

MEET THE **EXPERT** *in CLL*

MESTRE (VE), 19 OTTOBRE 2026

Aula Verde-Padiglione Giovanni Rama, Ospedale dell'Angelo



I vantaggi della terapia a durata fissa e la sostenibilità dei farmaci: il punto di vista dell'ematologo e del farmacista

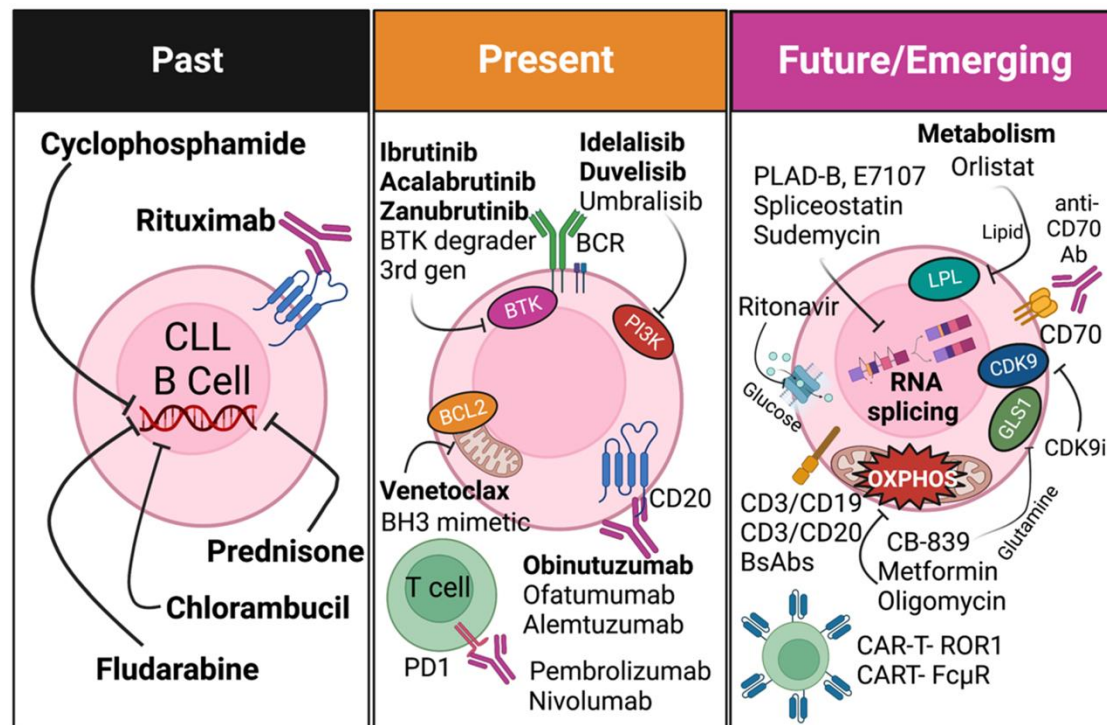
Alessia Salvador- farmacista Ospedale dell'Angelo AULSS3 Serenissima

Disclosures Alessia Salvador

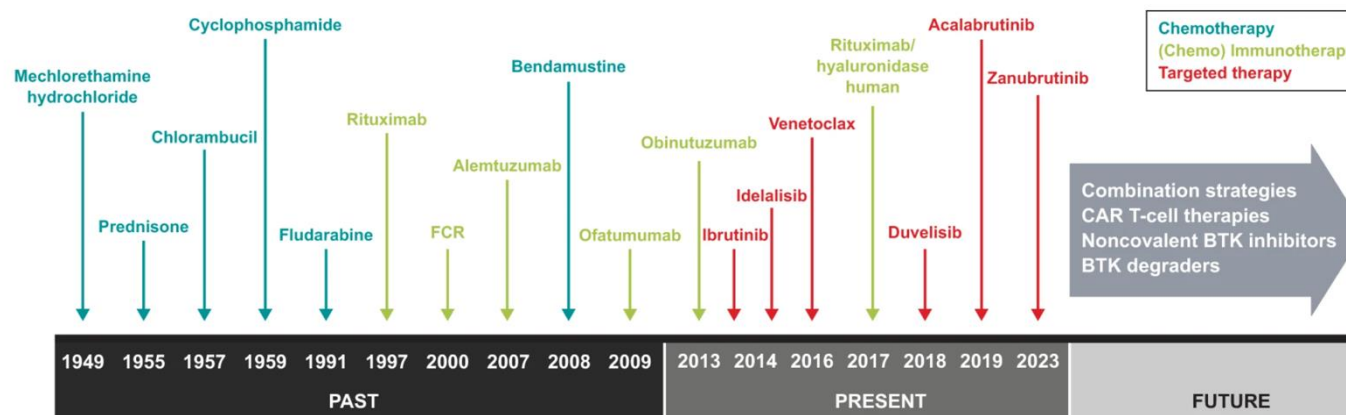
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Cancers **15**, 1583 (2023)



Cancer J. **13**, 141 (2023)

CAR chimeric antigen receptor, BTK Bruton tyrosine kinase, FCR fludarabine, cyclophosphamide, and rituximab.



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IL PUNTO DI VISTA DEL FARMACISTA

Farmacista
UFA



Farmacista
diretta



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Terapia continua

- Inibitori BTK
- Venetoclax

Terapia a durata fissa

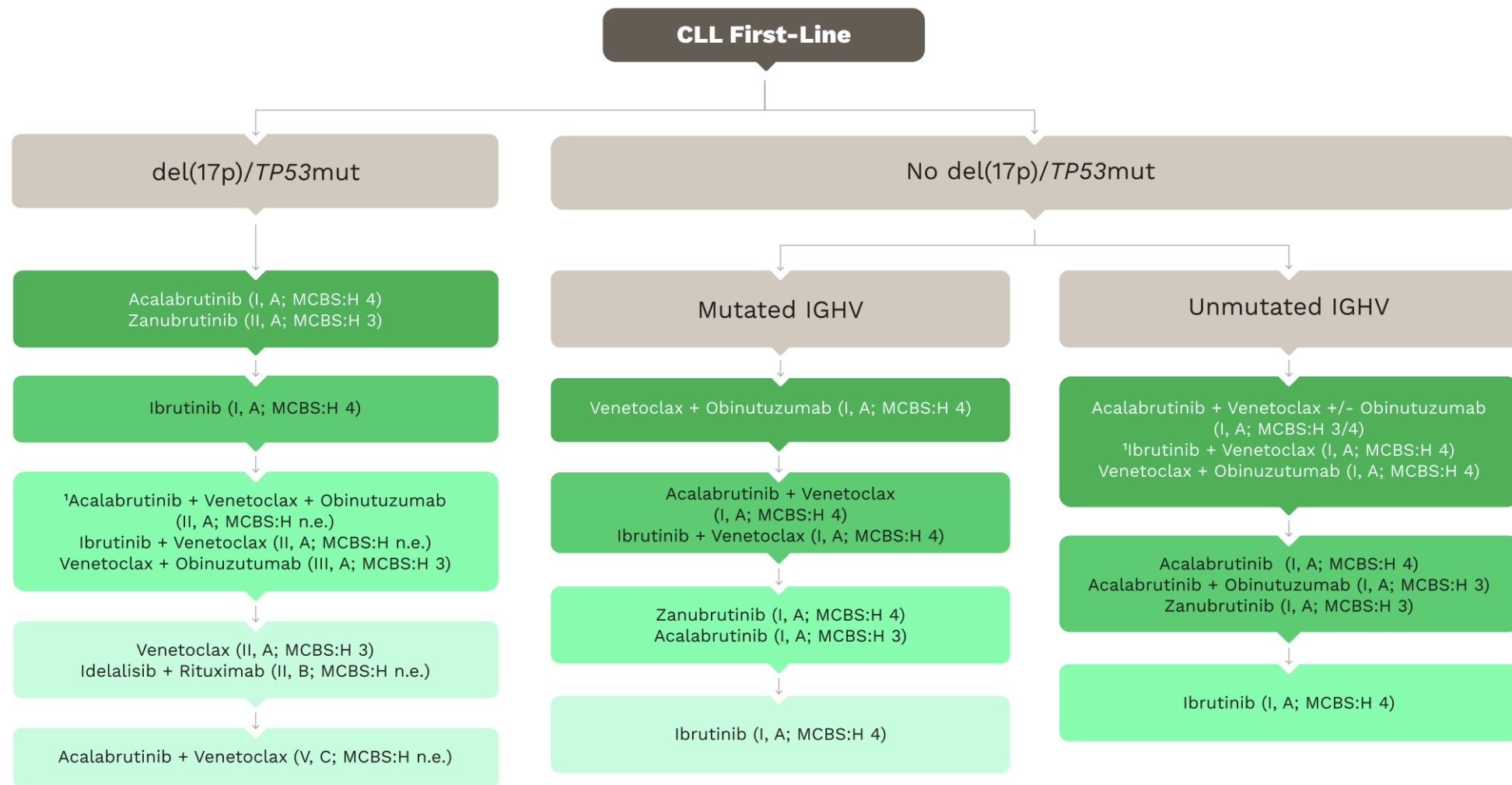
- Venetoclax + inibitori BTK (14-15 cicli)
- Venetoclax + Obinutuzumab (12 cicli)



		Key determinants of treatment selection	Secondary influences on treatment selection
PATIENT PREFERENCES		Attitude toward fixed-duration vs continuous therapy Willingness to visit hospital for treatment and follow-ups	Attitude to intravenous therapy Attitude to side effects
DISEASE FEATURES		Del(17p)/TP53 status IGHV status	Tumor burden* Complex karyotype
PATIENT CHARACTERISTICS & COMORBIDITIES		Age and fitness Cardiovascular status Renal status History of infections or immunosuppression	Potential for DDIs with existing medications Bleeding risk
LOGISTICS		Drug availability Patient's suitability for hospital-based treatment and monitoring Hospital capacity to provide TLS monitoring	Anticipated adherence to treatment

Fig. 1 Key factors to evaluate in first-line treatment selection for patients with CLL. *Particularly relevant when considering venetoclax-based regimens, owing to TLS risk. DDI drug–drug interaction, IGHV immunoglobulin heavy chain variable, TLS tumor lysis syndrome.





The order of each box listed reflects the ranking based on the recommendations, highlighted also by the different shades of green.

The order within each box is based on the MCBS:H score or otherwise preference, as the therapeutic choice should be guided not only by efficacy but also by comorbidities, drug interactions, logistics, and patient's preferences (see figure 2 "Heat map").

¹This combination has potentially more efficacy in an MRD-guided approach, but is not approved (see the text). N.e. = not evaluated.

HemaSphere. 2026;10:e70403



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CLL First-Line

Integrated vision of individual features to guide treatment decision

	Biological Profile			Infection risk	Ease of treatment	Concomitant comorbidities & comedication			
	M-IGHV	UM-IGHV	TP53mut/del(17p)			Cardio-vascular Disease	Impaired Renal Function	Anticoagulation/bleeding risk	Drug Interactions
Venetoclax - Obinutuzumab	A	A	B	C	C	A	B ²	A	Assess specific interactions
Venetoclax + Ibrutinib ¹	A	A	B	B	B	C	B ²	B ³	
Venetoclax + Acalabrutinib	A	A	B	B	B	B	B ²	B ³	
Venetoclax + Acalabrutinib + obinutuzumab	A	A	B	C	C	C	B ²	B ³	
Acalabrutinib	B	A	A	A	A	B	A ²	B ³	
Zanubrutinib	B	A	A	A	A	B	A ²	B ³	
Ibrutinib	B	A	A	A	A	C	A ²	B ³	

A= Strongly recommended; **B**= Recommended; **C**= consider alternatives.

