POST-NEW ORLEANS 2022
Novità dal Meeting della Società Americana di Ematologia

Novità dal Meeting della Società Americana di Ematologia

Milano
Teatro Dal Verme
2-3-4 Febbraio 2023

Linfoma di Hodgkin

Chiara Rusconi
Ematologia
Fondazione IRCCS Istituto Nazionale Tumori
Milano

DICHIARAZIONE

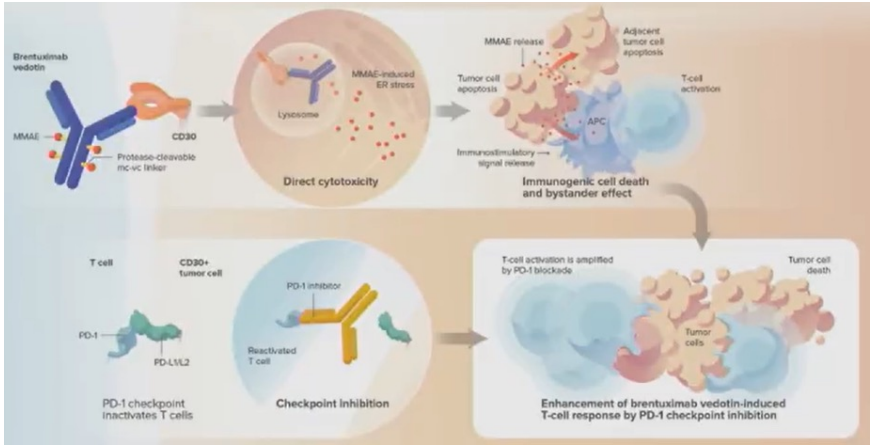
Chiara Rusconi

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario: **NIENTE DA DICHIARARE**
- Consulenza ad aziende con interessi commerciali in campo sanitario: **NIENTE DA DICHIARARE**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario: **CELGENE**
- Partecipazione ad Advisory Board: **TAKEDA, JANNSEN, ITALFARMACO**
- Titolarietà di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario: **NIENTE DA DICHIARARE**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario: **NIENTE DA DICHIARARE**
- Partecipazione a congressi: **TAKEDA, GILEAD, NOVARTIS, ROCHE**

AN+AD first line for Advanced Stage cHL

Lee H et al, abs 0314



synergistic effect BV+nivo

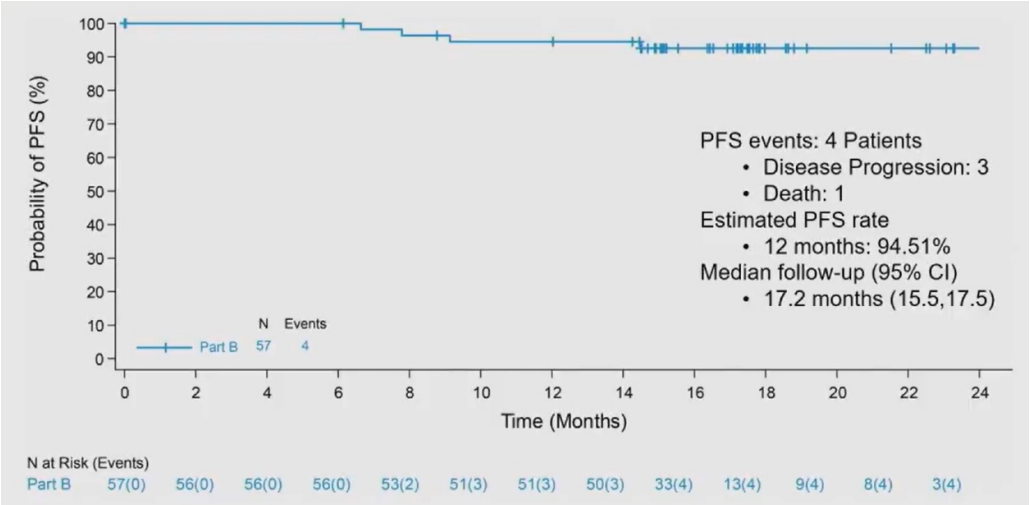
- SGN35-027 (NCT03646123) is an open-label, multiple part, multicenter, phase 2 clinical trial
- Part B enrolled patients with Stage II bulky mediastinal disease (≥10 cm), Stage III, or Stage IV cHL
- Patients received up to 6 cycles of AN+AD
  - BV 1.2 mg/kg, nivolumab 240 mg, doxorubicin 25 mg/m^2, and dacarbazine 375 mg/m^2
  - All study drugs were administered separately by IV infusions on Days 1 and 15 of each 28-day cycle for up to 6 cycles
- Primary endpoint is CR rate at EOT

Patient Demographics	Part B (N = 57)
Age, median (range)	35.0 (19, 78)
Age range, n (%)[a]	
<65 years	54 (95)
≥65 years	3 (5)
Race, n (%)[a]	
White	50 (88)
Black or African American	2 (4)
Asian	1 (2)
Multiple or Not Reported	4 (7)
Disease stage at diagnosis, n (%)[a]	
Stage II with bulk[b]	17 (30)
III	10 (18)
IV	29 (51)
Extranodal disease, n (%)[a]	28 (49)
International Prognostic Score, n (%)[a]	
0–1	13 (23)
2–3	32 (56)
4–7	12 (21)

