FDA Approves Mirdametinib for Treatment of Adults, Children With NF1-PN

Key Takeaways

- Mirdametinib is the first approved therapy for adults and a novel option for children with NF1-PN.
- The phase 2b ReNeu trial showed significant objective response rates in both adult and pediatric patients.
- Adverse events were reported, but the safety profile was considered manageable for both cohorts.
- Mirdametinib addresses a significant unmet need for patients with neurofibromatosis type 1-associated plexiform neurofibromas.

The approval is based on positive clinical trial results that indicated deep and durable reductions in plexiform neurofibroma.

The FDA granted regulatory approval to mirdametinib (Gomekli; SpringWorks Therapeutics), an investigational MEK inhibitor, for the treatment of adult and pediatric patients with neurofibromatosis type 1-associated plexiform neurofibromas (NF1-PN), according to a news release from the agency. The approval makes mirdametinib the first approved therapy for adults in this population and provides a novel best-in-class therapy for children with NF1-PN.1,2

Previously, the FDA granted priority review to mirdametinib upon accepting SpringWorks' new drug application for the treatment. Saqib Islam, CEO of SpringWorks, praised the granting of priority review, writing that the decision "brings us closer to our goal of delivering a transformative medicine to both adults and children with NF1-PN in the US and Europe." Now that mirdametinib has received full approval, it could fill a major unmet need for patients with the difficult-to-treat condition.2

The approval of mirdametinib is based in part on positive clinical trial results from the phase 2b ReNeu (NCT03962543) study, a multicenter, open-label trial that evaluated mirdametinib's safety and efficacy in adult and pediatric patients with inoperable NF1-PN. The primary end point was confirmed objective response rate (ORR), indicated by a reduction of target PN volume.3

A total of 114 patients (58 adults and 56 pediatrics) were enrolled in the trial, and all received mirdametinib. As of the data cut-off point, confirmed ORR during the treatment phase was 41% (95% CI, 29-55; $P < .001$ vs null) in adults and 52% (95% CI, 38-65; $P < .001$ vs null) in pediatric patients, according to the investigators. The median duration of treatment was 22 months for each cohort.3

Some adverse events (AEs) were reported across the study population, with the most frequent treatment-emergent AEs being dermatitis acneiform, diarrhea, nausea, and vomiting. Occasionally, patients experienced a severe AE, with 16% and 25% of adults and pediatrics experiencing grade 3 or higher AEs, respectively. Overall, the safety analysis demonstrated a manageable profile of AEs in both adults and children with NF1-PN.3

NF1 arises from loss-of-function variants in the NF1 gene, which encodes a critical suppressor of the MAPK pathway. NF1 is the most common form of neurofibromatosis, with approximately 100,000 patients living with the condition in the US. The clinical presentation of NF1 can be complex; it manifests as myriad symptoms across multiple organ systems. These signs can include abnormal skin pigmentation, tumor growth, skeletal deformities, and neurological complications.2

Patients with NF1 have a 30% to 50% lifetime risk of developing PN, which are tumors that grow along the peripheral nerve sheath and can cause severe pain, impairment, and disfigurement. Often diagnosed in the first 2 decades of a patient's life, PN tumors can be aggressive and are typically associated with significant morbidity.2

According to the FDA, mirdametinib can also cause left ventricular dysfunction and ocular toxicity, including retinal vein occlusion, retinal pigment epithelial detachment, and blurred vision. FDA investigators said mirdametinib should be withheld, prescribed with a reduced dosage, or permanently discontinued based on the severity of adverse reactions.1

REFERENCES

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