The rule of immunotherapy in the treatment of relapse Hodgkin lymphoma.

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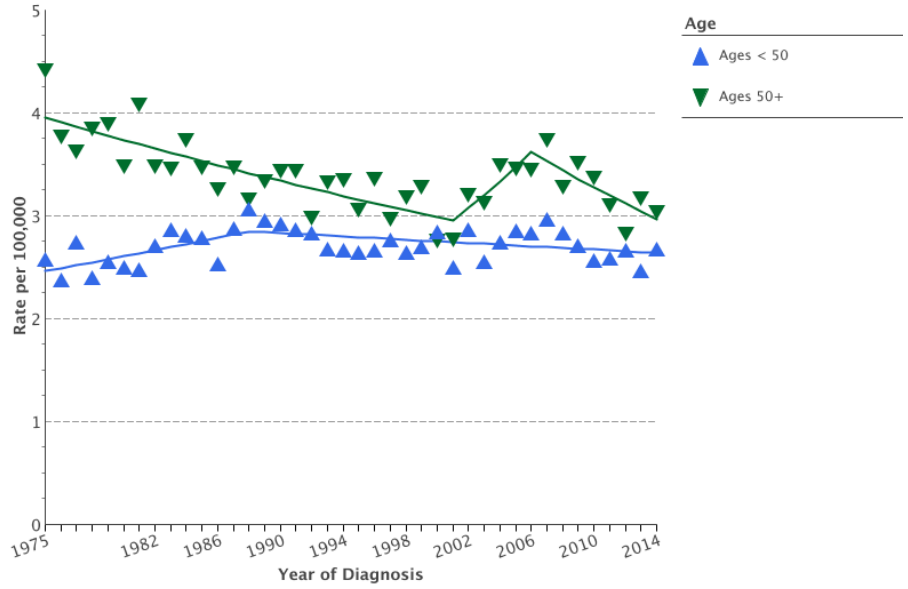
Objectives

- Understand the trends in Hodgkin lymphoma survival and outcome
- Ann Arbor staging for Hodgkin lymphoma
- How I treat early stage Hodgkin lymphoma
- Advances in early stage therapy
- How I treat advanced stage Hodgkin lymphoma
- Advances in advanced stage therapy
- How I treat relapsed refractory Hodgkin lymphoma
- Advances in relapsed refractory therapy
- Conclusions

Epidemiology

Hodgkin Lymphoma
Long-Term Trends in SEER Incidence Rates, 1975-2014
By Age
Both Sexes, All Races (includes Hispanic)



SEER 9 areas [http://seer.cancer.gov/registries/terms.html] (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, and Atlanta).
Rates are per 100,000 and are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).
The Annual Percent Change (APC) estimates were calculated from the underlying rates using the Joinpoint Trend Analysis Software [http://surveillance.cancer.gov/joinpoint], Version 4.4, January 2017, National Cancer Institute.
The APC's direction is "rising" when the entire 95% confidence interval (C.I.) is above 0, "falling" when the entire 95% C.I. is lower than 0, otherwise, the trend is considered stable.
Cancer sites are defined using the SEER Site Recode ICD-O-3/WHO 2008 Definition [https://seer.cancer.gov/siterecode/icdo3_dwhoheme/index.html].
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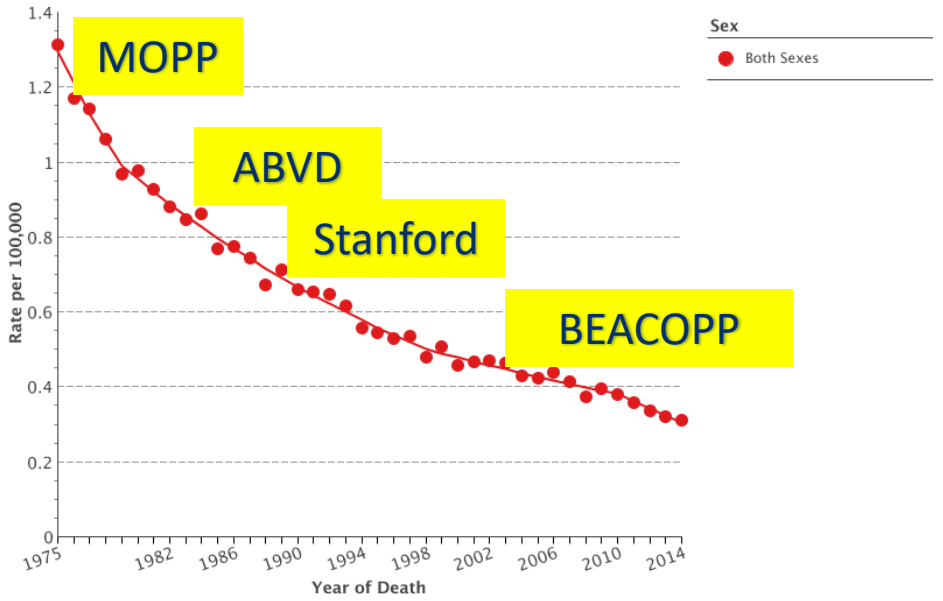
Hodgkin Lymphoma
Long-Term Trends in U.S. Mortality Rates, 1975-2014
By Sex
All Races (includes Hispanic), All Ages



US Mortality Files, National Center for Health Statistics, CDC.
Rates are per 100,000 and are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).
The Annual Percent Change (APC) estimates were calculated from the underlying rates using the Joinpoint Trend Analysis Software [http://surveillance.cancer.gov/joinpoint], Version 4.4, January 2017, National Cancer Institute.
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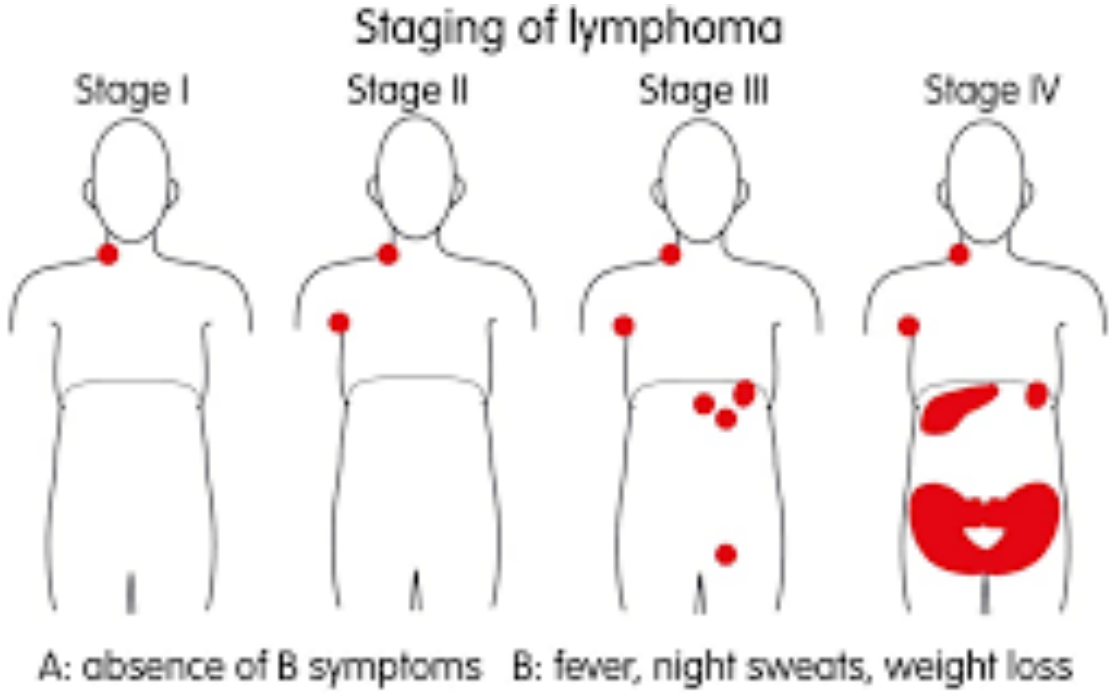
Cancer sites are defined using the SEER Cause of Death Recode 1969+ (04/16/2012).
Created by seer.cancer.gov/explorer/application.php on 01/20/2018 5:08 pm.

Staging

Stage	Involvement	Extranodal (E) Status
Limited		
I	One node or a group of adjacent nodes	Single extranodal lesions without nodal involvement
II	Two or more nodal groups on the same side of the diaphragm	Stage I or II by nodal extent with limited contiguous extranodal involvement
II bulky*	II as above with "bulky" disease	Not applicable
Advanced		
III	Nodes on both sides of the diaphragm; nodes above the diaphragm with spleen involvement	Not applicable
IV	Additional noncontiguous extralymphatic involvement	Not applicable

NOTE. Extent of disease is determined by positron emission tomography–computed tomography for avid lymphomas and computed tomography for nonavid histologies. Tonsils, Waldeyer's ring, and spleen are considered nodal tissue.

*Whether stage II buiky disease is treated as limited or advanced disease may be determined by histology and a number of prognostic factors.

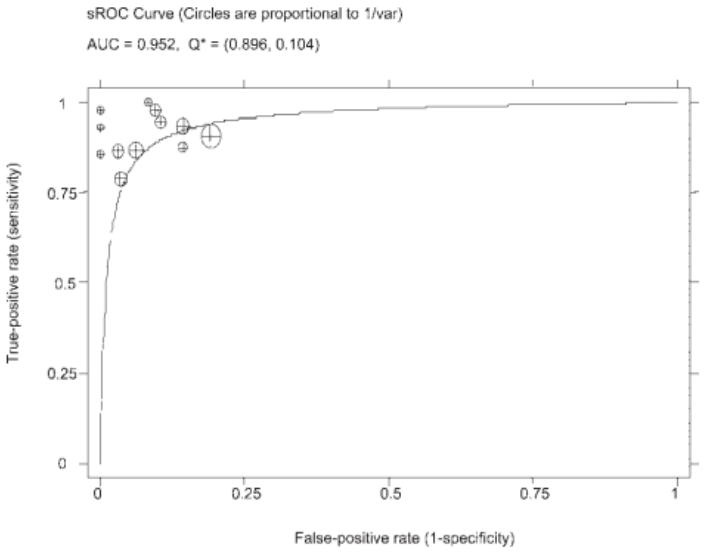


PET Scan

Summary True-Positive Rate, False-Positive Rate, and Maximum Joint Sensitivity and Specificity of FDG-PET in the Staging of Patients with Lymphoma (January 1995–June 2004)

	No. of studies	TPR (95% CI)	FPR (95% CI)	Maximum joint sensitivity and specificity (95% CI)
Patient-based data				
All	14	90.9 (88.0–93.4)	10.3 (7.4–13.8)	87.8 (85.0–90.7)
Excluding studies with lowest sensitivity and lowest specificity	12	91.8 (88.8–94.3)	9.5 (6.6–13.1)	89.6 (87.5–91.6)
Hodgkin disease	6	92.6 (88.4–95.6)	13.4 (8.0–20.6)	89.4 (84.5–94.3)
Non-Hodgkin lymphoma	5	89.4 (82.8–94.1)	11.4 (5.6–19.9)	85.0 (78.2–82.0)
Lesion-based data				
All	7	95.6 (93.9–97.0)	1.0 (0.6–1.3)	95.6 (93.1–98.1)
Excluding study with lowest specificity	6	95.1 (93.0–96.7)	1.0 (0.5–1.3)	95.8 (92.0–99.6)

FDG-PET: ^{18}F-2-deoxy-2-fluoro-D-glucose positron emission tomography; TPR: true-positive rate; 95% CI: 95% confidence interval; FPR: false-positive rate.



In an early meta-analysis published in Cancer in 2005:

- ROC curve have an AUC of 0.96
- Sensitivity of 93%
- Specificity of 87%.

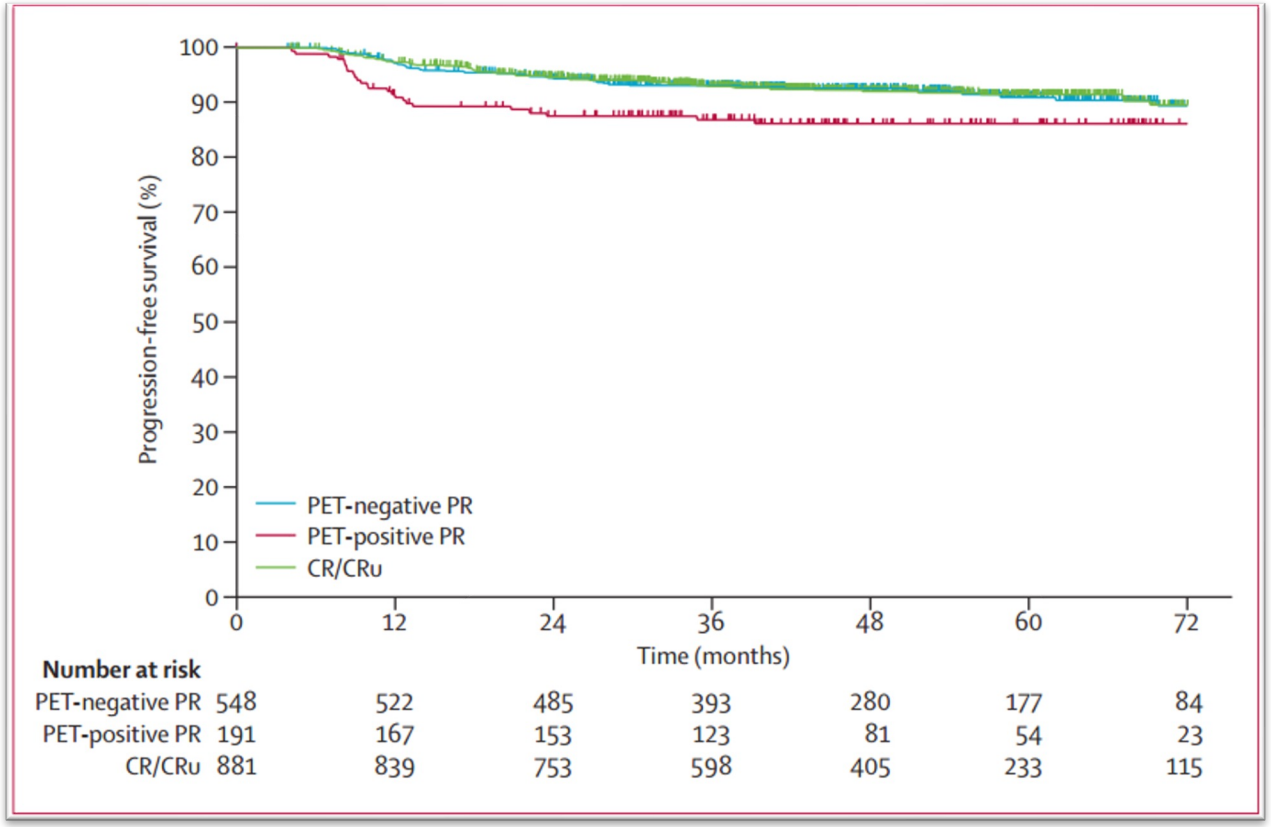
Isasi et al 2005

PET Scan

Rule in end of therapy prognosis:

HD 15 trial which compared three schedules of BEACOPP in Advanced cHL

- PET positivity was associated with inferior PFS of 86% at 4 years compared to 92% for negative PET.

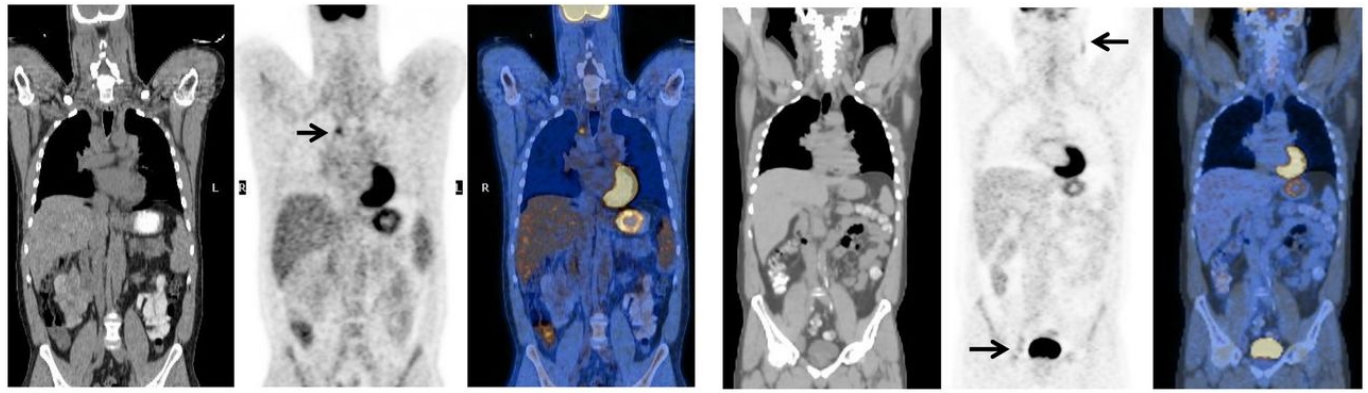


Sher et al 2009
Engert et al, 2012

PET Scan

Deauville Criteria:

(1) No abnormal uptake;
(2) Uptake ≤ mediastinal blood pool uptake;
(3) Uptake above the mediastinal blood pool uptake and ≤ liver blood pool uptake;
(4) Uptake moderately above the liver blood pool uptake;
(5) Uptake markedly above the liver blood pool uptake at any original lesion or appearance of new lesions



Score 4
Uptake > Liver

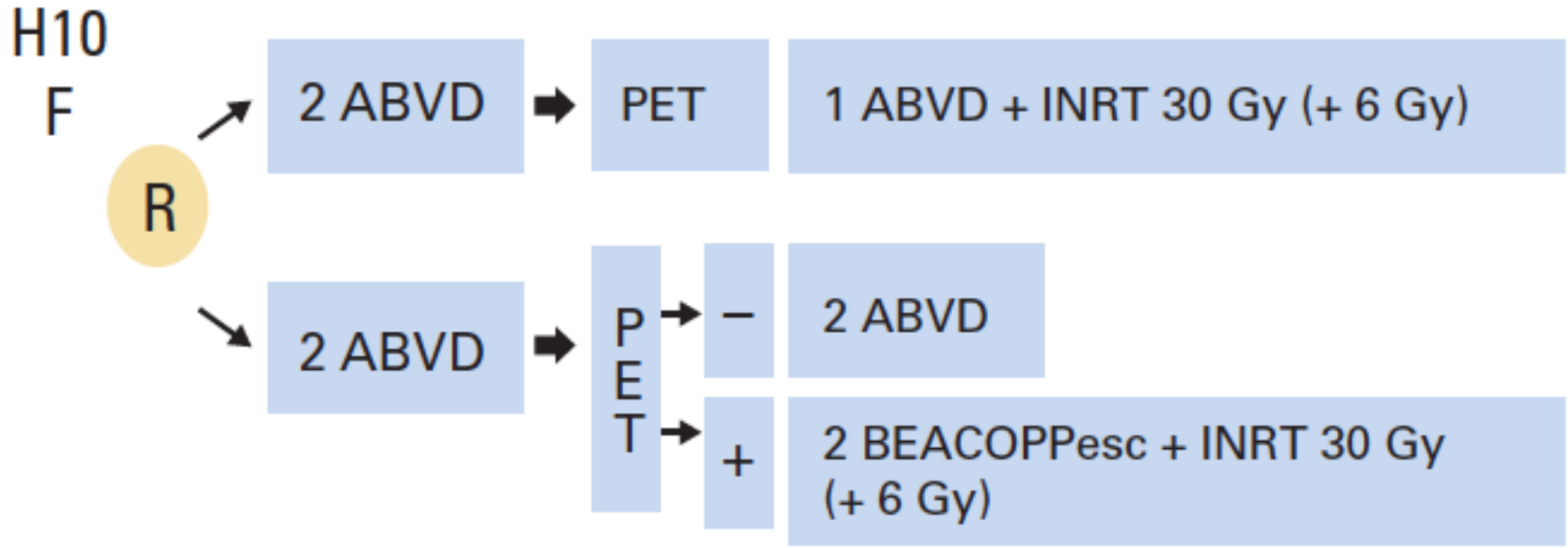
Positive by Deauville 5PS

Score 3
Uptake ≤ Liver

Negative by Deauville 5PS

Meignan et al, 2010
Meignan et al, 2012

Favorable early stage

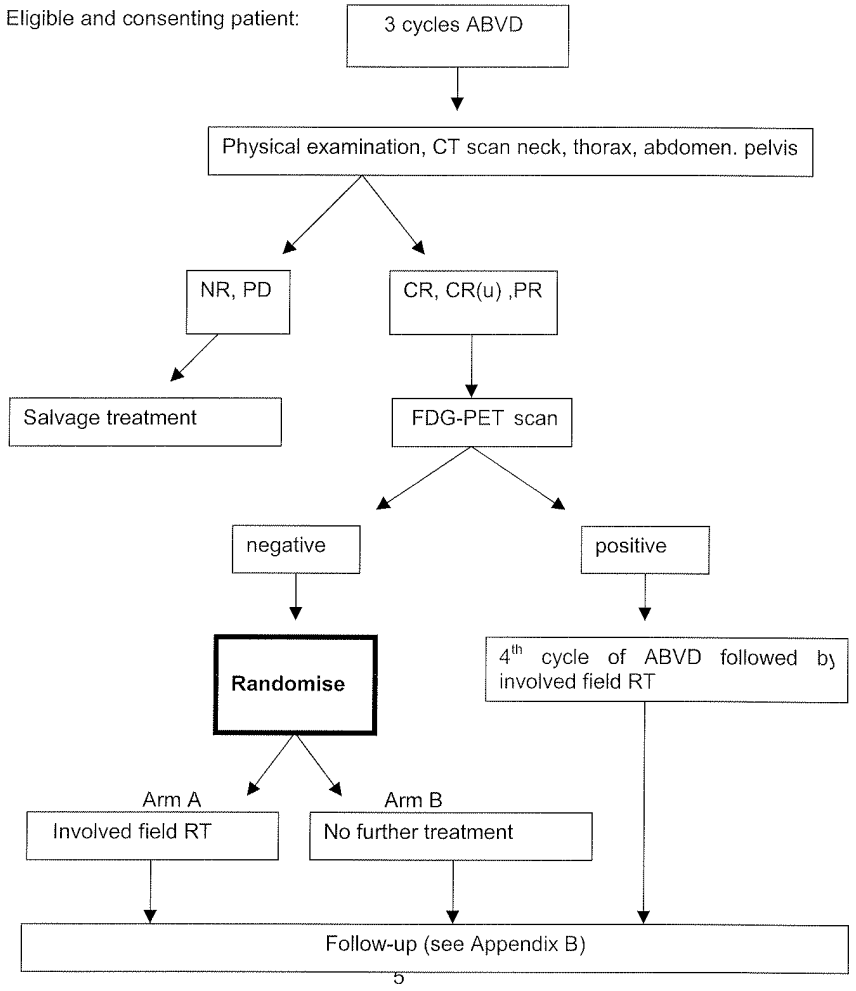


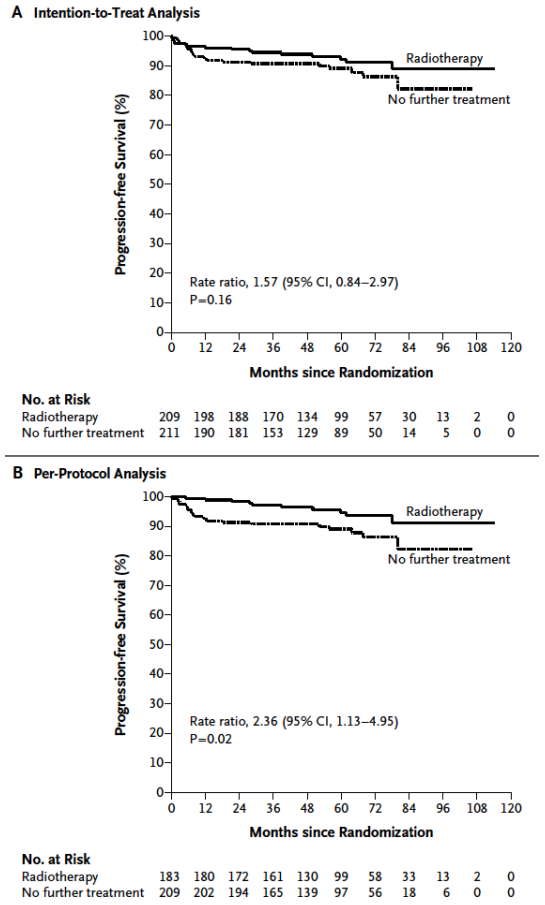
Subset	No. of Patients	No. of Observed Events	HR	Adjusted CI*	*P*†	1-Year PFS	
						%	Adjusted CI*
Favorable					.017		
Standard	188	1	1.00			100.00	
Experimental	193	9	9.36	2.45 to 35.73		94.93	91.89 to 96.85

It was stopped early after enrolling over 1130 patients, the reason is that the interim analysis failed to show non inferiority if radiation was omitted

Raemaeker 2014

Favorable early stage



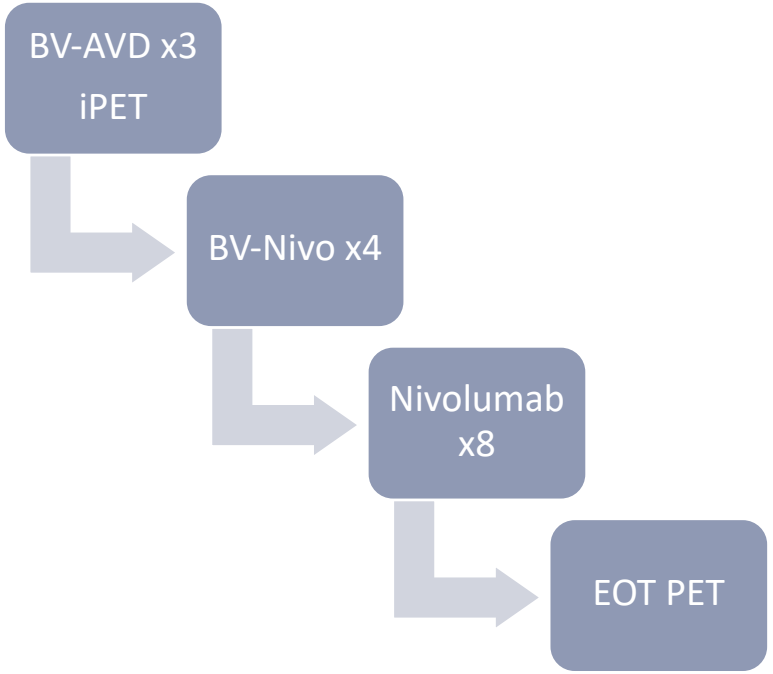


Radford 2015

BV-AVD > Nivo

Frontline PET-Directed Therapy with Brentuximab Vedotin Plus AVD Followed By Nivolumab Consolidation in Patients with Limited Stage Hodgkin Lymphoma

- A phase 2 single arm, multi-center study
- 83 patient with early stage cHL were enrolled
- 75 patients were evaluable
- Of those with negative iPET, CR 100% at EOT PET
- Of those with positive iPET, N=2, 1 patient achieved CR and other achieved CR after radiation



Park 2022

Unfavorable early stage

HD11 trial
16-75 yo
Stage I-II
Unfavorable diagnosis
At least 1 risk factor

- ABVD x4+ 30 IFRT

VS

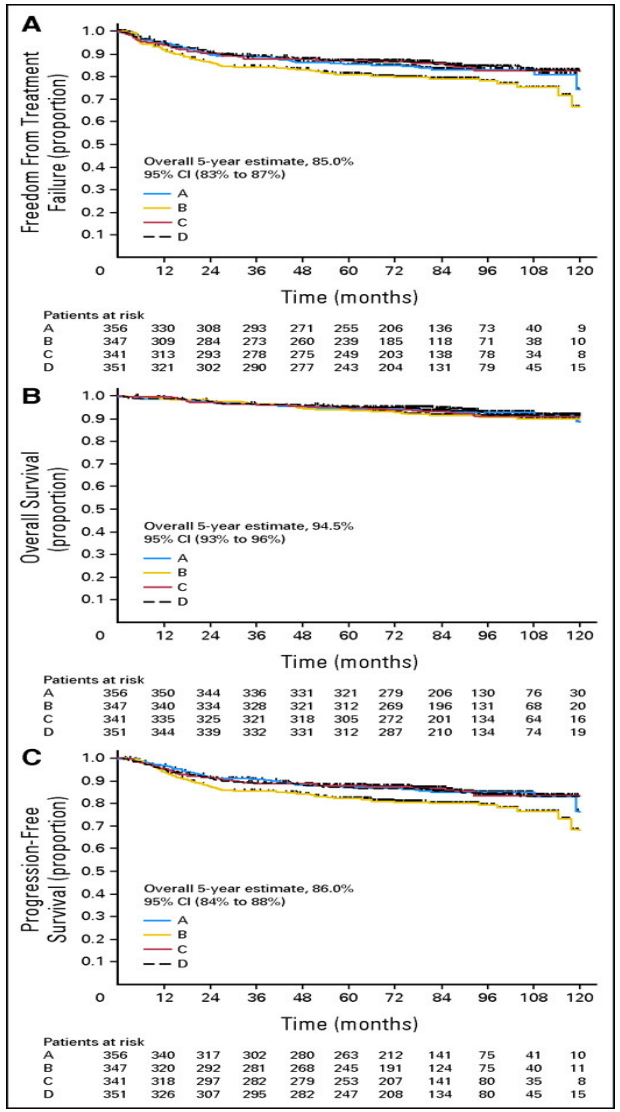
- ABVDx4+ 20 IFRT

VS

- BEACOPP x4+ 30 IFRT

VS

- BEACOPP x4+ 20 IFRT



Eich H T et al. JCO 2010;28:4199-4206

ANAD

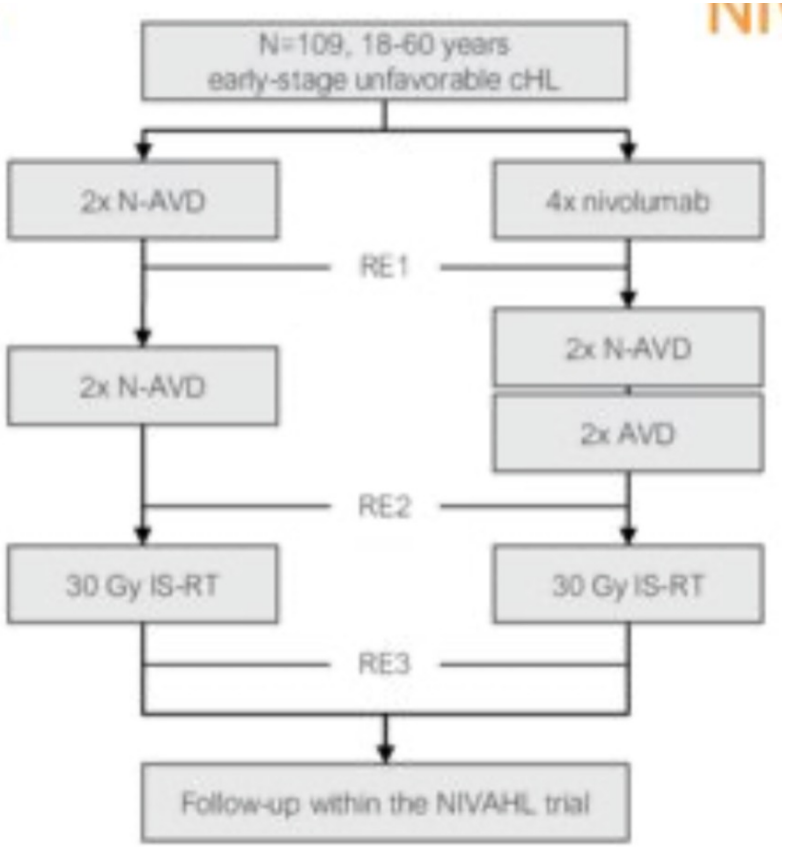
Part C Phase 2 Study of Brentuximab Vedotin, Nivolumab, Doxorubicin, and Dacarbazine (AN+AD) for Early-Stage Classic Hodgkin Lymphoma (Abstract #4230)

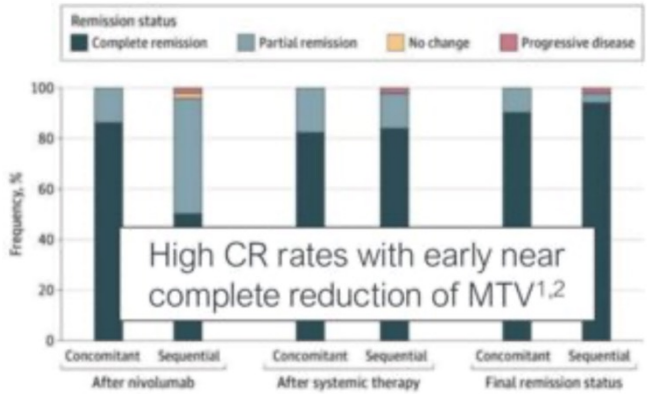
- Part C of SGN35-027 is evaluating the novel BV combination in 125 patients with early-stage (non-bulky Stage I or II) cHL.
- Of 125 patients in the study, 76 were included at the time of efficacy assessment.
- Results showed:
  - A 92% CR rate (95% CI: 83.6, 97.0) and a 95% ORR (95% CI: 87.1, 98.5) at end of treatment (N=76).
  - Follow up is ongoing and PFS results are not yet available.
  - The most frequently reported treatment-related TEAEs occurring in more than 30% of patients were nausea at 68% (85/125), peripheral sensory neuropathy at 42% (53/125), and fatigue at 38% (47/125).
  - Peripheral sensory neuropathy was primarily low grade (2% Grade ≥3), and no patients discontinued due to peripheral sensory neuropathy.

