Attending supervised interventions requiring periodic medical center visits can be burdensome and patients may decline participation, whereas, effective home-based exercise interventions that do not need regular medical center visits are likely to be more accessible and acceptable for patients with AS. Recently, increasing evidences have been accumulated that the wearable devices could facilitate patients with inflammatory arthritis by giving exercise instructions and improving self-efficacy. Therefore, patients with AS may benefit from an effective technology-assisted home-based exercise intervention.

**Objectives:** To investigate the efficacy of a comprehensive technology-assisted home-based exercise intervention on disease activity in patients with AS.

**Methods:** This study was a 16-week assessor-blinded, randomized, waiting-list controlled trial (ChiCTR1900024244). Patients with AS were randomly allocated to the home-based exercise intervention group and the waiting-list control group. A 16-week comprehensive exercise program consisting of a moderate intensity 84%-78% HRmax aerobic training for 30min($\pm$5 min per session) and a functional training for 60min on 3 days/week was given to patients in the intervention group immediately after randomization, with 15h training sessions for two consecutive days by a study physical therapist at baseline and Week 8. The aerobic exercise intensity was controlled by a Mio FUSE Wristband with a smartphone application. The functional training consisted of the posture training, range of motion exercises, strength training, stability training and stretching exercises. Patients in control group received standard care during the 16-week follow-up and started to receive the exercise program at Week 16. The primary outcome was ASDAS at Week 16. The secondary outcomes were BASDAI, BASFI, BSAI, ASAS HI, peak oxygen uptake, body composition and muscle endurance tests. The mean difference between groups in change from baseline was analyzed with the analysis of covariance.

**Results:** A total of 54 patients with AS were enrolled (26 in intervention group and 28 in control group) and 46 (85.2%) patients completed the 16-week follow-up. The mean difference of ASDAS between groups in change from baseline to 16-week follow-up was −0.2 (95% CI, −0.4 to 0.003, P = 0.032), and the mean change from baseline was −0.4 (95% CI, −0.5 to −0.2) in the intervention group vs. −0.1 (95% CI, −0.3 to 0.01) in the control group, respectively. Significant between-group differences were found between groups for BASDAI (−0.5 [95% CI, −0.9 to −0.2], P = 0.004), BASMI (−0.7 [95% CI, −1.1 to −0.4], P < 0.001), BASFI (−0.3 [95% CI, −0.6 to 0.01], P=0.035), peak oxygen uptake (2.7 [95% CI, 0.02 to 5.3] ml/kg/min, P=0.048) and extensor endurace test (17.8 [95% CI, 0.5 to 35.2], P=0.044) at Week 16. Between-group differences were detected in ASAS HI (−0.9 [95% CI, −1.7 to −0.1], P=0.030), body fat percentage (−1.0 [95% CI, −2.0 to −0.01] %, P=0.048) and visceral adipose tissue (−4.9 [95% CI, −8.5 to −1.4] cm², P=0.008) at Week 8, but not at Week 16. No significant between-group differences were detected in the total lean mass, time up and go test and the flexor endurance test during the follow-up.

**Conclusion:** Comprehensive technology-assisted home-based exercise has been shown to have beneficial effects on disease activity, physical function, spinal mobility, aerobic capacity, and body composition as well as in improving fatigue and morning stiffness of patients with AS.

**References:**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2020-eular.5100

### Advances in treating SLE and lupus nephritis

**OP0160 HYDROXYCHLOROQUINE BLOOD LEVELS AND RISK OF THROMBOTIC EVENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Hydroxychloroquine (HCQ) has a primary role in the treatment of systemic lupus erythematous (SLE). Beyond its pleiotropic immunomodulatory effects on Toll-like receptor and type I interferon signaling, HCQ use has been found to be protective for thrombosis in SLE (1). Optimal dosing of HCQ in SLE is unknown. The longitudinal measurement of HCQ blood levels may provide an opportunity to individualize weight-based dosing strategies and reduce risk of toxicity.

