**Supplementary method**

**Liver histology data**

Our center was part of the NASH Clinical Research Network and all biopsies were interpreted by dedicated liver pathologists who follow the standardized NASH CRN grading and staging scoring system. Biopsies were only included if judged by the pathologist as adequate for accurate interpretation based on the biopsy size and the number of portal tracts. Fifty random biopsies from our cohort were reviewed for quality of biopsy assessment. The median biopsy length was 1.8 cm and 96% of the specimens were 1.5 cm or greater. No inadequate number of portal tract was reported by the pathologists in these biopsy samples**.**

**Supplementary table 1 Full multivariable model** **of risk factors associated with HCC development in NAFLD patients with cirrhosis**

|  |  |
| --- | --- |
| **Factors** | **Multivariable analysis\***  |
| **HR** | **95% CI** | **P-value** |
|  Male gender | 3.65 | 2.22-6.00 | <0.001 |
|  Age | 1.06 | 1.03-1.09 | <0.001 |
|  Non-white race | 1.46 | 0.57-3.71 | 0.432 |
|  BMI | 1.04 | 1.01-1.07 | 0.011 |
|  Diabetes mellitus | 1.39 | 0.71-2.70 | 0.334 |
|  Smoker | 0.93 | 0.58-1.50 | 0.780 |
|  Alcohol user | 1.34 | 0.82-2.20 | 0.247 |
|  Bariatric surgery | 0.29 | 0.04-2.12 | 0.222 |
|  Liver decompensation | 1.02 | 0.60-1.73 | 0.932 |
|  MELD-Na score | 1.06 | 0.99-1.13 | 0.091 |
|  CTP score | 1.23 | 1.00-1.51 | 0.049 |
|  Statin user | 0.45 | 0.26-0.79 | 0.005 |
|  Aspirin user | 0.67 | 0.40-1.13 | 0.131 |
|  Metformin user | 0.99 | 0.53-1.75 | 0.910 |
|  Sulfonylurea user | 0.97 | 0.53-1.75 | 0.910 |
|  Insulin user | 0.80 | 0.43-1.50 | 0.490 |

\*Multivariable Cox proportional hazard model

Abbreviations: BMI , body mass index; MELD-Na, model for end-stage liver disease; CTP, Child-Turcotte-Pugh

**Supplementary table 2 Characteristics of cirrhotic NAFLD population who were lost to follow-up by statin user and non-statin user**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Characteristics** | **Total****(n = 178)** | **Statin user****(n = 57)** | **Non-user****(n = 121)** | **P-value** |
| Male gender, n(%) | 76 (42.7) | 27 (47.4) | 49 (40.5) | 0.39 |
| Age at diagnosis, year, mean±SD | 58.7 ± 11.2 | 59.7 ± 10.9 | 58.2 ± 11.3 | 0.43 |
| Race/ethnicity, n(%) |  |  |  | 0.10 |
|  White | 159 (89.3) | 54 (94.7) | 105 (86.8) |  |
|  Hispanic | 11 (6.2) | 2 (3.5) | 9 (7.4) |  |
|  Black | 4 (2.3) | 1 (1.8) | 3 (2.5) |  |
|  Other | 4 (2.3) | 0 (0) | 4 (3.3) |  |
| BMI (kg/m2), mean±SD | 36.0 ± 8.8 | 35.8 ± 7.5 | 36.0 ± 9.4 | 0.87 |
| Comorbidities, n(%) |  |  |  |  |
|  Diabetes | 130 (73.0) | 47 (82.5) | 83 (68.6) | 0.07 |
|  Hypertension | 131 (73.6) | 46 (80.7) | 85 (70.3) | 0.15 |
|  Hyperlipidemia | 82 (46.1) | 53 (93.0) | 29 (24.0) | <0.001 |
| Bariatric surgery, n(%) | 16 (9.0) | 5 (9.0) | 11 (9.1) | 1.00 |
| Smoking status, n(%) |  |  |  | 0.34 |
|  Non-smoker | 95 (53.4) | 27 (47.4) | 68 (56.2) |  |
|  Current smoker | 16 (9.0) | 4 (7.0) | 12 (9.9) |  |
|  Former smoker | 67 (37.6) | 26 (45.6) | 41 (33.9) |  |
| Alcohol status, n(%) |  |  |  | 0.56 |
|  Modest alcohol use | 36 (20.2) | 13 (22.8) | 23 (19.0) |  |
| MELD-Na, mean±SD | 9.2 ± 4.1 | 9.1 ± 3.9 | 9.3 ± 4.2 | 0.68 |
| CTP score, mean±SD | 6.0 ± 1.2 | 5.6 ± 1.0 | 6.1 ± 1.3 | 0.013 |
| Child-Pugh class, n(%) |  |  |  | 0.33 |
|  A | 128 (71.9) | 45 (79.0) | 83 (68.6) |  |
|  B | 49 (27.5) | 12 (21.1) | 37 (30.6) |  |
|  C | 1 (0.6) | 0 (0) | 1 (0.8) |  |
| Clinical decompensation, n(%) | 81 (45.5) | 17 (29.8) | 64 (52.9) | 0.004 |
| Laboratory data, mean±SD |  |  |  |  |
|  AST (U/L) | 43.3 ± 20.3 | 42.1 ± 16.8 | 43.9 ± 21.8 | 0.58 |
|  ALT (U/L) | 36.0 ± 20.3 | 35.5 ± 20.3 | 36.2 ± 22.9 | 0.84 |
|  Albumin (g/dl) | 3.8 ± 0.6 | 3.9 ± 0.5 | 3.7 ± 0.6 | 0.034 |
|  Total bilirubin (g/dl) | 1.0 ± 0.8 | 0.9 ± 0.5 | 1.0 ± 1.0 | 0.32 |
|  Platelet count (k/mcl) | 142.3 ± 80.9 | 155.6 ± 91.1 | 136.0 ±75.2 | 0.13 |
|  INR  | 1.1 ± 0.2 | 1.1 ± 0.1 | 1.2 ± 0.3 | 0.07 |
|  HbA1c\* (mmol/mol)  | 6.8 ± 1.5 | 7.0 ± 1.6 | 6.7 ± 1.4 | 0.34 |
|  HDL\* cholesterol (mg/dl) | 45.6 ± 21.2 | 48.4 ± 26.7 | 44.0 ± 17.2 | 0.26 |
|  LDL\* cholesterol (mg/dl) | 86.6 ± 35.1 | 88.7 ± 37.8 | 85.5 ± 33.6 | 0.62 |
|  Triglyceride\* (mg/dl) | 129.6 ± 84.7 | 139.8 ± 83.2 | 123.6 ± 85.4 | 0.29 |
|  AFP (ng/dl)\* | 4.5 ± 2.4 | 4.4 ± 3.0 | 4.5 ± 2.2 | 0.92 |
| Statin use |  |  |  |  |
|  Type of statin\*\* |  |  |  |  |
|  Lipophilic statin |  | 38 (66.7) |  |  |
|  Hydrophilic statin |  | 19 (33.3) |  |  |
|  cDDD, mean±SD\*\* |  | 1,178 ± 1,530 |  |  |
| Follow up time (years), mean±SD | 3.4 ± 2.5 | 3.5 ± 2.6 | 3.3 ± 2.4 | 0.61 |

\*Data not available for all subjects. Data available: HbA1c n=128, HDL cholesterol n=129, LDL cholesterol n=128, triglyceride n=129, AFP n=138
\*\*Data in statin users n=57

Statistical analysis: independent *t*-test for continuous variables; Chi-squared test for categorical variables

Abbreviations: NAFLD, non-alcoholic fatty liver disease; BMI , body mass index; MELD-Na, model for end-stage liver disease-Na; CTP, Child-Turcotte-Pugh; AST, aspartate aminotransferase; ALT, alanine aminotransferase; INR, international normalized ratio; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein; AFP, alpha-fetoprotein*;* cDDD, cumulative defined daily dose