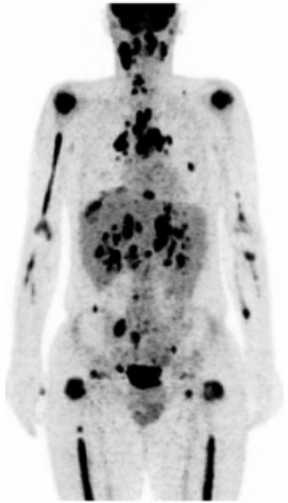




Nuevo Standard de tratamiento en Linfoma de Hodgkin avanzado en 1L: NIVO-AVD

Dra. Victoria Irigoín
Grupo Uruguayo de Linfoma (GULI)



Mujer **jóven (edad reproductiva)** LH clásico estadio avanzado, IPS alto riesgo



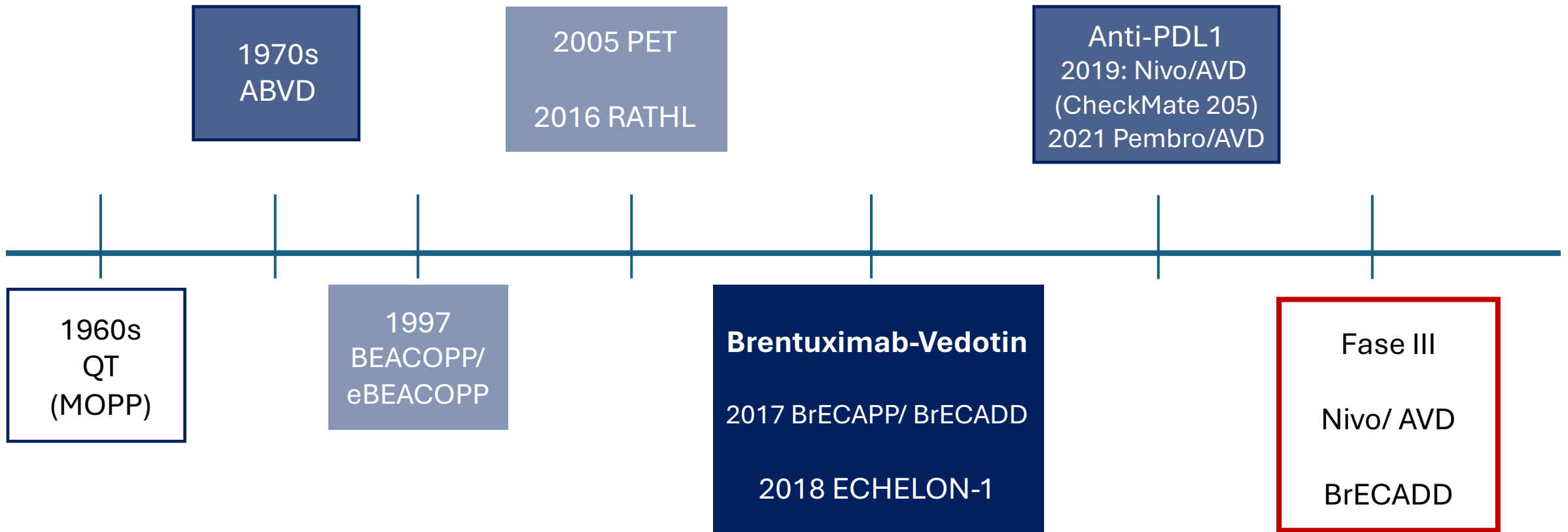
Objetivo?

Curación (con tratamiento de 1L)

Minimizar toxicidad a corto, mediano y largo plazo



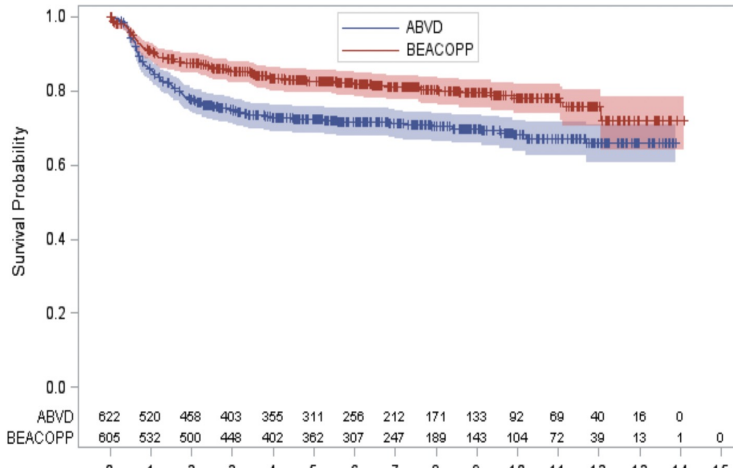
- Reducir mielotoxicidad
- Reducir toxicidad pulmonar
- Evitar irradiación mediastinal
- Preservar fertilidad
- Disminuir probabilidad de 2das neoplasias



AVBD o eBEACOPP?

