)	5-y: 82% (HR, 0.40; *P*<.0001)
	Bendamustine + rituximab	195 [del(17p), n=46; mutated *TP53*, n=51]		59 mo	72% (4% CR)	Median: 17 mo	5-y: 62%

Abbreviations: BR, bendamustine + rituximab; CLL, chronic lymphocytic leukemia; CR, complete response; HR, hazard ratio; IdR, idelalisib + rituximab; NR, not reached; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PS, performance status; SLL, small lymphocytic lymphoma.

ELEVATE-RR CV AEs

Eventi CV acalabrutinib vs ibrutinib: **24,1%** con **8,6%** di grado 3 e 4 vs **30%** con **9,5%** di grado 3 e 4

AF acalabrutinib vs ibrutinib **9,4%** vs **16%**

	Acalabrutinib (n = 266)		Ibrutinib (n = 263)	
Events	**Any Grade**	**Grade ≥ 3**	**Any Grade**	**Grade ≥ 3**
Hypertension events[a]	25 (9.4)	11 (4.1)	61 (23.2)	24 (9.1)
Events/100 person-months	0.444	0.133	1.243	0.435
Patients with a history of hypertension	16 (64.0)	9 (81.8)	30 (49.2)	16 (66.7)
Cardiac events	64 (24.1)	23 (8.6)	79 (30.0)	25 (9.5)
Ventricular arrhythmia or cardiac arrest	1 (0.4)	1 (0.4)	5 (1.9)	3 (1.1)
Cardiorespiratory arrest	1 (0.4)	1 (0.4)	0	0
Cardiac arrest	0	0	2 (0.8)	2 (0.8)
Ventricular arrhythmia	0	0	1 (0.4)	0
Ventricular extrasystoles	0	0	1 (0.4)	0
Ventricular fibrillation	0	0	1 (0.4)	1 (0.4)
Atrial fibrillation[b]	25 (9.4)[c]	13 (4.9)	42 (16.0)	10 (3.8)
Events/100 person-months	0.366	0.155	0.721	0.124
Age 75 years or older	8 (32.0)	6 (46.2)	11 (26.2)	4 (40.0)
Patients with a history of atrial fibrillation	10 (40.0)	6 (46.2)	5 (11.9)	2 (20.0)
Patients with risk factors[d]	23 (92.0)	12 (92.3)	32 (76.2)	8 (80.0)
Hypertension	15 (60.0)	6 (46.2)	23 (54.8)	6 (60.0)
Diabetes mellitus[e]	10 (40.0)	5 (38.5)	4 (9.5)	2 (20.0)
Myocardial infarction/ischemia	3 (12.0)	3 (23.1)	4 (9.5)	0
Cardiac disease[f]	2 (8.0)	2 (15.4)	5 (11.9)	2 (20.0)

Byrd et al, Acalabrutinib Versus Ibrutinib in Previously Treated Chronic Lymphocytic Leukemia: Results of the First Randomized Phase III Trial - 2021

