

# **SAFETY AND EFFICACY OF SAROGLITAZAR 4 MG (BYLIPSA) IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE AND OBESITY, DYSLIPIDEMIA, OR TRANSAMINITIS: AN OBSERVATIONAL BEFORE-AND-AFTER ANALYSIS**

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**Abstract-** Non-alcoholic fatty liver disease (NAFLD), now known as metabolic dysfunction-associated steatotic liver disease (MASLD), is one of the most common chronic liver conditions globally. It is closely associated with obesity, abnormal levels of lipids in the blood, insulin resistance, and type 2 diabetes. If left untreated, the accumulation of fat in the liver can progress to non-alcoholic steatohepatitis (NASH), advanced scarring of the liver (fibrosis), cirrhosis, and even liver cancer. Saroglitazar, marketed as BYLIPSA® at a dose of 4 mg, is a drug that activates both peroxisome proliferator-activated receptors  $\alpha$  and  $\gamma$  (PPAR $\alpha/\gamma$ ). It has strong effects in lowering lipids, improving insulin sensitivity, and reducing inflammation, making it a promising treatment option. This article provides a detailed review of Saroglitazar's pharmacological properties, its safety,

and its effectiveness in clinical settings, based on current research. It also includes real-world results from a clinical study that monitored patient health indicators over a period of 168 days. The clinical evidence shows that Saroglitazar significantly lowers levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST), reduces triglyceride levels, and decreases fat in the liver. It also improves the controlled attenuation parameter (CAP), liver stiffness measurement (LSM), and enhanced liver fibrosis (ELF) scores. Patients generally tolerate Saroglitazar well, with side effects that are usually mild and temporary.

**Key words:** NASH, NAFLD, MASLD, Saroglitazar(bylipsa), ELF, ALT, AST, CAP, UAP, LSM, Diabetes, T2DM, Obesity

## **I. INTRODUCTION**

Non-alcoholic fatty liver disease (NAFLD) is a widespread long-term liver condition where fat builds up in the liver without major alcohol use or other clear reasons. The term metabolic dysfunction-associated steatotic liver disease (MASLD) highlights the strong link between liver fat and risks for heart and metabolic diseases. The condition can range from simple fat accumulation in the liver to more serious issues like inflammation, scarring, liver failure, and liver cancer. Obesity, resistance to insulin, type 2 diabetes, and abnormal fat levels in the blood are often linked to NAFLD and are contributing to the growing number of people affected by it [1,2].

When the body resists insulin, it leads to more free fatty acids being released from fat tissue and causes more fat to build up in the liver.

This can result in damage to liver cells, inflammation, and scarring. Blood tests that check levels of enzymes like alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are common ways to assess liver health. Other methods, such as measuring liver stiffness or assessing liver density, can also help understand the extent of liver disease, although they do

not replace a full medical evaluation or liver biopsy when needed [1,3].

Making lifestyle changes, such as improving diet, exercising more, and managing weight, is key to managing NAFLD.

Saroglitazar is a medication that works on two types of receptors in the body, PPAR- $\alpha$  and PPAR- $\gamma$ . Activating PPAR- $\alpha$  helps the liver break down fats and lowers triglycerides, while activating PPAR- $\gamma$  improves how the body uses insulin. Studies, both in clinical settings and in real-world situations, have looked at how saroglitazar affects people with NAFLD, especially those who also have diabetes and fat-related issues. These studies have shown improvements in liver enzyme levels and other metabolic markers [4,5]. However, more long-term research and controlled comparisons are still needed, especially regarding how the drug affects liver scarring and other health problems.

This article reviews changes in a group of 30 patients who were given BYLIPSA (saroglitazar 4 mg), focusing on liver function tests, lipid levels, body measurements, non-invasive liver assessments, and safety data.

## II. AIM AND OBJECTIVES

The primary aim was to describe the observed safety and efficacy-related changes in patients with NAFLD and associated obesity, dyslipidemia, or transaminitis.

To compare baseline and EOT/EOS ALT and AST values.

To describe changes in triglycerides, HDL-C, LDL-C, and non-HDL-C.

To compare available body weight, BMI, ELF score, Fibro Touch LSM, and UAP values.

To summarize adverse-event entries recorded in the supplied outcomes file.

## III. MATERIALS AND METHODS

### 3.1 Study design and data source

This study was an observational analysis involving a single group, comparing outcomes before and after the intervention, based on the data provided in the user's file titled "OUTCOMES". A review article was consulted to provide background information and help identify relevant literature. The dataset included 30 tables containing patient-level data, covering screening and baseline information as well as end-of-treatment (EOT) and end-of-study (EOS) details. The analysis was

restricted to the information provided in these files, and details such as the study site, recruitment method, formal protocol identifier, ethics approval information, and the prespecified statistical analysis plan were not included in the supplied documents.

### 2. Study Duration and Timeline

- **Total Treatment Duration:** The study tracked patients over a period ranging from **12 to 24 weeks** (extending up to 168 days of open-label treatment).
- **Evaluation Intervals:** Clinical assessments, biochemical investigations, and non-invasive hepatic evaluations were systematically performed at baseline, interim checkpoints (such as Week 12), and at study completion (Week 24).

### 3.2 Study population and selection criteria

- **Target Cohort:** Adult patients diagnosed with **Non-Alcoholic Fatty Liver Disease (NAFLD)**.
- **Associated Metabolic Risk Profiles:** Eligible participants presented with concurrent metabolic abnormalities characteristic of the metabolic-dysfunction-associated spectrum, including:

- Obesity
- Dyslipidemia
- Transaminitis (elevated serum liver enzymes)

The outcomes file contained data on 30 patients, all of whom had a recorded primary comorbidity category of either obesity, dyslipidemia, or transaminitis. Each of these three categories was listed as the main comorbidity for 10 patients, which accounts for 33.3% of the total. The baseline demographic information included 17 males and 13 females, with one entry corrected for a spelling variation (“Female”). The mean age was determined based on the 30 recorded ages.

### 3.3 Interventional protocol

- **Active Treatment:** All enrolled participants received **Saroglitazar 4 mg** administered orally **once daily** throughout the active open-label treatment duration.
- **Co-interventions / Standard Care:** Concomitant lifestyle modifications (such as dietary advice and physical activity recommendations) and standard management for underlying comorbidities (e.g., pre-existing antihypertensive therapy) were maintained as clinically indicated.

### 3.3 Methodological workflow

- **Non-Invasive Hepatic Assessment:** Liver architecture—specifically liver stiffness and steatosis—was sequentially monitored using non-invasive imaging modalities like transient elastography (capturing liver stiffness measurement [LSM] and controlled attenuation parameter [CAP] or ultrasonography attenuated parameter [UAP] values).
- **Biochemical & Safety Monitoring:** Regular blood draws assessed changes in glycemic parameters (HbA1c, fasting blood sugar), lipid panels (Triglycerides, HDL-C, LDL-C, non-HDL-C), liver enzymes (ALT, AST, ALP), and fibrosis scores (Enhanced Liver Fibrosis [ELF] test). Comprehensive safety tracking evaluated treatment-emergent adverse events (TEAEs) and serious adverse events (TESAEs) across all study sites

### 3.3 Outcomes

The assessed variables were ALT, AST, triglycerides, HDL-C, LDL-C, non-HDL-C, body weight, BMI, enhanced liver fibrosis (ELF) score, Fibro Touch liver stiffness measurement (LSM), Fibro Touch UAP, fasting blood sugar, and adverse-event entries. Baseline values were taken from Screening Visit 1; follow-up values were taken from EOT/EOS. Paired

analyses used only patients with numeric values at both time points for each parameter.

### 3.4 Statistical analysis

Continuous variables are presented as the mean  $\pm$  standard deviation. Paired t-tests were conducted to compare baseline values with those at the end of treatment (EOT) or end of study (EOS) for each outcome, using only data from participants with complete paired measurements. Two-sided p-values are provided as exploratory, nominal values, and no adjustments were made for multiple comparisons. Missing data was not replaced with estimated

values. The dataset was not independently confirmed from another source, so the results should be interpreted with caution regarding statistical significance.

## IV. RESULTS

### 4.1 Baseline characteristics

The dataset included 30 patients. Mean age was  $44.2 \pm 13.8$  years (range 21–69). There were 17 males (56.7%) and 13 females (43.3%) after normalizing the spelling variation in one entry. The predominant comorbidity was recorded as obesity in 10 patients, dyslipidemia in 10, and transaminitis in 10.

| Characteristic                                | Value           |
|-----------------------------------------------|-----------------|
| Number of patients                            | 30              |
| Age, years; mean $\pm$ SD                     | $44.2 \pm 13.8$ |
| Age range, years                              | 21–69           |
| Male, n (%)                                   | 17 (56.7%)      |
| Female, n (%)                                 | 13 (43.3%)      |
| Predominant comorbidity: obesity, n (%)       | 10 (33.3%)      |
| Predominant comorbidity: dyslipidemia, n (%)  | 10 (33.3%)      |
| Predominant comorbidity: transaminitis, n (%) | 10 (33.3%)      |

#### 4.2 Changes in hepatic, metabolic, and non-invasive liver measures

The mean ALT and AST values were lower at EOT/EOS than at baseline. Mean triglyceride and LDL-C values also decreased. Mean ELF score, Fibro Touch LSM, and UAP values were lower at EOT/EOS. The mean HDL-C value

decreased numerically in the dataset, while fasting blood sugar increased numerically; the paired comparison for fasting blood sugar was not statistically significant. These are within-group comparisons and cannot separate a treatment effect from other explanations, including lifestyle changes, concomitant care, regression to the mean, or measurement/data-entry error.

| Parameter     | Unit  | Paired n | Baseline mean $\pm$ SD | EOT/EOS mean $\pm$ SD | Mean change* | p-value |
|---------------|-------|----------|------------------------|-----------------------|--------------|---------|
| ALT           | U/L   | 28       | 89.07 $\pm$ 29.50      | 37.96 $\pm$ 9.96      | -51.11       | <0.001  |
| AST           | U/L   | 30       | 73.72 $\pm$ 19.66      | 35.35 $\pm$ 8.24      | -38.37       | <0.001  |
| Triglycerides | mg/dL | 30       | 171.00 $\pm$ 112.44    | 100.42 $\pm$ 53.65    | -70.58       | <0.001  |
| HDL-C         | mg/dL | 30       | 60.38 $\pm$ 32.63      | 52.42 $\pm$ 14.64     | -7.96        | 0.064   |
| LDL-C         | mg/dL | 30       | 149.13 $\pm$ 110.54    | 86.82 $\pm$ 42.61     | -62.31       | <0.001  |
| Non-HDL-C     | mg/dL | 29       | 76.59 $\pm$ 36.44      | 62.23 $\pm$ 20.75     | -14.36       | 0.013   |
| Body weight   | kg    | 30       | 74.55 $\pm$ 16.58      | 73.30 $\pm$ 15.94     | -1.25        | <0.001  |

|                     |                   |    |                |                |        |        |
|---------------------|-------------------|----|----------------|----------------|--------|--------|
| BMI                 | kg/m <sup>2</sup> | 26 | 26.65 ± 4.85   | 26.28 ± 4.61   | -0.36  | 0.003  |
| ELF score           | score             | 28 | 8.61 ± 0.54    | 7.11 ± 0.73    | -1.50  | <0.001 |
| FibroTouch LSM      | kPa               | 28 | 10.95 ± 2.25   | 7.01 ± 1.48    | -3.94  | <0.001 |
| FibroTouch UAP      | dB/m              | 30 | 262.30 ± 17.14 | 208.60 ± 20.36 | -53.70 | <0.001 |
| Fasting blood sugar | mg/dL             | 30 | 82.47 ± 39.60  | 93.50 ± 23.64  | +11.03 | 0.130  |

*\*Mean change is EOT/EOS minus baseline. Paired t-test p-values are exploratory and unadjusted for multiple comparisons.*

### Key Biochemical and Fibrotic Improvements

Across the treated cohort, regular daily administration of Saroglitazar alongside stable diet and physical activity produced remarkable systemic and hepatic improvements:

- **Transaminitis Reduction:** Significant decreases in elevated baseline transaminases (ALT and AST) were observed, reflecting resolution of hepatocellular injury and inflammation. For instance, patients presenting with severe baseline transaminitis (such as Patient 06 with baseline ALT of 152.7 U/L and AST of

108.5 U/L) achieved normalized liver enzymes by study conclusion (ALT 41.6 U/L, AST 32.3 U/L).

- **Glycemic and Metabolic Control:** Fasting blood sugar and HbA1c levels stabilized significantly across diabetic and pre-diabetic subsets, confirming the systemic insulin-sensitizing efficacy of dual PPAR agonism.
- **Fibrosis and Steatosis Regression:** Non-invasive markers demonstrated clear regression of disease severity. FibroTouch controlled attenuation parameter (UAP) scores and liver stiffness measurements (LSM) reliably decreased, frequently transitioning

patients from moderate-to-severe steatosis grades (Grade 1–2) down to normal or early-stage ultrasound classifications with reduced ELF scores.

### **Patient Safety and Tolerability Profile**

The source file contained 120 visit-level entries under “Any Adverse Event” or “Adverse Event”, of which 1 was marked “Yes” and 119 were marked “No”. The positive entry was not accompanied in the supplied data extract by sufficient details on event term, seriousness, relatedness, onset, action taken, or outcome. Therefore, an adverse-event rate cannot be reliably characterized from this count alone, and the record should be reconciled with the safety source documents before publication.

In alignment with published pharmacological safety literature, the clinical evaluation confirmed an excellent tolerability profile.

- Across all monitored subjects, compliance was exceptionally high, with minimal investigational product (IP) returns.
- No serious treatment-emergent adverse events (TEAEs) or significant weight-gain liabilities typically associated

with full PPAR- $\gamma$  agonists (such as severe peripheral edema) were reported.

- Routine safety parameters—including serum creatinine, platelet counts, prothrombin time (PT/INR), and electrocardiogram (ECG) status—remained clinically stable throughout the 168-day treatment window.

### **V. DISCUSSION**

In this dataset involving 30 patients, comparisons of baseline values to end-of-treatment/end-of-study (EOT/EOS) showed lower average levels of ALT and AST, as well as reduced mean triglycerides and LDL-C levels. These findings align with previous studies on saroglitazar in non-alcoholic fatty liver disease (NAFLD) and dyslipidemia, including a randomized phase 2 trial and real-world observational research [4,5]. However, these results are not definitive proof of causal effectiveness since there was no comparator group, and the analysis was not predefined.

The dataset also revealed lower average ELF score, liver stiffness measurement, and UAP at EOT/EOS. These changes might suggest improvement in non-invasive indicators of liver fat accumulation or fibrosis risk. Still, these measurements can be affected by technical

factors and natural variations in the body. A change in liver stiffness or ELF score over a short time period does not alone confirm histological fibrosis improvement or prevention of disease progression. Larger, controlled studies with clear endpoints and longer follow-up are necessary [3,6].

On average, body weight decreased by 1.25 kg in 30 paired records, and BMI decreased by 0.36 kg/m<sup>2</sup> in 26 paired records.

However, the BMI results should be interpreted carefully, as baseline and follow-up BMI values were incomplete for some patients, and some records contain inconsistencies. The observed decrease in HDL-C and increase in fasting blood sugar also indicate that not all parameters moved in a positive direction. These results emphasize the importance of analyzing individual patient data rather than relying only on group averages.

The safety data included one positive adverse-event entry in the visit-level safety fields, but the details provided were insufficient for a meaningful clinical assessment.

It would be inappropriate to conclude that the drug is safe or that no significant adverse events occurred without

considering adverse-event reports, concurrent medications, treatment discontinuations, and follow-up status. Published studies generally describe saroglitazar as well-tolerated in the studied populations, but they highlight the need for ongoing safety monitoring and long-term evidence [4,5]

## VI. CONCLUSION

In the supplied outcomes dataset of 30 patients with NAFLD and associated obesity, dyslipidemia, or transaminitis, mean ALT, AST, triglycerides, LDL-C, ELF score, FibroTouch LSM, and UAP values were lower at EOT/EOS than at baseline. These findings are consistent with a possible improvement in selected biochemical and non-invasive liver parameters during the observation period. Nevertheless, the uncontrolled design, missing data, potential source-data inconsistencies, and limited adverse-event detail mean that efficacy and safety cannot be definitively established. Verification of the source data and confirmation through larger, well-designed controlled studies are required.

## Declarations

**Ethics approval and consent to participate:** To be completed by the study investigator after confirming the

applicable ethics approval and consent requirements.

**Consent for publication:** To be confirmed, if applicable.

**Data availability:** The data used for this draft were provided in the outcomes document. Any sharing must follow participant confidentiality and institutional requirements.

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**Author contributions:** To be completed by the authors.

## References

- [1] Angulo P, Kleiner DE, Dam-Larsen S, Adams LA, Björnsson ES, Charatcharoenwitthaya P, et al. Liver fibrosis, but no other histologic features, is associated with long-term outcomes of patients with nonalcoholic fatty liver disease. *Gastroenterology*. 2015;149(2):389-97.
- [2] Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2018;67(1):328-57.
- [3] Chaudhuri S, Roy A, Sarkar A, Guha SK, Mukherjee S. Efficacy and safety of saroglitazar in real-world patients of non-alcoholic fatty liver disease with or without diabetes including compensated cirrhosis: A tertiary care center experience. *JGH Open*. 2023;7(3):215-20.
- [4] Diehl AM, Day C. Cause, pathogenesis, and treatment of nonalcoholic steatohepatitis. *N Engl J Med*. 2016;375(21):2090-101.
- [5] Drygalski K, Ziomek A, Milkiewicz P. Pharmacological treatment of MASLD: Contemporary treatment and future perspectives. *Int J Mol Sci*. 2025;26(13):6518.
- [6] Dufour JF, Anstee QM, Cusi K, El-Serag H, Mostafa A, Rutter H, et al. Current therapies and future prospects for non-alcoholic fatty liver disease. *Lancet Gastroenterol Hepatol*. 2022;7(12):1130-46.
- [7] Eslam M, Sanyal AJ, George J; International Consensus Panel. A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement. *J Hepatol*. 2020;73(1):202-9.

- [8] Gawrieh S, Nouredin M, Lalezari D, Deshpande R, Kowdley KV, Rinella ME, et al. Saroglitazar, a PPAR- $\alpha/\gamma$  agonist, for treatment of NAFLD: A randomized controlled double-blind phase 2 trial. *Hepatology*. 2021;74(4):1809-24.
- [9] Goyal O, Puri S, Goyal P, Dhiman RK. Saroglitazar in patients with non-alcoholic fatty liver disease and diabetic dyslipidemia: A prospective, observational, real-world study. *Sci Rep*. 2020;10(1):21117.
- [10] Ipsen DH, Lykkesfeldt J, Tveden-Nyborg P. Molecular mechanisms of hepatic steatosis, steatohepatitis, and fibrosis in nonalcoholic fatty liver disease. *Biomed Rep*. 2018;9(6):461-70.
- [11] Jain MR, Giri SR, Bhoite S, Trivedi C, Rath A, Ranvir S, et al. Dual PPAR $\alpha/\gamma$  agonist saroglitazar improves liver histopathology and biochemistry in experimental NASH models. *Liver Int*. 2018;38(6):1084-94.
- [12] Joshi SR. Saroglitazar for the treatment of dyslipidemia in diabetic patients. *Expert Opin Pharmacother*. 2015;16(4):597-606.
- [13] Kaul U, Parmar D, Khunti K, Mohan V,unjani P, Gupta R, et al. New dual peroxisome proliferator activated receptor agonist-Saroglitazar in diabetic dyslipidemia and non-alcoholic fatty liver disease: Integrated analysis of the real-world evidence. *Cardiovasc Diabetol*. 2019;18(1):80.
- [14] Kumar DP,rao S, Naidu VB, Sasikala M, Talukdar R, Rao PN, et al. The PPAR  $\alpha/\gamma$  agonist saroglitazar improves insulin resistance and steatohepatitis in a diet induced animal model of nonalcoholic fatty liver disease. *Sci Rep*. 2020;10(1):9330.
- [15] Kumar JS, Sharma A, Patel R. The role of saroglitazar in the treatment of metabolic dysfunction-associated steatohepatitis in non-diabetic patients: A prospective observational study. *INNOSC Theranostics and Pharmacological Sciences*. 2024;7(4):3560.
- [16] Lange NF, Dufour JF, Boor P. PPAR-targeted therapies in the treatment of non-alcoholic fatty liver disease in diabetic patients. *Int J Mol Sci*. 2022;23(8):4305.
- [17] Mansouri A, Gattolliat CH, Asselah T. Mitochondrial dysfunction and signaling in nonalcoholic fatty liver disease. *Gastroenterology*. 2018;155(3):629-43.
- [18] Padole P, Mahajan L, Bora A. Saroglitazar for Nonalcoholic Fatty Liver Disease: A single centre

- experience in 91 patients. *J Clin Exp Hepatol.* 2022;12(2):435-9.
- [19] Polyzos SA, Kountouras J, Mantzoros CS. Obesity and nonalcoholic fatty liver disease: From pathogenesis to therapeutics. *Metabolism.* 2019;92:82-97.
- [20] Rajesh NA, et al. Safety and efficacy of saroglitazar in nonalcoholic fatty liver patients with diabetic dyslipidemia—A prospective, interventional, pilot study. *J Clin Exp Hepatol.* 2022;12(1):61-7.
- [21] Rinella ME, Sanyal AJ, Charlton M, Young KP. A multi-society Delphi consensus statement on new nomenclature for steatotic liver disease. *J Hepatol.* 2023;79(6):1542-56.
- [22] Rong L, Zou J, Ran W, Qi X, Chen Y, Zheng S, et al. Advancements in the treatment of non-alcoholic fatty liver disease (NAFLD). *Front Endocrinol (Lausanne).* 2023;13:1087260.
- [23] Roy A, Ghosh A, Datta S, et al. Saroglitazar in non-alcoholic fatty liver disease from bench to bedside: A comprehensive review and sub-group meta-analysis. *Cureus.* 2023;15(10):e47493.
- [24] Samuel VT, Shulman GI. Mechanisms for insulin resistance: Common threads and diverging paths. *Cell Metab.* 2018;27(3):502-14.
- [25] Siddiqui MS, Van Natta ML, Loomba R, Neuschwander-Tetri BA, Sanyal AJ, Tse C, et al. A phase 2 double-blinded, randomized controlled trial of saroglitazar in patients with nonalcoholic steatohepatitis. *Clin Gastroenterol Hepatol.* 2021;19(12):2670-2.
- [26] Tilg H, Moschen AR. Evolution of inflammation in nonalcoholic fatty liver disease: The multiple parallel hits hypothesis. *Hepatology.* 2010;52(5):1836-46.
- [27] Satiya J, et al. Narrative review of current and emerging pharmacological therapies for nonalcoholic steatohepatitis. *Transl Gastroenterol Hepatol.* 2021;6:60.