SAT0501

EARLY START OF BIOLOGICAL TREATMENT IN JUVENILE IDIOPATHIC ARTHRITIS: DOES A THERAPEUTIC WINDOW EXIST IN REAL LIFE?

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Background: Biological therapy (BT) has changed the treatment and perspectives of JIA patients but little is known about when is the best moment to start BT and the impact of this prompt initiation.

Objectives: To analyze the response to BT of Juvenile Idiopathic Arthritis (JIA) patients according to the time when the BT was started.

Methods: A retrospective, descriptive study was conducted on JIA patients followed up in a referral hospital that started BT up to 24 months after diagnosis from 2000 to 2018. Disease activity was measured, at 2 years after diagnosis, according to Wallace criteria for remission (absence of: active arthritis, active uveitis, fever, rash or any other manifestation attributable to JIA, normal CRP and ESR, PGA indicating no active disease) for at least 6 months.

Results: 55 JIA patients that started BT up to 24 months from diagnosis were analyzed. 69,1% were girls with a median age at diagnosis of 8 years old IQR(3-13), median age at the start of BT of 9 years old IQR(3-13). Regarding JIA categories: 25,5% were Oligoarticular Persistent (OligP), 18,2% Systemic JIA (sJIA), 16,4% Entesitis related Arthritis (ERA), 12,7% Psoriatic Arthritis (APso) and Polyarticular RF- (PolyRF-), 5,5% Oligoarticular Extended (OligE) and Polyarticular RF+ (PolyRF+), 3,6% Undifferentiated (Und). 20% of patients had uveitis during followup. Conventional DMARD (cDMARD) was indicated in 83,6% of patients (95,7% Methotrexate) at diagnosis [median 0 months IQR(0-2,3)]. At the end of followup (2 years) only 30,9% of patients continued with cDMARDs. The main causes of discontinuation were: adverse events (46,7%), remission (36,7%). TNF inhibitors were prescribed in 81,8% of patients and 18,2% of patients received two BT during the first 2 years from diagnosis. 54,5% of BT were indicated during the first 6 months from diagnosis, 27,3% from 7 to 12 months, 12,7% from 13 to 18 months, 5,5% from 19 to 24 months. After 2 years from diagnosis, 78,2% of patients were on remission and 21,8% active. Among patients with active disease: 75% had arthritis, 16,7% had uveitis and 8,3% had both. There were no differences regarding disease activity among patients with uveitis and neither taking cDMARDs. Regarding JIA categories: 66,7% of OligE, 57,1% of PolyRF- and 57,1% of APso patients were active at 2 years from diagnosis when compared to the other categories (p=0.004). Patients on remission at 24 months from diagnosis started sooner the BT than active patients [CI 95% (0,46-8,29) p=0,029]. The time when the BT was started was correlated to the activity at 2 years (K=-0,294 p=0,029). When the BT was prescribed after 7,5 months from diagnosis it was correlated, in a COR curve, with a higher probability of active disease at 2 years (S= 0,67 E= 0,63). There was a correlation, among patients on remission at 2 years, between prompt start of BT and less time to reach remission (K=-0,345 p=0,024). Patients with active disease at 2 years, regardless of moment of BT initiation, required more BT during follow-up (p=0,002).

Conclusion: Prompt initiation of BT was correlated with a better outcome. JIA patients that started BT early after diagnosis had a higher probability of remission after 2 years. Starting BT after 7,5 months was correlated with a higher probability of active disease at 2 years. Active disease at 24 months was correlated with persistent active disease during follow-up.

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SAT0502

LONG-TERM OBSERVATIONAL SAFETY SURVEILLANCE OF GOLIMUMAB TREATMENT FOR POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS—AN INTERIM ANALYSIS

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Background: Golimumab (GOL) is approved for treatment of polyarticular juvenile idiopathic arthritis (pJIA) in patients 2 years and older. Data on long-term safety in this indication are limited.

Objectives: Prospective monitoring of long-term safety and effectiveness of GOL in routine care using the German BIKER registry.

Methods: In this non-interventional study baseline and safety parameters were compared between patients initiating GOL and contemporary matched control cohorts starting either an alternative TNF inhibitor (TNFi) or methotrexate (MTX) without exposure to a biologic. Efficacy outcomes were JADAS10, JIA ACR scores, joint counts and Childhood Health Assessment Questionnaire disability-index (CHAQ-DI). Safety assessments were based on adverse event (AE) reports.

Results: From 2016 to 2019, 55 patients initiating GOL have been recruited and matched to 110 patients starting alternative TNFi and 47 biologic-naïve patients. Patients starting GOL had a longer disease duration (6.8y vs. 4.1 y and 1.0y; p<0.0001) and use of GOL was significantly more often second-line (85% vs 31% and 0%, p<0.0001). Disease activity was lower at baseline compared to MTX patients as indicated by active joint counts, JADAS10 and concomitant steroid use. Otherwise they were comparable with patients treated with other TNFi (Table 1).

Table 1 Comparison of GOL cohort with (1) other TNFi cohort and (2) MTX cohort.

	GOL N=55	Other TNFi N=110	MTX N=47	p-value # GOL vs TNFi/MTX
Gender female, n (%)	44 (80)	86 (78)	34 (72)	0.8/0.5
Age at baseline, mean (SD), years	13.6 (2.8)	13.6 (3.0)	13.1 (3.4)	1.0/0.4
Disease duration, mean (SD), years	6.8 (4.5)	4.1 (3.8)	1.0 (1.6)	<0.0001
RF neg. polyarthritis, n (%)	28 (51)	53 (48)	29 (62)	0.7/0.3
RF pos. polyarthritis, n (%)	6 (11)	18 (16.4)	11 (23.4)	0.5/0.1
Extended oligoarthritis, n (%)	20 (36.4)	37 (33.6)	6 (12.8)	0.7/0.007
Psoriatic arthritis	1 (1.8)	2 (1.8)	1 (2.1)	1.0/1.0
Pretreatment bDMARD n(%)	47 (85.5)	34 (30.9)	0	<0.0001
Concomitant steroids, n (%)	9 (16.4)	26 (23.6)	25 (53.2)	0.3/0.0001
Active joint count, mean (SD)	4.6 (4.0)	5.4 (6.1)	9.7 (6.5)	0.4/<0.0001
CHAQ DI, mean (SD)	0.4 (0.4)	0.5 (0.6)	0.6 (0.7)	0.3/0.07
ESR, mm/h, mean (SD)	20.4 (27.6)	15.4 (18.6)	21.4 (18.6)	0.2/0.8
JADAS10, mean (SD)	11.3 (6.0)	12.4 (5.8)	16.9 (5.4)	0.3/<0.0001
AE, n (rate/100PY; 95%CI)	45 (96; 72-128)	106 (114; 94-138)	39 (107; 78-146)	0.3/0.6
SAE, n (rate/100PY; 95%CI)	2 (4.2; 1.1-17)	5 (5.4; 2-13)	1 (2.7; 0.4-19)	0.8/0.7
Infectious AE, n (rate/100PY; 95%CI)	6 (12.8; 5.7-28)	11 (11.8; 6.5-21)	9 (24.5; 13-47)	0.9/0.2
Serious infections, n (rate/100PY; 95%CI)	0	2 (2.2; 0.5-8.6)	0	n.a.
Uveitis new manifestation	1 (2.1; 0.3-15)	2 (2.2; 0.5-8.6)	0	1.0/n.a.

In GOL treated patients a marked clinical response was noted at 6 months and beyond demonstrated by a significant decrease of the mean JADAS 10 from 11.3 to 6.4 (p=0.0008), as well as JIA ACR 30/50/70/90 response rates of 56/56/35/21%. JADAS remission and minimal disease activity was observed in 18% and 47% after 6 months and in 29% and 43% of patients after 12 months.

Rates of AE, SAE and infectious AE were comparable between the GOL cohort (96, 4.2 and 12.8/100PY), the alternative TNFi cohort (114, 5.4 and 11.8/100PY) and the MTX cohort (107, 2.7 and 24.5/100PY). SAE reported in the GOL cohort were uveitis and JIA flare (each 1). Two serious infections, both influenza, were reported in the alternative TNFi cohort, none in the GOL cohort. No case of pregnancy, malignancy or death was reported.

Conclusion: Interim results from this ongoing safety surveillance study indicate acceptable safety and tolerability of GOL in pJIA that is comparable to treatment with alternative TNFi or MTX. The long-term effectiveness data reinforce the established efficacy of GOL in pJIA treatment.

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SAT0503

SERIOUS INFECTION RISK IN PEDIATRIC PATIENTS WITH LOW IMMUNOGLOBULIN LEVELS FOLLOWING RITUXIMAB TREATMENT FOR GRANULOMATOSIS WITH POLYANGIITIS (GPA) OR MICROSCOPIC POLYANGIITIS (MPA)

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Background: Low immunoglobulin (Ig) levels can occur after rituximab treatment, but the clinical significance is not completely understood. Not all patients (pts) who develop low Ig levels after rituximab are at an increased risk of serious infection (SI), but factors such as pre-existing low Ig levels, prior biologic therapies, history of SI and other disease and age-related factors may increase the risk.

Objectives: To assess the risk of SI in pediatric pts with prolonged low IgG or IgM serum concentrations following rituximab treatment for GPA or MPA in a global clinical trial.

Methods: In the Phase 2a PePRS study (WA25615), pts aged ≥ 2 to ≤ 18 yrs with GPA or MPA received 4 weekly intravenous rituximab infusions of 375 mg/m² body surface area and concomitant oral glucocorticoid taper. After 6 months, pts could receive further rituximab and/or other immunosuppressants at the investigator's discretion during a minimum 12-month follow-up phase. Pts with IgG/IgM levels below age-specific reference ranges at baseline were excluded. Ig levels were measured every 4-12 wks. SI occurrence was assessed during/after low IgG or IgM. Prolonged low Ig was defined as IgG or IgM levels < lower limit of normal (LLN) reference range for age for a ≥ 4 -month period.

Results: All 25 pts completed 4 weekly rituximab infusions and the 6-month Remission Induction Phase; 24/25 pts completed ≥ 18 months of follow-up. 17 pts received additional rituximab treatment on or after Month 6. 11 pts received concomitant immunosuppressants (cyclophosphamide, azathioprine, mycophenolate mofetil) during the study. All pts had a decrease in IgG and IgM mostly after the first rituximab infusion. There was no consistent trend in IgG or IgM levels over time and no clear relationship between low IgG or IgM levels and the number of follow-up rituximab treatments. 18 pts (72%) had prolonged low IgG ≥ 4 months, of whom 5 had IgG levels < LLN at screening and/or baseline; in 7 pts, IgG levels returned to within normal range by study end. During or after prolonged low IgG, 6/18 pts experienced a total of 7 SIs. Three pts received treatment with intravenous Ig. 19 pts (76%) had prolonged low IgM, of whom 5 had IgM levels < LLN at screening and/or baseline. During or after prolonged low IgM levels, 6/19 pts experienced a total of 8 SIs. There were no deaths or study discontinuation due to SI. All pts with prolonged low IgG or IgM had past and/or concomitant treatment with steroids and/or immunosuppressants as potential contributory factors. Analysis of SI onset in relation to timing of low Ig was limited due to protocol-defined time points for Ig assessments.

Conclusion: In pediatric pts with GPA/MPA treated with rituximab, there was no consistent pattern in IgG or IgM levels over time. The majority of pts with prolonged low IgG or IgM did not experience any SIs; no increase in the number of SIs was observed over time or with multiple rituximab treatments. While no firm conclusions can be made on a possible relationship between prolonged low IgG or IgM and risk of SI following rituximab due to study limitations (low pt numbers, lack of placebo comparator), these observations are consistent with the known rituximab safety profile in adult pts with GPA/MPA.

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SAT0504

STING-ASSOCIATED VASCULOPATHY WITH ONSET IN INFANCY (SAVI SYNDROME) CAN MIMIC JUVENILE IDIOPATHIC ARTHRITIS.

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Background: STING-associated vasculopathy with onset in infancy (SAVI syndrome) can mimic Juvenile Idiopathic Arthritis.

Objectives: The aim of this study is to describe a detailed cohort of patients with SAVI syndrome and highlight the similarity, in some cases, of the phenotype of this disease with Juvenile Idiopathic Arthritis.

Methods: 3 patients diagnosed with SAVI syndrome from the institution Hospital Universitari Vall d'Hebron were recruited. Written informed parental consent was obtained for the use of clinical data and pictures reported. Demographic, clinical, analytical, lung function and previous and current treatment are described.

Results: Patient 1, a 11-year-old boy, was identified to carry a de novo p.V155M mutation in TMEM173. He presented at first month of life with recurrent bronchial infection and skin vasculitis lesions in nose, cheeks and toes. Arthritis affected hands, toes and knees but no erosions were found at X-Ray. Fever was not reported. High-resolution computed tomography (HRCT) of the lungs identified a nonspecific interstitial pneumonia (NSIP) and a lung biopsy showed lymphoid hyperplasia. Elevated inflammatory markers were reported and rheumatoid factor (RF), ACPA antibodies and antinuclear antibodies (ANA) were also positive. At the age of 6 years Ruxolitinib (RX) was introduced at the initial dose of 5 mg twice daily with an improvement of skin disease and lung function. Arthritis was well controlled and RX was well tolerated.

Patient 2, a 17-year-old girl, was identified to carry a de novo p.V155 mutation in TMEM173. She presented at the age of 3 with a severe polyarthritis of large and small joints. No fever, skin or respiratory symptoms were reported at the beginning of the disease. Laboratory tests were positive for RF and ACPA antibodies. She was diagnosed with Polyarticular JIA and was treated with steroids and Methotrexate without improvement. Few months later she reported dyspnoea with recurrent bronchial infections. HRCT showed NSIP and lymphoid interstitial pneumopathy was found at the lung biopsy. RX was initiated at the age of 17 years but at this time lung fibrosis was established. Moreover, RX was not well tolerated due to headache. She requires continuous domiciliary oxygen and has been included to lung transplant.

Finally, patient 3, a 29-year-old man, was recently diagnosed with a de novo p.V155 mutation in TMEM173. He presented at the age of 7 years with symmetrical polyarticular arthritis after a bronchial infection that course with fever. No skin manifestations were objectified. Autoimmune lab test was positive for RF, ACPA, and ANA. With the diagnosis of Polyarticular JIA he received different treatments with no response. Due to recurrent bronchial infections a HRCT was performed showing an ILD at bases and follicular bronchiolitis with NSIP pattern in a lung biopsy. Functional tests were worsening without any response to different treatments. SAVI syndrome was suspected, and genetic test was performed with positive result. RX was initiated but compliance was not good.

Conclusion: SAVI syndrome is a rare monogenic autoinflammatory disease with few cases reported in the literature. Disease phenotype could be different in every patient, with no presence of skin vasculitis lesions or fever. Patient 2 and 3, in contrast with patient 1, had severe articular and lung manifestations with no skin involvement. Furthermore, lab tests were positive for RF and ACPA and were misdiagnosed as JIA so genetic test was performed later in the follow-up. Being aware of the distinct phenotype of the disease could help the clinicians to make a PRONTO diagnostic and reassess the patients with these presentations that not respond well to conventional treatments.

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SAT0505

PLUTO TRIAL OF INTRAVENOUS BELIMUMAB IN PAEDIATRIC PATIENTS WITH CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS (CSLE): PATIENT RESPONSES OVER TIME

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Background: Belimumab (BEL) is a human monoclonal antibody that specifically inhibits B-cell activating factor (BAFF). PLUTO is an ongoing trial evaluating efficacy and safety of intravenous (IV) BEL in children ≥ 5 years of age with cSLE. Efficacy, and safety endpoints of PLUTO have been reported;¹ briefly, numerically more BEL vs PBO pts met the primary and major secondary efficacy endpoints. We present patient (pt) response to BEL over time.

Objectives: To evaluate changes in SLE Responder Index (SRI) 4 and SRI6 responses, and disease activity over 52 weeks, in paediatric pts receiving BEL, or placebo (PBO), plus standard SLE therapy (SST).