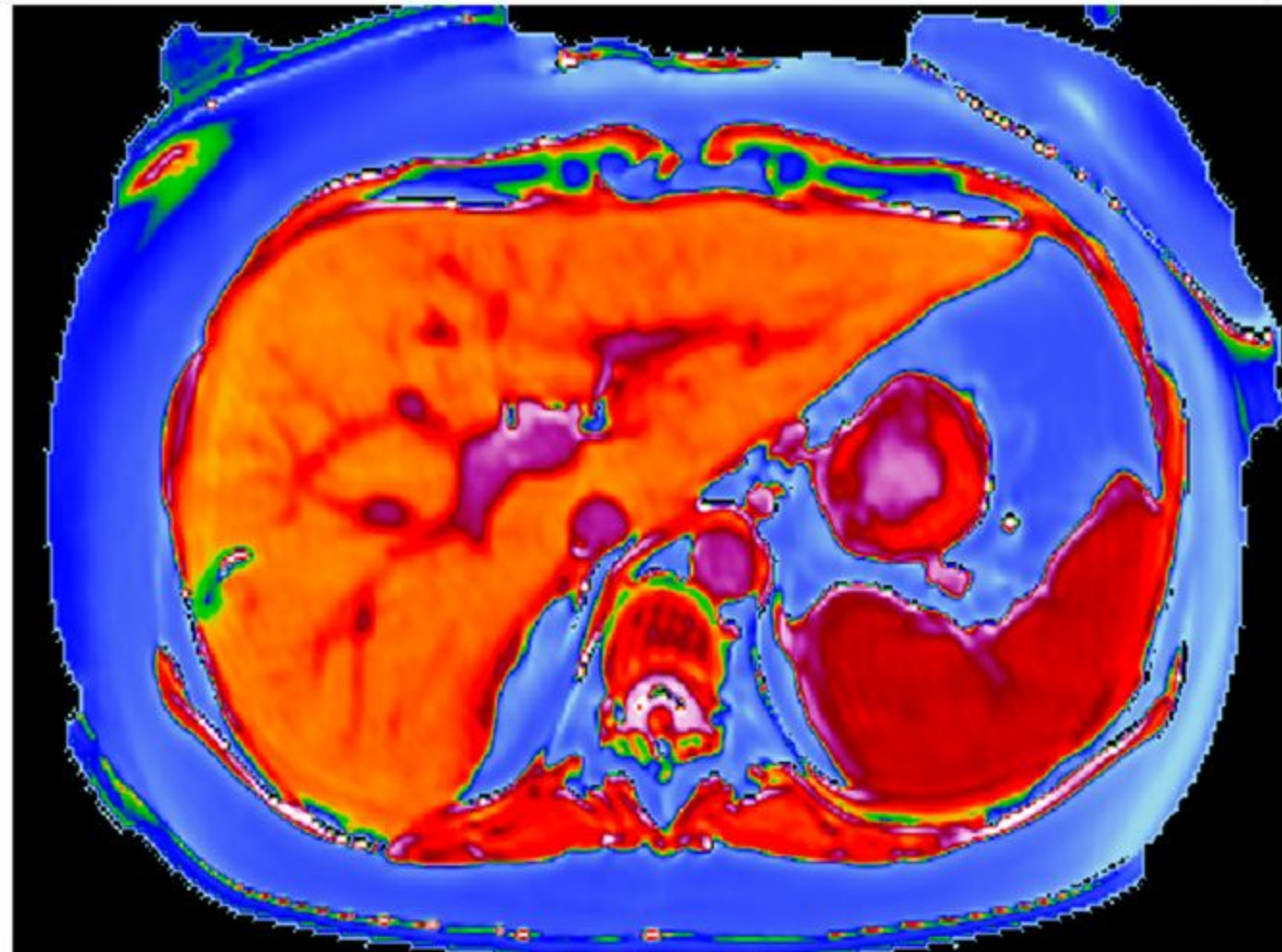


Liver*MultiScan* for monitoring treatment

response

June 2020



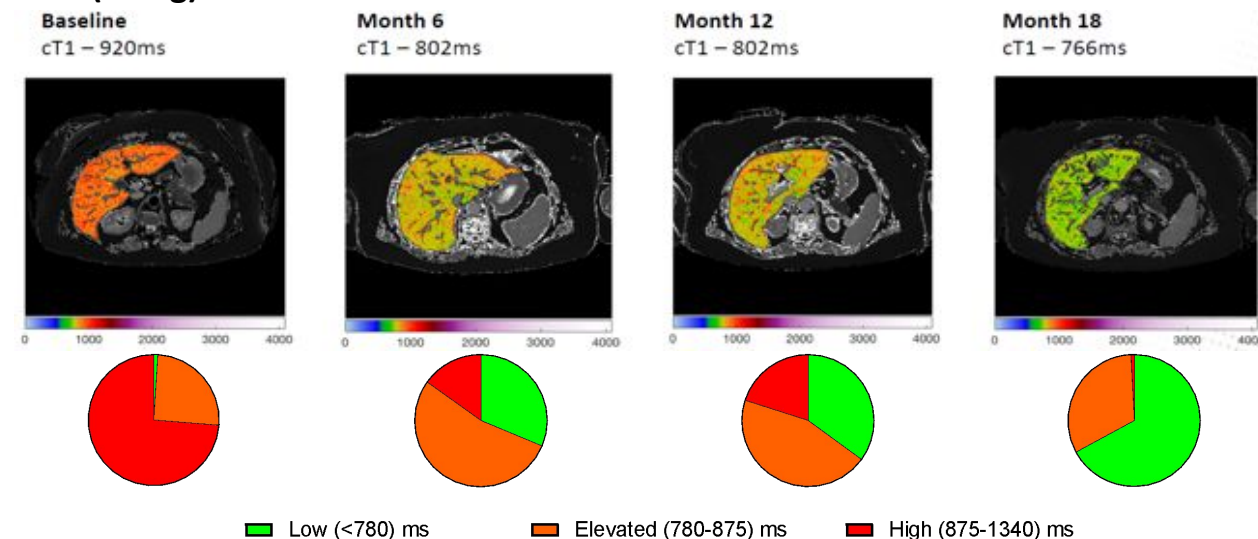
REGENERATE NASH Phase III Trial

Intercept Pharmaceuticals

Measuring OCA response with LiverMultiScan

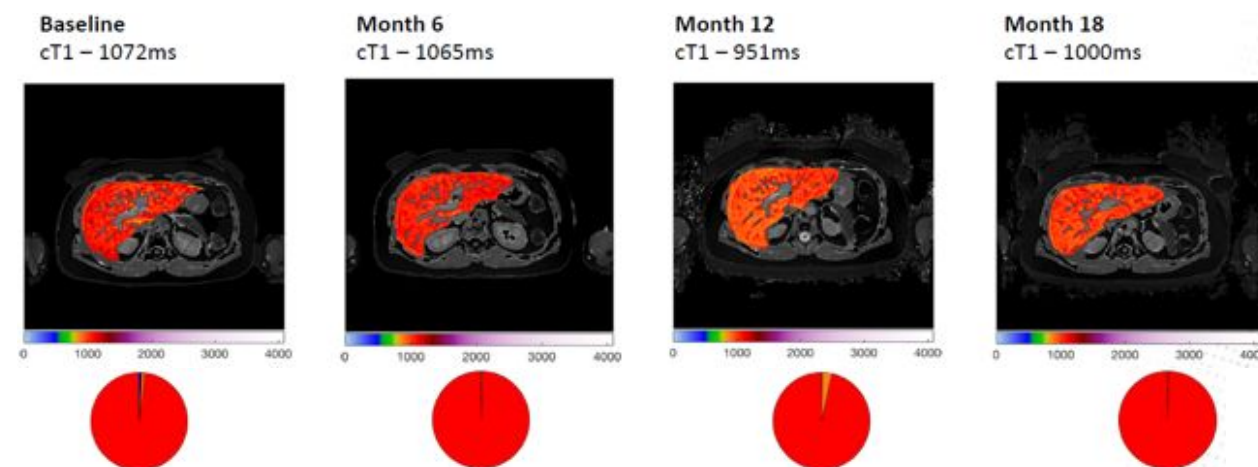
Quantitative imaging enables definitive assessment of treatment response

OCA (25mg)



cT1 (ms)	Baseline	Month 18
Low <780)	1%	67%
Elevated (780-875)	25%	32%
High (875-1340)	73%	<1%

