Objectives: The aims of this study were to evaluate AMH serum levels in a cohort of young adult women affected from JIA, to compare these levels between patients and healthy controls and to assess whether the presence of the disease and the influence of previous exposure to disease-modifying antirheumatic drugs (DMARDs) and of other disease parameters may affect the ovarian reserve.

Methods: Forty women with a diagnosis of JIA, aged 18 to 25 years and with regular menses, and 20 healthy women age-matched were evaluated. Anti-Müllerian Hormone serum levels were measured according to a 2-stage enzyme-linked immunosorbent assay (ELISA) technique using a commercially available kit (AMH Gen II ELISA; Beckman Coulter). Clinical and demographic characteristics, disease duration, previous and current therapies disease activity score on 44 joints (DAS), health assessment questionnaire (HAQ) were performed at the time of blood sample.

Results: JIA patients had a mean age of 21.4 ± 3.2 years, a disease duration of 11.5 ± 6.6 years, a DAS of 1.22 ± 0.58 , and 12 (30%) were smokers. No significant differences were found in our cohort of JIA and healthy subjects in AMH serum levels (5.6 ± 0.4 vs 6.6 ± 0.6 ng/ml, respectively, $p=0.5$).

Considering the JIA cohort, 23 patients (57.4%) were treated with methotrexate (MTX) for a mean period of 2.1 ± 3.1 years and 20 (50%) with anti-TNF drugs for 4.3 ± 2.3 years. Twelve JIA women (30%) were treated with both MTX and anti-TNF. No correlations were found between AMH serum levels and patients age ($p=0.6$), disease duration (years) ($p=0.67$) and duration of therapy with MTX ($p=0.5$) or anti-TNF ($p=0.11$).

Dividing JIA patients according to MTX use, no differences were observed between MTX users and non users patients in AMH levels (6.0 ± 0.5 vs 5.1 ± 0.5 ng/ml, respectively, $p=0.22$), age, disease duration and other clinical characteristics. Patients exposed to anti-TNF had AMH serum levels tendentially higher than non users patients (6.3 ± 0.6 vs 4.9 ± 0.5 ng/ml, respectively $p=0.07$).

Conclusions: In our JIA group of young adult JIA women, ovarian reserve seems not be changed by the presence of the disease, the long disease duration and the use of immunosuppressive drugs. These findings could be important for adult JIA patients.

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THU0500 PHOTOBIOSTIMULATION OF CHRONIC CERVICAL PAIN IN JUVENILE POLYARTHRITIS

C. Ailioaie, L.M. Ailioaie. Dept. of Medical Physics, Iasi, Romania, "Al. I. Cuza" University, Iasi, Romania

Background: Chronic pain management in juvenile arthritis constitutes a special provocation not only for the medical doctors, but also for the patients and parents. Despite the extensive use of the biological agents with high efficacy, combined with the multimodal therapies, chronic pain still remains an important issue for the public health, with implications on the activities of daily living and the scholar performances. Lasers could be used for transmitting biological messages and initiating metabolic changes within living cells: no more pain, much more energy, will contribute to muscular and joints repair.

Objectives: Aim of the present study was to evaluate the effects of photobiostimulation combined with DMARDs in patients with juvenile polyarthritis and chronic cervical pain.

Methods: 62 patients diagnosed with juvenile polyarthritis (ILAR criteria), 11.4 years mean age were randomly divided in Group I (42 patients treated with local laser biostimulation and methotrexate), comparatively with a Group II - control (20 patients) treated with methotrexate and placebo laser, for a period of 9 months. Group I received local laser biostimulation with a dose of 2.5 J/cm^2 in 14 latero-cervical painful points, corresponding to the 7 cervical vertebrae, 1 point on the insertion of sternocleidomastoid muscle on the styloid process, and 1 point on each loco-regional submandibular lymphatic ganglions, using a GaAlAs laser probe of 670 nm, 25 mW output power and a modulation frequency of 10 Hz. 45 joules were applied daily as laser treatment, 10 sessions per month, repeated 3 times, in the 9 months. For all the patients, the main medication was methotrexate in a dose of 0.6 mg/kg (maximum 20 mg) per week, steroids and symptomatic drugs, when necessary. Tutors and the older children have signed the informed consent. Measurement of the subjective pain was on VAS (0 – 100 mm), and objective pain was assessed with an electronic device, the Algometer Commender. The range of motion for flexion/extension, and the rotation to the left/right of the cephalic extremity was measured with Dualer IQ Inclinometer.

Results: In the end of study, the level of chronic pain estimated with Commender Algometer decreased by 74.6% in Group I, compared with only 41% in the control Group, and the range of motion in the affected cervical segment assessed with Dualer Inclinometer increased by 66% in the first Group, compared with only 34% in placebo group.

Conclusions: Laser biostimulation proved to be an effective method for the complex management of chronic pain in juvenile polyarthritis.

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THU0501 EFFICACY AND SAFETY OF METHOTREXATE AS MAINTENANCE THERAPY FOR CHILDREN WITH ANTI-N-METHYL-D-ASPARTATE RECEPTOR (NMDAR) ENCEPHALITIS: EXPERIENCE OF A SINGLE CENTER

D. Ramos-Bello, A.N. Rangel-Botello, G. Aguilera Barragan-Pickens, T.A. Luna-Zúñiga, A.J. Pedro-Martínez, G. Martínez-Flores, A. Bravo-Oro, C. Abud-Mendoza. Unidad regional de Reumatología y Osteoporosis, Hospital Central "Dr. Ignacio Morones Prieto" y Facultad de Medicina de la Uaslp, SLP, Mexico

Background: Autoimmune-mediated encephalitis (A-ME) in children remains as a diagnostic and therapeutic challenge (1). These patients have a 12% risk of relapse, which is usually more severe (2). We previously proposed the therapy with methotrexate (MTX) for this condition (3), and we are offering now additional data on its potential benefits.

Objectives: To describe the outcome of children with A-ME receiving MTX for at least one year after stabilization of symptoms.

Methods: In this retrospective study we recruited 11 patients (7 females) with A-ME, a mean age of 7.5 years (range 8 months - 14 years), and with a median follow up of 22 months. In all cases, anti-NMDAR antibodies (subunit NR1) were detected in the CSF. Data from these patients were collected by consulting medical records. Relapse of encephalitis was defined as new onset of symptoms occurring after at least 2 months of remission, in the absence of other CNS disease.

Results: Patients presented with seizures ($n=10$), behavioral changes ($n=11$), psychosis ($n=11$), speech problems ($n=10$), and autonomic/breathing dysregulation ($n=9$). Patients were initially treated with methylprednisolone pulses ($n=11$), rituximab ($n=6$), intravenous immunoglobulins ($n=4$), cyclophosphamide ($n=3$) and MTX ($n=11$). Complete remission was observed in all cases, and maintenance therapy with MTX (10 mg/m^2 BSA) was started in all them, with gradual tapering until it was stopped. Interestingly, no relapses have been observed in any case during the mean follow up. One patient had mild oral ulcers and other showed mild elevation of liver enzymes; both events remitted after discontinuing the treatment for a couple of weeks.

Conclusions: Since relapses in patients with A-ME are a relatively frequent, the immunosuppressive therapy to prevent them is fully justified (4). Moreover, MTX therapy in pediatric patients is safe and usually well tolerated (3,5,6). The recommended dose is less than 15 mg/m^2 BSA or 1 mg/kg , with a maximal dose of 40 mg and with folic acid supplementation. In this regard, our study suggests that MTX administration (10 mg/m^2 BSA) during at least one year is a viable and effective therapy for maintenance treatment of A-ME. Accordingly, we did not detect relapses in the 11 patients studied with a median follow up time of 22 months and with an acceptable safety profile.

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THU0502 EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH STILL'S DISEASE: A POOLED ANALYSIS OF SJIA DATA BY AGE GROUPS

E. Feist¹, P. Quartier², B. Fautrel³, R. Schneider⁴, P. Sfriso⁵, P. Efthimiou⁶, L. Cantarini⁷, K. Lheritier⁸, K. Leon⁹, C. Karyekar⁹, A. Speziale⁸.

¹Charité-Universitätsmedizin, Berlin, Germany; ²Necker-Enfants Malades Hospital; ³Pitié Salpêtrière Hospital, Paris, France; ⁴PRCSG, Cincinnati, United States; ⁵University of Padova, Padova, Italy; ⁶Weill Cornell Medical College, New York, United States; ⁷University of Siena, Siena, Italy; ⁸Novartis Pharma AG, Basel, Switzerland; ⁹Novartis Pharmaceuticals Corporation, East Hanover, United States

Background: Still's disease presents in paediatric and adult patients (pts) as a disease continuum with similar symptoms and pathophysiology.^{1,2}

Objectives: To evaluate the efficacy and safety of canakinumab (CAN), a selective human anti-IL1 β monoclonal antibody, in SJIA pts from pooled data across 3 age groups (grps): children, adolescent and adults (the latter representing adult-onset Still's disease [AOSD] population).

