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Ifetroban Shows Promise in Slowing Cardiac Decline in Duchenne Muscular Dystrophy

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Key Takeaways

- High-dose ifetroban improved LVEF in Duchenne muscular dystrophy patients, contrasting with declines in placebo and natural history cohorts.
- Transcriptomic profiling identified biomarkers correlating with LVEF improvements, suggesting mechanistic insights into ifetroban's cardioprotective effects.

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Findings from the phase 2 FIGHT DMD trial suggest an investigational oral thromboxane prostanoid receptor antagonist may preserve heart function in patients with DMD-associated cardiomyopathy.

John J. Parent, MD, MSCR

(Credit: Indiana University School of Medicine)

Recent findings from the randomized, placebo-controlled phase 2 FIGHT DMD trial (NCT03340675) demonstrated that high-dose ifetroban (Cumberland Pharmaceuticals), an oral thromboxane prostanoid receptor (TPr) antagonist, may help slow the progression of cardiomyopathy (CM) in patients with Duchenne muscular dystrophy (DMD). Over 12 months, results revealed that high-dose ifetroban treatment was associated with a modest improvement in left ventricular ejection fraction (LVEF), while placebo-treated patients experienced a decline that was consistent with the natural course of the disease.[1]

The trial enrolled 41 patients with DMD, who were randomly assigned to receive placebo (n = 11), low-dose ifetroban (100 mg, n = 12), or high-dose ifetroban (300 mg, n = 18) daily for 12 months. The primary efficacy measure, LVEF change from baseline, revealed a 1.8% (±5.4) increase in the high-dose group, compared with a 1.5% (±3.3) decline in the placebo group. Additionally, data from a matched natural history cohort (n = 24) showed a greater LVEF decline of 3.6% (±4.1) over the same period. Between-group analysis found a statistically significant difference in LVEF change, with high-dose ifetroban outperforming both placebo and natural history controls.[2]

Transcriptomic profiling identified several peripherally expressed biomarkers that correlated with LVEF improvements in ifetroban-treated patients, suggesting possible mechanistic insights into its cardioprotective effects. Overall, researchers reported that treatment was well-tolerated, with no serious or unexpected drug-related adverse events reported.

Presented by lead author John J. Parent, MD, MSCR, associate professor of clinical pediatrics at Indiana University School of Medicine, at the 2025 Muscular Dystrophy Association (MDA) Clinical & Scientific Conference, held March 16-19 in Dallas, Texas, these findings highlight ifetroban's potential as a therapeutic option for DMD-associated CM. Additionally, authors noted that long-term follow-up in an open-label extension study is ongoing to further assess the durability of its effects.

Building on promising clinical findings, preclinical research has further demonstrated the potential of TPr antagonism in improving cardiac outcomes for patients with muscular dystrophy. Prior to the recent phase 2 trial in DMD, animal studies provided key insights into ifetroban's cardioprotective mechanisms, reinforcing its potential as a therapeutic option.[3]

Published in the *Journal of the American Heart Association*, researchers tested ifetroban in 3 different mouse models of muscular dystrophy —mdx/utrn double knockout, mdx/mTR double knockout, and delta-sarcoglycan knockout—administering the drug via drinking water from weaning until study endpoints (10 weeks or 6 months, depending on the model). The treatment led to significant improvements in survival, with a 100% survival rate in ifetroban-treated mice, compared with lower rates in untreated groups (60%, 43%, and 90%, respectively).

Conducted by lead author James West, PhD, professor of medicine at Vanderbilt University Medical Center, and colleagues, ifetroban also improved cardiac function across all models. In mdx/utrn and mdx/mTR mice, it enhanced cardiac output, and in delta-sarcoglycan knockout mice, it normalized ejection fraction, fractional shortening, and other key measures of heart function. Additionally, TPr antagonism reduced cardiac fibrosis and normalized the expression of proteins and genes linked to DMD, suggesting a broader impact on disease pathology.

These findings provided a foundation for evaluating ifetroban in human DMD cardiomyopathy, supporting its potential role in mitigating the progressive cardiac decline seen in muscular dystrophy. With the recent phase 2 trial confirming its safety and efficacy in patients, ongoing long-term studies may be critical to understanding the full therapeutic potential of TPr antagonism in muscular dystrophy-related cardiomyopathy.

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