Grupo ONCOCLÍNICAS
Sua vida. Nossa vida.

INSTITUTO ONCOCLÍNICAS

HighLights ASCO 2017 Câncer de Pulmão

Apresentação

A Sociedade Americana de Oncologia Clínica (ASCO) foi fundada em 1964 e, desde então, tornou-se a principal organização voltada para profissionais que lidam diariamente com o câncer em todo o mundo.

Sua missão é promover o combate à doença, habilitando seus membros a oferecer o que existe de melhor em termos de tratamento para o seus pacientes. Para isso, investe maciçamente em pesquisa e é reconhecida por promover educação continuada de alto nível.

Todos os anos, a ASCO organiza seu Congresso, reunindo os mais renomados profissionais do mundo em todas as áreas da Oncologia. O contato direto com profissionais de destaque, o intenso compartilhamento de informações, assim como a troca de experiências cotidianas criam um ambiente favorável para o aprendizado.

O Grupo Oncoclínicas não poderia deixar de estar presente nesse evento, trazendo para seus pacientes e parceiros todas as novidades apresentadas. Em linha com nosso objetivo de nos transformar no melhor grupo de Oncologia do país, estivemos presentes com mais de 80 Oncologistas em Chicago, coletando os principais e mais atualizados dados científicos.

E por meio do Instituto Oncoclínicas conseguimos compilar as informações mais relevantes, transformando-as em um *slide kit* didático, versátil e inovador. É com prazer que disponibilizamos a vocês, nossos parceiros, o “Melhor da ASCO 2017”.

Cordialmente,
Instituto Oncoclínicas

PÓS 2017 ASCO ANNUAL MEETING
Making a Difference in Cancer Care WITH YOU

Grupo ONCOCLÍNICAS
Sua vida. Nossa vida.

INSTITUTO ONCOCLÍNICAS

CONFLITOS DE INTERESSE

Esses slides estão isentos de conflitos de interesses e possuem finalidade essencialmente educacional.

ROTEIRO

1. Tratamento Adjuvante do Câncer de Pulmão: Finalmente algo novo
2. Doença Avançada - ASCO 2017
3. Doença Avançada ALK + - ASCO 2017
4. Doença Avançada EGFR + - ASCO 2017
5. Doença Avançada – imunoterapia – ASCO 2017
6. Tratamento da Metástase cerebral – ASCO 2017
7. Mesotelioma e Imunoterapia

Tratamento Adjuvante do Câncer de Pulmão:

Finalmente algo novo

Tratamento Adjuvante

- Há décadas o padrão de tratamento adjuvante em câncer de pulmão é um doublet baseado em cisplatina.
- O benefício pela meta-análise LACE é cerca de 5% de ganho absoluto nesta estratégia.
- TKIs (direcionados a mutação do EGFR) demonstraram benefício limitado nos estudos prévios.
- Estudo ADJUVANT buscou analisar eficácia do gefitinibe em pacientes II-IIIA (N1-N2)

Gefitinib (G) versus vinorelbine / cisplatin (VP) as adjuvant treatment in stage II-IIIA (N1-N2) non-small-cell lung cancer (NSCLC) with *EGFR* activating mutation (ADJUVANT): A randomized, Phase III trial (CTONG 1104)

Yi-Long Wu,[1] Wen-Zhao Zhong,[1] Qun Wang,[2] Song-Tao Xu,[2] Wei-Min Mao,[3] Lin Wu,[4] Yi Shen,[5] Yong-Yu Liu,[6] Chun Chen,[7] Ying Cheng,[8] Lin Xu,[9] Jun Wang,[10] Ke Fei,[11] Xiao-Fei Li,[12] Jian Li,[13] Cheng Huang,[14] Zhi-Dong Liu,[15] Ke-Neng Chen,[16] Hong-Hong Yan,[1] Xue-Ning Yang[1]

[1]Guangdong General Hospital; [2]Fudan University Affiliated Zhongshan Hospital; [3]Zhejiang Cancer Hospital; [4]Hunan Cancer Hospital; [5]Affiliated Hospital of Medical College Qingdao University; [6]Liaoning Cancer Hospital; [7]Concord Hospital of the Fujian Medical University; [8]Jilin Cancer Hospital; [9]Jiangsu Cancer Hospital; [10]People's Hospital of Peking University; [11]Shanghai Pulmonary Hospital; [12]Tangdu Hospital; [13]Peking University Hospital; [14]Fujian Cancer Hospital; [15]Beijing Chest Hospital; [16]Beijing Cancer Hospital

PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17

Abstract 8500 presented by Y-L Wu
Guangdong Lung Cancer Institute , Guangdong General Hospital, China

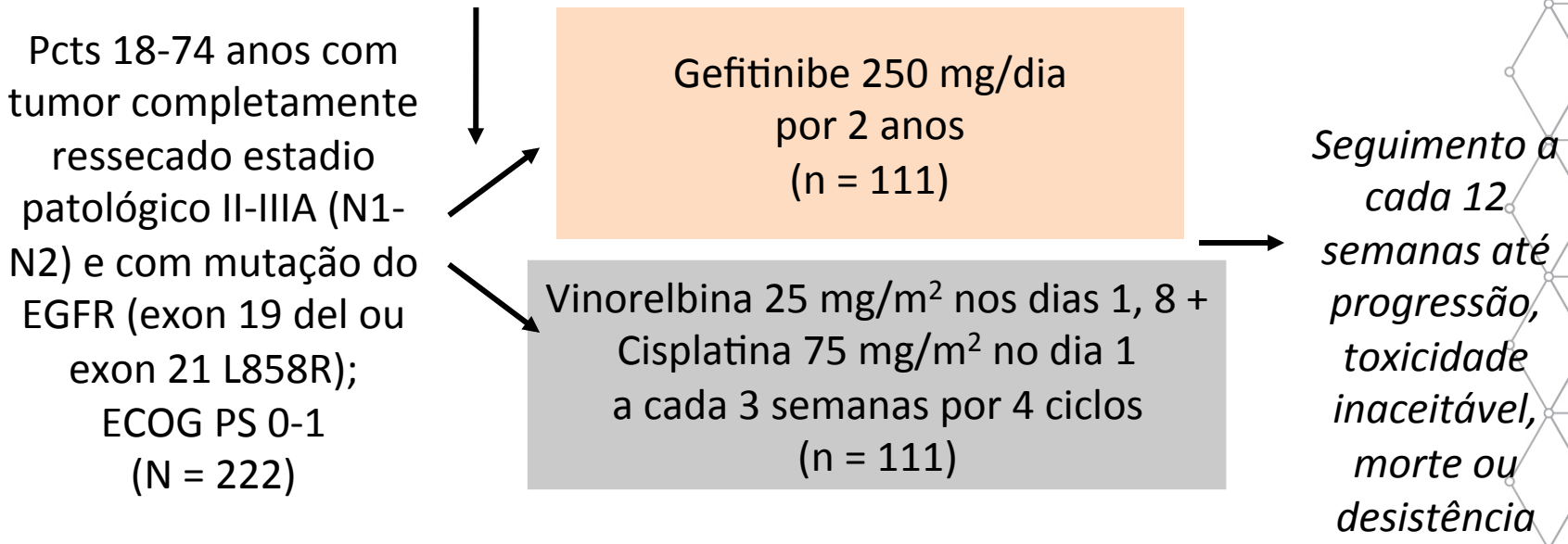
June 5,2017

Presented By Yi-Long Wu at 2017 ASCO Annual Meeting

ADJUVANT

- Estudo randomizado fase III

Estratificado pela mutação do EGFR *e pelo N*



- Desfecho primário: Sobrevida livre de Progressão (SLP)
- Desfecho secundário: 3-anos SLP, 5-anos SLP, Sobrevida Global (SG) , 5-anos OS, tolerância, analyses

Wu YL, et al. ASCO 2017. Abstract 8500.

Baseline demographics (ITT population)

	Vinorelbine plus cisplatin (n=111)	Gefitinib (n=111)
Age, years, median (range)	60 (26–76)	58 (32–74)
Female, n (%)†	65 (58.6)	65 (58.6)
Never smoker, n (%)	85 (76.6)	82 (73.9)
Baseline ECOG PS, n (%)		
1	85 (76.6)	72 (64.9)
Pathology stage, n (%)		
IIA	33 (29.7)	33 (29.7)
IIB	4 (3.6)	4 (3.6)
IIIA	71 (64.0)	72 (64.9)
Not available	3 (2.7)	2 (1.8)
Pathology, n (%)		
Adenocarcinoma	105 (94.6)	102 (91.9)
Squamous carcinoma	1 (0.9)	5 (4.5)
Adenosquamous carcinoma	3 (2.7)	2 (1.8)
Not available	2 (1.8)	2 (1.8)

†Sex was not available for two patients in the gefitinib arm and one patient in the vinorelbine plus cisplatin arm

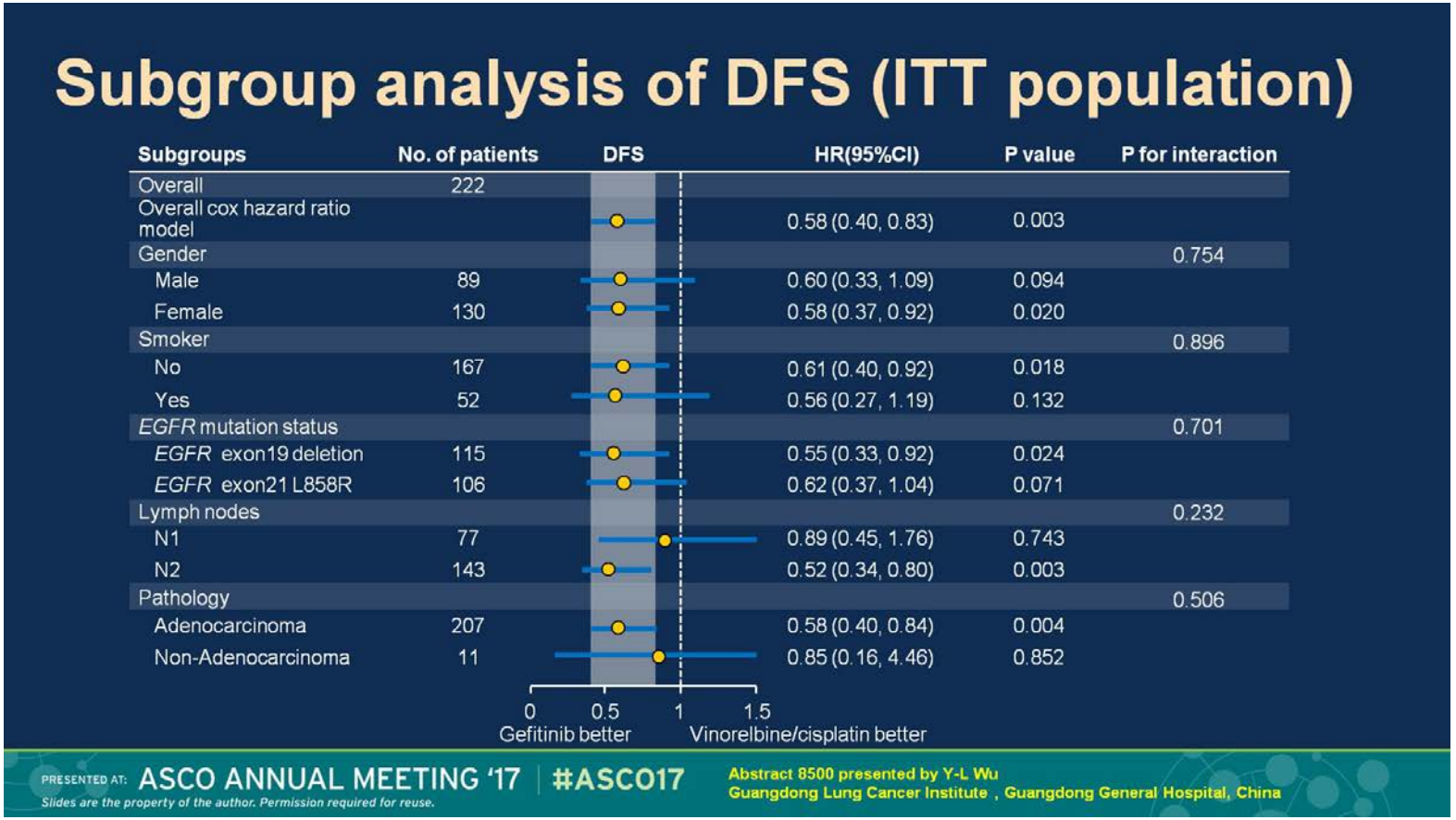
Abstract 8500 presented by Y-L Wu
Guangdong Lung Cancer Institute , Guangdong General Hospital, China

Presented By Yi-Long Wu at 2017 ASCO Annual Meeting

ADJUVANT: Sobrevida livre de Progressão (Desfecho Primário)

	Gefitinibe (n = 111)	Vinorelbina/ Cisplatina (n = 111)	HR (95% CI)	*P*
Mediana SLP, meses	28.7	18.0	0.60 (0.42-0.87)	.005
▪ Taxa 3-anos SLP %	34	27		

Wu YL, et al. ASCO 2017. Abstract 8500.



Não há um subgrupo específico que possamos caracterizar com maior eficácia.
Mesmo subgrupos de "não adenocarcinoma"e "fumantes", que não tiveram p significativo, possuem um número muito pequeno de pacientes para qq conclusão.

AEs in ≥10% of patients (safety population)

AE, n (%)	Gefitinib (n=106)		Vinorelbine plus cisplatin (n=87)	
	All grades	Grade ≥3	All grades	Grade ≥3
Total AEs	**61 (57.5)**	**13 (12.3)**	**70 (80.5)**	**42 (48.3)**
Neutropenia	3 (2.8)	0 (0.0)	46 (52.9)	30 (34.5)
Anemia	2 (1.9)	1 (0.9)	44 (50.6)	5 (5.7)
Leukopenia	4 (3.8)	0 (0.0)	41 (47.1)	14 (16.1)
Myelosuppression	0 (0.0)	0 (0.0)	12 (13.8)	3 (3.4)
Nausea	3 (2.8)	0 (0.0)	38 (43.7)	6 (6.9)
Vomiting	5 (4.7)	0 (0.0)	36 (41.4)	8 (9.2)
Anorexia	2 (1.9)	0 (0.0)	20 (23.0)	0 (0.0)
Rash	43 (40.6)	1 (0.9)	0 (0.0)	0 (0.0)
Elevated ALT	29 (27.4)	2 (1.9)	3 (3.4)	0 (0.0)
Elevated AST	12 (11.3)	2 (1.9)	1 (1.1)	0 (0.0)
Diarrhea	28 (26.4)	1 (0.9)	4 (4.6)	0 (0.0)
Cough	11 (10.4)	0 (0.0)	15 (17.2)	0 (0.0)
Fatigue	4 (3.8)	0 (0.0)	10 (11.5)	0 (0.0)
Fever	1 (0.9)	0 (0.0)	9 (10.3)	1 (1.1)

AE, adverse evevnt; ALT, alanine aminotransferase; AST, aspartate transaminase

Perfil de toxicidade usual para o gefitinibe

ADJUVANT: Conclusões

- Em pacientes operados estádio II-IIIA, o braço em uso do Gefitinibe alcançou melhor SLP em comparação a vinorelbina/cisplatina para aqueles pacientes com mutação do *EGFR.*
  - Mediana SLP: 28.7 vs 18.0 meses (HR: 0.60; 95% CI: 0.42-0.87; *P* = .005)
    - 3-anos DFS: 34% vs 27%
    - Dados de sobrevida glbal não disponíveis
- Gefitinibe apresentou tolerância usual
- Autores concluíram que o gefitinibe por 2 anos deve ser considerado como novo tratamento padrão para este perfil de pacientes.

Wu YL, et al. ASCO 2017. Abstract 8500.

Doença Avançada ASCO 2017

Doença Avançada – ALK + ASCO 2017

Alectinib vs crizotinib in treatment-naïve advanced *ALK*+ NSCLC: primary results of the global phase III ALEX study (LBA9008)

Alice Shaw[1], Solange Peters[2], Tony Mok[3], Shirish M. Gadgeel[4], Jin Seok Ahn[5], Sai-Hong Ignatius Ou[6], Maurice Perol[7], Rafal Dziadziuszko[8], Dong-Wan Kim[9], Rafael Rosell[10], Ali Zeaiter[11], Ting Liu[11], Sophie Golding[11], Bogdana Balas[11], Johannes Noe[11], Peter N. Morcos[12], and D. Ross Camidge[13] on behalf of the ALEX investigators

1. Massachusetts General Hospital, Boston, MA, USA; 2. Lausanne University Hospital, Switzerland; 3. Chinese University of Hong Kong, Hong Kong; 4. Karmanos Cancer Institute/Wayne State University, Detroit, MI, USA; 5. Sungkyunkwan University School of Medicine, Seoul, South Korea; 6.Chao Family Comprehensive Cancer Center, University of California, Irvine School of Medicine, Orange, CA, USA; 7. Department of Medical Oncology, Léon Bérard Cancer Center, Lyon, France; 8. Department of Oncology and Radiotherapy, Medical University of Gdansk, Gdansk, Poland; 9. Seoul National University Hospital, Seoul, South Korea; 10. Catalan Institute of Oncology, Barcelona, Spain; 11. F. Hoffmann-La Roche Ltd, Basel, Switzerland; 12. Roche Innovation Center, New York, USA; 13. University of Colorado, Denver, CO, USA

PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17

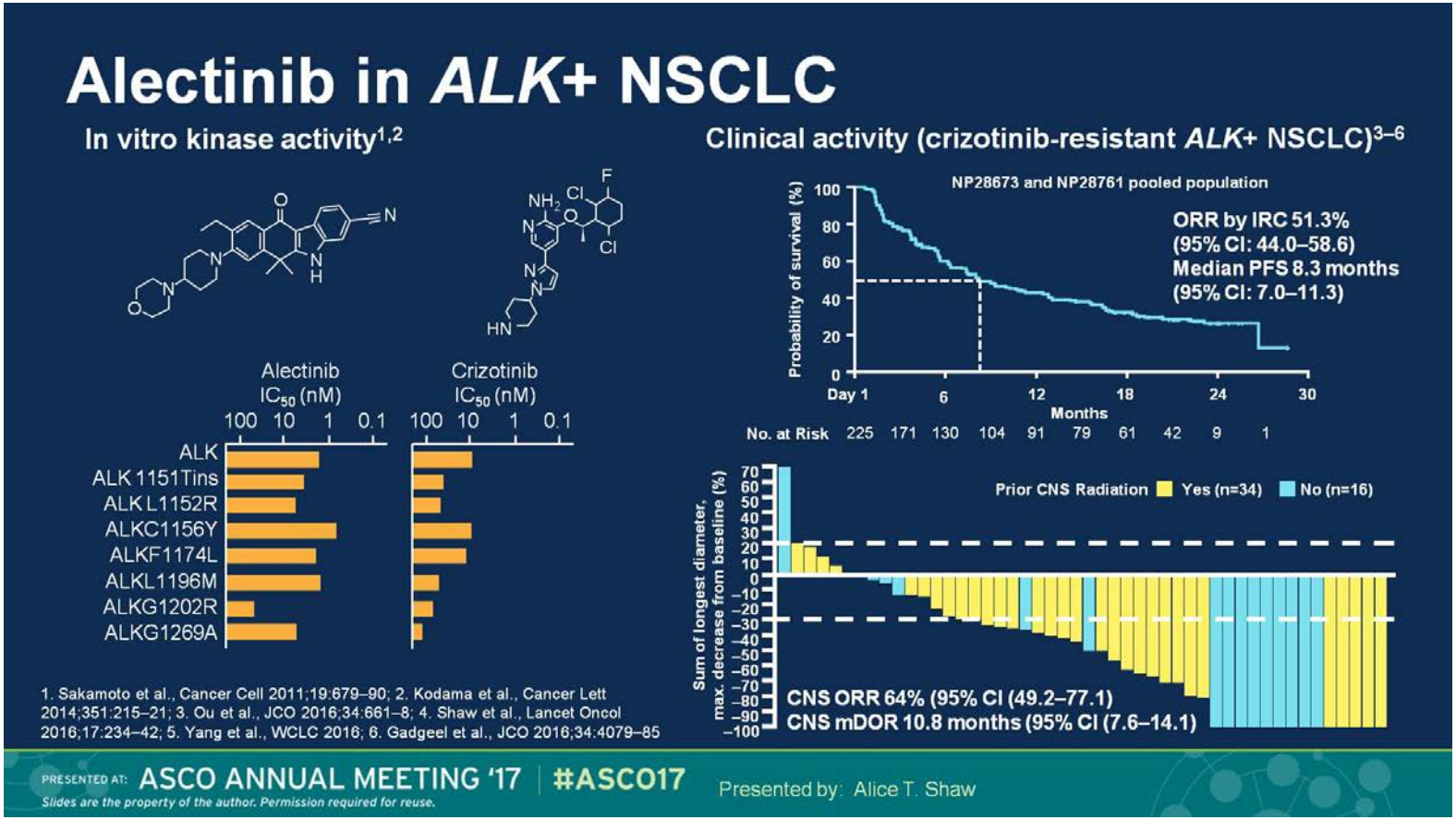
http://tago.ca/Lfq

Presented By Alice Shaw at 2017 ASCO Annual Meeting

BackGround para doença ALK+ NSCLC

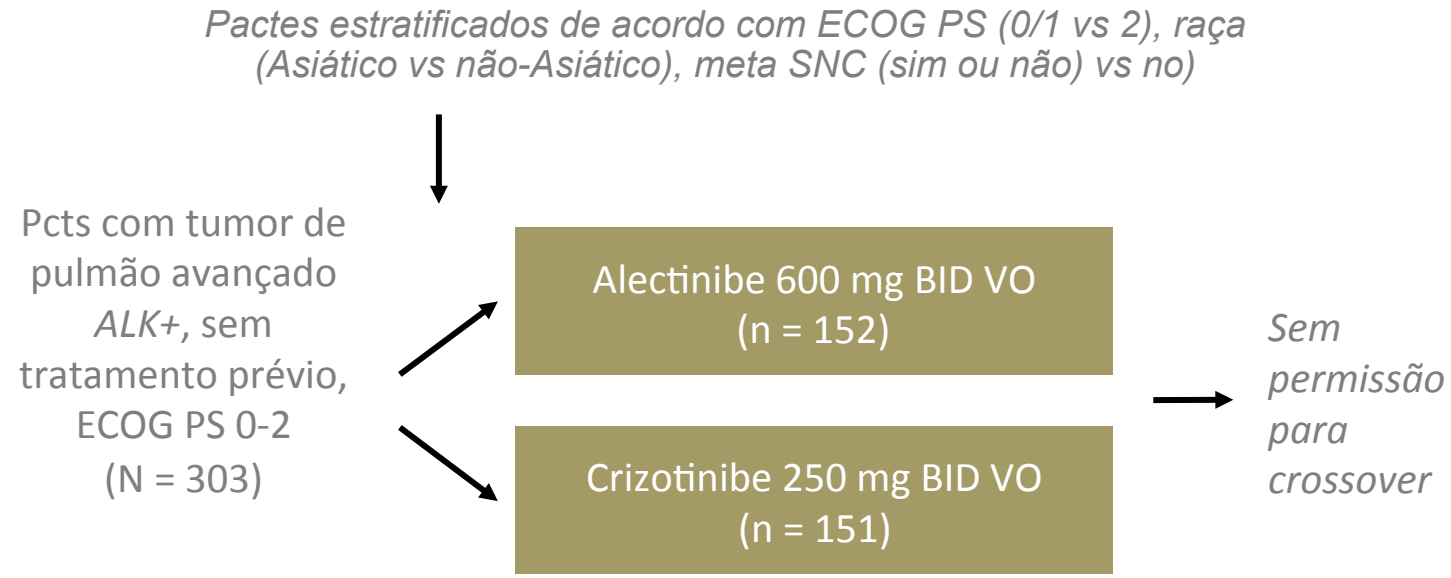
- Inibidores do *ALK+ são ativos e o tratamento padrão neste tipo de doença* [1]
- Crizotinibe é o tratamento padrão dem doença *ALK+*
  - Estudo de fase III PROFILE 1014 demonstrou superioridade do crizotinibe frente a terapia padrão da época com pemetrexed + cisplatina[2]
    - Desfechos do Crizotinibe , mediana de SLP: 10.9 meses; TxResp: 74%
  - *Progressão em SNC é comum em pacientes ALK+* recebendo crizotinibe[3]
- Alectinibe demonstrou atividade em pacientes refratários ao crizotinibe em estudos iniciais[4-6]

1. Kwak EL, et al. N Engl J Med. 2010;363:1693-1703. 2. Solomon BJ, et al. N Engl J Med. 2014;371:2167-2177. 3. Yoshida T, et al. Lung Cancer. 2016;97:43-47. 4. Ou SH, et al. J Clin Oncol. 2016;34:661-668. 5. Shaw AT, et al. Lancet Oncol. 2016;17:234-242. 6. Gadgeel SM, et al. J Clin Oncol. 2016;34:4079-4085. 7. Peters S, et al. N Engl J Med. 2017; [Epub ahead of print].



Presented By Alice Shaw at 2017 ASCO Annual Meeting

Estudo ALEX



- Desfecho Primário: sobrevida livre de progressão (SLP)
- Desfechos Secundários: SLP por IRC, tempo para progressão em SNC, taxa de resposta (TXR), sobrevida global, tolerância
- Mediana de seguimento do alectinibe de 18.6 meses e do crizotinibe de 17.6 meses

Peters S, et al. N Engl J Med. 2017;

Baseline characteristics

		Crizotinib (N=151)	Alectinib (N=152)
Age, years	Median (range)	54 (18–91)	58 (25–88)
Gender, n (%)	Female	87 (58)	84 (55)
	Male	64 (42)	68 (45)
Race, n (%)	Non-Asian	82 (54)	83 (55)
	Asian	69 (46)	69 (45)
ECOG PS, n (%)	0–1	141 (93)	142 (93)
	2	10 (7)	10 (7)
Smoking status, n (%)	Non-smoker	98 (65)	92 (61)
	Past smoker	48 (32)	48 (32)
	Active smoker	5 (3)	12 (8)
Histology, n (%)	Adenocarcinoma	142 (94)	137 (90)
	Other*	9 (6)	15 (10)

*Other histology included: large cell carcinoma, mixed with predominantly adenocarcinoma component, squamous cell carcinoma, undifferentiated

ECOG PS, Eastern Cooperative Oncology Group Performance status

Presented By Alice Shaw at 2017 ASCO Annual Meeting

Baseline CNS disease

		Crizotinib (N=151)	Alectinib (N=152)
CNS metastases by IRC (%)	Present	58 (38)	64 (42)
	Absent	93 (62)	88 (58)
CNS metastases treatment (%)	n	58	64
	None	36 (62)	37 (58)
	Whole brain RT	16 (28)	17 (27)
	Radiosurgery	4 (7)	5 (8)
	Other*	1 (2)	4 (6)
	Brain surgery	1 (2)	1 (2)

*1 patient in the alectinib arm received both radiosurgery and whole brain radiotherapy; 1 patient in the crizotinib arm and 3 patients in the alectinib arm had brain surgery combined with radiotherapy

CNS, central nervous system; IRC, Independent Review Committee, RT, radiotherapy

Presented By Alice Shaw at 2017 ASCO Annual Meeting

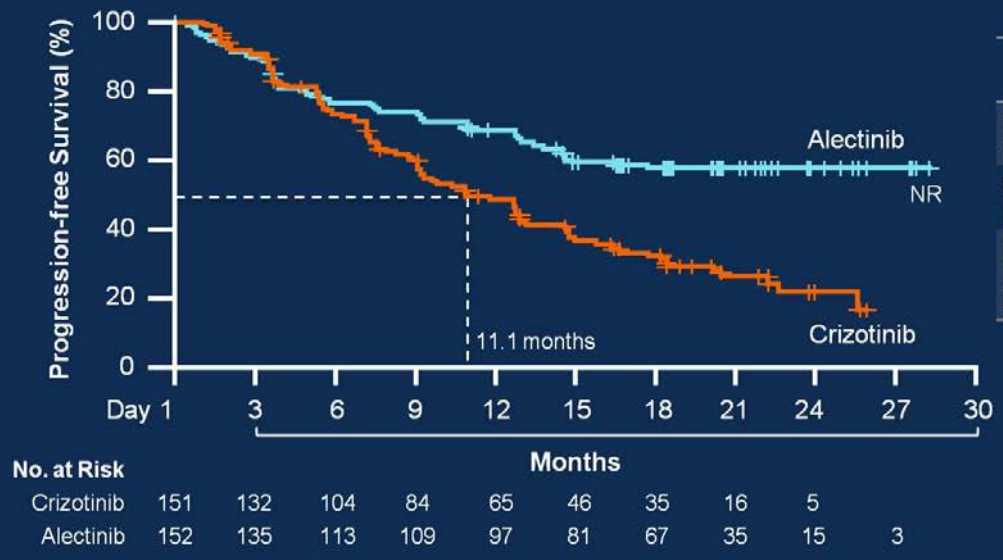
ALEX:TX Resposta

TX Resposta (ITT)	Alectinibe (n = 152)	Crizotinibe (n = 151)	HR (95% CI)	*P*
Tx Resposta Investigador, % (95% CI)	82.9 (76.0-88.5)	75.5 (67.8-82.1)	--	.09
CR, n (%)	6 (4)	2 (1)		
PR, n (%)	120 (79)	112 (74)		
SD, n (%)	9 (6)	24 (16)		
Mediana DuraçãoR meses (95%CI)	NA (NA)	11.1 (7.9-13.0)	0.36	--

TX Resposta (Lesão mensurável SNC)	Alectinibe (n = 21)	Crizotinibe (n = 22)
TX resposta pelo IRC, % (95% CI)	81 (58-95)	50 (28-72)
SNC respsota completa, n (%)	8 (38)	1 (5)
Mediana DuraçãoR, meses (95% CI)	17.3 (14.8-NA)	5.5 (2.1-17.3)

Peters S, et al. N Engl J Med. 2017;print].

Primary endpoint: PFS, investigator-assessed

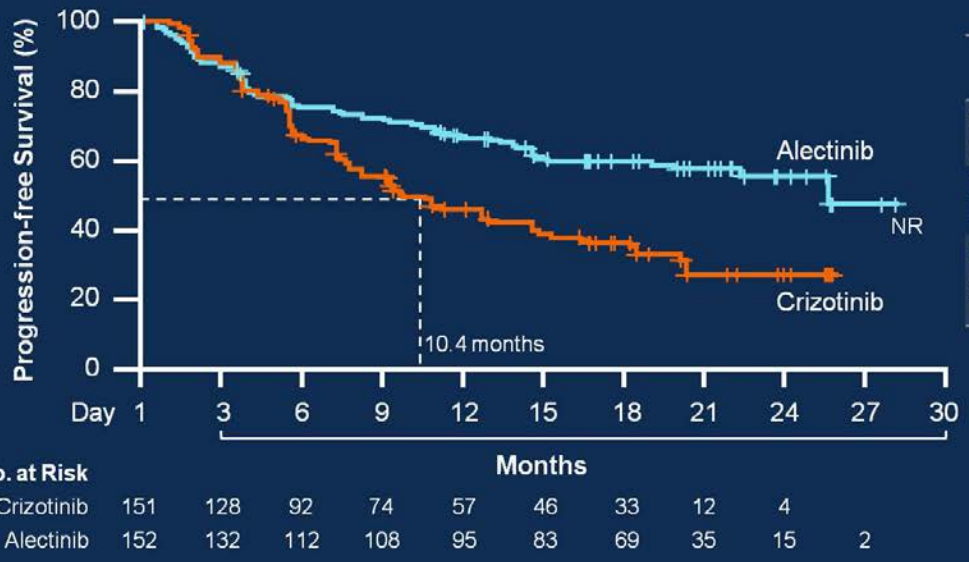


	Crizotinib (N=151)	Alectinib (N=152)
Patients with events, n (%)	102 (68)	62 (41)
Median PFS, months (95% CI)	**11.1** (9.1–13.1)	**NR** (17.7–NR)
HR (95% CI) P-value (log-rank test)	**0.47** (0.34–0.65) P<0.0001	

PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17 Presented by: Alice T. Shaw

Presented By Alice Shaw at 2017 ASCO Annual Meeting

Secondary endpoint: PFS, IRC-assessed



	Crizotinib (N=151)	Alectinib (N=152)
Patients with events, n (%)	92 (61)	63 (41)
Median PFS, months (95% CI)	**10.4** (7.7–14.6)	25.7 (19.9–NR)
HR (95% CI) P-value (log-rank test)	**0.50** (0.36–0.70) P<0.0001	

PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17 Presented by: Alice T. Shaw

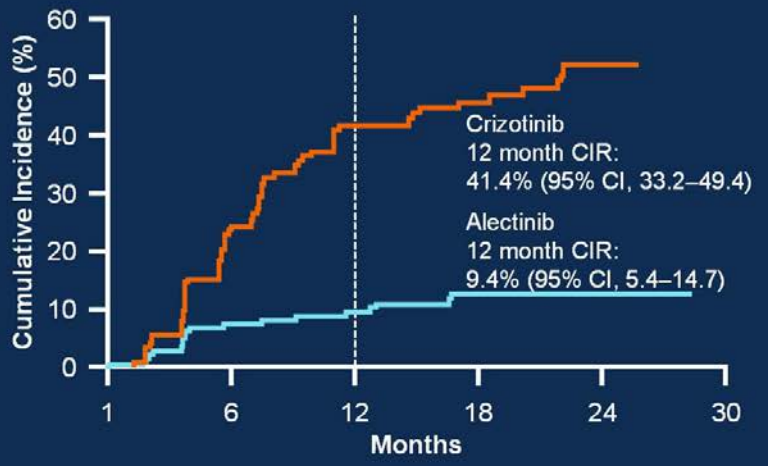
A Sobrevida livre de Progressão mais que dobrou com o uso do Alectinibe!

Secondary endpoint: Time to CNS progression (by IRC, ITT)

- A competing risk analysis with CNS progression, non-CNS progression and death as competing events was conducted
- For each patient, the first event of CNS progression, non-CNS progression or death was counted

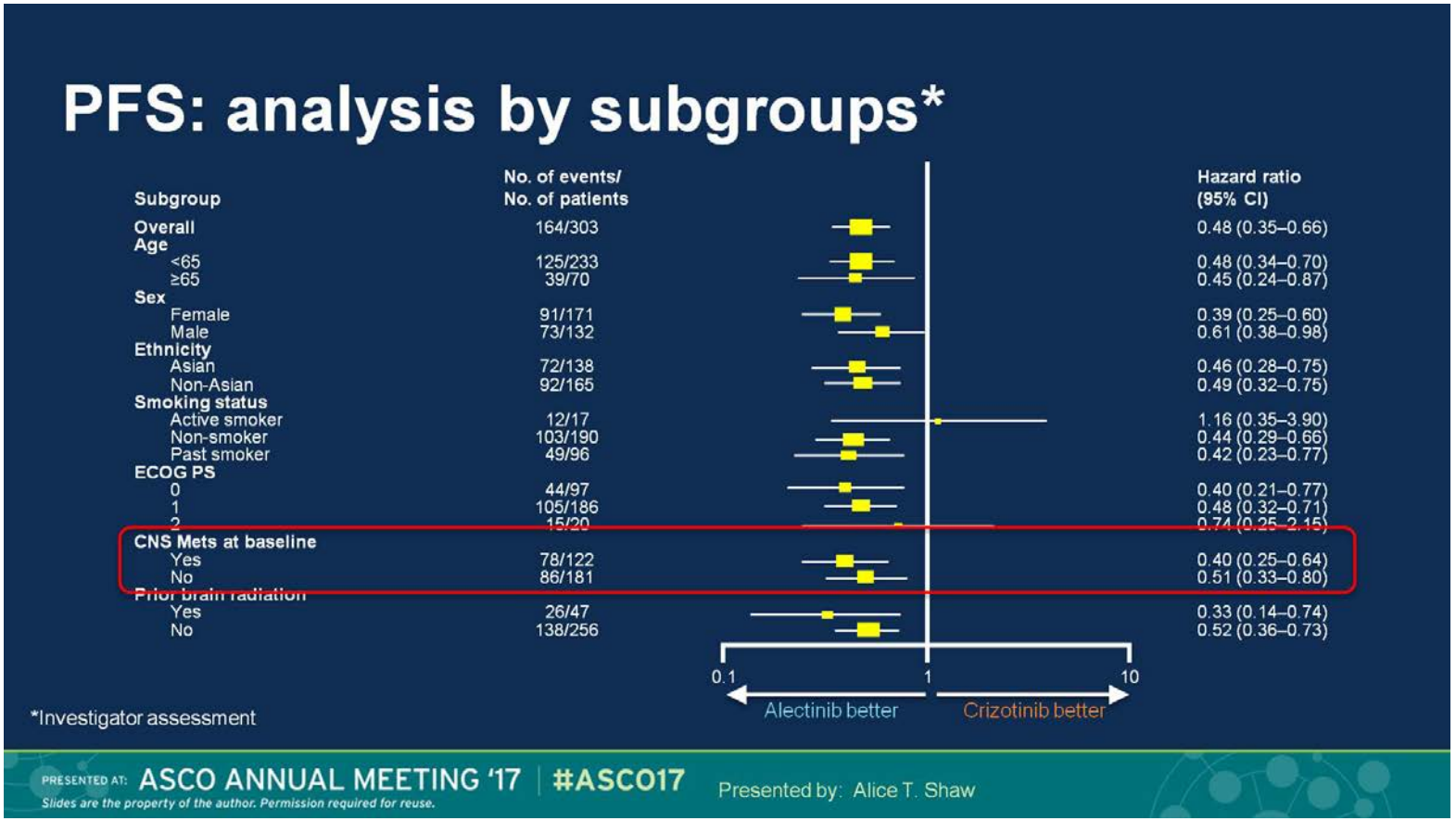
	Crizotinib (N=151)	Alectinib (N=152)
Patients with events, n (%)	68 (45)	18 (12)
Cause-specific HR (95% CI) P-value (log-rank test)	**0.16** (0.10–0.28) P<0.0001	

Cumulative incidence of CNS progression

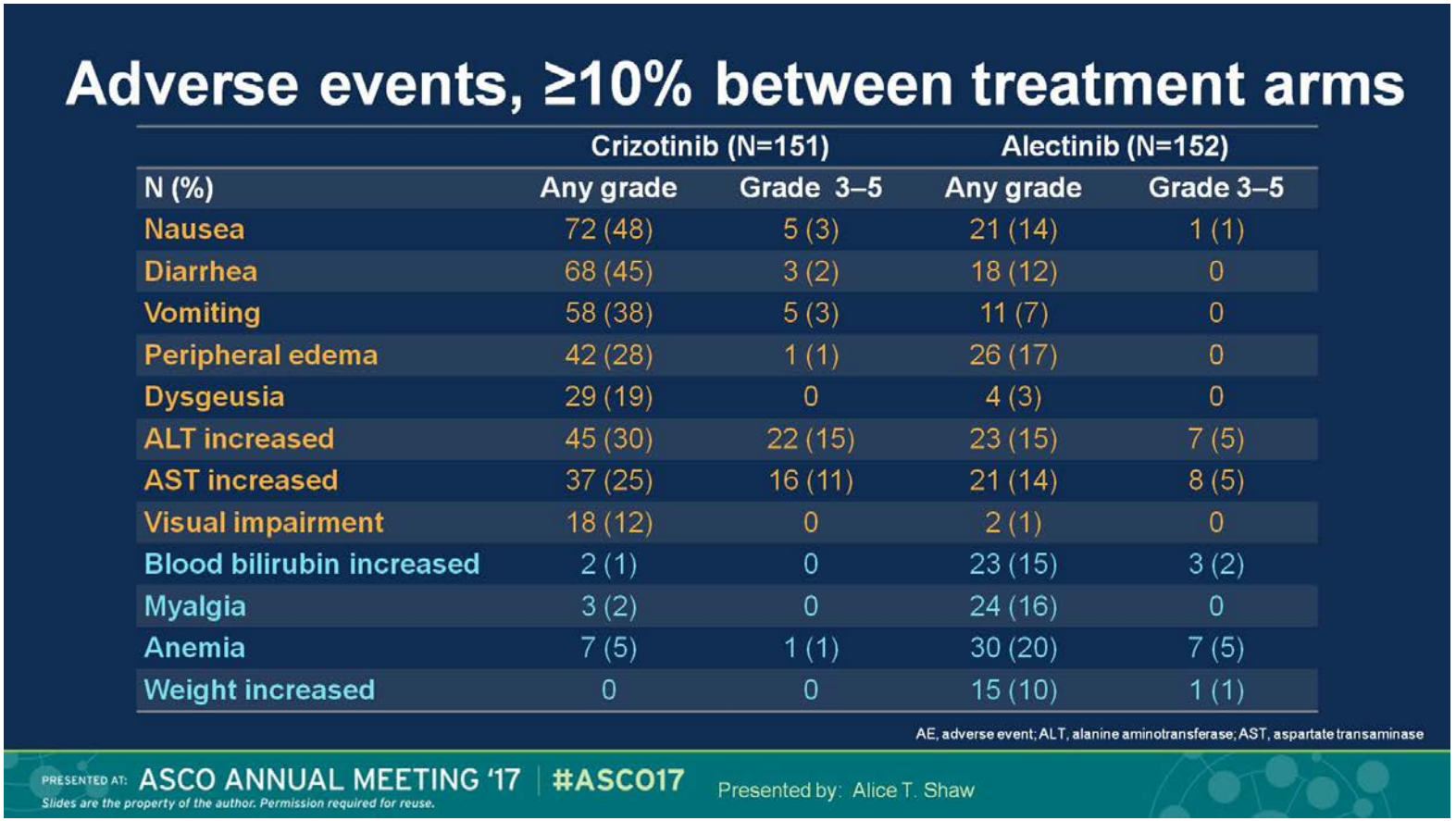


PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17 Presented by: Alice T. Shaw

Presented By Alice Shaw at 2017 ASCO Annual Meeting



Presented By Alice Shaw at 2017 ASCO Annual Meeting



Perfil de toxicidade favorável ao Alectinibe: menor toxicidade hepática e melhor tolerância GI

Conclusões

- Pacientes com tumores de pulmão avançado *ALK+*, a primeira linha de tratamento com alectinibe mostrou-se superior ao crizotinibe
  - Mediana de sobrevida livre de progressão: HR 0.47 (95% CI: 0.34-0.65; *P* < . 0001)
  - Melhor tempo para progressão em SNC
  - Toxicidade favorável

- Investigadores do estudo concluíram que alectinibe é o novo “standart of care”

Shaw A, et al. ASCO 2017. Abstract LBA9008.

Doença Avançada – EGFR + ASCO 2017

AURA-3 : Background

- Metastases em SNC ocorrem em cerca de 40% dos apceintes com mutação do EGFR no decorrer da sua evolução.
  - Metas SNC são um sinal de pior prognóstico.

Uso de TKIs tem um melhor desfecho comparativamente a quimioterapia para metas em SNC.

- Osimertinibe: tem ação em SNC
  - Usado hoje em segunda linha para quem tem a mutação do T790M.
- Esta apresentação enfoca o desfecho do osermetinibe neste estudo fase III comparativamente ao doublet de platina/pemetrexede para paceintes com a mutação do T790M+ e metastases em SNC.

AURA-3: Análise de desfechos SNC

Doença avançada ou irressecável que progrediu a Tki em pacientes com mutação do EGFR T790M (N = 419)

Osimertinib 80 mg QD (n = 279)	n = 75 (27%)	n = 30 (11%)
Quimioterapia com platina/alimta (n = 140)	n = 41 (29%)	n = 16 (11%)

- Desfechos: Resposta em SNC; Duração resposta SNC; SLP SNC

Mok T, et al. ASCO 2017. Abstract 9005.

AURA-3:Caracteristicas dos grupos

Caracteristicas	Osimertinibe (n = 75)	QT (n = 41)
Idade, anos	59 (34-82)	59 (20-79)
Homens, %	45	29
Raça, % ▪ Branco ▪ Asiático ▪ Outros	 31 68 1	 20 80 0
PS, % ▪ 0 ▪ 1	 29 71	 34 66
MutaçõesEGFR, % ▪ Ex19del ▪ L858R ▪ Other	 64 36 0	 49 41 7
	99	Adenocarcinoma
Radioterapia até a entrada do estudo, %	34	49

Mok T, et al. ASCO 2017. Abstract 9005.

AURA-3: Tx resposta e duração em SNC

In cFAS, CNS ORR better with osimertinib regardless of previous radiotherapy, but numbers small

Desfecho	Osimertinibe (n = 30)	QT(n = 16)	TX R (95% CI)
TX R SNC, % (95% CI)	70 (51-85)	31 (11-59)	5.13 (1.44-20.64); *P* = .015
Tempo para resposta SNC, semanas	6.1	6.1	
Mediana DurR, meses (95% CI)	8.9 (4.3-NC)	5.7 (NC-NC)	

TXR SNC, % (95% CI)	Osimertinibe (n = 75)	QT (n = 41)
Radioterapia SNC últimos 6 meses da randomização	64 (35-87) (n = 14)	22 (2-60) (n = 9)
Sem radiothrapia ou radioterapia ≥ 6 meses antes da radomização	34 (23-48) (n = 61)	16 (5-33) (n = 32)

Mok T, et al. ASCO 2017. Abstract 9005.

AURA-3:SLP em pacientes com e sem Meta SNC

Mediana SLP, Meses	Osimertinibe	QT	HR (95%CI)
SLP população total AURA-3			
▪ Pactes meta SNC	8.5 (n = 93)	4.2 (n = 51)	0.32 (0.21-0.49); *P* < .001
▪ Pactes sem meta SNC	10.8 (n = 186)	5.6 (n = 89)	0.40 (0.29-0.55); *P* < .001

Mok T, et al. ASCO 2017. Abstract 9005.

AURA-3:Resposta em pacientes com metas em Meninge

- 7 paientes com metastases em leptomeninge foram tratados com osimertinibe 80 mg : 4 tiveram respostas

Pact	RT prévia	Tipos de resposta		
		Score de RANO	SNC (RECIST v1.1)	Sistemico (RECIST v 1.1)
1	Não	CR	CR	PR
2	Não	CR	PR	PR
3	Não	PR	SD	SD
4	Não	PR	SD	SD
5	Não	SD	SD	PR
6	Sim	SD	SD	SD
7	Sim	SD	SD	SD

Mok T, et al. ASCO 2017. Abstract 9005.

AURA-3: Conclusões SNC

- Osimertinibe foi associado com significante melhora da taxa de resposta e da SLP em metas no SNC comparativamente a QT com platina/pemetrexede
- Respostas observadas independentemente de radioterapia prévia.
- Geralmente tempo para resposta de aproximadamente 6 semanas.
- Pacientes com metastases em meninge também tiveram resposta com a uso do osemertinibe.

Mok T, et al. ASCO 2017. Abstract 9005.

Dacomitinib versus Gefitinib for the First-Line Treatment of Advanced NSCLC (ARCHER 1050): A Randomized, Open-Label, Phase 3 Trial

Tony Mok,[1] Ying Cheng,[2] Xiangdong Zhou,[3] Ki Hyeong Lee,[4] Kazuhiko Nakagawa,[5] Seiji Niho,[6] Fumito Tsuji,[7] Rafael Rosell,[8] Jesus Corral,[9] Maria Rita Migliorino,[10] Adam Pluzanski,[11] Rolf Linke,[12] Eric Sbar,[13] Tao Wang,[14] Yi-Long Wu[15]

[1]State Key Laboratory of South China, Department of Clinical Oncology, Chinese University of Hong Kong, Hong Kong, China; [2]Jilin Provincial Cancer Hospital, Changchun, China; [3]First Affiliated Hospital of Third Military Medical University, Chongqing, China; [4]Chungbuk National University Hospital, Chungcheongbuk-do, Republic of Korea; [5]Kindai University Hospital, Osaka, Japan; [6]National Cancer Center Hospital East, Kashiwa, Japan; [7]SFJ Pharma Japan, Osaka, Japan; [8]Catalan Institute of Oncology, Barcelona, Spain; [9]Hospital Universitario Virgen del Rocio, Seville, Spain; [10]Pulmonary Oncology Unit, San Camillo-Forlanini Hospital, Rome, Italy; [11]The Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, Warsaw, Poland; [12]SFJ Pharmaceuticals Group, Pleasanton, CA; [13]Pfizer, Collegeville, PA; [14]Pfizer, Groton, CT; [15]Guangdong Lung Cancer Institute, Guangdong General Hospital & Guangdong Academy of Medical Sciences, Guangzhou, China

PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17

Presented by: Tony Mok, MD

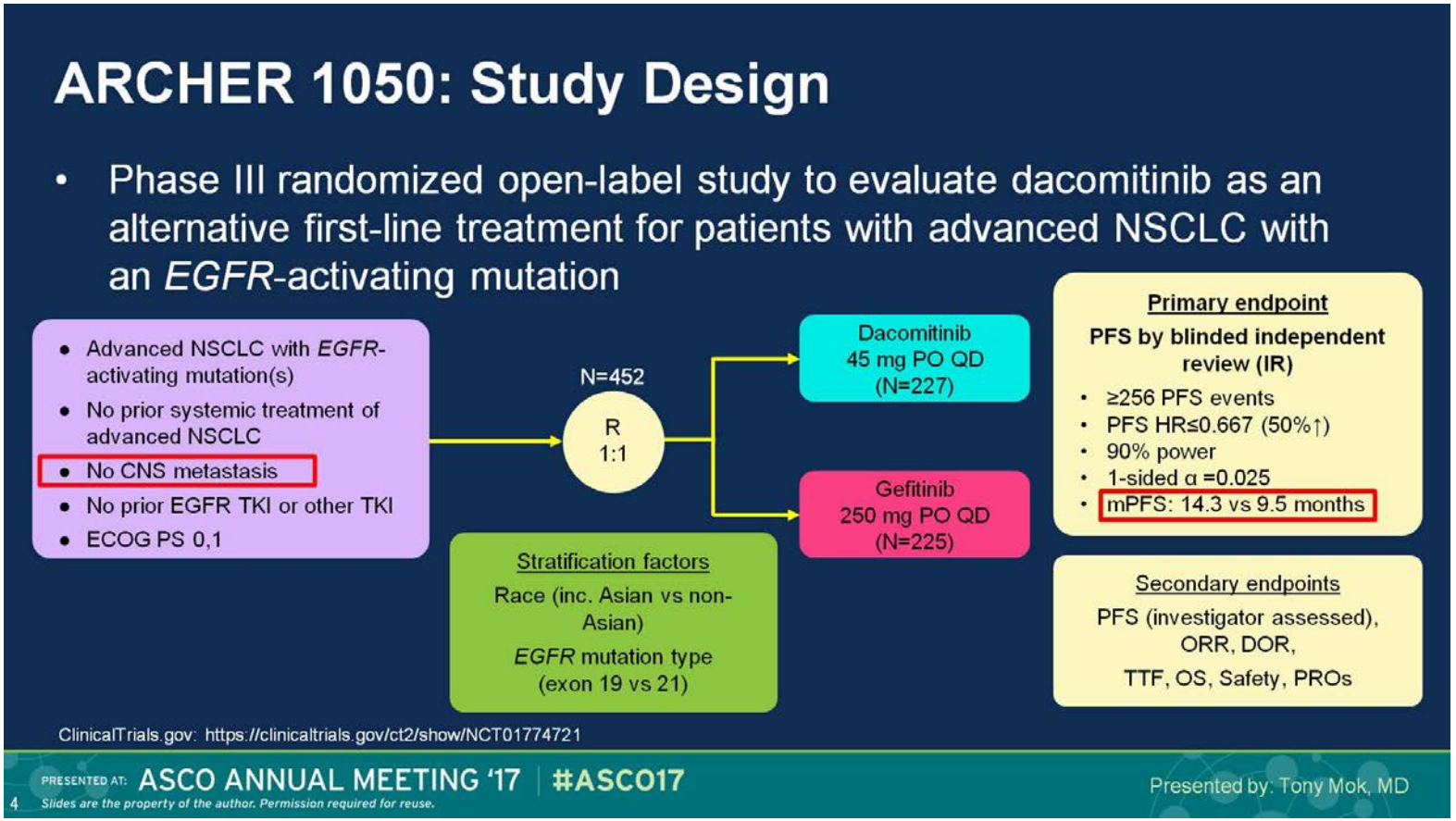
Presented By Tony Mok at 2017 ASCO Annual Meeting

Background

- Dacomitinib is a second-generation, irreversible epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor
  - Characterized by irreversible inhibition of three members of the ErbB family (EGFR/HER1, HER2, and HER4)
- A single arm phase 2 study (ARCHER 1017) of dacomitinib as first-line therapy in subgroup of patients with *EGFR*-activating mutation reported:
  - Response rate 75.6%
  - Median PFS 18.2 months
- Phase III ARCHER 1050 was designed to investigate dacomitinib versus gefitinib as first-line treatment in patients with advanced NSCLC harbouring *EGFR*-activating mutations

Engelman et al *Can Res* 2007; Janne et al *Lancet Oncology* 2014

- Dacometinibe é um inibidor irreversível do EGFR
- Estudo de comparação direta entre dois TKIs na primeira linha de tratamento do tumor de pulmão EGFR mutado avançado.

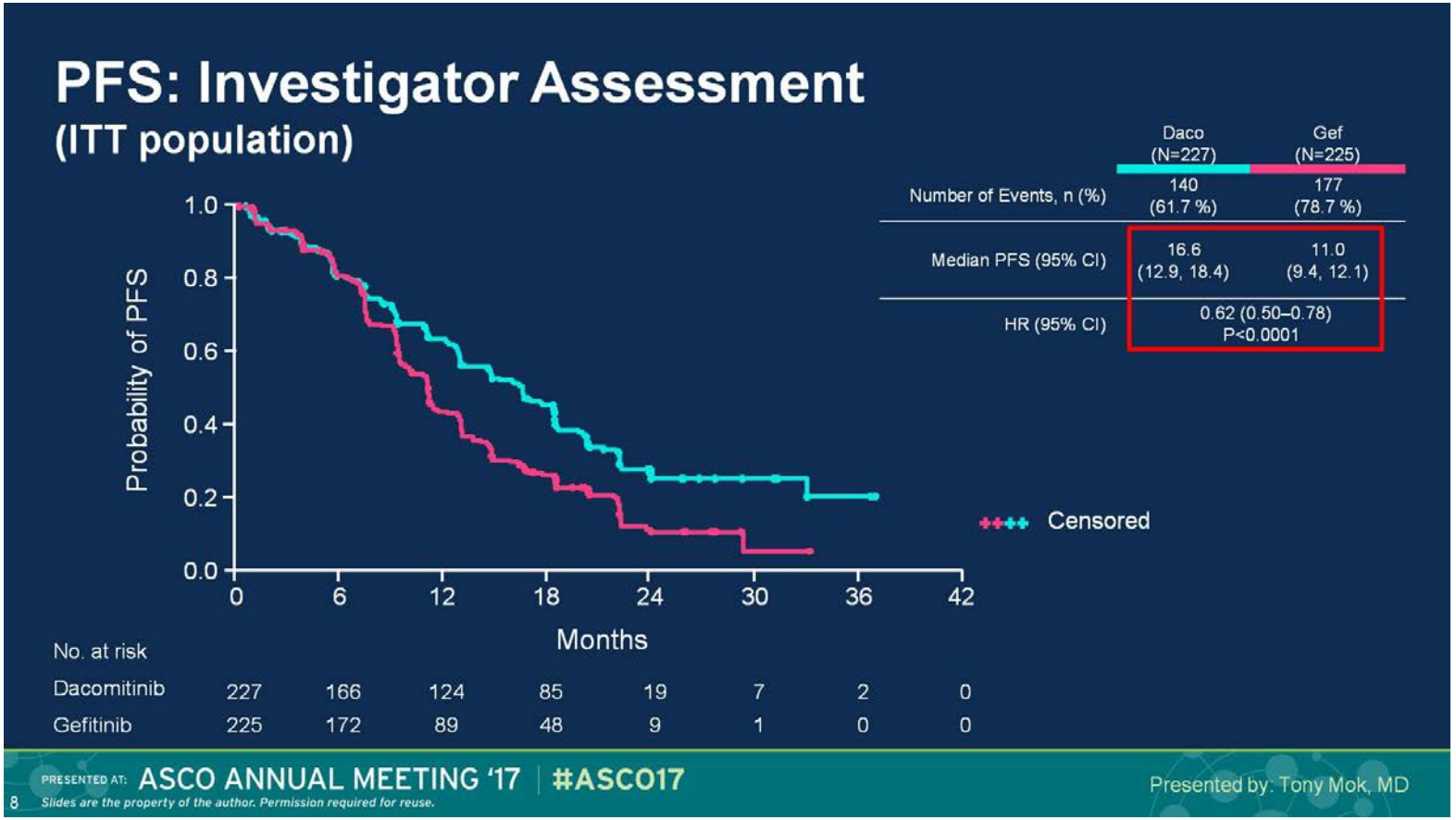


- Estudo 1:1 sem pacientes com metástase em SNC.

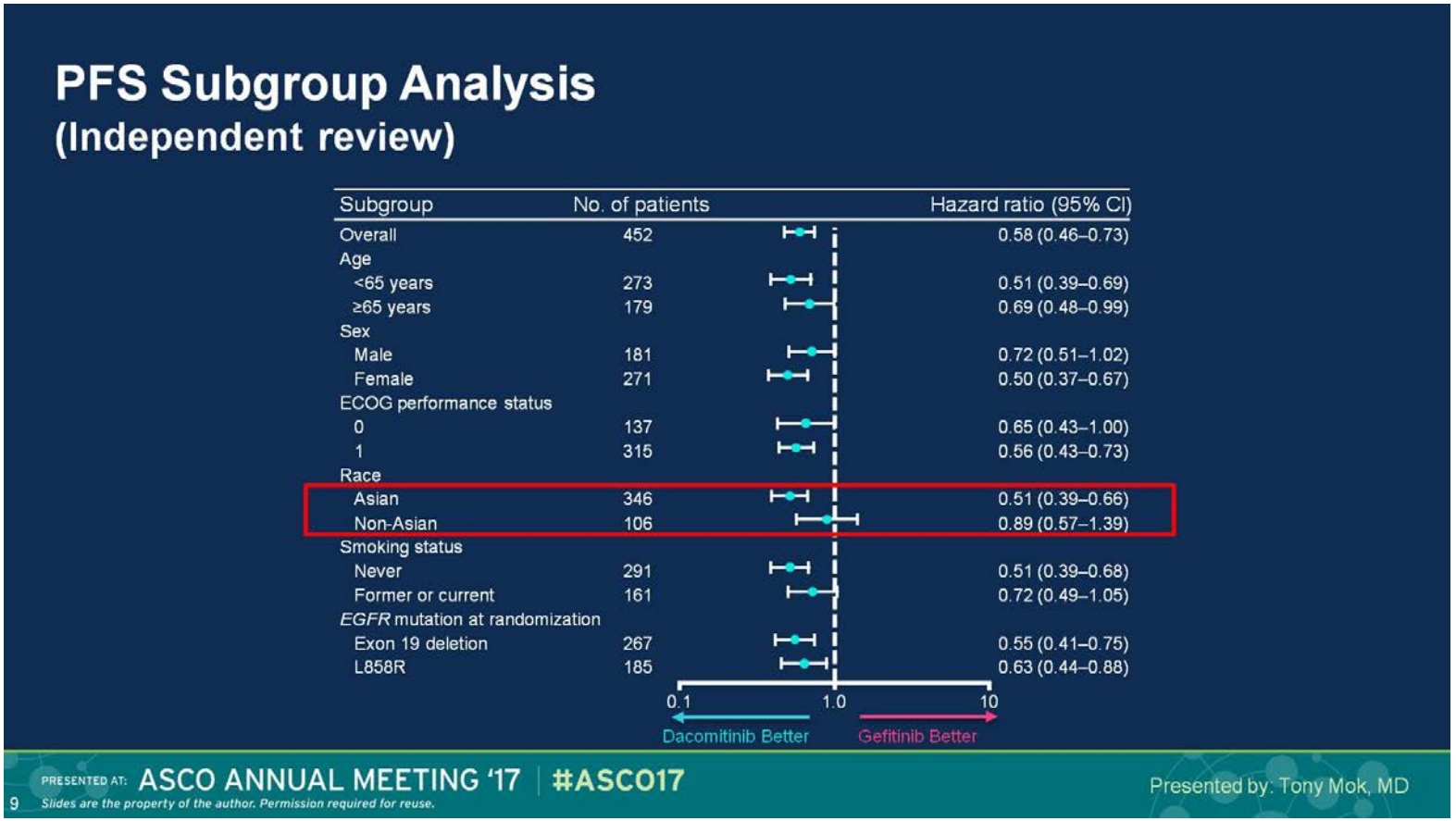
Baseline Patient Characteristics

Characteristic	Dacomitinib (n=227) (n[%])	Gefitinib (n=225) (n[%])
Age, years		
Median (range)	62 (28–87)	61 (33–86)
<65 years	133 (58.6)	140 (62.2)
≥65 years	94 (41.4)	85 (37.8)
Sex		
Male	81 (35.7)	100 (44.4)
Female	146 (64.3)	125 (55.6)
Ethnicity		
White	56 (24.7)	49 (21.8)
Black	1 (0.4)	0 (0.0)
Asian	170 (74.9)	176 (78.2)
ECOG PS		
0	75 (33.0)	62 (27.6)
1	152 (67.0)	163 (72.4)
Smoking status		
Never smoked	147 (64.8)	144 (64.0)
Ex-smoker	65 (28.6)	62 (27.6)
Smoker	15 (6.6)	19 (8.4)
EGFR status at randomization (per IVRS)		
Exon 19 deletion	134 (59.0)	133 (59.1)
L858R mutation in exon 21	93 (41.0)	92 (40.9)

- Maior parte da população do estudo é asiática.



- Houve uma diferença estatisticamente significativa em favor do dacometinibe



- Não há uma população específica para o benefício. A diferença entre asiáticos e não asiáticos pode se dever ao número de pacientes.

Best Overall Response
(Blinded Independent Review; ITT Population)

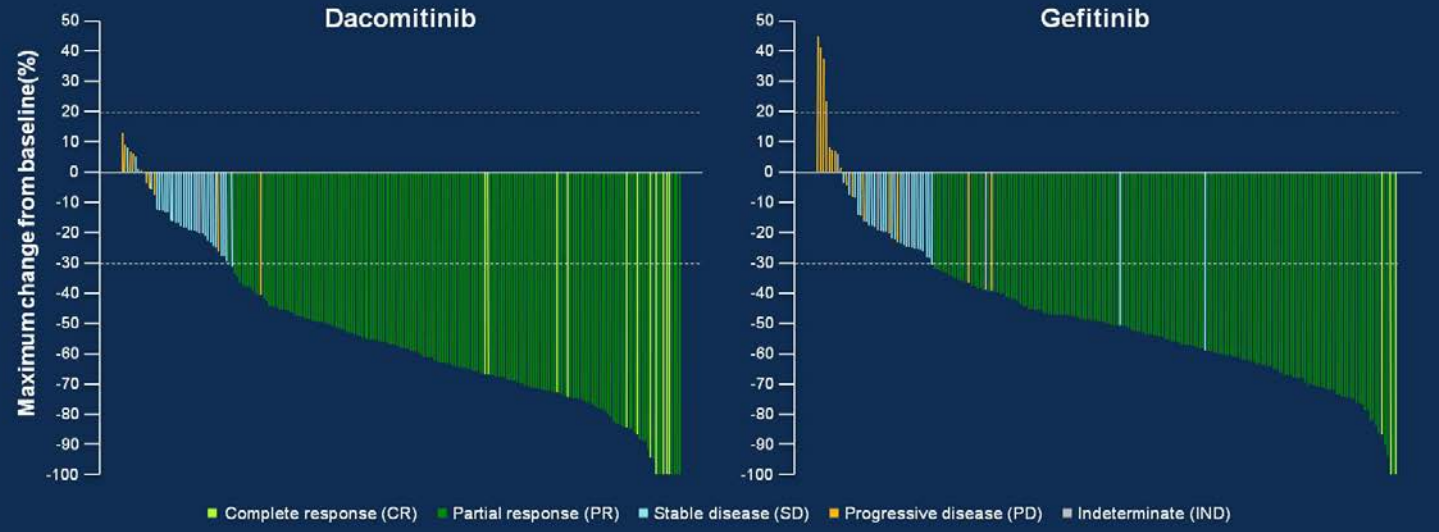
	Dacomitinib (n=227)	Gefitinib (n=225)
Objective response rate		
Percentage of patients	74.9	71.6
95% CI	68.7-80.4	65.2-77.4
P value[a]	0.3883	
Duration of response in responders[b]		
Median no. of months	14.8	8.3
95% CI	12.0-17.4	7.4-9.2
P-value[b]	<0.0001	

Overall survival was not mature, with only 36.9% of events at the time of data cutoff

[a]The P-value (2-sided) is from the Cochran–Mantel–Haenszel test stratified by *EGFR* mutation status at randomization (exon 19 deletion vs. the L858R mutation) and by race (Japanese vs. Chinese and other East Asian vs. Non-Asian). [b]The duration of response was calculated with the use of the Kaplan–Meier method from the time of the first documented response until the date of progression or the last RECIST assessment for patients who did not have disease progression.

- A taxa de resposta foi basicamente a mesma...
- Diferença foi o tempo de duração da resposta!

ORR: Tumor change per blinded IRC review



Shown are best responses in patients treated with dacomitinib or gefitinib. Each bar represents an individual patient's maximum reduction in target lesion size.

Adverse Events from Any Cause

Adverse event	Dacomitinib (N = 227)						Gefitinib (N = 224)					
	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
	Number of patients (percent)											
Diarrhea	198 (87.2)	113(49.8)	65 (28.6)	19 (8.4)	0	1 (0.4)	125 (55.8)	103 (46.0)	20 (8.9)	2 (0.9)	0	0
Paronychia	140 (61.7)	46 (20.3)	77 (33.9)	17 (7.5)	0	0	45 (20.1)	30 (13.4)	12 (5.4)	3 (1.3)	0	0
Dermatitis acneiform	111 (48.9)	37 (16.3)	43 (18.9)	31 (13.7)	0	0	64 (28.6)	43 (19.2)	21 (9.4)	0	0	0
Stomatitis	99 (43.6)	51 (22.5)	40 (17.6)	8 (3.5)	0	0	40 (17.9)	33 (14.7)	6 (2.7)	1 (0.4)	0	0
Decreased appetite	70 (30.8)	40 (17.6)	23 (10.1)	7 (3.1)	0	0	55 (24.6)	48 (21.4)	6 (2.7)	1 (0.4)	0	0
Dry skin	63 (27.8)	42 (18.5)	18 (7.9)	3 (1.3)	0	0	38 (17.0)	35 (15.6)	3 (1.3)	0	0	0
Weight decreased	58 (25.6)	31 (13.7)	22 (9.7)	5 (2.2)	0	0	37 (16.5)	22 (9.8)	14 (6.3)	1 (0.4)	0	0
Alopecia	53 (23.3)	41 (18.1)	11 (4.8)	1 (0.4)	0	0	28 (12.5)	26 (11.6)	2 (0.9)	0	0	0
Cough	48 (21.1)	39 (17.2)	9 (4.0)	0	0	0	42 (18.8)	36 (16.1)	5 (2.2)	1 (0.4)	0	0
Pruritus	45 (19.8)	27 (11.9)	17 (7.5)	1 (0.4)	0	0	31 (13.8)	24 (10.7)	4 (1.8)	3 (1.3)	0	0
ALT increased	44 (19.4)	37 (16.3)	5 (2.2)	2 (0.9)	0	0	88 (39.3)	45 (20.1)	24 (10.7)	19 (8.5)	0	0

Adverse events occurring in at least 15% of the patients in either study group in the safety population.
Events are listed in descending order of frequency in the dacomitinib group.

- Esta análise de tolerância mostra o perfil de maior toxicidade para o dacometinibe, especialmente para a diarréia e para os efeitos de pele

Serious Adverse Events (SAE)

	Total incidence of SAE	Treatment-related SAE	Permanent discontinuation due to treatment-related AEs	Death related to treatment
Dacomitinib (n=227)	62 (27.3%)	21 (9.3%)	22 (9.7%)	2 (0.9%)
Gefitinib (n=224)	50 (22.3%)	10 (4.5%)	15 (6.7%)	1 (0.4%)

- Cause of death related to treatment
  - Dacomitinib: 2 (1 related to untreated diarrhea, 1 related to untreated cholelithases/liver disease)
  - Gefitinib: 1 (related to sigmoid colon diverticulitis/rupture complicated by pneumonia)

Conclusions

- ARCHER 1050 is the first randomized Phase 3 study to compare a second-generation EGFR TKI with a standard first-generation EGFR TKI for first-line treatment of patients with advanced *EGFR*-mutated NSCLC
- Dacomitinib was superior to gefitinib with respect to PFS and DOR
  - Median PFS at 14.7 months is among the highest
- Incidence of diarrhea, skin rash and mucositis is higher with dacomitinib while incidence of hepatic toxicity is higher with gefitinib
- Incidence of AEs reported for dacomitinib was comparable to that reported for other dacomitinib studies; no new safety signals were identified
- Dose modification is more frequent with dacomitinib
- Patients treated with dacomitinib shared similar improvements in patient-reported measures of key disease-associated symptoms as the gefitinib group
- **Dacomitinib should be considered as a new treatment option for first-line management of patients with advanced *EGFR*-mutated NSCLC**

Presented by: Tony Mok, MD

- Esta conclusão de que o inibidor irreversível é mais eficaz vale para outros compostos também?

Doença Avançada – Imunoterapia ASCO 2017

Doença Avançada – Imunoterapia Pequenas Células

Nivolumab ± Ipilimumab in Advanced Small Cell Lung Cancer: First Report of a Randomized Cohort From CheckMate 032

Matthew D. Hellmann,[1] Patrick A. Ott,[2] Jon Zugazagoitia,[3] Neal Ready,[4] Christine L. Hann,[5] Filippo de Braud,[6] Scott Antonia,[7] Paolo A. Ascierto,[8] Victor Moreno,[9] Akin Atmaca,[10] Stefania Salvagni,[11] Matthew Taylor,[12] Asim Amin,[13] D. Ross Camidge,[14] Leora Horn,[15] Emiliano Calvo,[16] Weiguo Cai,[17] Justin Fairchild,[17] Margaret Callahan,[1] David Spigel[18]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA USA; [2]Dana-Farber Cancer Institute, Boston, MA, USA; [3]Hospital Universitario 12 de Octubre, Madrid, Spain; [4]Duke University Medical Center, Durham, NC, USA; [5]The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, Baltimore, MD, USA; [6]Fondazione IRCCS Instituto Nazionale dei Tumori Milano, Milan, Italy; [7]H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, USA; [8]Istituto Nazionale Tumori Fondazione Pascale, Naples, Italy; [9]START Madrid-FJD, Hospital Fundación Jiménez Díaz, Madrid, Spain; [10]Krankenhaus Nordwest GmbH Institut für Klinisch-Onkologische Forschung, Frankfurt am Main, Germany; [11]Policlinico Sant'Orsola – Malpighi University Hospital, Bologna, Italy; [12]Oregon Health & Science University, Portland, OR, USA; [13]Levine Cancer Institute, Carolinas Medical Center, Charlotte, NC, USA; [14]University of Colorado Cancer Center, Aurora, CO, USA; [15]Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; [16]START Madrid, Centro Integral Oncológico Clara Campal, Madrid, Spain; [17]Bristol-Myers Squibb, Princeton, NJ, USA; [18]Sarah Cannon Research Institute/Tennessee Oncology, PLLC, Nashville, TN, USA

PRESENTED AT: ASCO ANNUAL MEETING '17 #ASCO17

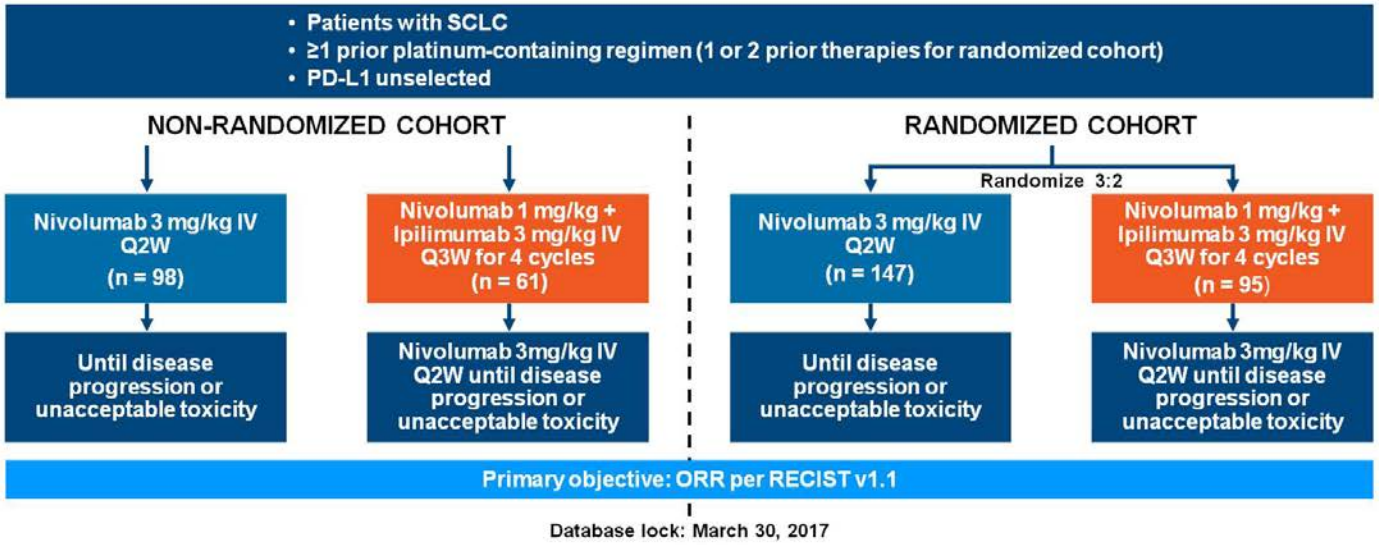
Presented By Matthew Hellmann at 2017 ASCO Annual Meeting

Nivolumab ± Ipilimumab in Advanced SCLC (CheckMate 032): Background

- Pacientes com tumores “Oat Cell” geralmente são de prognóstico muito reservado.
- CheckMate 032: estudo de fase I/II trial avaliando nivolumabe isolado ou com ipilimumabe em vários tipos de tumor, inclusive “oat cell” que progrediu a Qt prévia com platina.
  - Nivolumabe ± ipilimumabe já considerados para tratamento em alguns guidelines

Hellmann MD, et al. ASCO 2017. Abstract 8503. Antonia SJ, et al. Lancet Oncol. 2016;17:883-895.

CheckMate 032: Nivolumab ± Ipilimumab in Advanced SCLC
Phase I/II CheckMate 032 Study Design



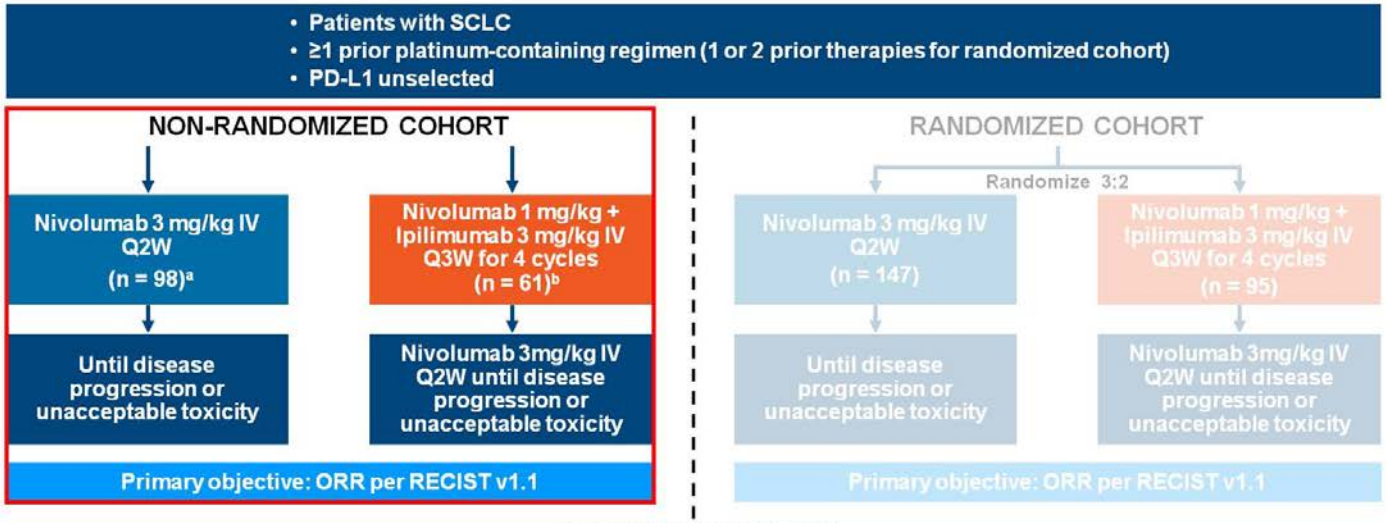
ORR = objective response rate; PD-L1 = programmed death ligand 1

3

Presented By Matthew Hellmann at 2017 ASCO Annual Meeting

CheckMate 032: Nivolumab ± Ipilimumab in Advanced SCLC

Phase I/II CheckMate 032 Study Design – Non-Randomized Cohort



Database lock: March 30, 2017

- Update includes response per blinded independent central review (BICR)
  - Additional follow-up of ~6 months from prior disclosure[8]

[a]Median follow-up 23.3 mo; [b]Median follow-up 28.6 mo
Follow-up was calculated as time from first dose to database lock

Presented By Matthew Hellmann at 2017 ASCO Annual Meeting

CheckMate032: Resposta no subgrupo não randomizado com Follow-up prolongado

Tx de Resposta	Nivolumabe (n = 98)	Nivolumabe + ipilimumabe (n = 61)
ORR, % ▪ PD-L1 ≥ 1% ▪ PD-L1 < 1%	11 9 14	23 10 32
Mediana para resposta, meses	1.4 (1.1-4.1)	2.0 (1.0-4.1)
Mediana da duração de resposta, meses	17.9 (2.8-34.6+)	14.2 (1.5-26.5+)
Resposta mantida aos 2 anos, %	45	36

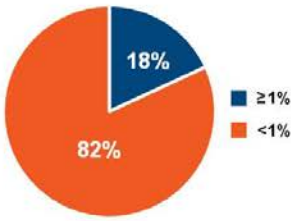
Hellmann MD, et al. ASCO 2017. Abstract 8503.

CheckMate 032: Nivolumab ± Ipilimumab in Advanced SCLC
Summary of Response per BICR – Non-Randomized Cohort

Summary of response

	Nivolumab (n = 98)	Nivolumab + Ipilimumab (n = 61)
ORR, % (95% CI)	**11** (6, 19)	**23** (13, 36)
Median time to response, mo (range)	1.4 (1.1–4.1)	2.0 (1.0–4.1)
Median DOR, mo (range)	17.9 (2.8–34.6+)	14.2 (1.5–26.5+)
Patients with ongoing responses at 2 yr,[a] %	45	36

Tumor PD-L1 expression in non-randomized cohort (n = 159)[b]



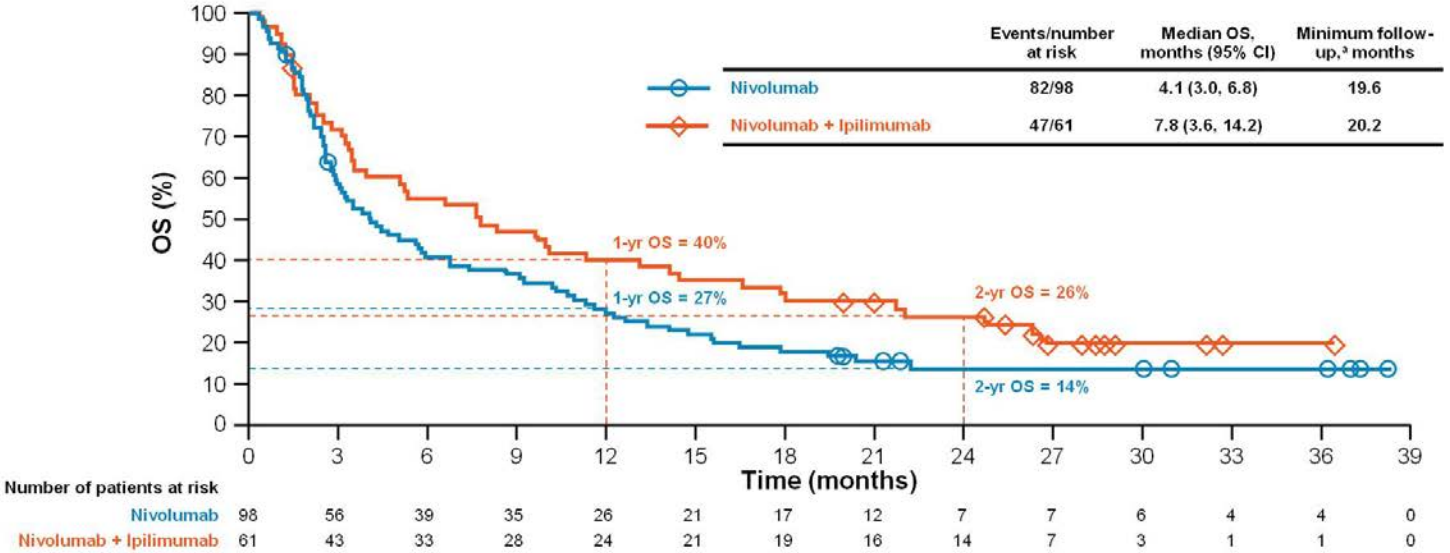
ORR by tumor PD-L1 expression

PD-L1 expression	ORR, % (n/N)	
	Nivolumab (n = 98)	Nivolumab + Ipilimumab (n = 61)
Less than 1%	14 (9/64)	32 (10/31)
1% or more	9 (1/11)	10 (1/10)

DOR = duration of response; ipi = ipilimumab; nivo = nivolumab; [a]Percentage of responders (nivo, n = 11; nivo + ipi, n = 14)
[b]Percentage of patients with quantifiable PD-L1 expression; PD-L1 expression was not evaluable/missing in 43 patients (27%)

Presented By Matthew Hellmann at 2017 ASCO Annual Meeting

CheckMate 032: Nivolumab ± Ipilimumab in Advanced SCLC
OS – Non-Randomized Cohort



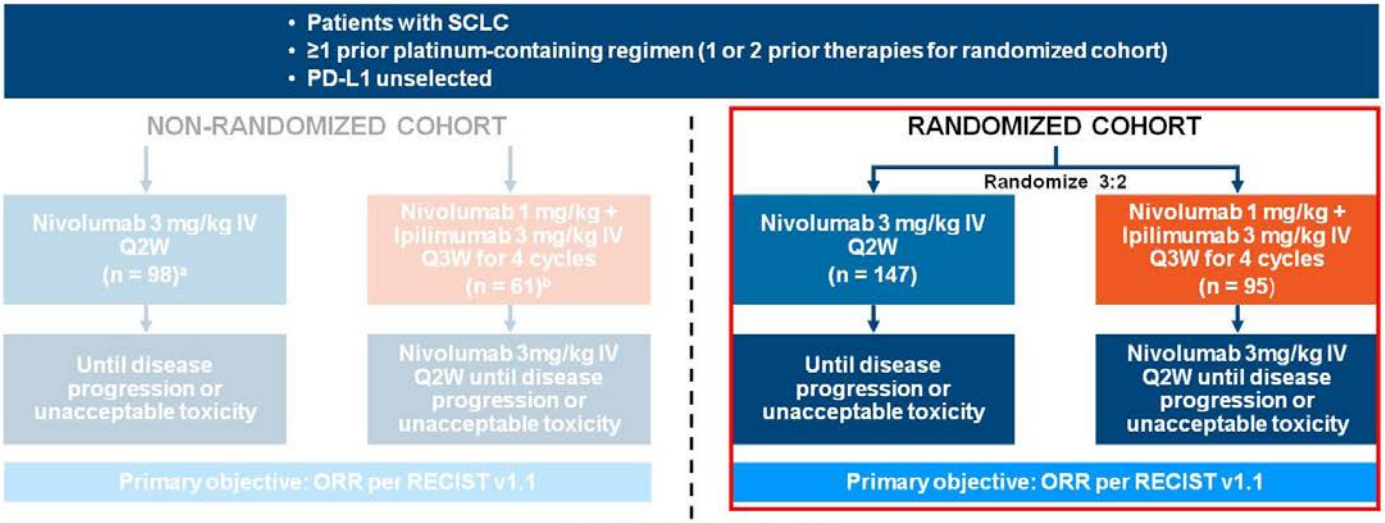
	Events/number at risk	Median OS, months (95% CI)	Minimum follow-up,[a] months
Nivolumab	82/98	4.1 (3.0, 6.8)	19.6
Nivolumab + Ipilimumab	47/61	7.8 (3.6, 14.2)	20.2

OS = overall survival; [a]Between first dose and database lock; follow-up shorter for patients who died prior to database lock

7

Presented By Matthew Hellmann at 2017 ASCO Annual Meeting

CheckMate 032: Nivolumab ± Ipilimumab in Advanced SCLC
Phase I/II CheckMate 032 Study Design – Randomized Cohort



Database lock: March 30, 2017

- Interim descriptive analysis of the randomized cohort
  - Median follow-up: nivo, 10.8 mo; nivo + ipi, 11.2 mo

[a]Median follow-up 23.3 mo; [b]Median follow-up 28.6 mo
Follow-up was calculated as time from first dose to database lock

Presented By Matthew Hellmann at 2017 ASCO Annual Meeting

CheckMate 032: Nivolumab ± Ipilimumab in Advanced SCLC Baseline Patient Characteristics – Randomized Cohort

	Nivolumab (n = 147)	Nivolumab + Ipilimumab (n = 95)
Median age, yr (range)	63.0 (29–83)	65.0 (41–91)
≥65 yr, %	44	51
Male, %	59	63
Prior treatment regimens, %		
1	67	67
2–3	33	33
Platinum sensitivity, %		
Sensitive	50	42
Resistant	49	57
Unknown/not reported	1	1
Smoking status, %		
Current/former smoker	92	95
Never-smoker	7	4
Unknown	1	1
ECOG PS, %		
0	33	28
1	67	71
Not reported	0	1

Presented By Matthew Hellmann at 2017 ASCO Annual Meeting

CheckMate 032: Eficácia

Desfechos	Coorte Randomizado		Coorte Não Randomizedo	
	Nivolumabe (n = 147)	Nivolumabe + Ipilimumabe (n = 95)	Nivolumabe (n = 98)	Nivolumabe + Ipilimumabe (n = 61)
TX resposta, %	12	21	11	23
TTR, meses	1.5	1.4	1.4	2.0
3-meses SLP, %	18	30	27	36
3-meses SG, %	65	64	59	72

Hellmann MD, et al. ASCO 2017. Abstract 8503.

