Neoadjuvant Nivolumab plus Platium-Doublet Chemotherapy vs Chemo for resectable (stage IB- IIIA) NSCLC: Association of Pathological Regression with Event Free Survival (EFS) in CheckMate 816

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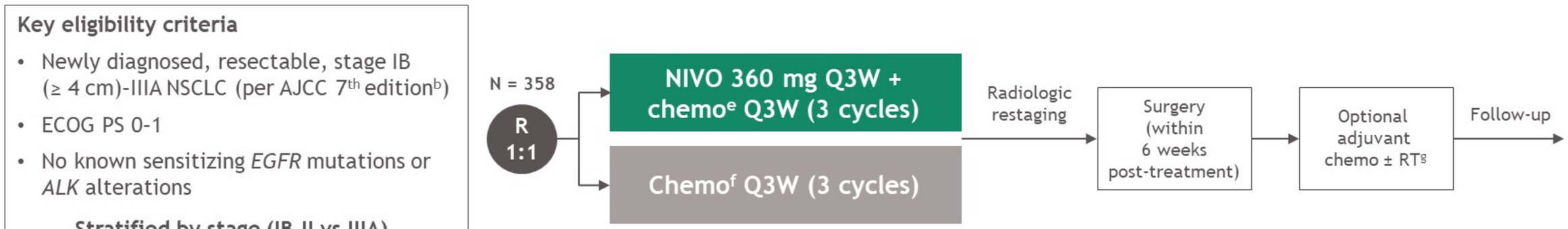
Neoadjuvant nivolumab + platinum-doublet chemotherapy vs chemotherapy for resectable (IB-IIIA) non-small cell lung cancer: association of pathological regression with event-free survival in CheckMate 816

Mariano Provencio-Pulla, et al. Poster LBA8511

- In CheckMate 816,[a] neoadjuvant NIVO + chemo significantly improved the primary endpoints of EFS and pCR vs chemo in patients with resectable NSCLC[1]
  - NIVO + chemo is now indicated in the United States as neoadjuvant treatment for adult patients with resectable (tumors ≥ 4 cm or node positive) NSCLC[2]
- Here, we present a post hoc analysis evaluating the association between pathological regression and EFS from CheckMate 816

