Novità nella terapia del linfoma di Hodgkin ricaduto/refrattario

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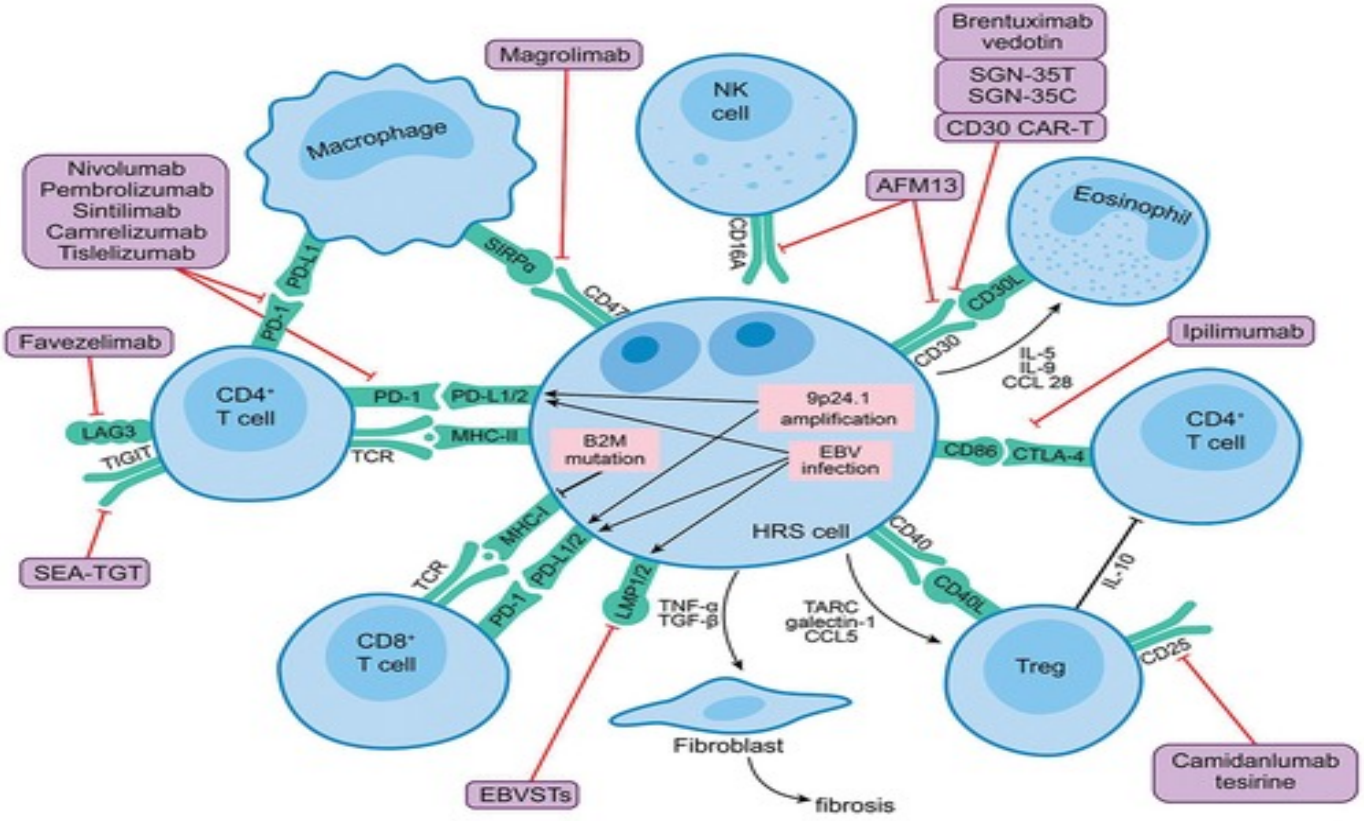
Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
TAKEDA							X
GENTILI							X
GRIFOLS							X
SANOFI						X	

Immunoterapie e bersagli biologici



Spinner et Al. Expert opinion on emerging drugs, 2024

Table 1. Immunotherapies and small molecules in development for classic Hodgkin lymphoma.

Compound	Company	Structure	Phase	Combinations	Mechanism of action in cHL
Immune checkpoint inhibitors					
Sintilimab	Innovent	Anti-PD-1 mAb	Phase 2	ICE	Enhance CD4+ T-cell responses, withdrawal of pro-survival signals, possible NK cell activation
Camrelizumab	Jiangsu Hengrui		Phase 2	Decitabine, AVD	
Tislelizumab	BeiGene		Phase 2	Gem/Ox, AVD	
Avelumab	Merck	Anti-PD-L1 mAb	Phase 1b	–	
Ipilimumab	Bristol Myers Squibb	Anti-CTLA-4 mAb	Phase 2	Nivolumab, BV	Potentiate T-cell responses
Favezelimab	Merck	Anti-LAG-3 mAb	Phase 2	Pembrolizumab	Overcome T-cell exhaustion
MK-4280A	Merck	Coformulated anti-PD-1 + LAG-3 mAb	Phase 3	–	Overcome T-cell exhaustion, potentiate T-cell responses
Magrolimab	Gilead	Anti-CD47 mAb	Phase 2	Pembrolizumab	Enhance phagocytosis, increase antigen presentation
IMM01	ImmuneOnco Biopharmaceuticals	SIRPα-Fc fusion protein	Phase 2	Tislelizumab	Enhance phagocytosis, increase antigen presentation
SEA-TGT	Seattle Genetics	Anti-TIGIT mAb	Phase 1	BV	Enhance T & NK cell responses
Immunomodulatory agents and small molecules					
Lenalidomide	Bristol Myers Squibb	CELMoD	Phase 2	Nivolumab, temsirolimus	Increase IL-2 production, enhance T & NK cell responses
Ruxolitinib	Incyte	JAK1/2 inhibitor	Phase 2	Nivolumab	Inhibit JAK/STAT signaling, synergize with PD-1 inhibitors
Ibrutinib	AbbVie	BTK/ITK inhibitor	Phase 2	Nivolumab	Enhance Th1 responses
Epigenetic modifying therapies					
Vorinostat	Merck	HDAC inhibitor	Phase 1	Pembrolizumab	Enhance antigen presentation, T-cell recruitment & function
Entinostat	Syndax		Phase 2	Pembrolizumab	
Decitabine	Otsuka	Hypomethylating agent	Phase 2	Camrelizumab	Increase tumor immunogenicity, T-cell infiltration, and overcome resistance to PD-1 inhibitors
Decitabine/cedazuridine (ASTX727)	Astex Pharmaceuticals		Phase 1	Nivolumab	
Azacitidine (CC-486)	Bristol Myers Squibb		Phase 1	Nivolumab	
Antibody-drug conjugates (ADCs)					
Camidanlumab tesirine	ADC Therapeutics	Anti-CD25 ADC	Phase 2	–	Deplete regulatory T cells, target CD25+ HRS cells
SGN-35T	Seattle Genetics	Anti-CD30 ADC	Phase 1	–	Target CD30+ HRS cells with novel linker and MMAE (35T) or camptothecin payload (35C)
SGN-35C	Seattle Genetics		Phase 1	–	
Bispecific antibodies (BsAbs)					
AFM13	Affimed	CD30/CD16A BsAb	Phase 2	Pembrolizumab, AB-101	Recruit NK cells to target CD30+ HRS cells
GEN3017	Genmab	CD30/CD3 BsAb	Phase 1/2	–	Recruit T cells to target CD30+ HRS cells
AZD7789	AstraZeneca	PD-1/TIM-3 BsAb	Phase 1/2	–	Overcome T-cell exhaustion, potentiate T-cell responses
IBI322	Innovent	CD47/PD-L1 BsAb	Phase 1	–	Enhance phagocytosis, increase antigen presentation, potentiate T-cell responses
Cellular therapies					
Autologous CD30 CAR-T	Tessa Therapeutics	Anti-CD30 CAR-T	Phase 2	–	Engineered autologous or allogeneic T cells targeting CD30+ HRS cells
Allogeneic CD30 CAR. EBVSTs (TT11X)	Tessa Therapeutics		Phase 1	–	
Allogeneic UCB-derived NK cells (AB-101)	Artiva	Cytokine-enhanced NK cells	Phase 2	AFM13	Allogeneic NK cell-mediated cytotoxicity, enhanced ADCC

Studio fase II CART anti CD30 in HD R/R

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%)

Bendamustine (90 mg/m²/day) x 2 days
or
Bendamustine (70 mg/m²/day) x 3 days
Fludarabine (30 mg/m²/day) x 3 days

Cyclophosphamide (500 mg/m²/day) x 3 days
Fludarabine (30 mg/m²/day) x 3 days

TABLE 3. Clinical Responses in Patients With Measurable Disease at the Time of Treatment

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 et al. JCO 2020

CART anti CD30 in HD R/R

Linfodeplezione a base di fludarabina

ORR 72%
CR 59%
PFS a 1 anno 36%
mPFS 14.8 mesi

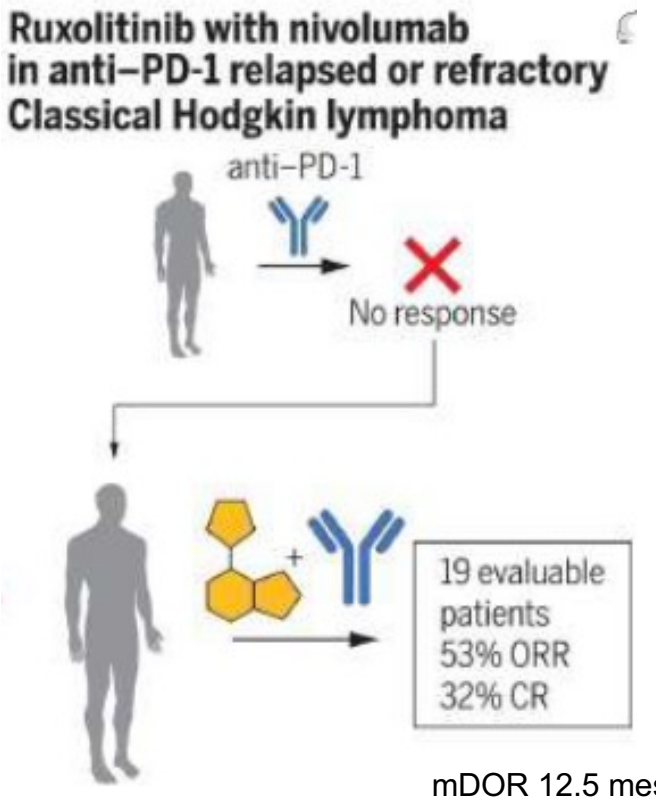
Eventi avversi : rash (48%) , citopenie
CRS grade 1 (24%)
ICANS 0

TABLE 2. Grade 3 or Higher Adverse Events and Adverse Events of Special Interest

Adverse Event	All Patients (N= 42)[a]	Benda (n = 8)[a]	Benda-Flu (n = 17)	Cy (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)