Methods: Data of CAN treated pts were pooled from 4 SJIA studies (NCT00426218, NCT00886769, NCT00889863, NCT00891046). CAN was ad-

ministered at 4 mg/kg every 4 weeks (wk). Efficacy parameters (adapted ACR [aACR] paediatric responses, juvenile idiopathic arthritis [JIA] ACR responses, pts with inactive disease), CRP levels over 12 wk and safety were assessed by age grp. One study [NCT00426218] was excluded for efficacy outcomes.

Results: 216 children (2–<12 years [y]), 56 adolescents (12–<16 y) and 29 adults (≥16 y) were analysed for efficacy outcomes. The efficacy parameters across the 3 age grps were largely comparable (Table 1). The safety profile of CAN was similar across age grps (Table 2). One death was reported (adolescents grp). Clinical, laboratory and immunogenicity data showed no notable differences between the age grps.

Table 1. Responses by age grp and time point

Age group	%	aACR paediatric; n/N (%)		JIA ACR; n/N (%)	
		Day 15	Day 85	Day 15	Day 85
Children	≥30	158/216 (73.1)	90/133 (67.7)	169/216 (78.2)	93/133 (69.9)
	≥70	109/216 (50.5)	77/133 (57.9)	111/216 (51.4)	77/133 (57.9)
	≥100	46/216 (21.3)	42/133 (31.6)	47/216 (21.8)	42/133 (31.6)
Adolescents	≥30	47/56 (83.9)	20/27 (74.1)	47/56 (83.9)	20/27 (74.1)
	≥70	33/56 (58.9)	18/27 (66.7)	33/56 (58.9)	18/27 (66.7)
	≥100	15/56 (26.8)	8/27 (29.6)	15/56 (26.8)	8/27 (29.6)
Adults	≥30	25/29 (86.2)	15/18 (83.3)	25/29 (86.2)	15/18 (83.3)
	≥70	19/29 (65.5)	13/18 (72.2)	19/29 (65.5)	12/18 (66.7)
	≥100	4/29 (13.8)	4/29 (13.8)	4/18 (22.2)	4/18 (22.2)
Age group		Inactive disease; n/N (%)		CRP, median; mg/L (n/N)	
		Day 15	Day 85	Day 15	Day 85
Children		40/216 (18.5)	32/133 (24.1)	12.00 (211/216)	9.75 (168/216)
Adolescents		18/56 (32.1)	10/27 (37.0)	10.00 (55/56)	8.40 (45/56)
Adults		6/29 (20.7)	8/18 (44.4)	4.50 (26/29)	7.80 (23/29)

Table 2. Adverse events (AEs)

	Children, n (%) N = 233	Adolescents, n (%) N = 60	Adults, n (%) N = 31
AEs (at least 1)	202 (86.7)	53 (88.3)	27 (87.1)
AEs leading to study drug discontinuation	26 (11.2)	10 (16.7)	6 (19.4)
AEs most common/special interest			
Infections and infestations	176 (75.5)	42 (70.0)	23 (74.2)
Gastrointestinal disorders	122 (52.4)	32 (53.3)	18 (58.1)
Musculoskeletal and connective tissue disorders	119 (51.1)	33 (55.0)	16 (51.6)
Opportunistic infections	3 (1.3)	4 (6.7)	1 (3.3)
Neutropenia	11 (4.7)	2 (3.3)	0
SAE (at least 1)	81 (34.8)	25 (41.7)	9 (29.0)

Conclusions: Pooled analyses indicate similar efficacy of CAN across all the age grps of children, adolescents and adult SJIA pts. There were no meaningful differences in safety profiles across the different age grp. These analyses suggest similar efficacy of CAN in AOSD pts as observed in the SJIA pts.

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THU0503 IDENTIFICATION OF OPTIMAL SUBCUTANEOUS (SC) DOSES OF TOCILIZUMAB IN CHILDREN WITH POLYARTICULAR-COURSE JUVENILE IDIOPATHIC ARTHRITIS (PCJIA)

F. De Benedetti¹, N. Ruperto², D. Lovell³, A.V. Ramanan⁴, R. Cuttica⁵, J.E. Weiss⁶, M. Henrickson³, H. Schmeling⁷, J. Anton⁸, K. Minden⁹, J. Hsu¹⁰, K. Bharucha¹¹, S. Wimalasundera¹², A.K. Kadva¹¹, R. Upmanyu¹², N.L. Mallalieu¹⁰, A. Martini², H. Brunner³. ¹IRCCS Ospedale Pediatrico Bambino Gesù, Rome; ²PRINTO Coordinating Ctr, Genoa, Italy; ³PRCSG, Cincinnati Children's Hosp Med Ctr, Cincinnati, United States; ⁴Bristol Royal Hosp for Children, Bristol, United Kingdom; ⁵Hosp Gral de Niños Pedro Elizalde, Buenos Aires, Argentina; ⁶Hackensack U Med Ctr, Hackensack, United States; ⁷Alberta Children's Hosp/U Calgary, Calgary, Canada; ⁸Hosp Sant Joan de Deu, Barcelona, Spain; ⁹Charité U Med Berlin, Berlin, Germany; ¹⁰Roche Innovation

Ctr, New York; ¹¹Genentech, S San Francisco, United States; ¹²Roche Products Ltd, Welwyn Garden City, United Kingdom

Background: Efficacy and safety of intravenous (IV) tocilizumab (TCZ) have been shown in patients (pts) with pcJIA.¹

Objectives: Determine appropriate dosing regimens of SC TCZ in pcJIA.

Methods: Pts were aged 1–17 y with pcJIA, inadequate response/intolerance to MTX and TCZ-naïve or receiving TCZ IV with adequate disease control. TCZ SC was administered open label by body weight (BW)–based dosing modeled on IV dosing in pcJIA and SC dosing in adult rheumatoid arthritis: pcJIA pts <30kg received TCZ 162mg every 3 wks (Q3W) and pts ≥30kg received TCZ 162mg Q2W for 52 wks. Safety, efficacy (exploratory) and model-computed pharmacokinetic (PK) and pharmacodynamic (PD) parameters were assessed.

Results: 52 pts were enrolled; 27 <30kg and 25 ≥30kg BW; 85% and 56% were TCZ naïve. Since no notable difference in steady state PK occurred in naïve vs non-naïve pts, pooled data are shown. Median C_{min} was similar between BW groups and higher than with TCZ IV (TCZ IV median C_{min}: 3.2 µg/mL for 10mg/kg <30kg BW and 7.3 µg/mL for 8mg/kg ≥30kg BW) ensuring adequate exposure from SC doses. Median C_{max} was lower from SC than IV dosing. Changes in PD parameters for TCZ-naïve pts were consistent with those for TCZ IV. JADAS-71 generally improved (Table), with trends consistent with those for TCZ IV. Infections were the most frequent adverse event (AE), reported in 36 pts; 2 serious infections occurred in 1 pt. Injection site reactions occurred in 15% pts in the <30kg group and 44% pts in the ≥30kg group. The most common symptoms were erythema, swelling, hematoma, pain and pruritus. No serious hypersensitivity, AE leading to withdrawal, opportunistic infection, serious hepatic AE or death occurred. Overall there were 4 serious AEs in 3 pts (7.9/100 pt-y, consistent with that for TCZ IV).

	TCZ 162mg SC Q3W, BW <30kg (n=27)	TCZ 162mg SC Q2W, BW ≥30kg (n=25)
Model-computed steady state PK parameters, median [range]		
C _{min} , µg/mL	13.4 [0.2, 52.3]	12.7 [0.2, 23.8]
C _{max} , µg/mL	62.4 [39.4, 121.1]	29.7 [7.6, 50.3]
AUC _{12weeks} , µg/mL×day	2998 [1465, 7708]	1933 [324, 3098]
Change from baseline to week 52 ^a in PD markers and efficacy, median [range]; TCZ-naïve pts		
IL-6, pg/mL	27.3 [3.5, 173.9], n=11	12.2 [-6.2, 30.9], n=9
sIL-6R, ng/mL	612.1 [399.4, 808.4], n=14	429.3 [245.5, 585.6], n=11
CRP, mg/L	-1.3 [-17.0, 0.5], n=21	-0.8 [-22.9, 0.0], n=12
ESR, mm/h	-11.0 [-40.0, 0.0], n=21	-6.0 [-35.0, 0.0], n=12
JADAS-71	-16.8 [-40.3, -4.4], n=21	-12.9 [-48.1, -2.3], n=12

^aWeek 51 for Q3W group. AUC, area under the concentration curve; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IL-6, interleukin-6; sIL-6R, soluble IL-6 receptor.

Conclusions: The BW-based TCZ SC dosing regimens for pcJIA provided adequate exposure to support efficacy comparable to that for TCZ IV, with an acceptable benefit-risk profile.

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