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Letter from Prof Rolf Stahel

Dear Colleagues

It is my pleasure to present this ETOP slide set which has been designed to highlight and summarise key findings in thoracic cancers from the major congresses in 2017. This slide set specifically focuses on the **ESMO 2017 Congress** and is available in 4 languages – English, French, Chinese and Japanese.

The area of clinical research in oncology is a challenging and ever changing environment. Within this environment we all value access to scientific data and research which helps to educate and inspire further advancements in our roles as scientists, clinicians and educators. I hope you find this review of the latest developments in thoracic cancers of benefit to you in your practice. If you would like to share your thoughts with us we would welcome your comments. Please send any correspondence to etop@etop.eu-org.

I would like to thank our ETOP members Drs Solange Peters and Martin Reck for their roles as Editors – for prioritising abstracts and reviewing slide content. The slide set you see before you would not be possible without their commitment and hard work.

And finally, we are also very grateful to Lilly Oncology for their financial, administerial and logistical support in the realisation of this complex yet rewarding activity.

Yours sincerely,
Rolf Stahel
President, ETOP Foundation Council

ETOP Medical Oncology Slide Deck Editors 2017

Focus: advanced NSCLC (not radically treatable stage III & stage IV)

Dr Solange Peters

Multidisciplinary Oncology Center, Lausanne Cancer Center, Lausanne, Switzerland

Focus: other malignancies, SCLC, mesothelioma, rare tumours

Dr Martin Reck

Department of Thoracic Oncology, Hospital Grosshansdorf, Grosshansdorf, Germany

Contents

- Biomarkers and screening
- Early stage and locally advanced NSCLC – Stages I, II and III
- Advanced NSCLC – Not radically treatable stage III and stage IV
  - 1st line
  - Later lines
- Other malignancies
  - SCLC and mesothelioma

Biomarkers

1295O: Blood-based biomarkers for cancer immunotherapy: Tumor mutational burden in blood (bTMB) is associated with improved atezolizumab (atezo) efficacy in 2L+ NSCLC (POPLAR and OAK) – Gandara DR, et al

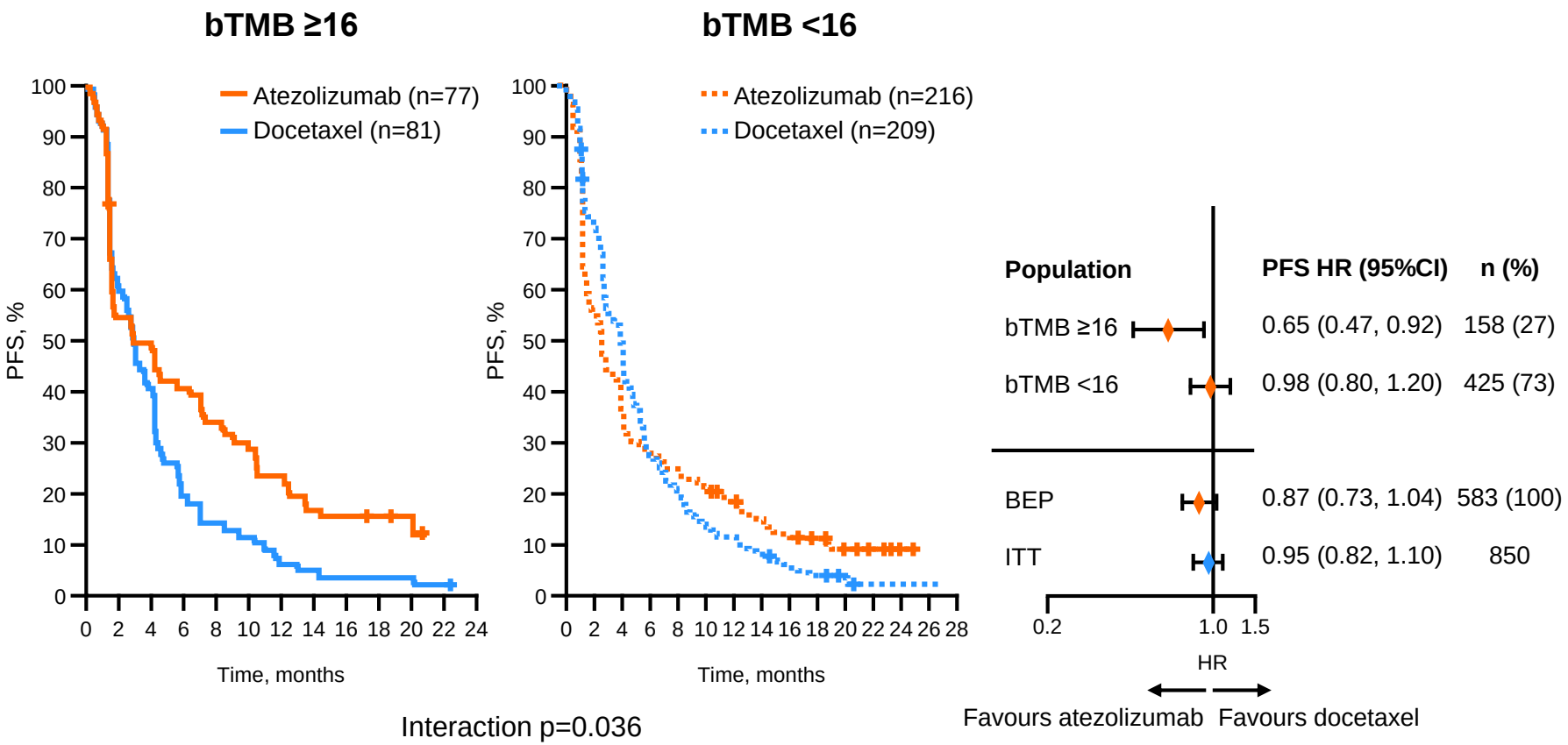
- **Study objective**
  - To validate a novel assay to measure blood tumour mutational burden (bTMB) and evaluate the association between bTMB and efficacy of atezolizumab
- **Methods**
  - A 394 gene-based NGS assay was used to retrospectively test plasma samples for bTMB from the phase 2 POPLAR study and phase 3 OAK study
    - 211/273 samples from POPLAR and 583/797 samples from OAK were biomarker-evaluable
  - The association between bTMB and atezolizumab efficacy was analysed and the cut-point of bTMB ≥16 was selected based on POPLAR, and validated in OAK

Gandara DR et al. Ann Oncol 2017;28(suppl 5):Abstr 1295O

1295O: Blood-based biomarkers for cancer immunotherapy: Tumor mutational burden in blood (bTMB) is associated with improved atezolizumab (atezo) efficacy in 2L+ NSCLC (POPLAR and OAK) – Gandara DR, et al

- **Key results**

Atezolizumab PFS benefit in bTMB subgroups: OAK



Interaction p=0.036

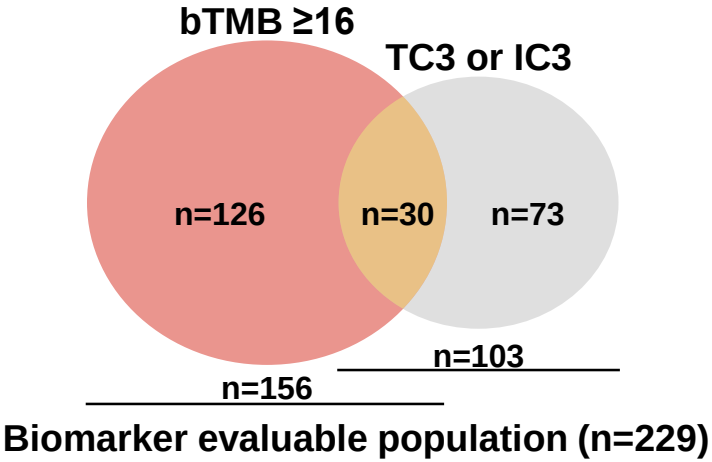
BEP, biomarker-evaluable population

Gandara DR et al. Ann Oncol 2017;28(suppl 5):Abstr 1295O

1295O: Blood-based biomarkers for cancer immunotherapy: Tumor mutational burden in blood (bTMB) is associated with improved atezolizumab (atezo) efficacy in 2L+ NSCLC (POPLAR and OAK) – Gandara DR, et al

- **Key results (cont.)**

Limited overlap between bTMB ≥16 and PD-L1 expression: OAK



	PFS HR (95%CI)	OS HR (95%CI)
bTMB ≥16	0.64 (0.46, 0.91)	0.64 (0.44, 0.93)
TC3 or IC3	0.62 (0.41, 0.93)	0.44 (0.27, 0.71)
bTMB ≥16 and TC3 or IC3	0.38 (0.17, 0.85)	0.23 (0.09, 0.58)

- **Conclusions**
  - This exploratory analysis demonstrated that TMB can be measured in blood
  - The cut-point of bTMB ≥16 was identified in POPLAR, and independently validated to predict PFS benefit in OAK
  - bTMB identified a unique patient population which was not significantly associated with PD-L1 status

Gandara DR et al. Ann Oncol 2017;28(suppl 5):Abstr 1295O

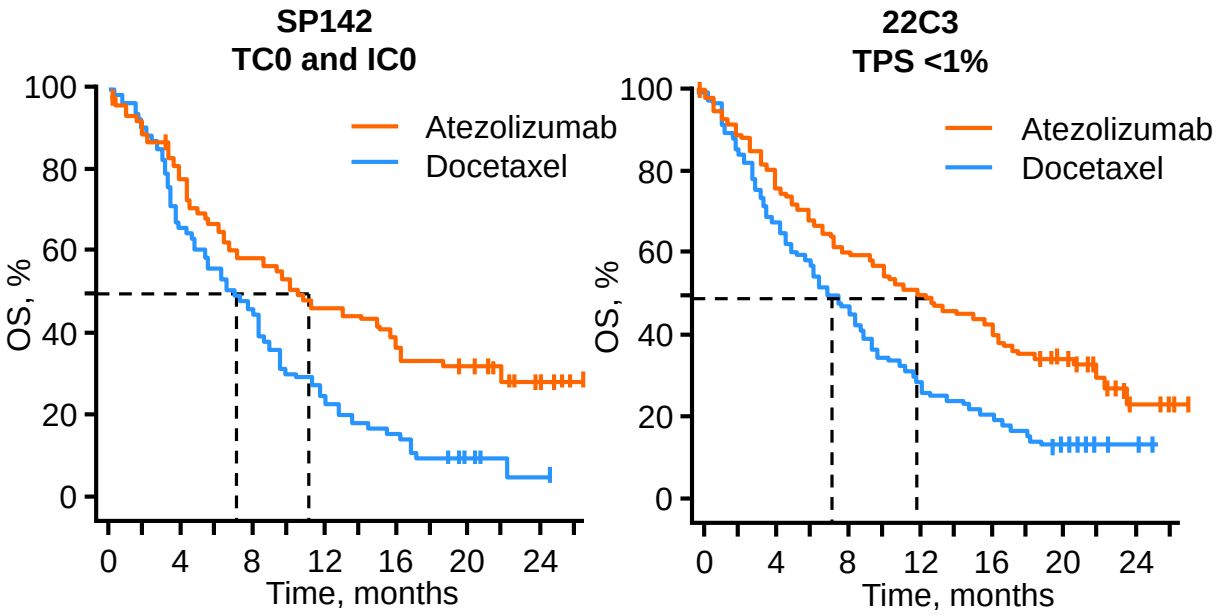
1296O: Clinical efficacy of atezolizumab (Atezo) in PD-L1 subgroups defined by SP142 and 22C3 IHC assays in 2L+ NSCLC: Results from the randomized OAK study – Gadgeel S, et al

- **Study objective**
  - To determine whether correlation between PD-L1 expression and OS is consistent across PD-L1 IHC assays (SP142 [Ventana] and 22C3 [Agilent/Dako])
- **Methods**
  - In samples from the OAK study (n=400), PD-L1 expression was assessed prospectively with the SP142 IHC assay in archival or fresh tumour samples from all patients, and retrospectively with 22C3 IHC assay
    - Only those with submitted tissue blocks were eligible due to a limited cut section stability for the 22C3 assay (biomarker-evaluable population [BEP])
  - Staining and scoring of PD-L1 expression was independently assessed at a central library according to each respective assay protocol

Gadgeel S et al. Ann Oncol 2017;28(suppl 5):Abstr 1296O

1296O: Clinical efficacy of atezolizumab (Atezo) in PD-L1 subgroups defined by SP142 and 22C3 IHC assays in 2L+ NSCLC: Results from the randomized OAK study – Gadgeel S, et al

- **Key results**
  - mOS for atezolizumab vs. docetaxel was 13.6 vs. 9.6 months (HR 0.73; 95%CI 0.62, 0.87) in the ITT population and 14.1 vs. 7.7 months (HR 0.56; 95%CI 0.44, 0.71) in the BEP
  - OS benefit observed in PD-L1 negative populations as defined by either assay



	SP142 TC0 and IC0	22C3 TPS <1%
Atezolizumab mOS, months (95%CI)	7.3 (5.2, 8.8)	7.3 (5.8, 8.8)
Docetaxel mOS, months (95%CI)	11.2 (7.1, 16.3)	12.1 (8.3, 16.0)
	SP142 Dx– (n=150)	**22C3 Dx– (n=218)**
OS HR (95%CI)	0.55 (0.37, 0.80)	0.61 (0.45, 0.84)

SP142 assay: TC0 and IC0, PD-L1 expression on <1% TC and IC
22C3 assay: TPS <1%, PD-L1 expression on <1% TC
Dx–, no or low PD-L1 expression

Gadgeel S et al. Ann Oncol 2017;28(suppl 5):Abstr 1296O

1296O: Clinical efficacy of atezolizumab (Atezo) in PD-L1 subgroups defined by SP142 and 22C3 IHC assays in 2L+ NSCLC: Results from the randomized OAK study – Gadgeel S, et al

- **Key results (cont.)**
  - Patients without PD-L1 expression by both IHC assays (n=115) show improved survival with atezolizumab compared with docetaxel with median OS of 9.9 vs. 7.7 months, respectively (HR 0.63 [95%CI 0.41, 0.97]; p=0.0347)
- **Conclusions**
  - The majority (77%) of those PD-L1-negative by the SP142 assay were also negative by the 22C3 assay
  - Patients defined as PD-L1-negative by either assay, or in both assays, continue to demonstrate improved OS with atezolizumab compared with docetaxel
    - Atezolizumab improves survival in patients with PD-L1-negative tumours irrespective of the assay used
  - These results also confirm the results from the OAK trial, with survival benefit with atezolizumab in all patients with NSCLC regardless of PD-L1 status

Gadgeel S et al. Ann Oncol 2017;28(suppl 5):Abstr 1296O

1306PD: Hyperprogressive disease (HPD) is frequent in non-small cell lung cancer (NSCLC) pts (pts) treated with anti PD1/PD-L1 monoclonal antibodies (IO) – Ferrara R, et al

- **Study objective**
  - To assess the prognostic value of hyperprogressive disease (HPD) and the correlation with clinical characteristics in patients with advanced NSCLC treated with anti-PD-1/PD-L1 therapy
- **Methods**
  - Retrospective review of 242 patients with NSCLC treated with anti-PD-1/PD-L1 therapy at 5 French institutions
  - HPD was defined as delta tumour growth rate >50% (i.e. >50% increase in tumour volume between baseline and post-treatment CT scans)
- **Key results**
  - 40/242 (16%) patients experienced HPD
  - OS was 13.4 months (95%CI 9.6, 42) for the overall population
    - For patients with HPD OS was 3.3 months (95%CI 1.8, 5.8) vs. 5.7 months (95%CI 4, 8.6) in those with PD but not HPD
- **Conclusions**
  - 16% of patients treated with anti-PD-1/PD-L1 therapy exhibited HPD
  - HPD was positively correlated with the number of metastatic sites prior to IO
  - HPD was associated with reduced OS

Ferrara R et al. Ann Oncol 2017;28(suppl 5):Abstr 1306PD

1307PD: Detection of driver and resistance mutations in leptomeningeal metastases of NSCLC by next-generation sequencing of cerebrospinal fluid circulating tumor cells – Li Y, et al

- **Study objective**
  - To evaluate methods of diagnosing and detecting mutations in leptomeningeal metastases (LM) of NSCLC
- **Methods**
  - Diagnoses of LM by the CellSearch Assay™, the Thinprep cytologic test (TCT) and brain MRI were compared in 21 patients
  - Next-generation sequencing of 416 cancer-associated genes was performed on cerebrospinal fluid circulating tumour cells (CSFCTCs) of 19 patients
- **Key results**
  - The highest sensitivity for LM diagnosis was with CSFCTCs by CellSearch (95.2%) compared with TCT (57.1%), MRI (47.6%) or MRI + TCT (90.5%)
  - The genetic profiles of CSFCTCs were highly concordant with molecular mutations identified in the primary tumour (17/19; 89.5%)
- **Conclusion**
  - In patients with LM of NSCLC, CSFCTCs may be a more effective method for diagnosing LM, and could be a potential method for performing liquid biopsy for gene profiles

Li Y et al. Ann Oncol 2017;28(suppl 5):Abstr 1307PD

1148PD: Immunotherapy in pts with concurrent solid organ transplant, HIV, and Hepatitis B and C – Tio M, et al

- **Study objective**
  - To evaluate the safety and efficacy of PD-1/PD-L1 immunotherapy in patients with solid organ transplant, HIV or hepatitis B/C
- **Methods**
  - Patients from 16 centres with a history of solid organ transplant, HIV or hepatitis B/C who were treated with PD-1/PD-L1 immunotherapy were included
  - Data on patient and tumour characteristics, toxicity, response and survival were collected
- **Key results**
  - 41 patients were included
    - Solid organ transplant: n=5 (liver, n=1; kidney, n=4)
    - HIV: n=10
    - Hepatitis B: n=12
    - Hepatitis C: n=14

Tio M et al. Ann Oncol 2017;28(suppl 5):Abstr 1148PD

1148PD: Immunotherapy in pts with concurrent solid organ transplant, HIV, and Hepatitis B and C – Tio M, et al

- **Key results (cont.)**

Group	Outcome
Solid organ transplant (n=5)	• Liver (n=1): acute grade 5 rejection after single cycle of pembrolizumab • Kidney (n=4): 1 PR, 3 PD; grade 2 pneumonitis (n=1)
HIV (n=10)	• 1 CR, 1 PR, 4 SD, 4 PD • 2 virologic response; 0 virologic failure • Immune-related AEs: grade 2 right facial palsy; grade 2 hypothyroidism; grade 2 nephritis; grade 1 diarrhoea (n=1 each)
Hepatitis B (n=12)	• 1 CR, 1 PR, 8 SD, 2 PD • 2 virologic response; 1 virologic failure (not on antiviral therapy) • Immune-related AEs: grade 2 pneumonitis; grade 2 rash; grade 1 rash; grade 1 vitiligo (n=1 each)
Hepatitis C (n=14)	• 2 CR, 1 PR, 8 SD, 3 PD • 0 virologic response; 0 virologic failure • Immune-related AEs: grade 4 colitis/duodenitis; grade 3 autoimmune hepatitis; grade 3 adrenal insufficiency; grade 1 rash; grade 1 arthralgia (n=1 each)

Tio M et al. Ann Oncol 2017;28(suppl 5):Abstr 1148PD

1148PD: Immunotherapy in pts with concurrent solid organ transplant, HIV, and Hepatitis B and C – Tio M, et al

- **Conclusions**
  - The data suggest that patients undergoing kidney transplantation and those with HIV or hepatitis B or C may benefit from and tolerate PD-1/PD-L1 immunotherapy
    - The acute rejection and death in the liver transplant patient is consistent with other case reports, and suggests that liver transplantation may be a contraindication to PD-1/PD-L1 immunotherapy
    - Despite case reports of rejection in kidney transplantation, PD-1/PD-L1 immunotherapy did not lead to rejection in 4 patients in this review
    - PD-1/PD-L1 immunotherapy did not appear to worsen viral control in HIV or hepatitis B or C patients
  - However, this is still a high risk treatment option that requires adequate and intensive patient information plus careful monitoring of potential AEs; immunotherapy in this patient group should only be considered by an experienced multidisciplinary team who are able to react promptly to the occurrence of potential AEs

Tio M et al. Ann Oncol 2017;28(suppl 5):Abstr 1148PD

Early and locally advanced NSCLC
Stages I, II and III

1273O: Results of the phase III IFCT-0302 trial assessing minimal versus CT-scan-based follow-up for completely resected non-small cell lung cancer (NSCLC) – Westeel V, et al

- **Study objective**
  - To investigate two programmes for follow-up after complete surgical resection in NSCLC

Key patient inclusion criteria

- Completely resected stage I, II, IIIA, and T4 N0–2 NSCLC
- After anatomic complete resection (within 8 weeks)
- All perioperative treatments allowed

(n=1775)

R

Minimal follow-up: History + physical examination, chest X-ray* (Control) (n=888)

Stratification

- Centre
- Stage
- Histology
- Perioperative treatments

Maximal follow-up: History + physical examination, chest X-ray, CT-scan + contrast, bronchoscopy (n=887)

Primary endpoint

- OS

Secondary endpoints

- DFS, survival from recurrence or 2nd primary tumour, HRQoL, cost-effectiveness

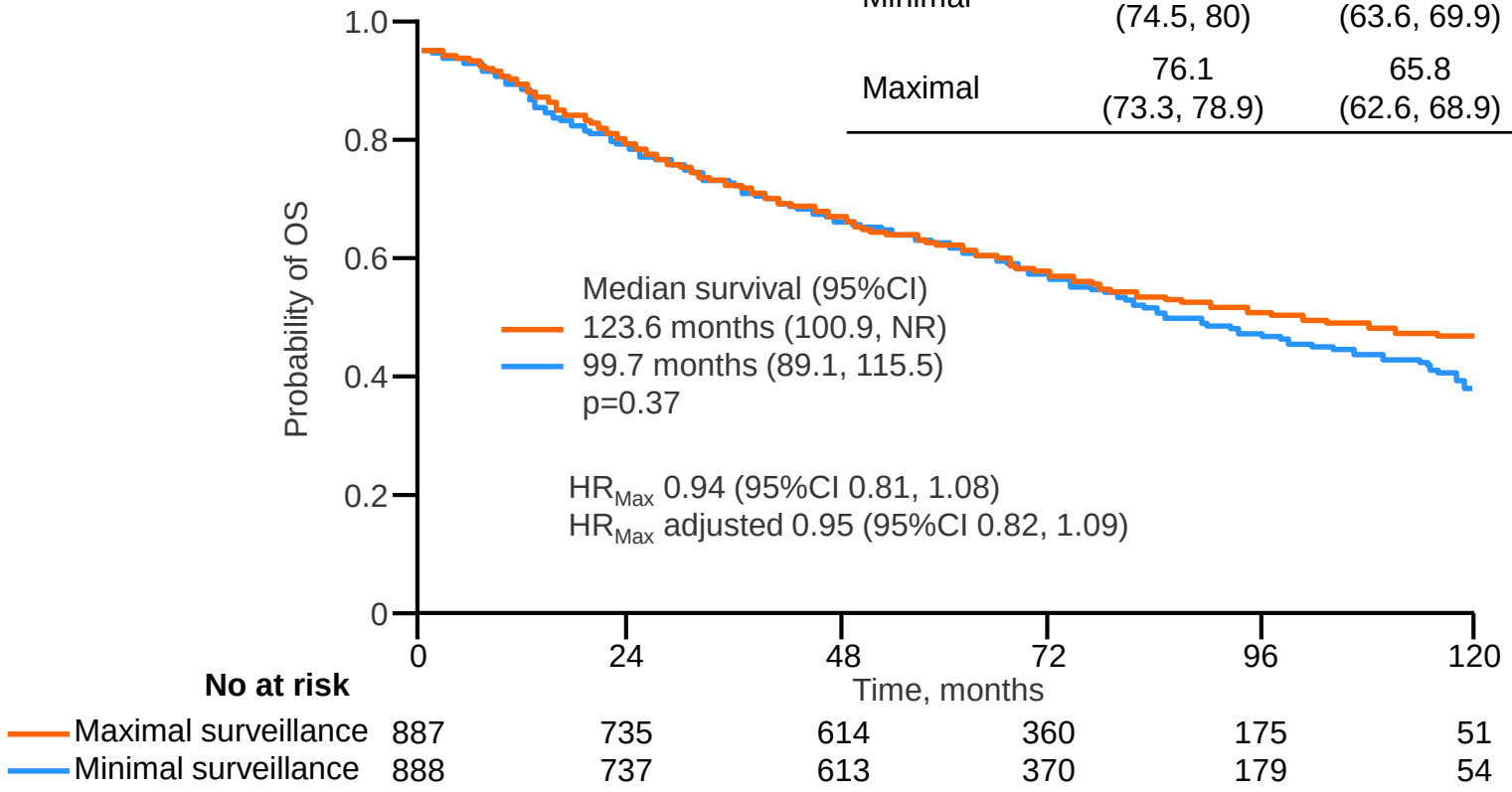
* CT scan allowed if symptoms or abnormal X-ray

Westeel V et al. Ann Oncol 2017; 28(suppl 5):Abstr 1273O

1273O: Results of the phase III IFCT-0302 trial assessing minimal versus CT-scan-based follow-up for completely resected non-small cell lung cancer (NSCLC) – Westeel V, et al

- **Key results**

Survival rate, % (95%CI)	3 years	5 years	8 years
Minimal	77.3 (74.5, 80)	66.7 (63.6, 69.9)	51.7 (47.8, 55.5)
Maximal	76.1 (73.3, 78.9)	65.8 (62.6, 68.9)	54.6 (50.9, 58.3)



Westeel V et al. Ann Oncol 2017; 28(suppl 5):Abstr 1273O

1273O: Results of the phase III IFCT-0302 trial assessing minimal versus CT-scan-based follow-up for completely resected non-small cell lung cancer (NSCLC) – Westeel V, et al

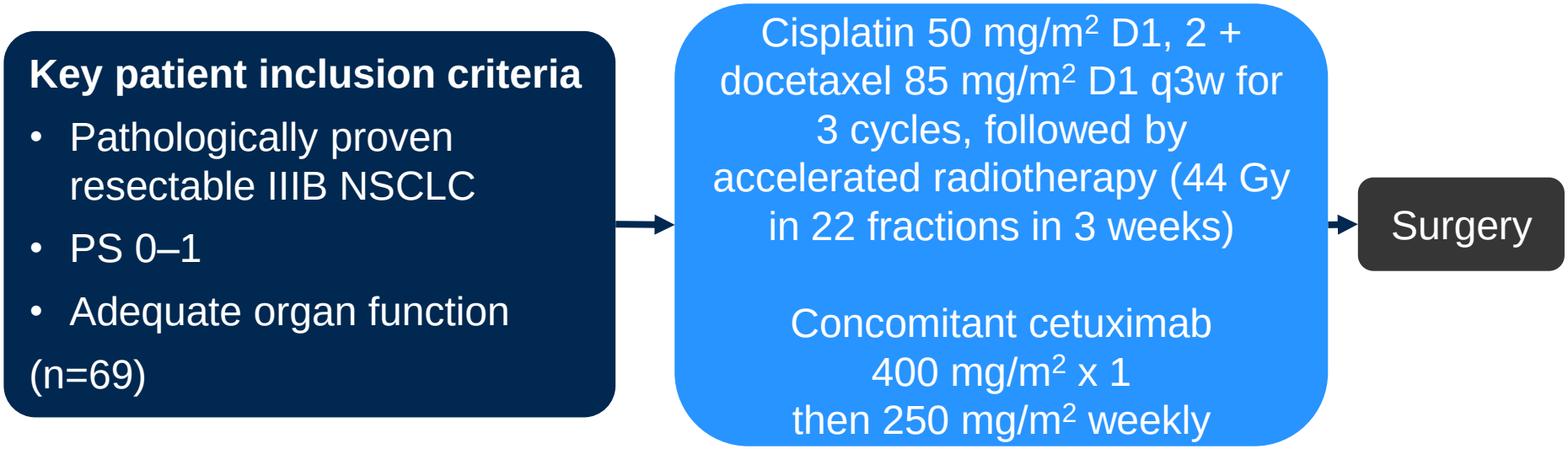
- **Key results (cont.)**
  - DFS was not significantly different between minimum and maximum follow-up at 5 years (54.1% vs. 49.7%); HR_{Max} adjusted 1.14 (95%CI 0.99, 1.31)

- **Conclusions**
  - This study represents the first large randomized trial evaluating follow-up after surgery for NSCLC
  - The results indicate no survival benefit of maximum follow-up, and suggest that CT scans every 6 months is probably not useful during the first 2 years

Westeel V et al. Ann Oncol 2017; 28(suppl 5):Abstr 1273O

1287PD: Preoperative chemotherapy and radiotherapy concomitant to cetuximab in stage IIIB NSCLC: A multicenter phase II SAKK – Curioni-Fontecedro A, et al

- **Study objective**
  - To evaluate the efficacy and safety of the addition of cetuximab to neoadjuvant chemoradiotherapy (CRT) followed by neoadjuvant accelerated radiotherapy



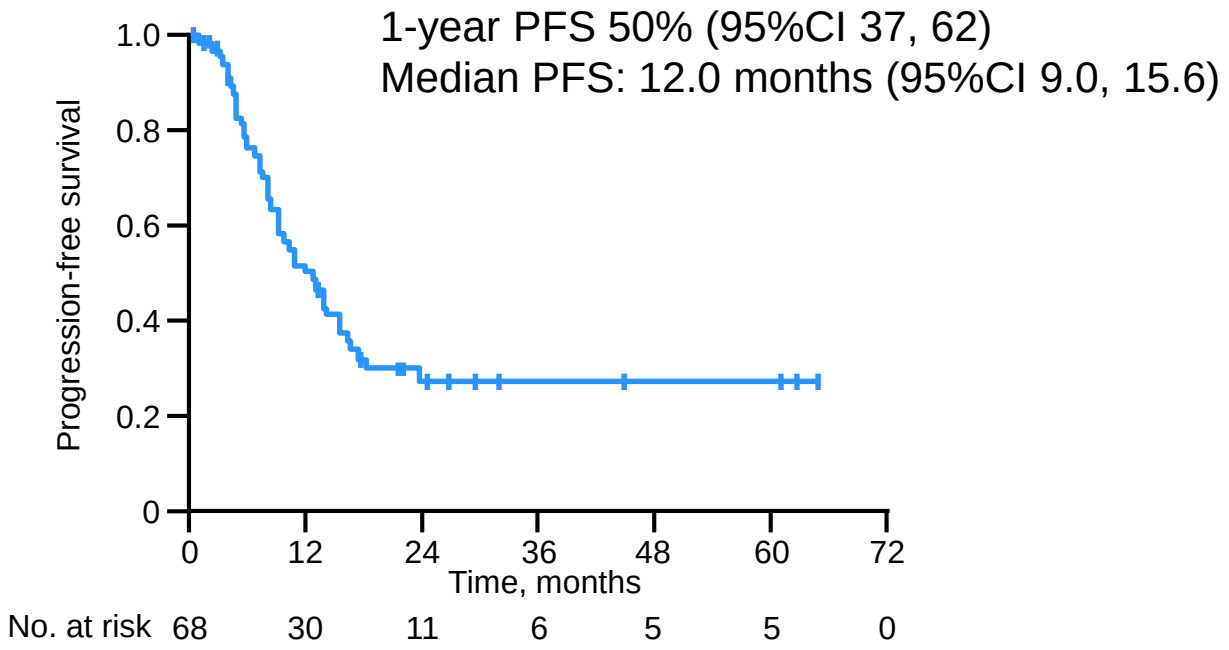
Primary endpoint(s)

- PFS at 1 year

Curioni-Fontecedro A et al. Ann Oncol 2017;28(suppl 5):Abstr 1287PD

1287PD: Preoperative chemotherapy and radiotherapy concomitant to cetuximab in stage IIIB NSCLC: A multicenter phase II SAKK – Curioni-Fontecedro A, et al

- **Key results**



Curioni-Fontecedro A et al. Ann Oncol 2017;28(suppl 5):Abstr 1287PD

1287PD: Preoperative chemotherapy and radiotherapy concomitant to cetuximab in stage IIIB NSCLC: A multicenter phase II SAKK – Curioni-Fontecedro A, et al

- **Key results (cont.)**
  - Response rate after chemo-immunotherapy was 57% (95%CI 44, 68) and after CRT-immunotherapy it was 64% (95%CI 51, 75)
  - Median OS was 21 months (95%CI 14, 25)
    - 2- and 3-year survival rates were 41% and 30%, respectively
- **Conclusions**
  - The results suggest that the treatment regimen is feasible as evidenced by the adherence to the protocol and the promising response rates, OS and PFS
  - The results support an aggressive approach, including surgery, in strictly selected patients with stage IIIB NSCLC

Curioni-Fontecedro A et al. Ann Oncol 2017;28(suppl 5):Abstr 1287PD

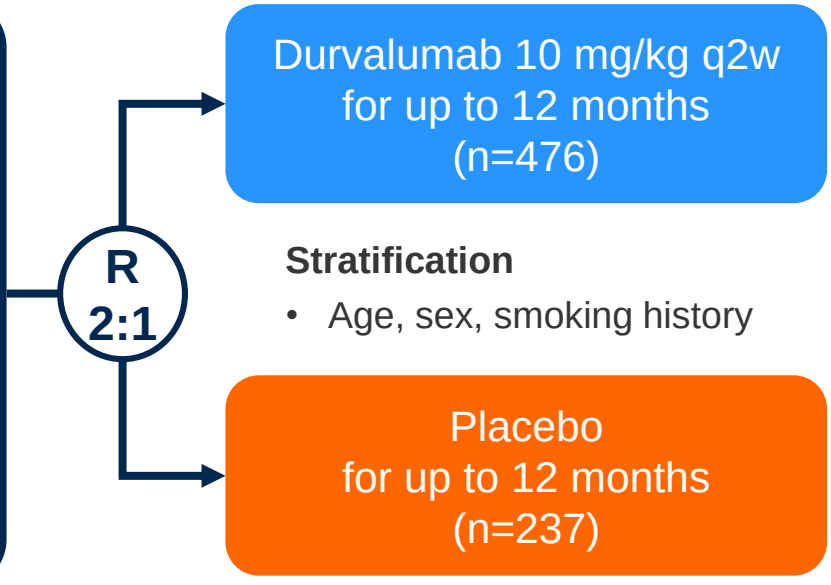
LBA1: PACIFIC: a double-blind, placebo-controlled Phase III study of durvalumab after chemoradiation therapy (CRT) in patients with stage III locally advanced, unresectable NSCLC – Paz-Ares L, et al

- **Study objective**
  - To evaluate the anti-PD-L1 durvalumab, in stage III, locally advanced, unresectable NSCLC

Key patient inclusion criteria

- Stage III, locally advanced, unresectable NSCLC
- Not progressed following platinum-based concurrent chemoradiation therapy (≥2 cycles)
- WHO PS 0–1
- Estimated life expectancy ≥12 weeks

(n=713)



Co-primary endpoints

- PFS (BICR, RECIST v1.1), OS

Secondary endpoints

- ORR (BICR), DoR (BICR), safety, PROs

Paz-Ares L et al. Ann Oncol 2017;28(suppl 5):Abstr LBA1

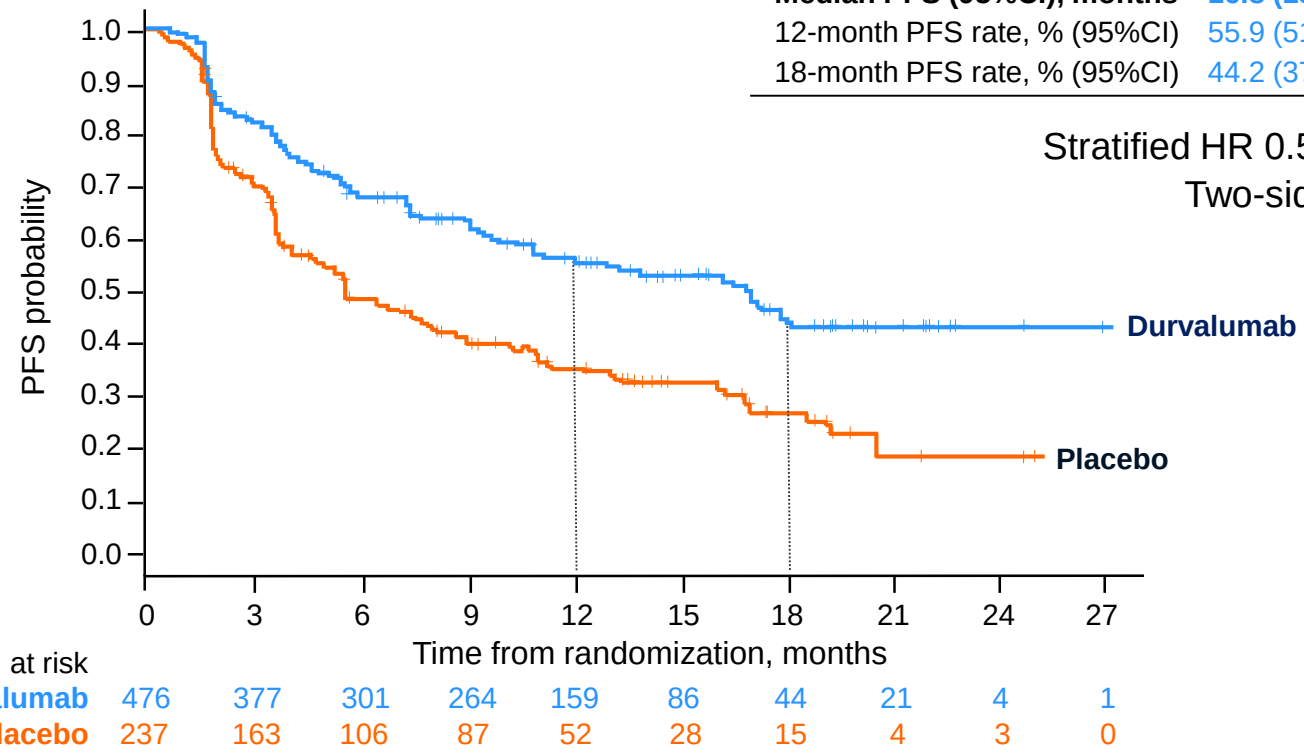
LBA1: PACIFIC: a double-blind, placebo-controlled Phase III study of durvalumab after chemoradiation therapy (CRT) in patients with stage III locally advanced, unresectable NSCLC – Paz-Ares L, et al

- **Key results**

PFS (BICR)

	Durvalumab (n=476)	Placebo (n=237)
Median PFS (95%CI), months	**16.8 (13.0, 18.1)**	**5.6 (4.6, 7.8)**
12-month PFS rate, % (95%CI)	55.9 (51.0, 60.4)	35.3 (29.0, 41.7)
18-month PFS rate, % (95%CI)	44.2 (37.7, 50.5)	27.0 (19.9, 34.5)

Stratified HR 0.52 (95%CI 0.42, 0.65)
Two-sided p<0.0001



No. at risk										
Durvalumab	476	377	301	264	159	86	44	21	4	1
Placebo	237	163	106	87	52	28	15	4	3	0

Paz-Ares L et al. Ann Oncol 2017;28(suppl 5):Abstr LBA1

LBA1: PACIFIC: a double-blind, placebo-controlled Phase III study of durvalumab after chemoradiation therapy (CRT) in patients with stage III locally advanced, unresectable NSCLC – Paz-Ares L, et al

- **Key results (cont.)**

	Durvalumab (n=443)	Placebo (n=213)	Treatment effect, HR (95%CI)
Best overall response, n (%)			
CR	6 (1.4)	1 (0.5)	
PR	120 (27.1)	33 (15.5)	
SD	233 (52.6)	119 (55.9)	
PD	73 (16.5)	59 (27.7)	
Non-evaluable	10 (2.3)	1 (0.5)	
Median DoR, months (95%CI)	NR	13.8 (6.0, NR)	0.43 (0.22, 0.84)
Ongoing response at data cut-off, %			
At 12 months	72.8	56.1	
At 18 months	72.8	46.8	

Paz-Ares L et al. Ann Oncol 2017;28(suppl 5):Abstr LBA1

LBA1: PACIFIC: a double-blind, placebo-controlled Phase III study of durvalumab after chemoradiation therapy (CRT) in patients with stage III locally advanced, unresectable NSCLC – Paz-Ares L, et al

- **Key results (cont.)**

AEs, n (%)	Durvalumab (n=475)	Placebo (n=234)
Any grade all-causality AEs	460 (96.8)	222 (94.9)
Grade 3/4	142 (29.9)	61 (26.1)
Grade 5	21 (4.4)	13 (5.6)
Leading to discontinuation	73 (15.4)	23 (9.8)
Any grade TRAEs	322 (67.8)	125 (53.4)
SAEs	136 (28.6)	53 (22.6)
Any grade immune-mediated AEs	115 (24.2)	19 (8.1)
Grade 3/4	16 (3.4)	6 (2.6)

Pneumonitis (grouped terms) or radiation pneumonitis, n (%)	Durvalumab (n=475)	Placebo (n=234)
Any grade	161 (33.9)	58 (24.8)
Grade 3/4	16 (3.4)	6 (2.6)
Grade 5	5 (1.1)	4 (1.7)
Leading to discontinuation	30 (6.3)	10 (4.3)

Paz-Ares L et al. Ann Oncol 2017;28(suppl 5):Abstr LBA1

LBA1: PACIFIC: a double-blind, placebo-controlled Phase III study of durvalumab after chemoradiation therapy (CRT) in patients with stage III locally advanced, unresectable NSCLC – Paz-Ares L, et al

- **Conclusions**
  - Durvalumab was associated with a statistically significant and robust improvement in PFS at a planned interim analysis
    - Improvement in PFS was observed across all prespecified subgroups
  - Durvalumab demonstrated a clinically meaningful benefit in ORR with durable responses vs. placebo
  - No new safety signals were identified, with the safety profile of durvalumab being consistent with its known safety profile as monotherapy in patient with more advanced disease
  - The results suggest that durvalumab is a promising new therapeutic option in patients with stage III, locally advanced, unresectable NSCLC who have completed concurrent chemoradiation

Paz-Ares L et al. Ann Oncol 2017;28(suppl 5):Abstr LBA1

Advanced NSCLC

Not radically treatable stage III and stage IV

First line

LBA49: Updated results from KEYNOTE-021 cohort G: a randomized, phase 2 study of pemetrexed and carboplatin (PC) with or without pembrolizumab (pembro) as first-line therapy for advanced nonsquamous NSCLC – Borghaei H, et al

- **Study objective**
  - To evaluate the efficacy and safety of pembrolizumab added to 1L carboplatin + pemetrexed in cohort G of KEYNOTE-021 after 5 additional months of follow-up
- **Methods**
  - 123 patients with untreated stage IIIB/IV NSCLC were randomized to pembrolizumab + pemetrexed + carboplatin or to pemetrexed + carboplatin, with optional pemetrexed maintenance
  - Median follow-up was 18.7 months
- **Key results**
  - ORR was significantly higher in the pembrolizumab vs. control group (56.7% vs. 31.7%; p=0.0029)
  - Median PFS was significantly higher in the pembrolizumab vs. control group (19.0 months [95%CI 8.5, NR] vs. 8.9 months [95%CI 6.2, 11.8]; p=0.0067)
  - Median OS was not reached in pembrolizumab arm and was 20.9 months in control arm (HR 0.59 [95%CI 0.34, 1.05]; p=0.03)
- **Conclusion**
  - The improvements in OS, PFS and ORR previously observed were maintained and continued to improve

Borghaei H et al. Ann Oncol 2017;28(suppl 5):Abstr LBA49

LBA2_PR: Osimertinib vs SoC EGFD-TKI as first-line treatment in patients with EGFRm advanced NSCLC (FLAURA) – Ramalingam S, et al

- **Study objective**
  - To assess efficacy and safety of osimertinib vs. SoC EGFR-TKI as 1L in patients with EGFRm advanced NSCLC

Key patient inclusion criteria

- Locally advanced or metastatic NSCLC
- Ex19del/L858R
- No prior EGFR-TKI/systemic anti-cancer therapy
- Stable CNS metastases allowed
- WHO PS 0–1

(n=556)

R 1:1

Osimertinib 80 mg/day (n=279) → PD

SoC EGFR-TKI* Gefitinib 250 mg or erlotinib 150 mg (n=277) → PD

Stratification

- Mutation status (Ex19del/L858R), race (Asian/non-Asian)

Primary endpoint

- PFS (by RECIST v1.1, by investigator)

Secondary endpoint

- ORR, DoR, DCR, depth of response, OS PROs, safety

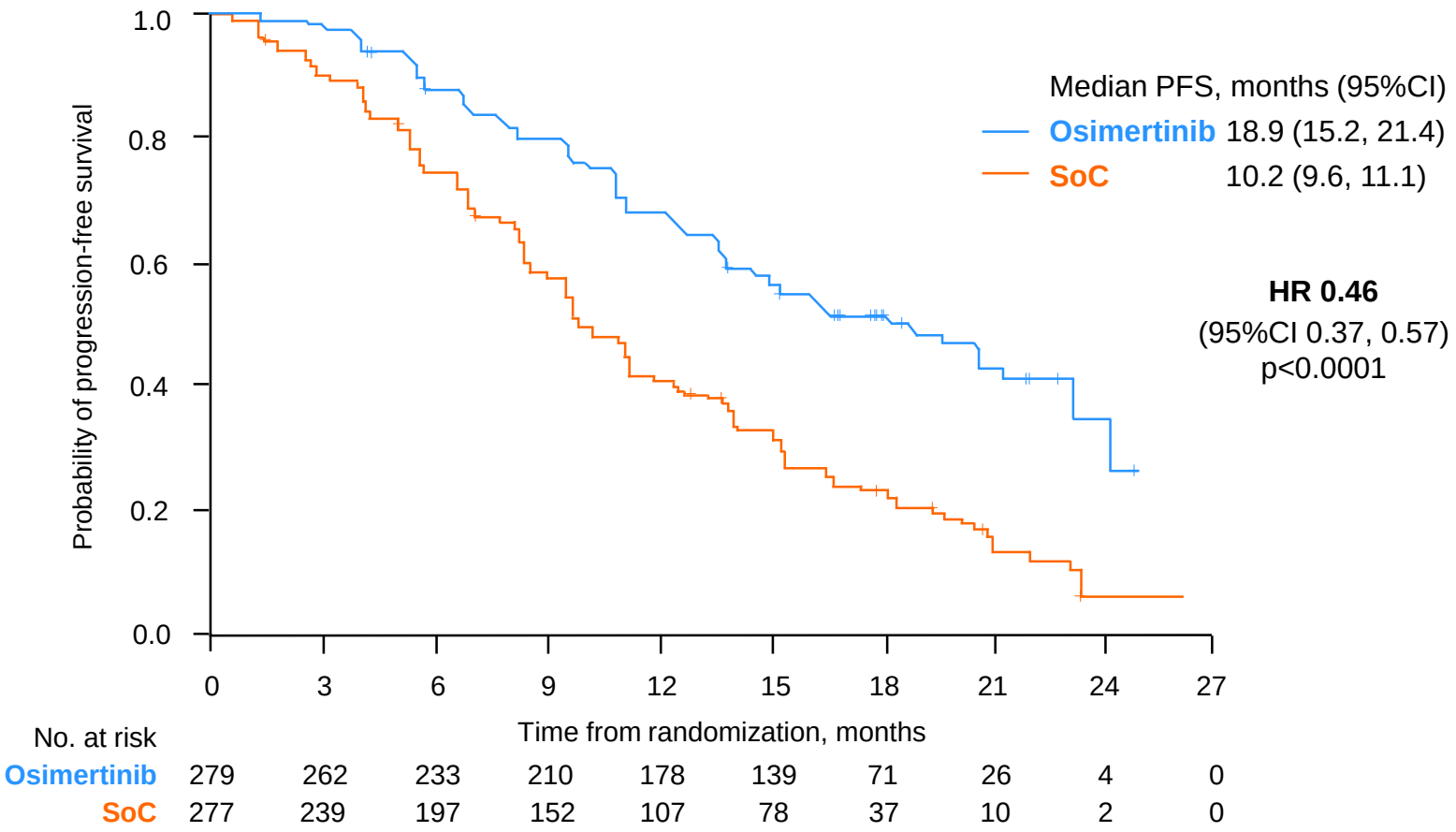
*Crossover to osimertinib was permitted upon central confirmation of progression and T790M positivity

