Objectives: To test the hypothesis that low or absent ERAP1 activity alters CD8 T cell immunogenicity through changes in the HLA-B51 peptidome and shapes the CD8 T cell immune response in affected subjects.

Methods: We generated HLA-B51* ERAP1 KO LCL clones using CRISPR-Cas9, performed mass spectrometry of the immunoprecipitated MHC-class I peptidome with subsequent computational deconvolution for HLA-B51-binding peptides. We then assessed single cell (ICS), bulk (ELISA) and proliferative (CFSE) CD8 effector (IFN γ , granzyme B, perforin) T cell responses through stimulation of allogeneic donor cells with WT vs KO LCL and determined ERAP1 haplotypes in 49 untreated Turkish BD subjects with ocular and/or major vascular involvement as well as healthy donors (HD) whose PBMC were profiled using 6 multicolour flow cytometry panels.

Results: WT and KO peptidomes differed significantly ($p < 0.0005$ Fisher's exact test) with a distinctive shift of peptide length frequencies exceeding 9-mer (binding optimum) in the KO vs WT. This held true for computationally deconvoluted HLA-B51 binders. IFN γ secretion from CD8 T cells stimulated with KO LCL was significantly different from WT (ICS, $p = 0.0006$; ELISA, $p = 0.0059$) as were CD8 T cell proliferation and ICS of perforin/granzyme B* CD8 T cells. Analysis of 133 T, B, NK and monocyte cell populations revealed predominance of CD8 T and NKT cell subset in HLA-B51+/Hap10+ BD vs HLA-B51+/Hap10- BD and HD, accounting for 80% of all populations reaching significance ($p < 0.05$, Mann-Whitney). Naive and effector memory CD8 T cell subsets were inversely correlated. Cohen's effect sizes were large (> 0.8) or very large (> 1.2).

Conclusion: We show that absence of functional ERAP1 alters human CD8 T cell immunogenicity. This is mediated by an HLA-class I peptidome with propensity for longer peptides above 9mer and suggests loss or de-novo presentation of peptide-HLA-B51 complexes to cognate CD8 TCR. The reciprocal changes in antigen-experienced vs naive CD8 T cell subsets in affected subjects point to biologic significance of HLA-B51/Hap10 in BD. Collectively, our findings suggest that an altered HLA-B51 peptidome modulates immunogenicity of CD8 effector T cells in ERAP1-Hap10 carriers with BD and identify targets for future drug development.

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Disclosure of Interests: Arshed F. Al-Obeidi: None declared, Ann Cavers: None declared, Yesim Ozguler: None declared, Olivier Manches: None declared, Hua Zhong: None declared, Berna Yurttas: None declared, Beatrix Ueberheide: None declared, Gulen Hatemi Grant/research support from: BMS, Celgene Corporation, Silk Road Therapeutics – grant/research support, Consultant of: Bayer, Eli Lilly – consultant, Speakers bureau: AbbVie, Mustafa Nevzat, Novartis, UCB – speaker, Matthias Kugler: None declared, Johannes Nowatzky: None declared
DOI: 10.1136/annrheumdis-2020-eular.3885

OP0033

OPTIMIZATION OF TOCILIZUMAB THERAPY IN GIANT CELL ARTERITIS. A MULTICENTER REAL-LIFE STUDY OF 134 PATIENTS

M. Calderón-Goercke¹, D. Prieto-Peña¹, S. Castañeda², C. Moriano², E. Becerra-Fernández², M. Revenga², N. Alvarez-Rivas², C. Galisteo², Á. Prior-Español², E. Galindez², C. Hidalgo², S. Manrique Arijia², E. De Miguel², E. Salgado-Pérez², V. Aldasoro², I. Villa-Blanco², S. Romero-Yuste², J. Narváez², C. Gomez-Arango², E. Perez-Pampín², R. Melero², F. Sivera², A. Olive², M. Álvarez del Burgo², L. Marena Rojas², C. Fernández-López², F. Navarro², E. Raya², B. Arca², R. Solans-Laque², A. Conesa², C. Vázquez², J. A. Román-Ivorra², P. Lluch², P. Vela-Casasempere², C. Torres-Martín², J. C. Nieto², C. Ordas-Calvo², C. Luna-Gomez², F. J. Toyos Sáenz de Miera², N. Fernández-Llanio², A. García², J. L. Hernández¹, M. A. González-Gay¹, R. Blanco¹. ¹HUM.Valdecilla, Santander, Spain; ²Reference Centers from Spain, Spain

Background: Tocilizumab (TCZ) is the only biological agent approved in Giant Cell Arteritis (GCA). There is general agreement on the initial and the standard maintenance dose of TCZ. However, information on duration and optimization of TCZ in GCA is scarce.

Objectives: Our aim was to assess efficacy and safety of TCZ therapy optimization in an unselected wide series of GCA in clinical practice.

Methods: Multicenter study, 134 patients with GCA who received TCZ due to inefficacy/adverse events of previous therapy. Once complete remission was reached and based on a shared decision between patient and physician TCZ was optimized in some cases. Optimization was done by decreasing the dose and/or prolonging the TCZ dosing interval progressively.

Results: 134 GCA patients treated with TCZ (101w/33m); mean age 73.0±8.8 years. TCZ was administered IV to 106 (79.1%) patients and SC to 28 (20.9%). TCZ was optimized in 43 (32.1%) patients. No demographic, clinical manifestations or laboratory data differences had been found at TCZ onset (TABLE). After a follow up of 12 [6-15.5] months, and a

complete remission for 6 [3-12] months; the first TCZ optimization was performed. Median prednisone dose at first TCZ optimization was 2.5 [0-5] mg/day. TCZ IV was optimized from 8 to 4mg/kg/4weeks in 12 of 106 (11.3%) and from 162mg/SC/week to 162mg/SC/2weeks in 9 of 28 (32.1%) cases. Five (11.6%) of the 43 optimized cases relapsed. In 4 cases, the relapses were treated increasing TCZ up to the pre-optimization dose, in 1 case the route of administration was change (4mg/kg/4week to 162mg/SC/week). In 8 of 43 optimized patients (18.6%), it was possible to withdraw TCZ after complete remission for 30 [16.25-45.75] months. Regarding adverse events and severe infections were similar in both groups. The mean TCZ treatment costs were lower in the optimized group.

Conclusion: Once remission is reached in GCA patients under TCZ treatment, optimization of TCZ may be performed. Based on our experience it could be performed by reducing the dose with IV TCZ or by prolonging dosing interval with SC TCZ.

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TABLE

	OPTIMIZED-TCZ GROUP (n=43)	NON-OPTIMIZED TCZ GROUP (n=91)	p
BASAL FEATURES AT TCZ ONSET			
GENERAL FEATURES			
Age, years, mean± SD	68.9±8.7	71.4±8.5	0.125
Sex, female/male n(%)	32/10	68/24	0.779
Time from GCA diagnosis to TCZ onset (months), median [IQR]	19.5[7.75-45]	10.5[4-25]	0.047
SYSTEMIC MANIFESTATIONS			
Fever, n(%)	1(2.4)	8(8.7)	0.176
Constitutional syndrome, n(%)	11(26.2)	19(20.7)	0.476
PMR, n(%)	18(42.9)	56(60.9)	0.052
ISCHEMIC MANIFESTATIONS			
Visual involvement, n(%)	5(11.9)	23(25)	0.084
Headache, n(%)	26(61.9)	42(45.7)	0.081
Jaw claudication, n(%)	1(2.4)	11(12)	0.072
CORTICOSTEROIDS AT TCZ ONSET			
Prednisone dose, mg/d mean (SD)	15.1±11.1	25±17.4	0.001
FOLLOW-UP ON TCZ THERAPY (MONTHS), MEDIAN [IQR]	24[18-27]	6 [3-18]	0.000
RELAPSES			
Relapses, n(%)	5(11.6)	5(5.5)	0.207
End follow-up remission, n(%)	40(93)	84(92)	0.99
Severe side effects, n(%)	14(32.6)	22(24.2)	0.307
Serious infections, n(%)	6(14)	10(11)	0.878
Cost, (mean) euros per year			
IV	7 538.4	11 726.4	-
SC	7 329.0	11 726.4	-

Disclosure of Interests: Monica Calderón-Goercke: None declared, D. Prieto-Peña: None declared, Santos Castañeda: None declared, Clara Moriano: None declared, Elena Becerra-Fernández: None declared, Marcelino Revenga: None declared, Noelia Alvarez-Rivas: None declared, Carles Galisteo: None declared, Águeda Prior-Español: None declared, E. Galindez: None declared, Cristina Hidalgo: None declared, Sara Manrique Arijia: None declared, Eugenio de Miguel Grant/research support from: Yes (AbbVie, Novartis, Pfizer), Consultant of: Yes (AbbVie, Novartis, Pfizer), Paid instructor for: yes (AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunenthal, Janssen, Sanofi), Speakers bureau: yes (AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunenthal, Janssen, Sanofi), Eva Salgado-Pérez: None declared, Vicente Aldasoro Speakers bureau: Roche, AbbVie, MSD, UCB, Pfizer, Menarini, Grunenthal, Gebro, Novartis, Janssen, Ignacio Villa-Blanco Consultant of: UCB, Speakers bureau: Novartis, MSD, Lilly, Susana Romero-Yuste: None declared, J. Narváez: None declared, Catalina Gomez-Arango: None declared, Eva Perez-Pampín: None declared, Rafael Melero: None declared, Francisca Sivera: None declared, Alejandro Olive: None declared, María Álvarez del Burgo: None declared, Luisa Marena Rojas: None declared, Carlos Fernández-López: None declared, Francisco Navarro: None declared, Enrique Raya: None declared, Beatriz Arca: None declared, Roser Solans-Laque: None declared, Arantxa Conesa: None declared, Carlos Vázquez: None declared, Jose Andrés Román-Ivorra: None declared, Pau Lluch: None declared, Paloma Vela-Casasempere: None declared, Carmen Torres-Martín: None declared, Juan Carlos Nieto Speakers bureau: Pfizer, AbbVie, MSD, Novartis, Janssen, Lilly, Nordic Pharma, BMS, Gebro, FAES Farma, Roche, Sanofi, Carmen Ordas-Calvo: None declared, Cristina Luna-Gomez: None declared, Francisco J. Toyos Sáenz de Miera: None declared, Nagore Fernández-Llanio: None declared, Antonio García: None declared, J. Luis Hernández: None declared, Miguel A González-Gay Grant/research support from: Pfizer, AbbVie, MSD, Speakers bureau: Pfizer, AbbVie, MSD, Ricardo Blanco Grant/research support from: AbbVie, MSD, and Roche, Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, and MSD
DOI: 10.1136/annrheumdis-2020-eular.2574

Lung diseases and other comorbidities in RA

OP0034

DOES THE RISK OF VENOUS THROMBOEMBOLISM VARY WITH DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS?

V. Molander¹, H. Bower¹, J. Askling¹. ¹Division of Clinical Epidemiology, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden