POST-NEW ORLEANS 2022
Novità dal Meeting della Società Americana di Ematologia

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Milano
Teatro Dal Verme
2-3-4 Febbraio 2023

COORDINATORI
Angelo Michele Carella
Pier Luigi Zinzani

BOARD SCIENTIFICO
Paolo Corradini
Mauro Krampera
Fabrizio Pane
Adriano Venditti

Novità dal Meeting della Società Americana di Ematologia

3ª Sessione
Leucemia Linfatica Cronica

- **17.35 Stato dell'arte** — **M. KRAMPERA**

Milano, 2 Febbraio 2023

DICHIARAZIONE

MAURO KRAMPERA

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Consulenza ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazione ad Advisory Board **(Novartis 2017 per AML, Janssen 2018 per MM)**
- Titolarietà di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Altro (**supporto per partecipazione a convegni o per moderazione/relazione: Abbvie, Incyte, Novartis, Roche, Janssen, Pfizer**)

Era Pizzoliana Primaria

CLB / FC / Benda

Era Pizzoliana Secondaria

FCR / BR

Era Pizzoliana Terziaria

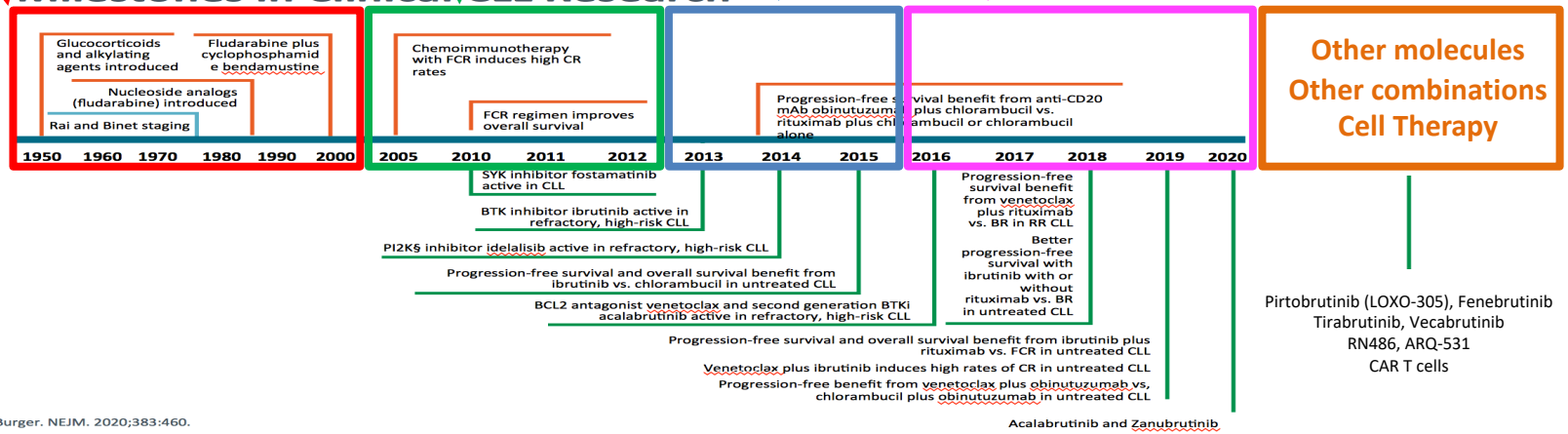
BTKIs (Ibrutinib/Idelalisib)

Era Pizzoliana Quaternaria

2nd gen BTKIs (Acalabrutinib/Zanubrutinib)
Venetoclax
Obinotuzumab

Futuro

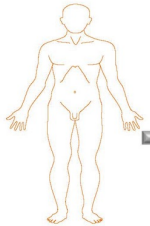
72 anni

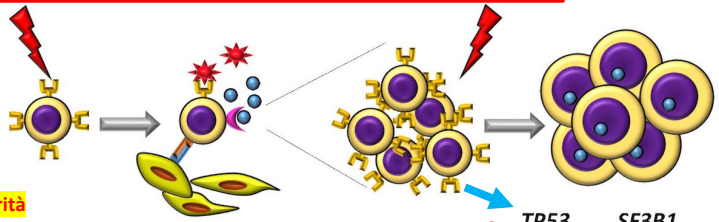


Burger. NEJM. 2020;383:460.

