991P - *EGFR* exon 20 insertions in non-small cell lung cancer (NSCLC): Impact of *TP53* mutation status and value of immune-checkpoint blockade (ICB)

Type: Abstract

Category: NSCLC, metastatic

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Background

About 4% of all *EGFR* mutations account as exon 20 insertions, which convey resistance to the first three generations of *EGFR*-tyrosine kinase inhibitors (TKIs). Recent research has revealed new drugs to target these mutations specifically. However, little is known about the impact of immune-checkpoint blockade (ICB) in this subgroup, especially in patients with co-occurring *TP53* mutations.

Methods

We analyzed co-occurring mutations in patients with *EGFR* exon 20 insertions and their influence on the efficacy of systemic treatment. The main focus was impact of ICB on overall survival (OS) in these patients with or without *TP53* mutations. Co-mutational status was assessed using next-generation-sequencing (NGS) panels. *TP53* mutations were further divided into truncating vs. non-truncating mutations.

Results

Real-world-data (RWD) of 159 advanced NSCLC patients with *EGFR* exon 20 insertion in the timeframe of 2014-2020 were analyzed. *TP53* mutation was the most common co-occurring mutation in 69 (43.7%) patients. OS of *TP53* wildtype patients was trended towards longer OS with 20 vs. 12 months, without reaching significance (p=0.092). No difference of OS referring to the subtype of *TP53* mutations was observed (p=0.412). In total, 66 pts were treated with ICB in one of the treatment lines reaching significantly longer OS of 22 vs. 10 months (p=0.018). In patients with co-occurring *TP53* mutation, patients who received ICB (n=33) had significantly longer OS than those without ICB exposure 16 vs. 8 months (p=0.048). Partly lack of significance might be explainable by a median follow-up time of 1498 days (4.1 years).

Figure 1: Baseline characteristics, treatment patterns and co-occurring mutations in the cohort

	N	%
Sex	**159**	
male	60	37.7%
female	99	62.3%
Age at diagnosis (years)		
mean	65.87 (range: 32-88)	
median	68	
Histology		
adenocarcinoma	153	96.2%
sqamous cell carcinoma	5	3.1%
other	1	0.6%
Smoking history		
yes	80	50.3%
no	61	38.4%
n/a	18	11.3%
ECOG performance status		
0-1	98	61.6%
>1	7	4.4%
n/a	54	34.0%
Tumor stage at diagnosis		
I	15	9.4%
II	7	4.4%
IIIA	13	8.2%
IIIB	6	3.8%
IV	118	74.2%

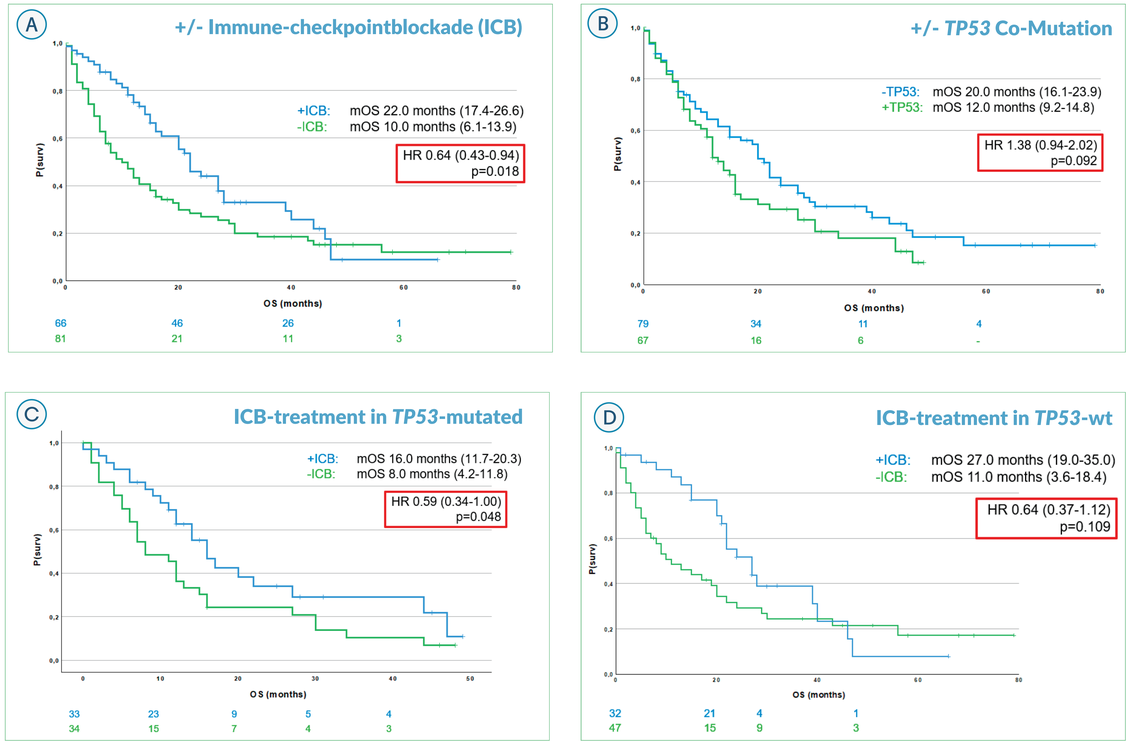
Treatment with ICB in any line		
yes	66	41.5%
ICB monotherapy	*41*	*62.1%*
ICB combinational therapy	*25*	*37.9%*
ICB from 1st line	*53*	*80.3%*
ICB from 2nd or further lines	*13*	*19.7%*
no	93	58.5%

Co-occurring mutations		
TP53	69/158	**43.7%**
truncating	*18*	*26.1%*
other	*51*	*73.9%*
KRAS	3/158	**1.9%**
PTEN	4/155	**2.6%**
BRAF	1/158	**0.6%**
CTNNB1	5/155	**3.2%**
DDR2	2/102	**0.0%**
FGFR3	1/107	**0.9%**
KEAP1	2/55	**3.6%**
PIK3CA	9/157	**5.7%**
PD-L1	52/110	**47.3%**

12 patients never reached stage IIIB/IV
- excluded from OS evaluation → n for OS = 147

Figure 2: Kaplan Meier curves demonstrating survival differences in subgroups

In brackets: 95% confidence interval. p-values estimated by Log rank, HR by Cox proportional hazards regression



Conclusions

Regardless of subtype, *TP53* co-mutation seems to be a strong negative prognostic factor in NSCLC pts with *EGFR* exon 20 insertions. However, in contrast to common *EGFR* mutations, these pts seem to benefit from the ICB, regardless of treatment line or regimen (mono- or combinational therapy).