ABSTRACT NUMBER: 0871

Disease-associated Central Nervous System Activation Predicts Good Clinical Response to Tumor Necrosis Factor Inhibition in Rheumatoid Arthritis Patients – "The PreCePRA Study"

Juergen Rech[1], Prof. Dr. Andreas Hess[2], Koray Tascilar[1], Dr. Hannah Schenker[3], verena schönau[1], Marina Sergeeva[2], Jutta Prade[2], Silke Kreitz[2], Mageshva Sulvakumar[2], Laura Konerth[2], Sandra Strobelt[2], Matthias Englbrecht[4], Prof. Dr. Dr. Axel Hueber[5], Eugen Feist[6], Prof. Dr. Mario Zaiss[1], Gerd Burmester[7], Frank Behrens[8], Dr. Michaela Koehm[9], Prof. Dr. Christoph Baerwald[10], Dr. Stephanie Finzel[11], Dr. Arnd Kleyer[12], Prof. Dr. Reinhard Voll[11], Dr. Julie Roesch[13], Prof. Dr. Arnd Doerfler[13], Prof. Dr. Nemanja Damjanov[14], Prof. José António P. Da Silva[15] and Georg Schett[16], [1]Department of Internal Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany, Deutsches Zentrum für Immuntherapie (DZI), Friedrich Alexander University Erlangen-Nuremberg and Universitätsklinikum Erlangen, Erlangen, Germany, Erlangen, Germany, [2]Institute for Experimental Pharmacology FAU Erlangen-Nürnberg, Erlangen, Germany, [3]Department of Internal Medicine 3 - Rheumatology and Immunology, Department of Internal Medicine 1 - Gastroenterology, Friedrich-Alexander University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany, Deutsches Zentrum für Immuntherapie (DZI), Friedrich Alexander University Erlangen-Nuremberg and Universitätsklinikum Erlangen, Erlangen, Germany, Erlangen, Germany, [4]Freelance Healthcare Data Scientist, Eckental, [5]Department of Internal Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany, + Rheumatologie, Klinik für Innere Medizin 5, Klinikum Nürnberg Nord, Prof.-Ernst-Nathan-Str. 1, 90419, Nürnberg, Deutschland, Erlangen, Germany, [6]Department of Rheumatology, Helios Clinic Vogelsang-Gommern, cooperation partner of the Otto von Guericke University Magdeburg, Gommern, Germany, [7]Department of Rheumatology and Clinical Immunology, Charité – Universitätsmedizin Berlin, Berlin, Germany, [8]University Hospital Goethe University Frankfurt and Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Frankfurt, Germany, [9]Goethe-University & Fraunhofer ITMP, Frankfurt, Germany, [10]Medizinische Klinik III - Bereich Rheumatologie, Liebigstraße 20, 04103 Leipzig, Leipzig, Germany, [11]Universitätsklinikum Freiburg, Klinik für Rheumatologie und Klinische Immunologie, Hugstetterstraße 55, 79106 Freiburg, Freiburg, Germany, [12]Department of Internal Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany, Deutsches Zentrum für Immuntherapie (DZI), Friedrich Alexander University Erlangen-Nuremberg and Universitätsklinikum Erlangen, Erlangen, Germany; Charité - Universitätsmedizin Berlin Med. Klinik mit Schwerpunkt Rheumatologie und Klinische Immunologie Berlin, Erlangen, Germany, [13]Department of Neuroradiology, Friedrich - Alexander - Universitaet Erlangen - Nuernberg and Universitaetsklinikum Erlangen , Erlangen , Germany, Erlangen, Germany, [14]Belgrade University School of Medicine, Institute Institute of Rheumatology, Belgrade, Belgrade, Serbia, [15]Head of Department Reumatologia. Hospitais da Universidade (SRHUC), Coimbra, Portugal, [16]Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany

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SESSION INFORMATION

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Title: **Abstracts: RA – Diagnosis, Manifestations, & Outcomes II: Bad Blood (Serologic and Imaging Biomarkers)**

Session Type: Abstract Session

Session Time: 3:00PM-4:30PM

Background/Purpose: Rheumatoid arthritis (RA) is an chronic inflammatory disease that is frequently treated with tumor necrosis factor inhibitors (TNFi). Little is known about predictors of response to TNFi. As clinical response in RA is measured by composite scores that contain a substantial number of subjective patients-orientated domains (pain, global disease perception) we speculated that patients with high disease representation in the central nervous system (CNS) may respond better to TNFi than patients in whom the disease is less represented in the CNS.

Methods: Phase 3,international multicenter, double-blind, placebo-controlled, parallel-group study with active RA patients. All patients underwent a functional MRI (fMRI) scan of the CNS at baseline measuring central nervous system CNS activation (voxels) by joint compression. Patients were stratified according to fMRI (high voxel, HV; low voxel, LV) and randomized 2:1 into treatment with the TNFi certolizumab-pegol (CZP) or placebo (PLB). The primary efficacy analysis compared the percentages of patients reaching low disease activity (LDA) according to DAS28 (≤3.2) at week 12. In addition, exploratory multi-parametric MRI assessment of brain anatomy and function was performed and analyzed with machine-learning approaches.
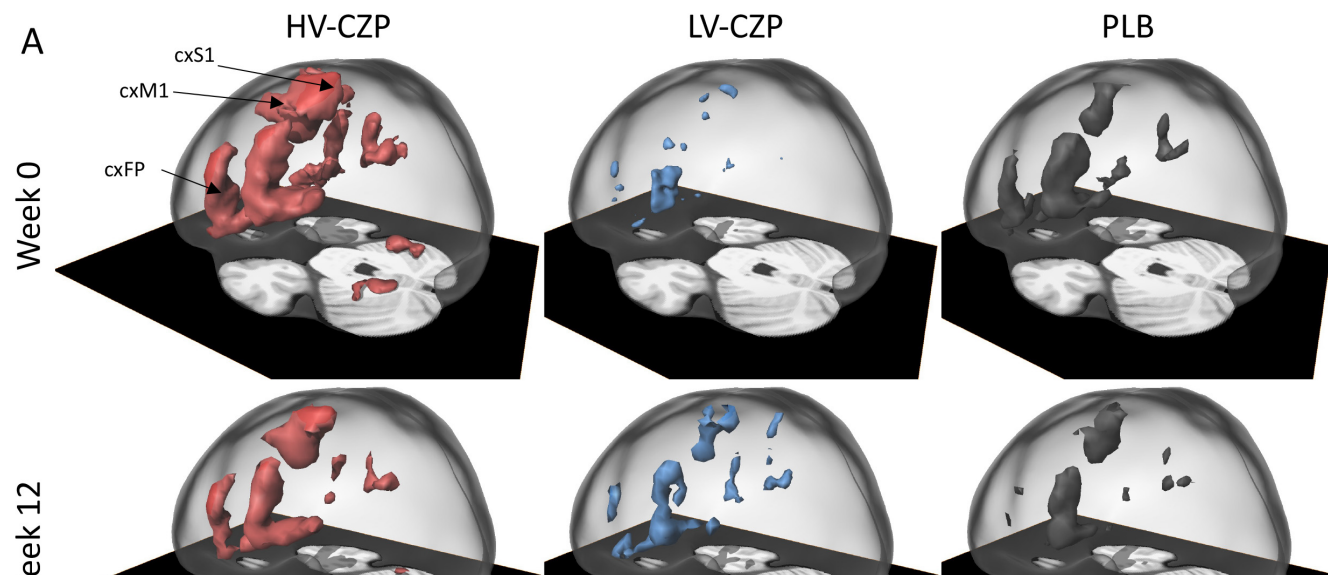
Results: 148 RA patients were screened and 139 patients were randomized to the HV-CZP arm(N=49), the LV-CZP arm (N=43) or PLB arm(N=47)patients. LDA was achieved by28/49 (57%) in HV-CZP,19/43 (44%) in LV-CZP and12/47 (26%) in PLB group at week 12. Response in the HV-CZP group but not in the LV-CZP group were significantly (p< 0.002) different from PLB group. HV-CZP and LV-CZP responses differed from placebo in patient-oriented outcomes (pain, patients global) but were similar in objective measures (CRP, joint swelling).The multi-parametric MRI together with machine learning confirmed, that only fMRI voxel size was able to separate CZP and PLB with an accuracy of 95.2%
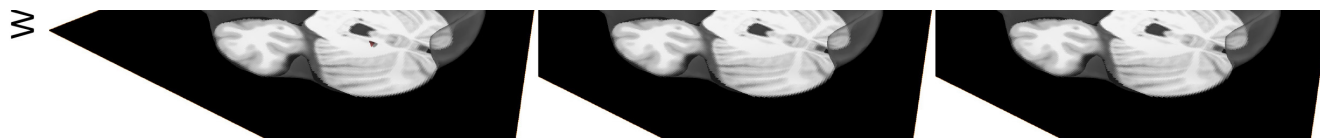
Conclusion: High disease-associated CNS activation,measured by fMRI,predicts good clinical response of RA patients to TNFi.
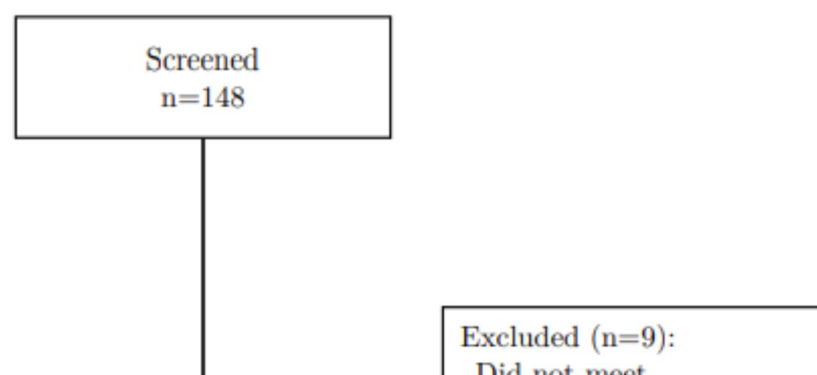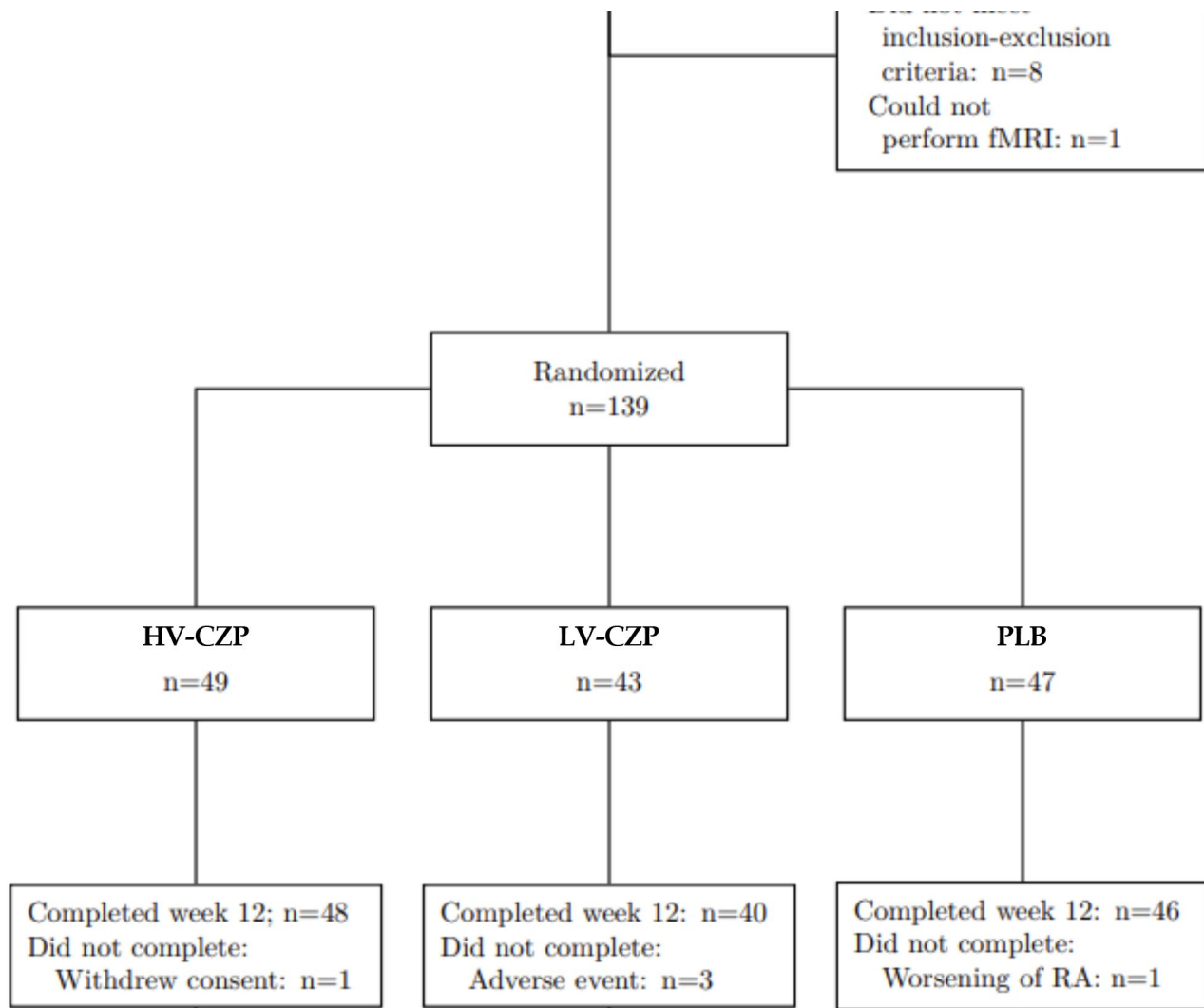
148 patients were screened in total, but 9 patients had to be excluded: 8 patients did not fulfill all inclusion criteria and 1 patient was not able to perform fMRI. Finally 139 patients were randomized into 3 groups: 92 patients received Certolizumab-Pegol (CZP), and were allocated to 2 different groups, stratified by the fMRI results at baseline: 49 patients were included in the high voxel count (HV-CZP)- group and 43 patients were included in the low voxel count (LV-CZP)- group. 47 patients were assigned to the placebo control (PLB) group.

3D surface visualization of activated volumes.

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