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.

Disclosure of Interest: None declared


THU0554 RITUXIMAB (RTX) IN PAEDIATIC 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, hematologic and renal diseases. The induced B cell depletion can lead to hypogammaglobulinemia and thus an increased risk of infection. B cell depletion is not always achieved, and this has a negative effect on therapeutic response. Anaphylaxis is a frequent side effect of RTX and has been associated with the occurrence of anti-drug antibodies (ADA) against RTX.

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*10^6/L or <2% of the total amount of lymphocytes).

Results: B cell measurements were performed in 5355 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) 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]). 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. Anaphylaxis was 2% of the total amount of lymphocytes.

Conclusions: Time-to-B-cell-repopulation after RTX did not significantly differ between different paediatric patient 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.

Key points: B cell depletion is not always achieved, and this has a negative effect on therapeutic response. Anaphylaxis is a frequent side effect of RTX and has been associated with the occurrence of anti-drug antibodies (ADA) against RTX. ADA against RTX is seen in 2% of the total amount of lymphocytes. Severe infections are 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.

REFERENCES:

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 (pJIA) were included in ICON after a median disease duration of 6 months (IQR: 3.0–11.1).

Methods: 4,440 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 9.6 (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=0.49, p=0.001). However, there was no significant association between the JADI scores and quality of life (PedsQL), and functional limitations (CHAQ, all r<0.05).

Results: Table 1 displays the distribution of patients in the different cohorts. In the AID group (n=1361), 18% of patients (58%) compared to 1845 events in 626 (46%) on MTX (OR 1.6 [1.0–2.4], p=0.031). No differences were noted for the number of infections, nausea or elevation of transaminases.

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