on arthritis in mice and (iii) to decipher the effect of ABX464 on human macrophages and T cells.

Methods: miR-124 was measured in human monocyte-derived macrophages (huMDM) treated with ABX464 for 4 days and in patients with ulcerative colitis included in a phase IIa RCT in blood and rectal biopsies at day 56 by TaqMan qPCR. Collagen-induced arthritis (CIA) was induced using usual protocol and ABX464 was given by gavage 2 weeks at 40mg/kg after the 2nd injection of collagen and Freund adjuvant. HuMDM were exposed to 5 µM of ABX464 or DMSO (control) for 4 days, during a M1-polarization. Cytokines and chemokines were assessed in supernatants using both Proteome Profiler Array and Luminex. PBMCs were exposed to ABX464 (5 µM) for 6 days. Th1 (IFN-γ+), Th17 (CCR6+IL-17+), Th2 (CRTH2+ IL-4+) and Tregs (CD25+CD125-/loFoxP3+) were assessed by flow cytometry. IL-6 receptor was assessed in CD4+ supernatant using ELISA.

Results: ABX464 increased miR-124 *in vitro* by 3.41 folds in huMDM (p=0.001) compared to DMSO. The phase IIa RCT conducted in 32 patients with moderate to severe active ulcerative colitis showed a good safety profile and significant clinical efficacy. A strong increase of miR-124 was observed both in blood and rectal biopsies of patients treated with ABX464 (637 and 769 folds respectively, compared to placebo, p<0.05). The use of ABX464 drastically decreased the incidence of arthritis from 52% (15/29 mice) to 10% (3/30 mice) in a CIA model. Macrophages treated with ABX464 produced significantly less MCP-1 (median decrease -67%, p=0.004), CXCL-1 (-18%, p=0.004) and SERPIN-E1 (-53%, p=0.004), as confirmed by the two techniques (n=9). ABX464 significantly decreased Th17 (-56%, p=0.02), while increasing Th2 (+21%, p=0.01). IL-6 soluble receptor was significantly decreased in supernatant of PBMCs treated with ABX464 (-43%, p=0.04).

Conclusion: We demonstrated that ABX464 increases miR-124 both *in vitro* and in ulcerative colitis patients. *In vitro*, ABX464 decreased the expression of miR-124 target genes, that is MCP-1, CXCL-1, SERPIN-E1 in macrophages and decreases the number of Th17 as well as IL-6 soluble receptor in CD4+ T cells. A phase IIa RCT is currently ongoing in patients with rheumatoid arthritis and inadequate response to methotrexate and/or TNF-inhibitors (n=60). Results are expected during 2020 summer.

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THE CHOICE OF bDMARD OR tsDMARD AS FIRST LINE THERAPY: DATA OF THE TARDIS-RA REGISTRY, A NATIONWIDE BELGIAN BIOLOGIC REGISTRY

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Background: The Tool for Administrative Reimbursement Drug Information Sharing (TARDIS) is an electronic platform combining data collection from all Belgian patients with Rheumatoid Arthritis (RA) on advanced therapy, together with a drug reimbursement request. Therapy choice after initial 2 classical synthetic DMARD failure is left to the treating rheumatologist in Belgium.

Objectives: To investigate first-line therapy choices for tumor necrosis factor inhibitor (TNFi) biologic (b) DMARDs, non-TNFi bDMARDs or targeted synthetic (ts) DMARDs via patient characteristics and initial treatment response in the TARDIS-RA registry.

Methods: All Belgian rheumatologist inserted patient data online when prescribing a b/tsDMARD. When data was entered for the first time, previous and current use of DMARD therapies was registered. Every next bDMARD or tsDMARD initiation, prolongation and discontinuation was registered electronically. First prolongation is 6 months for bDMARDs and 12 weeks for tsDMARDs, and yearly thereafter. Patients were selected for this analysis if they started a TNFi, non-TNFi or tsDMARD therapy between Jan 2018 and Jan 2019. Rituximab was excluded. Baseline characteristics of bionative patients per therapy were compared with Mann-Whitney U or Chi² tests were appropriate. Regression analyses, adjusted for age, DAS28 baseline and disease duration, evaluated DAS28 change, remission (DAS28<2.6) and low disease activity (LDA, DAS28<3.2) between b/tsDMARDs at first TARDIS follow-up.

Results: In 2018, 1263 bionative RA patients were included. Table 1 describes this population. Time until 1st follow-up differed between groups with 183 (181-184) days for bDMARD versus 84 (84-84) days for tsDMARD patients. Linear regression showed an effect of therapy type on DAS28 change in bionative patients (p=0.017). Logistic regression showed no difference per therapy for remission (p=0.090) nor low disease activity (p=0.123). Proportions of therapy prolongations at 1st follow up visit did not differ per therapy type.

Table 1. Baseline characteristics and treatment response of first-line TNFi, Non-TNFi or tsDMARDs

	TNFi	Non-TNFi	tsDMARD	p-value
Number patients	696 (57%)	293 (25%)	215 (18%)	
Age (years)	55, (45-64)	58, (51-68)	58, (49-66)	<0.001
Disease duration (years)	3, (1-7)	3, (1-9)	5, (2-13)	<0.001
DAS28 Baseline	4.8, (4.3-5.5)	5.1, (4.4-5.7)	4.7, (4.2-5.4)	0.010
DAS28 Change	2.2 (1.0-3.0)	2.2 (1.1-3.2)	1.9 (0.9-2.7)	0.014
Remission	296 (50%)	123 (49%)	78 (42%)	0.143
LDA	377 (64%)	153 (61%)	105 (56%)	0.196
Prolongation therapy	492 (82%)	219 (87%)	161 (86%)	0.158

Number given are median, (IQR) or number (proportion). TNFi = tumour necrosis factor inhibitor, ts= targeted synthetic, DAS = disease activity score, DAS28 change = DAS28 at 1st follow up visit minus DAS28 at baseline, remission = DAS28<2.6, LDA = low disease activity = DAS28<3.2, Prolongation = therapy was continued at 1st follow-up visit. Mann-Whitney U or Chi square tests were used where appropriate.

Conclusion: Initial therapy choices are partially driven by patient profile, although other factors such as patient preferences could not be verified. DAS28 change for tsDMARDs seemed less important versus bDMARDs, but can possibly be attributed to the preset evaluation moment being sooner for tsDMARDs versus bDMARDs aside of patient profile differences in age and disease duration. In contrast, proportion of remission, low disease activity and therapy prolongation did not differ by therapy.

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