ELEVATE-RR Bleeding

	Acalabrutinib (n = 266)		Ibrutinib (n = 263)	
Event	**Any Grade**	**Grade ≥ 3**	**Any Grade**	**Grade ≥ 3**
Diarrhea[a,b]	92 (34.6)	3 (1.1)	**121 (46.0)**	**13 (4.9)**
Headache[a,b]	**92 (34.6)**	**4 (1.5)**	53 (20.2)	0
Cough[a]	**77 (28.9)**	2 (0.8)	56 (21.3)	1 (0.4)
Upper respiratory tract infection	71 (26.7)	5 (1.9)	65 (24.7)	1 (0.4)
Pyrexia	62 (23.3)	8 (3.0)	50 (19.0)	2 (0.8)
Anemia	58 (21.8)	31 (11.7)	49 (18.6)	34 (12.9)
Neutropenia	56 (21.1)	52 (19.5)	65 (24.7)	60 (22.8)
Fatigue[b]	54 (20.3)	**9 (3.4)**	44 (16.7)	0
Arthralgia[a]	42 (15.8)	0	**60 (22.8)**	2 (0.8)
Hypertension[a,b]	23 (8.6)	11 (4.1)	**60 (22.8)**	**23 (8.7)**
Nausea	47 (17.7)	0	49 (18.6)	1 (0.4)
Pneumonia	47 (17.7)	28 (10.5)	43 (16.3)	23 (8.7)
Thrombocytopenia	40 (15.0)	26 (9.8)	35 (13.3)	18 (6.8)
Dyspnea	37 (13.9)	6 (2.3)	23 (8.7)	1 (0.4)
Bronchitis	34 (12.8)	3 (1.1)	23 (8.7)	2 (0.8)
Constipation	31 (11.7)	0	37 (14.1)	2 (0.8)
Contusion[a]	31 (11.7)	0	**48 (18.3)**	1 (0.4)
Nasopharyngitis	29 (10.9)	0	27 (10.3)	0
Dizziness	28 (10.5)	0	26 (9.9)	0
Vomiting	28 (10.5)	1 (0.4)	36 (13.7)	3 (1.1)
Peripheral edema	26 (9.8)	0	38 (14.4)	1 (0.4)
Rash	26 (9.8)	2 (0.8)	33 (12.5)	0
Myalgia	25 (9.4)	2 (0.8)	27 (10.3)	1 (0.4)
Atrial fibrillation[a]	24 (9.0)	12 (4.5)	**41 (15.6)**	9 (3.4)
Urinary tract infection[a]	22 (8.3)	3 (1.1)	**36 (13.7)**	6 (2.3)
Back pain[a]	20 (7.5)	0	**34 (12.9)**	2 (0.8)
Epistaxis	19 (7.1)	1 (0.4)	28 (10.6)	1 (0.4)
Muscle spasms[a]	16 (6.0)	0	**35 (13.3)**	2 (0.8)
Dyspepsia[a]	10 (3.8)	0	**32 (12.2)**	0

Emorragie con Acalabrutinib (38.0%) versus Ibrutinib (51.3%). **Incidenza di eventi emorragici maggiori confrontabile tra Acalabrutinib (4.5%) Ibrutinib (5.3%).**

Byrd et al, Acalabrutinib Versus Ibrutinib in Previously Treated Chronic Lymphocytic Leukemia: Results of the First Randomized Phase III Trial - 2021

Gennaio 2023

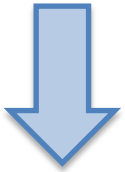
Hb	WBC	Ne	Ly	PLT
9,3 g/dl	81 560/mmc	940/mmc	66 170/mmc	47 000/mmc

