Associazione Italiana Radioterapia e Oncologia clinica

Società Italiana di Radiobiologia

LA RADIOTERAPIA BRIDGE PRIMA DELL' INFUSIONE DI CELLULE CAR-T NEL LINFOMA DIFFUSO A GRANDI CELLULE B. L'ESPERIENZA DI VICENZA

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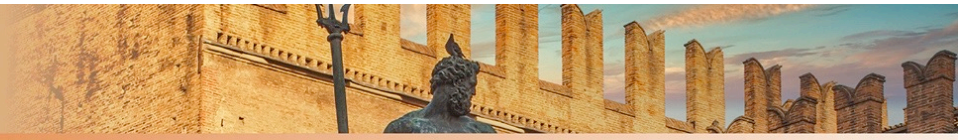

DICHIARAZIONE

Relatore: Spyridon Noulas

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 (NIENTE DA DICHIARARE)
- Titolarità 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)

CME ASTRO

International Journal of Radiation Oncology biology • physics
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Critical Review

Role of Radiation Therapy in Patients With Relapsed/Refractory Diffuse Large B-Cell Lymphoma: Guidelines from the International Lymphoma Radiation Oncology Group

CrossMark

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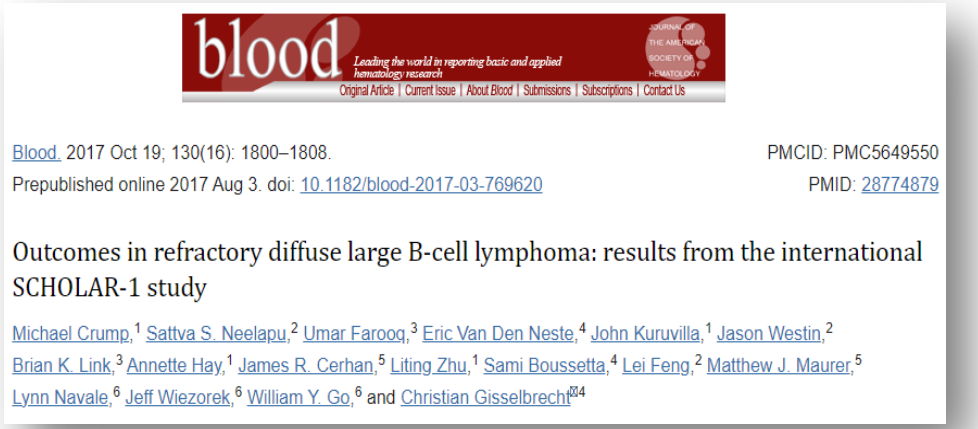
In patients with diffuse large B-cell lymphoma (DLBCL) treated with rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone (R-CHOP) chemotherapy, approximately **10%** to **15%** will have **primary refractory disease** and another **20%** to **25%** will develop a **relapse** after an initial response.



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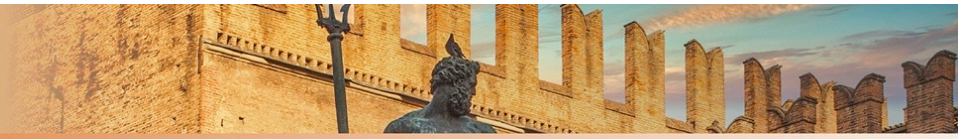
PMID: 28774879

Outcomes in refractory diffuse large B-cell lymphoma: results from the international SCHOLAR-1 study

Michael Crump,[1] Sattva S. Neelapu,[2] Umar Farooq,[3] Eric Van Den Neste,[4] John Kuruvilla,[1] Jason Westin,[2] Brian K. Link,[3] Annette Hay,[1] James R. Cerhan,[5] Liting Zhu,[1] Sami Boussetta,[4] Lei Feng,[2] Matthew J. Maurer,[5] Lynn Navale,[6] Jeff Wiezorek,[6] William Y. Go,[6] and Christian Gisselbrecht[✉4]