Non tutte le CLL nascono uguali

Caratteristiche comuni



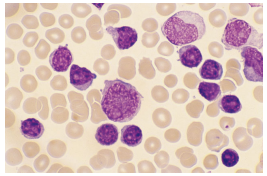


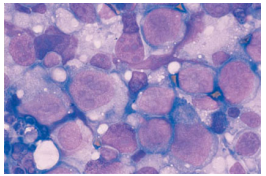
Peculiarità

Predisposition	Initiation	Promotion/Accumulation		
Polygenic	del13q	BCR		
IRF4, IRF8	+12		TLR	
Other	MYD88	CD38	VLA-4	
		NOTCH	CXCR4	

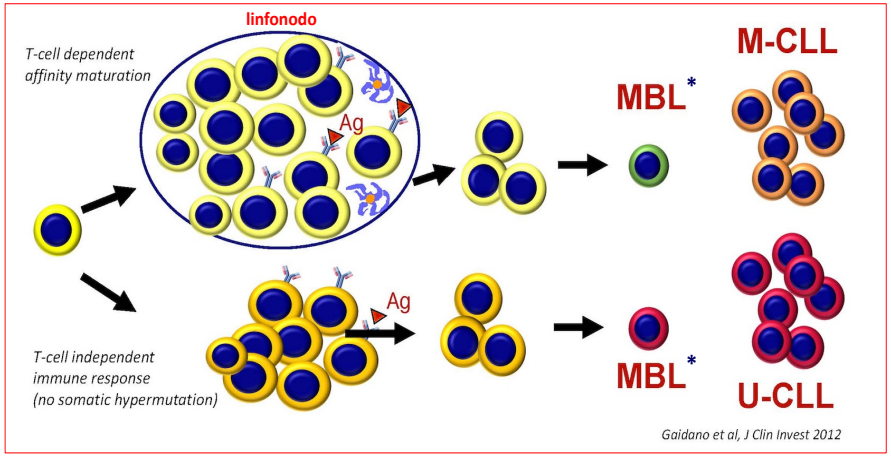
TP53 *SF3B1*
ATM
BIRC3
NOTCH1 *MYC*
ATM
CDKN2A
Other

Richter's Syndrome
- DLBCL-RT (90-95%)
- HL-RT (5-10%)
- Plasmablastic-RT (<1%)
- Poor prognosis (<1 year)





0.5-1% per year



Detoxification systems and metabolism

Catalase/ROS axis
Phosphoproteins
Metabolomics

Bcl-2 protein family

PRO: Bax, Bak, Bim, Bid, Puma
ANTI: Bcl-2, Bcl-xL, Mcl-1, Bfl-1

* Linfociti B clonali CD5+/Ig+ (k o l) <5.000/mmc in assenza di linfoadeno-epato-splenomegalia e citopenia

LLC : quando iniziare il trattamento?

Table 1. 2018 International Workshop on CLL (iwCLL) guidelines on indications for treatment [7].

Parameter	iwCLL indications for treatment[a]
Lymph nodes	Massive (i.e.,≥ 10 cm), progressive, or symptomatic
Liver and/or spleen size	Massive (i.e.,≥ 6 cm below the left costal margin), progressive, or symptomatic
Constitutional symptoms	Disease-related symptoms[b]
Circulating lymphocyte count	Progressive ≥ 50% over a 2-month period, or lymphocyte doubling time < 6 months[c]
Platelet count	Worsening thrombocytopenia < 100 x 109/L due to progressive marrow failure[d]
Hemoglobin	Worsening anemia < 10 g/dL due to progressive marrow failure[d]
Bone marrow	Progressive marrow failure as per above
Extranodal	Symptomatic or functional extranodal involvement (e.g., skin, kidney, lung, spine)

[a]Autoimmune complications (including autoimmune cytopenias) poorly responsive to corticosteroids or current treatment may represent an additional indication for change in treatment.
[b]Unintentional weight loss ≥ 10% within the previous 6 months; significant fatigue (ECOG performance scale ≥ 2), fevers (38.0 °C) for ≥ 2 weeks without evidence of infection; night sweats for ≥ 1 month without evidence of infection.
[c]Non-CLL factors that may contribute to lymphocytosis (e.g., infections and corticosteroids) should be excluded.
[d]Hemoglobin and platelet count cutoffs require consideration of the rate of decline. In certain patients, counts slightly below these levels may remain stable for an extended period and not require treatment initiation.

