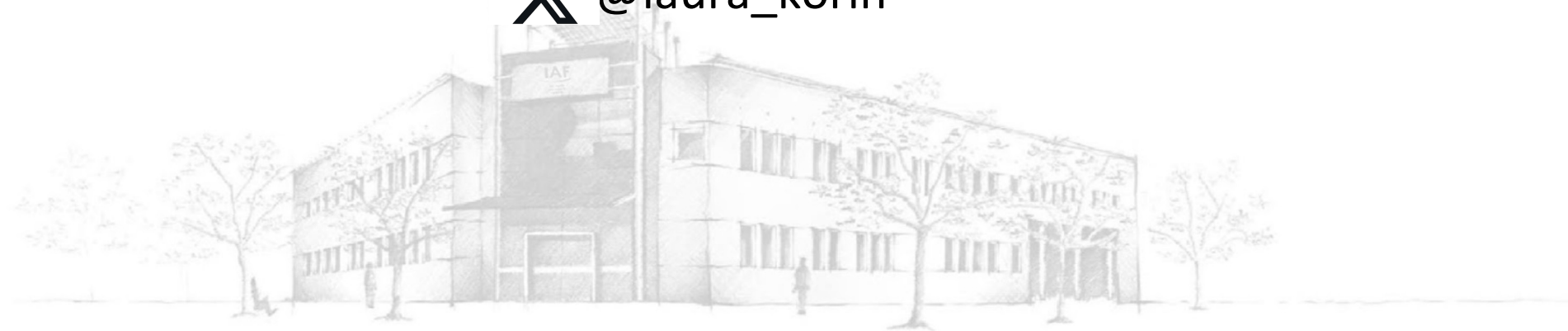


Inhibidores de check point pre TACPH en LH: derribando paradigmas

Lymphoma experience
12 de Abril 2024

Laura Korin
Médica Hematóloga
Instituto Alexander Fleming
X @laura_korin

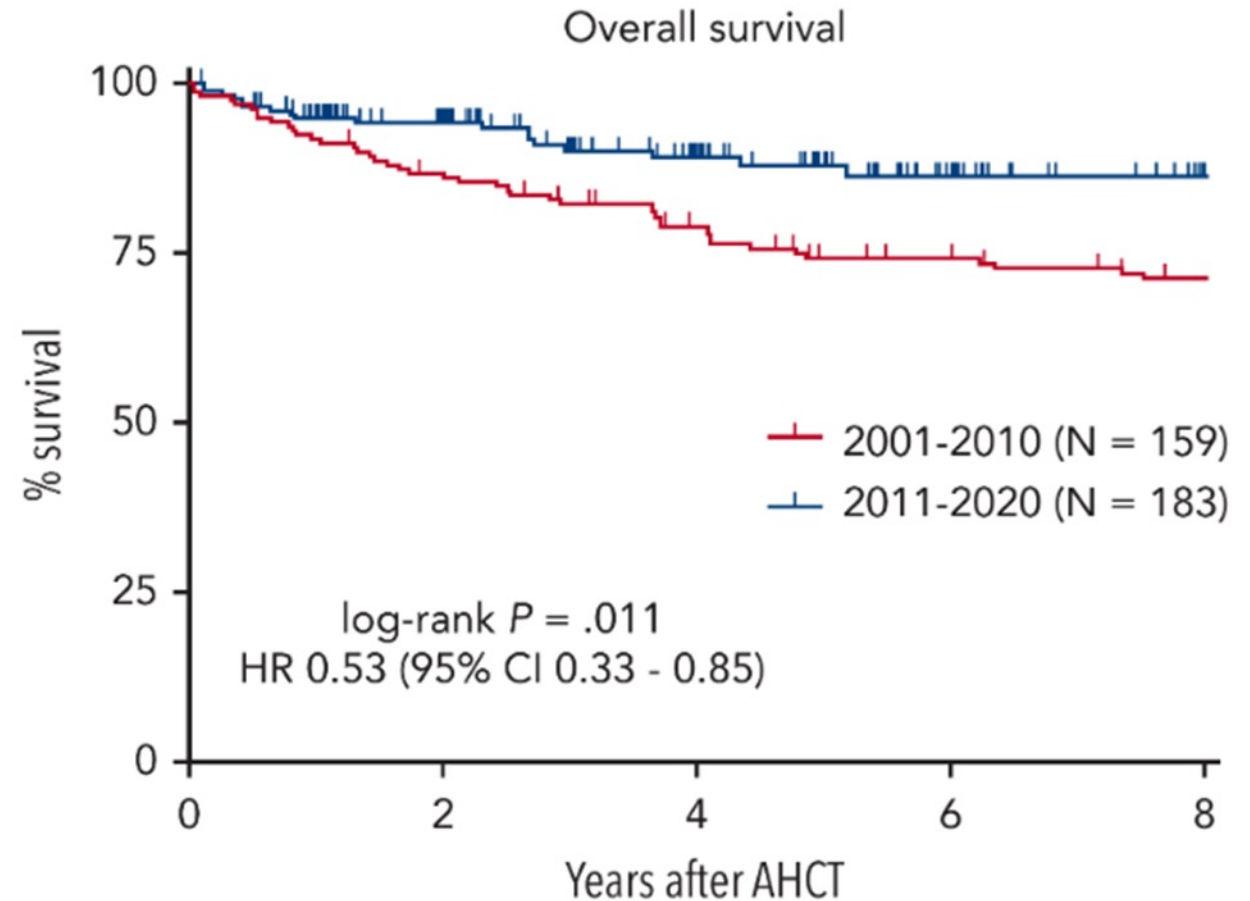


Conflictos de interés

Categoría	
Empleado	No
Consultor	No
Fondos de investigación	No
Honorarios por conferencia	Sandoz, Takeda, Pint-Pharma, Astra Zeneca
Formar parte del grupo de oradores	No
Honorarios por consultoría	Takeda, Roche, Raffo, Pint-Pharma, Abbvie
Otros	No

Mejoría de la supervivencia en LH R/R

	2001-2010	2011-2020
N	159	183
Use of novel agents in salvage therapy		
BV	0%	20%
PD-1 inhibitor	0%	15%
Pre-ASCT metabolic CR rate	42%	61%
Post-ASCT PFS	63.3%	73.1%
Post-ASCT OS	79.0%	89.1%
Receipt of radiation therapy	73%	32%



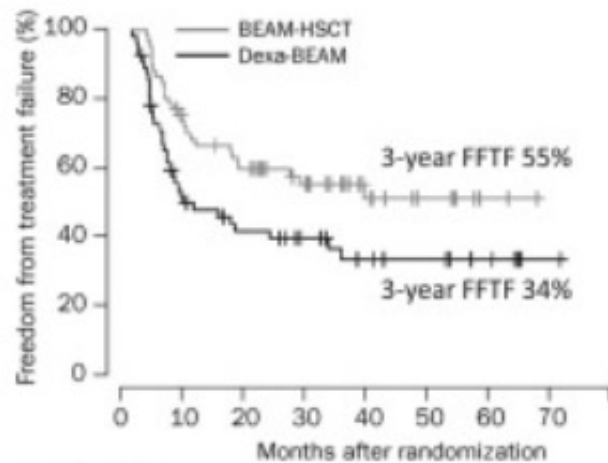
No. at risk:	159	137	119	105	95
	183	130	84	44	18