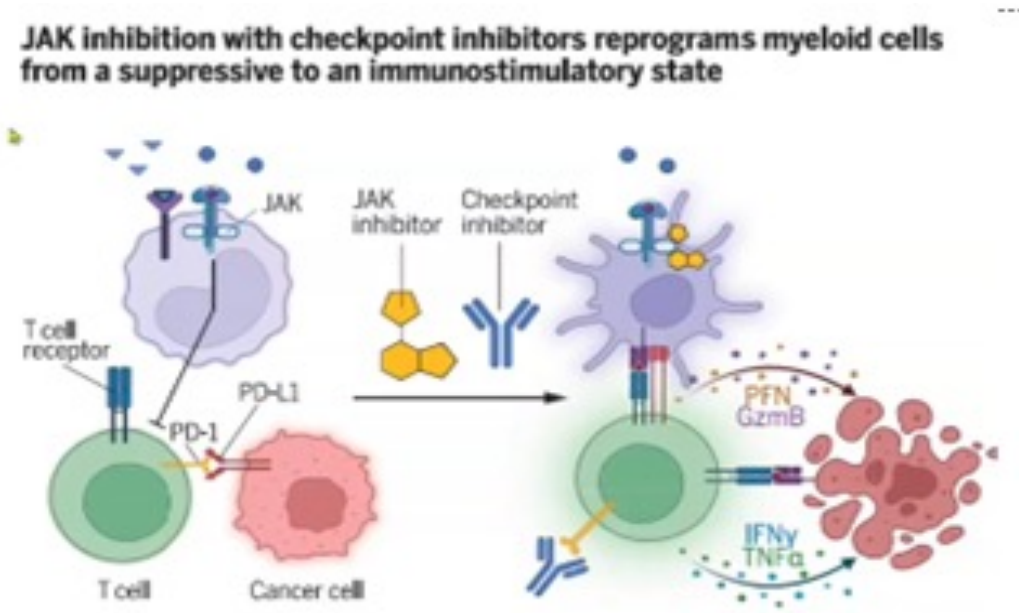
Ramos et al. JCO 2020

Agenti immunomodulanti+ inibitori di PD-1



mDOR 12.5 mesi

PFS a 2 anni 46%



Zak et Al. Science 2024

Favelizumab+ Pembrolizumab vs Pembrolizumab

Estimating Efficacy of Favezelimab Plus Pembrolizumab Relative to Pembrolizumab in Anti–PD-1–Refractory Hodgkin Lymphoma

Context of Research

Participants eligible from MK-4280-003 cohort 2 (NCT03598608)
- Received ≥2 doses of anti–PD-1 therapy
- Disease progression within 12 weeks of last dose of anti–PD-1
- Rx: pembrolizumab 200 mg + favezelimab 200 mg or 800 mg IV Q3W

Participants eligible from KEYNOTE-087 (NCT02453594)
- Received >2 doses of pembrolizumab beyond progression
- Disease progression within 12 weeks of last dose of pembrolizumab
- Rx: continued pembrolizumab 200 mg IV Q3W

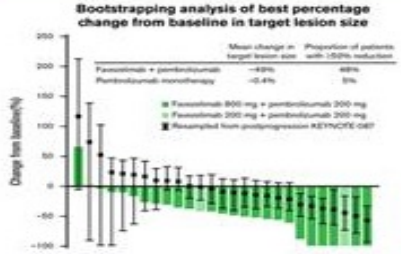
Relative contribution of favezelimab assessed
- Change in target lesion size
- Objective response rate (ORR)
- Bootstrapping method compared change in target lesion size

Main Outcomes

Best overall response per IWG 2007 criteria

	Favezelimab + pembrolizumab (MK-4280-003 cohort 2) n = 27	Pembrolizumab monotherapy (KEYNOTE-087) n = 81
ORR, % (95% CI)	37% (15%–51%)	2% (0%–6%)
Best response, n (%)		
Complete response	3 (11%)	0
Partial response	7 (26%)	2 (2%)
Stable disease	11 (41%)	23 (28%)
Progressive disease	6 (22%)	56 (69%)

Bootstrapping analysis of best percentage change from baseline in target lesion size



Conclusion: Favezelimab plus pembrolizumab had a higher response rate and greater reduction in tumor burden versus pembrolizumab alone in anti–PD-1–refractory classical Hodgkin lymphoma, suggesting favezelimab contributed substantially to efficacy in the MK-4280-003 study.

*Armand et al. DOI: 10.1182/**bloodadvances**.2024014654*

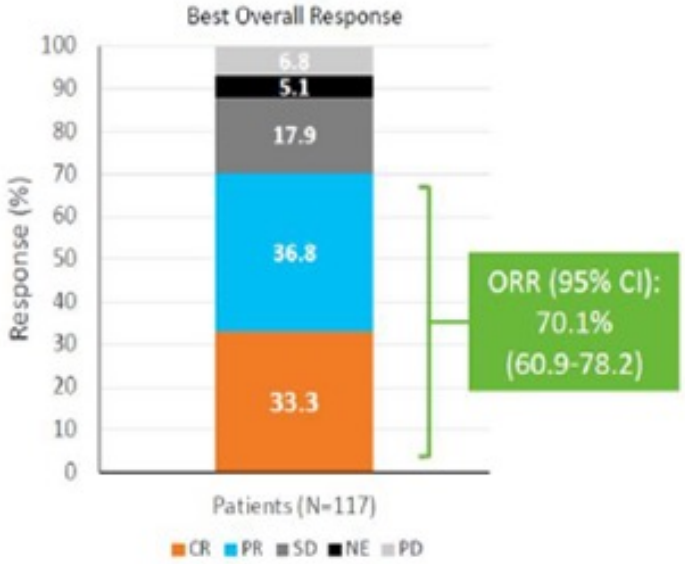
blood advances Visual Abstract

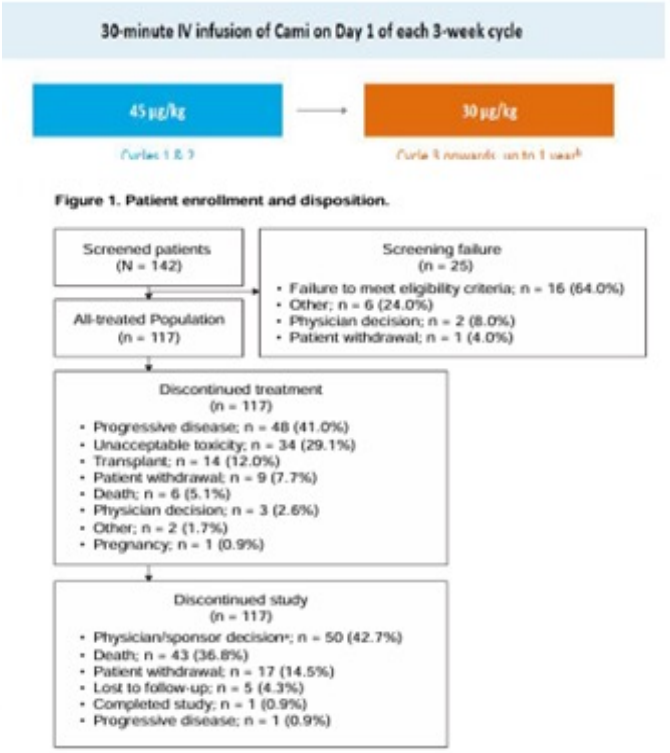
Analisi post HOC

ORR 31% vs 2.5%
Il 44% riduzione della lesione target >50% rispetto al 5%

Armand et Al. Blood Advance 2025

Studio di fase 2 con Camidanlumab Teresine in HD R/R





ORR 70%
CR 33%
mPFS 9.1 mesi

7% neurotossicità
poliradicolopatia

Herrera et Al. Blood Advance 2025

Un caso clinico di Linfoma di Hodgkin classico

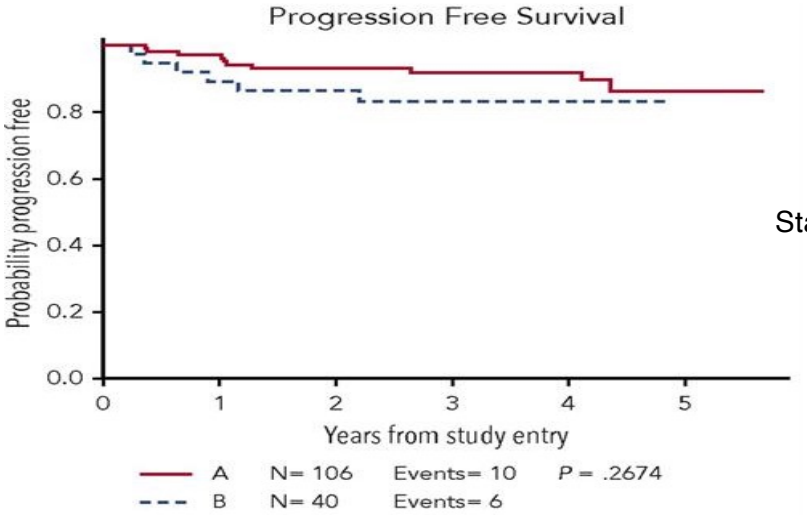
Donna 27 anni
2021 Linfoma di Hodgkin classico SN , stadio IIIS A per localizzazione nodale sovrasottodiaframmatica e splenica
Maggio 2021 avvio 6 ABVD RMC
Luglio 2021 recidiva splenica e nodale sottodiaframmatica
Febbraio 2022 salvataggio 2 BEGEV RMC
Maggio 2022 ASCT
Luglio 2022 consolidamento con Brentuximab per 16 cicli
Novembre 2025 CR

STANDARD OF CARE

RECIDIVA-REFRATTARIETÀ DOPO TERAPIA DI I^ LINEA

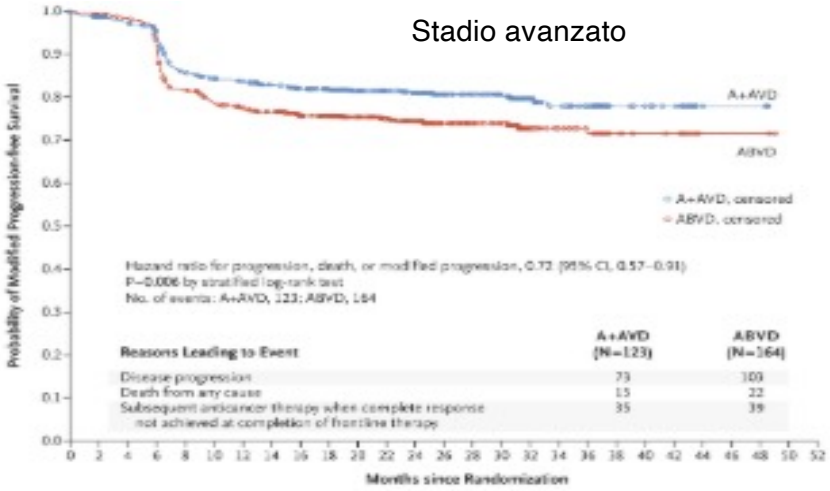
10% stadi iniziali

25% stadi avanzati



Stadio iniziale

Stadio avanzato



Connors JM et Al. N Engl J Med 2018; Stephens DM et Al. Blood 2019; Straus DJ et Al. Blood 2018

