IMMUNOTERAPIA NEL LINFOMA DI HODGKIN: CHE RUOLO HA OGGI ?

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Faenza 07/06/2018

ISTITUTO SCIENTIFICO ROMAGNOLO PER LO STUDIO E LA CURA DEI TUMORI

HODGKIN LYMPHOMA

GHSG Risk Allocation for HL

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	Stage (Ann Arbor)			
Risk factors	**IA, IB, IIA**	**IIB**	**IIIA, IIIB**	**IVA, IVB**
None	Early favorable		Advanced	
≥ 3 LK- Areas	Early unfavor-able			
Elevated ESR				
Large Med Mass				
Extranodal disease				

HODGKIN LYMPHOMA

EARLY STAGE: CHEMO+/-RT:

-PFS rates 3-5 years 82%-94%

ADVANCED STAGE: (ABVD,BEACOPP, STANFORD V)

-PFS rates 5 years 71%-86.4%

Gordon et al J Clin Oncol 2013
Engert et al J Clin Oncol 2009
Borchmann P et al J Clin Oncol 2011

Eich Ht et al J Clin Oncol 2010
Engert A et al N Eng J Med 2010
Radford J et al N Eng J Med 2015

HODGKIN LYMPHOMA

AUTOLOGOUS FOR RELAPSED/REFRACTORY DISEASE:

-PFS rates for RELAPSED: 50%-60%

-PFS rates for REFRACTORY: 40%-50%

About 50% Relapsed after autologous

Kewalramni et al Bone Marrow Transplant 2003
Hahn et al Biol Blood Marrow Transplant 2013

Schmitz et al Lancet 2002
Ferme' et al J Clin Oncol 2002
Gerrie et al Ann oncol 2014

HODGKIN LYMPHOMA

Survival in Hodgkin Lymphoma
Relapse After Autologous HSCT

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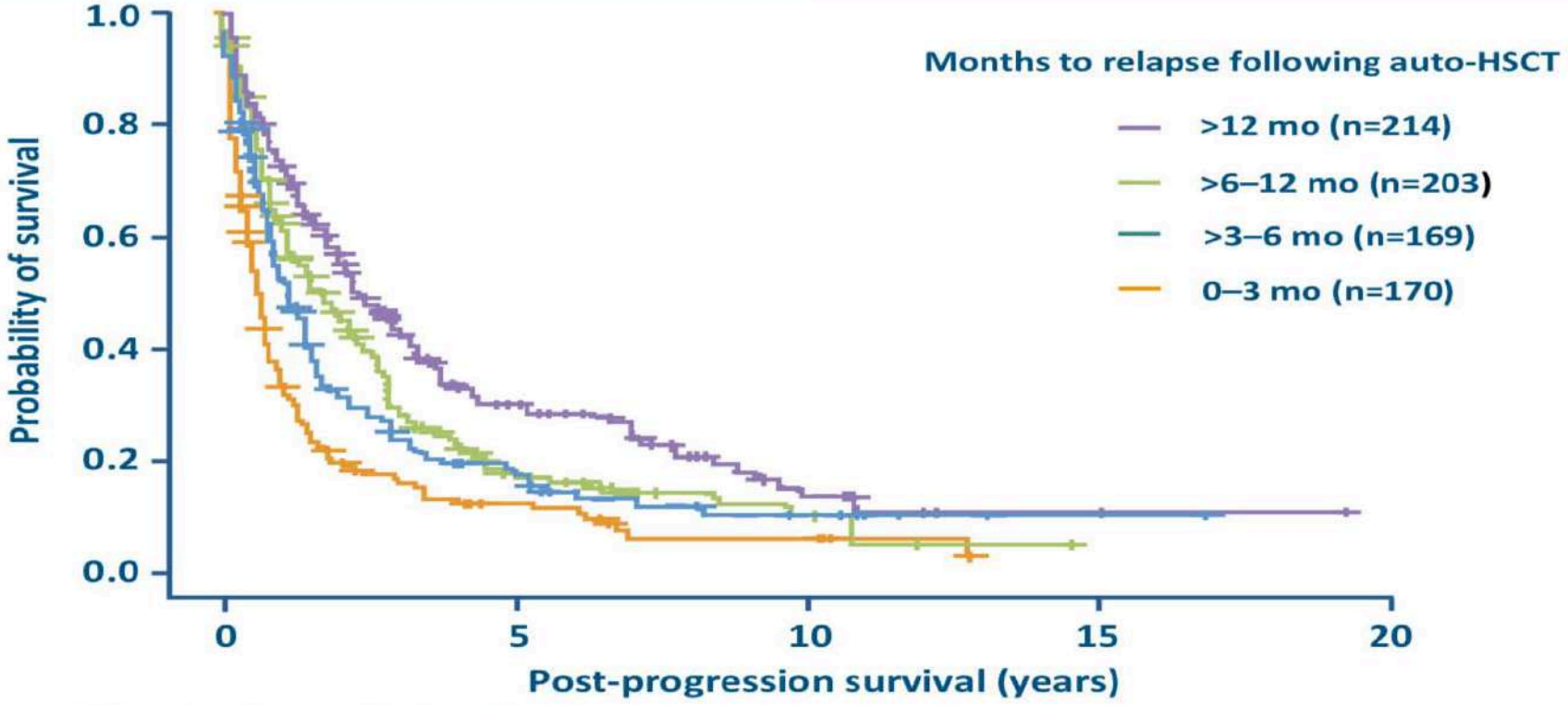


auto-HSCT = autologous hematopoietic stem cell transplant

Arai S et al. Leukemia & Lymphoma 2013;54:2531–2533.

HODGKIN LYMPHOMA

WHO IS THE RELAPSED/REFRACTORY PATIENT ?

HODGKIN LYMPHOMA

Biological Prognostic Factors Reported to Influence Hodgkin Lymphoma Outcome

Factor	Impact on prognosis
Assessment of Hodgkin-Reed Sternberg cells	
aberrant T-cell antigen expression, IHC/HRS	negative
FOXP3 expression, IHC/HRS	negative
CD20 expression, IHC/HRS	negative
BCL-XL, IHC/HRS	negative
p53, IHC/HRS	negative
HLA class II, IHC/HRS, loss	negative
presence of Epstein-Barr virus (EBV)	negative
Assessment of microenvironmental or circulating non-neoplastic cells, cytokines and membrane associated antigens	
fibroblast growth factor 2, IHC/circ	negative
syndecan-1, IHC/circ	negative
tumor-associated macrophages, IHC/TM	negative
CD68 expression, IHC/TM	negative
serum TARC, elevated	negative
serum galectin-1, elevated	negative
serum CD163, elevated	negative
serum IL-10, elevated	negative
serum IL-10 receptor, elevated	negative
serum IL-6, elevated	negative
serum CD30, elevated	negative
serum tumor necrosis factor (TNF), elevated	negative
serum TNF receptor, elevated	negative
serum CD4, elevated	negative
serum CD8, elevated	negative
serum CD25, elevated	negative
serum CD54, elevated	negative
Gene expression and miRNA profiling reflecting the tumor microenvironment	
gene expression profiling	positive or negative
global microRNA levels including MIR21, MIR30E, MIR30D and MIR92B	positive or negative
Host germline polymorphisms and mutations	
IL-10 specific polymorphism 592AA	negative
IL-6 specific polymorphism 174GG	negative

Presented By Joseph Connors at 2018 ASCO Annual Meeting

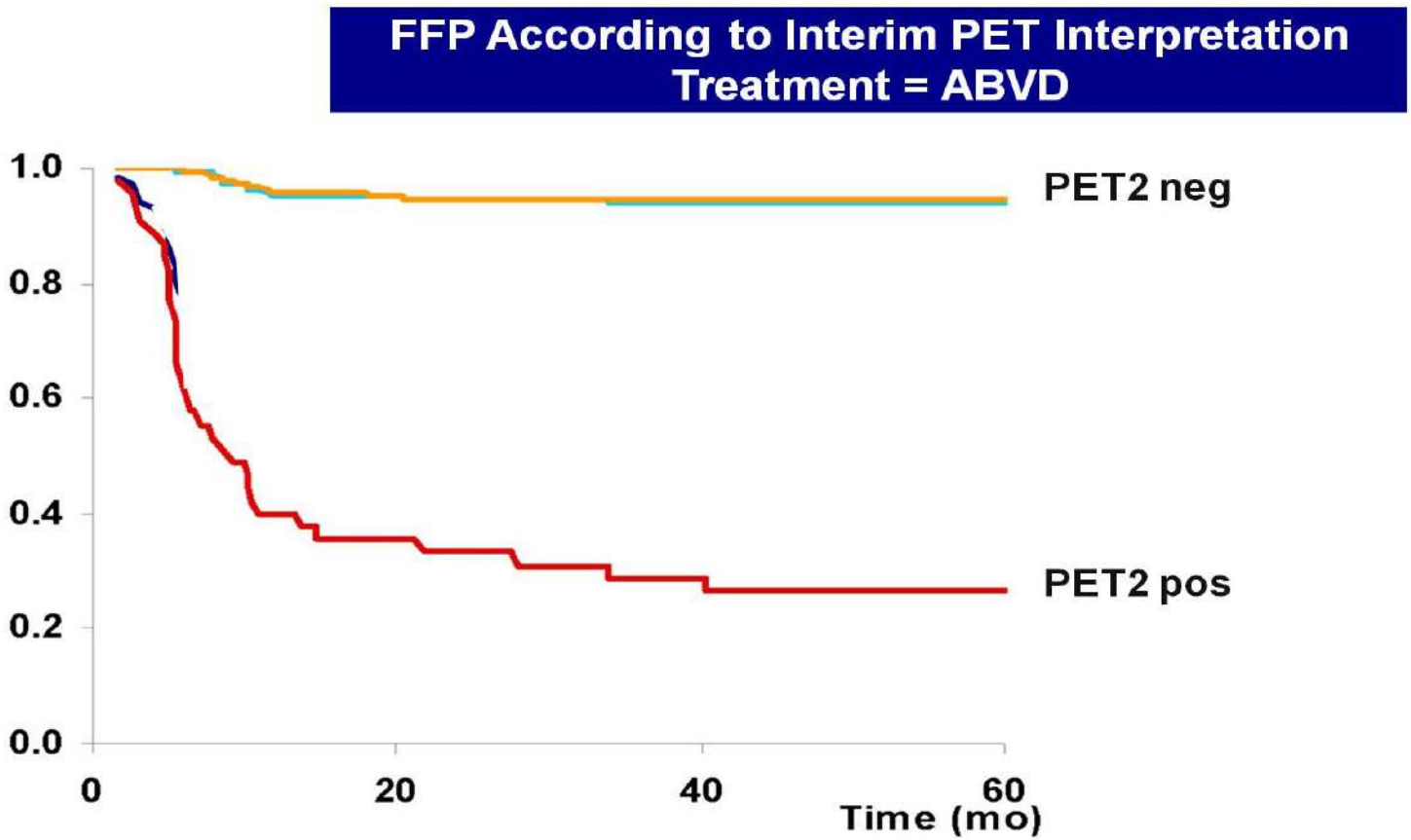
Connors. *Blood* 2015 125:1693

International Prognostic Factors Project on Advanced Hodgkin Lymphoma

Factor	Criteria in SI units
Age	> 44 y
Gender	male
Stage	IV
Albumin	< 40 g/L
WBC	> 15 x 10^9/L
Hemoglobin	< 105 g/L
Lymphs	< 0.6 x 10^9/L or < 8%

Hasenclever. *N Engl J Med.* 1998;339:1506

HODGKIN LYMPHOMA



adapted from Biggi. *J Nucl Med*. 2013;54:683.

Presented By Joseph Connors at 2018 ASCO Annual Meeting

HODGKIN LYMPHOMA

RISK FACTORS FOR RELAPSE AFTER AUTOLOGOUS :

-NUMBER OF PRIOR REGIMENS

-LESS THAN A PET CR BEFORE ASCT

-DURATION OF FIRST REMISSION < 12 MONTHS

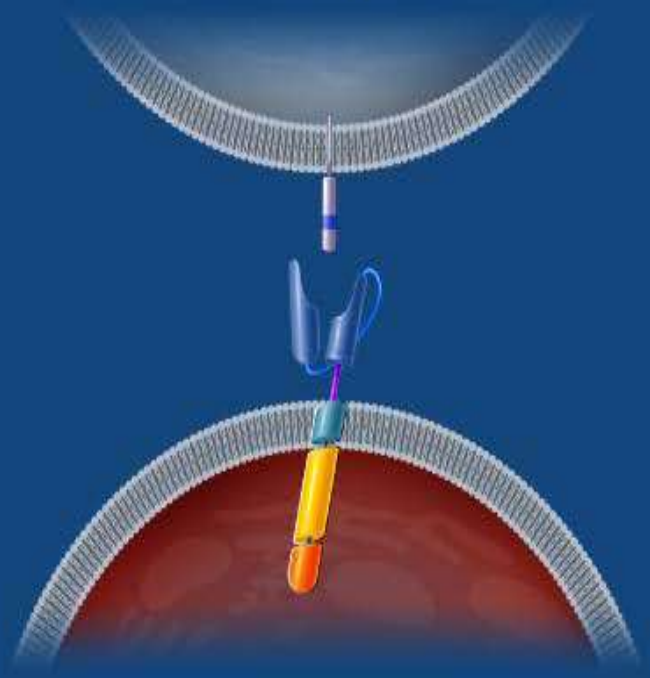
-Karnofsky< 90

-EXTRANODAL INVOLVEMENT

Spaepen et al Blood 2003
Hahn et al Biol Blood Marrow Transplant 2013

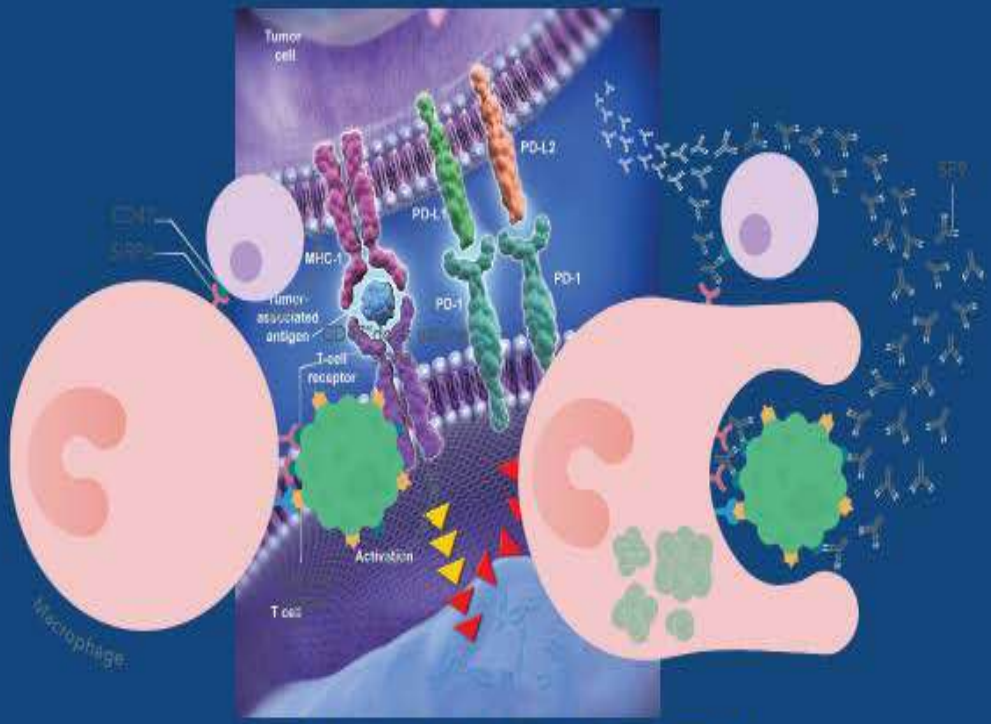
Modern Immunotherapy Approaches to Lymphoma

- Antigen Specific Anti-tumor Immunotherapy



Abramson ASCO 2018

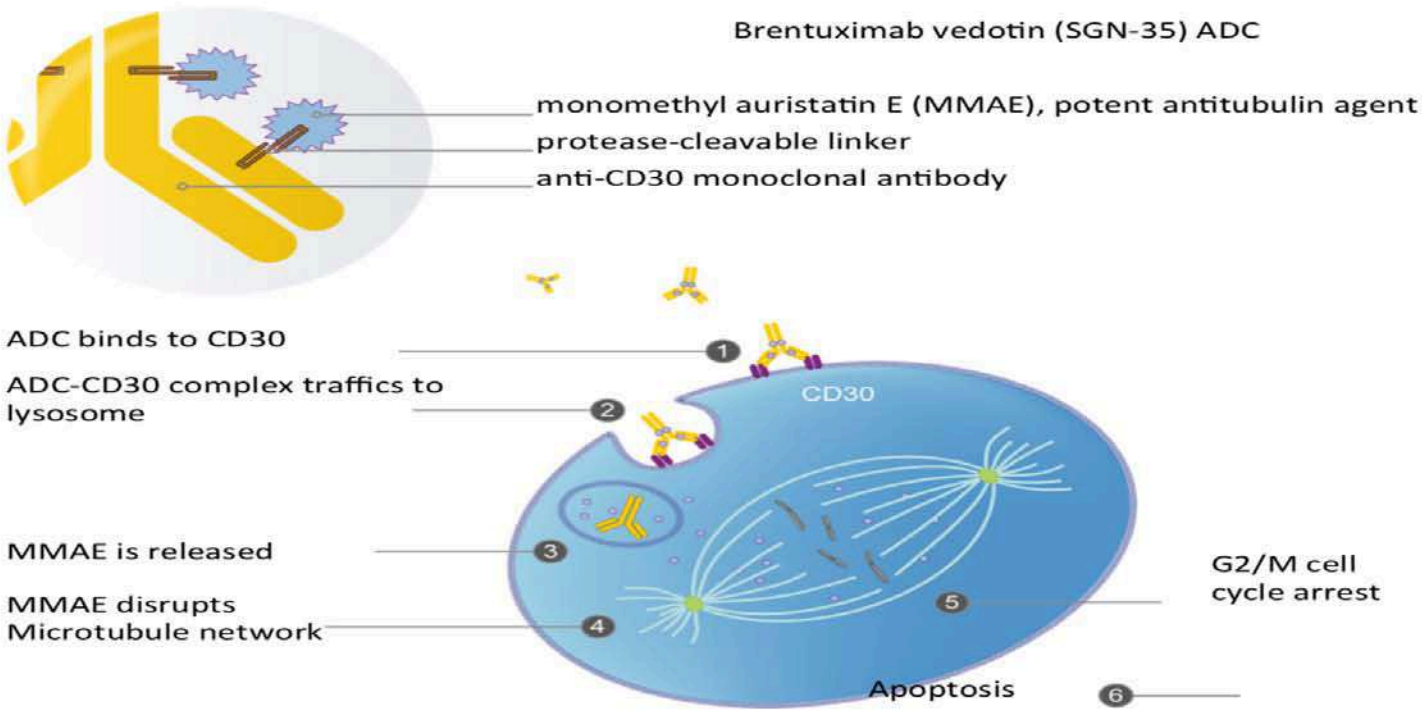
- Antigen Independent Anti-tumor Immunotherapy



Advani et al ASCO 2018 7504

HODGKIN LYMPHOMA

BRENTUXIMAB VEDOTIN (SGN-35) : MECHANISM OF ACTION



Younes A et al. N Engl J Med 2010; 363:1812-21 (appendix)

SGN35-003: 5-year follow-up from phase II study of brentuximab vedotin in R/R HL post-ASCT – Update *Blood* 2016(NCT00848926)

Endpoints: *Primary*: ORR (IFR); *Secondary:* CR rate, DOR, PFS, OS, safety

Patients: 102 pts with R/R CD30+ HL after ASCT; median age 31 yrs (15–77), median of 3.5 (1–13) prior chemotherapy regimens, 71% refractory to frontline therapy, 42% refractory to most recent treatment, 71% relapsed ≤1 yr post-ASCT

Dose and Schedule:

- All pts completed treatment Aug 2010, and were followed for PD/OS until end of study
  - Follow-up: every 3 mos for 2 yrs; every 6 mos yrs 3–5; every 12 months thereafter

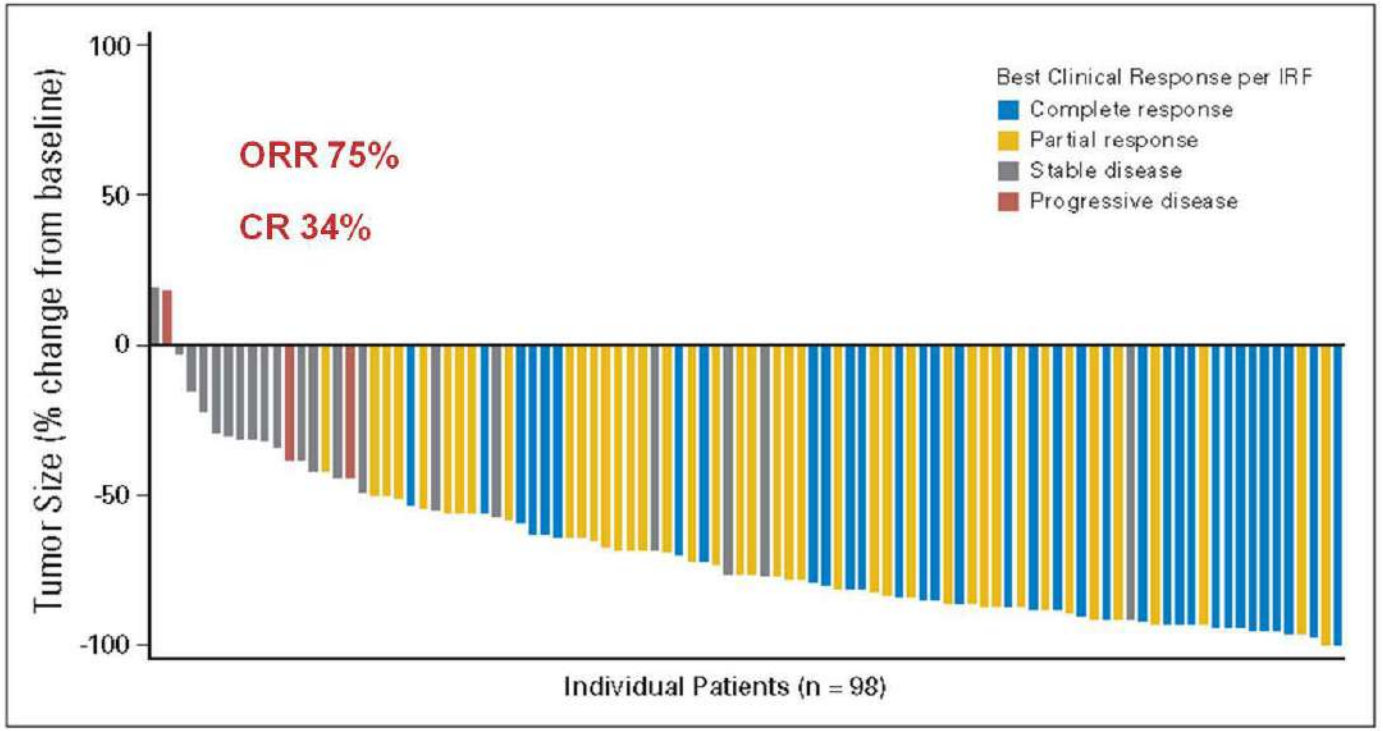
Efficacy: Median observation time from first dose at study closure (~5 yrs after EOT visit for last pt) was 35.1 mos (1.8–72.9)

Chen R, et al. Blood 2016

Previous publications: Chen R, et al. ASH 2015, Poster presentation from Abstract #2736

Younes A, et al. J Clin Oncol 2012;30:2183–9;
Gopal AK, et al. Blood 2015;125:1236–43

Brentuximab Vedotin Active in Relapsed HL



Younes, et al. *J Clin Oncol*. 2012; 30(18): 2183–2189.

