Abstract #: 02

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Title: Therapeutic drug monitoring of azathioprine and tacrolimus in SLE pregnancies: Preliminary results from the LEGACY cohort

Objective(s): In the prospective "Lupus prEGnAnCY (LEGACY)" cohort we evaluated azathioprine (AZA) and tacrolimus (TAC) levels at the first pregnancy (baseline) visit of women with systemic lupus erythematosus (SLE).

Method(s): LEGACY is a prospective cohort enrolling unselected SLE pregnancies ≤16 6/7 gestational weeks at 7 Systemic Lupus International Collaborating Clinics. We record demographics, disease activity, and drugs. In addition, whole blood samples are collected at baseline to determine AZA metabolites (e.g., erythrocyte-free 6-thioguanine, 6-TG) and trough TAC levels if applicable. The present study included Montreal LEGACY participants prescribed either AZA or TAC ≥3 months prior to their first pregnancy visit. We characterized AZA metabolite and TAC levels as continuous and categorical variables (i.e., non-adherent, sub-therapeutic, therapeutic, and supra-therapeutic, using established cut-offs in nonpregnant populations). We defined patients as non-adherent if they had undetectable or barely detectable levels despite appropriate dosing.

Result(s): Of 64 LEGACY pregnancies enrolled in Montreal, 23 (36%) and 6 (9%) were prescribed AZA and TAC, respectively. Among those prescribed AZA, only 9% had therapeutic levels, while 91% were sub-therapeutic or non-adherent. Compared to those with therapeutic levels, pregnancies with sub-therapeutic or non-adherent AZA levels were more likely to occur in women of non-Caucasian ethnicity/race, on steroids, with longer SLE duration, and with prior lupus nephritis. Among those prescribed TAC, 50% (3/6) had therapeutic levels, while 33% (2/6) and 17% (1/6) were sub-therapeutic and supra-therapeutic, respectively. No patient on TAC were identified as non-adherent. Less than half (43%) of pregnancies non-adherent to AZA were in Lupus Low Disease Activity State (LLDAS) at baseline as opposed to 71% of those with higher AZA levels (i.e., sub-therapeutic or therapeutic). Of the pregnancies with sub-therapeutic TAC levels, 50% (1/2) were not in LLDAS, while all (4/4) pregnancies with therapeutic or supra-therapeutic TAC levels were in LLDAS at baseline.

Conclusion(s): We observed that most SLE pregnancies prescribed AZA had sub-therapeutic levels, with nearly a third identified as non-adherent. Pregnancies with lower AZA and TAC levels may be less likely to achieve LLDAS. Despite low numbers, our preliminary results suggest the value of personalized drug monitoring as a novel approach to precision medicine in pregnant SLE women, that might improve efficacy, safety, and adherence in a high-risk population.