Asian J Biol Life Sci., 2026; 15(1):37-44.
https://ajbls.com

Review Article

# Advances in Therapeutic Strategies for Fibrodysplasia Ossificans Progressiva: From Symptom Management to Targeted Therapies

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**ABSTRACT**

Muscles, tendons, and ligaments are part of the soft tissues that can develop progressive heterotopic ossification in Fibrodysplasia Ossificans Progressiva (FOP), a very rare genetic disorder that follows an autosomal dominant pattern. About one in every two million people worldwide are affected by this condition. Because FOP can resemble other disorders such as sarcoma, fibromatosis, and congenital skeletal abnormalities, early diagnosis is often challenging. Current management mainly focuses on symptomatic treatment, including the use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) or COX-2 inhibitors for pain relief and short-term corticosteroids during acute flare-ups. The aim of this review is to summarize current understanding of the molecular basis of FOP, particularly the role of ACVR1 mutations, and to evaluate existing supportive treatments along with emerging targeted and gene-based therapeutic strategies that may help slow disease progression.

**Keywords:** ACVR1 gene mutation, Heterotopic Ossification (HO), Palovarotene, Fibrodysplasia Ossificans Progressiva (FOP).

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**Received:** 25-12-2025;
**Revised:** 11-02-2026;
**Accepted:** 06-04-2026.

## INTRODUCTION

Fibrodysplasia Ossificans Progressiva (FOP) is one of the rarest genetic disorders, characterized by progressive heterotopic ossification of soft connective tissues, including muscles, tendons, and ligaments (Katagiri *et al*., 2018; Kaplan *et al*., 2008; Smilde *et al*., 2022). The condition is primarily caused by a gain-of-function mutation in the ACVR1/ALK2 gene, which leads to inappropriate activation of the Bone Morphogenetic Protein (BMP) signalling pathway and abnormal skeletal tissue formation (National Organization for Rare Disorders, 2024; Kaplan *et al*., 2024). Although FOP follows an autosomal dominant pattern of inheritance, most cases arise from spontaneous mutations, making early detection particularly challenging (Kaplan *et al*., 2010).

Clinically, FOP is distinguished by congenital malformations of the great toes and episodic inflammatory flare-ups that trigger progressive ossification in soft tissues. Over time, this ectopic bone formation results in severe joint restriction, loss of mobility, and substantial functional disability (Smilde *et al*., 2022; Kaplan *et al*., 2010). By early adulthood, many patients require assistance with daily activities, and thoracic involvement can lead to respiratory compromise, which remains a major cause of morbidity and mortality.

Early diagnosis of FOP is often delayed because its initial manifestations can resemble other conditions such as soft-tissue sarcomas, juvenile fibromatosis, and other musculoskeletal abnormalities (Pignolo *et al*., 2011). Misdiagnosis frequently results in unnecessary biopsies or surgical interventions, which can worsen disease progression by triggering additional heterotopic ossification.

At present, no curative treatment exists for fibrodysplasia ossificans progressiva. Management strategies mainly focus on preventing trauma, controlling inflammation during flare-ups, and providing supportive care to preserve function and quality of life. However, recent advances in molecular genetics and pharmacology have transformed the therapeutic landscape of FOP. Increasing knowledge of ACVR1-mediated signaling pathways has led to the development of targeted therapies aimed at modifying disease progression rather than merely alleviating symptoms (Kaplan *et al*., 2012). These advances offer new hope for patients and underscore the importance of continued translational research in this rare but devastating condition.

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Manuscript TECHNOMEDIA

**DOI:** 10.5530/ajbls.20260086



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## METHODOLOGY

This review was conducted through a systematic literature search of major electronic databases including PubMed, Google Scholar, ScienceDirect, and Scopus. Relevant articles were identified using keywords such as "Fibrodysplasia Ossificans Progressiva", "ACVR1 mutation", "heterotopic ossification", "BMP signalling", "Activin A", and "FOP therapies".

Publications in the English language from 2010 to 2025 were considered for inclusion. The selection focused on review articles, original research studies, clinical trials, and consensus guidelines that discussed the clinical features, molecular mechanisms, and therapeutic strategies related to FOP.

Articles were screened initially by title and abstract, followed by full-text evaluation to ensure relevance to the objectives of this review. Studies that lacked scientific credibility, had insufficient data, or were not directly related to FOP were excluded. Data from the selected articles were analysed qualitatively and synthesized to provide a comprehensive overview of disease pathophysiology and emerging treatment approaches.

## REVIEW OF LITERATURE / DISCUSSION

### Clinical Signs of Fibrodysplasia Ossificans Progressiva

Fibrodysplasia ossificans progressiva is characterized by a distinctive pattern of clinical manifestations that usually begin in early childhood and progressively worsen with age. One of the earliest and most reliable diagnostic signs is congenital malformation of the great toes, typically presenting as shortened, valgus-deviated toes with a single phalanx (Rivera *et al*., 2024; Li and Yuan, 2025). This feature is present at birth and serves as a critical clue for early diagnosis.

Another hallmark of the disease is the occurrence of painful inflammatory flare-ups, which are often accompanied by localized swelling, warmth, and tenderness of soft tissues. These episodes frequently preceded the formation of heterotopic bone and may last from several days to weeks (Zhou *et al*., 2025; Kaplan and Pignolo, 2018). Flare-ups can occur spontaneously or be triggered by minor trauma, intramuscular injections, viral infections, or surgical procedures.

As the disease progresses, patients develop progressive heterotopic ossification, in which normal muscles, tendons, and ligaments are gradually replaced by mature bone. Ossification typically begins in the cervical spine, shoulders, and upper back, and later extends to the trunk and limbs, leading to severe restriction of joint mobility and functional impairment (Ebise *et al*., 2015).

Involvement of the craniofacial region may result in reduced jaw mobility, causing difficulties in eating, speaking, and maintaining oral hygiene. Additionally, abnormal bone formation in the thoracic cage can limit chest expansion, leading to restrictive lung disease, recurrent respiratory infections, and increased risk of cardiorespiratory complications, which remain a major cause of morbidity and mortality in affected individuals (Mozumder, 2025).

Other associated clinical features include conductive hearing loss due to ossification of middle ear structures, chronic pain, fatigue during flare-ups, and occasional neurological symptoms caused by nerve compression (Kitoh, 2020).

The major clinical features of fibrodysplasia ossificans progressiva are summarized in Table 1 and illustrated in Figure 1.

## PATHOPHYSIOLOGY OF FIBRODYSPLASIA OSSIFICANS PROGRESSIVA

### Genetic Mutation

- Fibrodysplasia ossificans progressiva is caused by a gain-of-function mutation in the ACVR1 gene (also known as ALK2).
- The most common mutation is R206H, which leads to abnormal activation of bone-forming pathways even in the absence of normal signals (International FOP Association, 2025; National Institute for Health and Care Research Innovation Observatory, 2025).

### Abnormal BMP Signaling Pathway

- ACVR1 encodes a receptor involved in the Bone Morphogenetic Protein (BMP) signaling pathway, essential for normal skeletal development.
- In FOP, this pathway becomes overactive, leading to excessive activation of SMAD proteins and inappropriate bone formation in soft tissues (Eekhoff *et al*., 2022; Ikrama *et al*., 2025).

### Role of Activin A

- Under normal conditions, Activin A inhibits bone formation.
- In FOP, the mutated ACVR1 receptor misinterprets Activin A as a bone-forming signal, triggering abnormal ossification (Rivera *et al*., 2024).
- This discovery has made Activin A major target for new therapies.

### Inflammatory Response and Flare-Ups

Tissue injury, infections, or mechanical stress activate immune cells such as:

- Macrophages.
- Mast cells.

- Lymphocytes.
- These cells release inflammatory mediators that create an environment favoring heterotopic ossification (Pignolo *et al.*, 2011; Kaplan *et al.*, 2012).

### Role of Fibro-Adipogenic Progenitors (FAPs)

FAPs are stem-like cells present in skeletal muscle that normally assist in tissue repair.

In FOP, due to defective ACVR1 signaling, these cells abnormally differentiate into:

- Chondrocytes.
- Osteoblasts.
- This leads to ectopic cartilage and bone formation (Rivera *et al.*, 2024).

