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ASSESSMENT OF PATIENT-REPORTED OUTCOMES IN PATIENTS WITH NASH TREATED WITH OBETICHOLIC ACID: RESULTS FROM REGENERATE PHASE 3 CLINICAL TRIAL

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INTRODUÇÃO

- Obeticholic acid (OCA) was shown to improve fibrosis without worsening of steatohepatitis in the interim analysis of the REGENERATE phase 3 clinical trial[1]
- Our aim was to assess patient-reported outcomes (PROs) in NASH patients and the effects of treatment with OCA

MATERIAL/MÉTODOS

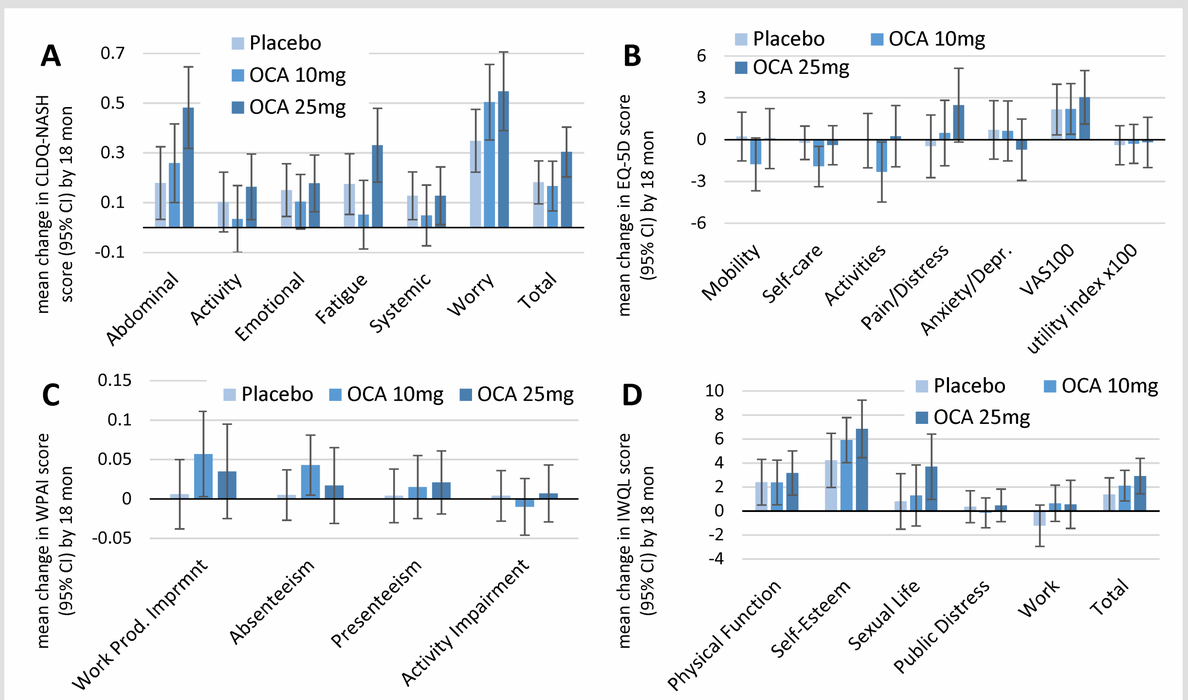
- Non-cirrhotic NASH patients were enrolled in a phase 3, double-blind, randomized, placebo-controlled, multicenter study of OCA (REGENERATE; #NCT02548351)
- The Chronic Liver Disease Questionnaire-NASH (CLDQ-NASH), Work Productivity and Activity Impairment (WPAI), EuroQol (EQ-5D), and Impact of Weight on Quality of Life-Lite (IWQL) were administered at baseline, 6, 12, and 18 months

RESULTADOS

Table 1. Clinico-demographic characteristics by REGENERATE treatment arm.

	Placebo	OCA 10 mg	OCA 25 mg	p	All
N	407	407	404		1,218
Age, years	53.6 ± 11.7	54.4 ± 11.0	54.2 ± 11.8	0.62	54.1 ± 11.5
Age at diagnosis, years	50.5 ± 12.0	51.0 ± 11.3	50.1 ± 12.4	0.68	50.5 ± 11.9
Enrolled in the U.S.	281 (69.0%)	280 (68.8%)	270 (66.8%)	0.76	831 (68.2%)
Male gender	176 (43.2%)	177 (43.5%)	171 (42.3%)	0.94	524 (43.0%)
White	338 (91.6%)	343 (90.7%)	325 (86.9%)	0.08	1006 (89.7%)
Employed	196 (59.2%)	174 (53.9%)	156 (48.9%)	0.0308	526 (54.1%)
Current smoker	35 (8.6%)	35 (8.6%)	40 (9.9%)	0.76	110 (9.0%)
Fibrosis stage 1	96 (23.6%)	95 (23.3%)	96 (23.8%)	0.99	287 (23.6%)
Fibrosis stage 2	142 (34.9%)	130 (31.9%)	139 (34.4%)	0.63	411 (33.7%)
Fibrosis stage 3	169 (41.5%)	182 (44.7%)	169 (41.8%)	0.60	520 (42.7%)
Type 2 diabetes	220 (54.1%)	219 (53.8%)	224 (55.4%)	0.88	663 (54.4%)
Baseline TZD/Glitazones/Vit. E	56 (13.8%)	57 (14.0%)	54 (13.4%)	0.97	167 (13.7%)
BMI, kg/m²	34.3 ± 5.9	33.9 ± 5.6	33.8 ± 5.5	0.62	34.0 ± 5.6
APRI score	0.737 ± 0.535	0.722 ± 0.498	0.735 ± 0.581	0.98	0.732 ± 0.539
ELF score	9.55 ± 0.93	9.63 ± 0.92	9.60 ± 0.93	0.37	9.59 ± 0.93
FIB-4 score	1.52 ± 0.83	1.55 ± 0.84	1.52 ± 0.82	0.71	1.53 ± 0.83
NAS score (0-8)	5.84 ± 1.11	5.82 ± 1.11	5.87 ± 1.08	0.83	5.85 ± 1.10
NAS: Ballooning (0-2)	1.69 ± 0.46	1.67 ± 0.47	1.68 ± 0.47	0.89	1.68 ± 0.47
NAS: Lobular inflammation (0-3)	2.19 ± 0.77	2.21 ± 0.73	2.22 ± 0.74	0.92	2.20 ± 0.75
NAS: Steatosis (0-3)	1.97 ± 0.85	1.94 ± 0.86	1.97 ± 0.88	0.86	1.96 ± 0.86

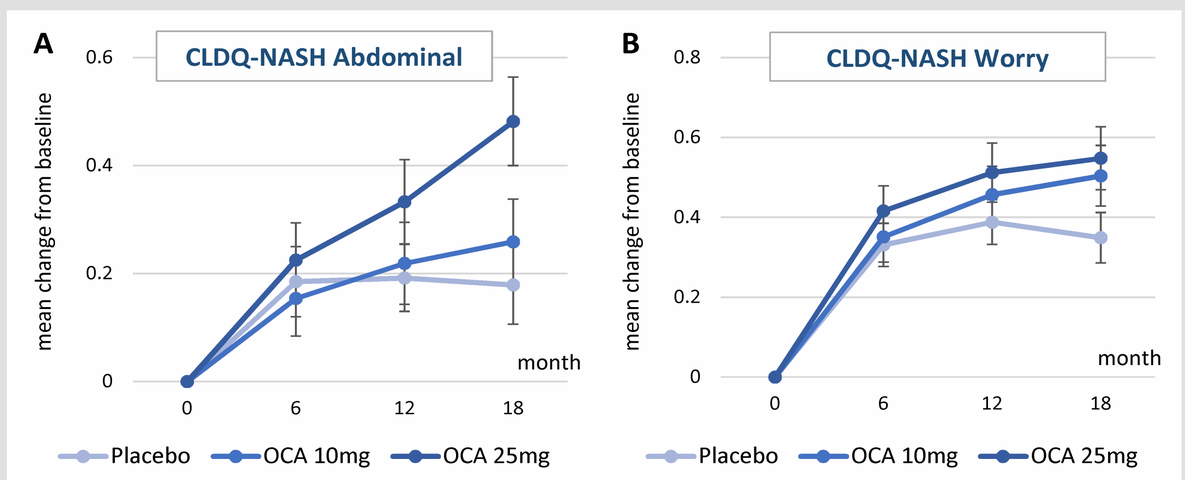
Figure 1. Changes in PRO scores from baseline to month 18 by treatment arm.



Note: The changes are shown as arithmetic means ± 95% CI. (A) CLDQ-NASH (range 1-7); (B) EQ-5D (transformed to 0-100); (C) WPAI (ranges 0-1, higher scores indicate worse impairment); (D) IWQL (transformed to 0-100).

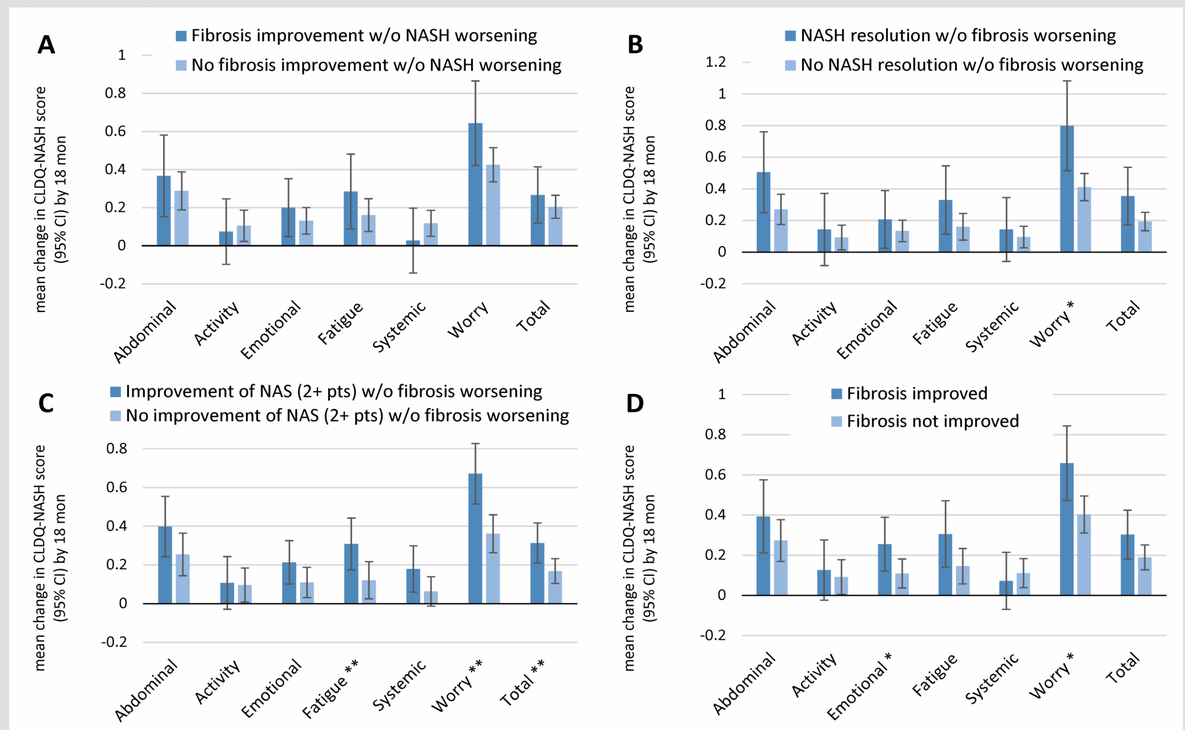
- There were 1,218 NASH patients; 43% had stage 3 fibrosis (**Table 1**)
- Patients were randomized to receive 10 mg (N=407) or 25 mg (N=404) of OCA or placebo (N=407) (**Table 1**)
- Baseline PRO scores were similar between three treatment groups (all p>.05)
- Baseline EQ-5D utility score 0.814 ± 0.173 was significantly lower than age- and country-matched population norm 0.855 (p<0.0001)

Figure 2. Mean changes from baseline in select PRO scores by treatment arm.



Note: The changes are shown as arithmetic means ± 95% CI.

Figure 3. Changes in CLDQ-NASH scores from baseline to month 18 by treatment outcome.



Note: The changes are shown as arithmetic means ± 95% CI; observed cases only; * p<0.05, ** p<0.01.

- During treatment, compared to baseline, consistent PRO improvement was observed: p<0.05 (by a sign rank test) for 12 out of 24 calculated domain and summary PRO scores by treatment month 18 in the pooled cohort (**Figure 1**)
- For 25 mg OCA, improvements in Abdominal and Worry domains of CLDQ-NASH over time were significantly greater than in the other treatment arms (p=0.013 and 0.043 by repeated measures ANOVA, respectively) (**Figure 2**); all other PRO score trends were similar between the two actively treated groups and placebo (p>0.05)
- In multivariate regression analysis, OCA 25 mg was independently associated with a greater improvement in CLDQ-NASH Abdominal score: β=0.26±0.10, p=0.006
- In patients who experienced fibrosis improvement, NAS score decrease (by ≥2 points), or NASH resolution, improvements exceeding the minimal clinically important difference threshold were noted in some CLDQ-NASH domains (MCID=0.3) (**Figure 3**)

CONCLUSÕES

- The baseline quality of life for non-cirrhotic patients with NASH is below population norms, suggesting that NASH is not an asymptomatic disease
- None of PRO domains measured during REGENERATE were negatively affected by OCA, while effective treatment of NASH could improve PRO scores

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1. Younossi Z, et al. International Liver Congress 2019; Vienna, Austria.

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