

Table S1. Signal-detected LMT-related indications.

Indication	Odds Ratio	95% Confidence Interval	<i>p</i> -Value
Hepatitis B	40.94	28.89–58.02	<.0001**
Chronic hepatitis B	38.53	21.87–67.88	<.0001**
Hepatic cirrhosis	36.97	25.83–52.93	<.0001**
Liver transplant	22.94	14.43–36.45	<.0001**
Chronic hepatitis C	22.01	18.67–25.95	<.0001**
Prophylaxis against transplant rejection	13.79	8.80–21.61	<.0001**
Immunosuppressant drug therapy	13.52	5.82–31.39	<.0001**
Hepatitis C	13.04	11.14–15.28	<.0001**
Fluid retention	12.82	5.52–29.76	<.0001**
Liver disorder	12.48	3.58–43.45	0.0179*
Ascites	11.54	4.02–33.11	0.0038*
Breakthrough pain	11.47	3.30–39.93	0.0209*
Carcinoid syndrome	11.05	3.18–38.46	0.0224*
Thrombocytopenia	8.89	3.10–25.49	0.0077*
Cardiovascular disorder	8.68	3.43–21.97	0.0020*
Cancer pain	8.42	4.82–14.73	<.0001**
Immunosuppression	7.17	3.09–16.6	0.0012*
Hypokalaemia	6.29	2.20–18.00	0.0193*
Gastric ulcer	5.75	2.48–13.30	0.0031*
Pain management	5.50	1.92–15.73	0.0272*
Angina pectoris	4.50	2.08–9.73	0.0038*
Growth hormone deficiency	4.35	1.52–12.44	0.0485*
Psoriasis	3.35	2.58–4.35	<.0001**
Prophylaxis against gastrointestinal ulcer	3.31	1.53–7.15	0.0156*
Diabetes mellitus	3.09	2.30–4.15	<.0001**
Type 2 diabetes mellitus	2.73	2.12–3.51	<.0001**
Hyperlipidaemia	2.67	1.56–4.57	0.0023*
Dyspepsia	2.51	1.22–5.14	0.0336*
Pulmonary arterial hypertension	2.42	1.62–3.61	0.0002*
HIV infection	2.01	1.25–3.21	0.0102*
Constipation	2.00	1.09–3.66	0.0480*
Rheumatoid arthritis	1.33	1.03–1.73	0.0421*

*: $p < 0.05$, **: $p < 0.0001$.

Table S2. Signal-detected LMT-related drugs.

Drug	Odds Ratio	95% Confidence Interval	p-Value
Daclatasvir	77.73	62.60–96.52	<.0001**
Asunaprevir	70.77	45.95–109	<.0001**
Entecavir	48.25	31.19–74.66	<.0001**
Cinnamomum cassia	35.89	13.96–92.27	<.0001**
Adefovir	33.87	18.25–62.84	<.0001**
Sofosbuvir	31.25	26.74–36.53	<.0001**
Quinine	29.58	12.63–69.3	<.0001**
Panax ginseng	28.15	11.00–72.08	<.0001**
Atractylodes lancea	27.38	9.44–79.46	0.0003*
Velpatasvir	26.52	16.86–41.69	<.0001**
Poria cocos	25.50	9.97–65.19	<.0001**
Telbivudine	24.82	10.62–58.01	<.0001**
Potassium aspartate	21.56	6.14–75.70	0.0065*
Docosahexaenoic acid	20.91	5.96–73.40	0.0069*
Ledipasvir	20.90	15.8–27.63	<.0001**
Glycyrrhiza spp.	19.88	7.80–50.66	<.0001**
Glecaprevir	18.81	11.53–30.69	<.0001**
Pibrentasvir	18.81	11.53–30.69	<.0001**
Albiglutide	18.42	7.23–46.92	0.0001*
Paritaprevir	17.42	13.15–23.08	<.0001**
Ombitasvir	17.36	13.10–23.01	<.0001**
Dasabuvir	15.70	11.43–21.57	<.0001**
Cefcapene	14.06	4.03–49.10	0.0144*
Levomefolic acid	13.10	3.75–45.70	0.0164*
Tocopherol	12.08	4.76–30.65	0.0006*
Bisacodyl	11.81	4.66–29.98	0.0007*
Enterococcus faecalis	11.64	3.34–40.59	0.0204*
Mianserin	11.60	4.57–29.42	0.0007*
Boceprevir	11.56	6.75–19.82	<.0001**
Ribavirin	11.53	9.96–13.34	<.0001**
Gliclazide	11.31	5.50–23.27	<.0001**
Cysteine	11.27	3.23–39.28	0.0217*
Elbasvir	10.80	4.65–25.07	0.0002*
Grazoprevir	10.78	4.64–25.02	0.0002*
Ursodeoxycholic acid	9.95	5.56–17.83	<.0001**
Clostridium butyricum	9.93	3.46–28.50	0.0058*
Eicosapentaenoic acid	9.89	3.45–28.40	0.0058*
Tolvaptan	9.87	6.15–15.83	<.0001**
Propranolol	9.40	5.25–16.84	<.0001**
Glycyrrhizic acid	9.24	2.65–32.15	0.0311*
Ritonavir	9.19	7.09–11.90	<.0001**
Telotristat	8.78	2.52–30.53	0.0342*
Etizolam	8.40	2.93–24.09	0.009*
Calcitriol	8.19	2.36–28.49	0.0386*
Rifaximin	7.97	3.44–18.48	0.0008*
Valine	7.80	2.24–27.11	0.0422*
Leucine	7.77	2.24–27.01	0.0425*
Thiamine	7.64	4.03–14.50	<.0001**

*: $p < 0.05$, **: $p < 0.0001$.

Table S2. Signal-detected LMT-related drugs (continued).

Drug	Odds Ratio	95% Confidence Interval	p-Value
Amino acids nos	7.56	2.64–21.66	0.012*
Isoleucine	7.52	2.16–26.13	0.045*
Ustekinumab	7.45	4.58–12.12	<.0001**
Peginterferon alfa-2b	7.24	5.30–9.89	<.0001**
Alogliptin	6.74	2.66–17.06	0.005*
Sennoside a+b	6.34	2.74–14.69	0.002*
Rabeprazole	6.24	3.29–11.83	<.0001**
Rebamipide	6.06	2.95–12.45	0.0003*
Simeprevir	5.78	3.44–9.70	<.0001**
Tacrolimus	5.67	3.99–8.07	<.0001**
Brotizolam	5.63	1.97–16.13	0.0256*
Insulin glargine	5.60	3.69–8.49	<.0001**
Lactulose	5.57	1.95–15.94	0.0264*
Lopinavir	5.52	2.69–11.33	0.0005*
Ranolazine	5.48	2.37–12.69	0.0038*
Mycophenolic acid	4.98	3.15–7.88	<.0001**
Saxagliptin	4.32	1.71–10.91	0.0219*
Abatacept	4.01	2.19–7.37	0.0004*
Sorafenib	4.01	2.18–7.36	0.0004*
Peginterferon alfa-2a	3.90	2.71–5.61	<.0001**
Loxoprofen	3.89	1.89–7.97	0.0038*
Macitentan	3.86	2.26–6.61	<.0001**
Sirolimus	3.86	1.53–9.75	0.0312*
Glimepiride	3.73	1.72–8.06	0.0091*
Tenofovir	3.71	2.47–5.58	<.0001**
Pravastatin	3.70	1.71–8.01	0.0094*
Octreotide	3.65	1.44–9.22	0.0371*
Secukinumab	3.64	1.92–6.89	0.0016*
Ascorbic acid	3.49	1.61–7.55	0.0123*
Magnesium oxide	3.33	1.62–6.83	0.0085*
Sitagliptin	3.23	2.11–4.94	<.0001**
Spirolactone	3.15	1.81–5.50	0.0009*
Ciclosporin	3.10	1.78–5.41	0.001*
Pyridoxine	3.04	1.32–7.04	0.0372*
Dapagliflozin	2.92	1.35–6.32	0.0263*
Somatropin	2.79	1.29–6.03	0.0319*
Infliximab	2.47	1.54–3.96	0.0011*
Bosentan	2.33	1.31–4.17	0.0197*
Lansoprazole	2.01	1.15–3.51	0.0399*
Metformin	1.86	1.20–2.88	0.0143*

*: $p < 0.05$, **: $p < 0.0001$.

Table S3. Molecular initiating events (MIEs) related to liver malignant tumor-inducing drugs.

AID	Molecular Initiating Events	Activity Type	ROR	95% Confidence Interval	p-Value
1259396	Estrogen Receptor- β	antagonist	8.08	0.91–71.73	0.040*
1259403	Estrogen Related Receptor	antagonist	4.65	1.72–12.61	0.002*
720552	p53	agonist	3.85	0.94–15.80	0.087
743139	Aromatase	antagonist	3.21	0.76–13.60	0.155
720516	ATAD5	genotoxic inducer	2.98	1.30–6.82	0.012*
1259404	Estrogen Related Receptor	agonist	2.96	1.33–6.56	0.010*
743241	Vitamin D Receptor	agonist	2.72	1.15–6.39	0.030*
1347030	Thyrotropin Releasing Hormone Receptor	agonist	2.69	1.22–5.95	0.018*
743199	Peroxisome Proliferator-Activated Receptor- γ	antagonist	2.52	1.00–6.36	0.060
1347033	human Pregnane X Receptor	agonist	2.40	0.83–6.88	0.113
743063	Androgen Receptor lbd	antagonist	2.24	0.94–5.32	0.079
743228	Heat Shock Response	activator	2.03	0.43–9.57	0.440
743091	Estrogen Receptor- α full	antagonist	1.91	0.85–4.34	0.145
1259387	Androgen Receptor with antagonist	agonist	1.89	0.82–4.33	0.143
743077	Estrogen Receptor- α lbd	agonist	1.87	0.86–4.07	0.121
1224894	Hypoxia (HIF-1)	agonist	1.87	0.85–4.11	0.160
743054	Androgen Receptor full	antagonist	1.80	0.67–4.670	0.322
1159531	Retinoid X Receptor- α	agonist	1.80	0.69–4.670	0.322
1347034	Caspase-3/7 in HepG2	inducer	1.78	0.82–3.893	0.168
743219	Antioxidant Response Element	agonist	1.77	0.79–3.98	0.213
743053	Androgen Receptor lbd	agonist	1.67	0.75–3.71	0.226
1259402	Estrogen Related Receptor with PGC	agonist	1.63	0.75–3.556	0.238
743122	Aryl Hydrocarbon Receptor	agonist	1.63	0.65–4.05	0.349
743067	Thyroid Receptor	antagonist	1.61	0.71–3.64	0.298
743226	Peroxisome Proliferator-Activated Receptor- δ	antagonist	1.52	0.70–3.32	0.325
743242	Vitamin D Receptor	antagonist	1.47	0.09–24.06	1.000
1259391	Estrogen receptor alpha with antagonist	agonist	1.47	0.09–24.06	1.000
1159528	Activator Protein-1	agonist	1.45	0.67–3.13	0.434
1259248	Estrogen Receptor- α with stimulator	antagonist	1.42	0.64–3.14	0.420
1259401	Estrogen Related Receptor with PGC	antagonist	1.30	0.60–2.83	0.555
720719	Glucocorticoid Receptor	agonist	1.23	0.56–2.72	0.688

*: $p < 0.05$.

Table S3. Molecular initiating events (MIEs) related to liver malignant tumor-inducing drugs (continued).

AID	Molecular Initiating Events	Activity Type	ROR	95% Confidence Interval	<i>p</i> -Value
1159518	NF- κ B	agonist	1.156	0.40–3.38	0.790
1224893	Constitutive Androstane Receptor	antagonist	1.044	0.310–3.53	1.000
743140	Peroxisome Proliferator-Activated Receptor- γ	agonist	1.027	0.45–2.344	1.000
1347032	Transforming Growth Factor- β	antagonist	0.852	0.36–2.04	0.826
720725	Glucocorticoid Receptor	antagonist	0.707	0.17–2.99	0.735
743227	Peroxisome Proliferator-Activated Receptor- δ	agonist	0.707	0.17–2.99	0.735
1347035	Transforming Growth Factor- β	agonist	0.707	0.17–2.99	0.735
1224892	Constitutive Androstane Receptor	agonist	0.636	0.27–1.50	0.396
743240	Farnesoid-X-Receptor	antagonist	0.473	0.05–4.70	0.644
1224896	histone variant H2AX	agonist	0.473	0.05–4.70	0.644
720637	Mitochondrial Membrane Potential	disruptor	0.447	0.11–1.76	0.353
743239	Farnesoid-X-Receptor	agonist	0.388	0.08–1.96	0.305
1159519	Endoplasmic Reticulum stress response	agonist	0.349	0.04–3.23	0.646
1259247	Androgen Receptor with stimulator	antagonist	0.291	0.06–1.42	0.194
1259392	Sonic Hedgehog signaling (Shh)	antagonist	0.274	0.03–2.43	0.398
743078	Estrogen Receptor- α lbd	antagonist	0.225	0.03–1.94	0.237
1224895	Thyroid Stimulating Hormone Receptor	agonist	0	-	0.269
1259388	Histone Decetylase (HDAC)	antagonist	0	-	0.078
1259395	Thyroid Stimulating Hormone Receptor	antagonist	0	-	0.144
1347031	Progesterone Receptor	antagonist	0	-	1.000
1347036	Progesterone Receptor	agonist	0	-	0.513
1347037	Caspase-3/7 in CHO-K1	inducer	0	-	0.079
1347038	Thyrotropin Releasing Hormone Receptor	antagonist	0	-	0.269
1259390	Sonic Hedgehog signaling (Shh)	agonist	-	-	-
1259394	Estrogen Receptor- β	agonist	-	-	-

*: $p < 0.05$.