### Endochondral Ossification Process

The abnormal bone in FOP forms through the same mechanism as normal bone development:

- Inflammation.
- Fibroblast recruitment.
- Cartilage formation (chondrogenesis).
- Replacement by mature bone.
- This process explains why heterotopic bone in FOP is structurally normal but anatomically misplaced (Kaplan *et al.*, 2012).

### Progressive and Irreversible Bone Formation

Continuous activation of osteogenic pathways results in:

- Joint ankylosis.
- Muscle replacement by bone.
- Severe restriction of movement.
- The disease is progressive and irreversible, with no natural regression (Smilde *et al.*, 2022; Kaplan *et al.*, 2010).

### Secondary Complications

Abnormal bone formation leads to multiple systemic problems:

- Thoracic involvement → restricted breathing.
- Jaw involvement → difficulty in eating and speaking.
- Spinal ossification → scoliosis and kyphosis.
- These complications significantly reduce quality of life and life expectancy (Kaplan *et al.*, 2010).

The molecular mechanisms involved in fibrodysplasia ossificans progressiva are illustrated in Figure 2.

## CURRENT THERAPEUTIC STRATEGIES OF FOP

### Symptomatic Management

Pain and inflammation are managed with NSAIDs or COX-2 inhibitors during flare-ups (Li and Yuan, 2025).

Short-term corticosteroids can be used in acute flare-ups affecting major joints or the jaw (Zhou *et al.*, 2025).

Avoidance of trauma, intramuscular injections, and surgery is critical, as these can trigger heterotopic ossification (Kaplan and Pignolo, 2018).

### Small-Molecule Inhibitors

Target ACVR1/BMP signaling to prevent abnormal ossification.

Examples include:

- Dorsomorphin derivatives.
- Selective ACVR1 kinase inhibitors.

Aim: reduce flare frequency and ectopic bone formation (Li and Yuan, 2025; Zhou *et al.*, 2025).

### Retinoic Acid Receptor (RAR) Agonists

Palovarotene (RARγ agonist) suppresses chondrogenesis and cartilage formation.

Clinical trials show reduced heterotopic ossification and flare severity (Vermeil *et al.*, 2025).

Limitations: caution in pediatric use due to growth effects.

### Biologics / Monoclonal Antibodies

Target Activin A, which abnormally activates mutant ACVR1.

**Table 1: Clinical features of fibrodysplasia ossificans progressiva (Katagiri *et al.*, 2018; Smilde *et al.*, 2022; Kaplan *et al.*, 2010).**

| Clinical symptom | Description |
|---|---|
| Malformations of the Great Toe | Deformed, short toes are a characteristic that is evident from birth. |
| Differential Ossification | Persistently aberrant bone in tendons, ligaments, and muscles; frequently brought on by trauma. |
| The stiffness of joints | Progressive loss of movement as a result of bone bridging between joints. |
| Common Locations of Onset | Starting in the neck, shoulders, and back, it usually spreads to the trunk and limbs. |

Example: Garetosmab neutralizes Activin A and prevents heterotopic bone formation (Ikrama *et al.*, 2025).

## mTOR and Other Pathway Inhibitors

Rapamycin (mTOR inhibitor) suppresses inflammation and ossification in preclinical studies.

Other experimental agents aim to modulate TGF-β, SMAD, and inflammatory signaling (Kitoh, 2020; Shaik, 2023).

## Gene- and RNA-Based Therapeutic Approaches

- CRISPR: potential correction of ACVR1 mutation in progenitor cells (Eekhoff *et al.*, 2022).
- RNA interference / antisense oligonucleotides: block mutant ACVR1 expression (Ikrama *et al.*, 2025).
- Currently experimental; safety and delivery remain challenges.

