Background: Tacrolimus (TAC), an immunosuppressant, can be used in second-line maintenance therapy for interstitial lung disease (ILD) in patients with dermatomyositis (DM) [1]. Although some studies reported the clinical efficacy of initial high-trough levels of TAC in combination with GC and IV Cy in induction therapy for severe DM-ILD [2], there have been no useful clinical tools for deciding suitable initial dose of TAC. Genotype of polymorphisms in cytochrome P450 (CYP) 3A5 enzyme was reported to play an important role in pharmacokinetics of TAC [3], and we made a formula for deciding initial dose of TAC according to CYP3A5 genotypes in our previous study. 

Objectives: In our previous study (retrospective study), we set the target trough according to the severity for nine DM-ILD patients, six of whom were CYP3A5 *3/*3 and investigated the dose of TAC that could attain the trough using their CYP3A5 genotyping. Using these results, we developed a formula for deciding initial daily dose of TAC (target trough weight / [(151.1, if CYP3A5 *3/*3) or (86.5, if CYP3A5 *1 allele)]). In this study, we prospectively examined the usefulness and accuracy of this formula.

Methods: We introduced TAC for new six DM-ILD patients who visited our hospital between November 2019 and May 2020 (prospective study). The starting dose of TAC was decided by using the formula. We assessed the association between predicted and observed trough concentration of TAC at first measurement date (from day 2 to day 4), using linear regression analysis. We also assessed the days for attaining the target trough concentration between the patients using the formula (prospective group) and six patients with CYP3A5 *3/*3 (retrospective group).

Results: CYP3A5 genotype of all six DM-ILD patients were *3/*3 and underwent the TAC treatment by using the formula. The predicted and observed trough concentration of first measurement date were significantly correlated in the patients (r=2. 897, p=0.0041) (Fig.1). Compared with our retrospective study, target trough was more quickly attained in patients of the prospective study (Fig.2).

Conclusion: The formula which we made for attainment target trough concentration based on CYP3A5 genotype was useful for deciding the starting dose of TAC. We also showed that we could attain the target trough concentration at early stage of initial treatment by using the formula.

REFERENCES:
Background: Antisynthetase syndrome (ASyS) may have different clinical phenotypes and outcomes associated with different anti-aminoacyl RNA-synthetase (anti-ARS) antibodies. Its wide clinical spectrum can include inflammatory myopathy, interstitial lung disease (ILD), arthritis, fever, mechanic’s hands, and Raynaud phenomenon (RP).

Objectives: To describe a nationwide, multicentre cohort of Portuguese patients with ASyS.

Methods: Retrospective analysis of patients with ASyS from nine Portuguese Rheumatology centers. Data on patients’ signs and symptoms, laboratory results, pulmonary radiological findings (computed tomography) and treatment (immuno-modulators) were collected.

Results: Among the 70 patients included, 42 patients (60%) were anti-Jo1–positive, 11 (15.7%) were anti-PL12–positive, 10 (14.3%) were anti-PL7–positive, 4 (5.7%) were anti-EJ–positive and 2 (2.9%) were anti-OJ–positive. In one patient it was not possible to identify the type of antibody. Antibody overlap was found in 15 patients (21.4%), who were positive for anti-Ro52 antibodies. The general clinical characteristics and outcomes associated with different anti-ARS antibodies are shown in Table 1. The diagnosis delay was greater in patients positive for anti-Jo-1, compared to anti-PL-12 and anti-PL-7. The follow-up was shorter for anti-PL-7-positive patients. Anti-PL7-positive patients had lower rates of arthritis when compared to anti-Jo-1 (p < 0.01). When compared with anti-Jo-1 ARS, myositis was less common in anti-PL12 (p = 0.04). ILD prevalence was similar in the different ARS subgroups. Glucocorticoids (GCs) were the most frequently used class of drugs. Pulmonary modulators (e.g. azathioprine, mycophenolate mofetil) were preferred when lung involvement occurred. Only two patients were treated with rituximab or mycophenolate mofetil when preferred when lung involvement occurred. Only two deaths were reported, being one associated with lung neoplasia.

Conclusion: This is the first study investigating the clinical phenotypes of Portuguese patients with ASyS. These results are generally concordant with data retrieved from international cohorts.

REFERENCES: