SpringWorks THERAPEUTICS

OGSIVEO™ (nirogacestat) is the FIRST and ONLY U.S. Food and Drug Administration (FDA) Approved Treatment for Adults with Desmoid Tumors

OGSIVEO is an oral, selective, small molecule gamma secretase inhibitor approved in the U.S. for the treatment of adult patients with progressing desmoid tumors who require systemic treatment.[1]

ABOUT DESMOID TUMORS

- Desmoid tumors are locally aggressive and invasive soft-tissue tumors that can lead to severe pain, loss of physical function and impact a person's quality of life.[2-7] These tumors are difficult to control and can be debilitating for people living with them.[3-5] When vital structures are impacted, desmoid tumors can be life threatening.[3,8]
- Although they do not metastasize, desmoid tumors are associated with recurrence rates of up to 77% following surgical resection.[9-10*]
- There are approximately 1,000-1,650 new cases diagnosed annually in the U.S.[11-13]
- Desmoid tumors are commonly diagnosed in people between 20 to 44 years of age and are 2-3 times more likely to be diagnosed in women than men.[8,11]

*Based on retrospective, observational data. Factors associated with local recurrence postsurgery include tumor location, age of the participant, tumor size, margin status, and prior recurrence.[9-10]

OGSIVEO HELPS ADDRESS A HIGH UNMET NEED

Until OGSIVEO, there was no FDA-approved therapy indicated for adults with desmoid tumors.[16]

Desmoid tumors are typically treated with off-label systemic treatments including chemotherapy and tyrosine kinase inhibitors, which are often poorly tolerated with inconsistent efficacy.[17-18]

Desmoid tumors are also treated with surgical resection, but surgery has become less common due to high rates of post-surgical recurrence.[9-10]

Desmoid tumor experts and treatment guidelines now recommend systemic therapies as first-line intervention instead of surgery for most tumor locations requiring treatment.[19-20]

OGSIVEO CLINICAL DATA

- The FDA approval of OGSIVEO was based on results from the Phase 3 Desmoid/Fibromatosis (DeFi) trial, an international, multicenter, randomized (1:1), double-blind, placebo-controlled trial, in adult patients who had progressing desmoid tumors with treatment-naïve, refractory, or recurrent disease (N = 142).[1,21] The trial results were published in the March 9, 2023 issue of *The New England Journal of Medicine*.[21]
- OGSIVEO achieved statistically significant and clinically meaningful improvements across the primary and all key secondary efficacy endpoints.[1,21]
- OGSIVEO met the primary endpoint of improving progression-free survival (PFS), demonstrating a statistically significant improvement over placebo, with a 71% reduction in the risk of disease progression (hazard ratio (HR) = 0.29 (95% CI: 0.15, 0.55); p< 0.001).[1,21]
- Median PFS was not reached in the OGSIVEO arm and was 15.1 months in the placebo arm.[1,21]
- Confirmed objective response rate (ORR) based on RECIST v1.1 was 41% with OGSIVEO versus 8% with placebo (p<0.001); the complete response rate was 7% in the OGSIVEO arm and 0% in the placebo arm.[1,21]
- The median time to first response was 5.6 months with OGSIVEO and 11.1 months with placebo.[21] PFS and ORR improvements were in favor of OGSIVEO regardless of baseline characteristics including sex, tumor location, tumor focality, treatment status, previous treatments, mutational status, and history of familial adenomatous polyposis.[21-22]
- OGSIVEO also demonstrated early and sustained improvements in patient-reported outcomes (PROs), including pain, desmoid tumor-specific symptoms, physical/role functioning, and overall quality of life. Differences in these PROs with OGSIVEO over placebo at Cycle 10 were statistically significant and clinically meaningful (P≥0.01).[21]
- The most common adverse events (≥15%)* reported in patients receiving OGSIVEO were diarrhea, ovarian toxicity, rash, nausea, fatigue, stomatitis, headache, abdominal pain, cough, alopecia, upper respiratory tract infection, and dyspnea. Please see Important Safety Information below, including Warnings & Precautions relating to diarrhea, ovarian toxicity, hepatotoxicity, non-melanoma skin cancers, electrolyte abnormalities, and embryo-fetal toxicity.[1]

*With a difference between arms of >5% compared to placebo.

Please see Important Safety Information below and click here for full Prescribing Information.

OGSIVEO PATIENT SUPPORT SERVICES

- SpringWorks is dedicated to helping patients with desmoid tumors access OGSIVEO and to providing support throughout their treatment journey.
- SpringWorks CareConnections™ is a comprehensive patient support program that offers personalized services to eligible OGSIVEO patients, including insurance coverage information and access support, financial assistance and personalized educational and emotional support.
- Physicians and patients can call 1-844-CARES-55 (1-844-227-3755) or visit springworkstxcares.com for more information.

For additional information, visit OGSIVEO.COM

Indication

OGSIVEO is indicated for adult patients with progressing desmoid tumors who require systemic treatment.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Diarrhea:** Diarrhea occurred in 84% of patients treated with OGSIVEO. Grade 3 events occurred in 16% of patients. Monitor patients and manage using antidiarrheal medications. Modify dose as recommended.
- **Ovarian Toxicity:** Female reproductive function and fertility may be impaired in patients treated with OGSIVEO. Impact on fertility may depend on factors like duration of therapy and state of gonadal function at time of treatment. Long-term effects on fertility have not been established. Advise patients on the potential risks for ovarian toxicity before initiating treatment. Monitor patients for changes in menstrual cycle regularity or the development of symptoms of estrogen deficiency, including hot flashes, night sweats, and vaginal dryness.
- **Hepatotoxicity:** ALT or AST elevations occurred in 30% and 33% of patients, respectively. Grade 3 ALT or AST elevations (>5 x ULN) occurred in 6% and 2.9% of patients. Monitor liver function tests regularly and modify dose as recommended.
- **Non-Melanoma Skin Cancers:** New cutaneous squamous cell carcinoma and basal cell carcinoma occurred in 2.9% and 1.4% of patients, respectively. Perform dermatologic evaluations prior to initiation of OGSIVEO and routinely during treatment.
- **Electrolyte Abnormalities:** Decreased phosphate (65%) and potassium (22%) occurred in OGSIVEO-treated patients. Phosphate <2 mg/dL occurred in 20% of patients. Grade 3 decreased potassium occurred in 1.4% of patients. Monitor phosphate and potassium levels regularly and supplement as necessary. Modify dose as recommended.
- **Embryo-Fetal Toxicity:** Oral administration of nirogacestat to pregnant rats during the period of organogenesis resulted in embryo-fetal toxicity at maternal exposures below human exposure at the recommended dose of 150 mg twice daily. Advise pregnant women of the potential risk to a fetus. Advise females and males of reproductive potential to use effective contraception during treatment with OGSIVEO and for 1 week after the last dose.

ADVERSE REACTIONS

- The most common (≥15%) adverse reactions were diarrhea, ovarian toxicity, rash, nausea, fatigue, stomatitis, headache, abdominal pain, cough, alopecia, upper respiratory tract infection, and dyspnea.
- Serious adverse reactions occurring in ≥2% of patients were ovarian toxicity (4%).
- The most common laboratory abnormalities (≥15%) were decreased phosphate, increased urine glucose, increased urine protein, increased AST, increased ALT, and decreased potassium.

DRUG INTERACTIONS

- **CYP3A4 Inhibitors and Inducers:** Avoid concomitant use with strong or moderate CYP3A4 inhibitors (including grapefruit products, Seville oranges, and starfruit) and strong or moderate CYP3A4 inducers.
- **Gastric Acid Reducing Agents:** Avoid concomitant use with proton pump inhibitors and H2 blockers. If concomitant use cannot be avoided, OGSIVEO can be staggered with antacids (e.g., administer OGSIVEO 2 hours before or 2 hours after antacid use).
- Consult the full Prescribing Information prior to and during treatment for important drug interactions.

Please click here for full Prescribing Information.

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