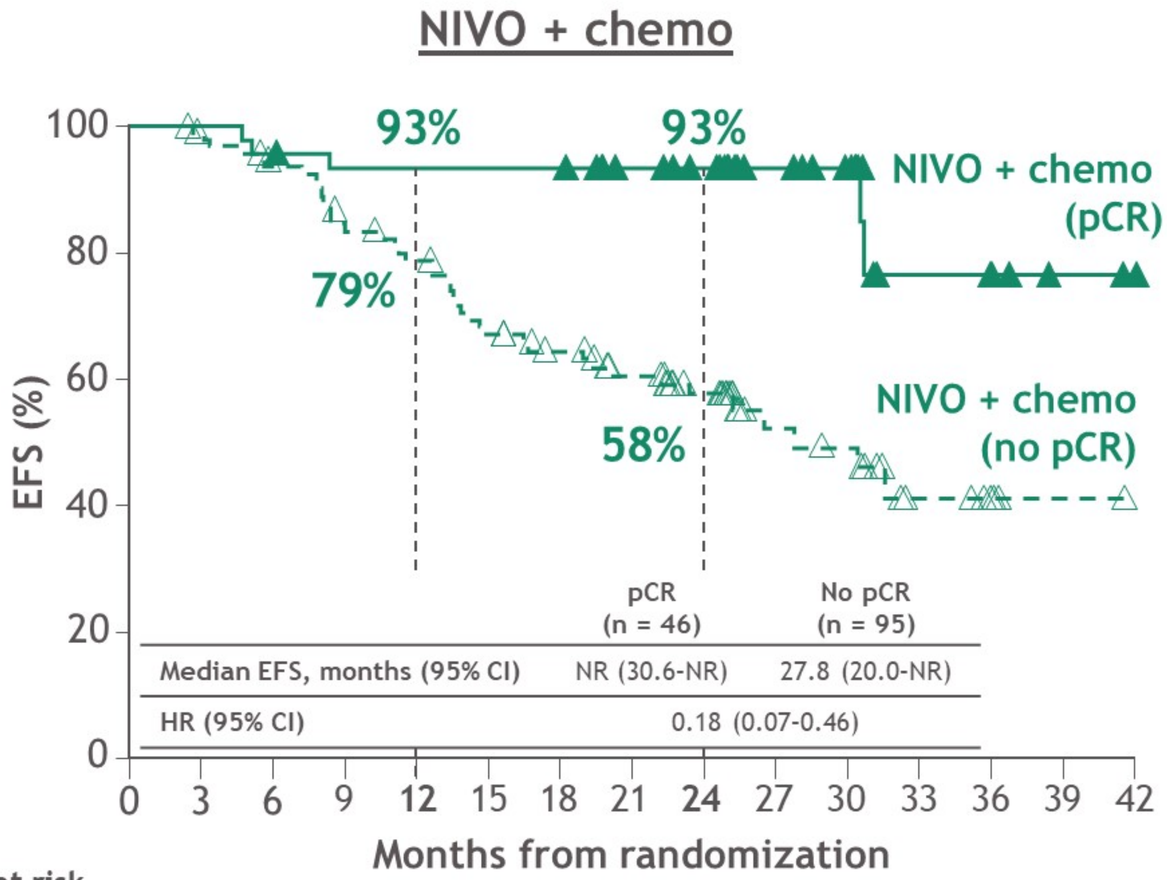


Database lock: September 16, 2020 (final analysis of pCR); October 20, 2021 (preplanned interim analysis 1 of EFS); minimum follow-up: 21 months.

[a]NCT02998528; [b]TNM Classification of Malignant Tumors 7th edition; [c]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); [d]Included patients with PD-L1 expression status not evaluable and indeterminate; [e]Non-squamous: pemetrexed + cisplatin or paclitaxel + carboplatin; squamous: gemcitabine + cisplatin or paclitaxel + carboplatin; [f]Vinorelbine + cisplatin, docetaxel + cisplatin, gemcitabine + cisplatin (squamous only), pemetrexed + cisplatin (non-squamous only), or paclitaxel + carboplatin; [g]Per healthcare professional choice.

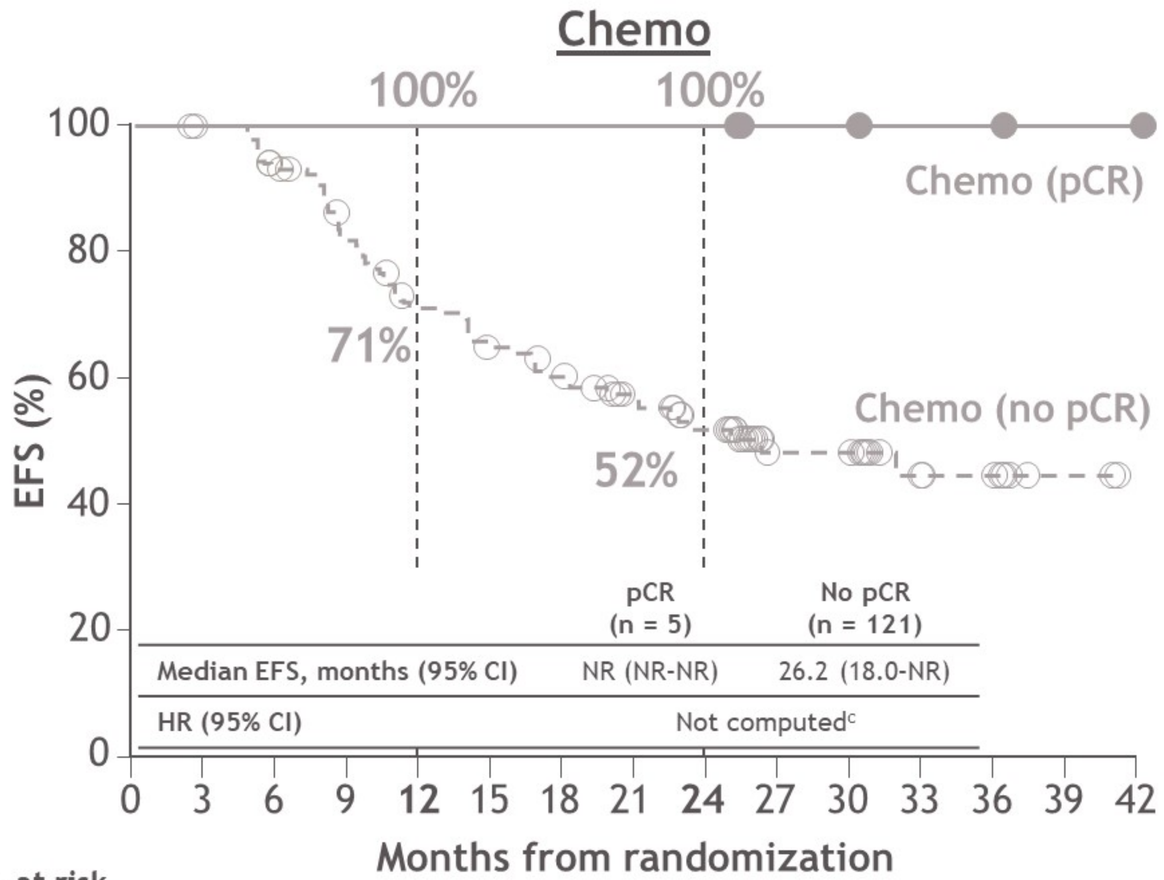
1. Forde PM, et al. *N Engl J Med* 2022; epub ahead of print. doi: 10.1056/NEJMoa2202170; 2. OPDIVO® (nivolumab) [package insert]. Princeton, NJ: Bristol Myers Squibb; March 2022.

EFS by pCR status[a] (primary tumor) in the path-evaluable patient population



No. at risk

pCR	46	46	43	42	42	42	42	37	34	20	15	7	4	2	0
No pCR	95	92	84	74	68	57	52	45	35	18	16	6	2	1	0



No. at risk

pCR	5	5	5	5	5	5	5	5	5	3	2	2	2	1	0
No pCR	121	119	108	93	79	71	64	53	44	21	20	10	8	2	0

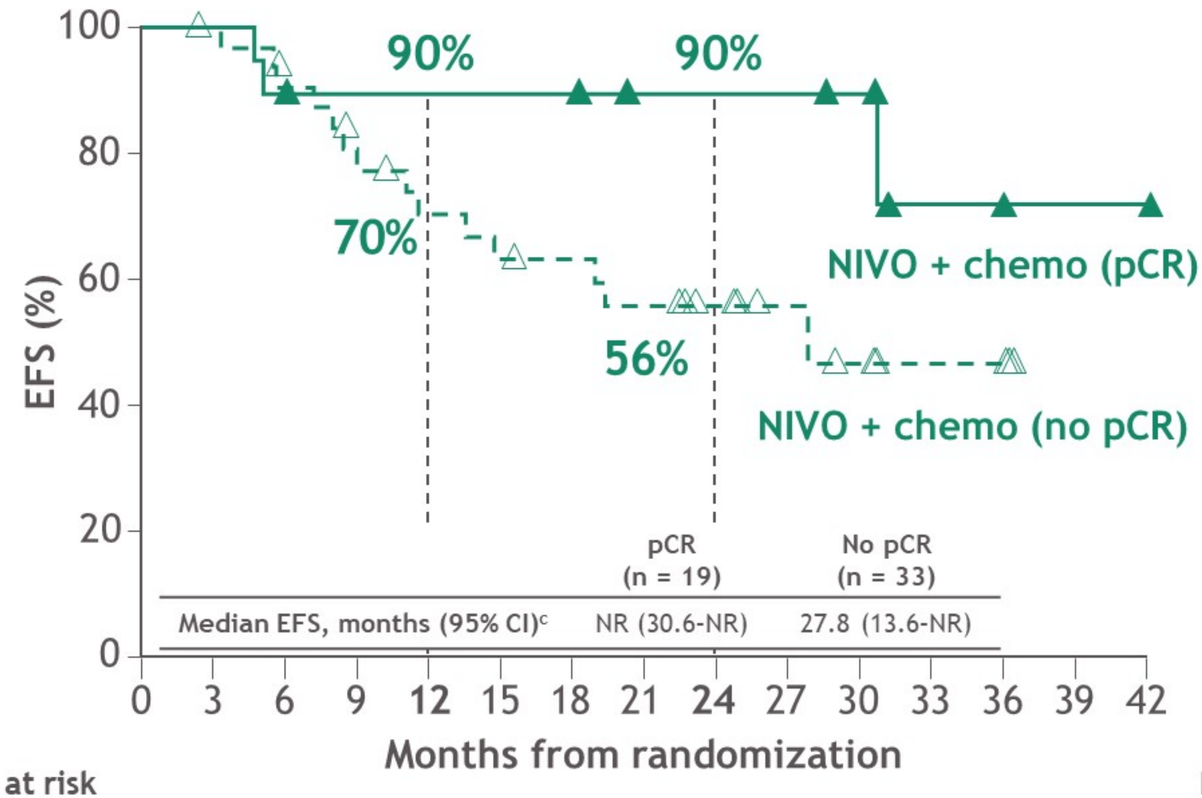
- EFS was also improved in patients with MPR[b] in the primary tumor compared with those without; HR (95% CI) was 0.26 (0.14–0.50) for NIVO + chemo and 0.48 (0.22–1.05) for chemo, respectively

