

representation as to the accuracy of the content. The authors are solely responsible for the content in their abstract including accuracy of the facts, statements, results, conclusion, citing resources etc.

POS0207

PREDICTORS OF ADVERSE PREGNANCY OUTCOMES IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME IN THE FRENCH PROSPECTIVE STUDY GR2

Keywords: Observational studies/registry, Pregnancy and reproduction, Epidemiology

A. Murarasu^{1,2}, G. Guettrot Imbert³, V. Le Guern³, E. Lazaro¹⁰, A. Deroux⁵, O. Souchaud-Debouverie¹¹, P. Orquevaux¹², V. Langlois¹³, N. Ferreira-Maldent¹, T. Goulenok⁷, L. Perard¹⁴, V. Poindron¹⁵, N. Martin Silva¹⁶, F. Sarrot-Reynauld⁵, N. Belhomme^{8,9}, E. Pannier¹⁷, A. Moltó, L. Sentilhes¹⁸, C. Le Ray^{6,17}, C. Deneux-Tharau⁶, Y. Nguyen^{2,4}, N. Costedoat-Chalumeau^{2,3}. ¹Service de médecine interne et immunologie clinique, CHRU de Tours, Tours, France; ²Université Paris Cité, équipe ECAMO, CRESS UMR 1153 INSERM, Paris, France; ³Assistance Publique-Hôpitaux de Paris, Service de Médecine Interne, Centre de Référence Maladies Auto-immunes et Systémiques Rares, Hôpital Cochin, Université de Paris Cité, Paris, France; ⁴Service de Médecine Interne, Hôpital Beaujon, APHP, Université de Paris Cité, Paris, France; ⁵Service de Médecine Interne, CHU Grenoble-Alpes, Grenoble, France; ⁶Université Paris Cité, Obstétrical Perinatal and Pediatric Lifelong Epidemiology Research Team (OPPaLE), CRESS U1153, INSERM, INRAE, Paris, France; ⁷Service de Médecine Interne, Hôpital Bichat Claude Bernard, APHP, Paris, France; ⁸Service de Médecine Interne et Immunologie Clinique, Hôpital Universitaire Sud, Rennes, France; ⁹Inserm, EHESP, Irset (Institut de Recherche en Santé, Environnement et Travail)-UMR_S 1085, Rennes, France; ¹⁰Service de Médecine Interne, Hôpital du Haut-Lévêque, Pessac, France; ¹¹Service de Médecine Interne, CHU Poitiers, Poitiers, France; ¹²Service de Médecine Interne, Hôpital Robert Debré, Reims, France; ¹³Service de Médecine Interne et Maladies Infectieuses, Hôpital Le Havre, Le Havre, France; ¹⁴Service de Médecine Interne, Centre Hospitalier Saint Joseph Saint Luc, Lyon, France; ¹⁵Service d'Immunologie Clinique, Nouvel Hôpital Civil, Strasbourg, France; ¹⁶Service de Médecine Interne, CHU de Caen, Caen, France; ¹⁷Assistance Publique-Hôpitaux de Paris, Service de Maternité Gynécologie Obstétrique Port-Royal, Université de Paris Cité, Hôpital Cochin, Paris, France; ¹⁸Service de Gynécologie Obstétrique, CHU de Bordeaux, Bordeaux, France

Background: Although significant maternal haemorrhages and thrombosis risks have been documented in pregnant patients with antiphospholipid syndrome (APS) [1], there is a lack of robust data on the frequency and the predictors of adverse pregnancy outcomes (APO). The main study on this subject is the prospective American study PROMISSE on 144 women who carry antiphospholipid antibodies (and not only APS) [2] and were treated with aspirin and/or heparin in 67.4% and 52.1% of cases respectively. An APO occurred in 28/144 women (19.4%). The presence of lupus anticoagulant was the main predictor of APO.

Objectives: To investigate the rate and the predictors of APO in women with definite APS, in the French prospective study on pregnancy and rare autoimmune disease, GR2.

Methods: We included: (1) the first ongoing pregnancies at 12 weeks, (2) conceived before March 2023, (3) in women with definite APS according to 2006 classification criteria [3]. We excluded women with proteinuria (ratio > 1 g/g), serum creatinine > 100 µmol/L, and multifetal pregnancy. APO included intrauterine fetal death (IUFD), neonatal death because of prematurity or placental insufficiency, placental insufficiency with delivery ≤34weeks, and/or a small for gestational age (SGA) ≤3rd percentile. APO explained by another cause than APS or missing data on APO were excluded.

Results: We analysed 257 pregnancies in 257 women: 123 (47.9%) of which with thrombotic APS. 121/238 of the women (50.8%) had lupus anticoagulant at the time of pregnancy, and 60 (23.3%) had systemic lupus erythematosus (SLE). Treatment included low-dose aspirin (n=252; 98.0%), low-molecular-weight heparin (n=251; 97.7%), and hydroxychloroquine (n=145; 56.4%) including 59 in case of associated SLE. APO were observed in 38 (14.8%) pregnancies: 8 (3.1%) IUFD, 20 (8.0%) delivery ≤34weeks due to placental insufficiency, 3 (1.2%) neonatal death, and/or 17 (6.8%) SGA. APO were more frequent in the presence of lupus anticoagulant (21.5% versus 8.6% in its absence; p=0.006), antiβ2GP1 antibody (21.9% versus 9.6% if negative; p=0.008) and triple-positive status (28.6% versus 10.2%; p<0.005). No association was found between APO and the coexistence of SLE or history of thrombosis.

In multivariate analysis, the only independent factor associated with APO was the presence of lupus anticoagulant (ORa=2.66, 95%CI [1.10-6.41]).

Conclusion: This is the largest prospective study on predictors of APO in women with definite APS. Despite the majority of women being treated, the rate of adverse pregnancy outcomes remains high at 14.8%. Presence of lupus anticoagulant was the main predictor of APO.

REFERENCES:

- [1] Murarasu, et al. *Lancet Rheumatol* (2022).
- [2] Lockshin, et al. *Arthritis Rheum* (2012).
- [3] Miyakis, et al. *J Thromb Haemost* (2006).

Acknowledgements: We also thank the French Society of Internal Medicine (SNFMI), the French Society of Rheumatology (SFR), and the filière de santé des maladies auto immunes et auto-inflammatoires rares (FAI2R) for their scientific and technical support. The GR2 study has received grants from patient associations (Lupus France; association des Sclérodermiques de France, association Gougerot Sjögren, Association Francophone contre la Polychondrite chronique atrophiante), from the AFM-Telethon, the SNFMI, the SFR, the CMEI commission for Research and Innovation of Cochin Hospital, the Ministère de la Santé (the Clinical Research Contract—Database CRBDD17003), Foundation for Research in Rheumatology, ORRICK society (Prix Véronique ROUALET).

Disclosure of Interests: Anne Murarasu grants by Chugai and GSK for attending meeting, Gaelle Guettrot Imbert: **None declared**, Véronique Le Guern: **None declared**, Estibaliz Lazaro: **None declared**, Alban Deroux: **None declared**, Odile Souchaud-Debouverie: **None declared**, Pauline Orquevaux: **None declared**, Vincent LANGLOIS: **None declared**, Nicole Ferreira-Maldent: **None declared**, Thiphaine Goulenok Advisory board for GSK company, Laurent Perard: **None declared**, Vincent Poindron: **None declared**, Nicolas Martin Silva: **None declared**, Françoise SARROT-REYNAULD: **None declared**, Nicolas Belhomme paid instructor for GSK, speaker for GSK, Astrazeneca, consultant for Astrazeneca, Emmanuelle Pannier: **None declared**, Anna Moltó: **None declared**, Loic Sentilhes: **None declared**, Camille Le Ray: **None declared**, Catherine Deneux-Tharau: **None declared**, Yann Nguyen: **None declared**, Nathalie Costedoat-Chalumeau paid consultant for Bristol Myers Squibb, grants from Roche and UCB to her institution.

DOI: 10.1136/annrheumdis-2025-eular.B1177

© The Authors 2025. This abstract is an open access article published in Annals of Rheumatic Diseases under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>). Neither EULAR nor the publisher make any representation as to the accuracy of the content. The authors are solely responsible for the content in their abstract including accuracy of the facts, statements, results, conclusion, citing resources etc.

Basic and Clinical Poster Tours: Pain in Rheumatic Musculoskeletal Diseases

POS0208

PROTEOMIC SIGNATURES IN CHRONIC WIDESPREAD PAIN

Keywords: Biomarkers, Artificial Intelligence

L. Chen¹, J. Xie¹, D. Prieto-Alhambra¹. ¹University of Oxford, Oxford, United Kingdom

Background: Effectively managing chronic widespread pain (CWP) remains a clinical challenge.

Objectives: This study aimed to uncover proteomic biomarkers that could improve the diagnosis and prognosis of different CWP types.

Methods: We analyzed 2,923 plasma proteins from 29,254 participants in the UK Biobank, with 1.6% reporting CWP, defined as pain all over the body. We first modelled univariate association of each protein with CWP using logistic regression. We then created a sparse proteomic score (S-ProtS) and a comprehensive proteomic score (C-ProtS) by combing the top 10 and all significant proteins, respectively, using XGBoosting machine learning algorithms. Both scores were compared with a clinical score (CS) derived from key factors, including sleeplessness, feelings of being “fed-up,” tiredness, stressful life events, and a body mass index >30, identified from previous literature [1]. The prospective association of the ProtS (quantile 5 vs quantile 1) and various pain mechanisms was estimated using Poisson regression.

Results: Overall, 811 proteins were associated with CWP after Bonferroni correction. Both S-ProtS and C-ProtS performed similarly to the CS in terms of discrimination, with AUCs of 0.82 (95% CI: 0.77–0.87), 0.88 (95% CI: 0.83–0.92) and 0.81(95% CI: 0.76–0.86), respectively. Incorporating S-ProtS into the CS model enhanced discrimination, yielding an AUC of 0.87 (95% CI: 0.83–0.91) for WCP. A model combining C-ProtS and CS reached the highest discrimination, with an AUC of 0.92 (95% CI: 0.88–0.94). Prospective associations were observed with nociceptive pain (RR of S-ProtS per 1 SD: 1.68 [95%CI:1.52-1.85]; RR of C-ProtS: 1.67 [1.52-1.84]) and particularly with fibromyalgia (RR of S-ProtS: 5.84 [4.29-7.94]; RR of C-ProtS: 5.53 [4.09-7.49]). In contrast, no associations were observed with nociceptive (RR of S-ProtS: 1.06 [0.81-1.38]; RR of C-ProtS: 0.80 [0.60-1.07]) or neuropathic pain (RR of S-ProtS: 1.78 [0.90-3.54]; RR of C-ProtS: 1.47 [0.70-3.07]).

Conclusion: Proteomic signatures improve clinical discrimination to classify and prospectively predict CWP overall and phenotypes. More research is needed to unravel the mechanistic effects of these proteins on the development and progression of CWP.

REFERENCES:

- [1] Tanguay-Sabourin C, Fillingim M, Guglietti GV, Zare A, Parisien M, Norman J, Sweatman H, Da-Ano R, Heikkala E; PREVENT-AD Research Group; Perez J, Karppinen J, Villeneuve S, Thompson SJ, Martel MO, Roy M, Diatchenko L, Vachon-Preseau E. A prognostic risk score for development and spread of chronic pain. *Nat Med.* 2023 Jul;29(7):1821-1831. doi: 10.1038/s41591-023-02430-4. Epub 2023 Jul 6. PMID: 37414898; PMCID: PMC10353938.

Acknowledgements: NIL.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2025-eular.A451

© The Authors 2025. This abstract is an open access article published in *Annals of Rheumatic Diseases* under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>). Neither EULAR nor the publisher make any representation as to the accuracy of the content. The authors are solely responsible for the content in their abstract including accuracy of the facts, statements, results, conclusion, citing resources etc.

POS0209

IMPACT OF TIRZEPATIDE ON MUSCULOSKELETAL PAIN AND RISKY ANALGESIC USE AMONG NON-DIABETIC INDIVIDUALS WITH OVERWEIGHT OR OBESE BODY HABITUS: A PROPENSITY SCORE-MATCHED, ACTIVE COMPARATOR, NEW USER DESIGN STUDY

Keywords: Pain, Real-world evidence, Epidemiology

G. Challenger¹, K. S. K. Ma¹, N. McCormick¹, M. Kohler¹, J. Yin¹, C. Yokose¹, S. Rai¹, F. Porterfield¹, A. Jorge¹, H. Choi¹. ¹Massachusetts General Hospital, Boston, United States of America

Background: Tirzepatide is a dual gastric inhibitory peptide (GIP)/glucagon-like peptide 1 (GLP-1) receptor co-agonist that is currently approved in the United States (U.S.) and European Union for weight loss among patients with obesity or those with body mass index (BMI) ≥ 27 kg/m² with weight-related comorbidities. It has been hypothesized that GLP-1-based therapies may improve osteoarthritis symptoms indirectly through weight loss resulting in reduced mechanical stress to joints as well as directly through anti-inflammatory mechanisms [1, 2, 3]. The STEP 9 clinical trial recently demonstrated that patients with obesity and knee osteoarthritis who received semaglutide treatment experienced improvement in knee pain and function, as well as reduced use of non-steroidal anti-inflammatory drugs (NSAIDs) [4]. Tirzepatide notably differs from semaglutide in its dual agonism and comparatively increased weight loss [5]. There is currently no data on musculoskeletal pain outcomes or risky analgesic use for patients receiving tirzepatide.

Objectives: The aim of the present study was to examine whether patients who initiated treatment with tirzepatide had improved joint pain and required less analgesic use than those receiving phentermine (the most commonly prescribed anti-obesity medication in the U.S.) thereafter.

Methods: We conducted a population-based cohort study using the TriNetX Research network, a large, multicenter network of U.S. electronic health records and claims data. International Classification of Diseases, Tenth Revision (ICD-10) codes identified non-diabetic patients with BMI ≥ 27 kg/m². Using the intention-to-treat method, we analyzed the overall rate of prespecified musculoskeletal pain encounters and risky analgesic use (i.e., NSAIDs and opioids), as well as cardiovascular endpoints following initiation of therapy with tirzepatide or phentermine, excluding patients with prior history of the outcomes of interest. Outcomes were defined as ≥ 1 encounter with applicable ICD-10 code occurring one day to any time after the index event. Nausea served as a positive control outcome. Propensity score matching included over 400 prognostic factors to adjust for demographics, comorbidities, medications, family history, surgical history, and baseline BMI; representative covariates are included in Table 1. Kaplan-Meier analysis and Cox proportional hazards models estimated the risk of the outcomes of interest.

Results: A total of 62,722 patients started on tirzepatide and 119,020 patients started on phentermine were included. After 1:1 propensity score matching, 27,930 patients in each group were comparable with well-balanced baseline characteristics (Table 1; all standardized mean differences < 0.1). Mean follow-up time was 276 days (with standard deviation of 278 days) among patients on tirzepatide compared with mean follow-up time of 318 days (with standard deviation of 296 days) among patients on phentermine. Patients receiving tirzepatide were significantly more likely to achieve a normal BMI level than those receiving phentermine, with hazard ratio (HR) of 3.02 (95% CI: 2.61, 3.49). Initiation of tirzepatide was associated with overall lower risk of joint pain with HR 0.91 (95%

CI: 0.84, 0.99), including low back pain (HR 0.89 with 95% CI: 0.80, 0.98), hip pain (HR 0.88 with 95% CI: 0.78, 0.999), and knee pain (HR 0.84 with 95% CI: 0.76, 0.93). Tirzepatide was also associated with a lower risk of NSAID (HR 0.88 with 95% CI: 0.81, 0.95) and opioid prescriptions (HR 0.86 with 95% CI: 0.79, 0.93). As expected, the risk of nausea was increased among those receiving tirzepatide (HR 1.22 with 95% CI: 1.10, 1.35), while risks of mortality and overall major adverse cardiac events (acute myocardial infarction, cerebral infarction, and/or mortality) were reduced (respectively, HR 0.48 with 95% CI of 0.28, 0.80; and HR 0.77 with 95% CI of 0.61, 0.99).

Conclusion: This large population-based study of non-diabetic patients with overweight or obesity demonstrates improvement in musculoskeletal pain requiring clinical care, and risky analgesic use as well as cardiovascular outcomes, among those receiving tirzepatide in comparison to patients receiving phentermine. This provides further support for the use of tirzepatide in patients with overweight or obesity to reduce musculoskeletal pain and the need for NSAID and opioid medications.

REFERENCES:

- [1] PMID: 35091584.
[2] PMID: 39476345.
[3] PMID: 35280931.
[4] PMID: 39476339.
[5] PMID: 38976257.

Table 1. Baseline Characteristics of Patients Receiving Tirzepatide versus Phentermine after 1:1 Propensity Score Matching

	Tirzepatide (n = 27,930)	Phentermine (n = 27,930)	Std diff.*
Age at index, mean (SD)	45.9 (12.9)	45.6 (13.1)	0.024
Male	16.7%	16.1%	0.016
Female	73.7%	74.3%	0.012
Unknown gender	9.6%	9.6%	0.001
Comorbidities			
Hypertension	40.0%	38.7%	0.026
Chronic kidney disease	2.6%	2.5%	0.007
Ischemic heart disease	5.4%	5.0%	0.021
Heart failure	2.0%	1.8%	0.015
Liver disease	11.9%	11.5%	0.013
Cerebrovascular disease	3.0%	2.8%	0.011
Nicotine dependence	13.1%	13.2%	0.002
Alcohol-related disorders	3.0%	2.8%	0.010
Osteoarthritis	24.8%	24.2%	0.016
Knee osteoarthritis	12.7%	12.6%	0.004
Knee pain	25.0%	24.9%	0.002
Low back pain	27.2%	26.9%	0.006
Medications			
Beta blockers	26.9%	26.2%	0.014
ACE inhibitors	14.3%	13.8%	0.014
NSAIDs	62.1%	62.1%	0.001
Opioid analgesics	58.4%	58.3%	0.003
Measures			
BMI, mean (SD)	37.9 (6.5)	37.8 (6.5)	0.026
A1c, mean (SD)	5.6 (1.2)	5.6 (1.3)	0.004

* Std diff. (standardized mean difference) < 0.1 indicates negligible difference between groups. Baseline characteristics were defined as occurring any time up to one day prior to the index event.

Table 2. Outcomes Among Patients Receiving Tirzepatide versus Phentermine

Pain/analgesic outcomes	Unmatched, HR (95% CI)	Matched, HR (95% CI)
Joint pain	1.00 (0.95, 1.05)	0.91 (0.84, 0.99)
Low back pain	0.84 (0.79, 0.89)	0.89 (0.80, 0.98)
Hip pain	1.08 (1.00, 1.16)	0.88 (0.78, 0.999)
Knee pain	0.93 (0.88, 0.995)	0.84 (0.76, 0.93)
NSAID script	0.84 (0.81, 0.89)	0.88 (0.81, 0.95)
Opioid analgesics	0.82 (0.78, 0.86)	0.86 (0.79, 0.93)
Other outcomes		
Mortality	0.74 (0.54, 1.02)	0.48 (0.28, 0.80)
Major adverse cardiac events	1.29 (1.11, 1.51)	0.77 (0.61, 0.99)
Nausea	1.33 (1.25, 1.41)	1.22 (1.10, 1.35)
Achieved normal BMI	3.24 (3.01, 3.50)	3.02 (2.61, 3.49)

Note: Phentermine serves as the reference group. Abbreviations: HR, hazard ratio; CI, confidence interval; NSAID, nonsteroidal anti-inflammatory drug

Acknowledgements: NIL.

Disclosure of Interests: Gregory Challenger: **None declared**, Kevin Sheng-Kai Ma: **None declared**, Natalie McCormick: **None declared**, Minna Kohler: **None declared**, Janeth Yin: **None declared**, Chio Yokose: **None declared**, Sharan Rai: **None declared**, Florence Porterfield: **None declared**, April Jorge: **None declared**, Hyon Choi Ani, Protalix, Horizon, LG Chem, Shanton, LG Chem. **DOI:** 10.1136/annrheumdis-2025-eular.B3530

© The Authors 2025. This abstract is an open access article published in *Annals of Rheumatic Diseases* under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>). Neither EULAR nor the publisher make any