Two Extended-Release Buprenorphine Doses Effective in High-Risk Opioid Use Disorder

— Maintenance with higher monthly dose level may provide an advantage in heavy fentanyl users

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Key Takeaways

- In a randomized trial, both 100-mg and 300-mg monthly maintenance doses of extended-release buprenorphine improved opioid abstinence in patients with high-risk opioid use, with no new safety signals.
- Post-hoc analysis suggested the 300-mg dose may be more effective in patients with heavy fentanyl use.
- Researchers said the findings in fentanyl users are "particularly relevant" given the increasing use of the potent synthetic opioid.

Two dose levels of maintenance treatment with extended-release buprenorphine (Sublocade) improved opioid abstinence in patients with high-risk opioid use disorder (OUD), a randomized trial showed.

After two buprenorphine injections during an induction phase, the proportion of responders (defined as weekly opioid abstinence of at least 80% for weeks 20-38) proved similar with eight monthly maintenance injections of a 300-mg buprenorphine dose versus a 100-mg dose (23.2% vs 20.2%, *P*=0.48), according to Robert Dobbins, MD, PhD, of Indivior in North Chesterfield, Virginia, and colleagues.

Prespecified subgroup analyses showed no significant differences between arms, the authors detailed in *JAMA Network Open*, but post-hoc data suggested the 300-mg dose was significantly better than the 100-mg dose among those who reported daily fentanyl use (24.3% vs 13.3%), using fentanyl 14 or more times per week (20.2% vs 8%), or both (22.2% vs 6.8%).

Those post-hoc results, "are particularly relevant because individuals with OUD in North America are increasingly exposed to highly potent synthetic opioids, such as fentanyl, a driver of high levels of opioid overdose deaths," the researchers concluded.

The trial results "lend further support of the efficacy and safety of higher doses of extended-release injectable buprenorphine for persons with OUD who use fentanyl," according to Sandra Springer, MD, of the Yale School of Medicine in New Haven, Connecticut, who noted that opioid withdrawal even with buprenorphine is of particular concern among fentanyl users.

"Including patient choice that provides education about the different formulations of buprenorphine and dosing strategies should be incorporated when treating OUD to reduce opioid use and promote long-term recovery," she wrote in an accompanying editorial.

However, Springer cautioned that "this was an industry-sponsored trial and had a very high retention rate, with 63.2% in both study arms receiving all 10 planned injections, higher than most OUD medication treatment trials."

The increased retention may have been due to the rapid induction protocol the researchers tested, which may have reduced opioid use and craving typically seen in OUD trials, she noted. During the open-label induction period, participants received a 4-mg transmucosal dose of buprenorphine plus two 300-mg extended-release buprenorphine injections a week apart.

That strategy "is not yet traditionally used in most standard outpatient clinic settings but should be considered as an option for persons who use fentanyl, given that rapid inductions are being found to be safe and effective," said Springer. She noted that the approach could face insurance hurdles in the U.S., however.

The opioid epidemic remains a crisis in the U.S. and is complicated by increasing use of synthetic opioids like fentanyl, which last year was involved in more than 46,000 deaths.

Extended-release buprenorphine is approved as a once-monthly subcutaneous injection for the treatment of moderate-to-severe OUD. A previous study cited by the study authors had suggested that a higher percentage of OUD patients using injectable drugs achieved abstinence at week 24 with the 300-mg versus the 100-mg buprenorphine maintenance regimen.

The TRANSFORM trial was a randomized, double-blind, multicenter trial comparing 100-mg and 300-mg once-monthly maintenance doses of extended-release buprenorphine in 28 outpatient treatment centers in the U.S. and Canada from October 2021 to June 2024.

Participants were treatment-seeking adults who met criteria for moderate or severe OUD for 90 days or more prior to informed consent, as well as meeting criteria for high-risk opioid use, defined as those who used fentanyl or fentanyl analogs, high-dose opioids, or injected opioids an average of 5 or more days per week in the previous 4 weeks.

The primary endpoint was the proportion of responders for weekly opioid use.

The open-label induction substudy randomized patients in a 2:1 ratio to rapid or standard induction with 4-mg transmucosal buprenorphine and two 300-mg buprenorphine injections. Randomization was stratified by the route of opioid use at screening (injection route: yes or no) and week 6 urine drug screening results (opioid use: negative or positive).

Four weeks after the second induction injection, 436 participants were randomized in a 1:1 ratio to receive eight additional maintenance doses of either the 100-mg (n=218) or 300-mg dose (n=217) every 4 weeks (one patient was lost to follow up). The mean age of participants was 41.6 years, and 57% were men. Follow-up included urine drug screenings and self-reported drug use.

Almost 75% of the study population used fentanyl, and more reported smoking opioids (42.8%) rather than injecting them (27.8%), reflecting a change in how people are using these drugs. There was a high level of polysubstance use, including amphetamine or methamphetamines and cocaine, and 32.9% reported having a previous overdose event.

There was one nonfatal opioid overdose and no serious hepatic events in the trial, which Springer said attested to the safety of the long-acting formulations of buprenorphine in a high-risk population.

Disclosures

The study was funded by Indivior, makers of the extended-release buprenorphine used in this trial.

Dobbins reported being an employee of Indivior and having a patent pending owned by Indivior. Co-authors reported relationships with Indivior, including employment, and Alkermes.

Springer reported paid scientific consultation and in-kind study drug donations from Alkermes, Braeburn, and Indivior, grants from the National Institutes of Health, and the Veterans Affairs Cooperative Studies Program outside the submitted work.

Primary Source

JAMA Network Open

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Secondary Source

JAMA Network Open

Source Reference: Springer SA "Is high-dose extended-release buprenorphine safe and effective for persons who use fentanyl?" JAMA Netw Open 2025; DOI: 10.1001/jamanetworkopen.2025.47965.

1 Comment