

BACKGROUND

Among adults in the general population with metabolic dysfunction-associated steatotic liver disease (MASLD) and non-cirrhotic liver fibrosis, the glucagon-like peptide-1 receptor agonist semaglutide improves steatohepatitis (MASH) but not liver fibrosis.

The OWLiver[®] Metabolomics algorithm is a non-invasive diagnostic tool validated against liver biopsy in general population cohorts and uses serum profiling to distinguish MASLD from No MASLD. Among persons with MASLD, it can also distinguish MASH and MASH with significant fibrosis (at-risk MASH) from No MASH.

We previously reported that 24 weeks of semaglutide reduced magnetic resonance imaging proton density fat fraction (MRI-PDFF)-quantified liver fat in people with HIV (PWH) that correlated strongly with weight loss. Here we report metabolomic profiles before and after semaglutide.

METHODS

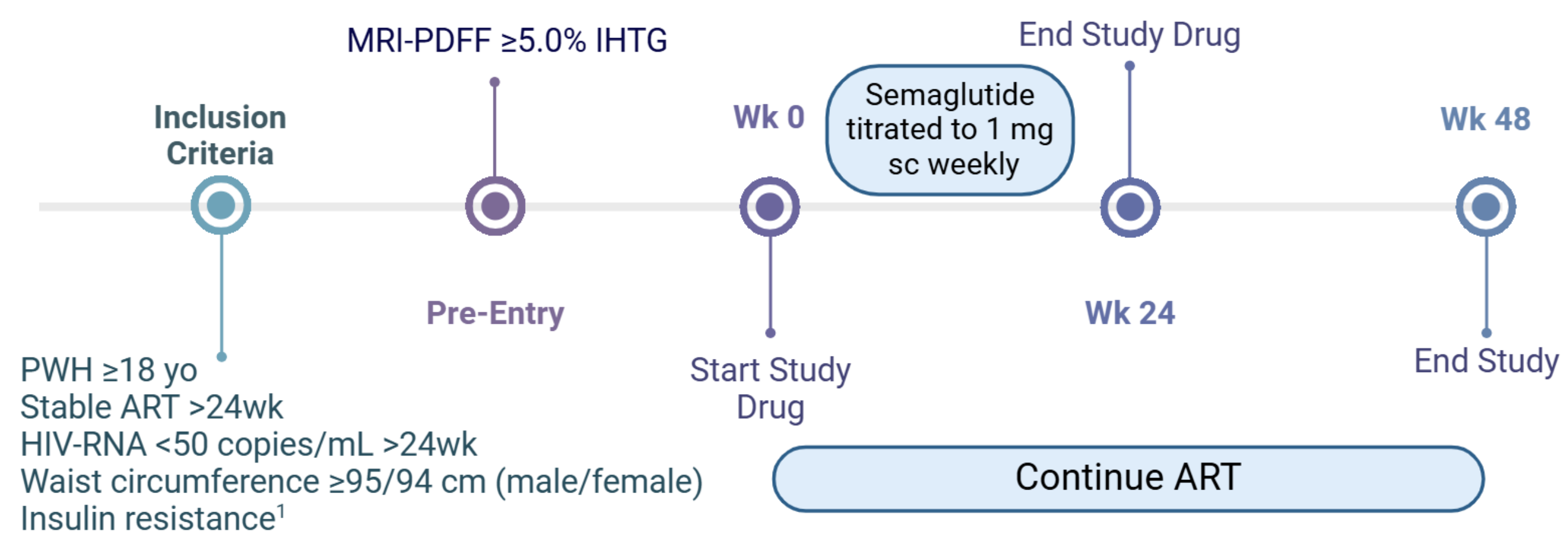


Fig. 1. A5371 The SLIM LIVER study schema.¹Fasting plasma glucose 100-125 mg/dL, HbA1c between 5.7 and <6.5%, or HOMA-IR >3.0. ART=antiretroviral therapy; IHTG= intrahepatic triglyceride content; MRI-PDFF=magnetic resonance imaging proton density fat fraction; Wk=week; sc=subcutaneously

Of 51 participants, 36 PWH with clinical response (>5 lb weight loss) to semaglutide had serum analyzed by ultra-high performance liquid chromatography-mass spectrometry at OWLiver[®] Metabolomics for OWLiver[®] disease staging.

RESULTS

Table 1. Clinical and Demographic Characteristics

Age (years)	52 (42, 59)
Race/ethnicity	
Non-Hispanic White	11 (31%)
Non-Hispanic Black	10 (28%)
Hispanic	14 (39%)
Cisgender/transgender female	16 (45%)
Body mass index (kg/m ²)	34 (31, 39)
Waist circumference (cm)	114 (106, 124)
INSTI-based ART	28 (77%)
CD4 ⁺ T-cell count/mm ³	700 (533, 795)

Table 1. Median (IQR) or frequency presented. INSTI=integrase strand transfer inhibitor; ART=antiretroviral treatment

RESULTS

Table 2. Changes in MASLD Disease Category on Semaglutide

Week 0 N (%)	Week 24 N (%)				24-week change	N (%)
	No MASLD	MASLD without MASH	MASH	At-risk MASH		
No MASLD	2 (6%)	1 (3%)	1 (3%)	(0%)	Improved	11 (31%)
MASLD without MASH	25 (69%)	4 (11%)	19 (53%)	1 (3%)	Worsened	3 (8%)
MASH	8 (22%)	2 (6%)	4 (11%)	2 (6%)	No change	22 (61%)
At-risk MASH	1 (3%)	(0%)	(0%)	1 (3%)		
Total	36 (100%)	7 (19%)	24 (67%)	4 (11%)		

Table 2. Some columns may not total exactly 100% due to rounding error. Green highlighting=movement into a better clinical category; Red highlighting=movement into a worse clinical category.

Figure 3. Participant-Level Changes by OWLiver[®] Diagnostic Algorithm Type

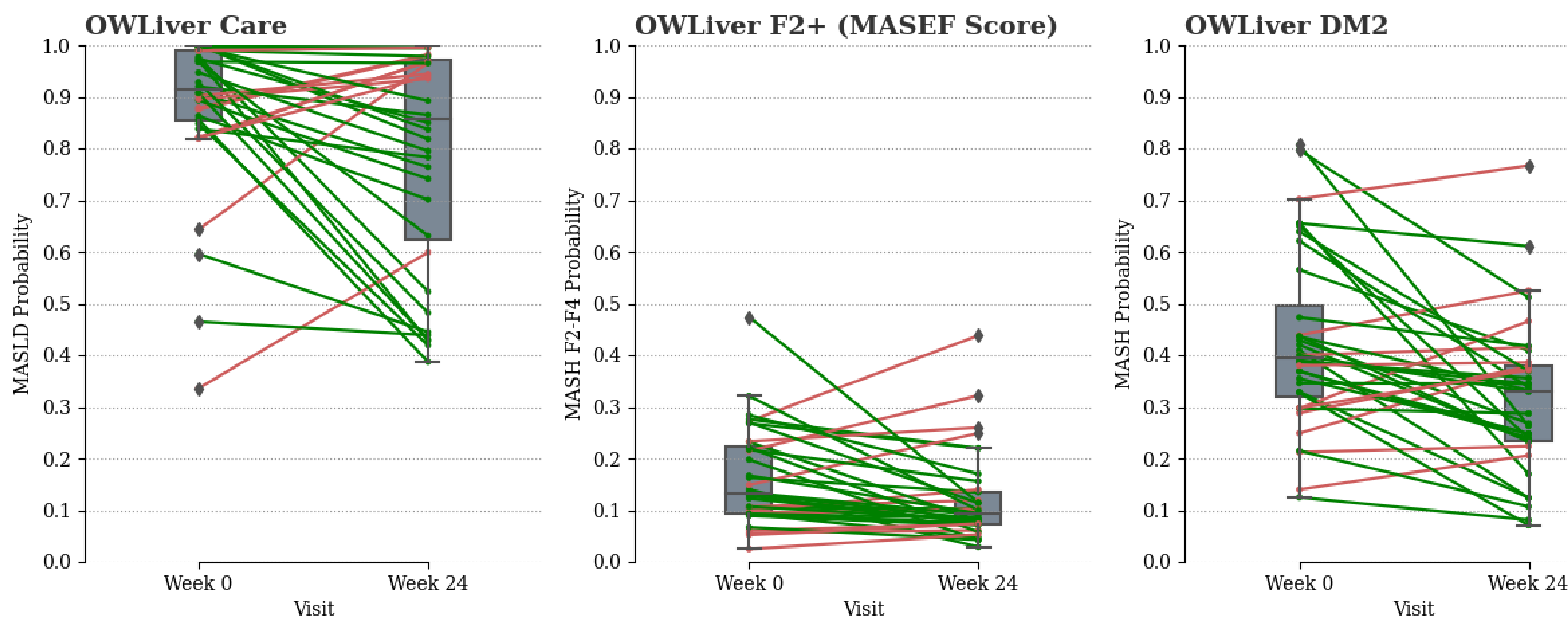


Fig. 3. OWLiver[®] Metabolomics algorithm. The results of the three algorithms included in the OWLiver[®] diagnostic panel (OWLiver Care, OWLiver F2+ and OWLiver DM2 tests) are a probability ranged from 0 to 1, and should be interpreted in a sequential order depending on the specific cutoff of each algorithm:

- The panel OWLiver Care identifies the presence or absence of MASLD (cutoff =0.5)
 - If the probability is lower than the cutoff (<0.5), the final diagnosis is No MASLD.
 - If the probability is higher than the cutoff (≥0.5), then OWLiver F2+ is evaluated.
- The panel OWLiver F2+ (also called Metabolomics-Advanced StEatohepatitis Fibrosis, MASEF Score) identifies participants with MASH and with significant fibrosis (cutoff=0.33)
 - If the probability is higher than the cutoff (≥0.33), the final diagnosis is “at-risk MASH” or MASH with F2-F4.
 - If the probability is lower than the cutoff (<0.33), then OWLiver DM2 is evaluated.
- The OWLiver DM2 panel identifies participants with MASLD or MASH (cutoff =0.5)
 - If the probability is higher than the cutoff (≥0.5), the final diagnosis is MASH.
 - If the probability is lower than the cutoff (<0.5), the final diagnosis is MASLD.

Figure 2. Changes in MASLD Disease Category on Semaglutide Using the OWLiver[®] Diagnostic Algorithm

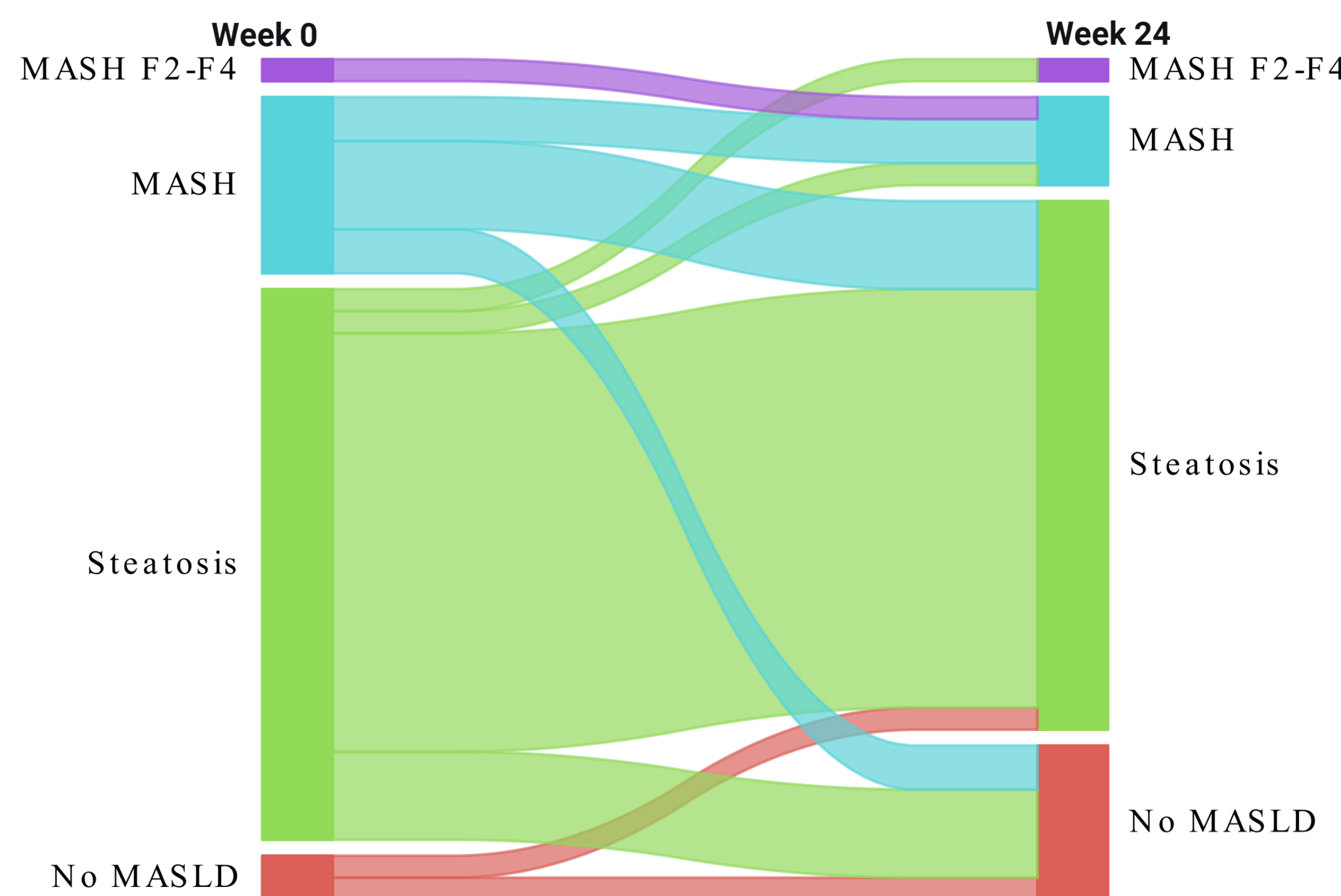


Fig.2. Sankey plot showing changes in MASLD disease category on semaglutide considering all three OWLiver[®] diagnostic tests.

CONCLUSIONS

- Among PWH and MRI-defined MASLD, 24 weeks of low-dose semaglutide led to significant improvement in MASLD disease severity in nearly 1/3 of participants and across all disease severity categories.
- While 61% did not change disease category, improvements within a category (such as from severe to mild MASLD) may have occurred.
- OWLiver[®] Metabolomics algorithms provide evidence of improvement in predicted histology without a requirement for liver biopsy and should be considered for disease staging in PWH.
- Studies of longer duration and higher dose semaglutide for MASLD are needed to determine if additional benefit can be gained.

ACKNOWLEDGEMENTS

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