The Role of Medications for the Management of Patients with NAFLD

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KEYWORDS

• Nonalcoholic fatty liver disease • Drug treatment • Antioxidants • Insuin-sensitizers
• PPAR agonists • Anti-fibrotic agents

KEY POINTS

- There is a recognized clinical need for an effective treatment of nonalcoholic fatty liver disease (NAFLD); current approaches remain suboptimal and no drug has so far been approved by International Agencies.
- Several factors complicate the development of novel pharmacotherapies, particularly the imprecision of surrogate markers, making histologic assessment compulsory.
- Incretin mimetics, farnesoid x-receptor blockers, peroxisome proliferator activated receptor α/δ agonists, and lysyl oxidase-like-2 inhibitory monoclonal antibodies are currently under scrutiny in randomized controlled trials.
- Although indicated by clinical guidelines, a careful follow-up and treatment of NAFLD is not the rule in the community. If, when, and how long drug therapy should be instituted and continued to reduce the burden of disease are being researched.

INTRODUCTION

Lifestyle changes are a mandatory strategy for the prevention and treatment of nonalcoholic fatty liver disease (NAFLD), but the results depend on individual subjects and therefore are largely unpredictable. Also, subjects who achieve a marked reduction

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of body weight tend to regain weight along the years; in this case recurrence and/or progression of disease may be very likely. This finding stimulated intensive research on pharmacologic treatment strategies and several randomized controlled trials having histology as treatment outcome have been published.[1–11] Several classes of drugs have been tested in the last 10 years, acting at different levels along the sequence of events from pure fatty liver to advanced disease (**Fig. 1**), but no drug has been so far been approved for the treatment of NAFLD. This finding opens a series of challenging questions that may be summarized, such as if, when, and how long should treatment be instituted/continued, considering that also with drugs the results are far from optimal? The situation is similar to that observed in other metabolic disorders largely linked to unhealthy lifestyles, namely, type 2 diabetes and obesity. International guidelines on the treatment of type 2 diabetes have never reached a general consensus as to the need to institute immediate pharmacologic treatment—with well-defined, effective, and safe drugs—soon after diagnosis, unless at risk of acute complications. In obesity all guidelines recommend systematic behavior treatment of weight loss before drug therapy—and very few drugs are approved by International Agencies. Drug therapy may also be effectively superimposed to drugs to increase the final results.[12]

The current scientific evidence on the principal drugs tested so far in several randomized controlled trials, divided according to their prevalent mechanism of action, is presented in **Table 1** and is reviewed in this chapter.

INSULIN SENSITIZERS

As insulin resistance is the basis for liver fat accumulation, insulin sensitizers probably remain the best pharmacologic option for NAFLD treatment.

Metformin

Metformin is a biguanide used widely in clinical practice as a first-line treatment for patients with type 2 diabetes mellitus for over 50 years. Metformin reduces blood

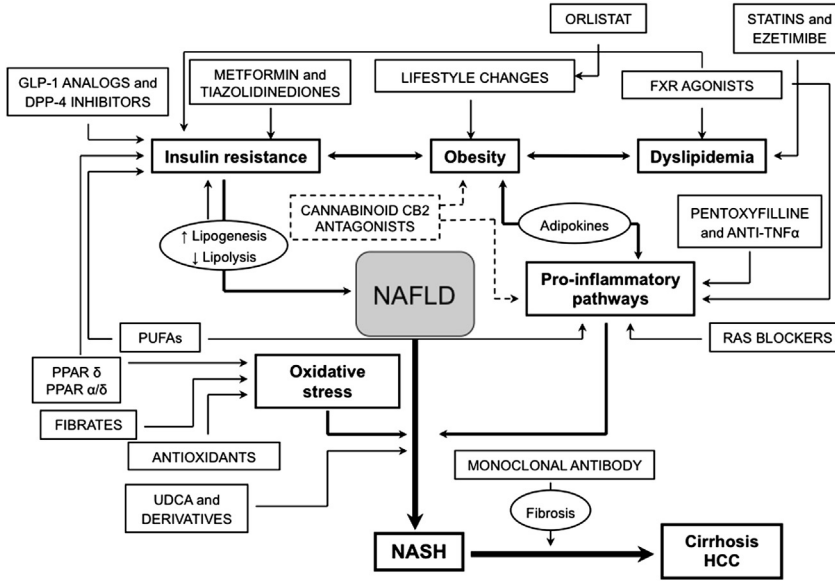

Fig. 1. The complex network of NAFLD pathogenesis and treatment.