Serum ferritin levels in patients with non-elevated Proton-Density Fat Fraction-derived $R2^*$ Liver Iron Concentration – an exploratory study of Revita-2 phase II trial data –

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Dysregulation of iron homeostasis has been associated with fatty liver disease and type 2 diabetes mellitus (T2DM)\(^1\).

Serum ferritin levels are positively correlated with elevated liver iron concentration (LIC)\(^2\).

The relationship between serum ferritin and LIC in patients with non-elevated LIC is not known.

• MRI-based proton density fat fraction (PDFF) can be used to quantify liver fat.

• T2* maps are generated as part of the PDFF measurements and can be used to estimate liver iron concentration (LIC).

• Vendor-derived PDFF sequences (e.g. Philips mDixonQuant, GE IDEAL-IQ) enable multi-site, multi-vendor, multi-field strength studies
DMR catheter is designed to perform submucosal lift and hydrothermal ablation of hyperplastic duodenal mucosa, promote healthy epithelial regrowth within 12 weeks, and reduce insulin resistance and hyperinsulinemia.\textsuperscript{1,2}

DMR is a well-tolerated procedure with few, self-limited side effects\(^3\)\(^-\)\(^5\)

Prior studies (eg, REVITA-1) showed a single DMR procedure durably improves hepatic and glycemic parameters through 2 years in patients with T2D, indicating potential benefit in T2D with concomitant NAFLD/NASH\(^3\)\(^-\)\(^6\)


REVITA-2 NCT02879383; DMR = duodenal mucosal resurfacing; NAFLD = nonalcoholic fatty liver disease; NASH = nonalcoholic steatohepatitis; T2D = type 2 diabetes.
Revita-2 is a phase II blinded, sham-controlled international multi-site multi-scanner vendor cross-over trial (NCT02879383).

Investigation of the effect of DMR on hepatic and glycaemic parameters in patients with sub-optimally controlled T2D across 7 sites (5 in EU, 2 in Brazil)

Trial endpoints include absolute and relative change in liver MRI-PDFF from baseline at 12 weeks (in patients with MRI-PDFF >5% at baseline)
To investigate the relationship between serum ferritin levels and *non-elevated* proton-density fat fraction (PDFF) derived R2* liver iron concentration (LIC) in patients with T2DM undergoing endoscopic Duodenal Mucosal Resurfacing (DMR).
Vendor-derived PDFF sequences (e.g. Philips mDixonQuant, GE IDEAL-IQ) were used for multi-site, multi-vendor, multi-field strength studies.
- Custom-developed online platform (Ambra Health, New York, USA)
- Circular ROIs measuring up to 20mm diameter
- Colocalised on PDFF maps and T2* maps
- LIC (µmol/g) estimated from T2* data as previously\(^1\)
- Absolute and relative (% of baseline) within-subject change in liver FF and LIC were assessed

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Baseline and 12-week post-treatment liver MRI scans with paired serum ferritin levels for initial open-label training (n=17) cohort, DMR (n=39) cohort, and Sham (n=23) cohort.
At baseline, a modest positive but significant correlation was demonstrated between LIC and serum ferritin.

All LIC measurements were <32 μmol/g consistent with normal (non-elevated liver iron).\(^1,2\)

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Open-label training cohort (n=17) – change in serum ferritin vs change in LIC 12 weeks post-treatment

$r = 0.3683, P = 0.1604$
DMR cohort (n=39) – change in serum ferritin vs change in LIC 12 weeks post-treatment

\[ r = 0.1075, \ P = 0.5146 \]
Sham treatment cohort (n=23) – change in serum ferritin vs change in LIC 12 weeks post-treatment

\[ r = -0.1319, P = 0.5484 \]
Even at non-elevated LIC levels, serum ferritin and LIC are positively correlated.

Poor correlations in LIC and serum ferritin in post-treatment changes may reflect mechanistic effects on hepatic iron metabolism as a result of DMR.