ORIGINAL INVESTIGATIONS

Use of palovarotene in pathogenetic therapy of fibrodysplasia ossificans progressiva: real-world clinical practice experience

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Fibrodysplasia ossificans progressiva (FOP) is an ultra-rare monogenic disease manifested by an uncontrolled process of generalized heterotopic ossification. The first and only drug that has demonstrated in clinical trials the ability to slow the growth of new ossifications is palovarotene (PVT), a selective agonist of the gamma subtype of the retinoic acid receptor (RARγ), which has been approved for the treatment of FOP in certain age groups in several countries. Published real-world data on its use are limited.

Objective: *to analyze the experience of using PVT in FOP in real-world Russian clinical practice, with an emphasis on detailed patients' characteristics description and assessment of treatment efficacy and safety.*

Material and methods. *Nineteen patients with severe FOP (mean age 12.4 years; 14 patients younger than 14 years) who met the selection criteria were chosen for PVT therapy. Progression of the total volume of heterotopic ossifications (HO) was assessed using low-dose whole-body computed tomography (LDCT). The number of flare-ups before and during therapy was analyzed. Functional status was assessed using the CAJIS and CHAQ scales. Adverse events (AEs) occurring during treatment were recorded.*

Results and discussion. *All 19 patients with FOP had the classic disease phenotype with a pathogenic variant of the ACVR1 gene. Of these, 15 are currently receiving PVT in the ongoing regimen in combination with the Janus kinase inhibitor tofacitinib (TOFA); in 8 of these patients, treatment duration exceeds 1 year (median 18 months). Another 4 patients are awaiting access to the drug. According to serial LDCT examinations with a 12-month interval, no substantial increase in the total HO volume was detected. No deterioration in functional status was observed during therapy. No serious AEs were recorded. In 14 of 15 patients, mucocutaneous AEs (dryness, pruritus, retinoid dermatitis) of varying severity were observed.*

Conclusion. *Preliminary analysis of PVT use in patients with FOP showed no significant progression of HO and, at the same time, a favorable safety profile. Complementarity of the pathogenetic effects of PVT and TOFA may become a new therapeutic strategy for FOP.*

Keywords: *fibrodysplasia ossificans progressiva; heterotopic ossification; palovarotene; tofacitinib.*
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Fibrodysplasia ossificans progressiva (FOP) is an ultra-rare genetic disease (prevalence about 1:1,000,000) with an autosomal dominant type of inheritance. FOP is caused by a pathogenic variant of the *ACVR1* gene, which causes activation of the bone morphogenetic protein signaling pathway, leading to the formation of foci of heterotopic ossification in muscles, fasciae, tendons, and ligaments with subsequent progressive limitation of functional capabilities, loss of the ability for self-care, and ultimately to severe disability up to complete immobility [1]. The course of FOP is characterized by episodes of painful inflammatory infiltrates (flare-ups), which can be spontaneous, but are more often provoked by triggers: household injuries, falls, intramuscular injections (including during vaccination), surgical interventions, dental manipulations, invasive diagnostic procedures, for example tissue biopsy [2, 3]. The most important condition for the prevention of iatrogenic heterotopic ossification (HO) is the early diagnosis of FOP. The disease can be suspected at birth, long before the appearance of HO, by the characteristic congenital malformation of the big toes, usually bilateral, with shortening and valgus deviation, however, the final diagnosis must be confirmed by the result of a molecular genetic study with the identification of a pathogenic variant of the ACVR1 gene [1]. Until recently, therapeutic possibilities were limited mainly to symptomatic and anti-inflammatory options, unable to prevent the formation of new HOs [4, 5]. Palovarotene (PVT) was the first drug with proven pathogenetic activity in FOP. Its action is based on the selective activation of the retinoic acid receptor gamma (RARγ), which leads to the inhibition of SMAD 1/5/8 phosphorylation and consequently to the suppression of ALK2/SMAD-dependent chondrogenesis and endochondral ossification [6].