Minimum follow-up: 21 months; median follow-up: 29.5 months.

[a]pCR: 0% RVT cells in the primary tumor in the path-evaluable patient population (patients who underwent surgery and had pathologically evaluable samples); [b]MPR: ≤ 10% RVT cells in the primary tumor in the path-evaluable patient population; [c]HR was not computed for the chemo arm due to only 5 patients having a pCR.

EFS by pCR status (primary tumor) and baseline stage of disease[a]: NIVO + chemo

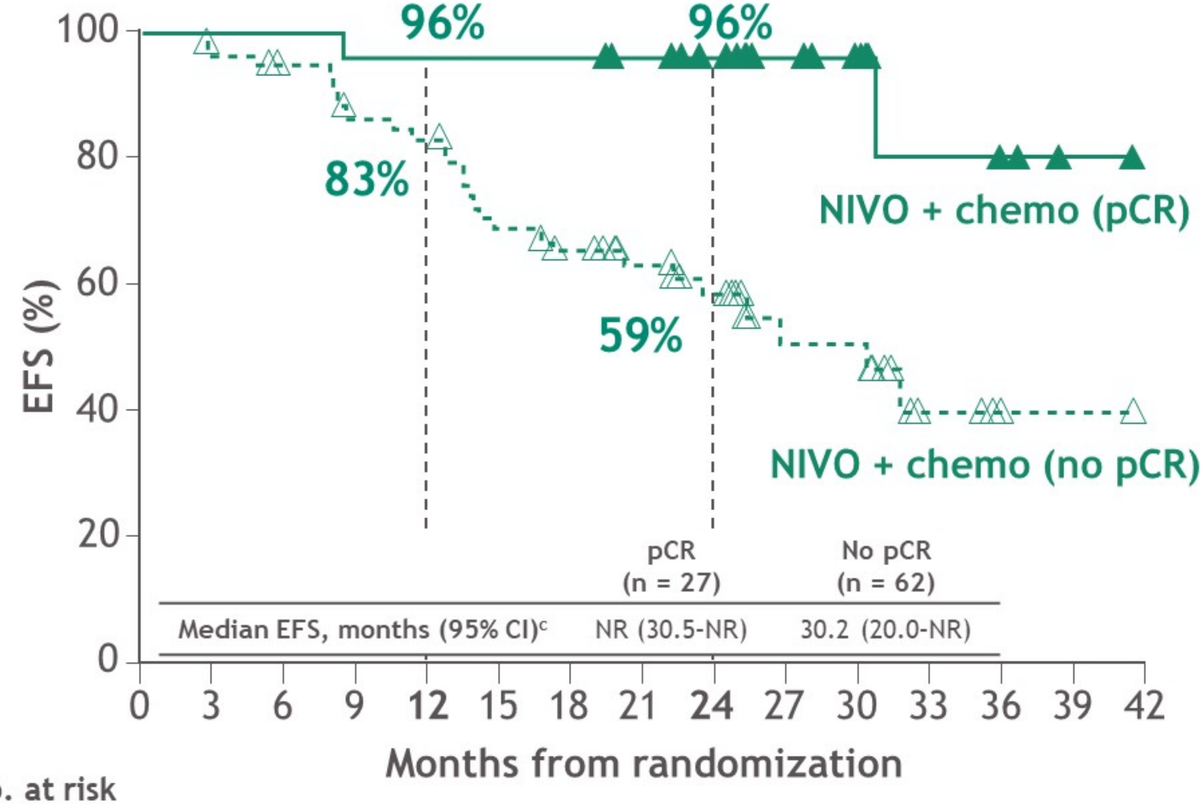
Baseline stage IB-II[b]



