- The iCHIP® microarray technology is being further developed to generate a clinically useful test to rule in a diagnosis of SLE relative to other related autoimmune diseases.

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AB1164 RABIOPRED, AN INNOVATIVE THERAGNOSTIC TOOL FOR PRECISION MEDICINE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Anti-TNF alpha biologicals are an important breakthrough in the treatment of Rheumatoid Arthritis (RA) patients. However, 30–40% of RA patients do not respond to these therapies. Therefore, there is an unmet need for a tool to predict treatment response that would help clinicians choose an optimal treatment for RA patients.

Objectives: Under the framework of Horizone2020 SME Instrument of European Commission, Firalis has identified and developed a panel of 2159 mRNA genes which can predict non-response to anti-TNF alpha therapy using the HTG EdgeSeq platform, an innovative combination of a nuclease protection assay & next generation sequencing (NGS).

Methods: RABIOPRED assay is a proprietary panel of Firalis signatures, which also includes targets selected by the *BTCure consortium*, to predict treatment response of anti-TNF alpha biologicals. In total 2175 targets were selected for the development and 2159 are successfully included in the panel. Each oligonucleotide is a 100-mer comprising a 25-mer "wing" at the 5' end and 3' end, and a 50-mer sequence in between that is complementary to the target mRNA. QC is checked for secondary structure and absence of homology with other sequences. Analytical parameters are assessed and repeatability of the RABIOPRED assay is validated on both Paxgene and purified RNA samples. Sample input is set at 32 µl for Paxgene RNA blood and 25 ng for extracted RNA.

Results: Mean correlation factor for 12 samples on 8 replicates for Paxgene and RNA samples are $R^2>0.97$ and $R^2>0.99$ respectively. First analysis and predictive modelling shows an AUC over 0.95 for the prediction of non-response to anti-TNF alpha. In the present work, we disclose the performance of the CE-IVD RABIOPRED assay based on more than 200 samples obtained from the prospective clinical studies, PRINT and RA-TNF. The algorithm will be further validated within the ongoing RABIOPRED Proof-of-Performance study (ClinicalTrials.gov Identifier: NCT03016260) in 720 patients treated by anti-TNF alpha biologicals (5 originators and 3 biosimilars) launched in December 2016. First version of the CE-IVD RABIOPRED assay will be available during Q2 2017 and open for testing.

Conclusions: We are showing that we can accurately measure mRNA expression with RABIOPRED assay using HTG-EdgeSeq NGS platform. Preliminary performance of the assay shows that it can efficiently predict treatment response to anti-TNF alpha biologicals. The algorithm will be later on validated in a multi-centric proof-of-performance clinical study.

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AB1165 THE MINIMAL CLINICALLY IMPORTANT DIFFERENCE (MCID) RAISES THE SIGNIFICANCE OF OUTCOME EFFECTS ABOVE THE STATISTICAL LEVEL

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Background: In measurement of outcome effects, the patient's subjective perception to feel a change in health defines clinical effectiveness irrespective of statistical significance. Nevertheless, many – especially pharmacological – studies argue with statistical effects alone.

Objectives: To review, develop, illustrate, and discuss current and proposed new concepts of effect quantification and significance.

Methods: Different methods for determining minimal clinically important differences (MCIDs) were reviewed and further developed focusing on their characteristics and (dis)advantages. The concepts were illustrated by empiric rehabilitation effects (evaluation study) and a randomized controlled trial (investigative study) in knee osteoarthritis.

Results: In controlled studies, empirical score differences between verum and placebo become statistically significant if sample sizes are sufficiently large. For example, a score difference of 5 points (scale 0–100) between the verum and the placebo effect becomes statistically significant, if the sample sizes are $n\geq33$ for each of both groups at a standard deviation=10 of the score differences (baseline to follow-up). MCIDs by contrast, are defined by patients' perceptions, which led to "anchoring" of effects by the "transition" item, where patients rate their change of health between baseline and follow-up in an evaluation study. The MCID for improvement by the "mean change method" is the difference of the mean change experienced by the "slightly better" group minus that of the "almost equal" group. The MCID can be expressed as absolute or relative score, as effects size (ES), standardized response mean (SRM) and standardized mean difference (SMD) (bivariate). It can further be adjusted by multivariate regression modeling. In our example of knee osteoarthritis, the MCID for pain relief was 8.74 score points (scale 0–100), 17.15% of the baseline score, ES=0.407, SRM=0.413, SMD=0.469. This is consistent to the range of 0.30–0.50 for MCIDs reviewed in literature. After adjusting for potential confounders, the MCID was 7.09 score points or an increase of 2.9% per score point to feel better obtained by logistic regression.

Conclusions: Absolute and relative MCIDs are easy to interpret and apply to data of investigative studies. MCIDs expressed as ES/SRM/SMD reduce bias, which mainly results from dependency on the baseline score. Multivariate linear and logistic regression modeling further reduces bias by adjustment for possible confounders and increase validity. Anchor-based methods use clinical/subjective perception to define MCIDs and should be clearly differentiated from distribution-based methods that provide statistical effect significance only.

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AB1166 QUANTUM BLUE® ADALIMUMAB: EVALUATION OF A POINT OF CARE RAPID TEST FOR THERAPEUTIC DRUG MONITORING OF SERUM ADALIMUMAB LEVELS

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease affecting approximately 1% of the population [1]. The pathogenesis of RA involves the overexpression of tumor necrosis factor alpha (TNFα) and other cytokines [2]. Adalimumab (ADA) is a human monoclonal antibody directed against TNFα and is highly effective in the treatment of RA. For efficient treatment trough levels of ADA need to be adjusted within a therapeutic window which is 5 to 10 µg/mL [3]. A rapid test allows faster reporting of trough levels, providing a great advantage over test formats that need samples to be sent to a central or service laboratory. Here we report on the technical performance evaluation of the Quantum Blue® Adalimumab lateral flow test.

Objectives: Development and performance evaluation of a rapid test for the monitoring of ADA trough levels in human serum at the point of care.

Methods: The sandwich lateral flow immunoassay uses a TNFα coated gold label and a highly specific monoclonal antibody immobilized on the test membrane to detect ADA in diluted human serum samples. Sensitivity of the assay was determined by calculating limit of detection (LoD) and limit of quantification (LoQ) according to CLSI EP17-A2 guideline. Moreover, the assay was evaluated regarding cross-reactivity with other therapeutic antibodies targeting TNFα, influence of rheumatoid factors (RF) and high dose hook effect. A method comparison was performed against a commercially available ELISA (RIDASCREEN® ADM Monitoring, R-Biopharm, Germany) to compare the trough level results of 40 patients treated with ADA. All statistical analyses were performed with Analyse-it for Excel.

Results: The Quantum Blue® Adalimumab test allowed analysis of serum samples within 15 minutes. The samples were diluted 1:20 in chase buffer before application onto a test cassette (volume 80 µL). The readout was performed with the Quantum Blue® Reader resulting in adalimumab concentration levels in the lower µg/mL range. The test exhibited a LoD of 0.2 µg/mL and a LoQ of 0.69 µg/mL. No high dose hook effect was detected for samples containing up to 1000 µg/mL ADA. The latter two data sets allowed a measuring range of 1 to 35 µg/mL of ADA in patient samples. Other therapeutic TNFα blockers, like infliximab and golimumab, showed no cross-reactivity with the Quantum Blue® Adalimumab test. RF showed no influence on correct measurement of ADA at all tested concentrations. The method comparison to a well-established commercial ELISA method revealed a slope of 1.12 and a regression coefficient (r^2) of 0.90 (by Passing-Bablok). A Bland-Altman analysis showed a bias of 1.9% confirming the overall excellent correlation of the two methods as well as the accuracy of our newly developed rapid test.

Conclusions: The BÜHLMANN Quantum Blue® Adalimumab assay enables the quantitative determination of ADA trough levels over the clinically relevant range in serum with a time to result of only 15 minutes. The assay exhibits an excellent accuracy and correlation to a well-established laboratory reference