Ramalingam S et al. Ann Oncol 2017;28(suppl 5):Abstr LBA2_PR

LBA2_PR: Osimertinib vs SoC EGFD-TKI as first-line treatment in patients with EGFRm advanced NSCLC (FLAURA) – Ramalingam S, et al

- **Key results**

PFS by investigator assessment

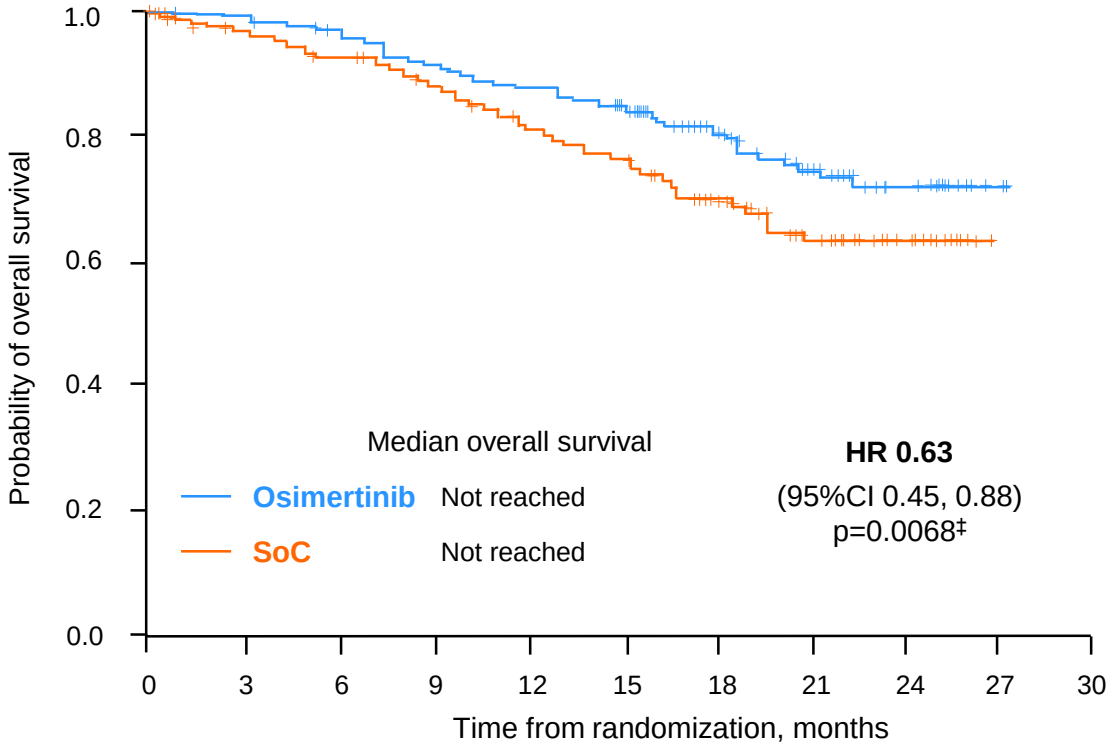


Ramalingam S et al. Ann Oncol 2017;28(suppl 5):Abstr LBA2_PR

LBA2_PR: Osimertinib vs SoC EGFD-TKI as first-line treatment in patients with EGFRm advanced NSCLC (FLAURA) – Ramalingam S, et al

- **Key results (cont.)**

OS interim analysis



‡A p-value of <0.0015 was required for statistical significance at current maturity

No. at risk											
Osimertinib	279	276	269	253	243	232	154	87	29	4	0
SoC	277	263	252	237	218	200	126	64	24	1	0

Ramalingam S et al. Ann Oncol 2017;28(suppl 5):Abstr LBA2_PR

LBA2_PR: Osimertinib vs SoC EGFD-TKI as first-line treatment in patients with EGFRm advanced NSCLC (FLAURA) – Ramalingam S, et al

- **Key results (cont.)**

All causality AE in ≥15% of patients, %	Osimertinib (n=279)			SoC (n=277)		
	Any grade	Grade 3	Grade 4	Any grade	Grade 3	Grade 4
Diarrhoea	161 (58)	6 (2)	0	159 (57)	6 (2)	0
Dry skin	88 (32)	1 (<1)	0	90 (32)	3 (1)	0
Paronychia	81 (29)	1 (<1)	0	80 (29)	2 (1)	0
Stomatitis	80 (29)	1 (<1)	1 (<1)	56 (20)	1 (<1)	0
Dermatitis acneiform	71 (25)	0	0	134 (48)	13 (5)	0
Decreased appetite	56 (20)	7 (3)	0	51 (18)	5 (2)	0
Pruritus	48 (17)	1 (<1)	0	43 (16)	0	0
Cough	46 (16)	0	0	42 (15)	1 (<1)	0
Constipation	42 (15)	0	0	35 (13)	0	0
AST increased	26 (9)	2 (1)	0	68 (25)	12 (4)	0
ALT increased	18 (6)	1 (<1)	0	75 (27)	21 (8)	4 (1)

Ramalingam S et al. Ann Oncol 2017;28(suppl 5):Abstr LBA2_PR

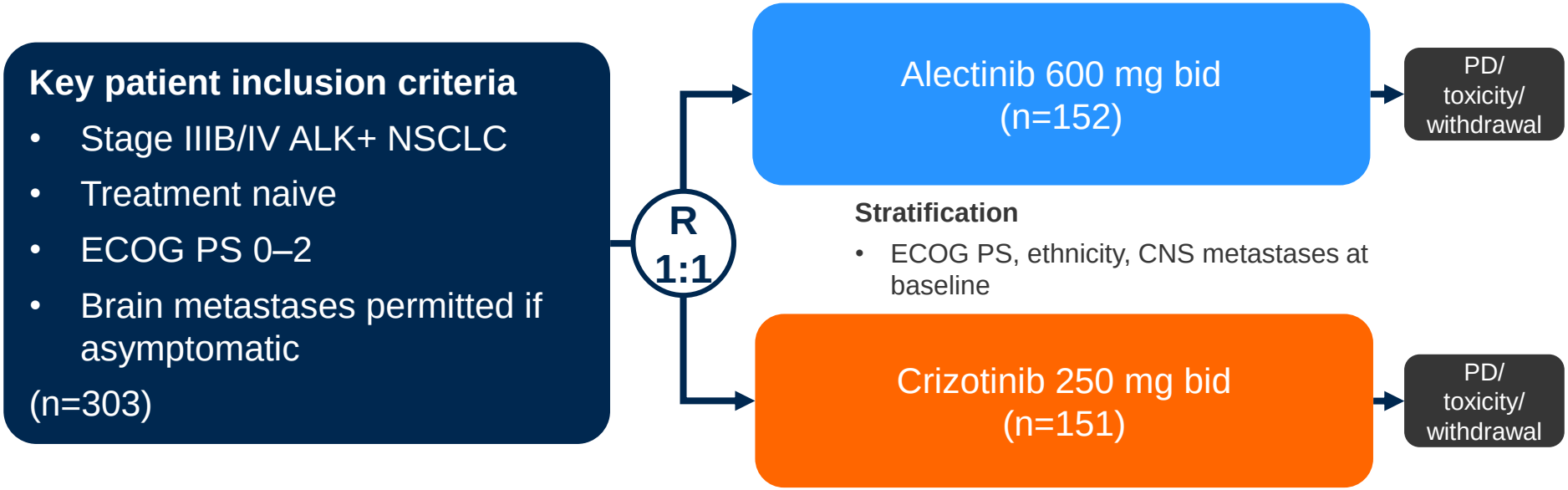
LBA2_PR: Osimertinib vs SoC EGFD-TKI as first-line treatment in patients with EGFRm advanced NSCLC (FLAURA) – Ramalingam S, et al

- **Conclusions**
  - Osimertinib resulted in a significant improvement in PFS over SoC
    - There was early separation of PFS KM curves, with a 54% reduction in risk of progression or death
    - There was consistent benefit in patients with and without CNS metastases at study entry
    - Osimertinib was associated with double the DoR vs. SoC
  - Interim OS results showed promising survival favouring osimertinib vs. SoC (p=0.0068), the difference was not significant as a p-value of <0.0015 was required for statistical significance
  - The safety profile of osimertinib was comparable to SoC, although with lower rates of grade ≥3 AEs and a lower discontinuation rate

Ramalingam S et al. Ann Oncol 2017;28(suppl 5):Abstr LBA2_PR

1298O_PR: Alectinib vs crizotinib in treatment-naïve ALK+ NSCLC: CNS efficacy results from the ALEX study – Gadgeel S, et al

- **Study objective**
  - To assess the systematic and CNS efficacy of alectinib vs. crizotinib as 1L therapy in patients with advanced/metastatic ALK+ NSCLC



Primary endpoint

- PFS (investigator assessed)

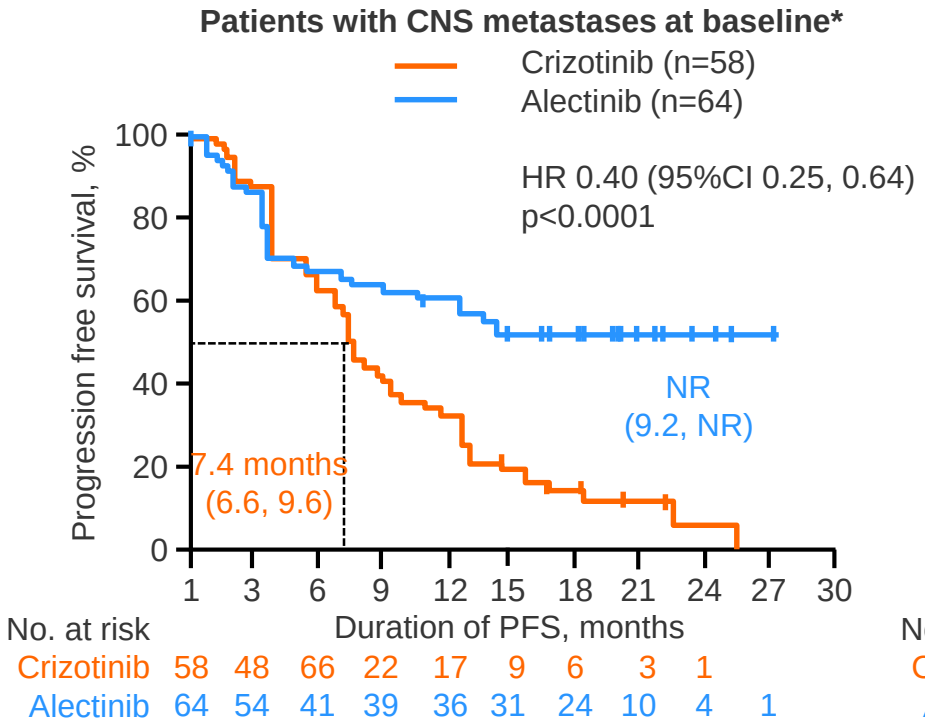
Secondary endpoints

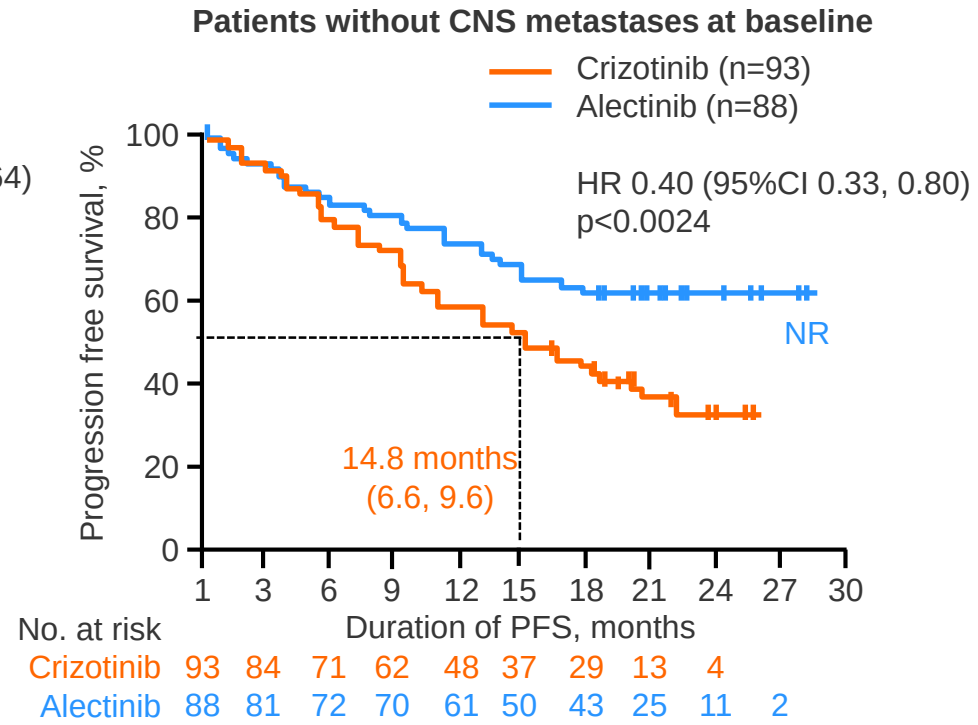
- Time to CNS progression, CNS ORR, CNS DoR

Gadgeel S et al. Ann Oncol 2017;28(suppl 5):Abstr 1298O_PR

1298O_PR: Alectinib vs crizotinib in treatment-naïve ALK+ NSCLC: CNS efficacy results from the ALEX study – Gadgeel S, et al

