



**Sarcoma  
Patient Advocacy  
Global Network**

# **Current Management of Desmoid Tumors: A Review**

**LAY SUMMARY**



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Authors of the original publication “Current Management of Desmoid Tumors. A Review” in JAMA Oncology, published online June 20, 2024. doi:10.1001/jamaoncol.2024.1805

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Sarcoma Patient Advocacy Global Network (SPAGN) is the global network of national Sarcoma Patient Advocacy Organizations. With nearly 70 member groups from 5 continents, SPAGN's network provides a common, international and influential patient voice for sarcoma patients everywhere. SPAGN works to improve the treatment and care of sarcoma patients through information and support, and by increasing the visibility of sarcoma with policymakers and the public.



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## EXECUTIVE SUMMARY

### *Why it matters*

Desmoid tumors (DT) are rare, aggressive tumors that can vary greatly in how they progress. In the past, surgery was the main treatment, but in recent years, there has been a shift towards less-invasive treatments. The 2023 guidelines focus on how local treatments, like surgery and radiotherapy, fit into the treatment algorithm, as well as new medications like  $\gamma$ -secretase inhibitors.

### *How the new guidelines were developed*

To update the global guidelines for treating DT a meeting was held in Milan, Italy, on June 30, 2023. It included over 90 experts and patient advocates. Research from MEDLINE and Embase databases was reviewed to support the guidelines. New guidelines include data on treatments like cryotherapy and the  $\gamma$ -secretase inhibitor nirogacestat, the first approved drug for DT. Treating DT is complex and should be done in specialized centers with a multidisciplinary team. The treatment plan should consider symptoms, risks, tumor location, disease complications, available treatments, and patient preferences.

### *What this means*

The options for treating DT are continually growing. It is crucial to choose the best treatment for each patient to control the tumor and improve patients' quality of life.



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*The treatment plan should consider symptoms, risks, tumor location, disease complications, available treatments, **and patient preferences.***

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## INTRODUCTION

A desmoid tumor (DT) is a rare type of tumor made up of fibroblastic cells. These tumors can behave in different and often unpredictable ways. DTs occur in about five out of every 1 million people each year, most commonly in women between 30 and 40 years old. These tumors can develop in various places in the body, including the abdomen. Around 5% to 10% of cases are linked to a genetic condition called familial adenomatous polyposis.

In the past decade, there has been a significant effort to standardize how DTs are treated. The Desmoid Tumor Working Group held a meeting with experts from around the world in 2023 to update global guidelines on the best ways to manage DT. The goal was to improve patient care and outcomes by reducing inconsistencies in treatment.

### **About the consensus initiative 2023**

The 2023 meeting focused on where to place local treatments, surgery, and radiotherapy in the treatment plan, as well as the use of new medical drugs like  $\gamma$ -secretase inhibitors. Experts from Europe, North and South America, Canada, Australia, and Japan, along with patients and advocates, participated in the meeting. The meeting was supported by the European Reference Network on Rare Adult Solid Cancers (EURACAN) and funded by the Desmoid Foundation Italy and the Desmoid Tumor Research Foundation (DTRF).

### **Methods: How we did it**

#### *Choosing the panel*

The panel for the discussion and guideline development in 2023 mainly consisted of the participants in the first global consensus meeting held in 2018. These included experts from various fields related to treating and caring for patients with DT, such as pathology, molecular biology, radiology, orthopedic surgery, surgical oncology, radiotherapy, medical oncology, pediatric oncology, and supportive care. We had representatives from sarcoma centers in Europe, the United States, Canada, Australia, and Japan.

We also included DT patients and representatives from patient organizations around the world. Since new topics and chapters were added to the updated guidelines, we expanded the panel to better represent different medical specialties and regions, and to increase patient involvement and advocacy.

## *Reviewing the evidence*

Before the consensus meeting, we conducted a literature search for randomized clinical trials (RCTs) on systemic therapies published since our last search in 2018. This helped gather data to support the recommendations.

## *Reaching consensus*

To create the 2023 guidelines, The Desmoid Tumor Working Group held a one-day, in-person meeting on June 30, 2023, in Milan, Italy. Based on the literature review and discussions, the group agreed on key management strategies for patients with DT, which are summarized in this article.

## **Key consensus statements**

### *Watching DTs without treatment (active surveillance)*

Recent studies from Europe have shown that monitoring newly diagnosed DT without immediate treatment (“active surveillance”) can be a safe and effective approach. This strategy helps to decide who needs treatment and who can avoid unnecessary aggressive treatments. These studies backed up previous data and agreed with the 2020 guidelines recommending active surveillance. The combined Italian and Dutch studies found that factors like genetic mutations, tumor size, and location could help identify patients who might not do well with just monitoring. This helps tailor follow-ups and decide when active treatment might be needed. However, it is recommended that all DT patients start with active surveillance before considering any aggressive treatments.

### *When surgery is needed for sporadic DTs*

In cases of sporadic DT, where there are complications like bleeding or obstruction, surgery is crucial. However, the goal is not always to completely remove the tumor (R0 resection) since this can lead to significant and unnecessary complications. For non-mesenteric DTs, if the disease progresses despite medical treatment or active surveillance, surgery might be an option when the risks are low (for example, in the abdominal wall). Surgery might also be considered if there is progression or residual disease after treatment that could cause further problems, particularly in mesenteric DTs.

## *Local treatments*

Cryoablation (freezing the tumor) is a promising local treatment for DTs. According to the CRYODESMO-01 trial, this method is recommended for growing DTs after trying at least two types of medical treatment or when the tumor causes pain or other symptoms. A team of specialists should discuss this option with the patient. Cryotherapy is not available everywhere and needs specialized skills. More research is encouraged to better understand the role of local treatments for DTs.

## *New drug treatments*

Randomized phase 3 trials have tested drugs like sorafenib and nirogacestat for DTs. Nirogacestat was the first drug approved for this condition. However, without comparative studies, we cannot definitively rank the effectiveness of current systemic treatments. Choosing a treatment should consider the specific side effects and time to treatment effect of each drug for the patient. Generally, starting with a treatment that has fewer side effects and then moving to more toxic options if necessary is a good approach.

DT often require multiple treatments over time. Having a variety of treatment options benefits both patients and doctors by providing multiple choices for different situations. Nirogacestat is of interest because it has few short-term side effects, but its long-term effects, especially on female reproductive health, are not well known. Efforts should be made to collect this information. Until then, women with the potential for pregnancy should be informed about the risks of early menopause or reduced fertility with nirogacestat.

There is no clear guideline on how long to use any of the available systemic treatments for DT. The Desmoid Tumor Working Group suggests that most treatments should be administered for at least six months (unless the disease worsens significantly) before assessing their effectiveness. For low-dose chemotherapy such as methotrexate and/or vinorelbine, longer treatment durations may be needed. More research is needed to determine the minimum effective treatment time and to understand the effects of stopping and resuming therapy during breaks in treatment.

An overview of different systemic treatments can be found in “The management of desmoid tumours: A joint global consensus-based guideline approach for adult and paediatric patients”, published 2020 in the European Journal of Cancer.

## Diagnosis of DTs: Updates in Pathology and Molecular Biology

To diagnose DT accurately, an expert in soft tissue pathology should be consulted. CTNNB1 and APC gene mutations do not occur together in DT, so finding a CTNNB1 mutation can help rule out Familial Adenomatous Polyposis (FAP). On the other hand, if a DT does not show CTNNB1 mutations, especially in tumors inside the abdomen, it could indicate FAP, and further testing (like a colonoscopy or genetic testing) might be needed. We recommend analyzing DT biopsy samples for mutations to confirm the diagnosis and guide further treatment. Using Next-Generation Sequencing (NGS) for this analysis can be more sensitive.

Further information on diagnostic methods can be found in **“The management of desmoid tumours: A joint global consensus-based guideline approach for adult and paediatric patients”** (2020).

## Hormonal contraception and pregnancy

Hormonal contraception is safe for people with DT, and having DT does not stop someone from having future pregnancies if the DT is not progressing. Since most DTs grow within two years, it is advisable to wait at least two years of no growth before planning a pregnancy, though this can be personalized. Pregnant individuals with DT should be monitored closely by both obstetricians and DT specialists. During pregnancy, there is about a 12% risk of DT progression, which increases to 15% one year after childbirth. For pregnancies after a DT diagnosis, the risk of progression is around 5% during pregnancy and 9% one year after childbirth.



Desmoid Tumor Working Group. European Journal of Cancer. 2020;127:96-107.



*Choosing a treatment should consider the specific side effects and time to treatment effect of each drug for the patient.*

### *When to use radiation therapy*

For DT patients whose disease is worsening or showing symptoms, and who cannot use systemic treatments or whose disease doesn't respond to them, local treatments like surgery, radiation therapy, or cryoablation should be considered. Radiation is preferred for large DTs that are too big for cryoablation and for patients where surgery would cause too many complications, especially older patients. Radiation is also often better than surgery for DTs in the arms or legs due to lower success rates with surgery. However, radiation should not be used as an adjuvant treatment after surgery. However, radiotherapy is recommended in only a limited number of specific indications.

### *Challenges in treating FAP-related DT*

Managing DTs in FAP (Familial Adenomatous Polyposis) cases still needs improvement. While preventive colectomy (removal of the colon) is the standard to avoid colon cancer, the best timing and surgical method are still debated. Prophylactic surgeries should be done at specialized centers to minimize risks. Surgeons experienced in familial polyposis or collaborating with sarcoma specialists should plan these surgeries.

After colectomy, high-risk FAP patients should be monitored closely, with MRI or CT scans every 6-12 months for five years, while low-risk patients might just need abdominal ultrasounds. Diagnosing DT in some FAP patients can be difficult, and sometimes medical treatment might be started without a biopsy. Once DT is confirmed, close monitoring is essential, especially for aggressive cases of DTs around the small bowel. A specialized team is crucial for managing these high-risk patients, and surgery should be limited to emergencies like perforation or blockage to avoid complications.

For DTs that continue to progress despite standard treatments, small bowel transplantation might be considered, but it should be done in specialized centers as it is experimental. Psychological and nutritional support should also be part of the care for FAP patients.



Radiation is preferred for large DTs that are too big for cryoablation and for patients where surgery would cause too many complications, especially older patients.

### *Treatment and monitoring for children*

When diagnosing DT in children, an initial period of active surveillance is recommended to understand how the tumor behaves. Treatment decisions should consider the disease's nature, extent, patient age, symptoms, quality of life, and potential risks. If treatment is needed, the choice is usually a weekly intravenous regimen of methotrexate and vinblastine. Alternatives include oral vinorelbine with or without methotrexate or a tyrosine kinase inhibitor for adolescents. Tumor resection should be avoided.

In life-threatening cases, treatment options could include vincristine, dactinomycin, or cyclophosphamide, or surgery might be required. Tyrosine kinase inhibitors should be used cautiously in children, with their long-term safety still under investigation. Gamma secretase inhibitors should be used only after ongoing trials confirm their safety and efficacy. Medical treatments are typically suggested for at least 6-12 months, though longer periods may be discussed.

### *The impact of an international tumor board*

Consensus papers help standardize treatment approaches for rare tumors but might not capture every patient's unique situation. For patients in less resourceful areas, presenting cases in a multidisciplinary setting might not always be possible. International virtual tumor boards, like the one launched by DTRF in 2017, provide a valuable platform for discussing complex cases. These boards include various specialists and have reviewed cases from 16 countries, offering reassurance to patients that their cases are thoroughly reviewed. They also help promote clinical trials and identify knowledge gaps in the disease.



*Since most DTs grow within two years, it is advisable to wait at least two years of no growth before planning a pregnancy, though this can be personalized.*



## Health-related quality of life

Providing interdisciplinary support is crucial for young patients with chronic diseases like DT. The condition can significantly affect many aspects of their lives, including social interactions, work, and relationships. Collaborative and personalized care should involve pain specialists, physiotherapists, psychologists, and social workers, all trained to handle the unique and unpredictable nature of DT.

## CONCLUSIONS

The 2023 update to the guidelines for treating DT includes several new aspects compared to the 2020 version. There is now more information available about local treatments like cryotherapy, which will become more important for physicians and patients dealing with DT. Specific indications for choosing surgery have also been discussed.

Additionally, a new drug called nirogacestat, which is the first approved medicine specifically for DT, has been added to the treatment plan. The options for treating DT are growing. It is very important to choose the right treatment approach for each DT patient to best control the tumor and improve his or her quality of life.

### READ FULL PUBLICATION HERE

*Current Management of Desmoid Tumors. A Review.*

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**IMPORTANCE** Desmoid tumor (DT) is a rare and locally aggressive monoclonal, fibroblastic proliferation characterized by a variable and often unpredictable clinical course. Previously, surgery was the standard primary treatment modality; however, within the past decade, a paradigm shift toward less-invasive management has been introduced and an effort to harmonize the strategy among clinicians has been made. To update the 2020 global evidence-based consensus guideline on the management of patients with DT, the Desmoid Tumor Working Group convened a 3-day consensus meeting in Milan, Italy, on June 30, 2023, under the auspices of the European Reference Network on Rare Adult Solid Cancers and Sarcoma Patient Advocacy Global Network, the Desmoid Foundation Italy, and the Desmoid Tumor Research Foundation. The meeting brought together over 90 adult and pediatric sarcoma experts from different disciplines as well as patients and patient advocates from around the world.

**OBSERVATIONS** The 2023 update of the global evidence-based consensus guideline focused on the positioning of local therapies alongside surgery and radiotherapy in the treatment algorithm as well as the positioning of the newest class of medical agents, such as  $\gamma$ -secretase inhibitors. Literature searches of MEDLINE and Embase databases were performed for English-language randomized clinical trials (RCTs) of systemic therapies to obtain data to support the consensus recommendations. Of the 18 full-text articles retrieved, only 4 articles met the inclusion criteria. The 2023 consensus guideline is informed by a number of new aspects, including data for local ablative therapies such as cryotherapy, other indications for surgery, and the  $\gamma$ -secretase inhibitor nirogacestat, the first representative of the newest class of medical agents and first approved drug for DT. Management of DT is complex and should be carried out exclusively in designated DT referral centers equipped with a multidisciplinary tumor board. Selection of the appropriate strategy should consider DT-related symptoms, associated risks, tumor location, disease morbidities, available treatment options, and preferences of individual patients.

**CONCLUSIONS AND RELEVANCE** The therapeutic armamentarium of DT therapy is continually expanding. It is imperative to carefully select the management strategy for each patient with DT to optimize tumor control and enhance quality of life.

**Author Affiliations:** Author affiliations are listed at the end of the article.

**Group Information:** A complete list of the members of the Desmoid Tumor Working Group appears in Supplement 2.

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