

# The role of immunotherapy in the first-line treatment of elderly advanced non-small cell lung cancer

Alessia Spagnuolo and Cesare Gridelli

**Table S1.** A. The KEYNOTE-010, KEYNOTE-024 and KEYNOTE-042 pooled analysis: overall survival following treatment with pembrolizumab or chemotherapy by patient age ( $\geq 75$  or  $< 75$  years) in the population with PD-L1 TPS  $\geq 1\%$  or  $\geq 50\%$  (a) and in an analysis of patients from each individual trial (b). B. FDA pooled analysis of randomized controlled trials with anti-PD-(L)1 combined with chemotherapy versus immunotherapy alone for first-line treatment of advanced NSCLC with PD-L1 score 1-49%.

1A				
a		Overall survival by age HR (95% CI)		
PD-L1 TPS ≥1% PD-L1 TPS ≥50%		Patients ≥ 75 years	Patients < 75 years	
		0.76 (0.56-1.02)	0.76 (0.69-0.84)	
		0.40 (0.25-0.64)	0.67 (0.57-0.78)	
b		Overall survival by age HR (95% CI)		
KEYNOTE-010 KEYNOTE-024 KEYNOTE-042		Patients ≥ 75 years	Patients < 75 years	
		0.72 (0.43-1.21)	0.64 (0.55-0.75)	
		0.49 (0.17-1.39)	0.64 (0.42-0.97)	
		0.89 (0.59-1.35)	0.79 (0.68-0.92)	
1B				
		Overall survival by age HR (95% CI)		
		Patients <65 years	Patients 65-74 years	Patients ≥75 years
		0.63 (0.43-0.92)	0.61 (0.38-0.97)	0.95 (0.42-2.14)

Abbreviations. CI: confidence interval; HR: hazard ratio; PD-L1 TPS: programmed death-ligand 1 tumor proportion score

**Table S2.** Overall survival by age of patients in randomized phase III clinical trials with mono-immunotherapy for advanced stage NSCLC.

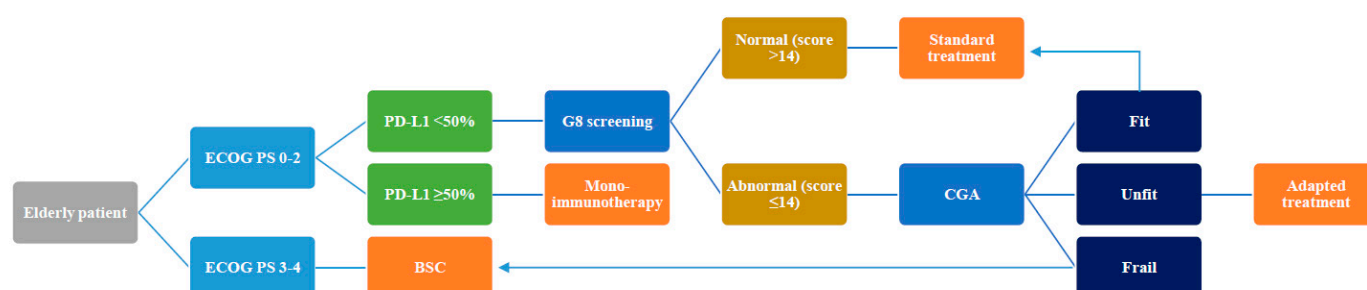
Study	Treatment line	PD-L1 expression	Intervention/arms	Overall survival by age HR (95% CI)
KEYNOTE-024	First-line	PD-L1 $\geq 50\%$	Pembrolizumab vs platinum-based chemotherapy	$< 65$ : 0.60 (0.38-0.96) $\geq 65$ : 0.64 (0.42-0.98)
KEYNOTE-042	First-line	PD-L1 $\geq 1\%$	Pembrolizumab vs platinum-based chemotherapy	$< 65$ : 0.81 (0.67-0.98) $\geq 65$ : 0.82 (0.66-1.01)
IMpower 110	First-line	PD-L1 $\geq 1\%$	Atezolizumab vs platinum-based chemotherapy	$< 65$ : 0.59 (0.34-1.04) 65-74: 0.63 (0.34-1.19) $\geq 75$ : 0.79 (0.18-3.56)
IPSOS	First-line	Stratification factor	Atezolizumab vs vinorelbine or gemcitabine	0.78 (0.63-0.97) $< 70$ : 0.75 (0.49-1.14) 70-79: 0.68 (0.49-0.94) $\geq 80$ : 0.97 (0.66-1.44)
EMPOWER-Lung 1	First-line	PD-L1 $\geq 50\%$	Cemiplimab vs platinum-based chemotherapy	$< 65$ : 0.66 (0.44-1.00) $\geq 65$ : 0.48 (0.30-0.76)

Abbreviations. CI: confidence interval; HR: hazard ratio; PD-L1: programmed death-ligand 1.

**Table S3.** Overall survival by age of patients in randomized phase III clinical trials with immunotherapy in combination regimens for advanced stage NSCLC.

Study	Treatment line	Intervention/arms	Overall survival by age HR (95% CI)
KEYNOTE-189	First-line	Platinum-based chemotherapy + pembrolizumab or placebo	<65: 0.43 (0.31-0.61)
			≥65: 0.64 (0.43-0.95)
			≥75: 1.54 (0.76-3.14)
KEYNOTE-407	First-line	Platinum-based chemotherapy + pembrolizumab or placebo	<65: 0.52 (0.34-0.80)
			≥65: 0.74 (0.51-1.62)
			≥75: 0.81 (0.43-1.55)
IMpower 150	First-line	Platinum-based chemotherapy and bevacizumab +/- atezolizumab	<65: 0.83 (0.65-1.04)
			65-74: 0.72 (0.54-0.97)
			≥75: 0.97 (0.58-1.62)
IMpower 130	First-line	Platinum-based chemotherapy +/- atezolizumab	<65: 0.79 (0.58-1.08)
			≥65: 0.78 (0.58-1.05)
			75-84: 0.54 (0.27-1.05)
IMpower 131	First-line	Platinum-based chemotherapy +/- atezolizumab	<65: 0.89 (0.68-1.15)
			65-74: 0.84 (0.63-1.13)
			≥75: 0.74 (0.45-1.23)
EMPOWER-Lung 3	First-line	Platinum-based chemotherapy + cemiplimab or placebo	<65: 0.57 (0.40-0.81)
			≥65: 0.88 (0.56-1.37)
CheckMate 227	First-line	Nivolumab + ipilimumab vs platinum-based chemotherapy	PD-L1 ≥1%:
			<65: 0.70 (0.56-0.89)
			65-74: 0.84 (0.65-1.08)
			≥75: 0.93 (0.58-1.49)
			PD-L1 <1%:
			<65: 0.69 (0.51-0.93)
CheckMate 9LA	First-line	Platinum-based chemotherapy + nivolumab + ipilimumab vs platinum-based chemotherapy	<65: 0.61 (0.47-0.80)
			65-74: 0.62 (0.46-0.85)
			≥75: 1.21 (0.69-2.12)
POSEIDON	First-line	Tremelimumab + durvalumab + platinum-based chemotherapy and durvalumab + platinum-based chemotherapy vs chemotherapy alone	<65: 0.79 (0.62-1.00)
			≥65: 0.74 (0.58-0.94) and
			<65: 0.86 (0.68-1.10)

Abbreviations. CI: confidence interval; HR: hazard ratio; PD-L1: programmed death-ligand 1.

**Figure S1.** Therapeutic algorithm for the first-line treatment of elderly advanced NSCLC. Abbreviations: BSC: Best Supportive Care; CGA: Comprehensive Geriatric Assessment; ECOG PS: Eastern Cooperative Oncology Group Performance Status; PD-L1: Programmed death-ligand 1.