- **Key results**





*All patients with CNS metastases, irrespective of radiotherapy

Gadgeel S et al. Ann Oncol 2017;28(suppl 5):Abstr 1298O_PR

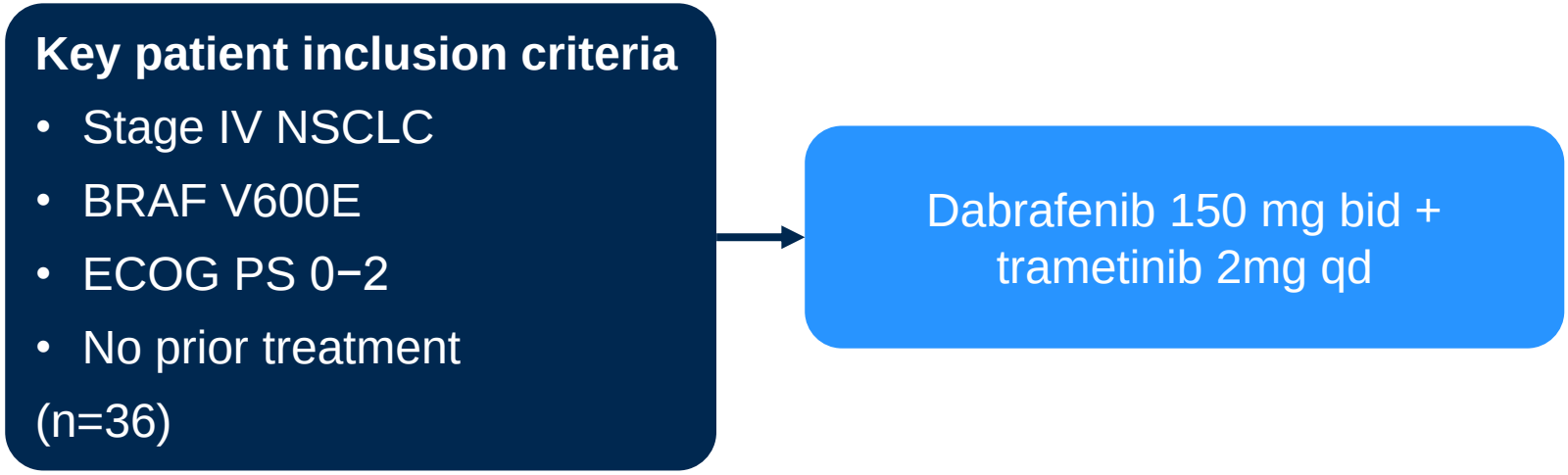
1298O_PR: Alectinib vs crizotinib in treatment-naïve ALK+ NSCLC: CNS efficacy results from the ALEX study – Gadgeel S, et al

- **Key results (cont.)**
  - Alectinib associated with superior efficacy vs. crizotinib for other CNS endpoints:
    - Improved intracranial ORR vs. crizotinib in patients with prior RT (85.7% vs. 71.4%) and without prior RT (78.6% vs. 40.0%)
    - Duration of CNS response longer in all subgroups with alectinib
    - Lower rate of CNS metastases at time of first progression (4.6% vs. 31.5%; HR 0.14 [95%CI 0.06, 0.33]; p<0.0001)
- **Conclusions**
  - In previously untreated patients with advanced ALK+ NSCLC, CNS activity was significantly superior with alectinib vs. crizotinib in patients with CNS disease, in those with and without prior CNS radiotherapy
  - Significantly fewer alectinib-treated patients had CNS metastases at the time of first progression, suggesting alectinib is protective against CNS progression
  - Overall, these results support alectinib for patients with previously untreated, advanced ALK+ NSCLC

Gadgeel S et al. Ann Oncol 2017;28(suppl 5):Abstr 1298O_PR

LBA51: Phase 2 trial (BRF 11328) of dabrafenib (D) plus trametinib (T) in patients (pts) with previously untreated BRAF V600E-mutant metastatic non-small cell lung cancer (NSCLC) – Planchard D, et al

- **Study objective**
  - To evaluate the efficacy and safety of 1L treatment with dabrafenib + trametinib in patients with BRAF V600E-mutant metastatic NSCLC (BRF113928 Cohort C)



Primary endpoint

- ORR (investigator-assessed)

Secondary endpoints

- DoR, PFS, OS, safety, PK

Planchard D et al. Ann Oncol 2017;28(suppl 5):Abstr LBA51

LBA51: Phase 2 trial (BRF 11328) of dabrafenib (D) plus trametinib (T) in patients (pts) with previously untreated BRAF V600E-mutant metastatic non-small cell lung cancer (NSCLC) – Planchard D, et al

- **Key results**

	Investigator assessed	IRC assessed
CR, n (%)	2 (6)	2 (6)
PR, n (%)	21 (58)	21 (58)
SD, n (%)	4 (11)	3 (8)
PD, n (%)	5 (14)	7 (19)
NE, n (%)	4 (11)	3 (8)
ORR, n (%) [95%CI]	**23 (64) [46, 79]**	**23 (64) [46, 79]**
DCR, n (%) [95%CI]	27 (75) [55, 88]	26 (72) [55, 86]
Median DoR, months (95%CI)	10.4 (8.3, 17.9)	15.2 (7.8, 23.5)
mPFS, months (95%CI)	10.9 (7.0, 16.6)	14.6 (7.0, 22.1)
mOS, months (95%CI)	24.6 (12.3, NE)	

Planchard D et al. Ann Oncol 2017;28(suppl 5):Abstr LBA51

LBA51: Phase 2 trial (BRF 11328) of dabrafenib (D) plus trametinib (T) in patients (pts) with previously untreated BRAF V600E-mutant metastatic non-small cell lung cancer (NSCLC) – Planchard D, et al

- **Key results (cont.)**

	All grades, n (%)	Grade 3/4, n (%)
Drug-related AE	32 (89)	13 (36)
Drug-related serious AE	16 (44)	10 (28)
AEs leading to discontinuation	7 (19)	3 (8)
AEs requiring dose interruption/delay	25 (69)	15 (42)

- **Conclusions**
  - In the first study of combined BRAF and MEK inhibition as 1L therapy in patients with BRAF V600E-mutant metastatic NSCLC, dabrafenib + trametinib demonstrated substantial anti-tumour activity and durable response
  - No new safety signals were identified; the safety profile of the combination was manageable and consistent with previous experience
  - Efficacy was similar to that reported in patients who had received prior treatment
  - Based on these results, the European Commission and the US FDA has approved the combination for patients with metastatic NSCLC harbouring this mutation regardless of prior treatment history

Planchard D et al. Ann Oncol 2017;28(suppl 5):Abstr LBA51

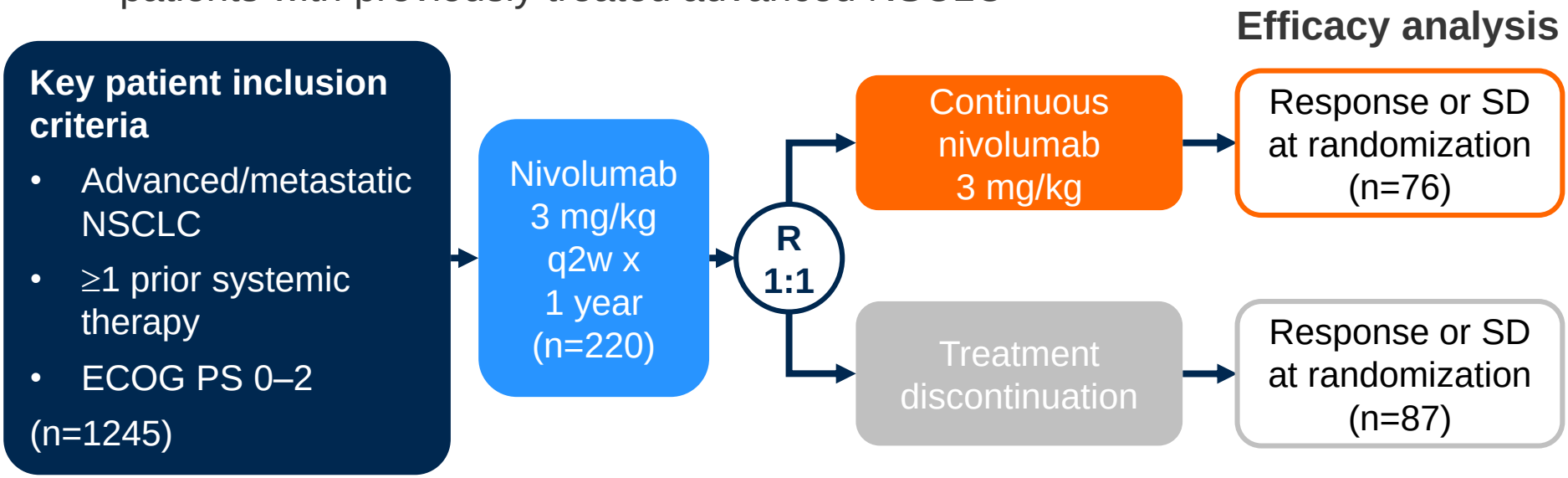
Advanced NSCLC

Not radically treatable stage III and stage IV

Later lines

1297O: Randomized results of fixed-duration (1-yr) vs continuous nivolumab in patients (pts) with advanced non-small cell lung cancer (NSCLC) – Spigel DR, et al

- **Study objective**
  - To evaluate the incidence of select high grade TRAEs and the clinical benefit of a fixed-duration (1 year) of nivolumab treatment vs. continuous treatment in patients with previously treated advanced NSCLC



Primary endpoint

- Select high grade TRAEs

Exploratory endpoints

- Safety/efficacy with continuous vs. 1-year treatment, biomarkers, PK

Spigel DR et al. Ann Oncol 2017;28(suppl 5):Abstr 1297O

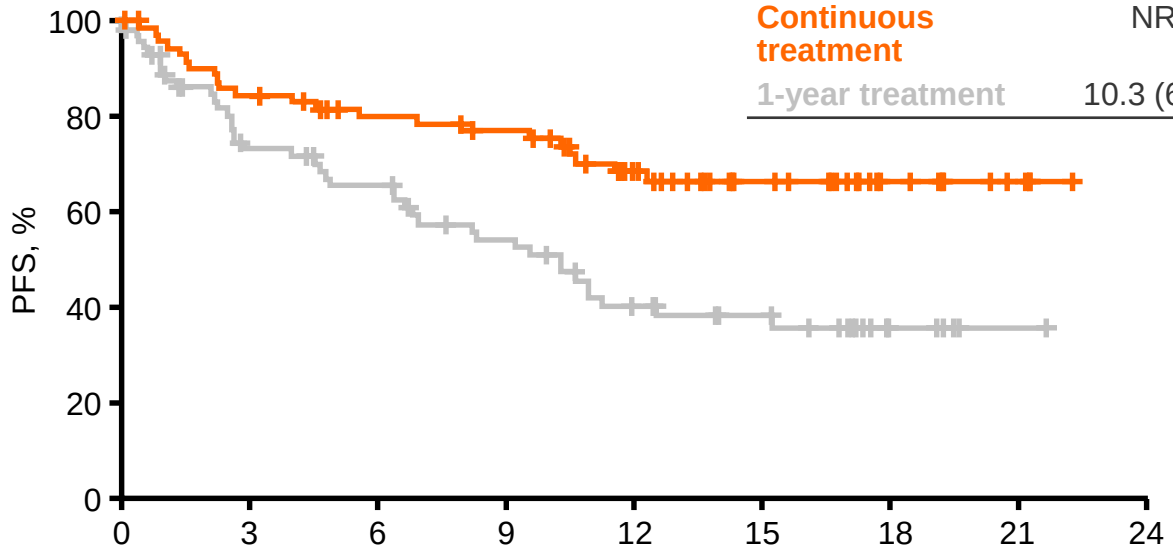
1297O: Randomized results of fixed-duration (1-yr) vs continuous nivolumab in patients (pts) with advanced non-small cell lung cancer (NSCLC) – Spigel DR, et al

- **Key results**

PFS from randomization (investigator-assessed response)

	Median, months (95%CI)	PFS rate, %	
		6-month	1-year
Continuous treatment	NR (NR)	80	65
1-year treatment	10.3 (6.4, 15.2)	69	40

HR 0.42 (95%CI 0.25, 0.71)



No. at risk

Continuous	76	60	53	49	35	22	10	3	0
1-year	87	50	43	33	21	16	5	1	0

Spigel DR et al. Ann Oncol 2017;28(suppl 5):Abstr 1297O

1297O: Randomized results of fixed-duration (1-yr) vs continuous nivolumab in patients (pts) with advanced non-small cell lung cancer (NSCLC) – Spigel DR, et al

- **Key results (cont.)**

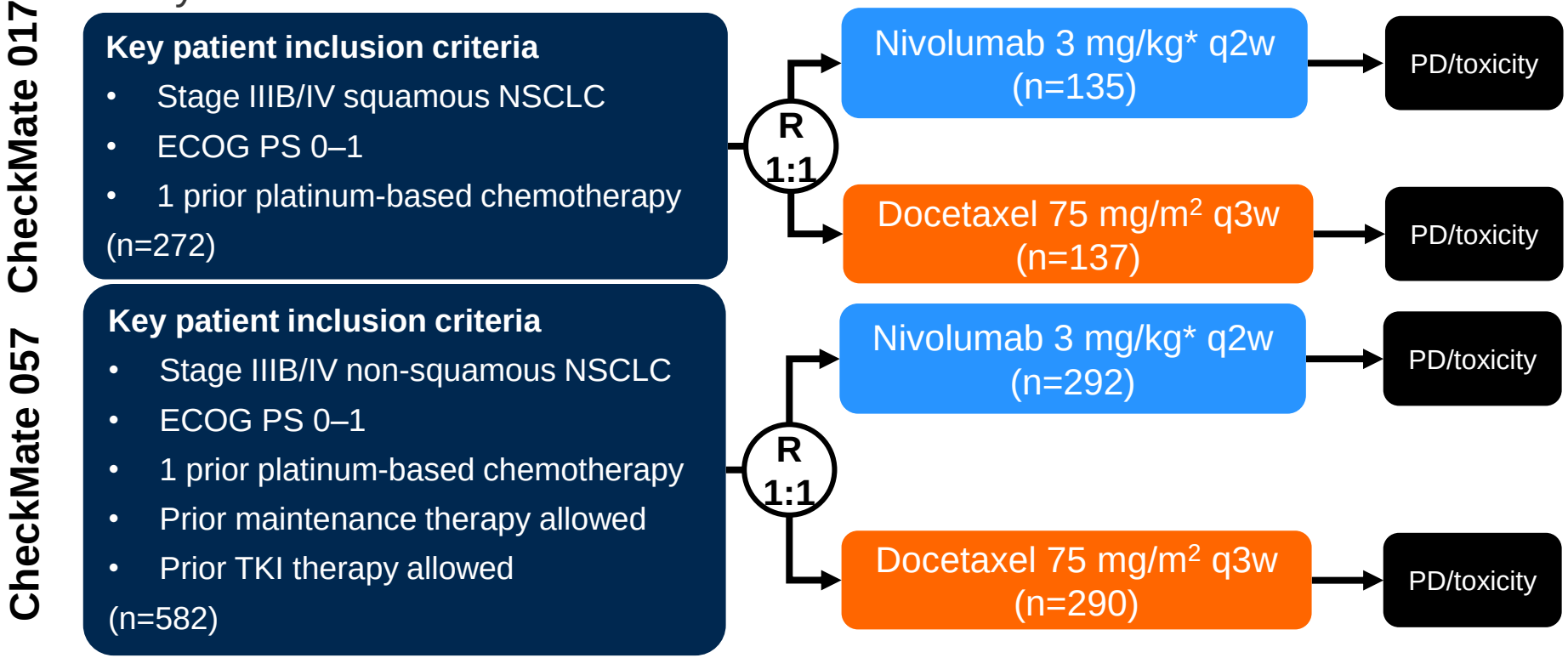
	Continuous treatment (n=107)		1-year treatment (n=113)	
AEs post-randomization, %	**Any grade**	**Grade 3/4**	**Any grade**	**Grade 3/4**
Treatment-related AEs	39	8	25	4
Treatment-related SAEs	5	4	2	1
Select treatment-related AEs	33	2	17	2
Treatment-related AEs leading to discontinuation	7	5	3	1

- **Conclusions**
  - Although the frequency of treatment-related AEs was higher with continuous vs. fixed duration (1-year) treatment, there were few new-onset events after the first year
  - Among those still on nivolumab at 1 year, continuing therapy was associated with significantly higher PFS vs. stopping therapy in responding patients
  - The CheckMate 153 results suggest that treatment until PD may be beneficial

Spigel DR et al. Ann Oncol 2017;28(suppl 5):Abstr 1297O

1301PD: Three-year follow-up from CheckMate 017/057: Nivolumab versus docetaxel in patients with previously treated advanced non-small cell lung cancer (NSCLC) – Felip E, et al

- **Study objective**
  - To assess the efficacy and safety of nivolumab in patients with NSCLC after >3 years



