serious infections were 4.6 and 3.5 per 100 pt-years, respectively. Additional results will be presented for original PBO pts.

Conclusion: Nearly half the pts treated with TCZ QW maintained CR for the entirety of part 2, though flares still occurred in the remaining pts once they discontinued TCZ treatment. Among pts who maintained CR in part 2, higher proportions of those originally assigned to TCZ were treatment-free compared with those originally assigned to PBO. Retreatment with TCZ restored CR in pts who experienced flare. Cumulative GC doses over 3 years were lower in pts originally assigned to TCZ than in those originally assigned to PBO. No new safety signals were observed with TCZ exposure in GCA pts during the 3-year study.

REFERENCES:

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OP0142

THE IMPACT OF DISEASE EXTENT AND SEVERITY DETECTED BY QUANTITATIVE ULTRASOUND ANALYSIS IN THE DIAGNOSIS AND OUTCOME OF GIANT CELL ARTERITIS: RESULTS FROM THE TEMPORAL ARTERIOBLOPSY VERSUS ULTRASOUND (TABUL) STUDY AND VALIDATION IN AN INDEPENDENT COHORT

Sara Monti1,2, Cristina Ponte3, Claudio Pereira4, Federica Rumi5, Greta Carrara5, Catherine Kleyer5, Andrew Hutchings5, Wolfgang A. Schmidt5, Bhaskar Dasgupta5, Roberto Caporali5,1, Carlomaurizio Montecucco1, Raashid Luqmani4.

Objective(s): To develop a quantitative CDS score to improve the diagnosis of GCA, and to correlate the score with histologic findings and clinical outcome. To determine the additional role of clinical signs/symptoms to the CDS score.

Methods: We selected patients with a positive CDS and a diagnosis of GCA recruited into the Temporal Artery (TA) Biopsy (TAB) vs Ultrasound in Diagnosis of GCA (TABUL) study. Due to linearity we fitted 4 different CDS models including combinations of the following items: number of sites and distribution of halos, average and maximum intima-media thickness (IMT) at the level of the TA and axillary arteries (AX) and halos bilaterality. We fitted 4 models with clinical and laboratory findings. We combined the best CDS and clinical models (according to the Akaike Information Criterion) to identify independent correlates of a TAB diagnosis for GCA and of clinical outcome at 6 months (visual loss + VDI ocular + glucocorticoids > 10 mg/day and/or need for immunosuppressants) and performed a 10-fold cross-validation of the model. We validated the clinical outcome model on an independent cohort referred to the fast-track ultrasound clinics of two European rheumatology centres.

Results: We included 135 patients with GCA from TABUL (female: 68%, age 73 ± 8) and 72 patients from an independent cohort (female: 46%, age 75 ± 7). The

[1] MMP (Matrix Metalloproteinase)-9 Producing Monocytes Enable T Cells to Invasive the Vessel Wall and Cause Vasculitis.


[4] Inhibition of JAK-STAT Signaling Suppresses Pathogenic Immune Responses in Medium and Large Vessel Vasculitis.


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Figure 1. CASA scores combining rheumatological and clinical models to stratify patients according to the risk of having a positive temporal artery biopsy.

OP0141

CD2 AS A POTENTIAL THERAPEUTIC TARGET FOR GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is a granulomatous vasculitis of medium and large arteries. In GCA-affected arteries, vascular wall is destroyed by tissue-infiltrating CD4 T cells and macrophages, which leads to intramural neoangiogenesis, intimal hyperplasia and luminal occlusion.

Objectives: This study aimed to examine how CD28 signaling plays a role in vasculitis induction and maintenance and which pathogenic processes are dependent on CD28-mediated T-cell activation.

Methods: We engrafted human arteries into immunodecient NSG mice and mice engrafted by transfusing GCA immune cells. Human artery-NSG chimeras were treated with anti-CD28 domain antibody or control Ab. Using tissue and transcriptome analysis, immunohistochemistry, flow cytometry and immunometabolic analysis, treatment effects were examined in vivo and in vitro.

Results: Treating such humanized mice with an anti-CD28 domain antibody profoundly reduced tissue-infiltrating T-cells and effectively suppressed vasculitis. Mechanistic studies revealed that CD28 regulated AKT signaling, T-cell proliferation and differentiation of IFN-γ and IL-21-producing effector T-cells. Blocking CD28 signaling disrupted T-cell metabolic functionality; particularly, glucose utilization. Expression of the glucose transporter Glut1 and of glycolytic enzymes as well as mitochondrial oxygen consumption all rely on CD28 signaling. CD28 blockade effectively suppressed vessel wall remodeling processes such as adventitial microvesSEL formation and intimal hyperplasia as well as induction and maintenance of CD4+CD103+ tissue-resident memory T cells.

Conclusion: CD28 stimulation provides a metabolic signal required for pathogenic effector functions in GCA, implicating CD28 signaling as a promising therapeutic target.

REFERENCES: