

Supplemental Table 1. Coronavirus disease 2019 vaccine-associated liver Injury: case series including autoimmune hepatitis and non-autoimmune hepatitis patients

Ref. No. (Published year)	No. of cases	Demographics (median age [range], M/F)	Pre-existing other autoimmune disorders, n (%)	Pre-existing liver diseases, n (%)	Pre-existing AIH, n (%)	COV ID-19 survivor, n (%)	Vaccine, n (%)	Injury after 1st/2nd/3rd/4th dose (%)	Pattern of injury (Hep/Chol/Mixed) (%)	The median (range) time from last vaccine dose to onset of liver injury (days)
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17 (2022)	46 77	mRNA: 52 [IQR 38-63], 1,449/1,024; Inactivated: 60 [IQR 49-68], 1,311/893	NA	mRNA: 77 (3.1); Inactivated: 93 (4.2)	NA	mRNA: 15 (0.6); Inactivated: 4 (0.2)	mRNA: 2,473 (53); Inactivated: 2,204 (47)	NA	NA	20 (IQR 11-33)
18 (2022)	17 7	70±14 ^I , 71/106	NA	NA	NA	NA	mRNA: 171 (97); Vector: 6 (3)	14/86/N A/NA	45/35/20	1st: 29±21 ^I ; 2nd: 45±25 ^I
19 (2022)	87	48 [18-79], 32/55	24 (28)	12 (14)	2 (2.3)	NA	mRNA: 67 (77); Vector: 20 (23)	46/54/N A/NA	84/6/10	15 (3-65)
20 (2022)	59	54 [19-92], 24/35	18 (31)	NA	NA	5 (8.5)	Last vaccine before liver	34/63/3 /NA	n = 58 95/0/5	24 (1-74) ^{II}

							injury: mRNA: 42 (71); Vector: 16 (27); Inactivate d: 1 (1.7)			
21 (2024)	47	57 (IQR 19-86), 17/30	12 (26)	NA	7 (15)	4 (8.5)	mRNA: 36 (77); Vector: 11 (23)	36/47/17 /NA	81/6.4/13	22 (IQR 11-41) ⁱⁱ
22 (2024)	23	Overall (n = 23): 58 [21-83], 6/17; High causality cases (n = 16): 63 [48-68], 4/12			Overall cases :5 (22); High causality cases: 5 (31)			High causality cases: 32/56/12 /NA	Overall cases: 70/13/17; High causality cases: 75/6/19	Overall cases: 20 (1-147) ⁱⁱⁱ ; High causality cases: 16 (1-47) ⁱⁱⁱ
23 (2022)	16	63 [25-74], 6/10	NA	8 (50)	4 (25)	NA	mRNA: 16 (100)	25/75/N A/NA	81/6.3/13	NA

24 (2023)	13	42 [22-67], 6/7	NA	1 (7.7)	NA	NA	Inactivate d: 13 (100)	69/31/N A/NA	92/7.7/0	NA
25 (2025)	12	58 [29-79], 4/8	NA	4 (33)	1 (8.3)	NA	mRNA: 12 (100)	17/50/17 /17	NA	10 (0-60) ⁱⁱⁱ
26 (2023) ^{iv}	7	46 [14-65], 4/3	2 (29)	5 (71)	1 (14)	1 (14)	mRNA: 6 (86); Vector: 1 (14)	29/71/N A/NA	n = 6 83/17/0	15 (1-42) ⁱⁱⁱ
27 (2023)	6	58 [21-85], 4/2	NA	0	0	0	mRNA: 6 (100)	50/50/N A/NA	100/0/0	8.5 (2-28) ⁱⁱⁱ
ⁱ Values shown as mean ± SD.										
ⁱⁱ Median duration (range) calculated from the date of vaccination to the diagnosis of liver injury.										
ⁱⁱⁱ Median duration (range) calculated from the date of vaccination to symptom onset.										
^{iv} One case excluded due to liver injury being primarily caused by COVID-19 infection.										
AIH: Autoimmune hepatitis; COVID-19: Coronavirus disease 2019; Hep: Hepatocellular injury; Chol: Cholestatic injury; Mixed, Mixed injury; IQR: Interquartile range; n: Number; NA: Not applicable or not available; No: Number; Ref: Reference.										

Supplemental Table 1. Coronavirus disease 2019-associated liver Injury: case series including autoimmune hepatitis and non-autoimmune hepatitis patients (Continued)

Ref. No. (Published year)	Clinical presentation	Autoimmune liver disease-related data	Pathology and/or diagnostic criteria	Therapy	Outcome	Rechallenge, n
17 (2022)	No severe or fatal ALI, peak ALT>20xULN (mRNA: 3.8%; Inactivated: 3.6%)	NA	NA	NA	Hospitalization rate: mRNA: 2.9%; vector: 3.5%, resolution by day 42: 99.2%	NA
18 (2022)	Peak mean ALT: 553 U/L; T. bil>2.5 mg/dL: 29%	NA	NA	NA	n=42: Normalized liver test: 48%	NA
19 (2022)	Grade 3-4 liver injury ³⁶ : 22%, LT due to ALF: 1.1%	n varied according to the test: ANA+: 67%;	n=44 for biopsy, Simplified IAIHG criteria for the Dx of AIH ³⁹ :	Steroid: 46 (53) ^I ; steroid/2nd IS: 11 (13) ^I ; PE including steroid;	SR: 47%; No relapse after withdrawal of IS: 12 (26) ^{I,II}	Same mRNA vaccine: 1 (liver failure required LT);

		ASMA+: 18%; AMA+: 6.0%; IgG>ULN: 67%	(Probable+definite): 77% METAVIR scoring system ⁴⁰ : Fibrosis stage<3: 93%	9 (10) ^I ; IVIG/steroid: 1 (1.1) ^I ; LT: 1 (1.1) ^I		different vaccine class: 2 (no relapse: 100%)
20 (2022)	Median ALT/ULN: 24; median T. bil/ULN: 4.7, ALF requiring LT: 1 (1.7) ^{37, I}	ANA+: 74%; ASMA+: 37%; Anti-LKM+: 7.7%; AMA+: 9.1%; ANCA+: 2.9%; IgG>16 g/L: 68%	n=59 for biopsy: mainly lobular hepatitis: 76%; mainly portal hepatitis: 17%; Ishak Fibrosis stage ⁴¹ <3: 88%, Simplified IAIHG criteria for the Dx of AIH ³⁹ (Typical+compatible): 81%, recently proposed AIH pathological criteria ⁴² :	n=54: Steroid: 47 (87) ^I ; steroid/azathioprine: 7 (13) ^I ; LT: 1 (1.7) ^I	SR: 8.5%; relapse after SR: 3.4%; remission with IS: 63% (successful IS withdrawal: 17%; IS withdrawal still ongoing: 39%; IS withdrawal failure: 6.8%); improvement but no remission with IS: 20%; non-liver-related death: 5.1%	n=15 ^{III} : Same vaccine class: 10 (no relapse: 60%, relapse including required LT: 30%); different vaccine class: 5 (no relapse: 80%)

			(Likely+Possible): 92%			
21 (2024)	Median ALT: 966 IU/mL; jaundice: 16 (42) ^{I, IV} , EASL criteria ³⁸ : ALF: 3 (6.4) ^I , death due to ALF: 1 (2.1) ^I ; ALF requiring LT: 1 (2.1) ^I	ANA+: 64%; ASMA+: 21%; AMA+: 11%; IgG>ULN: 30 (64) ^I	n=33 for biopsy, Simplified IAIHG criteria for the Dx of AIH ³⁹ : compatible AIH: 88% (de novo AIH: 70%), DILI: 9.1%, RUCAM score ³⁵ : at least possible association: 81%; at least probable association: 43%	IS: 41 (87) ^I ; steroid: 35 (75) ^I ; azathioprine: 31 (66) ^I ; MMF: 2 (4.3) ^I ; LT: 1 (2.1) ^I	SR: 13%; normalization of ALT: 72%; successful steroid withdrawal: 6 (15) ^{I, II} ; ALF-related death: 2.1%	n=25 Relapse (non severity): 7 (28) ^{I, V}
22 (2024)	High causality cases: median peak ALT: 655 U/L; T. bil>2.5	High causality cases: ANA+: 27%; ASMA+: 36%; IgG>1500	n=8 for biopsy (High and low causality cases): Ishak Fibrosis stage ⁴¹ <2: 100%, AIH-like hepatitis:	High causality cases: steroid including azathioprine: 6 (38) ^I	High causality cases: hospitalization: 25%; full recovery: 88%; successful steroid withdrawal: 4 (67) ^I ,	High causality cases: same vaccine class: 3 (liver injury

	mg/dL: 6 (37) ^I	mg/dL: 2 (13) ^I , candidate gene variants and haplotype: ERAP1 Hap6 haplotype 6; ERAP2 variant: rs1363907	5/8 (63%), DILI Causality assessment ^{35,43} : (highly likely+probable): n=16		^{II} no death ;	exacerbation: 33%)
23 (2022)	INR>1.5: 3 (19) ^I , no ALF	ANA+: at least 5 (31) ^I ; ASMA+: at least 4 (25) ^I	n=10 (63%) for biopsy: portal inflammation (100%); no significant fibrosis except 3 cirrhotic patients, Simplified IAIHG criteria for the Dx of	Steroid: 8 (50) ^I ; NAC: 2 (13) ^I ; EBD: 1 (6.3) ^I	SR: 38%; hospitalization: 63%; fully recovered: 25%; recovering: 75%	NA

			AIH ^{39, VI} : (probable): n=1			
24 (2023)	Median peak ALT/ULN: 17; median peak T. bil/ULN: 1.2, symptomatic at liver injury onset: 11 (85) ^I , grade 1-2, 3, 4 liver injury ^{36,VI} : 85%, 7.7%, 7.7%	ANA+: 8 (62%) ^I ; ASMA+: 3 (23%) ^I ; high serum IgG: 6 (50) ^{I, VII}	n=3 (23%) for biopsy, Simplified IAIHG criteria for the Dx of AIH ^{39, VI} : (Probable+definite): 6 (46) ^I	Steroid: 5 (NA) ^I ; LT: 1 (NA) ^I	Successful steroid withdrawal: 4 (80) ^{I, II}	NA
25 (2025)	Symptomatic: 9 (75) ^I : significantly elevated liver enzymes: 11 (92) ^I ;	n=9 Autoimmune antibodies+: 9	n = 12 (100%) for biopsy: portal/periportal and perisinusoidal fibrosis: 1 (8.3) ^I ; interface activity: 9	Steroid: 8 (67) ^I	SR: 4 (33) ^I ; remission with IS: 8 (67) ^I ; new-onset AIH: 1 (8.3) ^I ; lately diagnosed	NA

	median T. bil: 5.4 mg/dL		(75) ^I ; histologic variations: active hepatitis ^{VIII} : 10 (83) ^I ; interface activity: 9 (75) ^I ; resolving hepatitis: 1 (8.3) ^I ; bile duct injury: 1 (8.3) ^I ; cholestatic injury ^{VIII} : 1 (8.3) ^I		celiac disease and sarcoidosis: 1 (8.3) ^I	
26 (2023) ^{IX}	Median ALT: 344 U/L	ANA+: 4 (57) ^I ; ASMA+: 4 (57) ^I ; ANCA+: 2 (29) ^I ; IgG>1800 mg/dL: 3 (75)	n = 5 (71%) for biopsy: interface hepatitis: 4 (80) ^I ; plasma cell infiltrate: 3 (60) ^I ; fibrosis: 3 (60%), Revised IAIHG descriptive criteria ⁴⁴ :	Steroid: 3 (43) ^I ; steroid/azathioprine: 1 (14) ^I	SR: 3 (43) ^I ; remission with IS: 3 (75) ^I , ^{II} ; improvement with IS: 1 (25) ^{I,II}	Same vector vaccine: 1 (relapse or deterioration); same mRNA vaccine or same platform: 1 (relapse that may be due to

		^{I, VII} HLA-DRB1 (*11: 5, *03: 3, *07: 3, *15: 1) ^X	(Definite+Probable): 4 (80) ^{I, VII}			autonomous steroid discontinuation)
27 (2023)	Median ALT/ULN: 34; median ALP/ULN: 1.1; median T. bil/ ULN: 6.8	ANA+: 3 (50) ^I ; AMA+: 1 (17%) ^I ; Anti-actin Ab: 1 (50) ^{I, VII} ; increased IgG: 2 (40) ^{I, VII}	n = 6 (100%) for biopsy: interface hepatitis: 5 (83) ^I ; Ishak scoring system ⁴¹ : Fibrosis (F0): 6 (100) ^I , mean Ishak grading score ⁴¹ : 12.2, Simplified IAIHG criteria for the Dx of AIH ^{39, VI} : probable/definite AIH score: 3 (60) ^{I, VII}	Steroid: 5 (80) ^I	Remission: 6 (100) ^I	NA

^IData are presented as n (%).

^{II}Proportion calculated among subjects who received IS.

^{III}Two cases of re-exposure during elevated transaminase levels with immunosuppressive intervention were not classified as relapse.

^{iv} Percentage calculated among 38 symptomatic individuals only.
^v Higher relapse rate observed in patients not receiving immunosuppressants during vaccine rechallenge ($P = .007$).
^{vi} Assumed to be applied in the absence of direct citation.
^{vii} Measurements or assessments were performed in a subset of cases.
^{viii} One case showed overlapping characteristics of both entities.
^{ix} One case excluded due to liver injury being primarily caused by COVID-19 infection.
^x Data are presented as n.
⁺ denotes positive test results.
Ab: Antibody; AIH: Autoimmune hepatitis; ALF: Acute liver failure; ALI: Acute liver injury; ALP: Alkaline phosphatase; ALT: Alanine aminotransferase; AMA: Anti-mitochondrial antibody; ANA: Antinuclear antibody; ANCA: Anti-neutrophil cytoplasmic antibody; Anti-LKM: Anti-liver-kidney microsomal antibody; ASMA: Anti-smooth muscle antibody; COVID-19: Coronavirus disease 2019; DILI: Drug-induced liver injury; Dx: Diagnosis; EASL: European Association for the Study of the Liver; EBD: Endoscopic biliary dilation; ERAP: Endoplasmic reticulum aminopeptidase; HLA: Human leukocyte antigen; IAIHG: International Autoimmune Hepatitis Group; IgG: Immunoglobulin G; INR: International normalized ratio; IS: Immunosuppressants; IVIG: Intravenous immunoglobulin; LKM: Liver kidney microsome; LT: Liver transplantation; MMF: Mycophenolate mofetil; n: Number; NAC: N-Acetyl-L-cysteine; NA: Not applicable; No: Number; PE: Plasma exchange; Ref: Reference; rs: Reference sequence; RUCAM: Roussel Uclaf Causality Assessment Method; SR: Spontaneous remission or resolution; T. bil: Total bilirubin; ULN: Upper limit of normal.