02/01/2023 START C1 Acalabrutinib 100 mg x 2 vv/die

Gennaio 2023

Hb	WBC	Ne	Ly	PLT
9,3 g/dl	81 560/mmc	940/mmc	66 170/mmc	47 000/mmc

02/01/2023 START C1 Acalabrutinib 100 mg x 2 vv/die

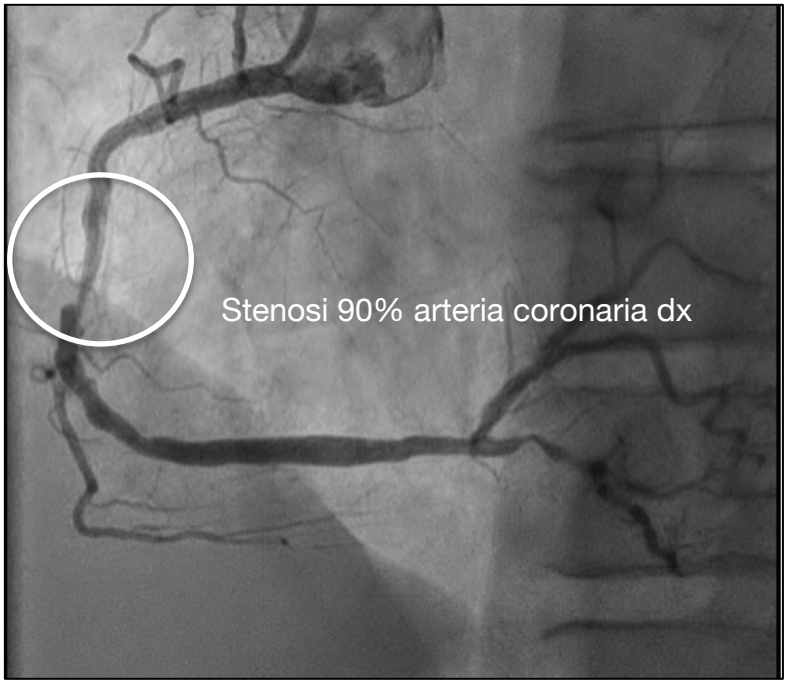


22/03/2023 + 2 mesi Acalabrutinib

Hb	WBC	Ne	Ly	PLT
12,1 g/dl	46 420/mmc	1550/mmc	41 080/mmc	62 000/mmc

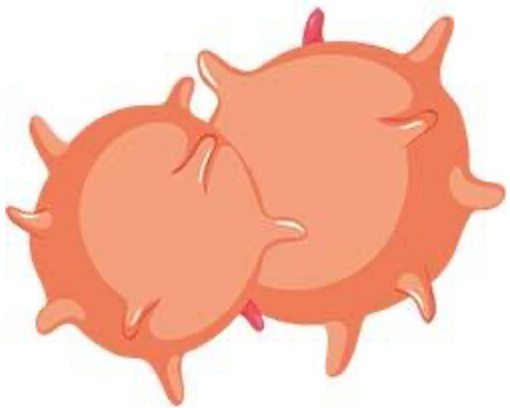
Aprile 2023

CORONAROGRAFIA → **coronaropatia trivasale** con stenosi subocclusiva lunga al tratto medio della discendente anteriore (IVA), occlusione totale della arteria circonflessa (CX) al tratto medio e stenosi del 90% del tratto medio della coronaria destra e subocclusiva della discendente posteriore.



Aprile 2023

- Eseguita rivascolarizzazione percutanea con posizionamento di 2 stent medicati (IVA e CDx).
- Posta indicazione a terapia per un anno con Plavix e cardio ASA



- Piastrinopenia
- Indicazione a trattamento per LLC con BTKi (TP53 mut)
- Necessità di doppia antiaggregazione prolungata

Rischio di sanguinamento

- Coronaropatia trivasale con posizionamento di stent medicati

Rischio CV

Cosa fare?

Hb	WBC	Ne	Ly	PLT
13,5 g/dl	13 320/mmc	1350/mmc	10 760/mmc	65 000/mmc

1. Sospendere Acalabrutinib?
2. Riprendere Acalabrutinib con doppia antiaggregazione?
3. Riprendere Acalabrutinib e sospendere un antiaggregante?
4. Zanubrutinib?

NCCN 2023

SUGGESTED TREATMENT REGIMENS[a,b,c,d]
CLL/SLL with del(17p)/*TP53* mutation
(alphabetical by category)
CIT is not recommended since del(17p)/*TP53* mutation is associated with low response rates.

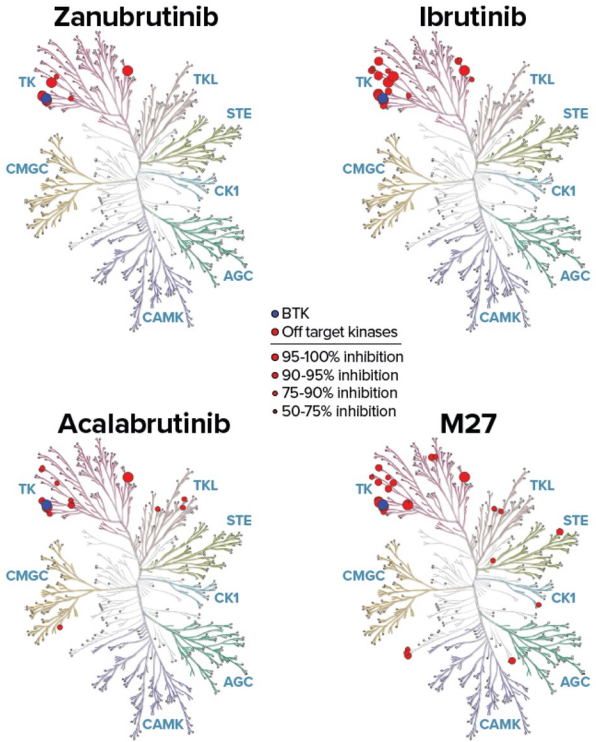
FIRST-LINE THERAPY[e]	
Preferred regimens	**Other recommended regimens**
• Acalabrutinib[f,*] ± obinutuzumab	• Alemtuzumab[t] ± rituximab
• Venetoclax[f,g] + obinutuzumab	• HDMP + rituximab
• Zanubrutinib[f,*]	• Ibrutinib[f,h,*]
	• Obinutuzumab
	• Ibrutinib[*] + venetoclax[f,g] (category 2B)