¹: This combination appears particularly effective in UM-IGHV when used within an MRD-guided strategy, but is not currently approved.

²: caution with CrCl < 50 mL/min for venetoclax and < 30 mL/min for BTKi. For venetoclax recommended TLS preventions should be followed in patients with CrCl 50 -79 mL/min.

³: contraindicated with anti-Vitamin K.

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Costo ex factory per ciclo			Costo ex factory per anno		Costo terapia totale atteso	Efficacia dimostrata (endpoint primario)
	Costo/ciclo da 28 gg	N cicli da 28 gg	Costo terapia/anno	N anni		
Acalabrutinib + Venetoclax	10.108	14	131.769	1,08	141.516	Superiore vs chemioimmunoterapia a scelta del PI
Ibrutinib + Venetoclax	9.775	15	127.425	1,15	146.626	Superiore vs G-Cl
Acalabrutinib	5.110	continuativo	66.609	5-6 anni (follow up 74.5 mesi)	333.045-399.654	Superiore vs G-Cl
Ibrutinib	5.110	continuativo	66.609	5-9 anni (follow up 9 anni)	333.045-599.481	Superiore vs Cl
Zanubrutinib	5.110	continuativo	66.609	5-6 anni (follow up 72 mesi)	333.045-399.654	Superiore vs R-Benda
Venetoclax + Obinutuzimab	7.214	12	86.572	1	86.572	Superiore vs G-Cl



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RESEARCH

Open Access

Organizational impacts of fixed-duration therapies for the management of patients with chronic lymphocytic leukemia in Italy

Carla Rognoni^{1*}, Giacomo Loseto², Antonio Cuneo³, Anna Maria Frustaci⁴, Francesca Romana Mauro⁵, Francesco Costa³ and Patrizio Armeni¹

Abstract

Background Chronic Lymphocytic Leukemia (CLL) is a common adult leukemia characterized by the progressive accumulation of dysfunctional lymphocytes. Recently introduced fixed-duration targeted therapies for previously untreated patients have demonstrated superior efficacy compared to chemotherapy, while offering time-limited treatment that improves patient quality of life and reduces the burden on healthcare systems compared to continuous therapies. This analysis examines the organizational impact of implementing first-line, fixed-duration CLL therapies, with focus on healthcare resource allocation, costs, and patient management.

Methods The regimens analyzed included ibrutinib + venetoclax (I + V, oral), venetoclax + obinutuzumab (Ven-Obi, oral/infusion), bendamustine + rituximab (BR, infusion), chlorambucil + obinutuzumab (Clb-Obi, oral/infusion), and fludarabine + cyclophosphamide + rituximab (FCR, infusion). Data were defined through product characteristics, published literature, expert opinion, and standard hospital procedures for drug administration, adverse event management, and treatment duration. A questionnaire administered in four Italian centers captured organizational aspects such as healthcare personnel time, patient assessment, treatment preparation and administration, and follow-up.

Results Personnel time and costs varied substantially across regimens, with administration mode (oral vs. infusion) emerging as a key driver. Time ranged from 4,899 min (81.6 h) for BR to 8,019 min (133.7 h) for Ven-Obi. Organizational costs ranged from €3,942 (BR) to €8,631 (Ven-Obi). The all-oral I + V combination showed a lower cost profile (€5,724) than Ven-Obi and was comparable to Clb-Obi, despite additional monitoring requirements.

Conclusions Treatment selection should balance efficacy with organizational and economic considerations. Findings highlight that oral therapies improve efficiency and patient convenience while reducing delivery costs.

Keywords Chronic lymphocytic leukemia, Fixed-duration therapy, Healthcare resource utilization, Organizational impact, Cost analysis, Economic evaluation

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Activity	Oral	Infusion
Preparatory phase insertion of CVC or peripheral catheter (if required))		x
Patient admission and informational communication		x
Clinical examinations at baseline (lab tests, CT scan, cardiological evaluation, blood tests)	x	x
Onco-hematological (assessment of treatment eligibility)		x
Pharmacy dispensing activities (e.g., patient check-in, counseling and medication package delivery)	x	
Pharmaceutical preparation processes (including dosing, safety risk evaluation, quality assurance checks)		x
Co-medications preparation		x
Drug administration in hospital setting		x
Observation and hospital discharge		x
Wastage management		x
Management of possible adverse events	x	x
Patient monitoring and laboratory tests during follow-up	x	x
Removal of CVC or peripheral catheter (at the end of the entire treatment)		x

CVC=central venous catheter



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Table 12 Mean time (minutes with ranges) per patient dedicated by the healthcare personnel for the entire treatment pathway

Treatment	Hematologist	Nurse	Pharmacist	Lab technician	Biologist	Radiologist	Employee at the centralized booking center	Social-Healthcare Operator	Vascular surgeon	Anesthesiologist	Case manager	MEAN PERSONNEL TIME PER CYCLE	OVERALL PERSONNEL TIME
I+V	1,432 (541-4,171)	1,289 (58-4,740)	525 (0-1,577)	2,391 (5-8,550)	150 (0-600)	40 (0-450)	108 (0-290)	439 (0-975)	0 (0-0)	0 (0-0)	0 (0-0)	425 (40-1,424) (15 cycles)	6,376 (604-21,353) (106.3 h)
Ven-Obi	1,280 (294-4,002)	3,189 (270-7,851)	816 (129-2,454)	1,913 (4-6,840)	120 (0-480)	33 (0-361)	93 (0-245)	561 (18-1,245)	5 (0-40)	6 (0-60)	2 (0-20)	668 (60-1,967) (12 cycles)	8,019 (715-23,598) (133.7 h)

Table 13 Overall costs (€) represented by mean values with ranges

Treatment	Healthcare personnel	Disposables for clinical tests to assess treatment eligibility	Disposables for treatments	Concomitant treatments (including TLS prevention)	Management of AEs	Disposables for clinical exams in the FUP	MEAN COST PER CYCLE	TOTAL COST
I+V	4,097 (622-13,529)	1,052 (469-1,634)	60 (0-157)	247 (0-493)	0 (0-0)	269 (154-1,008)	382 (83-1,121) (15 cycles)	5,724 (1,246-16,821)
Ven-Obi	4,869 (574-14,805)	892 (413-1,372)	780 (51-2,133)	1,867 (283-2,958)	7 (0-15)	215 (123-806)	719 (120-1,841) (15 cycles)	8,631 (1,444-22,089)