Prima linea di chemioterapia di salvataggio

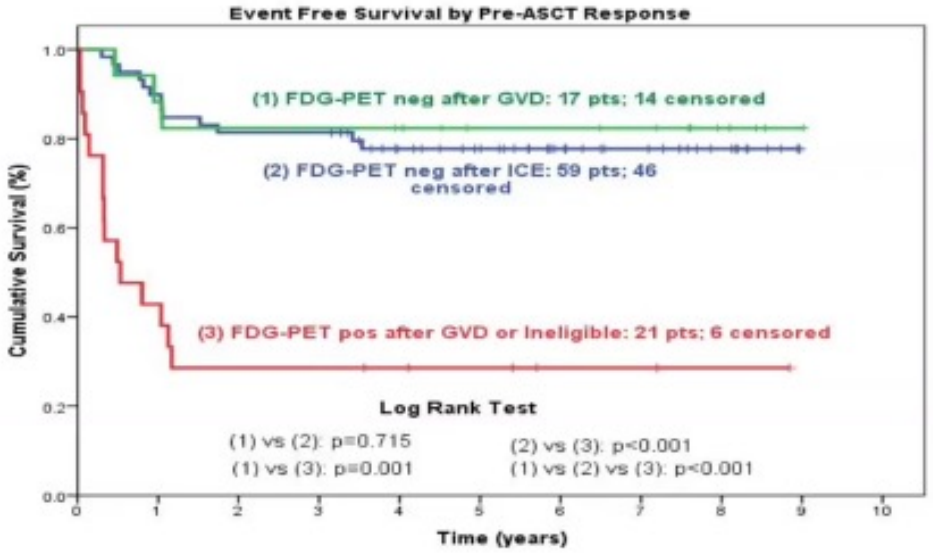
Table 1. Overview of first-salvage chemotherapy regimens since 2010

Study	N	Intervention	Refractory, n (%)	CR pre-ASCT	ORR pre-ASCT	PFS	OS
Josting et al (2010)[13] (RCT)	279	DHAP	0 (0)	CT: 24%	CT: 71%	3 years: 69% (no significant difference between arms)	3 years: 85% (no significant difference between arms)
Moskowitz et al (2010)[14]	105	ICE	48 (46)	PET/gallium: 61% CT: 33%	CT: 59%	4 years: 56%	4 years: 72%
Moskowitz et al (2012)[11]	97	ICE + GVD (PET-adapted sequential)	41 (42)	PET: 60% after ICE 78% after GVD	—	51 months: 70%	51 months: 80%
Labrador et al (2014)[15] (retrospective)	82	ESHAP	41 (50)	PET/gallium: 50%	PET/ gallium: 67%	Median PFS: 56 months	5 years: 73%
Santoro et al (2016)[16]	58	BeGEV	27 (46)	PET: 73%	PET: 83%	5 years: 59%	5 years: 78%

BeGEV, bendamustine, gemcitabine, and vinorelbine.

Driessen et Al. Hematology 2021

Importanza della CRM PET PRE ASCT



Fattore prognostico chiave CMR PRE ASCT

I pazienti con RMC prima del trapianto hanno una prognosi migliore

Se CRM PFS post ASCT intorno al 70-80%

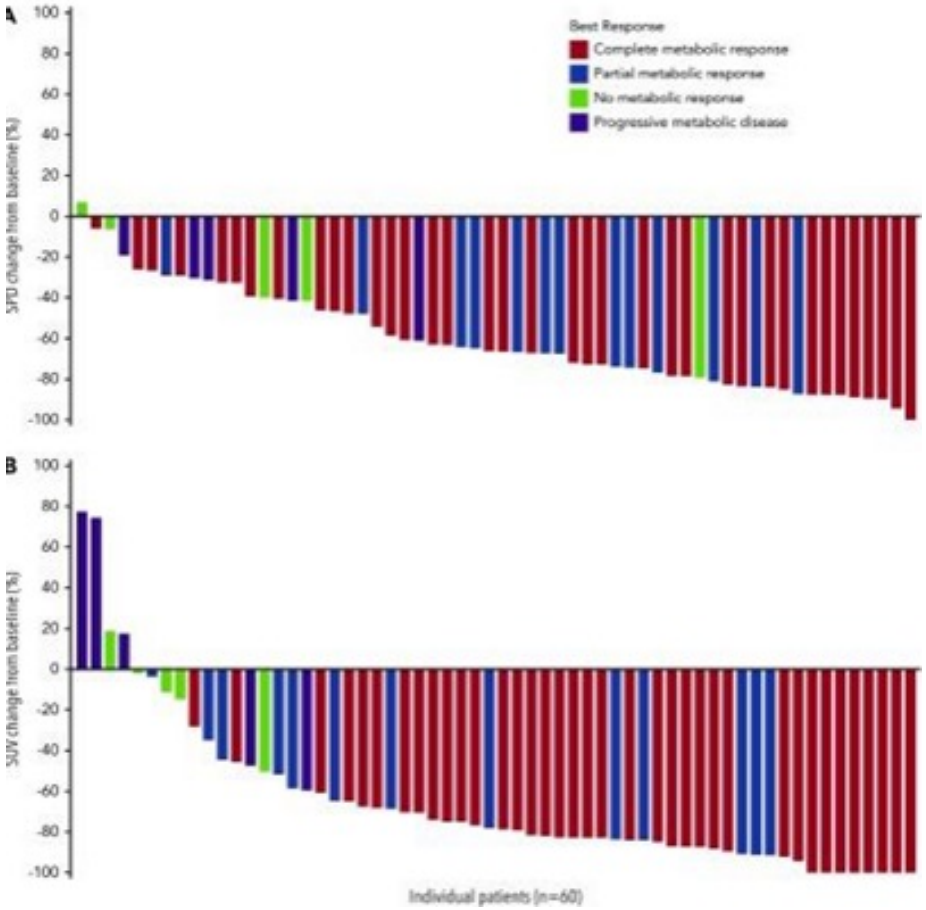
Moskowitz AJ et Al. Blood 2010 ; Linch DC et Al. Lancet 1993; Schmitz et Al. Lancet 2002

Terapie di salvataggio PET-adapted e BV based curano circa il 75% dei pazienti

	Regimen	n	% PET-neg	Post-transplant PFS/EFS
PET-adapted sequential therapy	ICE->GVD[1]	98	77%	78% @ 5 yrs
	BV->augICE[2]	65	83%	77%@ 5yrs
	BV->ICE[3]	56	66%	67% @ 2yrs
BV or bendamustine plus chemo combinations	BV-benda[4]	55	74%	70% % 2 yrs
	BV plus:			
	ICE[5]	39	74%	80% @ 2 yrs
	DHAP[6]	55	81%	74% @ 2 yrs (IIT)
	ESHAP[7]	66	70%	71% @ 30 m (IIT)
	Gem[8]	42	67%	NR
	BEGEV[10]	59	75%	77% @ 5yrs
	BV-nivolumab[9]	91	67%	77% @ 3 yrs (IIT)

Moskowitz C et Al.Blood 2012, Moskowitz AJ, ASH 2019; Herrera et Al. Ann Oncol 2018; LaCasce et al. Blood 2018 , Linch et Al. Lancet Hemat 2021; Kersten et Al. Hematologica 2021; Advani et Al. Blood 2021 ; Santoro et Al. Blood Adv 2021: Moskowitz AJ, JCO 2021

Brentuximab in combinazione con Nivolumab in HD R/R



62 pz
Dopo 4 cicli Bv+Nivo i pz procedevano con ASCT

ORR 82% CR 67 %
PFS a 3 anni 77%

E' un alternativa alla chemioterapia

Ben tollerato (neuropatia, rash , tiroiditi)

Herrera et Al. Blood 2018

Aggiunta di Brentuximab alla chemioterapia in pazienti con HD R/R

BV-cohort
BV +/− salvage chemotherapy

vs

Chemo-cohort
Standard salvage chemotherapy

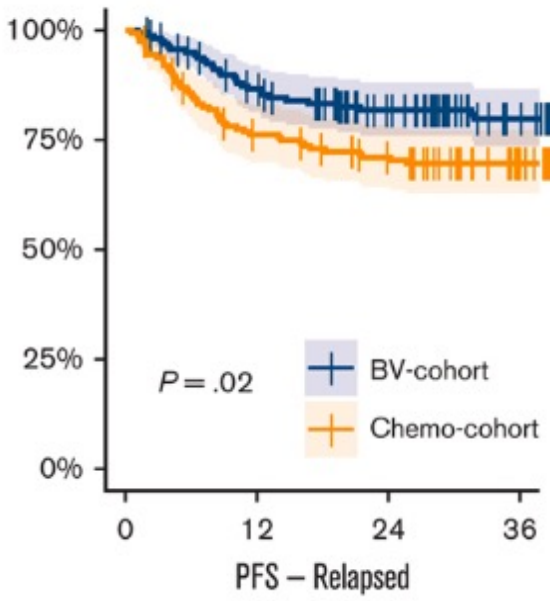
768 pz

Main outcomes:

- No significant differences in pre-ASCT CMR rate
- No significant differences in PFS

- Significant better OS in BV-cohort (92% vs 80%; $P < .001$), but likely due to treatment advances over time
- Sequential approach feasible, no PFS difference for patients with 1 or 2 lines of salvage treatment

- Relapsed patients: significant better PFS in BV-cohort (80% vs 70%, $P = .02$)
- Primary refractory patients: no difference in PFS and OS
- Patients with stage IV: significant better PFS in BV-cohort



Driessen et Al. Ash 2021; Driessen et Al. Blood Advance 2024

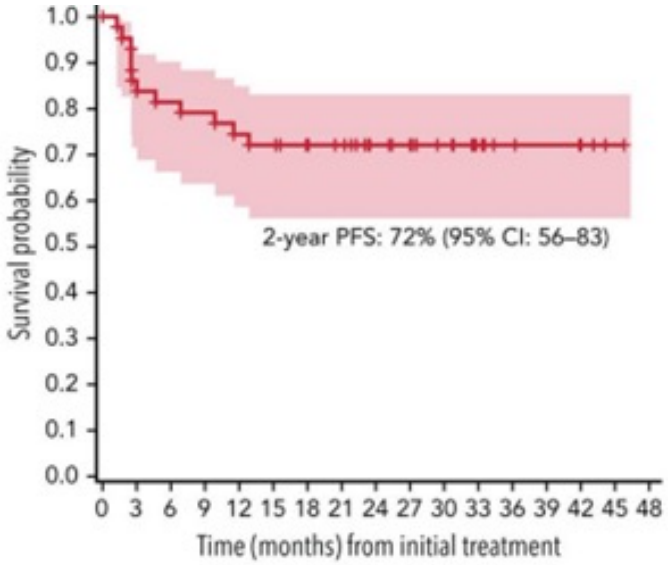
Terapie di salvataggio comprendenti inibitori PD1 raggiungono tassi di cura del 90 %

Regimen	n	% PET-neg	Post-transplant PFS/EFS
BV-nivolumab[1]	91	67%	91% @ 3 yr right after BV/nivo 77% @ 3yr (IIT)
Pembro-ICE[4]	37	86.5%	87.2% @ 2 yr
Nivo->NICE[3]	42	91%	90% @ 1 yr
Pembro-GVD[2]	38	95%	91% @ 5yr

Advani et Al. Blood 2021; Moskowitz AJ et Al . JCO 2021; Mei et Al. Blood 2022; Lock et Al. JAMA 2023

Nivolumab ICE terapia di salvataggio in HD R/R alto rischio

Characteristics	n (%)
Total	43 (100)
Male sex	26 (60)
Age (median, range), y	35 (18-70)
Stage at diagnosis	
I-II	17 (40)
III-IV	26 (60)
Frontline regimen	
A(B)VD	37 (86)
BV+AVD	2 (5)
BV→ABVD (sequential)	1 (2.3)
ABVD/BV+AVD	1 (2.3)
ABVE+PC	1 (2.3)
BEACOPP escalated	1 (2.3)
Stage at baseline	
I-II	17 (40)
III-IV	26 (60)
B symptoms at baseline	15 (35)
Extranodal disease at baseline	16 (37)
Bulky disease at baseline (>5 cm)	8 (19)
Prior radiation	5 (12)
Primary refractory	19 (44)
Relapsed	24 (56)



PFS a 2 aa 72%
OS a 2 aa 95%

Immunoterapia sembra senibilizzare alla chemioterapia

Dopo NIVO
ORR 81% CR71%

Dopo il termine della terapia NIVO+ICE
ORR 93% CR91%

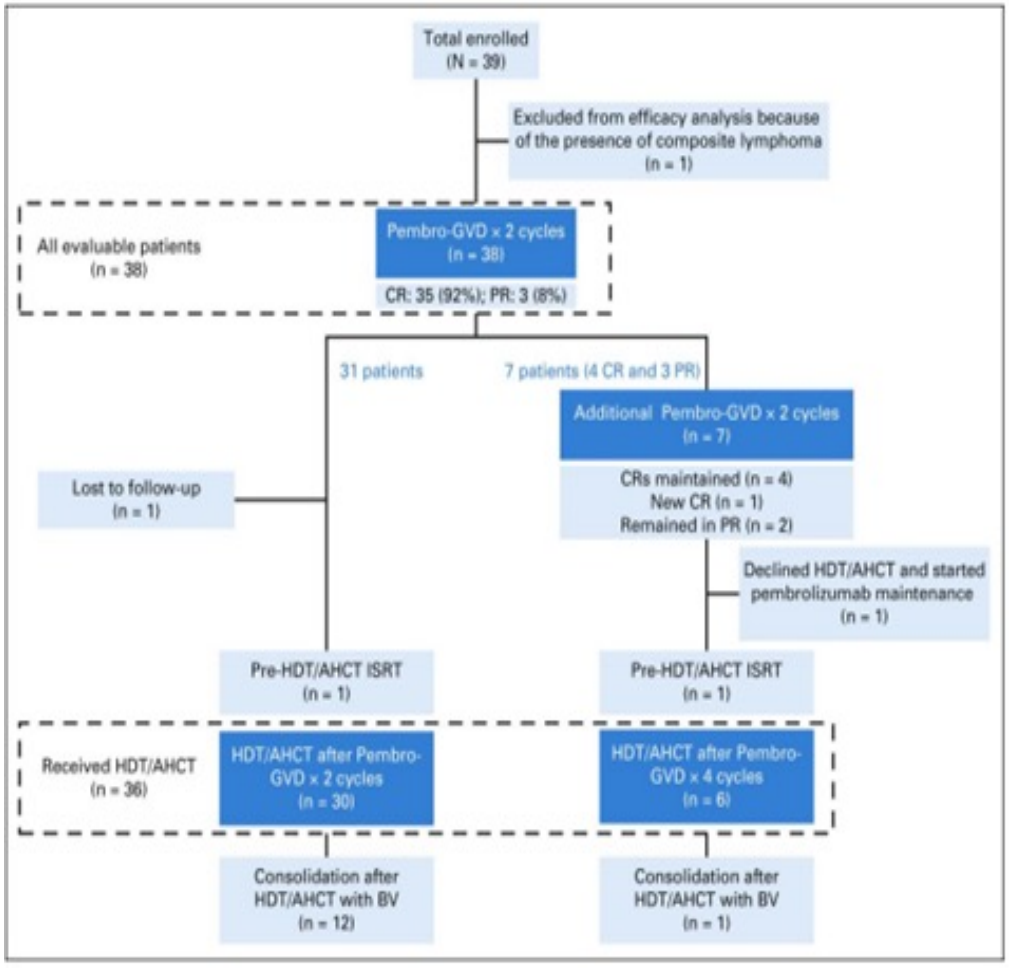
26 pz ASCT dopo solo NIVO

33 pz ASCT dopo il termine della terapia

Ben tollerato
Grado 3/4 nel 12 %
Ipo-ipertiroismo
Epatite
Colite

Mei et Al. Blood 2022

Pembrolizumab GVD come seconda linea di terapia per HD R/R



39 pz
41% refrattari
38% recidiva entro 12 mesi
CR dopo 4 cicli primary endpoint .
ORR 100% CR 95%

36 pz ASCT
13 pz mantenimento BV
PFS a 30 mesi 96%

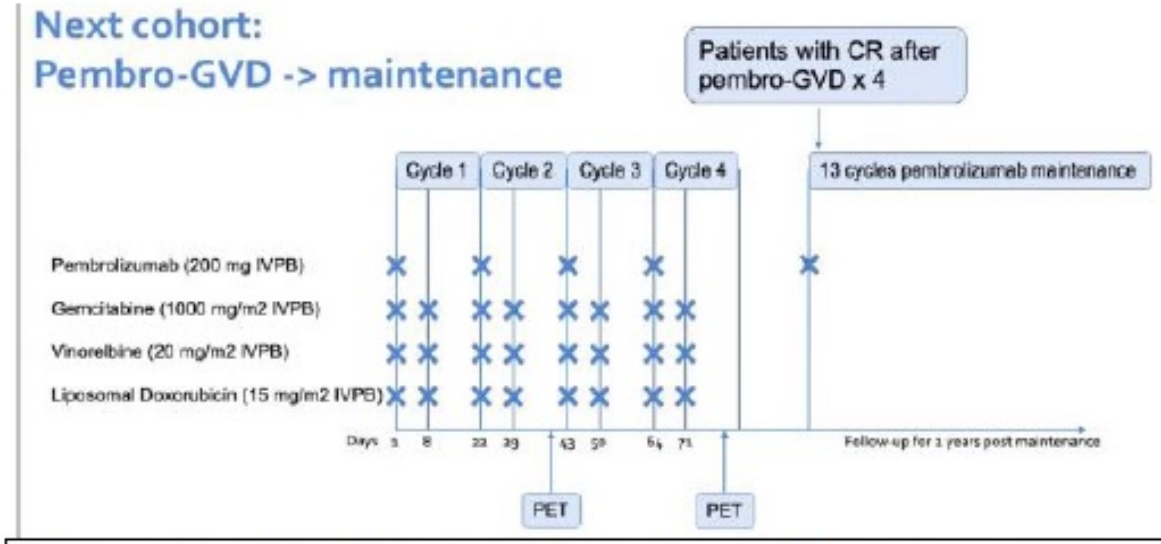
Ben tollerato

Grade 3/4 :	Transaminite	4
	Neutropenia	4
	Mucosite	2
	Tiroidite	1
	Rash	1

Moskowitz AJ et Al. J Clin Oncol 2021

Pembrolizumab GVD come seconda linea di terapia per HD R/R
Approccio chemo free ?

(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

10 relapses:
- 4 pts during pembro maintenance
- 3 pts within 6 months of last pembro
- 3 pts beyond 6 months of last pembro

9 pts proceeded to transplant following:
- BV/benda (n=1)
- BV-ICE (n=1)
- ICE (n=1)
- BV/nivo, ICE, RT (n=2)
- Pembro-GVD (n=2)
- Pembro-GVD, ICE (n=1)

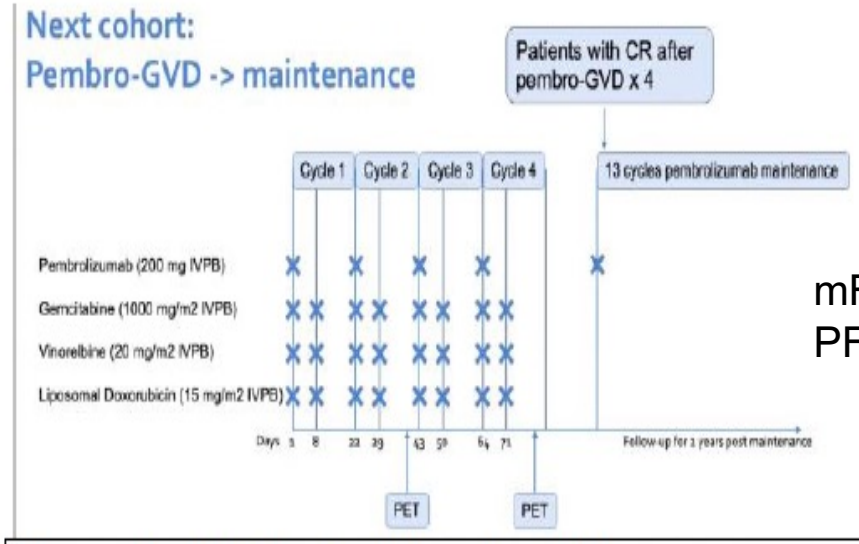
1 pt not transplanted due to comorbidities
- receiving palliative pembro plus gemcitabine, achieved CR

40 pz
36 pz CR (90%)
25 mantenimento
10 relapse

Moskowitz et Al . Blood 2024

Pembrolizumab GVD come seconda linea di terapia per HD R/R
Approccio chemo free ?

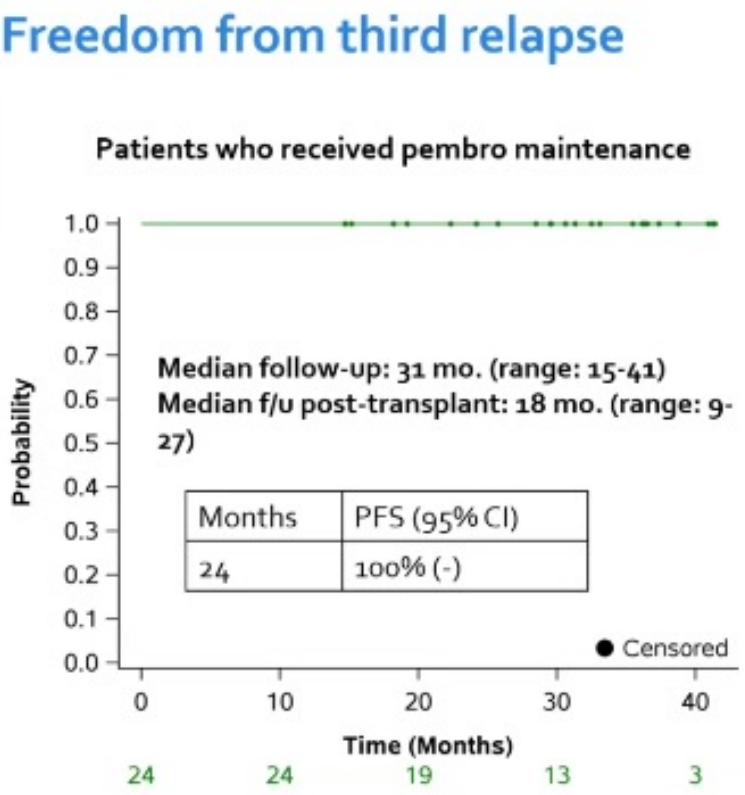
(patients in CR after Pembro-GVD x 4 will receive 13 cycles of Pembrolizumab manteinance)



Unprecedented CR rate with pembro GVD

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

mFU di 26 mesi
PFS a 2 anni 56%



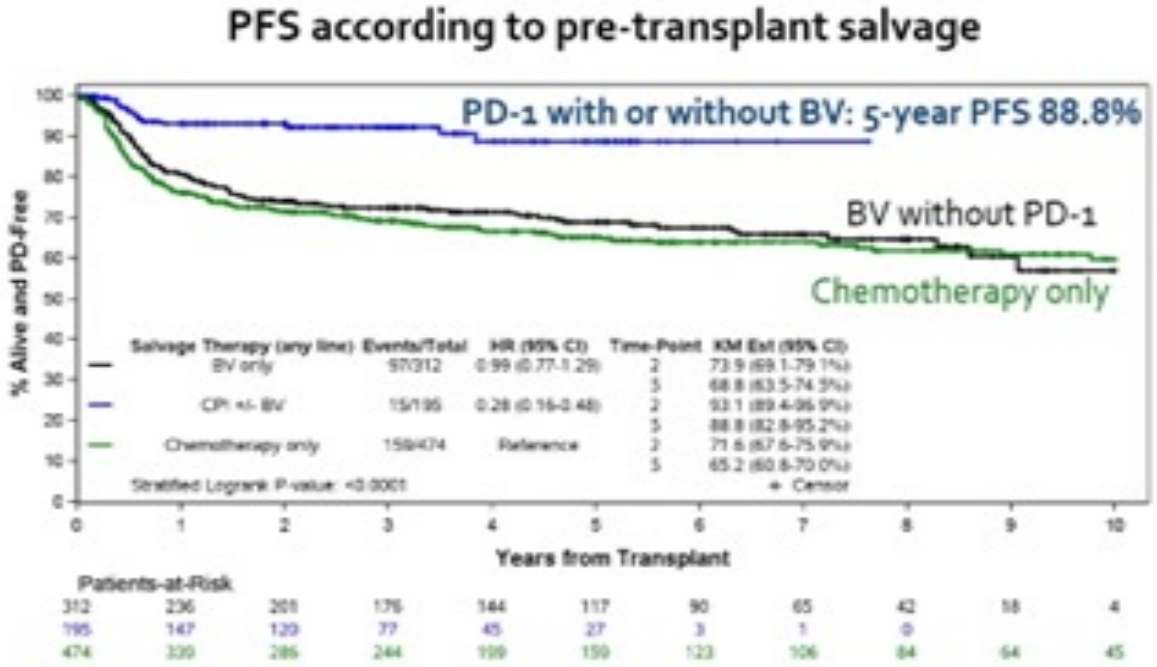
Moskowitz et Al . Blood 2024

Terapie di salvataggio basate su inibitori PD1 migliorano l'outcome

Studio multicentrico, retrospettivo

981 pz trapiantati 2010-2021
PRE asct
700 pz chemiotx
65 pz PD1 (62 pz Nivo+BV)

35% refrattari
35% malattia extranodale
35% sintomi B



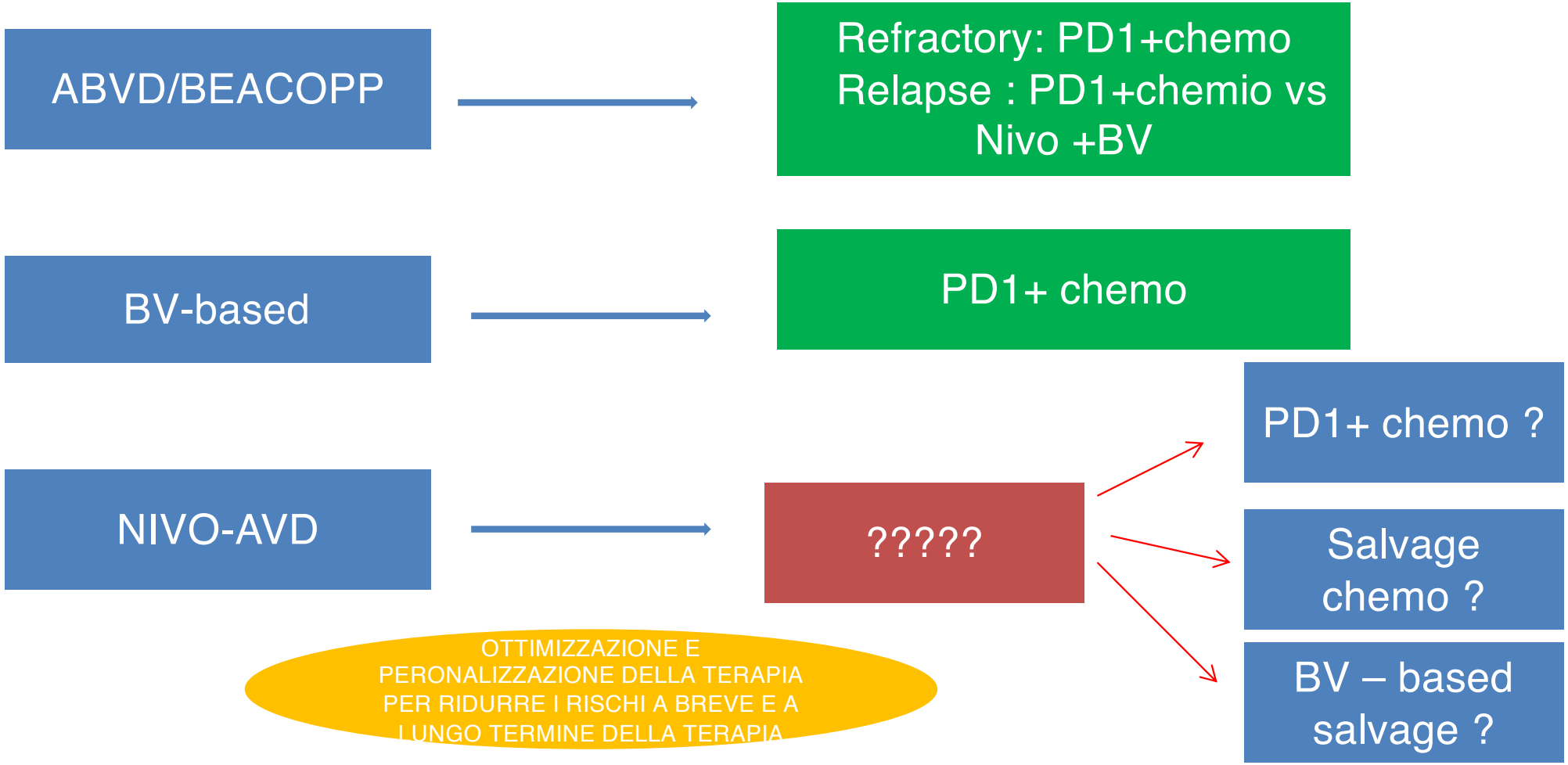
Desai et Al . ASH 2023

Table 2. Efficacy of PD-1 inhibitors in relapsed/refractory classic Hodgkin lymphoma

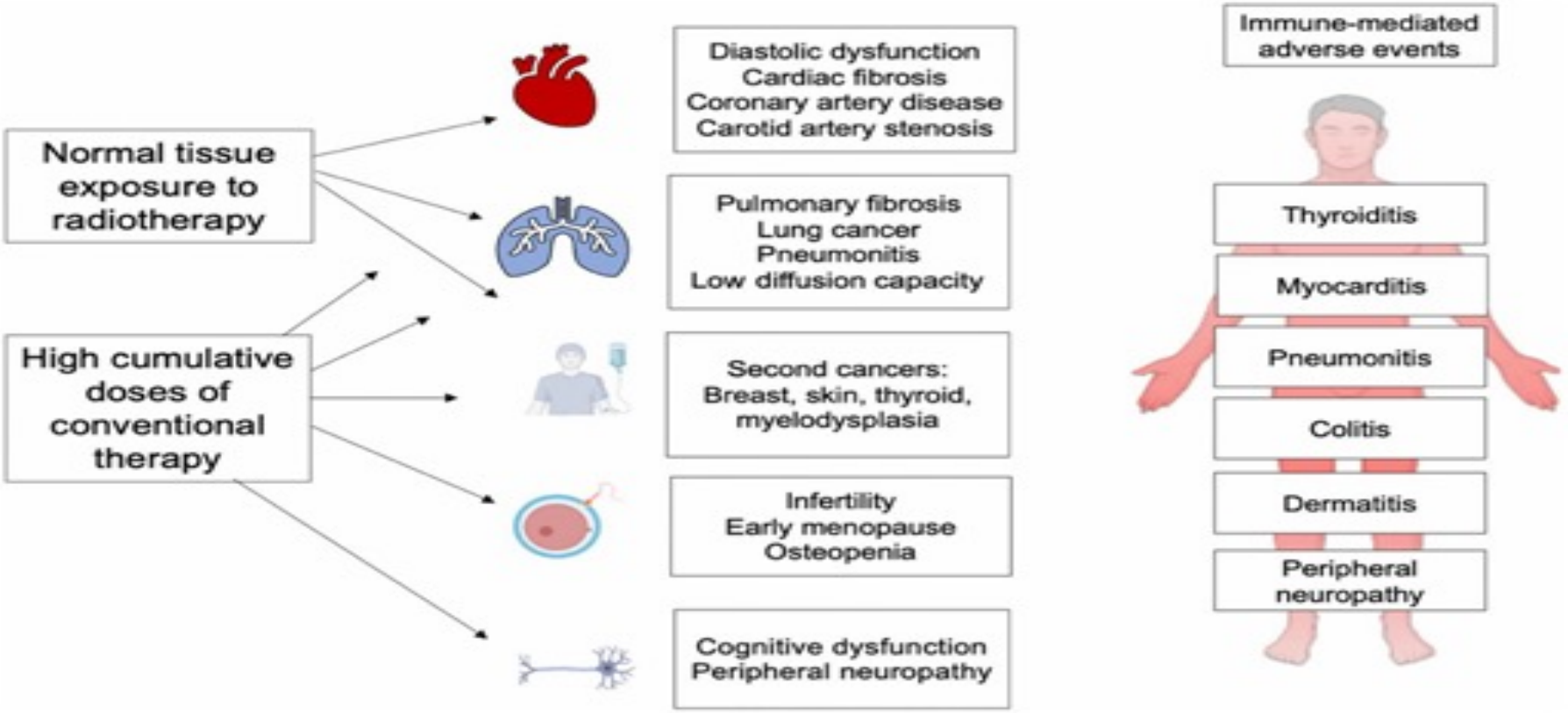
Author, year	Study design	Treatment setting	Number of patients	Key efficacy data	Key toxicity data
Moskowitz et al 2021[17] Moskowitz et al 2022[18]	Pembrolizumab-GVD × 2–4 cycles, followed by ASCT	ASCT eligible	39	ORR 100%, CR 95% 30-month PFS 96%	Grade ≥3 hepatoxicity 10%; grade ≥3 neutropenia 10%
Mei et al 2022[22]	Nivo × 3, Nivo × 3 and/or Nivo-ICE × 2, then ASCT	ASCT eligible	43	Nivo alone: ORR 89%, CR 78%, 2-year PFS 96% Nivo-ICE: ORR 100%, CR 89%, 2-year PFS 86%	1 case of grade 4 encephalitis; 1 case of grade 3 colitis
Bryan et al 2023[20]	Pembrolizumab-ICE × 2, pembro × 1	ASCT eligible	42	ORR 97.3%, CR 86.5%, 2-year PFS 87.2%	Grade ≥3 hepatoxicity 5%; grade ≥3 neutropenia 36%; 2 grade 5 events
Advani et al 2021[16]	BV+nivolumab	ASCT eligible	93	ORR 85%, CR 67%, 3-year PFS 77%	Grade ≥3 pneumonitis 3%, grade ≥3 rash 1%, grade ≥3 AST elevation 1%, Guillain-Barre syndrome 1%
Ding et al 2023[28]	Tislelizumab+GemOx × 6–8, followed by tislelizumab maintenance	Relapsed/refractory; majority without prior ASCT	30	ORR 100%, CR 96.7%, 12-month PFS 86%	Grade ≥3 neutropenia 3%, grade ≥3 transaminase elevation 3%
Kuruvilla et al 2021[32]	BV vs pembrolizumab	After prior ASCT or ineligible for ASCT	153	Median PFS 13.2 vs 8.3 mos	Grade ≥3 pneumonitis 4% (1 grade 5 event); grade ≥3 neutropenia 2%
Chen et al 2019[38] Armand et al 2023[39]	KEYNOTE-087: pembrolizumab every 3 weeks up to 2 years	After prior ASCT/BV or salvage chemo/BV or ASCT	210	ORR 71.4%, median DOR 16.6 mos, median PFS 13.7 mos, median OS NR, 5-year OS 70.7%	Grade ≥3 neutropenia 2.4%; grade ≥3 pericarditis 1%; grade ≥3 diarrhea 1%
Ansell et al 2023[30] Armand et al 2018[39]	CheckMate 205: Nivo every 2 weeks until progression or unacceptable toxicity	After prior BV or ASCT or ASCT/BV	243	ORR 71.2%, median DOR 18.2 mos, median PFS 15.1 mos, median OS NR, 5-year OS 71.4%	Grade ≥3 hepatitis 4.9%; grade ≥3 colitis 2.1%; grade ≥3 pneumonitis 0.8%

ASCT, autologous stem cell transplant; AST, aspartate aminotransferase; BV, brentuximab vedotin; CR, complete response; DOR, duration of response; GemOx, gemcitabine, oxaliplatin; GVD, gemcitabine, vinorelbine, liposomal doxorubicin; ICE, ifosfamide, carboplatin, etoposide; mos, months; NR, not reached; ORR, objective response rate; PFS, progression-free survival.