Reasons for treatment discontinuation	
Completed treatment	52 (90)
Progressive disease	0
Adverse event	4 (7)
Investigator decision	1 (2)

Overall Response at EOT per Investigator, n (%)	Part B (N = 57)
ORR (CR+PR)[a,b]	53 (93)
95% CI for objective response rate	(83.0, 98.1)
Complete response (CR)[a,b]	50 (88)
95% CI[c] for CR rate	(76.3, 94.9)
Partial response (PR)[a,b]	3 (5)
95% CI[c] for PR rate	(1.1, 14.6)
Stable disease (SD)[a,b]	0
Progressive disease (PD)[a,b]	2 (4)
Indeterminate response (IR)[d]	1 (2)
Not evaluable (NE)[e]	1 (2)

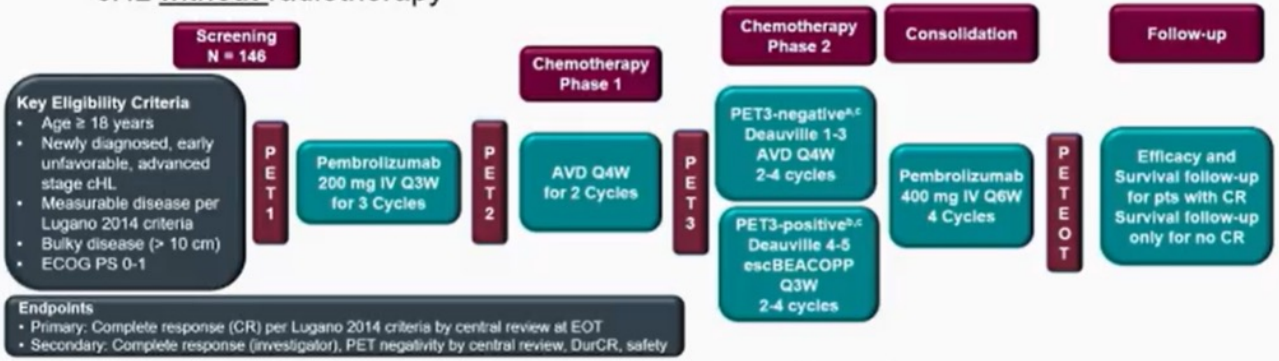
PFS



Treatment-Related Treatment-Emergent Adverse Events, n (%)	Part B (N = 57)	
	Any Grade (>10%)	Grade ≥3 (>2%)
Any event	56 (98)	21 (37)
Nausea	37 (65)	–
Fatigue	27 (47)	2 (4)
Peripheral sensory neuropathy	25 (44)	2 (4)
Alopecia	20 (35)	–
Diarrhea	18 (32)	–
Constipation	15 (26)	–
Alanine aminotransferase increased	10 (18)	7 (12)
Headache	10 (18)	–
Vomiting	9 (16)	–
Bone pain	8 (14)	–
Stomatitis	8 (14)	
Aspartate aminotransferase increased	7 (12)	2 (4)
Decreased appetite	7 (12)	–
Myalgia	7 (12)	–
Dyspepsia	6 (11)	–
Neutropenia	6 (11)	5 (9)
Rash maculo-papular	6 (11)	–
Colitis	–	2 (4)
Neutrophil count decreased	–	2 (4)
Pneumonitis	–	2 (4)
Pyrexia	–	2 (4)

Phase 2 KEYNOTE-C11 Study
(NCT05008224)

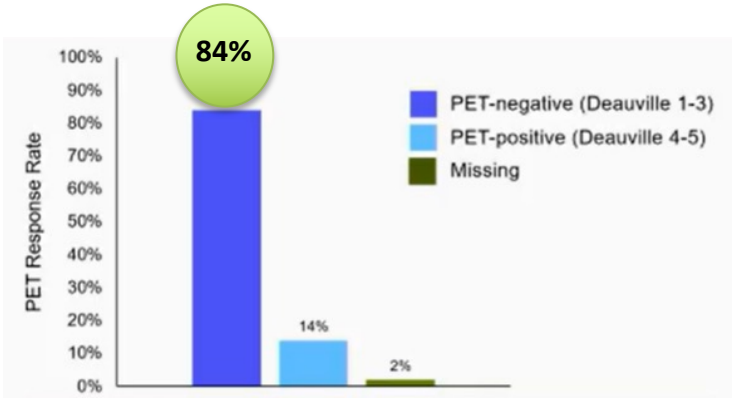
- Global study initiated in 2021
  - Evaluates the safety and efficacy of a PET-adapted regimen of sequential pembrolizumab monotherapy followed by AVD or escBEACOPP and pembrolizumab consolidation in untreated, early unfavorable or advanced-stage cHL *without* radiotherapy



- Primary end point: Investigator-assessed PET3 negativity rate of first 50 patients
- **The study will continue further enrollment if ≥ 25 of first 50 patients are PET3 negative (PET3 negativity rate ≥50%)**

