FPN – 1107P

BRAF mutations and fusions in a real-world cohort of NSCLC patients

Jiaxin Niu[1], Elizabeth Mauer[2], Alexander S. Barrett[2], Arya Ashok[2]

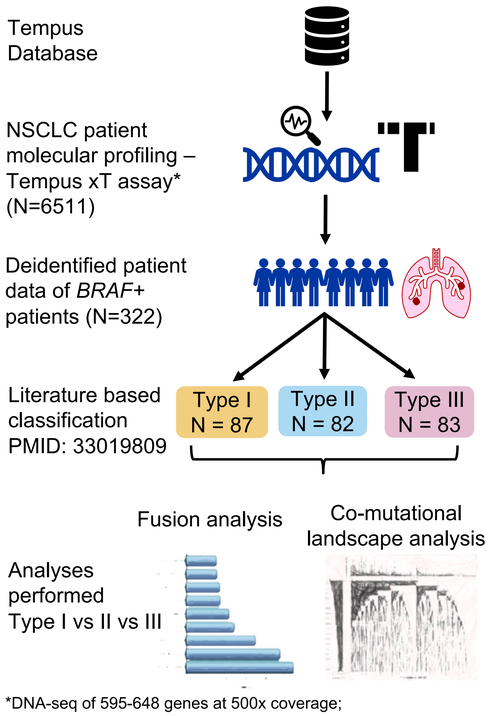
[1]Banner MD Anderson, Gilbert, AZ USA; [2]Tempus Labs, Inc., Chicago, IL

INTRODUCTION

- BRAF V600E (type I) mutant non-small cell lung cancer (NSCLC) is well characterized
- Less is known about other types of BRAF mutations or BRAF fusions in this population
- Previous studies have suggested that different types of BRAF mutations may have varied clinical implications, motivating further study to guide therapeutic options in clinical practice.

We characterize the type of BRAF and co-occurring mutations as well as BRAF fusions in a real-world NSCLC cohort using comprehensive genomic profiling (CGP)

METHODS



*DNA-seq of 595-648 genes at 500x coverage; Whole-exome capture RNA-seq

SUMMARY

- **DNA and RNA-seq analysis showed that BRAF Class II and Class III mutations are associated with distinct genomic characteristics as compared to Class I, such as more frequent concurrent RAS and NF1 mutations.**
- BRAF fusions were also detected, predominantly via RNA sequencing

RESULTS

- Genomic analysis identified several significant differences in the co-mutational landscape of distinct BRAF classes including EGFR, KRAS, and NF1 (q<0.05)
- Pathogenic EGFR mutations were more prevalent in class I (20%) vs class II (6.1%) and class III (7.2%)
- By contrast, KRAS mutations were more prevalent in class II (13%) and class III (19%) compared to class I (3.4%)
- NF1 mutations were more prevalent in class II (9.8%) and class III (12%) vs class I (2.3%)
- DNA and RNA gene fusion analysis identified 13 patients with reported pathogenic BRAF fusions; of these, 11/13 were only identified via RNA-seq

Patient Demographics

Patient Characteristic	Type I N = 87	Type II N = 82	Type III N = 83	p-value
Age				0.9
Median (IQR)[1]	68 (62, 74)	67 (60, 76)	69 (61, 76)	
Range	48,89	41,88	46,92	
Unknown	9	8	8	
Gender				0.7
Female	49 (56%)	42 (51%)	42 (51%)	
Male	38 (44%)	40 (49%)	40 (49%)	
Unknown	0	0	1	
Race				0.3
White	40 (73%)	40 (75%)	33 (67%)	
Black/African American	11 (20%)	10 (19%)	12 (24%)	
Asian	3 (5.5%)	0 (0%)	1 (2%)	
Alaska Native	1 (1.8%)	0 (0%)	0 (0%)	
Other	0 (0%)	3 (5.7%)	3 (6.1%)	
Unknown	32	29	34	
Ethnicity				0.8
Non-Hisp/Latino	30 (91%)	23 (96%)	34 (94%)	
Hispanic/Latino	3 (9.1%)	1 (4.2%)	2 (5.6%)	
Unknown	54	58	47	
Smoking Status				**<0.0001**
Current/former smoker	60 (76%)	73 (97%)	71 (95%)	
Never smoker	19 (24%)	2 (2.7%)	4 (5.3%)	
Unknown	8	7	8	

[1]*IQR: Interquartile range*

Table 1. Demographic characteristic information for all patients included in this study

BRAF Alteration Status

Characteristic	N = 322[1]
Type I	87 (27%)
Type II	82 (25%)
Type III	83 (26%)
other mutation	22 (6.8%)
CN loss	26 (8.1%)
CN amplification	8 (2.5%)
DNA and RNA fusion	2 (0.6%)
RNA fusion	11 (3.4%)
CN amplification and RNA fusion	1 (0.3%)

[1]*n (%)*

Table 2. Status of BRAF alterations in patients

Somatic Co-mutations

Characteristic	Type I, N = 87[1]	Type II, N = 82[1]	Type III, N = 83[1]	q-value[3]
TP53	40 (46%)	56 (68%)	55 (66%)	0.010
SETD2	28 (32%)	3 (3.7%)	3 (3.6%)	<0.001
EGFR	**10 (11%)**	**0 (0%)**	**1 (1.2%)**	**0.011**
KRAS	3 (3.4%)	11 (13%)	16 (19%)	0.010
STK11	0 (0%)	13 (16%)	15 (18%)	<0.001
KEAP1	2 (2.3%)	5 (6.1%)	12 (14%)	0.011
NF1	2 (2.3%)	8 (9.8%)	10 (12%)	0.048

[1]*n (%)*, [2]*Pearson's Chi-squared test*, [3]*False discovery rate correction for multiple testing*

Table 3. Somatic co-mutations showing prevalence of somatic gene alterations between the three BRAF types. Note - Copy number gain and loss omitted for EGFR.

Immune Markers

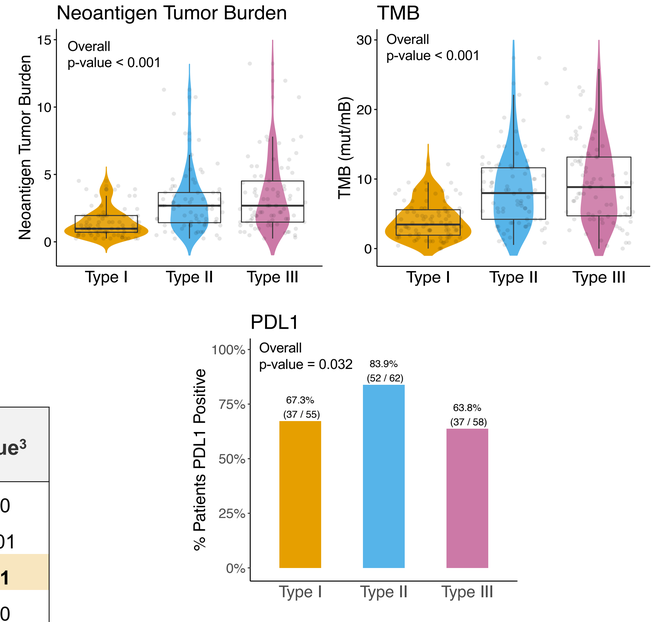


Figure 1. A comparison of the BRAF mutation types with resect to Neoantigen tumor burden, TMB and PD-L1 expression levels. The overall (Types I vs II vs III) p-values were significant (<0.005)

Acknowledgements: We thank Amrita A. Iyer, Ph.D, for assistance with poster preparation and review.

Correspondence: Jiaxin.Niu@bannerhealth.com