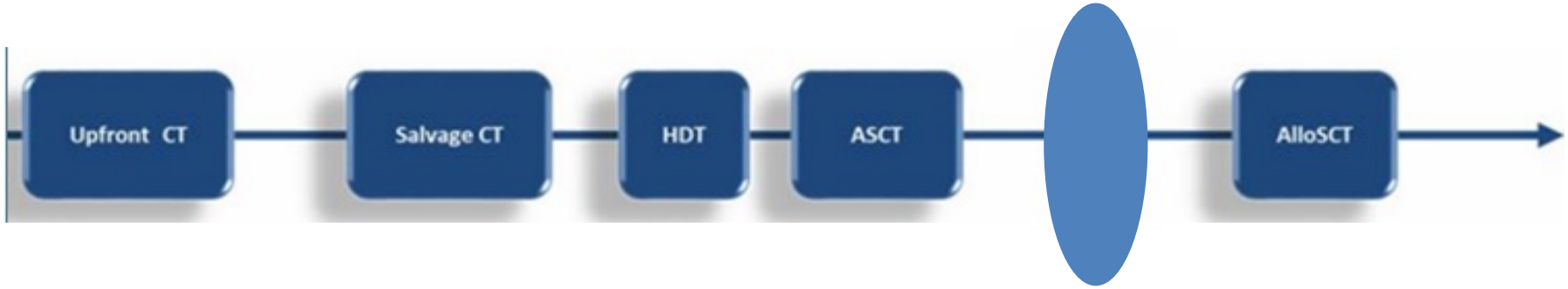
Qual'è la prossima terapia di salvataggio ?



Tossicità a breve e lungo termine della terapia dell'Hodgkin



Possibile scenario nel HD R/R
LA RECIDIVA POST TRAPIANTO AUTOLOGO



- Keynote-013
- Keynote-087
- Keynote-204
- Checkmate-205

Milrod et Al. Frontiers in Oncology 2024

Regimen arm	Pembrolizumab	Pembrolizumab	Nivolumab	Tislelizumab
Trial	Keynote 087	Keynote 204	Checkmate 205	NCT03209973
Median FU	5 years	2 years	5 years	33.8 mo
Participants #	210	151	243	70
Participant characteristics	• Median number of previous therapies: 4 • Relapsed after autoSCT: 71%	• Median number of previous therapies: 2 • Relapsed after autoSCT: 37%	• Median number of previous therapies: 4 • Relapsed after autoSCT: 100%	• Median number of previous therapies: 3 • Relapsed after autoSCT: 18.6%
ORR	**71.4%**	**65.6%**	**71.2%**	**87.1%**
CR	27.6%	25%	21.4%	67.1%
DOR	16.6 mo	20.7 mo	18.2 mo	31.3 mo
PFS	**63.6%** at 6 mo **72.4%** at 12 mo **31.4%** at 4 y	**53.9%** at 12 mo **35.7%** at 24 mo	**68%** at 12 mo **50%** at 24 mo **39%** at 4 y	**31.5** mo
OS	**99.5%** at 6 mo **96.2%** at 12 mo **81.4%** at 4 y	**90.9%** at 12 mo **80.5%** at 24 mo	**93%** at 12 mo **87%** at 24 mo **81%** at 4 y	Not reached

Milrod et Al.Frontiers in Oncology 2024

Brentuximab in monoterapia in pazienti recidivati dopo ASCT

Table 2. Key Response Results

Parameter	No. of Patients (N = 102)	%
Objective response	76	75
Complete remission	35	34
Partial remission	41	40
Stable disease	22	22
Progressive disease	3	3
Not evaluable	1	1
Duration of objective response, months		
Median	6.7	
95% CI	3.6 to 14.8	
Duration of response for patients with complete remission, months (n = 35)		
Median	20.5	
95% CI	10.8 to NE	
Progression-free survival, months		
Median	5.6	
95% CI	5.0 to 9.0	
Overall survival, months		
Median	22.4	
95% CI	21.7 to NE	

Abbreviation: NE, not estimable.

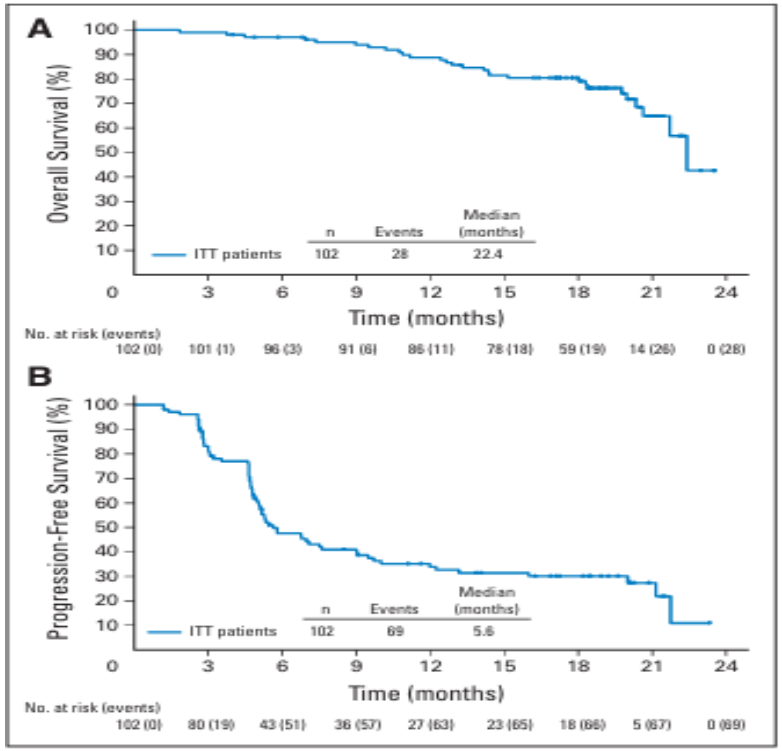


Fig 2. Secondary end points of overall survival (A) and progression-free survival (B). ITT, intent to treat.

102 pz
Mediana n terapie precedenti 2
ORR 75%
CR 34%

mPFS 5.6 mesi

mDOR in CR 21.7 mesi

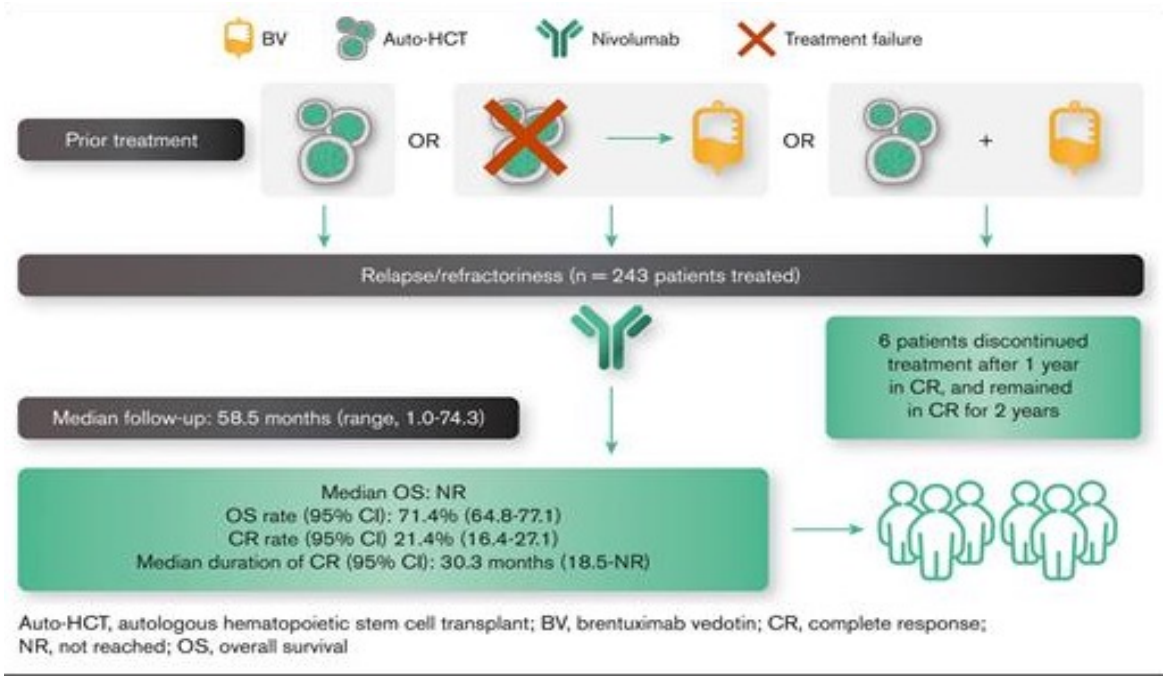
Younes et Al. JCO 2012

Nivolumab in HD R/R dopo ASCT Check Mate 205

Studio registrativo, multicentrico multicorte (Europa, Nord America), fase 2
243 pz
Mediana LOT 4
3 coorti

-A BV naive
-B BV after ASCT
-C BV before and after ASCT

Follow up 5 anni ~
ORR 71% CR 21.4%
Tempo mediano alla risposta 2 mesi
mPFS 15.1 mesi
OS non raggiunta



Younes et al. Lancet Oncol 2016; Armand et al, J Clin Onco 2018; Ansell et al. Blood Adv 2023

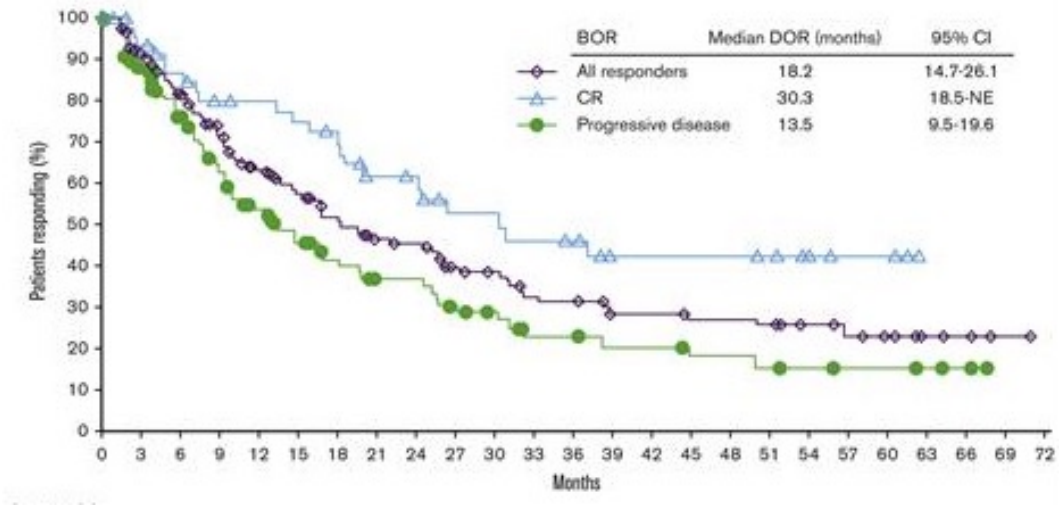
Nivolumab in HD R/R dopo ASCT CHECK MATE 205

mDOR 18,2 mesi
DOR CR 30,3 mesi

65 pz deceduti , 36 per PD
57 pz in CR sono stati sottoposti ad allo-HCT (a 2 anni CR 50%)

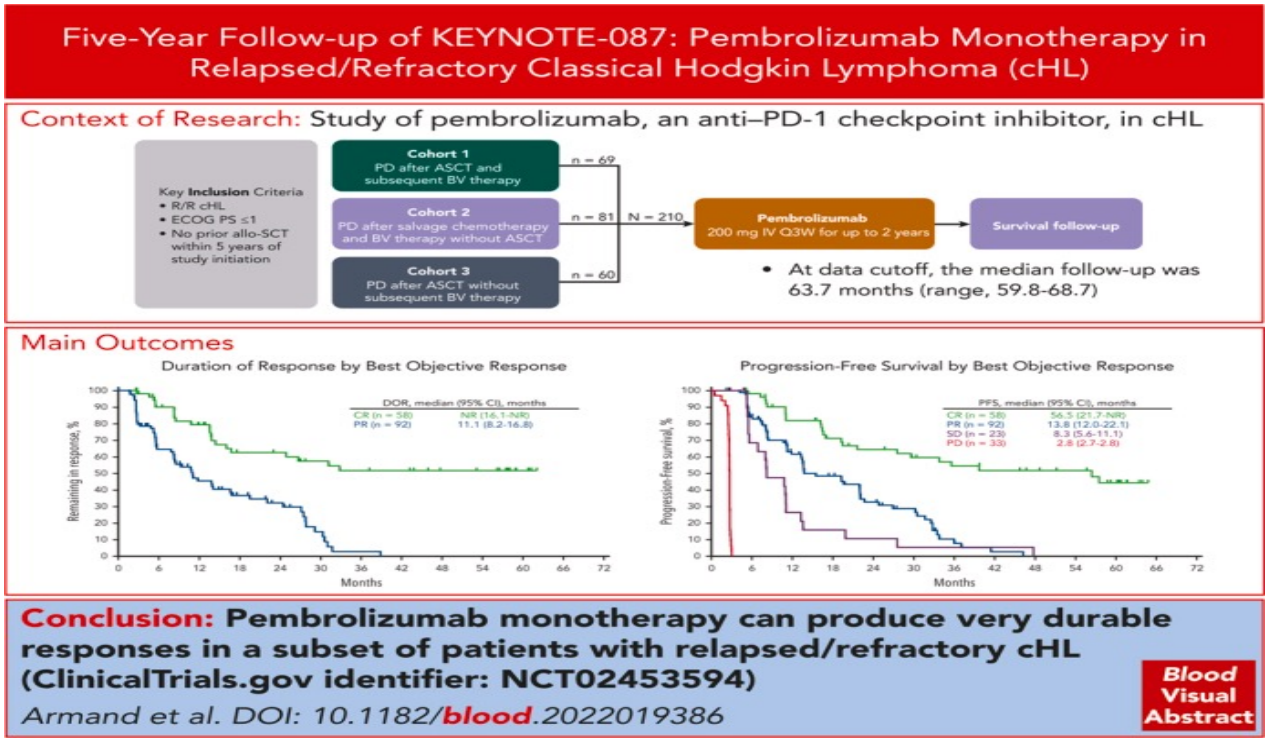
12 pz in CR persistente > 1aa
STOP

6 in follow up per 48 mesi
3 PD
3 ritrattati (2 CR e 1 PR)



Younes et al. Lancet Oncol 2016; Armand et al, J Clin Onco 2018; Ansell et al. Blood Adv 2023

Pembrolizumab in RR HD KEYNOTE -087



ORR 71%
mFU 62.2 mesi
mPFS 13.7 mesi
mOS NR

CR
mDOR NR
51% DOR>60 mesi
mPFS 56.6 mesi
mOS NR
Risposta duratura

I tassi di PFS e OS a 5 anni dei pz che hanno raggiunto la CR sono stati rispettivamente del 44.3% e del 82.7 %

Kuruvilla et Al. Lancet Oncol 2021; Chen et A. Blood 2019, Armand et Al. Blood 2023

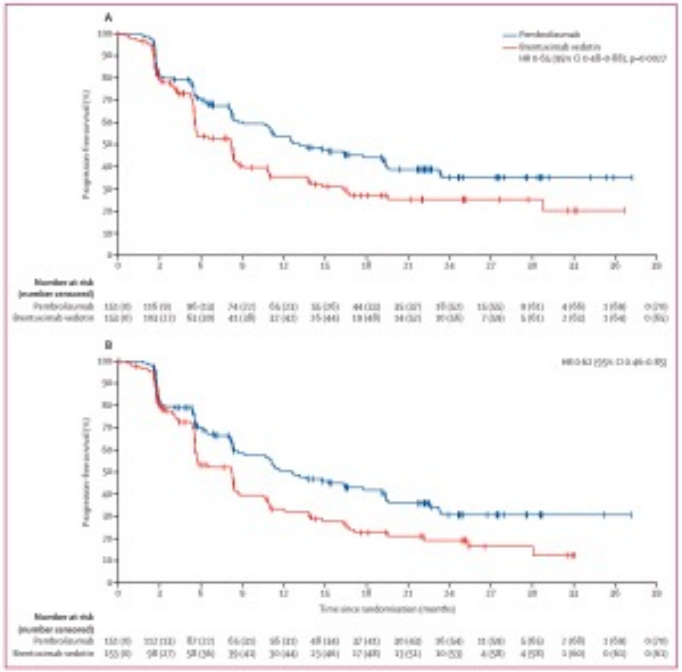
PEMBROLIZUMAB versus BRENTUXIMAB in R/R HD , studio di fase 3 randomizzato , multicentrico KEYNOTE-204

304 pz
mFU di 2 anni
44% malattia refrattaria
37 % ASCT
18% 1 LOT

PEMBROLIZUMAB (dopo 2 LOT) ORR 68% CR26%
mPFS 13.2 mesi m DOR 20.7 mesi

BRENTUXIMAB (dopo 3 LOT)
ORR 50% CR 26% mPFS 8.3 mesi mDOR 13.8 mesi

Tempo mediano alla risposta 2.8 mesi simile in entrambi i bracci
Refrattari mPFS 13.5 mesi con Pembro vs 5.5 mesi Brentuximab
No dati di sopravvivenza



Kuruvilla er A. Lancet Oncol 2021 ; Kuruvilla er A. Leuk lymphoma 2025

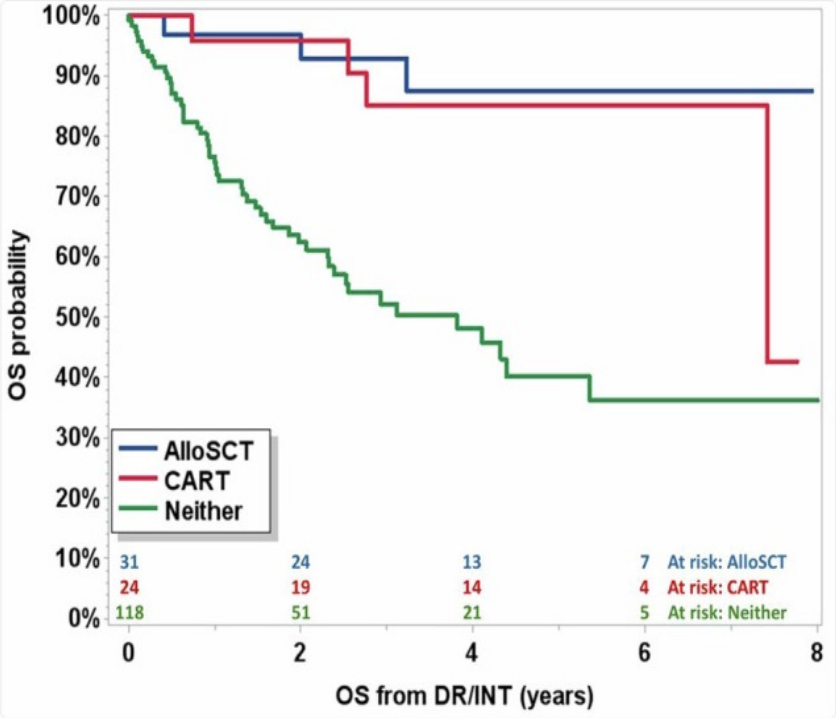
OUTCOMES IN PATIENTS WITH DR/INT cHL: a real world analysis from 15 U.S. academic centers

173 pz

Brentuximab dopo una mediana di 2 linee di terapia
61% BV monotx
14% BV+ Nivo
ORR 56% (21%CR 35%PR) mPFS 166 gg

Anti PD1 dopo mediana di 3 linee di terapia 78% monotx (72% Nivo; 28% Pembrolizumab)
ORR 55% (19%CR 36%PR) mPFS 225 gg

mOS2 (sopravvivenza dal tempo della DR/INT) 7.4 anni



Vooheers et al. Blood Cancer J 2025 Mar 26;15(1):45

OUTCOMES IN PATIENTS WITH DR/INT cHL: a real world analysis from 15 U.S. academic centers

mOS 1 (sopravvivenza dalla diagnosi) 14.8 anni

Non c'è differenza in OS1 fra DR e INT

mOS 1 AFTER ASCT 19.1 years vs NO ASCT 8.6 years

- RECHALLENGE anti PD1 dopo DR/INT mPFS 237 giorni

- RECHALLENGE BV dopo DR/INT mPDF 183 giorni

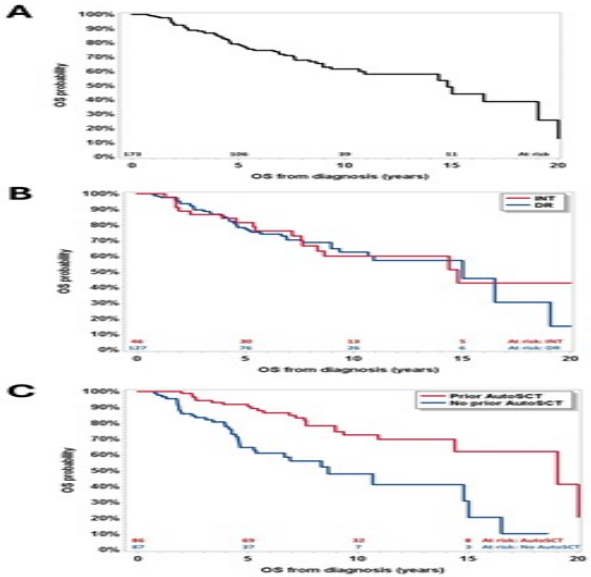
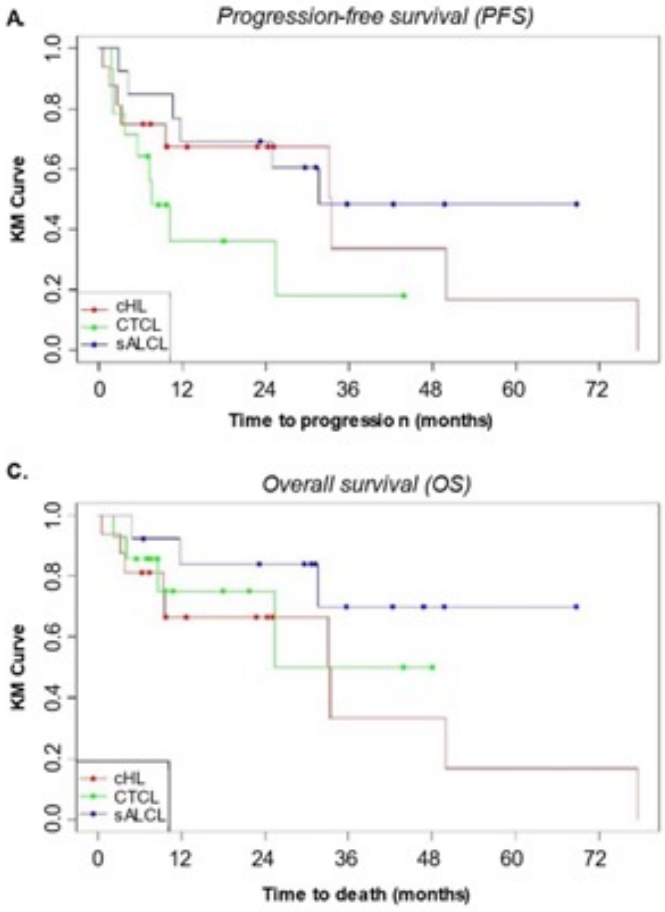
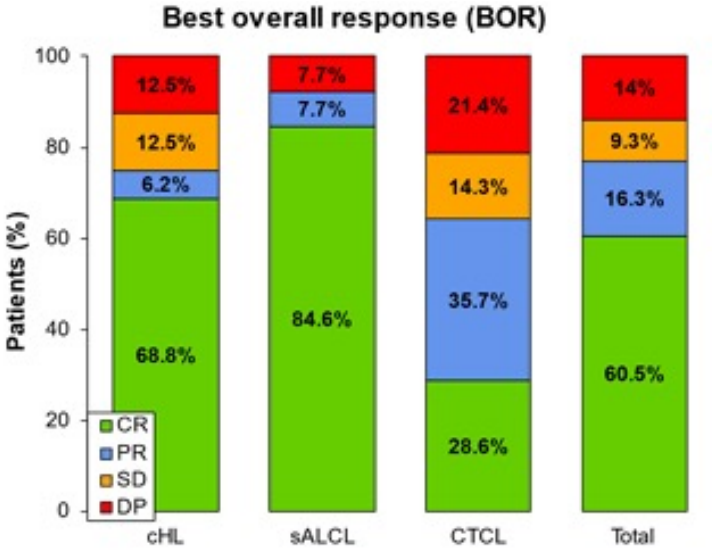


Fig. 1 Overall survival from diagnosis (OS-1). **A** the full cohort, **(B)** cohort stratified by INT (red) or DR (blue), **(C)** cohort stratified by prior ASCT (red) or no prior ASCT (blue) at the time of DR/INT.

Vooheers et al. Blood Cancer J 2025 Mar 26;15(1):45

Studio Believe : ritrattamento con Brentuximab





43 pz
16 cHL
13 sALCL
14 CTCL

Sureda et Al. Cancer 2025

CPI risensibilizzano alla chemioterapia

Chemotherapy after PD-1 inhibitors in relapsed/refractory Hodgkin lymphoma: Outcomes and clonal evolution dynamics

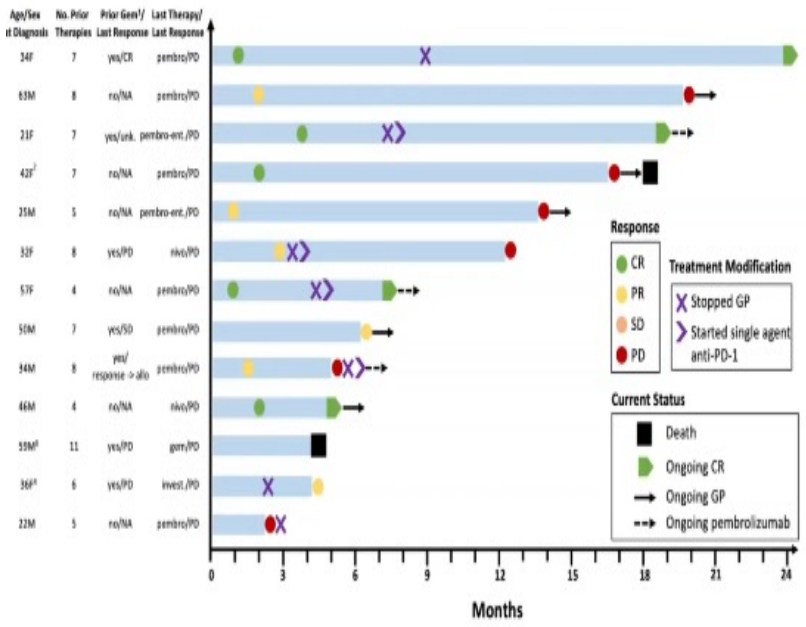
Eleonora Calabretta[1,2] | Anna Guidetti[3,4] | Francesca Ricci[2] | Martina Di Trani[1] | Chiara Monfrini[3] | Massimo Magagnoli[2] | Stefania Bramanti[2] | Davide Maspero[5,6] | Lucia Morello[2] | Michele Merli[7] | Alice Di Rocco[8] | Alex Graudenzi[6,9] | Enrico Derenzini[10,11] | Marco Antoniotti[5,9] | Davide Rossi[12,13,14] | Paolo Corradini[3,4] | Armando Santoro[1,2] | Carmelo Carlo-Stella[1,2]

28 pz trattati con anti-PD-1 (marzo 2017–novembre 2020).
mediana 4 linee precedenti
100% brentuximab; 64% ASCT
Risposta alla chemioterapia somministrata dopo anti-PD-1 : ORR 93% CR 82% PR 11%
mFU 21 mesi, **a 2anni PFS 70.7%** e **OS 80%**
25/28 bridged verso trapianto allo-SCT o ASCT

Effectiveness of chemotherapy after anti-PD-1 blockade failure for relapsed and refractory Hodgkin lymphoma

Beatrice Casadei [1], Lisa Argnani [1], Alice Morigi [1], Ginevra Lolli [1], Alessandro Broccoli [1], Cinzia Pellegrini [1], Laura Nanni [1], Vittorio Stefoni [1], Paolo E Coppola [1], Matteo Carella [1], Michele Cavo [1], Pier Luigi Zinzani [1]

Gemcitabina + Pembrolizumab dopo fallimento di CPI in HD RR



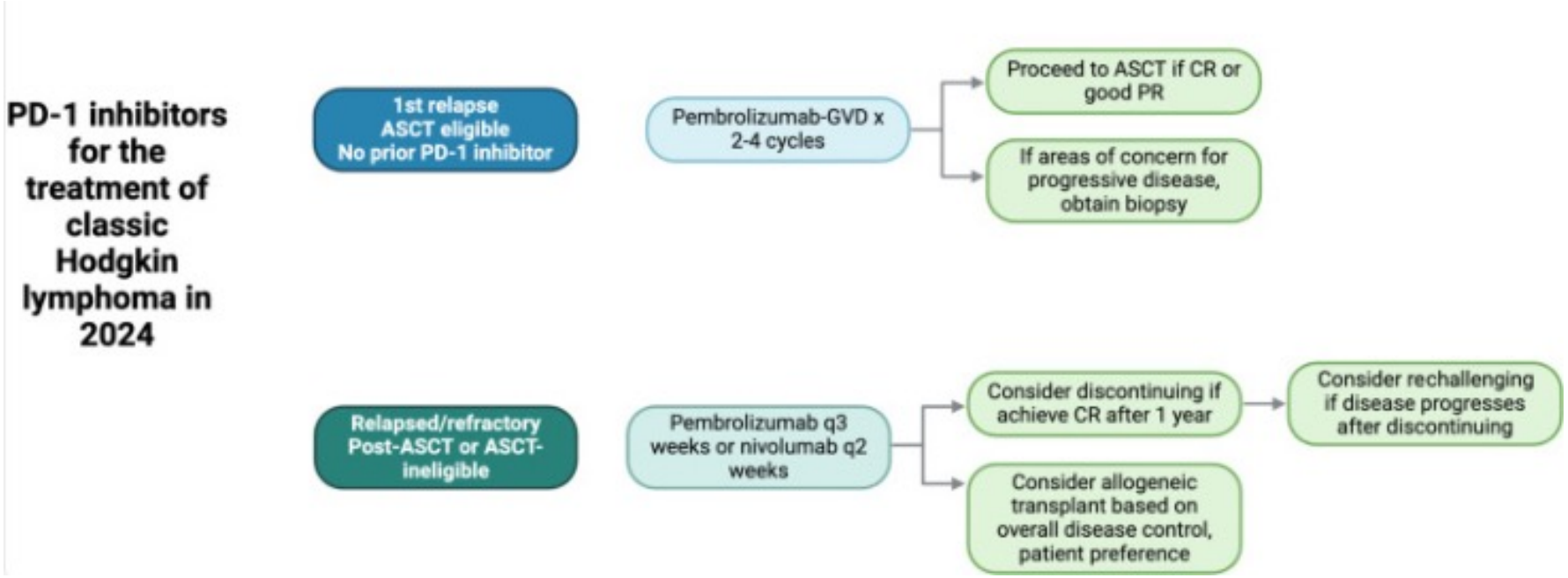
- N=13 (11 progressed on PD-1)
- ORR: 85%
- CR: 38%

Details of prior therapies	
Any checkpoint inhibitor	13 (100)
Pembrolizumab	11 (85)
Nivolumab	9 (69)
Brentuximab vedotin	13 (100)
Gemcitabine	7 (54)
History of HDT/ASCR	10 (77)
History of AlloSCT	3 (23)
Last therapy prior to GP	
Checkpoint inhibitor	11 (85)
Monotherapy	9 (69)
Combined with entinostat	2 (15)
Other	2 (15)
Response to last therapy	
POD	13 (100)
Other	0 (0)

Gemcitabina :
Deplezione della cellule di derivazione mieloide soppressorie
Aumento degli antigeni del MCH I

Stuver et Al. British J of Haematology 2024

Gli inibitori di PD-1 hanno cambiato lo standard di cura del linfoma di Hodgkin classico ?



Kuczmarski, Lynch ASH Ed program 2024

CONCLUSIONI

Brentuximab Vedotin e anticorpi anti PD-1 sono componenti principali delle strategie terapeutiche di prima e seconda linea

Le terapie basate sull'utilizzo di anticorpi anti PD-1 hanno trasformato il paradigma terapeutico del Linfoma di Hodgkin

Le combinazioni con anticorpi anti PD-1 (con chemioterapia o BV) determina risposte profonde e durature nel pre ASCT

Gli anticorpi di nuova generazione (ac anti CD25, CAR-T, bispecifici) sono promettenti nella malattia resistente a BV / anticorpi anti PD-1

Direzione futura per trattare i pazienti con strategie chemo free, immunoterapia target per ridurre al massimo le tossicità tardive