Advani R et al, abs 0731

Characteristics, n (%)	Pembrolizumab Monotherapy N = 146
Median age, years (range)	34.5 (18-78)
≥ 65 years	19 (13)
Male	79 (54)
White	126 (86)
ECOG 0	111 (76)
ECOG 1	35 (24)
Region	
US	21 (14)
EU	50 (34)
Rest of World	75 (51)
Disease Stage	
Early unfavorable by GHSG criteria[a]	62 (42)
Advanced	84 (58)
Bulky disease[b]	32 (22)



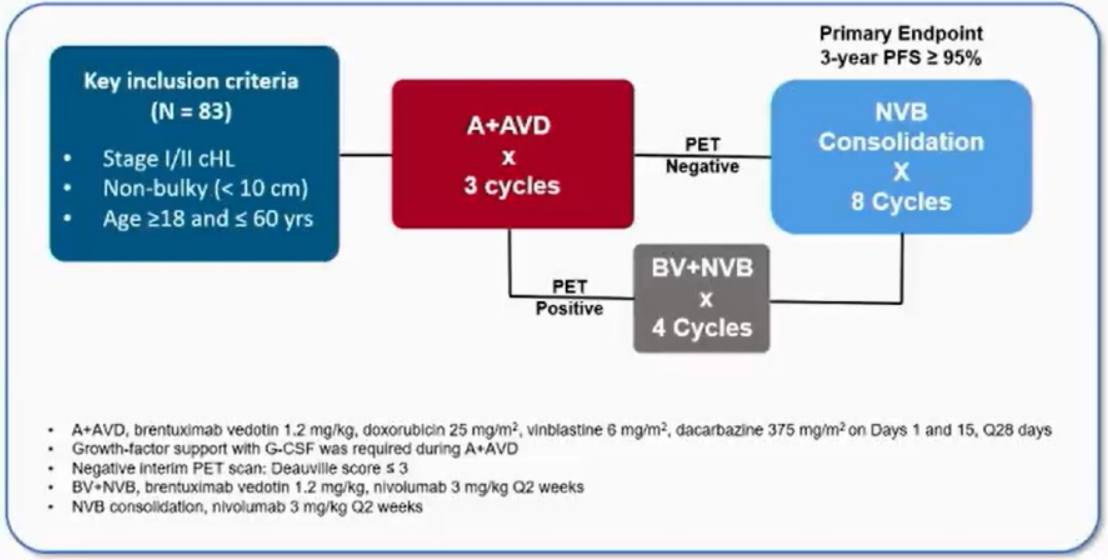
Advani R et al, abs 0731

Advani R et al, abs 0731

	Pembrolizumab[a]		AVD		escBEACOPP	
AEs	**N = 146**		**N = 116**		**N = 3**	
All	22%		7%		0	
Grade ≥3	5%		1%		0	
Led to death	0		0		0	
Led to discontinuation	3%		0		0	
AEs	**Grade 1-2**	**Grade ≥3**	**Grade 1-2**	**Grade ≥3**	**Grade 1-2**	**Grade ≥3**
Hyperthyroidism	9%	0	3%	0	0	0
Hypothyroidism	3%	0	3%	0	0	0
Infusion reactions	4%	2%	1%	0	0	0
Severe skin reactions	0	1%	1%	1%	0	0
Encephalitis	0	2%	0	0	0	0
Thyroiditis	1%	0	0	0	0	0

- Mid-treatment, this PET-adapted regimen showed promising antitumor activity and no safety concerns
  - Therapy was well tolerated; most treatment-related AEs were grade 1-2
  - 9% of patients who received pembrolizumab induction had a treatment interruption

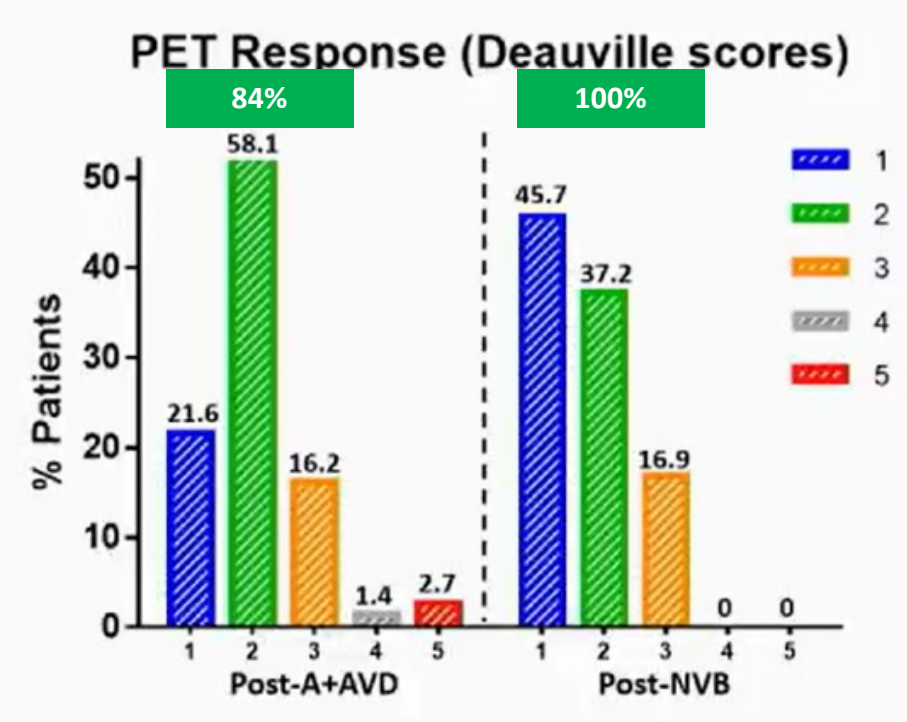
ACCRU-LY-1601: Multicenter, Open-label, Phase 2 Trial



