

## **Blood platelet RNA profiles do not enable for nivolumab response prediction at baseline in patients with non-small cell lung cancer**

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### Contents

Table S1 - Patient characteristics per hospital

Table S2 - Patient characteristics per randomized group

Table S3 - ANOVA comparison nivolumab responders versus non-responders (separate file)

Table S4 – Patient characteristics per sample (separate file)

Figure S1 - ThromboSeq bioinformatics QCs

Figure S2 - Post-hoc analyses

**Table S1 - Patient characteristics per hospital**

	NKI (N=128)	AUMC (N=59)	UMCG(N=99)	Total (N=286)	P-value
<b>Patient</b>					
Male sex – No. (%)	66 (51.6)	39 (66.1)	53 (53.5)	158 (55.2%)	0.167 <sup>A</sup>
Age (yr) – Mean (95% CI)	63.6 (62.0-65.2)	63.9 (61.7-66.1)	65.0 (62.9-67.1)	64.1 (63.0-65.3)	0.535 <sup>B</sup>
Smoking status	17 (13.3)	3 (5)	4 (4)	24 (8.4)	0.015 <sup>C</sup>
Never / Current / Stop - No. (%)	29 (22.7) 78 (60.9)	14 (23.7) 31 (52.5)	15 (15.1) 80 (80.8)	58 (20.3) 189 (66.1)	
Pack Years – Mean (95% CI)	34.7 (30.8-38.6)	31.3 (27.2-35.4)	34.7 (31.2-38.1)	34.2 (31.9 – 36.5)	0.613 <sup>B</sup>
WHO Performance status ≥ 2 – no / total known patients	13 /122	6 / 45	14 / 99	33 / 266	0.729 <sup>B</sup>
Platelet not normal range* – no. / total known patients	21 /128	13 / 57		34 /185	0.299 <sup>A</sup>
Platelet Count Baseline – Mean (95% CI)	319.1 (297.6-340.5)	369.2 (332.4 – 406.1)		334.5(315.7-353.3)	0.015 <sup>B</sup>
Brain metastasis (yes)	29	9	22	60	0.494 <sup>A</sup>
<b>Pathology – no.</b>					
Adenocarcinoma	95	44	62	201	0.000 <sup>A</sup>
Squamous cell carcinoma	22	10	37	59	
Other	11	2	0	13	
Unknown	0	3	0	3	
<b>PD-L1 – no.</b>					
Unknown	102	25	99	226	0.644 <sup>C</sup>
Negative	15	23		38	
Positive 1 – 50%	8	7		15	
Positive >50%	3	4		7	
<b>Previous treatment – no.</b>					
CCRT – no.	16	13		29	0.213 <sup>A</sup>
Platinum chemotherapy	110	46		156	
Unknown	2	0	99	101	
<b>Line of treatment – no.</b>					
1	2	1		3	0.792 <sup>A</sup>
2	100	44		144	
>2	25	14		39	
Unknown	1	0	99	100	
Previous RT / total known patients	79/126	41/57	1/2	121/185	0.332 <sup>A</sup>
Thoracic RT / total known patients	48/126	31/57	0/2	79/185	0.042 <sup>A</sup>
<b>Medication Platelet – no.</b>					
None	79	41		120	0.024 <sup>C</sup>
Acetylsalicylic acid	20	12		32	
Other	29	4		33	
Unknown	0	2	99	101	
<b>Survival</b>					
Responder – no.	38	20	30	88	0.865 <sup>A</sup>
Mean OS (days) (95% CI)	291.8 (251.8-331.8)	295.8 (232.7-358.9)	227.3 (189.2-265.5)	270.4 (244.7-296.2)	0.057 <sup>B</sup>
Mean PFS (days) (95% CI)	201.2 (159.3-243.1)	211.0 (152.8-269.1)	164.5 (124.7-204.3)	190.5 (164.5-216.48)	0.345 <sup>B</sup>

**Table S1 - Patient characteristics per hospital**

Abbreviations: N: Number of patients; NKI: Netherlands Cancer Institute; AUMC: Amsterdam University Medical Centers – Location VuMC; UMCG: University Medical Center Groningen; no.: Number of patients, yr: years; 95% CI: 95% confidence interval; WHO performance-status score: World Health Organization performance status score, this is a score ranging from 0 to 5, where 0 indicates no symptom, 1 indicates mild symptoms and above 1 indicates greater disability; PD-L1: Programmed death ligand 1; CCRT: chemoradiation therapy; RT: radiation therapy; OS: Overall Survival; PFS: Progression Free Survival.

\* Either below under limit of normal or above limit of normal, as defined by the clinical laboratory. In the Netherlands a normal platelet count is between 150-350 platelets x 10<sup>9</sup> / liter (150.000-350.000 platelets per microliter).

Used statistical tests: <sup>A</sup>: Chi Square, <sup>B</sup>: One way ANOVA, <sup>C</sup>: Fisher-Freeman Halton exact test

**Table S2 - Patient characteristics per randomized group**

	Training N=88	Evaluation N=91	Validation N=107	Total (N=286)	P-value
<b>Patient</b>					
Male sex – No. (%)	49	47	62	158 (55.2%)	0.680 <sup>A</sup>
Age (yr) – Mean (95% CI)	64.7 (62.7-66.6)	63.9 (62.0 – 65.8)	63.9 (61.9-65.85)	64.1 (63.0-65.3)	0.811 <sup>B</sup>
Smoking status Never / Current / Stop - No. (%)	6 19 59	4 16 68	14 23 62	24 58 189	0.119 <sup>C</sup>
Pack Years – Mean (95% CI)	36.1 (31.8-40.2)	31.8 (28.0 – 35.5)	35.1 (30.9-39.2)	34.2 (31.9 – 36.5)	0.289 <sup>B</sup>
WHO Performance status ≥ 2 – no. / total known patients	10/80	13/84	10/102	33/266	0.519 <sup>C</sup>
Platelet not normal range <sup>A</sup> – no. / total known patients	10/57	11/61	13/61	34/185	0.971 <sup>A</sup>
Platelet Count Baseline – Mean (95% CI)	312.6 (280.2- 344.9)	335.1(303.4-366.9)	352.7 (318.6-386.7)	334.5(315.7- 353.3)	0.229 <sup>B</sup>
Brain metastasis (yes)	18	18	24	60	0.902 <sup>A</sup>
<b>Previous treatment – no.</b>					
Adenocarcinoma	57	67	77	201	0.305 <sup>A</sup>
Squamous cell carcinoma	27	20	22	59	
Other	2	4	7	13	
Unknown	2	0	1	3	
<b>PD-L1 – no.</b>					
Unknown	88	76	62	226	0.949 <sup>C</sup>
Negative		9	29	38	
Positive 1 – 50%		4	11	15	
Positive >50%		2	5	7	
<b>CCRT – no.</b>					
CCRT – no.	8	11	10	29	0.890 <sup>A</sup>
Platinum chemotherapy	48	50	58	156	
Unknown	32	30	39	101	
<b>Line of treatment – no.</b>					
1	2	0	1	3	0.827 <sup>A</sup>
2	42	50	52	144	
>2	12	11	16	39	
Unknown	32	30	38	100	
Previous RT / total known patients	35/57	40/59	46/69	121/185	0.759 <sup>A</sup>
Thoracic RT / total known patients	22/57	26/59	31/69	79/185	0.749 <sup>A</sup>
<b>Medication Platelet – no.</b>					
None	41	36	43	120	0.702 <sup>A</sup>
Acetylsalicylic acid	8	15	9	32	
Other	7	10	16	33	
Unknown	32	30	39	101	
<b>Survival</b>					
Responder	26	28	34	88	0.935 <sup>A</sup>
Mean OS (days) (95% CI)	276.7 (225.7- 327.7)	273.9 (226.9-320.8)	262.4 (223.7-301.2)	270.4 (244.7- 296.2)	0.891 <sup>B</sup>
Mean PFS (days) (95% CI)	189.8 (138.7- 240.8)	185.3 (146.6-224.1)	190.5 (164.5-216.5)	190.5 (164.5- 216.48)	0.931 <sup>B</sup>
<b>Hospital</b>					
NKI	39	43	46	128	0.983 <sup>A</sup>
AUMC	18	18	23	59	
UMCG	31	30	38	99	

**Table S2 - Patient characteristics per randomized group**

Abbreviations: N: Number of patients no.: Number of patients. yr: years; 95% CI: 95% confidence interval; WHO performance-status score: World Health Organization performance status score. this is a score ranging from 0 to 5. where 0 indicates no symptom. 1 indicates mild symptoms and above 1 indicates greater disability; PD-L1: Programmed death ligand 1; CCRT: chemoradiation therapy; RT: radiation therapy; OS: Overall Survival; PFS: Progression Free Survival. ; NKI: Netherlands Cancer Institute; AUMC: Amsterdam University Medical Centers; UMCG: University Medical Center Groningen;

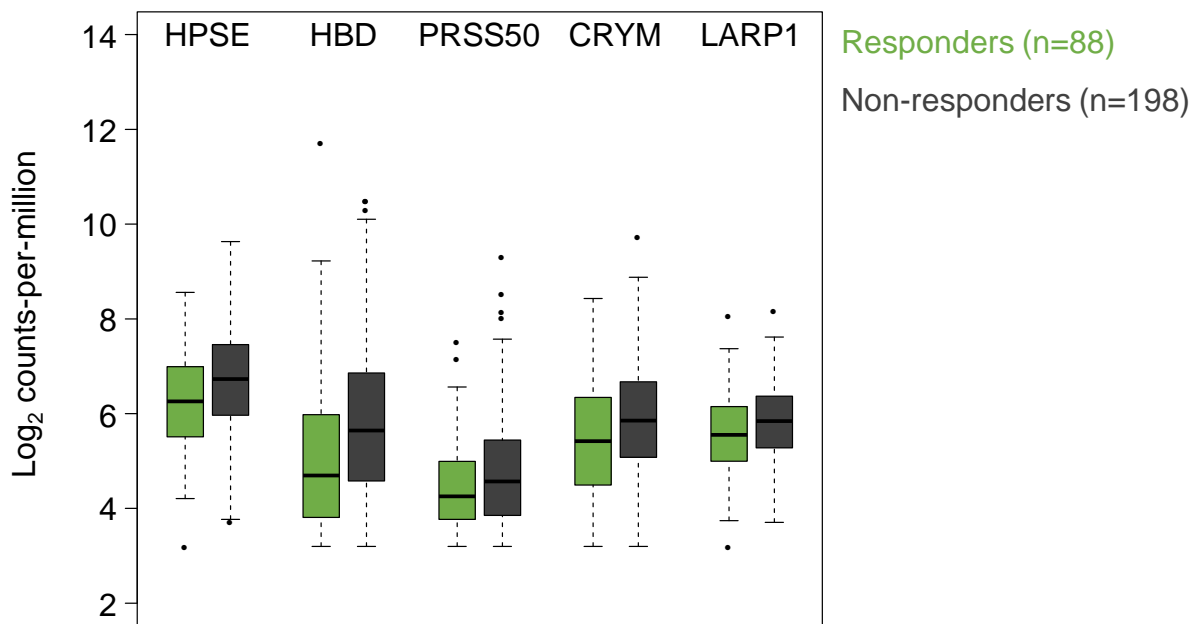
<sup>A</sup>. Either below under limit of normal or above limit of normal. as defined by the clinical laboratory. In the Netherlands a normal platelet count is between 150-350 platelets x 10<sup>9</sup> / liter (150.000-350.000 platelets per microliter).

Used statistical tests: <sup>A</sup>: Chi Square, <sup>B</sup>: One way ANOVA, <sup>C</sup>: Fisher-Freeman Halton exact test



Supplemental Figure 2

A



B

