Background: Giant cell arteritis (GCA) is a chronic disease, and affected patients suffer from relapses and glucocorticoid (GC)-related toxicity. Targeted therapies are emerging with the aim of achieving better disease control and reducing GC exposure. Blocking IL-6 receptor with tocilizumab has been a major advance in the treatment of GCA. However, approximately 40% of patients treated with tocilizumab in combination with GCs experience a flare or tocilizumab-related adverse event. Blocking GM-CSF receptor α with mavrilimumab significantly reduced risk of relapse and improved sustained remission at week 26 vs placebo in a Phase 2 trial. Not all patients satisfactorily respond to any therapy, indicating heterogeneity in leading pathogenic pathways among patients. For these reasons, it is crucial to understand the specific impact of targeted therapies on vascular lesions.

Objectives: In this study we investigated transcriptomic changes induced by tocilizumab or mavrilimumab in ex vivo cultured arteries from patients with GCA.

Methods: Temporal artery sections obtained for diagnostic purposes from 11 patients with histopathologically-confirmed GCA and 3 controls were cultured ex vivo and exposed to placebo, mavrilimumab, or tocilizumab (both at 20 µg/mL) for 5 days. Of 11 GCA donors, 2 had received no treatment prior to biopsy, 2 had received a single prednisone (60 mg) dose, and the remaining 6 had received treatment; in prednisone-treated patients, mean (SEM) treatment duration was 17.9 ± 8.7 days. A separate cohort of patients (consisting of five newly diagnosed patients with GCA, age- and sex-matched with the previous cohort) was used to validate 7 transcripts by real time PCR. Genes expressed in at least one comparison across groups (Figure 1A). 15 transcripts were lower, and 2 were higher in the tocilizumab group vs placebo; 3 transcripts were lower, and 2 were higher in the tocilizumab group vs placebo. Most changes elicited between treatments were unique, but CXCL1 was common (Figure 1B). None remained significant after correction for multiple comparisons. The effects of mavrilimumab and tocilizumab on GNAS, CXCL1, IL8, IL2, IRF3, MRC1 and BCL6 expression by Nanostring were consistent with the effect assessed using real time PCR in the separate validation cohort (Figure 1C).

Conclusion: Mavrilimumab and tocilizumab have a different transcriptomic impact on cultured arteries from patients with GCA, with some overlapping effects, although differential effects may have been attenuated by prior GC use. A better understanding of the impact of targeted therapies on vascular inflammation is needed to improve treatment options for patients with GCA.

Acknowledgements: The authors would like to thank: the Genomics core facility of the Institut d’Investigacions Biomèdiques August Pi I Sunyer (IDIBAPS) and Emily Plummer, PhD, Kiniksa Pharmaceuticals, for her invaluable contribution. The study was funded by Kiniksa Pharmaceuticals, Ltd. With support from: Fundación Clínica Barcelona, Fundación Privada Cellex, IDIBAPS, Universitat de Barcelona, Vasculitis Foundation, Marie Curie Actions, and Gobierno de España, Ministerio de Economía, Industria, y Competitividad.

Disclosure of Interests: Marc Corbera-Bellalta: None declared, Farah Kamberovic: None declared, Ferar Araujo: None declared, Roser Alba-Rovira: None declared, Georgina Espigol-Frigole Consultant of: Consulting for Janssen and Hoffmann-La Roche; Grant/research support from: Meeting attendance support from Boehringer Ingelheim, Marco Alba: None declared, Sergi Prieto-Gonzalez-Speakers bureau: Lecturer for Roche. Grant/research support from: Meeting attendance support from Idalfarmo and CSL Behring. José Hernández-Rodriguez-Speakers bureau: Lecturing for Novartis, Consultant of: Consulting for Sobi. Grant/research support from: Meeting attendance support from Sobi and Novartis, Patricia Pérez-Galan: None declared, Kent Bendongesa Shareholder of: Kiniksa Pharmaceuticals Corp., Employee of: Kiniksa Pharmaceuticals Corp., John F. Paolini Shareholder of: Kiniksa Pharmaceuticals Corp., Employee of: Kiniksa Pharmaceuticals Corp., Maria C. Cid Speakers bureau: Educational from GSK and Vifor, Consultant of: Consulting for Janssen, GSK, and Abbvie, Grant/research support from: Research grant from Kiniksa; meeting attendance support from Roche and Kiniksa.


POS0251 MYOFIBROBLASTS MAINTAIN TH1 AND TC1 POLARIZATIONS IN GIANT CELL ARTERITIS

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