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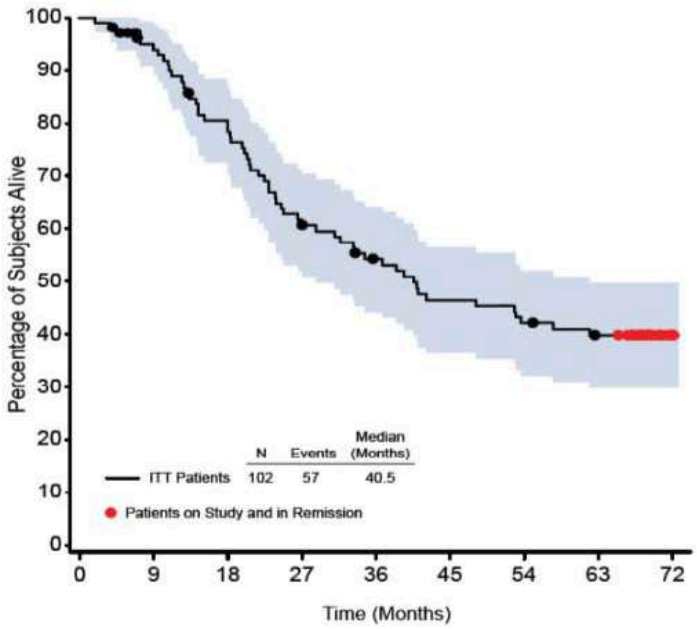
SGN35-003: 5-year follow-up from phase II study of brentuximab vedotin in R/R HL post-ASCT – Update *Blood* 2016(NCT00848926)

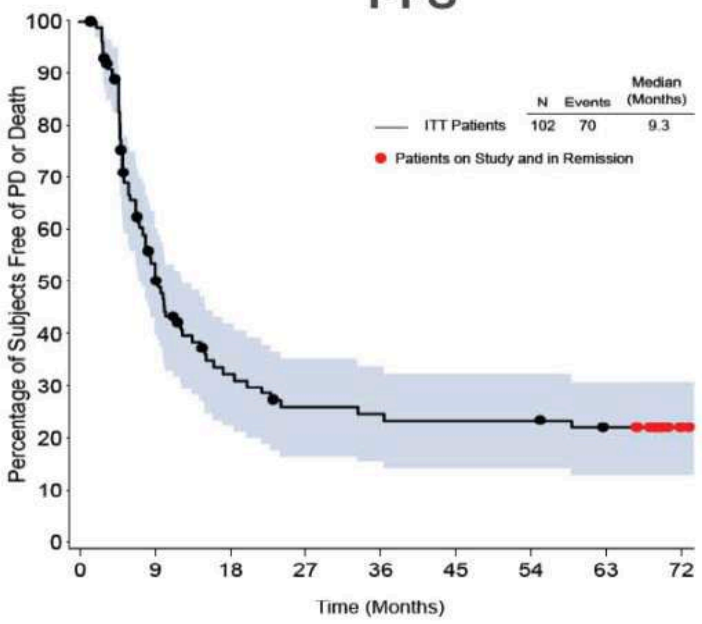
Efficacy (cont'd): ORR: 72%; CR rate: 33% (per investigator)

OS



Median OS: 40.5 mos
(95% CI: 28.7, 61.9 [1.8–72.9+])
5-yr OS: 41%
(95% CI: 31%, 51%)

PFS

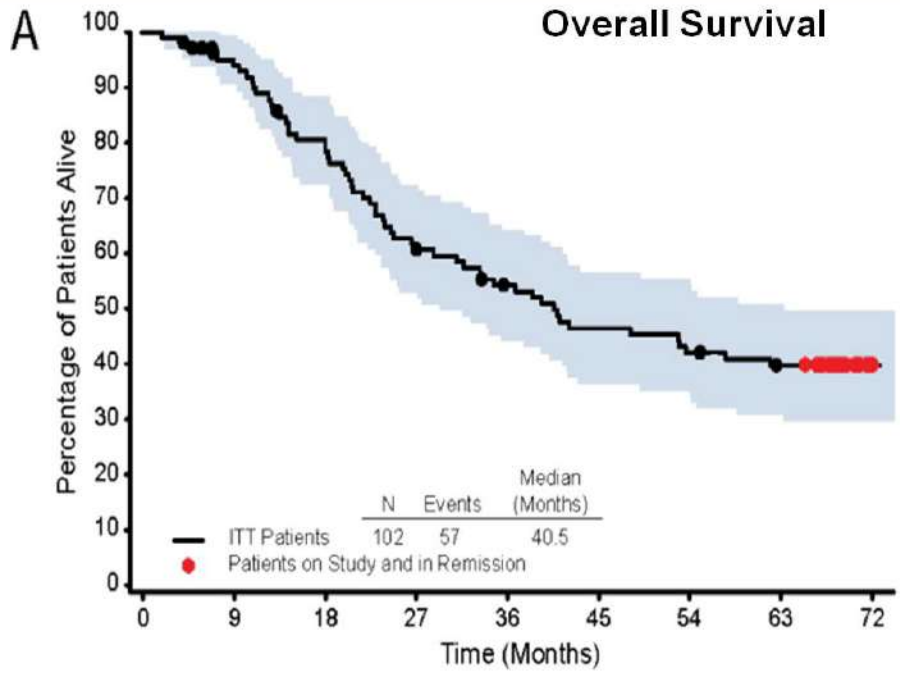


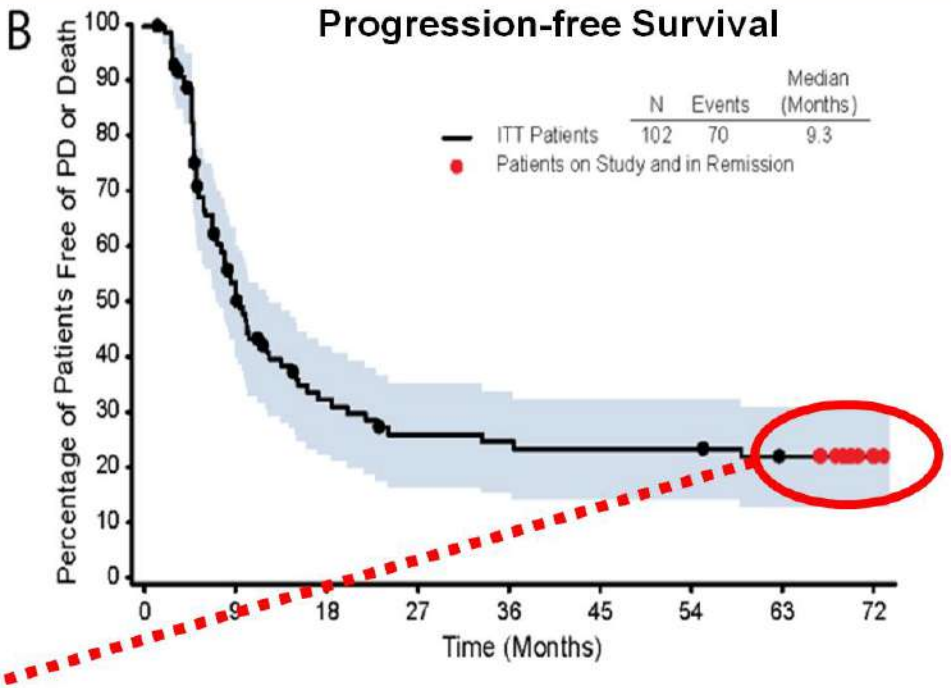
Median PFS: 9.3 mos
(95% CI: 7.1, 12.2)
5-yr PFS: 22%
(95% CI: 13%, 31%)

Chen R,, et al. *Blood* 2016

1. Previous publications: Chen R, et al. ASH 2015, Poster presentation from Abstract #2736
Younes A, et al. J Clin Oncol 2012;30:2183–9;
Gopal AK, et al. Blood 2015;125:1236–43

Brentuximab Vedotin in Relapsed/Refractory HL





n = 13

4 transplant after Bv

9 no addn'l Tx

Brentuximab vedotin may be able to cure Hodgkin lymphoma that is incurable with standard or intensive dose chemotherapy

Chen. *Blood.* 2016;128:1562

SGN35-003: 5-year follow-up from phase II study of brentuximab vedotin in R/R HL post-ASCT[1] – Update *Blood* 2016(NCT00848926)

Safety: Pts received a median of 9 cycles (1–16) of brentuximab vedotin

- Gr ≥3 AE in ≥5% of pts were 20% neutropenia, 8% sensory PN, 8% thrombocytopenia, 6% anemia

Reason for treatment discontinuation, n (%)*	CR (n=34)	PR (n=39)
Completed treatment	12 (35)	4 (10)
PD	4 (12)	23 (59)
AE	9 (26)	5 (13)
Investigator decision	7 (21)	4 (10)
Pt decision	2 (6)	3 (8)

Treatment-emergent PN	N=102
Pts experiencing PN, n (%)	56 (55%)
PN outcome, %	**n=56**
Complete resolution	73%
Improvement	14%
Ongoing PN Gr ≤2 at last follow-up, n (%)	15 (27%)
Grade ≥3 PN at last follow-up	0

Chen R, et al. Blood 2016

Previous publications: Chen R, et al. ASH 2015, Poster presentation from Abstract #2736

Younes A, et al. J Clin Oncol 2012;30:2183–9;
Gopal AK, et al. Blood 2015;125:1236–43

*1 patient was not evaluable for response

SALVAGE BEFORE TRANSPLANT

Single Agent BV in Second Line Salvage: Response Rate

	Best response to BV, N=37	Response to combination chemotherapy (ICE/DICE/IGEV/GND) post-BV, N=18	Disease Status at AHCT, N=33	
ORR	25/37 (68%)	16/18 (89%)		
CR	13/37 (35%)	11/18 (61%)	24/33 (73%)	
PR	12/37 (32%)	5/18 (28%)	9/33 (27%)	
SD	10/37 (27%)	1/18 (6%)	1/33 (3%)	
PD	2/37 (5%)	1/18 (6%)		

Chen et al. Biol Blood Marrow Transplant. 2015 Dec; 21(12): 2136–2140

NYU Langone Health

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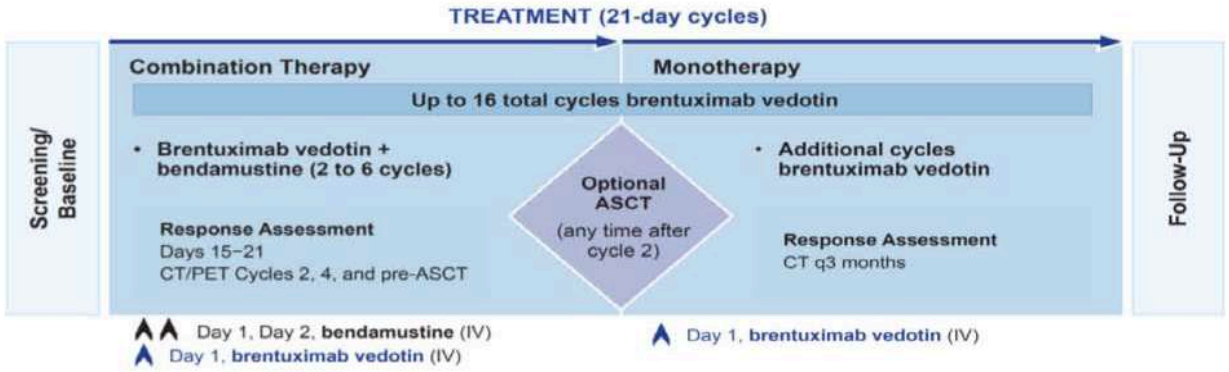
SALVAGE BEFORE TRANSPLANT

SGN35-016: Phase I/II trial of brentuximab vedotin combined with bendamustine in R/R HL: *updated 2-yr results* (NCT01874054)

Study Design:



Safety: Median 2 cycles (1–6) of brentuximab vedotin 1.8 mg/kg + bendamustine 90 mg/m^2, median 10 cycles (1–14) of single-agent brentuximab vedotin (n=31; 25 ASCT pts, 6 non-ASCT pts). 3 pts died, due to progression of HL (2 pts) or septic shock after transplant (1 pt)

- IRRs were observed in 58% of pts overall, most common symptoms (≥15%) were pyrexia, chills, dyspnea, flushing, and nausea
- Protocol was amended to require premedication with corticosteroids and antihistamines, the use of which decreased the severity of IRRs:

Toxicity, %	Pre-amendment n=25	Post-amendment n=30
Discontinuation	24	7
SAE	24	10
Gr ≥3	32	17

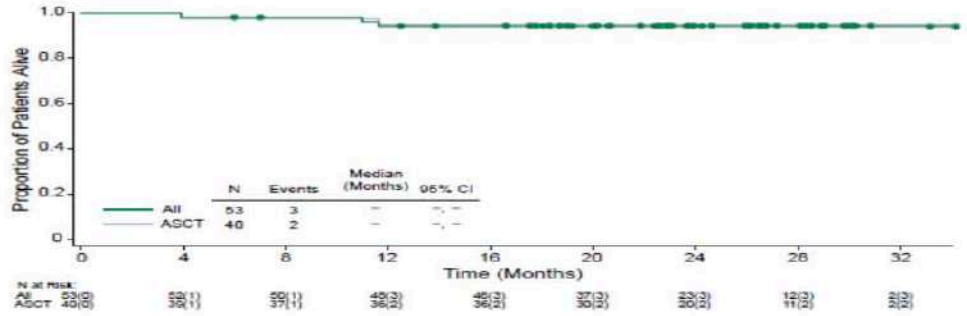
LaCasce et al, ISHL 2016 Poster #P020, Updated from LaCasce et al, ASH 2014, Abstract #293

SALVAGE BEFORE TRANSPLANT

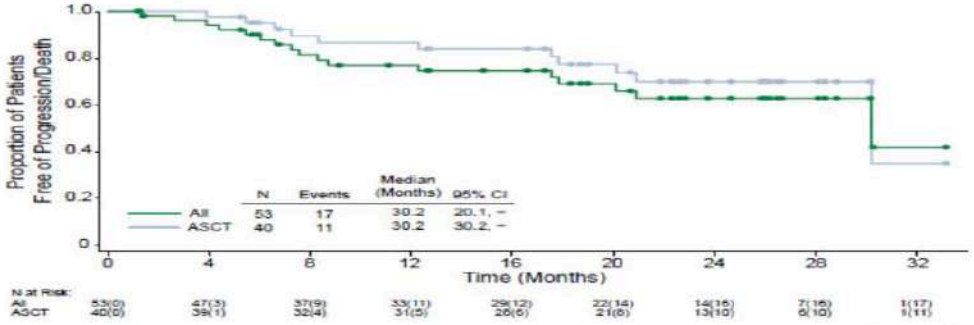
SGN35-016: Phase I/II trial of brentuximab vedotin combined with bendamustine in R/R HL: *updated 2-yr results* (NCT01874054)

Response (Cont'd): Median follow-up: ~23 mos from first dose (N=53), 21 mos from ASCT (n=40)

OS – all patients and ASCT subset



PFS – all patients and ASCT subset



Overall estimated 24-month PFS:

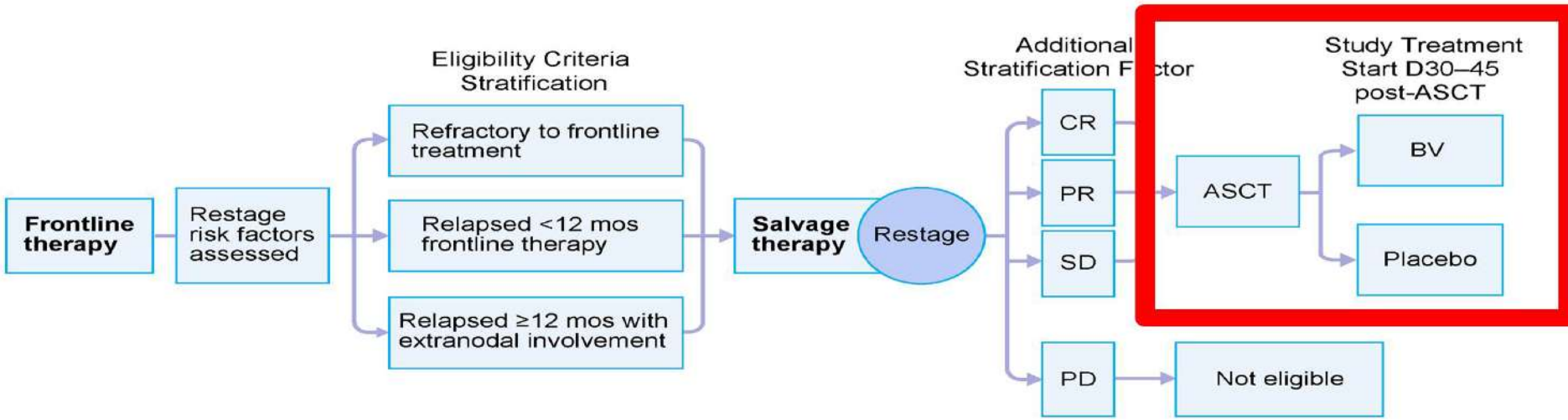
- All pts: 63% (95% CI: 46, 76)
- ASCT: 70% (95% CI: 51, 83)
- 93% (13/14) of pts observed for ≥24 mos remain progression free

LaCasce et al, ISHL 2016 Poster #P020, Updated from LaCasce et al, ASH 2014, Abstract #293

CONSOLIDATION POST ASCT

Aethera Study Design and Key Eligibility Criteria

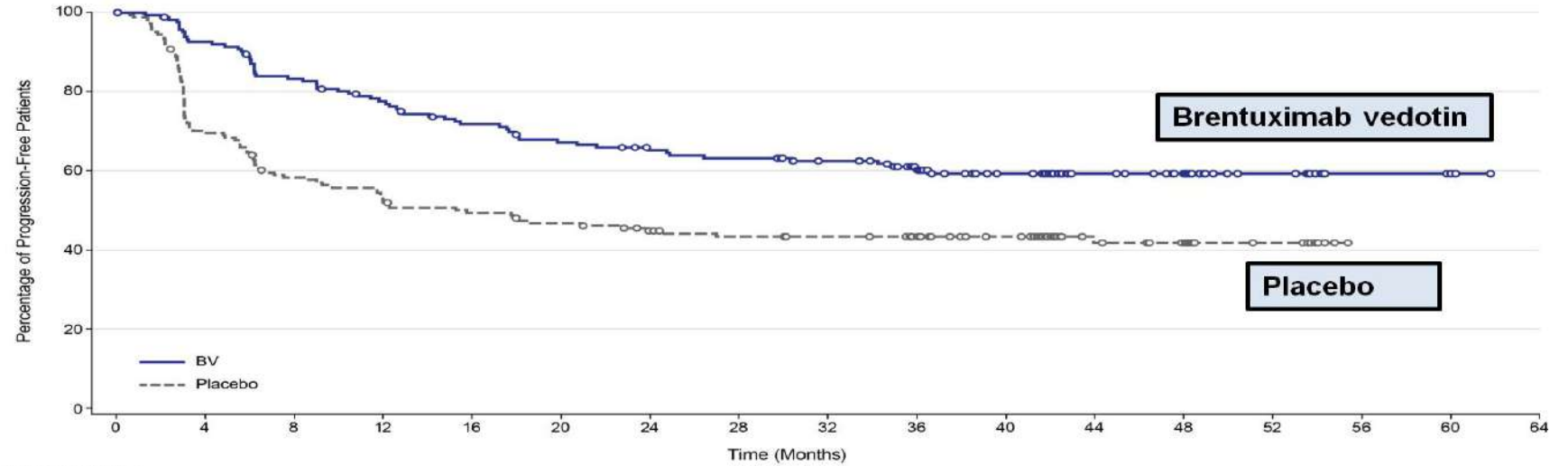
- **329 patients were randomized at 78 sites in North America and Europe**



Moskowitz. *Lancet.* 2015;385:1853.

CONSOLIDATION POST ASCT

PFS per Investigator—3 Years Since Last Patient Randomized



N at Risk (Events)

BV	165 (0)	149 (12)	133 (27)	122 (36)	111 (45)	103 (52)	97 (55)	94 (58)	87 (59)	74 (61)	56 (63)	39 (63)	32 (63)	13 (63)	4 (63)	3 (63)	0 (63)
Placebo	164 (0)	113 (48)	92 (67)	83 (76)	77 (81)	72 (85)	65 (88)	61 (90)	59 (90)	54 (90)	44 (90)	26 (91)	22 (91)	9 (91)	0 (91)	0 (91)	0 (91)

	Median Treatment Cycles	Median PFS (months)	HR
BV	15	—	0.517
Placebo	15	15.8	

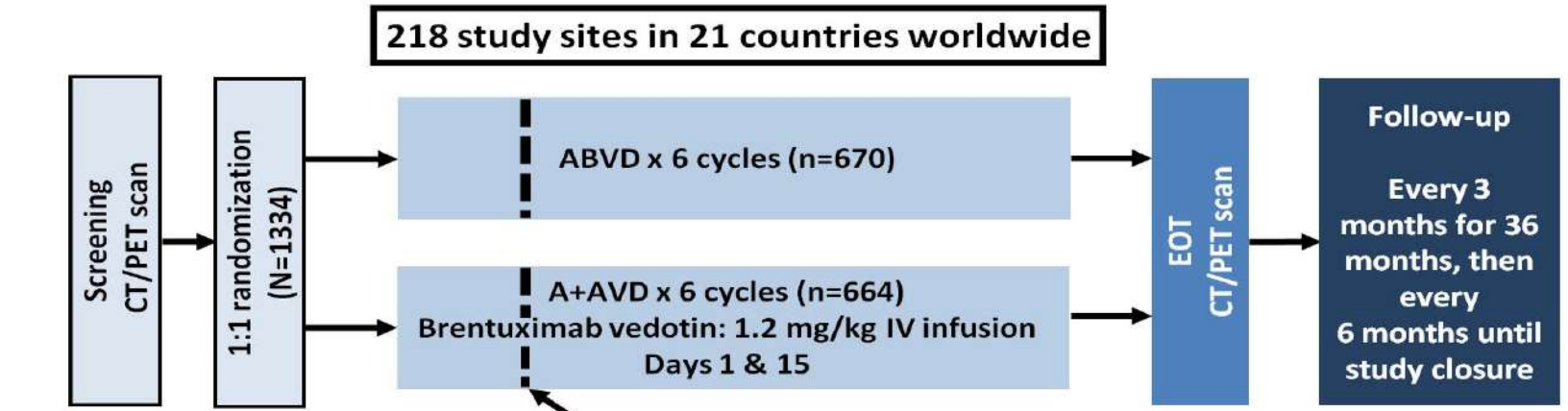
*Includes clinical assessments of lymphoma.

Moskowitz. *Lancet*. 2015;385:1853. Updated Lugano ICML 2017

Presented By Joseph Connors at 2018 ASCO Annual Meeting

FIRST LINE

ECHELON-1: Open-label, global, randomized, phase 3 study of A+AVD versus ABVD in patients with newly diagnosed advanced cHL



- Inclusion criteria
  - cHL stage — III or IV
  - ECOG PS — 0, 1 or 2
  - Age — ≥18 years
  - Measurable disease
  - Adequate liver and renal function

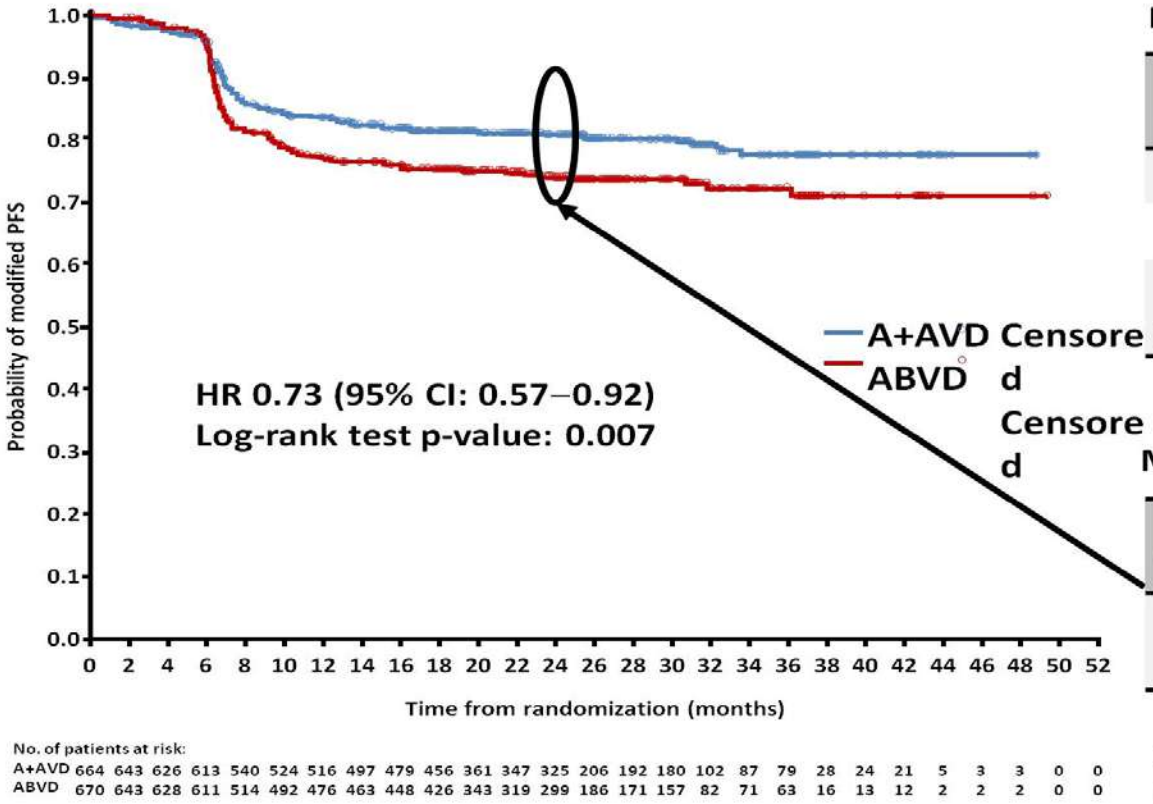
cHL, classic Hodgkin lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; EOT, end-of-treatment; PFS, progression-free survival

Connors. *N Engl J Med* 2018;378:331.

Presented By Joseph Connors at 2018 ASCO Annual Meeting

FIRST LINE

Modified PFS per investigator



Number of events

Category	A+AVD N=123	ABVD N=164
Progression	73	103
Death	15	22
Modified progression	35	39

Modified PFS estimates

Time	A+AVD (95% CI)	ABVD (95% CI)
2-year	81.0 (77.6–83.9)	74.4 (70.7–77.7)

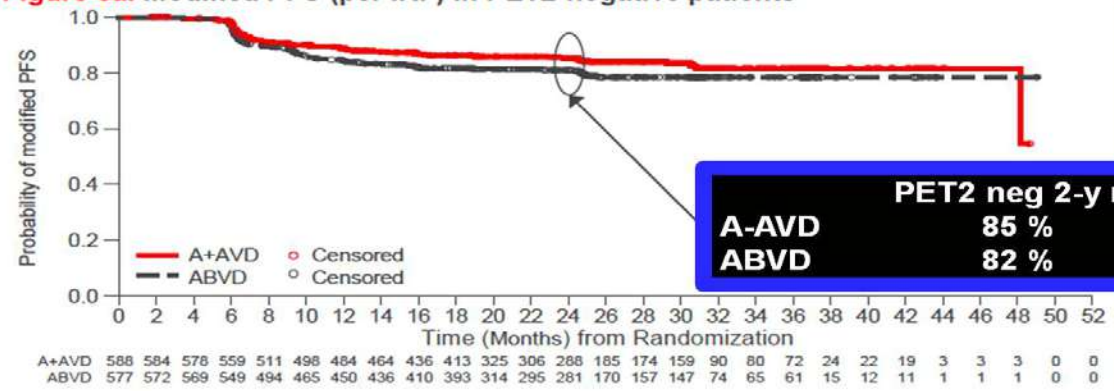
Median follow-up (range): 25.0 months (0.0–49.3)

Connors. *N Engl J Med* 2018;378:331.

FIRST LINE

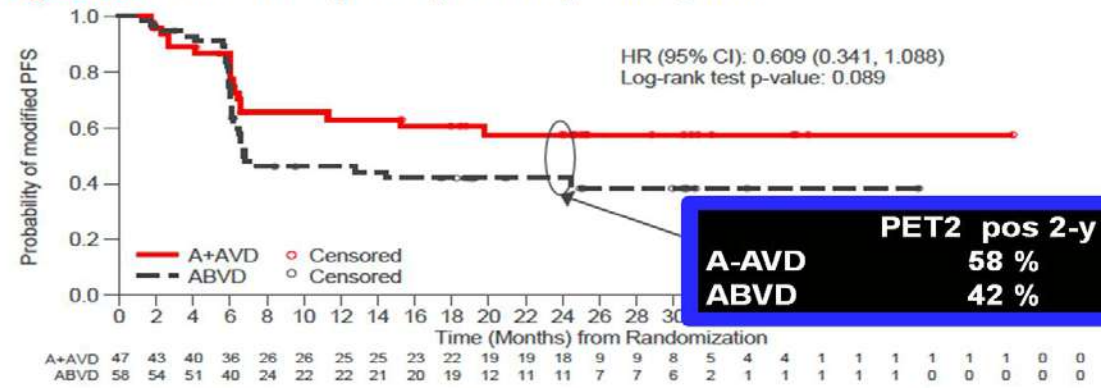
Impact of A-AVD vs ABVD on mPFS: PET2 neg vs PET2 pos

Figure 6a. Modified PFS (per IRF) in PET2-negative patients



PET2 neg 2-y mPFS	
A-AVD	85 %
ABVD	82 %

Figure 6a. Modified PFS (per IRF) in PET2-positive patients



PET2 pos 2-y mPFS	
A-AVD	58 %
ABVD	42 %

*Unstratified Cox model
Note: 1 patient in the A+AVD arm and 4 in the ABVD arm switched to alternative frontline therapy due to unacceptable response

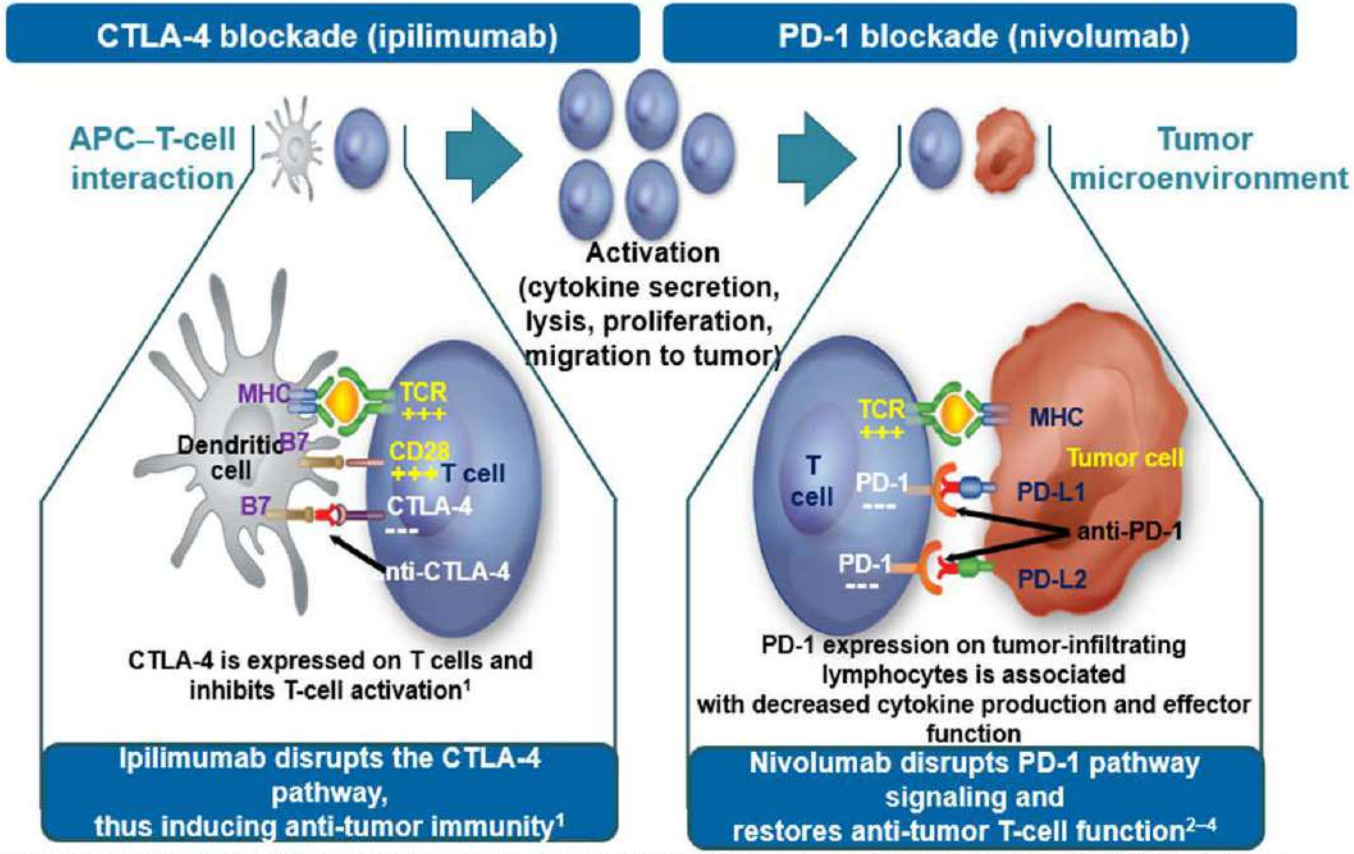
Impact of A-AVD primarily seen in PET2 positive cases

Chen. ASCO 2018, abstract 7539, poster Monday 4 June 2018

Presented By Joseph Connors at 2018 ASCO Annual Meeting

CHECKPOINT INHIBITORS

Nivolumab and Ipilimumab Mechanism of Action



1. Pardoll DM. *Nat Rev Cancer* 2012;12:252–64. 2. Brahmer JR et al. *J Clin Oncol* 2010;28:3167–75. 3. Hamanishi J et al. *Proc Natl Acad Sci U S A* 2007;104:3360–5. 4. Wang C et al. *Cancer Immunol Res* 2014;2:1–11

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CHECKPOINT INHIBITORS

Immunomodifiers in Lymphoma
Selection

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Antibody	Target	Company
Nivolumab	PD1	BMS
Pembrolizumab	PD1	MSD
REGN2810	PD1	Regeneron
Durvalumab	PD-L1	Celgene
Avelumab	PD-L1	Pfizer
Ipilimumab	CTLA-4	BMS

CHECKPOINT INHIBITORS

Results of PD1 Blocking Antibodies in Relapsed HL

Results of Phase-II Studies

Post ASCT and Brentuximab Vedotin

Drug	Dose/Schedule	N	% ORR	% CR	1st Author/Ref
Pembrolizumab (humanized IgG4)	200 mg IV Q 3wks	69	72%	21%	Chen, R & C. Moskowitz JCO 2017
Nivolumab (Fully human IgG4)	3 mg/kg IV Q 2 wks	80	66%	9%	Younes, A/Lancet Oncology 2016

CHECKPOINT INHIBITORS

Results of PD1 Blocking Antibodies in Relapsed HL

Results of Phase-II Studies

Post ASCT but No PRIOR Brentuximab Vedotin

Drug	Dose/Schedule	N	% ORR	% CR	1st Author/Ref
Pembrolizumab (humanized IgG4)	200 mg IV Q 3wks	60	67%	21%	Chen, R & C. Moskowitz JCO 2017
Nivolumab (Fully human IgG4)	3 mg/kg IV Q 2 wks	63	68%	22%	Fanale, M/ ICML2017

CHECKPOINT INHIBITORS

Phase 2 CheckMate 205
Study Design

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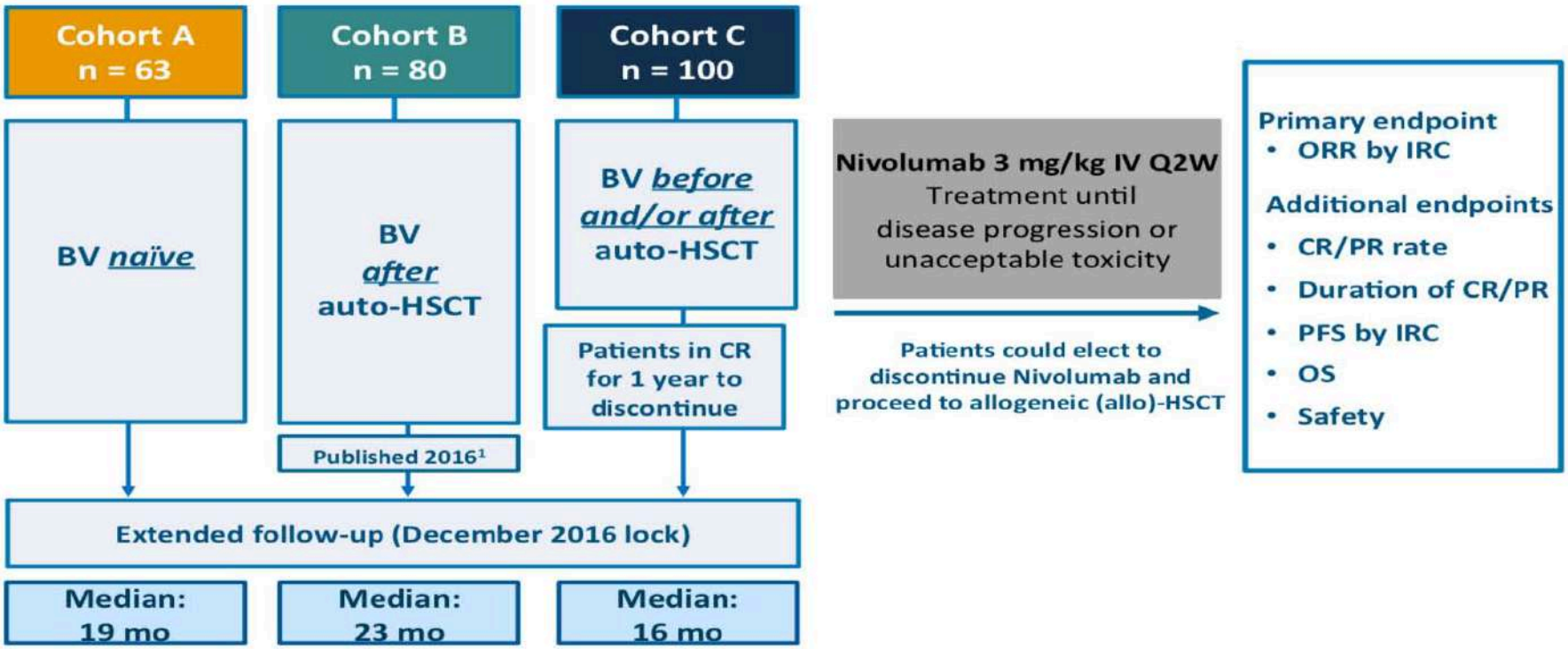

CR = complete response; DOR = duration of response; IRC = Independent Radiology Review Committee; ORR = objective response rate; OS = overall survival; PFS = progression-free survival; PR = partial response; Q2W = every 2 weeks.

1. Younes A et al, Lancet Oncol 2016;17:1283–94

CHECKPOINT INHIBITORS

Phase 2 CheckMate 205

Best Overall Response

GHSG www.ghsg.org

	BV naïve (Cohort A) n = 63	BV after auto-HSCT (Cohort B) n = 80	BV before and/or after auto-HSCT (Cohort C) n = 100	Overall n = 243
Objective resp.[a] % (95% CI)	65 (52, 77)	68 (56, 78)	73 (63, 81)	69 (63, 75)
Best overall response, %				
Complete remission[b]	29	13	12	16
Partial remission	37	55	61	53
Stable disease	24	21	15	19
Progressive disease	11	8	10	9
Unable to determine	0	4	2	2

Per investigator assessment, 33% pts achieved CR and 39% PR

[a]Defined according to 2007 International Working Group criteria. Responses were assessed by IRC; [b]All CRs

CHECKPOINT INHIBITORS

Phase 2 CheckMate 205

Safety Outcomes after Extended Follow-up

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Patients with drug-related AEs (≥10%), serious AEs (≥1%), or AEs leading to discontinuation (≥1%)	Overall population n = 243	
Drug-related AEs, %	**Any grade**	**Grade 3–4**
Fatigue	23	1
Diarrhea	15	1
Infusion-related reaction	14	<1
Rash	12	1
Drug-related serious AEs, %		
Infusion-related reaction	2	<1
Pneumonitis	1	0
Drug-related AEs leading to discontinuation, %		
Pneumonitis	2	0
Autoimmune hepatitis	1	1

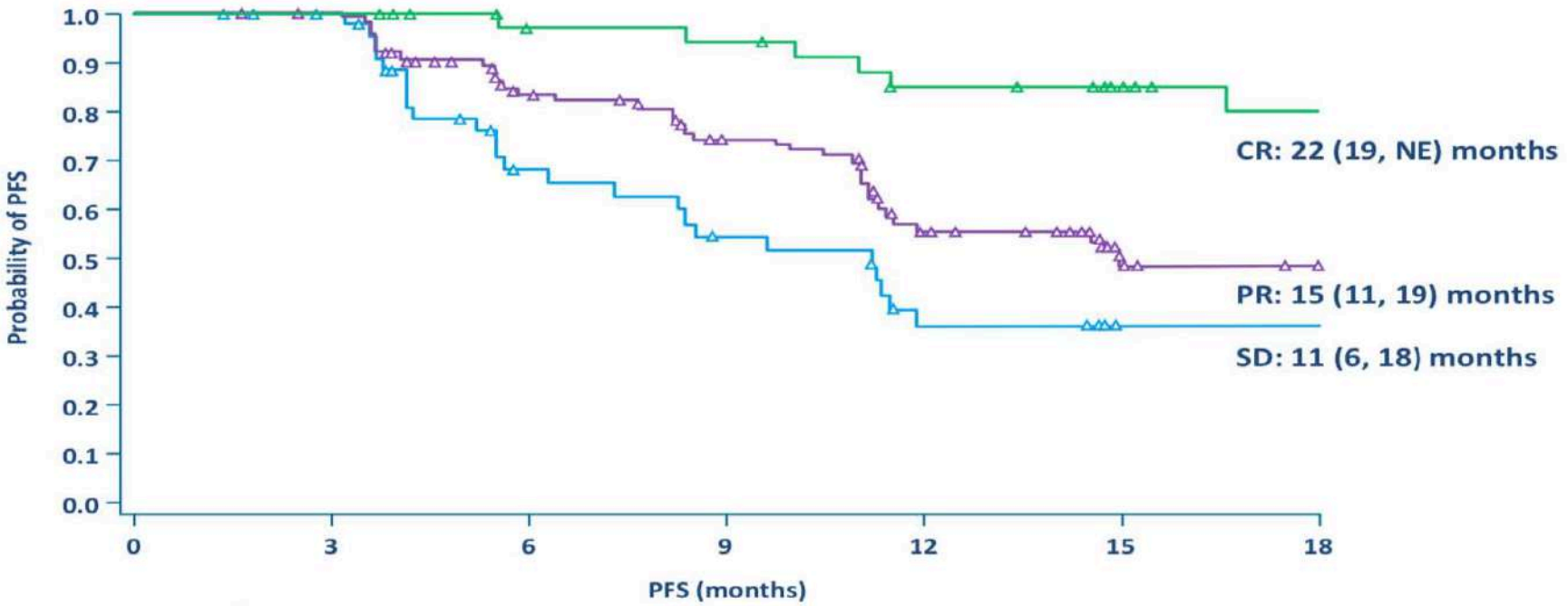
Engert et al, EHA 2017

CHECKPOINT INHIBITORS

Phase 2 CheckMate 205

PFS by Best Overall Response

GHSG
www.ghsg.org



Number of patients at risk

CR	40	40	33	32	27	20	16
PR	128	126	89	71	46	25	21
SD	47	44	25	19	11	8	8

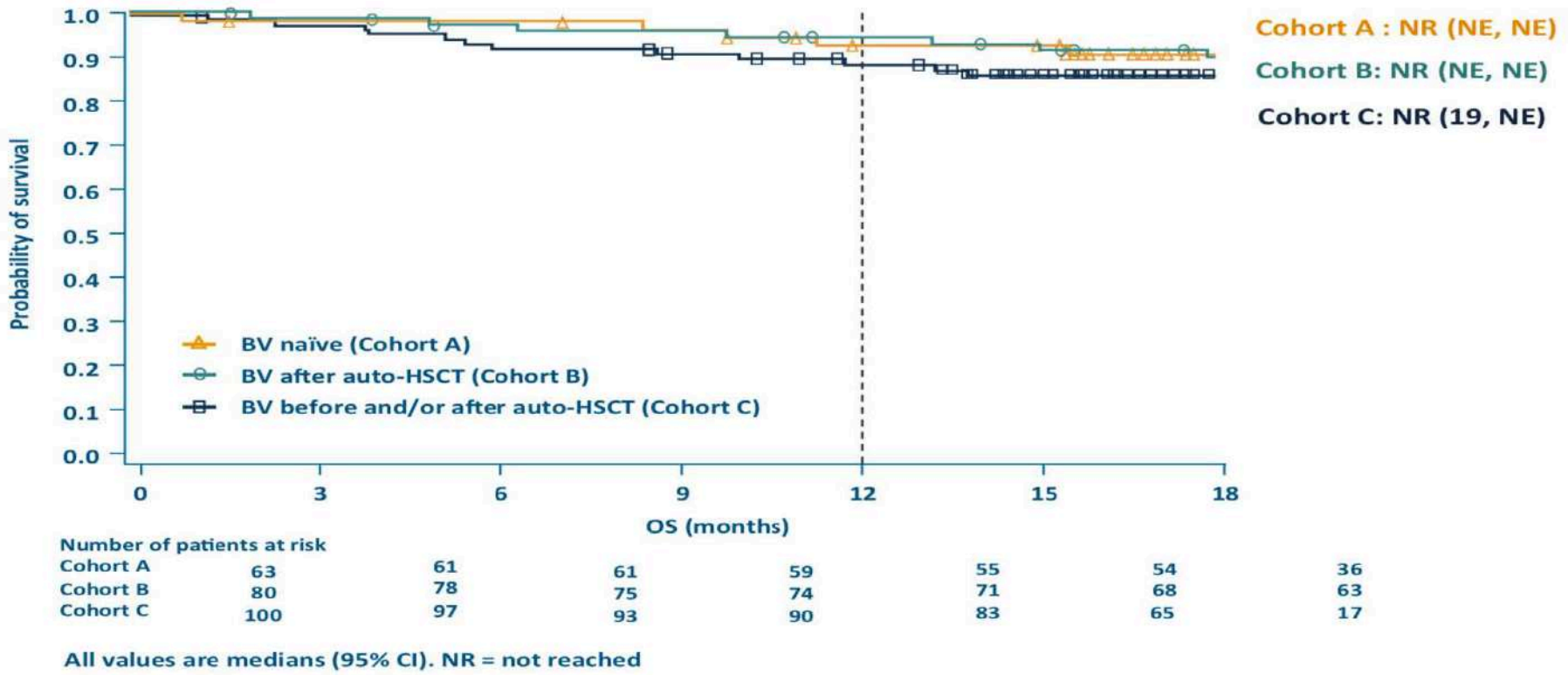
Median (95% CI) PFS for overall patients (N = 243) was 15 (11, 19) months

Engert et al, EHA 2017

CHECKPOINT INHIBITORS

Phase 2 CheckMate 205
Overall Survival

GHSG
www.ghsg.org

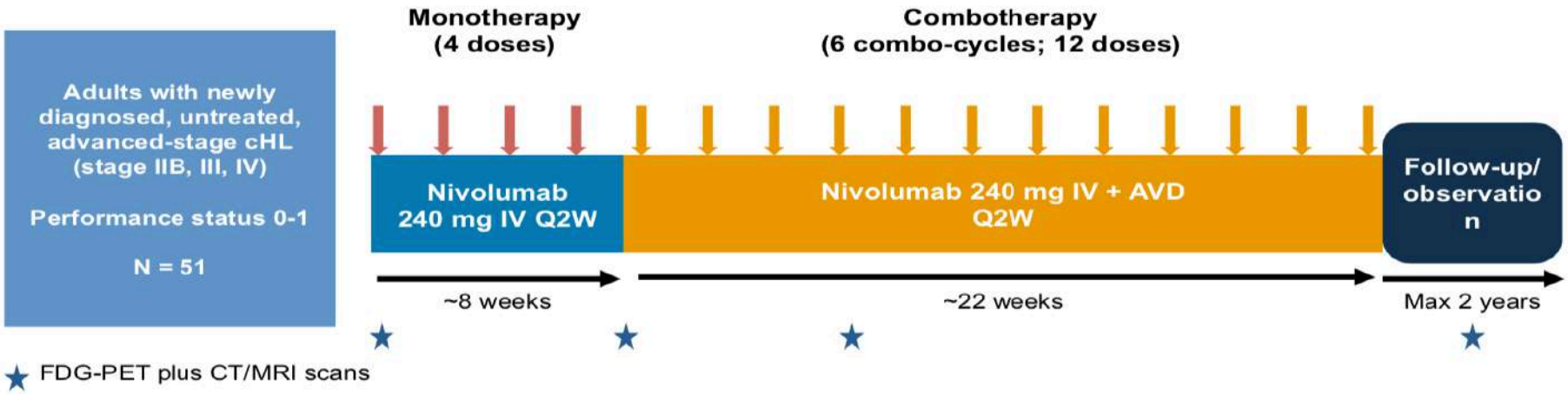


All values are medians (95% CI). NR = not reached

	Cohort A	Cohort B	Cohort C	Overall
12-month OS, %	93 (83-98)	95 (87-98)	90 (82-94)	92 (88-95)

CHECKPOINT INHIBITORS

Phase 2 CheckMate 205 Study Design: Nivolumab in Newly Diagnosed cHL[1]



Primary Endpoint
- Safety and tolerability (Grade 3-5 TRAEs)

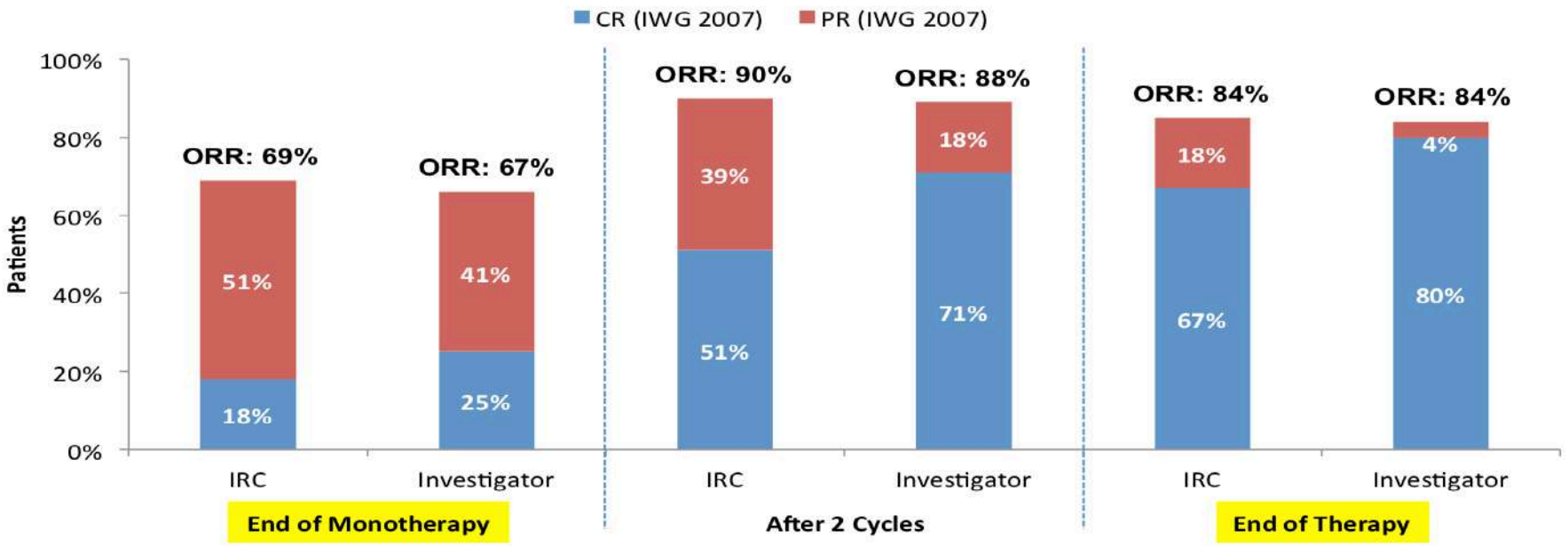
Additional Endpoints
- Discontinuation rate
- CR and ORR by IRC
- CR and ORR by investigator
- mPFS
- OS

Responses were assessed using the IWG 2007 criteria.
At database lock (October 2017), median duration of follow-up was 11.1 months.
Bleomycin excluded due to potential overlapping pulmonary toxicity.

1. Ramchandren R et al. *Blood*. 2017;130:Abstract 651.

CHECKPOINT INHIBITORS

Response per IRC and Investigator: ITT Population[1]



- At end of therapy, ORR per investigator for the ITT population was 84%, with 80% of patients achieving CR
- Five patients were nonevaluable at end of therapy[a]

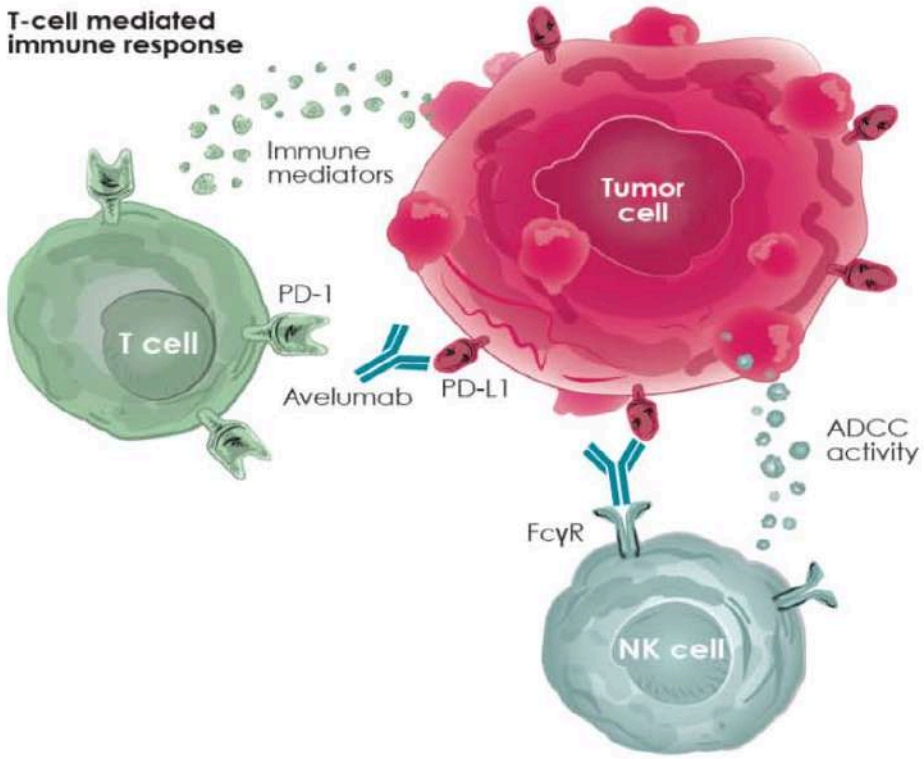
[a] No evaluable scan in at least one on-study time point.
Biopsies were not required for patients to be considered to have progressive disease.
Values may not add together due to rounding.

1. Ramchandren R et al. *Blood*. 2017;130:Abstract 651.

CHECKPOINT INHIBITORS

Avelumab

- Human anti–PD-L1 IgG1 mAb
- Inhibits PD-L1/PD-1 interactions,[1] leaving PD-L2/PD-1 pathway intact
  - Unlike anti–PD-1antibodies that target T cells, avelumab targets tumor cells
- Half-life ≈4 days; >90% target occupancy dosing Q2W at 10 mg/kg[1]
- Induces ADCC against tumor cells in vitro[2,3]
- Antitumor activity in lung, bladder, renal, and other malignancies[4-6]
- FDA-approved treatment for metastatic Merkel cell carcinoma and advanced urothelial carcinoma progressed after platinum-containing chemotherapy[7]



CHECKPOINT INHIBITORS

Study design: JAVELIN Hodgkin (NCT02603419)

Phase 1b, open-label, multicenter, multiple-dose, randomized, parallel-arm trial

Eligible patients

- Histologically confirmed cHL with R/R disease
- Disease progression following either auto-SCT or **allo-SCT**, or SCT-ineligible

R
1:1:1:1:1

Lead-in phase
Target enrollment:
n=6/cohort

Avelumab

Cohort	Dose (IV)	Schedule
A	70 mg	Q2W
B	350 mg	Q2W
C	500 mg	Q3W
D	500 mg	Q2W
E	10 mg/kg	Q2W

Selection criteria for dose-expansion phase

- >90% mean target occupancy after 1 treatment cycle
- ≥3 objective responses

Select endpoints

- Primary
  - Target occupancy
  - Pharmacokinetics
- Secondary
  - Safety*
  - Objective response[1]

Data cutoff date for this presentation: April 21, 2017

allo, allogeneic; **auto**, autologous; **cHL**, classical Hodgkin lymphoma; **IV**, intravenous; **NCI CTCAE**, National Cancer Institute Common Terminology Criteria for Adverse Events; **R**, randomize; **Q2W**, every 2 weeks; **Q3W**, every 3 weeks; **SCT**, stem cell transplant.
* Per NCI CTCAE v4.03.

1. Cheson BD, et al. J Clin Oncol. 2007;25(5):579-86.

CHECKPOINT INHIBITORS

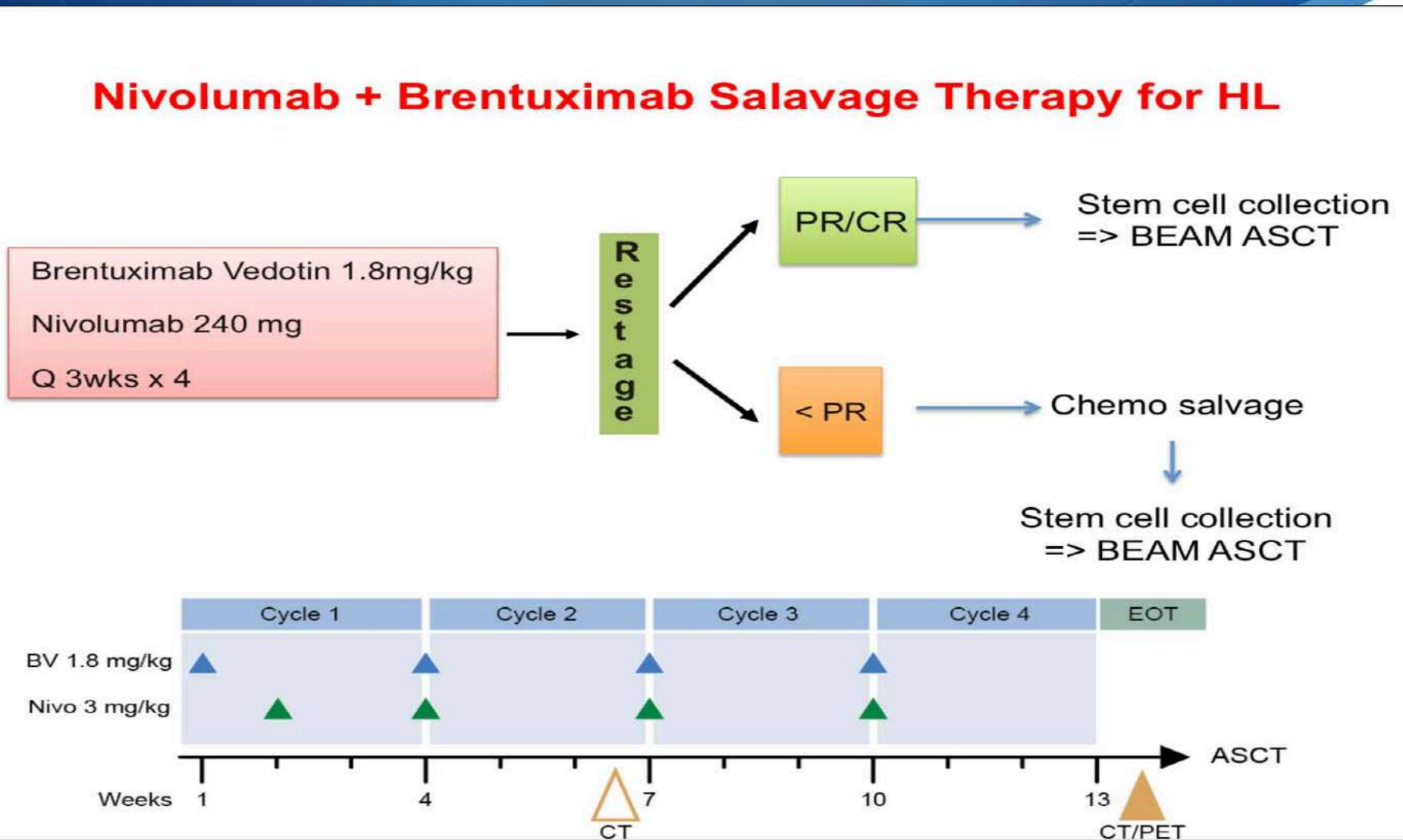
Best overall response

- ORR was 41.9%, including CR in 16.1% and PR in 25.8%
- Median time to response was 1.5 months (range 1.4-6.2)

BOR n (%)	Overall population N=31
CR	5 (16.1)
PR	8 (25.8)
SD	9 (29.0)
PD	5 (16.1)
NE*	4 (12.9)
ORR, %	41.9
DCR, %	71.0

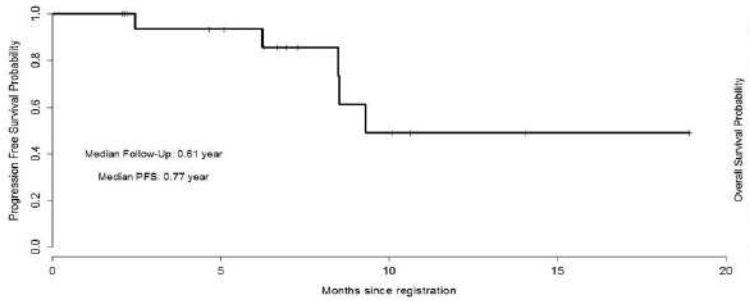
BOR, best overall response; **CR**, complete response; **DCR**, disease control rate; **NE**, not evaluable; **ORR**, objective response rate; **PD**, progressive disease; **PR**, partial response; **SD**, stable disease.
* Patients had no post-baseline assessments for reasons other than death.

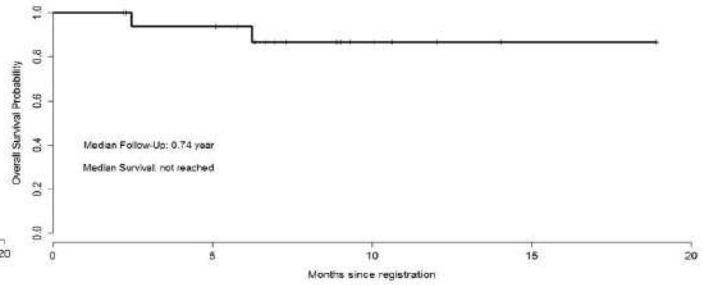
CHECKPOINT INHIBITORS combinations



CHECKPOINT INHIBITORS combinations

PFS and OS BV+ Nivo





6-month PFS: 93%
(95%CI: 82-100%)

Median follow-up = 0.74 years
Median OS not reached

ECOG-ACRIN cancer research group

NYU Langone Health

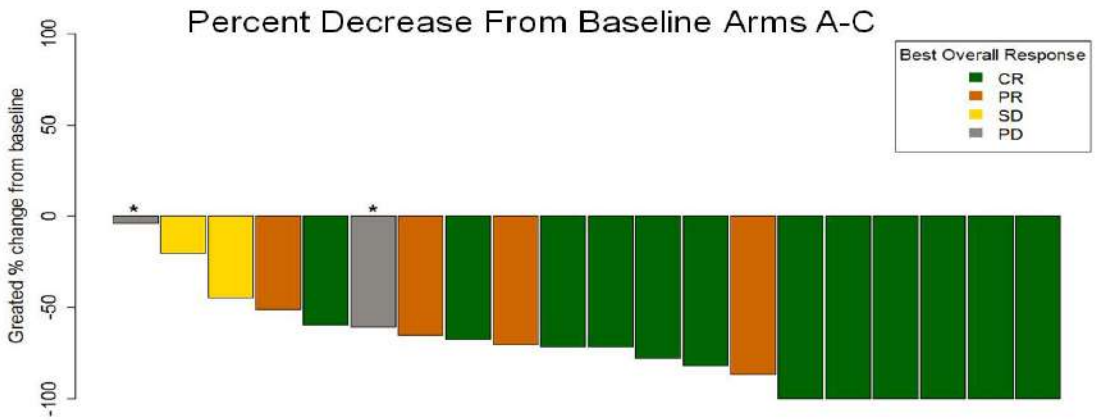
Presented By Catherine Magid Diefenbach at 2018 ASCO Annual Meeting

CHECKPOINT INHIBITORS combinations

BV + /- Ipilimumab is Highly Active

BV + IPI 21 Response Eligible Patients

Evaluable Pts.	ORR	CR	PR	SD	IE* for Response	PD
N = 21	16 (76%)	10 (48%)	6 (29%)	2 (10%)	1 (5%)	2 (10%)



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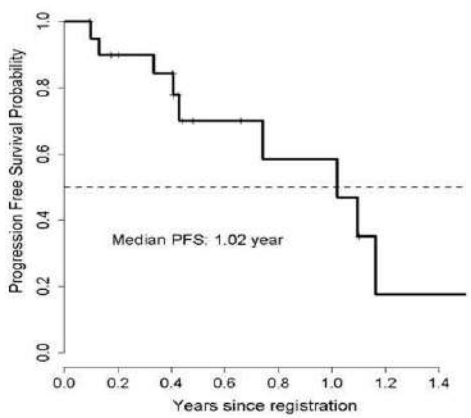
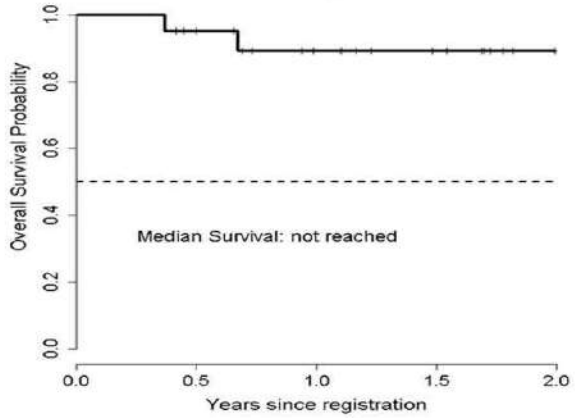
CHECKPOINT INHIBITORS combinations

PFS and OS Arms BV + Ipi





Time of evaluation	PFS% (95% CI)	OS % (95% C.I)
0.5 year	70 % (51-97%)	95% (87-100%)
1 year	58% (36-95%)	89% (76-100%)
Median PFS	1.02 yr (0.74 --)	Not reached

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IMMUNOTHERAPY

WHAT' S THE RIGHT ALGORITM?

WHAT'S THE RIGHT LINE?

(First? Salvage?After ASCT?

Bridge to Allo?)

AlloSCT

- 3 year OS approximately 50%
- High TRM (20%)
- Morbidity
- Hospitalization
- KNOWN CURABILITY

VS.

CBD

- Immune toxicity
- Low TRM
- Low Morbidity
- No Hospitalizations
- Relapses seen at 2+ years
- Curability unknown

COULD YOU STRATIFY PATIENTS BASED ON RISK OR ON BIOLOGY?

NYU Langone Health

CONCLUSIONS

HODGKIN DISEASE IS HIGHLY CURABLE DISEASE WITH CHEMOTHERAPY.

HOWEVER SOME PATIENTS ARE PRIMARY REFRACTORY OR RELAPSE AFTER FIRST LINE THERAPY OR ASCT

ASCT LEADS TO 3 YEARS PFS RATE OF 40%TO 60 % ACCORDING TO REFRACTORY OR RELAPSE PATIENTS

MEDIAN OS AFTER ASCT RELAPSE WAS 1 TO 2 YEARS

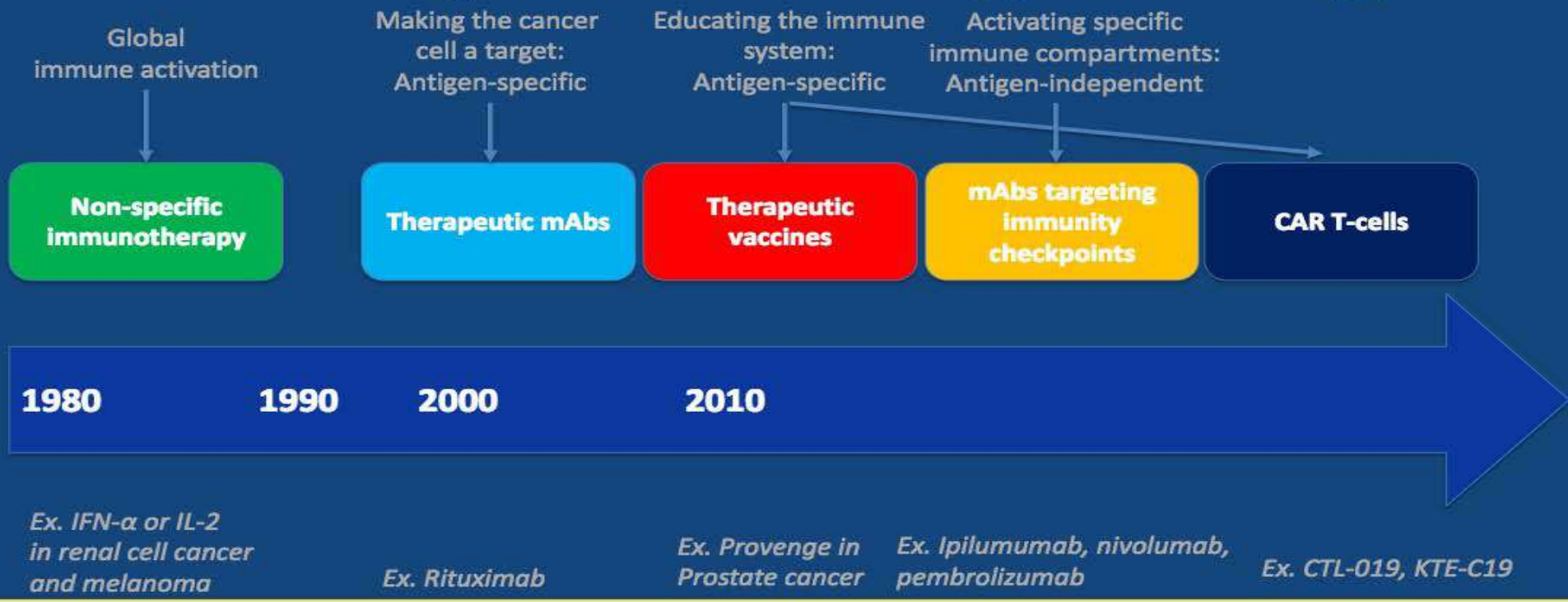
CONCLUSIONS

NEW AGENTS ARE CHANGING THE HYSTORY OF THE DISEASE

AND NOW PROBABLY THE INDICATION TO ALLO WILL BE CONTROVERSIAL IN CHECKPOINT INHIBITORS ERA, IN RELAPSED PATIENTS AFTER AUTO.

THE TREATMENT ALGORITHM IS RAPIDLY CHANGING TOWARD A COMBO THERAPY WITH IMMUNO AND CHEMOTHERAPY OR IMMUNOTHERAPY ALONE.

Brief History of Immunotherapy in Oncology



GRAZIE PER L'ATTENZIONE