Hampel PJ, Parikh SA. CLL treatment algorithm 2022. Blood Cancer J 2022;12:161

CLL - International Prognostic Index (CLL-IPI)

Prognostic Factor		Points
Del17p on FISH or *TP53* mutation		4
Unmutated *IGHV* genes		2
Serum β2 microglobulin >3.5 mg/L		2
Rai Stage I-IV		1
Age >65 years		1

CLL-IPI (Cumulative Points)	n	Median (Years)	5-Year TTFT Estimated Risk	10-Year TTFT Estimated Risk
Low (0-1)	574	Not reached	23%	40%
Intermediate (2-3)	578	3.7	58%	74%
High (4-6)	435	2.1	77%	83%
Very High (7-10)	99	0.7	87%	Not estimable

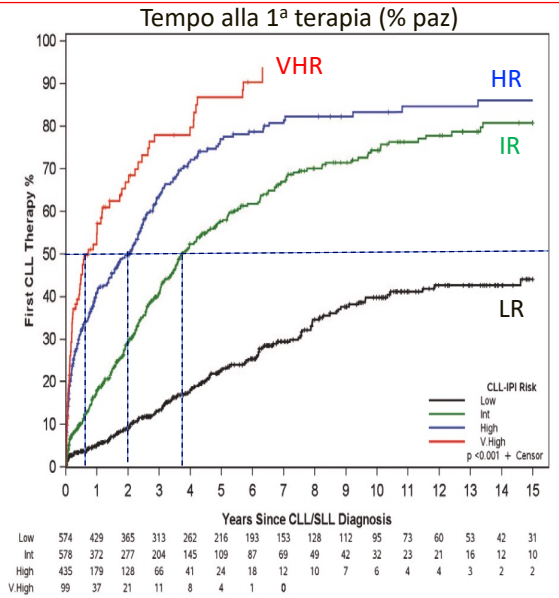
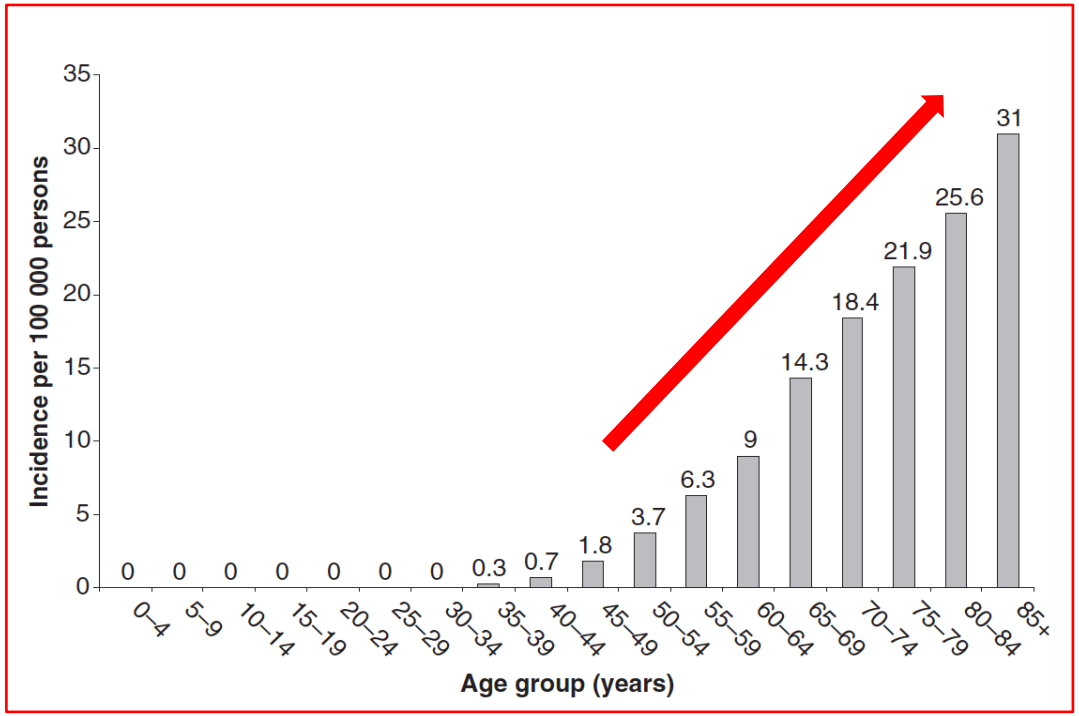


Fig. 2 The CLL-International Prognostic Index (CLL-IPI) and Time to First Therapy (TTFT) among newly diagnosed CLL patients seen at Mayo Clinic, Rochester, MN. Calculation of the CLL-IPI facilitates prognostic discussions regarding TTFT with newly diagnosed patients with CLL. FISH fluorescence in situ hybridization, IGHV immunoglobulin heavy chain gene, TTFT time to first therapy.

Hampel PJ, Parikh SA. CLL treatment algorithm 2022. Blood Cancer J 2022;12:161

E' fondamentale identificare alla diagnosi la classe di rischio del paziente per scegliere la terapia più efficace, in grado di modificare la storia naturale della malattia

Fattore ETA'



Definizione di anziano

LLC e trattamento

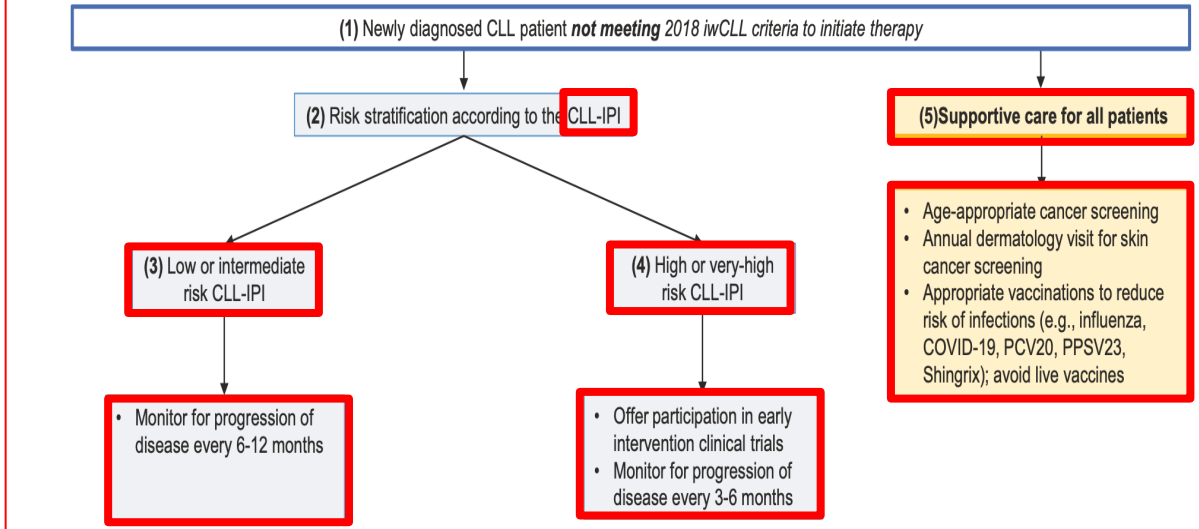


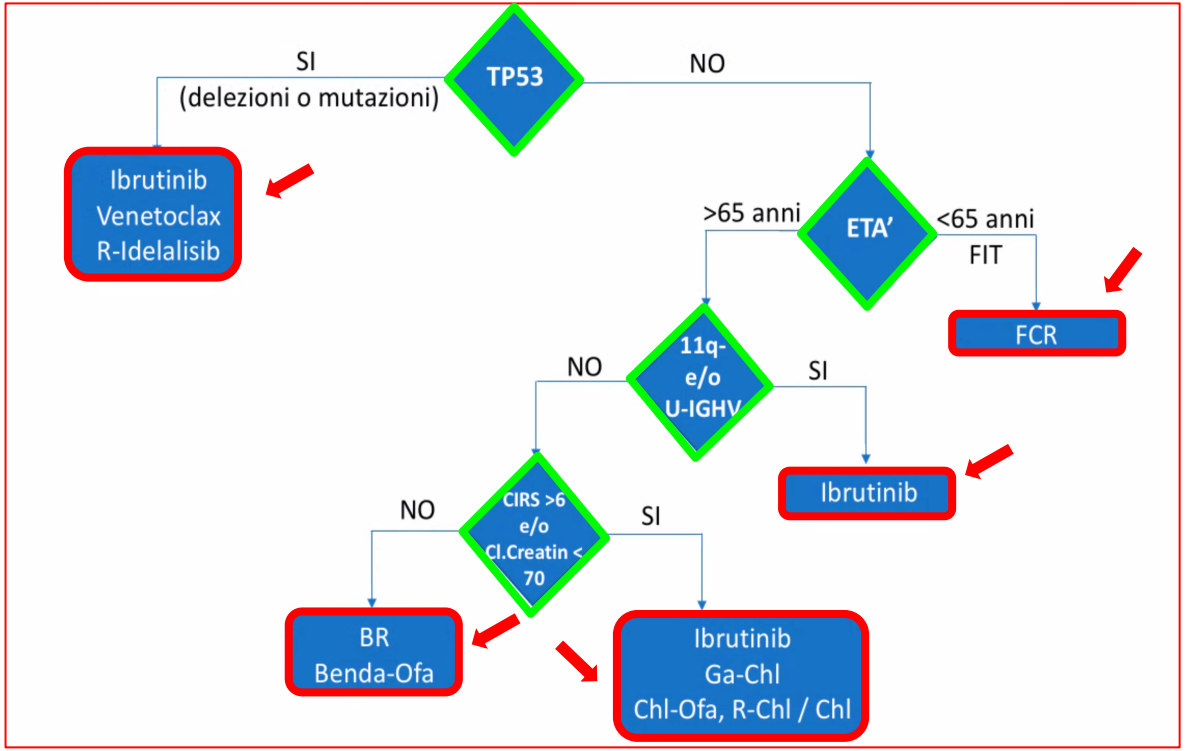
Fig. 1 Approach to the management of patients with newly diagnosed CLL who do not meet the 2018 International Workshop for Chronic Lymphocytic Leukemia (iwCLL) criteria for therapy. Management is guided by risk-stratification, while including supportive care is necessary for all patients with a CLL diagnosis.

Hampel PJ, Parikh SA. CLL treatment algorithm 2022. Blood Cancer J 2022;12:161

LLC e trattamento – Pazienti "naïve"

*PDTA LLC **2018***

RETE EMATOLOGICA VENETA
Sinergia per Condividere ASSISTENZA FORMAZIONE RICERCA



LLC e trattamento – Pazienti "naïve"