No. at risk

pCR	19	19	16	16	16	16	16	14	14	7	6	2	1	1	0
No pCR	33	32	28	24	20	18	17	15	11	6	4	2	1	0	0

Baseline stage IIIA[b]



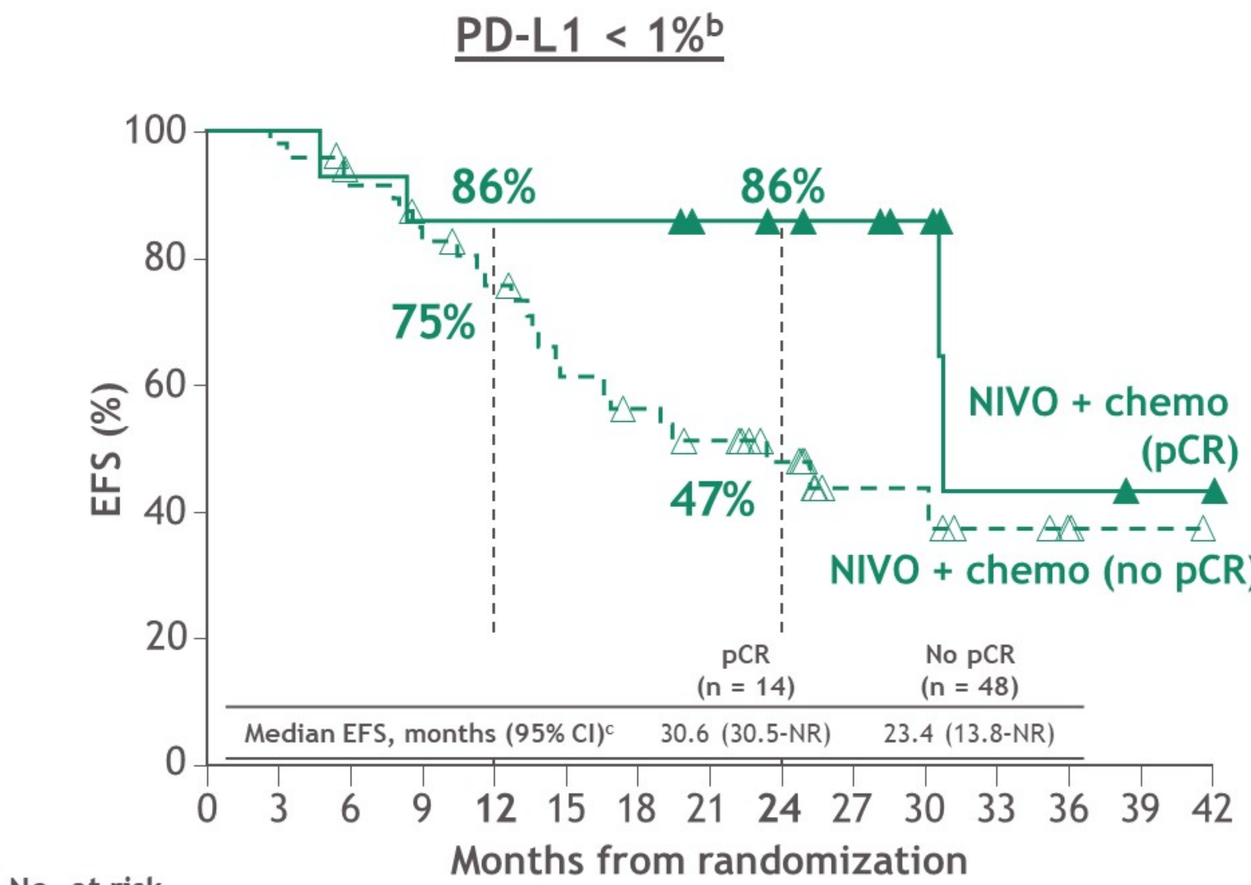
No. at risk

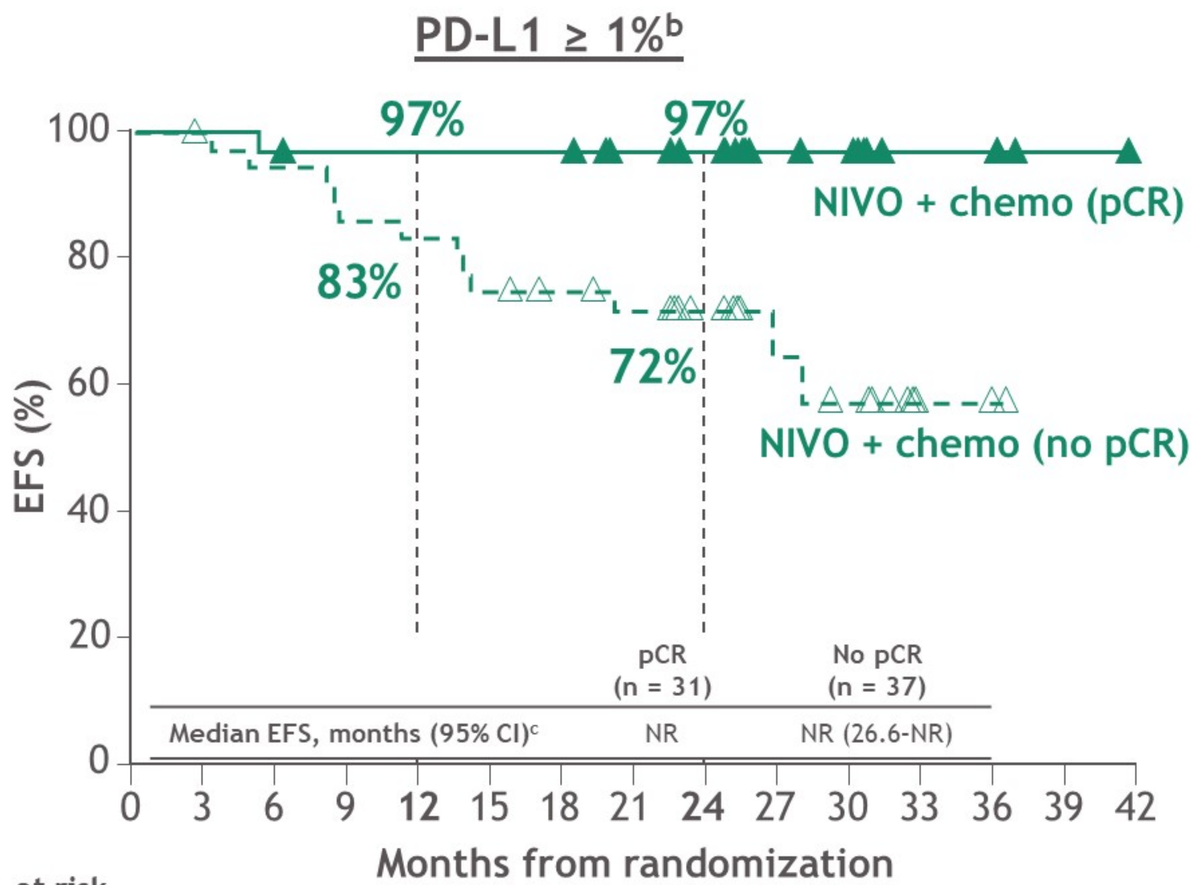
pCR	27	27	27	26	26	26	26	23	20	13	9	5	3	1	0
No pCR	62	60	56	50	48	39	35	30	24	12	12	4	1	1	0

Minimum follow-up: 21 months; median follow-up: 29.5 months.

[a]Path-evaluable patient population; [b]Subgroup analyses were not performed for the chemo arm because of small sample sizes; [c]HRs were not computed because of low number of events for the pCR subgroups.

