

Effect of CYP2D6 and ABCB1 polymorphisms on pharmacokinetics and efficacy of aripiprazole in pediatric tic disorders

Yingying Xin, MM^{1,#}, Liuliu Gao, MM^{2,#}, Sichan Li, MM², Jun Wang, MM², Chen Chen, MM³, Yali Tuo, MM², Gang Nie, MD², Ruizhen Li, MD¹, Dan Sun, MD⁴, Yongli Fu, MM⁵, Yang Wang, MM^{6,*}, Zhisheng Liu, MD^{4,*}

1. Department of Child Health, Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science & Technology, Wuhan 430016, China.

2. Department of Pharmacy, Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science & Technology, Wuhan 430016, China.

3. Department of Pharmacy, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Hubei Wuhan, China.

4. Department of Neurology, Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science & Technology, Wuhan 430016, China.

5. Department of Pharmacy, Wuhan Mental health Center, Tongji Medical College, Huazhong University of Science & Technology, Wuhan 430016, China.

6. Office of Clinical Trial Institution, Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science & Technology, Wuhan 430016, China.

Yingying Xin and Liuliu Gao contributed equally to this paper.

***Corresponding authors: Yang Wang (cattop3211@qq.com, Tel: 027-82308909) & Zhisheng Liu (liuzsc@126.com, Tel: 027-82433435) contributed equally to this paper.** Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science and Technology, Hubei Wuhan 430016, China.

Table S5 Summary of the latest researches on the correlation between CYP2D6/ABCB1 gene polymorphisms and pharmacokinetics of ARI

Gene	Research	Variants(phenotypes/genotypes)	Associated	Not associated
CYP2D6	Zhang et al ^[14] (2021)	rs1135840	C _{max} , T _{max} and AUC _{0-∞} of ARI	T _{1/2}
		rs28371702	T _{max} and AUC _{0-∞}	C _{max} , T _{1/2}
		rs1058164, rs28371699	C _{max} , T _{max} and AUC _{0-∞} , T _{1/2}	—
		EMs (extensive metabolizers) & IMs (intermediated metabolizers)	T _{1/2} , AUC _{0-∞}	C _{max} , T _{1/2}
	Belmonte et al ^[15] (2018)	PMs (poor metabolizers)	C _{max} , T _{1/2}	
ABCB1	Belmonte et al ^[15] (2018)	G2677T/A (rs2032582)	CL/F of ARI AUC _{0-t} of DARI	AUC _{0-t} , C _{max} , T _{1/2} of ARI CL/F, C _{max} , T _{1/2} of DARI
		C1236T (rs1128503)	CL of ARI AUC _{0-t} and C _{max} of the DARI	—
		C3435T(rs1045642)	Ratio of DARI/ARI	ARI&DARI AUC _{0-t} , C _{max} , T _{1/2} , CL/F
	Rafaniello et al ^[27] (2018)	2677TT/3435TT	concentration/dose(C/D)	—

PMs, poor metabolizers; IMs, intermediated metabolizers; EMs, extensive metabolizers; CL/F, apparent clearance rate