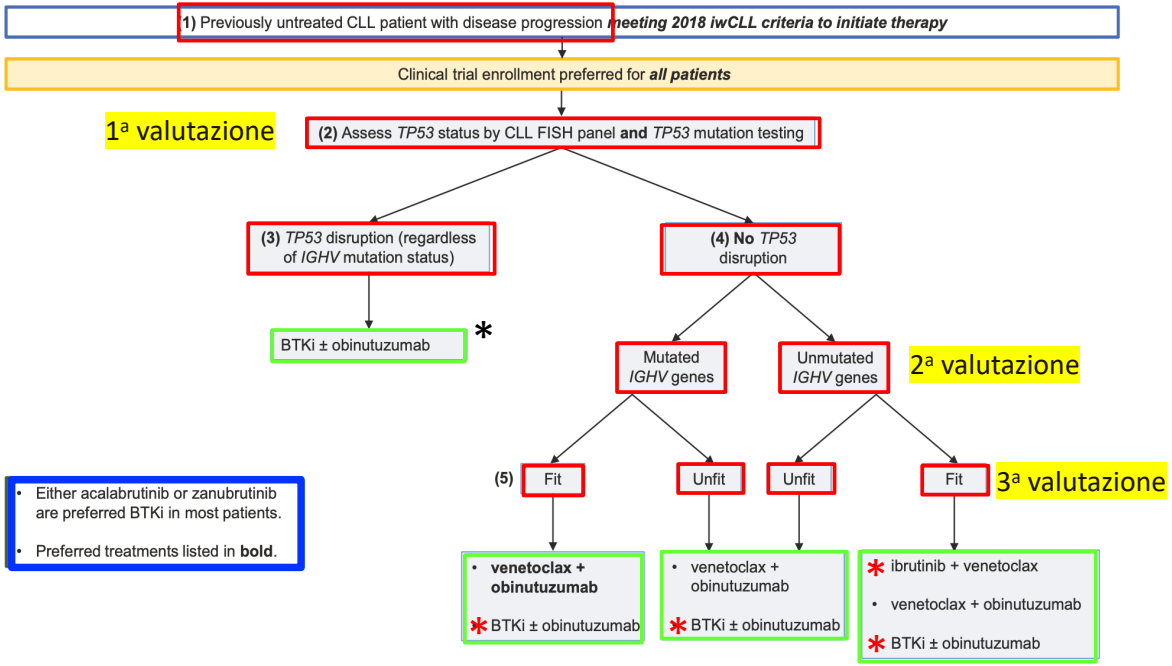


Fig. 3 Approach to the management of patients with previously untreated CLL who meet the 2018 International Workshop for Chronic Lymphocytic Leukemia (iwCLL) criteria for therapy. BTKi Bruton tyrosine kinase inhibitors, IGHV immunoglobulin heavy chain gene.

Hampel PJ, Parikh SA. CLL treatment algorithm 2022. Blood Cancer J 2022;12:161

* In Italia l'associazione non è ancora rimborsabile

C'è ancora spazio per l'immuno-chemioterapia?

LLC e trattamento – Pazienti già trattati

(previa rivalutazione dello stato mutazionale di TP53 e IgHV)

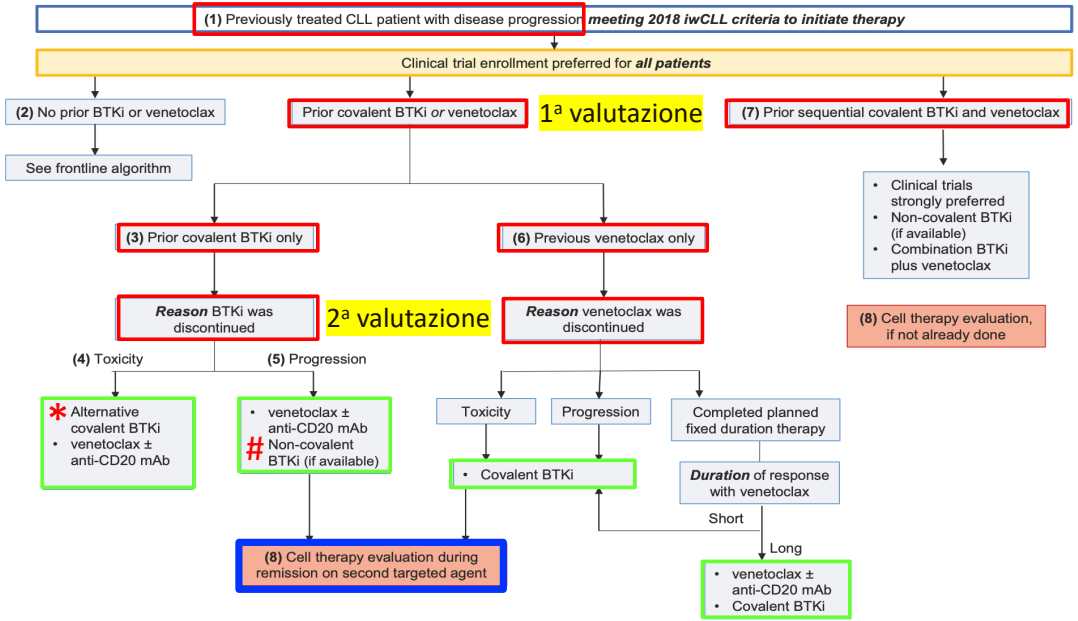


Fig. 4 Approach to the management of patients with relapsed CLL who meet the 2018 International Workshop for Chronic Lymphocytic Leukemia (iwCLL) criteria for therapy. BTKi Bruton tyrosine kinase inhibitors, IGHV immunoglobulin heavy chain gene, mAb monoclonal antibody.

