First year results from the prospective German pregnancy register Rhekiss

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Background

There is still limited evidence on the safety of a substantial number of drugs in pregnancy and lactation. With the increasing number of new options to treat inflammatory rheumatic diseases, there is a growing need for systematic collection of prospective real-world data on drug safety in pregnancy and lactation. Prospective randomized studies are not conducted in women who are pregnant or wish to conceive. Therefore, systematic and prospective observation in daily care is the only possibility to gather these data.

Purpose

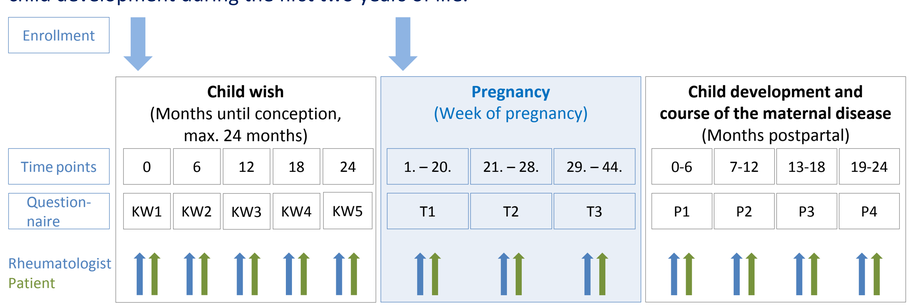
To determine the safety of various drug treatments during pregnancy and the influence of the underlying rheumatic disease on outcome and child development.

Methods

Rhekiss is a prospective web-based longitudinal observational cohort study. Patients can be included via the rheumatologist until week 20 of their pregnancy or when they seek advice from their rheumatologist with a concrete wish to become pregnant.

At baseline, sociodemographic parameters, prior pregnancies, and comorbidities are reported.

During observation, rheumatologists and patients report on all given drug treatments, details on the course of the maternal disease, the development of the pregnancy (including sonography examination results), maternal or fetal complications during pregnancy, pregnancy outcomes, and child development during the first two years of life.

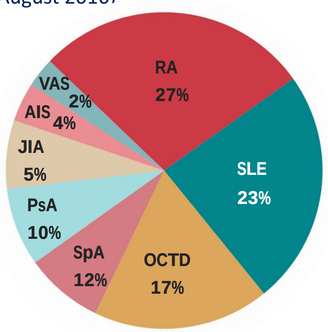


The register is designed as uniform platform with specific modules for various inflammatory rheumatic diseases. Only pseudonymized data are used, data security issues conform with regulatory authorities have been implemented.

We thank all participating rheumatologists who have enrolled patients, especially: Henes J, Aries P, Lorenz HM, Glaser C, Späthling-Mestekemper S, Kreher G, Günzel J, Specker C, Schnorfeil M, Käßer U, Zeuner R, Baraliakos X, Saar P, Mewes S, Krause D

Results

Since the start of the register on the 15th of September 2015, already 364 patients have been enrolled by 99 rheumatologists. At time of analyses, questionnaires were available from 259 patients. 232 of them were already pregnant at inclusion, 27 have been enrolled in the pre-pregnant (child wish) module (which started on the 10th of August 2016)



RA: Rheumatoid arthritis
SLE: Systemic lupus erythematosus
OCTD: Other connective tissue disease
SpA: Spondyloarthritis
PsA: Psoriatic arthritis
JIA: Juvenile idiopathic arthritis
AIS: Autoinflammatory syndromes
VAS: Systemic vasculitis

Figure 1: Distribution of diagnoses among patients enrolled.

	RA	SLE	OCTD	SpA	PsA	JIA	AIS
N	70	61	44	32	26	12	10
Age (years)	32.9	32.2	33	33.1	31.8	31	31.3
Duration of disease (years)	7.3	7.2	6.1	5.8	7.1	24	10
Severity of disease (1-5)	2.7	2.3	2.2	2.4	2.4	2.4	2.5
Physician global (0-10)	2.6	1.4	1.7	2.5	2.8	1.7	3.2
Pregnancy week	14.1	12.7	13.1	15.2	12.6	12.6	13.3
Patients with 1st pregnancy	52%	51%	57%	53%	65%	64%	56%
Pregnancy was planned	91%	82%	89%	79%	82%	88%	33%
Rheumatologic consultation before pregnancy	84%	82%	72%	73%	86%	100%	100%

Table 1: Characteristics of pregnant patients at inclusion, stratified by diagnose, only for diagnoses with ≥ 10 patients. Values are mean, if not otherwise specified.

	bDMARD naïve	bDMARD stopped before pregnancy (mean weeks before pregnancy)	bDMARD at pregnancy start (mean weeks of pregnancy when stopped)
No. of pregnancies by diagnoses	**RA/SpA/PsA/JIA:** 47 **SLE/OCTD:** 78 **All:** 131	**RA/SpA/PsA/JIA:** TNFi: 12 (31 w) Tocilizumab: 3 (33 w) Abatacept: 1 (15 w) Stelara: 1 (2 w) **SLE/OCTD:** TNFi: 1 (27 w) Belimumab: 1 (23 w) **All:** 20 (28 w)	**RA/SpA/PsA/JIA:** TNFi: 32 (6 w) Rituximab: 1 (5 w) Tocilizumab: 3 (6 w) **SLE/OCTD:** Belimumab: 2(2 w) **All:** 40 (6 w)

Table 2: Patients exposure to biologic DMARDs before and during pregnancy.

Adverse events during pregnancy were reported 60 times in 39 patients; 29 of them (in 15 patients) were **hospitalized serious adverse events**. The most severe serious events were premature labor/rupture of membranes (4 (SLE), 1 (AIS)), HELLP syndrom (1 (SLE), 4 (OCTD)), postpartal cerebral insult (OCTD) and a herpes zoster triggered macrophage activating syndrom (AIS).

The most frequently reported **non-serious events** were bleedings (8), infections (7) and hypertension (5). Complications during pregnancy and also post partum were most frequent in patients with SLE than in patients with other diagnoses.

Outcome: So far, the pregnancy outcome was reported in 94 patients. In 4 patients a spontaneous abortion in week 10, 5, 9 and 14 was reported (2 RA, SLE, OCTD). In one pregnancy (SLE), malformations were detected by sonography leading to elective abortion in week 17. All other pregnancies ended in livebirths. One patient (SLE) developed a severe HELLP syndrome with termination of the pregnancy in week 23 (bDMARD naive, treated with AZA and HCQ throughout pregnancy). The very small newborn (470 gramm at birth) died on day 14 due to sepsis.

Conclusion

The German pregnancy register Rhekiss was initiated to fill the knowledge gap on the course and outcomes of pregnancies in patients with rheumatic diseases as well as on the current use and the safety of treatments during pregnancy and lactation. The fast uptake of patients in the register shows that there is a substantial need for and a high interest in real-life data to guide treatment decisions. Further analyses of the register data will concentrate on specific aspects or diseases.

Funding Rhekiss is a collaborative project of the DRFZ Berlin and the Rheumazentrum Rhein-Ruhr e.V. Düsseldorf, jointly funded by both institutions. *www.rhekiss.de*

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