

CHOPN

Kaplanovy-Meierovy křivky přežití
pro jednotlivé SNP

SNP v genu *IL10*:

IL10₋₁₀₈₂ rs1800896 T>C

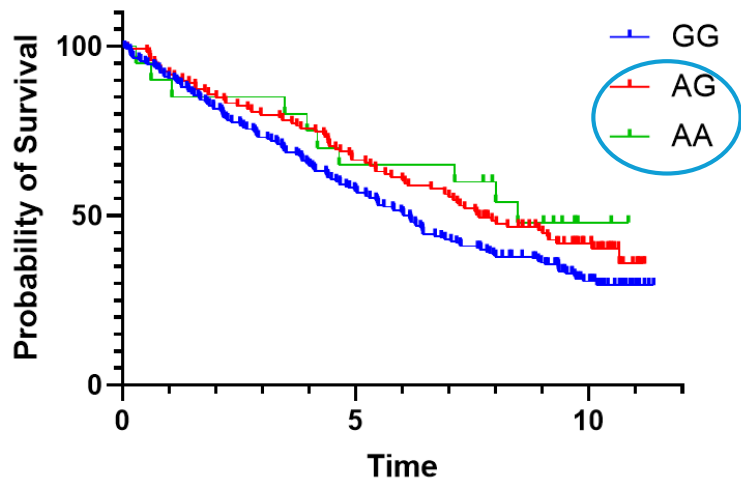
IL10₋₈₁₉ rs1800871 A >G

IL10₋₅₉₂ rs1800872 T >G

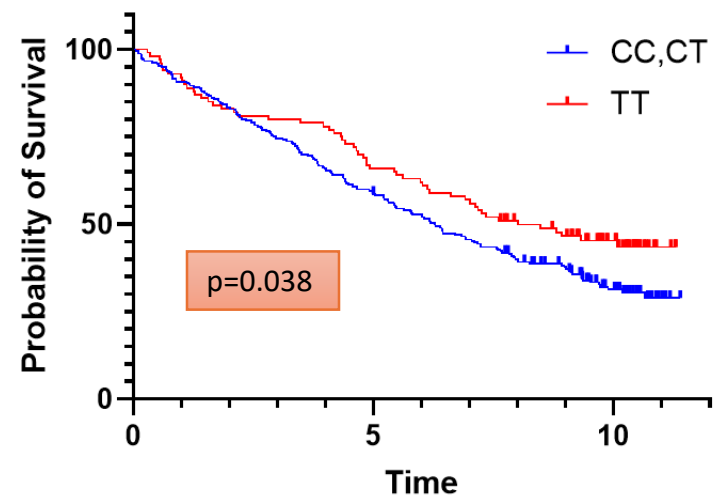
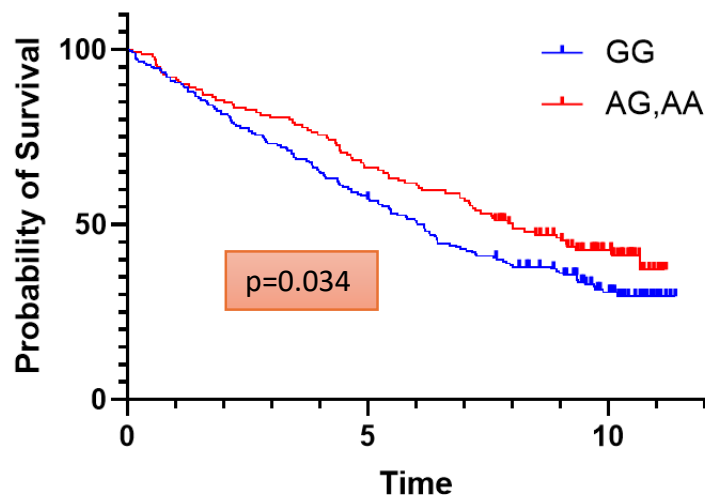
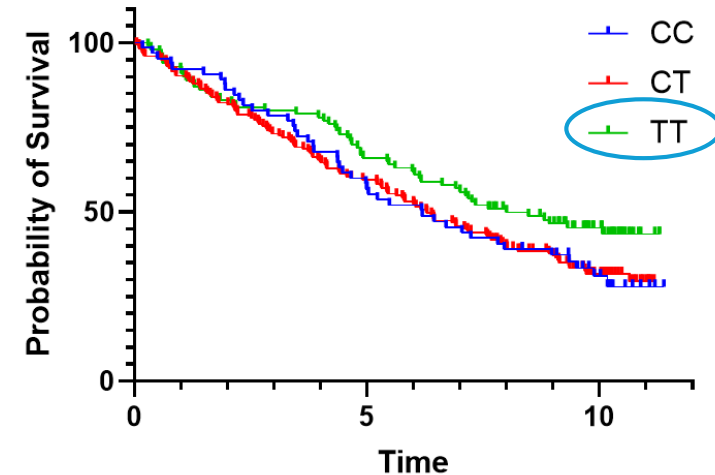
rs1800871 a rs1800872 se dědí společně (asociace s BMI u pacientů s CHOPN a ovlivnění délky přežití různé podle BMI – viz samostatné prezentace)

Vyskytují se 3 haplotypy:
TAT, TGG, CGG

IL10-819 rs1800871



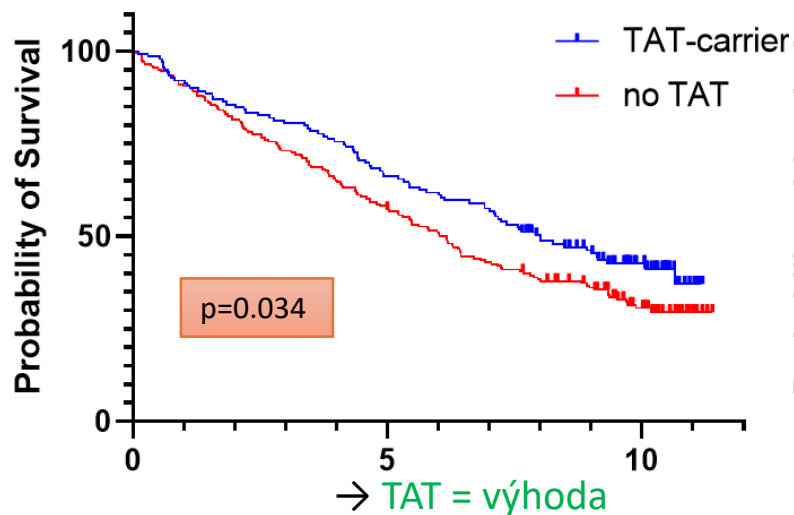
IL10-1082 rs1800896



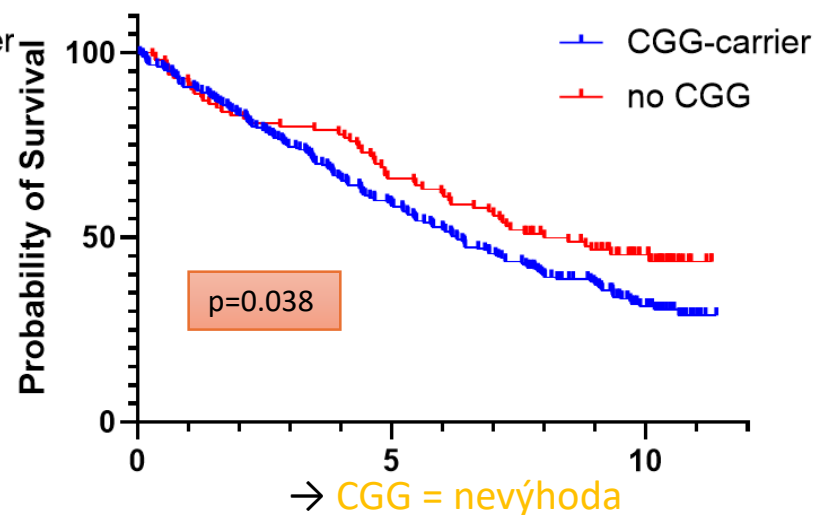
Median survival	
GG	6,163
AG,AA	8,003
Hazard Ratio (logrank)	A/B
Ratio (and its reciprocal)	1,345
95% CI of ratio	1,029 to 1,760

