PARIS 2022 ESMO congress

A randomized phase II study of preoperative nivolumab plus relatlimab or nivolumab in patients with resectable non-small-cell lung cancer

NEOpredict-Lung

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DECLARATION OF INTERESTS

Professor Martin Schuler declares the following interests

Personal fees (Advisory boards)

- Amgen, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, GlaxoSmithKline, Janssen, Merck Serono, Novartis, Roche, Sanofi, Takeda

Personal fees (Speaker at CME symposia)

- Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Janssen, Novartis, Roche

Research funding to institution

- AstraZeneca, Bristol Myers Squibb

Background

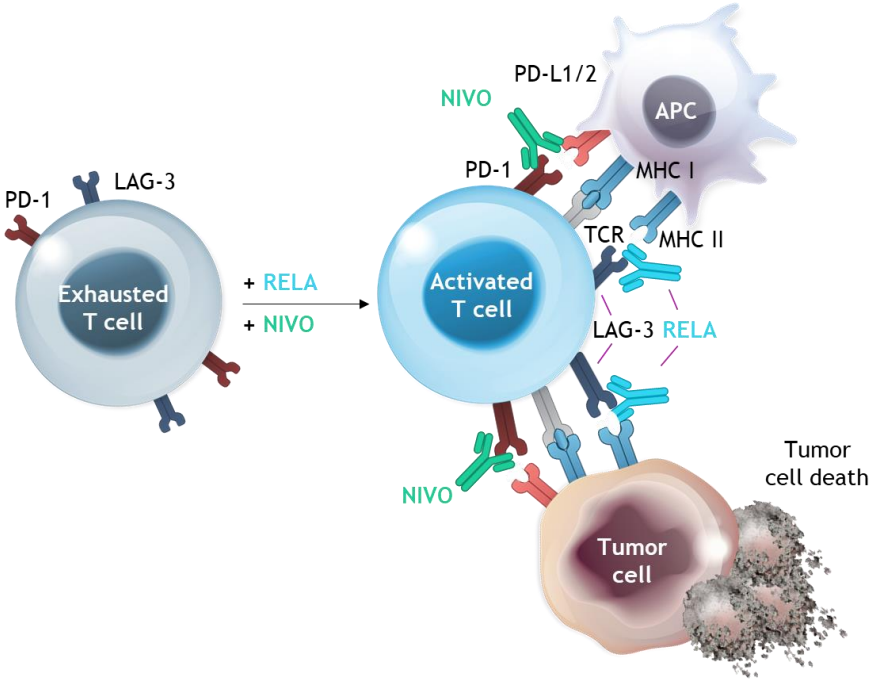
Preoperative immune checkpoint inhibition

- Monoclonal antibodies targeting PD-1, PD-L1 and CTLA-4 have demonstrated clinical activity in patients with non-small-cell lung cancer in the metastatic, adjuvant and neoadjuvant setting
- Still many patients derive no durable treatment benefit and predictive biomarkers in addition to PD-L1 are missing
- Preoperative immune checkpoint inhibitor therapy provides a window for early response assessment and correlative biomarker research on novel agents and combinations with sufficiently established clinical safety profile

Background and study design

NEOpredict-Lung (NCT04205552)

- Randomized phase II study in patients with resectable non-small-cell lung cancer exploring the feasibility, safety and early efficacy of combined preoperative treatment with nivolumab and relatlimab, a monoclonal antibody targeting LAG-3 with established efficacy in metastatic melanoma
- Reference arm with nivolumab monotherapy
- Primary study endpoint: Feasibility of curatively intended surgery within 43 days (continuously assessed)
- Secondary endpoints (selected): Radiological and histopathological response rates, DFS and OS at 12 months, safety, R0 resection rate



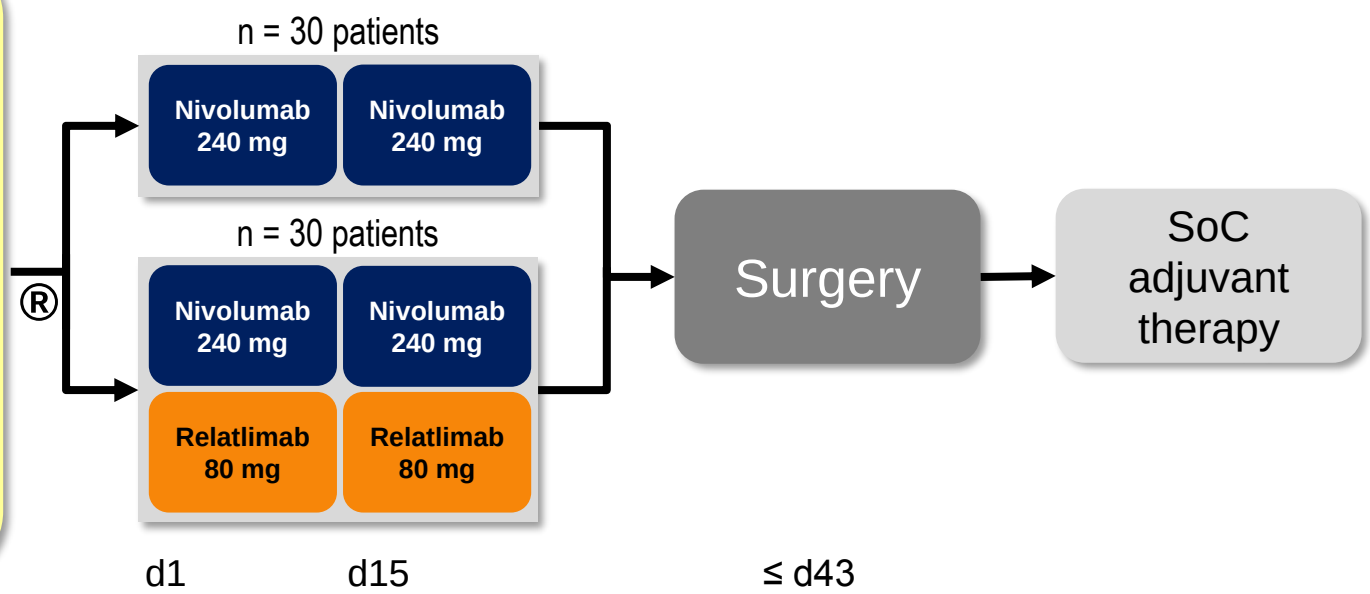
Lipson EJ, et al. Poster presentation at the Society for Immunotherapy of Cancer (SITC) Annual Meeting; November 9–13, 2016; National Harbor, MD, USA. Abstract P232

Study design

NEOpredict-Lung (NCT04205552)

Key eligibility

- Histologically confirmed non-small-cell lung cancer
- Stage I B, II or III A (UICC 8th edition)
- Curative resectability as determined by the multidisciplinary lung cancer board
- Sufficient organ function



Patient characteristics and disposition

	Nivolumab	Nivolumab/Relatlimab
n (female, male)	30 (15, 15)	30 (13, 17)
Age (median, range)	64 (43-77) years	65 (43-81) years
Histology		
▪ Adenocarcinoma	13	15
▪ Squamous cell carcinoma	10	9
▪ Adenosquamous	2	2
▪ Other	5	4
UICC stage (8th edition)		
▪ I B	9	10
▪ II A	6	1
▪ II B	11	16
▪ III A	3	3
▪ III B	1	0
PD-L1 status [TPS]		
▪ < 1%	6	8
▪ 1-49%	14	15
▪ ≥ 50%	10	7

Treatment-related adverse events

	Nivolumab		Nivolumab/Relatlimab	
	all	grade ≥ 3	all	grade ≥ 3
Anemia	2 (7%)	-	-	-
Atrial fibrillation	1 (3%)	1 (3%)	-	-
Hyperthyroidism	5 (17%)	1 (3%)	4 (13%)	-
Hypothyroidism	2 (7%)	-	3 (10%)	-
Gastrointestinal	1 (3%)	-	2 (7%)	-
Hepatic	1 (3%)	1 (3%)	1 (3%)	1 (3%)
Proteinuria	1 (3%)	-	-	-
Pneumonitis	-	-	2 (7%)	-
Chills/fever	2 (3%)	-	-	-
Rash	1 (3%)	-	-	-

NCI CTCAE version 5

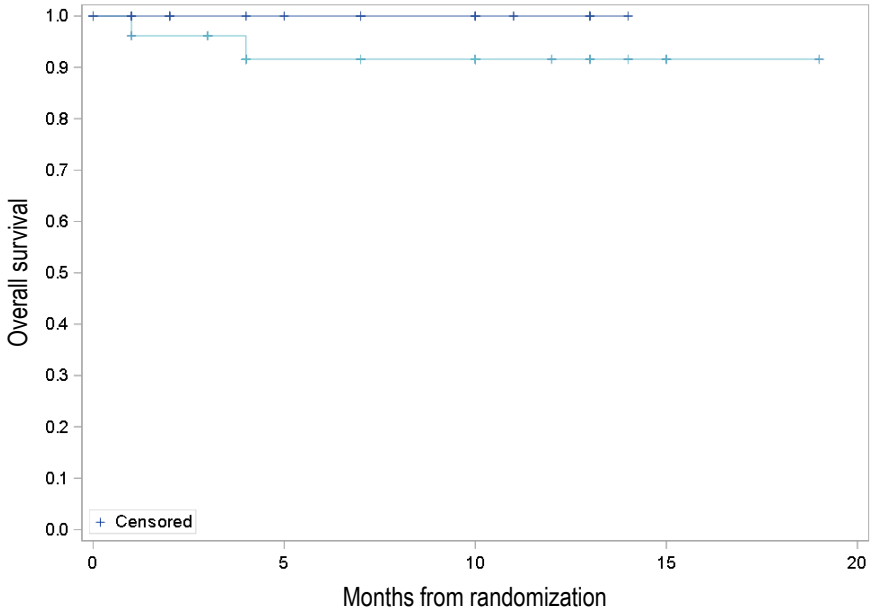
Primary and secondary endpoints

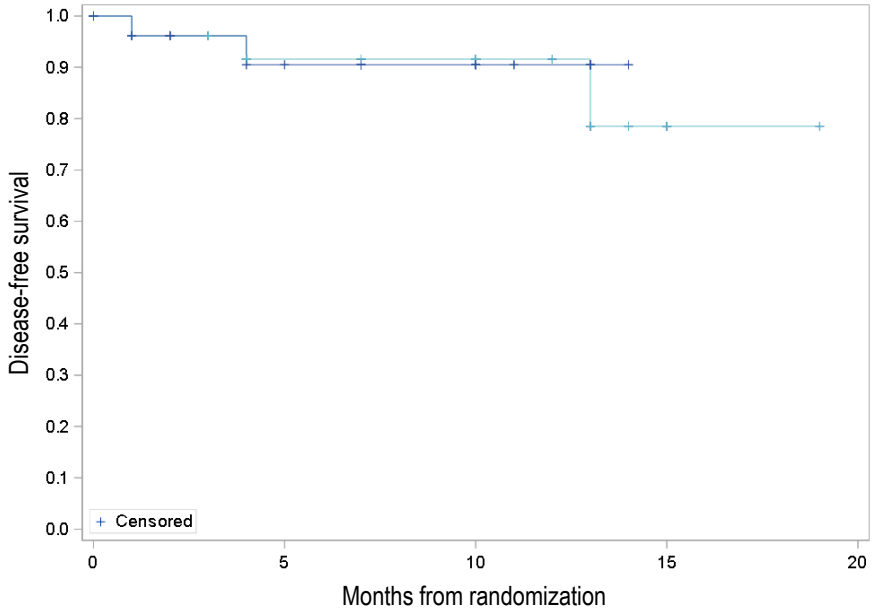
	Nivolumab	Nivolumab/Relatlimab
Primary endpoint:		
▪ Feasibility (surgery ≤ d43)	100%	100%
Secondary endpoints:		
▪ ORR (RECIST version 1.1)	10%	27%
▪ ORR (PERCIST version 1.0)*	38%	38%
▪ Complete/major pathological response**	27%	30%
▪ DFS at 12 months	92% (70-98%)	91% (66-98%)
▪ OS at 12 months	92% (70-98%)	100%
▪ R0 resection rate**	100%	97%

* Exploratory endpoint; preoperative FDG-PET/CT conducted at one study site (31 patients)
** Evaluable patients (pleural carcinosis detected at surgery in 2 patients)

Overall survival and disease-free survival

Median follow-up 5.68 months

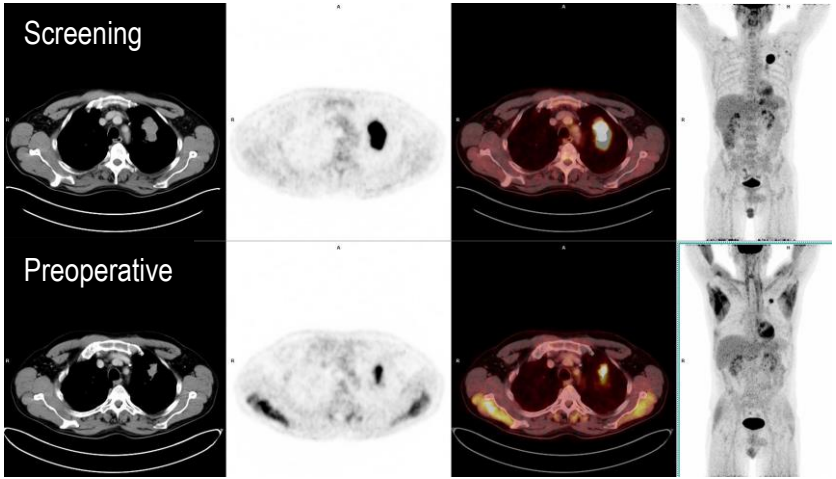




Nivolumab/Relatlimab Nivolumab

Radiologic and metabolic responses

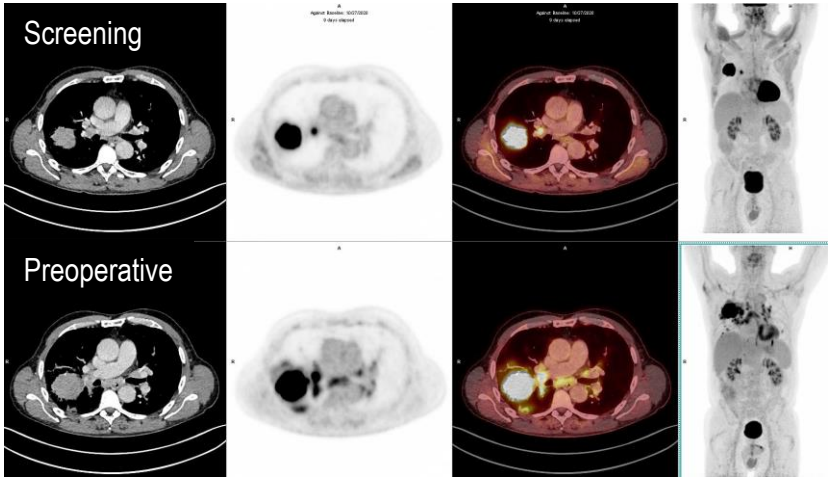
001-R-037 LUAD Nivolumab/Relatlimab



Preoperative stage: cT3 cN0 M0

PERCIST: partial response
Postoperative stage: ypT1a ypN0 M0 R0
Pathological response: 30% vital tumor cells

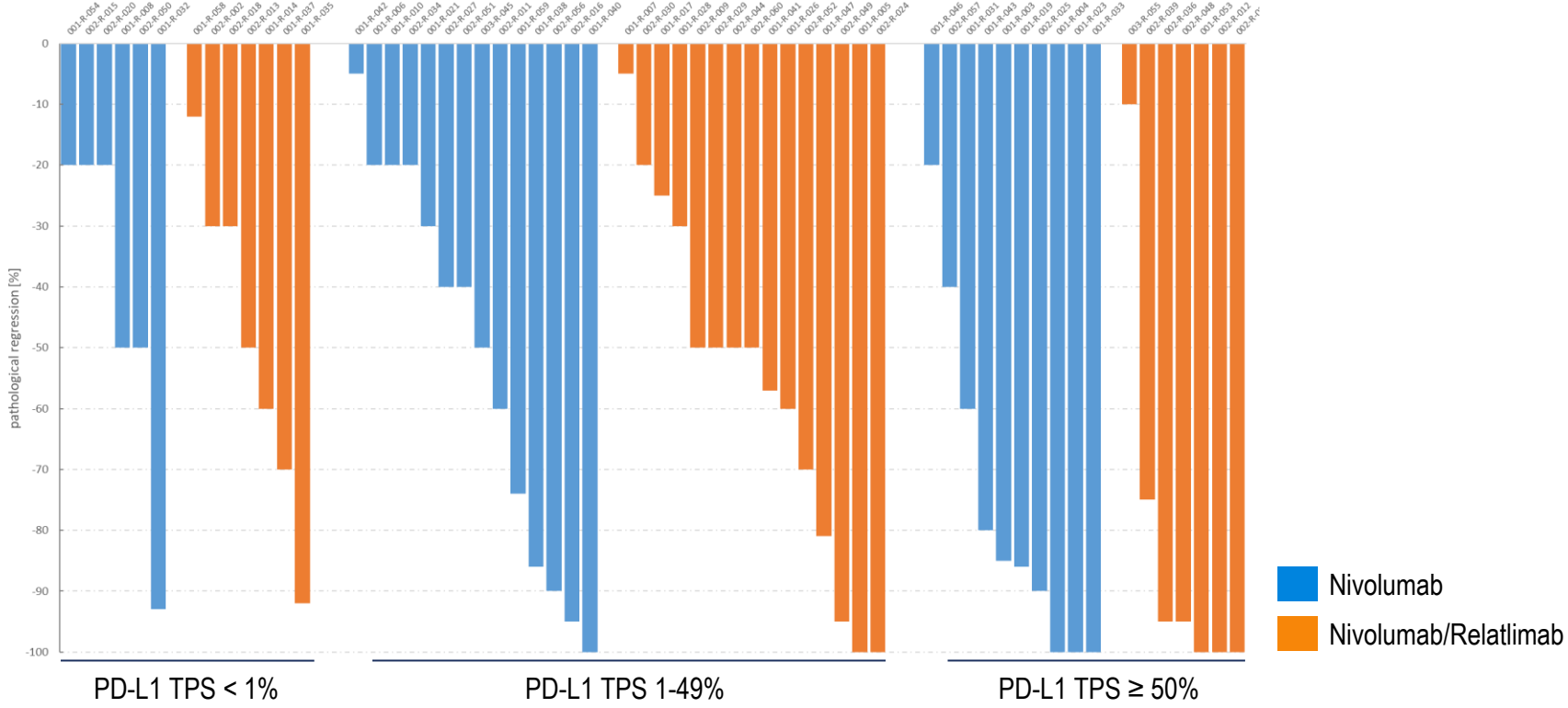
001-R-006 LUAD Nivolumab



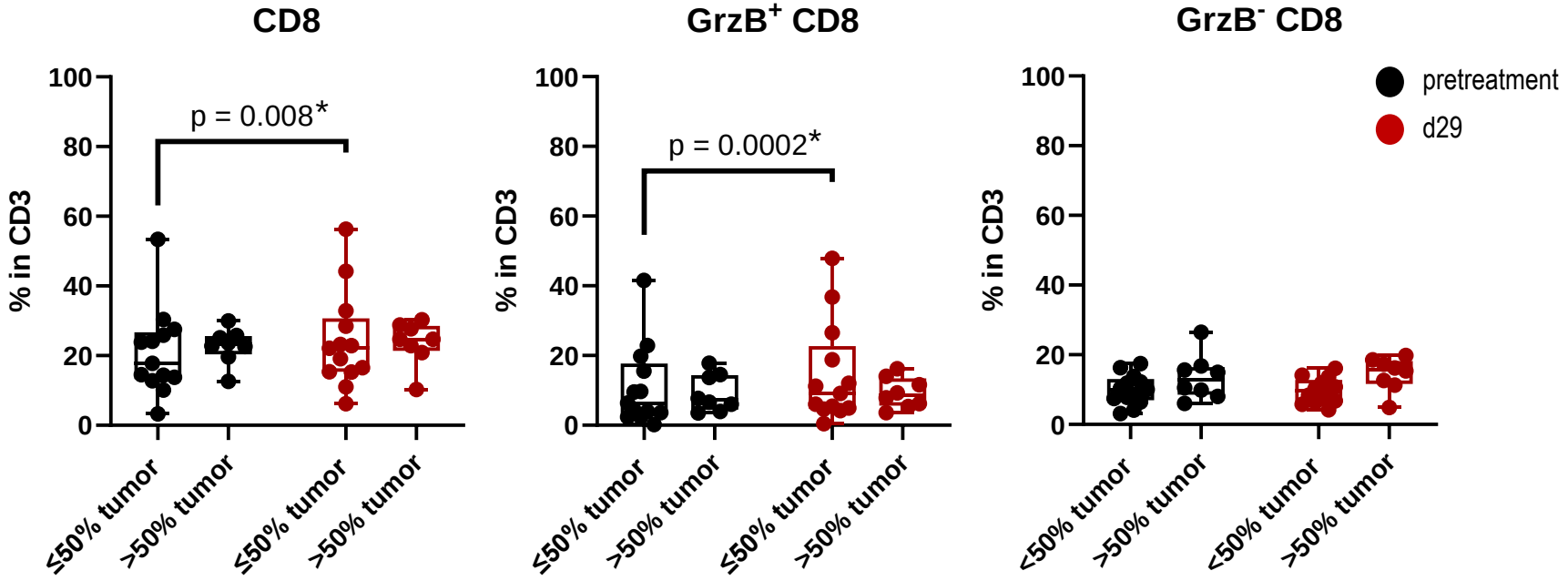
Preoperative stage: cT3 cN0 M0

PERCIST: progressive disease
Postoperative stage: ypT3 ypN0 M0 R0
Pathological response: 80% vital tumor cells

Histopathological responses



Increase in peripheral blood effector T cells in patients with ≤ 50% vital tumor cells in resected lung cancer



* Exploratory endpoint, p-values only indicating trend.

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Summary and conclusions

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- Preoperative combined immune checkpoint inhibitor therapy with two courses (q14d) of nivolumab (240 mg) plus relatlimab (80 mg) is safe and feasible in patients with curatively resectable non-small-cell lung cancer
- Preliminary efficacy signal of combined therapy with nivolumab/relatlimab
- Comprehensive correlative studies and biomarker analyses ongoing
- Protocol has been amended to explore a higher dose of relatlimab for increased LAG-3 target occupancy

Acknowledgments

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Universitätsmedizin Essen
Westdeutsches Tumorzentrum Essen

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