SUPPLEMENTAL MATERIAL

Supplemental Table 1. Pharmacogenomic Studies in Pediatric Cardiac Transplantation

Authors	Drug	N*	Patient Base	Outcome(s)	Gene(s)	Variant(s)	Findings
Zheng, 2002[1]	Tacrolimus	69	Children's Hospital of Pittsburgh	Steroid dependency at 1 year	*ABCB1*	rs1045642 rs2032582	rs1045642 CC homozygotes with increased steroid dependency (67% vs. 38%, p=0.04)
				Drug concentration			No associations to tacrolimus concentration
Zheng, 2003[2]	Tacrolimus	65	Children's Hospital of Pittsburgh	Dose adjusted drug concentration	*ABCB1*	rs1045642 rs2032582	rs1045642 CC homozygotes with lower drug level at 6m (p=0.028), 12m (p=0.033) rs2032582 GG homozygotes with lower drug level at 6m (p=0.017), 12m (p=0.014)
					CYP3A5	rs776746	Compared to *CYP3A5*3/*3, *1/*3* with lower Tacrol level at 3m (p=0.014), 6m (p=0.017), 12m (0.015)
Zheng, 2004[3]	Tacrolimus	70	Children's Hospital of Pittsburgh	Steroid dependency at 1 year	*ABCB1*	rs1045642 rs2032582	rs1045642 CC homozygotes with increased steroid dependency (67% vs. 38%, p=0.04, AOR 0.249 [0.063-0.983])
				Drug concentration			No difference in drug concentrations
					CYP3A5	rs776746	No associations
Gijsen et al, 2011[4]	Tacrolimus	39	Toronto, Ontario, Canada	Dose per kg/12 hours	*ABCB1*	rs1045642 rs1128503 rs2032582	No associations
				Trough concentration Dose adjusted concentration	*CYP3A5*	rs776746	Compared to *CYP3A5*3/*3, *1* carriers with higher dose (0.14 vs 0.06 mg/kg/12 hours, p=0.001), lower trough (7.7 vs 9.8 ng/ml, p=0.032), and lower dose adjusted concentration (45.34 vs 177.78 ng/ml per mg/kg/12 hours, p=0.001)
Gijsen et al, 2013[5]	Tacrolimus	60	Toronto, Ontario, Canada	Dose to reach target concentration	*CYP3A4*	rs35599367	*CYP3A4*22* carriers with 30% lower doses (p=0.016)
					CYP3A5/ CYP3A5	rs35599367 rs776746	Poor CYP3A metabolizers with 17% lower doses than intermediate (p=0.023), and 48% less than extensive metabolizers (p<0.0001)
Ohmann, 2010[6]	MMF/MPA	59	Children's Hospital of Pittsburgh	Drug discontinuation GI intolerance Bone marrow toxicity	*IMPDH1*	rs2288553 rs2288549 rs2278293 rs2278294 rs2220875	rs2278294 A and rs2228075 A carriers with more GI intolerance (p=0.029 and p=0.002; AORs 0.28 [0.09-0.90], 0.16 [0.05-0.55], respectively)

					IMPDH2	rs11706052	rs11706052 G carriers with increased bone marrow toxicity (p=0.046, AOR 0.26, [0.02-1.19])
					ABCC2	rs717620	rs717620 A carriers with higher rate of discontinuation of MMF/MPA due to any cause (p=0.021, AOR 0.22, 95%CI 0.06-0.77) and with more GI intolerance (p<0.001, AOR 0.025 [0.002-0.27])
Ohmann, 2010[7]	MMF/MPA	59	Children's Hospital of Pittsburgh	Gastrointestinal intolerance	*IMPDH1*	rs2288553 rs2288549 rs2278293 rs2278294 rs2228075	*IMPDH1* haplotype B (TCTTT) associated with GI intolerance (59% in carriers vs 22% in non-carriers, p=0.005)
Burckart, 2014[8]	MMF/MPA	290	Pediatric Heart Transplantation Study (6 institutions)	Rejection with hemodynamic compromise Graft failure Death	*ABCC2*	rs717620	rs717620 GG homozygotes with increased rejection with hemodynamic compromise and late rejection with hemodynamic compromise (p<0.05, hazard ratios: 1.80 and 4.57, respectively)

*N = Number included in study. Number with genotype and phenotype data available for each outcome may be slightly lower
AOR – Adjusted Odds Ratio; MMF – mycophenolate mofetil; MPA – mycophenolic acid

Supplemental References

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