Lung Cancer UPDATES
ASCO HIGHLIGTHS
04-08 JUNIO 2021

Iniciativa científica de:
GECP
lung cancer research

CPNCP estadio III irresecable.
Biopsia líquida en CPNM estadio precoz.

Dr. Ernest Nadal
ICO Hospitalet

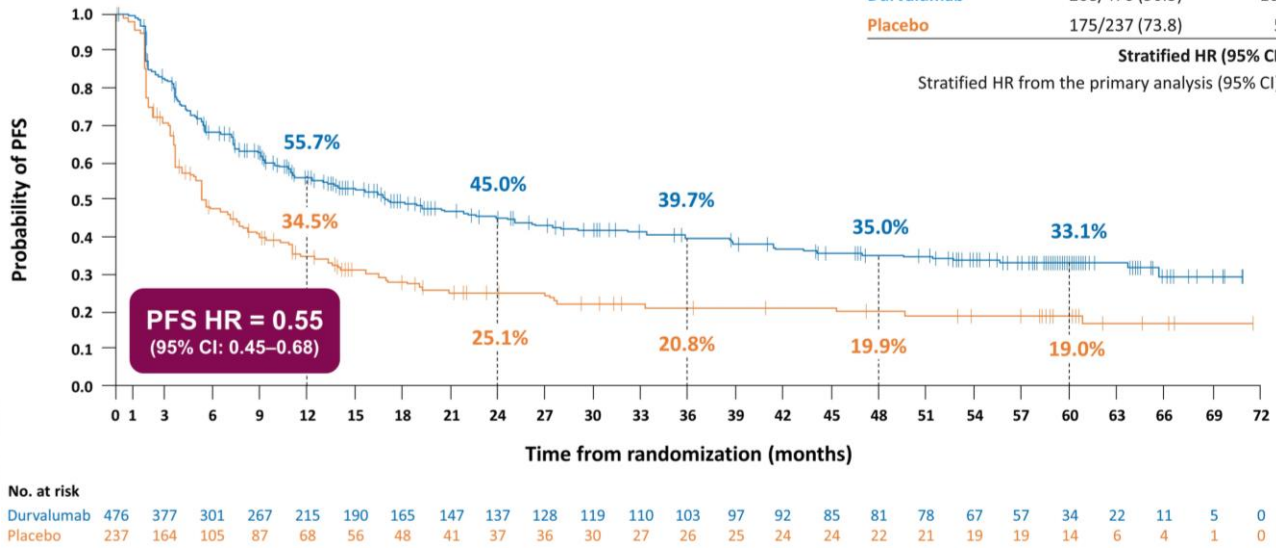
An update from the PACIFIC trial: 5y OS & PFS outcomes

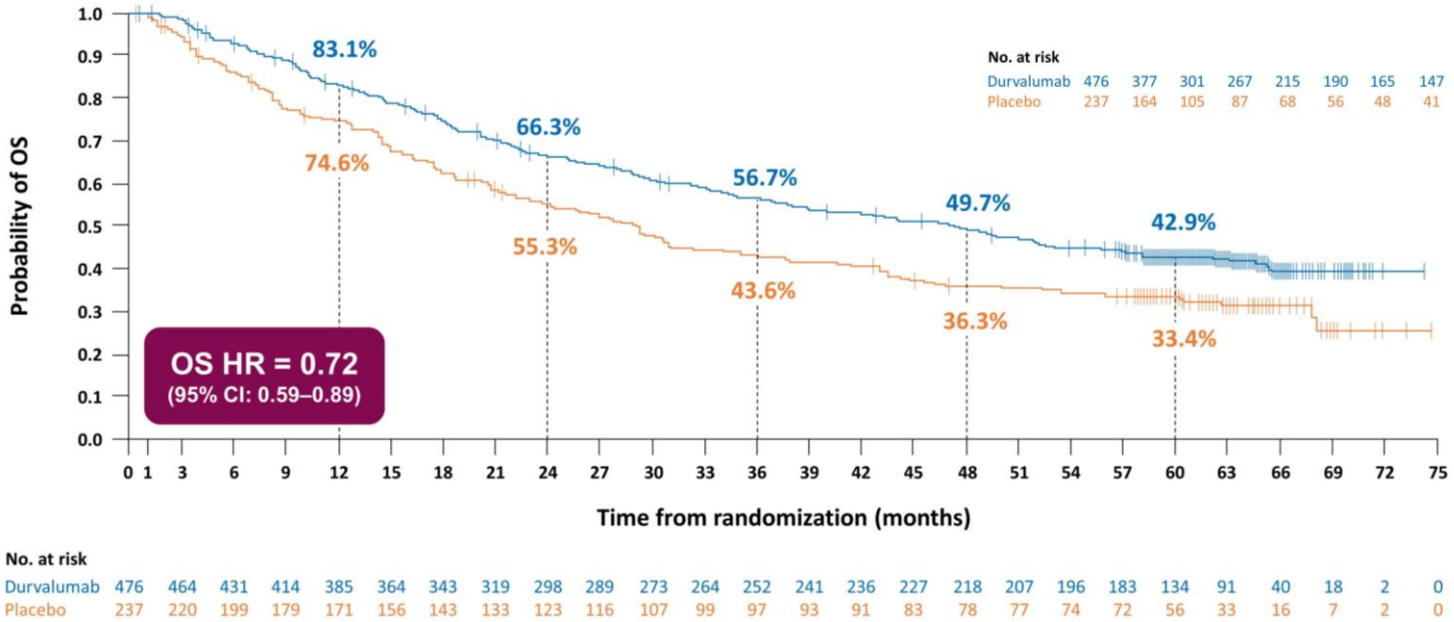
Benefit in survival outcomes is consistent at latter timepoints

	No. of events/ total no. of patients (%)	Median PFS (95% CI), months
Durvalumab	268/476 (56.3)	16.9 (13.0–23.9)
Placebo	175/237 (73.8)	5.6 (4.8–7.7)

Stratified HR (95% CI): 0.55 (0.45–0.68)

Stratified HR from the primary analysis (95% CI):[1] 0.52 (0.42–0.65)





	No. of events/ total no. of patients (%)	Median OS (95% CI), months
Durvalumab	264/476 (55.5)	47.5 (38.1–52.9)
Placebo	155/237 (65.4)	29.1 (22.1–35.1)

Stratified HR (95% CI): 0.72 (0.59–0.89)

Stratified HR from the primary analysis (95% CI):[1,2] 0.68 (0.53–0.87)

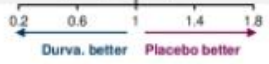
Spigel et al. ASCO 2021

An update from the PACIFIC trial: 5y OS & PFS outcomes

Updated OS & PFS were consistent with the primary analysis results

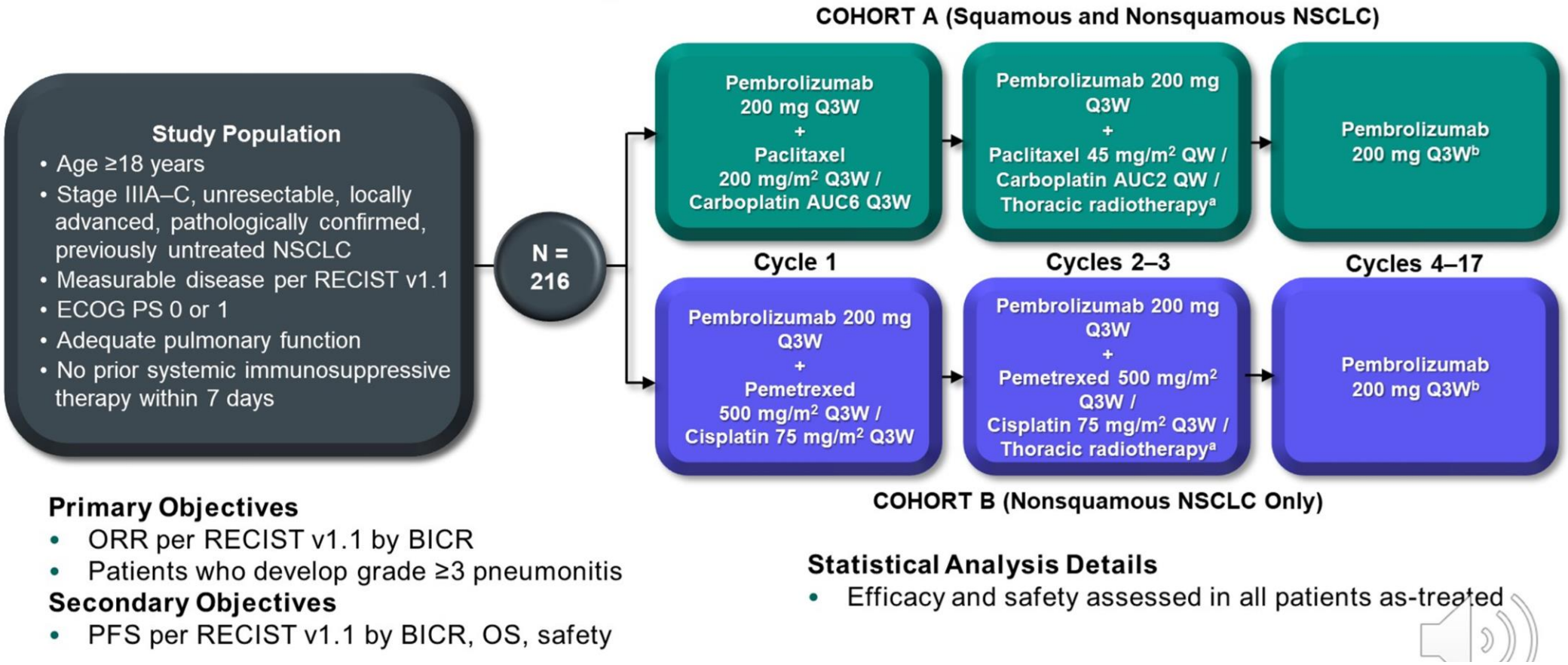
Figure 4. 5-year OS and PFS (BICR) by subgroup (ITT)

	OS			PFS		
	No. of events / No. of patients (%)			No. of events / No. of patients (%)		
	Durvalumab	Placebo	Unstratified HR (95% CI)	Durvalumab	Placebo	Unstratified HR (95% CI)
All patients	264/476 (55.5%)	155/237 (65.4%)	0.72 (0.59–0.87)	268/476 (56.3%)	175/237 (73.8%)	0.58 (0.48–0.70)
Sex						
Male	192/334 (57.5%)	112/166 (67.5%)	0.75 (0.59–0.95)	192/334 (57.5%)	122/166 (73.5%)	0.61 (0.48–0.76)
Female	72/142 (50.7%)	43/71 (60.6%)	0.64 (0.44–0.94)	76/142 (53.5%)	53/71 (74.6%)	0.52 (0.36–0.74)
Age at randomization						
<65 years	130/261 (49.8%)	79/130 (60.8%)	0.66 (0.50–0.87)	140/261 (53.6%)	100/130 (76.9%)	0.46 (0.36–0.60)
≥65 years	134/215 (62.3%)	76/107 (71.0%)	0.79 (0.60–1.05)	128/215 (59.5%)	75/107 (70.1%)	0.76 (0.57–1.01)
Smoking status						
Smoker	244/433 (56.4%)	140/216 (64.8%)	0.75 (0.61–0.93)	246/433 (56.8%)	158/216 (73.1%)	0.61 (0.50–0.75)
Non-smoker	20/43 (46.5%)	15/21 (71.4%)	0.42 (0.21–0.82)	22/43 (51.2%)	17/21 (81.0%)	0.33 (0.17–0.63)
Disease stage						
IIIA	136/252 (54.0%)	91/125 (72.8%)	0.61 (0.47–0.80)	132/252 (52.4%)	95/125 (76.0%)	0.53 (0.40–0.69)
IIIB	121/212 (57.1%)	61/107 (57.0%)	0.86 (0.63–1.17)	130/212 (61.3%)	77/107 (72.0%)	0.64 (0.48–0.85)
Tumor histologic type						
Squamous	138/224 (61.6%)	67/102 (65.7%)	0.82 (0.61–1.09)	138/224 (61.6%)	74/102 (72.5%)	0.71 (0.54–0.94)
All other	126/252 (50.0%)	88/135 (65.2%)	0.62 (0.47–0.81)	130/252 (51.6%)	101/135 (74.8%)	0.48 (0.37–0.63)
Best response to prior treatment						
Complete response	6/9 (66.7%)	3/7 (42.9%)	Not calculated*	5/9 (55.6%)	4/7 (57.1%)	Not calculated*
Partial response	118/237 (49.8%)	68/112 (60.7%)	0.71 (0.52–0.95)	126/237 (53.2%)	85/112 (75.9%)	0.56 (0.43–0.74)
Stable disease	135/223 (60.5%)	81/115 (70.4%)	0.70 (0.53–0.92)	133/223 (59.6%)	84/115 (73.0%)	0.57 (0.44–0.76)
Prior definitive CT						
Cisplatin	134/266 (50.4%)	81/129 (62.8%)	0.65 (0.50–0.86)	146/266 (54.9%)	94/129 (72.9%)	0.55 (0.42–0.71)
Carboplatin	121/199 (60.8%)	69/102 (67.6%)	0.81 (0.60–1.09)	114/199 (57.3%)	76/102 (74.5%)	0.62 (0.47–0.83)
***EGFR* mutation status**						
Positive	17/29 (58.6%)	8/14 (57.1%)	0.85 (0.37–1.97)	21/29 (72.4%)	11/14 (78.6%)	0.82 (0.39–1.71)
Negative	166/317 (52.4%)	109/165 (66.1%)	0.66 (0.52–0.84)	169/317 (53.3%)	124/165 (75.2%)	0.52 (0.41–0.65)
Unknown	81/130 (62.3%)	38/58 (65.5%)	0.85 (0.57–1.24)	78/130 (60.0%)	40/58 (69.0%)	0.74 (0.51–1.09)
PD-L1 expression level						
≥25%	51/115 (44.3%)	27/44 (61.4%)	0.52 (0.32–0.82)	61/115 (53.0%)	33/44 (75.0%)	0.44 (0.29–0.67)
<25%	111/187 (59.4%)	64/105 (61.0%)	0.90 (0.67–1.23)	105/187 (56.1%)	77/105 (73.3%)	0.64 (0.48–0.86)
Unknown	102/174 (58.6%)	64/88 (72.7%)	0.68 (0.50–0.93)	102/174 (58.6%)	65/88 (73.9%)	0.60 (0.44–0.82)
1–24% (post-hoc analysis)	52/97 (53.6%)	29/47 (61.7%)	0.73 (0.46–1.14)	50/97 (51.5)	36/47 (76.6%)	0.51 (0.33–0.78)
≥1% (post-hoc analysis)	103/212 (48.6%)	56/91 (61.5%)	0.61 (0.44–0.85)	111/212 (52.4%)	69/91 (75.8%)	0.47 (0.35–0.64)
<1% (post-hoc analysis)	59/90 (65.6%)	35/58 (60.3%)	1.15 (0.75–1.75)	55/90 (61.1%)	41/58 (70.7%)	0.80 (0.53–1.20)



Spigel et al. ASCO 2021

Keynote-799: Phase 2 trial of pembrolizumab plus platinum chemoradiotherapy for unresectable locally advanced stage III NSCLC



Primary Objectives

- ORR per RECIST v1.1 by BICR
- Patients who develop grade ≥3 pneumonitis

Secondary Objectives

- PFS per RECIST v1.1 by BICR, OS, safety

Statistical Analysis Details

- Efficacy and safety assessed in all patients as-treated

Jabbour et al. ASCO 2021

Keynote-799: Phase 2 trial of pembrolizumab plus platinum chemoradiotherapy for unresectable locally advanced stage III NSCLC

Total Population	Cohort A (Squamous and Nonsquamous) n = 112		Cohort B (Nonsquamous) n = 102	
ORR, % (95% CI)	**70.5 (61.2–78.8)**		**70.6 (60.7–79.2)**	
CR	4 (3.6)		5 (4.9)	
PR	75 (67.0)		67 (65.7)	
SD	20 (17.9)		23 (22.5)	
PD	1 (0.9)		0	
Not evaluable[a]/No assessment[b]	2 (1.8) / 10 (8.9)		0 / 7 (6.9)	
DOR, median (range),[c] mo	NR (1.7+ to 19.7+)		NR (1.8+ to 21.4+)	
DOR ≥12 mo,[c] %	79.7		75.6	
PFS,[c] median (95% CI), mo	NR (16.6–NR)		NR (NR–NR)	
12-mo PFS rate, %	67.1		71.6	
OS,[c] median (95% CI), mo	NR (NR–NR)		NR (21.9–NR)	
12-mo OS rate, %	81.3		87.0	
PD-L1 Status	**TPS <1% (n = 21)**	**TPS ≥1% (n = 66)**	**TPS <1% (n = 28)**	**TPS ≥1% (n = 40)**
ORR, n (%)	14 (66.7)	50 (75.8)	20 (71.4)	29 (72.5)
Histology	**Nonsquamous (n = 39)**	**Squamous (n = 73)**	**Nonsquamous (n = 102)**	**Squamous (n = 0)**
ORR, n (%)	27 (69.2)	52 (71.2)	72 (70.6)	NA

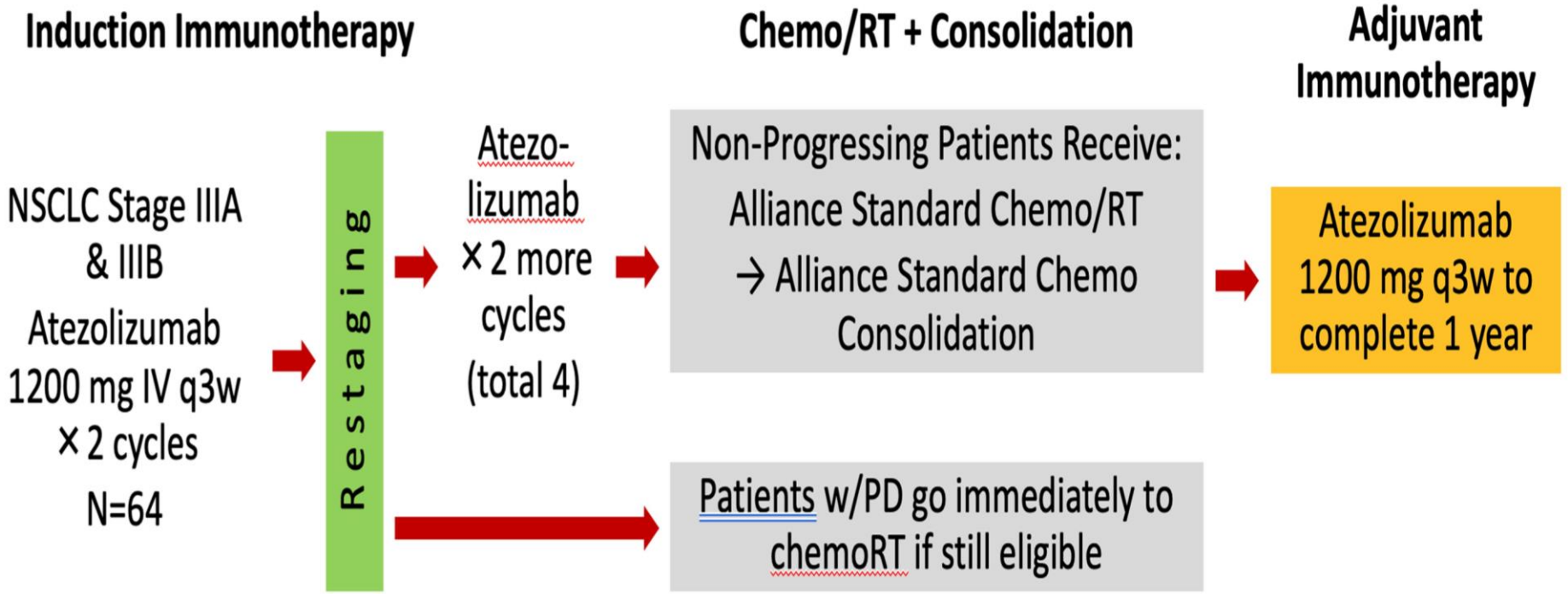
Jabbour et al. ASCO 2021

Keynote-799: Phase 2 trial of pembrolizumab plus platinum chemoradiotherapy for unresectable locally advanced stage III NSCLC

	Cohort A (Squamous and Nonsquamous) n = 112	**Cohort B** (Nonsquamous) n = 102
Grade ≥3 pneumonitis (all cause),[a,b] n (%) [95% CI]	**9 (8.0) [3.7–14.7]**	**7 (6.9) [2.8–13.6][c]**
Treatment-related AEs, n (%)	105 (93.8)	99 (97.1)
Grades 3–5	72 (64.3)	51 (50.0)
Led to death[b]	4 (3.6)	1 (1.0)
Led to discontinuation of any treatment component	38 (33.9)	19 (18.6)
Immune-mediated AEs and infusion reactions, n (%)	58 (51.8)	42 (41.2)
Grades 3–5	18 (16.1)	9 (8.8)
Led to death[b]	4 (3.6)	1 (1.0)
Led to discontinuation of any treatment component	21 (18.8)	11 (10.8)

Jabbour et al. ASCO 2021

AFT-16: Phase 2 trial of neoadjuvant and adjuvant atezolizumab and chemoradiation for stage III NSCLC



- 64 pts with unresectable stage III NSCLC, PS 0-1, no active autoimmune disease or significant organ dysfunction enrolled at 13 ALLIANCE sites from 11/2017 to 7/2019.
- 62 pts receiving at least 1 dose of atezolizumab are included in this analysis.

Ross et al. ASCO 2021

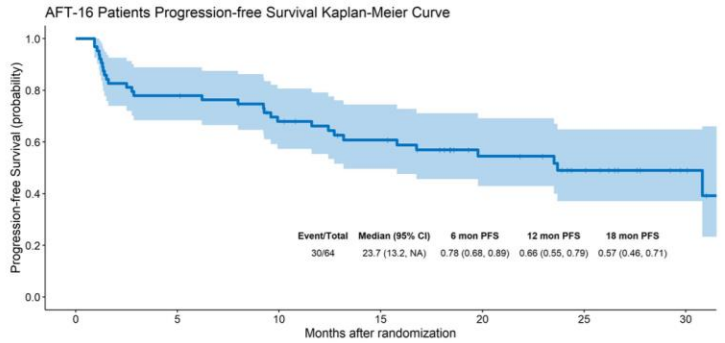
AFT-16: Phase 2 trial of neoadjuvant and adjuvant atezolizumab and chemoradiation for stage III NSCLC

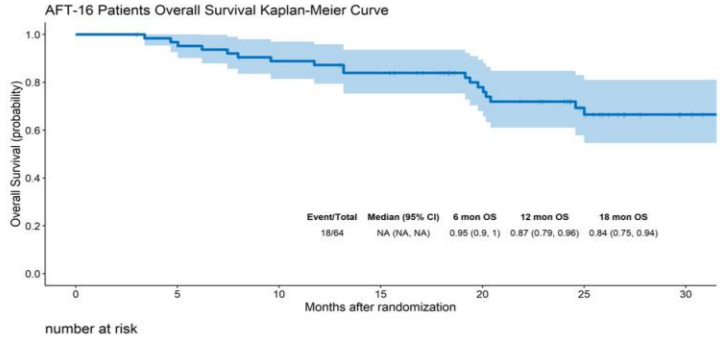
Pt characteristics:

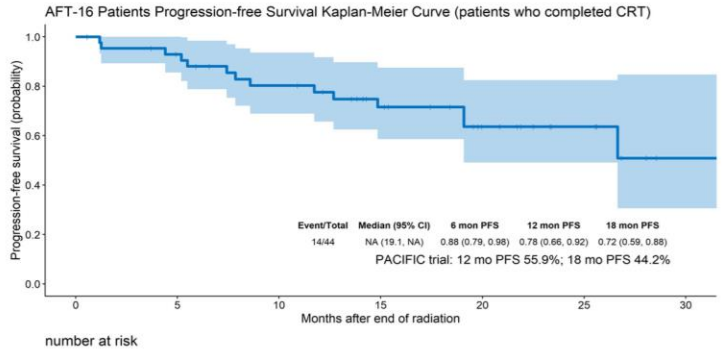
- Median age 63.9 y, 51.6% female, 77.4% white, 61.3% former and 11.3% never-smokers and 56.5% ECOG PS = 1

Outcomes:

- Median PFS = 23.7 mo
- PFS at 12 & 18 mo 66% and 57%
- OS at 18 mo = 84% (CI 75-94%)
- 1 ea gr 3 pneumonitis/pneumonia/colitis
- 1 gr 4 Guillain-Barre syndrome
- PFS was assessed from end of CRT in an exploratory analysis
- PFS 12 and 18 mo from end of CRT was 78% and 72% respectively (55.9% and 44.2% PFS at 12 & 18 mo reported for PACIFIC)







Ross et al. ASCO 2021

Indirect comparison of studies evaluating concurrent chemoradiotherapy and ICI in unresectable stage III NSCLC

	PACIFIC[1]	NICOLAS[2]	DETERRED (part 2)[3]	KN799[4]	AFT-16[5]
1y PFS	56%	53.7%	57%	67-72%	78%(*)
1y OS	81%	75.7%	79%	81-87%	87%
G3-5 TRAEs	29.9%	9-18%	67%	50-64%	NA
G≥3 pneumonitis	3.4%	11.7%	3%	7-8%	3.1%
G5 AEs	4.4%	6%	NA	3.6%	NA

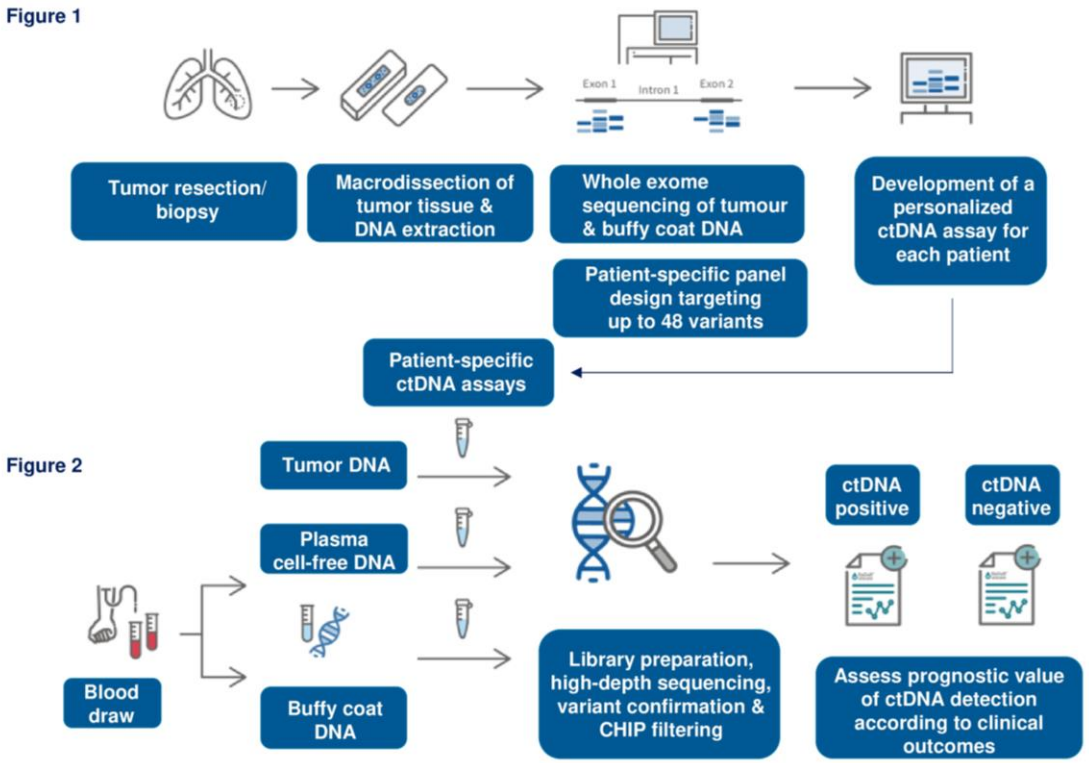
(*) for patients who completed radiotherapy

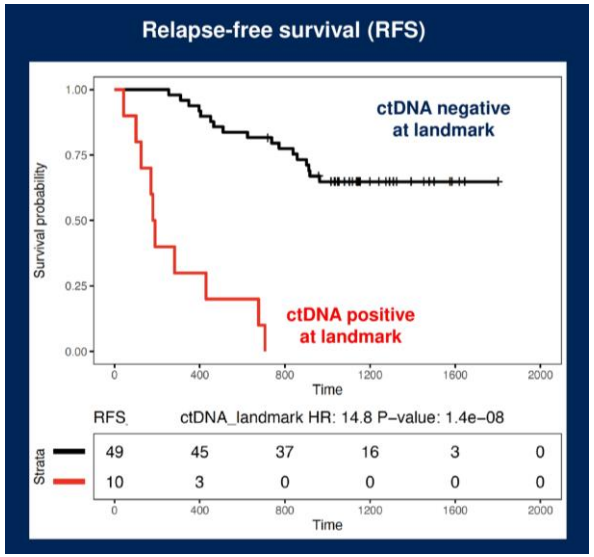
1) Spiegel et al. ASCO 2021; 2) Peters et al. J Thorac Oncol 2021; 3) Lin et al. ASCO 2019; 4) Jabbour et al. ASCO 2021

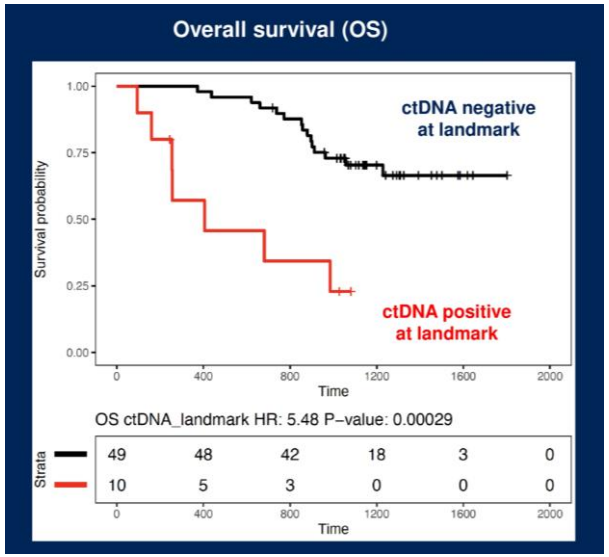
Residual ctDNA after treatment predicts early relapse in patients with early stage NSCLC

ctDNA detection after curative treatment is associated with shorter DFS

N=88 pts (78% surgery; 22% chemorad)



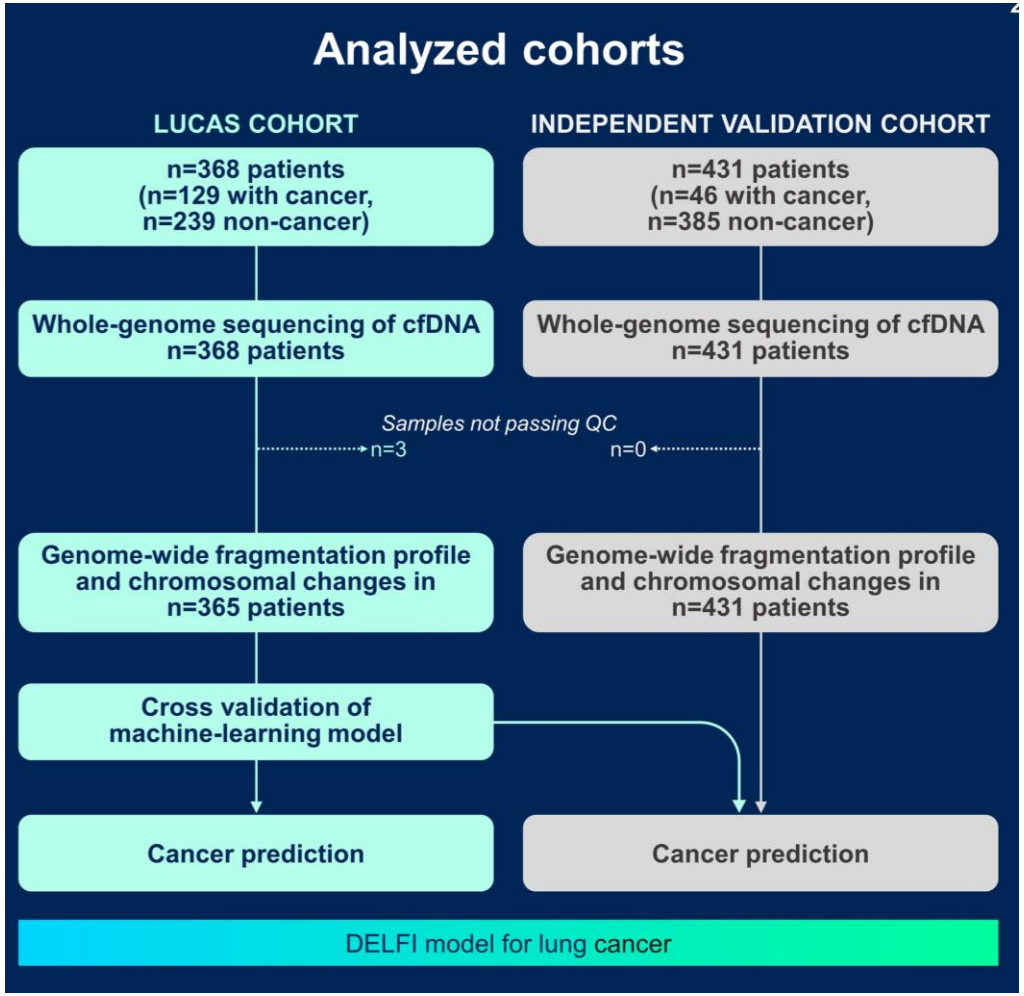


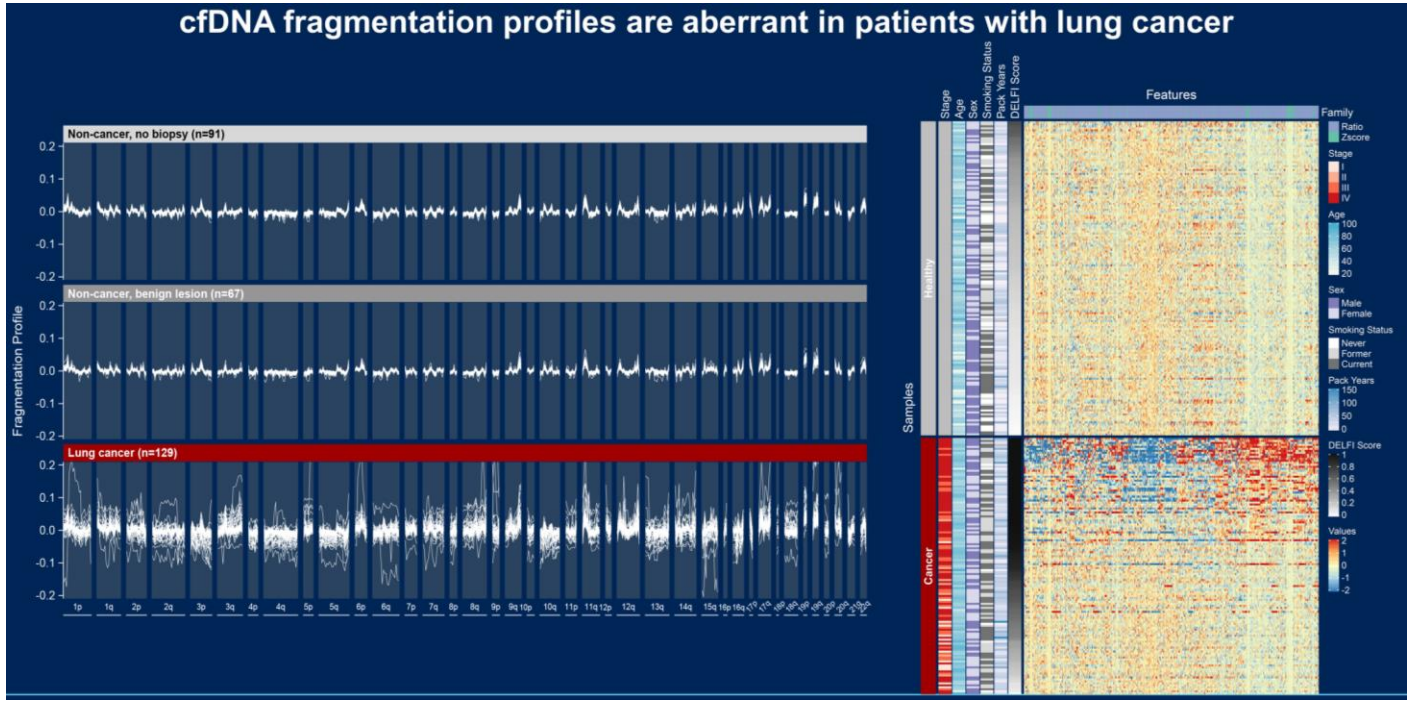


Gale et al. ASCO 2021

Early detection of lung cancer using cell-free DNA fragmentation

cfDNA fragmentation is highly variable in lung cancer patients compared with non-cancer subjects which have more consistent fragmentation patterns

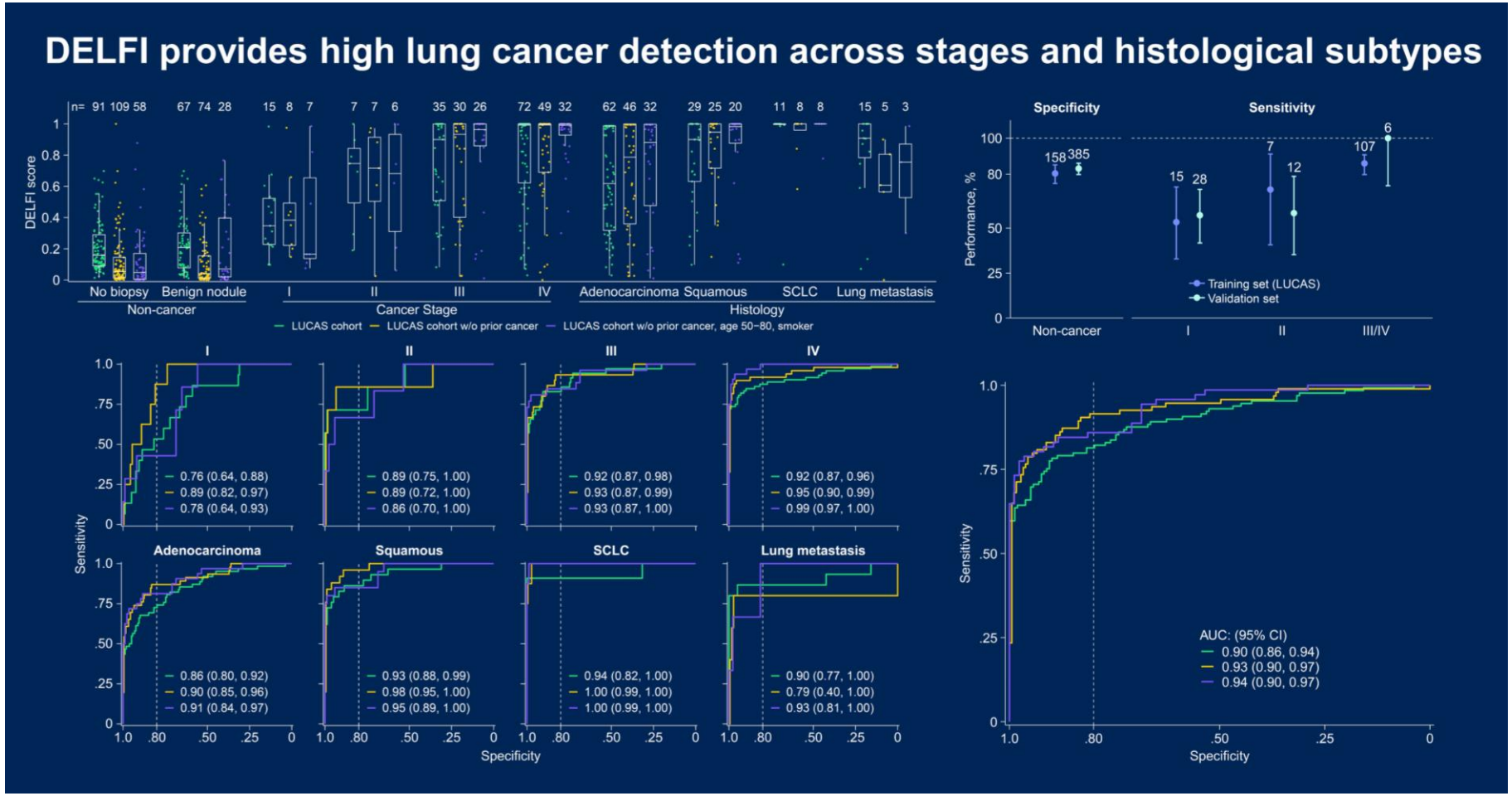




Mathios et al. ASCO 2021

Early detection of lung cancer using cell-free DNA fragmentation

cfDNA fragmentation can distinguish lung cancer individuals across stages and histological subtypes and DELFI score is associated with overall survival



Mathios et al. ASCO 2021

Muchas gracias por vuestra atención