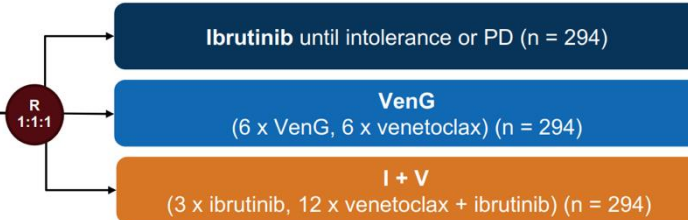


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CLL-17

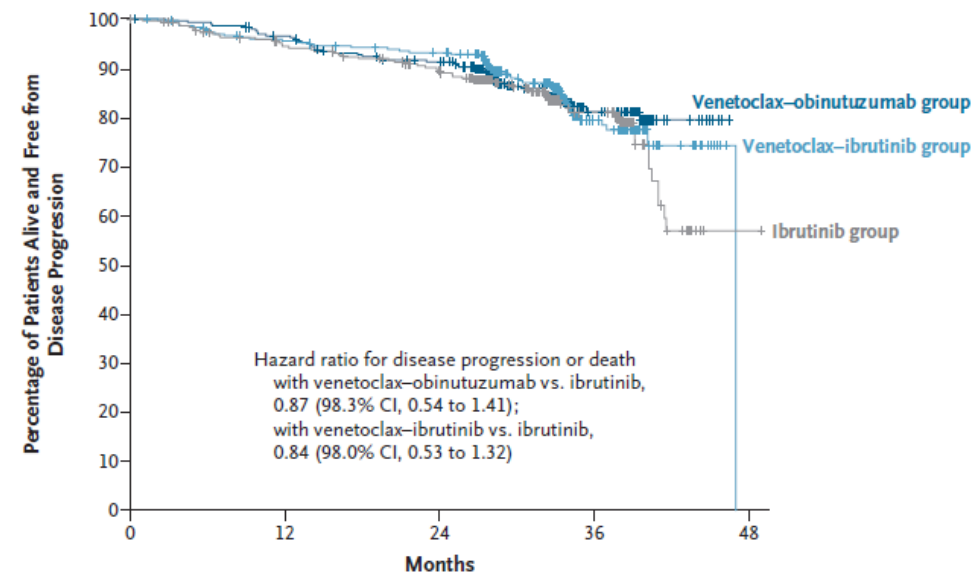
Patients with previously untreated CLL, including fit and unfit patients and patients with del(17p)/TP53mut (N = ~862)



- **Primary endpoint:** PFS
- **Key secondary endpoints:** response, MRD, and OS

	n=909
V+O	303
I+V	305
I	301
Median obs. Time (month)	34,2
Median age (range)	66 (34-90)
Male	67,80%
Median CIRS (range)	3 (0-18)
Creatinine clearance <70 mL/min	33,70%
del(17p) and/or TP53 mut	7,60%
uIGHV	56,50%
CK (>3 aberrations)	19,20%
High CLL-IPI	53,80%
Very high CLL-IPI	6,50%

3-yr PFS	
V+O	81%
I+V	79%
I	81%
uMRD <10-4 ITT C18D1	
V+O	73%
I+V	47%
I	0%
3-yr PFS uIGHV	
V+O	76%
I+V	79%
I	80%
3-yr OS	
V+O	92%
I+V	96%
I	96%
3-yr PFS del17/TP53mut	
V+O	62%
I+V	69%
I	79%



Adverse Event (AE)	VO	VI	I
Infections G≥3	35%	25%	25%
Febrile neutropenia	5%	2.3%	0%
Neutropenia G≥3	37%	22%	8%
COVID-19 infection (G≥3)	38% (14%)	42% (8%)	39% (7%)
Cardiac disorders	13.9%	23.8%	34.6%
SPM	11.5%	11.2%	18.5%

Al-Sawaf et al. abs25-2071, ASH 2025; Al-Sawaf O et al, NEJM 2026



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PRO TERAPIA CONTINUATIVA	PRO TERAPIA A DURATA FISSA
FACILITA' DI SOMMINISTRAZIONE	IL PAZIENTE ASSUME I FARMACI SOLO PER AL MASSIMO 15 CICLI
DATI DI EFFICACIA A PIU' LUNGO TERMINE	EFFETTI AVVERSI LIMITATI AL PERIODO DI ASSUNZIONE DEI FARMACI
del(17p)/ TP53mut	COSTO MINORE

CONTRO TERAPIA CONTINUATIVA	CONTRO TERAPIA A DURATA FISSA
IL PAZIENTE ASSUME IL FARMACO IN MODO CONTINUATIVO	MAGGIORI ACCESSI IN OSPEDALE NELLA FASE DI TITOLAZIONE DEL VENETOCLAX
ACCUMULO EFFETTI AVVERSI	REGIME PIU' COMPLESSO
COSTO MAGGIORE	REAZIONI INFUSIONALI NELLA COMBINAZIONE CON OBINU



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Grazie per l'attenzione



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