Zanubrutinib approvato da FDA gennaio 2023
disponibile in uso compassionevole in Italia

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) - Version 3.2023 — June 12, 2023

BGB-3111-215 – Updated Analysis

- Zanubrutinib ha dimostrato una selettività migliore rispetto a Ibrutinib e a Acalabrutinib e il suo metabolita M27
- Zanubrutinib ha un profilo di tollerabilità favorevole in pazienti precedentemente risultati intolleranti a ibrutinib e/o acalabrutinib



1. Burger JA. Cancer J. 2019;25(6):386-393. 2. Stephens DM, Byrd JC. Blood. 2019;133(12):1298-1307. 3. Guo Y, et al. J Med Chem. 2019;62(17):7923-7940. 4. Shadman M, et al. Lancet Haematol. 2023;10(1):e35-e45. 5. Shadman M, et al. Blood. 2021;138(suppl 1):1410-1413..

Shadman M et al. Poster presented at EHA 2023; abstract number: P683

Table 2. Phase III Randomized Studies of Small Molecule Inhibitor Therapy for Relapsed/Refractory CLL/SLL

Trial	Regimen	Patients n	Patient Characteristics	Median Follow-Up	ORR	PFS	OS
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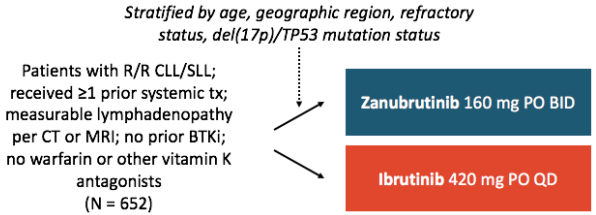
Abbreviations: BR, bendamustine + rituximab; CLL, chronic lymphocytic leukemia; CR, complete response; HR, hazard ratio; IdR, idelalisib + rituximab; NR, not reached; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PS, performance status; SLL, small lymphocytic lymphoma.

NCCN Guidelines® Insights: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma, Version 3.2022

Eventi cardiologici - ALPINE



FA/Flutter atriale **5.2%** (zanubrutinib) vs **13.3%** (ibrutinib)

Event, n (%)	Zanubrutinib (n = 324)	Ibrutinib (n = 324)
Cardiac AEs	69 (21.3)	96 (29.6)
Serious cardiac AEs*	6 (1.9)	25 (7.7)
Fatal cardiac events	0	6 (1.9)
Cardiac AEs leading to treatment discontinuation	1 (0.3)	14 (4.3)
▪ Ventricular extrasystoles	1 (0.3)	0
▪ Atrial fibrillation	0	5 (1.5)
▪ Cardiac arrest	0	2 (0.6)†
▪ Cardiac failure	0	2 (0.6)
▪ Cardiac failure acute	0	1 (0.3)†
▪ Congestive cardiomyopathy	0	1 (0.3)†
▪ Myocardial infarction	0	1 (0.3)†
▪ Palpitations	0	1 (0.3)
▪ Ventricular fibrillation	0	1 (0.3)

Hillman et al, ALPINE: zanubrutinib versus ibrutinib in relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma - 2020

Brown. ASH 2022. Abstr LBA-6. Brown. NEJM. 2022;[Epub]. Slide credit: clinicaloptions.com

Bleeding - ALPINE

Emorragie zanubrutinib vs ibrutinib **42,3%** con grado 3 e 4 **3,4%** vs **41,4%** con grado 3 e 4 **3,7%**

Emorragie maggiori zanubrutinib vs ibrutinib **3,7%** vs **4,3%**

Table 5: Safety Summary in ALPINE[2]