Primary endpoint

- OS

Secondary endpoints

- PFS, ORR, efficacy by PD-L1 expression, safety, QoL

*Optional switch to flat dose nivolumab 480 mg q4w

Felip E et al. Ann Oncol 2017;28(suppl 5):Abstr 1301PD

1301PD: Three-year follow-up from CheckMate 017/057: Nivolumab versus docetaxel in patients with previously treated advanced non-small cell lung cancer (NSCLC) – Felip E, et al

- **Key results**

	CheckMate 017 (squamous)		CheckMate 057 (non-squamous)	
	Nivolumab (n=135)	Docetaxel (n=137)	Nivolumab (n=292)	Docetaxel (n=290)
3-year OS rate, %	16	6	18	9
HR (95%CI)	0.62 (0.48, 0.80)		0.73 (0.62, 0.88)	
3-year PFS rate, %	12	NC	10	<1
HR (95%CI)	0.63 (0.48, 0.82)		0.89 (0.74, 1.06)	
ORR, % (95%CI)	20 (14, 28)	9 (5, 15)	19 (15, 24)	12 (9, 17)
Median DoR, months (95%CI)	25.2 (9.8, NE)	8.4 (3.6, 14.0)	18.3 (8.4, NE)	5.6 (4.4, 6.9)
Response ongoing, n/N (%)	7/27 (26)	0/12 (0)	13/56 (23)	0/36 (0)

- **Conclusion**
  - After 3 years of follow-up, nivolumab continued to provide OS and PFS benefits in patients with advanced squamous and non-squamous NSCLC

Felip E et al. Ann Oncol 2017;28(suppl 5):Abstr 1301PD

1303PD: Nivolumab in previously treated pts with metastatic squamous NSCLC: Results of a European single-arm, phase 2 trial (CheckMate 171) including pts aged 70 years and with poor performance status – Popat S, et al

- **Study objective**
  - To evaluate the efficacy and safety of nivolumab monotherapy following progression on platinum-based chemotherapy

Key patient inclusion criteria

- Advanced/metastatic squamous NSCLC
- ≥1 prior platinum-based systemic therapy
- No untreated CNS metastases

(n=809)

→ Nivolumab 3 mg/kg IV q2w → PD or toxicity

Primary endpoint

- Incidence of select grade 3–4 TRAEs

Safety endpoints

- Safety, OS, ORR (by investigator)

Popat S et al. Ann Oncol 2017;28(suppl 5):Abstr 1303PD

1303PD: Nivolumab in previously treated pts with metastatic squamous NSCLC: Results of a European single-arm, phase 2 trial (CheckMate 171) including pts aged 70 years and with poor performance status – Popat S, et al

- **Key results**

Select TRAEs in ≥1%, n (%)	All patients (n=809)		≥70 years (n=279)		ECOG PS 2 (n=98)	
	Any	Grade 3–4	Any	Grade 3–4	Any	Grade 3–4
Skin	98 (12)	5 (1)	40 (14)	1 (<1)	13 (13)	0
Endocrine	70 (9)	6 (1)	23 (8)	2 (1)	4 (4)	0
Gastrointestinal	63 (8)	7 (1)	28 (10)	3 (1)	9 (9)	0
Hepatic	33 (4)	8 (1)	11 (4)	1 (<1)	7 (7)	1 (1)
Pulmonary	30 (4)	5 (1)	10 (4)	2 (1)	2 (2)	0
Hypersensitivity/ infusion-related	13 (2)	0	4 (1)	0	3 (3)	0
Renal	12 (1)	3 (<1)	10 (4)	2 (1)	1 (1)	1 (1)

Popat S et al. Ann Oncol 2017;28(suppl 5):Abstr 1303PD

1303PD: Nivolumab in previously treated pts with metastatic squamous NSCLC: Results of a European single-arm, phase 2 trial (CheckMate 171) including pts aged 70 years and with poor performance status – Popat S, et al

- **Key results (cont.)**

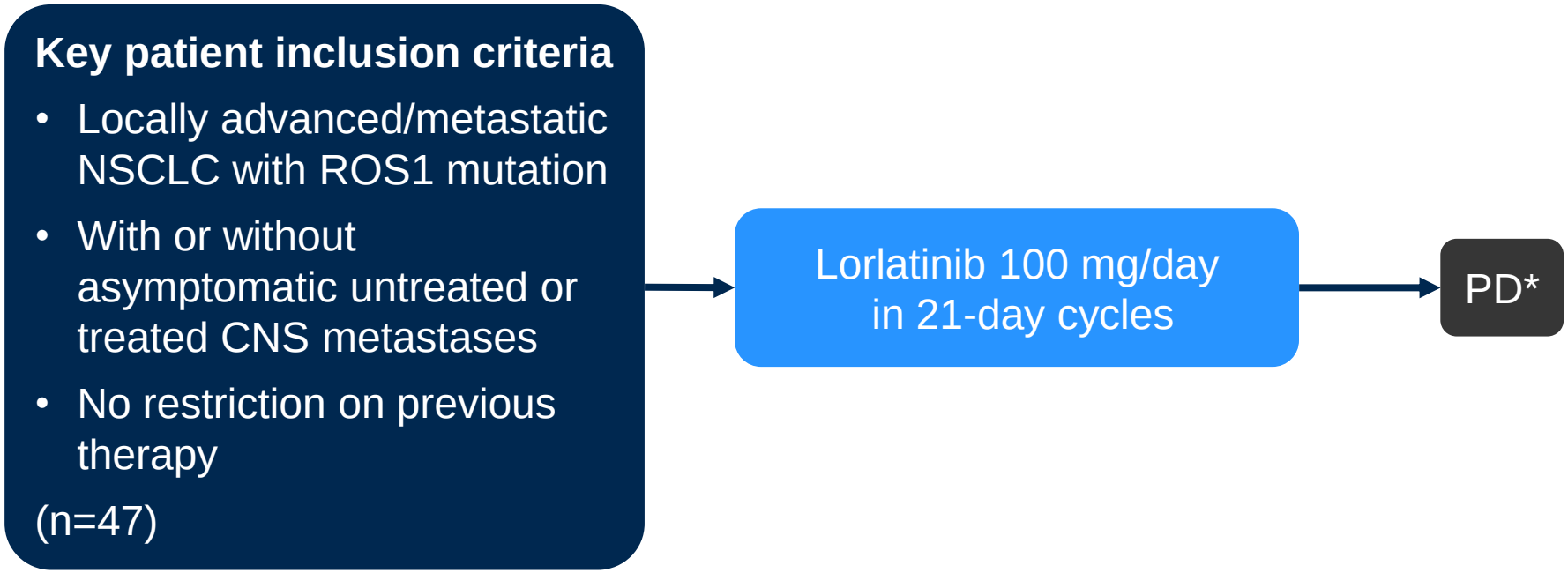
	All patients (n=809)	≥70 years (n=279)	ECOG PS 2 (n=98)
Median OS, months (95%CI)	9.9 (8.7, 13.1)	11.2 (7.6, NA)	5.4 (3.9, 8.3)
3-month OS rate, % (95%CI)	81 (78, 83)	78 (73, 83)	65 (54, 74)
6-month OS rate, % (95%CI)	67 (63, 70)	66 (59, 71)	46 (34, 57)

- **Conclusions**
  - Nivolumab is well tolerated and effective in previously treated patients with squamous NSCLC
  - Nivolumab was similarly tolerated in patients ≥70 years, or those with ECOG PS 2, compared to the overall population
  - The results support the use of nivolumab in patients with advanced, squamous NSCLC, including those ≥70 years and those with ECOG PS 2

Popat S et al. Ann Oncol 2017;28(suppl 5):Abstr 1303PD

1308PD: Preliminary efficacy and safety of lorlatinib in pts (Pts) with ROS1-positive non-small cell lung cancer (NSCLC) – Besse B, et al

- **Study objective**
  - To evaluate the efficacy and safety of lorlatinib in patients with ROS1-positive NSCLC



Primary endpoints

- ORR (RECIST v1.1), intracranial ORR

Secondary endpoints

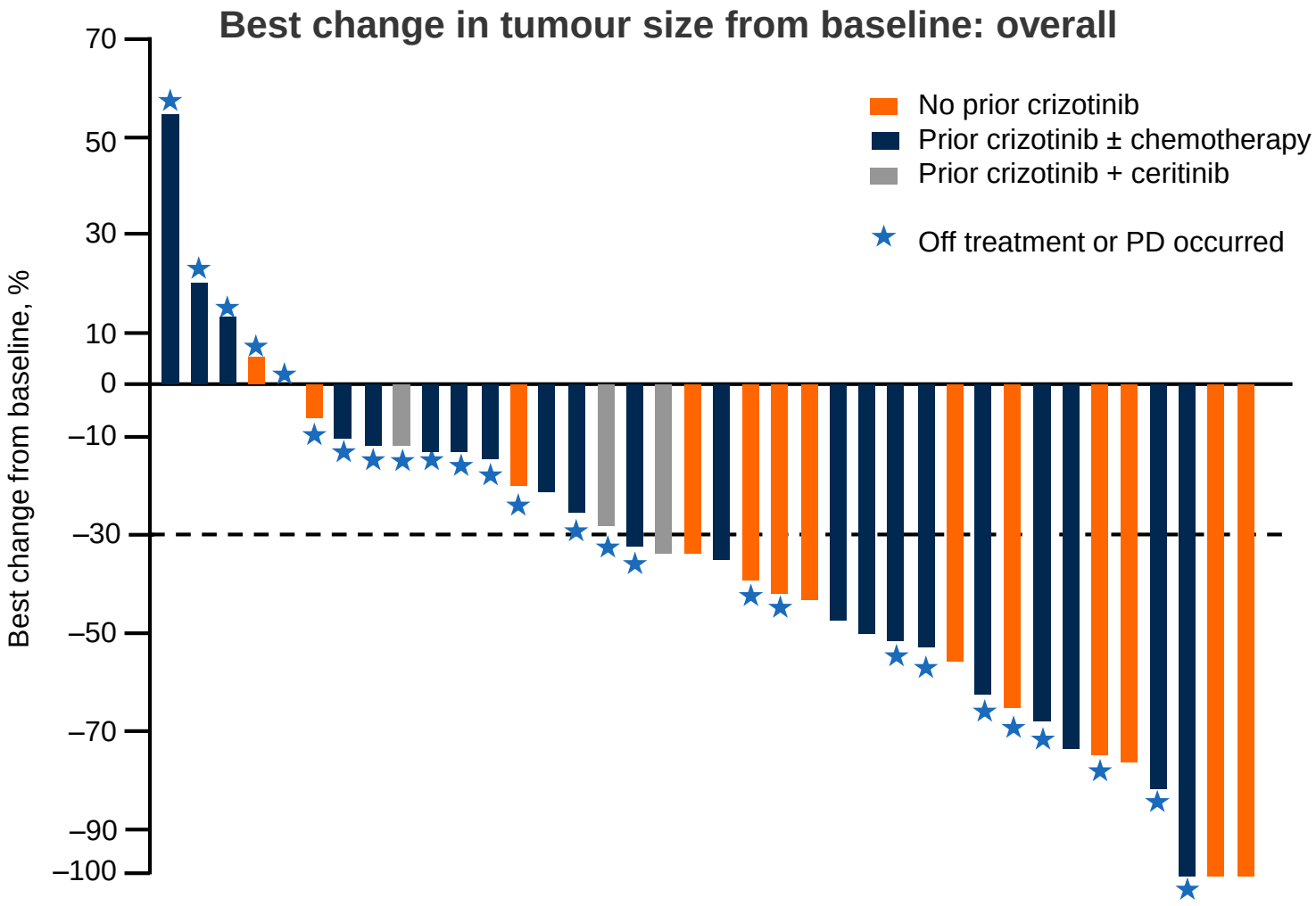
- DoR, PFS, safety

*Treatment was permitted to continue after PD if the patient was still experiencing clinical benefit

Besse B et al. Ann Oncol 2017;28(suppl 5):Abstr 1308PD

1308PD: Preliminary efficacy and safety of lorlatinib in pts (Pts) with ROS1-positive non-small cell lung cancer (NSCLC) – Besse B, et al

- **Key results**



Besse B et al. Ann Oncol 2017;28(suppl 5):Abstr 1308PD

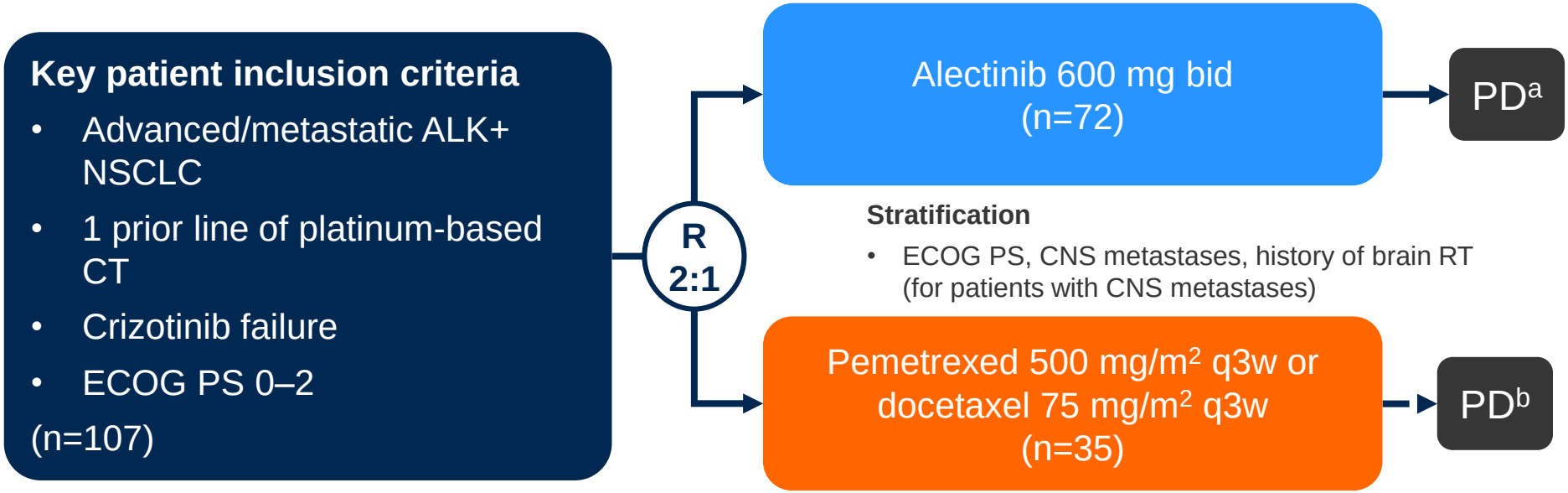
1308PD: Preliminary efficacy and safety of lorlatinib in pts (Pts) with ROS1-positive non-small cell lung cancer (NSCLC) – Besse B, et al

- **Key results (cont.)**
  - 53% of included patients had CNS metastases, and 66% had received prior crizotinib
  - Response
    - ORR in ROS1-positive patients was 36.2% (95%CI 22.7, 51.5); 22/47(46.8%) had best response of SD
    - Intercranial ORR was 56.0% (95%CI 30.2, 59.9), 9 patients had CR
    - Median DoR was 9.9 months (95%CI 6.9, 12.5)
  - Safety
    - Most TRAEs were grade 1 or 2; there were no grade 4–5 events
    - The most common TRAEs were hypercholesterolaemia (83%) and hypertriglyceridaemia (55%)
- **Conclusions**
  - Lorlatinib demonstrated clinical activity in patients with ROS1-positive NSCLC, including those with CNS involvement and those who had received prior crizotinib therapy
  - Treatment was generally well tolerated, with the most common TRAE being lipid elevations that were managed with lipid-lowering medication

Besse B et al. Ann Oncol 2017;28(suppl 5):Abstr 1308PD

1299O_PR: Primary results from the phase III ALUR study of alectinib versus chemotherapy in previously treated ALK+ non-small-cell lung cancer (NSCLC) – Novello S, et al

- **Study objective**
  - To compare alectinib with standard chemotherapy in patients with advanced/ metastatic ALK+ NSCLC after crizotinib failure



Primary endpoint

- PFS (investigator assessed)

Secondary endpoints

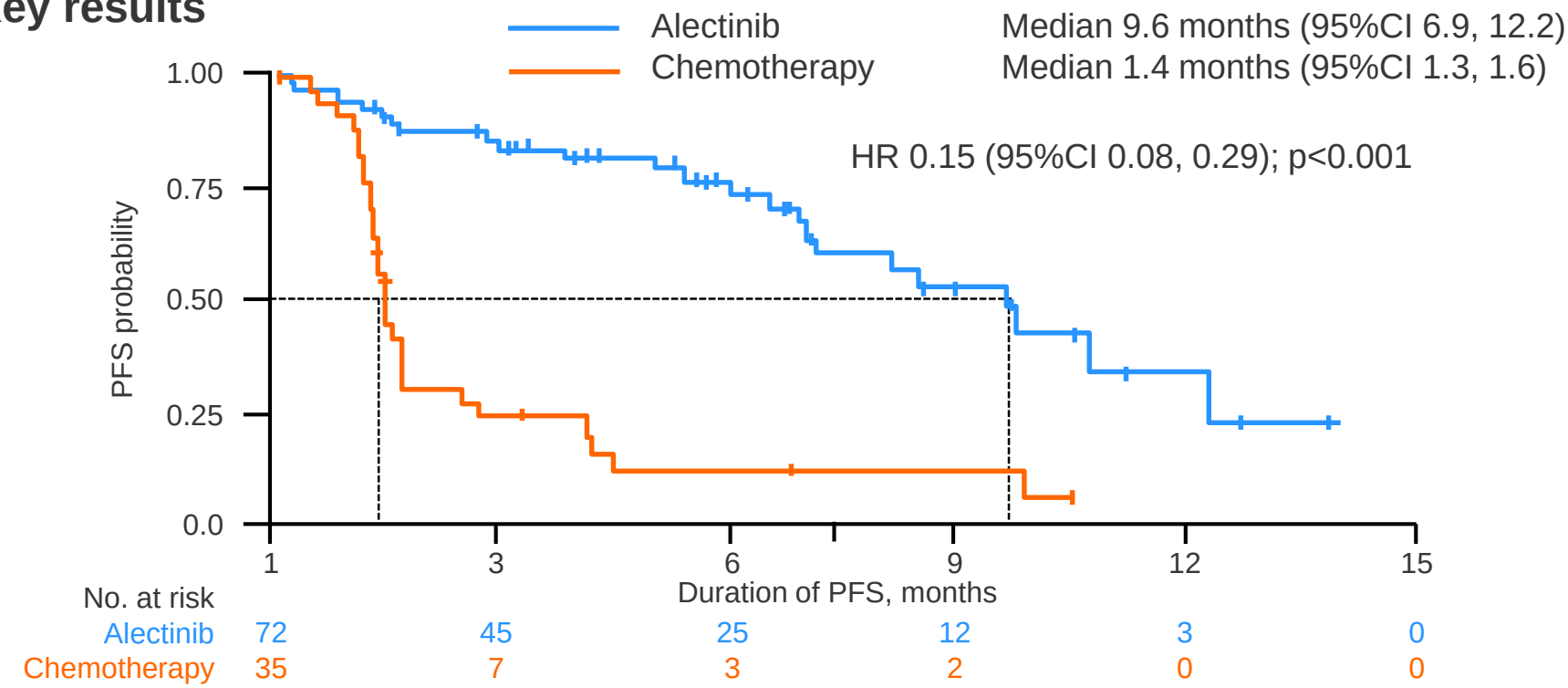
- CNS ORR, PFS (IRC-assessed), ORR, DCR, DoR, OS, safety

[a]Optional continuation of alectinib if clinical benefit
[b]Crossover to alectinib allowed

Novello S et al. Ann Oncol 2017;28(suppl 5):Abstr 1299O_PR

1299O_PR: Primary results from the phase III ALUR study of alectinib versus chemotherapy in previously treated ALK+ non-small-cell lung cancer (NSCLC) – Novello S, et al

- **Key results**



  - At data cut-off (26.01.17), median follow-up was 6.5 months with alectinib and 5.8 months with chemotherapy
  - Median time on treatment was 20 weeks (range 0.4–62.1) in the alectinib arm and 6 weeks (range 1.9–47.1) in the chemotherapy arm

Novello S et al. Ann Oncol 2017;28(suppl 5):Abstr 1299O_PR

1299O_PR: Primary results from the phase III ALUR study of alectinib versus chemotherapy in previously treated ALK+ non-small-cell lung cancer (NSCLC) – Novello S, et al

- **Key results (cont.)**
  - Improved PFS in all subgroups: age, sex, race, ECOG PS, CNS metastases at baseline, prior radiotherapy

CNS response in patients with baseline measurable CNS disease		
	Alectinib (n=24)	**Chemotherapy (n=16)**
CNS ORR by IRC, % (95%CI)	54.2 (33, 74)*	0 (0, 21)
CNS best overall response, n (%)		
CR	1 (4.2)	0
PR	12 (50)	0
SD	6 (25)	5 (31.3)
PD	3 (12.5)	8 (50.0)
Not evaluable	2 (8.3)	3 (18.8)

*p<0.001 vs. chemotherapy

Novello S et al. Ann Oncol 2017;28(suppl 5):Abstr 1299O_PR

1299O_PR: Primary results from the phase III ALUR study of alectinib versus chemotherapy in previously treated ALK+ non-small-cell lung cancer (NSCLC) – Novello S, et al

- **Key results (cont.)**

Event, n (%)	Alectinib (n=70)		Chemotherapy (n=34)	
AE (all grades)	54 (77.1)		29 (85.3)	
Serious AEs	13 (18.6)		5 (14.7)	
Grade 3−5 AEs	19 (27.1)		14 (41.2)	
AEs leading to discontinuation	4 (5.7)		3 (8.8)	
AEs leading to dose reduction	3 (4.3)		4 (11.8)	
AEs leading to dose interruption	13 (18.6)		3 (8.8)	
Most common AEs (≥10%), n (%)	**All grades**	**Grade ≥3**	**All grades**	**Grade ≥3**
Fatigue	4 (5.7)	0	9 (26.5)	3 (8.8)
Constipation	13 (18.6)	0	4 (11.8)	1 (2.9)
Nausea	1 (1.4)	0	6 (17.6)	1 (2.9)
Neutropenia	2 (2.9)	0	5 (14.7)	4 (11.8)
Anaemia	10 (14.3)	1 (1.4)	4 (11.8)	2 (5.9)

Novello S et al. Ann Oncol 2017;28(suppl 5):Abstr 1299O_PR

1299O_PR: Primary results from the phase III ALUR study of alectinib versus chemotherapy in previously treated ALK+ non-small-cell lung cancer (NSCLC) – Novello S, et al

- **Conclusions**
  - Alectinib was associated with significantly improved PFS vs. chemotherapy in patients with ALK+ NSCLC previously treated with crizotinib
  - Alectinib showed promising efficacy for CNS metastases (ORR 54.2% vs. 0% with chemotherapy)
  - The safety and tolerability profile compared favourably with chemotherapy despite longer treatment with alectinib vs. chemotherapy (20 vs. 6 weeks)
  - Overall, these results confirm the previously demonstrated benefit of alectinib in this patient group

Novello S et al. Ann Oncol 2017;28(suppl 5):Abstr 1299O_PR

Other malignancies

SCLC and mesothelioma

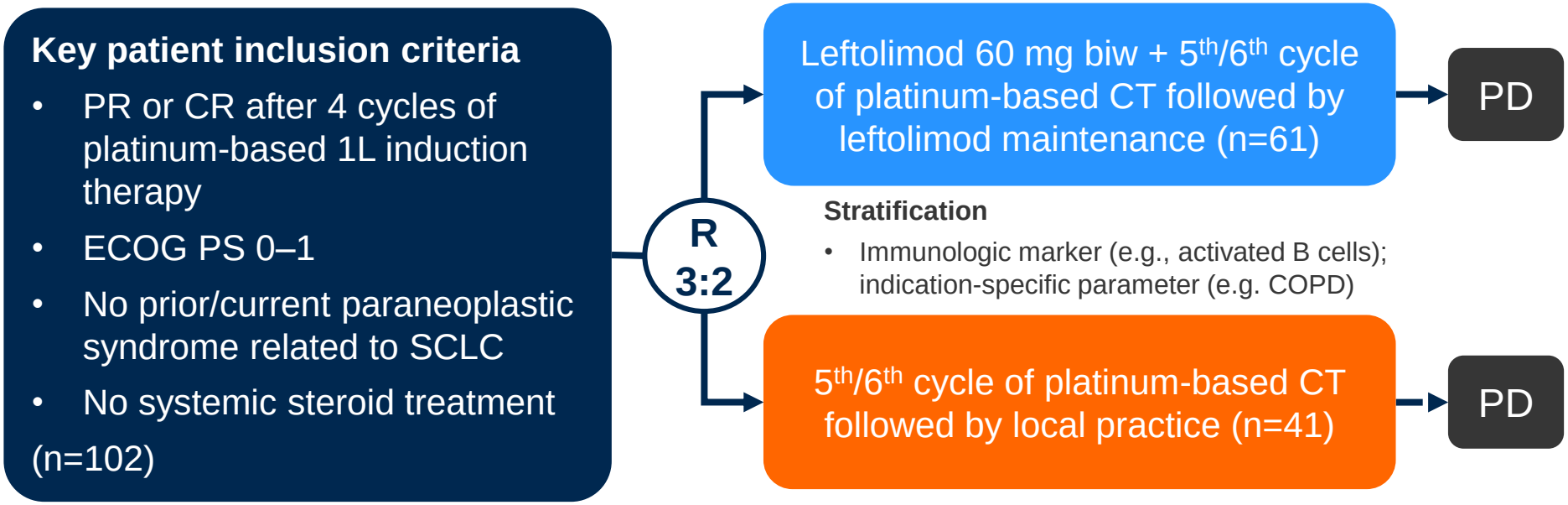
1531PD: Clinical outcomes for EGFR-mutant adenocarcinomas (AC) that transform to small cell lung cancer (SCLC) – Marcoux N, et al

- **Study objective**
  - To characterize the clinical course of patients whose EGFR-mutant lung adenocarcinomas transform to SCLC at the time of acquired resistance
- **Methods**
  - Retrospectively review of records of 16 patients with EGFR-mutant SCLC at one centre
  - Demographics, disease features, and clinical outcomes are summarised
- **Key results**
  - All genotyped patients kept their founder EFGF mutation; all were T790M negative
  - mPFS for initial therapy after transformation was 3.3 months (95%CI 1.2, 5.6)
  - mOS from initial diagnosis was 38 months (95%CI 22.1,44.1) and from time of SCLC transformation was 8.8 months (95%CI 4.9, 14.7)
  - The most common therapy after transformation to SCLC was platinum-etoposide (n=9)
- **Conclusion**
  - Further evaluation of these patients is needed to identify optimal treatment regimens

Marcoux N et al. Ann Oncol 2017;28(suppl 5):Abstr 1531PD

1527O: Top-line data from the randomized phase 2 IMPULSE study in small-cell lung cancer (SCLC): Immunotherapeutic maintenance treatment with lefitolimod – Thomas M, et al

- **Study objective**
  - To evaluate the efficacy and safety of lefitolimod in SCLC



Primary endpoint

- OS (ITT population)

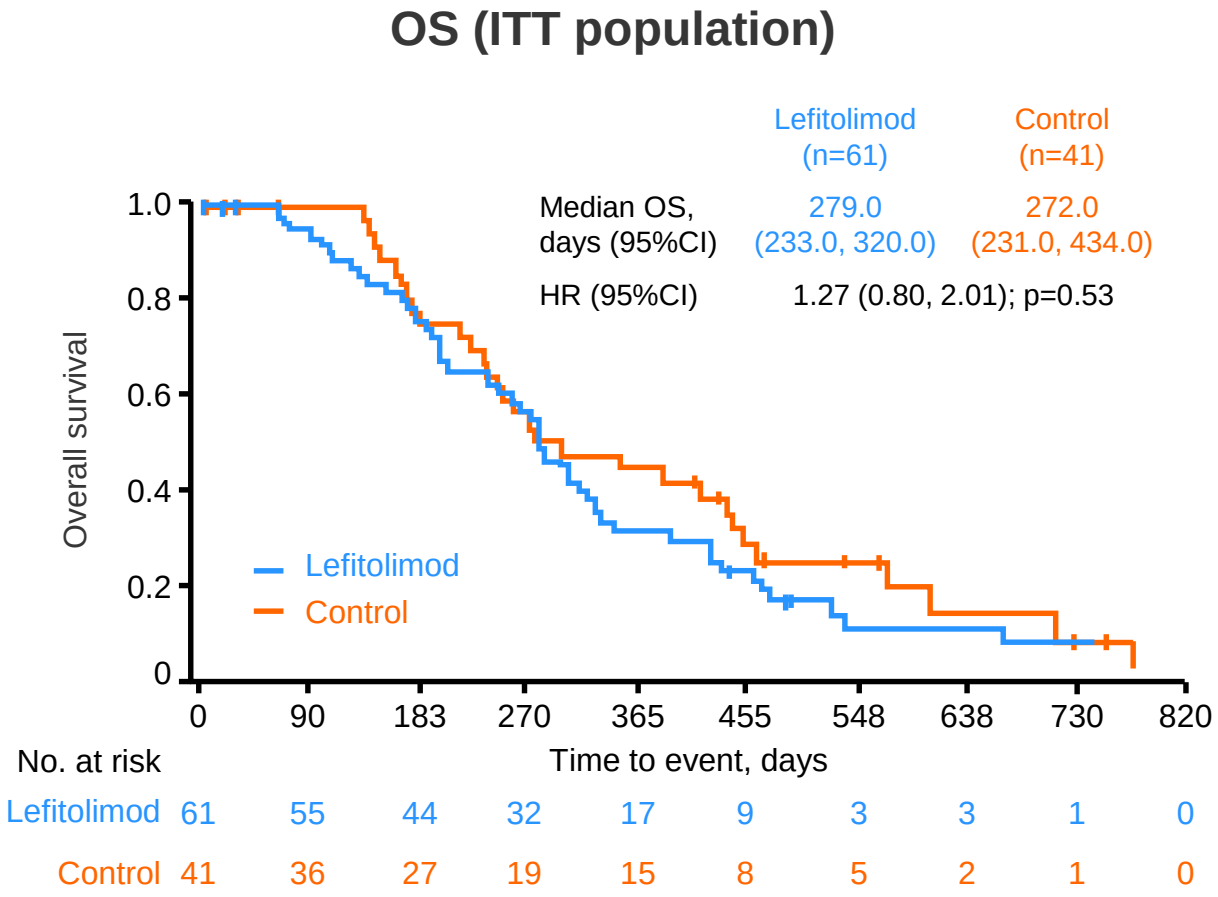
Secondary endpoints

- PFS, ORR, PD response, safety, OS (subgroups)

Thomas M et al. Ann Oncol 2017;28(suppl 5):Abstr 1527O

1527O: Top-line data from the randomized phase 2 IMPULSE study in small-cell lung cancer (SCLC): Immunotherapeutic maintenance treatment with lefitolimod – Thomas M, et al

