Table S1 Inclusion and exclusion criteria of surgical and non-surgical trials

Study ID & year	**Study design**	**Intervention**	**Outcome Parameters**	**Duration (weeks) follow up-biopsy and n**	**N biopsy proven NASH**	**Histological Scoring**	**Inclusion criteria**	**Exclusion criteria**
Almeida et al. 2006	Prospective comparative study, Self-paired design	RYGB	Histopathological components (steatosis, necroinflammatory activity and fibrosis)	94 ±33.6 N=16	N= 4	Brunt et al. Modified Matteoni et al. (NASH 3-4)	• Diagnosed NASH and RYGB >1 year before • (INR) ≤1.4 • platelet count ≥80,000/mm3 • partial thromboplastin time ≤10 sec- onds in relation to the reference value • Signed informed consent	• alcohol consumption (>20 g/day for women or >30 g/day for men) • Drug use • Anticoagulant or antiplatelet-aggregation drugs
Chaim et al.	Retrospective and longitudinal observational cohort study	RYGB	Histopathological characteristics of obese Brazilian patients and assessment of the efects of bariatric surgeyr on the attenuation on liver disease	84 ±88 N=30	N=10	SAF Score (Rinella et al., 2019)	• BMI>30 kg/m^2 • RYGB and consecutive liver biopsies	• Sclerosing cholangitis • Viral hepatitis • Schistosomiasis • Hemochromatosis • Primary biliary cirrhosis
Lassailly et al. 2015 Lille Bariatric Cohort	Prospective cohort	Gastric Bypass, LAGB, RYGB and Sleeve Gastrectomy	Primary endpoint: disappearance of NASH Secondary endpoint: change in overall NAFLD activity score and individual components	240 N=82	N=81	Brunt Score 1999 and NAS score 2005 Kleiner Fibrosis scale	• BMI>35 • One comorbidity resistant to med. treatment for >5 years • social security insurance coverage • age over 18 years old	• Medical or psychological contraindications for bariatric surgery • alcohol consumption (>20 g/day for women or >30 g/day for men) • History of excessive drinking in the last 2 years • Use of hepatotoxic drugs • Chronic liver disease (Hep B, Hep C and haemochromatosis)
Dixon et al. 2004	Prospective cohort	LAGB	Histological features of NAFLD after weight loss induced by LAGB	94 N=36	N=23	Modified Brunt et al.	• BMI>35 • Paired liver biopsies baseline and after weight loss (consequent laparoscopy and fibrosis >2 in index biopsy)	• Hemochromatosis Wilson's disease, autoimmune liver disease • history of alcoholism • hep B or C • hepatotoxic medication • other specific liver disease
Froylich et al. 2016	Comparative	RYGB & Sleeve gastrectomy	Changes in NAS score, NAS	81,6 N=23	N=15	NAS score Fibrosis semiquantitative	• Pre- and postoperative liver biopsies • n.a	• hepatitis C infection • autoimmune hepatitis • insufficient tissue biopsy

			components and fibrosis stage			grade score bei Brunt et al., 1999		• biliary cirrhosis or biliary cholangitis at the time of the second biopsy
Mathurin et al. 2009 Lille Bariatric Cohort	Prospective Cohort	Gastric Banding, Gastric Bypass	Long-term evaluation of steatosis, ballooning, inflammation, global NAS and fibrosis	84 and 240 N=267	N=99	NAS score and Kleiner Fibrosis grade	• BMI>35 • One comorbidity drug resistant for >5 years	• Medical or psychiatrical contraindication for bariatric surgery • alcohol consumption (>20 g/day for women or >30 g/day for men) History of excessive drinking in the last 2 years • Use of hepatotoxic drugs • Chronic liver disease (Hep B, Hep C and haemochromatosis)
Salman et al. 2019	Prospective cohort	Sleeve gastrectomy	Histological changes in NAS Improvement in other metabolic comorbidities and liver enzymes	52 N=94	N=50	NAS score	• BMI >40 or 35 with comorbidities • Informed consent	• Unwilling to change lifestyle after surgery • Pregnancy • Secondary causes of liver disease • History of alcohol intake or possible drug-induced liver disease
Salman et al. 2020	Prospective cohort	One-anastomosis gastric bypass	Effect of OAGB on NASH status and fibrosis severity	60 N=62	N=62	NAS score	• 18-60 years • BMI >40 or 35 with comorbidities	• Medical conditions hindering anaesthesia • No motivation to modify lifestyle post-op • Regular medication of alcohol consumption • Secondary causes for liver disease • Pregnancy
Schönfels et al. 2019	Retrospective comparison	RYGB and Sleeve gastrectomy	Comparing the results of gastric bypass and SG on histologic improvement scored by NAS	27.14 N=53	N=11	Modified Brunt NAS score	• consent	• n.a.
Vargas et al. 2012	Prospective Cohort	RYGB	Amount of steatosis, portal and lobular inflamma- tion, fibrosis score and grade of NASH	65±4 N=26	N=25	Modified Brunt Score (2005)	• BMI > 40 with significant medical, physical or psychosocial disability	• History of alcoholism • Alcohol consumption (>20 g/day for women or >30 g/day for men) • Evidence of hepatitis B or C or • History of another specific liver disease

Tai et al. 2012	Prospective Cohort	RYGB	NAS, NAS components, fibrosis Changes in metabolic syndrome and insuline resistance	52 N=21	N=15 (intermediate and definite NASH)	NAS score Kleiner Fibrosis score (2005)	• Morbidly obese Chinese patients with BMI ≥ 40 kg/m^2 or BMI ≥35 kg/m^2 with comorbidity • Written informed consent	• Alcohol intake of more than 20 g/d • Chronic hepatitis B or C virus infection • Hepatotoxic drugs • Other known liver diseases such as Wilson's disease, hemochromatosisα1-antitrypsin deficiency • Autoimmune hepatitis • Malignant diseases
Nikai et al. 2020	Prospective Cohort	LSG	Resolution of NASH, change of NAS components, fibrosis	52 N=34	N=28	NAS Brunt Score (2005) → The trial investigators developed their own fibrosis assessment score to validate in addition to the Brunt classification, however results were reported with NAS	• 18-65 years of age • Biopsy proven NASH • Severe obesity (BMI>35kg/m^2) • at least one comorbidity with resistance to medical treatment (hypertension, T2DM, dyslipidemia, OSAS)	• History of alcohol abuse • Secondary obesity (drug-induced or due to endocrine diseases) • Presence of major psychiatric disorders
LEAN Trial 2016	RCT, two arms	Liraglutide 1.8 mg/week vs. Placebo	Primary endpoint: resolution of steatohepatitis (disappearance of hepatocyte ballooning) without worsening of fibrosis Secondary endpoint: changes in the overall NAS, individual components of the NAS and the Kleiner fibrosis sage	48 weeks I: 23 P: 22	I: 23 P: 22	NAS Score Kleiner/Brunt 2005	• 18–70 years of age • body-mass index (BMI) of 25 kg/m^2 at screening • histological evidence of non-alcoholic steatohepatitis on the basis of liver biopsy obtained within 6 months of screening. • stable glycaemic control (glycated haemoglobin [HbA1c] <9·0% • written informed consent	• Alcohol consumption (>20 g/day for women or >30 g/day for men) • Poor glycaemic control (HbA1c> 9·0%) • Child- Pugh B/C cirrhosis, • Other causes of liver disease • Confounding concomitant drug use (Including insulin, incretin mimetics, thiazolidinediones, vitamin E) • Medical history of pancreatitis and pancreatic or thyroid carcinoma
FLINT Trial 2015	RCT, two arms	Obeticholic acid 25 mg/d vs. Placebo	Primary endpoint: decrease in NAS by at least 2 points without worsening of fibrosis Secondary endpoint: resolution of non-alcoholic	72 weeks I: 102 P: 98	I: 102 P: 98	NAS Score Kleiner/Brunt 2005	• >18 years of age • histological evidence of definite or borderline non-alcoholic steatohepatitis based upon a liver biopsy obtained 90 days or less before randomisation	• Cirrhosis • Other causes of liver disease • Alcohol consumption (>20 g/day for women or >30 g/day for men),

			steatohepatitis, change in NAS, changes in the individual scores for hepatocellular ballooning, steatosis, lobular and portal inflammation, and fibrosis				• NAS >4 with a score of 1 or more in each component of the score	
Promrat et al. 2008	RCT, two arms	Lifestyle intervention vs. Control	Primary endpoint: improvement in NASH activity score (NAS) of at least 3 points or post treatment NAS of 2 points or less	48 weeks I: 18 C: 10	I: 18 C: 10	NAS Score Kleiner/Brunt 2005	• Elevated alanine or aspartate aminotransferase values (ALT >41 or AST>34 U/L) • BMI between 25-40 kg/m^2	• Significant alcohol consumption (> 1 standard drink per day) • Contraindications to obtaining a liver biopsy • Inability to walk 2 blocks or a quarter of a mile without stopping • Pregnancy • Engagement in an active weight loss program or taking weight- loss medication • Substance abuse • Significant psychiatric problems • Other form of liver disease
Ratziu et al. 2015	RCT, three arms	Elafibranor 120 mg. vs. 80 mg. vs Placebo	Primary endpoint: reversal of NASH without worsening of fibrosis (i.e., disappearence of ballooning) Secondary endpoint : changes in NAS (including the proportion of patients with a 2-point decrease); changes and improvements in individual histologic scores of steatosis, ballooning, inflam-mation, and fibrosis	52 weeks E120: 78 E80: 82 P: 77	E120: 78 E80: 82 P: 77	NAS Score Kleiner/Brunt 2005	• 18 to 75 years of age • histologic diagnosis of noncirrhotic NASH confirmed by a central pathologist	• Alcohol consumption (>20 g/day for women or >30 g/day for men), • Secondary causes of NASH • Other chronic liver disease
Bril et al. 2019	RCT, three armed	Vitamin E Vitamin E + Pioglitazone Placebo	Primary endpoint: 2-point decrease of NAS Secondary endpoint: Resolution of NASH wothout worsening of	18 months a) 36 b) 37 c) 32	d) 36 e) 37 f) 32	NAS Score Kleiner/Brunt	• T2DM • Biopsy proven NASH	• Use of thiazolidinediones, glucagon-like peptide 1 agonists, sodium–glucose cotrans- porter 2 inhibitors, or vitamin E

			fibrosis, individual NAS scores, metabolic parameters					• Other liver diseases (or abnormal laboratory findings, e.g., AST or ALT threefold or greater than the upper limit of normal) • Hepatotoxic drugs (amiodarone, tamoxifen, methotrexate, etc.) • Type 1 diabetes mellitus • Severe heart, pulmonary, or renal disease
Kheong et al. 2017	RCT, two arms	Silymarin vs. Placebo	Primary endpoint: Decrease of >30% in NAS Secondary endpoint: individual components of NAS, fibrosis, resolution of NASH	48 weeks a) 49 b) 50	c) 49 d) 50	NASH Crn Criteria	• >18 years of age • Biopsy proven NASH (NAS>4)	• Alcohol consumption • Hepatitis B or C • Other liver diseases • Cirrhosis
PIVENS Trial 2010	RCT, three arms	Pioglitazone vs. Vitamin E vs. Placebo	Primary endpoint: improvement by 1 or more points in hepatocellular ballooning, no increase in the fibrosis score, either a decrease in NAS to 3 or less or a decrease in NAS of at least 2 points Secondary endpoint: changes in the overall NAS, as well as in individual component scores for steatosis, lobular inflammation, hepatocellular ballooning, and fibrosis	96 weeks Pio: 70 Vit: 80 P: 72	Pio: 70 Vit: 80 P: 72	NAS Score Kleiner/Brunt 2005	• >18 years of age • Non-diabetic • NAS >5 or definite NASH with NAS > 4 confirmed by central pathologist • Score of at least 1 for hepatocellular ballooning	• Alcohol consumption (>20 g/d for women or >30 g/d for men) at least 3 consecutive months during the prev. 5 years • Cirrhosis • Hepatitis C • Other liver diseases • Heart failure (NYHA II to IV) • Drugs known to cause steatohepatitis
Torres et al. 2011	RCT, three arms	Rosiglitazone vs. Rosiglitazone+ Metformin vs. Rosigllitazone+ Losartan	Primary endpoint: Improvement in steatosis, hepatocellular inflammation, or fibrosis, a minimum	48 weeks R: 26 RM: 28 RL: 35	R: 26 RM: 28 RL: 35	NAS Score Kleiner/Brunt 2005	• 18-70 years of age • biopsy- proven NASH (presence of inflammation and ballooning)	• Heart failure NYHA III or IV • Insulin-requiring diabetics, • Patients with a his- tory of TZD,

			1-point improvement in each quartile graded Secondary endpoint: overall changes in steatosis, hepato-cellular inflammation, hepatocyte ballooning, fibrosis, NAS, insulin, and alanine aminotransferase (ALT)				• (Liver biopsy must have been within the 6 months before enrollment)	metformin, or ARB use in the 3 months before enrollment • Alcohol consumption (>20 g/day for women or >30 g/day for men) • Serum creatinine greater than 1.4, • Known hyper- sensitivity to a study drug, • Known history of diabetic ketoacidosis, • Pregnant or breast-feeding females • Viral hepatitis • Wilson's disease • Autoimmune hepatitis, hemochromatosis, primary biliary cirrhosis, or primary sclerosing cholangitis
Younossi et al. 2019	RCT, three arms	Obeticholic acid 10 mg/d vs. Obeticholic acid 25 mg/d vs. Placebo	Primary endpoint: Fibrosis improvement (>1 stage) w/no worsening of NASH and NASH Resolution w/no worsening of fibrosis	72 weeks OA 10: 253 OA 25: 243 P: 252	253 243 252	NAS Score Kleiner/Brunt	• >18 years • Histologically proven NASH (biopsy <6 months from randomization) • NAS>4 • Fibrosis stage >F2 or F1 with 1 comorbidity (obesity, type 2 DM) • Informed consent	• Cirrhosis • Other liver disease • Clinically relevant alcohol consumption (women >2 units/d or men > 4 units/d) • HbA1c >9.5% • Bilirubin >1.5 mg/dL
Harrison et al. 2019	RCT, two arms	Resmetiron (MGL-3196) 80 mg/d orally vs. Placebo	Primary endpoint: Effect of Resmetiron on hepatic fat Secondary endpoint: Effects on liver histology, serum lipids, ALT, biomarkers of inflammation and fibrosis	36 weeks R: 74 P: 33	R: 74 P: 33	NAS Score Kleiner/Brunt	• >18 years • NASH suggestive diagnose based on presence of metabolic syndrome and elastography controlled fibrosis + steatosis or proven NASH in liver biopsy • NAS>4 (…)	• Cirrhosis • Other liver diseases • Alcohol consumption • Drug intake associated with NAFLD • Hypothyreoidism • HbA1c >9,5% or use of GLP-1 analogues (…)
Harrison et al. 2019 EMMINENCE Trial	RCT, four-arms	a) MSDC-0602K 62.5 mg (3x d orally) b) MSDC-0602K 125 mg c) MSDC-0602K 250 mg b) d) Placebo	Primary endpoint: hepatic histological improvement in NAS defined as ≥2-point NAS decrease with a ≥1-point reduction in either ballooning or lobular inflammation and no increase in	12 months N=400	a) 99 b) 98 c) 101 d) 94	NAS Score Kleiner/Brunt	• > 18 years. • Biopsy proven NASH (NAS ≥ 4 with a score of at least 1 in each component of NAS. • Histological evidence of liver fibrosis (fibrosis score of F1 to F3) • liver within 9 months prior to or during Screening	• Cirrhosis • Other liver diseases • History of liver transplant • Current or history of recent (≤ 6 months) use of ursodeoxycholic acid • Antidiabetic medication other than

			fibrosis stage at 12 months Secondary endpoints: NASH resolution (hepatocellular ballooning score of 0, lobular inflammation score of 0–1, no increase in fibrosis), fibrosis improvement, change in NAS				• AST ≥ 20 U/L • FibroScan with CAP score ≥ 270 db/m and kPa ≥8.5 • HbA1c ≤9.5%. • Body Mass Index (BMI) ≤ 50 kg/m^2 • Informed consent (…)	metformin, glp-1 agonist, SGLT2 inhibitors, sulfonylureas, or DPP4 inhibitors 3 months prior to (…)
Harrison et al. 2019	RCT, three armed	Emricasan 5 mg Emricasan 50 mg Placebo	Primary endpoint: improvement of at least 1 point in fibrosis stage without worsening of NASH at week 72 Secondary endpoint: NASH resolution, changes of NA components inflammation, Mallory denk bodies and portal inflammation	72 weeks a) 107 b) 106 c) 105	a) 107 b) 106 c) 105	NASH CRN criteria	• >18 years • Biopsy proven NASH (NAS>) • Fibrosis stage 1-3 • Biopsy 6 months prior to screening	• Alcohol consumption (current or history), >20g/d for females or >30g/d males) • Use of hepatotoxic drugs • HbA1c ≥9% • Presence of cirrhosis or fibrosis >4 • Other liver diseases • Liver transplant • Prior or planned bariatric surgery