CheckMate 032: Nivolumab ± Ipilimumab in Advanced SCLC
Summary of Safety – Pooled Cohorts

	Nivolumab (n = 245)		Nivolumab + Ipilimumab (n = 156)	
	Any grade, %	Grade 3–4, %	Any grade, %	Grade 3–4, %
Any TRAEs	**55**	**12**	**73**	**37**
TRAEs leading to discontinuation	**3**	**2**	**13**	**10**
Select TRAEs by category				
Skin	16	<1	36	6
Endocrine	8	0	21	3
Hepatic	6	2	12	6
Gastrointestinal	5	0	24	8
Hypersensitivity/infusion reaction	5	0	1	0
Pulmonary	3	2	4	3
Renal	1	<1	1	0
Grade 3–4 select TRAEs that resolved, %[a]	45		78	

- Median time to resolution of grade 3–4 select TRAEs ranged from 1.8 wk (gastrointestinal events) to 16.3 wk (hepatic events) in the nivolumab + ipilimumab arm and from 3.4 wk (pulmonary events) to not reached (renal and hepatic events) in the nivolumab arm
- There were a total of 5 treatment-related deaths[b]
  - 4 with nivolumab + ipilimumab (due to myasthenia gravis, pneumonitis, seizures/encephalitis, and autoimmune hepatitis)[c]
  - 1 with nivolumab (due to pneumonitis)

TRAE = treatment-related adverse event; [a]Percentage of total number of grade 3-4 select TRAEs across categories (nivo + ipi, n = 40; nivo, n = 11); [b]In addition, there was one death in the nivo + ipi arm for which both disease progression and colitis were felt to be contributing factors; [c]A previously reported death due to renal failure was subsequently determined to not be related to treatment

Presented By Matthew Hellmann at 2017 ASCO Annual Meeting

CheckMate 032: Nivolumab ± Ipilimumab in Advanced SCLC Summary

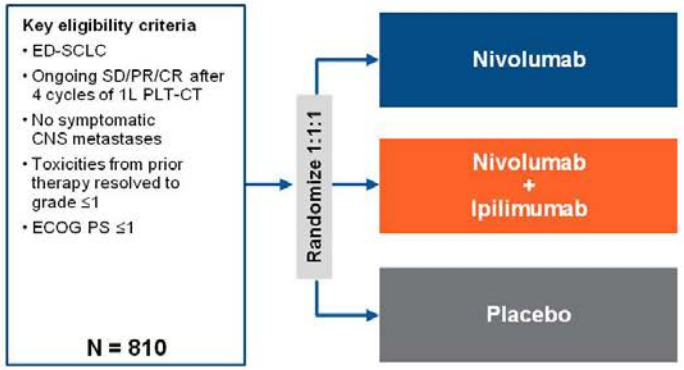
- With BICR and longer follow-up in the non-randomized cohort, responses remained durable and survival promising
  - 2-yr OS: nivolumab + ipilimumab, 26%; nivolumab, 14%
- In a randomized, phase 2 cohort of 242 patients, initial efficacy was consistent with that in the non-randomized cohort
  - ORR: nivolumab + ipilimumab, 21%; nivolumab, 12%
- Responses observed regardless of platinum sensitivity, line of therapy or PD-L1 status
- Grade 3/4 TRAEs and deaths were more common with nivolumab + ipilimumab than with nivolumab
- Additional exploratory analyses are ongoing (QoL, biomarkers) towards improving predictors of response to immunotherapy in SCLC and optimizing management

Presented By Matthew Hellmann at 2017 ASCO Annual Meeting

Ongoing Phase 3 Studies With Nivolumab ± Ipilimumab in SCLC

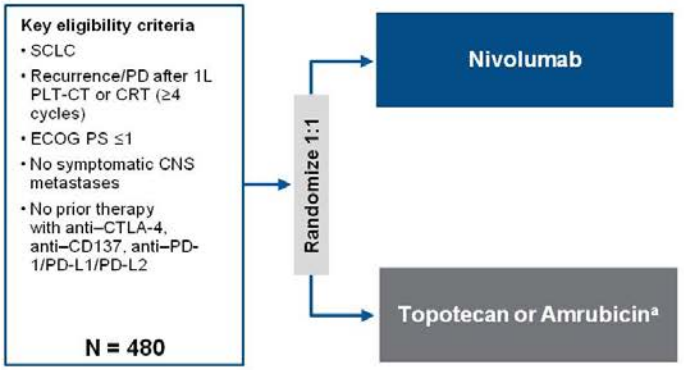
CheckMate 451: study design[10]

- *Currently enrolling patients*



- **Primary outcome measures:**
  - OS, PFS
- **Secondary outcome measures:**
  - OS and PFS descriptive analyses: nivolumab vs nivolumab + ipilimumab

CheckMate 331: study design[11]



- **Primary outcome measures:**
  - OS
- **Secondary outcome measures:**
  - PFS, ORR

1L = first-line; CT = chemotherapy; CRT = chemoradiation therapy; CTLA-4 = cytotoxic T lymphocyte antigen-4; PD-1 = programmed-death 1; PD-L2 = PD ligand 2
PLT = platinum-based; [a]Where locally approved

19

Presented By Matthew Hellmann at 2017 ASCO Annual Meeting

Doença Avançada - Imunoterapia Não Pequenas Células

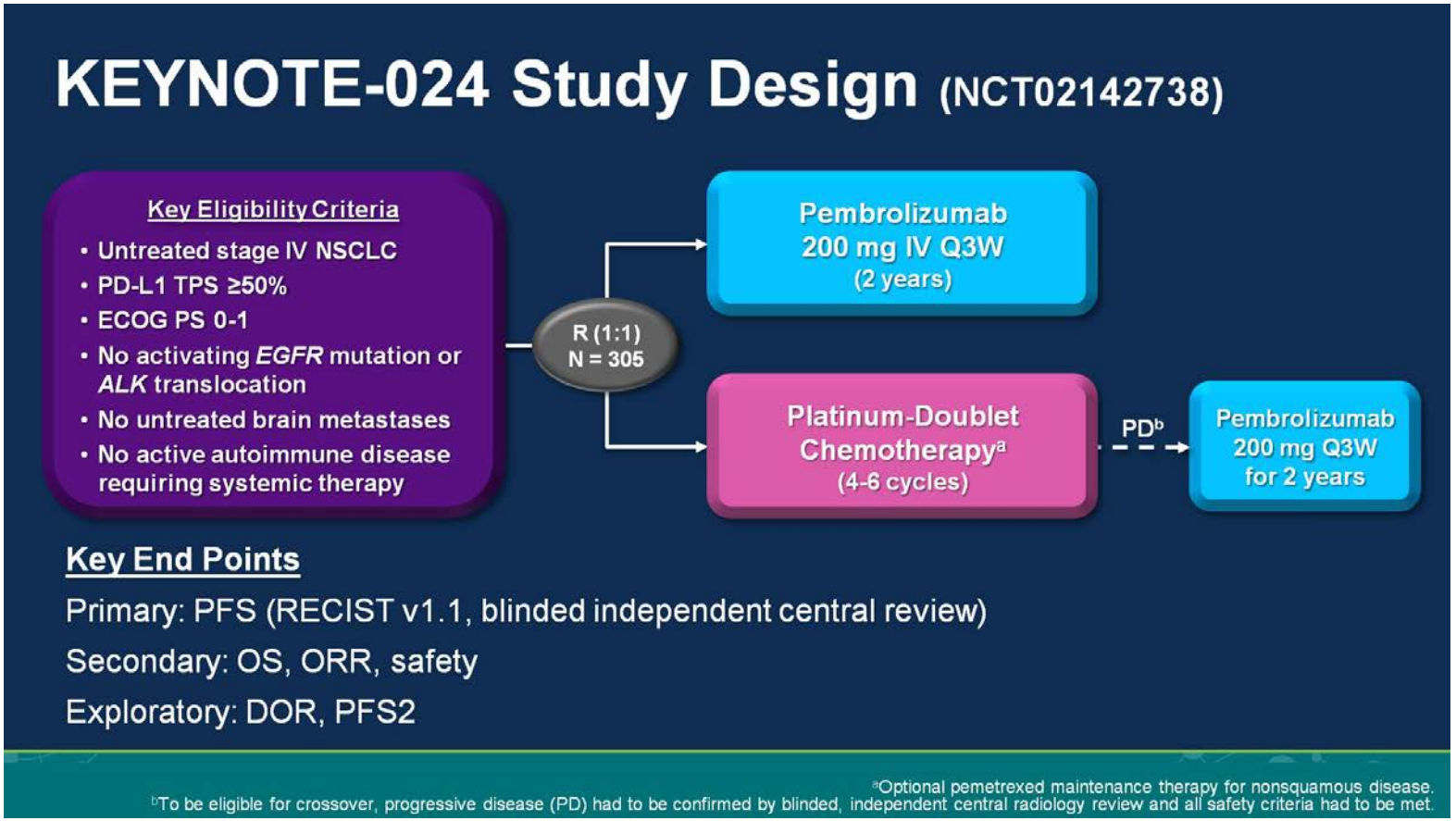
Progression After the Next Line of Therapy (PFS2) and Updated OS Among Patients With Advanced NSCLC and PD-L1 TPS ≥50% Enrolled in KEYNOTE-024

Julie R. Brahmer,[1] Delvys Rodríguez-Abreu,[2] Andrew G. Robinson,[3] Rina Hui,[4] Tibor Csőszi,[5] Andrea Fülöp,[6] Maya Gottfried,[7] Nir Peled,[8] Ali Tafreshi,[9] Sinead Cuffe,[10] Mary O'Brien,[11] Suman Rao,[12] Katsuyuki Hotta,[13] Melanie A. Leiby,[14] Jessica McLean,[14] Yue Shentu,[14] Reshma Rangwala,[14]* Martin Reck[15]

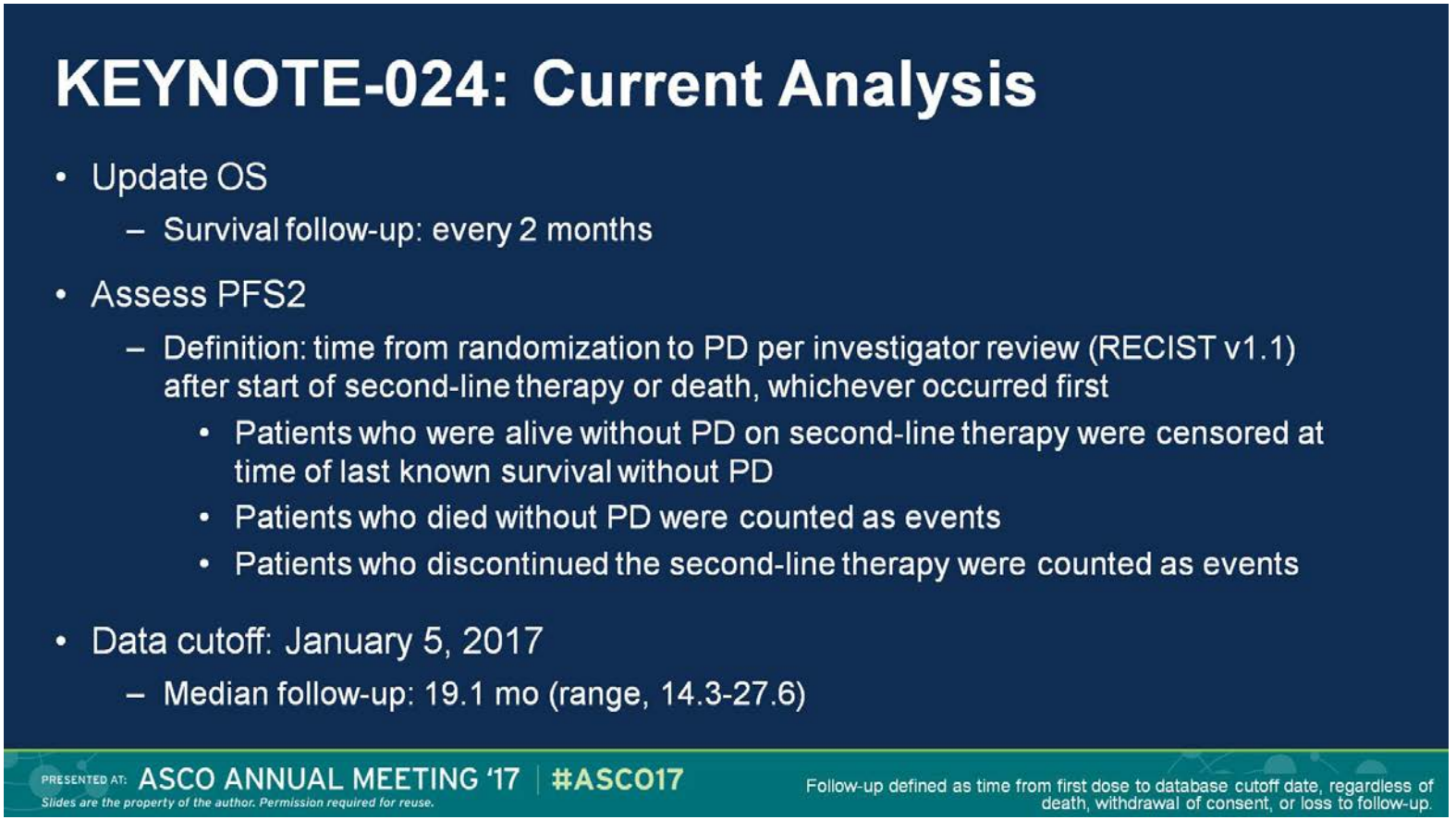
[1]Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD, USA; [2]Hospital Universitario Insular de Gran Canaria, Las Palmas, Spain; [3]Cancer Centre of Southeastern Ontario at Kingston General Hospital, Kingston, ON, Canada; [4]Westmead Hospital and the University of Sydney, Sydney, NSW, Australia; [5]Jász-Nagykun-Szolnok County Hospital, Szolnok, Hungary; [6]Országos Korányi TBC és Pulmonológiai Intézet, Budapest, Hungary; [7]Meir Medical Center, Kfar-Saba, Israel; [8]Davidoff Cancer Center, Tel Aviv University, Petah Tikva, Israel; [9]Southern Medical Day Care Centre, Wollongong, NSW, Australia; [10]St. James's Hospital and Cancer Trials Ireland (formerly ICORG – All Ireland Cooperative Oncology Research Group), Dublin, Ireland; [11]The Royal Marsden Hospital, Sutton, Surrey, UK; [12]MedStar Franklin Square Hospital, Baltimore, MD, USA; [13]Okayama University Hospital, Okayama, Japan; [14]Merck & Co., Inc., Kenilworth, NJ, USA; [15]Lung Clinic Grosshansdorf, Airway Research Center North (ARCN), member of the German Center for Lung Research (DZL), Grosshansdorf, Germany. *Former employee.

PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17

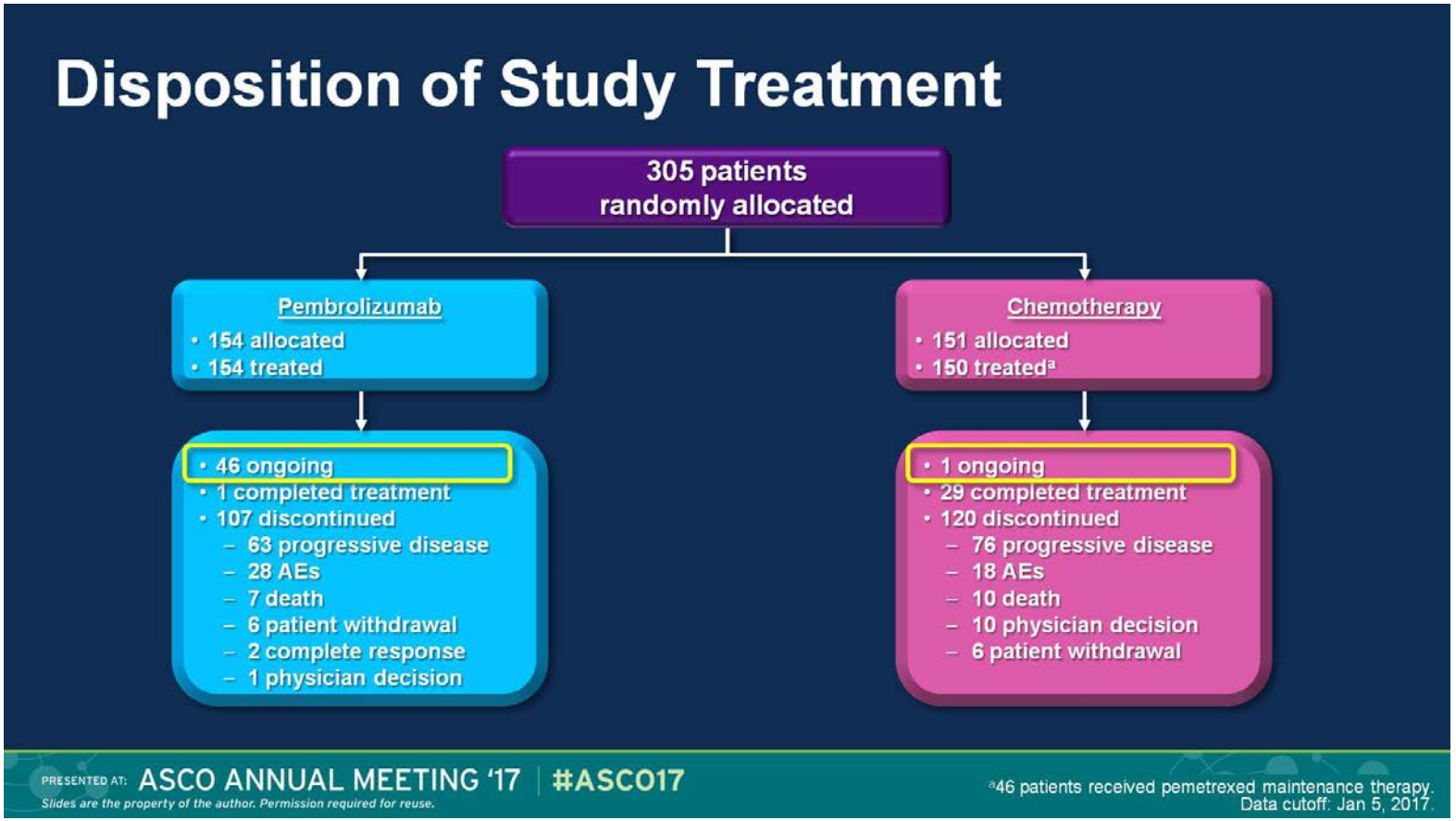
Presented By Julie Brahmer at 2017 ASCO Annual Meeting



KEYNOTE 024 em seu desenho original



- Esta análise procurou avaliar sobrevida livre de progressão após a primeira linha de tratamento. Ou seja, avaliar o desfecho dos pacientes que realizaram imunoterapia em segunda linha.



Presented By Julie Brahmer at 2017 ASCO Annual Meeting

First Subsequent Systemic Therapy: Pembrolizumab Arm (N = 48)

	Patients, n (%)[a]	Treatment Duration, median (range)
Platinum doublet	42 (87.5)	3.6 mo (1 d to 10.7+ mo)
Carboplatin + pemetrexed ± bevacizumab[b]	17 (35.4)	
Carboplatin + paclitaxel ± bevacizumab[c]	9 (18.8)	
Carboplatin + gemcitabine	8 (16.7)	
Cisplatin + pemetrexed	5 (10.4)	
Cisplatin + gemcitabine	2 (4.2)	
Platinum + pemetrexed	1 (2.1)	
Other	6 (12.5)	2.8 mo (1 d to 10.0+ mo)
Cisplatin	2 (4.2)	
Cabozantinib	1 (2.1)	
Carboplatin	1 (2.1)	
Cytarabine	1 (2.1)	
Pemetrexed + bevacizumab	1 (2.1)	

PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17

[a]Percentages calculated out of the number of patients who received subsequent therapy.
[b]1 patient received carboplatin + pemetrexed + bevacizumab.
[c]3 patients received carboplatin + paclitaxel + bevacizumab.
Data cutoff: Jan 5, 2017.

- Esta análise procurou avaliar sobrevida livre de progressão após a primeira linha de tratamento. Ou seja, avaliar o desfecho dos pacientes que realizaram imunoterapia em segunda linha.

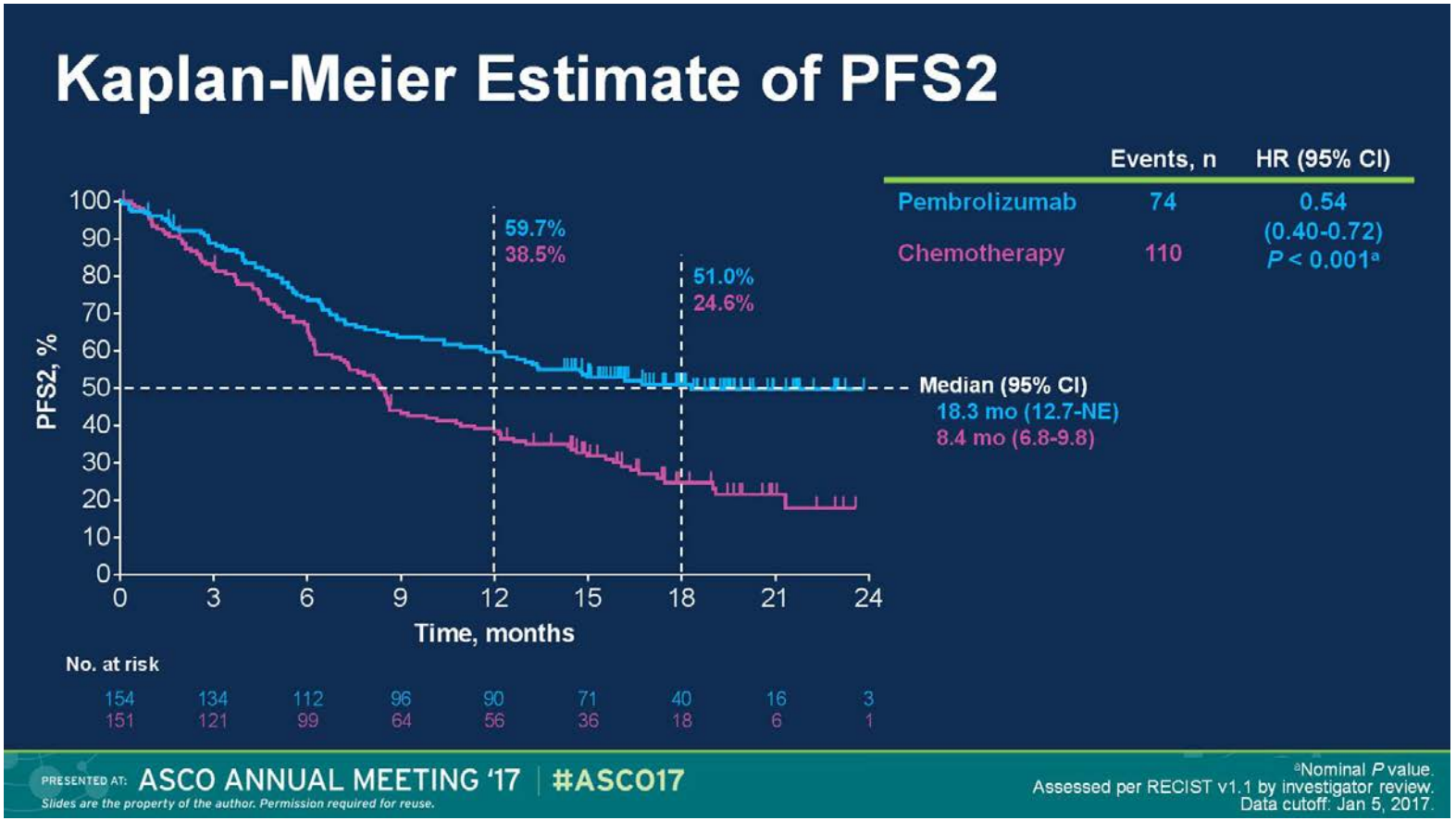
First Subsequent Systemic Therapy: Chemotherapy Arm (N = 97)

	Patients, n (%)[a]	Treatment Duration, median (range)
Crossover to pembrolizumab	79 (81.4)	4.2 mo (1 d to 20.3+ mo)
Anti–PD-1 outside of crossover	12 (12.4)	3.0 mo (1 d to 11.3+ mo)
Nivolumab	9 (9.3)	
Pembrolizumab	3 (3.1)	
Other	6 (6.2)	1.9 mo (1 d to 5.2 mo)
Pemetrexed	2 (2.1)	
Carboplatin + gemcitabine	1 (1.0)	
Carboplatin + paclitaxel	1 (1.0)	
Docetaxel	1 (1.0)	
Paclitaxel	1 (1.0)	

PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17

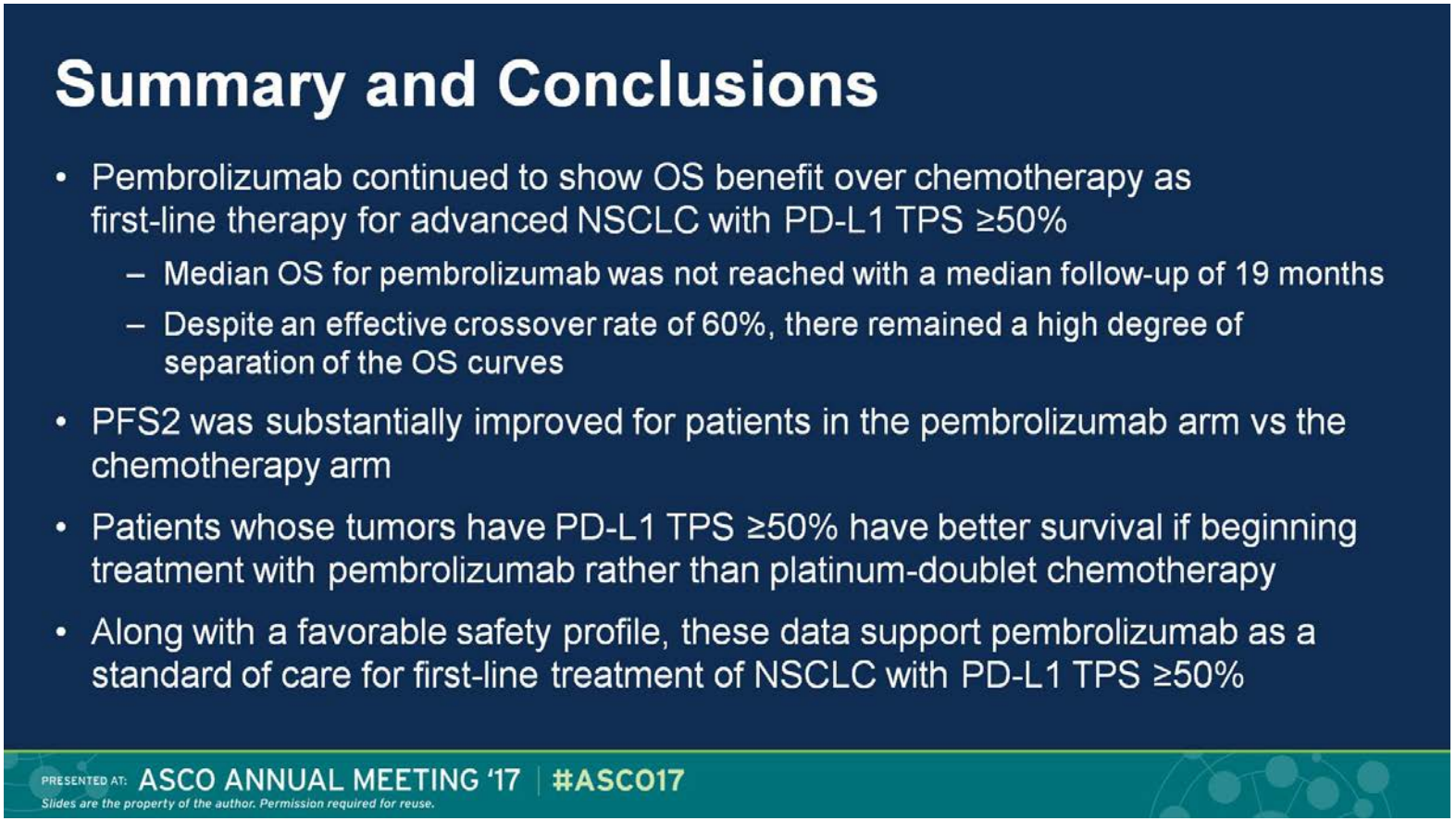
[a]Percentages calculated out of the number of patients who received subsequent therapy. Data cutoff: Jan 5, 2017.

- A maior parte dos pacientes submetidos a tratamento com quimitoerapia foram depois expostos a imunoterapia. .



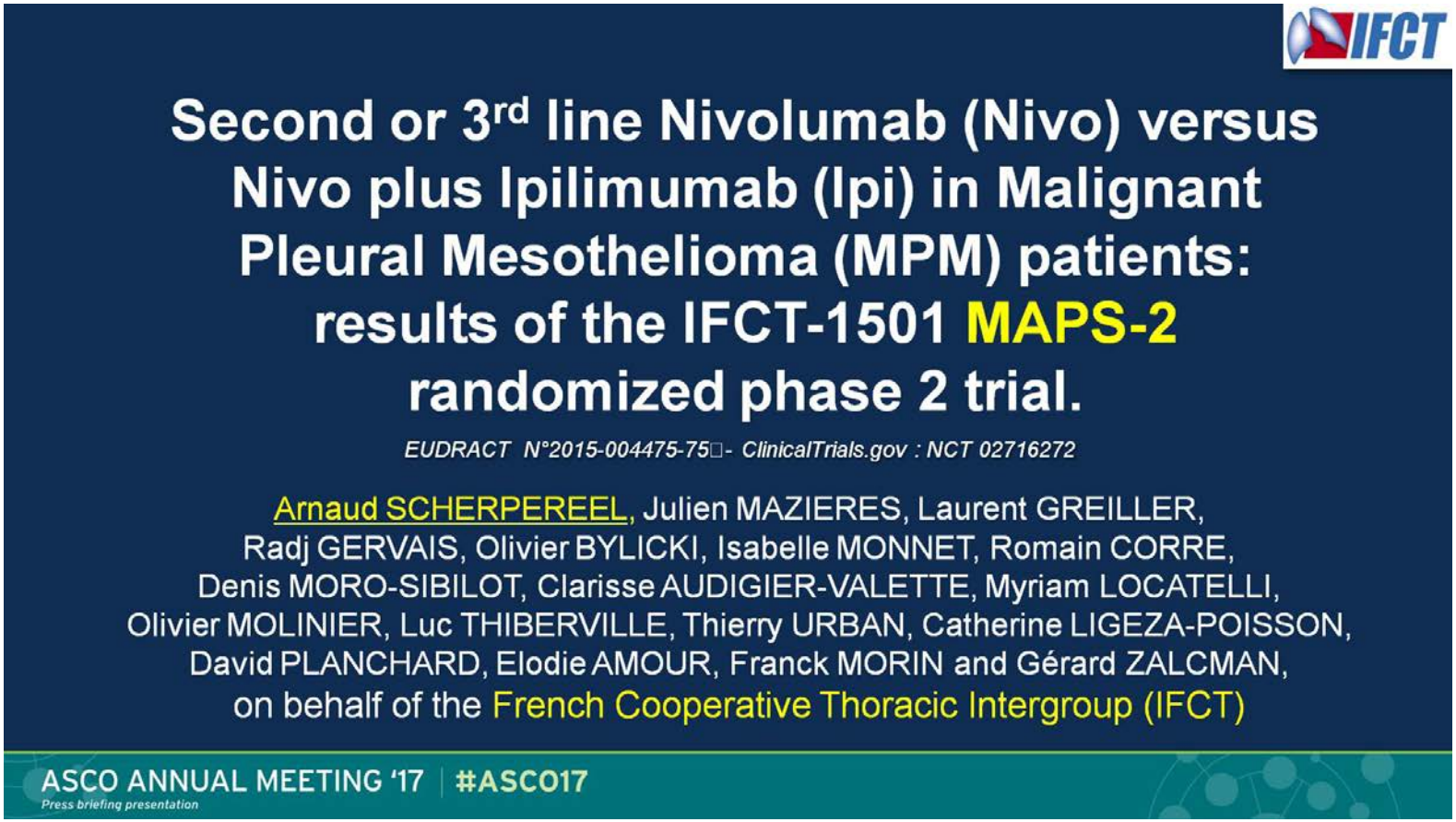
- A resposta da imunoterapia em segunda linha foi conforme esperado. Melhor do que a quimioterapia…e com reposta duradouras nos repondedores

PÓS 2017 ASCO ANNUAL MEETING
Grupo ONCOCLÍNICAS
Sua vida. Nossa vida.
INSTITUTO ONCOCLÍNICAS



- Nos pacientes selecionados deste estudo, com expressão do PDL1 acima de 50%, pembrolizumabe se mostrou a melhor alternativa terapêutica também em segunda linha.

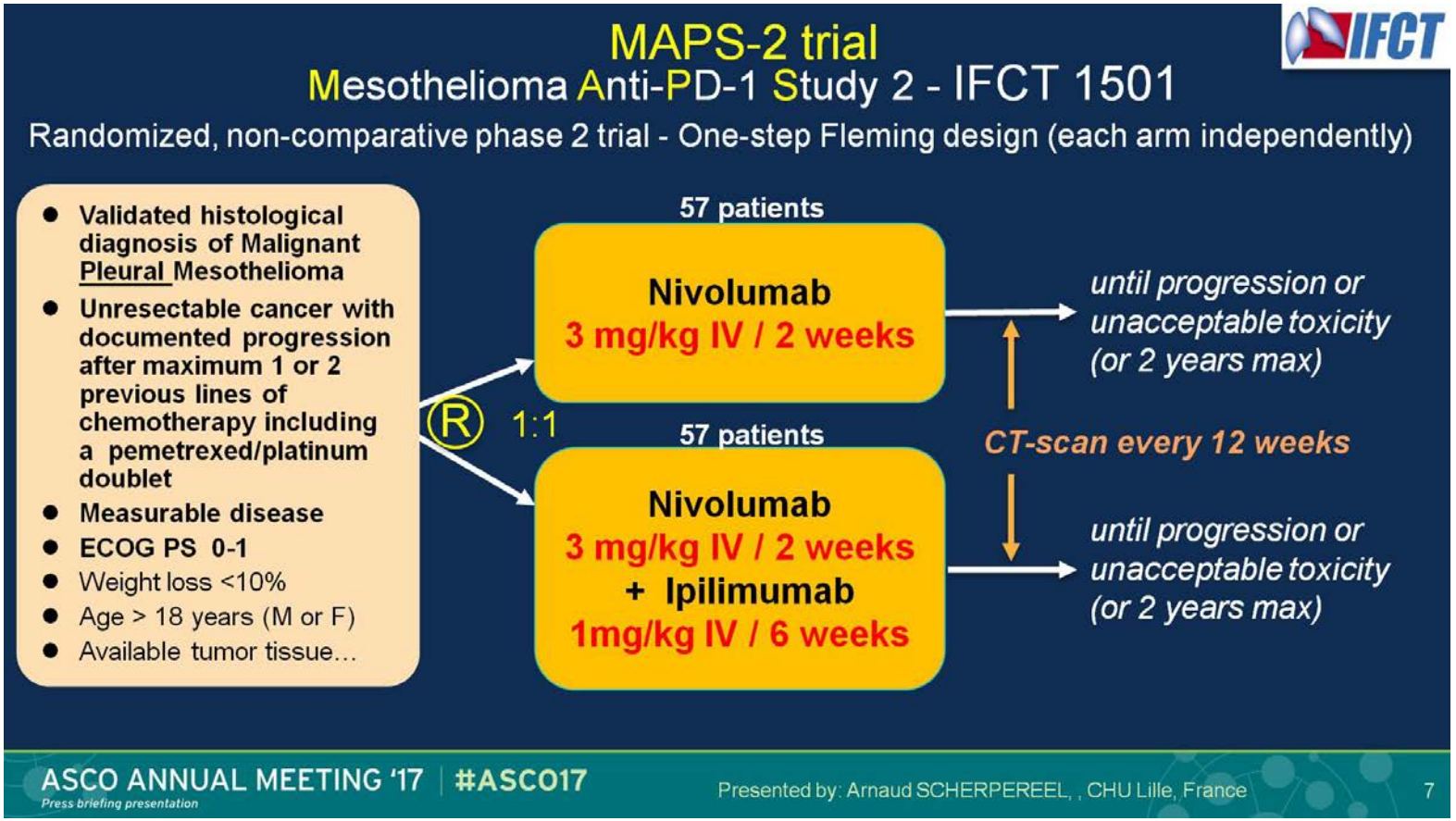
Mesothelioma
ASCO 2017



Presented By Arnaud Scherpereel at 2017 ASCO Annual Meeting

MAPS-2 Background

- Mesotelioma avançado e uma doença rara e agressiva.
  - Pacientes virgens de tratamento o tratamento padrão é a aassociação de bevacizumabe ao doublet pemetrexede/cisplatina ou o doublet isolado (18.8 meses e 16.1 meses de sobrevida global retorspectivamente).
- Em pacientes com mesotelioma, aproximadamente 20% a 60% dos tumores são positivos para o PD-L1.