- **Key results**



Thomas M et al. Ann Oncol 2017;28(suppl 5):Abstr 1527O

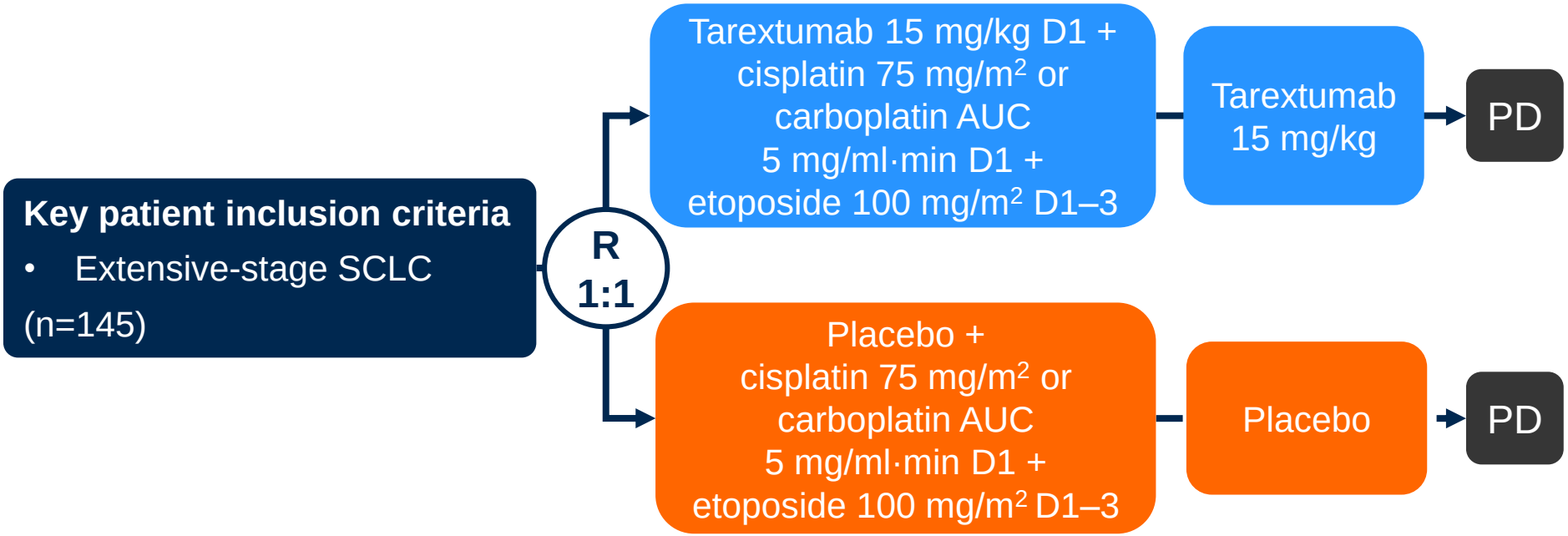
1527O: Top-line data from the randomized phase 2 IMPULSE study in small-cell lung cancer (SCLC): Immunotherapeutic maintenance treatment with lefitolimod – Thomas M, et al

- **Key results (cont.)**
  - There were no grade 4 or 5 AEs reported, grade 3 headache was reported by 2 (3.3%) patients with lefitolimod, grade 3 cough, asthenia, nausea, back pain and dyspnoea were reported by 1 (1.7%) patient each in the lefitolimod group
  - OS signal in patients with low activated B cells at baseline (n=38)
    - Median OS 284 vs. 232 days for lefitolimod vs. control (HR 0.59 [95%CI 0.29,1.21])
- **Conclusions**
  - There was no difference in OS between groups for the overall ITT population
  - There was a strong OS signal in a predefined subgroup with low activated B cells
  - Assessment of the PD marker confirmed the mode-of-action of lefitolimod
  - There was a favourable safety profile with lefitolimod

Thomas M et al. Ann Oncol 2017;28(suppl 5):Abstr 1527O

1530PD: Results of a randomized, placebo-controlled, phase 2 study of tarextumab (TRXT, anti-Notch2/3) in combination with etoposide and platinum (EP) in patients (pts) with untreated extensive-stage small-cell lung cancer (ED-SCLC) – Daniel DB, et al

- **Study objective**
  - To investigate the efficacy of the combination of tarextumab, an anti-Notch 2/3 antibody, and etoposide in patients with previously untreated SCLC



Primary endpoint

- PFS (ITT)

Secondary endpoints

- PK, immunogenicity, OS, ORR, safety, efficacy in biomarker groups

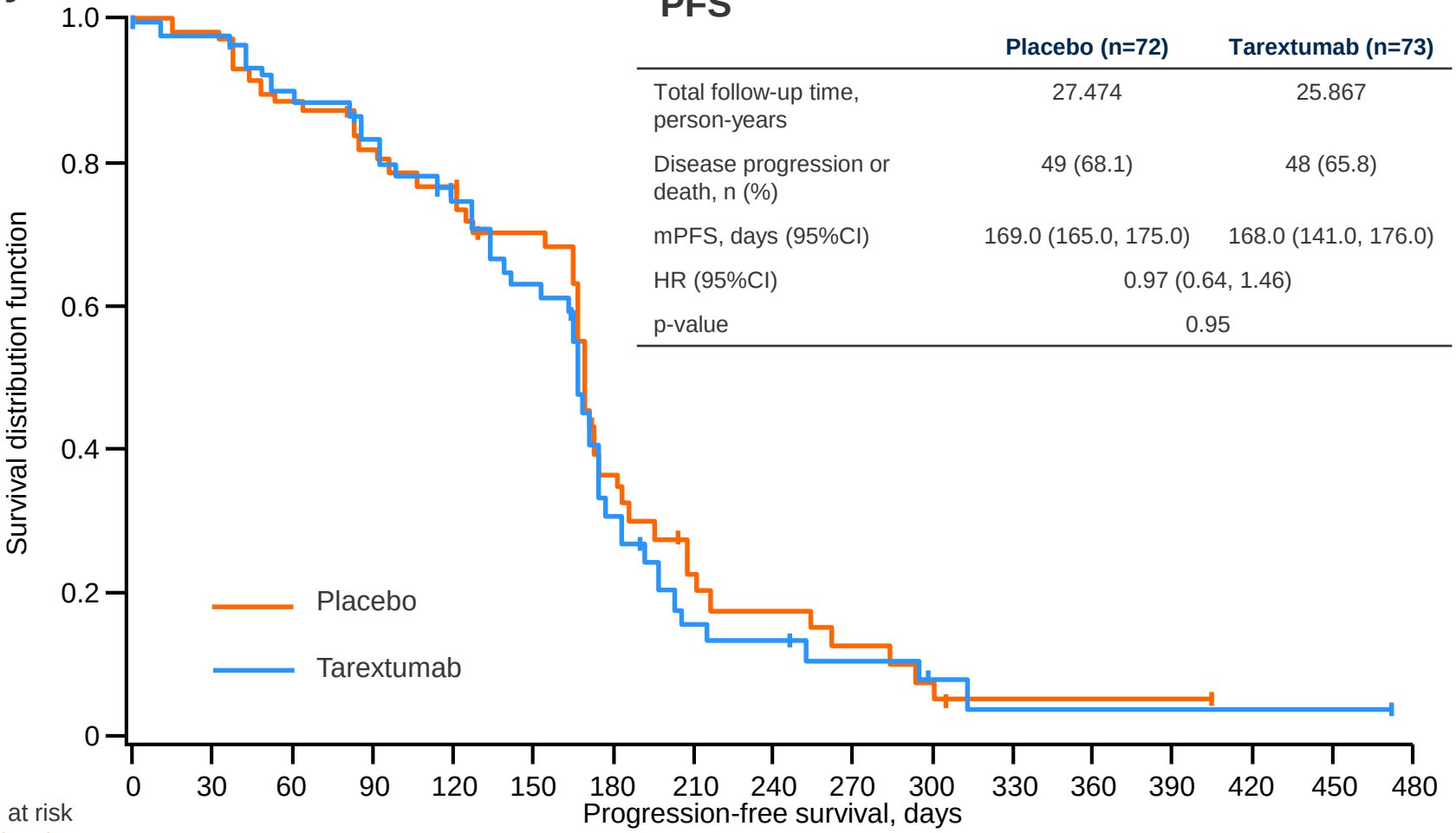
Daniel DB et al. Ann Oncol 2017;28(suppl 5):Abstr 1530PD

1530PD: Results of a randomized, placebo-controlled, phase 2 study of tarextumab (TRXT, anti-Notch2/3) in combination with etoposide and platinum (EP) in patients (pts) with untreated extensive-stage small-cell lung cancer (ED-SCLC) – Daniel DB, et al

- **Key results**

PFS

	Placebo (n=72)	Tarextumab (n=73)
Total follow-up time, person-years	27.474	25.867
Disease progression or death, n (%)	49 (68.1)	48 (65.8)
mPFS, days (95%CI)	169.0 (165.0, 175.0)	168.0 (141.0, 176.0)
HR (95%CI)	0.97 (0.64, 1.46)	
p-value	0.95	



No. at risk																	
Placebo	72	67	58	50	47	38	16	8	7	5	2	1	1	1	0	0	0
Tarextumab	73	63	55	47	42	33	15	7	6	4	2	1	1	1	1	1	0

Daniel DB et al. Ann Oncol 2017;28(suppl 5):Abstr 1530PD

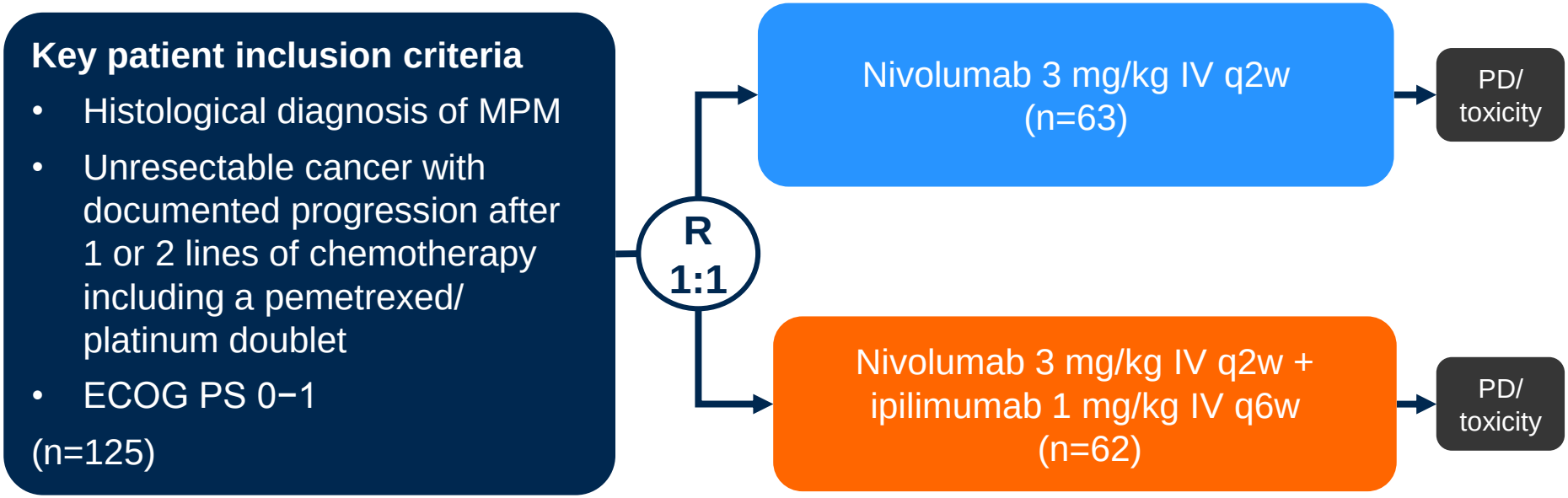
1530PD: Results of a randomized, placebo-controlled, phase 2 study of tarextumab (TRXT, anti-Notch2/3) in combination with etoposide and platinum (EP) in patients (pts) with untreated extensive-stage small-cell lung cancer (ED-SCLC) – Daniel DB, et al

- **Key results (cont.)**
  - Median survival (284.0 vs. 314.0 days; HR 1.01 [95%CI 0.68, 1.51]; p=0.95), and ORR (50% vs. 51%; OR 0.924 [95%CI 0.452, 1.887]; p=0.8275) were not significantly different between tarextumab- and placebo-treated patients
  - Adverse events were more common in tarextumab- vs. placebo-treated patients (91.3% vs. 76.5%), including more diarrhoea (63.8% vs. 20.6%) and thrombocytopenia (42.0% vs. 10.3%)
- **Conclusions**
  - Tarextumab + platinum-based therapy was not associated with improved outcome (PFS, OS, ORR) in previously untreated SCLC
  - Biomarker analysis did not identify predictive markers for treatment efficacy
  - Tarextumab was associated with an increase in toxicity compared to placebo

Daniel DB et al. Ann Oncol 2017;28(suppl 5):Abstr 1530PD

LBA58_PR: Second or 3rd line nivolumab (Nivo) versus Nivo plus ipilimumab (Ipi) in malignant pleural mesothelioma (MPM) patients: updated results of the IFCT-1501 MAPS2 randomized phase 2 trial – Zalcman G, et al

- **Study objective**
  - To evaluate the efficacy and safety of 2L or 3L nivolumab monotherapy vs. nivolumab + ipilimumab in patients with malignant pleural mesothelioma



Primary endpoint

- DCR at 12 weeks in first 54 accrued patients in each group

Secondary endpoints

- Toxicity, PFS, OS, QoL

Zalcman G et al. Ann Oncol 2017;28(suppl 5):Abstr LBA58_PR

LBA58_PR: Second or 3rd line nivolumab (Nivo) versus Nivo plus ipilimumab (Ipi) in malignant pleural mesothelioma (MPM) patients: updated results of the IFCT-1501 MAPS2 randomized phase 2 trial – Zalcman G, et al

- **Key results**

	In first 108 eligible patients		ITT population	
	Nivo (n=54)	Nivo + Ipi (n=54)	Nivo (n=63)	Nivo + Ipi (n=61)
OR, % (95%CI)	18.5 (8.2, 28.9)	27.8 (15.8, 39.7)	17.5 (8.1, 26.8)	25.8 (14.9, 36.7)
SD, % (95%CI)	25.9 (14.2, 37.6)	22.2 (11.1, 33.3)	22.2 (12.0, 32.5)	25.8 (14.9, 36.7)
DCR, % (95%CI)	**44.4 (31.2, 57.7)**	**50.0 (36.7, 63.3)**	**39.7 (27.6, 51.8)**	**51.6 (39.2, 64.1)**
Grade 3 TRAE, %			12.7	22.9
Grade 4 TRAE, %			0	3.3
Grade 5 TRAE, %			0	4.9[a]

  - OR was higher in patients with PD-L1 expression ≥1% vs. PD-L1 negative patients (39.0% vs. 12.1%; p=0.003 [both treatment arms combined])
  - QoL data favoured the monotherapy arm for global, pain, anorexia, and interference items and favoured the combination arm for general, symptom distress scales but the differences were not significant

[a]Fulminant hepatitis, encephalitis, acute kidney failure (n=1 each) Zalcman G et al. Ann Oncol 2017;28(suppl 5):Abstr LBA58_PR

LBA58_PR: Second or 3rd line nivolumab (Nivo) versus Nivo plus ipilimumab (Ipi) in malignant pleural mesothelioma (MPM) patients: updated results of the IFCT-1501 MAPS2 randomized phase 2 trial – Zalcman G, et al

- **Key results (cont.)**
  - mPFS was 4.0 months (95%CI 2.8, 5.7) and 5.6 months (95%CI 3.2, 8.4) for the nivolumab and nivolumab + ipilimumab groups, respectively
  - mOS was 13.6 months (95%CI 6.7, NR) and NR for the nivolumab and nivolumab + ipilimumab groups, respectively
- **Conclusions**
  - Both nivolumab monotherapy and nivolumab + ipilimumab meaningfully increased DCR at 12 weeks compared to historical control or previous non-immunotherapy clinical trials
  - Toxicity was manageable, although there were 3 potential toxic deaths in the combination therapy arm
  - There were non-significant differences in QoL for some items but results of long-term and longitudinal data are needed

Zalcman G et al. Ann Oncol 2017;28(suppl 5):Abstr LBA58_PR