damage (in 36 joints or joint groups) and the JADI-E extraarticular damage (in 5 different organs/systems: ocular, musculoskeletal excluding joints, cutaneous, endocrine, any organ/system).

Results: A total of 953 patients (67.2% female, mean age 7.9 years (SD 4.8)) with JIA were included in ICON after a median disease duration of 6 months (IQR: 3.0–11.1). About half of the patients (46%) had oligoarthritis, followed by rheumatoid factor-negative polyarthritis (RF-PA) (26%) and enthesitis-related arthritis (11%). The mean disease activity score cJADAS10 was 9.8 (6.2) and the mean CHAQ was 0.57 (0.69) at enrolment. Any damage was reported for 58 patients (8.6%) at the 3-year-Follow-up (FU) (mean JADI-A 0.17, mean JADI-E 0.06, JADI-A >0: 6.1%, JADI-E >0: 3.1%). At the 4 year (mean JADI-A 0.17, mean JADI-E 0.07) and 6-year-FU (mean JADI-A 0.13, mean JADI-E 0.12), 8.6% and 10.7% of patients had any damage. The number of patients with articular damage did not change during FU (6-year-FU: 6.5%), whereas the proportion of patients with extra-articular damage slightly increased (6-year-FU: 5.0%). At the 6-year-FU, the most frequently scored joints were the knee joints, followed by the wrist. JADI-E was dominated by eye damage. Among the JIA categories, patients with RF-PA showed most frequently damage (16.7%), followed by patients with enthesitis-related arthritis (15.4%) and extended oligoarthritis (14.3%) at the 6 year FU. The JADI-A score significantly correlated ($r=0.27$, $p<0.001$) with the number of active joints and JADI-E with the cJADAS10 ($r=0.14$, $p=0.041$). However, there was no significant association between the JADI scores and quality of life (PedsQL), and functional limitations (CHAQ, all $r<0.05$).

Conclusions: About one in ten patients with JIA has developed any damage three, four and six years after disease onset. Thus, a relevant increase in damage over time does not occur under current therapeutic conditions. Articular and extra-articular damage is similarly frequent.

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THU0553

TNF-INHIBITOR AND LEFLUNOMIDE COMBINATION THERAPY IN POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS IN CLINICAL PRACTICE – LESSONS FROM THE GERMAN BIOLOGICS JIA REGISTRY (BIKER)

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Background: Leflunomide has been shown to be a safe and effective therapy for adult rheumatoid arthritis.

Objectives: Safety and efficacy of combination of TNF inhibitors with leflunomide versus methotrexate for treatment of polyarticular-course juvenile idiopathic arthritis (pcJIA) were assessed in the prospective BIKER registry 2000–2016.

Methods: 3 cohorts of pcJIA patients ageing 3–17 years were analysed: Patients receiving leflunomide starting a TNF inhibitor, ¹ a TNF inhibitor starting leflunomide, ² methotrexate starting a TNF inhibitor. ³ Efficacy was determined using the JADAS response criteria, JADAS-10 minimal disease activity (MDA) and remission. Safety assessments were based on adverse events reports from the responsible physician.

Results: We identified 94 patients treated with Leflunomid-TNF-inhibitor in combination. 44 started a TNF-inhibitor on background Leflunomide, 50 started Leflunomide on background TNF inhibitor. 1361 patients starting a TNF-inhibitor on background Methotrexate served as control group. Differences in patients' characteristics at baseline limit direct comparison. Patients of cohort 3 had higher CRP, patients of cohort 2, already treated with a biologic, had lower disease activity parameters such as mean active joint count, physician and patient global disease activity judgement and JADAS10. At month 6, upon MTX +TNFi 54.6%/41.7%/19.6% and upon LEF +TNFi 35.0%/36.2%/13.8% reached JADAS improvement/JADAs minimal disease activity/JADAs remission. Thus significantly more patients with MTX +TNFi reached JADAS improvement (OR 2.22 [1.44–3.44]; $p<0.001$) while there comparable rates of patients reached JADAS-MDA and JADAS-remission. In the LEF cohorts, there were 95 adverse events in 54 patients (58%) compared to 1845 events in 626 (46%) on MTX (OR 1.6 [1.0–12.4] $p=0.031$). No differences were noted for the number of infections, nausea or elevated transaminases.

Abstract THU0553 – Table 1. Baseline patients' and disease characteristics

	Cohort 1 (n=44) LEF+TNFi	Cohort 2 (n=50) TNFi+LEF	Cohort 3 (n=1361) MTX+TNFi
Female	28 (64%)	40 (80%)	937 (68.8%)
Age at disease onset, median (IQR)	6.9 (2.1;11.3)	6.2 (1.8;9.6)	7.4 (2.9;11.5)
Disease duration, median (IQR)	6.3 (3.0;8.5)	5.1 (2.0;7.2)	4.1 (1.3;6.0)
ANA positive, n (%)	19 (43%)	28 (56%)	647 (47.5%)
CRP, median (IQR)	14.8 (3;22)	9.5 (0.6;4.5)	20.8 (1.4;23)

Active joint count, median (IQR)	6.2 (2;7.8)	3.5 (0;5.3)	7.3 (2;9)
Physician global, median (IQR)	5.3 (3.6;7.0)	2.6 (4.3;3.2)	5.4 (3.2;7.6)
Patient global, median (IQR)	4.4 (1.7;6.7)	2.9 (0.6;5.0)	4.4 (2.0;6.5)
CHAQ-DI, median (IQR)	0.59 (0;1)	0.5 (0;0.8)	0.7 (0.1;1.1)
JADAS10, median (IQR)	17 (13.1;19.2)	9.7 (12.5;3.5)	15.2 (11.5;22.5)

Abstract THU0553 – Table 2. Improvement at month 6 and tolerability

	Cohort 1 +2 LEF+TNFi	Cohort 3 MTX +TNFi	OR (Cohort 3 vs. 1+2)	P
JADAS improvement	35.1%	54.6%	2.2 [1.4–3.4]	<0.001
JADAS MDA (≤ 3.8)/ remission (≤ 1)	36.2%/13.8%	41.7%/19.6%		n.s.
AE (rate)	160 (57.4%)	1845 (46%)	0.63 [0.41–0.96]	0.031
Infections (rate)	37 (23.4%)	410 (22.2%)		n.s.
Nausea (rate)	9 (5.3%)	156 (8.5%)		n.s.
Elevated transaminases (rate)	8 (5.3%)	112 (6.1%)		n.s.

Conclusions: Combination with both leflunomide and methotrexate to treatment with TNF-inhibitors resulted in clinically meaningful improvements with a comparable rate of patients reaching JADAS-MDA and JADAS-remission at month 6 of treatment. Leflunomide turned out to be a well-tolerated alternative to methotrexate for polyarticular JIA.

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THU0554

RITUXIMAB (RTX) IN PAEDIATRIC DISEASES: DESCRIBING ITS PHARMACODYNAMICS WITH A FOCUS ON B-CELL DEPLETION AND REPOPULATION, INFECTIONS AND ANTI-DRUG ANTIBODIES

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Background: Rituximab (RTX) is increasingly used in rheumatologic, ^{1,2} hematologic³ and renal diseases.⁴ The induced B cell depletion can lead to hypogammaglobulinemia and thus an increased risk of infection.⁵ B cell depletion is not always achieved, and this has a negative effect on therapeutic response.⁶ Anaphylaxis is a frequent side effect of RTX and has been associated with the occurrence of anti-drug antibodies (ADA) against RTX.⁷

Objectives: To describe in different paediatric patient groups the pharmacodynamics of RTX in children by outcome variables, i.e. success of B-cell depletion and time of B cell repopulation, as well as the risk factors for severe infections and anaphylaxis.

Methods: Patient data of children who received RTX between 2008 and 2017 at our centre were retrospectively collected. Three patient subgroups were defined: autoimmune diseases (AID), immune dysregulation (ID) and renal diseases (RD). B cell repopulation was defined as a number above the cut-off value of B cell depletion ($=0.050 \times 10^6/l$ or $<2\%$ of the total amount of lymphocytes).

Results: B cell measurements were performed in 53/55 patients. B cell depletion was not achieved in 9 patients. In the 35 patients with B cell repopulation, median time until repopulation was 155 days (IQR 105–222): in the AID group (n=12) 129 days (IQR 77.5–243, $p=0.363$), in the ID group (n=5) 172 days (IQR 154–181, $p=0.574$) and in the RD group (n=18) 163 days (IQR 121–229, $p=0.847$). After RTX treatment, in 36 patients IgG levels were measured of which 14 (39%) had low IgG levels on at least one occasion (median 7 g/L [range 0.6–38.1 g/L]). Severe infections leading to hospitalisation occurred in 15 (27%) cases. An allergic reaction during or directly after RTX infusion was observed in 27 patients (49%). Anaphylaxis, defined as a systemic allergic reaction, characterised by impairment of airway, breathing, circulation or consciousness, occurred in 10 of these patients (18% of total cohort). Seven patients were tested for anti-RTX antibodies of whom 6 tested positive: 5 patients in the AID-group and one patient with renal disease. Allergic reactions occurred in all 6 while RTX failed to induce B cell depletion in 4 of these.

Conclusions: Time-to-B-cell-repopulation after RTX did not significantly differ between different paediatric patients groups. Severe infections were common (27%) in the cohorts studied. It is unclear from our data whether this is merely related to RTX treatment. Presence of ADA against RTX seems to predict failure of B-cell depletion and/or anaphylaxis after RTX treatment.

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