Patient number	Gender, Age (years), Cancer type	Immune checkpoint inhibitor molecule	Other concomitant irAEs	Latency of toxicity (weeks)	ALT Peak (IU/L)	AST / ALT	Total Bilirubin Peak (µmol/L)	Alkaline Phosphatase Peak (IU/L)	Clinical phenotype	Delay for immuno-suppression (in weeks)	Immunosuppressive therapy
1	Male in his 70s Mesothelioma	Anti-CTLA-4[1] / anti-PD-1[2] combination	Rash	7	662	0.33	16	110	IrH	5	Corticosteroids 2mg/kg, MMF
2	Male in his 50s, Renal cell carcinoma	Anti-CTLA-4[1] / anti-PD-1[2] combination	None	3	294	0.54	17	133	IrH	3	Corticosteroids 1mg/kg
3	Male in his 60s, Melanoma	Anti-CTLA-4[1] / anti-PD-1[2] combination	None	8	456	0.56	9	373	IrH	2	Corticosteroids 1mg/kg, MMF
4	Female in her 40s, Melanoma	Anti-PD-1[3]	Thyroiditis, hypophysitis	1	384	0.67	11	123	IrH	2	Corticosteroids 1mg/kg
5	Male is his 70s, Melanoma	Anti-PD-1[3]	Pleuritis, colitis, hypophysitis, vitiligo	23	1121	0.59	20	504	IrH	5	Corticosteroids 1mg/kg, MMF
6	Male in his 30s, Melanoma	Anti-CTLA-4[1] / anti-PD-1[2] combination	None	8	1224	0.43	63	186	IrH	3	Corticosteroids 2mg/kg, MMF, Tocilizumab
7	Female in her 60s, Small cell lung carcinoma	Anti-CTLA-4[1] / anti-PD-1[2] combination	Thyroiditis	12	948	0.71	14	205	IrH	No immuno-suppression	None
8	Female in her 60s, Uveal melanoma	Anti-CTLA-4[1] / anti-PD-1[2] combination	Thyroiditis	10	1630	0.6	76	374	IrH	0	Corticosteroids 2mg/kg, MMF, Infliximab
9	Female in her 20s, Uveal melanoma	Anti-CTLA-4[1] / anti-PD-1[2] combination	None	3	773	1.89	37	743	IrCH	3	Dexamethasone 16mg/day
10	Male in his 50s, Melanoma	Anti-CTLA-4[1] / anti-PD-1[2] combination	Neuropathy	6	1486	0.59	21	242	IrH	0	Corticosteroids 2mg/kg, MMF
11	Male in his 60s, Squamous cell lung carcinoma	Anti-PD-1[2]	Vitiligo	4	572	0.46	28	520	IrCH	3	Corticosteroids 2mg/kg, MMF
12	Male in his 80s, Melanoma	Anti-PD-1[3]	None	6	695	2.05	289	727	IrCH	0	Corticosteroids 1mg/kg, MMF
13	Female in her 60s, Lung adenocarcinoma	Anti-PD-1[3]	None	6	125	0.7	41	1395	IrC	No immuno-suppression	None

14	Male in his 40s, Melanoma	Anti-CTLA-4[1] / anti-PD-1[2] combination	Adrenal insufficiency, rash, colitis, thyroiditis	10	261	1.03	11	371	IrH	2	Corticosteroids 1mg/kg, Infliximab
15	Female in her 60s, Serous-type ovarian cancer	Anti-PD-L1[4]	None	32	190	0.72	7	45	IrH	1	Corticosteroids 1mg/kg
16	Male in his 70s, Prostate adenocarcinoma	Anti-CTLA-4[1] / anti-PD-1[2] combination	Colitis, thyroiditis	26	167	0.85	10	385	IrC	0	Corticosteroids 1mg/kg, Infliximab
17	Female in her 50s, Melanoma	Anti-PD-1[2]	Thyroiditis	72	569	0.5	11	510	IrH followed by irC[+]	24	Corticosteroids 2mg/kg
18	Male in his 60s, Prostate adenocarcinoma	Anti-CTLA-4[1] / anti-PD-1[2] combination	None	10	371	0.58	12	356	IrH	0	Corticosteroids 1mg/kg
19	Female in her 60s, Melanoma	Anti-CTLA-4[1] / anti-PD-1[2] combination	Thyroiditis, adrenal insufficiency, rash	5	283	1.08	16	610	IrCH	3	Corticosteroids 2mg/kg
20	Female in her 70s, Melanoma	Anti-CTLA-4[1] / anti-PD-1[2] combination	None	30	276	0.67	11	288	IrC	1	Corticosteroids 1mg/kg, MMF
21	Female in her 60s, Uveal melanoma	Anti-CTLA-4[1] / anti-PD-1[2] combination	Rash	4	132	1.09	26	144	IrH	No immuno-suppression	None
22	Male in his 80s, Squamous cell lung carcinoma	Anti-PD-1[3]	Nephritis	10	655	1.33	54	969	IrCH	1	Corticosteroids 2mg/kg, Tocilizumab
23	Male in his 40s, Melanoma	Anti-PD-1[3]	Thyroiditis	49	855	0.18	18	177	IrH	2	Dexamethasone 4mg/day
24	Male in his 60s, Squamous cell lung carcinoma	Anti-PD-1[3]	None	19	331	0.53	178	1018	IrC	2	Corticosteroids 2mg/kg, Tocilizumab
25	Female in her 70s, Cholangio-carcinoma	Anti-CTLA-4[1] / anti-PD-1[2] combination	Thyroiditis	4	210	1.16	10	274	IrCH	2	Corticosteroids 1mg/kg
26	Female in her 60s, Lung adenocarcinoma	Anti-PD-1[3]	None	2	1623	0.34	89	724	IrCH	2	Corticosteroids 1mg/kg, Tocilizumab
27	Male in his 70s, Urothelial carcinoma	Anti-PD-1[3]	Pneumonitis, nephritis	55	145	0.69	22	266	IrCH	Given 1 week before ALT increase for pneumonitis	Corticosteroids 1mg/kg, Tocilizumab

Supplementary Table 1. Clinical and biological characteristics of each irH and irC patient.

Description of each ICI patient, from their demographic and oncological data to their main laboratory values and immunosuppressive regimen. Patients 9 and 12 are in grey as these patients' biopsies were unreadable due to ischemic hepatitis and presence of radioembolic beads after SIRT.

[1] Ipilimumab; [2] Nivolumab; [3] Pembrolizumab; [4] Durvalumab

[+] Patient 17 received her immunotherapy two years prior to liver biopsy. She first developed irH one month following her immunotherapy. Two years later she developed irC without having received any additional immunotherapy and was biopsied at that point.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTLA-4, cytotoxic T-lymphocyte associated protein 4; irAE, immune-related adverse event; irC, immune-related cholangitis; irCH, immune-related cholangiohepatitis; irH, immune-related hepatitis; MMF, mycophenolate mofetil; PD-1, programmed cell death 1; PD-L1, programmed cell death ligand 1; SIRT, selective internal radiation therapy.

Patient	ICI	ALT Peak (U/l)	ALP Peak (U/l)	Total Bilirubin Peak (µmol/l)	Clinical Phenotype	Serological Markers	Histological Pattern
9	Anti-CTLA-4[1] and anti-PD-1[2]	773	743	37	Hepatitis	IgG 15.3 g/l ANA 1/160 SMA 1/160 Anti-actin 29 U/l	Acute portal and lobular hepatitis
14	Anti-CTLA-4[1] and anti-PD-1[2]	261	371	11	Hepatitis	IgG NA ANA 1/80 SMA 1/160 Anti-actin 40 U/l	Acute portal and lobular hepatitis
17	Anti-PD-1[2]	569	510	11	Hepatitis followed by cholangitis	IgG 14 g/l ANA 1/640 SMA 1/640 Anti-actin 108 U/l IgM 2.94 g/l Positive anti-M2	PBC like pattern
22	Anti-PD-1[3]	655	969	54	Mixed pattern	IgG 10 g/l ANA 1/320 Negative SMA anti-actin 27 U/l	Chronic portal hepatitis with biliary obstruction features

Supplementary Table 2. Biological and histopathological characteristics of ICI patients presenting with elevated serological markers for autoimmune liver disease.

[1] Ipilimumab; [2] Nivolumab; [3] Pembrolizumab

ALP, alkaline phosphatase; ALT, alanine aminotransferase; ANA, anti-nuclear antibody; SMA, smooth muscle antibody; CTLA-4, cytotoxic T-lymphocyte associated protein 4; ICI, immune checkpoint inhibitor; IgG, immunoglobulin G; IgM, immunoglobulin M; INR, international normalized ratio; irAE, immune-related adverse event; irC, immune-related cholangitis; irH, immune-related hepatitis; PBC, primary biliary cirrhosis; PD-1, programmed cell death 1.

Patient	Gender, Age (years)	Disease	History of Autoimmune Disease	Increased IgGs	Presence of anti-Smooth Muscle antibodies	Presence of other autoantibodies	ALT Peak	AST/ALT	Bilirubin Peak	GGT Peak	Alkaline Phosphatase Peak	Treatment
1	Female in her 40s	Autoimmune Hepatitis	Graves' disease	yes	+ 1/640	Anti-actin: 78 U	757	0.7	125	52	124	Corticosteroids, Azathioprine (intolerant), MMF 2g/day
2	Female in her 60s	Autoimmune Hepatitis	none	yes	+ 1/80	Anti-actin: 31 U	1944	0.7	359	969	431	Corticosteroids 1mg/kg/day, Azathioprine
3	Female in her 40s	Autoimmune Hepatitis	Type 1 diabetes	yes	+ 1/5120	Anti-actin: 109 U	210	1.1	10	186	125	Corticosteroids, Azathioprine, MMF 2g/day
4	Female in her 50s	Autoimmune Hepatitis	Autoimmune thyroiditis, DRESS syndrome	yes	+ 1/80	Negative anti-actin, Positive anti-SLA	1098	0.7	53	607	164	Corticosteroids 1mg/kg/day, Azathioprine
5	Female in her 60s	Autoimmune Hepatitis	none	yes	+ 1/640	Anti-actin 61 U	1895	0.4	327	500	153	Corticosteroids, MMF 1g/day
6	Female in her 20s	Autoimmune Hepatitis	Graves' disease	yes	+ 1/80	Anti-actin 15 U	1437	0.7	345	106	142	Corticosteroids 1mg/kg/day, Azathioprine
7	Female in her 30s	Autoimmune Hepatitis	none	yes	none	Anti-actin 64 U	3301	0.9	388	87	116	Corticosteroids 1mg/kg/day, Azathioprine
8	Female in her 70s	Autoimmune Hepatitis	none	no	+ 1/80	Anti-actin 34 U	198	0.7	44	289	185	Corticosteroids 1mg/kg/day, Azathioprine
9	Female in her 50s	Autoimmune Hepatitis	Lymphocytic colitis	yes	+ 1/5120	Anti-actin 124 U	165	0.8	33	120	190	Corticosteroids, Azathioprine, MMF 1.44g/day
10	Male in his 50s	Autoimmune Hepatitis	none	no	+ 1/320	Anti-actin 42 U	707	0.2	54	546	167	Corticosteroids 1mg/kg/day, Azathioprine
11	Female in her 20s	Autoimmune Hepatitis	Rheumatoid polyarthritis	yes	+ 1/2560	Anti-actin 123 U	285	0.5	11	90	242	Corticosteroids 1mg/kg/day, Azathioprine
12	Female in her 40s	Primary Biliary Cholangitis	Rheumatoid polyarthritis	no	none	Positive anti-mitochondria and anti-M2	49	0.8	5	167	240	Ursodeoxycholic acid 15mg/kg
13	Female in her 40s	Primary Biliary Cholangitis	none	no	none	Positive anti-mitochondria and anti-M2	80	0.6	11	339	330	Ursodeoxycholic acid 15mg/kg
14	Female in her 60s	Primary Biliary Cholangitis	Rheumatoid polyarthritis	yes	none	Positive anti-mitochondria and anti-M2	74	0.6	7	101	250	Ursodeoxycholic acid 15mg/kg

Supplementary Table 3. Clinical and biological characteristics of AIH and PBC patients

Description of each AIH and PBC patient. Eleven patients were diagnosed with AIH and three with PBC.

AIH, autoimmune hepatitis; ALT, alanine aminotransferase; AST, aspartate aminotransferase; DRESS, drug rash with eosinophilia and systemic symptoms; GGT, gamma-glutamyltransferase; IgG, immunoglobulin G; MMF, mycophenolate mofetil; PBC, primary biliary cholangitis; SLA, soluble liver antigen.

Patient	Lesional Pattern	Portal inflammation (0-3)	Interface hepatitis (0-3)	Bile duct injury (0-1)	Ductular reaction (0-3)	Biliary metaplasia (0-3)	Lobular inflammation (0-3)	Lobular necrosis (0-3)	Emperi-polesis (0-1)	Rosettes (0-1)	Granulomas (0-2)	Bilirubino-stasis (0-1)	Centrilobular injury (0-3)	Severity score	Plasma cells (0-2)	Eosinophils (0-2)	Neutrophils (0-2)	Fibrosis (METAVIR)	CD4/CD8 (ratio)
1	Lobular hepatitis	1	0	0	1	0	2	2	0	0	0	0	3	8	1	0	1	F1	-
2	Portal and lobular hepatitis with underlying NASH	1	1	0	1	1	1	0	0	0	1	0	0	3	1	1	1	F1	>1
3	Lobular hepatitis	1	0	0	1	1	2	1	0	0	0	0	2	6	1	1	1	F1	<1
4	Portal hepatitis	2	2	1	2	0	0	1	0	0	0	0	0	5	1	0	1	F2	<1
5	Mild portal hepatitis	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	F1	1
6	Portal and lobular hepatitis	2	1	0	0	0	3	1	0	0	1	0	1	8	1	1	1	F0	-
7	Portal and lobular hepatitis	2	1	1	2	0	2	2	0	0	2	0	1	8	1	2	1	F0	>1
8	Portal and lobular hepatitis	3	3	1	1	0	3	2	0	0	2	0	2	13	1	2	1	F0	<1
10	Portal and lobular hepatitis	1	1	0	1	0	2	2	0	0	1	0	1	7	1	0	1	F1	1
11	Portal hepatitis with biliary obstruction features	2	1	1	2	1	1	1	0	0	0	0	1	6	1	0	2	F2	<1
13	Mild portal hepatitis with biliary obstruction features	1	0	1	2	0	1	0	0	0	0	0	0	2	0	1	1	F1	1
14	Portal and lobular hepatitis	3	3	1	1	1	2	2	0	0	2	0	1	11	2	2	2	F1	1
15	Lobular hepatitis	1	0	0	0	0	1	1	0	0	1	0	0	3	0	1	0	F0	1

16	Portal hepatitis with biliary obstruction features	2	0	1	2	1	0	0	0	0	0	0	0	2	0	1	2	F1	1
17	Primary biliary cholangitis	2	1	1	2	2	1	1	0	0	1	0	0	5	1	1	2	F1	1
18	Portal hepatitis	3	3	1	1	0	1	1	0	0	1	0	0	8	0	2	1	F1	1
19	Portal and lobular hepatitis	2	1	1	2	0	2	1	0	0	1	0	0	6	0	2	2	F1	1
20	Primary biliary cholangitis	2	1	1	2	0	1	1	0	0	1	0	0	5	1	1	1	F1	>1
21	Portal and lobular hepatitis	1	1	0	1	0	2	2	0	1	1	0	1	7	0	0	0	F1	1
22	Portal hepatitis with biliary obstruction features	2	2	1	2	1	1	1	0	0	0	1	0	6	1	1	2	F1	1
23	Other[5]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	F0	1
24	Biliary obstruction features	1	1	1	3	3	1	1	0	0	0	1	0	4	0	0	2	F2/F3	1
25	Portal hepatitis with primary biliary cholangitis features	3	2	1	2	2	1	1	0	0	0	0	0	7	1	2	2	F2	>1
26	Primary biliary cholangitis	3	1	1	2	0	1	1	0	0	1	0	0	6	1	2	2	F1	>1
27	Portal hepatitis with biliary obstructions features	2	1	1	3	3	1	1	0	0	0	0	0	5	1	1	1	F2/3	>1

Supplementary Table 4. Histopathology and immunohistochemistry of irH and irC

Description of each patient in the ICI group.

[1] Ipilimumab; [2] Nivolumab; [3] Pembrolizumab; [4] Durvalumab

[5] Biological and clinical characteristics of irH, though liver biopsy predominantly showed macrovesicular steatosis.

CD4, cluster of differentiation 4; CD8, cluster of differentiation 8; CTLA-4, cytotoxic T-lymphocyte associated protein 4; F, fibrosis; irC, immune-related cholangitis; irH, immune-related hepatitis; NASH, non-alcoholic steatohepatitis; PD-1, programmed cell death 1, PD-L1, programmed cell death ligand 1.

Patient	Disease	Lesional Pattern	Portal inflammation (0-3)	Interface hepatitis (0-3)	Bile duct injury (0-1)	Ductular reaction (0-3)	Biliary metaplasia (0-3)	Lobular inflammation (0-3)	Lobular necrosis (0-3)	Emperipolesis (0-1)	Rosettes (0-1)	Granulomas (0-1)	Bilirubinostasis (0-1)	Centri-lobular injury (0-3)	Plasma cells (0-2)	Eosinophils/ neutrophils (0-1)	Fibrosis (METAVIR)	CD4-CD8 (ratio)
1	Autoimmune hepatitis																	
2	Autoimmune hepatitis	Portal and lobular hepatitis	3	3	1	2	0	3	3	1	1	0	1	0	1	1/2	F2	-
3	Autoimmune hepatitis	Portal and lobular hepatitis	3	3	1	2	1	2	2	0	0	0	0	0	2	1/1	F2	>1
4	Autoimmune hepatitis	Portal and lobular hepatitis	3	3	0	2	0	2	1	0	1	0	1	0	2	1/1	F0	-
5	Autoimmune hepatitis	Portal and lobular hepatitis	3	2	0	2	0	2	2	1	1	0	0	0	2	1/1	F2	-
6	Autoimmune hepatitis	Portal and lobular hepatitis	3	2	0	2	0	3	2	1	1	0	0	0	2	1/2	F2	>1
7	Autoimmune hepatitis	Portal and lobular hepatitis	2	1	0	2	1	1	1	0	0	0	0	1	1	1/2	F3/F4	>1
8	Autoimmune hepatitis	Mild portal and lobular hepatitis	1	0	0	0	0	1	1	0	0	0	0	0	1	0/0	F0	1
9	Autoimmune hepatitis	Macrovacuolar steatosis with moderate portal and lobular hepatitis	2	2	1	2	1	1	1	1	0	0	0	0	2	1/1	F1	1
10	Autoimmune hepatitis	Portal and lobular hepatitis	3	2	0	1	0	2	2	1	0	0	0	1	2	2/2	F2	>1
11	Autoimmune hepatitis	Mild portal hepatitis	1	0	0	0	0	1	0	0	0	0	0	0	1	0/0	F0	1
12	Primary biliary cholangitis	Mild portal hepatitis	1	0	0	0	0	0	0	0	0	0	0	0	1	0/0	F1	>1
13	Primary biliary cholangitis	Biliary lesions with ductopenia	1	1	1	1	3	1	0	0	0	0	0	0	0	0/0	F2	-
14	Primary biliary cholangitis	Inflammatory biliary lesions	1	0	1	0	0	0	0	0	0	0	0	0	2	0/0	F0	-

Supplementary Table 5. Histopathology and immunohistochemistry of AIH and PBC

Description of AIH and PBC patients.

AIH, autoimmune hepatitis; CD4, cluster of differentiation 4; CD8, cluster of differentiation 8; F, fibrosis; PBC, primary biliary cholangitis.