- Primary endpoint: Determine 3-year PFS
  - Historical control PFS rate of ~ 90%
  - Sample size of 78 subjects needed to detect 3-year PFS of 95% (90% power)

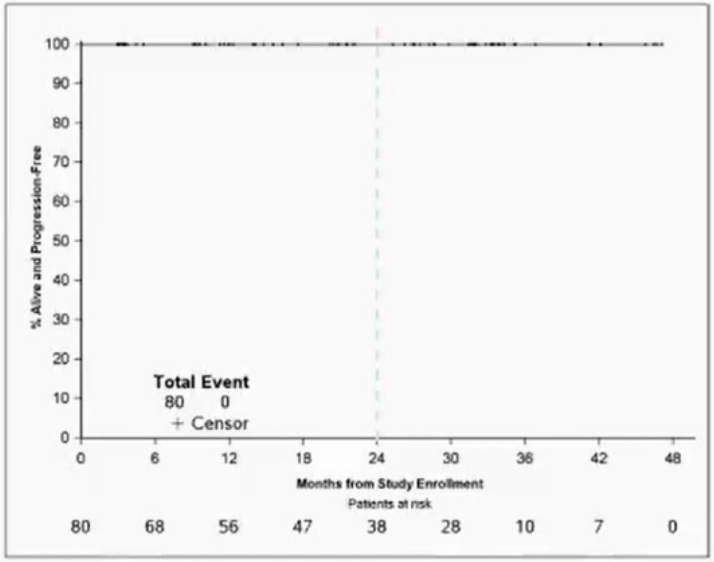
Park SI et al, abs 0728

Patient Characteristics	Number (n = 80)
Age (range), median, years	31 (19–60)
Female, n (%)	40 (50.0%)
Race, n (%)	
Asian	4 (5.0%)
Black or African American	4 (5.0%)
White	66 (82.5%)
Unknown	6 (7.5%)
ECOG PS, n (%)	
0	60 (75.0%)
1	20 (25.0%)
Stage, n (%)	
1	9 (11.3%)
2	71 (88.8%)
B symptoms, n (%)	26 (32.5%)



Park SI et al, abs 0728

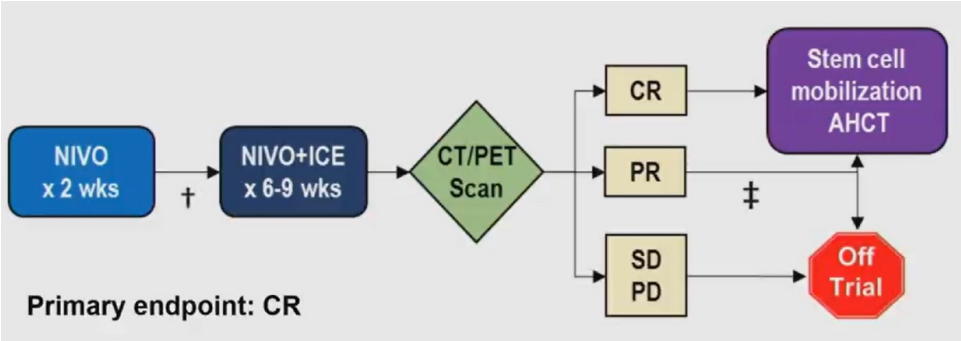
Major AEs	A+AVD % (n = 80)		BV+Nivo % (n = 2)		NVB Consolidation % (n = 73)	
	G1-2	G3-4	G1-2	G3-4	G1-2	G3-4
Neutropenia	7.6	32.6	-	-	5.5	2.7
Anemia	8.8	2.5	-	-	6.8	-
Peripheral sensory neuropathy	35.1	1.3	-	-	30.1	-
Constipation	25.1	1.3	50.0	-	6.9	-
Diarrhea	13.8	3.8	-	-	8.2	1.4
Elevated ALT	21.3	8.8	-	-	8.2	-
Elevated lipase	2.6	2.6	-	-	1.4	5.5
Pancreatitis	-	2.5	-	-	-	-
Colitis	-	1.3	-	-	-	-
Hyperglycemia	1.3	1.3	-	-	-	-
Congestive heart failure	-	1.3	-	-	-	-
Hypothyroidism and endocrine	-	-	-	-	6.9	1.4



Follow-up Time	Number (months)
Patient number (n = 80)	
Median	28.4
Range	2.9 – 47.9
IQR	13.2 – 36.6

Park SI et al, abs 0728

NICE-cohort B

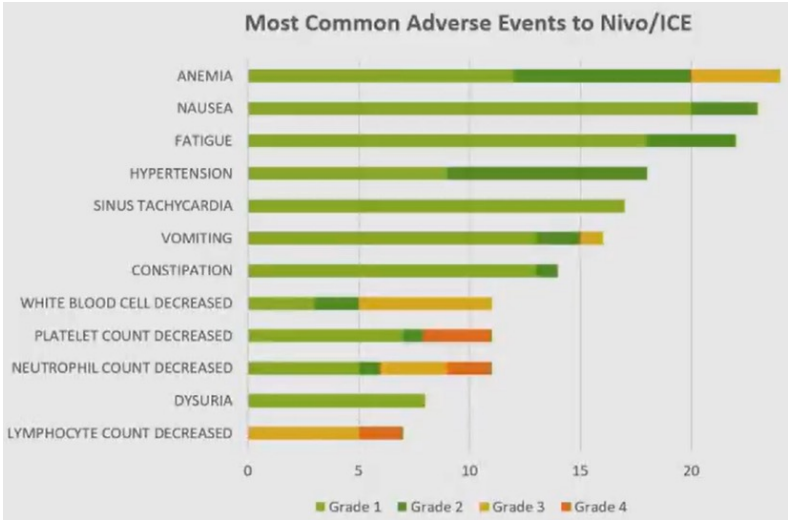


Baseline Characteristics	N (%)
Total	35
Stage III-IV at diagnosis	18 (51)
B symptoms at relapse	6 (17)
Bulky disease (> 5cm) at relapse	4 (11)
Extranodal involvement at relapse	10 (29)
BV in 1L	6 (17)
Primary refractory	23 (66)

- **ORR 100%**
  - CR 89%, PR 11%
  - 28 patients received 3 cycles (i.e. nivo x 1, nivo + ICE x 2)
- 32 patients proceeded to autoHCT
  - 8 received post-transplant maintenance
  - Median time to neutrophil and platelet engraftment 11 days (range: 9-14 for both)

CRR: 89%

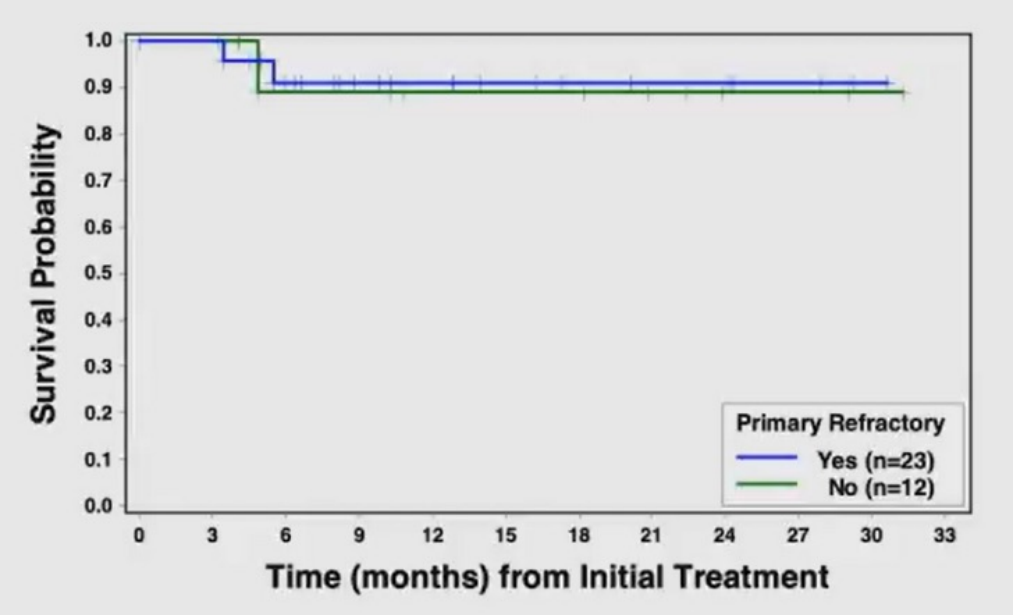
Mei M et al, abs 0318



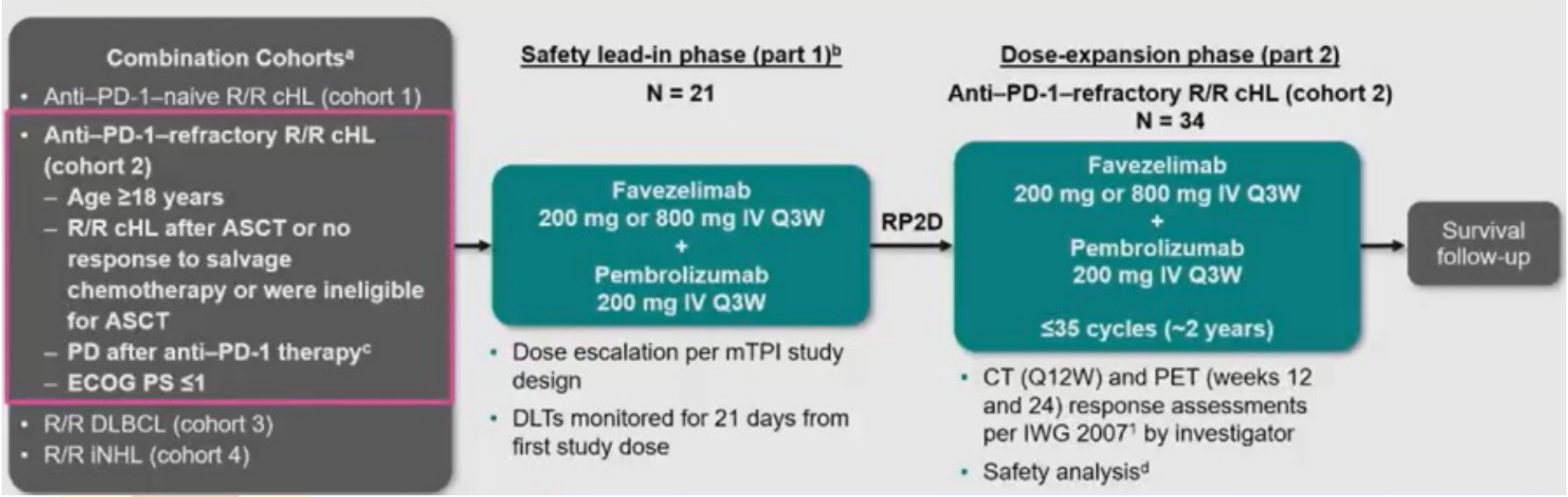
All toxicities to nivo alone grade 1 except 1 case each of grade 2 hypertension, pruritis, fatigue

4 cases of engraftment syndrome (14%)

PFS

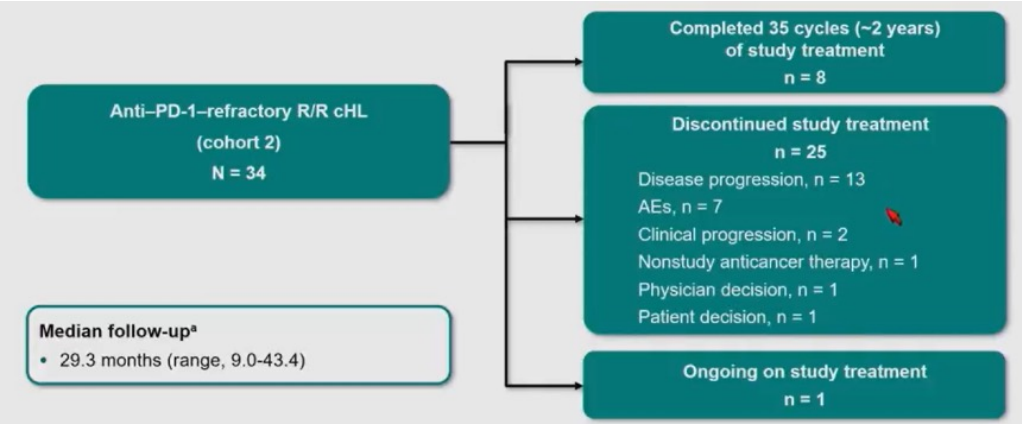


Mei M et al, abs 0318



- LAG-3 is involved in T-cell regulation and is coexpressed with PD-1 on anergic T cells[2]
- Dual blockade of PD-1 and LAG-3 has shown antitumor activity in advanced melanoma, leading to FDA approval in this indication[3,4]

Timmerman J et al, abs 0728

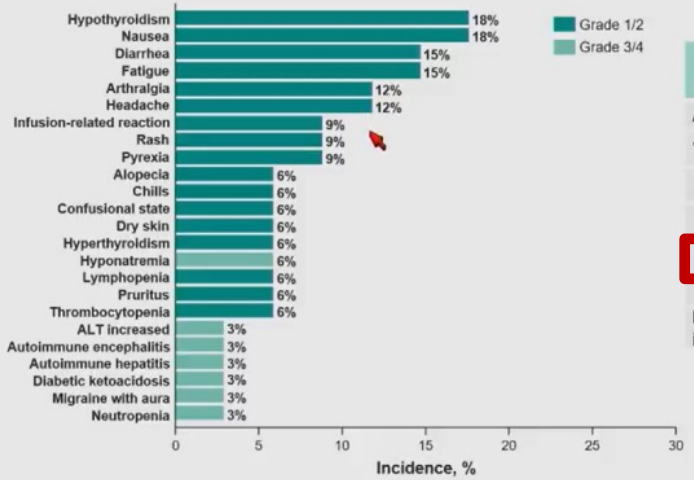


Median age: 37 (range: 25-79)
Previous ASCT: 74%

	Cohort 2 N = 34
Disease subtype	
Nodular sclerosis cHL	27 (79)
Mixed cellularity cHL	4 (12)
Data missing	3 (9)
Prior line of therapy	
Second line	1 (3)
Third line	1 (3)
Fourth line	4 (12)
Fifth line or more	28 (82)
Most recent line of therapy	
Anti–PD-1–based	17 (50)
Not anti–PD-1–based	17 (50)

Timmerman J et al, abs 0728

Treatment-Related AEs in ≥5% and All Grade 3 or 4 Events

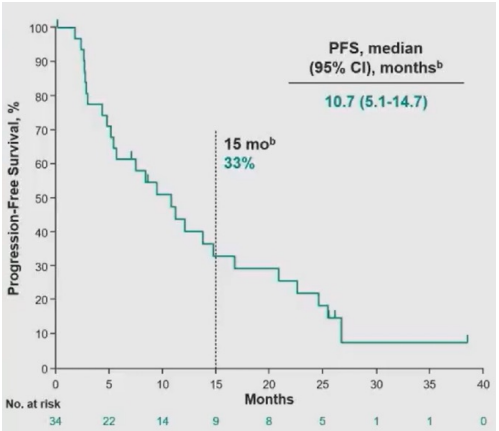


Events, n (%)	Total N = 34
All-cause AEs	34 (100)
Treatment-related AEs	28 (82)
Grade 3/4[a]	6 (18)
Serious	6 (18)
Discontinuations	6 (18)
Deaths[b]	0 (0)
Immune-mediated AEs and infusion reactions	17 (50)

1 patient who underwent allo-HSCT after completion of study treatment had a grade 3 AE unrelated to study treatment (acute GVHD) that resolved

Timmerman J et al, abs 0728

	Total population N = 34
ORR, n (% [95% CI])[b]	10 (29 [15-48])
Best overall response, n (%)	
Complete response	3 (9)
Partial response	7 (21)
Stable disease	12 (35)
Progressive disease	7 (21)
Not available[c]	5 (15)



CHARIOT Study

Phase 2, Multi-center, Single Arm of Autologous CD30.CAR-T in Patients With Relapsed/Refractory (r/r) cHL (NCT#04268706)

Study Population

Patients with r/r cHL:

- 12-75 years old
- Failed ≥3 lines of therapy:
  - Chemotherapy
  - Brentuximab vedotin,® and
  - PD-1 inhibitor®

May have received an autologous or allogeneic stem cell transplant

Study Treatment
(Pilot: n = >12, Pivotal: n = 82)

LD (3 days)*

- Fludarabine 30 mg/m²/day
- Bendamustine 70 mg/m²/day

CD30.CAR-T*

Allowable dose range:
2.0 - 2.7 × 10⁸ cells/m²

Endpoints

Primary

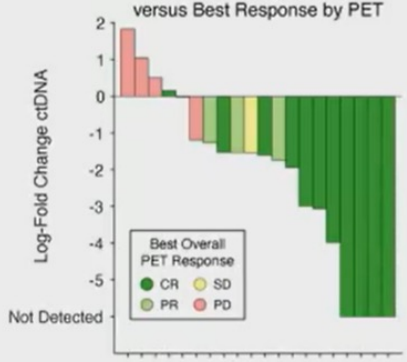
- Pilot: Safety
- Pivotal: ORR

Secondary

- Pilot:
  ORR, DOR, PFS, OS, HRQoL
- Pivotal:
  Safety, DOR, PFS, OS, HRQoL

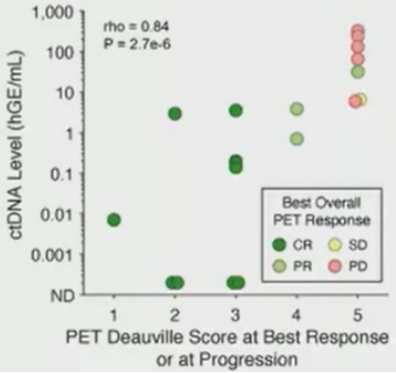
Response Category

Log-Fold Change in ctDNA versus Best Response by PET



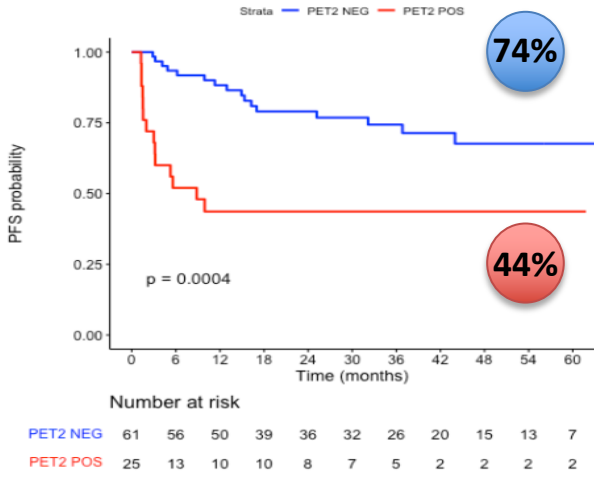
Deauville 5-point scale

ctDNA Level Versus Deauville 5-Point Scale



Kurtz DM et al, abs 0984

DECISIONAL ROLE OF INTERIM PET IN RELAPSED/REFRACTORY CLASSICAL HODGKIN LYMPHOMA TREATED WITH BEGEV CHEMOTHERAPY AS FIRST SALVAGE