**Table 2: Major ongoing and recent clinical trials in Fibrodysplasia Ossificans Progressiva (FOP) (International FOP Association, 2025; Ikrama *et al.*, 2025; Vermeil *et al.*, 2025).**

| Drug | Type/Mechanism | Formulation | Phase Trial | Key Objective | Status |
|---|---|---|---|---|---|
| Palovarotene | RARγ agonist that stops cartilage formation | Oral capsule | Phase 3 | Reduce flare-ups and extra bone growth | Approved for limited use; ongoing monitoring |
| Garetosmab | Anti-Activin A monoclonal antibody | Intravenous | Phase 3 (LUMINA-1) | Block faulty ACVR1 signals; reduce new bone growth | Ongoing; promising early results |
| Fidrisertib (IPN60130) | Selective ACVR1 kinase inhibitor | Oral tablet | Phase 2 (FALKON) | Block mutant ACVR1 activity; slow flare-ups | Recruiting participants worldwide |
| Zilurgisertib | ACVR1 pathway inhibitor | Oral tablet | Phase 2 | Stop extra bone growth, especially in children | Active; early safety confirmed. (National Organization for Rare Disorders, 2024; Kaplan *et al.*, 2010). |
| BCX9250 | Small-molecule ACVR1 inhibitor | Oral tablet | Phase 1 | First human study; safe dosage determined | Phase 1 finished; moving to Phase 2 |
| KER-047 | BMP pathway inhibitor | Oral tablet | Phase 1/2 | Test safety and efficacy in stopping abnormal bone growth | Active; good early tolerance |
| DS-6016a | Novel ACVR1/SMAD inhibitor | Oral tablet | Phase 1 | Reduce SMAD activation to stop bone formation | Preclinical and early Phase 1 |
| Saracatinib | Src kinase inhibitor (used for cancer) | Oral tablet | Phase 2 (STOPFOP) | Block harmful signals; reduce flare intensity | Ongoing in Europe and the U.S. |
| Andecaliximab | Anti-fibrotic monoclonal antibody | Intravenous | Phase 2 | Reduce inflammation and tissue scarring | Enrolling patients |
| Rapamycin | mTOR pathway inhibitor | Oral tablet | Pilot trial | Prevent extra bone growth by lowering inflammation | Early testing |

### Ongoing Clinical Trials

Several trials are evaluating the efficacy and safety of:

- Palovarotene.
- Fidrisertib (ACVR1 inhibitor).
- Garetosmab (Activin A antibody) (International FOP Association, 2025; National Institute for Health and Care Research Innovation Observatory, 2025; Vermeil *et al*., 2025).

### Supportive Care

Physical therapy is used cautiously to maintain mobility without causing trauma.

Nutritional support and respiratory monitoring are recommended for patients with thoracic involvement (Kaplan and Pignolo, 2018).

The major ongoing and recent clinical trials investigating therapeutic approaches for fibrodysplasia ossificans progressiva are summarized in Table 2, providing an overview of current pharmacological strategies and their developmental status.

## FUTURE DIRECTIONS AND RESEARCH GAPS

### Advanced Technology in the Study of FOP

Emerging technologies are enhancing our understanding of FOP and guiding the development of more precise interventions:

### Gene Therapy and Genome Editing

The goal is to improve safety and precision by targeting progenitor cells that drive heterotopic ossification using CRISPR/Cas9 and RNA interference (RNAi) technologies, delivered via AAV9 vectors (National Institute for Health and Care Research Innovation Observatory, 2025).

### Molecular Drug Design

High-throughput and structure-based approaches have led to the development of selective inhibitors such as Fidrisertib,

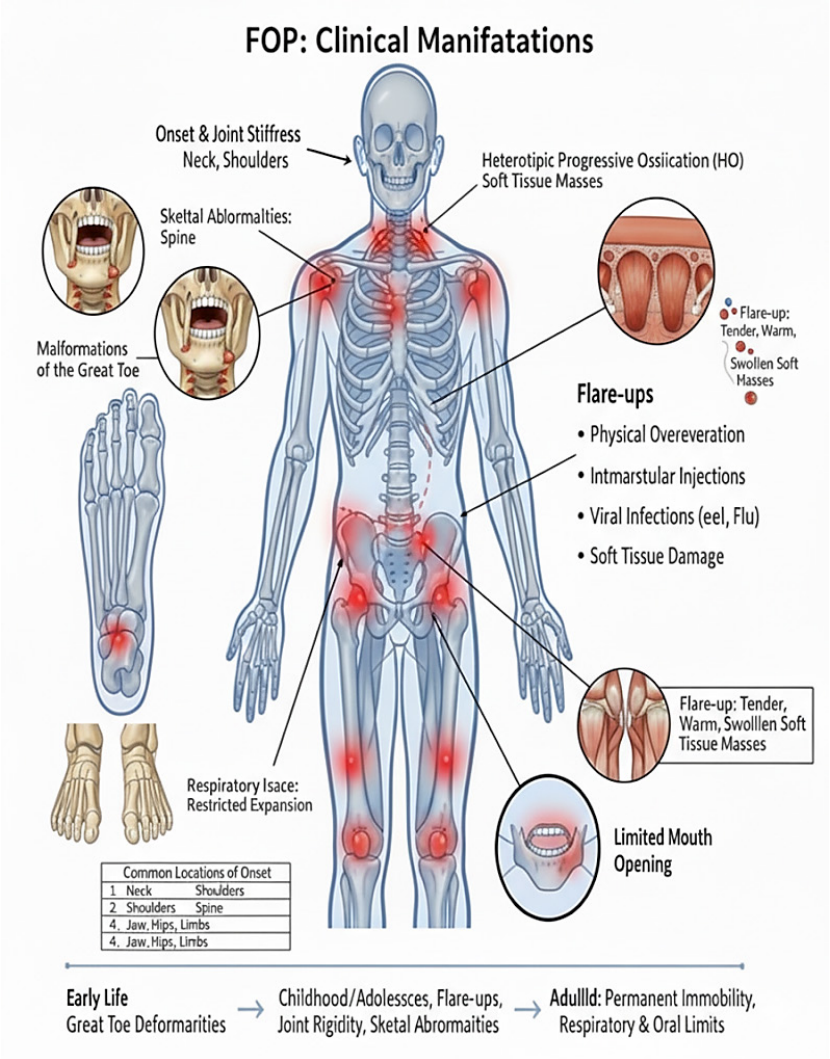


**Figure 1:** Clinical manifestations of fibrodysplasia ossificans progressiva.

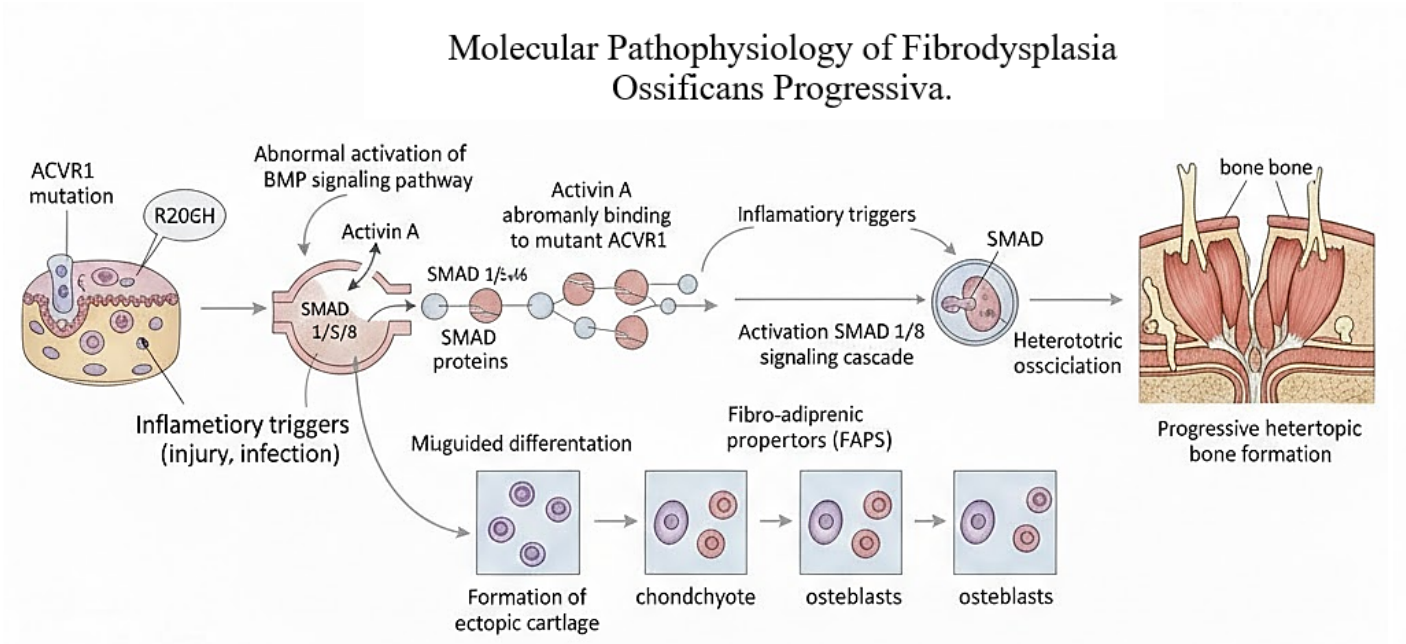


**Figure 2:** Molecular Pathophysiology of Fibrodysplasia Ossificans Progressiva.

Palovarotene, and Garetosmab, optimizing efficacy while minimizing off-target effects (Eekhoff *et al.*, 2022).

## Advanced Imaging Techniques

MRI, CT, and molecular imaging facilitate early detection of flare activity and heterotopic ossification, improving disease monitoring (Vermeil *et al.*, 2025).

## Platforms for Biomarkers

Proteomics and metabolomics are employed to identify biomarkers for therapy monitoring, flare prediction, and early diagnosis (Ikrama *et al.*, 2025; Shaikh, 2023).

## FOP Treatment Challenges

Despite advancements, several challenges limit the effectiveness of current and emerging therapies:

## No Curative Therapy

Existing treatments delay heterotopic ossification or reduce flare frequency but cannot reverse disease progression (Ikrama *et al.*, 2025).

## Handling Flares

Inflammatory pathways underlying flare-ups are poorly understood, and flare triggers remain unpredictable (Eekhoff *et al.*, 2022; Ikrama *et al.*, 2025).

## Safety Concerns

Potential off-target effects or immune reactions from gene/biologic therapy, as well as risks like premature growth plate closure from drugs such as Palovarotene (Vermeil *et al.*, 2025).

## Variability in Disease Expression

Differences in HO location, flare timing, and severity complicate clinical trial design and therapeutic targeting.

Delivering molecular/genetic therapies specifically to affected progenitor cells without affecting healthy tissue remains challenging (Vermeil *et al.*, 2025).

## Rarity of Disease

Limited patient numbers hinder validation of new therapies and restrict the scale of clinical trials (Shaikh, 2025).

