OP0060

SAFETY PROFILE OF ETANERCEPT IN LONG-TERM USE IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Background: Etanercept is the most frequently used biologic drug in patients with JIA. Children and adolescents with JIA are treated with etanercept often over long periods of time, sometimes even into adulthood. The knowledge about its long-term safety, especially with regard to the occurrence of new-onset immune-mediated diseases and malignancies, is still limited.

Objectives: To investigate the exposure-adjusted rates of adverse events (AE) and serious AE (SAE) in patients with JIA with long-term use of etanercept.

Methods: Patients with JIA who were enrolled in the German biologic register BiKeR and were born before 30.05.2000 (at least 18 years of age at this date) were considered for this analysis. The follow-up register JuMBO ensures the long-term follow-up into adulthood. An AE or SAE was attributed to etanercept when the treatment was either ongoing or terminated in less than 3 month prior to the event. The incidence of malignancies was estimated in patients who were ever exposed to etanercept with at least one dose.

Results: Of 4546 patients who were currently enrolled in BiKeR a total of 2584 JIA patients were eligible for the JuMBO register (>18 years). Among those, 1765 (68%) were ever exposed to etanercept and observed for a mean of 6.8±4.9 years (including 1101 into adulthood). The majority of them had polyarthritis (35%), followed by enthesitis-related arthritis (20%) and extended oligoarthritis (17%). The patients were exposed to etanercept for a total of 4.2 years (mean, 6,726 exposure years, EY); 518 patients were continuously treated with etanercept for at least 5 years (4,534 EY). In total, 124 autoimmune events (1.84/100EY) and 7 other immune disorders (0.10/100EY) were reported in 102 (5.8%) and 7 (0.4%) patients with onset on average 10.2 years after JIA onset, and 6.8 years after start with etanercept, respectively. The number of selected immune-mediated events and the exposure-adjusted rates are given in the table. In addition, 11 malignancies (0.10 events/100 person-years) were reported in patients ever exposed to etanercept. Among those (mean age at onset 20.3 years), 4 malignancies were reported in childhood and 7 in young adulthood. Three patients were also exposed to other biologics before the incidence of malignancy. The malignancies occurred on average 12.1 years after JIA onset, 10.4 years after start with a first DMARD and 7.5 years after first exposure to etanercept.

Conclusion: This is the first long-term large safety study in prospectively followed JIA patients with focus on new-onset immune-mediated diseases and malignancies in etanercept. The study also highlights that it is important to prospectively collect data on adverse events under treatment with biologics in JIA, in particular with respect to the risk of malignancies in young adulthood.

Table 1. Adverse and serious adverse events under treatment with etanercept

	All patients ever treated with etanercept, n=1765		Patients continuously treated with etanercept for at least 5 years, n=518	
	Number of patients	Number of reported events (rate / 100 EY)	Number of patients	Number of reported events (rate / 100 EY)
Serious adverse events	218 (7.3%)	320 (4.76)	116 (22.4%)	189 (4.17)
All infections	285 (16.1%)	469 (6.97)	124 (23.9%)	238 (5.25)
Medically important infections	56 (3.2%)	69 (1.03)	31 (6.0%)	43 (8.95)
Autoimmune disorder events	102 (5.8%)	124 (1.84)	49 (9.5%)	59 (1.30)
Uveitis	72 (4.1%)	87 (1.29)	37 (7.1%)	43 (8.95)
Inflammatory bowel diseases	22 (1.2%)	28 (0.42)	8 (1.5%)	11 (2.24)
Demyelinating disorders	3 (0.2%)	3 (0.04)	2 (0.4%)	2 (0.04)
Autoimmune hepatitis	1 (0.1%)	1 (0.01)	1 (0.2%)	1 (0.02)
Autoimmune thyroiditis	1 (0.1%)	1 (0.01)	1 (0.2%)	1 (0.02)
Encephalitis autoimmune	1 (0.1%)	1 (0.01)	0	0 (0.00)
Histiocytosis haematophagic	1 (0.1%)	1 (0.01)	0	0 (0.00)
Incident immune disorders	7 (0.4%)	7 (0.10)	6 (1.2%)	6 (0.13)
Vasculitides	2 (0.1%)	2 (0.03)	2 (0.4%)	2 (0.04)
Psoriasis	4 (0.2%)	4 (0.06)	3 (0.6%)	3 (0.07)
Erythema nodosum	1 (0.1%)	1 (0.01)	1 (0.2%)	1 (0.02)

Disclosure of Interests: Jens Klotsche: None declared, Ariane Klein: None declared, Martina Niewerth: None declared, Gerd Ganser: None declared, Peer Aries: None declared, Marisa Walther: None declared, Peter Haas Grant/research support from: Pfizer, Gernot Keyßer: None declared, Gerd Horneff: None declared, Kirsten Minden Consultant for: AbbVie

DOI: 10.1136/annrheumdis-2019-eular.5509

OP0061

CONSUMER PERSPECTIVE ON PAEDIATRIC RHEUMATOLOGY CARE AND SERVICE DELIVERY: RESULTS FROM AN EARLY JUVENILE IDIOPATHIC ARTHRITIS (JIA) COHORT STUDY

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Background: Timely access to specialized and multidisciplinary care is a core principle in the management of JIA patients and crucial to achieve the best possible outcome for children and adolescents with JIA.

Objectives: To assess satisfaction with access to specialized care and used health care services of families with children with JIA and to identify factors associated with unmet needs.

Methods: Parents of JIA patients enrolled in the early JIA cohort study ICON completed the Child Healthcare Questionnaire on Satisfaction, Utilisation and Needs (CHC-SUN)¹ and the Family Burden Questionnaire (FaBel) 3 months after enrolment. The socioeconomic status, disease activity, patients' functional ability and quality of life were also assessed. Factors associated with unmet needs were identified by logistic regression analysis.

Results: Data were available from 835 families with children diagnosed with JIA 3 months (median, IQR 1-6) after symptom onset and cared for by paediatric rheumatologists (68% females). At assessment (4.6 months after diagnosis, median), 67% of patients received non-steroidal anti-inflammatory drugs, 50% received conventional synthetic DMARDs and 8% biologic DMARDs. In addition, the following health care services were utilized: 84% physiotherapy, 23% occupational therapy, 21% supply with physical aids, 17% telephone counselling, 15% health education, 13% social worker services, and 11% psychological counselling. Unmet needs were most frequently reported for health education (19%), rehabilitation services (11%), psychological counselling (11%), self-help groups (10%), and lowest for physiotherapy (2%). Unmet needs varied depending on the type of service and JIA category (Table). They were more frequently observed in families with higher burden as indicated by FaBel, but were not associated with migration background and socioeconomic status. Most parents were generally satisfied with their child's health care (satisfied 30%, very satisfied 42%, extremely satisfied 23%). Satisfaction was highest with the behaviour of doctors and lowest with school-related services (e.g. 36% not or partly satisfied with teachers' knowledge about the child's illness) and diagnosis/information (e.g. 29% not or partly satisfied with the time required for the diagnosis).

