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AUTHOR CORRECTION

Author Correction: Hepatic Impairment Physiologically Based Pharmacokinetic Model Development: Current Challenges

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The original version of this article unfortunately contained a mistake. Equal contribution note and Tables 1 and 2 are missing in the original article. Tables 1 and 2 are shown here.

The original article has been corrected.

Beatrice Han and Agnes Han contributed equally.

The original article can be found online at https://doi.org/10.1007/s40495-021-00266-5.

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Table 1 Summary of hepatic impairment impact on physiological parameters associated with drug absorption, distribution, metabolism, and excretion

	HI-induced physiological changes	Impact on PK parameter(s)	Compounds and drugs of interest	Highlighted issues	References
Absorption	Altered bile salt concentration	Decrease in ka and fa of poorly soluble drugs	Poorly soluble drugs; BCS II and BCS IV drugs, e.g., erlotinib	Lack of reported bile salt concentration changes associated with HI	29; 30; 33
Distribution	Decreased levels of AAG and albumin	Increased fraction unbound	Telaprevir; naproxen; erythromycin	Not applicable	41; 42; 17
	Ascites	Increased volume of distribution and half life; decreased Cmax	Gentamicin; cefodizime	Current PBPK models do not account for the effect of ascites on distribution	17; 50; 49
Metabolism	Shunting (reduced hepatic blood flow)	Decreased presystemic elimination and first pass metabolism; increased drug systemic bioavailability	Drugs experiencing extensive first pass metabolism; ibrutinib	Not applicable	18; 19; 24
	General decrease in CYP expression but variable individual CYP enzyme changes (see Table 2)	Increased exposure in cirrhotic patients	Sorafenib; imatinib	Existing literature disagrees significantly on HI-induced CYP enzyme changes	See Table 2
	Undetermined Aldehyde Oxidase (AO) level changes	Undetermined	Capmatinib	Clearance of AO substrates is difficult to predict	58; 60
	General lowered UGT expression with severe HI; minimal effects with moderate/mild HI; variable levels of specific UGT enzymes (see Table 2)	Minimal impact on PK for moderate and mild HI	Depaglifozin	See Table 2	See Table 2
Excretion	Variable changes in of hepatobiliary transporter expression (see Table 2)	Variable changes in clearance	Atorvastatin, cervastatin, nelfinavir	Considerable disagreement in current literature exists over transporter expression in HI patients	74; 75 See Table 2 for transporter-specific references
	HI-induced hepatorenal syndrome/acute renal failure	Decreased renal clearance	Rivaroxaban	HI associated fluctuations in creatinine levels induces inaccurate GFR estimates	78; 79

Table 2 Summary of HI-induced changes in drug-metabolizing enzymes and drug transporters

Metabolism	Enzyme	Disease stage	Expression level change with HI relative to healthy volunteer	References
	CYP3A4	General liver cirrhosis	Decrease	13; 17
	CYP1A2	General liver cirrhosis	Decrease	17
		NAFLD	Decrease	54
	CYP2A6	General liver cirrhosis	Decrease	17
		NAFLD	Increase	54
	CYP2B6	General liver cirrhosis	Decrease	17
	CYP2C8	General liver cirrhosis	Decrease	17
		General liver cirrhosis	No change	13
	CYP2C9	General liver cirrhosis	Decrease	17
		Alcoholic and HCV cirrhotic livers	Decrease	64
		General liver cirrhosis	No change	13
		NAFLD	Increase	54
	CYP2C18	General liver cirrhosis	Decrease	17
	CYP2C19	General liver cirrhosis	Decrease	17
		NAFLD	Decrease	54
	CYP2D6	General liver cirrhosis	Decrease	17
		NAFLD	Decrease	54
	CYP2E1	General liver cirrhosis	Decrease	17
		NAFLD	Decrease	54
	UGT			
	UGT1A6	Alcoholic cirrhosis and HCV cirrhosis	Decrease to less than 25%	64
	UGT1A4	Alcoholic cirrhosis and HCV cirrhosis	Decrease to less than 25%; Decrease was larger for alcoholic cirrhosis vs. HCV cirrhosis	64
	UGT2B7	Alcoholic cirrhosis and HCV cirrhosis	Decrease to less than 25%	64
	UGT1A9	General liver cirrhosis	Decrease	65
	Other enzymes			
	ADH1A	Alcoholic cirrhosis	Decrease to less than 25%	64
	ADH1B	Alcoholic cirrhosis	Decrease to less than 25%	64
	AOX1	Alcoholic cirrhosis	Decrease to less than 25%	64
	CES1A2	Alcoholic cirrhosis	Decrease to less than 25%	64

Table 2 (continued)

Metabolism	Enzyme	Disease stage	Expression level change with HI relative to healthy volunteer	References
Excretion	**Transporters**			
	OCT1	Hep C cirrhosis	38% decreased expression	12
		CPC	65% decreased expression	73
	OATP2B1	HCV	Decreased	75
		NASH	Increased	75
		PBC	Decreased	76
		Alcoholic cirrhosis	No change	12
		CPC	63% decreased expression	73
	OATP1B3	Hep C cirrhosis	Decreased	12
	MRP2	HCV	Decreased	75
		NASH	Increased	75
		PBC	No change	76
		Alcoholic cirrhosis	No change	12
		Hep C cirrhosis	Decreased	12
		CPC	70% decreased expression	73
	MRP3	NASH	Increased	75
		Alcoholic cirrhosis	32% increased expression	12
	MRP4	CPC	Increased	73
		Primary biliary cholangitis	2.9-fold higher expression	73
	NTCP	PBC	Decreased	76
		Hep C cirrhosis	36% decreased expression	12
		CPC	34% decreased expression	73
	BSEP	PBC	No change	76
		Hep C cirrhosis	Decreased	12
	MDR1	PBC	Increased	76
	MDR3	PBC	Increased	76
	P-gp	HCV	Increased	75
		Alcoholic cirrhosis	No change	12
		Hep C Cirrhosis	Decreased	12
		CPC	2. 6-fold higher expression	73
	MATE1	Alcoholic cirrhosis	No change	12
		Hep C cirrhosis	Increased	