Placebo

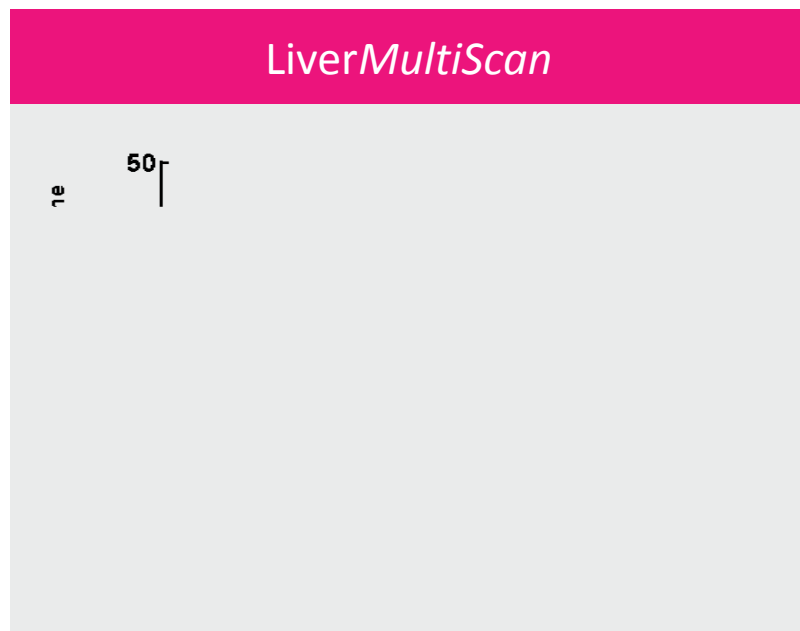


cT1 (ms)	Baseline	Month 18
Low <780)	<1%	<1%
Elevated (780-875)	1%	3%
High (875-1340)	>98%	>97%

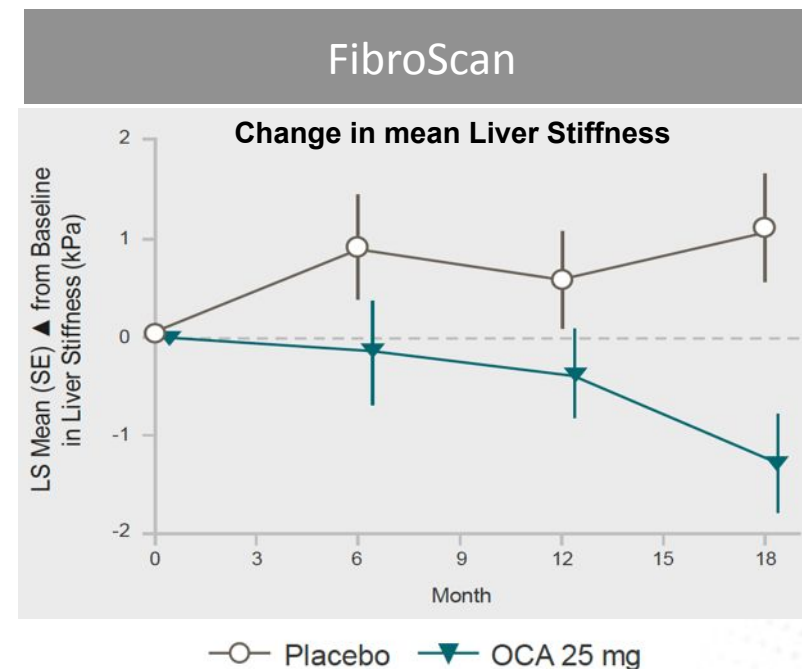
Measuring OCA response with LiverMultiScan vs. FibroScan

LiverMultiScan shows NASH resolution within 6 months

Month 18 interim analysis from Intercept Phase III NASH study (REGENERATE)



LiverMultiScan detects response within **6 months**



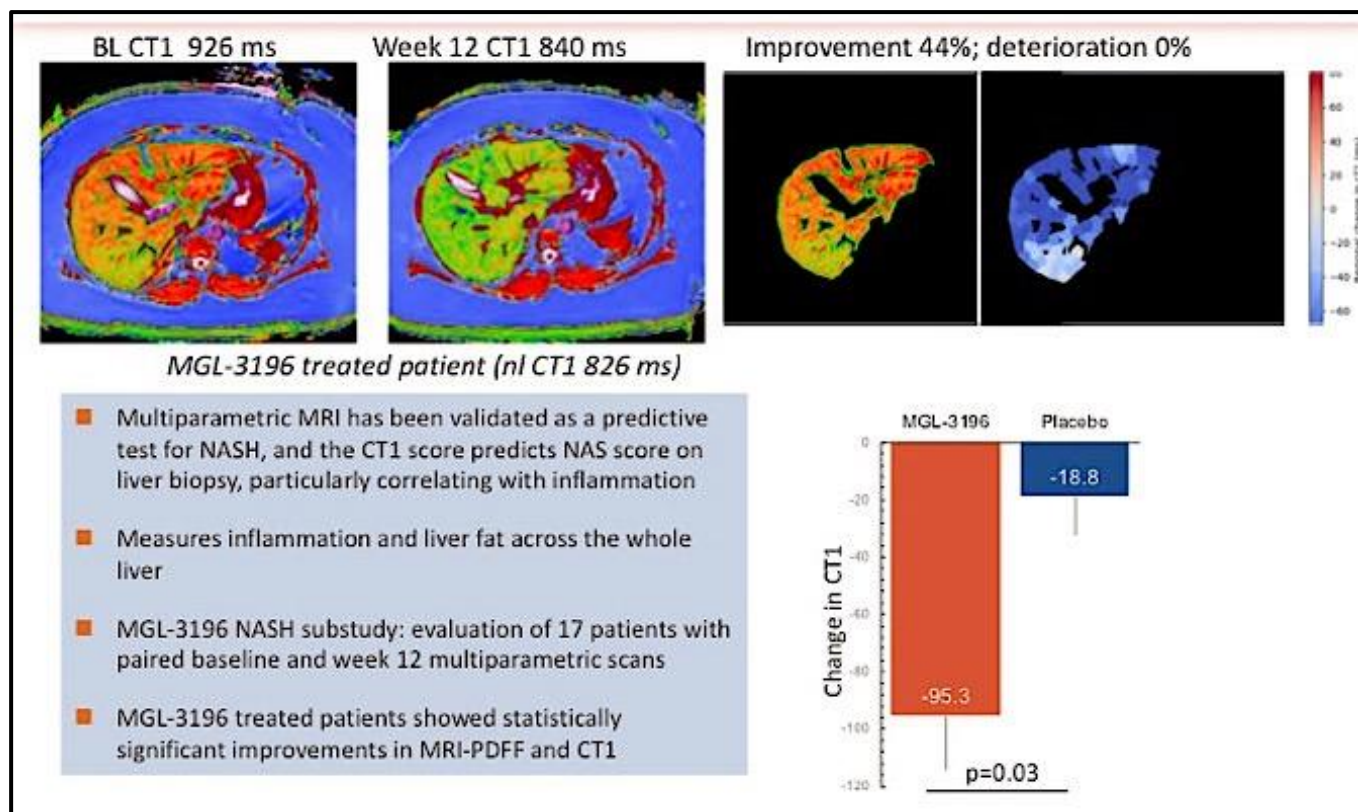
FibroScan requires **18 months** to detect difference

Resmetirom (MGL-3196) NASH Phase II Trial

Madrigal Pharmaceuticals

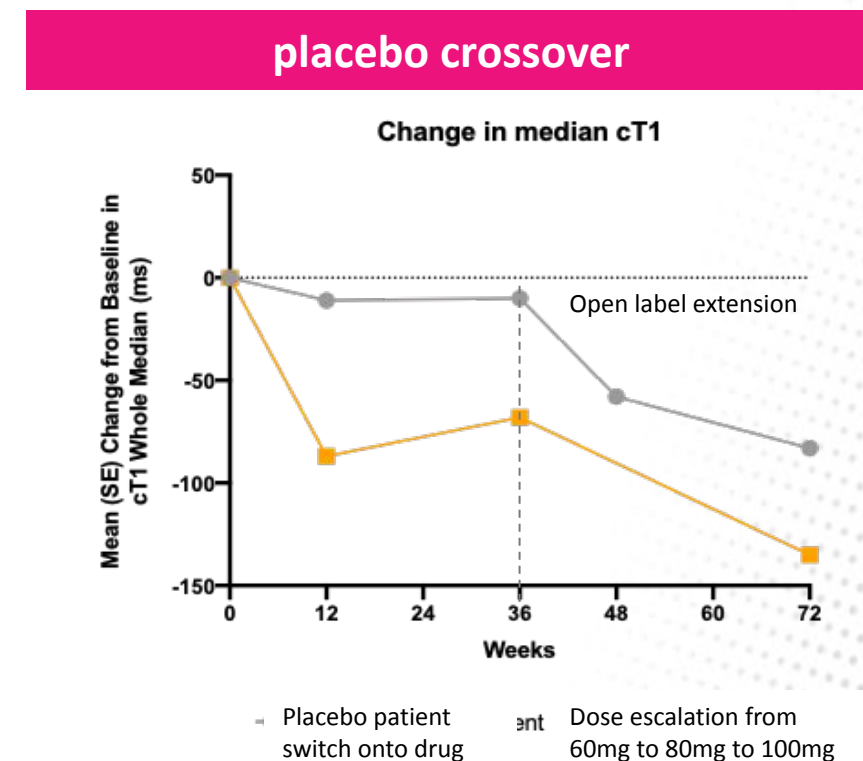
Measuring treatment change in 12 weeks

Phase II NASH study with MGL-3196 and open label extension



Significant decrease in fibroinflammatory disease (cT1), after 12 weeks (n=17)

Harrison SA et al. EASL 2018 (oral presentation)



cT1 detected efficacy at Week 12 in a placebo crossover

Taub R, AASLD 2019 (oral presentation)

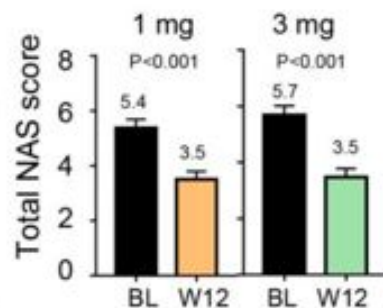
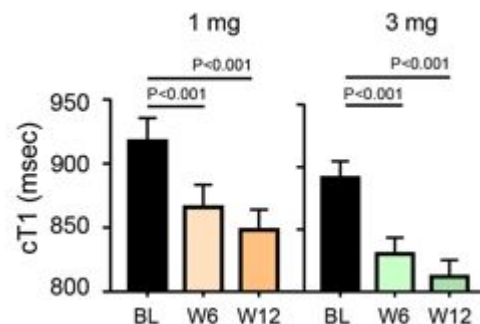
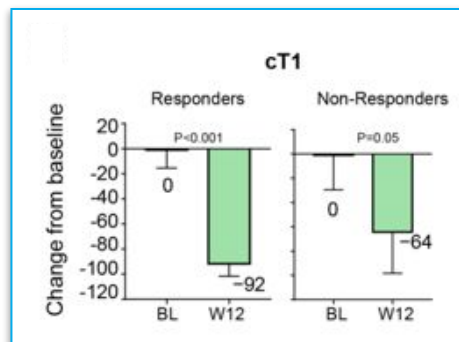
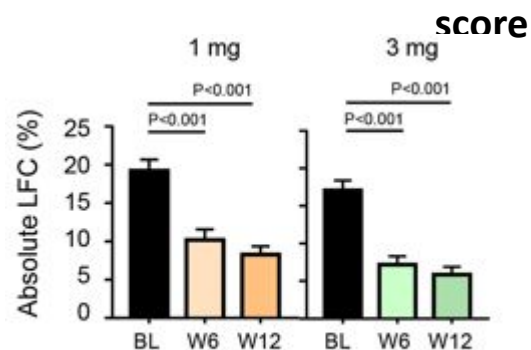
NGM282 Phase II NASH Trial

NGM Bio

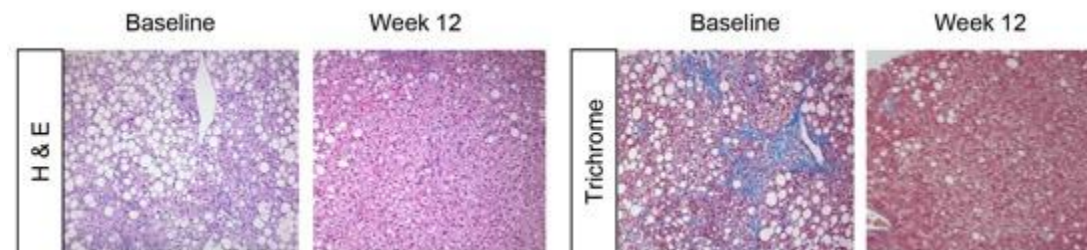
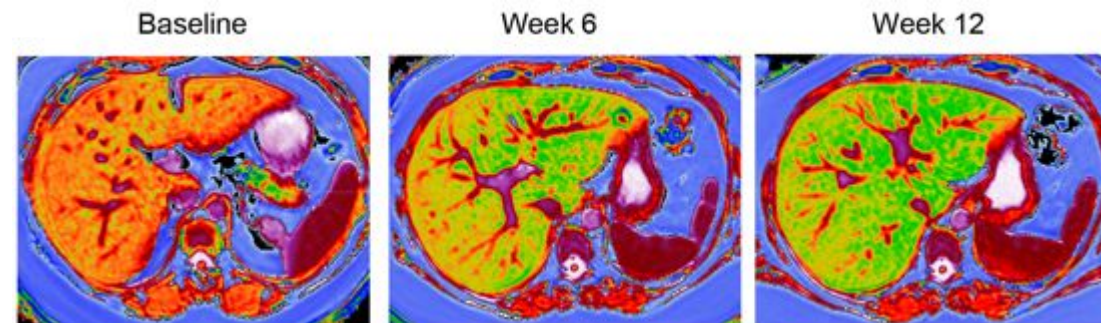
Measuring treatment change in 6 weeks

Liver*MultiScan* as an endpoint in drug development NGM-282

Change in cT1 and LFC correlated with reduction in NAS



Improvement in cT1 observed in 6 weeks



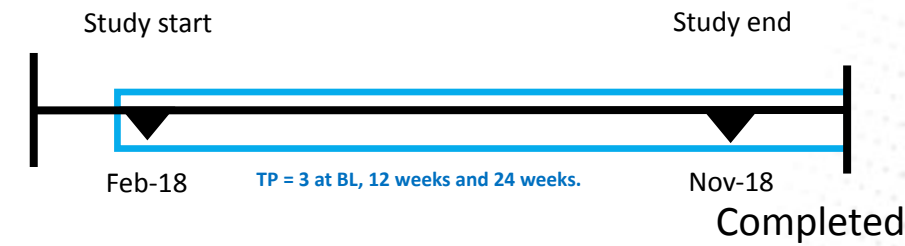
In NGM-282 Phase 2 study, cT1 has been shown to detect changes in 6 weeks that correlated with histological response.

NAFLD LiLi



NAFLD LiLi

Lifestyle Induced Weight loss and Liraglutide in the Treatment of Non-Alcoholic Steatohepatitis



Study design: Interventional study assessing the effects of either lifestyle management Vs GLP1RA (Liraglutide) upon NASH over a 12-week period.

Enrolment criteria:

- Non-diabetic (HbA1c < 48mmol/mol)
- Aged 18-75 years
- BMI of 25-40 kg/m²
- Diagnosis of NAFLD (imaging, histology)

Analysis: data has not been published:

- Weight significantly impacts changes to cT1.
- Age has small but significant effect whilst gender and lifestyle do not.

Status: Study complete.

Objectives:

- To assess the effects of either lifestyle management or Liraglutide on liver health.

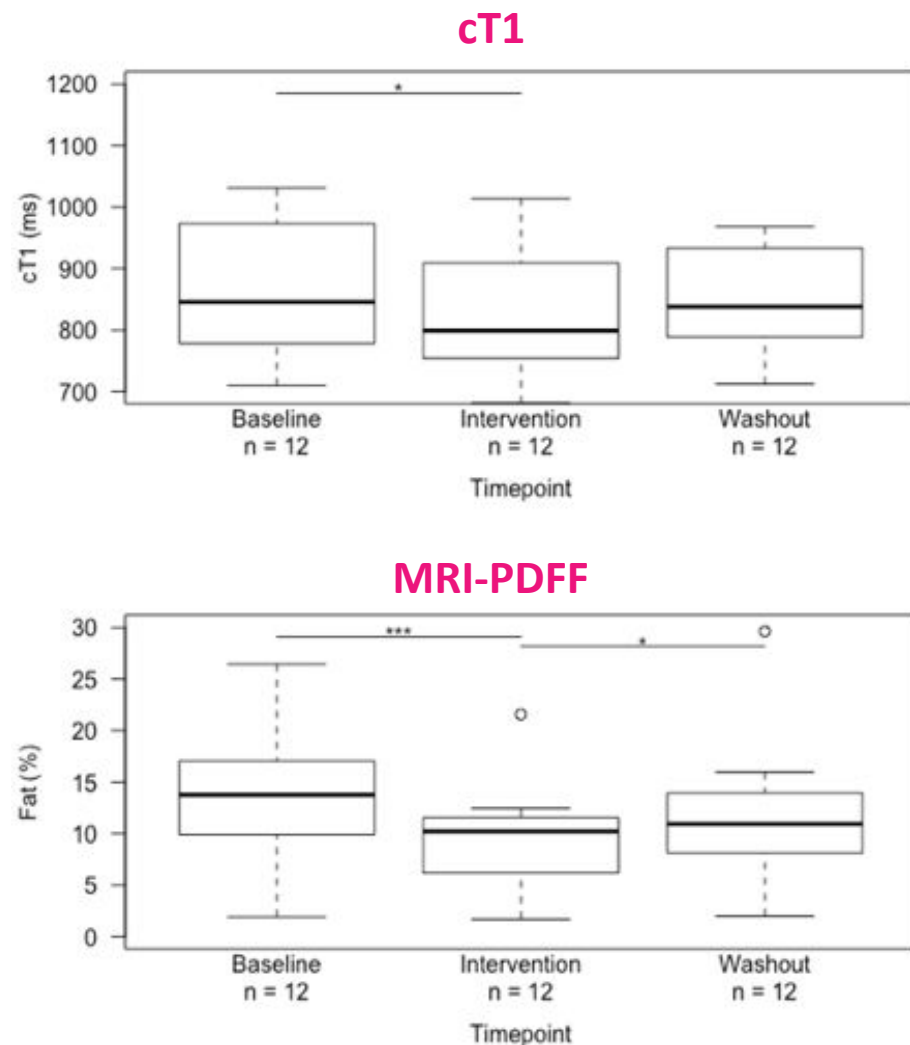
Primary endpoints are measures of weight and steatosis as assessed by:

- Liver fat content (¹H-MRS)
- Weight loss

GLP1-RA intervention reduces liver cT1 and PDFF

Monitoring liver-specific response to diabetic treatment

LiverMultiScan



- Non-diabetic patients with NAFLD (HbA1c <48 mmol/mol)
- 12-week treatment with a GLP1-RA
- Both liver fibroinflammation and steatosis significantly reduced and partially restored if treatment discontinued

MODIFY



Longitudinal Assessment of Multiple Organs in Patients With Type 2 Diabetes (MODIFY)

Investigating the utility of ATLAS metrics in monitoring T2D and ability to predict outcomes



MRI



Blood



Urine



ECHO
(Optional)



Online
questionnaire

TP1: Baseline

- Atlas
- Bloods
- Urine
- Anthropometrics
- (Echocardiogram)

TP2: 9-months

- Atlas
- Bloods
- Urine
- Anthropometrics

F1: 1 yr

- Clinical events

F2: 3 yr

- Clinical events

F2: 5 yr

- Clinical events

n=150

Adults >18 yr with any T2D from community, primary, secondary care

Primary objective

- Investigate the degree of liver fibroinflammation in a large cohort of patients with T2D, using multi-parametric MRI.
- Endpoint = MRI metrics for liver fibroinflammation in patients with T2D compared with the same metrics in healthy, non-diabetic individuals at baseline.

Secondary objectives

- Other liver abnormalities (such as fat infiltration) & abnormality in other organs (pancreas, spleen, kidneys, aorta) using multi-parametric abdominal MRI.
- Quantify changes in multiple organs over 9 months using MRI and biochemical biomarkers.
- Impact of multi-parametric abdominal MRI on type 2 diabetes management.
- Prognostic information provided by abdominal imaging for longer-term evaluation of clinical outcomes (after 1, 3 5 years).

<https://clinicaltrials.gov/ct2/show/NCT04114682>

Liver*MultiScan* can be used to screen for steatohepatitis in T2D

- Scans from 48 patients with confirmed T2D compared to 100 healthy UK Biobank participants
- T2D had significantly higher values for
 - Liver PDFF
 - Liver cT1
- Prevalence of steatohepatitis in 50% of T2D
- BMI positively associated with cT1 and PDFF