Table: Unmet needs reported by parents of children with various JIA categories

	OA	RF-PA	RF-PA	ERA	PA	SoDA	Other JIA	P-value
N	189	228	13	87	32	29	17	
Age at assessment, years*	5.1 (6.6)	7.2 (8.6)	12.7	12.8	10.8	6.9 (8.4)	10.9	<0.001
CHC-SUN ¹	7.0 (6.0)	13.5	11.8	7.5 (9.6)	10.5	10.5	9.8 (8)	<0.001
	(10.0)	(14.0)	(14.0)	(13.0)	(14)			
CHC-SUN ²	0.0 (0.0)	0.3 (1.0)	0.4 (1.0)	0.1 (0.0)	0.13	0.13	0.13	<0.001
				(1.0)				
Most frequently reported unmet needs (n %)								
Health education	16.2	21.1	46.2	16.7	13.8	25.9	20.0	0.11
Psychological counselling	7.5	12.9	15.4	13.0	10.3	12.0	16.0	0.31
Rehabilitation services	10.5	11.2	33.3	7.6	3.4	15.4	14.3	0.13
Self-help groups	9.3	11.5	7.7	7.6	10.3	14.8	14.0	0.84
Telephone counselling	7.8	7.5	7.7	6.4	13.3	11.5	8.0	0.92
Occupational therapy	7.8	9.1	7.7	6.3	6.7	7.4	6.1	0.99

* median (IQR)

Conclusion: There are, although infrequently, unmet needs and dissatisfaction with health services among families with children who have JIA and receive specialized care. Whether these deficits are relevant for long-term JIA outcomes will be further investigated in the ICON study.

REFERENCE:

[1] Schmidt S, Thyen U, Chaplin J, Mueller-Godeffroy E; European DISAB-KIDS Group. Cross-cultural development of a child health care questionnaire on satisfaction, utilization, and needs. *Ambul Pediatr.* 2007;7:374-82.

Acknowledgement: Funding by Federal Ministry of Research: 01 ER 1504A

Disclosure of Interests: Michaela Heinrich: None declared, Jens Klotsche: None declared, Claudia Sengler: None declared, Martina Niewerth: None declared, Frank Weller-Heinemann: None declared, Peter Haas Grant/research support from: Pfizer, Gerd Horneff: None declared, Toni Hospach Speakers bureau: Chugai, Roche, Novartis, Kirsten Moenkemoeller: None declared, Angelika Thon: None declared, Ivan Foeldvari Consultant for: Chugai, Novartis, Kirsten Minden Consultant for: AbbVie

DOI: 10.1136/annrheumdis-2019-eular.5028

WEDNESDAY, 12 JUNE 2019

Myositis and SSc: Clinical highlights 2019

OP0062

IDENTIFICATION OF SIX DERMATOMYOSITIS SUBGROUPS USING PRINCIPAL COMPONENT ANALYSIS-BASED CLUSTER ANALYSIS

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Background: Dermatomyositis (DM) is a heterogeneous disease with a wide range of clinical manifestations. Bohan and Peter suggested four subtypes of DM: idiopathic DM, juvenile DM, DM associated with cancer, and DM associated with other connective tissue diseases. Different DM subtypes have distinct clinical manifestations, responses to therapy and prognoses.

Objectives: The aim of the present study was to identify the clinical subtypes of DM by applying cluster analysis.

Methods: We retrospectively reviewed the medical records of 720 DM patients and selected 21 variables for analysis, including clinical characteristics, laboratory findings, and comorbidities. Principal component analysis (PCA) was first conducted to transform the 21 variables into independent principal components. Patient classification was then performed using cluster analysis based on the PCA-transformed data. The relationships among the clinical variables were also assessed.

Results: We transformed the 21 clinical variables into 9 independent principal components by PCA and identified 6 distinct subgroups. Cluster A was composed of two sub-clusters of patients with classical or moderate DM. Cluster-B patients were older and had malignancies. Cluster C was characterized by interstitial lung disease (ILD), skin ulcer, and minimal muscle involvement. Cluster D included patients with prominent lung, muscle, and skin involvement. Cluster E contained DM patients with other connective tissue diseases. Cluster F included all patients with myocarditis and prominent myositis and ILD. We found significant differences in treatment across the six clusters, with clusters C, D, and E being more likely to receive aggressive immunosuppressive therapy.

Conclusion: We applied cluster analysis to a large group of DM patients and identified six clinical subgroups, underscoring the need for better phenotypic characterization to help develop individualized treatments and improve prognosis.

REFERENCES:

- [1] Bohan, A. and J.B. Peter, Polymyositis and dermatomyositis (first of two parts). *N Engl J Med*, 1975. 292(7): p. 344-7.
- [2] Bohan, A. and J.B. Peter, Polymyositis and dermatomyositis (second of two parts). *N Engl J Med*, 1975. 292(8): p. 403-7.
- [3] Marie, I., Morbidity and mortality in adult polymyositis and dermatomyositis. *Curr Rheumatol Rep*, 2012. 14(3): p. 275-85.
- [4] Callen, J.P., Dermatomyositis. *The Lancet*, 2000. 355(9197): p. 53-57.

Fig. 1

Dermatomyositis Unsupervised combination of the Dermatomyositis Patients into Distinct Clusters

Fig. 2

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.385

OP0063

SAFETY OF MYCOPHENOLATE MOFETIL TREATMENT IN SYSTEMIC SCLEROSIS IN REAL LIFE: REPORT FROM A SINGLE CENTER LARGE COHORT OBSERVATIONAL STUDY

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Background: Mycophenolate mofetil (MMF) has been increasingly used in the treatment of early diffuse cutaneous Systemic Sclerosis (dcSSc) and SSc-associated interstitial lung disease (SSc-ILD), and a recent Randomized Controlled Trial confirmed its efficacy and safety in SSc-ILD. However, the safety of this drug in the long term use has not been assessed in a real life setting.

Objectives: We aimed to analyze the period prevalence and the type of adverse events (AEs) associated to MMF treatment in a single center large cohort.

Methods: Charts of all SSc patients meeting the 2013 ACR/EULAR classification criteria consecutively visited at our outpatient clinic from January 1st 2017 to December 31st 2017 were retrospectively analyzed. Demographics, clinical, serological, functional, imaging data, treatments, and AEs were recorded. Patients were subgrouped according to the immunosuppressant (IS) taken during the observation period (e.g. MMF, azathioprine- AZA, or cyclophosphamide- CYC, no IS). The period prevalence of AEs was calculated and correlations of between AEs and patient features were investigated by univariate and multivariate analyses.

Results: Two-hundred and thirty-seven patients were included (92.4% were females, aged 56.4±11.3 years, with a median disease duration of 17 years, range 1-60). Among them, 85 (35.9%) were taking MMF, 34 (14.3%) AZA or CYC, 118 (49.8%) had no current IS treatment. Prevalence of the dcSSc subset was higher in the MMF group (34.1% versus 17.6% in the AZA/CYC group and 5.9% in the no IS group; p<0.05), while prevalence of ILD was similar in the MMF and in the AZA/CYC group and higher than the no IS group (89.4% and 82.3% versus 41.5%; p<0.05 for both), as well as the prevalence of the anti-topoisomerase I antibody positivity (60.7% and 52.9% versus 26.3%; p<0.05). Both patients treated with MMF and AZA/CYC had more frequently concomitant low-dose glucocorticoid (GC) therapy than patients without IS (76.5% for both groups versus 39%; p<0.05). In regard of total AEs, their prevalence was higher in the MMF group (71.7% versus 67% in the AZA/CYC group and 49% in the no IS group; p<0.05 MMF vs no IS). In particular, patients treated with MMF had a higher prevalence of total infectious AEs (55.7% versus 30.4% in the AZA/CYC group and 27.6% in the no IS group; p<0.05), predominantly airway infections (41.2% of all infectious AEs). Given so, we investigated the correlations of the infectious AEs in the MMF group with ILD, smoking history, and concurrent GC. However, we didn't find any significant association with these variables. When we looked for correlations of infectious AEs in the MMF group with other disease features, we found that they were correlated with the duration of the disease (median= 4 years; r=0.25; p=0.02) and with the presence of digital ulcers and/or pitting scars (r=0.22; p=0.03). No AE required hospitalization and resolved after treatment suspension.