EFS by pCR status (primary tumor) and tumor PD-L1 expression[a]: NIVO + chemo





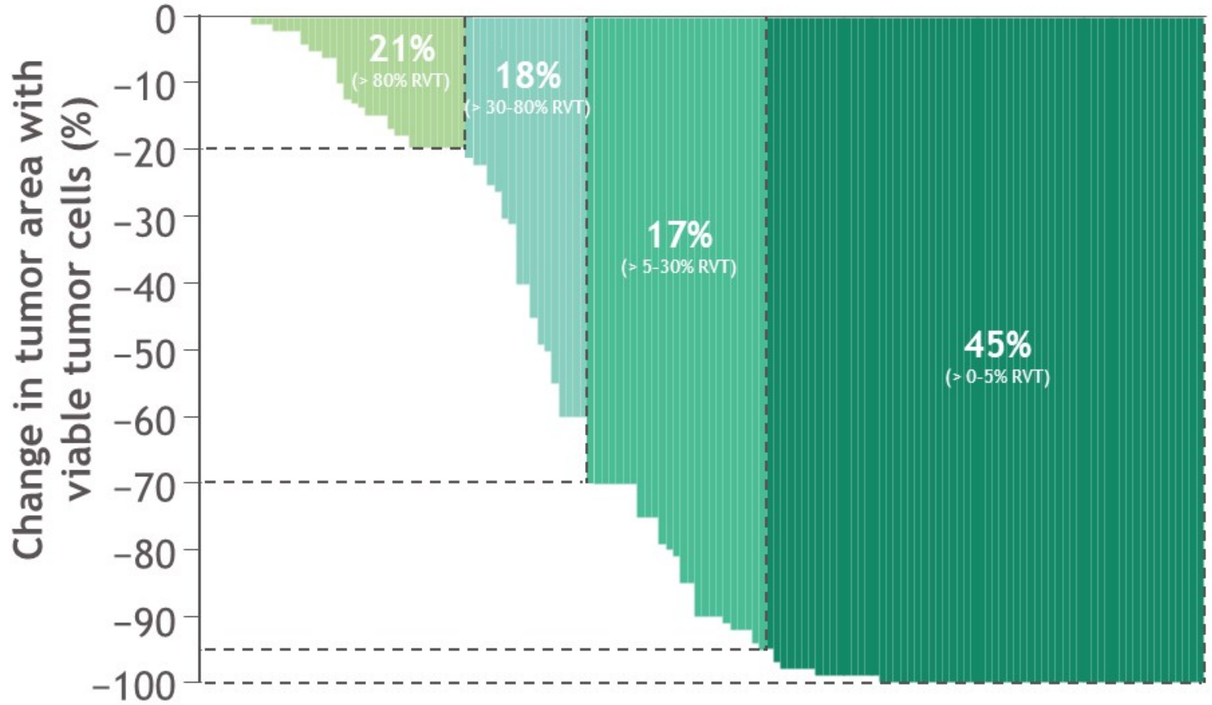
Minimum follow-up: 21 months; median follow-up: 29.5 months.

[a]Path-evaluable patient population; [b]Subgroup analyses were not performed for the chemo arm because of small sample sizes; [c]HRs were not computed because of low number of events for the pCR subgroups.

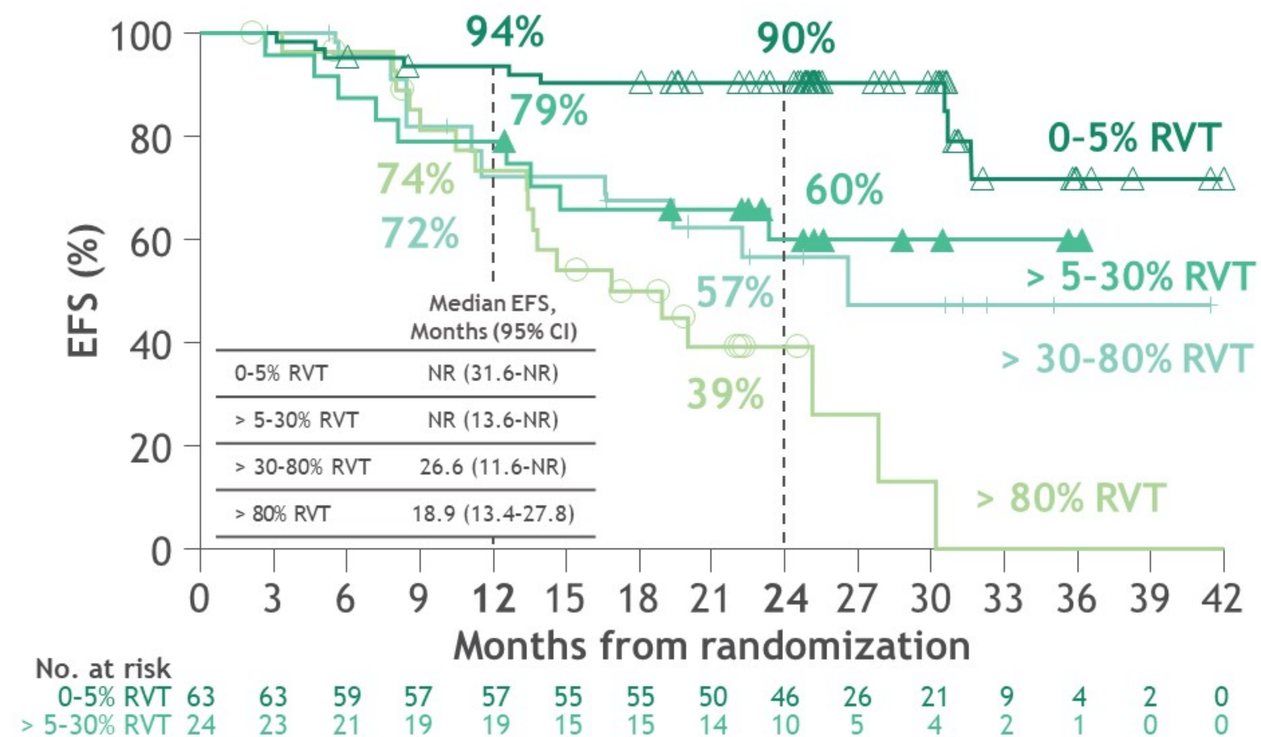
EFS by depth of pathological regression (primary tumor)[a]: NIVO + chemo

- Based on a ROC curve analysis, depth of pathological regression (measured by %RVT) as a continuous variable in the primary tumor appeared to be predictive of EFS at 2 years for NIVO + chemo (AUC = 0.74), but not for chemo (AUC = 0.54)

Depth of pathological regression (%RVT in the primary tumor): NIVO + chemo



EFS by %RVT categories: NIVO + chemo



Minimum follow-up: 21 months; median follow-up: 29.5 months.

[a]Path-evaluable patient population.

Safety

Patients (%)	All treated		pCR (primary tumor)[b]		No pCR (primary tumor)[b]		MPR (primary tumor)[b]		No MPR (primary tumor)[b]	
	NIVO + chemo (n = 176)	Chemo (n = 176)	NIVO + chemo (n = 46)	Chemo (n = 5)	NIVO + chemo (n = 95)	Chemo (n = 121)	NIVO + chemo (n = 72)	Chemo (n = 22)	NIVO + chemo (n = 69)	Chemo (n = 104)
Any grade TRAEs[a]	82	89	85	100	84	88	79	96	90	86
Grade 3-4 TRAEs[a]	34	37	30	40	37	35	31	32	39	36

- Incidence of TRAEs in the NIVO + chemo arm was similar in patients with or without pCR/MPR and consistent with all treated patients

[a]Includes events reported between the first neoadjuvant dose and 30 days after the last neoadjuvant dose as per Common Terminology Criteria for Adverse Events Version 4.0; Medical Dictionary for Regulatory Activities Version 24.0; [b]pCR and MPR assessed in path-evaluable patient population.

Conclusions

- This post hoc analysis from CheckMate 816 provides the first in-depth assessment of pathological regression and EFS in a phase 3 trial with neoadjuvant immunotherapy
- EFS was improved with neoadjuvant NIVO + chemo and chemo in patients with pCR or MPR in the primary tumor relative to those without
  - In the NIVO + chemo arm, EFS improvement in patients who had a pCR was observed regardless of baseline stage of disease or tumor PD-L1 expression
- Patients with deeper pathological regression in the primary tumor with neoadjuvant NIVO + chemo appeared to have better EFS outcomes at 2 years
- Neoadjuvant NIVO + chemo showed a similar safety profile in patients with or without pCR/MPR and was overall consistent with previous reports
- These results from CheckMate 816, along with previously reported data, continue to support pathological response as an early indicator of EFS benefit with neoadjuvant NIVO + chemo

For complete information, please see poster LBA8511.

Acknowledgments

- The patients and families who have made the study possible
- The clinical study teams who participated
- Dako, an Agilent Technologies, Inc. company (Santa Clara, CA), for collaborative development of the PD-L1 IHC 28-8 pharmDx assay
- Bristol Myers Squibb (Princeton, NJ) and Ono Pharmaceutical Company Ltd. (Osaka, Japan)
- The study was supported by Bristol Myers Squibb
- All authors contributed to and approved the presentation; writing and editorial assistance were provided by Ashvanti Valji, PhD, of Caudex, London, UK, funded by Bristol Myers Squibb

Thank You