New
Drugs
In Hematology
October 1, 2018

Hodgkin Lymphoma

Nivolumab

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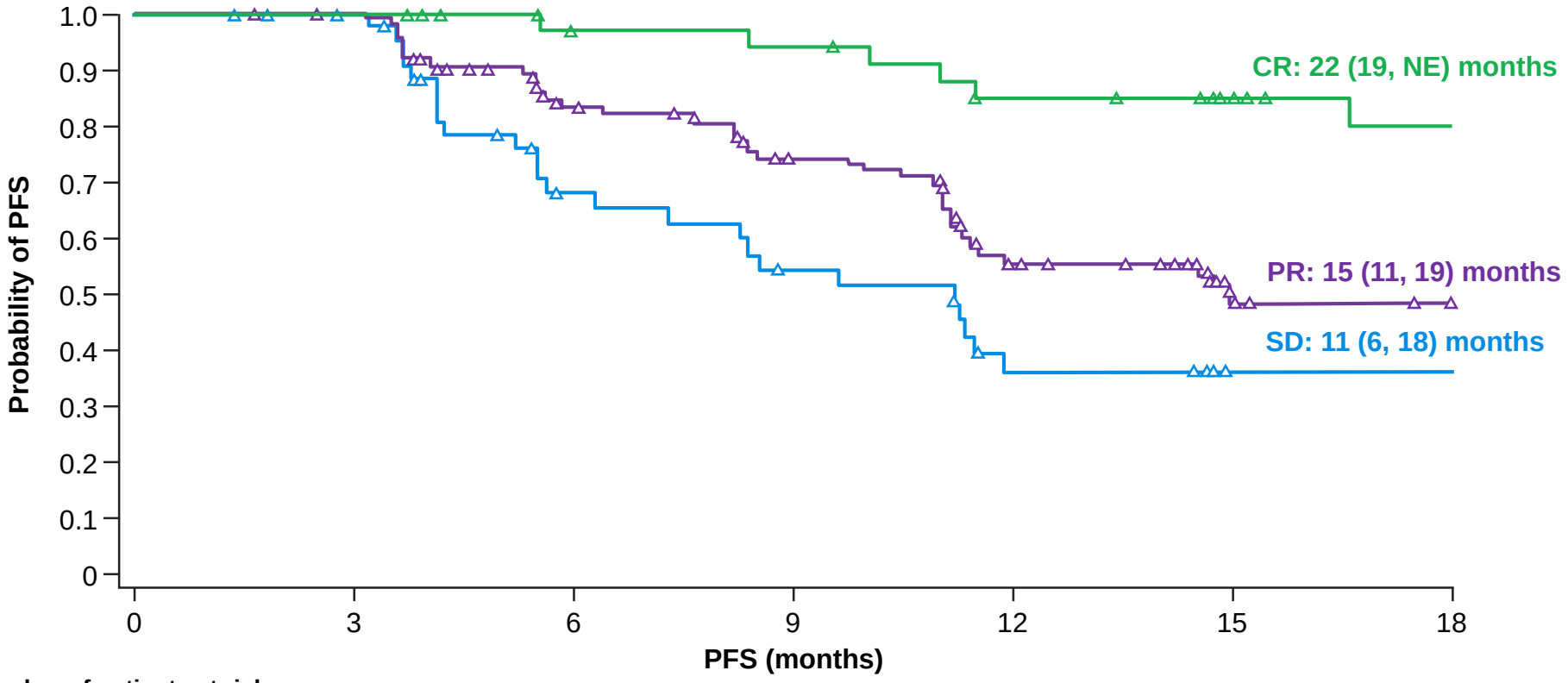
Nivolumab

- Clinical Activity
- Response Assessment
- Treatment Beyond Progression
- Flare

Nivolumab for Relapsed cHL

Progression-Free Survival by Best Overall Response



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

International Working Group consensus response evaluation criteria in lymphoma (RECIL 2017)

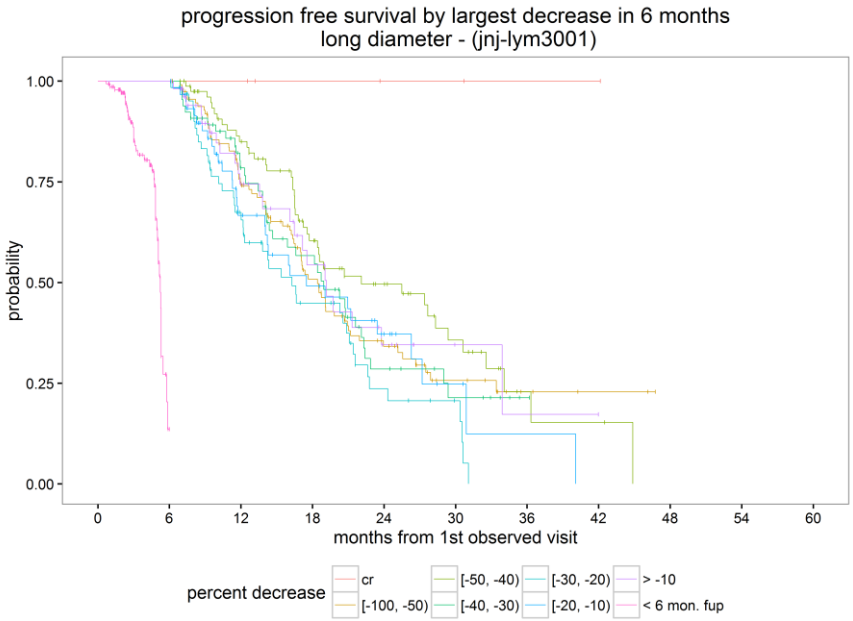
A Younes P Hilden B Coiffier A Hagenbeek G Salles W Wilson J.F. Seymour K Kelly J Gribben M Pfreunschuh F Morschhauser H Schoder A.D. Zelenetz J Rademaker R Advani N Valente C Fortpied T.E. Witzig L.H. Sehn A. Engert R.I. Fisher P-L Zinzani M. Federico M. Hutchings C. Bollard M. Trneny Y.A. Elsayed K Tobinai J.S. Abramson N Fowler A Goy M Smith S Ansell J Kuruvilla M Dreyling C Thieblemont R.F. Little I Aurer M.H. J. Van Oers K Takeshita A Gopal S Rule S de Vos I Kloos M.S. Kaminski M Meignan L.H. Schwartz J.P. Leonard S.J. Schuster V.E. Seshan

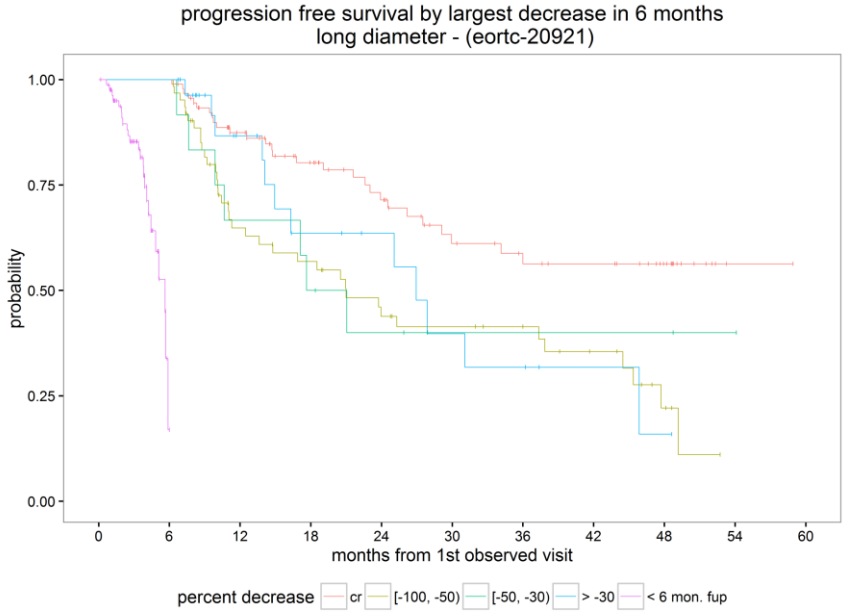
50 co-authors
38 Academic centers
4 Pharmaceutical companies

