L'ANTIGENE CD30 COME TARGET TERAPEUTICO NEI LINFOMI

UPDATE IN EMATOLOGIA
GENOVA
19 DICEMBRE 2023

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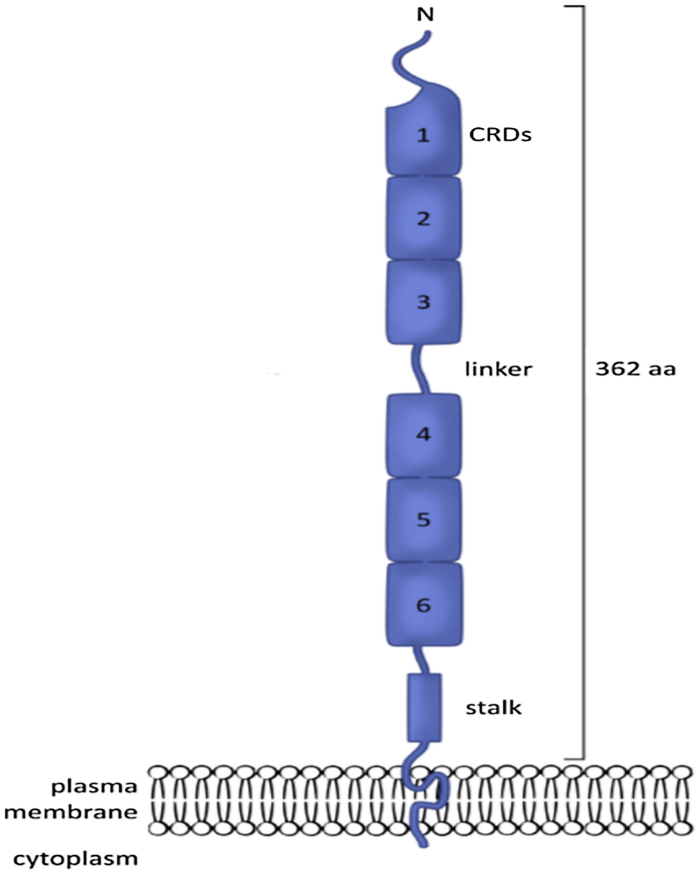
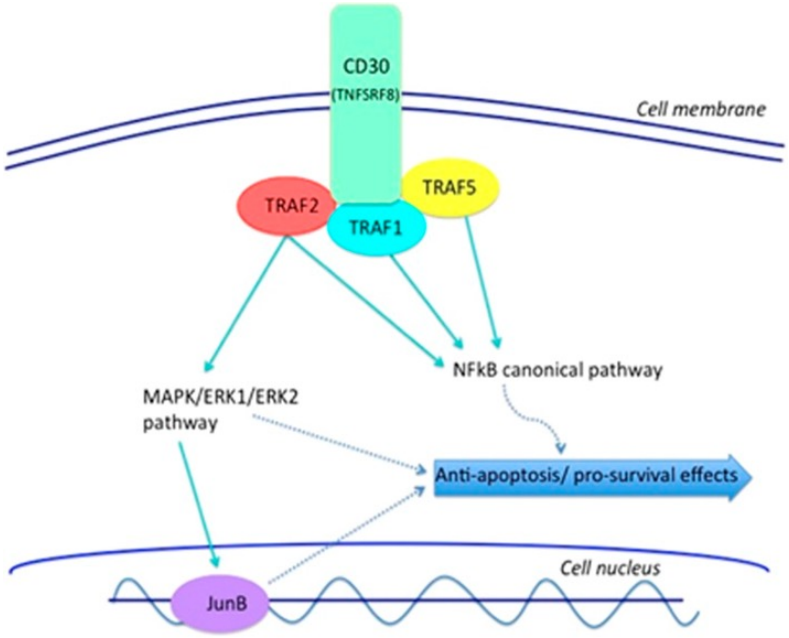
Clinica Ematologica

CD30 (TNFRSF8)



- 120KDa type I transmembrane glycosylated protein
- In healthy tissues, CD30 expression in restricted to a subsed of activated T and B lymphocytes located around the B cell centre follicles and the edge of germinal centres
- The natural ligand is CD153, a glycoprotein of the TNF family expressed on activated T cells, B cells, neutrophiles, eosinophils, mast cells.



BR J HAEMATOL, VOLUME: 201, ISSUE: 6, PAGES: 1033-1046, FIRST PUBLISHED: 11 MAY 2023, DOI: (10.1111/BJH.18841)
VAN DER WEYDEN CA ET AL BLOOD CANCER J. 2017

PTCL	Proportion of patients with CD30 expression, % (n/total *n* of patients with lymphoma subtype)							
	CD30 cut-off	**PTCL-NOS**	**AITL**	**ATLL**	**ENKTL**	**ALK- ALCL**	**ALK+ ALCL**	**EATL**
Karube K et al. 2008 [122]	≥20%	11% (NS)	32% (NS)	24% (NS)	64% (NS)	58% (NS)		
Weisenburger DD et al. 2011 [123]	≥20%	32% (69/217)						
Sabattini E et al. 2013 [124]	≥25%	52% (45/87)	21% (9/42)		70% (7/10)			100% (9/9)
Bossard C et al. 2014 [125]	≥5%	58% (82/141)	63% (61/97)	56% (5/9)	46% (13/28)	100% (19/19)	100% (61/61)	50% (7/14)
Lamarque M et al. 2016 [126]	≥5%	90% (9/10)	100% (1/1)	0% (0/1)		100% (14/14)	56% (5/9)	100% (1/1)
Kawamoto K et al. 2018 [127]	≥25%				57% (55/97)			
Wang G-N et al. 2017 [128]	≥1%				70% (86/122)			
CTCL	**CD30 cut-off**	**CTCL**	**MF**	**T-MF**	**SS**			
Karube K et al. 2008 [122]	20–70%	9% (unknown)						
Sabattini E et al. 2013 [124]	≥25%		13% (4/32)	100% (9/9)				
Benner MF et al. 2012 [129]	>25%			47% (47/100)				
Klemke CD et al. 2015 [130]	≥5%				33% (11/49)			
B-cell lymphomas	**CD30 cut-off**	**DLBCL**						
Salas MQ et al. 2020 [114]	>20%	19% (41/216)						
Rodrigues-Fernandes CI et al. [4]	>20%	2.5–37% (NS)						
Slack GW et al. 2014	≥20%	12% (47/385)						

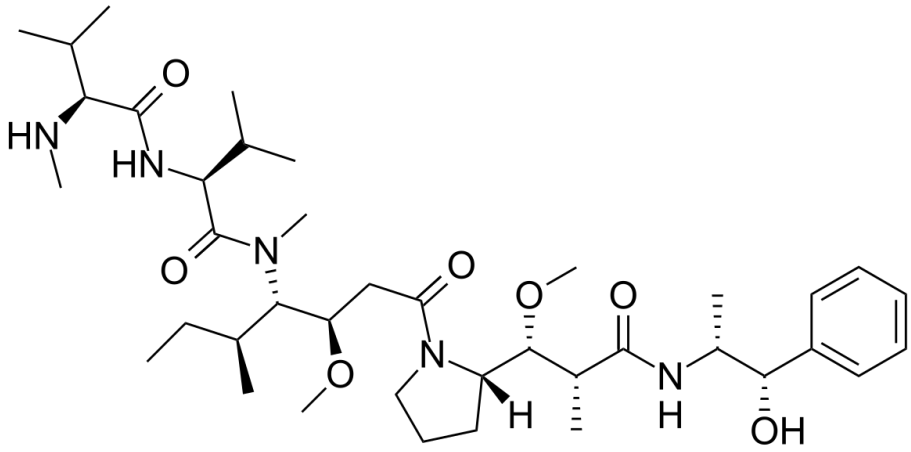
SUMMARY RESULTS OF PHASE I/II CLINICAL TRIALS TARGETING CD30

Drug	Disease	Antibody type	Phase	Number of evaluable patients	PR	CR	%PR + CR
MDX-060	HL, ALCL	Humanized	I	HL = 63	2	2	6%
				ALCL = 9	2	0	22%
SGN-30	HL, ALCL	Chimeric	I	24	0	0	0
SGN-30	HL, ALCL	Chimeric	II	HL = 38	0	0	0
				ALCL = 41	5	2	17%
Xmab2513	HL	Humanized	I	13	1	0	7%
131I-Ki4	HL	Murine	I	22	5	1	27%

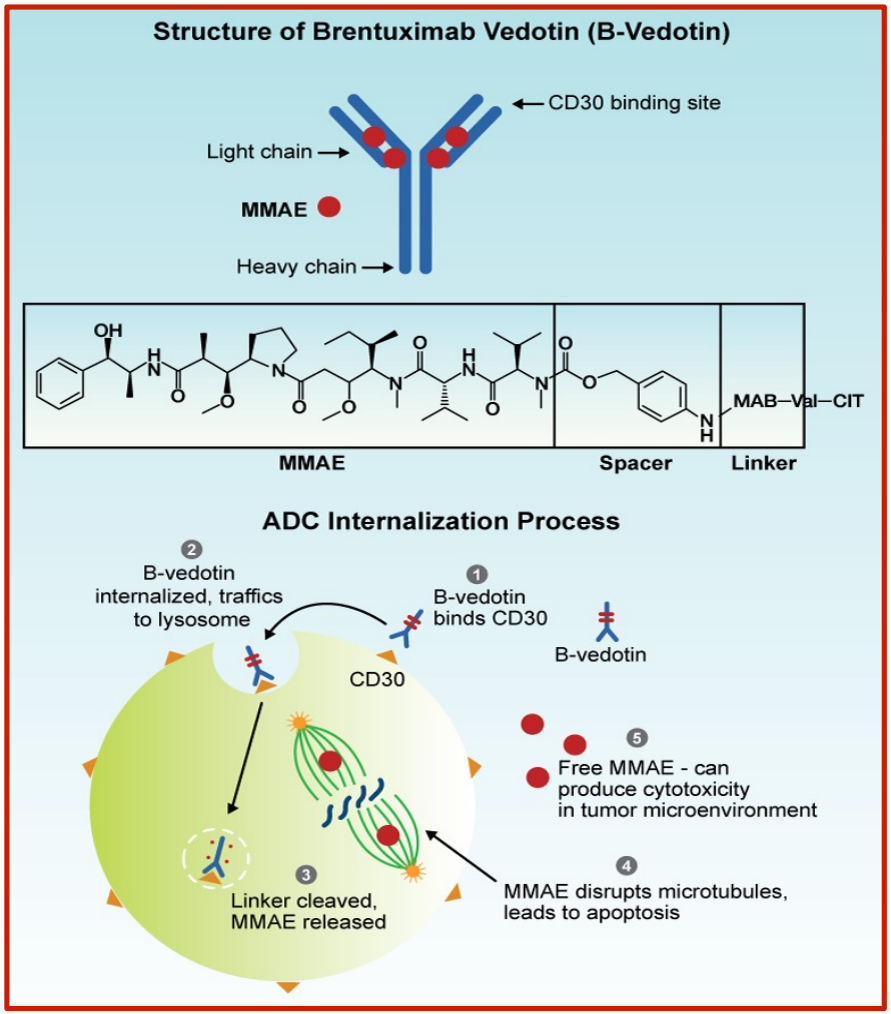
YOUNES, A: CURR OPIN ONCOL. 2011

THE AURISTATINS – TUBULINE POLYMERASE INHIBITOR

The parent antintubulin agent Dolastatin 10 isolated from the Indian Ocean *Dolabella Auricularia*



MMAE



In addition to BV's primary MOA non-clinical studies highlight other contributory mechanisms of action, including :

- Antibody dependent phagocytosis (ADCP)
- Bystander effects on nearby cells in the tumor microenvironment due to released MMAE
- Immunogenic cell death (ICD) due to endoplasmic reticulum (ER) stress that drives exposure of immune-activating molecules

BRENTUXIMAB VEDOTIN INDICAZIONI

HL

- in associazione con doxorubicina, vinblastina e dacarbazina (AVD) per pazienti adulti non precedentemente trattati affetti da linfoma di Hodgkin (HL) CD30+ in Stadio III o IV
- (trattamento di pazienti adulti affetti da HL CD30+ ad aumentato rischio di recidiva o progressione in seguito a trapianto di cellule staminali autologhe)
- trattamento di pazienti adulti affetti da linfoma di Hodgkin (HL) CD30+ recidivante o refrattario:

1. in seguito ad ASCT, oppure
2. 2. in seguito ad almeno due precedenti regimi terapeutici, quando l'ASCT o la polichemioterapia non è un'opzione terapeutica.

sALCL

- in associazione con ciclofosfamide, doxorubicina e prednisone (CHP) per pazienti adulti non precedentemente trattati
- trattamento di pazienti adulti affetti da sALCL recidivante o refrattario.

CTCL

- trattamento di pazienti adulti affetti da linfoma cutaneo a cellule T (CTCL) CD30+ sottoposti ad almeno 1 precedente terapia sistemica

BV FOR THE FIRST LINE TREATMENT IN CHL: ECHELON1-PFS AND OS WITH BV + AVD VS ABVD

Selected inclusion criteria:

- Aged ≥18 years
- Stage III or IV

N=1,334
Median age: 36 years

BV + AVD 6 × cycles (n=664)

ABVD 6 × cycles (n=670)

PET scan at Cycle 2

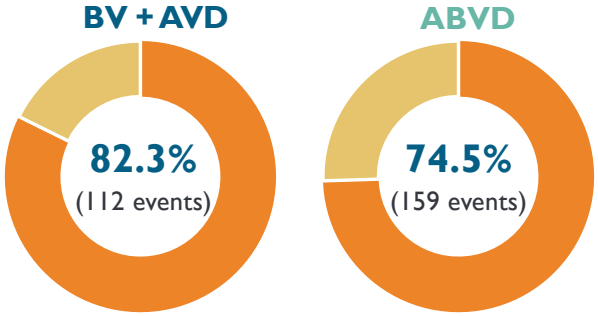
EoT CT/PET scan at Cycle 6

Follow-up every 3 months for 12 months, then every 6 months until trial closure

Primary endpoint:
mPFS by IRF

PFS

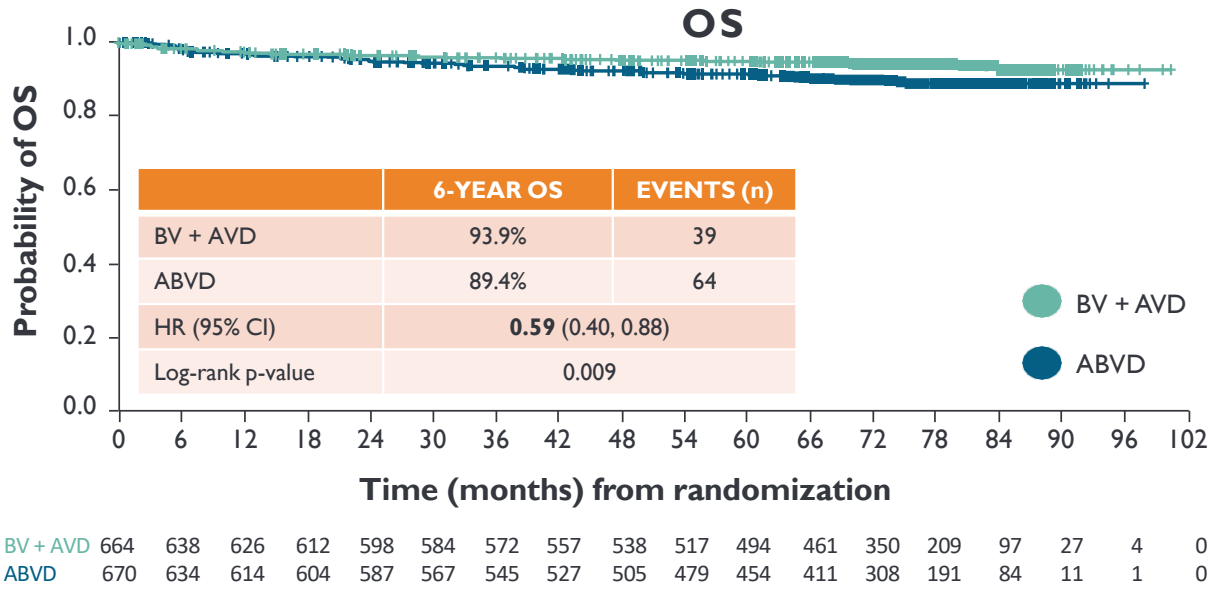
6-year PFS



HR (95% CI): 0.68 (0.53, 0.86)

These data support the primary analysis of the primary endpoint
2-year mPFS: 82.1% vs 77.2% (HR: 0.77 [95% CI: 0.60, 0.98])

OS



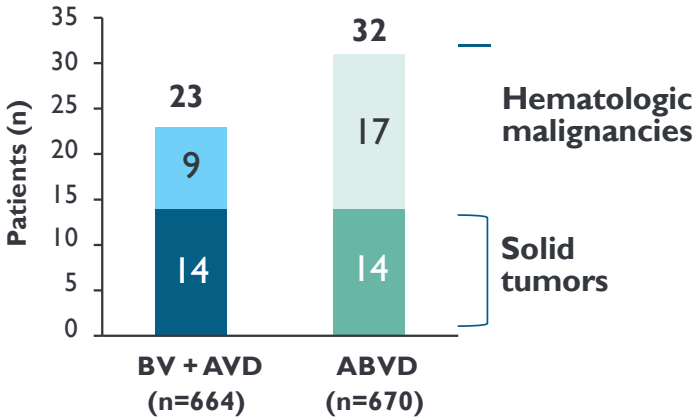
	6-YEAR OS	EVENTS (n)
BV + AVD	93.9%	39
ABVD	89.4%	64
HR (95% CI)	**0.59** (0.40, 0.88)	
Log-rank p-value	0.009	

BV + 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

1. ANSELL SM, ET AL. N ENGL J MED 2022;387:310–20; 2. CONNORS JM, ET AL. N ENGL J MED 2018;378:331–44

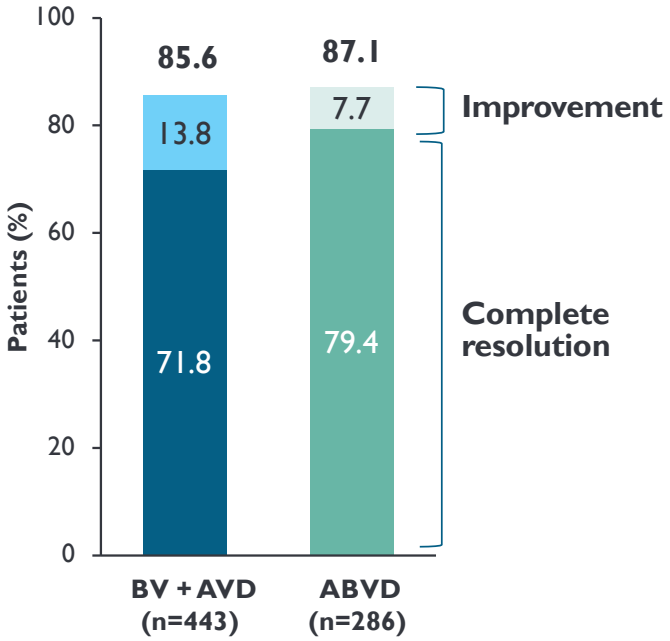
ECHELON-1: 6-YEAR SAFETY PROFILE WITH BV + AVD VS ABVD

Second malignancies

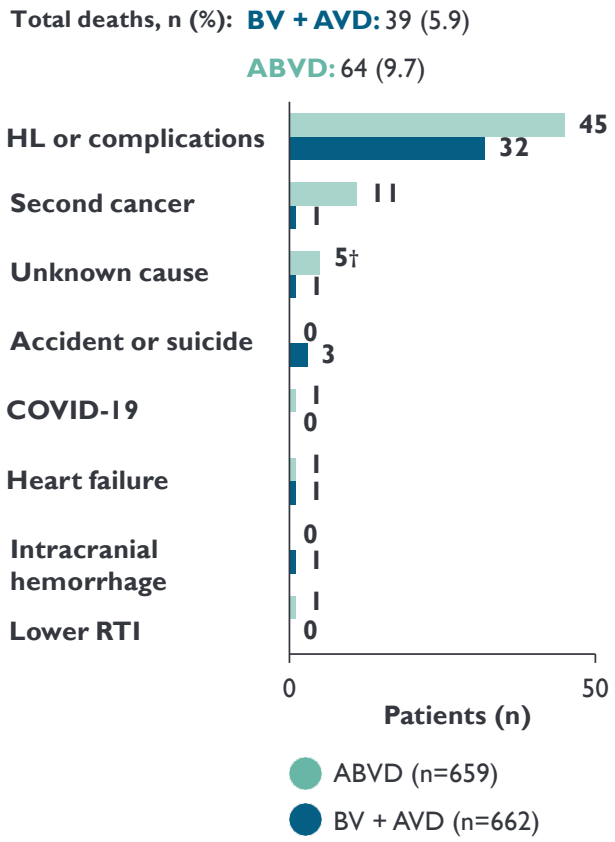


42% of second malignancies occurred in patients **aged ≥60 years**, even though these patients constituted ~14% of the total trial population

Peripheral neuropathy



Deaths



1.ANSELL SM, ET AL. N ENGL J MED 2022;387:310–20; 2. CONNORS JM, ET AL. N ENGL J MED 2018;378:331–44

AHOD1331: BV-AVE-PC VS ABVE-PC IN PEDIATRIC PATIENTS

AHOD1331: OPEN-LABEL, RANDOMIZED, PHASE 3 TRIAL OF BV-AVE-PC vs ABVE-PC IN PEDIATRIC PATIENTS WITH NEWLY DIAGNOSED HIGH-RISK cHL

Previously untreated advanced cHL

BV-AVE-PC

ABVE-PC × 2

Interim PET

BV-AVE-PC

ABVE-PC × 3

ENDPOINTS

Primary: EFS

Secondary:

- Interim response
- Use of involved-site RT
- Clinician-reported chemotherapy-induced PN

N=600
Median age: 15.6 years

Key inclusion criteria:

- Aged 2–21 years
- Stage IIB with bulk tumor, or Stage IIIB, IVA, or IVB
- No nodular lymphocyte-predominant disease
- No immunodeficiency

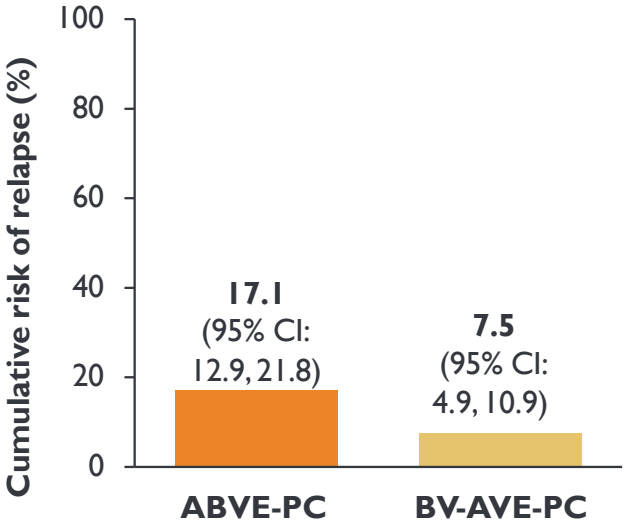
RT:

Limited to slow responding regions or large mediastinal adenopathy

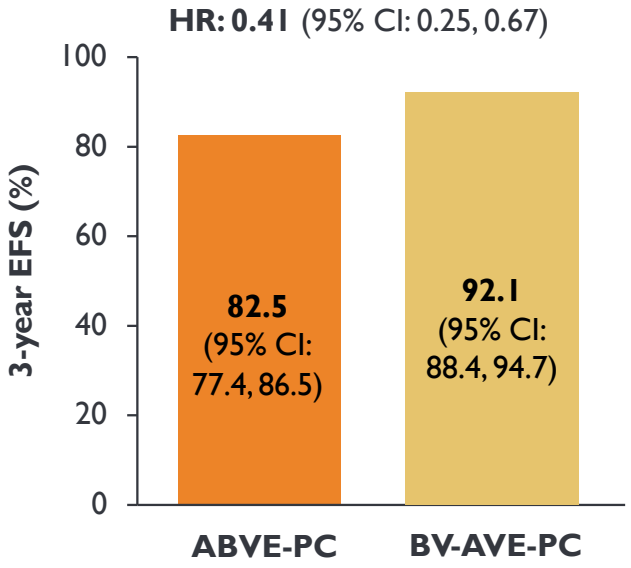
CASTELLINO SM, ET AL. N ENGL J MED 2022;387:1649–60

AHOD1331: SURVIVAL OUTCOMES AND SAFETY PROFILE

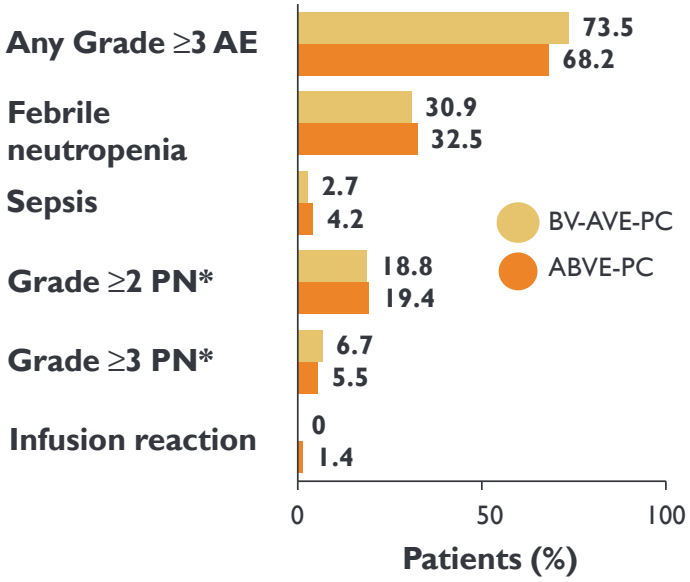
Cumulative incidence of relapse



EFS



Safety profile (Grade ≥3 AEs)



BV-AVE-PC demonstrated reduced relapse rates and improved EFS vs ABVE-PC in pediatric patients with cHL

CASTELLINO SM, ET AL. N ENGL J MED 2022;387:1649–60

*ABVE-PC, doxorubicin + bleomycin + vincristine + etoposide + prednisone + cyclophosphamide; AE, adverse event; BV-AVE-PC, brentuximab vedotin + doxorubicin + vincristine +etoposide + prednisone + cyclophosphamide; CI, confidence interval; EFS, event-free survival; HR, hazard ratio; PN, peripheral neuropathy

BRECADD: INVESTIGATIONAL FRONTLINE REGIMEN FOR HL

escBEACOPP		BrECADD	REGIMEN CHANGES	RATIONALE
Bleomycin 10 mg/m^2	B Br	**BV** 1.8 mg/kg	Omitted bleomycin	Reduce risk of bleomycin-induced pneumonitis
			Added BV	Improve specificity of regimen to CD30-bearing HL cells
Etoposide 200 mg/m^2	E	**Etoposide** 150 mg/m^2	Reduced dose	Reduce overall dose intensity of the polychemotherapy regimen, aiming to reduce risk of second malignancies (MDS and AML)
Doxorubicin 35 mg/m^2	A	**Doxorubicin** 40 mg/m^2	Moderately increased dose	Maintain cumulative effective chemotherapy dose in context of reduction in etoposide dose
Cyclophosphamide 1,250 mg/m^2	C	**Cyclophosphamide** 1,250 mg/m^2	No changes	–
Vincristine 1.4 mg/m^2 (max. 2 mg)	O –	—	Omitted	Vincristine MoA overlaps with that of MMAE (cytotoxic conjugate component of BV) Reduce risk of vincristine-associated Grade 3/4 polyneuropathies
Procarbazine 100 mg/m^2	P D	**Dacarbazine** 250 mg/m^2	**7-day** procarbazine regimen replaced with **2-day** dacarbazine regimen	Reduce risk of second malignancies (MDS and AML) Reduce gonadal toxicity
Prednisone 40 mg/m^2	P D	**Dexamethasone** 40 mg	**14-day** prednisone regimen replaced by **4-day** dexamethasone	Reduce risk of serious infection during aplasia phase (Days 6–10 of each chemotherapy cycle)

The BrECADD regimen is an investigational, rationally designed, CD30-intensified frontline regimen that aims to maintain the efficacy of escalated BEACOPP while reducing toxicity

BrECADD, brentuximab vedotin + etoposide + cyclophosphamide + doxorubicin + dacarbazine + dexamethasone; BV, brentuximab vedotin; CD30, cluster of differentiation 30; escBEACOPP, escalated bleomycin + etoposide + doxorubicin + cyclophosphamide + vincristine + procarbazine + prednisone

GERMAN HODGKIN STUDY GROUP. HD21 STUDY PROTOCOL V8.0, JULY 2021

HD21: GERMAN PHASE 3 TRIAL OF BRECADD VS ESCBEACOPP

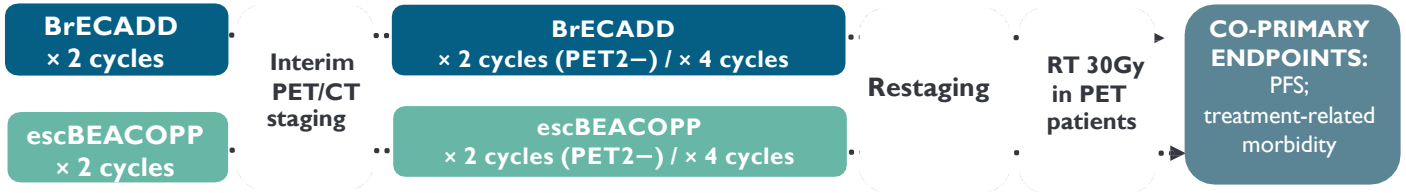
RANDOMIZED, PHASE 3 TRIAL OF BrECADD VS escBEACOPP IN NEWLY DIAGOSED cHL

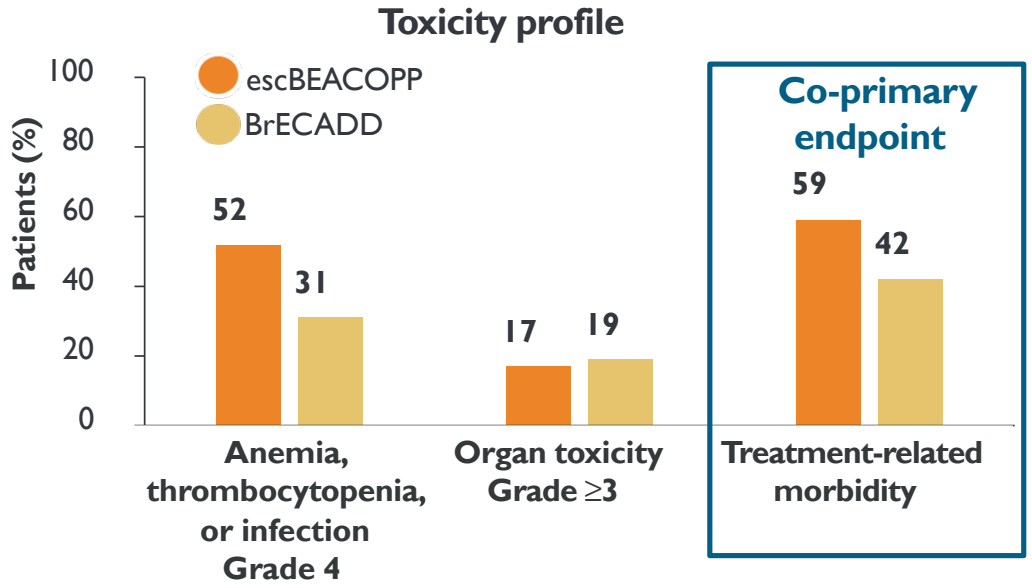
Newly diagnosed cHL

Selected inclusion criteria:

- Aged 18–60 years
- Stage IIB, III, and IV

N=1,500





NCI/SWOG 1826 TRIAL OF NIVOLUMAB + AVD VS BV + AVD

RANDOMIZED PHASE 3 TRIAL OF NIVOLUMAB + AVD VS BV + AVD IN PATIENTS WITH NEWLY DIAGNOSED ADVANCED-STAGE cHL

Newly diagnosed cHL

N=940

BV + AVD × 6 cycles

Nivolumab + AVD × 6 cycles

RT to residual FDG-avid areas in patients with DS 4–5, ≥30% reduction in max. transverse diameter, and residual LN ≥2.5 cm*

ENDPOINTS

Primary:
- PFS

Secondary:
- EFS
- OS
- CR
- Safety and tolerability

Stratification:
- Age, IPS, EoT eligible

Key inclusion criteria:
- Aged ≥12 years
- Stage III–IV
- Bidimensionally measurable disease

BV + AVD

BV 1.2 mg/kg on Days 1 and 15
Doxorubicin 25 mg/m^2 on Days 1 and 15
Vinblastine 6 mg/m^2 on Days 1 and 15
Dacarbazine 375 mg/m^2 on Days 1 and 15

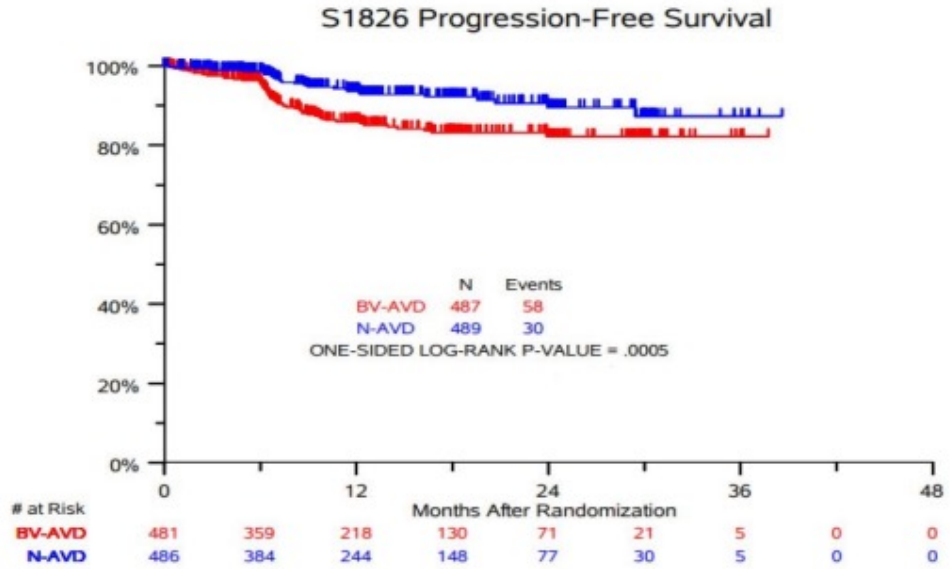
Nivolumab + AVD

Nivolumab 240 mg on Days 1 and 15
Doxorubicin 25 mg/m^2 on Days 1 and 15
Vinblastine 6 mg/m^2 on Days 1 and 15
Dacarbazine 375 mg/m^2 on Days 1 and 15

1HERRERA A, ET AL. BLOOD 2020;136(SUPPL 1):23–4; 2. CLINICALTRIALS.GOV, NCT03907488 (ACCESSED MAY 2023)

Nivolumab(N)-AVD Improves Progression-Free Survival Compared to Brentuximab Vedotin(BV)-AVD in Advanced Stage (AS) Classic Hodgkin Lymphoma (HL): Results of SWOG S1826

Herrera et al.



The 1-y PFS per ITT

N-AVD: 94%, versus BV-AVD: 86%

[HR 0.48, 99% CI 0.27-0.87, one-sided p=0.0005)

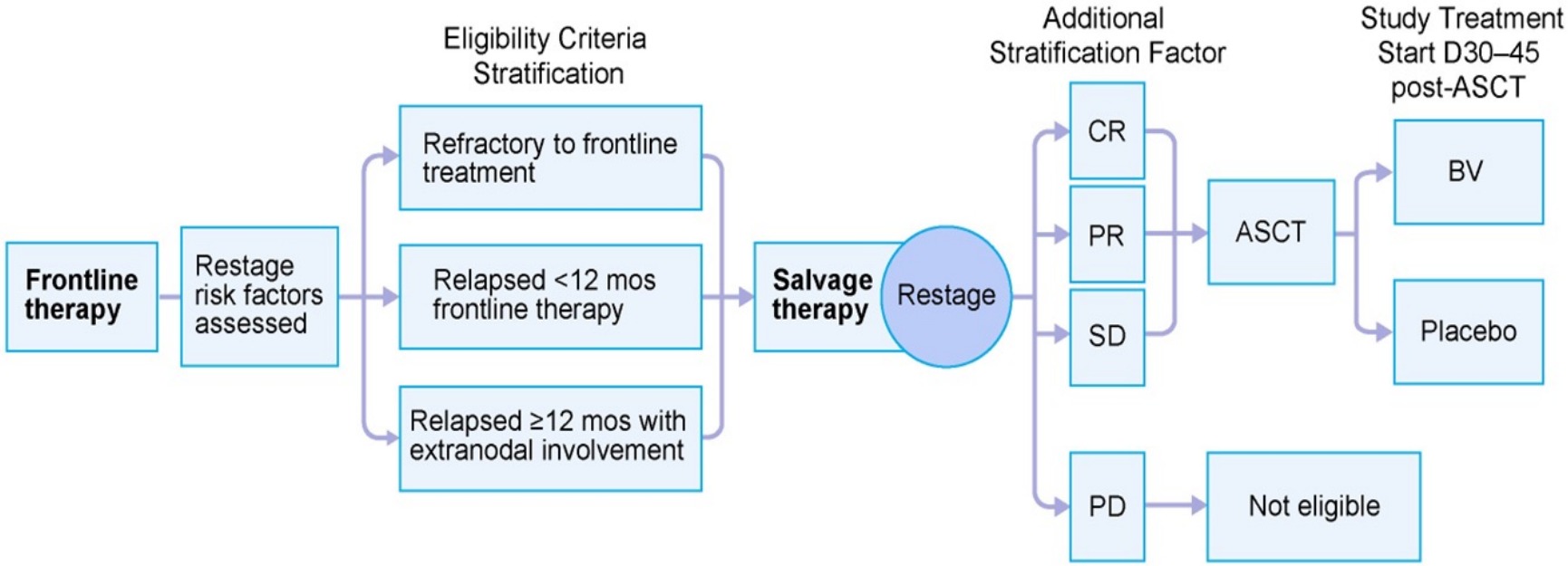
Nota bene:

significance was reached at a 99% CI due to interim analysis

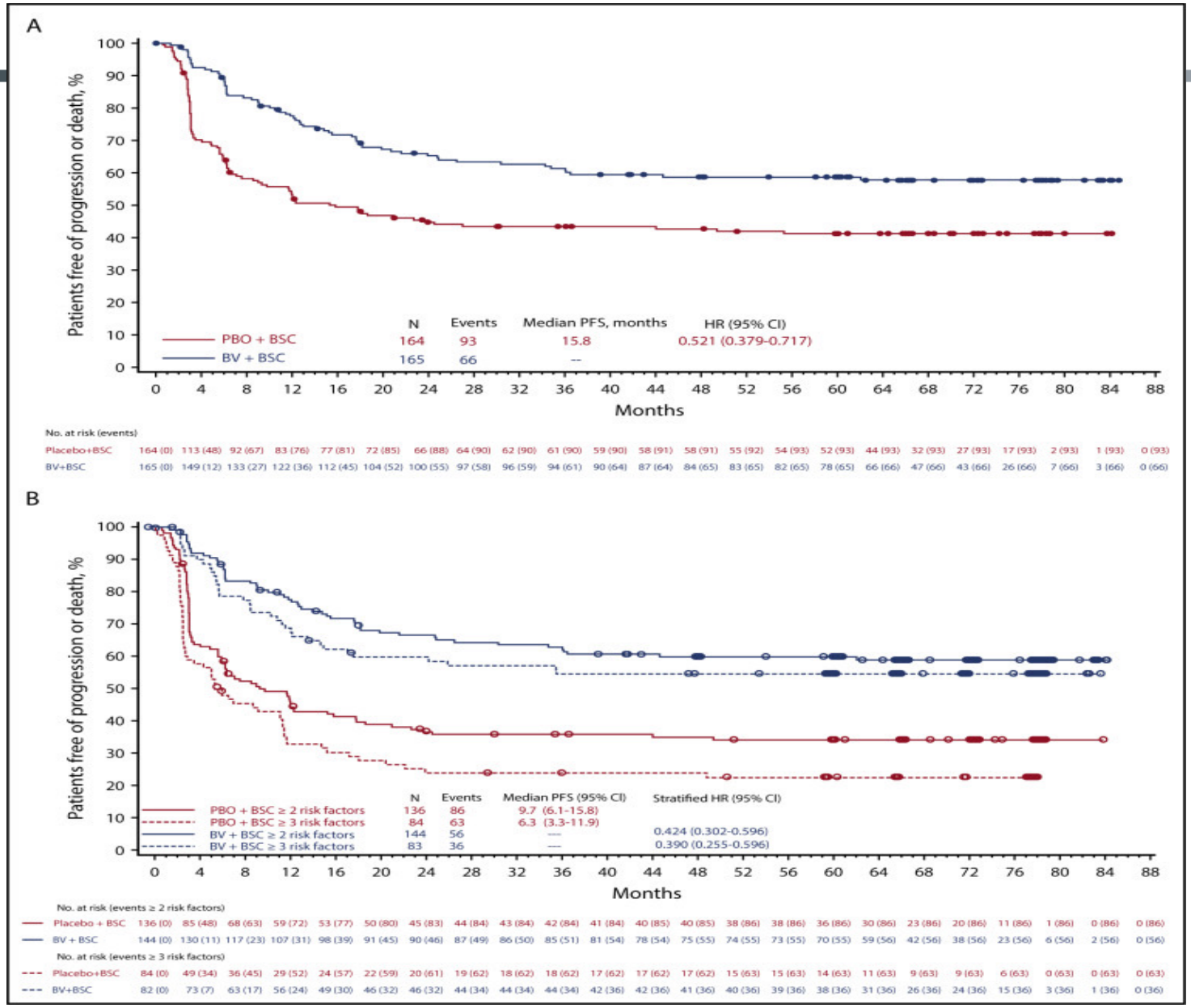
cons RTx was used only in very few patients

The AETHERA study

329 patients were randomised at 78 sites in North America and Europe



5 Years PFS


A
Patients free of progression or death, %
Months
N Events Median PFS, months HR (95% CI)
PBO + BSC 164 93 15.8 0.521 (0.379-0.717)
BV + BSC 165 66 --
No. at risk (events)
Placebo+BSC 164 (0) 113 (48) 92 (67) 83 (76) 77 (81) 72 (85) 66 (88) 64 (90) 62 (90) 61 (90) 59 (90) 58 (91) 58 (91) 55 (92) 54 (93) 52 (93) 44 (93) 32 (93) 27 (93) 17 (93) 2 (93) 1 (93) 0 (93)
BV+BSC 165 (0) 149 (12) 133 (27) 122 (36) 112 (45) 104 (52) 100 (55) 97 (58) 96 (59) 94 (61) 90 (64) 87 (64) 84 (65) 83 (65) 82 (65) 78 (65) 66 (66) 47 (66) 43 (66) 26 (66) 7 (66) 3 (66) 0 (66)
B
Patients free of progression or death, %
Months
N Events Median PFS (95% CI) Stratified HR (95% CI)
PBO + BSC ≥ 2 risk factors 136 86 9.7 (6.1-15.8)
PBO + BSC ≥ 3 risk factors 84 63 6.3 (3.3-11.9)
BV + BSC ≥ 2 risk factors 144 56 ---- 0.424 (0.302-0.596)
BV + BSC ≥ 3 risk factors 83 36 ---- 0.390 (0.255-0.596)
No. at risk (events ≥ 2 risk factors)
Placebo + BSC 136 (0) 85 (48) 68 (63) 59 (72) 53 (77) 50 (80) 45 (83) 44 (84) 43 (84) 42 (84) 41 (84) 40 (85) 40 (85) 38 (86) 38 (86) 36 (86) 30 (86) 23 (86) 20 (86) 11 (86) 1 (86) 0 (86) 0 (86)
BV + BSC 144 (0) 130 (11) 117 (23) 107 (31) 98 (39) 91 (45) 90 (46) 87 (49) 86 (50) 85 (51) 81 (54) 78 (54) 75 (55) 74 (55) 73 (55) 70 (55) 59 (56) 42 (56) 38 (56) 23 (56) 6 (56) 2 (56) 0 (56)
No. at risk (events ≥ 3 risk factors)
Placebo+BSC 84 (0) 49 (34) 36 (45) 29 (52) 24 (57) 22 (59) 20 (61) 19 (62) 18 (62) 18 (62) 17 (62) 17 (62) 17 (62) 15 (63) 15 (63) 14 (63) 11 (63) 9 (63) 9 (63) 6 (63) 0 (63) 0 (63) 0 (63)
BV+BSC 82 (0) 73 (7) 63 (17) 56 (24) 49 (30) 46 (32) 46 (32) 44 (34) 44 (34) 44 (34) 42 (36) 42 (36) 41 (36) 40 (36) 39 (36) 38 (36) 31 (36) 26 (36) 24 (36) 15 (36) 3 (36) 1 (36) 0 (36)

ALTERNATIVES TO CHOP AS INITIAL THERAPY IN PTCL

Results with CHOP as initial therapy for PTCL are generally poor, with few patients achieving CR or durable remission. However, several alternative strategies to CHOP have had limited success

ADDING ETOPOSIDE TO CHOP (CHOEP)

- **Meta-analysis of five studies (N=1,560)[1]**
  - No difference in CR or
  - ORR with CHOP vs CHOEP
  - Significantly increased AEs with CHOEP vs CHOP

ADDING TARGETED AGENTS TO CHOP IN FRONTLINE

- **Targeted agents include:**
  - Alemtuzumab
  - Romidepsin
  - Brentuximab vedotin
  - Azacitidine
  - Duvelisib

ASCT AS CONSOLIDATION

- No RCTs vs chemotherapy, although prospective studies showed promising results

. Deng S, et al. Onco Targets Ther 2019;12:2335–42;

HEMATOLOGIST 2021;18:5; 10. MEHTA-SHAH N, ET AL. J CLIN ONCOL 2022;40:16; 11. REIMER P. ADV HAEMATOL 2010;2010:320624

ECHELON-2: TRIAL DESIGN

PLACEBO-CONTROLLED, DOUBLE-BLIND, GLOBAL, PHASE 3 TRIAL TO COMPARE THE EFFICACY AND SAFETY OF BV + CHP VS SoC CHOP IN PATIENTS WITH PREVIOUSLY UNTREATED CD30+ PTCL

CD30+ PTCL

N=452
Median age: 58 years

BV + CHP × 6–8 cycles

CHOP × 6–8 cycles

ENDPOINTS

Primary:
- **PFS**

Secondary:
- **PFS in patients with sALCL**
- **CR rate at EoT**
- **OS**
- **ORR**
- **Safety**

Key inclusion criteria:
- Previously untreated, CD30+ PTCL
- Age ≥18 years
- ECOG PS ≤2
- No primary cutaneous CD30+ T-cell LPD or lymphoma, or MF

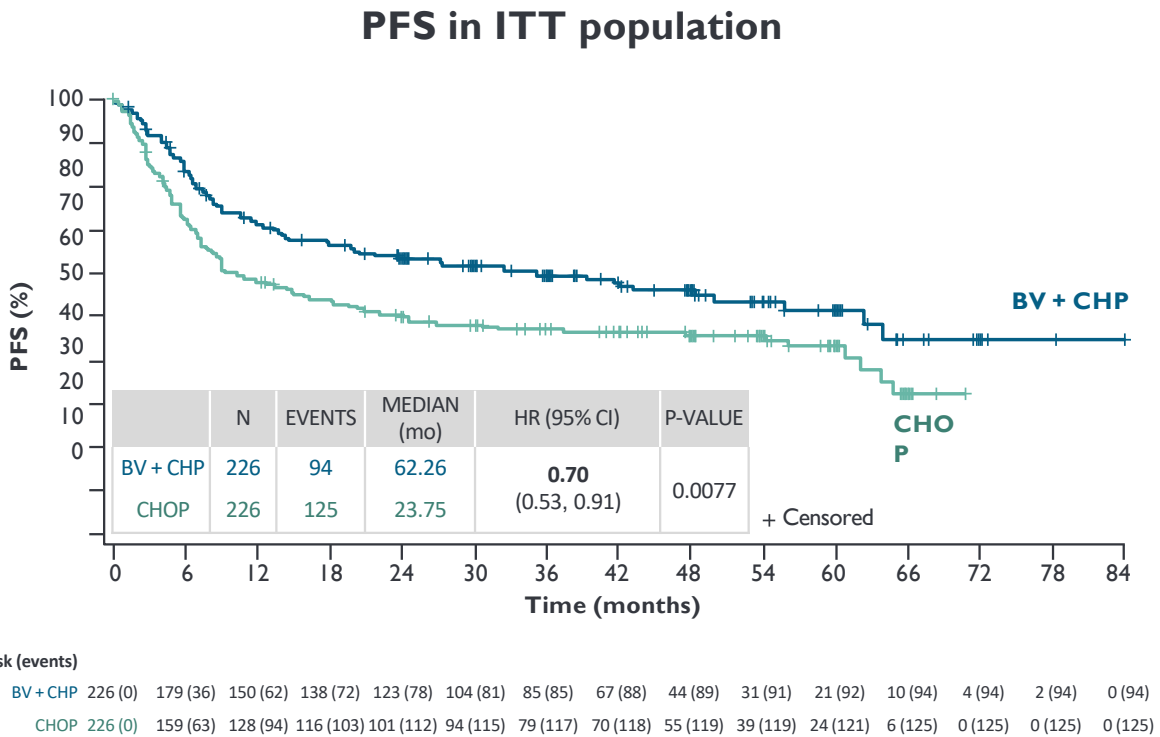
BV + CHP[1]:
- BV 1.8 mg/kg IV Day 1 Q3W
- Cyclophosphamide 750 mg/m² IV Day 1 Q3W
- Doxorubicin 50 mg/m² IV Day 1 Q3W
- Prednisone 100 mg PO Days 1–5 of each 21-day cycle
- Vincristine placebo

CHOP[1]:
- Cyclophosphamide 750 mg/m² IV Day 1 Q3W
- Doxorubicin 50 mg/m² IV Day 1 Q3W
- Vincristine 1.4 mg/m² (maximum 2 mg) IV Day 1 Q3W
- Prednisone 100 mg PO Days 1–5 of each 21-day cycle
- BV placebo

BV + CHP, brentuximab vedotin + cyclophosphamide + doxorubicin + prednisone; CD30, cluster of differentiation 30; CHOP, cyclophosphamide + doxorubicin + vincristine + prednisone; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance score; EoT, end of treatment; IV, intravenously; LPD, lymphoproliferative disorder; MF, mycosis fungoides; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PO, orally; PTCL, peripheral T-cell lymphoma; Q3W, every 3 weeks; R, randomization; sALCL, systemic anaplastic large cell lymphoma; SoC, standard of care

HORWITZ S, ET AL. LANCET 2019;393:229–40; 2. CLINICALTRIALS.GOV, NCT01777152 (ACCESSED MAY 2023)

ECHELON-2 PRIMARY ENDPOINT: PFS



	N	EVENTS	MEDIAN (mo)	HR (95% CI)	P-VALUE
BV + CHP	226	94	62.26	**0.70** (0.53, 0.91)	0.0077
CHOP	226	125	23.75		

N at risk (events)

BV + CHP	226 (0)	179 (36)	150 (62)	138 (72)	123 (78)	104 (81)	85 (85)	67 (88)	44 (89)	31 (91)	21 (92)	10 (94)	4 (94)	2 (94)	0 (94)
CHOP	226 (0)	159 (63)	128 (94)	116 (103)	101 (112)	94 (115)	79 (117)	70 (118)	55 (119)	39 (119)	24 (121)	6 (125)	0 (125)	0 (125)	0 (125)

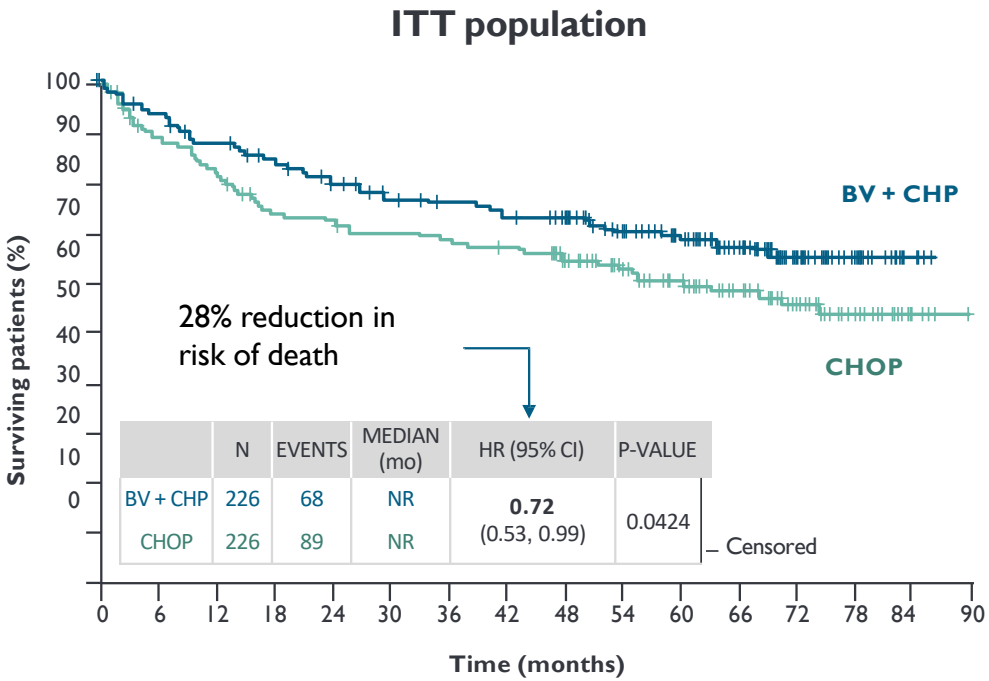
30% reduction in the risk of progression events was observed with BV + CHP vs CHOP with long-term follow-up (median follow-up: 66.8 mo)

Figure adapted from Horwitz S, et al

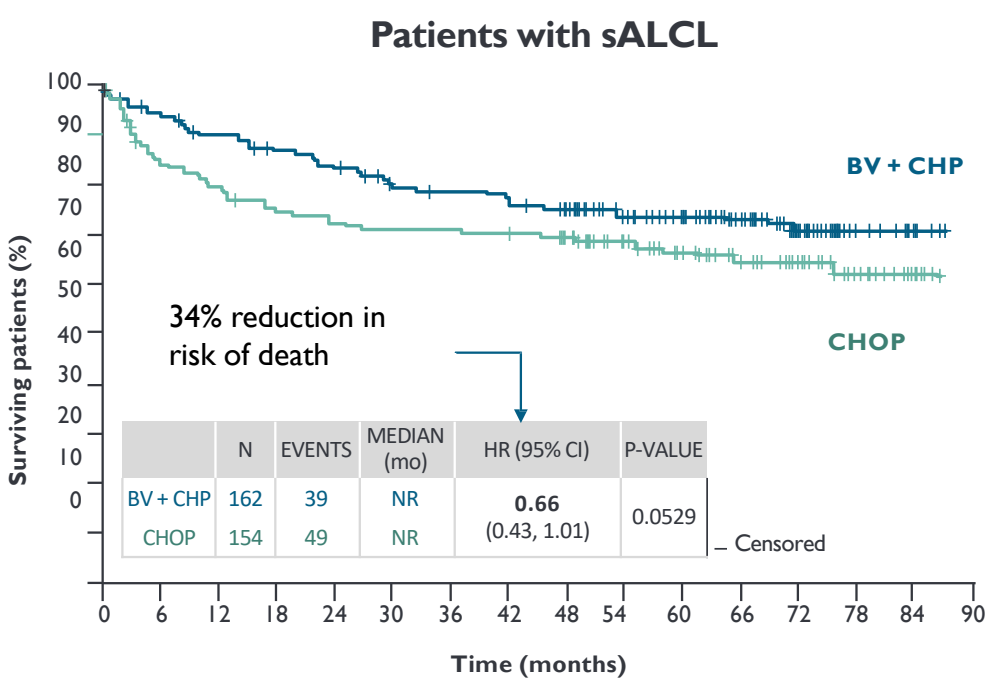
BV + CHP, brentuximab vedotin + cyclophosphamide + doxorubicin + prednisone; CHOP, cyclophosphamide + doxorubicin + vincristine + prednisone; CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; PFS, progression-free survival

HORWITZ SM, ET AL. ANN ONCOL 2022;33:288–98

ECHELON-2



	N	EVENTS	MEDIAN (mo)	HR (95% CI)	P-VALUE
BV + CHP	226	68	NR	**0.72** (0.53, 0.99)	0.0424
CHOP	226	89	NR		



	N	EVENTS	MEDIAN (mo)	HR (95% CI)	P-VALUE
BV + CHP	162	39	NR	**0.66** (0.43, 1.01)	0.0529
CHOP	154	49	NR		

Significant improvement in OS was observed through 5 years in the ITT population, with a numerical OS improvement in the sALCL subgroup

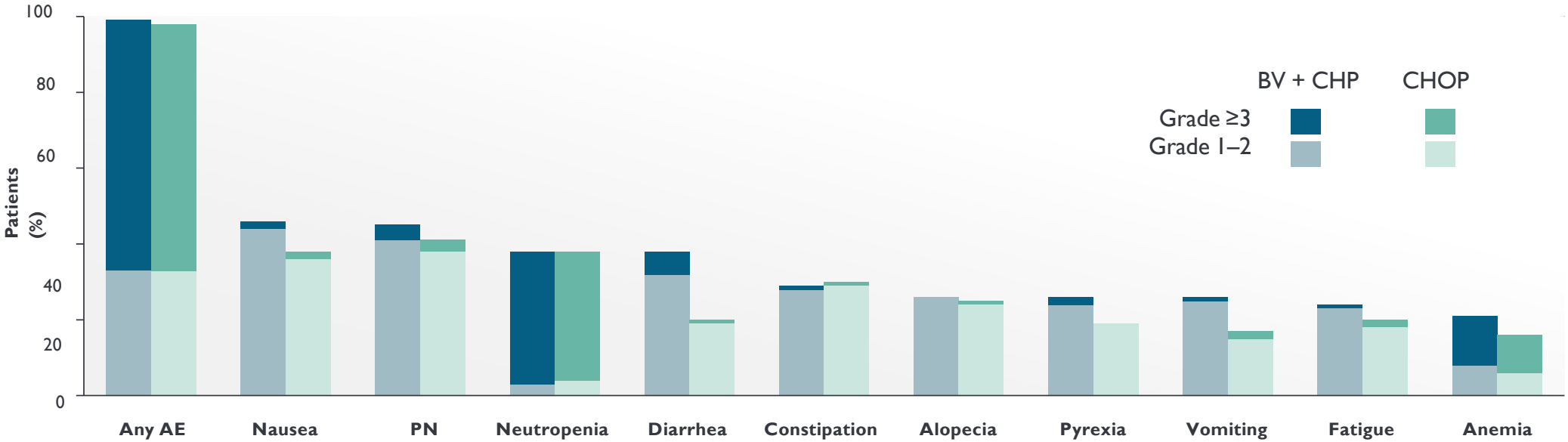
Figure adapted from Horwitz S, et al,

BV + CHP, brentuximab vedotin + cyclophosphamide + doxorubicin + prednisone; CHOP, cyclophosphamide + doxorubicin + vincristine + prednisone; CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; NR, not reached; OS, overall survival; sALCL, systemic anaplastic large cell lymphoma

HORWITZ SM, ET AL. ANN ONCOL 2022;33:288–98

ECHELON-2: SAFETY PROFILE

Adverse events in ≥20% of patients



The safety of BV + CHP was consistent with the previously established safety profile

Rate and severity of neutropenia were similar with BV + CHP and CHOP, and lower in the subgroup of patients receiving primary prophylaxis with G-CSF

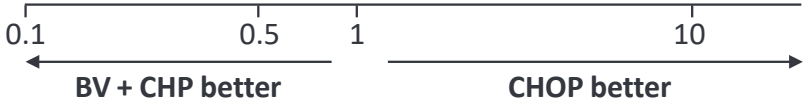
Rate and severity of febrile neutropenia were also similar with BV + CHP and CHOP

BV + CHP continued to have a manageable safety profile at 5 years; similar resolution of PN was seen in both arms

HORWITZ S, ET AL. LANCET 2019;393:229–40; 2. ANSELL SM, ET AL. N ENGL J MED 2022;387:310–20; 3. HORWITZ SM, ET AL. ANN ONCOL 2022;33:288–98

ECHELON-2: 5-year survival by disease indication subgroup

ITT subgroups	Event/N BV + CHP	Event/N CHOP	HR (95% CI)
Overall survival	68/226	89/226	0.72 (0.53, 0.99)
Disease indication			
ALK-positive sALCL	5/49	10/49	0.48 (0.16, 1.40)
ALK-negative sALCL	34/113	39/105	0.71 (0.44, 1.12)
ATLL	2/4	3/3	0.70 (0.11, 4.27)
AITL	12/30	8/24	1.01 (0.40, 2.55)
EATL	1/1	2/2	Not estimable
PTCL-NOS	14/29	27/43	0.75 (0.37, 1.48)
sALCL	39/162	49/154	0.66 (0.43, 1.01)
Non-sALCL	29/64	40/72	0.76 (0.46, 1.23)



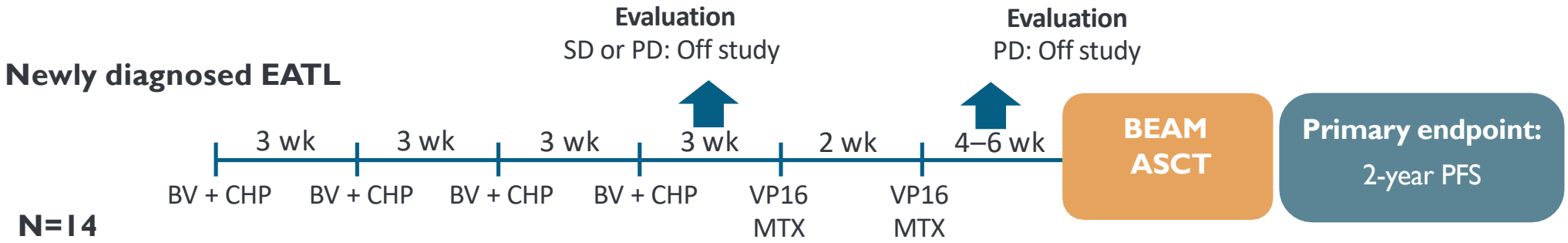
Note: Patient numbers were small in many subgroups. The study was not powered to compare efficacy between individual histologic subtypes, and small subgroup sizes preclude definitive determination of the treatment effect in the non-ALCL population

Trends for improved response with BV + CHP vs CHOP were observed across most disease indication subgroups

HORWITZ SM, ET AL. ANN ONCOL 2022;33:288–98

BRENTUXIMAB IN EATL

EATL-001: A PROSPECTIVE PHASE 2 TRIAL (SIBON D, ET AL. BLOOD 2021;138[SUPPL 1]:136)



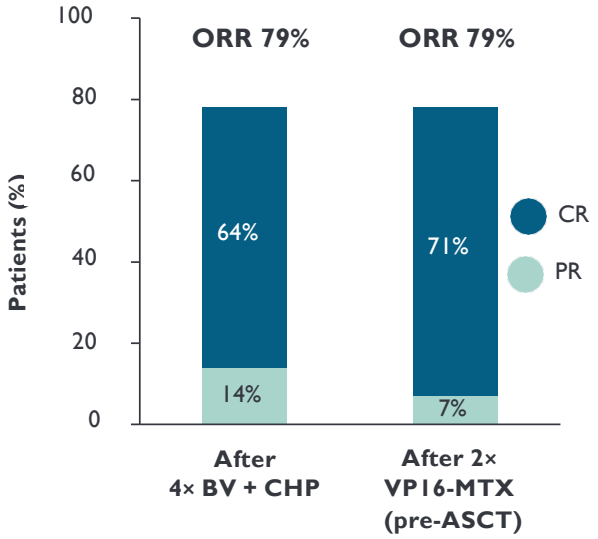
Key inclusion criteria:

- Pathologically confirmed newly diagnosed EATL
- CD30+ (≥10% of neoplastic cells by central review)
- Aged 18–65 years
- ECOG PS 0–3

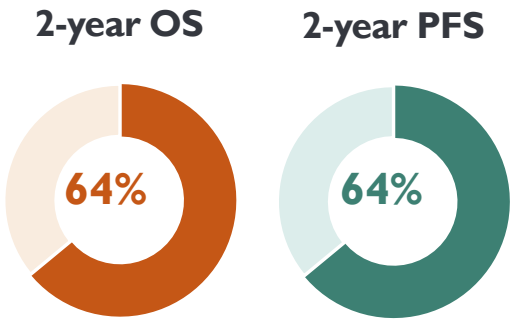
Median follow-up: 2.7 years

SIBON D, ET AL. BLOOD 2021;138(SUPPL 1):136

Response rates (Lugano criteria)

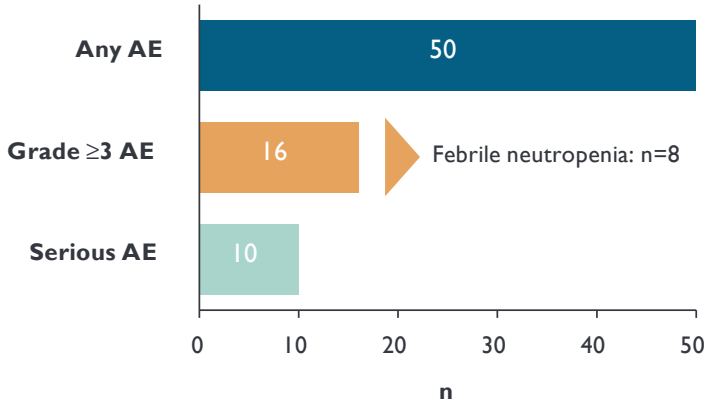


OS and PFS



Median follow-up: 2.7 years

Safety summary



No deaths or treatment discontinuations due to AEs

Indirect comparison with historical controls suggest promising survival outcomes vs existing treatments

SIBON D, ET AL. BLOOD 2021;138(SUPPL 1):136

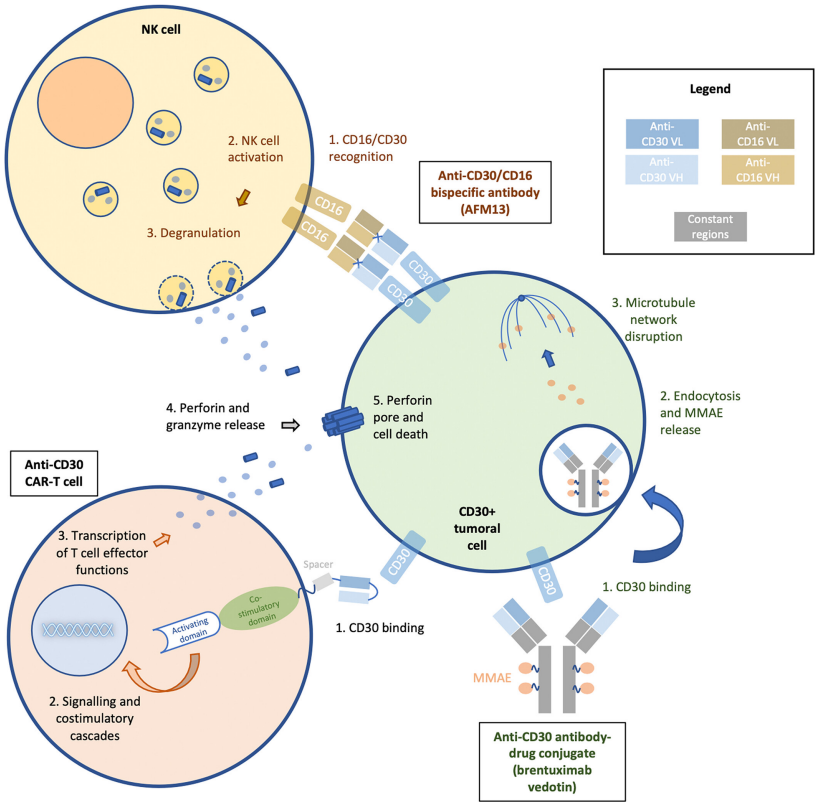
CAR-T

- Phase I/II study, 41 patients with R/R HL treated with second-generation anti-CD30 CAR-T cells
  Lymphodepletion regimens bendamustine, bendamustine + fludarabine or cytarabine + fludarabine.
  No overall response was detected in any of the patients with active disease who underwent lymphodepletion with bendamustine alone. Patients with the evaluable disease who received fludarabine-based lymphodepletion had high rates of durable responses, with an ORR of 72%, including a CR in 59% of these patients, and the one-year PFS was 41% (Ramos et Al.)
- 18 patients with R/R HL PR was achieved in 39% of patients and stable disease was achieved in 33%

BISPECIFIC ANTIBODIES (BSABS)

- A bispecific antibody (bsAb) against CD30/CD16 (murine anti-CD30 HRS3 Ab conjugated with the anti-CD16 A9 Ab) was developed, with one arm reportedly binding the CD30 antigen, and the other recruiting NK by binding the CD16 receptor. In clinical trials in humans, nine of the 15 patients with refractory HL treated with HRS-3/A9 every 3–4 days (1 mg/m^2 to 64 mg/m^2/infusion) developed anti-drug antibodies (ADA) that may compromise the efficacy and impact the safety profile. Indeed, four patients suffered allergic reactions on reinfusion and were excluded from further treatment. Complete and partial remission was observed in one patient each.
- AFM13, a first-in-class tetravalent bispecific antibody with two binding sites for CD30 and two for CD16 (anti-CD30 Ab derived from the murine HRS-3 and human anti-CD16a Abs;
- AFM13 was studied in a phase I dose-escalation study (AFM13-101) in 28 patients with heavy prior treatment for R/R CD30+ HL. AFM13 was infused weekly for 4 weeks, at doses of 0.01–7 mg/kg. Adverse events were generally mild to moderate.

  The best clinical response was a PR, observed in only 11.5% of patients. Following the administration of AFM13 at a dose of ≥1.5 mg/kg, the ORR was 23% and the overall disease control rate was 77% in subjects with heavy prior treatment. ADA was detected in 15 of 28 patients, and they had the potential to neutralize the treatment in 50% of cases.



GRAZIE PER L'ATTENZIONE