Adverse Event, n (%)	Zanubrutinib (n=324)		Ibrutinib (n=324)	
Any Grade ≥3 TEAEs	218 (67.3)		228 (70.4)	
Serious AEs	136 (42)		162 (50)	
Grade 5 AEs	33 (10.2)		36 (11.1)	
Leading to dose reduction	40 (12.3)		55 (17)	
Leading to dose interruption	162 (50)		184 (56.8)	
Leading to treatment discontinuation	50 (15.4)		72 (22.2)	
Adverse Events of Interest*	**Any Grade**	**Grade ≥3**	**Any Grade**	**Grade ≥3**
Infections	231 (71.3)	86 (26.5)	237 (73.1)	91 (28.1)
Opportunistic infection	7 (2.2)	5 (1.5)	10 (3.1)	5 (1.5)
Hemorrhage	137(42.3)	11 (3.4)	134 (41.4)	12 (3.7)
Major hemorrhage	12 (3.7)	11 (3.4)	14 (4.3)	12 (3.7)
Neutropenia†	95 (29.3)	68 (21)	79 (24.4)	59 (18.2)
Hypertension	76 (23.5)	49 (15.1)	74 (22.8)	44 (13.6)
Anemia	50 (15.4)	7 (2.2)	53 (16.4)	8 (2.5)
Thrombocytopenia	42 (13)	11 (3.4)	50 (15.4)	17 (5.2)
Secondary primary malignancies	40 (12.3)	22 (6.8)	43 (13.3)	17 (5.2)
Skin cancers	21 (6.5)	7 (2.2)	28 (8.6)	4 (1.2)

Hillman et al, ALPINE: zanubrutinib versus ibrutinib in relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma - 2020

SEQUOIA TRIAL

Eventi CV **15,3%** con **4,5%** di grado 3 e 4

FA **4,5%**

Table 6: Safety Summary in SEQUOIA Cohort 2 (n=111)[1]

Adverse Event, n (%)	Any Grade	Grade ≥3
Most Common (>15%) TEAE		
Bleeding*	57 (51.3)	6 (5.4)
URTI	23 (20.7)	0
Arthralgia	22 (19.8)	1 (0.9)
Neutropenia/neutrophil count decreased	20 (18)	17 (15.3)
Cardiac events*	17 (15.3)	5 (4.5)
Adverse Event of Interest		
Anemia	103 (92.8)	46 (41.4)
Infections	79 (71.2)	19 (17.1)
Bleeding	57 (51.4)	6 (5.4)
Major bleeding	8 (7.2)	6 (5.4)
Other cancers	24 (21.6)	7 (6.3)
Dermatologic other cancers	17 (15.3)	2 (1.8)
Neutropenia	21 (18.9)	18 (16.2)
Diarrhea	19 (17.1)	1 (0.9)
Hypertension	12 (10.8)	6 (5.4)
Thrombocytopenia	8 (7.2)	1 (0.9)
Arthralgia	6 (5.4)	0 (0.0)
Myalgia	6 (5.4)	1 (0.9)
Atrial fibrillation	5 (4.5)	4 (3.6)

* Pooled terms

Tam CS et al Zanubrutinib versus bendamustine and rituximab in untreated chronic lymphocytic leukaemia and small lymphocytic lymphoma (SEQUOIA): a randomised, controlled, phase 3 trial. Lancet Oncol. 2022

Tabella riassuntiva eventi CV e Emorragie

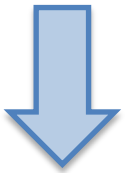
	ALPINE- ibru	ALPINE- zanu	SEQUOIA- zanu coorte 1 e 2	ELEVATE- ibru	ELEVATE - acala
Emorragie maggiori	4.3%	**3.7%**	**5-7.2%**	5.3%	4.5%
Piastrinopenia G 3 e 4	5.2%	**3.4%**	**2.1-0.9%**	6.8%	9.8%
Eventi CV	29.6%	**21%**	**15.3%**	30%	24.1%
FA	10.1%	**2.5%**	**3.3-4.5%**	16%	9.4%

Tam CS et al Zanubrutinib versus bendamustine and rituximab in untreated chronic lymphocytic leukaemia and small lymphocytic lymphoma (SEQUOIA): a randomised, controlled, phase 3 trial. Lancet Oncol. 2022
Byrd et al, Acalabrutinib Versus Ibrutinib in Previously Treated Chronic Lymphocytic Leukemia: Results of the First Randomized Phase III Trial - 2021
Hillman et al, ALPINE: zanubrutinib versus ibrutinib in relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma - 2020

Giugno 2023

Hb	WBC	Ne	Ly	PLT
12,5 g/dl	9 600/mmc	1500/mmc	7 500/mmc	70 000/mmc

- Sta bene, in stretto follow-up
- Piccole emorragie muco cutanee
- Piastrinopenia stabile



W&W

Take Home Messages:

- Attenta valutazione del profilo CV
- La scelta ottimale del farmaco è influenzata da fattori biologici e dalle comorbilità del paziente
- Valutare attentamente il profilo di safety

Thank you for your attention!