#484 Association between BTLA polymorphisms and NSCLC risk

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IINTRODUCTION

Importance of immune checkpoints molecules in NSCLC was proven by the introduction of blockade of these receptors in routine treatment. B and T lymphocyte attenuator (BTLA) is another immune checkpoint molecule that regulates immune response. Our previous studies showed a significant association between BTLA gene variants and susceptibility to renal cell carcinoma and chronic lymphoblastic leukemia [1,2]. The aim of this study was to verify the hypothesis that BTLA polymorphic variants are associated with susceptibility to NSCLC in the Polish population.

PATIENTS AND METHODS

Genomic DNA was isolated from the venous blood of 383 patients diagnosed with NSCLC and 475 controls. Using TaqMan probes we genotyped seven BTLA SNPs: rs1982809, rs1844089, rs9288952, rs9288953, rs2705511, rs2633582, and rs11921669 on ViiA 7 Real-Time PCR System. The statistical analysis was performed using the SHEsis program (http://analysis.bio-x.cn/myAnalysis.php) [3,4].
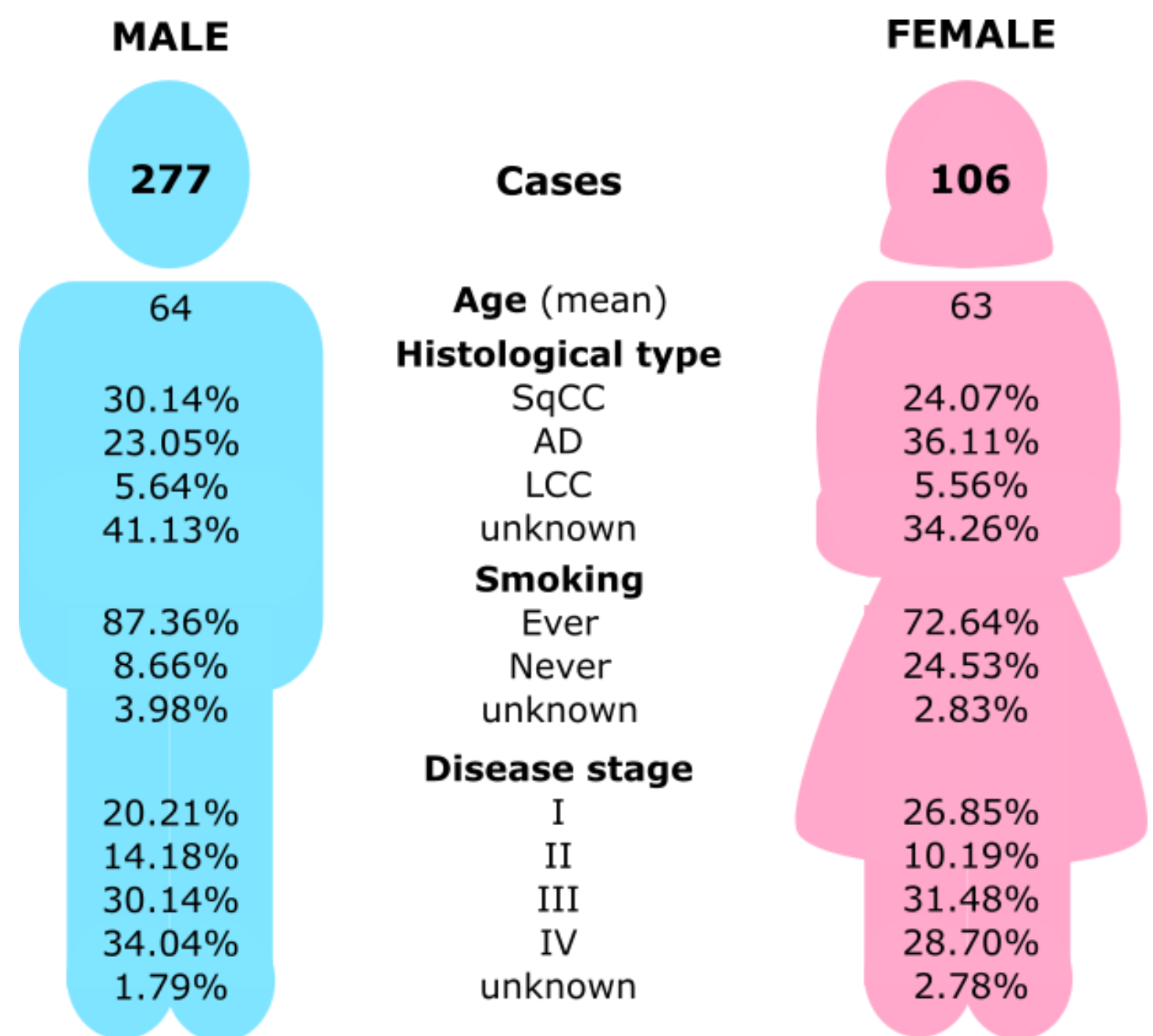

Fig 1. Characteristics of NSCLC group.
SqCC – squamous cell carcinoma; AD – adenocarcinoma; LCC – large cell carcinoma

Reference

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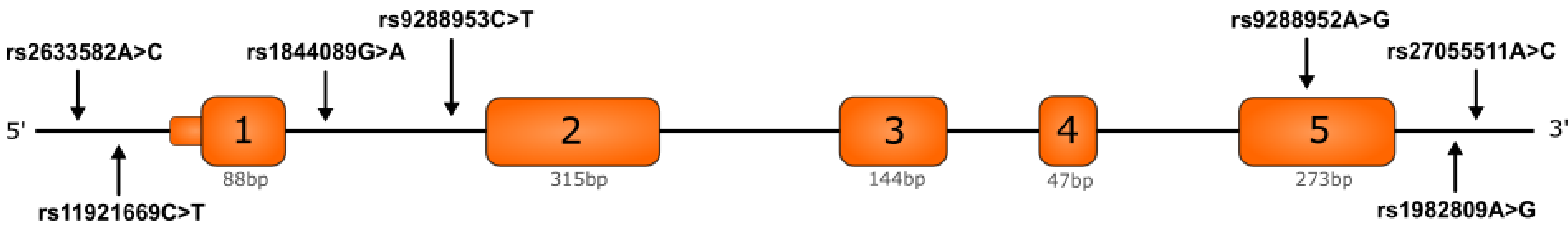
Fig 2. Structure of *BTLA* gene and localization of studied BTLA single nucleotide polymorphisms. Orange boxes indicate exons and black lines introns, 5'UTR and 3'UTR regions.

Statistical analysis of genotypes and alleles distributions for all investigated BTLA SNPs showed that SNP rs1982809 might be associated with susceptibility to NSCLC. In particular presence of G allele at rs1982809 (AG+GG genotypes) was more frequent in NSCLC group compared to controls (45.3% vs 38.8%, p=0.057). Allele distribution showed that the presence of allele G in rs1982809 significantly increases NSCLC risk (OR=1.25, p=0.046). For other studied polymorphisms in the overall analysis, we did not observe differences between NSCLC patients and controls.

The global distributions of the haplotypes did not differ significantly between the cases and controls. However, we noticed that the global distribution of the haplotypes differs significantly between the never-smokers and smokers (p=0.0003).
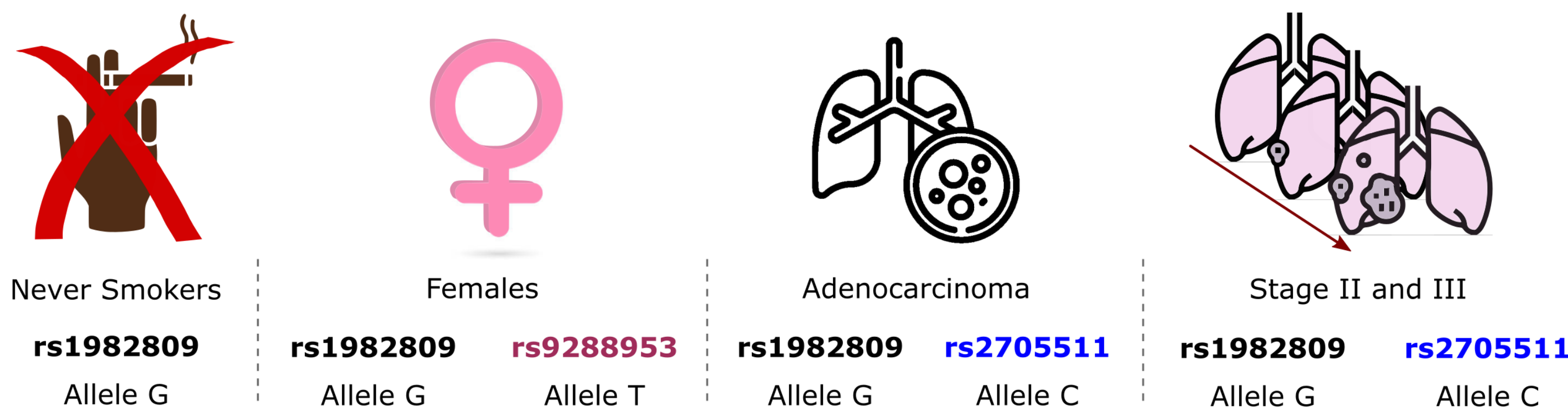

Fig 3. BTLA allele variants associated with increased NSCLC susceptibility in subgroup analysis.

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Disclosure Information

Presenter; Anna Andrzejczak

In relation to this presentation, the author has no conflict of interest that needs to be disclosed

RESULTS

SNP	Genotype	Allele	Cases N	Cases %	Controls N	Controls %	p value
rs1982809	AA		209	54.71	290	61.18	0.140
	AG		146	38.22	159	33.54	
	GG		27	7.07	25	5.27	
	AG+GG		173	45.29	184	38.82	**0.057**
		A	564	73.82	739	77.95	**0.046**
		G	200	26.18	209	22.05	
rs9288953	CC		87	36.10	186	39.83	0.595
	CT		121	50.21	217	46.47	
	TT		33	13.69	64	13.70	
	CC+CT		208	86.31	403	86.30	0.997
		C	295	61.20	589	63.06	
		T	187	38.80	345	36.94	0.494
rs2705511	AA		208	54.59	274	57.81	0.531
	AC		143	37.53	170	35.86	
	CC		30	7.87	30	6.33	
	AA+AC		351	92.13	444	93.67	0.380
		A	559	73.36	718	75.74	
		C	203	26.64	230	24.26	0.261

SNP	Genotype	Allele	Cases N	Cases %	Controls N	Controls %	p value
rs9288952	AA		337	88.22	421	88.82	0.780
	AG		42	10.99	51	10.76	
	GG		3	0.79	2	0.42	
		A	716	93.72	893	94.20	
		G	48	6.28	55	5.80	0.677
rs1844089	GG		320	85.11	395	83.33	0.385
	AG		56	14.89	77	16.24	
	AA		0	0.00	2	0.42	
		G	696	92.55	867	91.46	
		A	56	7.45	81	8.54	0.409
rs2633582	AA		322	84.29	265	85.76	0.192
	AC		56	14.66	44	14.24	
	CC		4	1.05	0	0.00	
		A	700	91.62	574	92.88	
		C	64	8.38	44	7.12	0.387
rs1192166	CC		362	95.01	298	96.13	0.408
	CT		17	4.46	12	3.87	
	TT		2	0.52	0	0.00	
		C	741	97.24	608	98.06	
		T	21	2.76	12	1.94	0.321

Table 1. BTLA polymorphisms genotypes and alleles frequencies in NSCLC patients and controls.

In the subgroup analysis, we found that in patients with adenocarcinoma (AD) genotypes distribution of rs1982809 was significantly different compared to controls (p=0.048). Moreover, we noticed the trend for overrepresentation of rs2705511[C] allele (AC+CC genotypes) in patients with AD (53% vs 43.4%, p=0.079). After stratification by gender, we observed an association between the presence of rs9288953[T] allele (CT+TT genotypes) and NSCLC susceptibility (74.6% vs 54.4%, p=0.004) in females. Moreover, the distribution of the genotypes differs between female patients and controls (p=0.01). After stratification by smoking status, allele distribution analysis showed that the presence of allele G in rs1982809 significantly increases NSCLC risk (OR=1.6, p=0.043) in never-smoking patients. Additionally, we observed that the presence of rs1982809 and rs2705511 correlate with the stage of the disease. In patients at stage II allele distribution analysis showed overrepresentation of rs1982809[G] and rs2705511[C] alleles (31.4% vs 22%, p=0.03; 33% vs 24.3%, p=0.055). Presence of rs1982809[G] allele (AG+GG genotypes) and rs2705511[C] allele (AC+CC genotypes) were more frequent in patients at stage III (54.3% vs 38.8%, p=0.0025; 52.2% vs 42.2%, p=0.053) compared to controls.

CONCLUSION

Results of our study show that rs1982809 in *BTLA* gene might be considered a low penetrating risk factor for NSCLC susceptibility in the Polish population.

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