SESSIONE 2

Tavola rotonda esperti a confronto: il ruolo dell'algoritmo terapeutico nel paziente affetto da linfoma della zona marginale, macroglobulinemia di Waldenström, linfoma follicolare

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Zanubrutinib demonstrated durable disease control in patients with relapsed/refractory marginal zone lymphoma

MZL subtype	Response	2-Year Rates		
		Response Duration	PFS	OS
Nodal (n = 25)	ORR 76%; CR 20%; PR 56%	78%	73%	80%
Splenic (n = 12)	ORR 67%; CR 8%; ORR 58%	Not estimable	64%	92%
MALT (n = 25)	ORR 64%; CR 40%; PR 24%	75%	77%	92%

HRQOL

Patients experienced sustained improvements from baseline in HRQOL with greatest benefits at 18 to 24 months

High-risk patients
- Stage III/IV disease: 87%
- Bulky (>5 cm) disease: 37%
- Age ≥75 years: 28%

Zanubrutinib had a favorable safety profile
- Most common grade ≥3 TEAE: neutropenia/neutrophil count decreased (12%)
- Cardiac TEAEs (any grade) uncommon: atrial fibrillation/flutter (3%), hypertension (4%)
- Grade ≥3 bleeding: 1 patient
- No new safety signals observed

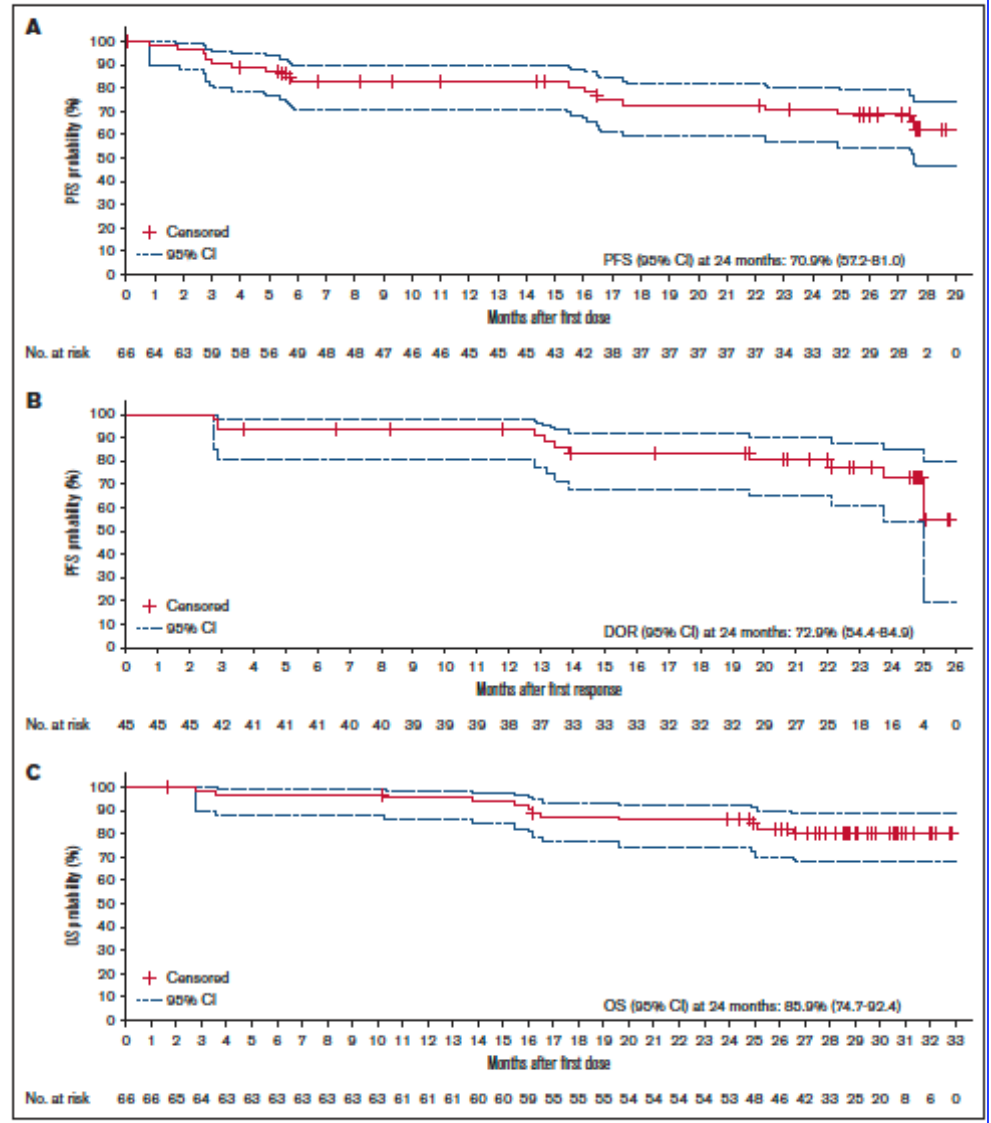

Figure 1. Kaplan-Meier analyses. (A) PFS, (B) DOR, and (C) OS (efficacy analysis set). NR, not reached.