**Objectives:** Examine the association of HCQ blood levels with thrombotic events in a longitudinal SLE cohort.

**Methods:** 812 SLE patients with HCQ blood level measured prior to the thrombotic events were included: 93% Caucasian, 4% African American, 4% Caucasian. HCQ blood levels were quantified by liquid chromatography-tandem mass
Thrombotic Events are Associated with Lower Mean HCQ Blood Level

<table>
<thead>
<tr>
<th>Thrombotic Event</th>
<th>Mean HCQ Blood Level (± Std. Dev.)</th>
<th>No Event</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any thrombosis</td>
<td>695 ± 464</td>
<td>887 ± 562</td>
<td>0.029</td>
</tr>
<tr>
<td>Any venous thrombosis</td>
<td>682 ± 374</td>
<td>881 ± 560</td>
<td>0.19</td>
</tr>
<tr>
<td>DVT/PE only</td>
<td>615 ± 384</td>
<td>881 ± 559</td>
<td>0.055</td>
</tr>
<tr>
<td>Any arterial thrombosis</td>
<td>708 ± 539</td>
<td>882 ± 558</td>
<td>0.13</td>
</tr>
<tr>
<td>Stroke</td>
<td>720 ± 643</td>
<td>880 ± 557</td>
<td>0.029</td>
</tr>
</tbody>
</table>

Conclusion: HCQ blood levels are inversely associated with risk of any thrombosis and of venous thrombosis in patients with SLE in a prospective analysis. Reduction of HCQ dosing, as suggested by the American Academy of Ophthalmologists (2), could reduce or eliminate the benefit of hydroxychloroquine to prevent thrombosis.

References:

Acknowledgments: The Hopkins Lupus Cohort is supported by NIH Grant RO1 AR069572.

Disclosure of Interests: Michelle A Petri Grant/research support from: GSK, Eli Lilly and Company, Consultant of: Eli Lilly and Company, Maximilian Konig: None declared, Jessica Li: None declared, Daniel Goldman: None declared. DOI: 10.1136/annrheumdis-2020-eular.1236

OP0161

ASSOCIATION OF BASELINE CYTOTOXIC GENE EXPRESSION WITH USTEKINUMAB RESPONSE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic Lupus Erythematosus (SLE) is a clinically and biologically diverse disease, for which only one new therapy has been approved in the past 60 years. In a phase 2 trial on patients with mild-to-moderate SLE, ustekinumab (UST) improved clinical and laboratory measures of disease activity compared with placebo (PBO).1

Objectives: We previously reported an association of IFN-γ reduction with response to UST,1 suggesting an impact on the IL12/Th1 axis. To extend these findings, we performed unbiased transcriptomic analysis from baseline whole blood samples to identify genes that discriminate UST responders (UST-R) from non-responders (UST-NR) using the primary endpoint of Systemic Lupus Erythematosus Responder Index (SRI)-4 at week 24 to define response.

Methods: UST was studied in a Ph2 PBO-controlled study of 102 patients with seropositive SLE and active disease despite standard therapy. Patients were randomized 3:2 to receive IV UST 90mg or PBO every 8 weeks. Whole blood gene expression at baseline was measured via microarray using RNA samples from 100 patients, as samples from 2 patients failed quality control. An unbiased approach was used to identify gene signatures present at baseline that associate with UST response. Recombinant IL-12 or IL-23 was incubated in vitro with whole blood from 6 healthy donors for 24h and RNA-Seq was performed to determine the effect of these treatments on representative genes comprising the UST response signature.

Results: A non-biased machine learning algorithm identified a 9-gene whole blood signature composed primarily of cytokotic cell-associated transcripts (PRF1, KLRL1, GZMH, NKG7, NLNY, FGFBP2, TRGC2, TARP, TRGV2) that was enriched at baseline in UST-R vs UST-NR. By Gene Set Variation Analysis, the cytokotic signature enrichment in UST-NR was less at baseline than both UST-R and a healthy control cohort (P=0.0087, P=0.056, respectively), whereas UST-R cytokotic gene enrichment was similar to healthy controls (P>0.31). No significant difference in cytokotic signature enrichment was observed at baseline between PBO responders and PBO non-responders or healthy controls (Figure). Enrichment levels of the cytokotic gene signature remained stable over time in PBO and UST-NR groups while a trend of decreased cytokotic signature was observed in UST-R, although never reaching levels seen in UST-NR. To begin to understand the relationship between IL-12 and IL-23, the targets of UST, and the cytokotic signature, whole blood was stimulated with these cytokotines in vitro. Recombinant IL-12, but not IL-23, resulted in increased expression of representative members of this cytokotic gene signature.

Conclusion: We identified a novel cytokotic signature in baseline blood samples that associated with UST response in SLE. The observation that IL-12 can increase this signature in vitro and that IL-12 is a robust inducer of cytokotic cell activity2 as well as IFN-γ3 suggests an important role of IL-12 blockade in the mechanism of action of UST in SLE.

References: