CHOPN

Kaplanovy-Meierovy křivky přežití

pro jednotlivé SNP

SNP v genu *IL10:*

***IL10*$_{-1082}$ rs1800896** T>C

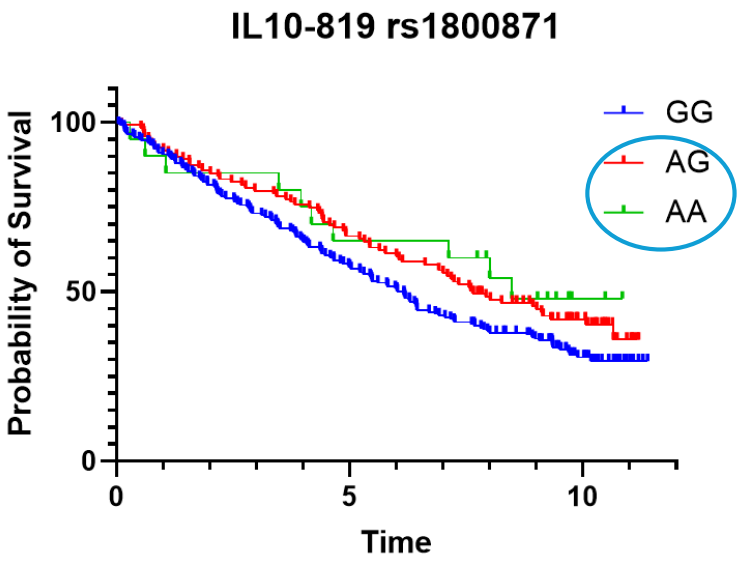
***IL10*$_{-819}$ rs1800871** A >G

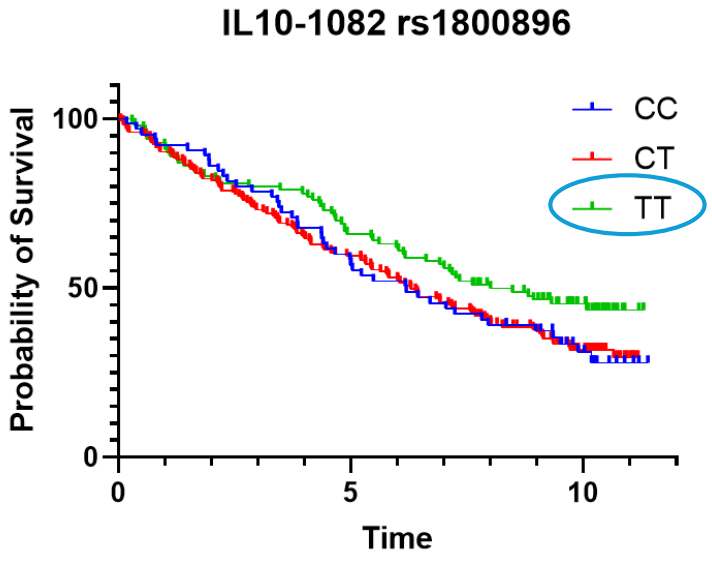
***IL10*$_{-592}$ rs1800872** T >G

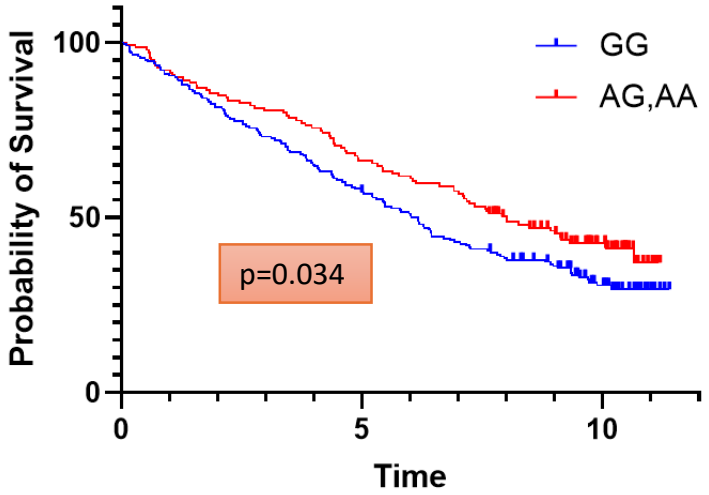
rs1800871 a rs1800872 se dědí společně (asociace s BMI u pacientů s CHOPN a ovlivnění délky přežití různé podle BMI – viz samostatné prezentace)

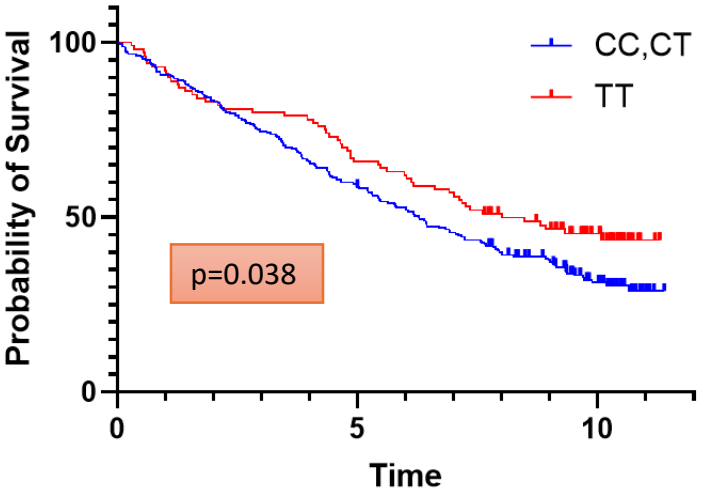
Vyskytují se 3 haplotypy:

TAT, TGG, CGG





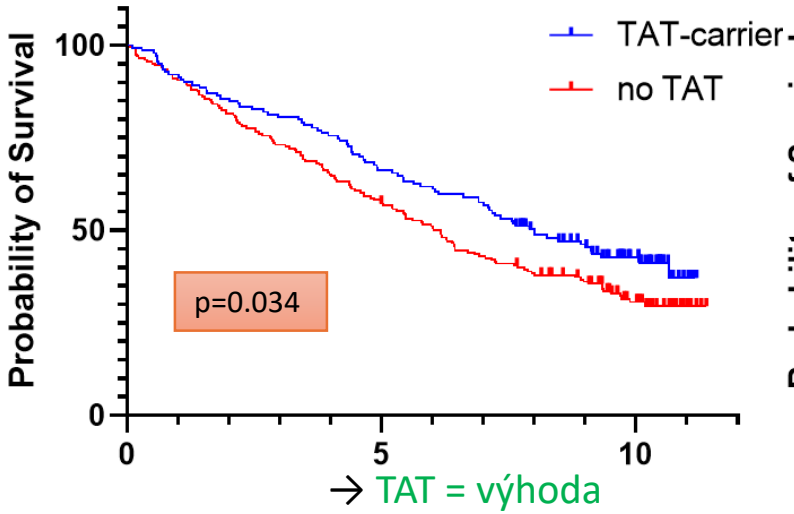




Median survival	
GG	6,163
AG,AA	8,003
Hazard Ratio (logrank)	A/B
Ratio (and its reciprocal)	1,345
95% CI of ratio	1,029 to 1,760

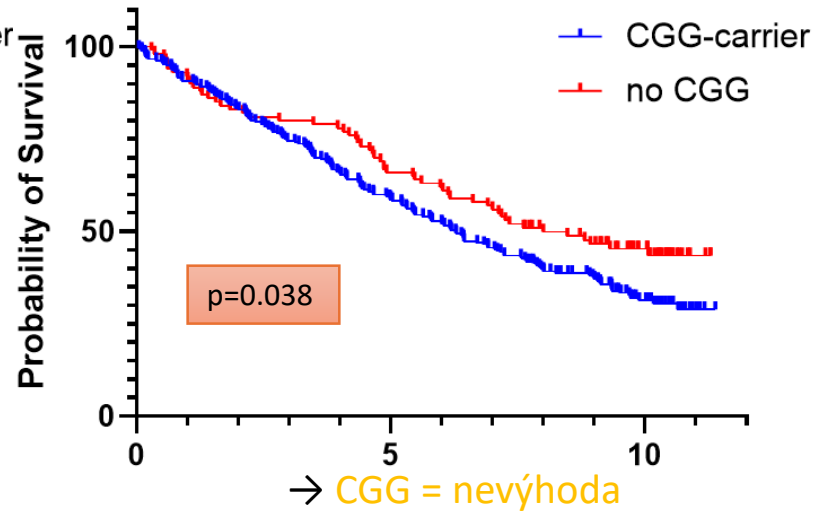
Median survival	
CC,CT	6,278
TT	8,003
Hazard Ratio (logrank)	A/B
Ratio (and its reciprocal)	1,380
95% CI of ratio	1,037 to 1,836

IL10 haplotyp TAT



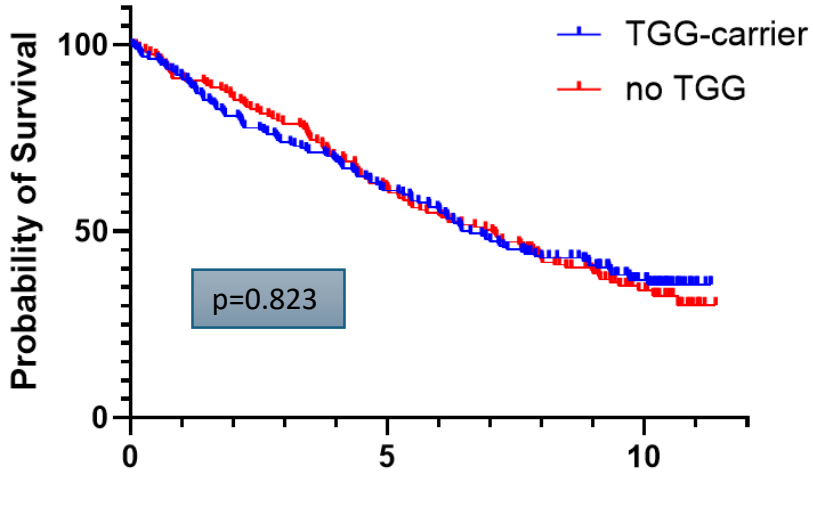
→ TAT = výhoda

IL10 haplotyp CGG

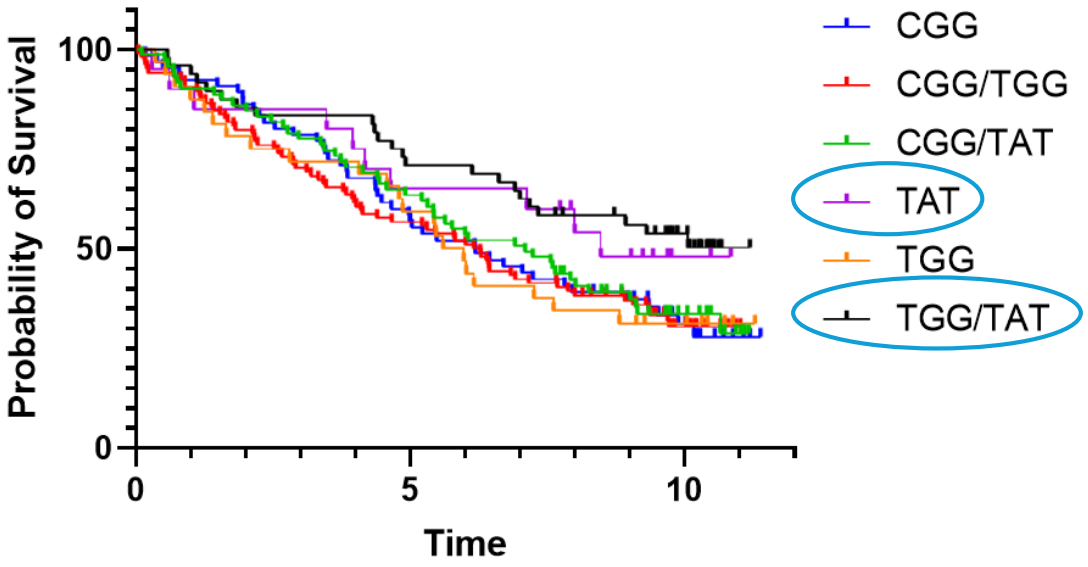


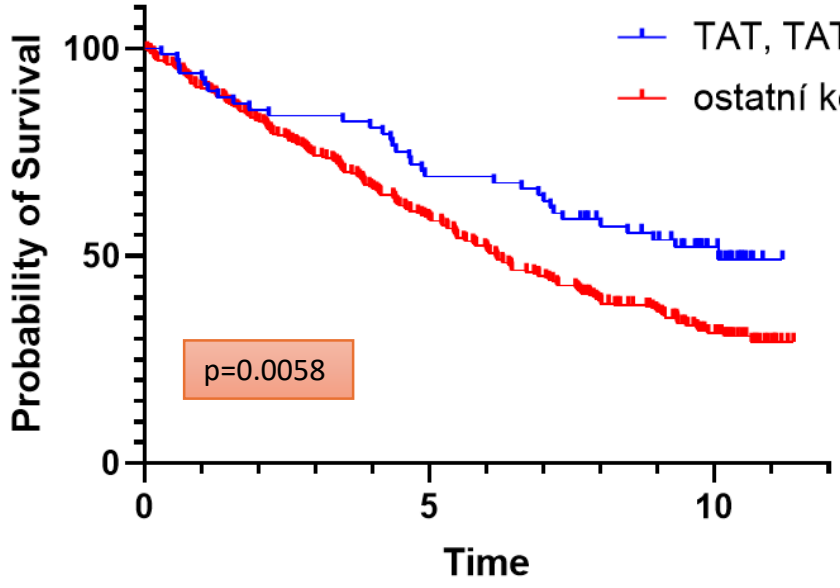
→ CGG = nevýhoda

IL10 haplotyp TGG



IL10 haplotypy





Median survival	
TAT, TAT/TGG	10,07
ostatní kombinace	6,166
Hazard Ratio (logrank)	B/A
Ratio (and its reciprocal)	1,674
95% CI of ratio	1,220 to 2,296

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

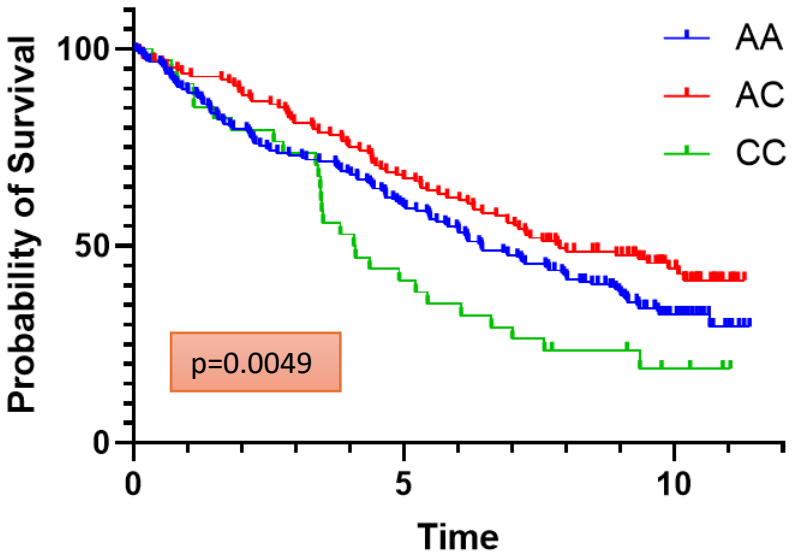
3) mMRC
nosič haplotypu CGG ($IL10_{-1082}$ CC nebo CT genotyp) častější u vyššího stupně mMRC
0-1 (n=87) vs. 2-3 (n=234): 60,9 % vs. 73,9 %, p=0,023
0-2 (n=219) vs. 3-4 (n=102): 66,7 % vs. 78,4 %, p=0,032

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

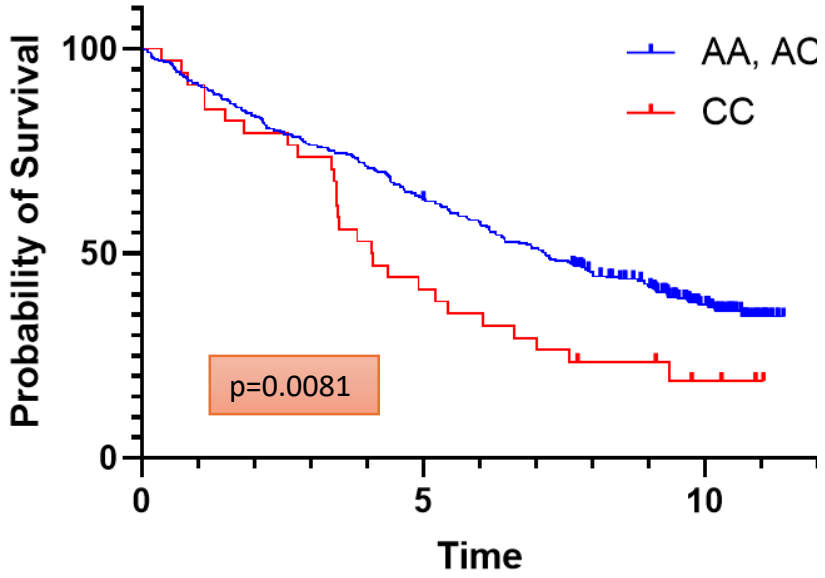
5) Fenotyp BCOS (n=52) vs. **no BCOS** (n=214)
nosičství haloptypu TAT častější (trend) u no BCOS: 44,4 % vs. 30,8 %, p=0,074 (=trend)

SNP v genu *IL2* (rs2068762, rs2069763)

$IL2_{-330}$ rs2069762 A>C

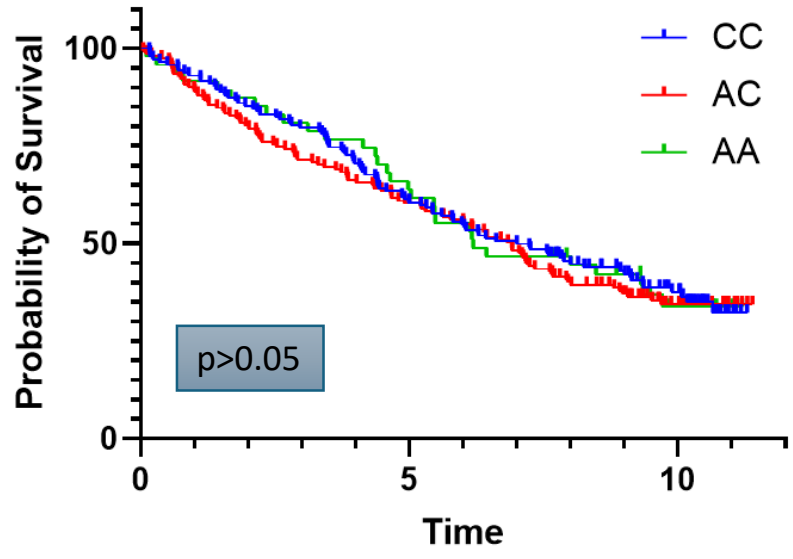


	AA	AC	CC
Median survival	6,42026	7,87953	4,08761



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



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*

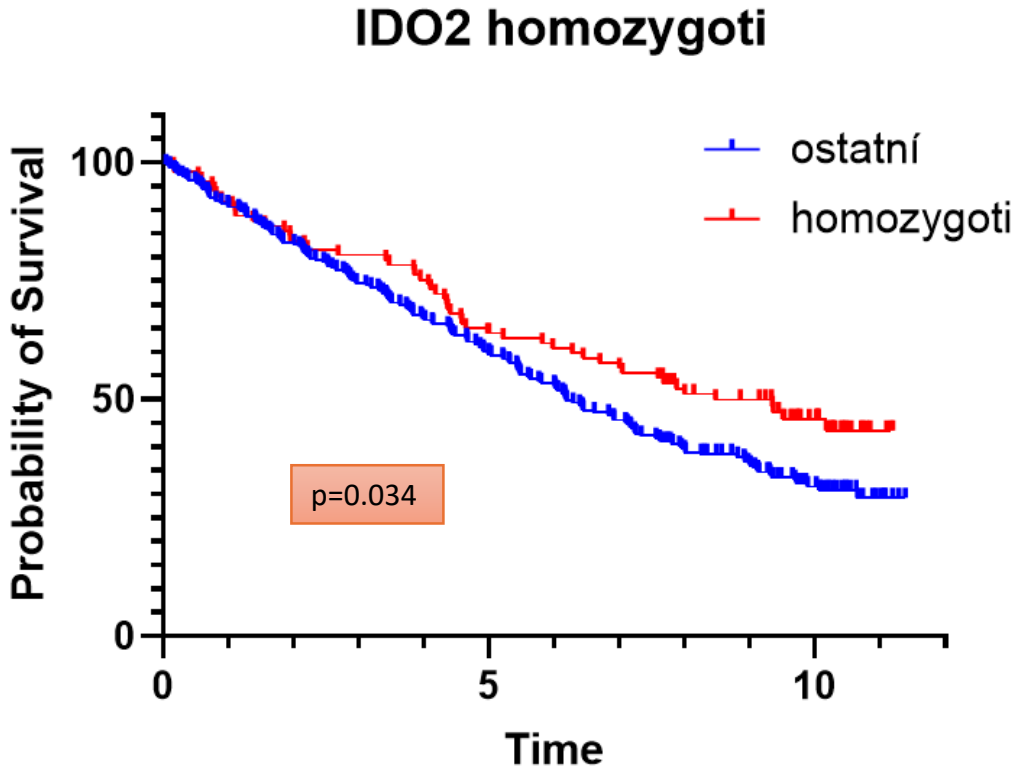
***IDO2* rs10109853** C>T (R248W)

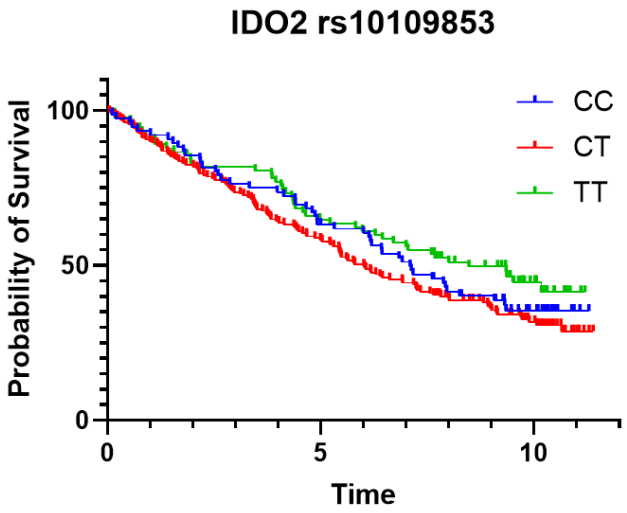
alela *T = nižší aktivita enzymu IDO2

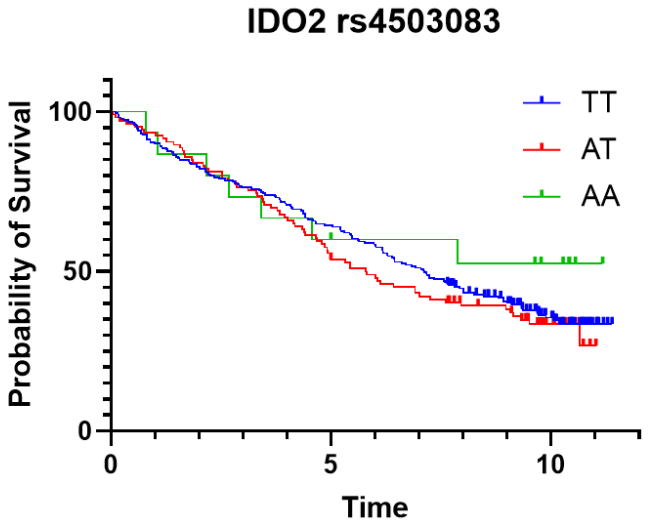
***IDO2* rs4503083** T>A (Y359X)

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







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

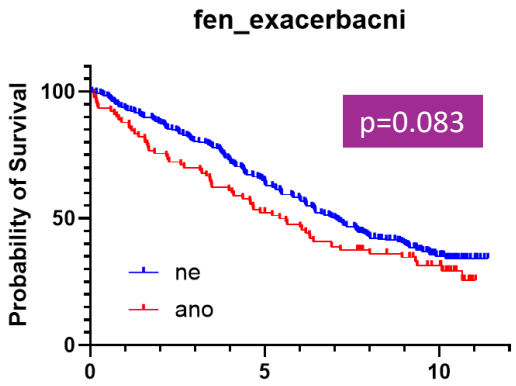
AA homozygoti častější u CAT<18: 6,7 % vs. 1,6 %, p=0,040

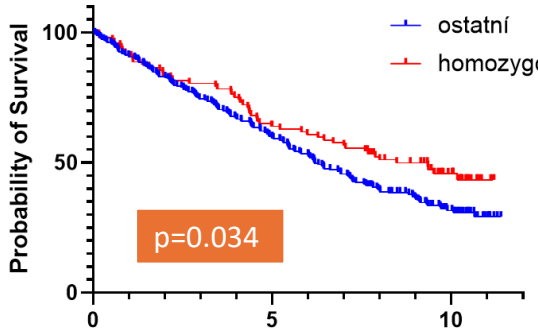
4) BMI <27,5 (n=127) vs. **BMI≥27,5** (n=175)

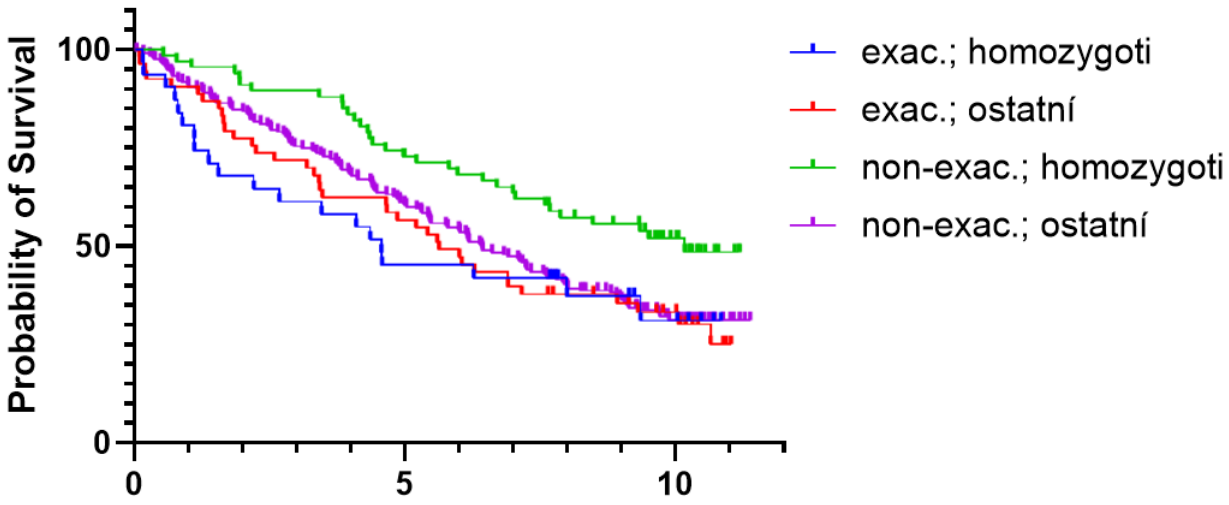
rs10109853 C>T (R248W) TT homozygot častější (trend) u BMI≥27,5: 28,6 % vs. 18,9 %, p=0,054 (=trend)

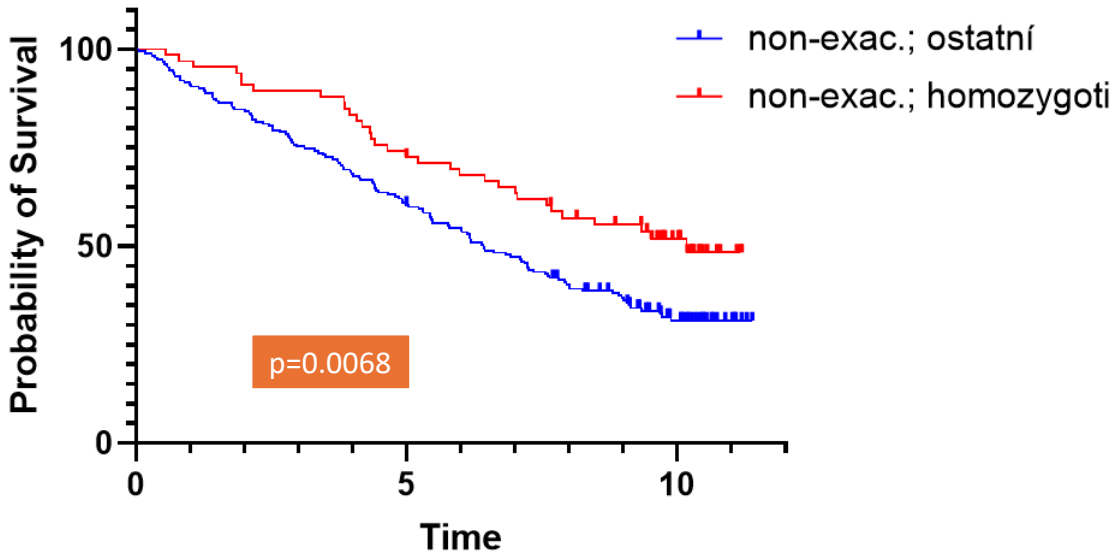
VIZ DÁLE

Homozygoti IDO2 R248W nebo Y359X



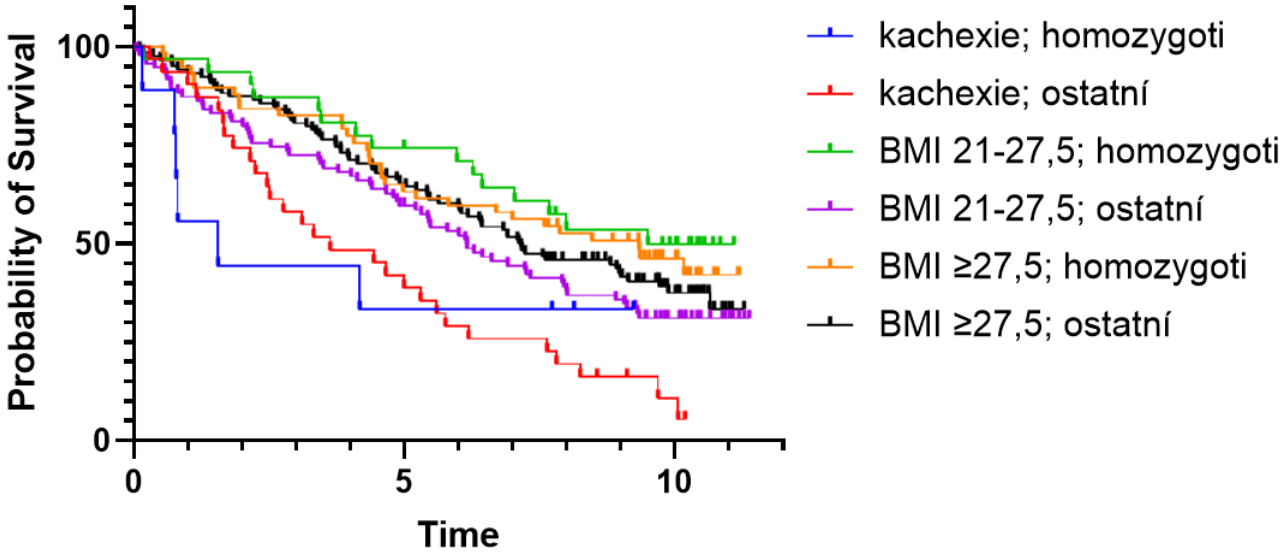




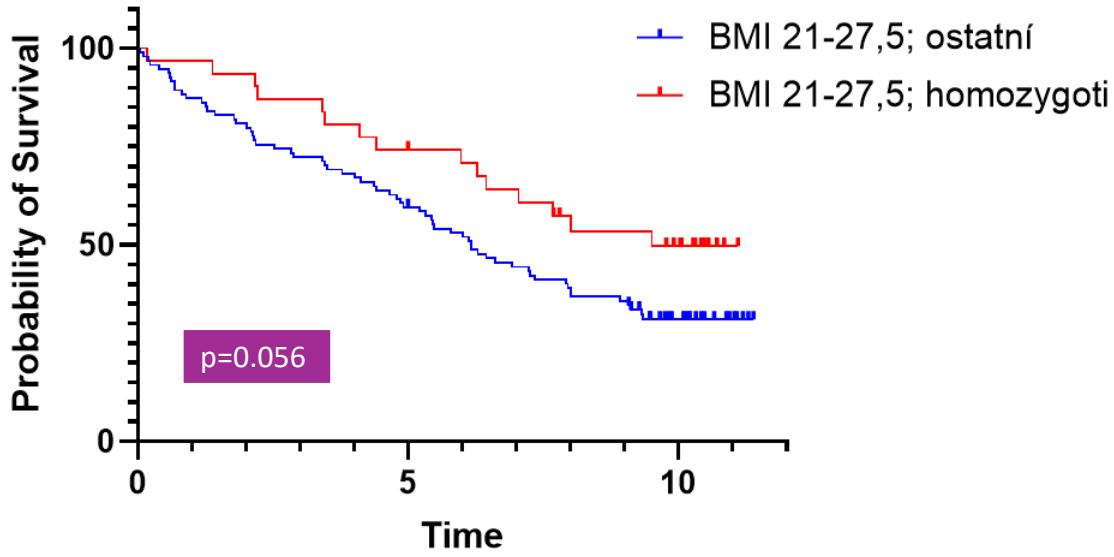


	exac.; homozygoti	exac.; ostatní	non-exac.; homozygoti	non-exac.; ostatní
Median survival	4,57221	5,6345	10,1793	6,42026

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



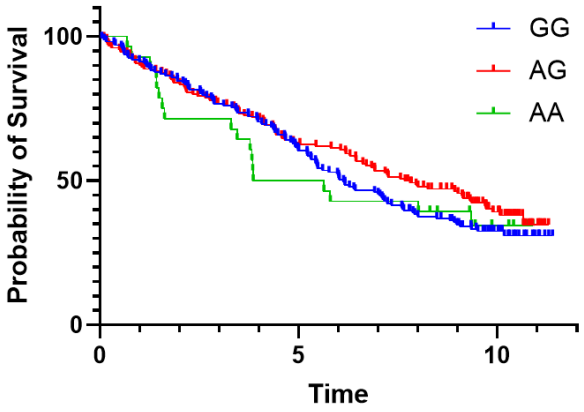
	Median survival
kachexie; homozygoti	1,56
kachexie; ostatní	3,63
BMI 21-27,5; homozygoti	9,51
BMI 21-27,5; ostatní	6,16
BMI ≥27,5; homozygoti	9,35
BMI ≥27,5; ostatní	7,16



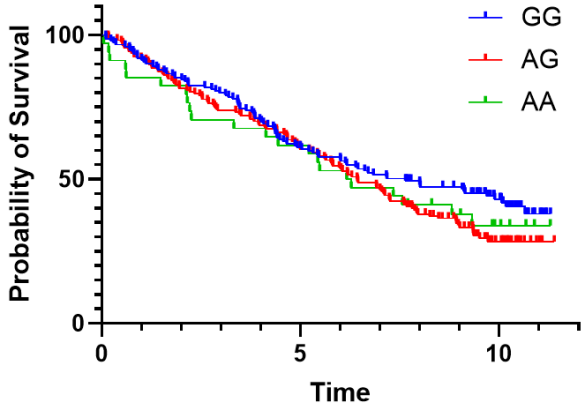
Median survival	
BMI 21-27,5; homozygoti	9,511
BMI 21-27,5; ostatní	6,163
Hazard Ratio (Mantel-Haenszel)	B/A
Ratio (and its reciprocal)	1,610
95% CI of ratio	0,9876 to 2,623

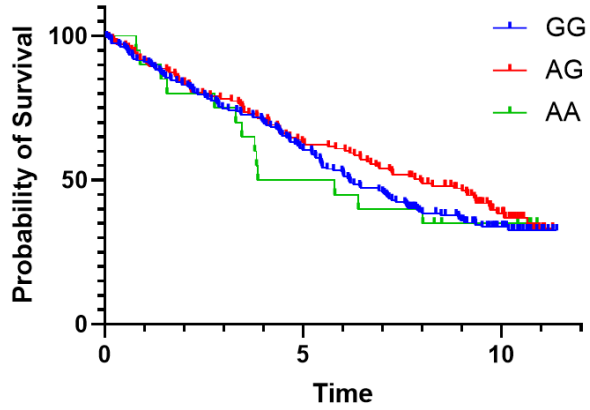
SNP v genech *IL1* genového klastru:

1) SNP v genu *IL1A:* ***IL1A*$_{-889}$ rs1800587**

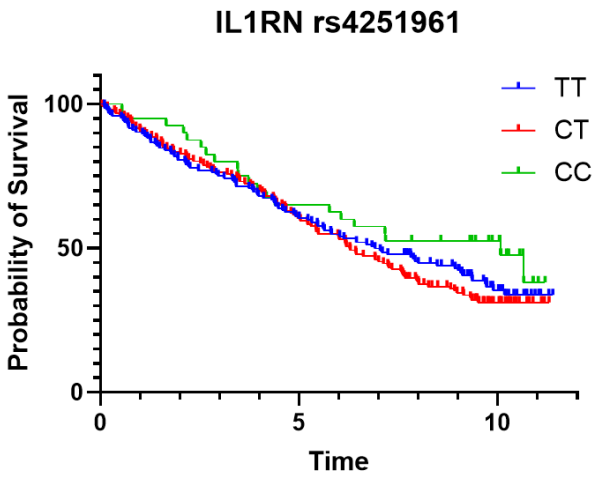


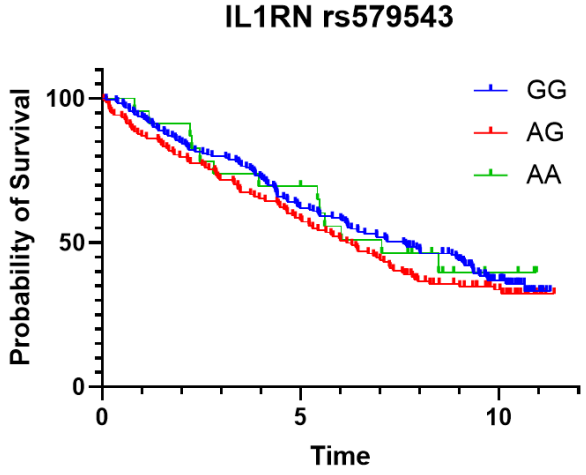
2) SNP v genu *IL1B:* ***IL1B*$_{-511}$ rs16944, *IL1B*$_{+3962}$ rs1143634**

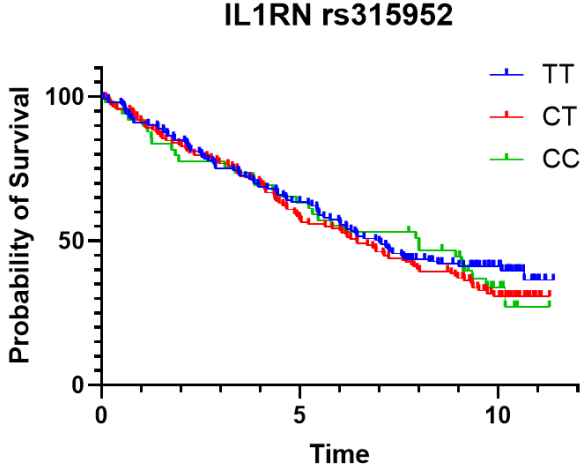




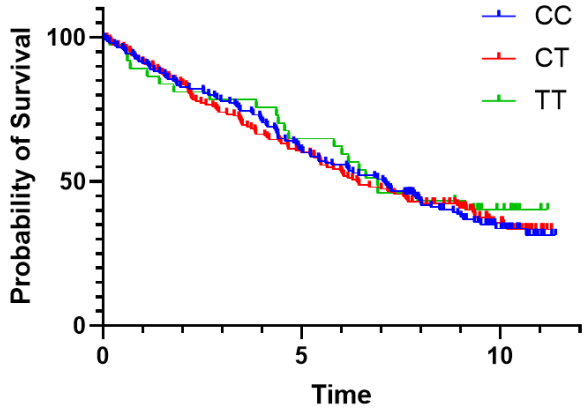
3) SNP v genu ***IL1RN*: *rs4251961, rs579543, rs315952***





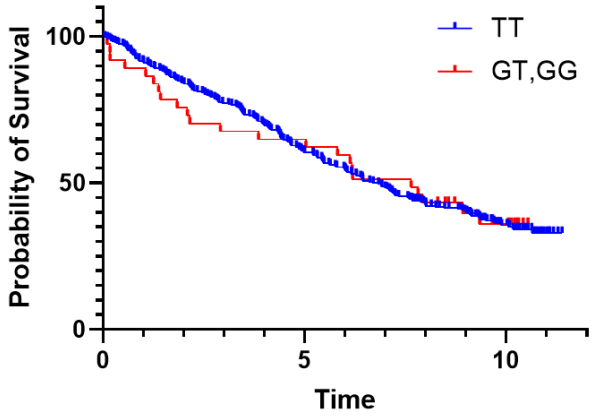


4) SNP v genu ***IL1R1 rs2234650***



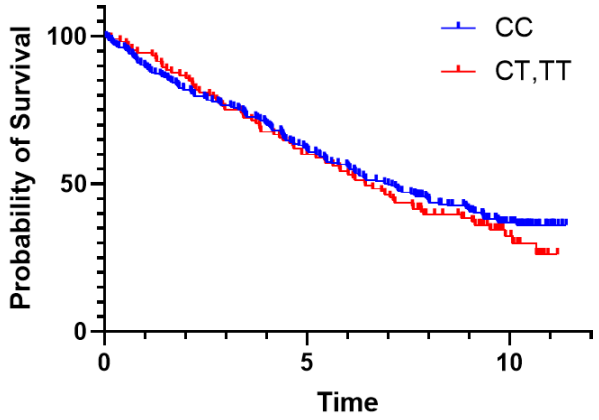
SNP v genech *IL4 a IL4R*:

***IL4*$_{-1098}$ rs2243248**

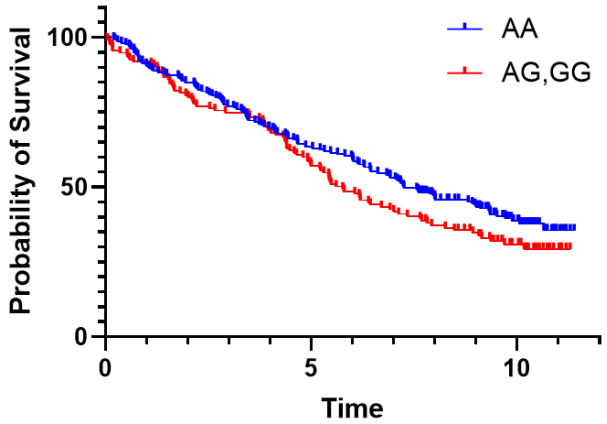


***IL4*$_{-590}$ rs2243250, *IL4*$_{-33}$ rs2070874**

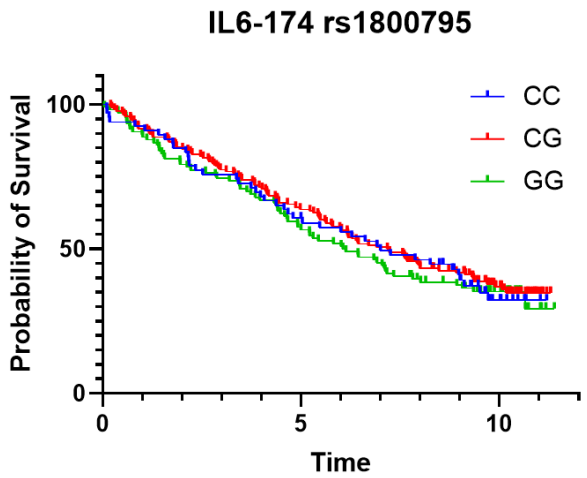
2 SNP ve vazbě



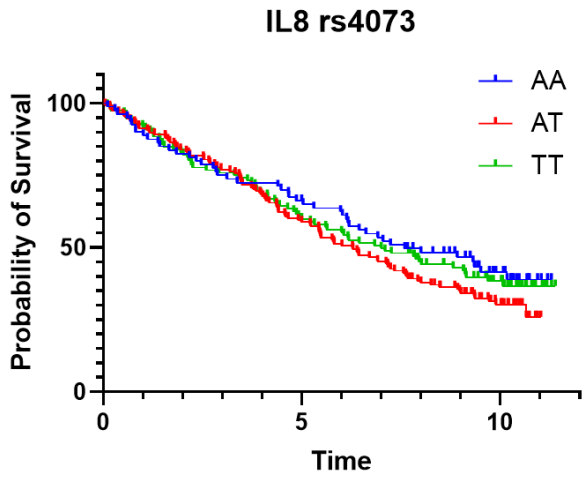
***IL4Rα*$_{+1902}$ rs1801275**



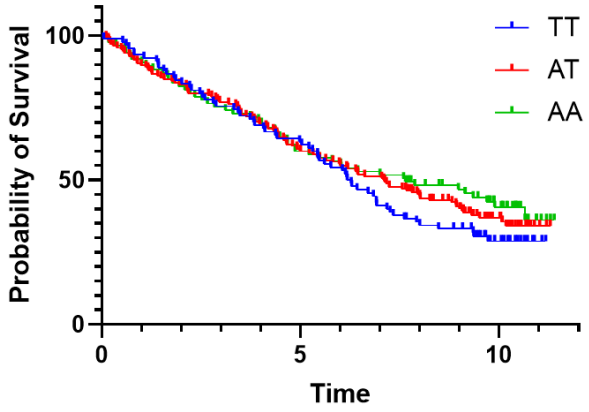
SNP v genu *IL6*: ***IL6*$_{-174}$ rs1800795, *IL6*$_{+565}$ rs1800797** (2 SNP ve vazbě)



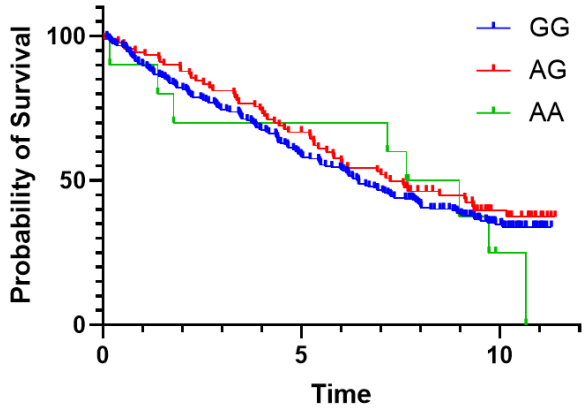
SNP v genu ***CXCL8* (IL8): rs4073, rs2227307** (2 SNP ve vazbě)

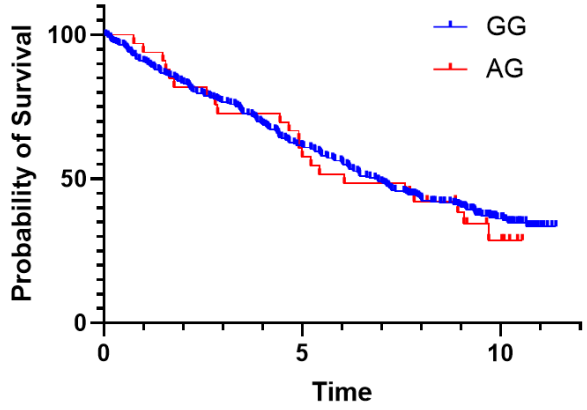


SNP v genu pro interferon γ: ***INFG*$_{+874}$ rs2430561**

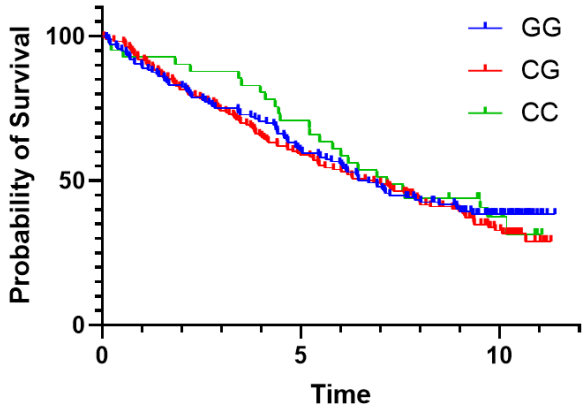


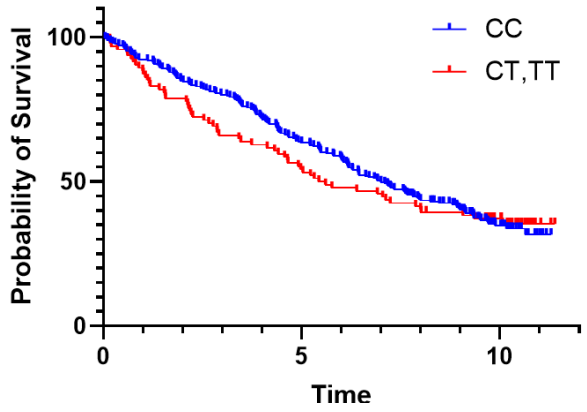
SNP v genu pro TNF-α: **TNFA$_{-308}$ rs1800629 , TNFA$_{-238}$ rs361525**



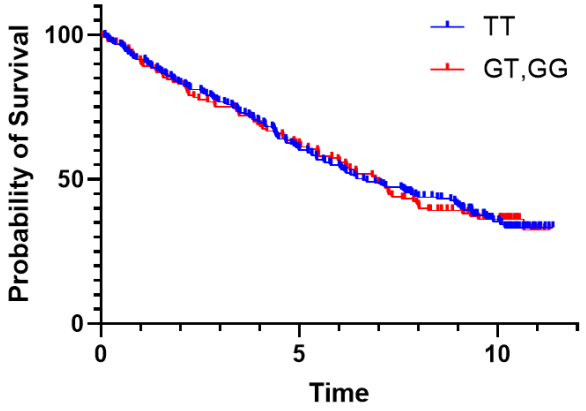


SNP v genu *MBL2*: ***MBL2*$_{-550}$ rs11003125**, **MBL2$_{cd54}$ rs1800450**

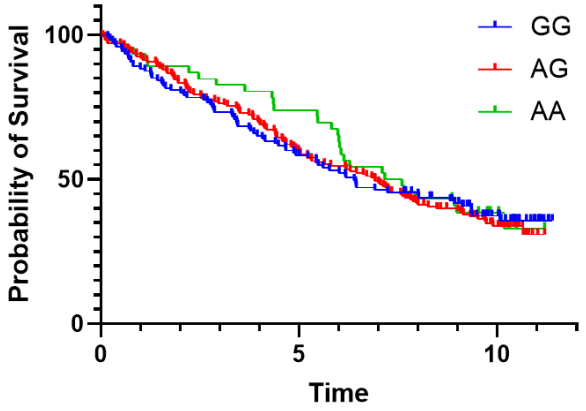




SNP v genu *IL12*: ***IL12*$_{-1188}$ rs3212227**



SNP v genu ***IL17A* rs2275913**

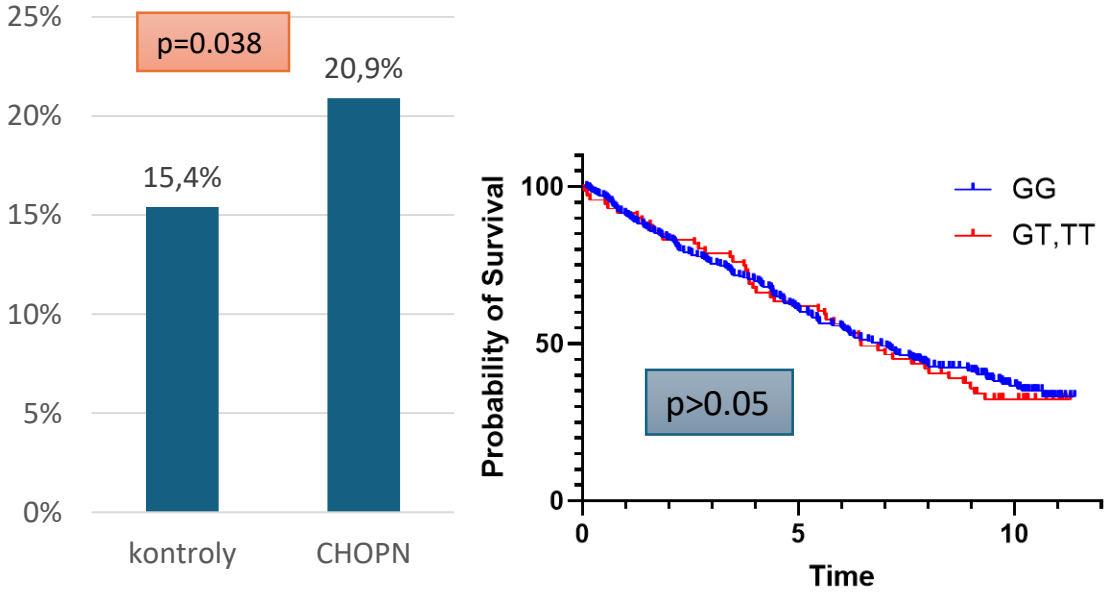


SNP predisponující k CHOPN (1)

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

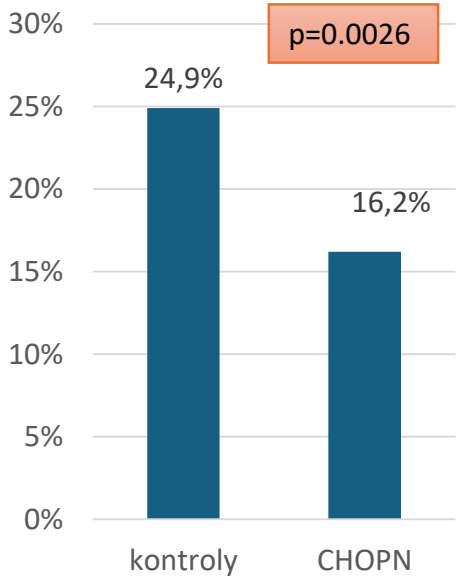
MUC5B rs35705950 G>T

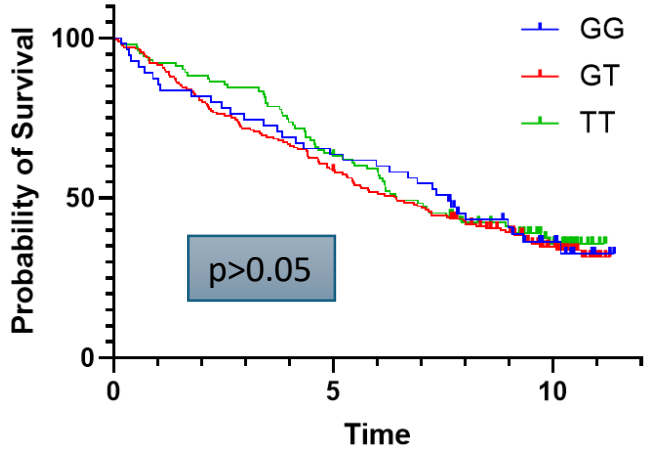
Nosičství alely *T



DSP rs2076295 T>G

Genotyp GG

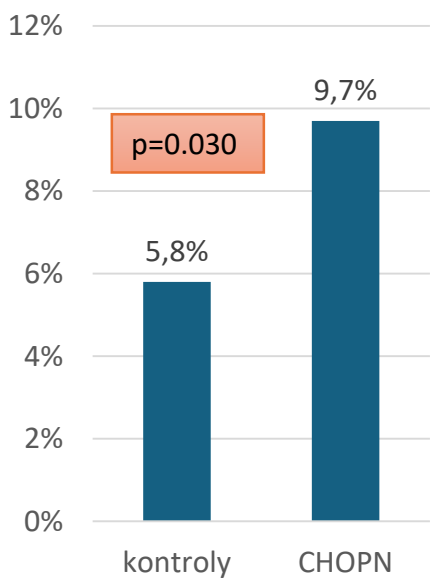


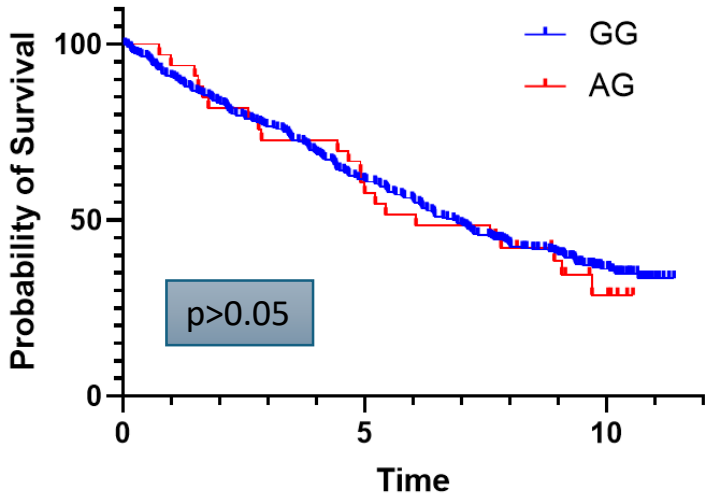


SNP predisponující k CHOPN (2)

TNFA (TNFα$_{-238}$) rs361525 G>A

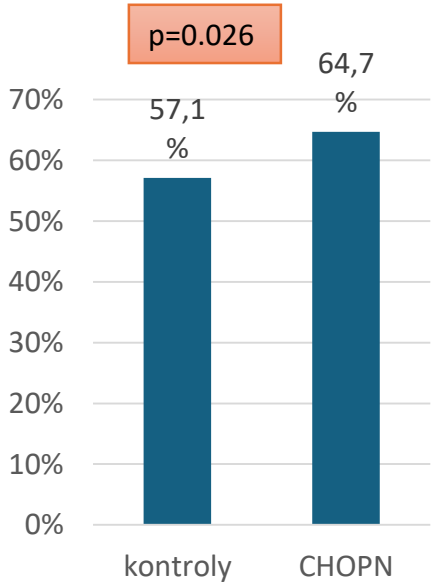
Nosičství alely *A

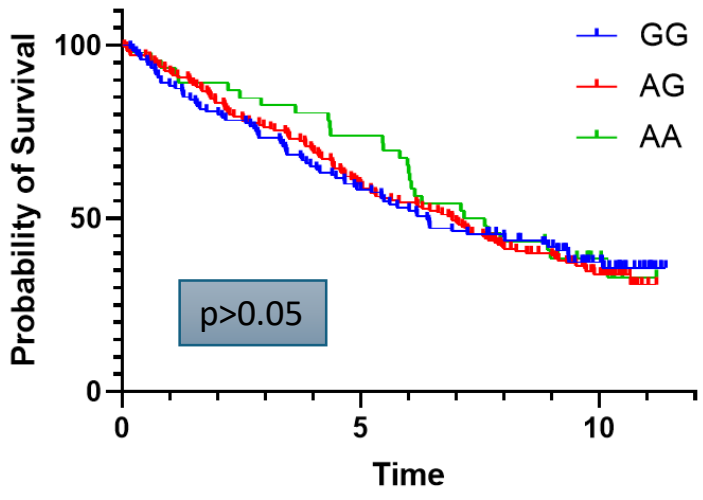




IL17A rs2275913 G>A

Nosičství alely *A





nosičství alely *A nejvíce u pacientů s kachexií (23,7%)
a se srdečním selháním (16,7%)

SNP predisponující k CHOPN (3)

SNP, jejichž frekvence se liší při srovnání pacientů s CHOPN (celá kohorta, n=340) a zdravými kontrolami (n=520) neovlivňují délku přežití ani není jejich frekvence rozdílná při rozdělení pacientů do podskupin podle fenotypů, plicních funkcí atd. (kromě TNF_{-238} u kachexie a srdečního selhání)