The therapeutic potential of PVT was consistently studied in a large-scale international clinical research program, which included a randomized placebo-controlled phase II study (NCT02190747), an open-label extension (with the administration of the drug to patients who received placebo) clinical study PVO-1A-202 (NCT02279095), as well as a phase III clinical study MOVE (NCT03312634), in which the comparison group consisted of patients included in the natural history study (NHS, NCT02322255) [6–9]. In the phase II clinical study, in patients with FOP receiving PVT during flare-ups, according to computer tomography data at the 12th week, the average volume of new HO in the groups with different PVT dosing regimens was 1.3×10^3 and 3.8×10i mmi (dose 5/2.5 and 10/5 mg, respectively) compared to 18.0×10^3 mmi in the placebo group, however, these differences

were not statistically significant (p=0.12) [6]. Despite the insufficiently convincing results, primarily due to the small size of the compared groups, which is typical for such a rare disease, the authors concluded that the drug is potentially effective. In the phase III study MOVE, the ability of PVT to slow the progression of HO during long-term therapy (up to 48 months) was confirmed, including both a maintenance dose regimen and intensified therapy during flare-ups. Under such a regimen applied for up to 48 months, the annual increase in new HO averaged 9.4 cm^3, which is 54–60% lower than in the natural history cohort (20.3 cmi/year). Special attention when using PVT was paid to studying the potentially negative impact on growth plates inherent to all retinoids, which necessitates taking into account the age and stage of skeletal maturation. In the MOVE study, premature closure of growth plates was recorded in 21 (37%) of 57 patients under 14 years of age. In this regard, the instructions for medical use of the drug, including the Russian one (September 2024), recommend starting therapy at an age no earlier than 8 years for girls and 10 years for boys, while performing regular monitoring of bone age and linear growth indicators. The complex multifaceted aspects of FOP pathogenesis are naturally and inextricably linked with the physiological processes of bone formation, which creates objective difficulties with developing an effective means of suppressing heterotopic ossification without a negative impact on normotopic bone.

Table 1. Clinical and demographic characteristics of patients with FOP

Indicator	Value
Sex, n (%):	
female	13 (68,4)
male	6 (31,6)
Age at the time of PVT prescription:	
M (min–max), years	12.4 (8–17,9)
<14 years, n (%)	14 (74)
Anthropometric indicators at the time of PVT prescription, M (min – max):	
height, cm	151 (129–180)
body weight, kg	45 (25–78)

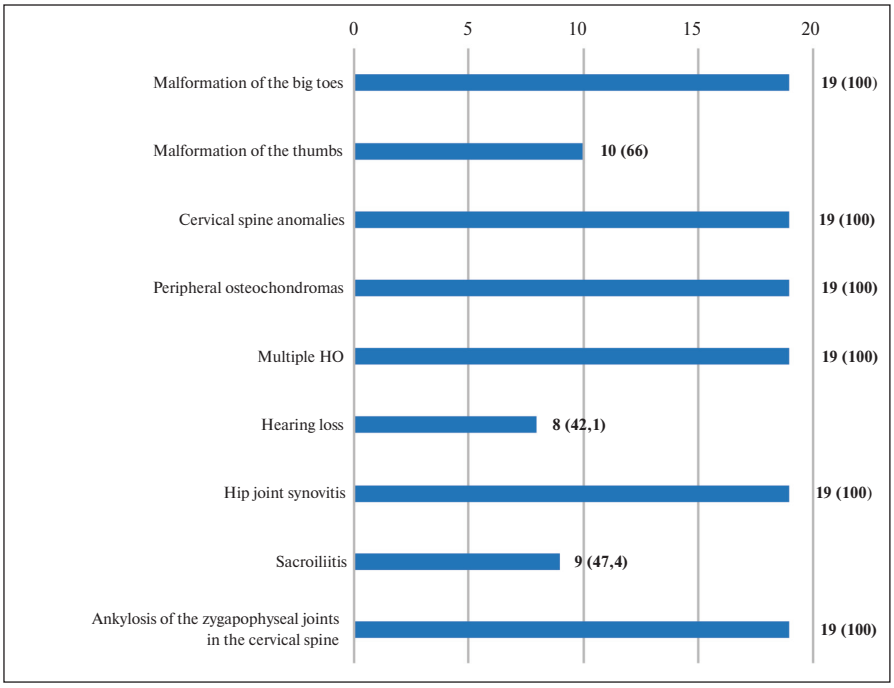

Fig. 1. *Phenotypic and rheumatologic characteristics of patients with FOP, n (%)*

The multiplicity of potential points of application capable of inhibiting excessive osteogenesis has been widely discussed in the literature of recent years, including the possibility of drug combinations acting on various molecular targets. As noted in the guidelines of the International Clinical Council on FOP (International Clinical Council on FOP, ICC) 2024 and in other recent publications, the inflammatory phase of a flare-up precedes chondrogenesis and the subsequent development of HO [4, 5]. In this context, the use of Janus kinase inhibitors, in particular tofacitinib (TOFA), which suppresses intracellular signal transmission from pro-inflammatory cytokines, is justified for reducing inflammatory activity. Thus, the drug has a universal anti-inflammatory effect in patients with a severe refractory course of FOP [10]. The multitarget therapy strategy assumes a synergistic effect of TOFA (suppression of the inflammatory process at the early stage of HO formation, i.e., during the flare-up period) and PVT (blocking the late stage of HO, endochondral ossification by inhibiting the RARγ/SMAD-dependent pathway) [11]. The first Russian experience of using PVT in combination with TOFA in 2 patients with active FOP proved successful and was described in 2025 [12]. The gradually accumulating clinical experience of pathogenetic therapy in a cohort of Russian patients is of great practical importance for the treatment of this severe disease with a focus on the choice of therapy regimen, safety monitoring, and evaluation of effectiveness, while the absence of publications in the world literature on the use of PVT in patients with FOP outside of clinical research programs creates conditions for the priority of Russian medicine at the international level.

The **goal** of the study is to analyze the Russian experience of using PVT in FOP under real clinical practice conditions with an emphasis on a detailed characterization of patients, evaluation of the effectiveness and safety of therapy.

Materials and methods. From October 2022 to December 2025, patients selected for the prescription of PVT pathogenetic therapy at the FSBSI V.A. Nasonova Research Institute of Rheumatology were included in an open cohort study. All patients underwent laboratory and instrumental studies standard for rheumatological practice, as well as low-dose computed tomography (LDCT) of the whole body. For each patient, a conclusion was drawn up justifying the need for PVT prescription and the dosing regimen. Based on the received conclusion, a package of documents was prepared for drug provision from the funds of the Circle of Kindness State Foundation. PVT was prescribed in accordance

with the officially approved instructions: in a maintenance dose regimen (3–5 mg/day depending on body weight) or in a dose intended for managing an exacerbation—a flare-up (4 weeks at a dose of 12.5–20 mg/day and 8 weeks at a dose of 6–10 mg/day depending on body weight).

Inclusion criteria: genetically confirmed diagnosis of FOP; presence of active manifestations of FOP; female patients from 8 to 18 years old and male patients from 10 to 18 years old.

The diagnosis was established according to the following criteria: clinical picture of the disease (congenital malformation of the big toes, presence of HO areas) in combination with a pathogenic variant in the ACVR1 gene confirmed by the results of a molecular genetic study at the FSBSI Academician N.P. Bochkov Research Centre for Medical Genetics.

Non-inclusion criteria: refusal of PVT therapy.

The effectiveness of therapy was assessed by the change in the total volume of heterotopic ossification (in cmi) according to the whole-body LDCT data with volumetric measurement. In patients with a PVT therapy duration of more than 12 months, the values of this indicator were compared during a follow-up study with a 12-month interval. To determine disease activity, the number of clinically manifest exacerbations (flare-ups) occurring during the observation period was analyzed.

Visualization of HO was performed using non-contrast LDCT on a 128-slice computed tomography scanner GE Revolution EVO (GE HealthCare). For the scanning program, the following parameters were selected: voltage: 100 kV, current: 85 mA, slice thickness: 1.25 mm. On the GE Revolution EVO workstation, to view images in DICOM PACS format, the Volume Viewer program was used with slice-by-slice segmentation of all HO separately in several anatomical regions. HO volume was determined by segmenting each axial slice using semi-automatic algorithms; additionally, manual contouring was used for optimization (AW Server, version 3.2). HO volumes (in mm^3) were calculated separately for each anatomical region and then summed for the total body volume.

The effectiveness of therapy was additionally assessed by the functional status of the patients using the CHAQ questionnaire (Childhood Health Assessment Questionnaire) [13] and the Cumulative Analogue Joint Involvement Scale for FOP (CAJIS) [14]. In addition, the dynamics of anthropometric indicators (height), data from clinical and laboratory monitoring (clinical, biochemical blood tests), as well as the frequency and nature of adverse events (AEs) during PVT therapy and concomitant therapy were analyzed.

Statistical data processing. The calculation of the required sample size at the study planning stage was not performed. Data analysis was performed using the Statistica statistical software package, version 12.0 (StatSoft Inc., USA). Quantitative indicators were described indicating the median and interquartile range (Me [25th; 75th percentiles]) or the mean value depending on the nature of the distribution and data volume. To compare quantitative whole-body LDCT data (total HO volume) recorded during visits 1 (at the time of PVT prescription) and 2 (12 months after PVT prescription), the Wilcoxon test was used.

The study was approved by the local ethics committee (protocol №2 dated 01/27/2022). Upon hospitalization, informed consent was obtained from each patient and their legal representative for the anonymous use of their medical data for scientific purposes. The information presented in this article is anonymized; identifying information has been removed.

Table 2. Therapy prior to PVT initiation in patients with FOP (n=19), n (%)

Drug	Number of patients
NSAIDs	19 (100)
GC:	
oral	10 (53)
intravenous (pulse therapy)	11 (58)
Bisphosphonates	7 (37)
TOFA	18 (95)

Note. NSAIDs: nonsteroidal anti-inflammatory drugs; GC: glucocorticoids.

Results. The study included 19 patients (68% female) with FOP who were prescribed PVT pathogenetic therapy. All patients had a confirmed presence of a pathogenic variant of the *ACVR1* gene: in 18 c.617G>A (p.Arg206His), in 1 female patient the ultra-rare variant c.1067G>A (p.Gly356Asp). Clinical and demographic characteristics of the patients are presented in Table 1.

All 19 patients corresponded to the classic FOP phenotype. The distribution of clinical manifestations and radiological signs is presented in Fig. 1.

Based on the examination results, which revealed signs of arthritis of the large joints and sacroiliitis, a competing rheumatological diagnosis (juvenile chronic arthritis in 10 or juvenile ankylosing spondylitis in 9) was justified in all patients.

The full range of drugs used at various stages of management of patients with FOP is reflected in Table 2. At the time of this analysis, 15 patients are receiving PVT, and 4 are waiting for the drug. In more than half of the patients (n=9, 60%), PVT was prescribed at a maintenance dose, and in 6 (40%), an increased dose regimen during an exacerbation (flare-up) was additionally used. The average duration of therapy is 18 months (from 1 to 32 months). 7 patients have been receiving PVT for less than 1 year, 2 for less than 2 years, 6 for more than 2 years. The key indicators at the time of prescribing PVT therapy in all 15 patients with FOP sequentially included in the analyzed group are presented in Table 3.

To evaluate the pathogenetic effect of PVT and HO growth, whole-body LDCT was performed with fixed time intervals of measurement, optimally annually. To date, a total of 8 patients (5 female and 3 male) have been receiving PVT therapy for more than 1 year. The results of their dynamic observation were selected for the final analysis with an assessment of the total HO volume according to whole-body LDCT data, the dynamics of functional status using the functional CAJIS scale, and the CHAQ questionnaire during two consecutive visits: at the time of PVT prescription and after 12 months (Table 4). The average values of these indicators at the time of the baseline visit and 12 months after the start of PVT therapy are presented in Table 5

For all analyzed indicators during 12 months of PVT therapy, no increase ($p>0.05$) was revealed in HO volume, CAJIS and CHAQ values (see Table 5, Fig. 2).

From the moment PVT was prescribed, flare-ups of FOP were noted in 4 patients. At the same time, no increase in HO volume was revealed in them, just as in the other 4 patients who remained stable while taking the drug. The detailed characteristic of AEs for each patient is reflected in Table 3. During the treatment

Table 3. Baseline characteristics at PVT initiation, dosing regimen, and AEs

Patient №	Sex	Age, years	Height, cm	Body weight, kg	HO volume, cm^3	Date of starting t PVT treatmen	Duration of therapy, months	Use of flare-up regimen	AEs
1	F.	14	161	52	49,7	23.04.2023	32	No	Dry skin, minor itching
2	F.	10,1	147	35	271,2	30.09.2023	27	No	Dry skin, cheilitis
3	M.	17,9	180	60	622,65	15.07.2023	29	Yes	Severe itching and dermatitis when using the increased dose
4	F.	14,3	150	59	710	18.12.2023	24	Yes	Severe peeling, itching, hyperemia of the skin when using the increased dose
5	M.	10,1	144	37	56,69	16.11.2023	25	Yes	Retinoid dermatitis, severe peeling when using the increased dose
6	F.	11	156	39	46,9	15.02.2024	22	No	Dry skin
7	F.	13,6	150	45	297,13	15.04.2023	32	Yes	Retinoid dermatitis
8	M.	12,9	155	41	182,1	15.04.2024	20	No	Dry skin
9	M.	13,1	165	65	359,45	01.12.2024	13	No	Short-term dyspeptic phenomena, dry skin
10	F.	13,2	129	25	Н. д.	26.12.2024	12	No	Short-term dyspeptic phenomena, dry skin
11	F.	17	166	56	9,2	15.04.2025	8	No	Exacerbation of KJ and hip joints arthritis, dry skin
12	F.	8,9	133	28	89,67	03.02.2025	10	No	Dry skin
13	F.	8,1	147	73	231,2	01.12.2024	13	Yes	Dyspeptic phenomena, increased transaminase levels (<3 norms), dry skin
14	F.	10,7	160	44	147,25	01.06.2025	7	Yes	Dry skin and mucous membranes when using the increased dose
15	F.	8,1	122	28	26,81	15.11.2025	1	No	No

Note. V1: visit 1; V2: visit 2.

Table 4. Total HO volume and CAJIS and CHAQ scores in 8 patients with FOP receiving PVT for more than 12 months

Patient №	Age at time of PVT prescription, months	Duration of treatment, months	HO volume, V1	CAJIS, V1	CHAQ, V1	HO volume, V2	CAJIS, V2	CHAQ, V2
1	168	32	49,7	9	2	53,79	10	2,25
2	122	27	271,2	7	1,875	271,4	7	1,875
3	215	29	622,65	16	2,5	622,8	13	2,5
4	172	24	710,0	11	2,5	711,5	11	2
5	122	25	56,69	4	1,875	60,55	6	1,625
6	132	22	46,9	10	1,625	47,2	10	1,625
7	163	32	297,13	6	1,875	297,4	6	1,75
8	155	20	182,1	11	2,625	182,1	11	2,625

Note. V1: visit 1; V2: visit 2.

period, no serious AEs were registered, therefore the drug was not discontinued in any patient. In 14 out of 15 patients, mucocutaneous manifestations, class-specific for the entire group of retinoids, were observed with varying degrees of severity depending on the PVT dose. In 11, mild skin changes occurred: dryness, cheilitis, and short-term itching. In 4 patients receiving PVT at an increased dose (during the flare-up regimen), more significant skin manifestations of the retinoid dermatitis type were observed with erythema, peeling with severe itching, which regressed after adjusting the drug dose and using emollients. In 3 patients, short-term dyspeptic phenomena were noted (nausea, diarrhea, vomiting), which resolved independently. In 1 female patient with comorbid grade 3 obesity and fatty hepatosis, a short-term increase (<3 norms) in alanine aminotransferase and aspartate aminotransferase was recorded. In another female patient aged 17.5 years, who initially did not receive TOFA, an exacerbation of arthritis developed during the first month of PVT therapy, confirmed by ultrasound and magnetic resonance imaging data of the joints, possibly within the natural course of the disease during late (after 15 years of age) manifestation of clinical FOP symptoms or due to the mediated pro-inflammatory effect of retinoids. After adding TOFA to the therapy, a reduction in arthritis manifestations was achieved.

During the treatment, linear growth indicators were measured at baseline and after 12 months of therapy. The average height at the baseline visit was 155.43±11.2 cm, after 12 months 158.45±10.6 cm, the average annual growth increase 3.025±2.4 cm/year, which indicates the absence of significant growth suppression during PVT therapy. Growth indicators corresponded to age norms for this age group (average Z-score: -0.42±0.85), which indicates the absence of a negative impact of PVT on the linear growth of patients when used in the specified doses. Personalized data reflecting growth dynamics are presented in Table 6.

Table 5. Median and mean values of total HO volume and CAJIS and CHAQ scores in patients with FOP (n=8)

Indicator	Baseline	After 12 months
Total HO volume, cm^3:		
Me [25th; 75th percentiles]	226,7 [54,9; 378,51]	226,7 [58,8; 378,51]
M (min–max)	279,5 (46,9–710,0)	280,5 (46,9–710,0)
Total CAJIS score:		
Me [25th; 75th percentiles]	9,5 [6,75; 11,0]	10,0 [6,7; 11,0]
M (min–max)	9,25 (4–16)	9,25 (4–13)
Total CHAQ score:		
Me [25th; 75th percentiles]	1,94 [1,88; 2,5]	1,94 [1,84; 2,3]
M (min–max)	2,1 (1,625– 2,625)	2,0 (1,625–2,625)

Discussion. The present work includes all Russian patients with FOP who underwent PVT therapy, and to date, is the only publication in the world dedicated to real clinical practice of its use. The path to obtaining evidence of PVT effectiveness proved difficult, as the specifics of the disease development and its exceptional rarity complicated the choice of clinical study methodology with the definition of primary and secondary endpoints within a classic randomized placebo-controlled design [6]. Changing the design to an open-label mode in the phase III study MOVE and

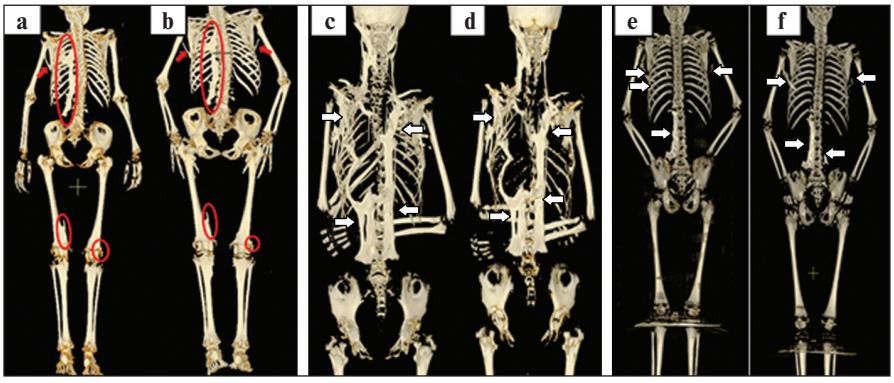

Fig. 3. *Assessment of total HO volume based on whole-body LDCT during PVT therapy in patients № 1, 2, and 5 at baseline (a, c, d) and after 12 months (b, e, f). Patient № 1, 14 years: a – 49.7 cm^3, b – 53.79 cm^3. Patient № 2, 11 years: c – 271.2 cm^3, d – 271.4 cm^3. Patient № 5, 10 years: e – 56.69 cm^3, f – 60.55 cm^3*

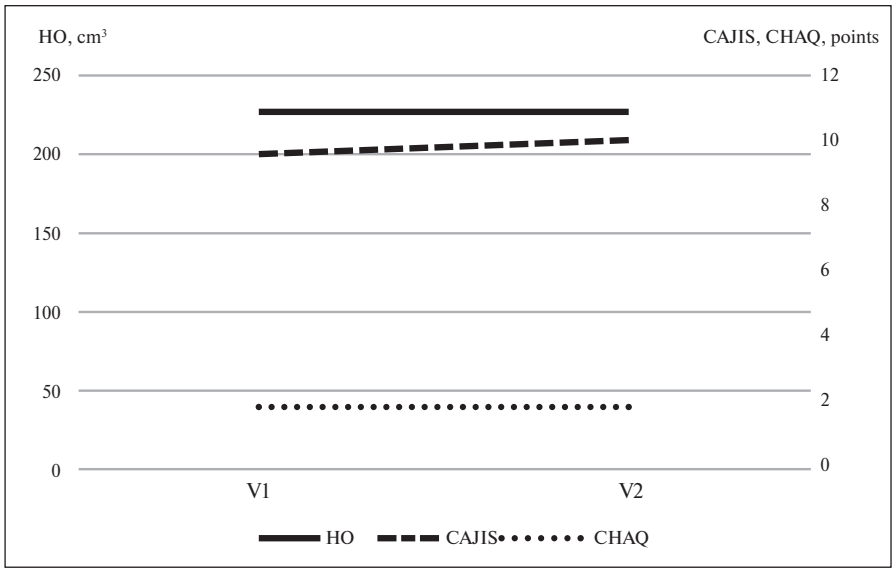

Fig. 2. *Changes in the median total HO volume, CAJIS, and CHAQ over 12 months of PVT therapy*

conducting a parallel study of patients with the natural course of the disease (NHS) as a comparison group allowed proving the effectiveness of PVT in terms of inhibiting the growth of new HO. It should be emphasized that in 29% of patients receiving PVT, a decrease in HO volume was recorded, whereas in the natural history group, such dynamics were noted only in 5% of cases, although these indicators were not originally included in the effectiveness criteria in the study endpoints. It is worth noting that Russian centers were not included in the program of international clinical studies, despite our repeated appeals to their organizers; nevertheless, several Russian patients, at the initiative of a patient organization, were participants in the FOP natural history study [9]. This allows us with confidence to use the published data of the specified observational study for comparison with our results, especially in part of the predicted increase in HO volume according to LDCT data.

Our preliminary results of PVT use proved to be very encouraging and generally comparable with the data from the MOVE study. Thus, in one 14-year-old female patient who started PVT therapy in 2023, the HO increase was only 2.73 cmi (from 49.7 to 53.79 cm^3) over 1.5 years, and in another patient 10 years after the start of PVT use, the HO increase was 4.95 cm^3/year, which turned out to be significantly lower than the rate of HO increase before the start of therapy (very fast growth of HO volume from 1.234 to 56.69 cm^3 in 9 months). The conducted analysis showed that the prescription of PVT allows slowing the rate of HO increase in patients with FOP. In patients with an initial HO volume <100 cm^3, their stability or moderate increase in volume (on average 7.5%) was noted, and in patients with an initial HO volume >200 cm^3, complete stabilization of the process (absence of increase). Unlike the MOVE study, which evaluated the increase in new heterotopic ossification, our observations analyzed the total volume of HO, and the results we obtained demonstrated even greater effectiveness in terms of reducing the rate of HO progression than in the international MOVE study. We believe that this may be related to the combined therapy used in all our patients. The synergistic effect of the two drugs acting on different stages of FOP pathogenesis (the retinoid pathway and JAK/STAT-dependent inflammation) likely provides a more pronounced inhibition of HO progression, which suggests potential advantages of combined therapy for patients with FOP. It is important to note that the greatest effectiveness of PVT and preservation of patients' functional capabilities can naturally be achieved with early initiation of therapy, at stages preceding the formation of massive HO. The dynamic CAJIS analysis showed a predominant stabilization of indicators, however, in individual patients, changes were fixed in both directions: both a decrease in CAJIS values (improvement) and their increase. CHAQ parameters, with stable indicators of total HO volume in most patients, remained unchanged, while in some cases, small multidirectional shifts (both improvement and worsening) were observed, which may reflect the influence of pain, FOP activity, limitation of mobility, and household activity in specific periods that do not always coincide with the moments of filling out the questionnaire. In general, it can be noted that CAJIS/CHAQ indicators demonstrated a predominantly stable functional status with moderate individual variability.

One of the important aspects of safety in retinoid therapy, widely discussed in the literature, is the potential acceleration of growth plate closure in bones. In our observations, no significant negative impact of PVT was revealed on the dynamics of linear growth in adolescent patients. In 7 (87.5%) of 8 patients during the therapy period, growth increase was maintained (average increase 0.8±0.3 cm/year), while in one boy who started PVT treatment at the age of 10, growth increased by 5 cm during the first year, and by a total of 8 cm over 2 years. This indicates the absence of a pronounced suppressive effect of PVT on growth zones at the doses used. The unique experience of our center, including the observation of 65 patients with FOP, most of whom have now reached adulthood, indicates that this disease is often associated with tall stature, and the periods of maximum HO progression coincide with periods of linear growth, while large HO affecting several segments of the musculoskeletal system are the leading cause of gross body deformities.

Of considerable importance for the interpretation of our study results is the nature of concomitant therapy. In all patients, along with PVT, anti-inflammatory therapy was used, which corresponds to the real clinical practice of managing patients with active FOP. Taking into account the pathogenesis of the disease [11], it is advisable to consider the obtained results as a reflection of the complementary influence of the two directions of therapy. At the same time, targeted anti-inflammatory therapy could potentially contribute to reducing the frequency and/or severity of flare-ups, while PVT, through its effect on the late stages of endochondral bone formation, to the stabilization of HO volume, which was reflected in the minimization of the increase in total HO volume according to serial LDCT data in most patients. Taking into account the study design, small sample size, and the lack of a control group, it is impossible to isolate the quantitative contribution of each therapy component, but it should be noted that the use of TOFA in almost all patients preceded the prescription of PVT and did not contradict the necessity of using the latter.

Table 6. Changes in linear growth parameters in patients with FOP receiving PVT

Patient №	Sex	Age at time of PVT prescription, years	Height at time of PVT prescription, cm	Height after 12 months of PVT therapy, cm	Height after 24 months of PVT therapy, cm
1	Female	14,0	161,0	161,0	161,0
2	Male	10, 2	147,0	153,0	155,0
3	Male	17,9	180,0	182,0	182,0
4	Female	14,3	150,0	152,0	152,0
5	Male	10,2	144,0	149,6	–
6	Female	11,0	156,0	159,0	–
7	Female	13,6	150,0,	150,0	–
8	Male	12,9	155,0	161,0	–

Nevertheless, the very structure of the observed effect (predominant stability of the total HO volume with moderate variability in functional scales) supports the clinical hypothesis that controlling the inflammatory phase of flare-ups and blocking endochondral ossification can mutually reinforce each other, forming a practical strategy for managing patients with active FOP.

Conclusion. The results of the observational study on the use of PVT allow us to conclude that it is possible to slow the progression of heterotopic ossification in patients with FOP. Taking into account the pathogenesis of the disease, it seems reasonable to consider the strategy of the combined use of PVT and TOFA as a synergistic multi-target therapy model.

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