GIORNATE EMATOLOGICHE VICENTINE

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Palazzo Bonin Longare - Vicenza

L’uso dei nuovi agenti anticorpali nel trattamento del linfoma di Hodgkin

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Disclosures of Vittorio Ruggero Zilioli

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Beigene							X
Gentili						X	
Italfarmaco						X	
Janssen					X		X
Kite/Gilead	X					X	
Lilly					X		
MSD						X	
Roche			X			X	X
Servier						X	
Sobi					X		
Takeda					X	X	X

Brentuximab Vedotin

Anti-PD1

New options

Brentuximab Vedotin **Anti-PD1** **New options**

diagnosis	first line	second line	consolidation	salvage therapy

Brentuximab Vedotin	**Anti-PD1**	**New options**
R/R cHL	R/R cHL	Camidanlumab teserine
Post autoSCT	Post autoSCT	Anti-PD1 + epigenetic modifiers
Second line	Second line	Anti-PD1 + AntiLAG3
First line	First line	AntiPD1 + bispecific Ab
		AntiCD30+ CART

diagnosis	first line	second line	consolidation	salvage therapy

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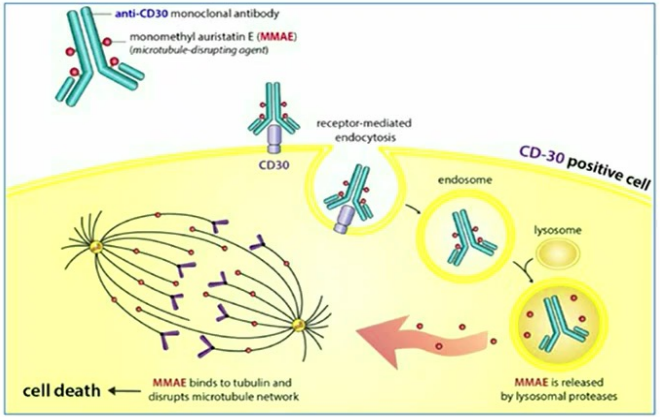
Brentuximab Vedotin



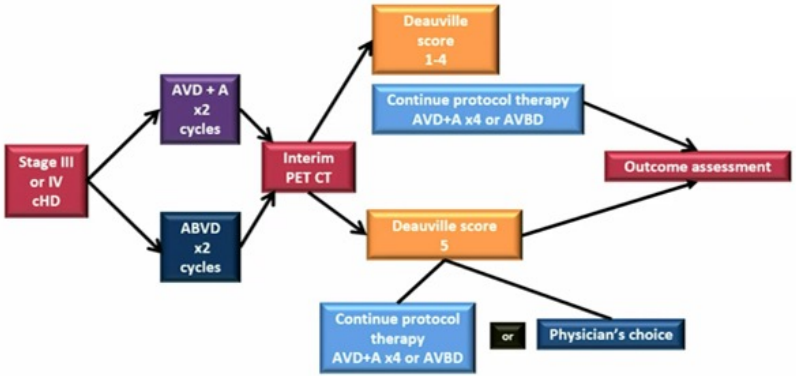
diagnosis	first line	second line	consolidation	salvage therapy

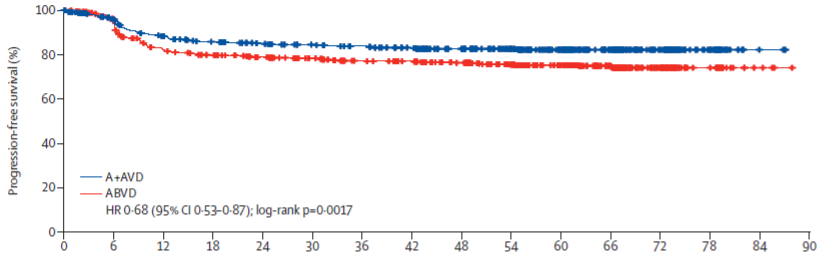
Brentuximab Vedotin

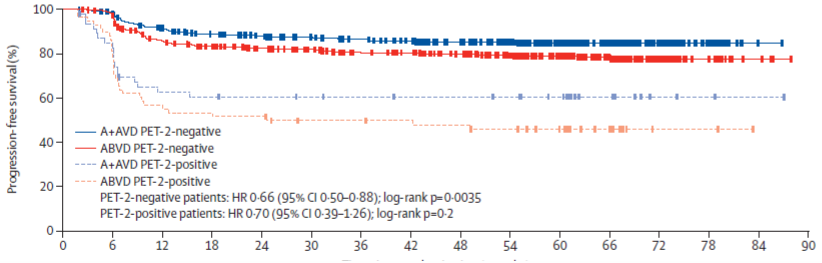
diagnosis	first line	second line	consolidation	salvage therapy

Brentuximab vedotin with chemotherapy for stage III or IV classical Hodgkin lymphoma (ECHELON-1): 5-year update of an international, open-label, randomised, phase 3 trial

David J Straus, Monika Długosz-Danecka, Joseph M Connors, Sergey Alekseev, Árpád Illés, Marco Picardi, Ewa Lech-Maranda, Tatyana Feldman, Piotr Smolewski, Kerry J Savage, Nancy L Bartlett, Jan Walewski, Radhakrishnan Ramchandren, Pier Luigi Zinzani, Martin Hutchings, Javier Munoz, Hun Ju Lee, Won Seog Kim, Ranjana Advani, Stephen M Ansell, Anas Younes, Andrea Gallamini, Rachael Liu, Meredith Little, Keenan Fenton, Michelle Fanale, John Radford





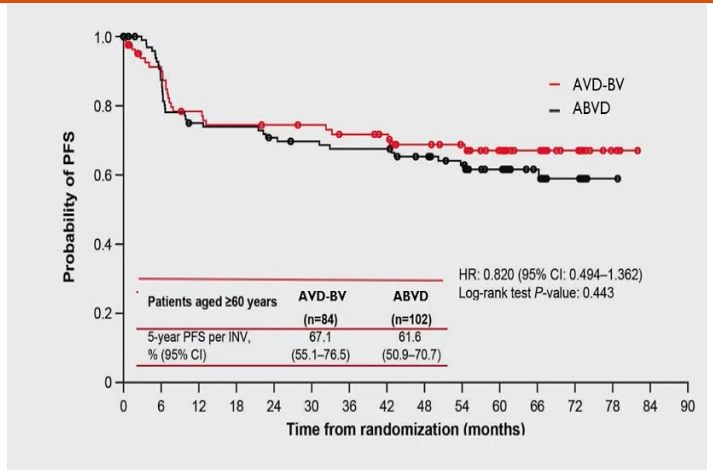


AVD plus concurrent BV

186 (14%) pts ≥ 60y, median 67; ECOG 2 11% (vs 3%)
80% BV dose mod, 71% bleo dose mod (28% discon)
TRM 3.6% (vs 5.1% ABVD) / 37% FN (vs 17%)
18% Grade 3-4 PN (vs 3% in <60y)
2% lung toxicity (vs 13%)

Bleomycin-free regimen as good as ABVD

Evens AM et al, Haematologica 2022

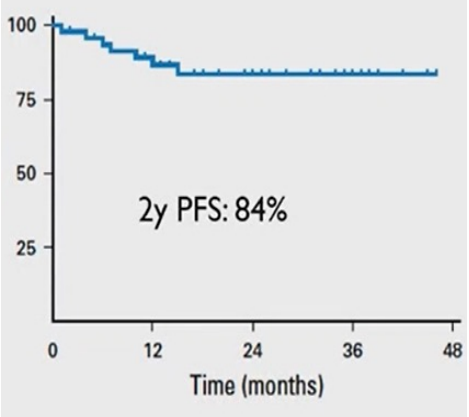


AVD plus sequential BV

48 pts, median age 69 (60-88)
77% completed 6 cycles AVD
33% Grade 2 PN (4% G3)
8% febrile neutropenia

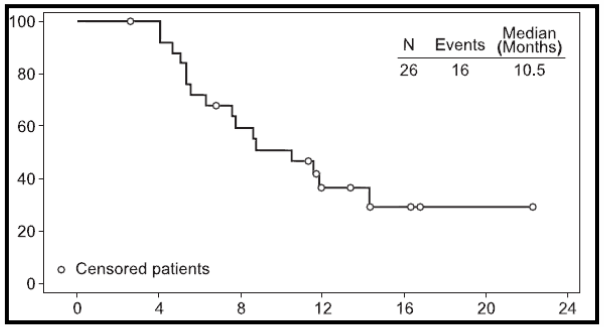
Tolerable, apparently high efficacy

Evens AM et al, J Clin Oncol 2018

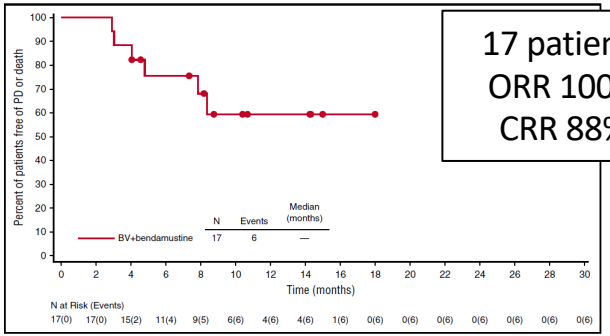


BV mono & BV-plus therapies

BV monotherapy

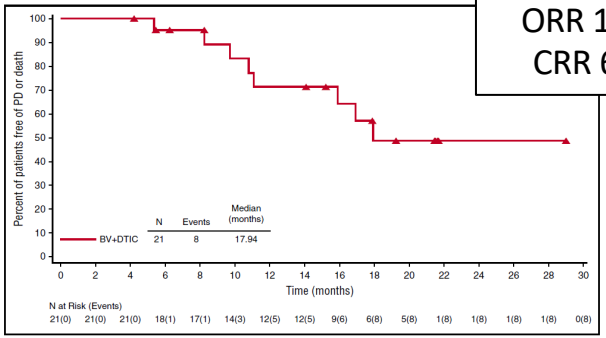


BV + BENDA

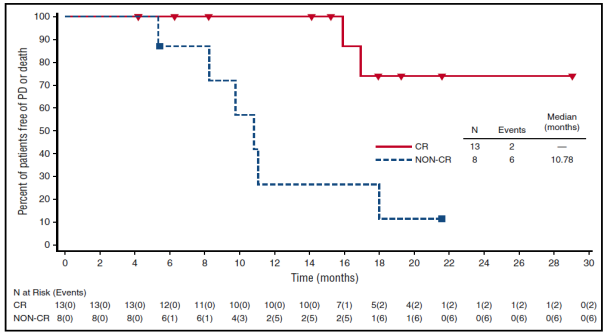


17 patients
ORR 100%
CRR 88%

BV + DACARBAZINE



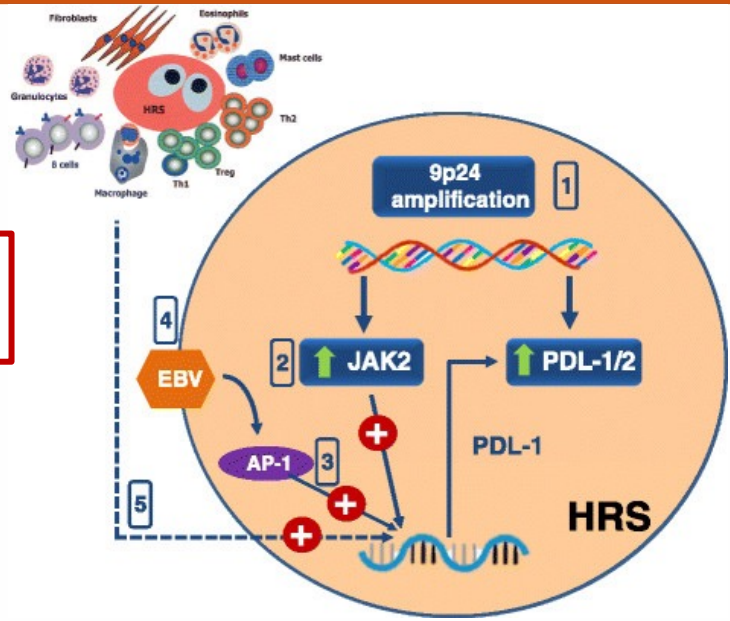
19 patients
ORR 100%
CRR 68%



BV monotherapy not effective
BV plus benda toxic
BV plus dacarbazine good option!

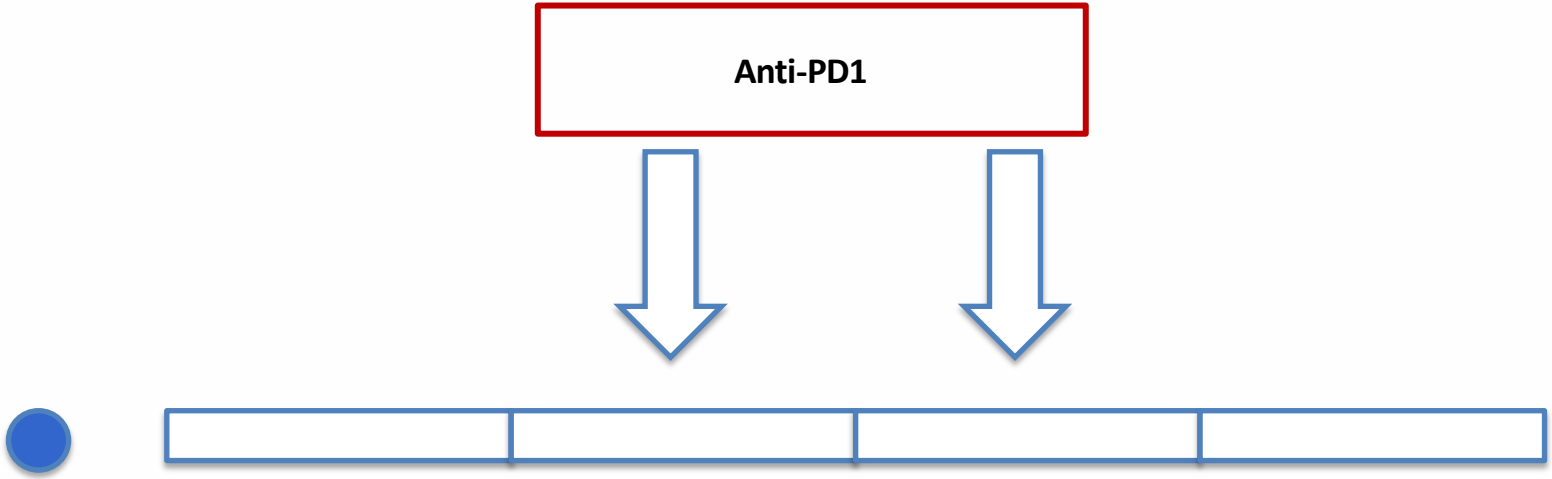
Around 30%
Grade 3 PN

Forero-Torres A et al, 2015
Friedberg JW et al, 2017



Anti-PD1

diagnosis	first line	second line	consolidation	salvage therapy

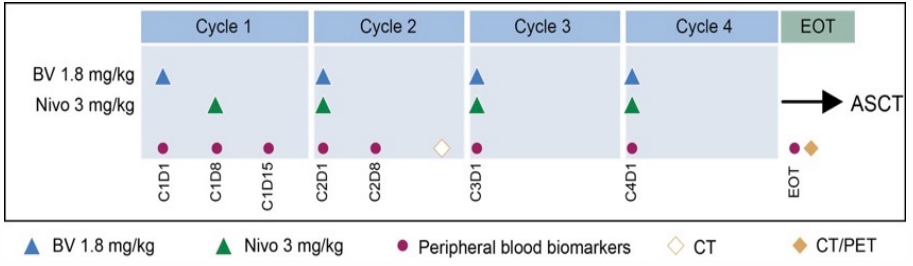


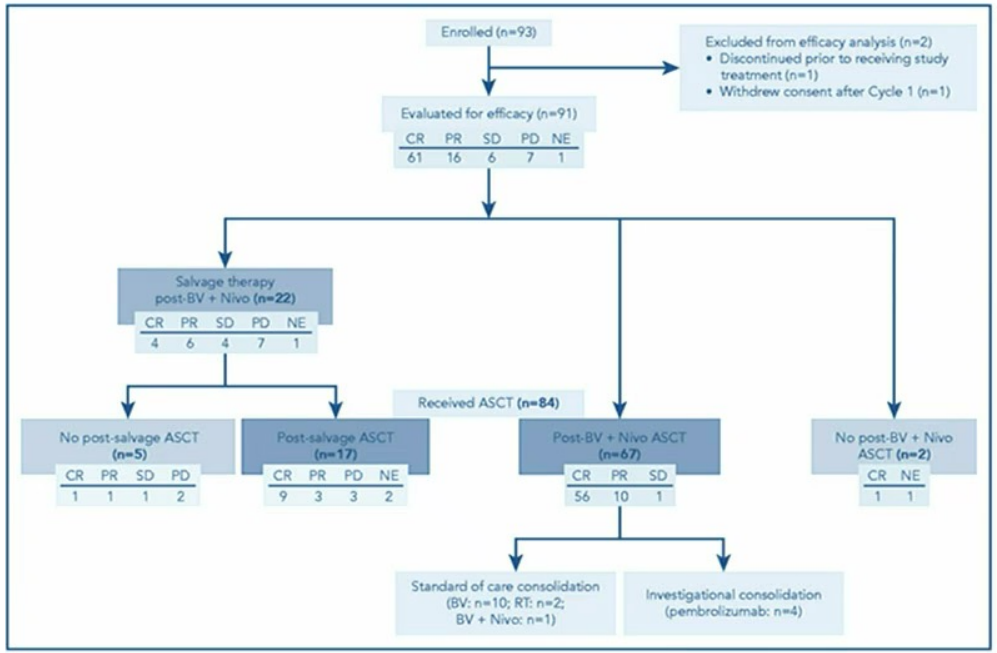
diagnosis	first line	second line	consolidation	salvage therapy

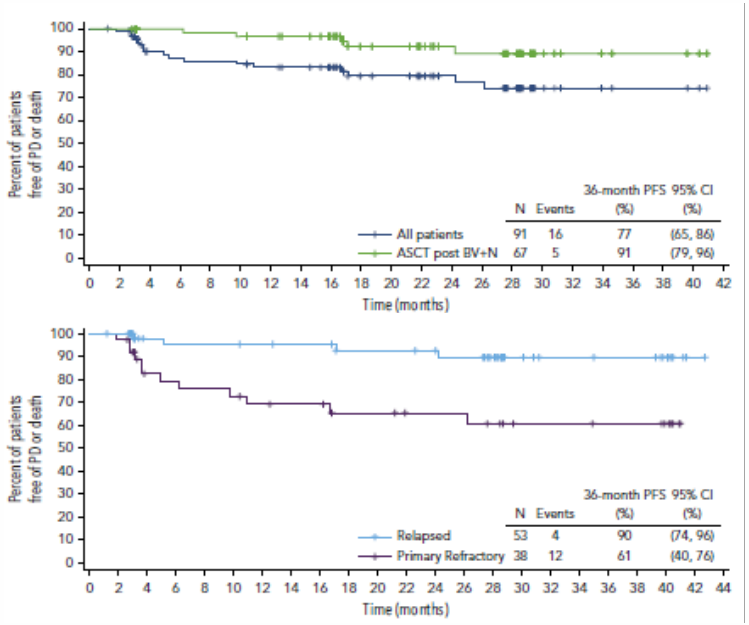
CLINICAL TRIALS AND OBSERVATIONS

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

Ranjana H. Advani,[1] Alison J. Moskowitz,[2] Nancy L. Bartlett,[3] Julie M. Vose,[4] Radhakrishnan Ramchandren,[5] Tatyana A. Feldman,[6] Ann S. LaCasce,[7] Beth A. Christian,[8] Stephen M. Ansell,[9] Craig H. Moskowitz,[10] Lisa Brown,[11] Chiyu Zhang,[11] David Taft,[11] Sahar Ansari,[11] Mariana Sacchi,[12] Linda Ho,[11] and Alex F. Herrera[13]







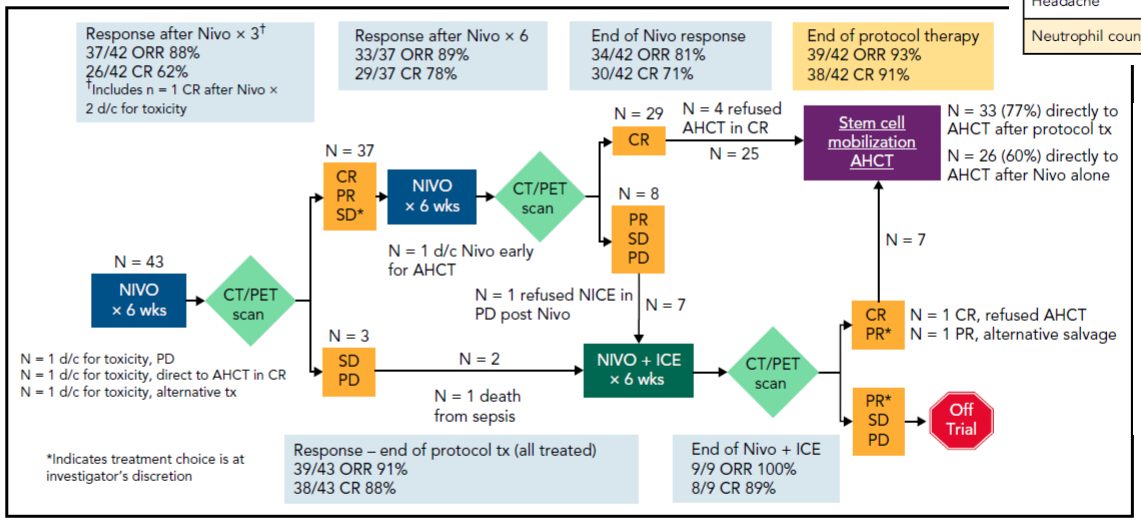
Advani RH et al, Blood 2021

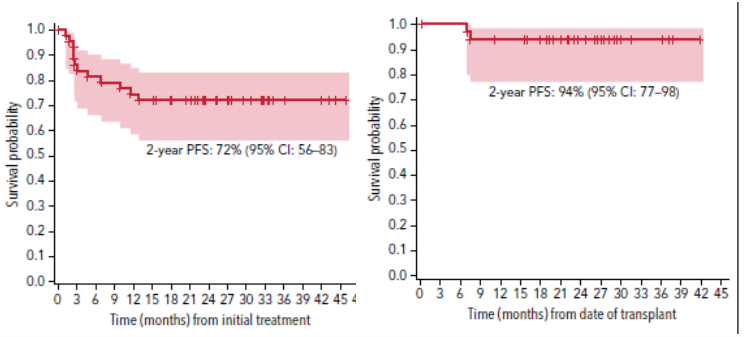
CLINICAL TRIALS AND OBSERVATIONS

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

Matthew G. Mei,[1,*] Hun Ju Lee,[2,*] Joycelynne M. Palmer,[3] Robert Chen,[1] Ni-Chun Tsai,[3] Lu Chen,[3] Kathryn McBride,[1] D. Lynne Smith,[1] Ivana Melgar,[1] Joo Y. Song,[4] Kimberley-Jane Bonjoc,[5] Saro Armenian,[6] Mary Nwangwu,[7] Peter P. Lee,[7] Jasmine Zain,[1] Liana Nikolaenko,[1] Leslie Popplewell,[1] Auayporn Nademanee,[1] Ammar Chaudhry,[5] Steven Rosen,[1] Larry Kwak,[1] Stephen J. Forman,[1] and Alex F. Herrera[1]

AEs	Grade 1	Grade 2	Grade 3	Grade 4	All
Fatigue	12	2	0	0	14
Rash maculopapular	7	1	0	0	8
Arthralgia	6	1	0	0	7
Fever	5	2	0	0	7
Nausea	7	0	0	0	7
White blood cell decreased	4	3	0	0	7
Alanine aminotransferase increased	6	0	0	0	6
Headache	5	0	0	0	5
Neutrophil count decreased	4	1	0	0	5





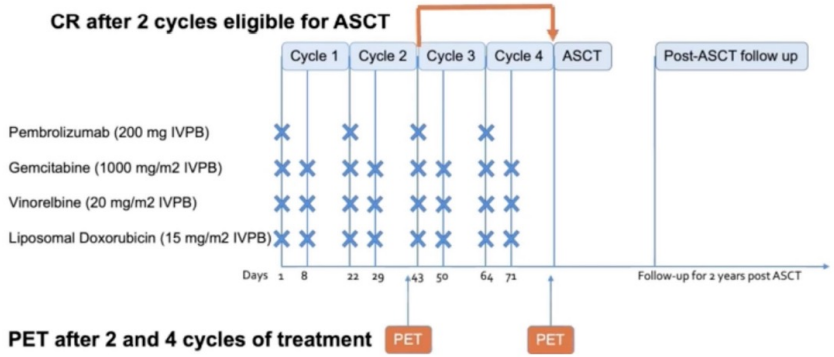
Mei MG et al, Blood 2022

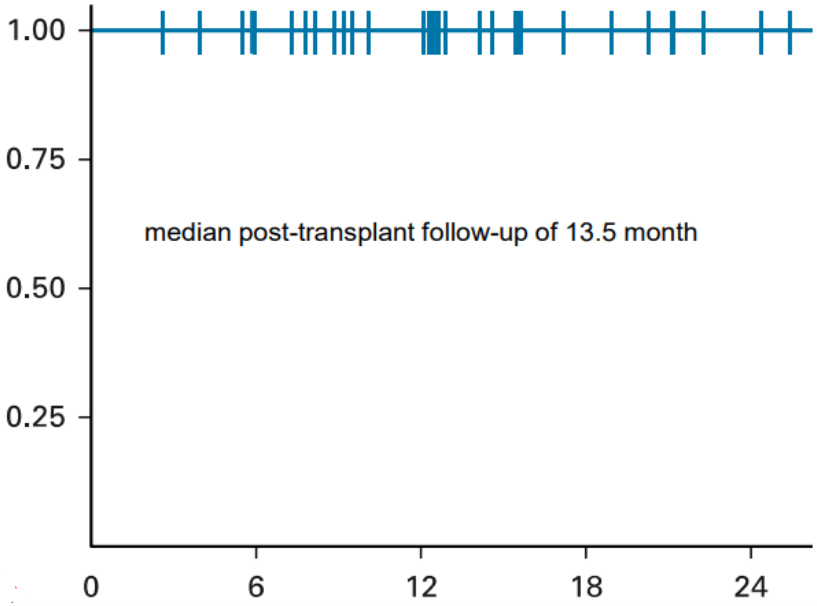
rapid communications

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

Alison J. Moskowitz, MD[1]; Gunjan Shah, MD[2]; Heiko Schöder, MD[1]; Nivetha Ganesan, MPH[1]; Esther Drill, PhD[3]; Helen Hancock, NP[1]; Theresa Davey, PA[1]; Leslie Perez, RN[1]; Sunyoung Ryu, RN[1]; Samia Sohail, MBS[1]; Alayna Santarosa, MPH[1]; Natasha Galasso, MSW[1]; Rachel Neuman, MBA[1]; Brielle Liotta, BS[1]; William Blouin, MBA[1]; Anita Kumar, MD[1]; Oscar Lahoud, MD[1]; Connie L. Batlevi, MD[1]; Paul Hamlin, MD[1]; David J. Straus, MD[1]; Ildefonso Rodriguez-Rivera, MD[1]; Colette Owens, MD[1]; Philip Caron, MD[1]; Andrew M. Intlekofer, MD[1]; Audrey Hamilton, MD[1]; Steven M. Horwitz, MD[1]; Lorenzo Falchi, MD[1]; Erel Joffe, MD[1]; William Johnson, DO[1]; Christina Lee, MD[1]; M. Lia Palomba, MD[1]; Ariela Noy, MD[1]; Matthew J. Matasar, MD[1]; Georgios Pongas, MD[4]; Gilles Salles, MD[1]; Santosha Vardhana, MD[1]; Beatriz Wills Sanin, MD[1]; Gottfried von Keudell, MD[1]; Joachim Yahalom, MD[1]; Ahmet Dogan, MD[1]; Andrew D. Zelenetz, MD[1]; and Craig H. Moskowitz, MD[4]

- **Primary endpoint**: CR (by Deauville 3) rate after 2-4 cycles



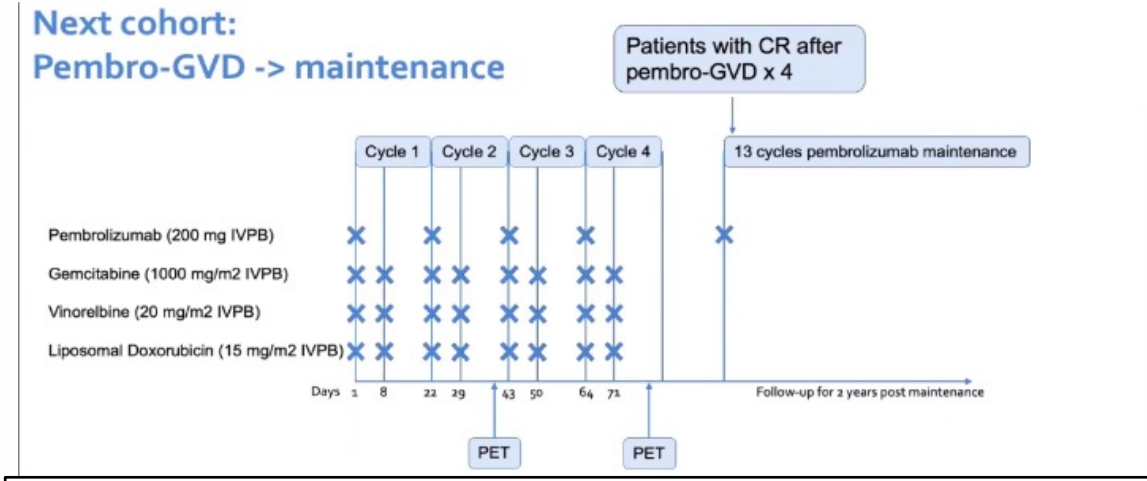


36/38 CR -> 95%

Moskowitz AJ et al, J Clin Oncol 2021

Moving towards an ASCT-free approach?

(patients in CR after Pembro-GVD x 4 will receive 13 cycles of Pembrolizumab manteinance)



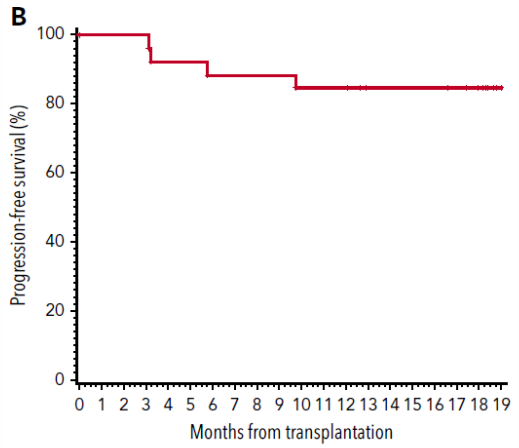
Unprecedented CR rate with pembro GVD

ASCT could be shifted to third line setting for those who need it

Moskowitz AJ et al, ASH 2020

PD-1 blockade with pembrolizumab for classical Hodgkin lymphoma after autologous stem cell transplantation

Philippe Armand,[1] Yi-Bin Chen,[2] Robert A. Redd,[3] Robin M. Joyce,[4] Jad Bsat,[1] Erin Jeter,[1] Reid W. Merryman,[1] Kimberly C. Coleman,[1] Parastoo B. Dahi,[5] Yago Nieto,[6] Ann S. LaCasce,[1] David C. Fisher,[1] Samuel Y. Ng,[1] Oreofe O. Odejide,[1] Arnold S. Freedman,[1] Austin I. Kim,[1] Jennifer L. Crombie,[1] Caron A. Jacobson,[1] Eric D. Jacobsen,[1] Jeffrey L. Wong,[1] Sanjay S. Patel,[7] Jerome Ritz,[1] Scott J. Rodig,[7] Margaret A. Shipp,[1] and Alex F. Herrera[8]



18-mos PFS 82%
18-mos OS 100%
Promising results in HR R/R cHL pts
Need for randomized trial

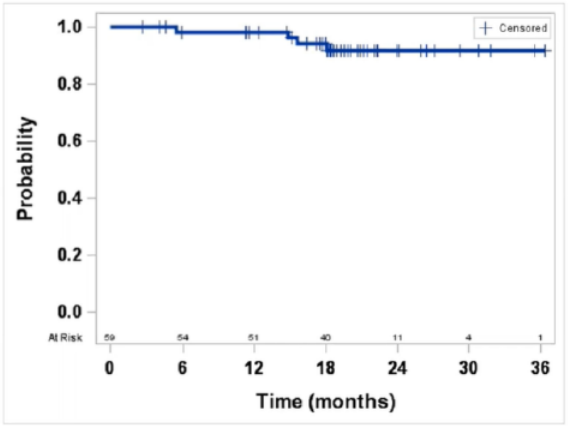
Armand P et al, Blood 2019

AHCT according to institutional standards → 30-75 days after AHCT → **BV 1.8 mg/kg + nivo 3 mg/kg every 21 days for 8 cycles**

If one drug discontinued for toxicity, other could be continued

PET-CT: after AHCT/baseline, Cycle 4 Day 15, EOT, 12 and 18 months after initiation

Progression-free survival



19-month PFS in all patients (n=59): 92% (95 CI 79–97)

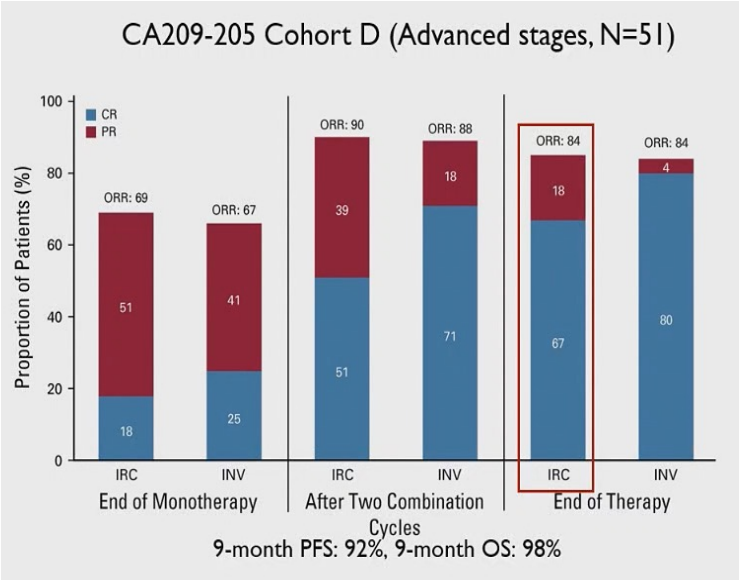
BV + Nivo for 8 cycles
→ tolerable approach
→ promising approach

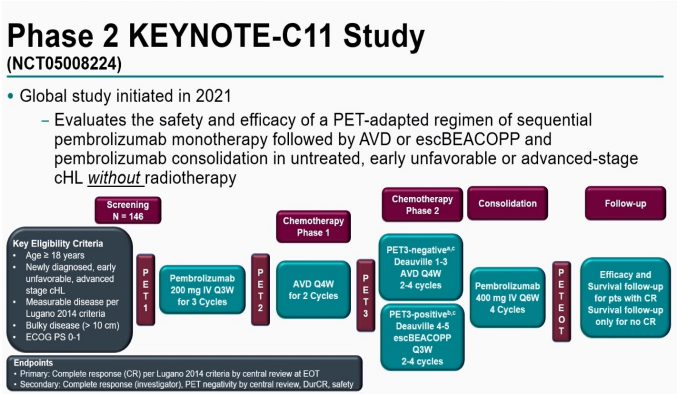
Herrera AF et al, ASH 2020

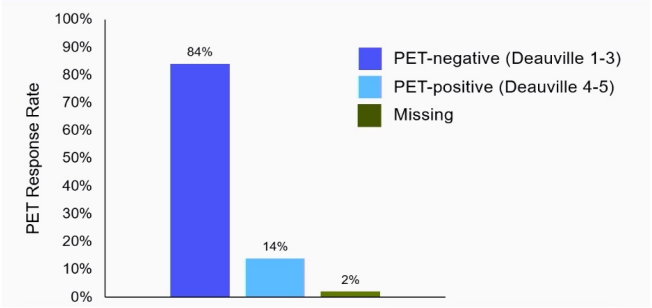

Anti-PD1
diagnosis
first line
second line
consolidation
salvage therapy

Improving first line treatment efficacy

4 x NIVO → 6 x NIVO+AVD

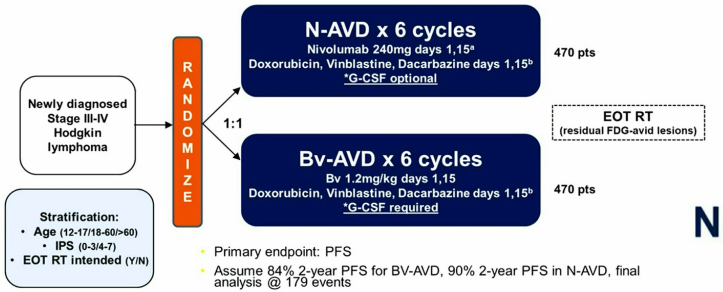






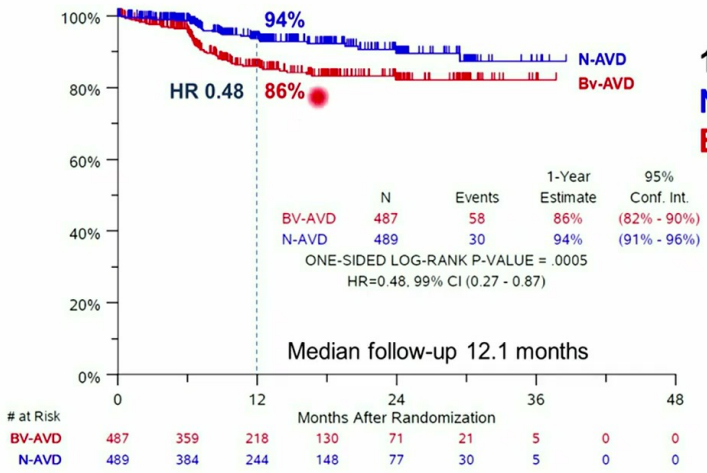
Advani RH et al, ASH 2022
Ramchandren R et al, 2019

S1826 Study Design



- Primary endpoint: PFS
- Assume 84% 2-year PFS for BV-AVD, 90% 2-year PFS in N-AVD, final analysis @ 179 events

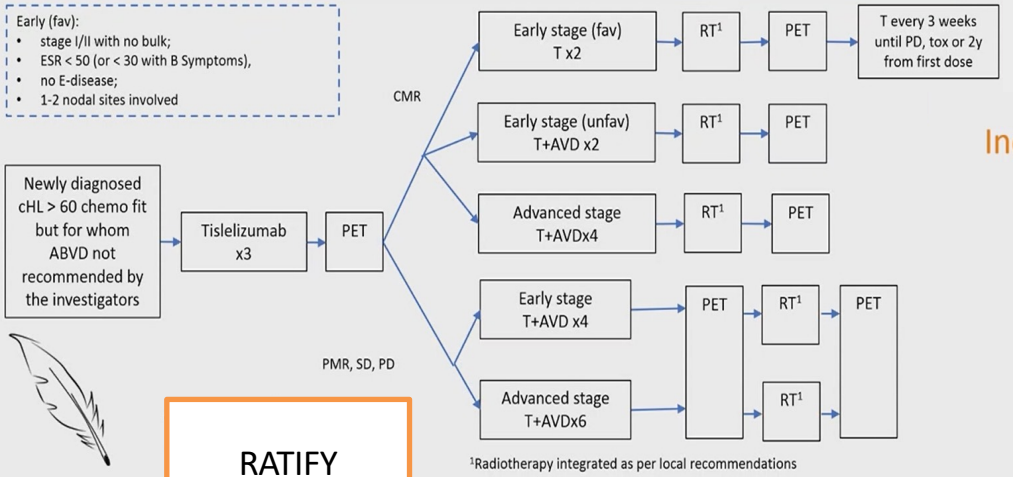
N-AVD improves PFS compared to Bv-AVD



Herrera AF et al, ASCO 2023

Sparing toxicity

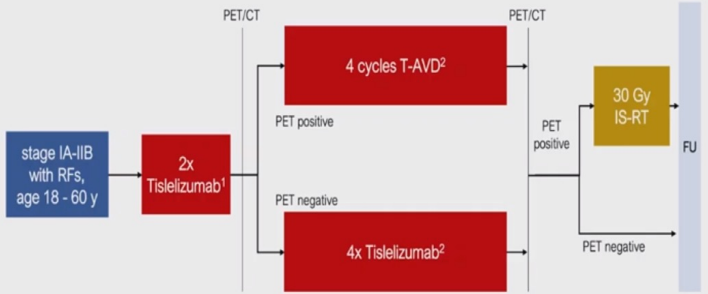
Reducing chemotherapy burden



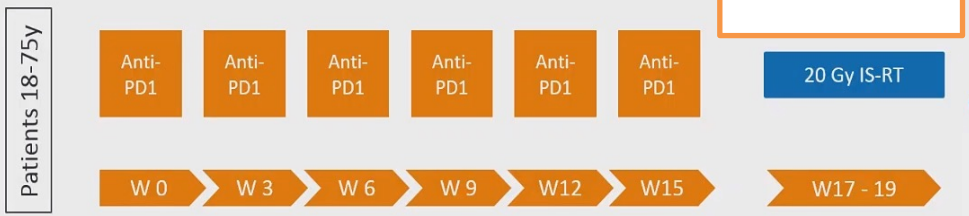
RATIFY

HD20

Individualized Immunotherapy in Early-Stage Unfavourable cHL (INDIE): HD20 pilot, status FPI planned for Q1 2023



HD19

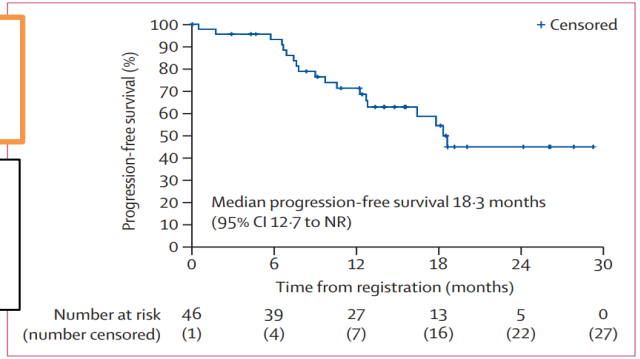


GHSG

Enabling non-fit patients to receive effective therapy

BV plus Nivo
ACCRU

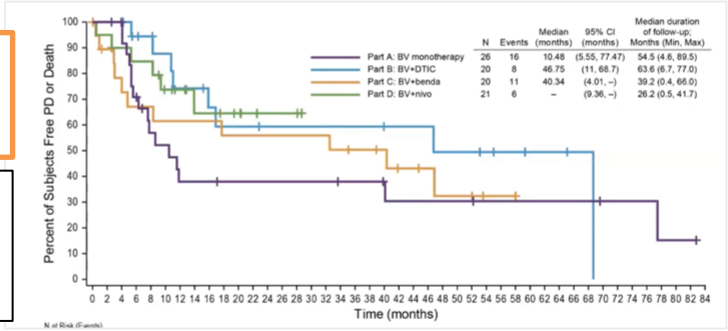
46 patients
ORR 64%
CRR 52%



Cheson BD et al, 2020

BV plus Nivo
SGN35-015

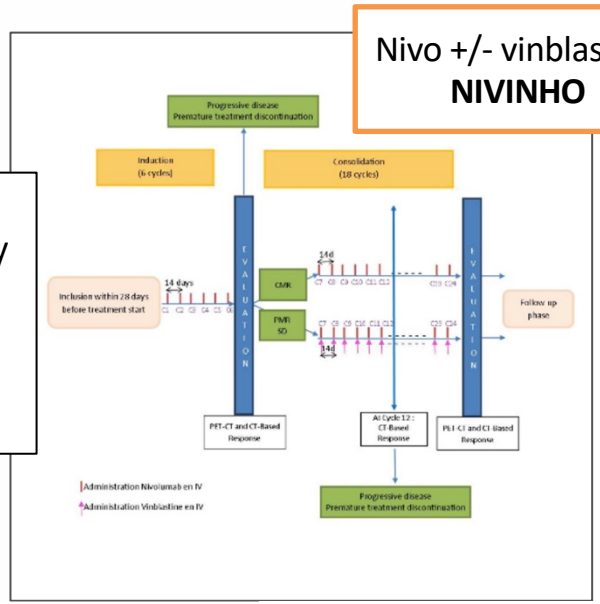
18 patients
ORR 95%
CRR 79%

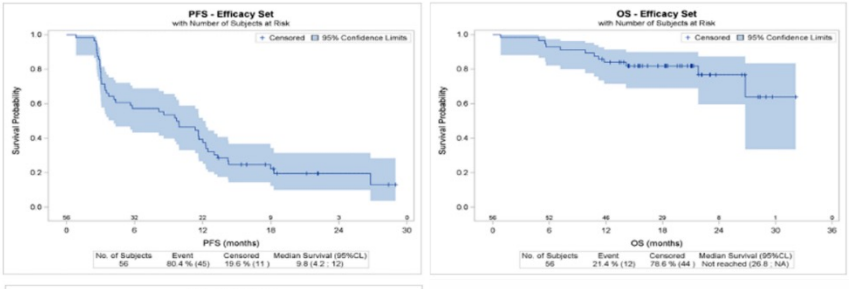


Yasenchak C, ASH 2020

Nivo +/- vinblastine
NIVINHO

56 pts
median 75y
CIRS-G 10
ORR 47%
CR
29%(16%)





Lazarovici J et al, ASH 2021

New options

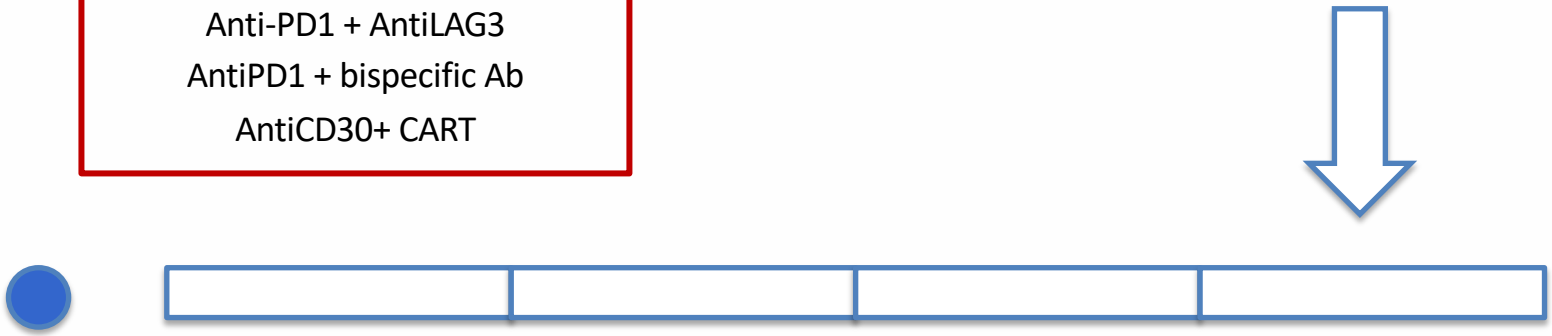
Camidanlumab teserine

Anti-PD1 + epigenetic modifiers

Anti-PD1 + AntiLAG3

AntiPD1 + bispecific Ab

AntiCD30+ CART



diagnosis	first line	second line	consolidation	salvage therapy

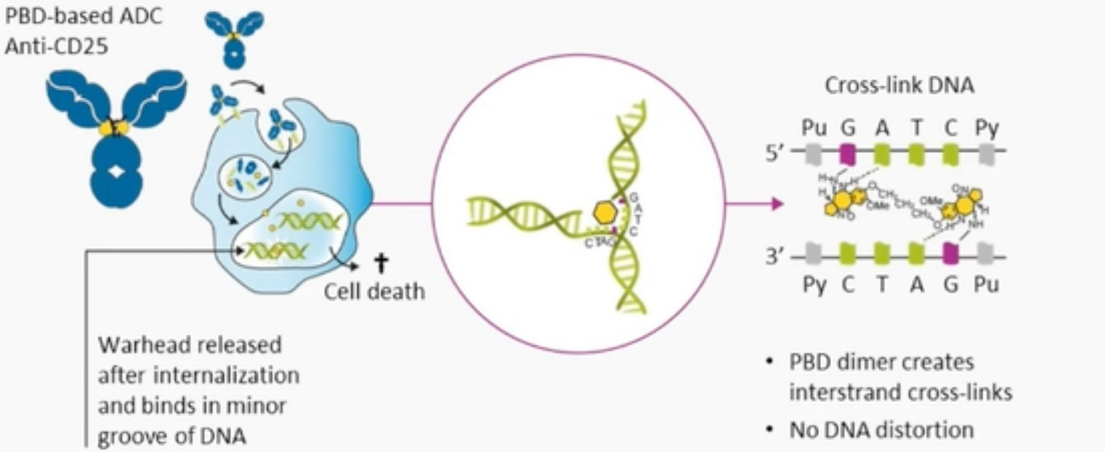
CAMIDANLUMAB TESIRINE (CAMI)
anti-CD25 antibody drug conjugate

Cami composition

- Human IgG1 anti-CD25 mAb stochastically conjugated to PBD dimer warhead

Mechanism of action[1–3]

- Death of CD25-expressing tumor cells
- Depletion of CD25-expressing T cells in HL tumor microenvironment
- Possible bystander killing of CD25-negative cells



1. Hartley JA. *Expert Opin Investig Drugs* 2011;20:733–44; 2. Flynn MJ, et al. *Mol Cancer Ther* 2016;15:2709–21; 3. Zammarchi F, et al. *J ImmunoTher Cancer* 2020;8:e000860.
ADC, antibody-drug conjugate; **IgG**, immunoglobulin G; **mAb**, monoclonal antibody; **PBD**, pyrrolobenzodiazepine.

KEY INCLUSION CRITERIA

Age ≥ 18 years (16 in US)
R/R cHL w > 3 prior LOT (2 if ASCT ineligible)
Measurable disease
ECOG 0 – 2
Adequate organ function

Camidanlumab Tesirine
45 µg/Kg

Cycle 1 & 2

Camidanlumab Tesirine
30 µg/Kg

Cycle 3 onwards

ORR per central review[2]	N=117
ORR, % (95% CI)	70.1 (60.9–78.2)
CR, %	33.3
PR, %	36.8
SD, %	17.9
PD, %	6.8
Not evaluable, %	5.1

Median DOR 13.7 months at a median follow-up of 10.7 months; median PFS: 9.1 months

Most common Grade ≥3 TEAEs (≥5% of patients)[a]	
Hypophosphatemia	6 (11.8)
Gamma-glutamyltransferase increased	5 (9.8)
Alanine aminotransferase increased	3 (5.9)
Maculopapular rash	3 (5.9)

No. of patients who experienced TEAEs
49 (96.1%)

No. of patients with Grade ≥3 TEAEs
32 (62.7%)

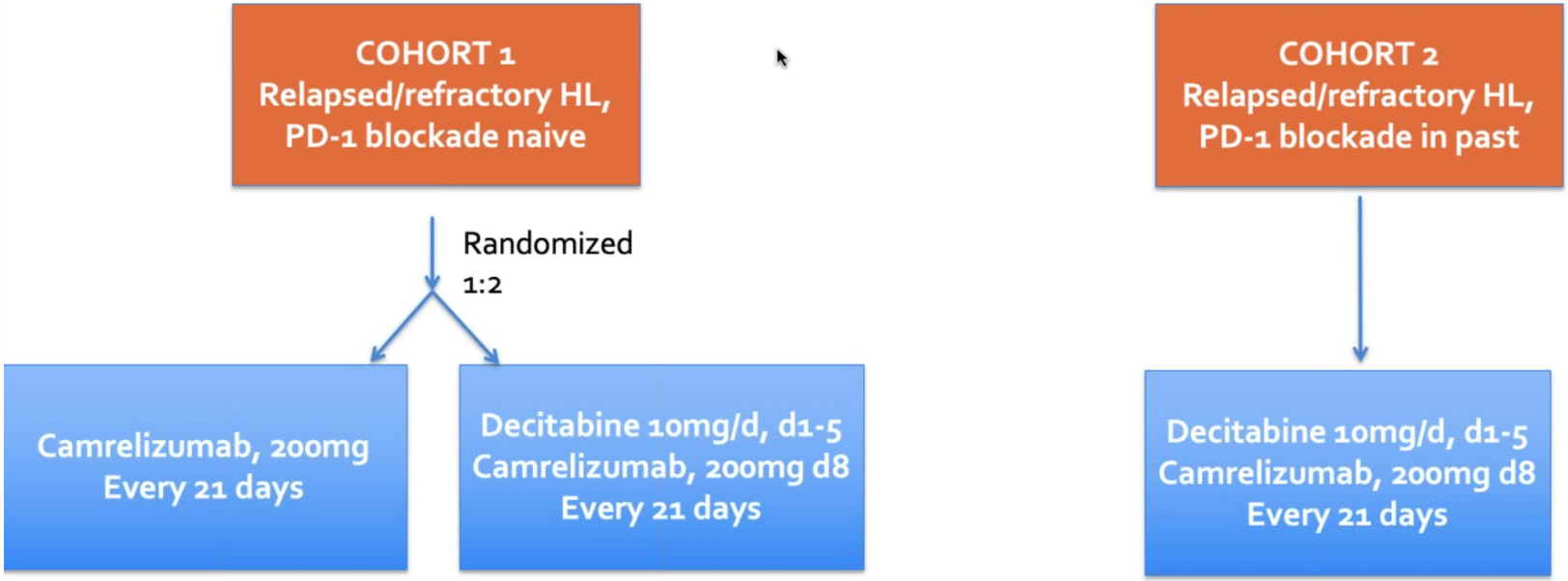
TEAEs leading to dose reduction/delay
6 (11.8%)

TEAEs leading to treatment withdrawal
7 (13.7%)

- No. of cases of GBS/polyradiculopathy: **3 (6.4%)**

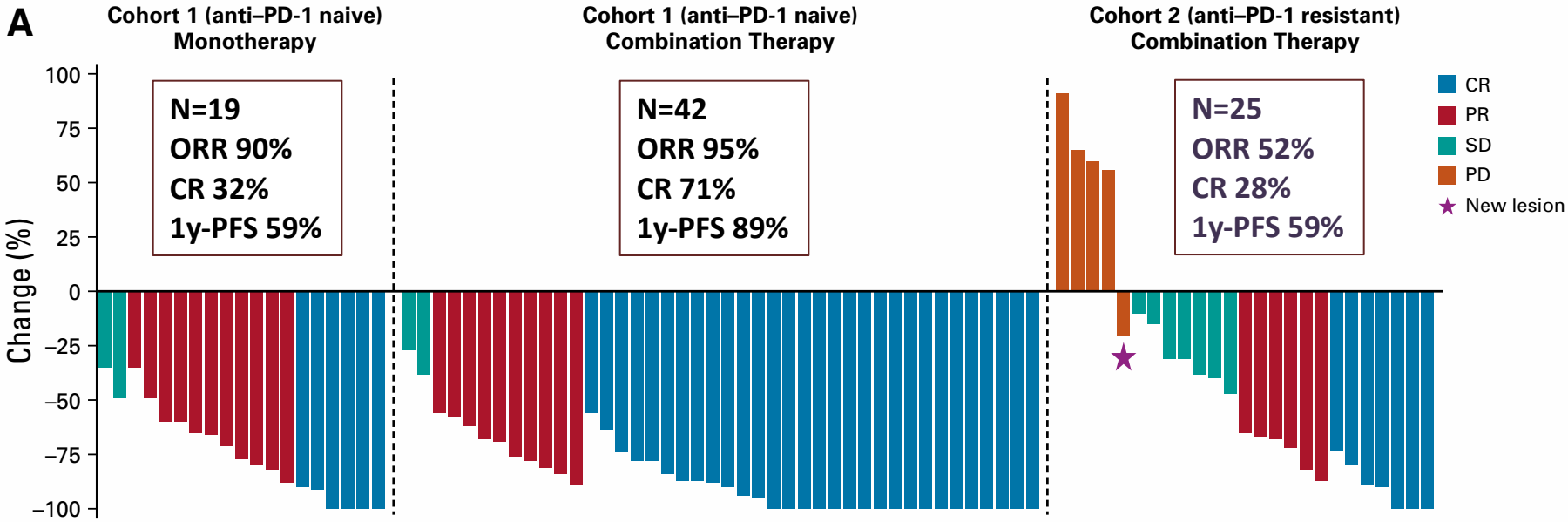
Zinzani P et al, ICML 2021; Carlo-Stella C et al, EHA 2022

Two-arm, open-label, phase II study: Low-dose decitabine plus anti-PD1 antibody Camrelizumab



Nie et al JCO, 2019

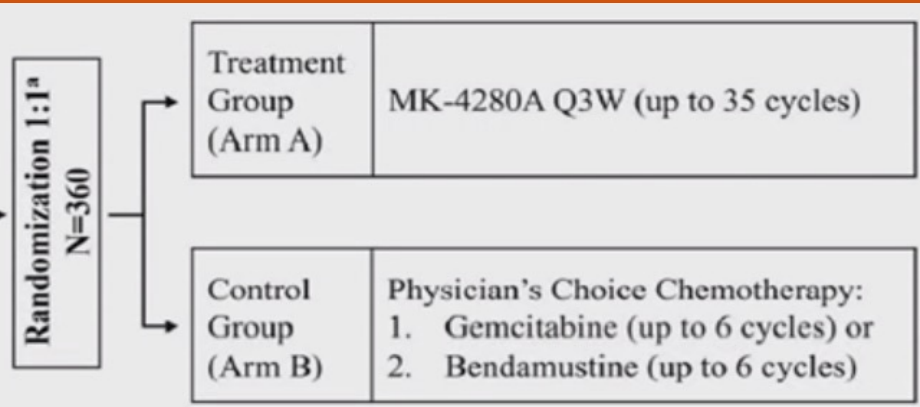
Low-dose decitabine plus anti-PD1 antibody Camrelizumab

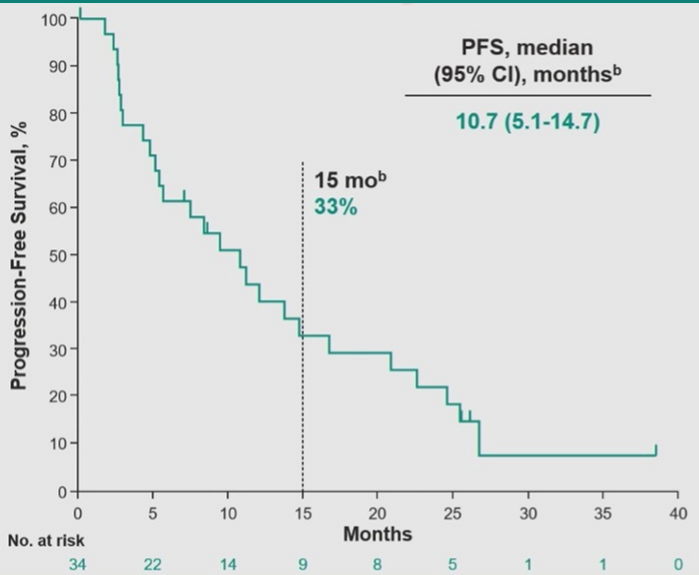


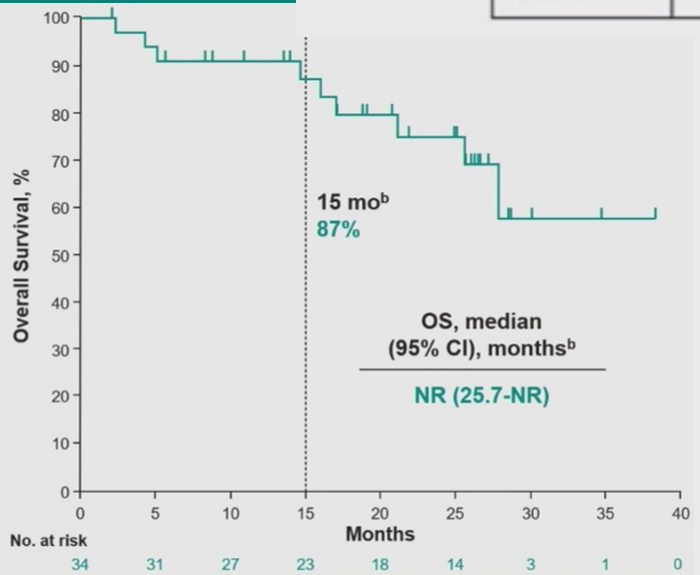
Nie et al JCO, 2019

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

John Timmerman[1]; David Lavie[2]; Nathalie A. Johnson[3]; Abraham Avigdor[4]; Peter Borchmann[5]; Charalambos Andreadis[6]; Ali Bazargan[7]; Gareth P. Gregory[8]; Colm Keane[9]; Inna Tzoran[10]; Vladan Vucinic[11]; Pier Luigi Zinzani[12]; Rachel Marceau West[13]; Pallavi Pillai[13]; Alex F. Herrera[14]







- 28-Day Window
- Informed Consent
- Confirm Eligibility
  - Key Eligibility:
    - PD-1/L1-refractory R/R cHL
    - ECOG PS 0-2
    - Auto-SCT ineligible or failed
    - BV ineligible, failed or discontinued due to toxicity

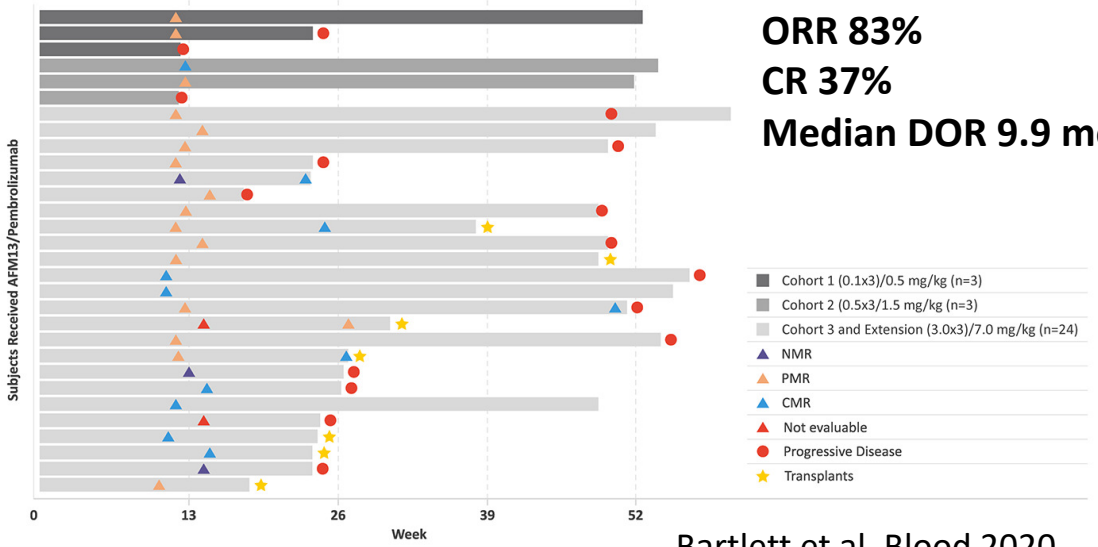
A phase 1b study of AFM13 in combination with pembrolizumab in patients with R/R HL

→ AFM13 is a bispecific, tetravalent innate cell engager that activates NK cells and macrophages via CD16A to target CD30+ lymphoma cells

→ AFM13 in combination with pembrolizumab for HL patients was well-tolerated with adverse events that were generally manageable

Characteristics	N=30
Median age (range)	33.5 (18, 73)
Relapsed	13 (43%)
Refractory	17 (57%)
Prior lines of therapy ≥ 4	16 (53%)
Prior ASCT	12 (40%)
BV as last prior therapy	13 (43%)

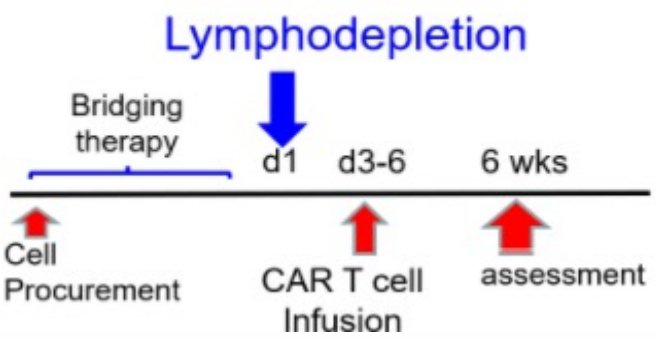
*prior anti PD1 excluded



ORR 83%
CR 37%
Median DOR 9.9 mo

Bartlett et al, Blood 2020

Anti-CD30 CAR-T



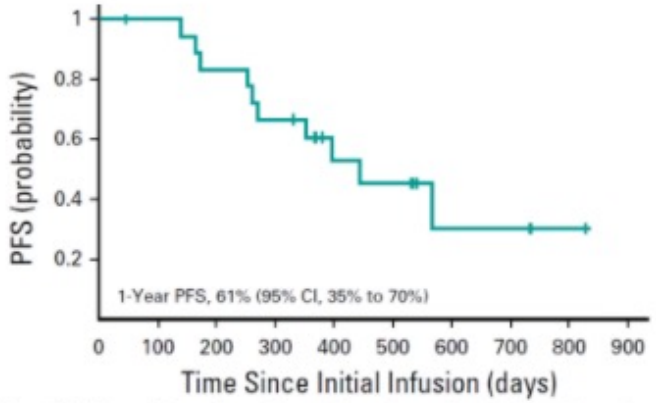
- Phase 1 trials run in parallel at BCM and UNC
- 41 HL, Median 35 yrs (range 17-69)
  - Median 7 regimens (range 2 -23)
  - BV (38; 90%), CPI (34; 81%), SCT (32; 76%), Allo (10; 24%)
- Primary Objective: safety
- Secondary: response per Lugano
  - Initial assessment at week 6

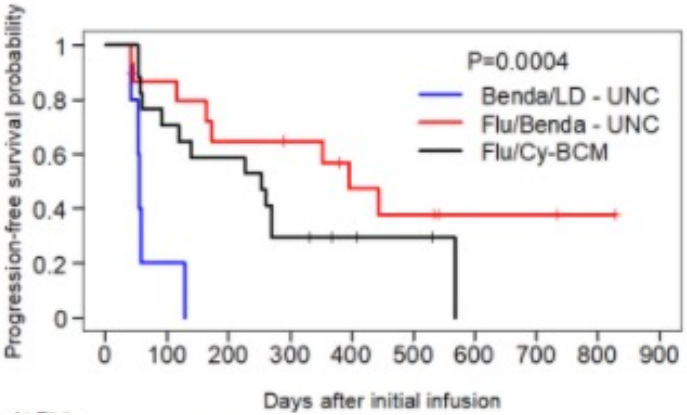
Bendamustine (90 mg/m^2/day) x 2 days
or
Bendamustine (70 mg/m^2/day) x 3 days
Fludarabine (30 mg/m^2/day) x 3 days

Cyclophosphamide (500 mg/m^2/day) x 3 days
Fludarabine (30 mg/m^2/day) x 3 days

Characteristics	All patients N=42
Prior BV	38 (90%)
Progression on BV	32 (84%)
Prior CPI	34 (81%)
Prior ASCT	32 (76%)
Prior AlloSCT	10 (24%)

Ramos et al, JCO 2020





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 et al, JCO 2020

Brentuximab Vedotin

Known efficacy and good safety profile

Recent approval in first line

Anti-PD1

Good efficacy in R/R cHL

Favorable safety profile

New SOC in first line?

New options

For “unmet need”

Mainly immunotherapy

(new targets, combos, bispecific, CART)

Sistema Socio Sanitario
Ospedale Niguarda
Regione Lombardia

Erika Meli - Cristina Muzi - Emanuele Ravano
Erika Ravelli - Roberto Cairoli

Thank you!