Minimal essential text

(Key findings + graphics)

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The Use of Tocilizumab in 40 Patients With Polyarticular Juvenile Idiopathic Arthritis: the Results of a Retrospective Study

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Background*. The issue of a therapy of children with juvenile idiopathic arthritis (JIA) with intolerance or insufficient effectiveness of methotrexate remains actual.* ***Objective****: Our aim was to study the efficacy and safety of tocilizumab in patients with polyarticular JIA.* ***Methods****. In a retrospective study, we studied the results of the use of tocilizumab in patients with active polyarticular JIA (5 active joints) resistant to prior therapy with methotrexate or a combination of methotrexate with other nonbiologic disease-modifying anti-inflammatory drugs.* ***Results****. The data of 40 children (83% girls) with the onset median of polyarticular JIA of 4.8 (2.9, 8.1) years and the interval between the disease onset and the initiation of tocilizumab therapy of 5.7 (1.8, 8.5) years was analyzed. Tocilizumab was used as an intravenous infusion of 8 mg/kg (with a weight _ 30 kg) or 10 mg/kg (with a weight < 30 kg) every 4 weeks. The duration of tocilizumab monotherapy in 5 (13%) children was 1,109 days (452; 1,542). The stages of inactive disease (according to the criteria of C. Wallace, 2004) in 6 months of tocilizumab therapy reached 6 (15%) patients, in 42 months — 32 (80%) patients. In 3 patients, tocilizumab was canceled due to persistent remission. After 6 months of treatment, there was a marked decrease in erythrocyte sedimentation rate, C-reactive protein concentration, number of leukocytes and platelets (in all cases, p < 0.001) to normal values, which persisted throughout the whole period of drug administration. Predictors for achieving inactive disease were the initial (at the onset of tocilizumab therapy) number of peripheral blood leukocytes < 9.0×10^9/l [relative risk (RR) 1.92; 95% confidence interval (CI) 0.9–4.6)] and the absence of prior biological therapy (RR 1.92, 95% CI 0.9–4.6). The most frequent side effects of tocilizumab therapy were transient hypercholesterolemia (in 13), hypertriglyceridemia (in 4), transient grade II neutropenia (in 1).*
Conclusion*. The long-term efficacy and relative safety of tocilizumab in children with polyarticular JIA have been showed.*
Key words*: children, polyarticular juvenile idiopathic arthritis, tocilizumab, interleukin 6.*
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RESULTS

Table 1. Characteristics of studied population (*n* = 40)

Girls, n (%)	33 (83)
Onset age of JIA, years	4,8 (2,9; 8,1)
Number of active joints, n	16 (6; 26)
JIA categories, n (%) • extended oligoarthritis • polyarthritis	 6 (15) 34 (85)
Hemoglobin, g/l	123 (112; 126)
White blood cells, 10^9/l	8,1 (7,2; 10,2)
Platelets, 10^9/l	372 (306; 450)
Erythrocyte sedimentation rate, mm/h	29 (11; 48)
C-reactive protein, mg/l	14,4 (3,0; 45,0)
Uveitis (active or in inactive), n (%)	5 (13)
Treatment*, n (%): • NSAID • Systemic corticosteroids • Methotrexate • Cyclosporin A • Leflunomid • Methotrexate+ Cyclosporin A • Methotrexate + Leflunomid	 26 (65) 14 (35) 37 (93) 7 (18) 9 (23) 6 (15) 9 (23)
Previous biologic treatment , n (%): • One biologic • Two biologics: ✓ TNFα ✓ abatacept	21 (53) 10 (25) 11 (28) 5 (13) 6 (15)
Onset age of tocilizumab, years	11,5 (8,5; 14,3)
JIA duration*, years	5,7 (1,8; 8,5)
JIA duration, days min-max, days	1109 (452; 1542) 184–2142

Note. * — on the start of tocilizumab treatment. JIA — juvenile idiopathic arthritis, NSAID — non-steroid anti-inflammatory drugs.

Table 2. Additional treatment outcomes

Treatment parameters		**n (%)**
Treatment outcomes	Inefficacy in arthritis Inefficacy in uveitis Adverse effects (infectious dideases) Receive tocilizumab at the last visit	5/40 (13) 2/40 (5) 1/40 (3) 29/40 (73)
Treatment (at the last visit)	NSAID Systemic corticosteroids Tocilizumab (monotherapy) Tocilizumab + methotrexate	0 0 5 (15) 30 (75)

	Tocilizumab + leflunomide Tocilizumab + methtrexate + leflunomide	2 (5) 1 (3)

Table 3. Dynamics of JIA activity on the tocilizumab treatment

Parameter	**Исходно (n =40)**	**6 мес (n =36)**	**12 мес (n =28)**	**18 мес (n =24)**	**24 мес (n =20)**	**30 мес (n =19)**	**36 мес (n =16)**	**42 мес (n =14)**
Number of active joints, n	16 (6; 26)	4 (2; 11)	1 (0; 5)	2 (0; 5)	0 (0; 2)	0 (0; 2)	0 (0; 2)	0 (0; 0)
p	-	0,001	0,001	0,001	0,001	0,001	0,001	0,005
Hemoglobin, g/l	123 (112; 126)	129 (120; 133)	131 (126; 140)	135 (128;142)	133 (127; 138)	130 (124; 140)	133 (123; 143)	137 (129; 147)
p	–	0,001	0,001	0,001	0,002	0,001	0,002	0,008
White blood cells, $\times 10^9$/l	8,1 (7,2; 10,2)	5,6 (4,7; 7,2)	5,5 (5,0; 6,0)	5,4 (4,9; 7,2)	5,4 (4,8; 7,7)	5,7 (4,9; 6,5)	6,1 (5,4; 7,9)	5,7 (5,1; 7,1)
p	–	0,001	0,001	0,005	0,03	0,03	0,07	0,07
Platelets, $\times 10^9$/л	372 (306; 450)	258 (189; 322)	248 (206; 285)	254 (206; 299)	248 (210; 282)	220 (191; 265)	253 (199; 293)	262 (248; 319)
p	–	0,001	0,001	0,001	0,001	0,001	0,004	0,11
Erythrocyte sedimentation rate, mm/h	29 (11; 48)	3,0 (2; 5)	3,0 (2; 5)	3,0 (2; 5)	2,0 (2; 3)	2,0 (2; 3)	2,0 (2; 3)	2,0 (2; 2)
p	–	0,001	0,001	0,001	0,001	0,001	0,001	0,008
C-reactive protein, mg/l	14,4 (7,5; 44,2)	0,5 (0,3; 2,4)	0,4 (0,2; 0,5)	0,3 (0,2; 0,5)	0,4 (0,2; 0,5)	0,6 (0,2; 3,2)	0,4 (0,6; 1,3)	0,4 (0,3; 0,5)
p	–	0,001	0,001	0,001	0,001	0,001	0,004	0,003
Remission, n (%)	0	5/33 (15)	10/27 (37)	10/21 (48)	12/19 (63)	11/18 (61)	9/15 (60)	8/10 (80)
*p**	–	0,016	0,001	0,001	0,001	0,001	0,001	0,001

Low disease activity,n (%)	0	8/33 (24)	14/27 (52)	10/21 (48)	13/19 (68)	13/18 (72)	12/15 (80)	9/10 (90)
*p**	–	0,001	0,001	0,001	0,001	0,001	0,001	0,001

Note. P-value related to comparison of each parameter to initial parameter: *p* — Wilcoxon matched paired test to quantative variables , *p** — McNemar's test — for categorical variables . JIA — juvenile idiopathic arthritis.

Table 4. Dynamic of serum lipids on the tocilizumab treatment

Parameters	**Before tocilizumab**	**6 months**	**12 months**	**18 months**	**24 months**	**30 months**	**36 months**
Cholesterin, mmol/l	4,4 (4,0; 4,8)	4,8 (4,6; 5,5)	4,5 (4,1; 4,9)	4,5 (3,8; 5,0)	4,2 (3,9; 4,9)	4,2 (3,9; 5,1)	4,2 (3,9; 4,7)
Hypercholesterinemia, n (%)	11/23 (49)	13/15 (87)[#]	8/13 (62)	5/8 (63)	4/10 (40)	5/11 (46)	3/7 (43)
Triglycerids, mmol/l	0,90 (0,64; 1,00)	1,00 (0,70; 1,16)	1,00 (0,77; 1,40)	1,20 (0,72; 1,40)	1,35 (0,66; 1,60)	1,08 (0,90; 1,26)	0,70 (0,66; 0,90)
Hypertriglyceridemeia, n (%)	0/14 (0)	2/10 (20)	3/8 (38)*	2/7 (29)	4/7 (57)*	1/6 (17)	0/4 (0)

Note. * — $p < 0,05$, calculation related to initial parameters with McNemar test.

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Not specified.

CONFLICT OF INTERESTS
Mikhail M. Kostik — receiving fees for lecturing from Pfizer, Ebbvi, Roche, Novartis.
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