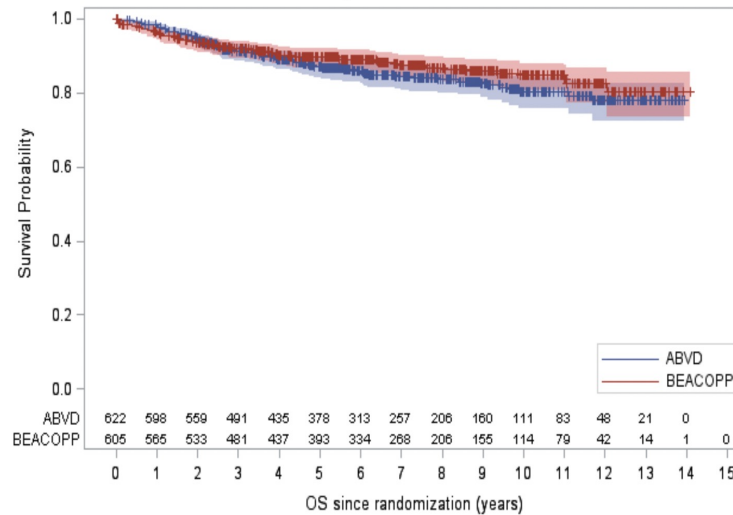
PFS by randomization arm - ITT set

With Number of Subjects at Risk and 95% Confidence Limits



OS by randomization arm - ITT set

With Number of Subjects at Risk and 95% Confidence Limits



All four studies

	ABVD (N = 624)	BEACOPP (N = 589)
--	-------------------	----------------------

Secondary cancer (n patients)

No	599 (96.0)	553 (93.9)
Yes	25 (4.0)	36 (6.1)

Type of cancer (n patients)

MDS/AML	0	13
NHL	9	5
Myeloproliferative	2	0
Myeloma	1	0
Lung	4	6
Breast	1	0
Colorectal	2	3
Other/unknown	8	9

> tasa de esterilidad
con BEACOPP 1-3

	Dose (mg/m ²)	Administration	Days
Doxorubicin	25	i.v.	1 + 15
Bleomycin	10	i.v.	1 + 15
Vinblastine	6	i.v.	1 + 15
Dacarbazine	375	i.v.	1 + 15

ANALISIS DE CASOS

	Dose (mg/m ²)	Administration	Days
Bleomycin	10	i.v.	8
Etoposide	200	i.v.	1-3
Doxorubicin	35	i.v.	1
Cyclophosphamide	1250	i.v.	1
Vincristine	1.4 ^a	i.v.	8
Procarbazine	100	p.o.	1-7
Prednisone	40	p.o.	1-14
G-CSF		s.c.	From day 8

1 Harel S et al. Haematologica. 2011;96(11):1692-9.

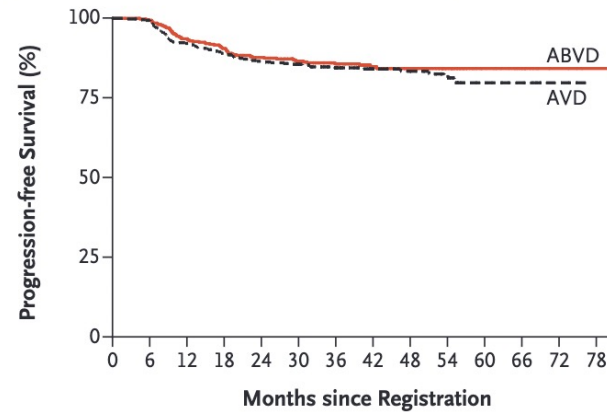
2 Behringer K, et al. J Clin Oncol. 2013;31(2):231-9.

3 Colpi GM, et al. Eur J Obstet Gynecol Reprod Biol. 2004;113(SUPPL.):S2-S6

RATHL

83.7% PET interim
neg
ABD con adaptación se

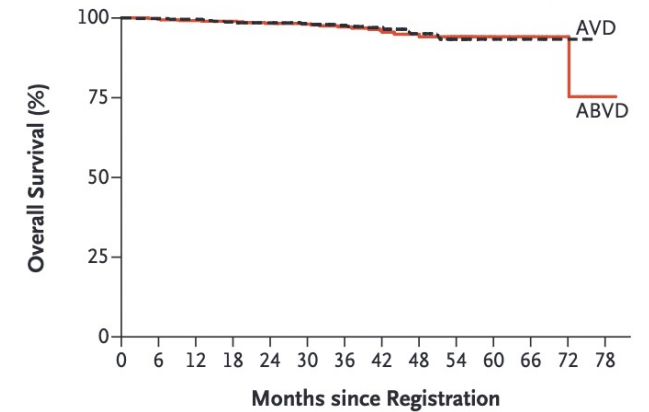
A Progression-free Survival among Patients with Negative PET Findings



No. at Risk

ABVD	470	464	433	417	394	340	262	169	100	67	26	14	4	1
AVD	465	455	419	396	376	327	264	182	112	68	28	16	3	0

B Overall Survival among Patients with Negative PET Findings



No. at Risk

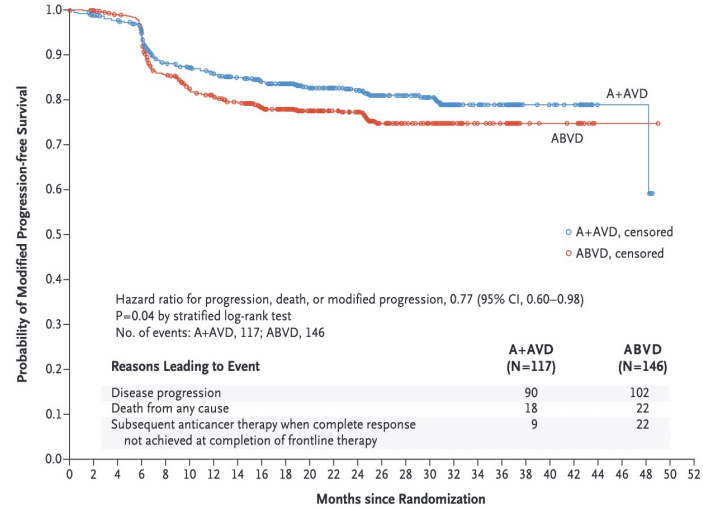
ABVD	470	464	459	456	441	385	298	197	119	79	33	16	5	1
AVD	465	457	450	438	421	371	298	209	126	72	29	16	3	0

1,7% diferencia en SLP con menor toxicidad

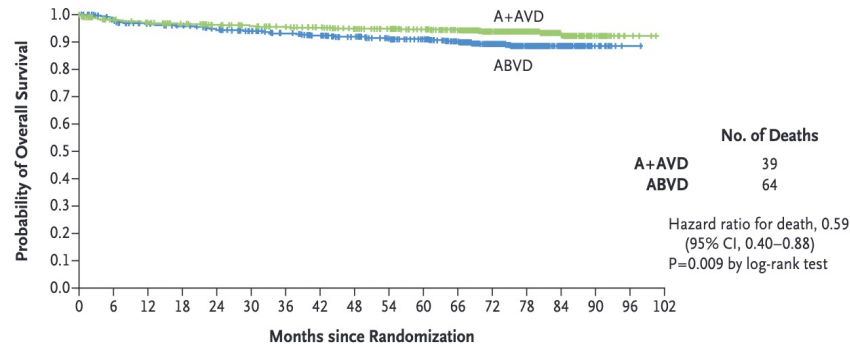
ECHELON-1

AVD

A Modified Progression-free Survival as Assessed by Independent Review Committee



No. at Risk	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50
A+AVD	664	637	623	600	541	528	513	493	463	439	347	328	309	196	185	169	96	85	77	26	24	21	4	4	0	0
ABVD	670	636	626	593	521	490	474	459	432	413	326	306	292	177	164	153	76	66	62	16	13	12	1	1	1	0



No. at Risk	0	6	12	18	24	30	36	42	48	54	60	66	72	78	84	90	96	102
A+AVD	664	638	626	612	598	584	572	557	538	517	494	461	350	209	97	27	4	0
ABVD	670	634	614	604	587	567	545	527	505	479	454	411	308	191	84	11	1	0

Events	A+AVD (N = 662)	ABVD (N = 659)
	no. (%)	
Grade ≥3 adverse event	549 (83)	434 (66)
Serious adverse event	284 (43)	178 (27)
Neutropenia		
Any grade	382 (58)	295 (45)
Grade ≥3	357 (54)	260 (39)
Peripheral sensory neuropathy		
Any grade	189 (29)	111 (17)
Grade ≥3	31 (5)	3 (<1)

Age	A+AVD	ABVD	Hazard Ratio (95% CI)
<60 yr	93/580 (16.0)	117/568 (20.6)	0.73 (0.56–0.96)
≥60 yr	24/84 (28.6)	29/102 (28.4)	1.00 (0.58–1.72)
<65 yr	99/604 (16.4)	128/608 (21.1)	0.74 (0.57–0.96)
≥65 yr	18/60 (30.0)	18/62 (29.0)	1.01 (0.53–1.94)
<45 yr	70/451 (15.5)	83/423 (19.6)	0.73 (0.53–1.01)
≥45 yr	47/213 (22.1)	63/247 (25.5)	0.86 (0.59–1.25)
Baseline Ann Arbor stage			
Stage III	40/237 (16.9)	43/246 (17.5)	0.92 (0.60–1.42)
Stage IV	77/425 (18.1)	102/421 (24.2)	0.71 (0.53–0.96)

Connors JM et al. N Engl J Med 2018.
 Straus DJ et al. Lancet Haematol 2021;

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Nivolumab+AVD in Advanced-Stage Classic Hodgkin's Lymphoma

A.F. Herrera, M. LeBlanc, S.M. Castellino, H. Li, S.C. Rutherford, A.M. Evens, K. Davison, A. Punnett, S.K. Parsons, S. Ahmed, C. Casulo, N.L. Bartlett, J.M. Tuscano, M.G. Mei, B.T. Hess, R. Jacobs, H. Saeed, P. Torka, B. Hu, C. Moskowitz, S. Kaur, G. Goyal, C. Forlenza, A. Doan, A. Lambie, P. Kumar, S. Chowdhury, B. Brinker, N. Sharma, A. Singh, K.A. Blum, A.M. Perry, A. Kovach, D. Hodgson, L.S. Constine, L.K. Shields, A. Prica, H. Dillon, R.F. Little, M.A. Shipp, M. Crump, B. Kahl, J.P. Leonard, S.M. Smith, J.Y. Song, K.M. Kelly, and J.W. Friedberg

S1826 Study Design

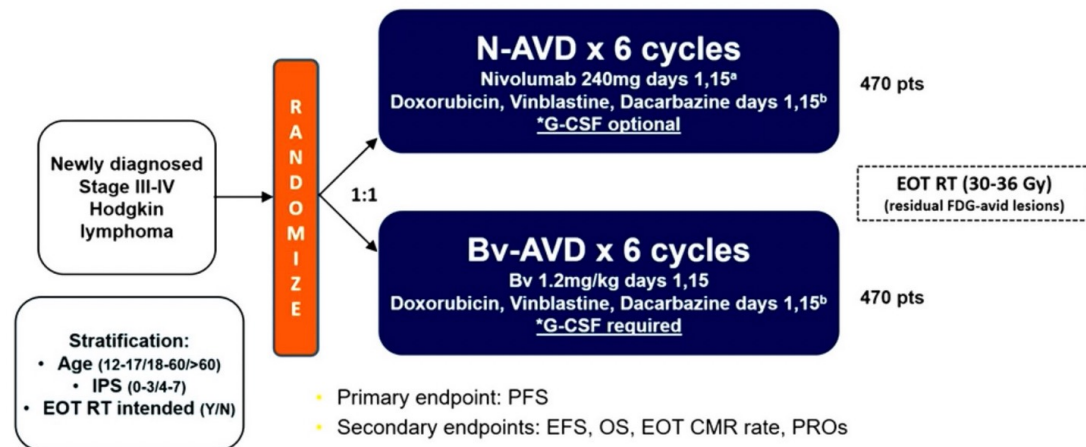


Table 1. Characteristics of the Patients at Baseline (Modified Intention-to-Treat Population).*

Characteristic	N+AVD (N = 487)	BV+AVD (N = 483)
Age		
Median (range) — yr	27.6 (12.0–83.7)	26.8 (12.0–81.7)
Distribution — no. (%)		
12–17 yr	118 (24)	118 (24)
18–60 yr	321 (66)	318 (66)
>60 yr	48 (10)	47 (10)
Female sex — no. (%)	216 (44)	210 (43)
Race or ethnic group — no. (%)†		
White	372 (76)	361 (75)
Black	58 (12)	56 (12)
Asian	11 (2)	17 (4)
Other or unknown	46 (9)	49 (10)
Hispanic	66 (14)	58 (12)
Disease stage — no. (%)		
III	185 (38)	168 (35)
IV	302 (62)	315 (65)
B symptoms present — no. (%)‡	288 (59)	273 (57)
IPS — no. (%)§		
0–3	332 (68)	328 (68)
4–7	155 (32)	155 (32)
Bulky disease — no. (%)¶	156 (32)	127 (26)
HIV-positive status — no. (%)	11 (2)	5 (1)

Table 2. Adverse Events of Any Grade (Modified Intention-to-Treat Population).*

Event	N+AVD (N = 482)	BV+AVD (N = 476)	
	number (percent)		
Nausea	312 (65)	331 (70)	
Fatigue	228 (47)	242 (51)	
Neutrophil count decreased	272 (56)	160 (34)	
Anemia	190 (39)	217 (46)	
Peripheral sensory neuropathy	139 (29)	266 (56)	*
Constipation	193 (40)	204 (43)	
ALT increased	160 (33)	201 (42)	
White-cells decreased	197 (41)	128 (27)	
Vomiting	134 (28)	157 (33)	
AST increased	125 (26)	160 (34)	
Diarrhea	100 (21)	129 (27)	
Alopecia	103 (21)	124 (26)	
Lymphocyte count decreased	103 (21)	109 (23)	
Mucositis, oral	107 (22)	100 (21)	
Platelet count decreased	52 (11)	86 (18)	
Fever	62 (13)	61 (13)	

* ≥ 23% vs 32%

Adverse Event Type	N-AVD	BV-AVD
	n = 482	n = 476
	Grade ≥ 3	Grade ≥ 3
	No (%)	No (%)
Neutrophil count decreased	232 (48%)	126 (26%)
White blood cell decreased	73 (15%)	61 (13%)
Anemia	29 (6%)	43 (9%)
Lymphocyte count decreased	30 (6%)	41 (9%)
Febrile neutropenia	28 (6%)	33 (7%)
ALT increased	22 (5%)	23 (5%)
Peripheral sensory neuropathy	5 (1%)	39 (8%)
AST increased	12 (2%)	14 (3%)
Platelet count decreased	9 (2%)	16 (3%)
Sepsis	8 (2%)	16 (3%)

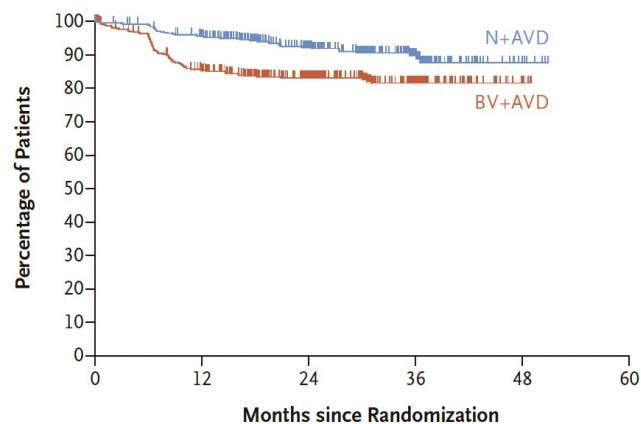
Hipo/ hipertiroidismo post tto: 7% vs 3%

Discontinuación tto por EA 9% vs 12%

Función gonadal preservada ¹

Uso de RT:
3 pac en Nivo
4 en BV

A Progression-free Survival



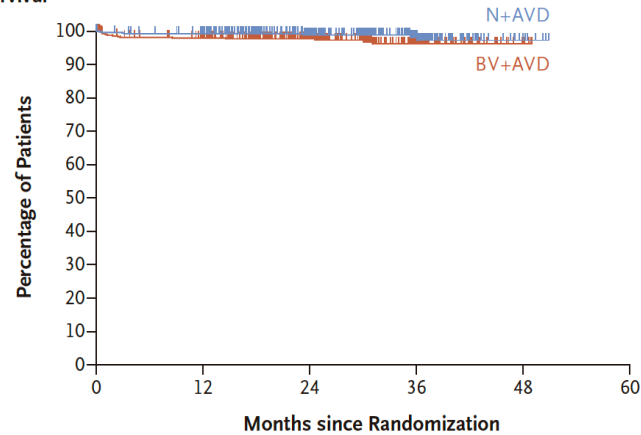
	Disease Progression or Death <i>no. of patients</i>	2-Year Estimate for Progression-free Survival (95% CI) <i>percent</i>
N+AVD	41	92 (89–94)
BV+AVD	81	83 (79–86)

Hazard ratio, 0.45 (95% CI, 0.30–0.65)

No. at Risk

N+AVD	487	450	281	101	9	0
BV+AVD	483	392	244	97	7	0

B Overall Survival

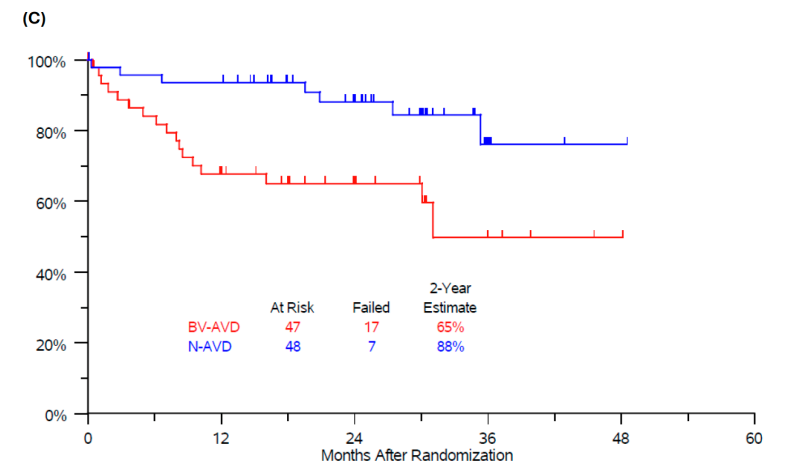
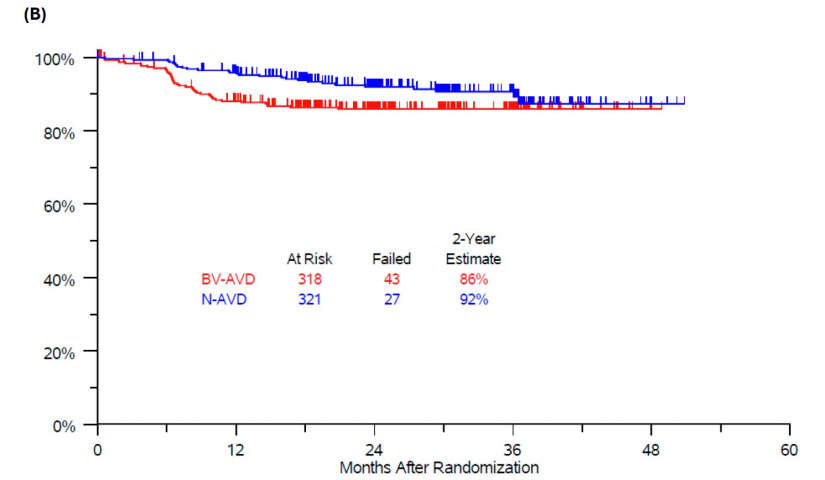
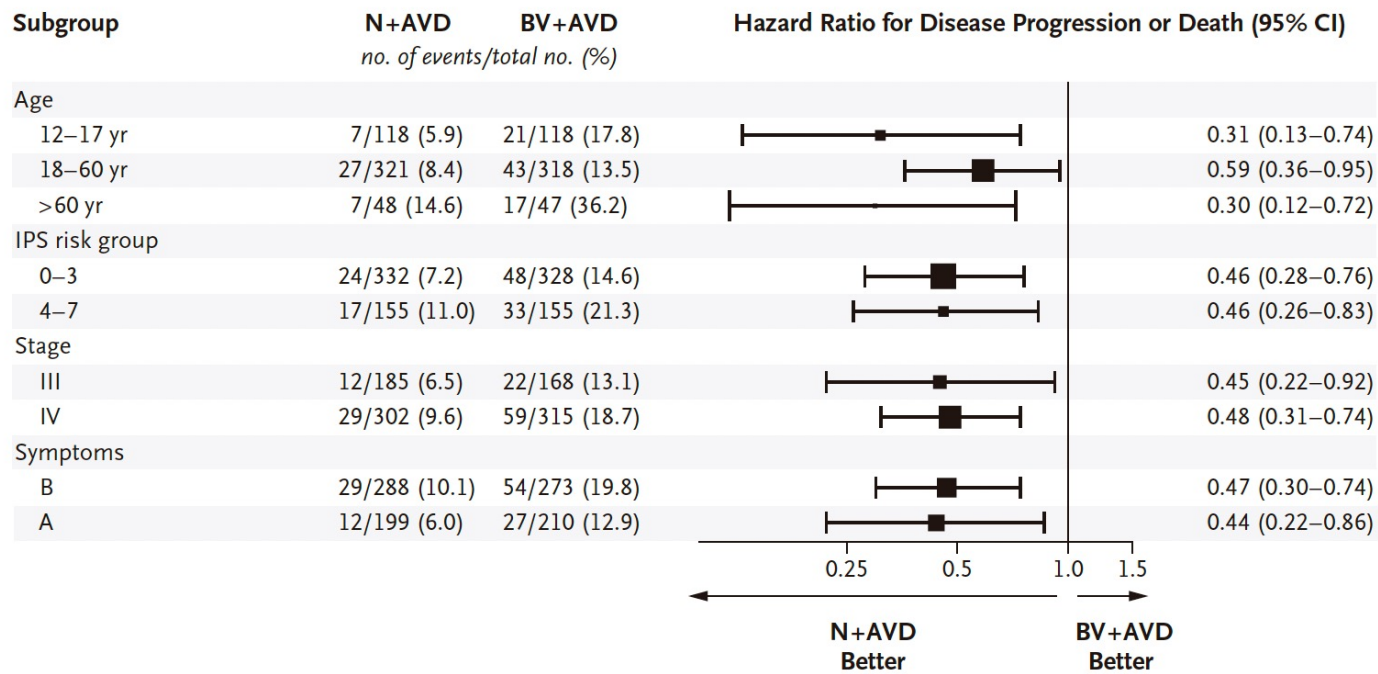


	Death <i>no. of patients</i>	2-Year Estimate for Overall Survival (95% CI) <i>percent</i>
N+AVD	7	99 (97–100)
BV+AVD	14	98 (96–99)

Hazard ratio, 0.39 (95% CI, 0.15–1.03)

No. at Risk

N+AVD	487	467	300	110	9	0
BV+AVD	483	447	274	107	7	0

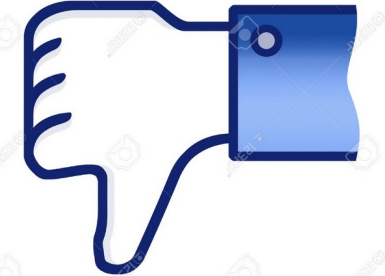




- Seguro y efectivo en TODOS los pacientes (incluso en > 60 años) HISPANOS incluidos!!
- Mínimo uso de RT posterior
- Esquema conocido, sencillo de administrar
- SEGURO
- No requiere PET interim (acceso NO es universal en LA)
- NO compromiso fertilidad

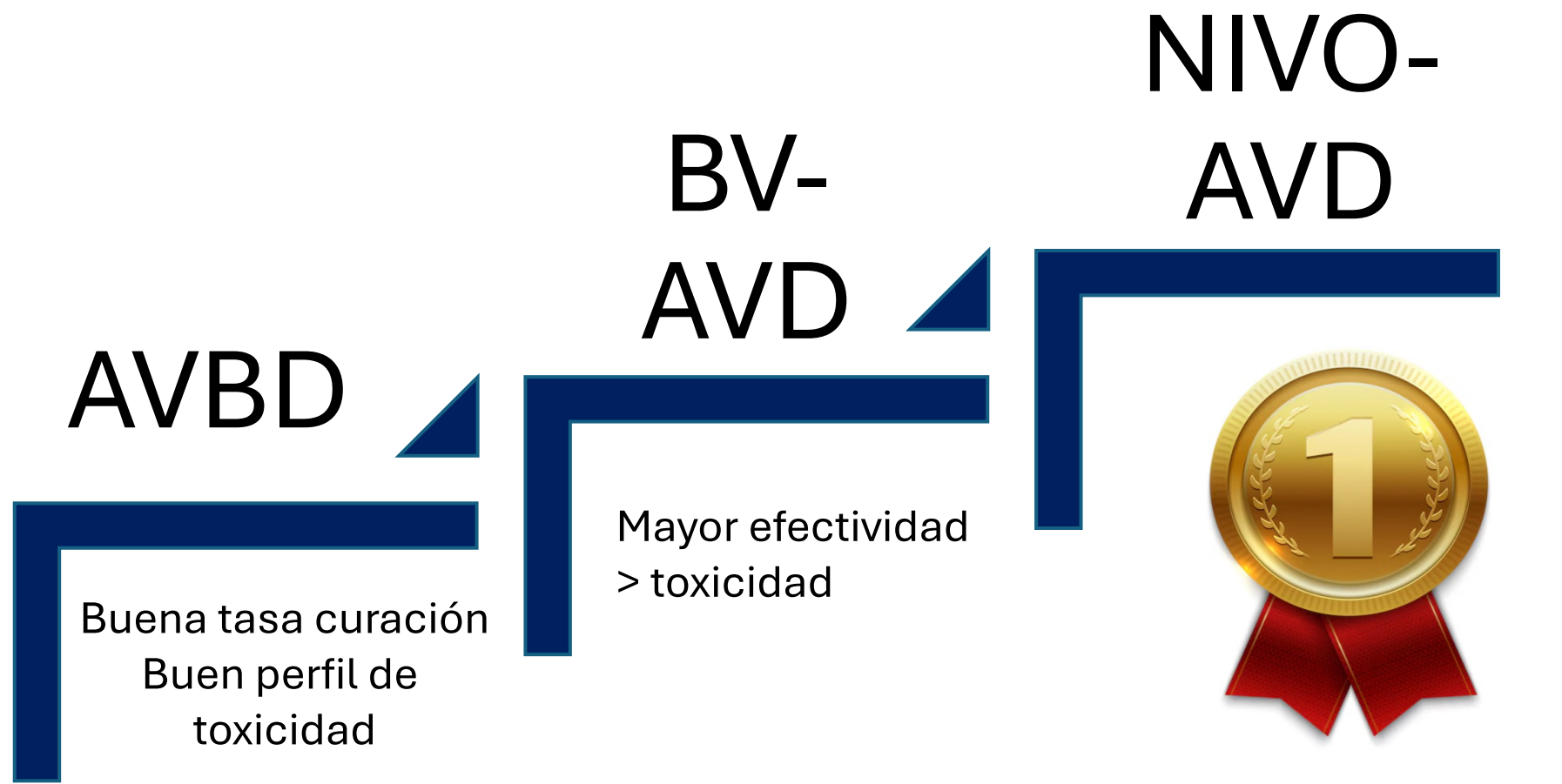


- Seguimiento aún corto
(pero cuándo ocurren la mayoría de las recaídas de L. Hodgkin?)



- Precio

Pero más barato de BV!!
(al menos en Uruguay)



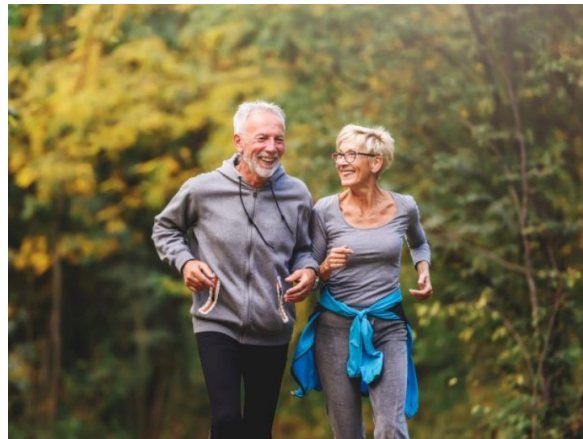
Nivo-AVD “ es la raja”

“En la guerra y en el amor todo se vale”

John Lyly 1579

Charles Bukowski

En el Linfoma de Hodgkin no





Gracias!