## Limitations in Monitoring

The Lack of standardized, long-term assessment tools makes evaluating disease progression and therapy efficacy difficult (Ikrama *et al.*, 2025).

# CONCLUSION

Fibrodysplasia Ossificans Progressiva (FOP) is a rare and debilitating genetic disorder characterized by progressive heterotopic ossification, leading to severe disability and reduced quality of life. Current therapeutic strategies, including RARγ agonists, ACVR1 inhibitors, and anti-inflammatory agents, provide symptomatic relief and reduce flare frequency but cannot reverse disease progression. Ongoing and recent clinical trials have expanded our understanding of potential pharmacological

interventions, while advanced technologies such as gene therapy, genome editing, molecular drug design, and biomarker-based monitoring offer promising avenues for more precise and personalized treatments.

Despite these advancements, significant challenges remain, including unpredictable flare triggers, variability in disease expression, safety concerns with emerging therapies, limited patient populations, and the lack of standardized long-term monitoring tools. Addressing these gaps through continued research, innovative therapeutic development, and improved clinical trial design is essential to improve outcomes for individuals with FOP.

In summary, while substantial progress has been made in understanding FOP and developing potential interventions, future research must focus on curative strategies, safe and targeted therapies, and robust monitoring approaches to ultimately transform patient care.

## ACKNOWLEDGEMENT

The authors acknowledge MET's Institute of D. Pharmacy for providing academic support and resources for the completion of this review.

## ABBREVIATIONS

**FOP:** Fibrodysplasia Ossificans Progressiva; **ACVR1:** Activin A Receptor Type 1; **HO:** Heterotopic Ossification; **BMP:** Bone Morphogenetic Protein; **NSAIDs:** Non-Steroidal Anti-Inflammatory Drugs; **COX-2:** Cyclooxygenase-2; **ALK2:** Activin Receptor-Like Kinase 2; **SMAD:** Mothers Against Decapentaplegic Homolog; **FAPs:** Fibro-Adipogenic Progenitors; **RARγ:** Retinoic Acid Receptor Gamma; **IL-1:** Interleukin-1; **mTOR:** Mammalian Target of Rapamycin; **MRI:** Magnetic Resonance Imaging; **CT**: Computed Tomography; **AAV:** Adeno-Associated Virus; **CRISPR/Cas9:** Clustered Regularly Interspaced Short Palindromic Repeats/CRISPR-associated Protein 9.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## FINANCIAL SUPPORT AND SPONSORSHIP

None.

## AUTHOR CONTRIBUTIONS

Rutuja Sudam Binnar contributed to the conceptualization, literature review, and manuscript drafting.

Rahul Nimba Patil assisted in data compilation and manuscript editing.

Mohammad Rizwan Niyazuddin Shaikh provided critical revision and overall supervision.

## SUMMARY

This review highlights recent advances in understanding the molecular basis of fibrodysplasia ossificans progressiva and evaluates emerging targeted therapies aimed at modifying disease progression. Continued translational research and global collaboration are essential for developing safe, long-term, disease-modifying treatments.

## REFERENCES

Eekhoff, E. M. W., de Ruiter, R. D., Smilde, B. J., Schoenmaker, T., de Vries, T. J., Netelenbos, C., Hsiao, E. C., Scott, C., Haga, N., Grunwald, Z., De Cunto, C. L., di Rocco, M., Delai, P. L. R., Diecidue, R. J., Madhuri, V., Cho, T.-J., Morhart, R., Friedman, C. S., Zasloff, M., (2022). Gene therapy for fibrodysplasia ossificans progressiva: Feasibility and obstacles. Human Gene Therapy, 33 (15–16), 782–788. https://doi.org/10.1089/hum.2022.023

Hino, K., Ikeya, M., Horigome, K., Matsumoto, Y., Ebise, H., Nishio, M., Sekiguchi, K., Shibata, M., Nagata, S., Matsuda, S., & Toguchida, J. (2015). Neofunction of ACVR1 in fibrodysplasia ossificans progressiva. Proceedings of the National Academy of Sciences of the United States of America, 112(50), 15438–15443. https://doi.org/10.1073/pnas.1510540112

Ikrama, M., Usama, M., Israr, S., Humayon, M., Umair Javaid, M. U., Abbas, S., & Haider, M. A. (2025). Future of fibrodysplasia ossificans progressiva management: A systematic review of investigational therapies. Rheumatology & Autoimmunity, 5(1), 28–36. https://doi.org/10.1002/rai2.12168

International FOP Association. (2025). Ongoing clinical trials in fibrodysplasia ossificans progressiva.

Kaplan, F. S., & Pignolo, R. J. (2018). FOP: From biomolecules to hope. New England Journal of Medicine, 379(5), 439–447.

Kaplan, F. S., Chakkalakal, S. A., & Shore, E. M. (2012). Fibrodysplasia ossificans progressiva: Mechanisms and models of skeletal metamorphosis. Disease Models and Mechanisms, 5(6), 756–762. https://doi.org/10.1242/dmm.010280

Kaplan, F. S., Pignolo, R. J., Mukaddam, M. A., Baujat, G., Bravo, A. H., Brown, M. *et al.* (2024). The medical management of fibrodysplasia ossificans progressiva: Current treatment considerations. Proceedings of the Int Clin Council FOP, 3, 1–159.

Kaplan, F. S., Xu, M., Glaser, D. L., Collins, F., Connor, M., Kitterman, J., Sillence, D., Zackai, E., Ravitsky, V., Zasloff, M., Ganguly, A., & Shore, E. M. (2008). Early diagnosis of fibrodysplasia ossificans progressiva. Pediatrics, 121(5), Article e1295–e1300. https://doi.org/10.1542/peds.2007-1980

Kaplan, F. S., Zasloff, M. A., Kitterman, J. A., Shore, E. M., Hong, C. C., & Rocke, D. M. (2010). Early mortality and cardiorespiratory failure in patients with fibrodysplasia ossificans progressiva. The Journal of Bone and Joint Surgery. American Volume, 92(3), 686–691. https://doi.org/10.2106/JBJS.I.00705

Katagiri, T., Tsukamoto, S., Nakachi, Y., Kuratani, M., & Shaikh, U. (2018). Recent topics in fibrodysplasia ossificans progressiva. Endocrinology and Metabolism, 33(3), 331–338. https://doi.org/10.3803/EnM.2018.33.3.331

Kitoh, H. (2020). Clinical aspects and current therapeutic approaches for FOP. Biomedicines, 8(9), Article 325. https://doi.org/10.3390/biomedicines8090325

Li, Q. C., & Yuan, Q. (2025). Targeting to BMP9 to restrain flare-up of fibrodysplasia ossificans progressiva. EMBO Molecular Medicine, 17(1), 1–2. https://doi.org/10.1038/s44321-024-00180-5

Mejias Rivera, L., Shore, E. M., & Mourkioti, F. (2024). Cellular and molecular mechanisms of heterotopic ossification in fibrodysplasia ossificans progressiva. Biomedicines, 12(4), Article 779. https://doi.org/10.3390/biomedicines12040779

Mozumder, K. (2025). Fibrodysplasia ossificans progressiva (FOP): Genetic mechanisms, clinical features, and emerging therapeutic approaches. IOSR Journal of Pharmacy and Biological Sciences, 20(5), 21–27.

National Institute for Health, & Care Research Innovation Observatory. (2025). Fidrisertib for fibrodysplasia ossificans progressiva: Health technology briefing. University of Newcastle.

National Organization for Rare Disorders (NORD). (2024). Fibrodysplasia ossificans progressiva—Symptoms, causes, treatment. Rare disease database.

Pignolo, R. J., Shore, E. M., & Kaplan, F. S. (2011). Fibrodysplasia ossificans progressiva: Clinical and genetic aspects. Orphanet Journal of Rare Diseases, 6, 80. https://doi.org/10.1186/1750-1172-6-80

Shaikh, U. (2023). Novel therapeutic targets for fibrodysplasia ossificans progressiva. Human Gene Therapy, 34 (11–12), 732–742.

Shaikh, U., Khan, A., Kumari, P., Ishfaq, A., Ekhator, C., Yousuf, P., Halappa Nagaraj, R., Raza, H., Ur Rehman, U., Zaman, M. U., Lakshmipriya Vetrivendan, G., Nguyen, N., Kadel, B., Sherpa, T. N., Ullah, A., & Bellegarde, S. B. (2023). Novel therapeutic targets for

fibrodysplasia ossificans progressiva: Emerging strategies and future directions. Cureus, 15(7), Article e42614. https://doi.org/10.7759/cureus.42614

Smilde, B. J., Botman, E., de Ruiter, R. D., Smit, J. M., Teunissen, B. P., Lubbers, W. D., Schwarte, L. A., Schober, P., & Eekhoff, E. M. W. (2022). Monitoring and management of fibrodysplasia ossificans progressiva: Current perspectives. Orthopedic Research and Reviews, 14, 113–120. https://doi.org/10.2147/ORR.S337491

Verheij, V. A., Diecidue, R. J., Botman, E., Harrington, J. D., Haga, N., Hidalgo-Bravo, A., Delai, P. L. R., Madhuri, V., Al Mukaddam, M., Zhang, K., Cho, T.-J., Morhart, R., Keen, R., De Cunto, C. L., Friedman, C. S., Grunwald, Z., Zasloff, M., Netelenbos, J. C., Hsiao, E., (2025). Palovarotene in fibrodysplasia ossificans progressiva: Review and perspective. Expert Opinion on Pharmacotherapy, 26(3), 291–299. https://doi.org/10.1080/14656566.2025.2452938

Zhou, Y., Shi, C., & Sun, H. (2025). Advancements in mechanisms and drug treatments for fibrodysplasia ossificans progressiva. Journal of Zhejiang University. Science. B, 26(4), 317–332. https://doi.org/10.1631/jzus.B2300779

**Cite this article:** Binnar RS, Patil RN, Shaikh MRN. Advances in Therapeutic Strategies for Fibrodysplasia Ossificans Progressiva: From Symptom Management to Targeted Therapies. Asian J Biol Life Sci. 2026;15(1):37-44.