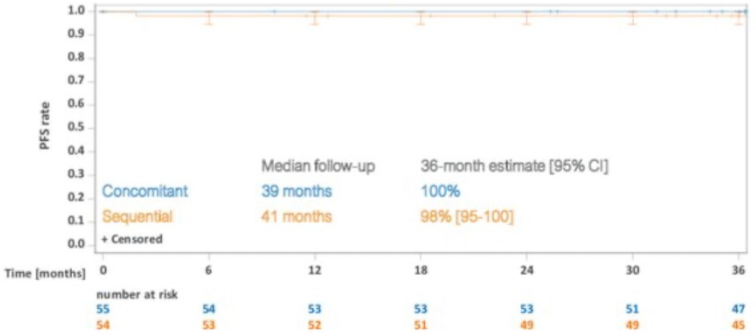
Lee 2022

Nivo-AVD

Nivolumab and AVD in Early-Stage Unfavorable Hodgkin Lymphoma: Follow-up Analysis of the Randomized GHSG Phase II Nivahl Trial





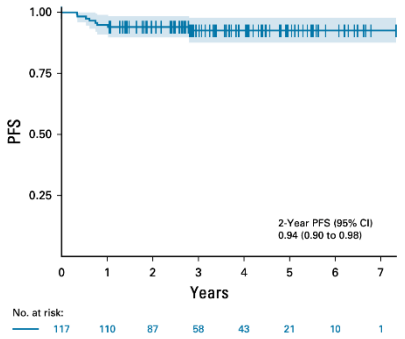


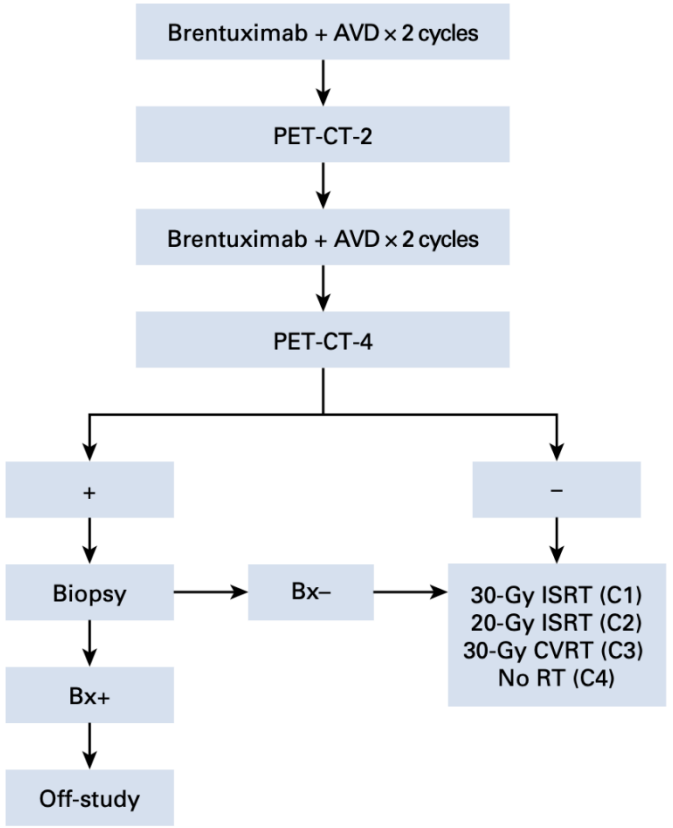
Brockelmann 2022

BV-AVD

Brentuximab Vedotin Combined with Chemotherapy in Newly Diagnosed, Early-Stage, Unfavorable-Risk Hodgkin Lymphoma: Extended Follow-up with Evaluation of Baseline Metabolic Tumor Volume and PET2

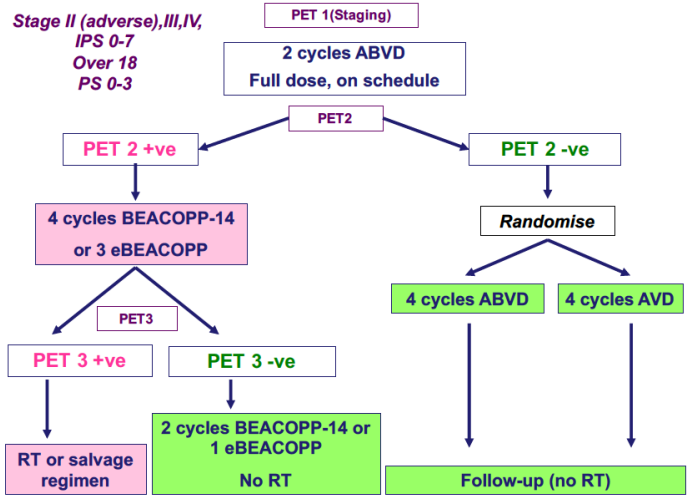
- Cohort 1 (C1) bulky mediastinal mass, ESR ≥ 50 mm/h or ≥ 30 mm/h if B symptoms, extranodal involvement, > 2 lymph node sites, or infradiphragmatic disease.
- Cohort 2 (C2) The same criteria applied to C2, except for bulk being defined by the Memorial Sloan Kettering (MSK) definition (maximal transverse or coronal diameter of the largest mass > 7 cm).
- In C3 and C4, all patients were required to have MSK criteria bulk.
- All cohorts received BV-AVD x 4.
- Treatment was safe: less than 5% dose delays, or modification
- Grade 3 NF happened in 8%, G3 PN happened in 3%
- CR was 93%, 100%, 93%, 97% respectively for the four cohorts

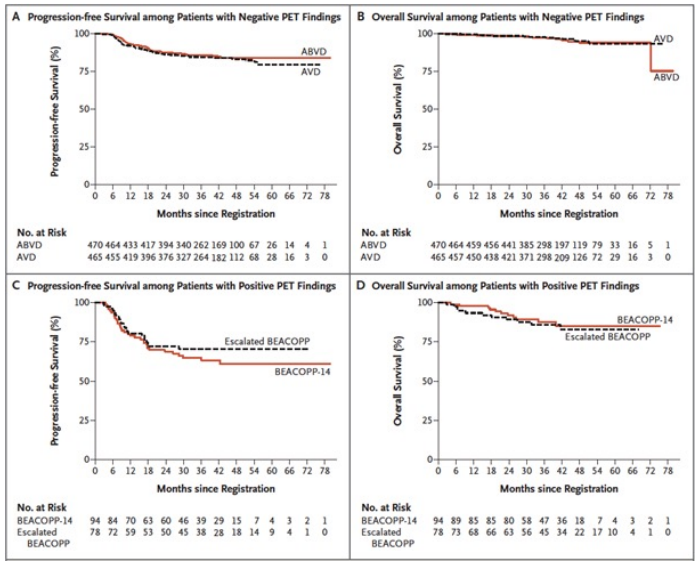




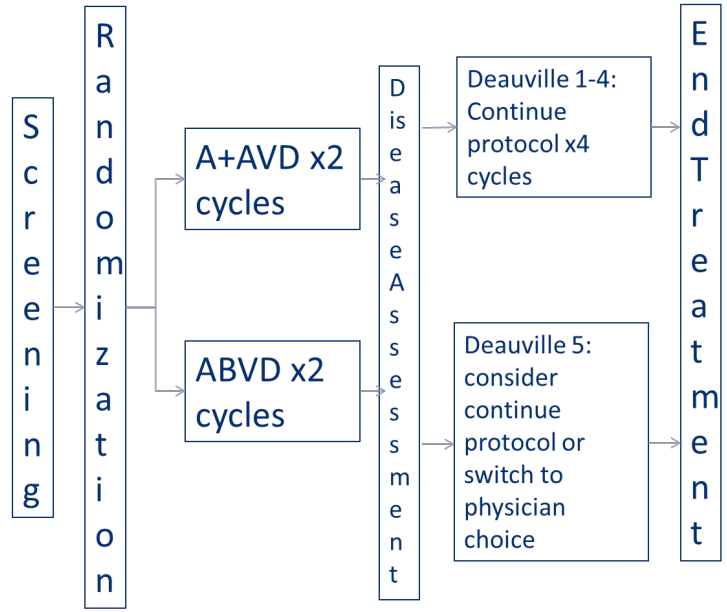
Stuver 2022

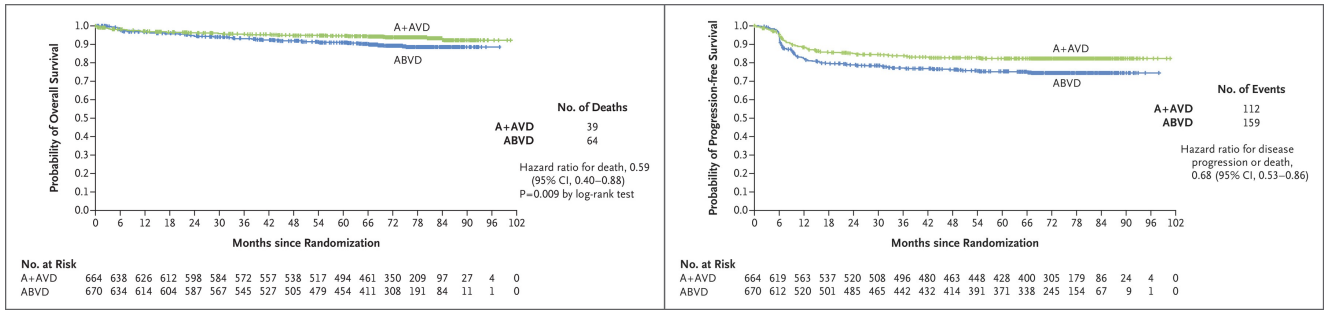
Advanced stage disease





Johnson 2016





Ansell 2022

ANAD

Brentuximab Vedotin, Nivolumab, Doxorubicin, and Dacarbazine (AN+AD) for Advanced Stage Classic Hodgkin Lymphoma: Updated Efficacy and Safety Results from the Single-Arm Phase 2 Study (SGN35-027 Part B)

- SGN35-027 (NCT03646123) is an open-label, multiple part, multicenter, phase 2 clinical trial. In Part B, enrolled pts had Ann Arbor stage I or II cHL with bulky mediastinal disease (defined as ≥10 cm) or stage III or IV cHL.
- Pts were treated with up to 6 cycles of AN+AD
- CR rate was 88% (95% CI: 76.3, 94.9) at EOT.
- ORR was 93% (95% CI: 83.0, 98.1) at EOT.
- With a median follow-up of 15.1 months,
  - 4 pts (7%) had progressive disease and 1 pt (2%) died.
  - The estimated PFS rate was 93% (95% CI: 81.6, 97.2) at 12 months.
- PN was reported in 42%, only 2 pts (4%) experienced ≥ Grade 3 peripheral sensory neuropathy, of which were considered treatment-related.
- No TEAEs led to death, and no cases of febrile neutropenia were reported.

Lee 2022

Relapse/Refractory cHL

Regimen	Response evaluation (cycles)		Overall response rate		Complete remission		Relapsed HD response rate		Refractory HD response rate		TRM rate (%)	Reference
	No.	*n*	No.	%	No.	%	No.	%	No.	%		
DHAP	2	102	89	88	21	21	78	92	11	65	0	Present study
ASHAP	2–3	57	39	70	19	34	n.e.	–	n.e.	–	0	6
ESHAP	4	22	16	73	9	41	16	73	0	0	5	5
Dexa-BEAM	1–5	55	33	60	17	31	19	70	14	52	4	19
Mini-BEAM	2	44	37	84	14	32	33	85	9	82	0	4
CEVD	4	32	18	52	14	44	5	100	8	53	0	20
MINE	2–5	100	73	73	34	34	54	93	41	49	3	21
MIME	n.e.	47	30	63	11	23	n.e.	n.e.	n.e.	n.e.	9	22
CEP	6	23	17	74	13	56	19	83	4	0	0	23
IV	2–8	26	20	77	10	38	15	79	5	71	4	24
ICE	2	65	57	88	17	26	n.e.	n.e.	n.e.	n.e.	0	7

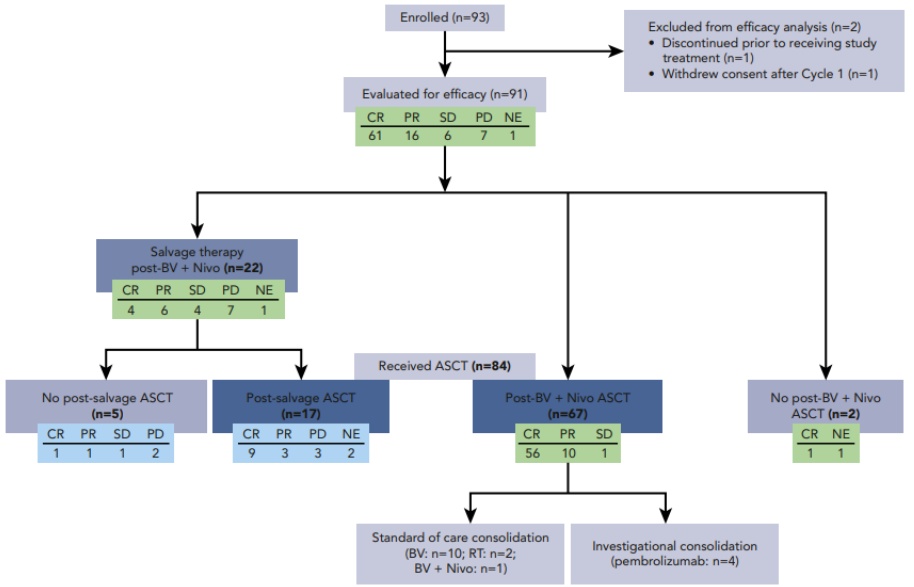
HD, Hodgkin's disease; TRM, treatment-related mortality; ASHAP, doxorubicin/solumedrol/high-dose cytarabine/cisplatinum; BEAM, BCNU (bis-chloro-ethyl nitrosourea)/etoposide/cytarabine/melphalan; CEP, CCNU (cyclohexyl chloroethylnitrosourea)/etoposide/prednimustine; CEVD, CCNU/etoposide/vindesine/dexamethasone; dexa-BEAM, dexamethasone/BCNU/etoposide/cytarabine/melphalan; DHAP, dexamethasone/high-dose cytarabine/cisplatinum; ESHAP, etoposide/high-dose cytarabine/cisplatinum; ICE, ifosfamide/carboplatin/etoposide; IV, ifosfamide/vinorelbine; MIME, methyl-GAG/ifosfamide/methotrexate/etoposide; MINE, mitoguazone/ifosfamide/vinorelbine, etoposide; mini-BEAM, BCNU/etoposide/cytarabine/melphalan; n.e., not evaluated.

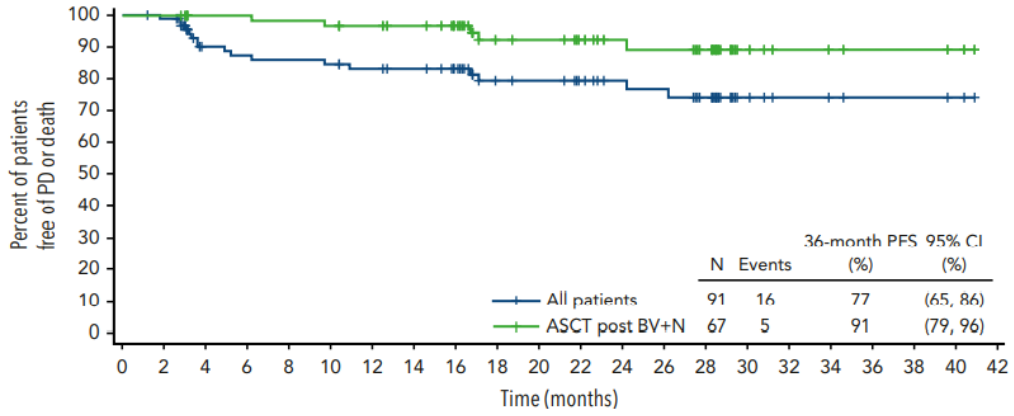
Josting 2002

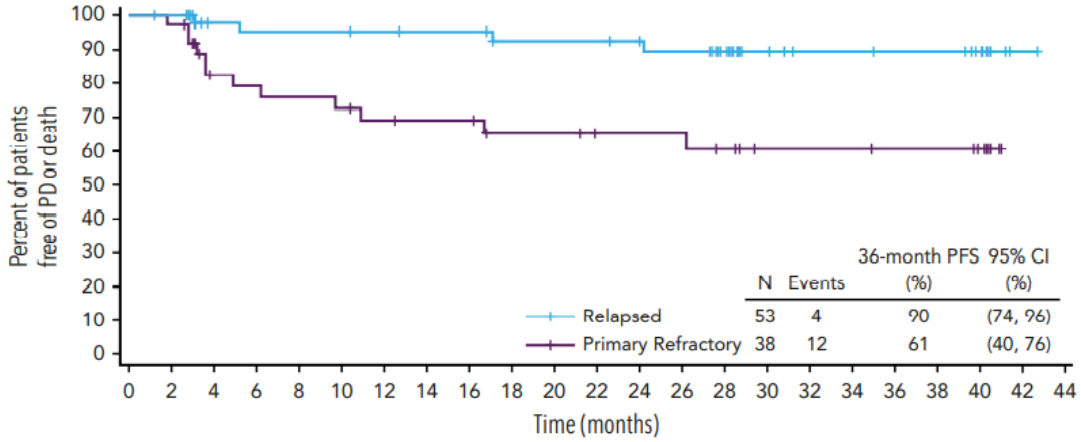
BV-Nivo

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

- This multicenter, single-arm, phase 1-2 trial (NCT02572167) enrolled adults with biopsy-proven primary refractory (ie, not achieving a CR or progression <3 months after CR) or relapsed Hodgkin lymphoma (HL; progression ≥3 months after CR).
- 93 patients enrolled
- ORR (85%), CR (67%)
- PFS at 3 years (77%)
- PFS at 3 years for PR patients proceeding to Auto SCT (N=10) is (67%)



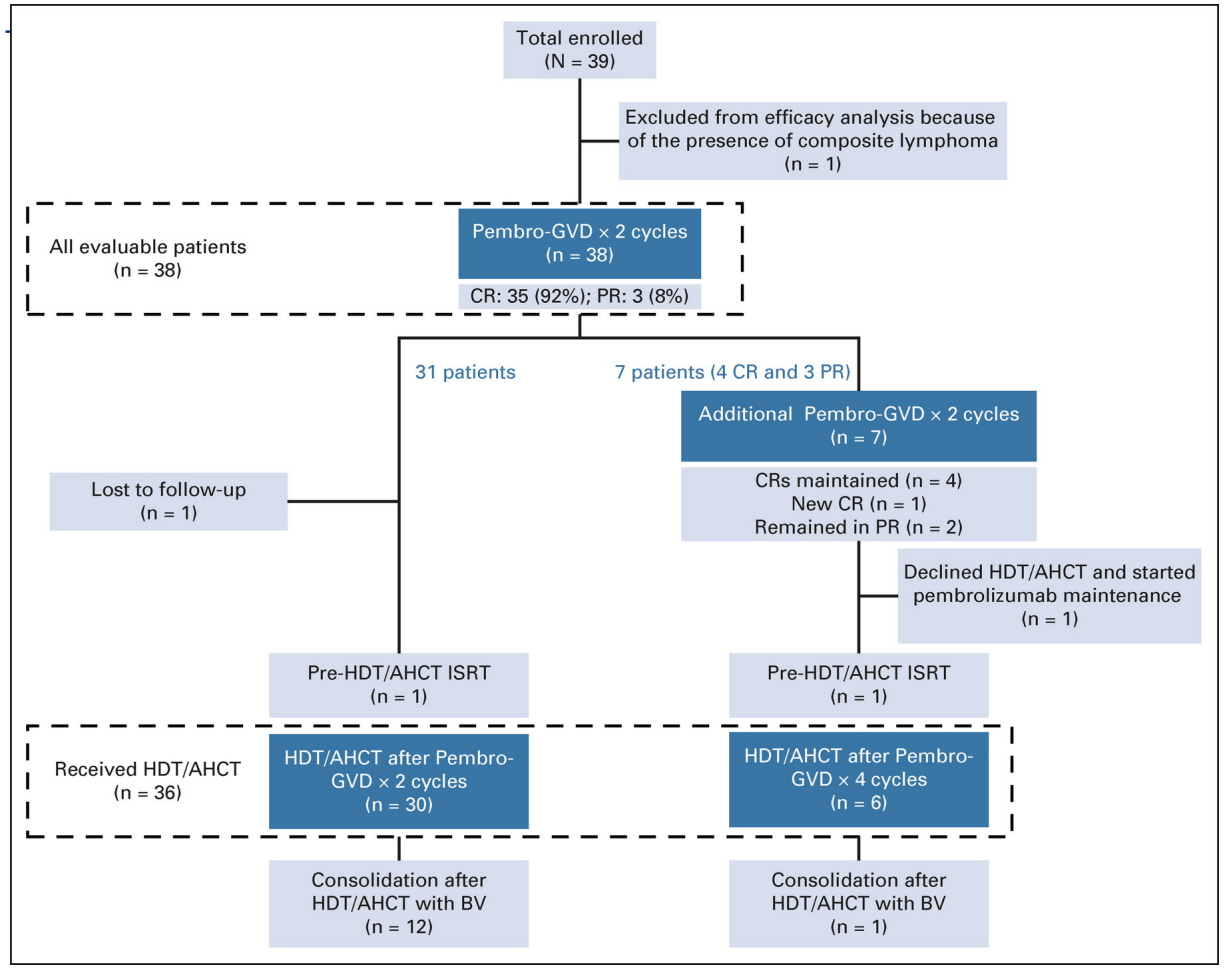




Advani 2021

GVD-Pembro

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



Moskowitz 2021

TABLE 3. Efficacy

Characteristic	Pembro-GVD × 2 (n = 38)[a]	Pembro-GVD × 4 (n = 7)	Pembro-GVD Overall (n = 38)
ORR, % (95% CI)	100 (91 to 100)	100 (59 to 100)	100 (91 to 100)
CR, % (95% CI)	92 (79 to 98)	71 (29 to 96)	95 (82 to 99)
PR, % (95% CI)	8 (2 to 21)	29 (4 to 71)	5 (1 to 18)
Best response, No. (%)			
CR	35 (92)	5 (71)	36 (95)
PR	3 (7.9)	2 (29)	2 (5.3)

Abbreviations: CR, complete response; HDT/AHCT, high-dose therapy and autologous hematopoietic cell transplantation; HL, Hodgkin lymphoma; ORR, overall response rate; pembro-GVD, pembrolizumab plus gemcitabine, vinorelbine, and liposomal doxorubicin; PET, positron emission tomography; PR, partial response; RICE, rituximab, ifosfamide, carboplatin, and etoposide.

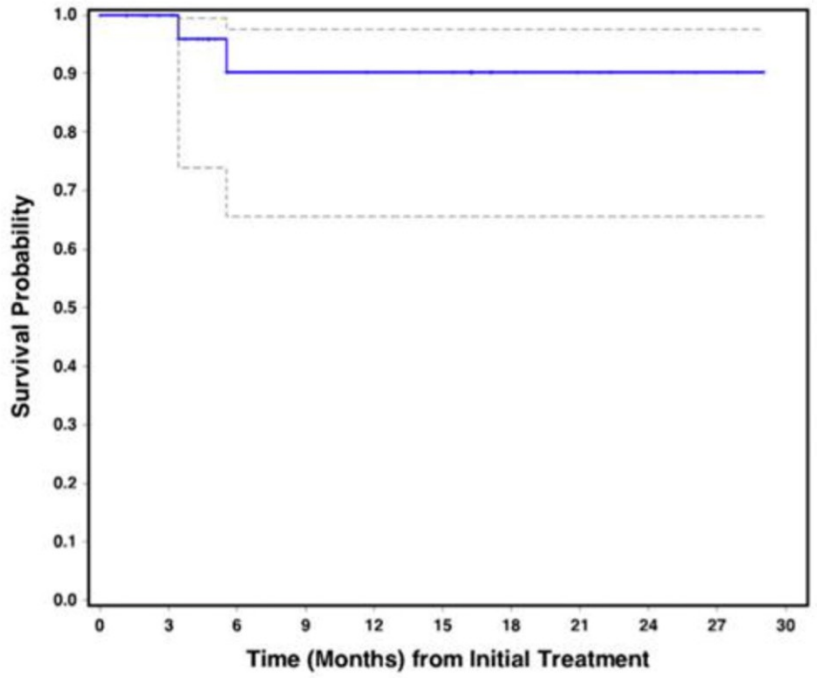
[a]One patient was excluded from the efficacy analysis because of the presence of composite lymphoma. This patient achieved CR in areas of biopsy-confirmed HL, but biopsy of residual PET-avid disease after pembro-GVD × 4 showed transformed follicular lymphoma. Upon rereview of the patient's baseline biopsies, it was determined that follicular lymphoma was present at the time that HL was initially diagnosed. The patient was subsequently treated with RICE × 3 cycles followed by HDT/AHCT. The patient is currently 9 months out from transplant and remains in remission.

Nivo-ICE

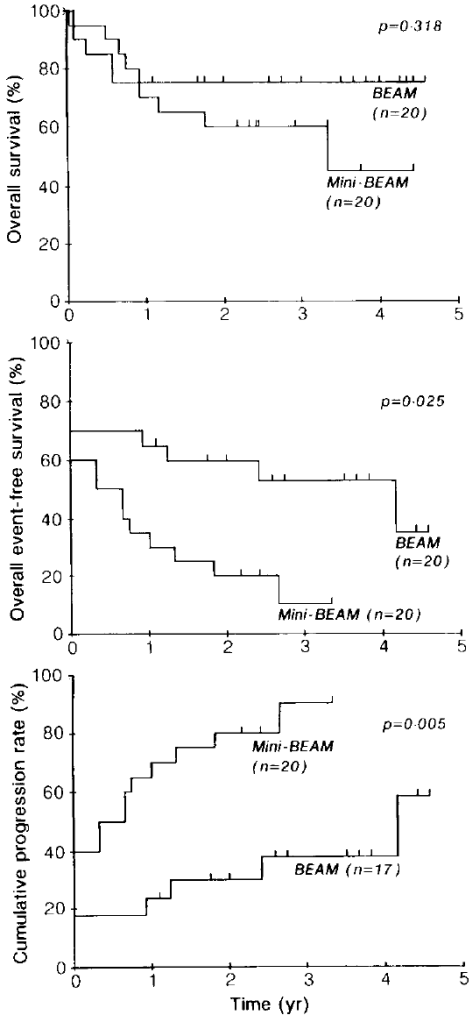
Nivolumab Plus ICE As First Salvage Therapy in High-Risk Relapsed/Refractory Hodgkin Lymphoma

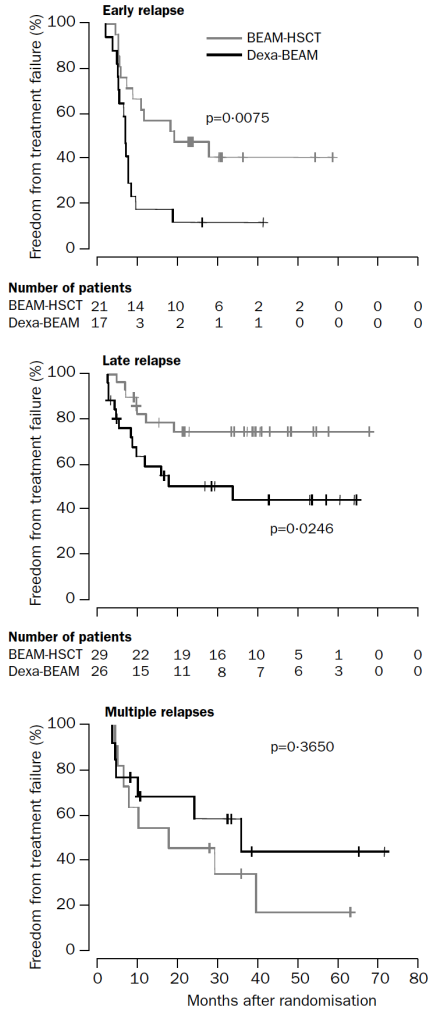
- Cohort B of this trial included using N-ICE to all patients with RR cHL in first relapse.
- Patients received Nivolumab 240mg, 2 weeks later received NICE x2-3 cycles
- 35 patients were enrolled, 32 patients we evaluable for response
- ORR 100%, CR 88%
- 29/32 underwent Auto SCT
- 24% received post Auto consolidation with (4 BV, 2 Nivo, 1 Ipi-Len)
- 1 year PFS for the entire cohort is 90%, OS 100%
- 1 year PFS for auto SCT patients is 100%

Figure 1: Progression-free Survival

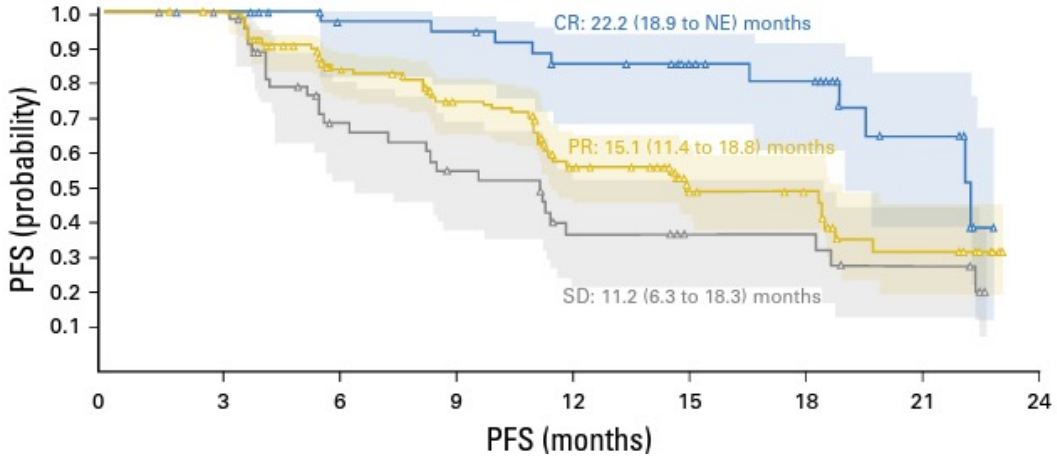


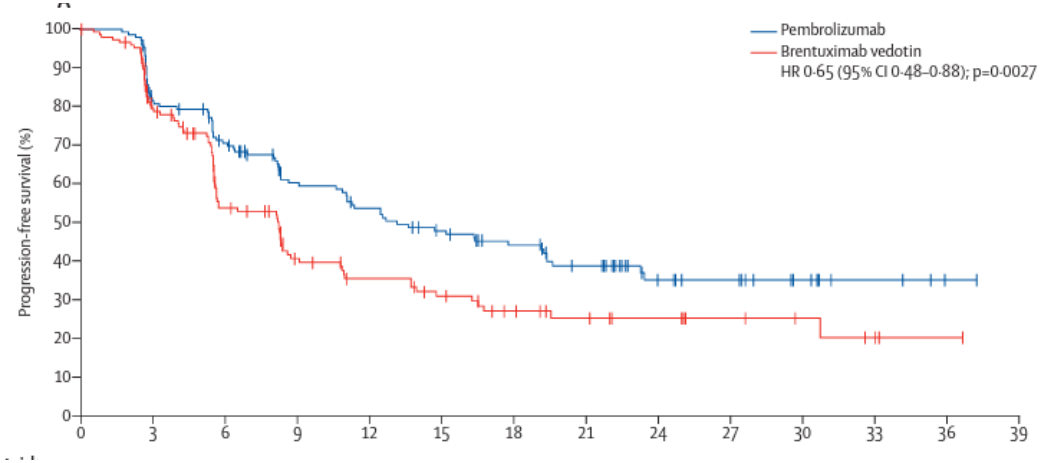
Relapse/Refractory cHL





Linch 1993
Schmitz 2002



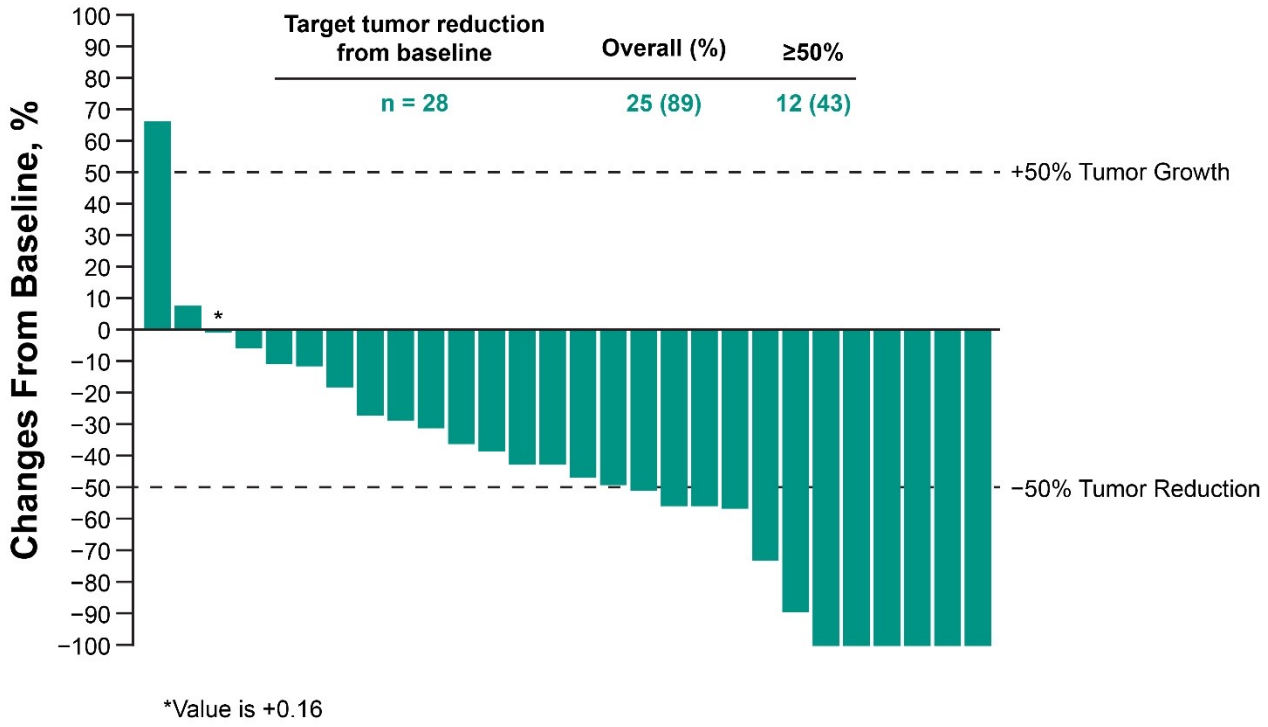


Kuruvilla 2021
Bekoz 2020

Favezelimab

Updated Results from an Open-Label Phase 1/2 Study of Favezelimab (anti–LAG-3) Plus Pembrolizumab in Relapsed or Refractory Classical Hodgkin Lymphoma after Anti–PD-1 Treatment

- Cohort 1 included PD1 naïve patients
- Cohort 2 included PD1 resistant patients
- The most common TRAE (≥10%):
  - hypothyroidism (18%)
  - nausea (18%)
  - diarrhea (15%)
  - fatigue (15%,),
  - arthralgia (15%)
  - headache (12%)
- In Cohort 1, ORR 80%, CR 33%, PR 47%
- In Cohort 2, After a median follow-up of 19.0 months, 10 pts had objective response (ORR, 29% [95% CI, 15-48]; complete response [CR], 3 [9%]; partial response [PR], 7 [21%]).

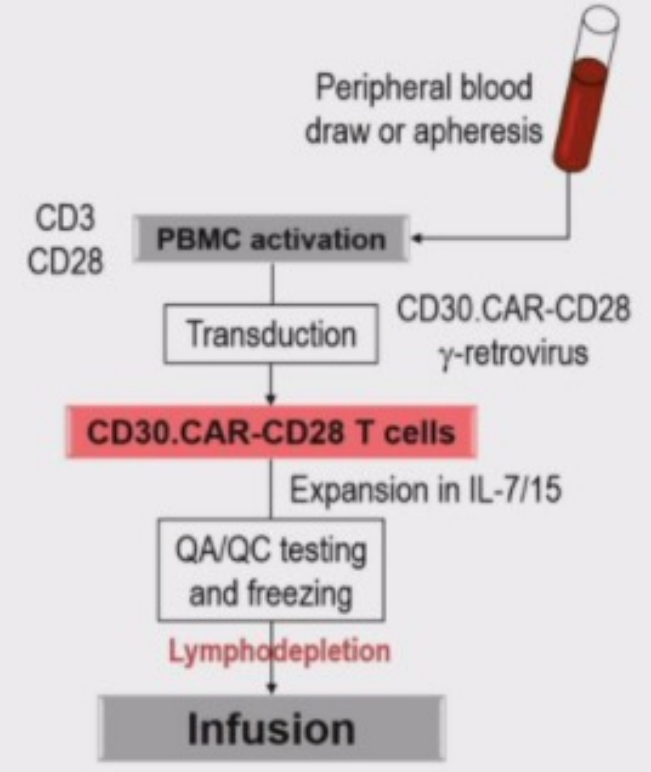


Timmerman 2022

CD-30 CAR T cells

Eligibility:

- r/r CD30 lymphomas after 2 lines.
- Having CD 30 was mandatory
- UNC (N=25) and BCM (N=17).
- Autologous CD30.CAR-Ts manufactured at each Institution using the same clinical grade gammaretroviral vector and following the same SOP
- Bridging chemotherapy was allowed
- Patients who achieved a complete remission (CR) with bridging therapy were allowed to receive lymphodepletion and CAR-T infusion at UNC, but not at BCM.



Ramos 2020

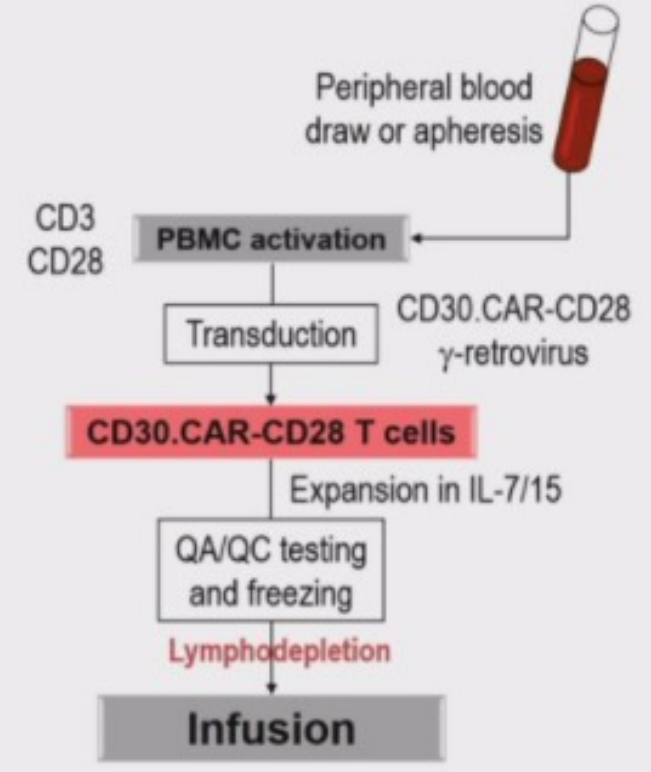
CD-30 CAR T cells protocol:

Lymphodepletion:

- UNC: cyclophosphamide 500 mg/m2/day and Flu 30 mg/m2/day for 3days
- BCM: Benda 90mg/m2/day for 2 days was used for the first cohort, Benda 70 mg/m2/day and Flu 30 mg/m2/day for 3 days were used for the second cohort.

CART cells dose:

- UNC: 1x108 CAR-Ts/m2 or 2x108 CAR-Ts/m2.
- BCM: 2x107 CAR-Ts/m2, 1x108 CAR-Ts/m2 or 2x108 CAR-Ts/m2
- Expansion cohort: 2x108 CAR-Ts/m2.
- A second infusion of CD30.CAR-Ts was allowed in patients who had stable disease (SD) or partial response (PR) after the first treatment.



Ramos 2020

CD-30.CAR T cells patient characteristics

The most common therapies used for bridging were:

- Bendamustine (32%)
- Nivolumab (25%)
- BV (7%)
- Gemcitabine-based regimens (11%).

Characteristic	All Patients (N = 42)[a]	Benda (n = 8)[a]	Benda-Flu (n = 17)	Cy-Flu (n = 17)[a]
HL subtype				
NS	32 (76)	6 (75)	10 (59)	16 (94)
MC	4 (10)	2 (25)	2 (12)	0
NOS	6 (14)	0	5 (29)	1 (6)
Stage at diagnosis				
I-II	14 (33)	1 (13)	7 (41)	6 (35)
III-IV	28 (67)	7 (88)	10 (59)	11 (65)
Median age (range), years	35 (17-69)	49 (23-67)	32 (23-45)	36 (17-69)
Male sex	28 (67)	5 (63)	13 (76)	10 (59)
ECOG PS $\geq$ 1	34 (81)	5 (63)	12 (71)	17 (100)
Median No. of prior therapies (range)	7 (2-23)	7.5 (5-17)	8 (3-23)	5 (2-10)
Bridging therapy	28 (67)	8 (100)	10 (59)	10 (59)
Prior BV	38 (90)	8 (100)	16 (94)	14 (82)
Progression on BV[b]	32 (84)	6 (75)	12 (75)	14 (100)
Prior CPI	34 (81)	7 (88)	13 (76)	14 (82)
Prior aSCT	32 (76)	7 (88)	14 (82)	11 (65)
Prior alloSCT	10 (24)	2 (25)	8 (47)	0 (0)
CAR-T cells/m^2				
2×10^7	3 (7)	0	0	3 (18)
1×10^8	9 (21)	3 (38)	0	6 (35)
2×10^8	30 (71)	5 (63)	17 (100)	8 (47)

Ramos 2020

CD-30.CAR T cells toxicity

- **NO DLTs**.
- **CRS**:
  - 10 patients (24%)
  - More frequent with the cyclophosphamide-based conditioning regimen than with the Benda-based regimen (41% v 12%).
  - All were grade 1 and resolved spontaneously
  - The median time of onset: 10 (range, 7-24 days)
  - Median duration was 4 days (range, 1-6 days).
- **Neurotoxicity**: It was not observed.
- **Rash**: Twenty patients (48%) developed a nonpruritic, nontender, maculopapular skin rash, which was more commonly found in patients receiving cyclophosphamide (82%) versus Benda (24%). None of the rashes required specific treatment, and all resolved spontaneously within 7-10 days.

Adverse Event	All Patients (N= 42)[a]	Benda (n = 8)[a]	Benda-Flu (n = 17)	Cy-Flu (n = 17)[a]
Lymphopenia	42 (100)	8 (100)	17 (100)	17 (100)
Leukopenia	24 (57)	3 (38)	8 (47)	13 (76)
Anemia	5 (12)	0	2 (12)	3 (18)
Hypoalbuminemia	3 (7)	0	0	3 (18)
Hyponatremia	2 (5)	0	0	2 (12)
Hyperkalemia	0	0	0	1 (6)
Dyspnea	1 (2)	0	0	1 (6)
Rash (any grade)	20 (48)	2 (25)	4 (24)	14 (82)
Headache	1 (2)	0	0	1 (6)
Pharyngitis	1 (2)	0	1 (6)	0
Lung infection	1 (2)	0	1 (6)	0
Neutropenia	20 (48)	2 (25)	7 (41)	11 (65)
Grade 3/4 neutropenia not resolved by day 28	4 (10)	0	2 (12)	2 (12)
Prolonged grade 3/4 neutropenia (not resolved by month 3)[b]	0	0	0	0
Thrombocytopenia	11 (26)	1 (13)	7 (41)	3 (18)
Grade 3/4 thrombocytopenia not resolved by day 28	10 (24)	0	7 (41)	3 (18)
Prolonged grade 3/4 thrombocytopenia (not resolved by month 3)[b]	4 (10)	0	3 (18)	1 (6)
Cytokine release syndrome (all grade 1)	10 (24)	1 (13)	2 (12)	7 (41)

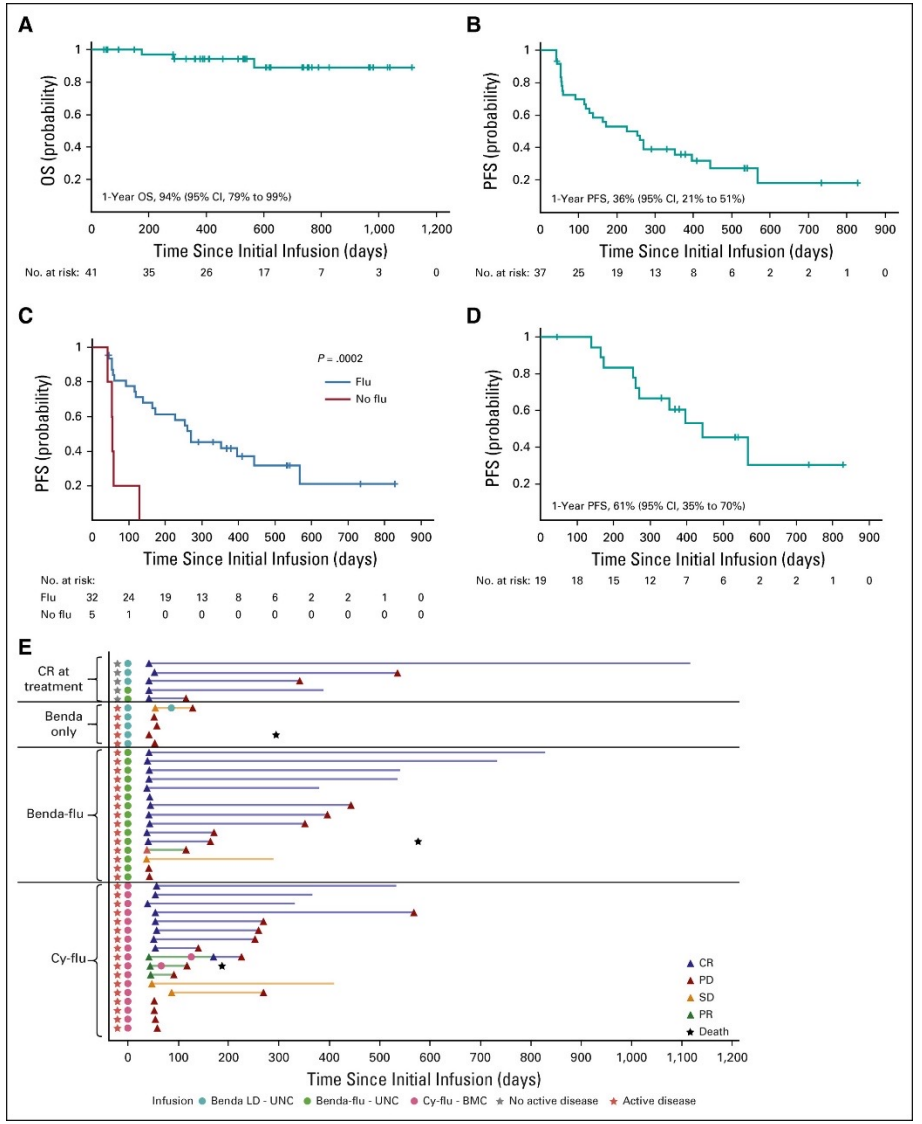
Ramos 2020

CD-30.CAR T cells Efficacy

- CD30.CAR-T persistence, measured as area under the curve, was higher in patients receiving 2x108 CAR-Ts/m2 than in patients receiving 2x107 CAR-Ts/m2 or 1x108 CAR-Ts/m2 (P , .001) regardless of type of lymphodepletion
- The 1-year PFS for patients with measurable disease was 41% (95% CI, 24% to 58%) for all patients who received fludarabine-based lymphodepletion.
- The 1-year OS for all 41 patients was 94% (95% CI, 79% to 99%)

Response	All Patients (N = 37)	Benda (n = 5)	Benda-Flu (n = 15)	Cy-Flu (n = 17)
ORR				
CR + PR	23 (62)	0 (0)	12 (80)	11 (65)
Response rate				
CR	19 (51)	0 (0)	11 (73)	8 (47)
PR	4 (11)	0 (0)	1 (7)	3 (18)
SD	4 (11)	1 (20)	1 (7)	2 (11)
PD	10 (27)	4 (80)	2 (13)	4 (24)

Ramos 2020



CHARIOT trial

- CHARIOT trial is designed based on preliminary results of the previous CD30.CART cells.
- Pilot segment including at minimum 12 patients (for which accrual is complete)
- Pivotal segment planned to enroll approximately 82 patients to obtain at least 67 CD30.CAR-T-treated patients.
- LD chemotherapy using bendamustine and fludarabine.
- CD30.CAR-T-related toxicities include:
  - Grade 1 cytokine release syndrome in 1 patient
  - Grade 1 maculopapular rash in 1 patient
  - Grade 2 ventricular tachycardia in 1 patient.
- The ORR at Day 42 after CD30.CAR-T infusion was 100% (5/5).
- CR and partial response (PR) rates were observed in 4 (80%) and 1 (20%) patients, respectively.

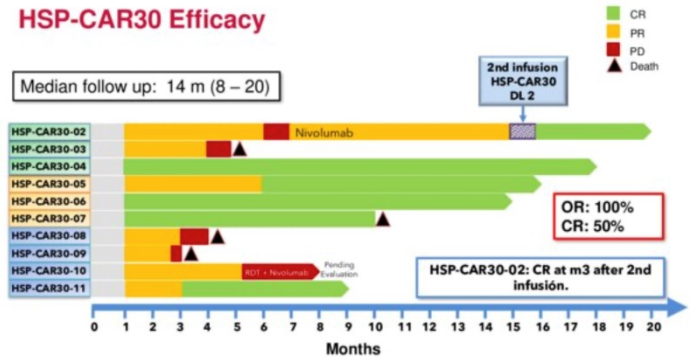
Characteristics	All patients (N=15)
Age, median (range)	35 (21-57)
Sex, % (No)	
• Male	10/15 (66.7)
• Female	5/15 (33.3)
cHL subtype, No (%)	
• Nodular sclerosis	10/14 (71.4)
• Mixed cellularity	4/14 (29.6)
Stage at enrolment, No (%)	
• I-II	2/13 (15.4)
• III-IV	11/13 (84.6)
ECOG Performance Status, No (%)	
• 0	12/15 (80.0)
• 1	3/15 (20.0)
Number of prior systemic therapies, Median (range)	6 (4-19)
Types of prior therapies, No (%)	
• Prior BV	11/13 (84.6)
• Prior Checkpoint Inhibitors	12/13 (92.3)
• Prior Autologous/ Allogeneic HSCT	12/14 (85.7)
Bridging therapies, No (%)	4/12 (33.3)

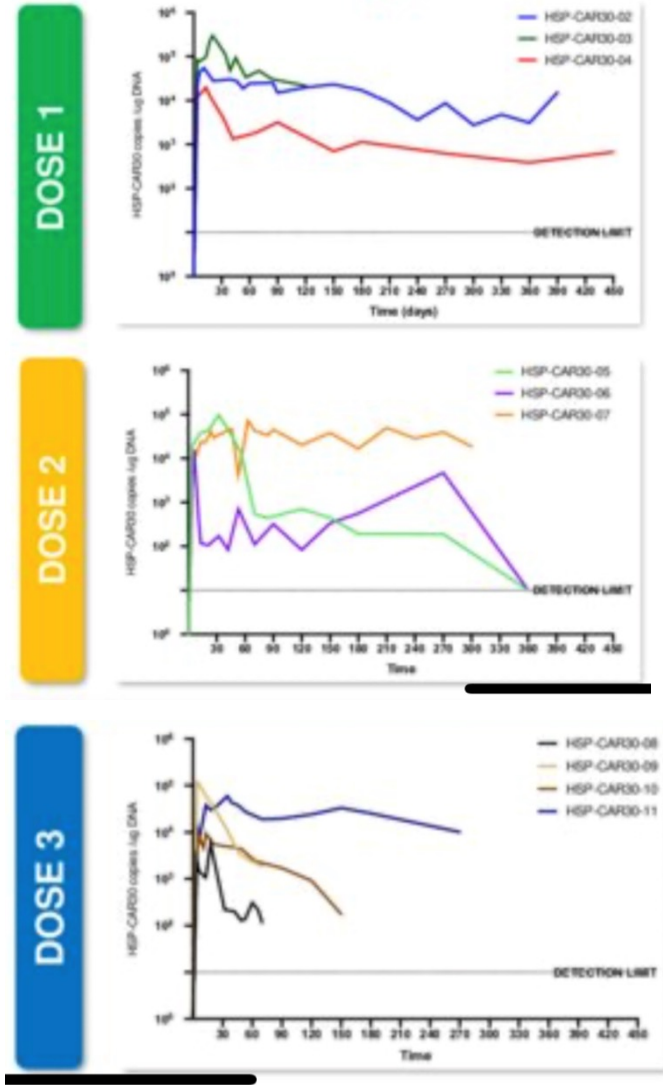
Ahmad 2021

HSP CAR30

Phase 1 Clinical Trial of Memory-Enriched Academic HSP-CAR30 for the Treatment of Relapsed/Refractory Hodgkin Lymphoma and CD30⁺ T-Cell Lymphoma: Clinical and Biological Studies

- HSP-CAR30 are enriched in memory T-cells to ensure persistence, and enhancement of antitumor efficacy.
- 3 dose levels were used, 3x106, 5x106, and 10x106 CAR30/kg
- HSP-CAR30 were manufactured in 10 days.
- Median prior lines 5 (3-7), refractory to prior line 6/10, prior ASCT 6/10
- CRS: 6/10 (all g1), no ICANs
- Mean time to peak expansion was 21 (4-63 days)
- HSP-CAR30 were detects in 6/6 patients at 9 months and 2/4 at 12 months



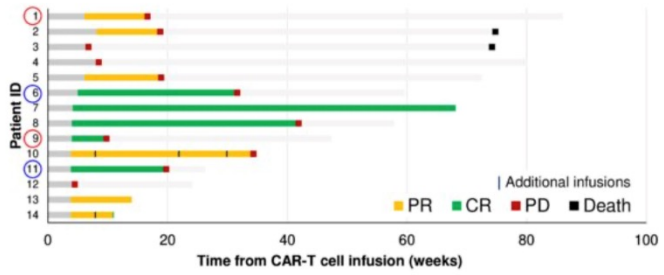


Gonzalez 2022

CD30.CAR EBVSTs

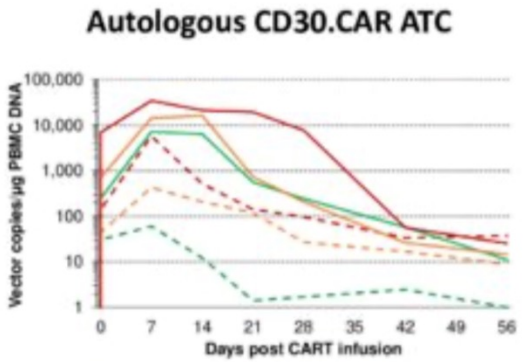
CD30.CAR-Modified Epstein-Barr Virus-Specific T Cells (CD30.CAR EBVSTs) Provide a Safe and Effective Off-the-Shelf Therapy for Patients with CD30-Positive Lymphoma

- To avoid GVHD, Virus Specific T cells are manufactured
- To avoid host rejection, anti-CD30 receptors are inserted to eliminate allo reactive CD30+ve T cells.
- 3 dose levels were used: 4 x107, 1x108, 4x108 CARs/kg
- 14 patients with cHL were treated.
- CR: 6/14, PR: 5/14
- Reasons for clinical response without persistence:
  - Rejected following response
  - Localizes to tumor

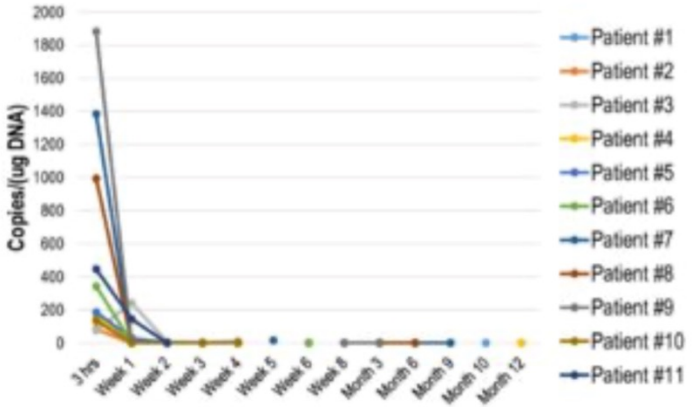


- 79% ORR (11/14), complete responses in 43% (6/14)

Quach 2022



Ramos CA, et al. JCI (2017) & JCO (2020)



- Detected CD30.CAR transgene with real time qPCR
- Autologous CD30.CAR ATCs show prolonged persistence
- Allogeneic CD30.CAR EBVSTs show rapid loss in blood

Conclusions

- Outcome of Hodgkin lymphoma continue to improve over the years.
- Understanding staging is essential to decide on therapy given the vast differences in management in a highly curable disease.
- PET scan is essential at initial diagnosis and follow up
- Incorporation of novel targeted immunotherapies is coming to early stage Hodgkin lymphoma
- The use of BV improves survival in frontline setting.
- Relapsed disease treatment with immunotherapy is more tolerable and leads to better outcome.
- Cellular therapies are catching up in Hodgkin lymphoma.

Thank you

Questions?

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