Median survival	
CC,CT	6,278
TT	8,003
Hazard Ratio (logrank)	A/B
Ratio (and its reciprocal)	1,380
95% CI of ratio	1,037 to 1,836

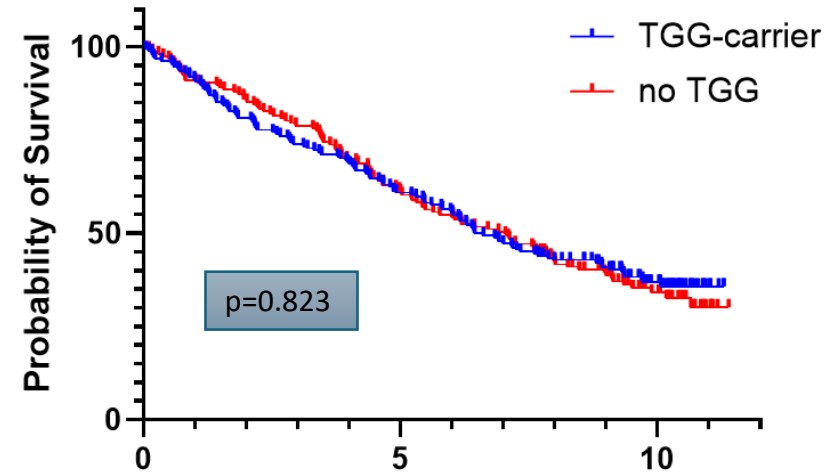
IL10 haplotyp TAT



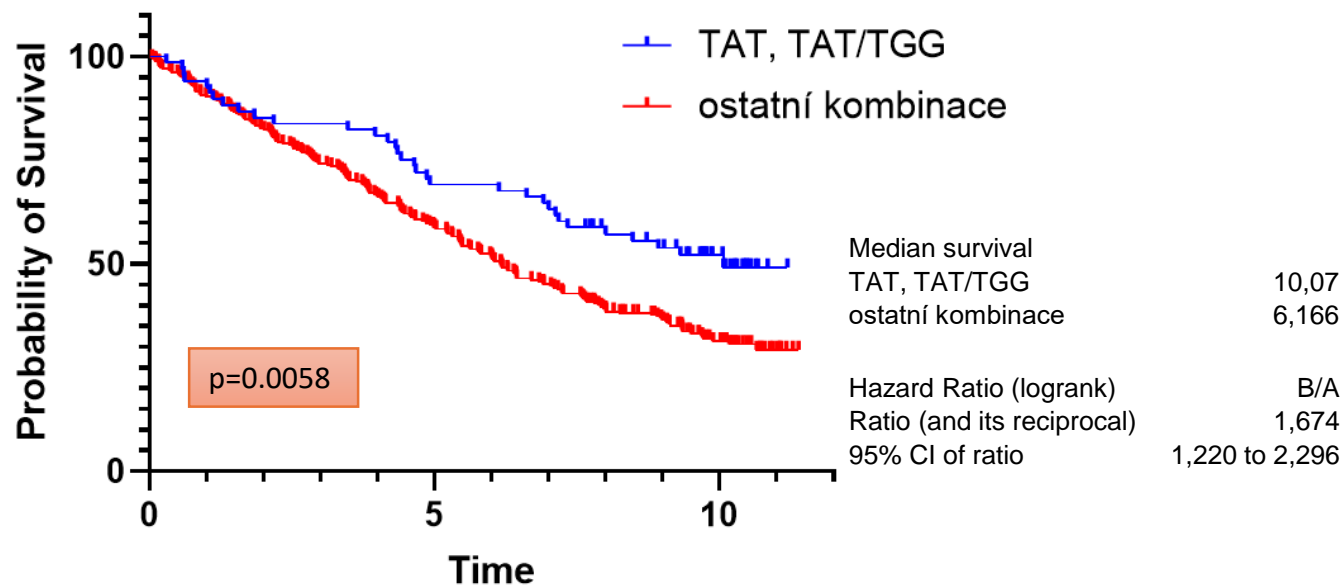
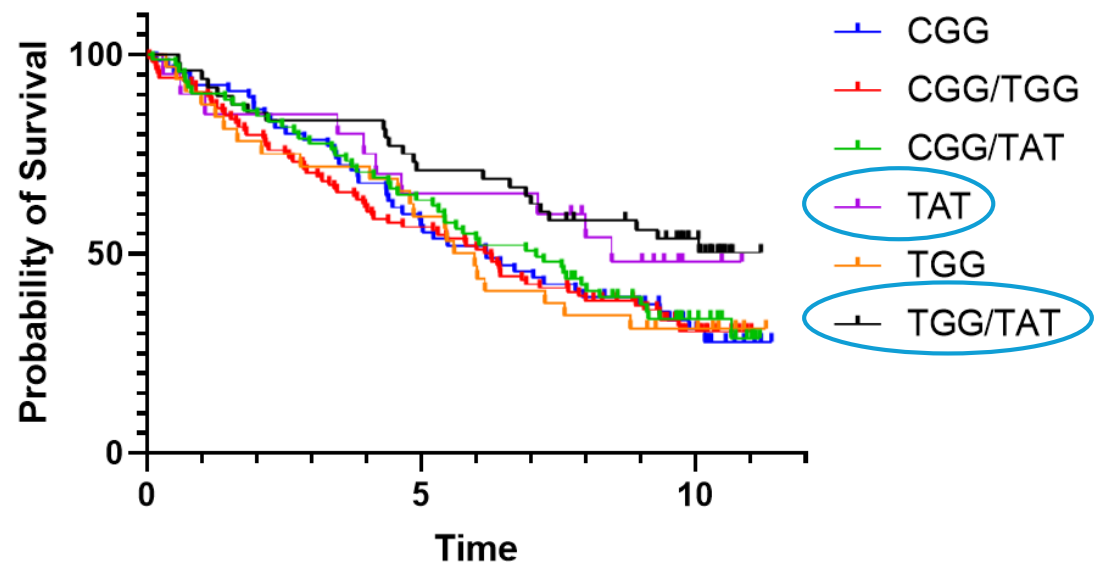
IL10 haplotyp CGG



IL10 haplotyp TGG



IL10 haplotypy



Zastoupení *IL10* SNP v podskupinách pacientů

1) BMI <27,5 (n=127) vs. BMI ≥27,5 (n=175)

nosičství halotypu TAT častější u BMI ≥27,5: 48,0% vs. 33,3%, p=0,0060

2) fenotyp exacerbační (n=84) vs. non-exacerbator (n=256)

CGG homozygot (IL10₋₁₀₈₂ CC genotyp) častější u non-exacerbátorů (!): 22,7 % vs. 8,3%, p=0,0038

3) mMRC

nosič haplotypu CGG (IL10₋₁₀₈₂ CC nebo CT genotyp) častější u vyššího stupně mMRC

0-1 (n=87) vs. 2-3 (n=234): 60,9 % vs. 73,9 %, p=0,023

0-2 (n=219) vs. 3-4 (n=102): 66,7 % vs. 78,4 %, p=0,032

4) Srdeční selhání (n=60) vs. ostatní (n=280)

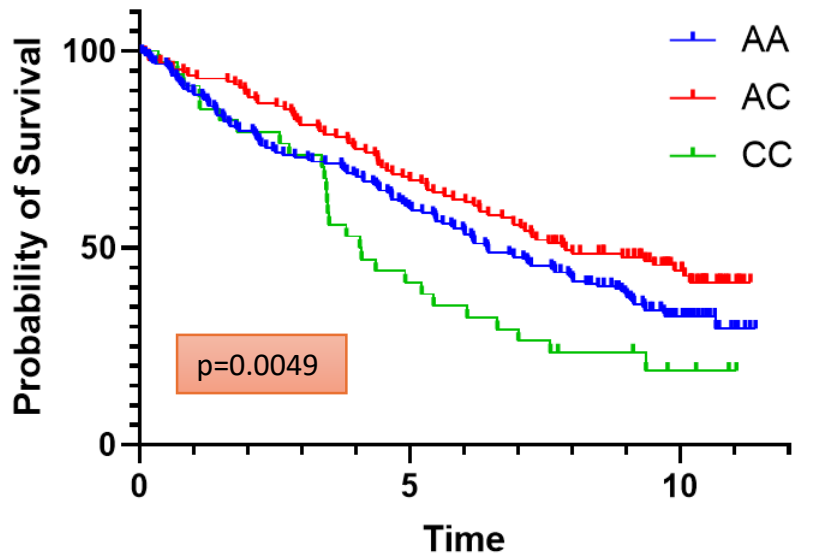
CGG homozygot (IL10₋₁₀₈₂ CC genotyp) častější u srdečního selhání: 28,3 % vs. 17,1 %, p=0,045

5) Fenotyp BCOS (n=52) vs. no BCOS (n=214)

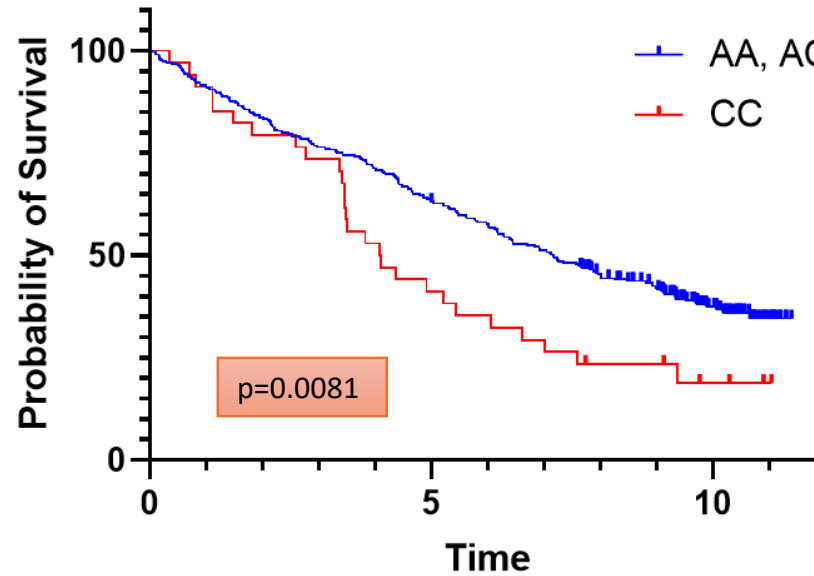
nosičství halotypu TAT častější (trend) u no BCOS: 44,4 % vs. 30,8 %, p=0,074 (=trend)

SNP v genu *IL2* (rs2068762, rs2069763)

IL2₋₃₃₀ rs2069762 A>C

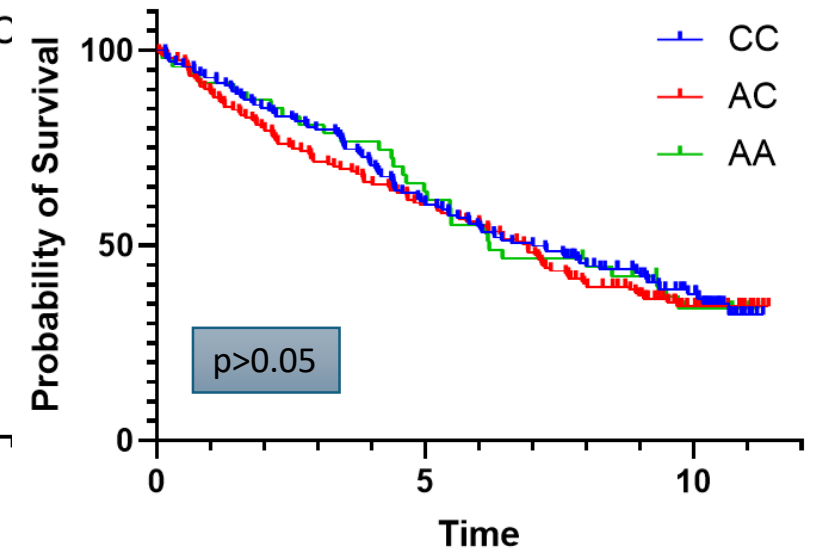


Median survival	AA	AC	CC
	6,42026	7,87953	4,08761



Median survival	AA, AC	7,165
	CC	4,088
Hazard Ratio (logrank)	B/A	
Ratio (and its reciprocal)		1,711
95% CI of ratio		1,038 to 2,821

IL2₊₁₆₆ rs2069763 C>A



p>0.05

Zastoupení $IL2_{-330}$ v podskupinách pacientů

1) Srdeční selhání (n=60) vs. ostatní (n=280)

CC homozygoti častější u pacientů se srdečním selháním: 20,0 % vs. 7,9 %, $p=0,0044$
nosičství alely *C: 61,7 % vs. 44,6 %, $p=0,017$

2) CHOPN kategorie 2017: A+B (n=219) vs. C+D (n=117)

CC homozygoti častější u pacientů v kategoriích C+D: 14,5 % vs. 7,3 %, $p=0,034$
nosičství alely *C: 54,7 % vs. 43,8 %, $p=0,057$ (=trend)

SNP v genu *IDO2*

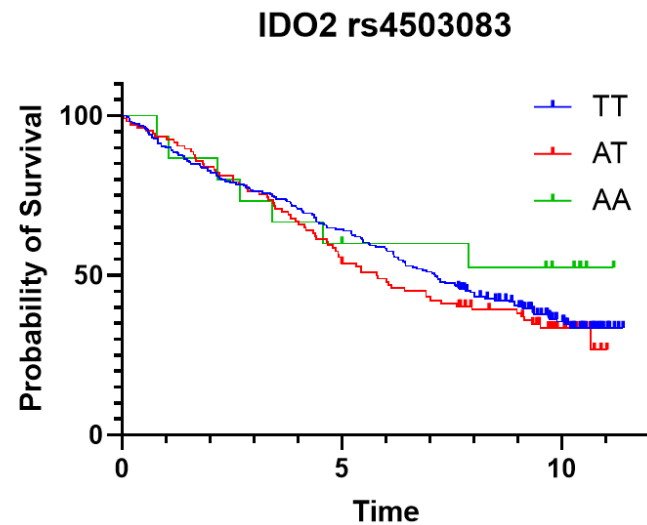
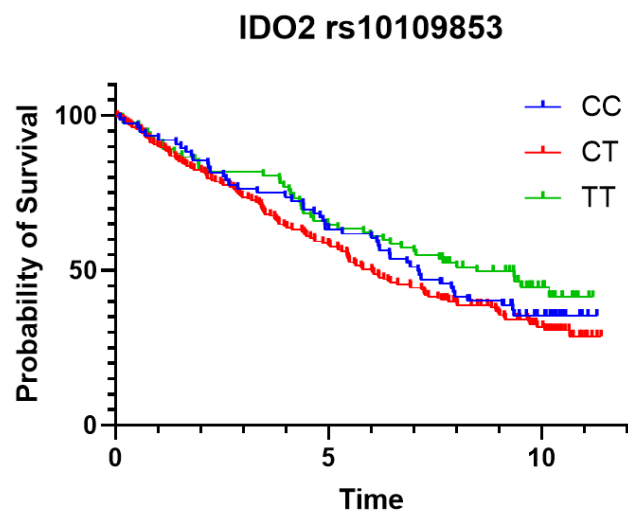
IDO2 rs10109853 C>T (R248W)

alela *T = nižší aktivita enzymu *IDO2*

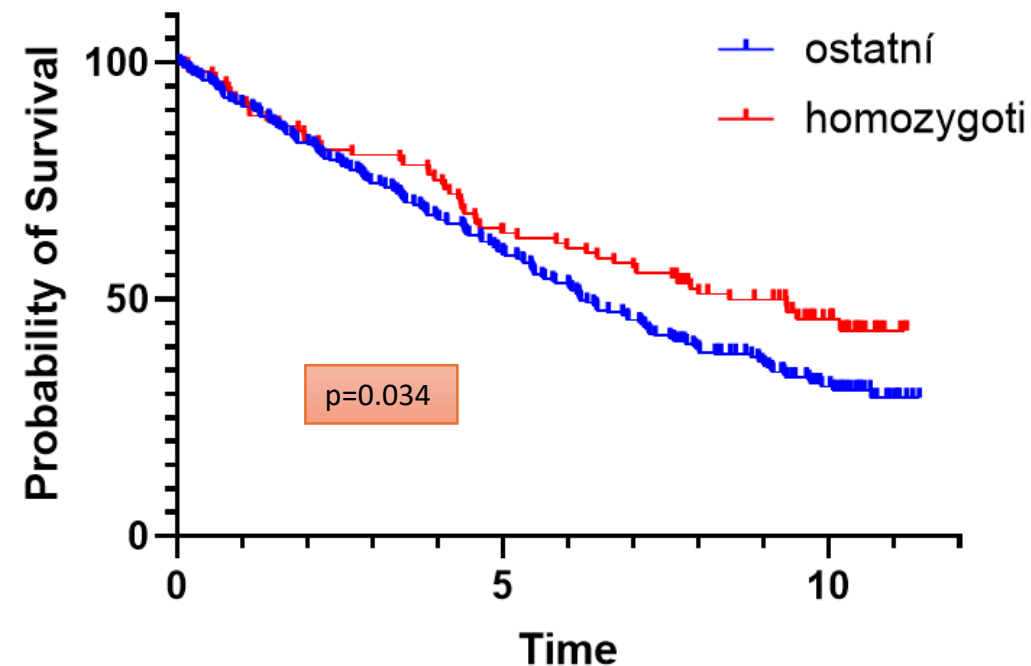
IDO2 rs4503083 T>A (Y359X)

alela *A = předčasný stop kodon

- *IDO2* (indolamine-2,3-dioxygenase) is an enzyme that is used for catabolism of tryptophan.
- Homozygoti rs1019853 TT a rs4503083 AA nemají ani jednu funkční alelu
→ snížená nebo žádná aktivita enzymu *IDO2*



IDO2 homozygoti



Median survival	
ostatní	6,193
homozygoti	8,476
Hazard Ratio (logrank)	A/B
Ratio (and its reciprocal)	1,398
95% CI of ratio	1,047 to 1,866

Zastoupení *IDO2* SNP v podskupinách pacientů

1) fenotyp exacerbační (n=84) vs. non-exacerbator (n=256)

rs10109853 C>T (R248W) TT homozygot častější u exacerbátorů (!): 34,5 % vs. 26,7 %, p=0,010

VIZ NÁSLEDUJÍCÍ STRANA

2) mMRC

rs4503083 T>A (Y359X) - AA homozygoti častější u nižšího stupně mMRC

0-1 (n=87) vs. 2-3 (n=234): 9,2 % vs. 3,0 %, p=0,019

3) CAT≥18 (n=122) vs. CAT<18 (n=195)

rs4503083 T>A (Y359X) - nosičství alely *A častější u CAT<18: 40,0 % vs. 27,9 %, p=0,028

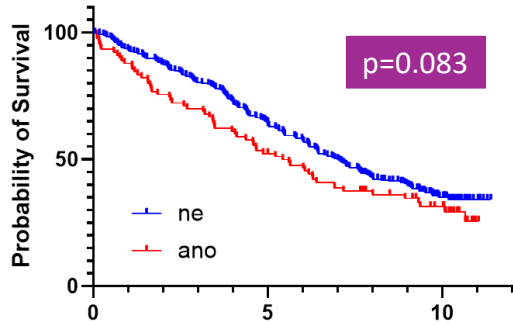
AA homozygoti častější u CAT<18: 6,7 % vs. 1,6 %, p=0,040

4) BMI <27,5 (n=127) vs. BMI≥27,5 (n=175)

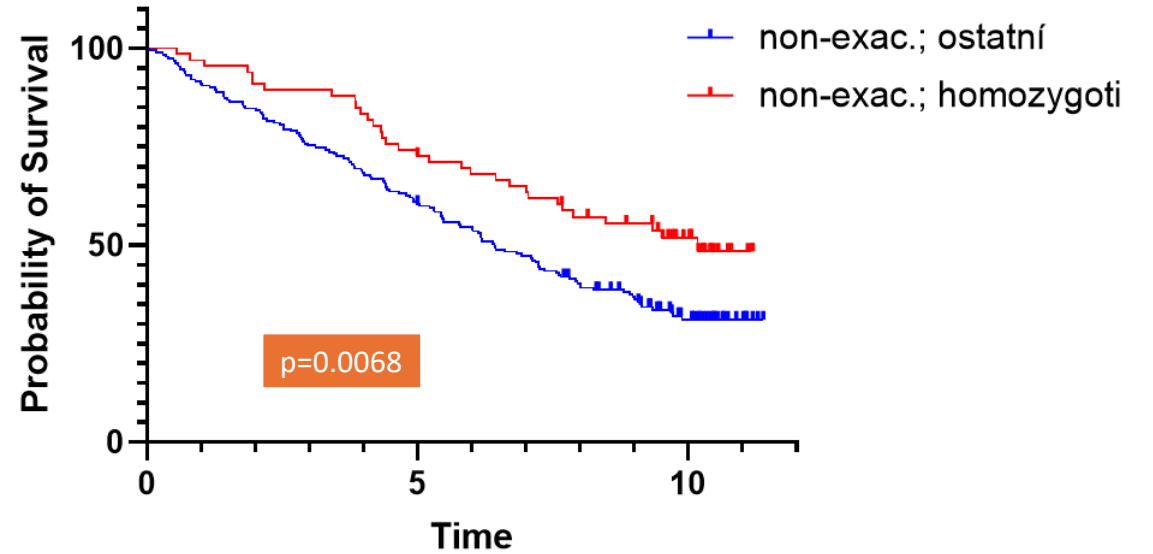
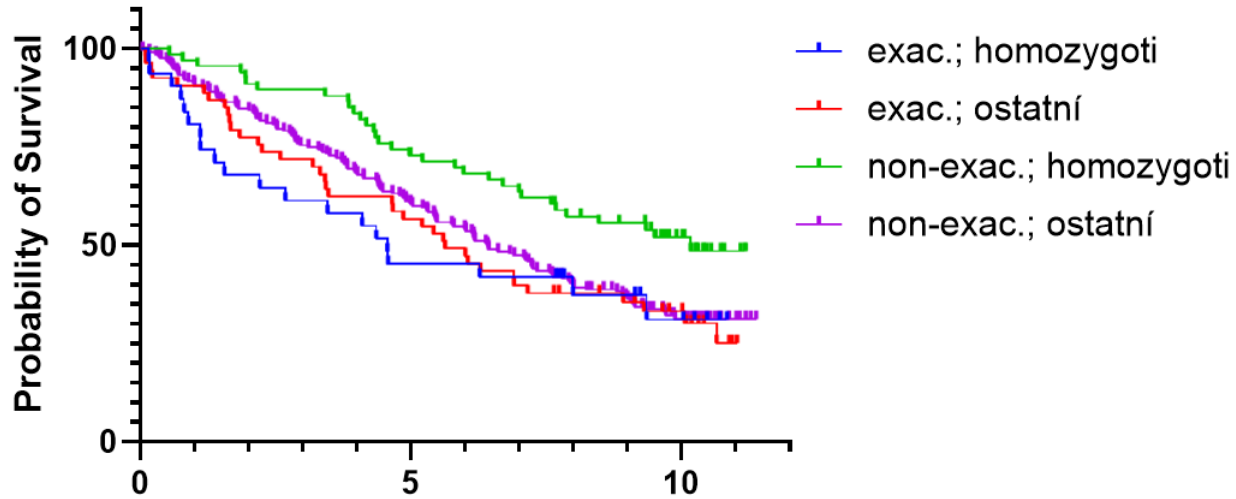
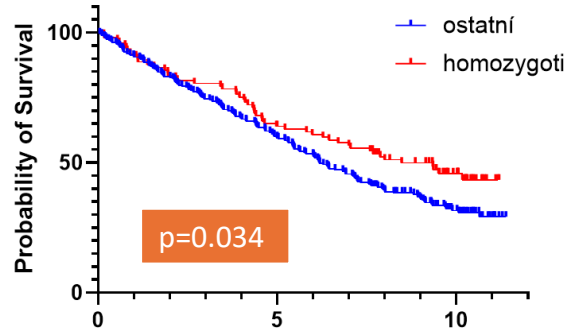
rs10109853 C>T (R248W) TT homozygot častější (trend) u BMI≥27,5: 28,6 % vs. 18,9 %, p=0,054 (=trend)

VIZ DÁLE

fen_exacerbacni

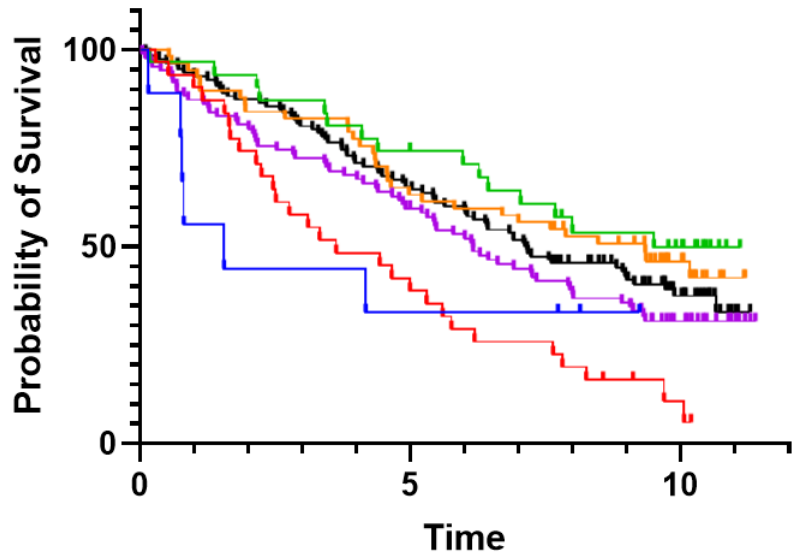


Homozygoti IDO2 R248W nebo Y359X



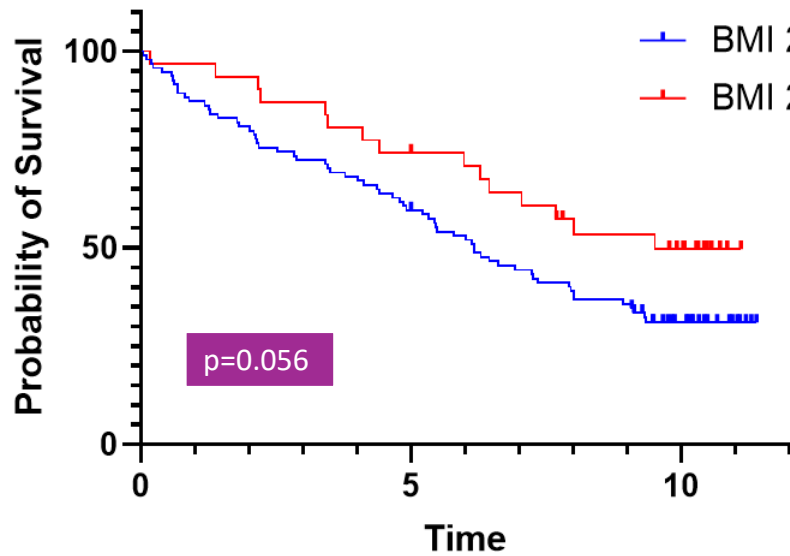
Median survival	exac.; homozygoti	exac.; ostatní	non-exac.; homozygoti	non-exac.; ostatní
	4,57221	5,6345	10,1793	6,42026

Median survival	
non-exac.; homozygoti	10,18
non-exac.; ostatní	6,420
Hazard Ratio (logrank)	B/A
Ratio (and its reciprocal)	1,696
95% CI of ratio	1,208 to 2,382



- kachexie; homozygoti
- kachexie; ostatní
- BMI 21-27,5; homozygoti
- BMI 21-27,5; ostatní
- BMI ≥27,5; homozygoti
- BMI ≥27,5; ostatní

	Median survival
kachexie; homozygoti	1,56
kachexie; ostatní	3,63
BMI 21-27,5; homozygoti	9,51
BMI 21-27,5; ostatní	6,16
BMI ≥27,5; homozygoti	9,35
BMI ≥27,5; ostatní	7,16

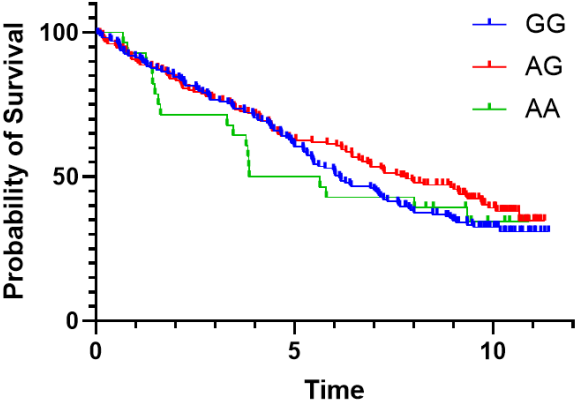


- BMI 21-27,5; ostatní
- BMI 21-27,5; homozygoti

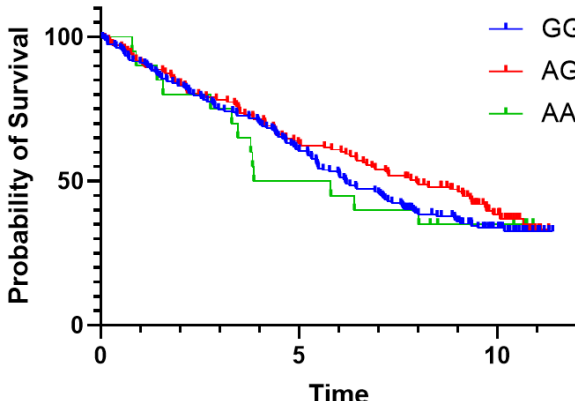
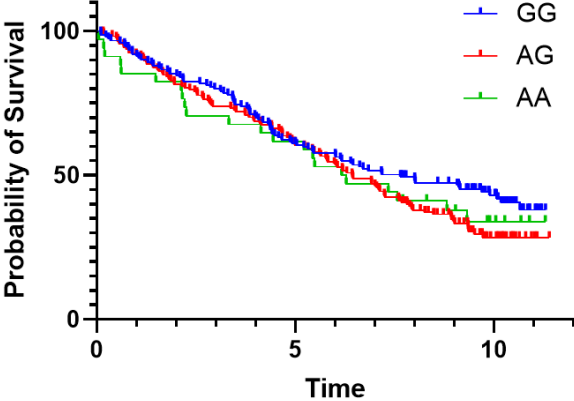
Median survival	
BMI 21-27,5; homozygoti	9,511
BMI 21-27,5; ostatní	6,163
Hazard Ratio (Mantel-Haenszel)	B/A
Ratio (and its reciprocal)	1,610
95% CI of ratio	0,9876 to 2,623

SNP v genech *IL1* genového klastru:

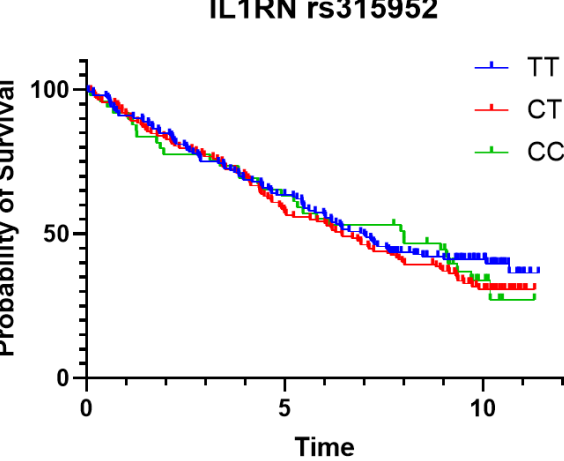
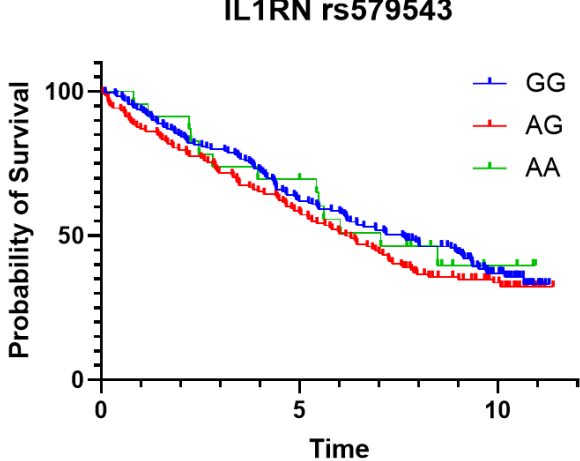
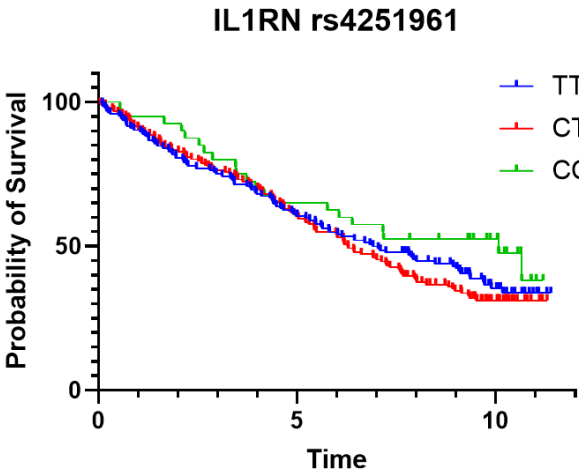
1) SNP v genu *IL1A*: *IL1A*₋₈₈₉ rs1800587



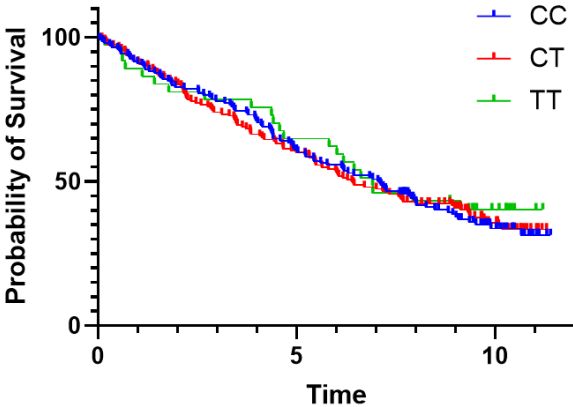
2) SNP v genu *IL1B*: *IL1B*₋₅₁₁ rs16944, *IL1B*₊₃₉₆₂ rs1143634



3) SNP v genu *IL1RN*: rs4251961, rs579543, rs315952

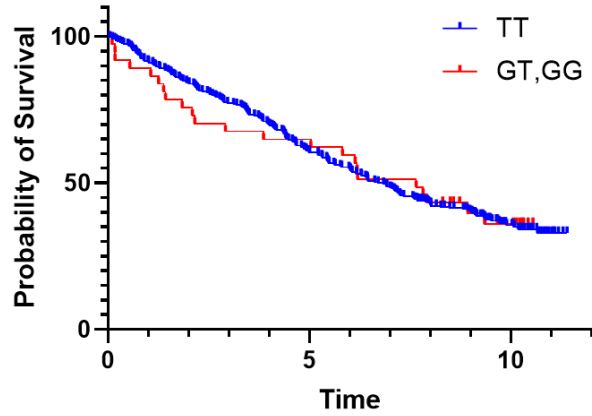


4) SNP v genu *IL1R1* rs2234650



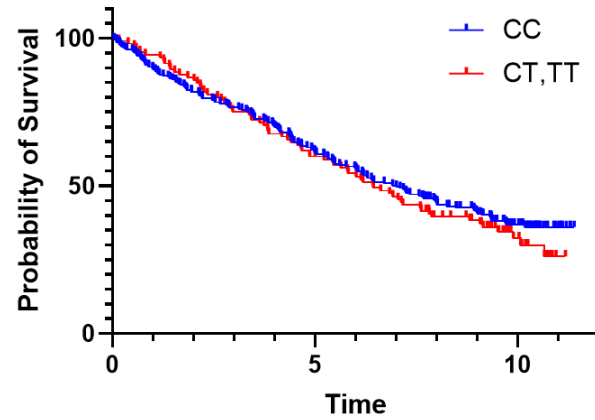
SNP v genech *IL4* a *IL4R*:

IL4₋₁₀₉₈ rs2243248

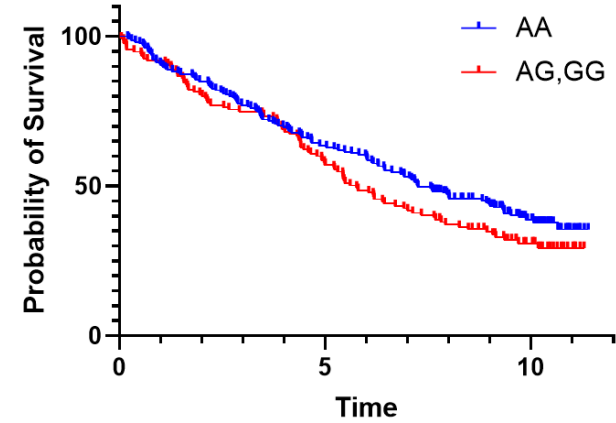


IL4₋₅₉₀ rs2243250, *IL4*₋₃₃ rs2070874

2 SNP ve vazbě

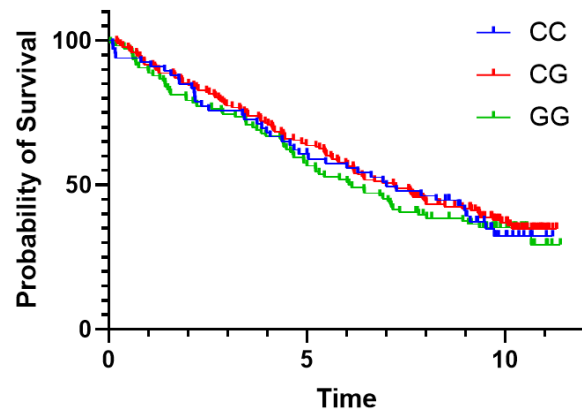


IL4Rα₊₁₉₀₂ rs1801275



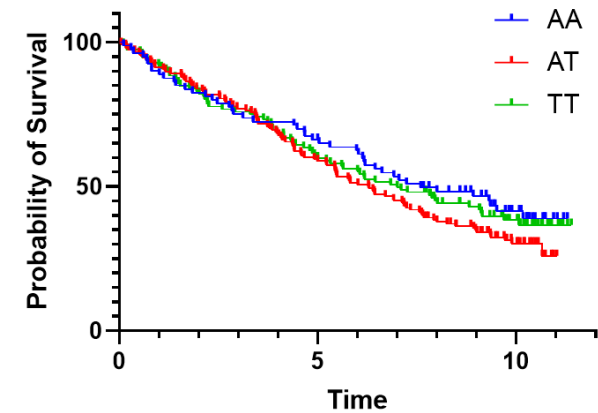
SNP v genu *IL6*: *IL6*₋₁₇₄ rs1800795, *IL6*₊₅₆₅ rs1800797 (2 SNP ve vazbě)

IL6₋₁₇₄ rs1800795

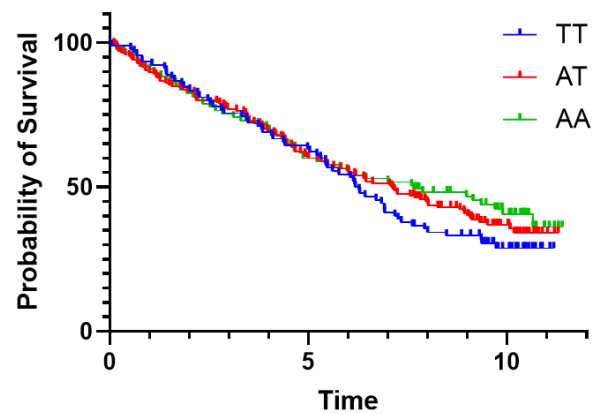


SNP v genu *CXCL8* (*IL8*): rs4073, rs2227307 (2 SNP ve vazbě)

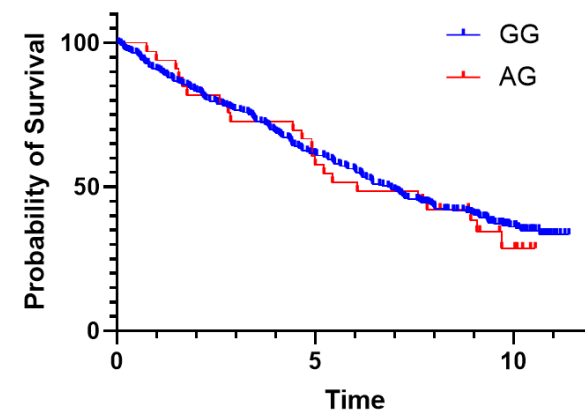
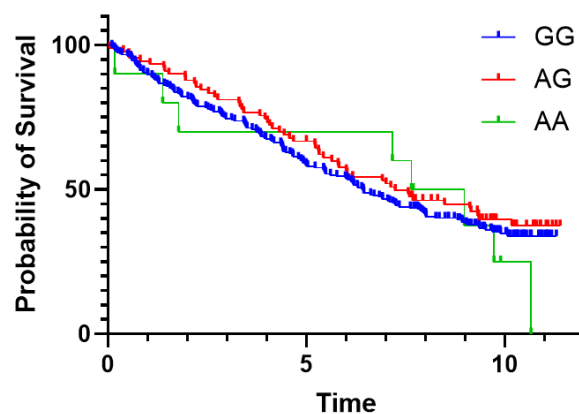
IL8 rs4073



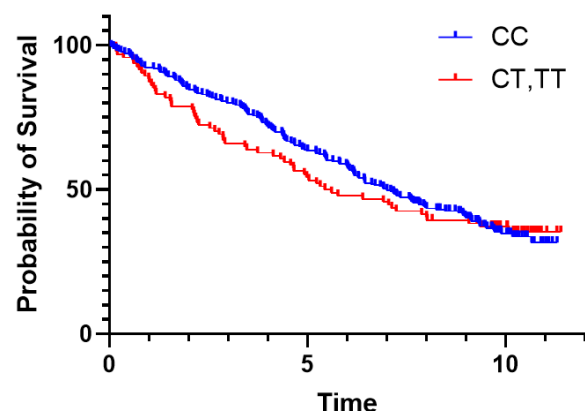
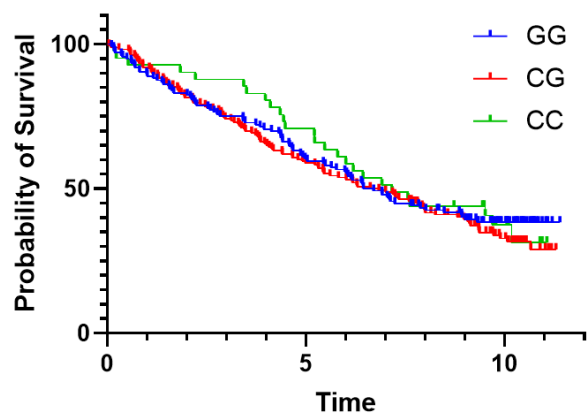
SNP v genu pro interferon γ : *INFG*₊₈₇₄ rs2430561



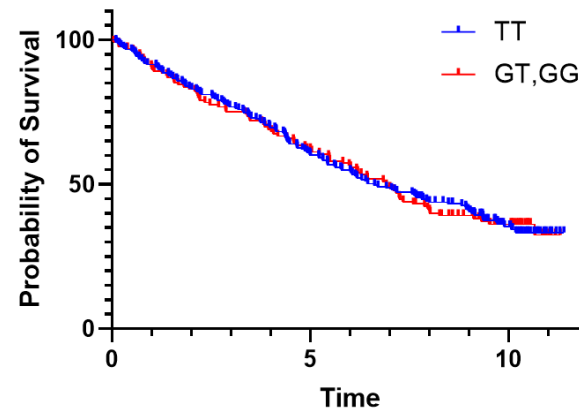
SNP v genu pro TNF- α : *TNFA*₋₃₀₈ rs1800629 , *TNFA*₋₂₃₈ rs361525



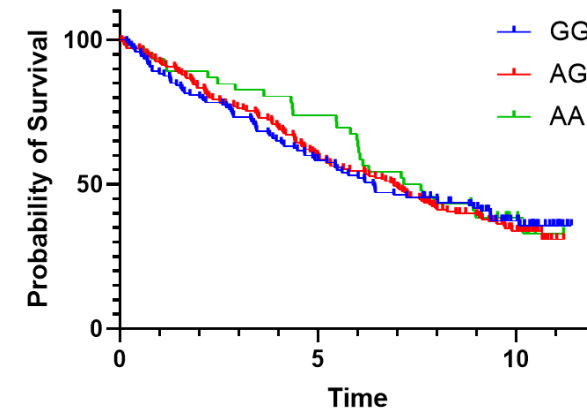
SNP v genu *MBL2*: *MBL2*₋₅₅₀ rs11003125, *MBL2*_{cd54} rs1800450



SNP v genu *IL12*: *IL12*₋₁₁₈₈ rs3212227



SNP v genu *IL17A* rs2275913

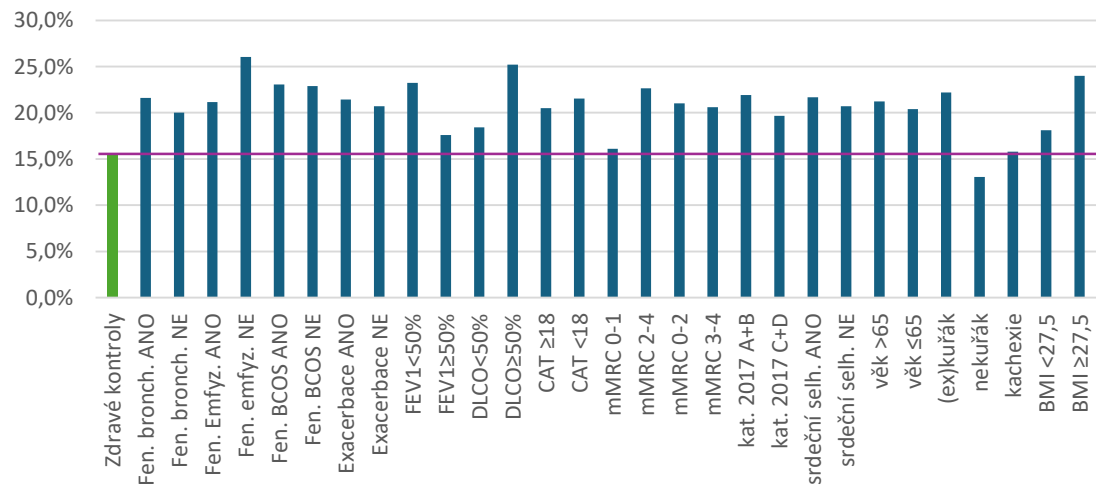
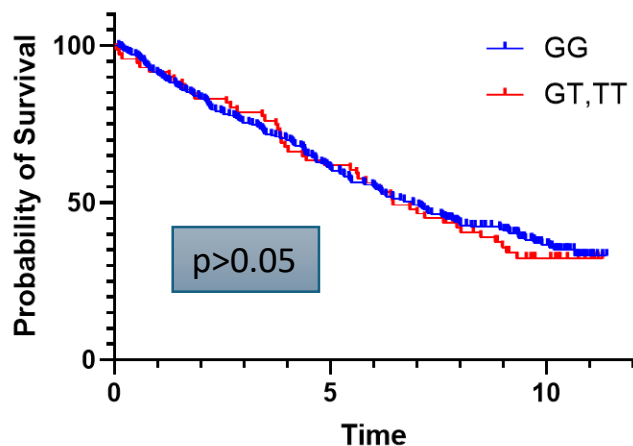
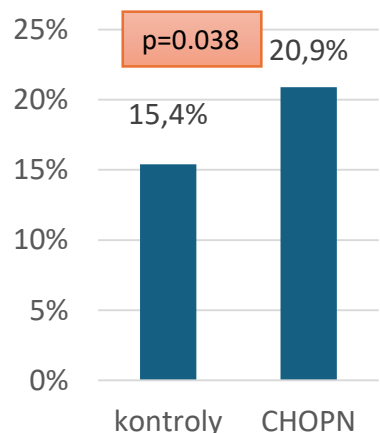


SNP predisponující k CHOPN (1)

rozdíl ve frekvenci alel mezi pacienty (celá kohorta) a zdravými kontrolami ($p \geq 0,05$)

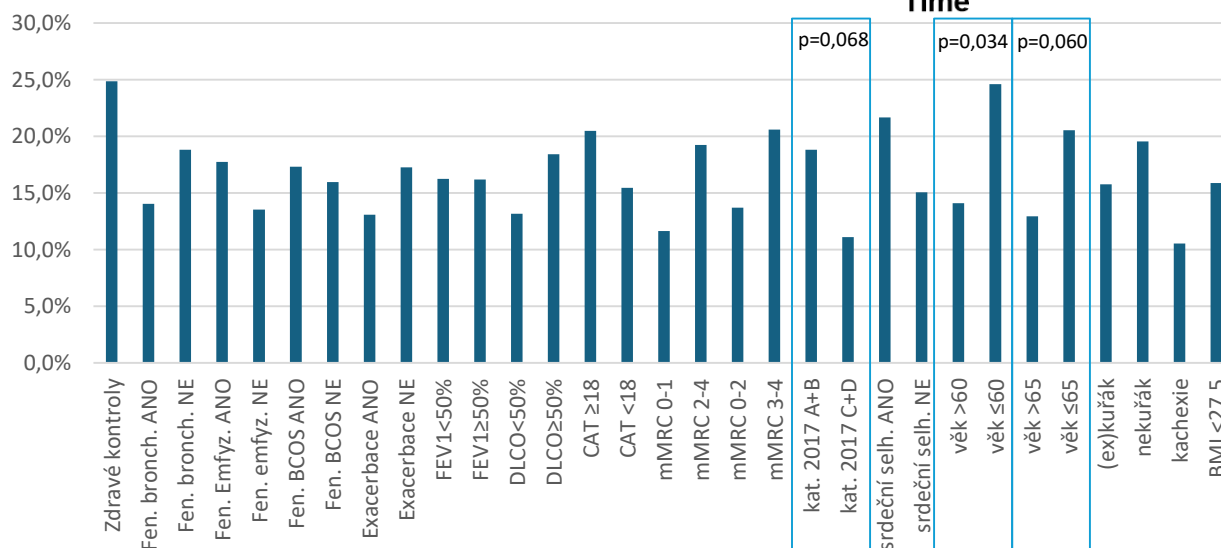
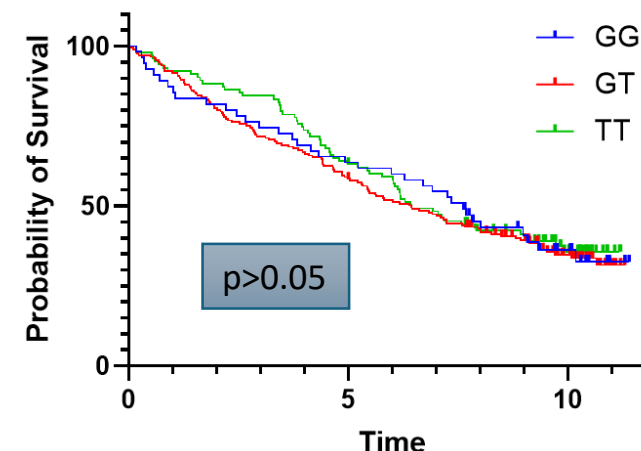
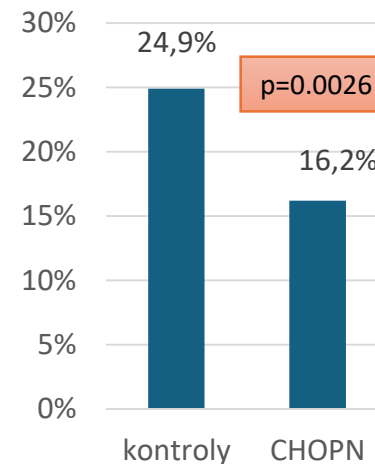
MUC5B rs35705950 G>T

Nosičství alely *T



DSP rs2076295 T>G

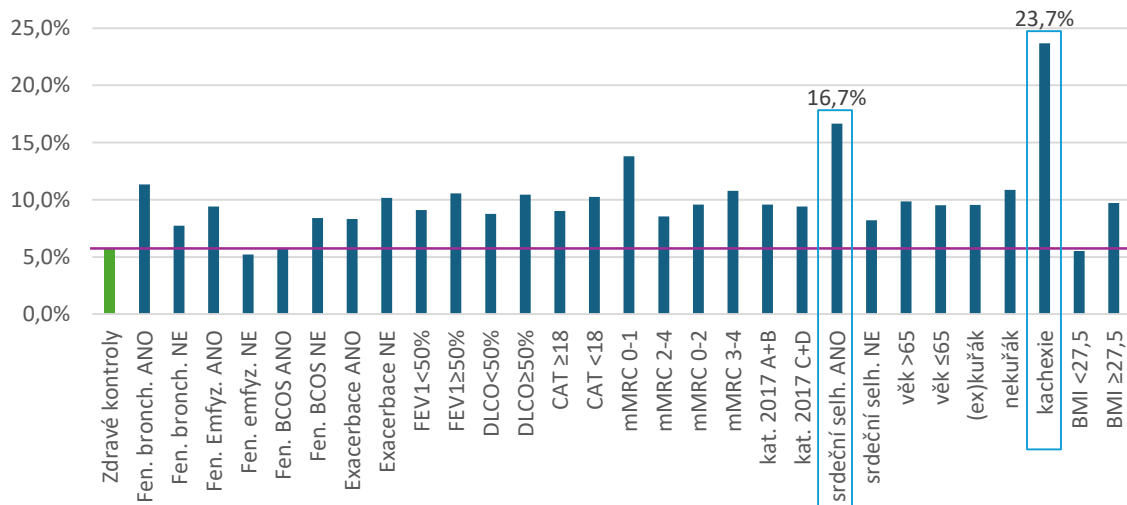
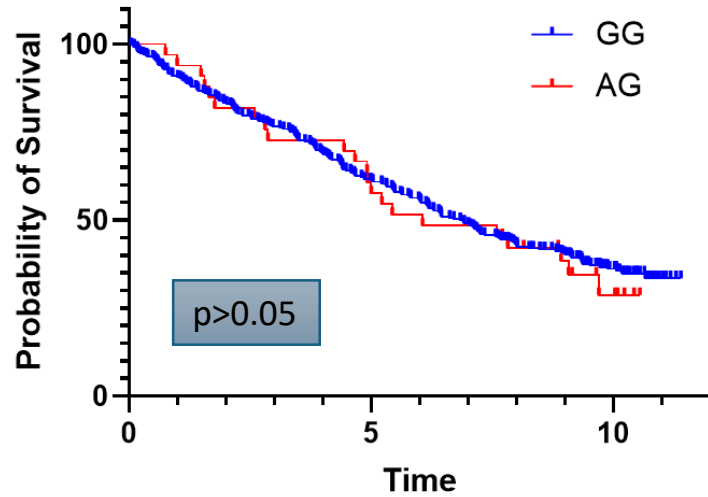
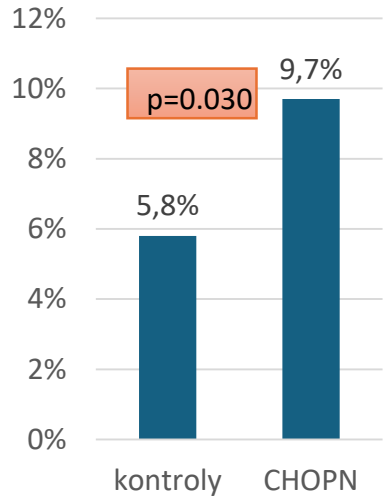
Genotyp GG



SNP predisponující k CHOPN (2)

TNFA (TNF α ₋₂₃₈) rs361525 G>A

Nosičství alely *A



IL17A rs2275913 G>A

Nosičství alely *A