Safety and efficacy of zanubrutinib in relapsed/refractory marginal zone lymphoma: final analysis of the MAGNOLIA study

Stephen Opat,[1] Alessandra Tedeschi,[2] Bei Hu,[3] Kim M. Linton,[4] Pamela McKay,[5] Sophie Leitch,[6] Morton Coleman,[7] Pier Luigi Zinzani,[8] Jie Jin,[9] Mingyuan Sun,[10] Magdalena Sobieraj-Teague,[11] Peter Browett,[12] Xiaoyan Ke,[13] Catherine Thieblemont,[14] Kirit Ardeshna,[15] Fontanet Bijou,[16] Patricia Walker,[17] Eliza A. Hawkes,[18] Shir-Jing Ho,[19] Keshu Zhou,[20] Zhiyu Liang,[21] Jianfeng Xu,[22] Chris Tankersley,[23] Richard Delaune,[24] Melannie Co,[23] and Judith Trotman[25]

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In Italia, Ibrutinib è disponibile ai sensi della Legge 648/96 nelle forme di MZL marginale recidivati/refrattari dopo almeno una linea di chemio-immunoterapia con anti-CD20: ORR del 58%, con mDOR di 27,6 mesi, mPFS di 15,7 mesi, mOS non raggiunta.

Table 3. Guide for selecting BTKis for the treatment of WM

	Preference	Alternative
BTKi options for initial therapy		
Convenience/compliance	Ibrutinib Zanubrutinib* Tirabrutinib*	Acalabrutinib
Deep IgM response needed (ie, IgM demyelinating neuropathy, cryoglobulinemia, and cold agglutinemia)	Zanubrutinib†	Ibrutinib Acalabrutinib Tirabrutinib‡
BNS	Ibrutinib Tirabrutinib‡	Zanubrutinib
History or predisposition to arrythmia	Zanubrutinib§	
History or predisposition to bleeding	Zanubrutinib§	
Neutropenic or pancytopenic	Ibrutinib	
$MYD88^{WT}$	Zanubrutinib	
$CXCR4^{Mut}$	Zanubrutinib	Ibrutinib plus rituximab
TP53 alteration	Zanubrutinib	Ibrutinib
BTKi options for switchover		
Intolerant to ibrutinib for adverse events other than atrial fibrillation	Dose-reduction of Ibrutinib Zanubrutinib Acalabrutinib‖	Pirtobrutinib¶
Intolerant to ibrutinib due to atrial fibrillation	Zanubrutinib	Pirtobrutinib¶
Acquired resistance to a cBTKi	Pirtobrutinib	

How I use genomics and BTK inhibitors in the treatment of Waldenström macroglobulinemia

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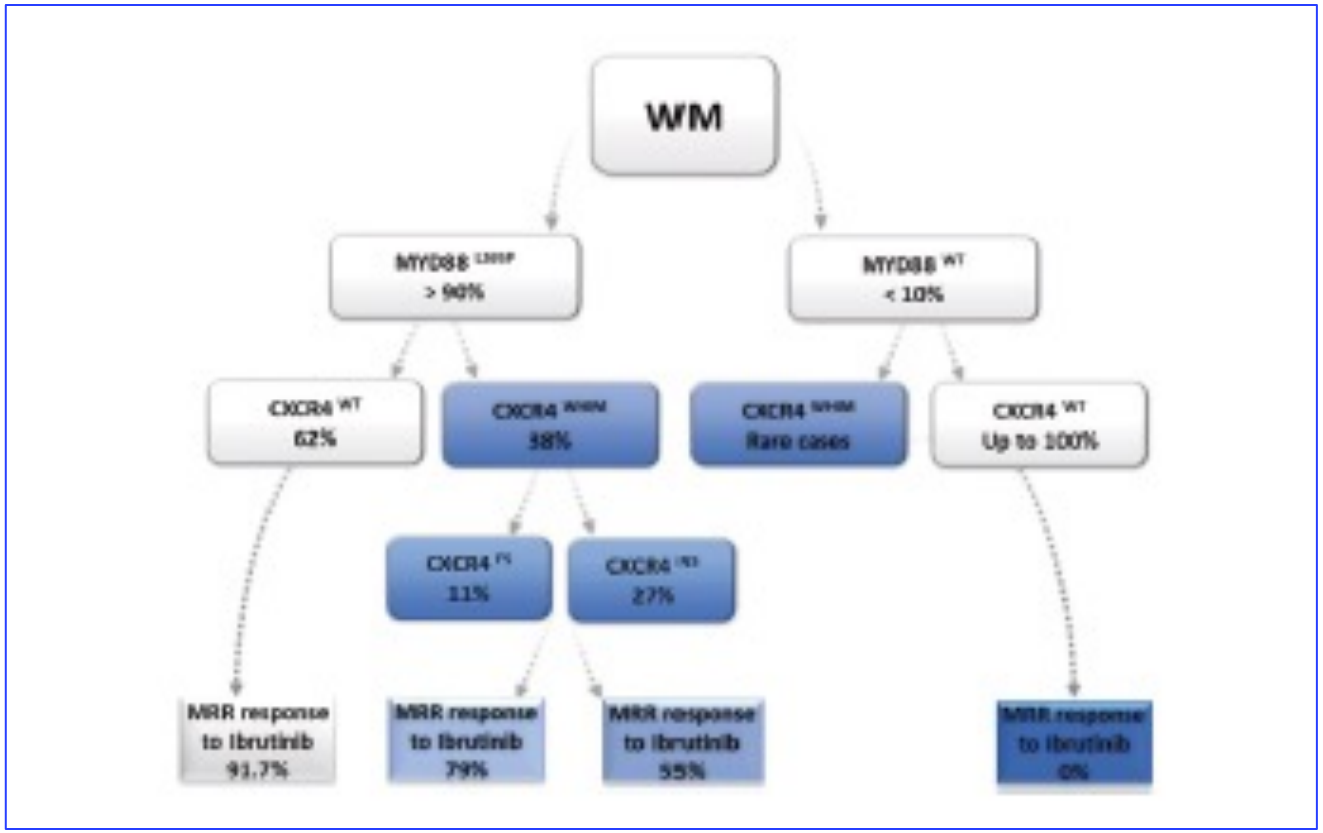
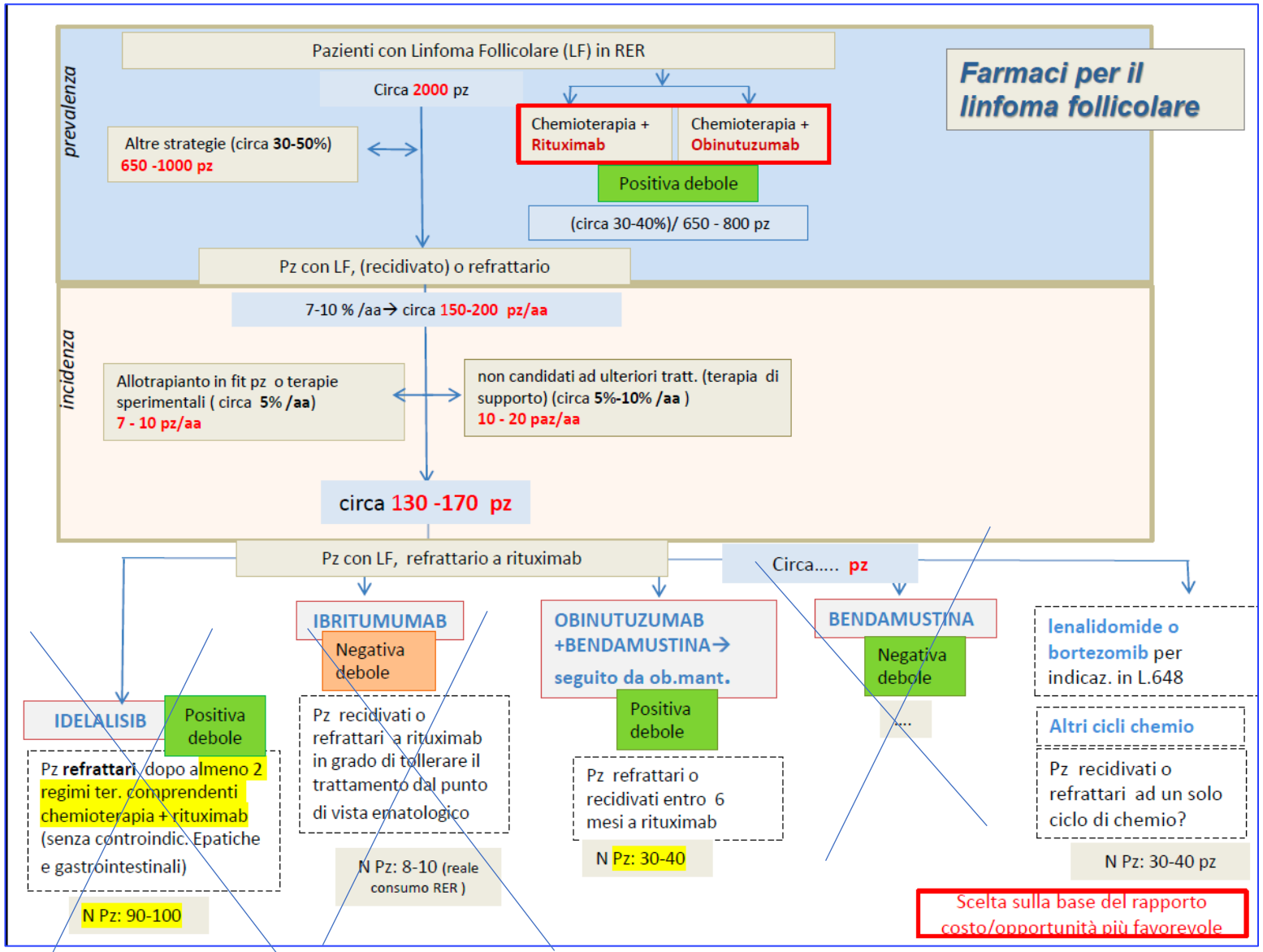


GREFO, RETTIFICA DETERMINAZIONE n. 13164 del 18/07/2019



AUTO-TX

1. Disease progression within 24 months of receiving front line chemo-immunotherapy;
2. No evidence of histo-transformation;
3. Achievement of CR/PR to salvage second line therapy.

Second CR/PR, durable remissions with 10-yr PFS about 50%

Rituximab+lenalidomide (R2)

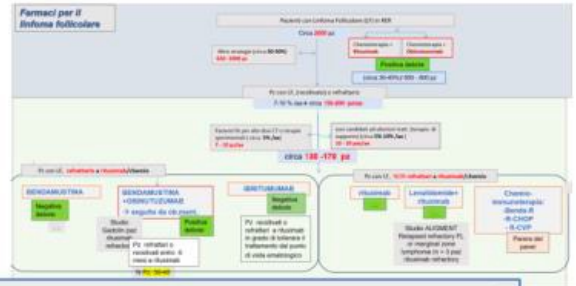
Augment population received one line of therapy with only 16% with refractory disease

Dose adjustement for renal failure necessary and cytopenia

PFS of 39.4 mos with median follow-up of 28.3 mos

Farmaci per il linfoma follicolare
Focus: dopo 2 linee di terapia

GReFO
4 dicembre 2023



Trattamenti dopo due precedenti linee di terapia

N Pz: 90-100

Idelalisib — Parere del panel

mosunetuzumab — Positiva debole

Tisagenlecleucel (TISA-CEL) — Positiva debole

Zanubrutinib +obinutuzumab

Titolo studio	Idelalisib Fase II, non controllato	Mosunetuzumab Fase II, non controllato			Tisagenlecleucel (ELARA) Fase II, non controllato	
Qualità delle prove	Bassa	Bassa			Bassa	
Follow up mediano	6 anni	18 mesi	update abstract a 27 mesi	Update a 3 aa abstract	9,9 mesi	28,9 mesi
n. paz.	72	90			97	
ORR (CR)	55,6% (16,7%)	80% (60%)	77,% (60%)	77,8% (60%)	86,2% (69,1%)	86% (68%)
PFS mediana % PFS	11 mesi	NR -- NR	NR -- a 24 m: 51,4%	24 m --- A 36 mesi: 43,2%	NR -- A 12 m: 67%	NR -- A 24 m: 57%
OS mediana --- %OS	61,2 m	---	---	NR -- A 36 m. 82,4%	NR ---	NR -- A 24 m: 88%

Previous lines of therapy	
Median (range)	3 (2-11)
2-3, No. (%)	104 (72)
>3, No. (%)	41 (28)
Refractory to most recent line of therapy, No. (%)	47 (32)
PD ≤24 months of starting first line of therapy, No. (%)	50 (34)

Median PFS 28 mos with median follow up of 20,3 mos

Parere del panel: **Uso residuale** (sulla base del bilancio benefici/rischi, utilizzo di **idelalisib** potrebbe avvenire in casi selezionati, in pazienti in buone condizioni generali e che abbiano esaurito le alt[illegible]pzioni terapeutiche).

Il trattamento con **Mosunetuzumab** è da preferire in pazienti che presentino recidive tardive (lunga durata delle risposte ai precedenti trattamenti) o nei pazienti più anziani.

Il trattamento con **Tisacel** è da preferire in pazienti che presentano recidiva precoce alle precedenti linee di terapia e nei pazienti più giovani

Bordo tratteggiato: f. non ancora rimborsato AIFA

53% POD24

63% POD24;
37% auto-tx

Farmaci per il linfoma follicolare

Focus: dopo 3 linee di terapia

Trattamenti dopo almeno tre precedenti linee di terapia

Mosunetuzumab	Tisa-cel	Axi-cel	Idelalisib
Positiva debole	Positiva debole	Positiva debole	Parere del panel Uso residuale
B/R: favorevole	B/R: favorevole	B/R: incerto-favorevole	

Titolo studio	Mosunetuzumab Fase II, non controllato			Tisagenlecleucel (ELARA) Fase II, non controllato		Axicel (Zuma-5) Fase II, non controllato	
Qualità delle prove	Bassa			Bassa		Bassa	
Follow up mediano	18 mesi	27 mesi	3 aa	9,9 mesi	28,9 mesi	17,5m/23,3 m	41,7 m
n. paz.	90			97		124 con LF	
Mortalità correlabile al trattamento	(1 paz) 1,6%						
Incidenza di EA grado III-IV	67,7% (50% Mosun related)			71,1% 40,2% Tisacel related		86%	
Interruzione del trattamento in assenza di progressione di malattia	4,8% (1,6% Mosenut related)			---		---	
CRS di qualsiasi grado	44%			49%		82%	
CRS di grado 3-4	2 paz			0		7%	

Mosunetuzumab: Bilancio B/R favorevole; non sono attualmente disponibili dati su un follow up a lungo termine sull'efficacia nel paziente precedentemente trattato con CART.

Il bilancio B/R fra i **due CAR-T** è risultato diverso in considerazione dei dati di safety dello studio registrativo che mostrano un vantaggio a favore di Tisa-cel per minore numero di CRS e ICAN di grado >=3 rispetto ad axi-cel.

Worse efficacy with prior exposure to bendamustine

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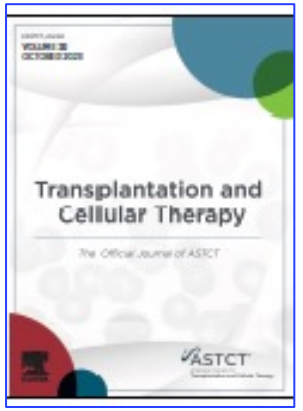
4 dicembre 2023

The American Society of Transplantation and Cellular Therapy and the European Society of Blood and Marrow Transplantation

Clinical Practice Recommendations for HSCT and Celluar Therapies for Follicular Lymphoma.

Clinical Practice Recommendations for Hematopoietic Cell Transplantation and Cellular Therapies in Follicular Lymphoma: A Collaborative Effort on behalf of The American Society of Transplantation and Cellular Therapy and the European Society of Blood and Marrow Transplantation

Madiha Iqbal , Ambuj Kumar , Peter Dreger , Julio Chavez , Craig S. Sauter , Anna M. Sureda , Veronika Bachanova , Richard T. Maziarz , Martin Dreyling , Sonali M. Smith , Caron Jacobson , Bertram Glass , Carla Casulo , Olalekan O. Oluwole , Silvia Montoto , Ranjana Advani , Jonathon Cohen , Gilles Salles , Nada Hamad , John Kuruvilla , Brad S. Kahl , Mazyar Shadman , Abraham S. Kanate , L. Elizabeth Budde , Manali Kamdar , Christopher Flowers , Mehdi Hamadani , Mohamed A. Kharfan-Dabaja



Highlights/Key recommendations

- Autologous-HCT is recommended as an option for consolidation therapy in patients with progression of disease within 24 months of receiving front line chemoimmunotherapy and who do not have evidence of histological transformation and achieve a CR or PR to salvage second line therapy.
- CAR-T should be considered a treatment option for patients who do not achieve CR or PR after second or subsequent lines of therapy.
- Allogeneic-HCT can be considered as consolidative treatment in select cases of relapsed chemosensitive FL patients who have received 3 or more lines of systemic therapy and are in the following clinical scenarios: post CAR-T failure; lack of access to CAR-T; concomitant therapy related myeloid neoplasm or bone marrow failure syndrome.