For patients with refractory DLBCL, the objective response rate was **26%** (complete response rate, **7%**) to the next line of therapy, and the **median overall survival** was **6.3 months**. **Twenty percent** of patients were **alive at 2 years**



	ZUMA-1[1,2]	JULIET[3]
CAR T-cell agent	Axicabtagene ciloleucel	Tisagenlecleucel
Study phase	II	II
Patient population	Adults with refractory DLBCL	Adults with R/R DLBCL
Patients pheresed/ treated, n	111/101	165/111
Bridging therapy, %	None allowed in pivotal trial, often used in standard practice	92
ORR, % CR, %	82 54	52 40

Long-term safety and activity of axicabtagene ciloleucel in refractory large B-cell lymphoma (ZUMA-1): a single-arm, multicentre, phase 1–2 trial

Frederick L Locke, Armin Ghobadi, Caron A Jacobson, David B Miklos, Lazaros J Lekakis, Olalekan O Oluwole, Yi Lin, Ira Braunschweig, Brian T Hill, John M Timmerman, Abhinav Deol, Patrick M Reagan, Patrick Stiff, Ian W Flinn, Umar Farooq, Andre Goy, Peter A McSweeney, Javier Munoz, Tanya Siddiqi, Julio C Chavez, Alex F Herrera, Nancy L Bartlett, Jeffrey S Wiezorek, Lynn Navale, Allen Xue, Yizhou Jiang, Adrian Bot, John M Rossi, Jenny J Kim, William Y Go, Sattva S Neelapu**

The median duration of response was **11.1 months** and the median progression-free survival was **5.9 months**

1. Neelapu. NEJM. 2017;377:2531. 2. Locke. Lancet Oncol. 2019;20:31. 3. Schuster. NEJM. 2019;380:45

Il flusso dei pazienti presso il G.O.M. CART

PAZIENTI VALUTATI: 65
dicembre 2019 – aprile 2022

LINFOCITOAFERESI: 24

2 non infusi per PD;
1 non infuso per «early termination»

PZ INFUSI: 21
13 Tisa-Cel + 8 Axi-Cel

ESCLUSI DAL PROGRAMMA:
41 pazienti

n 16 per CRITERI AIFA (incluso ECOG, conta linfocitaria, conta piastrinica, coinvolgimento SNC, dati anamnestici)

n 8 per MALATTIA RAPIDAMENTE PROGRESSIVA

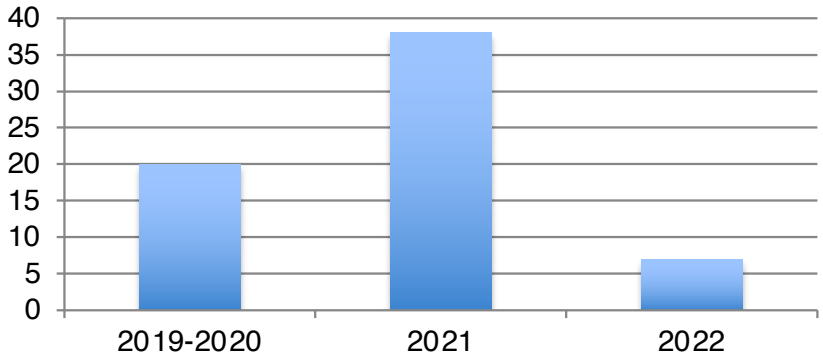
n 10 per ISTOLOGIA FUORI INDICAZIONE

n 9 per INDICAZIONE ASCT

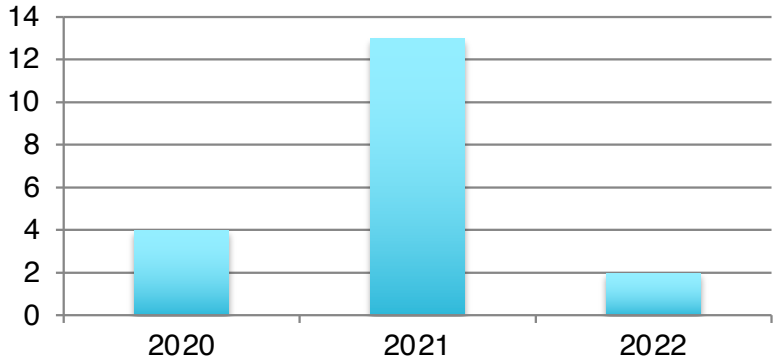
n 1 per scelta del paziente

prima infusione maggio 2020

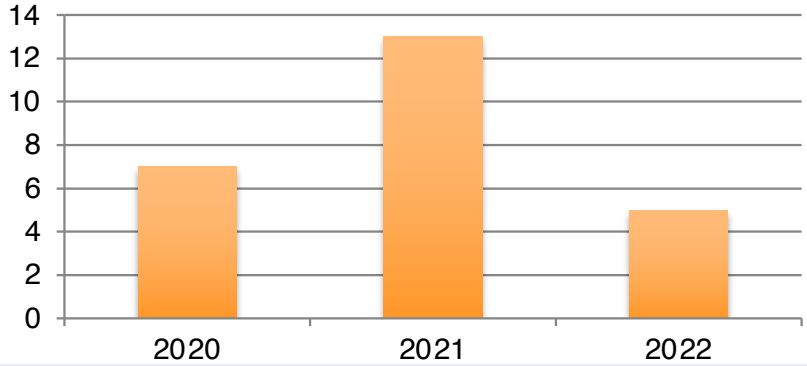
Richieste di valutazione

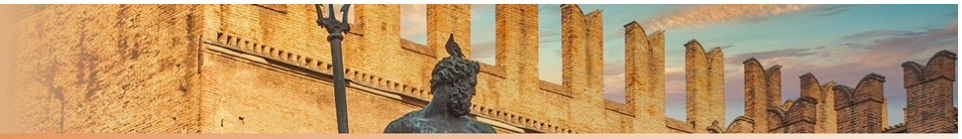


Infusioni



Linfocitoaferesi





Caratteristiche pz. candidati a CART

Totale pazienti sottoposti a Linfocitoaferesi	N=24 (%)
Diagnosi: - DLBCL - High grade/DHL - tFL	 12 (50%) 8 (33%) 4 (17%)
Prodotto infuso (21 pz) - Tisa-Cel - Axi-Cel	 13 (61%) 8 (39%)
Collection failure	**0 pz**
Final product failure	**3 pz**
Stato della malattia alla valutazione per CART - Primary refractory - Relapsed	 22 (92%) 2 (8%)

Caratteristiche pz. candidati a CART

Totale pazienti sottoposti a infusione di CART	N=21 (%)
Età, median (range)	62 (29-69)
Sesso (male)	9/21 (47%)
Stadio III/IV	7/21 (26%)
ECOG=1	6/21 (21%)
Tumor Bulk	10/21 (42%)
Siti extranodali (1-2)	8/21 (42%)
IPI 3-4	6/21 (32%)
Numero di precedenti terapie: 2 3 >3	 11/21 (57%) 7/21 (32%) 3/21 (11%)
Previous ASCT	6/21 (32%)

Terapia Bridge

100% dei pazienti sottoposti a bridge

Tipo di terapia bridge

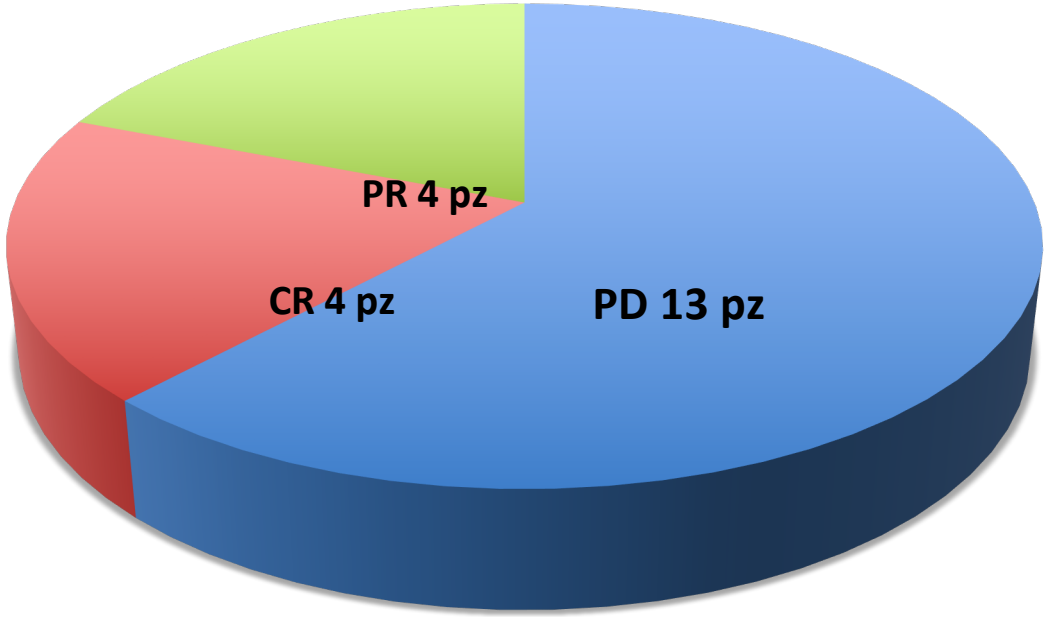
- R-BAC
- R-VEMP
- IEV
- R-ICE
- Rituximab + Dexa
- Pembro
- Lenalidomide/R-Lenalidomide
- RT
- Dexa

- RT + terapia sistemica concomitante(8)
- RT alone (4)
-Terapia sistemica (9)
- Necessità di più linee di bridge (4)

RT bridge

Totale pazienti sottoposti ad RT-bridge	N=12 (%)
Età, median (range)	60 (29-69)
Sesso (male)	5/12 (42%)
Sito RT	
-Laterocervicale -Addome -Pelvi -Mammella	2 (16%) 7 (59%) 2 (16%) 1 (9%)
Dose RT -20Gy/5f -30Gy/10f -36Gy/18f	 5 (41%) 4 (33%) 3 (26%)
Tecnica RT -3D -VMAT	 5 (41%) 7 (59%)
Terapia sistemica associata -R-BAC -Lenalidomide -Desametasone	 5 (41%) 2 (16%) 1 (9%)

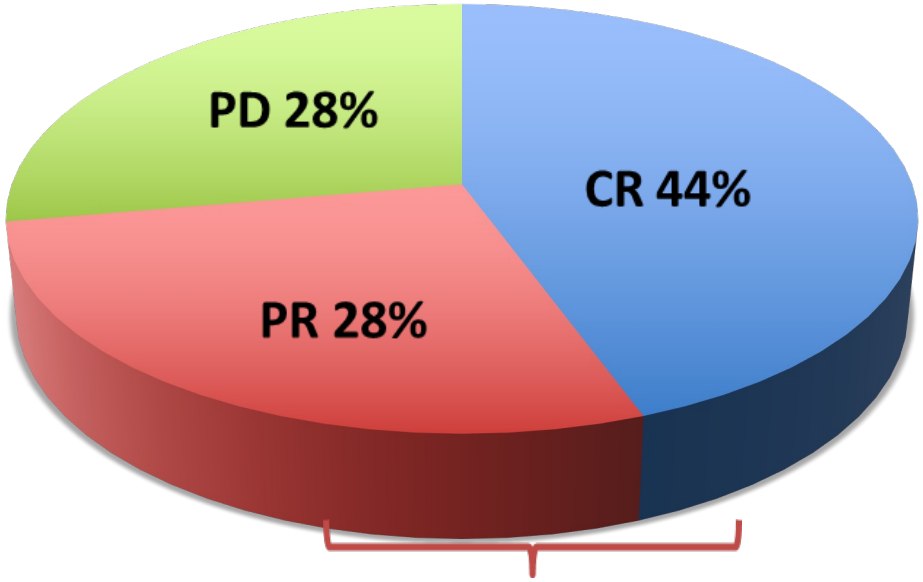
Stato di malattia alla linfodeplezione



Bridging RT

8 pz PD «out of field»

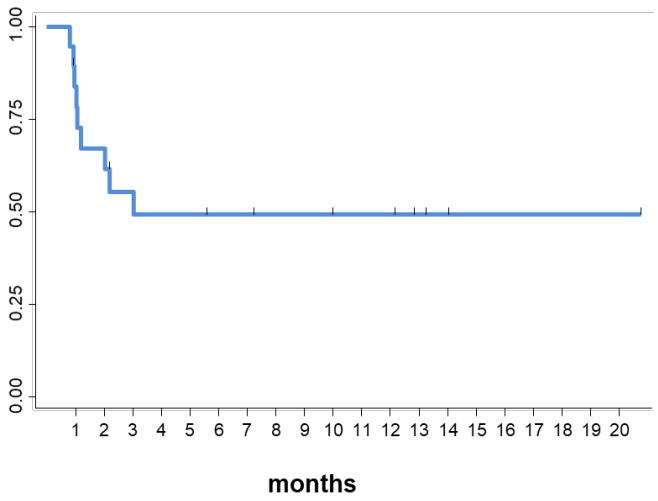
Risposta a 30 giorni



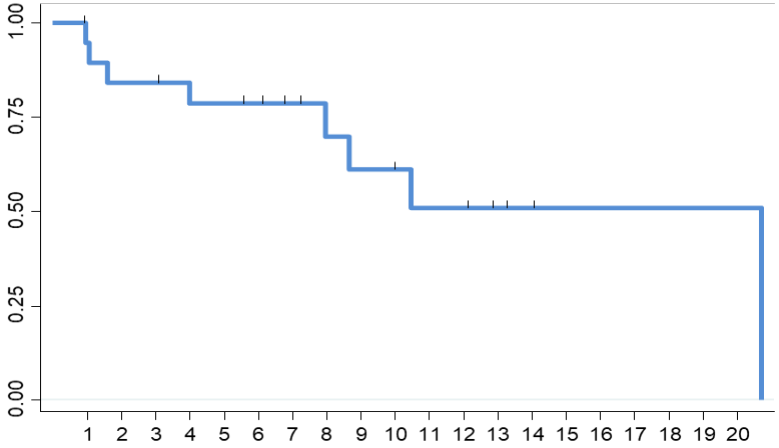
ORR 72%

I primi risultati – efficacia

PFS 6 m: 49% (95% CI: 25-67)



OS 6 m: 51% (95% CI: 22-74)



Median follow-up 7 months (1-20.7 months)

Safety

TOXICITY N=21	N (%)	G3-G4
CRS	16/21 (76%)	0
ICANS	2/21 (9%)	1 (5%)
Tocilizumab use	15/21 (71%)	/
Steroid use	6/21 (28%)	/
ICU admission	2/21 (9%)	/
Infections	3/21 (15%)*	

Nessuna tossicità RT associata G3 o superiore

*2 infections in the first 30 days; 1 patient with COVID disease 2 months after CART infusion

Conclusioni

La radioterapia «bridge», associata o meno a terapia sistemica concomitante, puo' essere somministrata con sicurezza prima dell'infusione di cellule CAR-T.

Ulteriori studi futuri si rendono necessari per definire le caratteristiche ottimali della RT (dose totale, dose/frazione, tempistiche).


Grazie!!