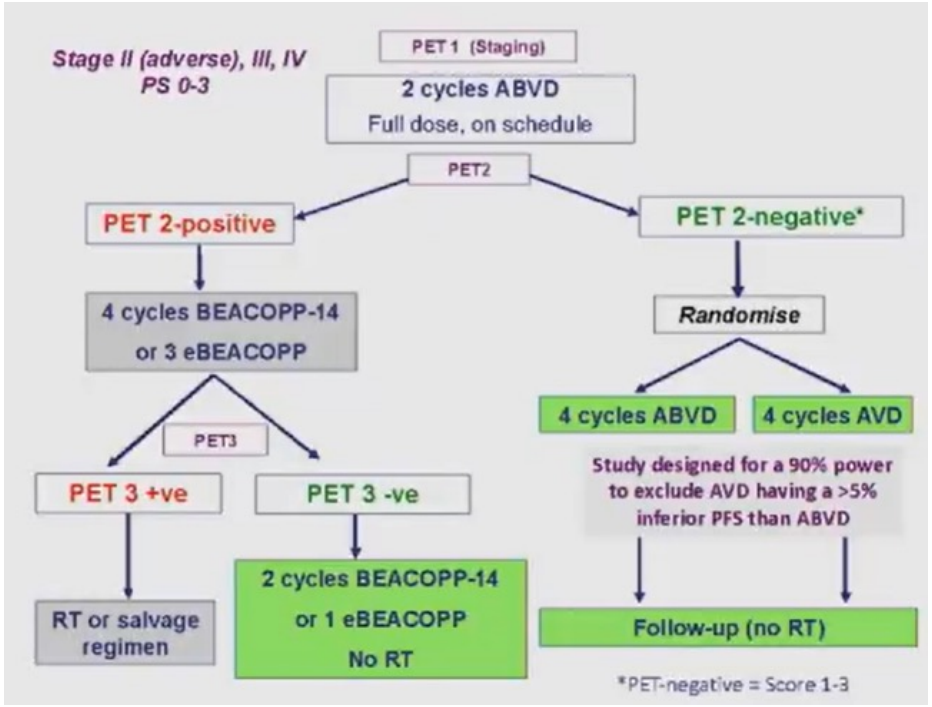
	Comparison	HR (CI 95%)	Wald p-value
PET2 result	POS vs NEG	3.14 (1.50-6.57)	0.002
Extranodal involvement	YES vs NO	1.48 (0.70-3.13)	0.310
Primary refractory & early relapse	YES vs NO	1.24 (0.58-2.64)	0.580

Rusconi C, Ricci F et al, abs 2929

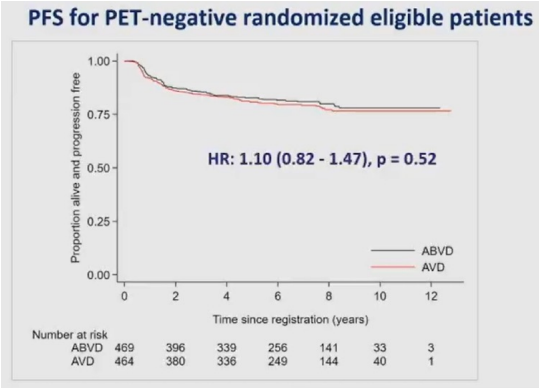
cHL@ASH2022: summary

- Firstline treatment: CPI together with brentuximab-vedotin and chemotherapy (concomitant or sequential schedule) allowed to obtain very high remission rate, but more extended follow-up is needed for survival and long-term cure rate
- Nivo-ICE as first salvage allowed to achieve in a high-risk population a CRR of 89% and a PFS@1 year over 90% without unexpected safety events, also in the post-autotransplant period
- New strategy under fast development for multi-refractory patients (i.e. anti-LAG3 plus pembro)

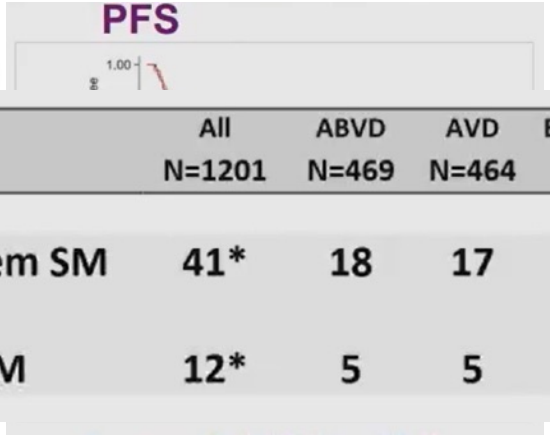
Grazie per l'attenzione!



PET-ve



PET+ve



	All N=1201	ABVD N=469	AVD N=464	BEACOPP N=172
Non haem SM	41*	18	17	3
Haem SM	12*	5	5	1

Luminari S et al, abs 0728