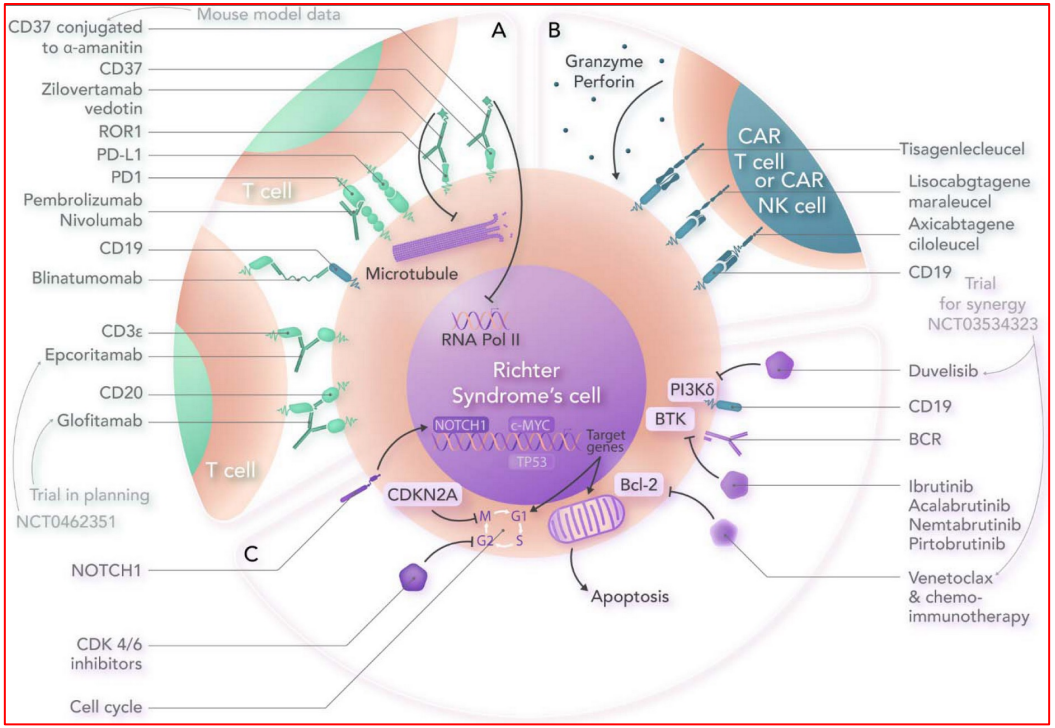
Hampel PJ, Parikh SA. CLL treatment algorithm 2022. Blood Cancer J 2022;12:161

* Non ancora rimborsabile in Italia

\# Pirtobrutinib (non ancora disponibile in Italia)

Cosa si fa quando tutti gli inibitori sono stati utilizzati?

Sindrome di Richter – Quale trattamento?



Philip A. Thompson,Tanya Siddiqi, Treatment of Richter's syndrome, Hematology Am Soc Hematol Educ Program, 2022

Sessions			201. Granulocytes, Monocytes, and Macrophages (COVID-19 in CLL)	331. Thrombotic Microangiopathies/ Thrombocytopenias and COVID-19-related Thrombotic/Vascular Disorders: Clinical and Epidemiological (ERIC Study)	603. Lymphoid Oncogenesis: Basic	605. Molecular Pharmacology and Drug Resistance: Lymphoid Neoplasms	623. Mantle Cell, Follicular, and Other Indolent B Cell Lymphomas: Clinical and Epidemiological	624. Hodgkin Lymphomas and T/NK cell Lymphomas: Clinical and Epidemiological (HL risk in CLL)	626. Aggressive Lymphomas: Prospective Therapeutic Trials (Richter)	627. Aggressive Lymphomas: Clinical and Epidemiological (Richter)	637. MDS: Clinical and Epidemiological (sMDS in CLL)	641. CLL: Basic and Translational	642. CLL: Clinical and Epidemiological	703. Cellular Immunotherapies: Basic and Translational (CAR T)	704. Cellular Immunotherapies: Early Phase and Investigational Therapies (CAR T and bispecific in CLL)	802. Chemical Biology and Experimental Therapeutics (new Inhibitors)	803. Emerging Tools, Techniques and Artificial Intelligence in Hematology (in silico/liquid IF/WGS)	902. Health Services Research – Lymphoid Malignancies (costs, therapy duration, control quality challenges & barriers)	905. Outcomes Research – Lymphoid Malignancies (QoL, Place in Therapy, Real world, sustainability)
Plenary Abstracts	p. 1-2	0																
Oral Abstracts	p. 3-186	42				4	1			2		12	18				4	1
Poster Abstracts	p. 186-854	141	1	1	1	3		1	3	1	1	39	63	1	4	1	4	7	10
Online Publication Only	p. 854-1042	42								1		14	20	1				3	3
	TOTAL	225	1	1	1	7	1	1	3	4	1	65	101	2	4	1	4	14	14

EXPLORE THE 2022 PROGRAM

- Education Program
- Education Spotlight Sessions
- Scientific Program
- Scientific Spotlight Sessions
- Special Scientific Symposia
- Scientific Workshops
- Poster Walks
- General Sessions
- Sessions on Diversity, Equity, and Inclusion
- Special Interest Sessions
- Trainee Activities and Services

Maximizing Outcomes in CLL

Sunday, December 11, 2022, 9:30 a.m. - 10:45 a.m.
Ernest N. Morial Convention Center, 265-268

The therapy of CLL has undergone a revolution in the last decade with the availability of highly effective targeted therapies. The options continue to expand with next generation inhibitors and combination therapy. The variety of available options can be confusing and their optimal use over a patient's entire disease course is still often unclear. More and more patients are developing disease progression after both BTK inhibitors and venetoclax and represent a new significant unmet need. Additionally, Richter's syndrome, the transformation of CLL to an aggressive lymphoma, remains a major clinical challenge with poor outcomes and is also a significant unmet need.

Dr. Jennifer Brown will discuss the selection of initial therapy in CLL, including BTK inhibitors with or without anti-CD20 antibody and venetoclax-obinutuzumab, as well as recent data on combination therapy, with a focus on BTK inhibitor-venetoclax based combinations. She will discuss the key unanswered questions and challenges in frontline therapy.

Dr. Lydia Scarfo will focus on the growing population of patients with CLL who have been treated with both BTK inhibitors and venetoclax, a population which represents a major unmet clinical need. Her discussion will include the role of non-covalent BTK inhibitors, and cellular therapy (mainly CAR T cell approaches), as well as novel promising investigational agents and strategies.

Dr. Tanya Siddiqi will discuss Richter's syndrome, the transformation of CLL to an aggressive lymphoma, an event which occurs typically in patients with high risk features. There remains no known effective standard of care and hence clinical trial enrollment is preferred when possible. Novel treatment approaches using combinations of small molecule targeted agents, antibody-based therapy, and/or CAR-T cell therapy appear to be more beneficial than chemoimmunotherapy alone.

CHAIR:

Jennifer R. Brown, MD, PhD
Dana-Farber Cancer Institute
Boston, MA

SPEAKERS:

Jennifer R. Brown, MD, PhD
Dana-Farber Cancer Institute
Boston, MA
Selecting Initial Therapy in CLL

Lydia Scarfò
Ospedale San Raffaele
Milano, Italy
Novel Therapies and Combinations in CLL Refractory to BTK Inhibitors and Venetoclax

Tanya Siddiqi, MD
City of Hope National Medical Center
Duarte, CA
Treatment of Richter's Syndrome

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Novel Genomic Blood Cancer Entities - Part 2

4:15 p.m. - 4:59 p.m. Central time
Ernest N. Morial Convention Center, 298-299

MODERATOR:

Elli Papaemmanuil, PhD
Memorial Sloan Kettering Cancer Center
NEW YORK, NY

SPEAKERS:

Elli Papaemmanuil, PhD
Memorial Sloan Kettering Cancer Center
NEW YORK, NY
Introductory Remarks

Jeffery Klco, MD, PhD
Saint Jude Children's Research Hospital
Memphis, TN
Ubtf Tandem Duplications As a Novel Sutype of Pediatric Acute Myeloid Leukemia

Phillip Nguyen
Peter MacCallum Cancer Centre
Melbourne, Australia
Ubtf Tandem Duplications in Myeloid Malignancy in Adults - Expansion of Phenotype?

Pauline Robbe, PhD
University of Oxford
Oxford, United Kingdom
Subclassifying CLL Using Whole Genome Sequencing

Daniel Nörenberg, MD
Charité Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, Berlin Institute of Health
Berlin, Germany
PMBCL - a Distinct Genomic Entity

Novità dal Meeting della Società Americana di Ematologia

3ª Sessione
Leucemia Linfatica Cronica

• 17.35 Stato dell'arte	M. KRAMPERA
• 17.45 Biologia e prognosi	G. GAIDANO
• 18.05 Trattamento di prima linea	P. GHIA
• 18.25 Terapie di salvataggio	F.R. MAURO
• 18.45 Discussione	

Milano, 2 Febbraio 2023