4 Imaging experts
3 statisticians

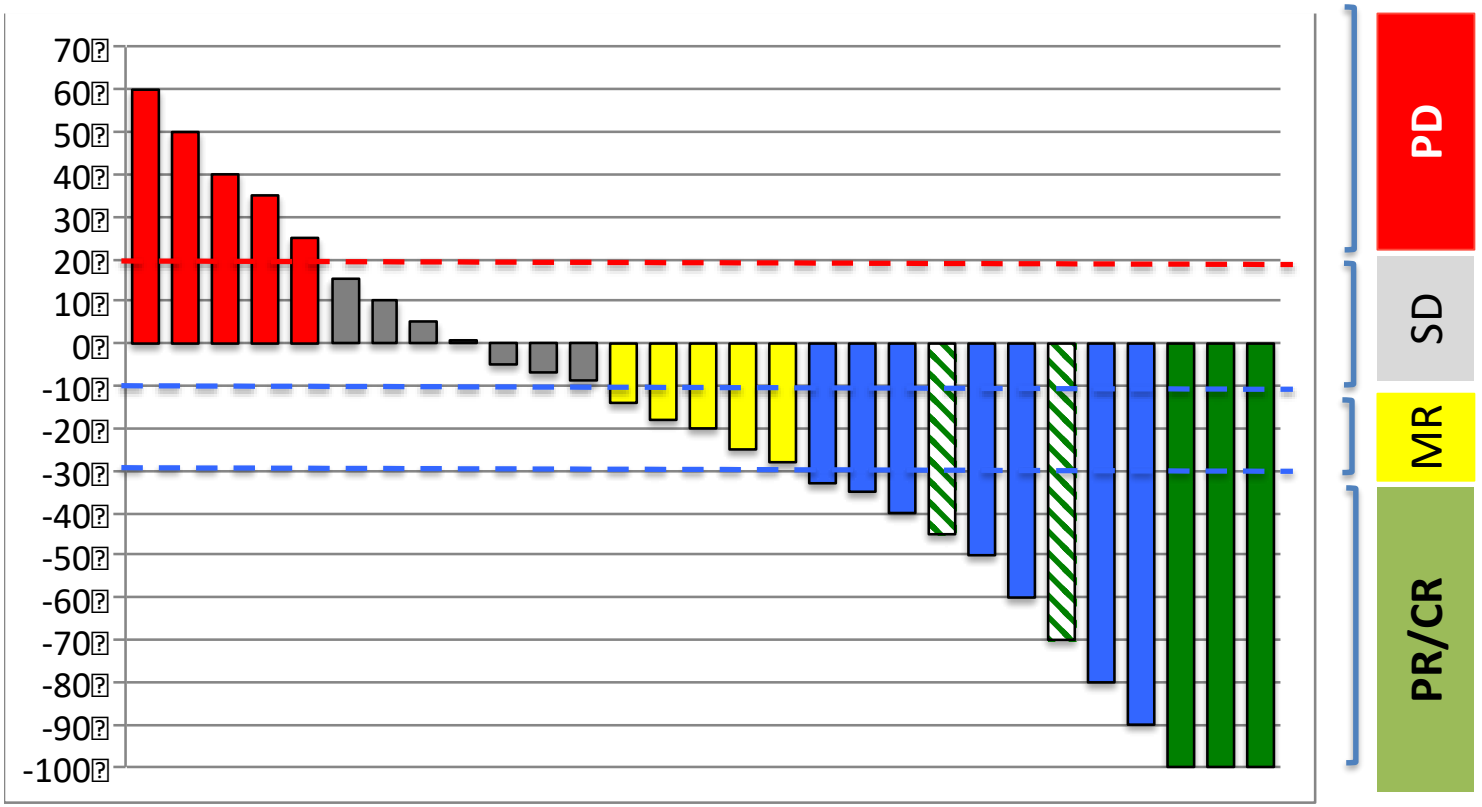
Ann Oncol, April 3, 2017

With the Exception of a CR, the depth of response has no impact on PFS





RECIL 2017



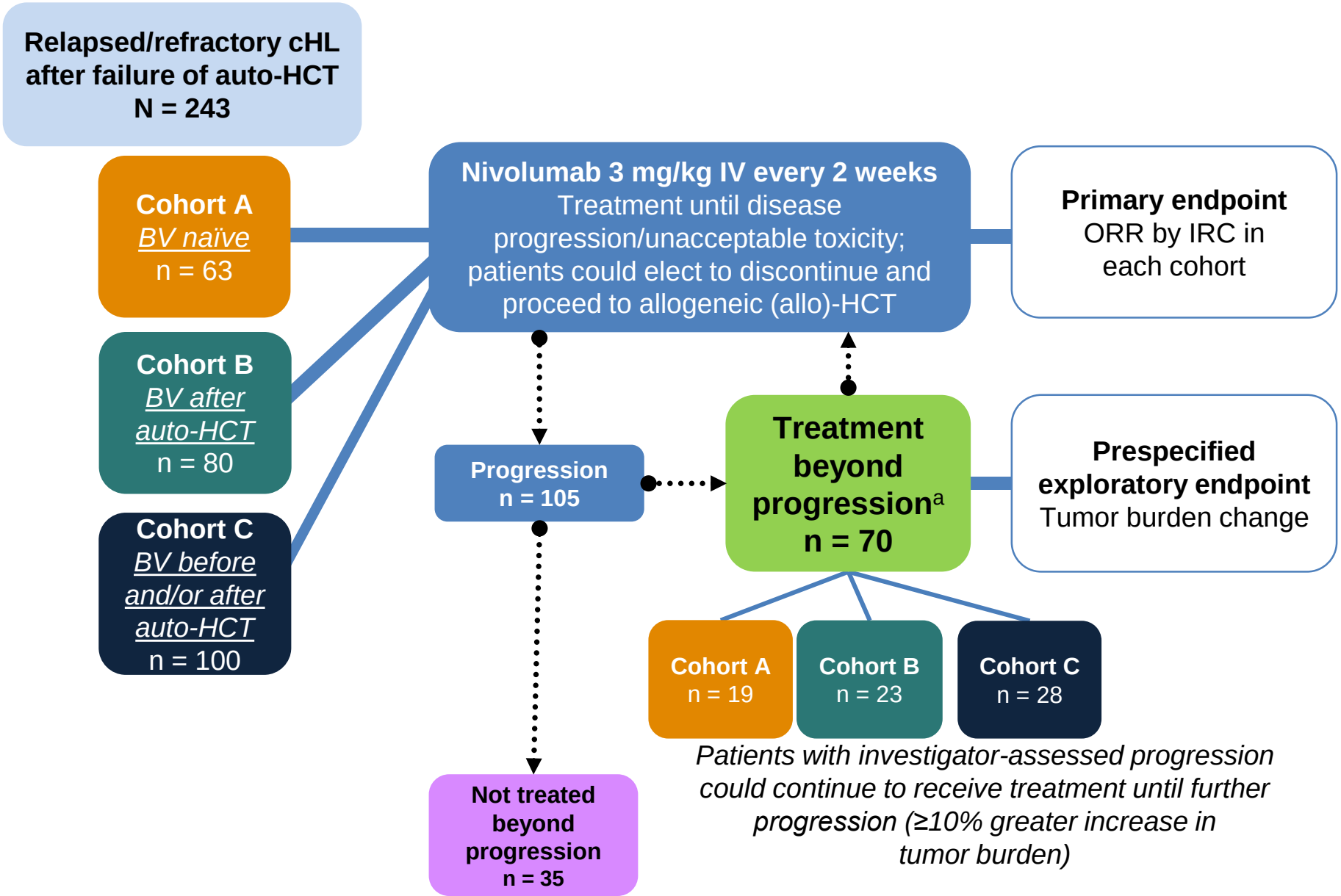
Younes A et al, Annals of Oncology 2017

Atypical Responses to Checkpoint Inhibitor Therapy

- In cHL, patients who have radiographic PD while on chemotherapy do not benefit from continued treatment beyond PD
- In contrast, atypical response patterns including pseudo-progression with checkpoint inhibitors led to clinical benefits in some patients with solid tumors who had been treated beyond PD
- A protocol amendment to the CheckMate 205 study (July 2014) allowed patients with stable performance status and perceived clinical benefit to be treated beyond investigator-assessed disease progression (TBP)
  - Disease progression was classified into 3 categories (IWG 2007 criteria)

1) Increase in overall tumor burden[a]
2) Non-target lesion growth[b]
3) Development of new lesion[c]

Phase 2 CheckMate 205 Study Design



Patient Demographics

Characteristic	All patients N = 243	TBP n = 70	Non-TBP n = 35
Age, years	34 (18–72)	37 (18–72)	34 (23–63)
Male, %	58	67	54
ECOG PS at baseline, % 0 1	 54 46	 61 39	 34 66
Stage IV disease at initial diagnosis, %	27	27	17
Previous lines of therapy	4 (2–15)	3 (2–5)	4 (3–9)
Time from diagnosis to first dose of nivolumab, years	4 (1–31)	6 (1–30)	3 (1–31)
Time from first dose of nivolumab to initial progression date, months		6 (1–22)	7 (1–22)
B symptoms at baseline, %	22	20	34
Bulky disease at baseline, %	20	19	23
Extra lymphatic involvement at baseline, %	43	46	51

Characteristics of Progressive Disease in Patients Treatment Beyond Progression (TBP)

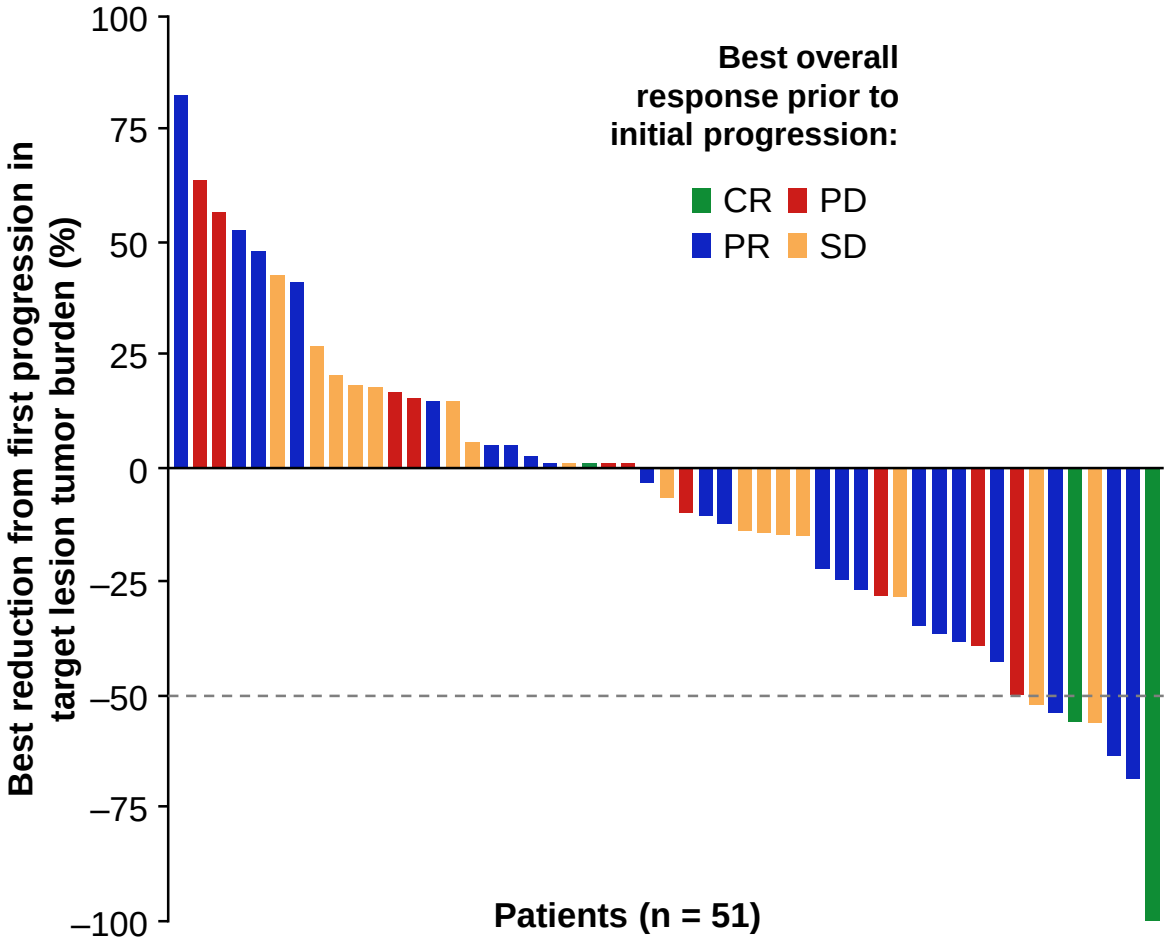
Characteristics of progressive disease, n (%)[a,b,c]	**TBP n = 70**	**Non-TBP n = 35**
Increase in overall tumor burden[d]	13 (19)	7 (20)
Non-target lesion growth[e]	17 (24)	2 (6)
Development of new lesion[f]	47 (67)	13 (37)

Best Overall Response (BOR) Prior to Initial Progression

Best overall response prior to progression, n (%)	TBP n = 70	Non-TBP n = 35
Complete remission	5 (7)	XX
Partial remission	31 (44)	XX
Stable disease	20 (29)	XX
Progressive disease	13 (19)	XX
Non-evaluable	1 (1)	XX

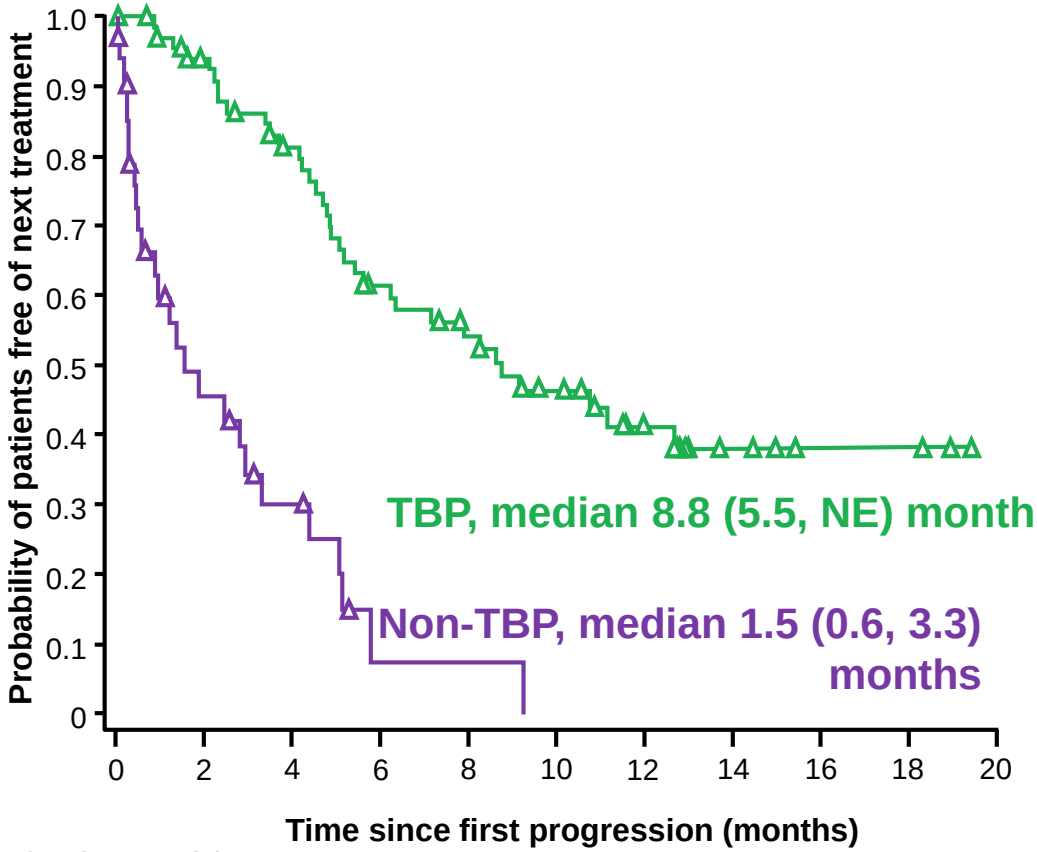
Change in Target Lesion Burden With Nivolumab TBP

51 patients were evaluable for post-progression tumor burden change at database lock



Patients with target lesion reductions, n (%)[a]	TBP n = 70
No reduction	24 (34)
Any reduction	27 (39)
>25%	16 (23)
>50%	7 (10)
100%	1 (1)

Time From Initial Progression to Next Therapy in Patients TBP

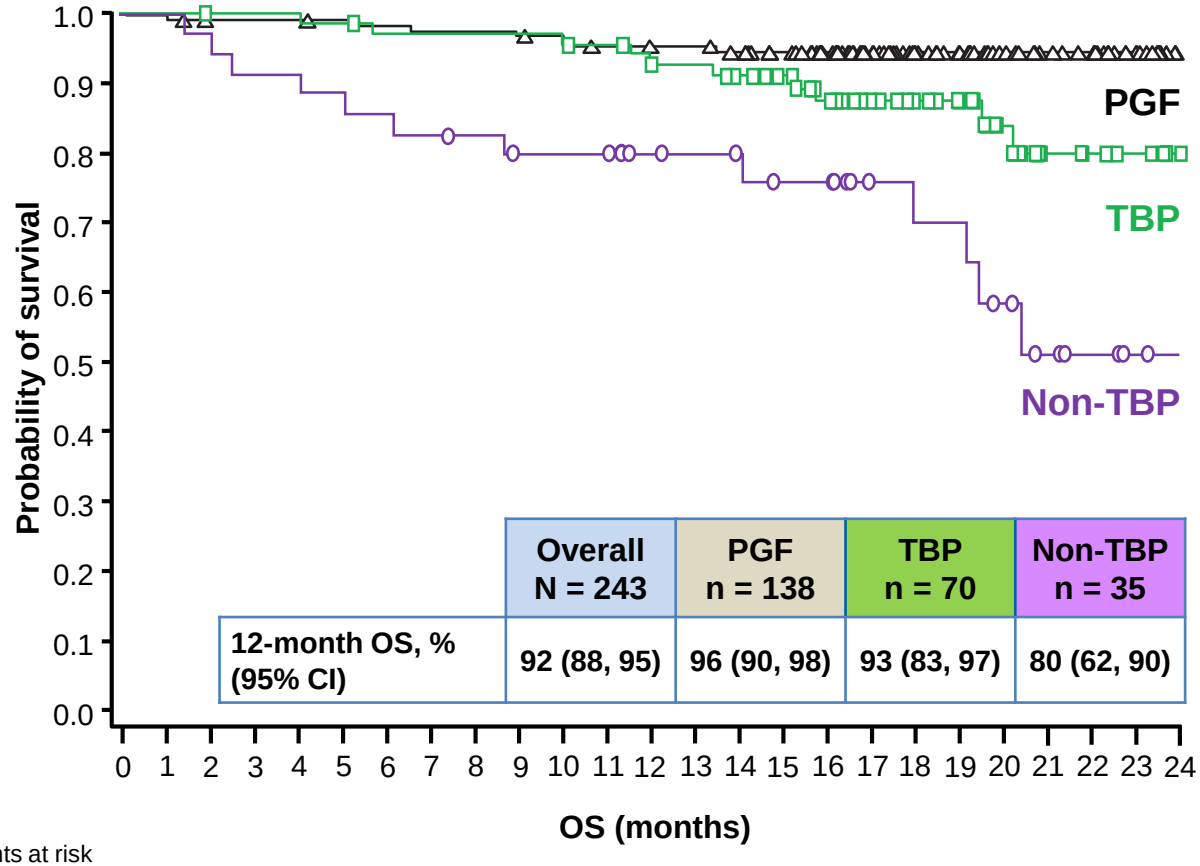


Number of patients at risk

TBP	70	35	13	3
Non-TBP	35	1	0	0

- 21/70 (30%) patients remain on TBP at database lock
- The number of patients TBP who discontinued due to disease progression was 39/70 (56%)

Overall Survival



Number of patients at risk

PGF	138	135	135	133	132	129	126	123	105	74	54	45	15
TBP	70	69	69	66	66	66	60	57	44	30	21	14	7
Non-TBP	35	34	32	30	28	26	23	21	19	12	9	4	1

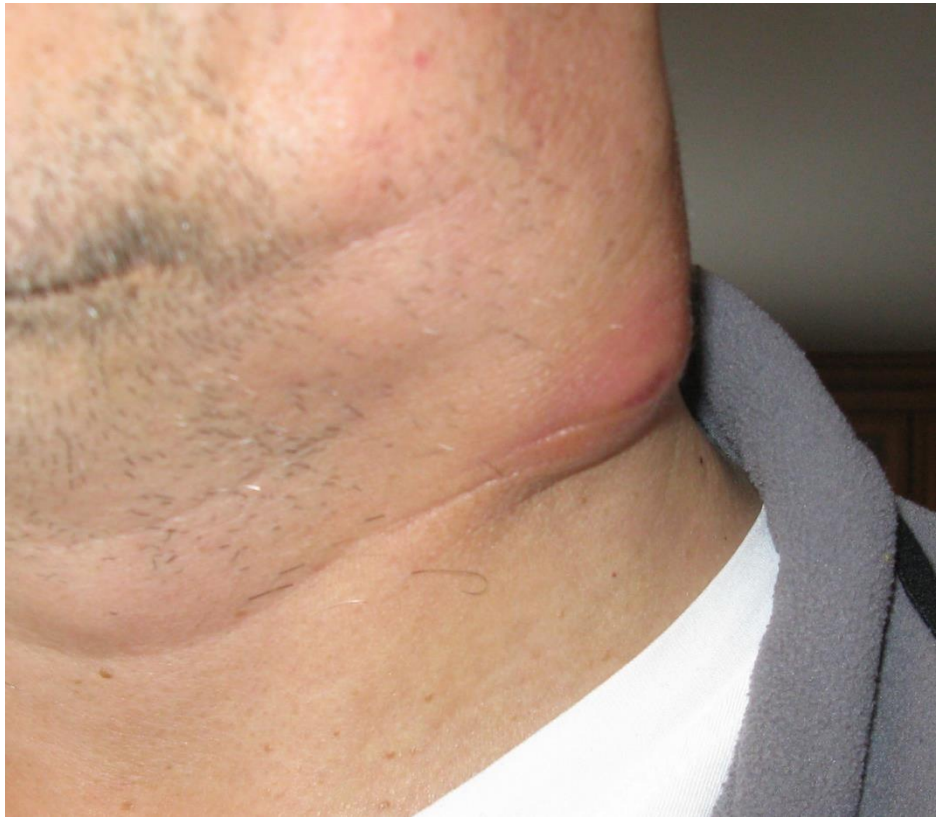
PGF, progression-free patients

Summary of Nivo TBP in cHL

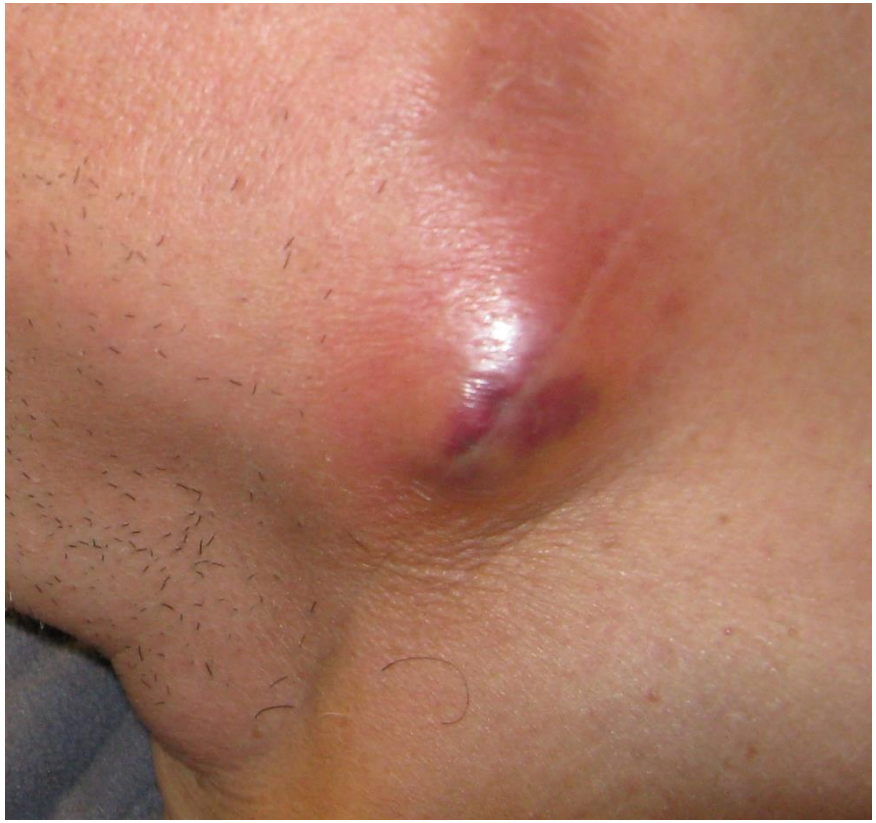
- In CheckMate 205, 70 of 105 (67%) eligible patients with investigator-assessed disease progression were TBP
  - New lesions were the most common cause (67%) of progression in patients TBP
- Stable reductions in tumor burden were seen with continued nivolumab treatment in patients TBP
- OS from first dose of study drug was 93% at 12 months for patients TBP (vs 80% for non-TBP)
- Median time from progression to next therapy was 9 months for patients TBP (vs 2 months for non-TBP)

Pt with relapsed FL
1st dose of Nivo 2/15/2016 at 10 a.m

2/15 2 PM

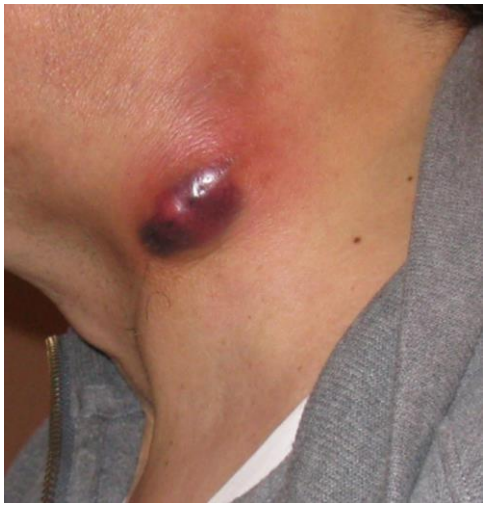


2/15 10 PM

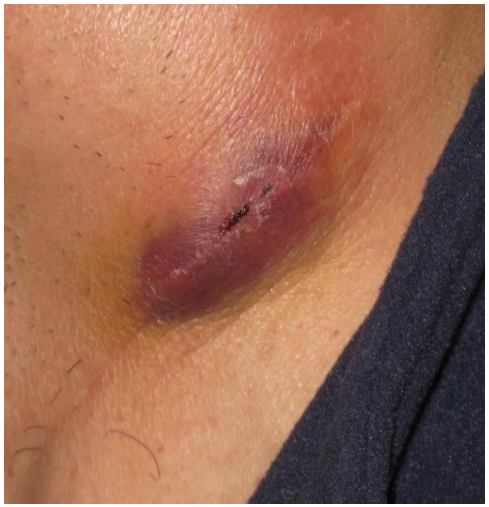


Pt with relapsed FL
1st dose of Nivo 2/15/2016 at 10 a.m

Day 2



Day 4



Day 10