- Primary endpoint: 12-wk DCR per BICR with modified RECIST criteria for MPM
- Secondary endpoints: safety, PFS, OS, QoL, predictive utility of tumor PD-L1 score, prognostic utility of biomarkers

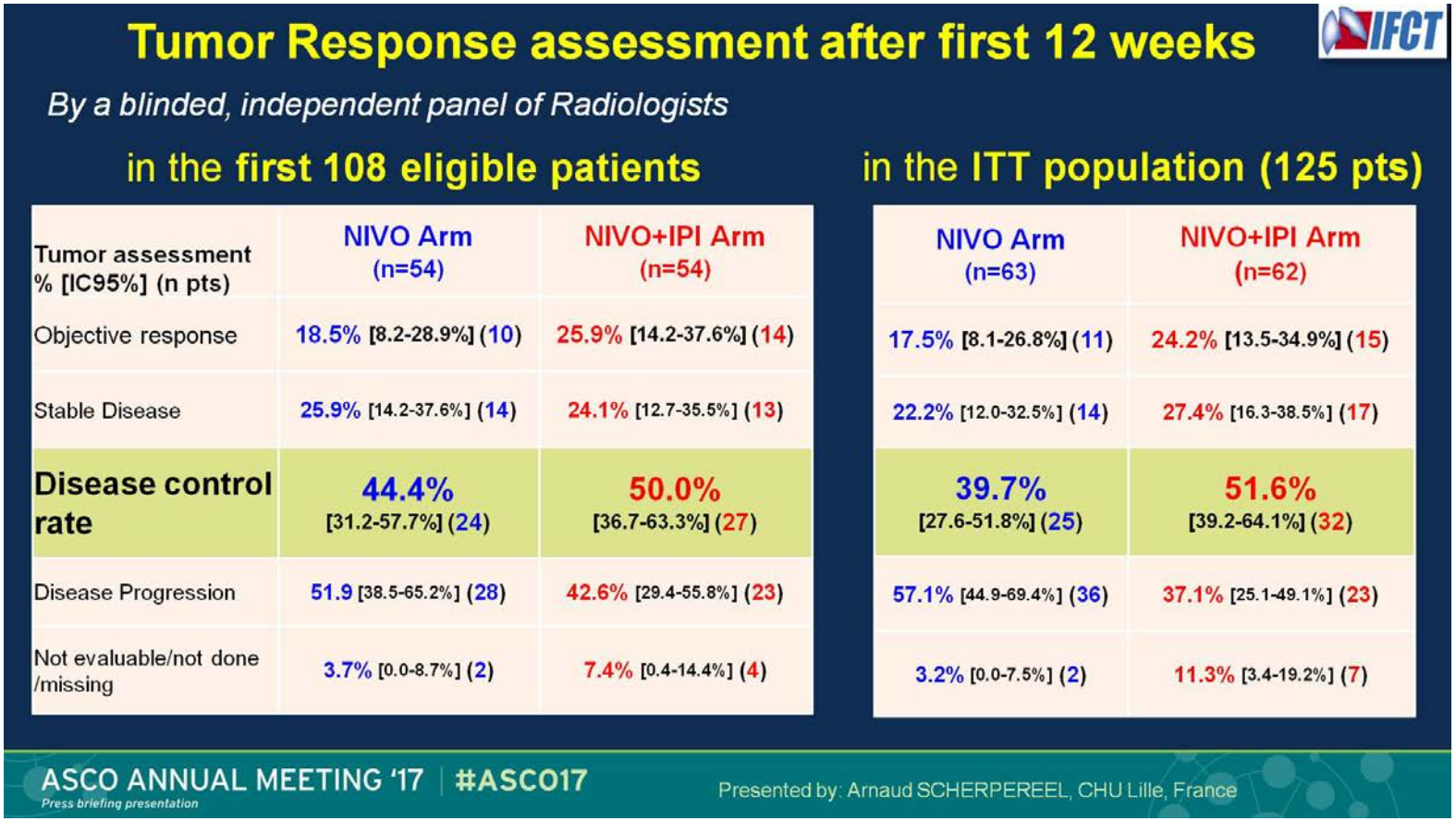
Patients baseline characteristics (1)	Nivo Arm (n=63)	Nivo+Ipi Arm (n=62)
Gender N (%)		
Male	47 (75)	53 (85)
Female	16 (25)	9 (15)
Age (years)		
Mean +/- SD	71.2 ± 9.4	70.4 ± 9.0
Median [Range]	72.3 [32.5-87.2]	71.2 [48.1-88.1]
Histologic subtype N (%)		
Epithelioïd	51 (81)	53 (85)
Sarcomatoid or Mixed (biphasic)	12 (19)	9 (15)
Performance Status N (%)		
0	19 (31)	25 (40)
1	42 (69)	36 (58)
2	0	1 (2)
Smoking status N (%)		
Smoker / Never Smoker	33 (53) / 29 (47)	35 (56) / 27 (44)
Number of prior line(s) N (%)		
1	44 (70)	43 (69)
2	16 (25)	18 (29)
>2	3 (5)	1 (2)

IFCT

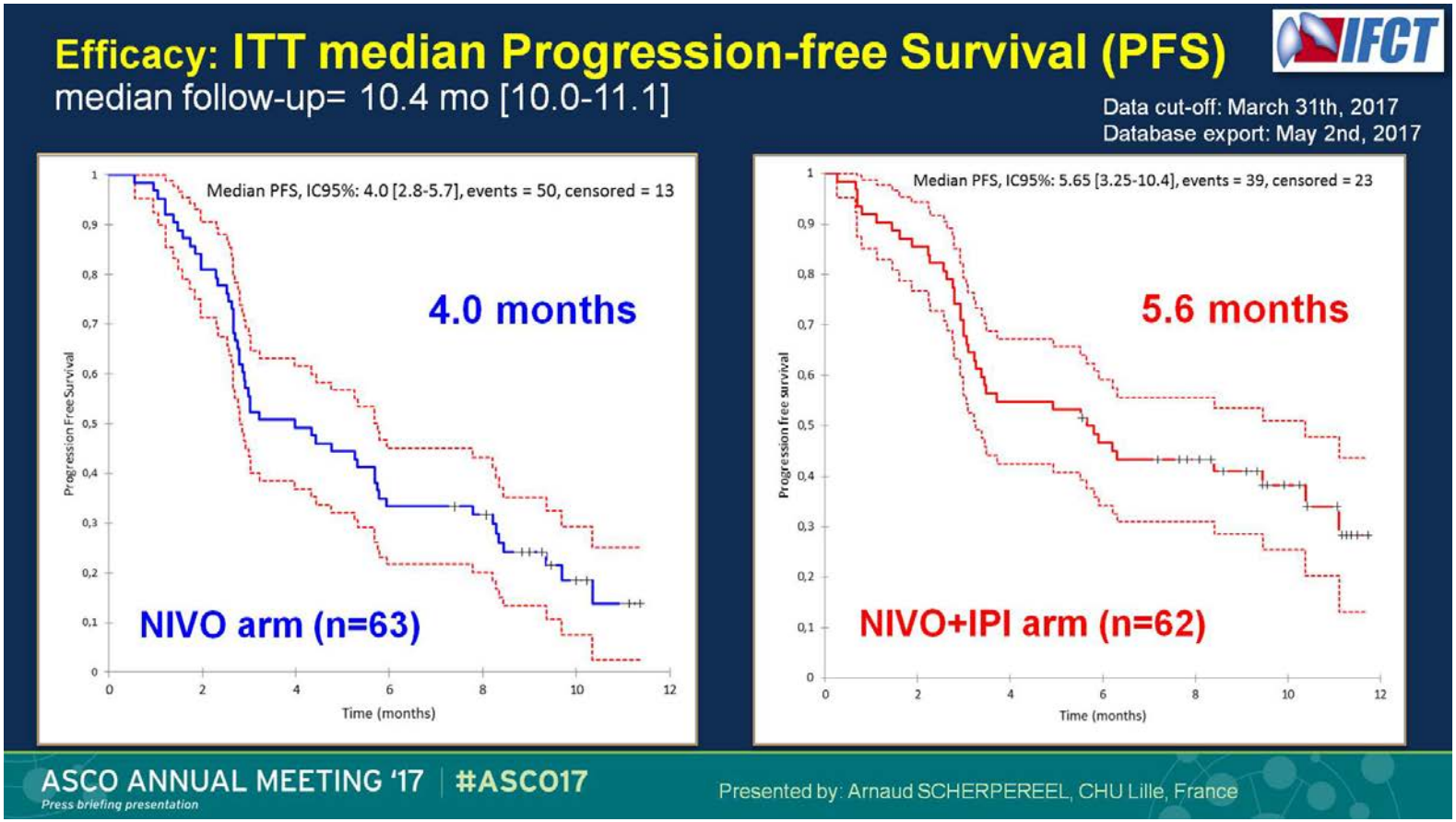
ASCO Press briefing

Presented by: Arnaud SCHERPEREEL, CHU Lille, France

Presented By Arnaud Scherpereel at 2017 ASCO Annual Meeting



Resposta em quase metade dos pacientes em cada braço.

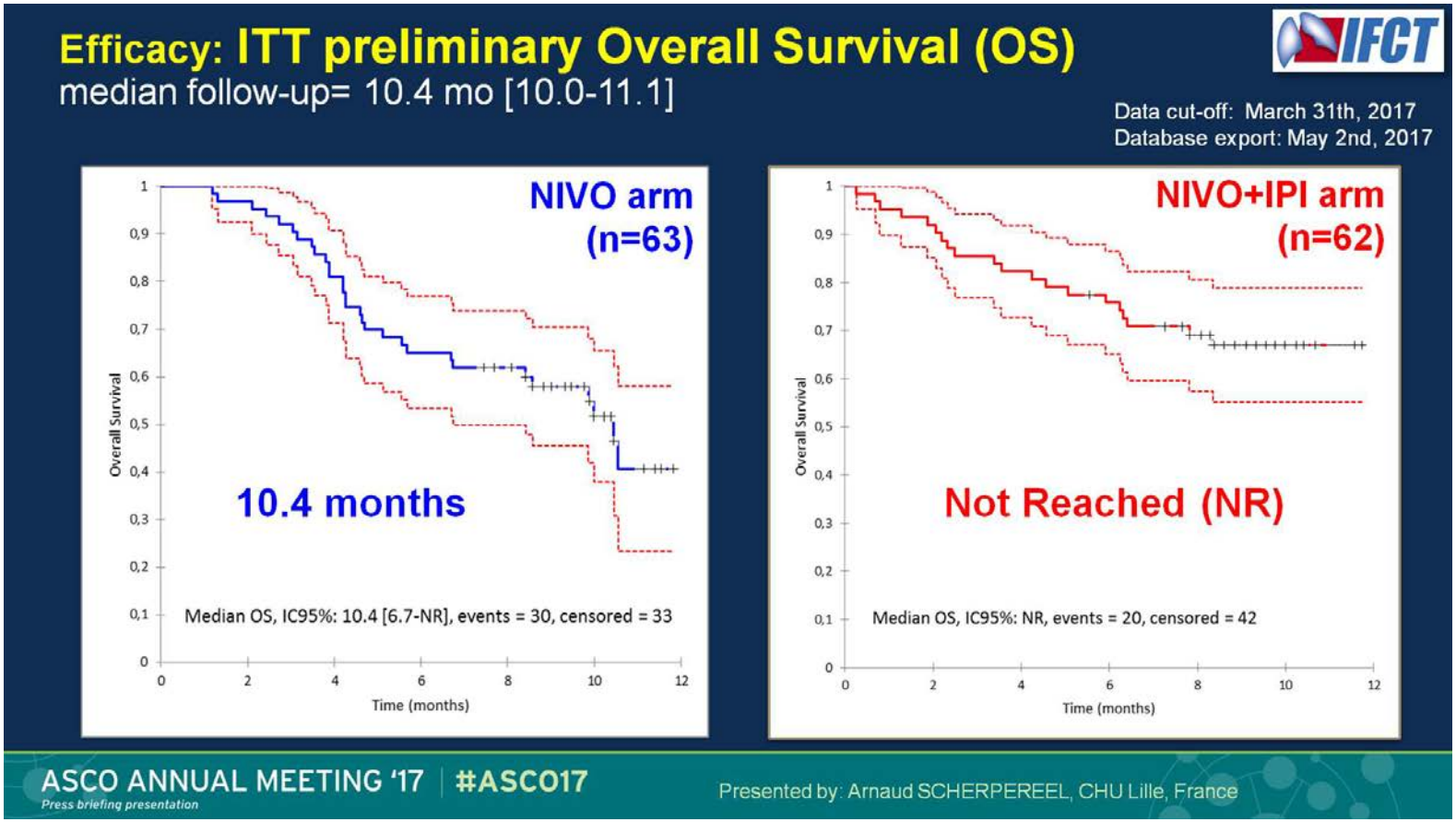


Presented By Arnaud Scherpereel at 2017 ASCO Annual Meeting

PÓS 2017 ASCO ANNUAL MEETING

Grupo ONCOCLÍNICAS Sua vida. Nossa vida.

INSTITUTO ONCOCLÍNICAS



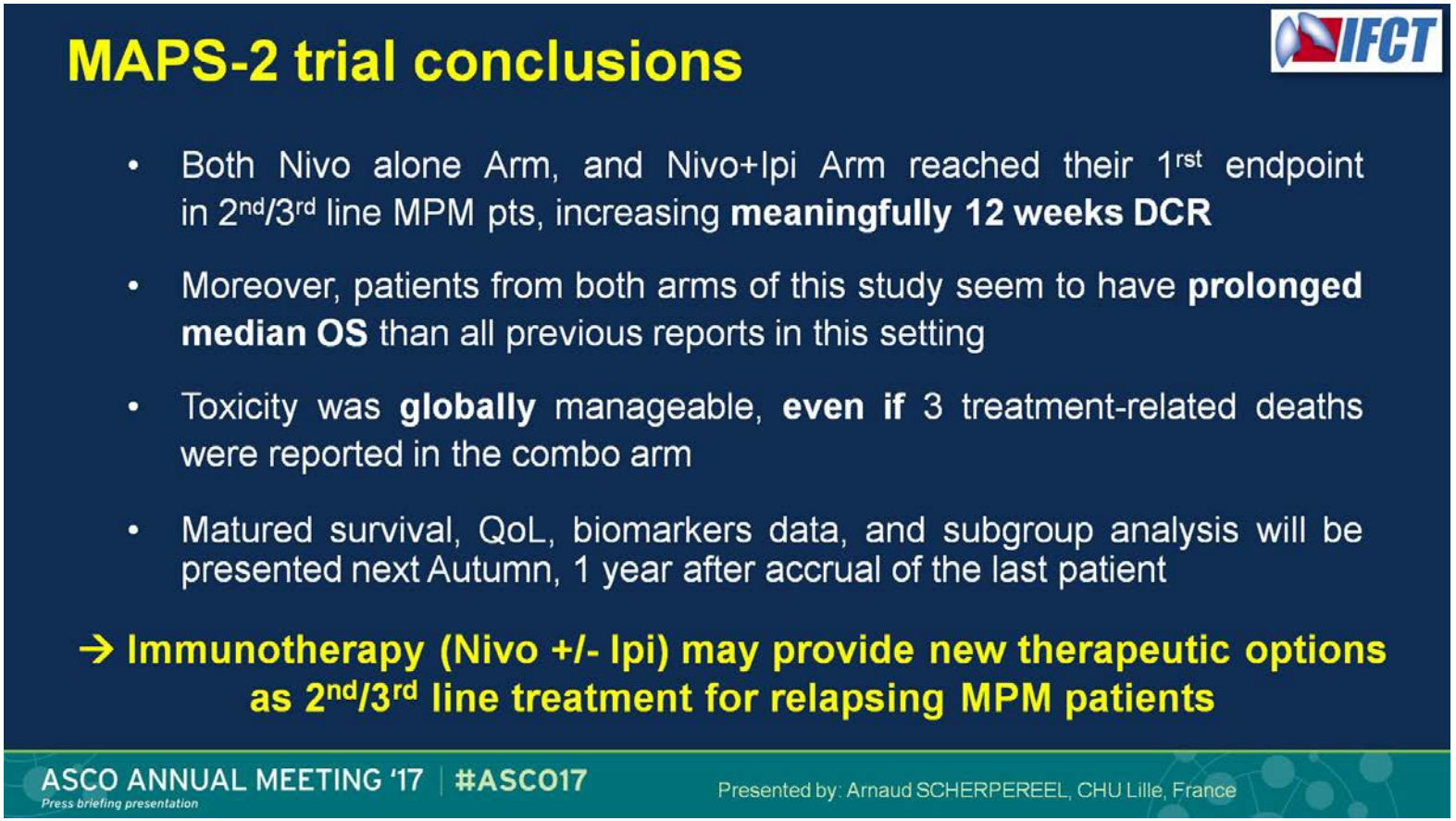
Presented By Arnaud Scherpereel at 2017 ASCO Annual Meeting

MAPS-2 Conclusões

- Em pacientes com mesotelioma avançado após 1-2 esquemas prévios de quimioterapia, tanto nivolumabe quanto a associação de nivo + ipilimumabe atingiram o desfecho estabelecido:
  - Tx controle de doença em12 semanas nos primeiros 108 pacientes: nivo, 44.4%; nivo + ipi, 50.0%
- Sobrevida global de nivolumabe e nivolumabe + ipilimumabe foi elevada (10.4 meses vs Não atingida)
- Efeitos colaterais esperados para a imunoterapia

Efeitos grau 3 e 4: nivo, 9.5%; nivo + ipi, 18.0%

Scherpereel A, et al. ASCO 2017. Abstract LBA8507.



Presented By Arnaud Scherpereel at 2017 ASCO Annual Meeting