

Appropriate Clinical Management to Improve Outcomes for Patients with Fibrodysplasia Ossificans Progressiva (FOP)



Clinical Pearls: Medical Care for Patients with FOP

Avoid unnecessary medical interventions

Intramuscular (IM) injections and some surgical procedures can cause heterotopic ossification (HO) formation.

Glucocorticoids can treat acute flare-ups

Use glucocorticoids to treat pain and swelling in acute flare-ups, but do not use them chronically.

Coordinate care across medical specialties

Include consultation with an FOP expert, easily available via The International Clinical Council on FOP (www.iccfop.org).

Things to Consider When Managing and Treating Patients With FOP



Use Caution

- Medically necessary surgeries may be okay when guided by a team familiar with FOP
- Dental procedures (ie, over-extension of the jaw)
- Subcutaneous (SC) injections and peripheral IV insertions may be okay when administered by an experienced team member
- Ambulation and transfers, especially when shoulders and elbows are locked



Avoid

- Muscle trauma
- Unnecessary medical procedures, particularly elective surgeries and IM injections (medications or vaccines)
- Endotracheal intubation (can cause submandibular/jaw flare-ups)



Treatments Not Recommended

- Bone marrow transplant
- Chemotherapy: actinomycin, vincristine, vinblastine, cyclophosphamide, doxorubicin, and ifosfamide
- Radiation therapy
- Chronic immunosuppression
- Rosiglitazone
- Narcotics

Available* and Investigational Treatments for Patients With FOP

Clinical Target	Treatment	Mechanism of Action	FDA Regulatory Status as of July 2020
Activin A; BMPs	Garetosmab	Activin A antibody	Under investigation (phase 2 clinical trials)
ACVR1 (ALK2) gene	BCS9250, BLU-782, KER-047	ALK2 inhibition	Under investigation (phase 1 clinical trials)
ACVR1 (ALK2) gene, p.R206H mutation	Saracatinib	ALK2 inhibition	Under investigation (phase 2 clinical trials)
HO	Palovarotene	RAR-γ agonist	Under investigation (phase 3 clinical trials)
Inflammation	Montelukast	Leukotriene inhibitor to block inflammatory mediators; complementary action to cyclo-oxygenase inhibitors	Available for off-label use for FOP (approved for use to treat other disorders)
	<ul style="list-style-type: none"> • Glucocorticoids • NSAIDs (selective and non-selective COX-2 inhibitors) 	Minimize/reduce inflammation	Available for off-label or over the counter use for FOP (approved for use to treat other disorders)
Spontaneous flare-ups	Rapamycin	mTOR inhibitor for immunosuppression	Under investigation (phase 2 clinical trials)
	Cromolyn	Mast cell stabilizers to reduce mast cell degranulation	Available for off-label use for FOP (approved for use to treat other disorders)
	Amino-bisphosphonate (pamidronate, zoledronate)	Antiangiogenic, possibly anti-inflammatory; potential inhibition of early angiogenic fibroproliferative lesion	Available for off-label use for FOP (approved for use to treat other disorders)
Tissue hypoxia	Imatinib	HIF1-inhibitor, selective tyrosine kinase inhibitor	Available for off-label use for FOP (approved for use to treat other disorders)
	Apigenin	Naturally occurring HIF1-inhibitor	Available over-the-counter nutraceutical

* As of July 2020, there are no FDA-approved treatments for FOP. Available treatments are currently utilized in an off-label or over-the-counter manner.

Abbreviations:

ACVR1 - activin receptor type-1; ALK2 - activin receptor-like kinase-2; BMPs - bone morphogenetic proteins; COX-2 - cyclooxygenase-2; HIF1 - hypoxia-inducible factor 1; mTOR - mammalian target of rapamycin; NSAIDs - nonsteroidal anti-inflammatory drugs; RAR-γ - retinoic acid receptor gamma.

Resources Available for Patients



Coordinate care across medical specialties while consulting with an FOP expert:

The International Clinical Council (ICC) on FOP:

<https://www.iccfop.org/for-patients/fop-doctors-and-specialists/>



Stay connected and up-to-date on clinical trials:

ClinicalTrials.gov:

<https://clinicaltrials.gov>

International FOP Association (IFOPA):

https://www.ifopa.org/ongoing_clinical_trials_in_fop



Provide information to patients and families living with FOP:

IFOPA:

<https://www.ifopa.org>

(online support groups, mentoring program)

Finding Magic Mountain book by Carol Zapata-Whelan

Summary

Outcomes for patients with FOP can be improved with appropriate clinical management.

Faculty



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