Mejoria de la supervivencia en LH R/R

Hitos del tto pre trasplante

TACPH como standard en R/R

A Transplant years: 1993-1997

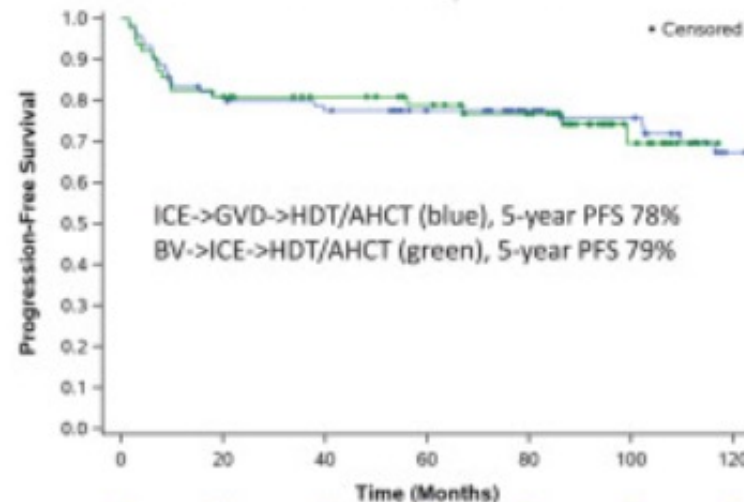


Number of patients

BEAM-HSCT	61	43	34	25	13	8	7	0
Dexa-BEAM	56	27	20	15	10	8	5	1

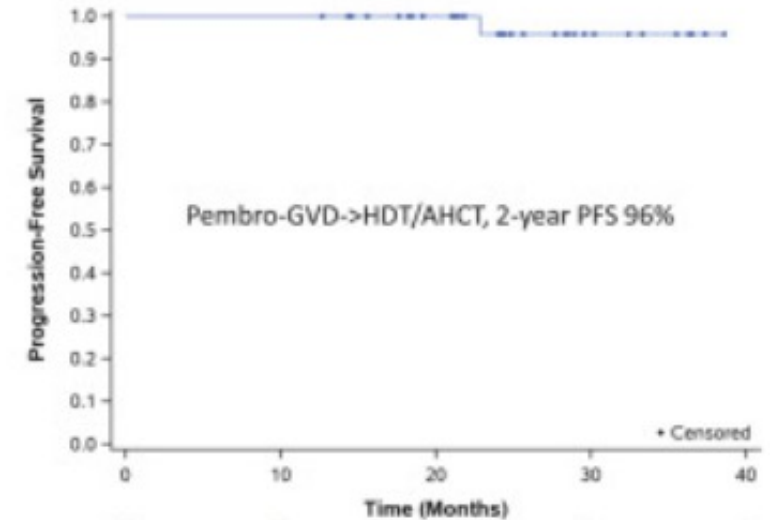
RMC como f. pronóstico

B Transplant years: 2004-2014



Esquemas de rescate con ICP

C Transplant years: 2018-2020



Moskowitz Hematology Am Soc Hematol Educ Program. 2022

Agenda

Hay que ir al TACPH
con un PET negativo

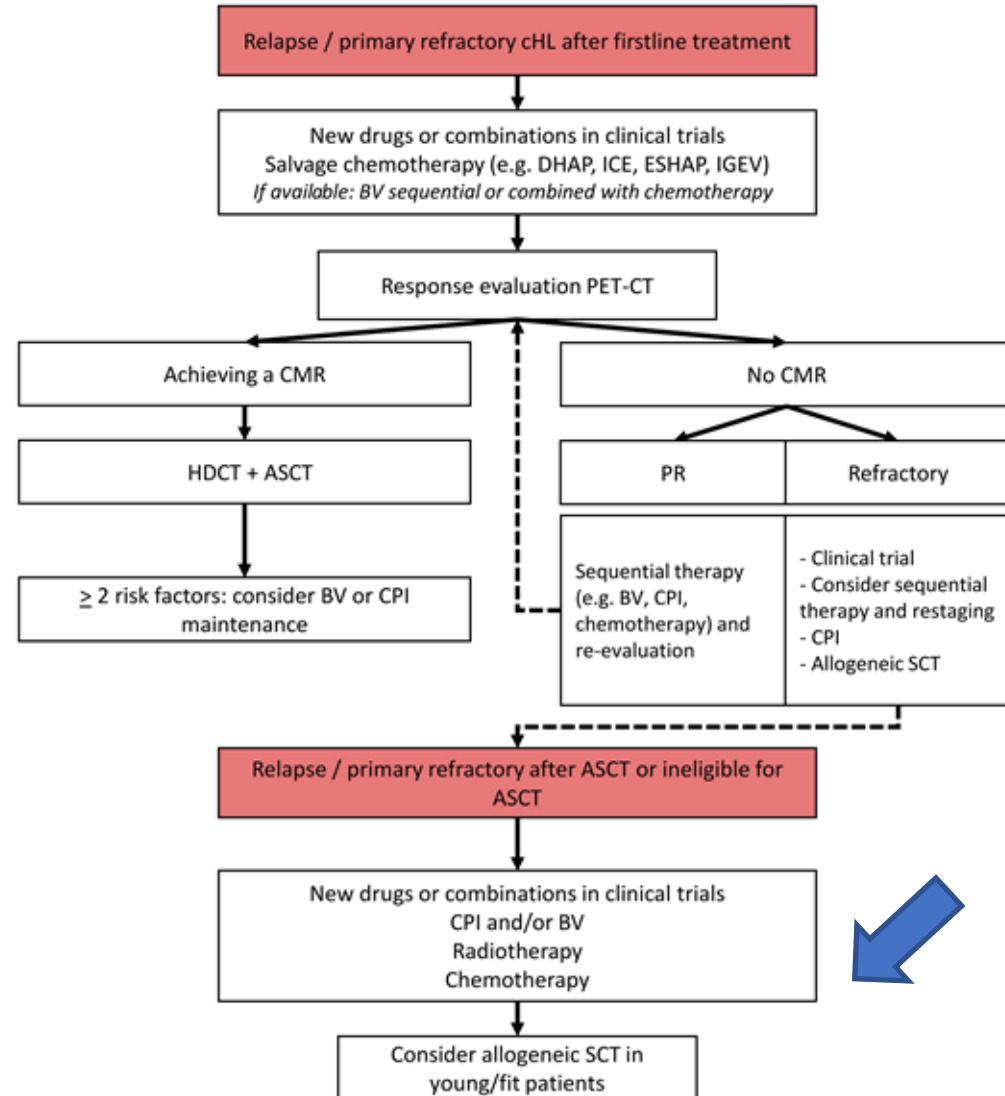
TACPH sólo con
quimiosensibilidad

Alto riesgo: consolidación
post TACPH



TACPH: alternativa válida sólo para pac quimiosensibles en la era de los ICP?

Paradigma histórico

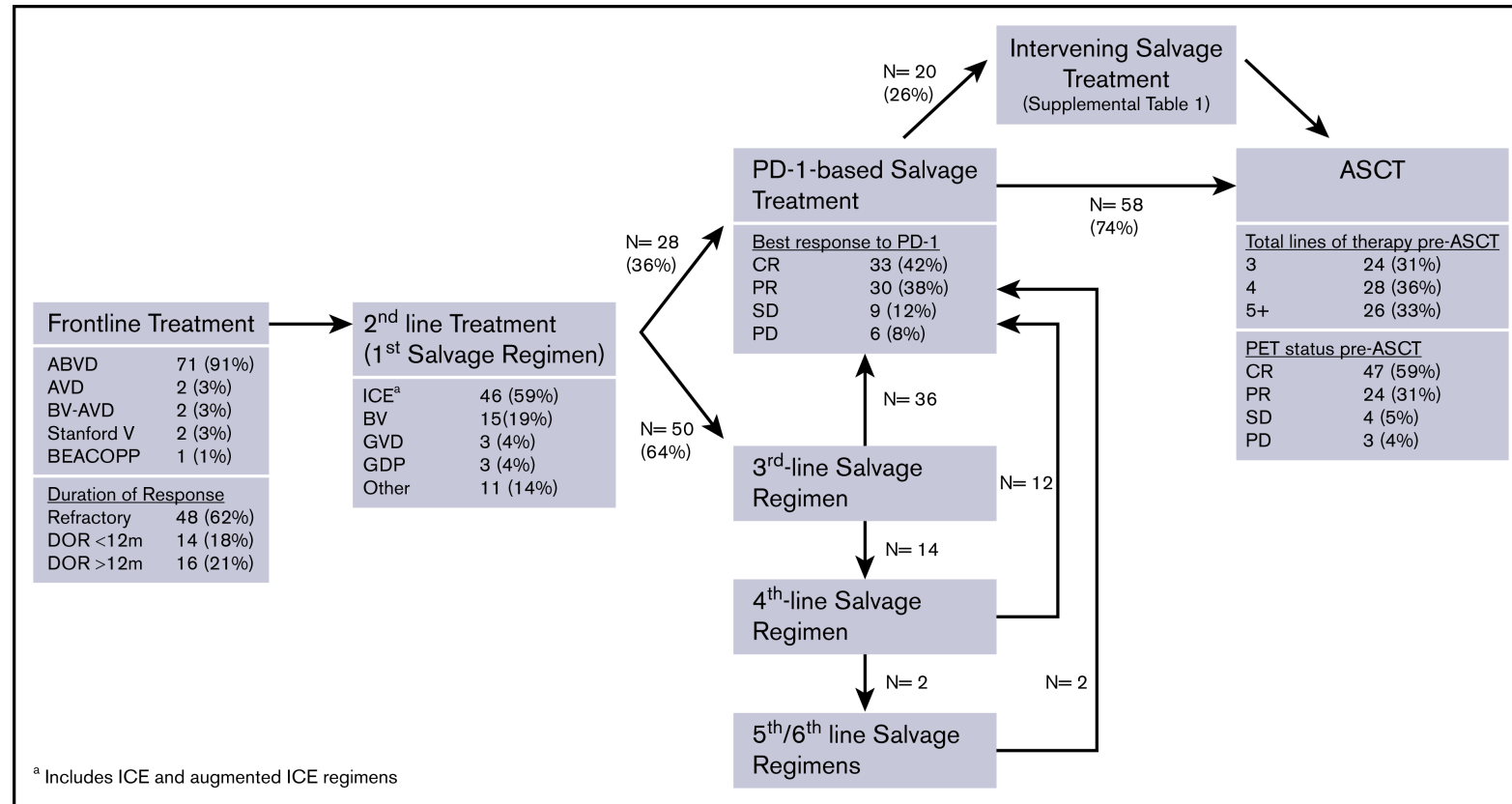


Driessen et al. Hematology Am Soc Hematol Educ Program. 2021

TACPH: alternativa válida sólo para pac quimiosensibles en la era de los ICP?

Experiencia EEUU

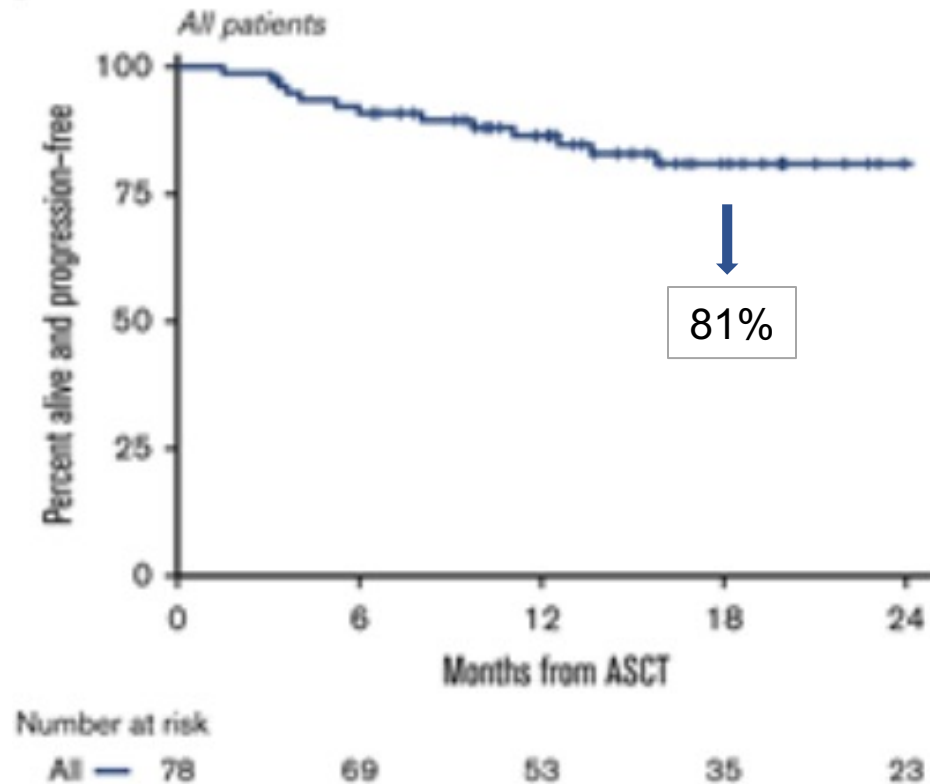
Autologous stem cell transplantation after anti-PD-1 therapy for multiply relapsed or refractory Hodgkin lymphoma



Merryman et al. Blood 2021

TACPH: alternativa válida sólo para pac quimiosensibles en la era de los ICP?

Experiencia EEUU



Merryman et al. Blood 2021

Autologous stem cell transplantation after anti-PD-1 therapy for multiply relapsed or refractory Hodgkin lymphoma

Term	N (%)	18-month PFS (95% CI)	HR (95% CI)	p-value
Age at time of ASCT				
10-year increment	78 (100)	-	1.69 (1.18, 2.41)	0.004
Refractory to pre anti-PD-1 treatment				
No	23 (29)	87 (72 - 100)	Reference	
Yes	55 (71)	78 (67 - 91)	1.73 (0.49, 6.15)	0.40
Refractory to two lines prior to anti-PD-1 treatment				
No	36 (46)	84 (72 - 98)	Reference	
Yes	42 (54)	78 (66 - 93)	1.33 (0.47, 3.73)	0.59
Refractory to three lines prior to anti-PD-1 treatment				
No	60 (77)	85 (75 - 96)	Reference	
Yes	18 (23)	67 (48 - 92)	2.22 (0.79, 6.25)	0.13
Refractory to all prior lines of therapy before anti-PD-1 treatment				
No	49 (63)	83 (72 - 95)	Reference	
Yes	29 (37)	78 (64 - 95)	1.20 (0.43, 3.39)	0.72
Refractory to two or more lines of salvage therapy				
No	48 (62)	85 (74 - 97)	Reference	
Yes	30 (38)	75 (60 - 93)	1.72 (0.62, 4.77)	0.30
Line received anti-PD-1 therapy				
Line 1-3	28 (36)	95 (87 - 100)	Reference	
Line 4+	50 (64)	73 (61 - 88)	3.69 (0.83, 16.42)	0.087
PD-1 regimen				
Combination	18 (23)	84 (65 - 100)	Reference	
Monotherapy	59 (77)	81 (72 - 93)	1.20 (0.26, 5.50)	0.82
PD-1 responders				
Response	63 (81)	88 (80 - 98)	Reference	
Non response	15 (19)	51 (30 - 86)	6.31 (2.28, 17.48)	< 0.001
Patients who received intervening salvage therapy				
No	58 (74)	88 (80 - 98)	Reference	
Yes	20 (26)	58 (37 - 90)	3.58 (1.28, 10.06)	0.015
Pre-ASCT PET response				
Negative	47 (60)	85 (74 - 97)	Reference	
Positive	31 (40)	75 (60 - 93)	2.00 (0.72, 5.52)	0.18
ASCT conditioning regimen				
Other	25 (32)	87 (73 - 100)	Reference	
BEAM	53 (68)	78 (67 - 92)	1.46 (0.46, 4.60)	0.52
No. of PD-1 half-lives				
0-5	67 (87)	84 (75 - 94)	Reference	
>5	10 (13)	60 (36 - 100)	2.85 (0.90, 8.97)	0.074

TACPH: alternativa válida sólo para pac quimiosensibles en la era de los ICP?

731.AUTOLOGOUS TRANSPLANTATION: CLINICAL AND EPIDEMIOLOGICAL | NOVEMBER 28, 2023

High Progression Free Survival Rates in Patients with Multiply Relapsed/Refractory Hodgkin Lymphoma Undergoing Autologous Stem Cell Transplant after Checkpoint Inhibitors: Results from Grupo Argentino De Trasplante De Medula Osea y Terapia Celular (GATMO-TC)

Laura Korin, Martin Castro, Silvina Palmer, Lautaro Sardu, Ana Basquiera, Sebastian Yantorno, Sol Jarchum, Maria Flavia Flavia Figueroa, Magali Colucci, María Eugenia Funes, Gonzalo Bentolila, Martin Saslavsky, Alejandra Banchieri, Maria Belén Rosales Ostriz, Romina Penalba, Micaela Quarchione, Gregorio Jaimovich, Gustavo Milone, Adriana Vitriu, Maria Cecilia Foncuberta

Experiencia argentina

N: 41, 15 centros.
-56% ref 1arios
-19,5% rec temprana

Tto de rescate entre ICP y TACPH (n:5)

Tto con ICP

Monoterapia 36 (87,8 %)
Nivo 21 (51,2%) / Pembro 20 (48,8%)
Mediana de líneas: 4 (2-6)
Mediana de ciclos: 7 (2-34)
RTA
EE 1 (2,4%)
EP 3 (7,3%)
RC 28 (68,3%)
RP 9 (22%)

TACPH

Lineas pre TAMO
2.....3 (7,3 %)
3.....9 (22%)
4.....16 (39%)
5 o +.....13 (31,7%)

PET pre TACPH
RC 31 (75,6%)
RP 10 (24,4%)

Mediana de días al TACPH post ICP: 60 (3-183)

Blood (2023) 142 (Supplement 1): 2220.

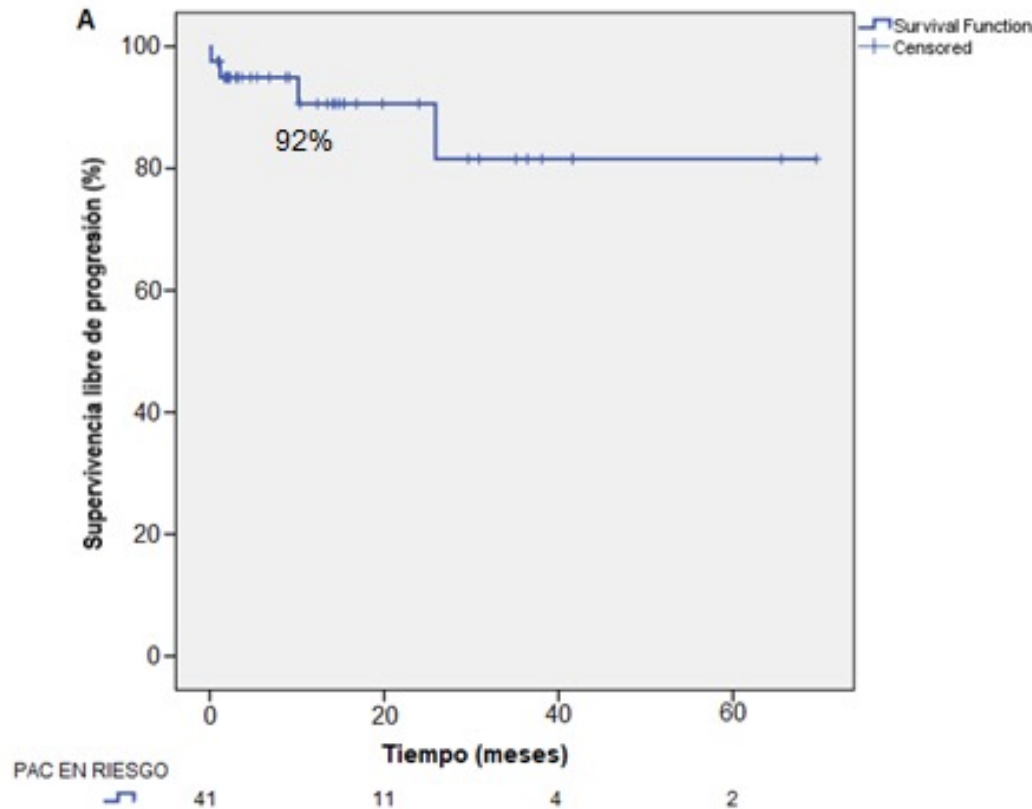
TACPH: alternativa válida sólo para pac quimiosensibles en la era de los ICP?

Experiencia argentina

731.AUTOLOGOUS TRANSPLANTATION: CLINICAL AND EPIDEMIOLOGICAL | NOVEMBER 28, 2023

High Progression Free Survival Rates in Patients with Multiply Relapsed/Refractory Hodgkin Lymphoma Undergoing Autologous Stem Cell Transplant after Checkpoint Inhibitors: Results from Grupo Argentino De Trasplante De Medula Osea y Terapia Celular (GATMO-TC)

Laura Korin, Martin Castro, Silvina Palmer, Lautaro Sardu, Ana Basquiera, Sebastian Yantorno, Sol Jarchum, Maria Flavia Flavia Figueroa, Magali Colucci, María Eugenia Funes, Gonzalo Bentolila, Martin Saslavsky, Alejandra Banchieri, Maria Belén Rosales Ostriz, Romina Penalba, Micaela Quarchione, Gregorio Jaimovich, Gustavo Milone, Adriana Vitriu, Maria Cecilia Foncuberta



Mediana de seguimiento de 12,3 meses (0,1-69)

2 pacientes recayeron

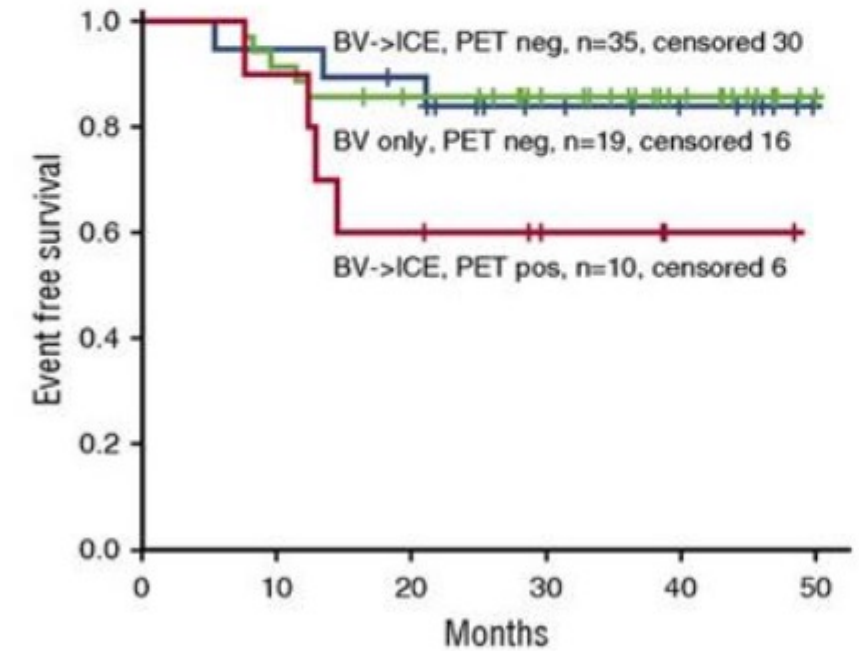
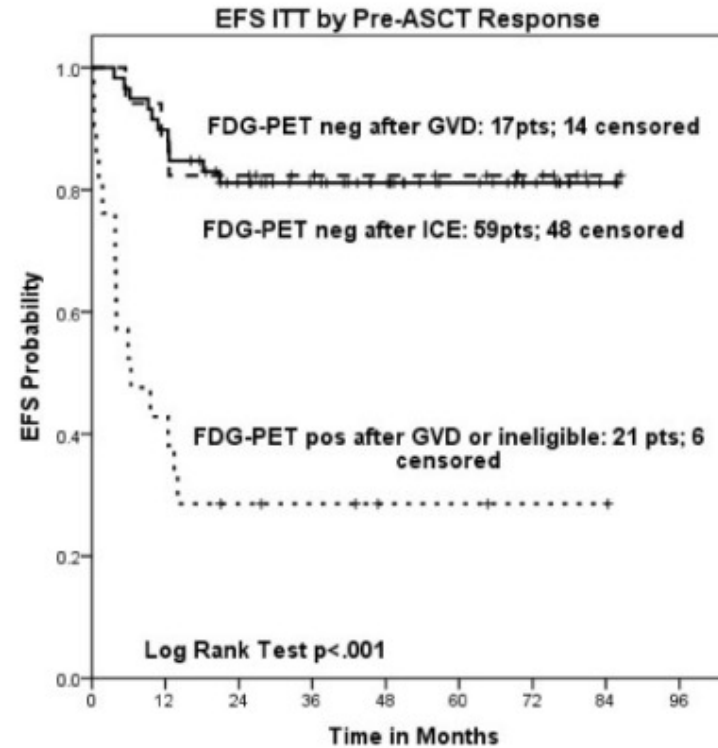
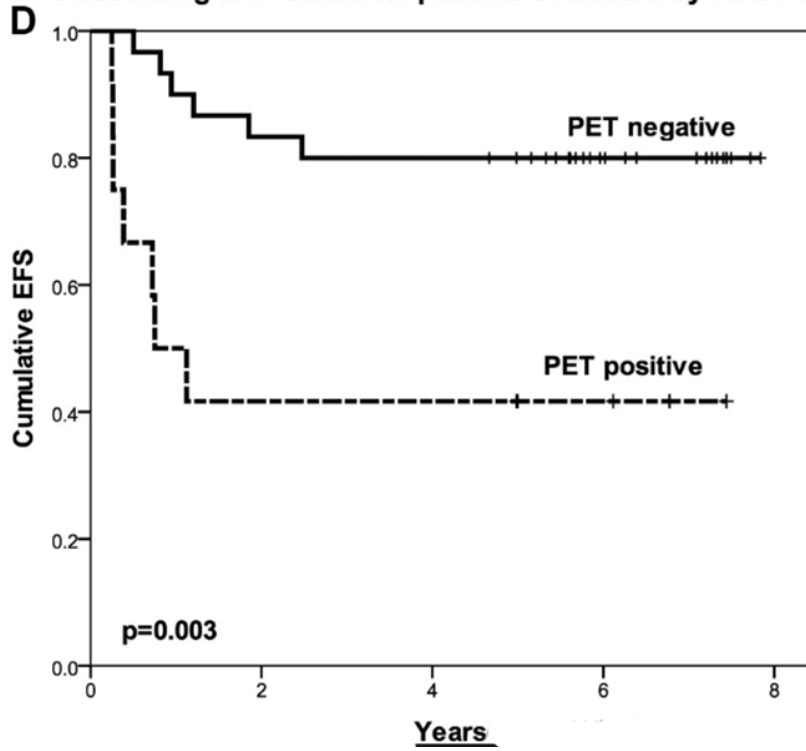
3 pacientes fallecieron
1 x progresion
1x MRT
1 x infeccion tardia

Blood (2023) 142 (Supplement 1): 2220.

Hitos del TACPH en LH R/R

Remisión completa metabólica pre TACPH

EFS according to FI status for patients evaluated by FDG-PET



Moskowitz et al, Blood 2010.

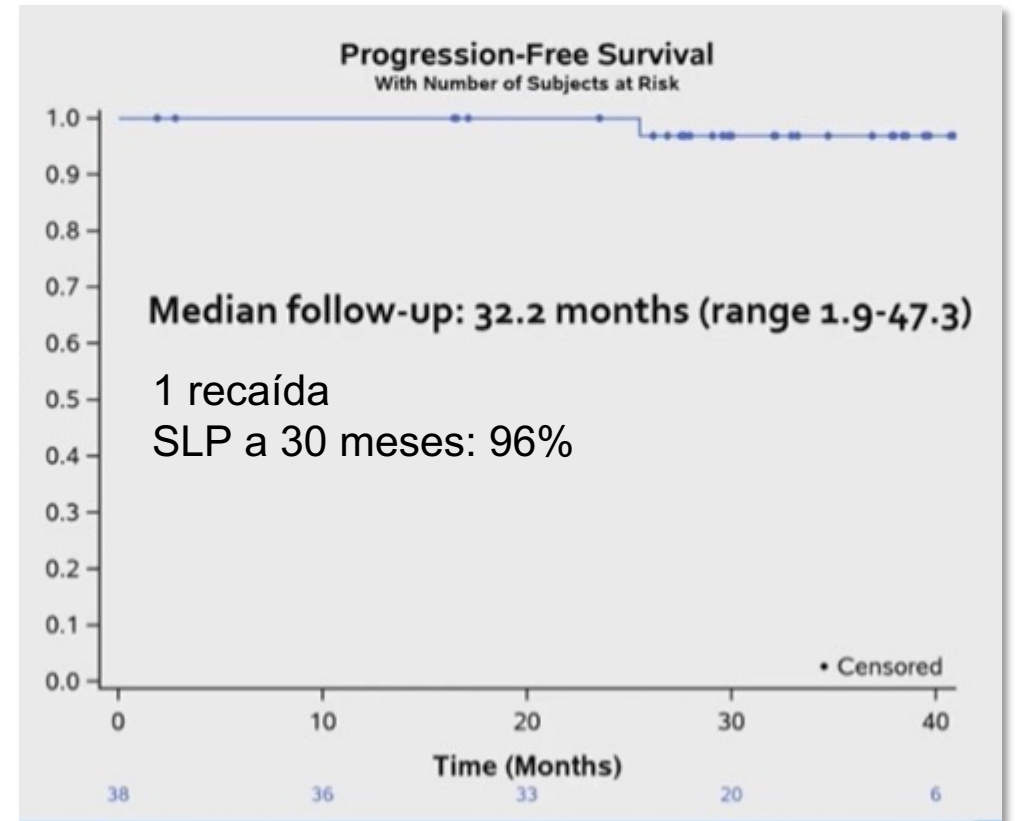
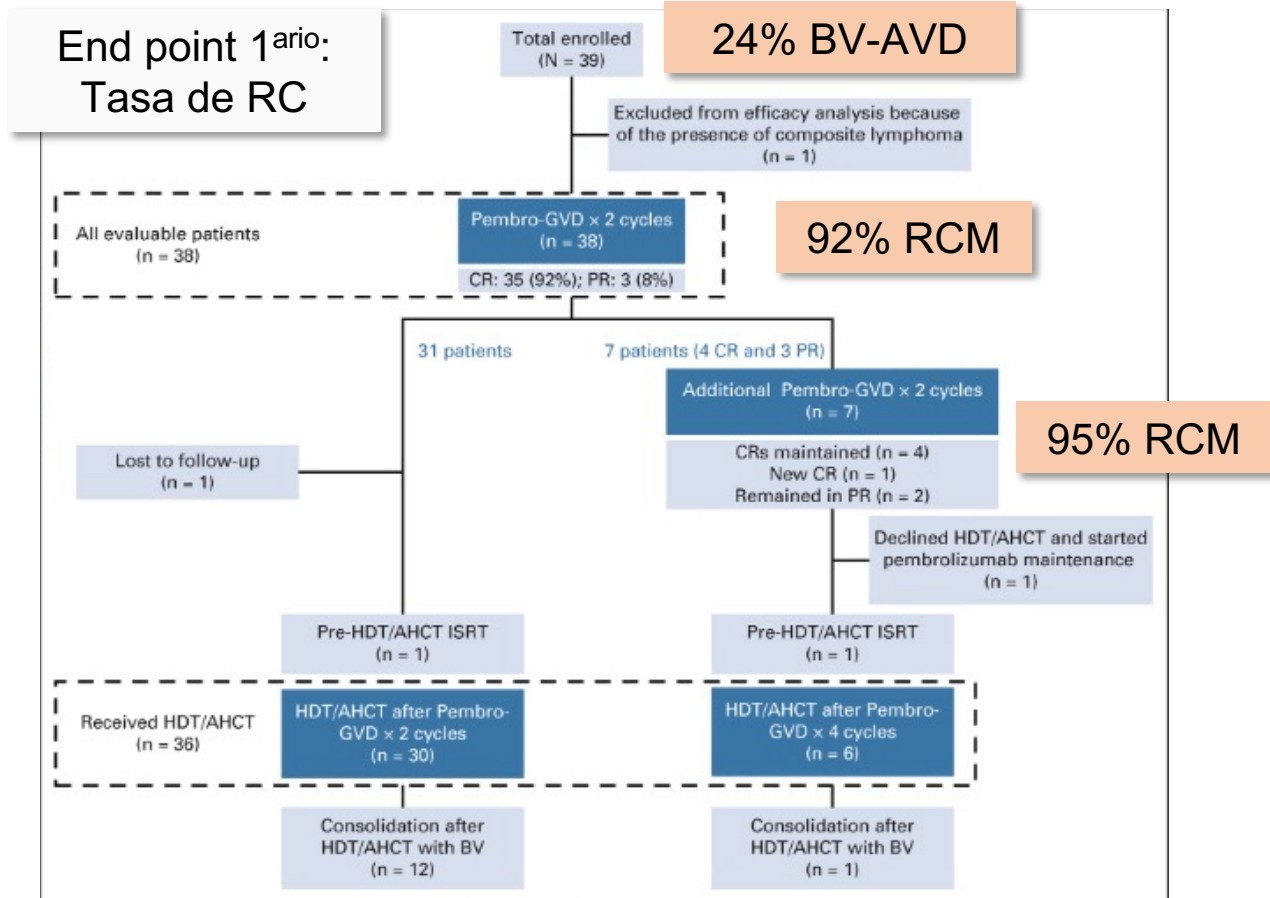
Moskowitz et al, Blood 2012.

Moskowitz et al, Blood 2017.

En búsqueda del PET neg pre TACPH

Intensificar tto de rescate (ICP en 2da línea)

Phase II Trial of Pembrolizumab Plus Gemcitabine, Vinorelbine, and Liposomal Doxorubicin as Second-Line Therapy for Relapsed or Refractory Classical Hodgkin Lymphoma

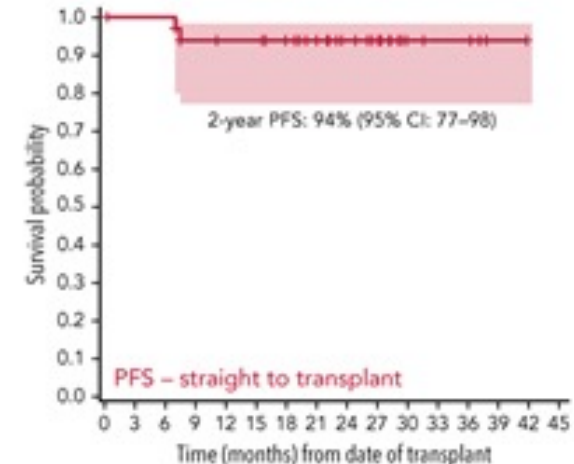
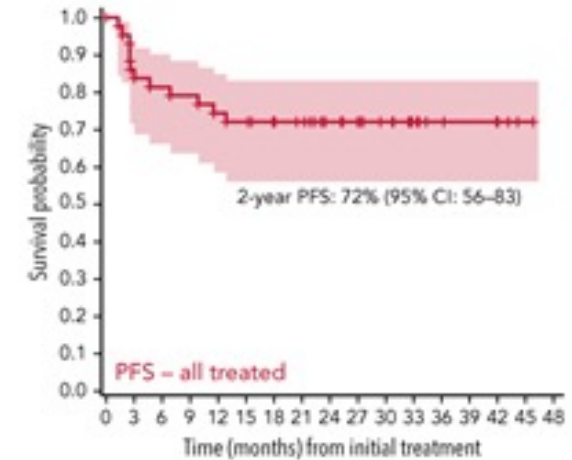
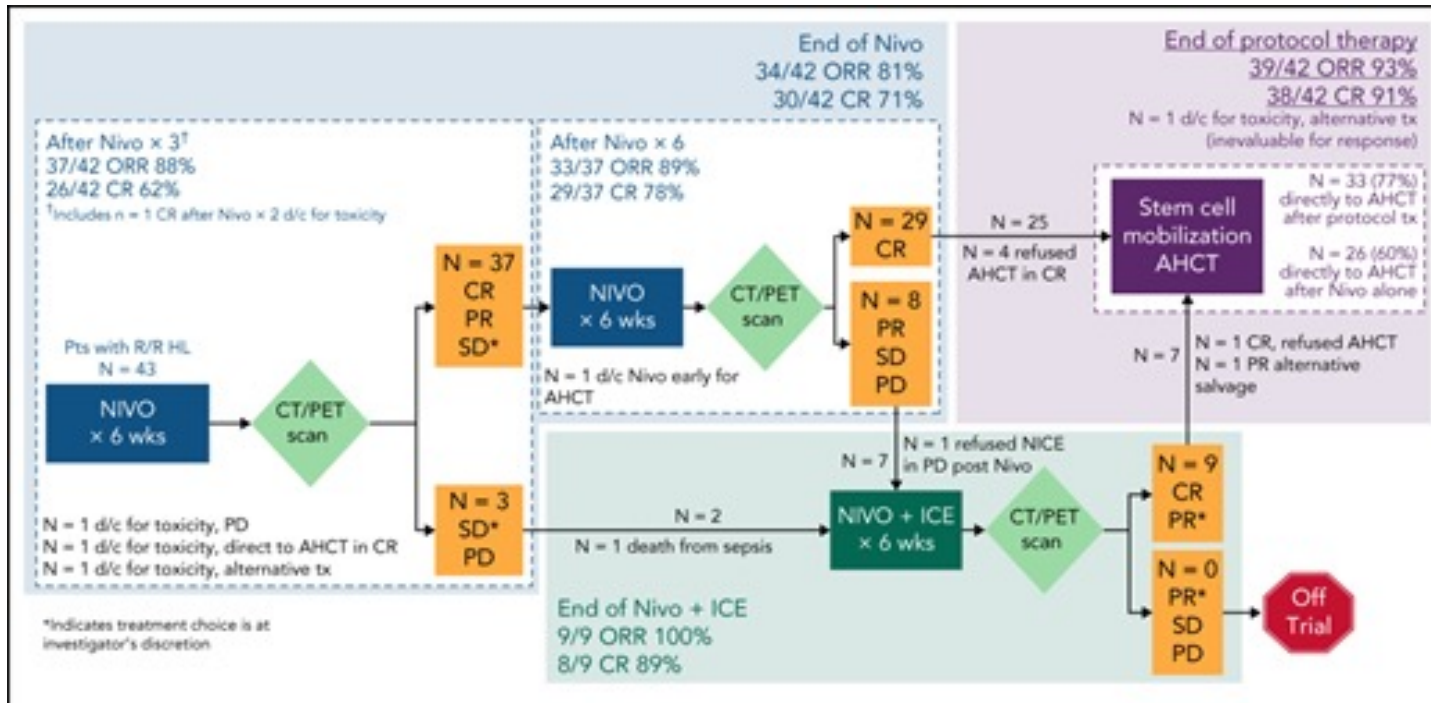


Moskowitz et al. JCO 2021
Moskowitz et al. ISHL 12

En búsqueda del PET neg pre TACPH

Intensificar tto de rescate (ICP en 2da línea)

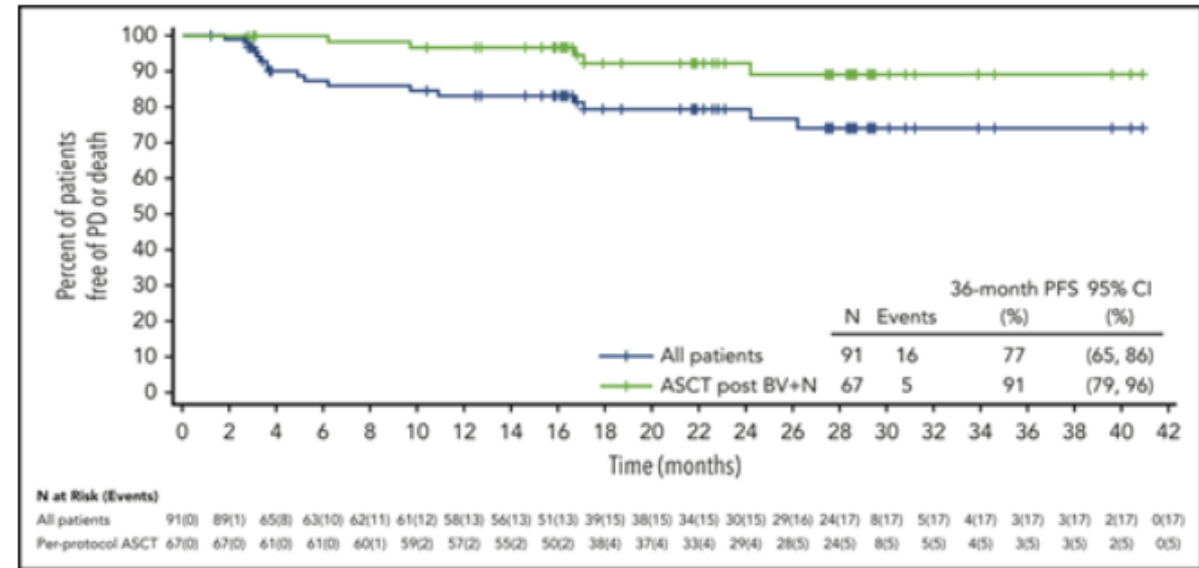
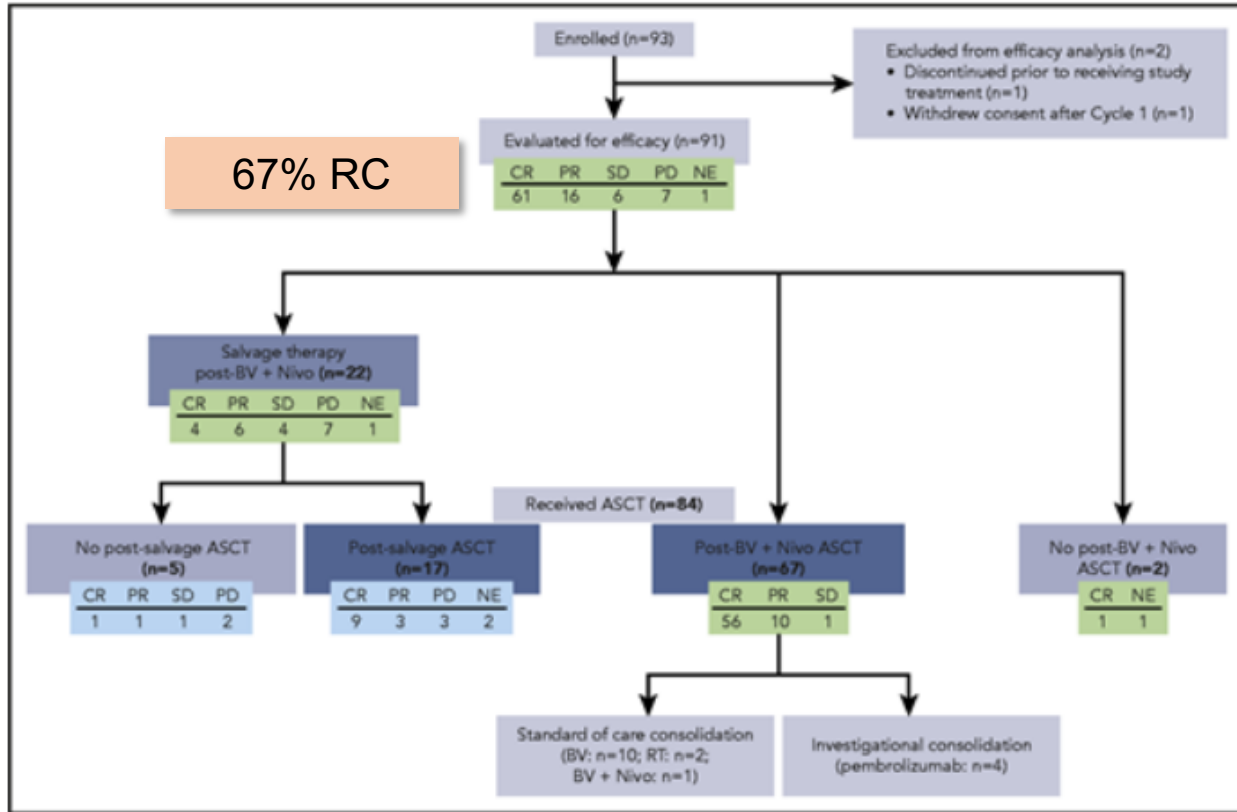
Response-adapted anti-PD-1-based salvage therapy for Hodgkin lymphoma with nivolumab alone or in combination with ICE



En búsqueda del PET neg pre TACPH

Intensificar tto de rescate (ICP + Bv en 2da línea)

Brentuximab vedotin in combination with nivolumab in relapsed or refractory Hodgkin lymphoma: 3-year study results



Advani et al. Blood 2021

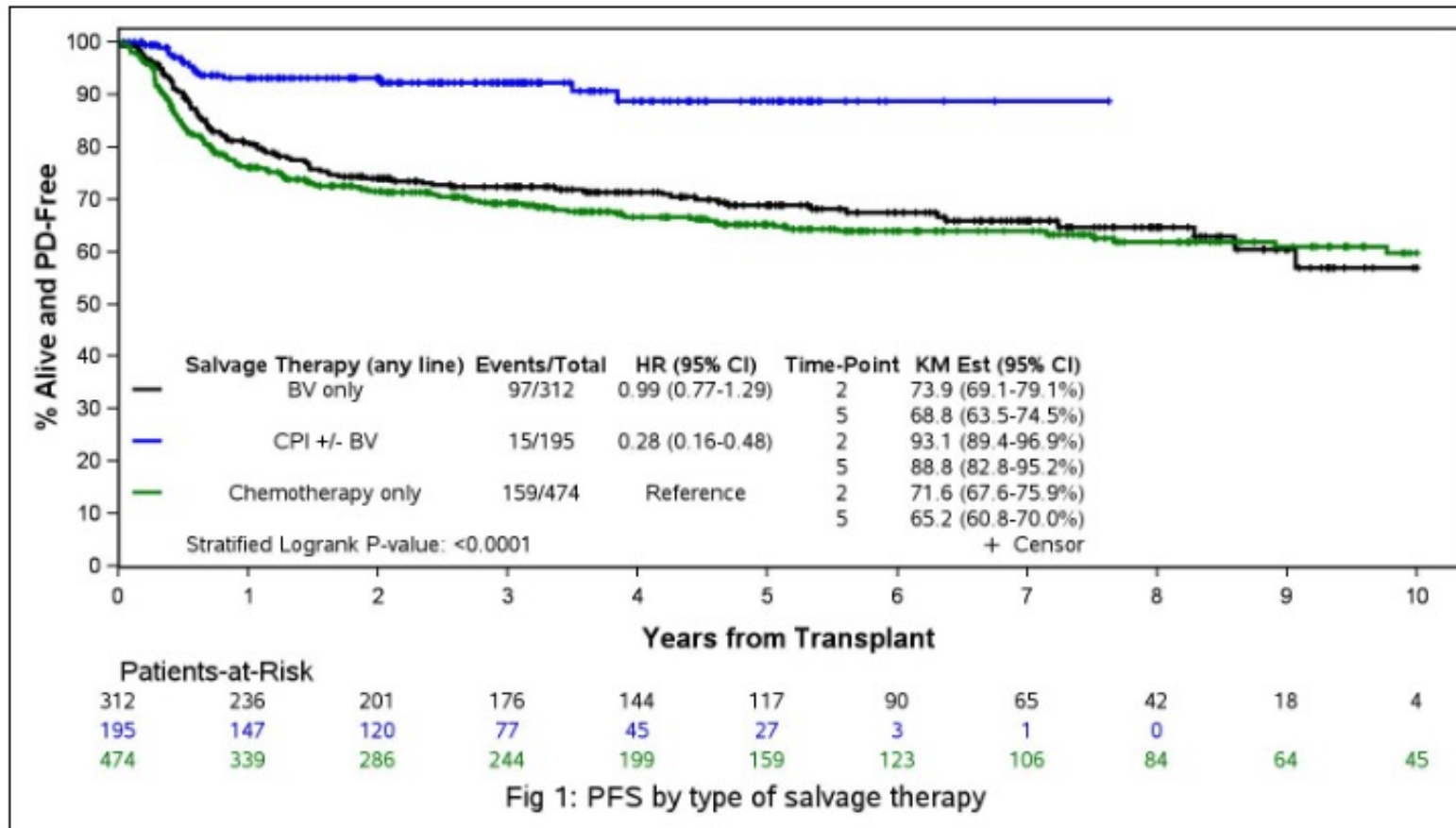
En búsqueda del PET neg pre TACPH

624.HODGKIN LYMPHOMAS AND T/NK CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL | NOVEMBER 28, 2023

PD-1 Blockade before Autologous Stem Cell Transplantation Improves Outcomes in Relapsed/Refractory Classic Hodgkin Lymphoma: Results from a Multicenter Cohort

Sanjal H. Desai, Reid W. Merryman, Harsh Shah, Levi D. Pederson, Susan M. Geyer, Nivetha Ganesan, Tiffany Chang, Tamer Othman, Ayo S Falade, Gunjan L. Shah, Urshila Durani, Kelsey Baron, Shin Yeu Ong, Steve M Ansell, Philippe Armand, Siddharth Iyengar, Ivana Micallef, Alison Moskowitz, Alex F. Herrera, Robert Stuver, Matthew Genyeh Mei

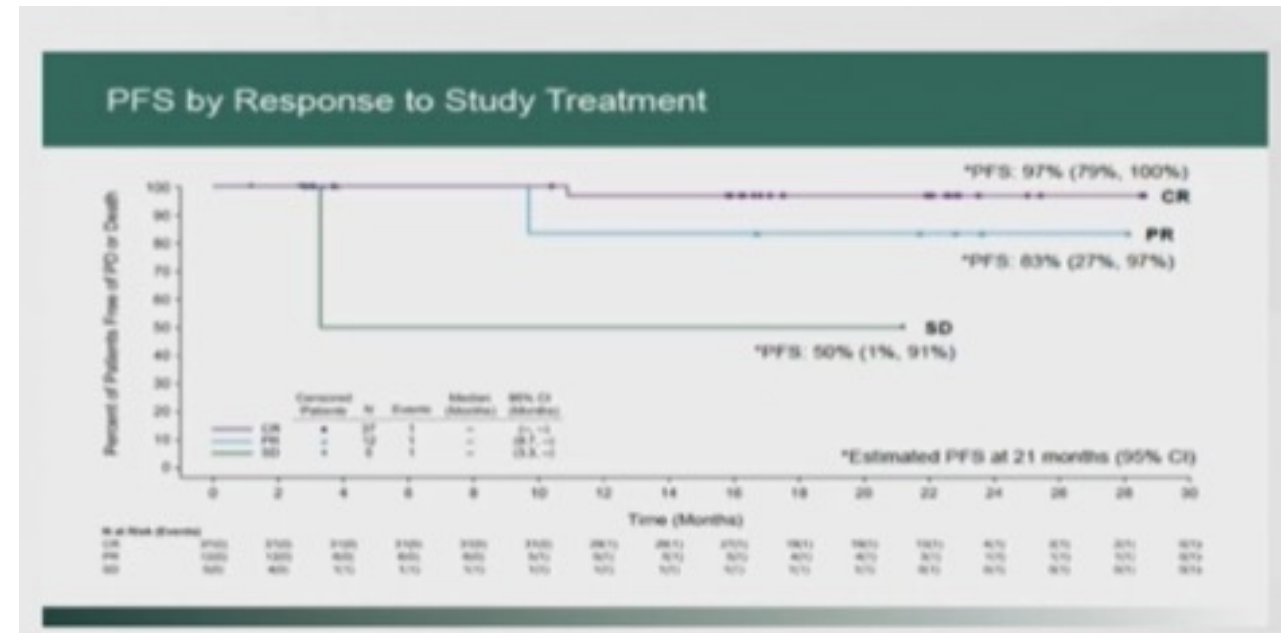
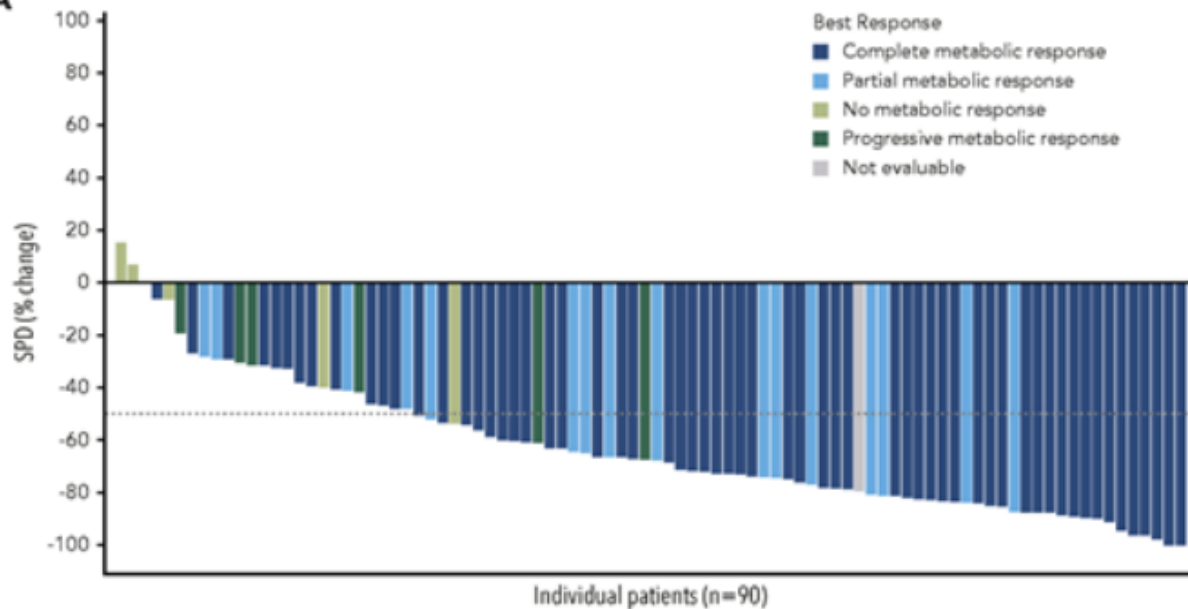
Outcomes de acuerdo a la terapia de rescate



La RMC sigue siendo el objetivo a alcanzar en la era de los ICP?

Post 2^{da} línea de tto

Brentuximab vedotin in combination with nivolumab in relapsed or refractory Hodgkin lymphoma: 3-year study results

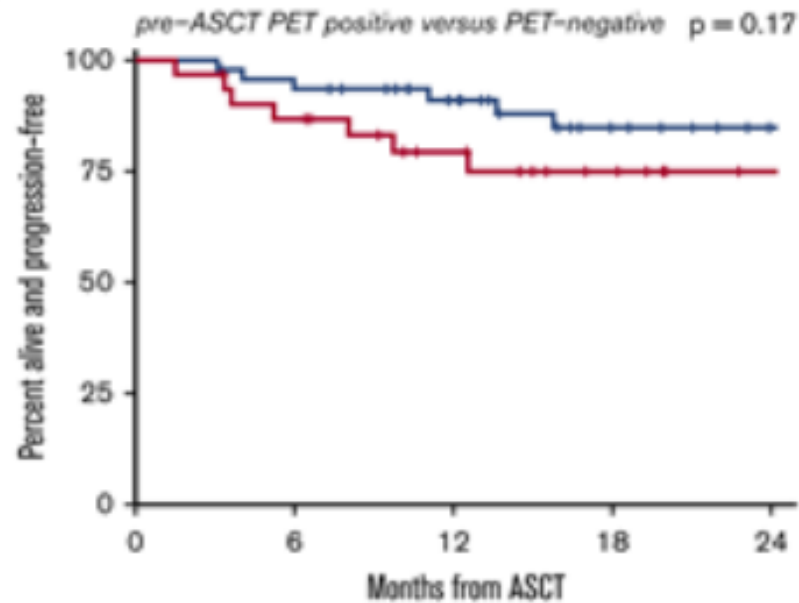


Advani et al. Blood 2021

La RMC sigue siendo el objetivo a alcanzar en la era de los ICP?

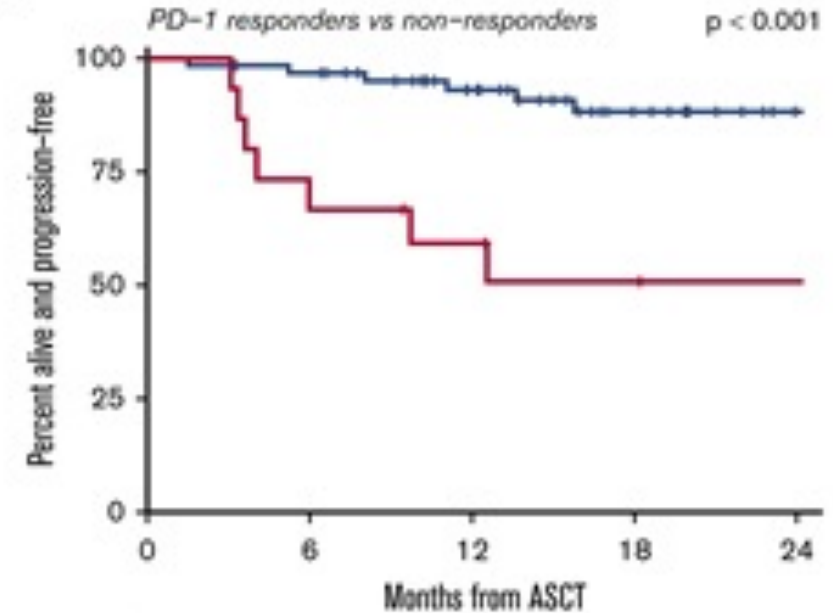
En R/R a varias líneas de tto

Autologous stem cell transplantation after anti-PD-1 therapy for multiply relapsed or refractory Hodgkin lymphoma



Number at risk

Negative	47	43	34	22	15
Positive	31	26	19	13	8



Number at risk

Response	63	59	45	29	18
Non response	15	10	8	6	5

Merryman et al. Blood 2021

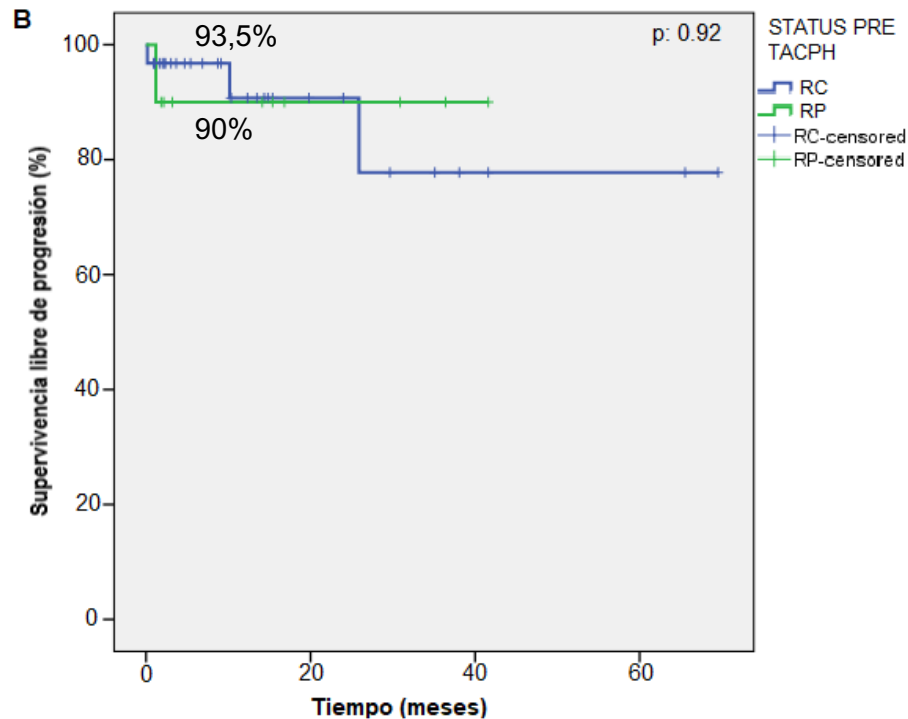
La RMC sigue siendo el objetivo a alcanzar en la era de los ICP?

En R/R a varias líneas de tto: Experiencia argentina

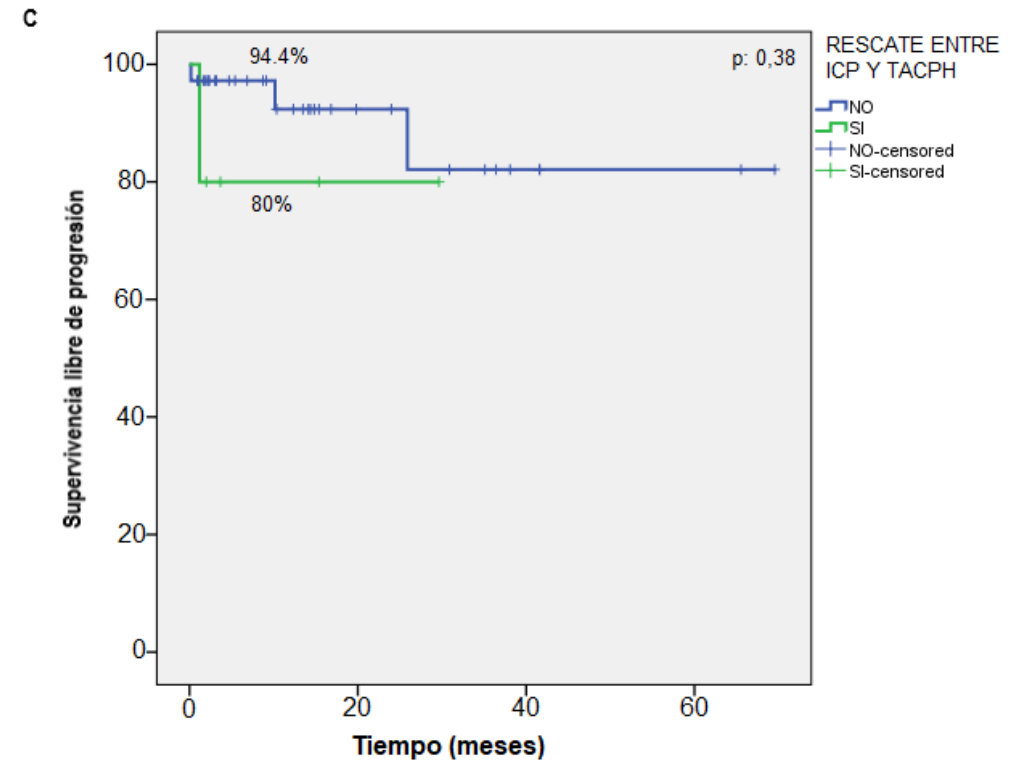
731.AUTOLOGOUS TRANSPLANTATION: CLINICAL AND EPIDEMIOLOGICAL | NOVEMBER 28, 2023

High Progression Free Survival Rates in Patients with Multiply Relapsed/Refractory Hodgkin Lymphoma Undergoing Autologous Stem Cell Transplant after Checkpoint Inhibitors: Results from Grupo Argentino De Trasplante De Medula Osea y Terapia Celular (GATMO-TC)

Laura Korin, Martin Castro, Silvina Palmer, Lautaro Sardu, Ana Basquiera, Sebastian Yantorno, Sol Jarchum, Maria Flavia Flavia Figueroa, Magali Colucci, María Eugenia Funes, Gonzalo Bentolila, Martin Saslavsky, Alejandra Banchieri, Maria Belén Rosales Ostriz, Romina Penalba, Micaela Quarchione, Gregorio Jaimovich, Gustavo Milone, Adriana Vitriu, Maria Cecilia Foncuberta



PAC EN RIESGO		0	25	50	60
RC	31	8	3	2	
RP	10	3	1	0	



PAC EN RIESGO		0	25	50	60
NO	36	10	4	2	
SI	5	1	0		

Blood (2023) 142 (Supplement 1): 2220.

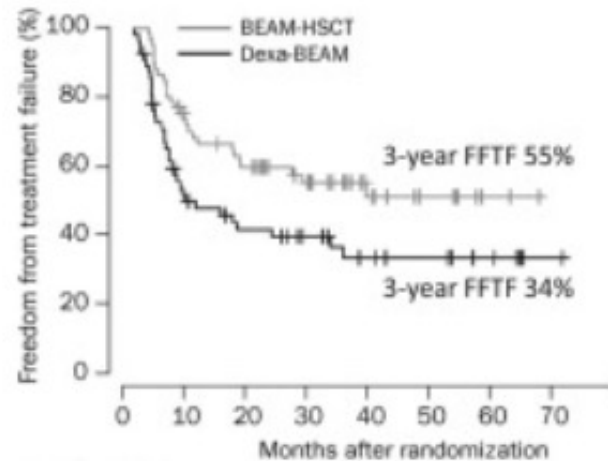
Podemos ser menos intensivos y omitir la consolidación post TACPH si rescatamos con ICP?

Es aún relevante la consolidación en el 2023?

Curación histórica: 50%

Curación posible 2023: 90%

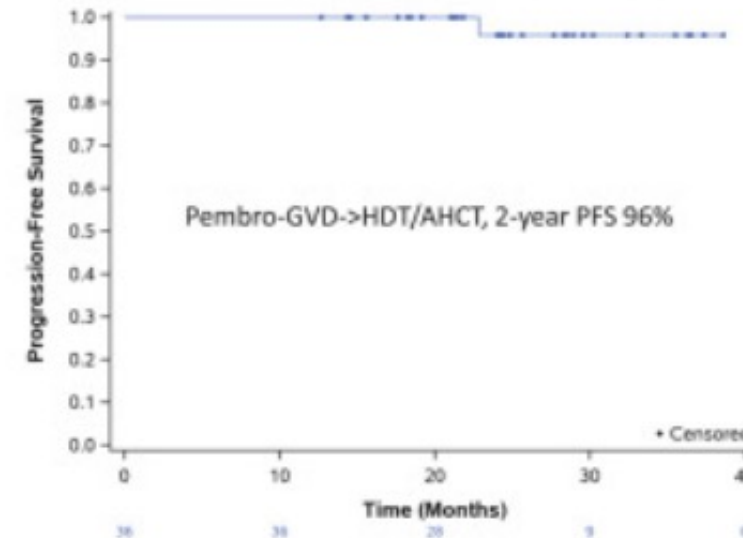
A Transplant years: 1993-1997



Number of patients

BEAM-HSCT	61	43	34	25	13	8	7	0
Dexa-BEAM	56	27	20	15	10	8	5	1

C Transplant years: 2018-2020



Podemos ser menos intensivos y omitir la consolidación post TACPH si rescatamos con ICP?

Qué data tenemos de los estudios con ICP en 2^{da} línea?

	Pembro-GVD	Nivo-ICE	Bv-Nivo
N de pacientes	38	43	91
N pac. alto riesgo (%)	31 (81)	19 ref 1 ^{arios} (44)	65 (71)
TACPH	36 (95)	33 (77%)	84 (92)
N consolidación (%)	13 (34)	22 (51)	15 (16)
Drogas de consolidación	BV (13)	BV (7), BV+ ICP (14), ICP (1)	BV (10), Bv+nivo (1), Pembro (4)
SLP	2 ^a y medio: 96%	2 ^a : 77%, 94% para los que procedieron directo al TACPH	3 ^a : 77%, 91% para los que procedieron directo al TACPH.

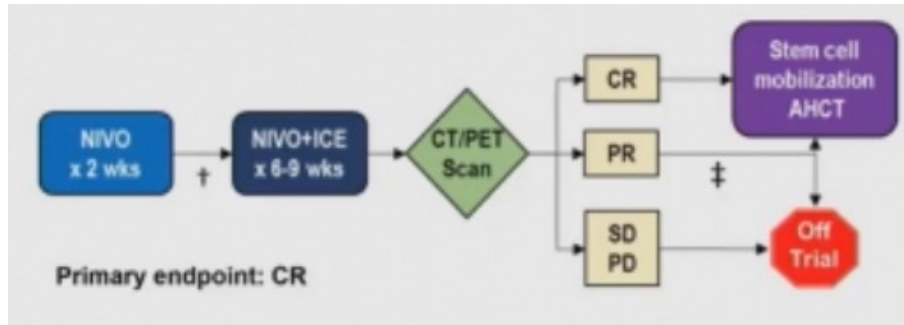
Moskowitz et al. JCO 2021
 Mei et al. Blood 2022
 Advani et al. Blood 2021

Podemos ser menos intensivos y omitir la consolidación post TACPH si rescatamos con ICP?

Qué data tenemos en pacientes de alto riesgo?

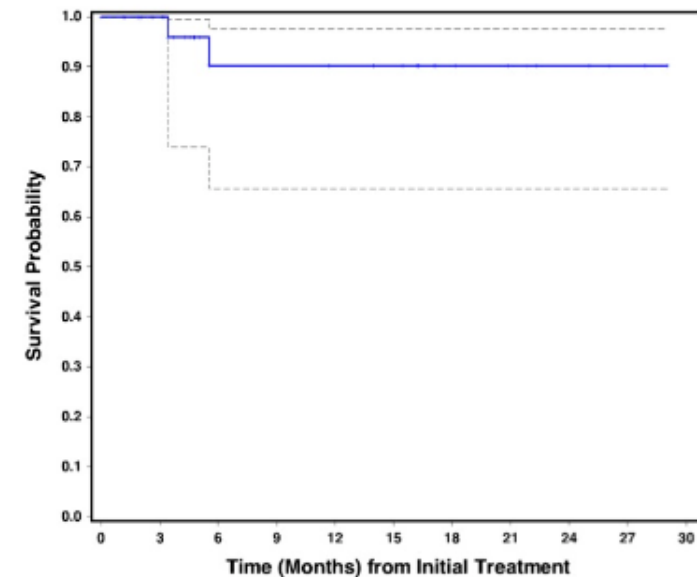
Nivolumab Plus ICE As First Salvage Therapy in High-Risk Relapsed/Refractory Hodgkin Lymphoma

N:35, RCM: 88%



Variable	N (%)
Male gender	21 (60)
Age	30 (19-70)
Stage at Baseline	
I-II	19 (55)
III-IV	16 (45)
B Symptom at Baseline	
No	29 (83)
Yes	6 (17)
Extranodal Disease at Baseline	10 (29)
Primary refractory	23 (66)
Frontline regimen	
ABVD	29 (83)
BV+AVD	6 (17)
Stage at diagnosis	
I-II	17 (49)
III-IV	18 (51)
Prior radiation	5 (14)
Prior brentuximab vedotin	6 (17)

Figure 1: Progression-free Survival



Alto riesgo según AETHERA +:

- Síntomas B
- 1L con Brentuximab (17%)

Solo 24% recibió consolidación (13% con Bv)

Podemos ser menos intensivos y omitir la consolidación post TACPH si rescatamos con ICP?

624.HODGKIN LYMPHOMAS AND T/NK CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL | NOVEMBER 28, 2023

Efficacy of Brentuximab Vedotin Maintenance Therapy Following Autologous Stem Cell Transplantation in Patients with Relapsed/Refractory Classical Hodgkin Lymphoma with and without Pre-Transplant Exposure to Novel Agents

Ayo S Falade, Robert A. Redd, Harsh Shah, Kelsey Baron, Siddharth Iyengar, Sanjal H. Desai, Stephen M Ansell, Ivana Micallef, Adrienne Nedved, Nivetha Ganesan, Tiffany Chang, Gunjan L. Shah, Robert Stuver, Alison Moskowitz, Matthew Genyeh Mei, Tamer Othman, Shin Yeu Ong, Alex F. Herrera, Philippe Armand, Reid W. Merryman

Qué data tenemos post rescate con drogas nuevas?

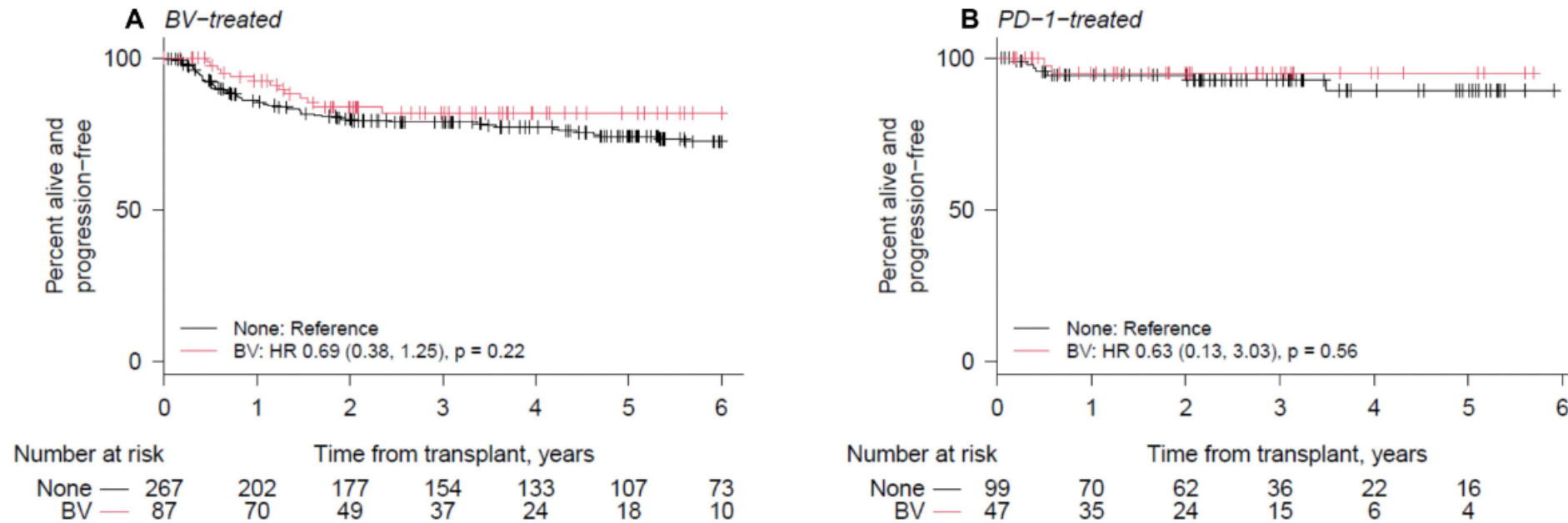


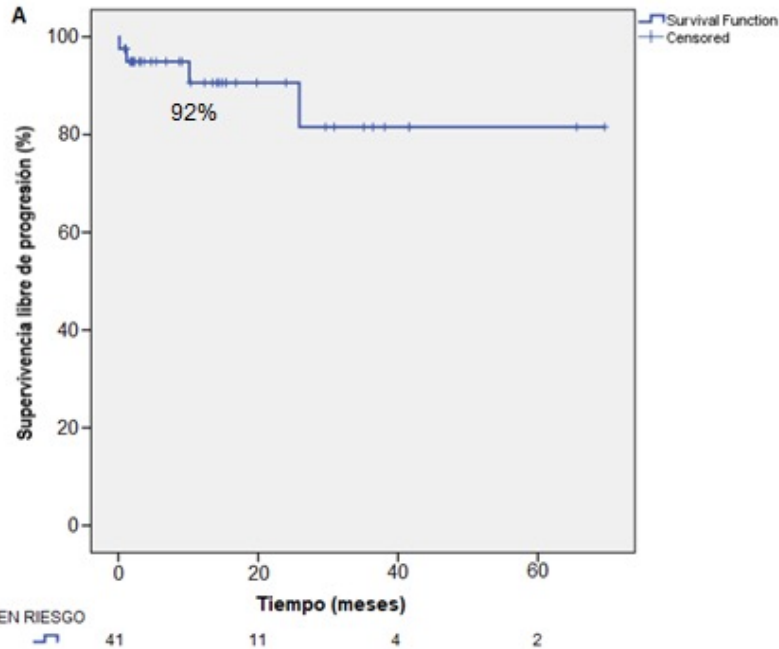
Figure: Progression-free survival with and without BV maintenance among **A)** Patients receiving BV before ASCT, and **B)** Patients receiving PD-1 before ASCT. BV-refractory patients were excluded from these analyses.

Podemos ser menos intensivos y omitir la consolidación post TACPH si rescatamos con ICP?

Qué data tenemos en pacientes R/R a multiples líneas?: experiencia argentina

731.AUTOLOGOUS TRANSPLANTATION: CLINICAL AND EPIDEMIOLOGICAL | NOVEMBER 28, 2023

High Progression Free Survival Rates in Patients with Multiply Relapsed/Refractory Hodgkin Lymphoma Undergoing Autologous Stem Cell Transplant after Checkpoint Inhibitors: Results from Grupo Argentino De Trasplante De Medula Osea y Terapia Celular (GATMO-TC)



FR AETHERA, n (%)

1: 6 (14,6)

2: 15 (36,6)

3: 10 (24,4)

≥4: 10 (24,4)

Consolidación post TACPH , n (%)

NO: 34 (82,9)

Brentuximab: 3 (7,3)

ICP: 4 (9,8)

Radioterapia: 2 (2,4)

Korin et al. Blood (2023) 142 (Supplement 1): 2220.

*“Cambia lo superficial,
cambia también lo profundo,
cambia el modo de pensar,
cambia todo en este mundo”*

*Todo cambia
Julio Numhauser*



Conclusiones

- ✓ El TACPH es una alternativa válida en pacientes quimiorrefractarios que responden a ICP, independientemente de las líneas de tto previas.
- ✓ Los ICP han demostrado aumento en las tasas de RMC pre TACPH (NO en RCT)
- ✓ La rta a ICP parece ser el factor pronóstico mas importante preTACPH y NO el status del PET. Considerar aún en RP.
- ✓ La consolidación post TACPH esta siendo desafiada en el contexto de la alta eficacia de la 2da línea con ICP + TACPH
- ✓ Se necesita profundizar en trabajos colaborativos que evaluen la experiencia del mundo real en LATAM con estas estrategias.

Muchas gracias x su atención!



X @laura_korin

