線上國際會議報告

2022歐洲風濕病醫學會年會
開會心得報告

服務機關：臺中榮民總醫院
姓名職稱：曾智偉 主治醫師
(線上)派赴國家/地區：丹麥
出國(線上會議)期間：2022/06/01-2022/06/03
報告日期：2022/06/02

摘要（含關鍵字）

歐洲風濕病醫學會年會自1947由歐洲抗風濕病聯盟 (英文全名 the European Alliance of Associations for Rheumatology, 縮寫 EULAR)舉辦的年會，算算聯盟成立到現今已經有75年歷史，因為疫情的關係算是第一次同時合併有線上跟實地參與開會的方式。歐洲抗風濕病聯盟是一個包含病友、醫護人員、科學家等等組成的非營利性學術組織，致力於促進、推動、跟支持風濕與肌肉骨骼相關疾病的研究、預防與治療。EULAR 現有45個科學學會組織組成，每年有18000名以上世界各地來參加的代表，是世界上風濕病學一年一度最重要的大會。也是各個風濕病專家們齊聚在一起分享新的治療的方式的地方。會中我分享『捷抑炎能有效降低 MDA5快速進展型間質性肺炎的死亡率』，希望透過發表自己的研究，讓自己也能融入相關領域的發展。

關鍵字：EULAR、MDA5。

目　次

內文

一、 目的

參與2022在丹麥舉行的歐洲風濕病醫學會年會 EULAR，借助論文發表機會，與與會的會員互相觀摩學習精進發炎性肌炎患者共病照護模式並爭取加入國際肌炎評估臨床研究的會議小組 International Myositis Assessment & Clinical Studies Group (IMACS)，以期未來參與更多國際上肌炎相關研究。

二、 過程

會議日期在2022年6月01日到6月03日。

開會期間配合政策去科博館幫忙兒童疫苗 BNT 施打，整個科大家白天的時候除了醫院常規以外還再加上兒童疫苗快打站，傍晚再上線參加歐洲風濕病醫學會年會，還好歐洲的會議大部分都是當地早上10點半才開始有很多大型的會議跟主題，只有很少數的一兩場是早上8點半開始，以前都看著資深醫師們去這些大型的風濕病醫學會，這次第二次親自參加才發現原來裡面 EULAR 裡面更新的知識每年都有不同的變化，雖然沒能獲選口頭報告自己的題目，但是自己的研究能被選上放在年會雜誌的最後面還是值得高興。最值得注意的是，跟亞太風濕病醫學會(APLAR)不同：我們每篇被選入的文章每一篇後面都有自己的 DOI，不像 APLAR 官方雜誌 IJRD 把所有的 Abstract 文章只用一個 DOI 做註記；這方面讓我在跟合作的日本教授來往 Email 時總覺得亞太風濕病學會的 Abstract 很沒有價值。

參加國際風濕病年會是希望可以在未來找到在相關領域 IMACS 這個組織在去年三月 Frederick W. Miller, M.D., Ph.D 退休之後，開始新陳代謝；邀請了 Lisa Rider , M.D.、Professor David Isenberg 以及英國曼徹斯特大學的 Hector Chinoy Ph.D., FRCP 出任領導，過去的肌炎疾病活動度多在 Lisa Rider 在10多年前的文章奠定基礎，但是這個位於美東的研究組織卻邀請了英國的教授來出任領導，而 Lisa 等比較資深的醫師似乎慢慢地在美國或是歐洲的相關肌炎討論會中較少出現了。看起來世代交替在進行。在今年的年會中沒有看到 Hector Chinoy 有演講但是多篇的跨國研究幾乎都有掛 Hector Chinoy 的名字。

跟以往在其他會議上看到的一樣年會 Myositis 的 update 都由瑞典卡洛林斯卡大學的 IE Lundberg 教授在主持。

可以注意到的是另外一外在英國曼徹斯特大學訓練畢業的 Latika Gupta，一位也算年輕的風濕病醫師，仔細注意的話還會發現原來跟 Hector Chinoy 同一間大學出來，Gupta 在亞太風濕病醫學會很活躍，對於肌炎很有興趣，應該是受到老師的鼓勵，建立起來了印度的 Registry。未來除了是個學習的對象也是可以進行合作的選擇醫師。

三、 心得

感謝院方支持，也期待未來能夠真的在疫情過後能夠親臨歐洲會議現場參與。我在年會發表的題目是捷抑炎能有效降低MDA5快速進展型間質性肺炎的死亡率。其實這篇文章我們只有比較了17位患者，研究的內容剛好就在疫情發生前就完成，陸續經過整理後我們也嘗試投了幾家主要的風濕病醫學期刊，但是病人數太少，所以被退了多次。希望經過這次年會的洗禮，聽取各方的建議後能夠早日登出。

MDA5快速進展型間質性肺炎的是在2004年 SARS 風暴的時候才發現的，而且 MDA5本身就是跟病毒的感染很有關係，所以在新冠發生的那一年，北京剛開始盛行的時候就有提到他們MDA5的病人量也逐漸增多，都是同輩且同樣有興趣的北京協和醫院風濕科王遷醫師，在當年一次的歐盟檢測試劑的學術就提到了他也同樣觀察到這樣的現象，也提醒我做好準備應付新冠來襲。我們對於 MDA5快速進展型間質性肺炎治療的方式應該也可以用於新冠肺炎治療的參考，其中我們所採納追蹤的 Biomarker 基本上跟新冠大同小異，加上自己發現其它對於肺纖維化有幫忙的 Biomarker，一直希望這些方法能夠被別人看見。

本科在過去的死亡個案中我們歸納發現到了在病患死亡之前的感染很多都有共通的地方就是巨細胞病毒的感染，也就是因為太多個案都有同樣的困擾，因此當我們碰到來勢洶洶的快速進展型間質性肺炎的時候，就提早準備投予預防性的抗生素跟抗病毒藥物。因為沒有用過這樣的經驗，我還請教了腎臟科對於巨細胞病毒感染的預防以及腎臟移植後肺囊蟲預防的方式，我採用了腎臟科醫師對於腎臟移植時的那種萬分小心，下定決心下次再碰到同樣的患者一定會盡早使用這些藥物或是頻繁的檢查有沒有這些感染避免太晚發現。

我採用了新的治療方式納入了使用在類風濕性關節炎患者的小分子藥物；俗稱口服生物製劑的捷抑炎用在患者身上，使用的時候還特別在科內的會議裡面提出來跟陳怡行主任、黃文男主任，及謝佳偉醫師討論我們該怎麼使用這樣的小分子藥物用在皮肌炎患者身上。無獨有偶的在去年底的美國風濕病醫學會年會，約翰霍普金斯的醫師已經很成功的使用捷抑炎把10位皮肌炎患者的皮膚給治療的非常成功。

今年剛剛過完的五月份，剛好是新冠疫情在全台蔓延的時刻，聽到病人剛出院當天卻又送回急診確診新冠再次入院的消息，病患出院前逐漸復原的腰大肌膿瘍又再一次惡化，甚至到休克影響到了腎功能，心裡就像是(現在電視節目每天都在講)上億的俄製先進坦克 T90被萬把塊的標槍飛彈打到一樣，之前的付出前功盡棄。聽到護理站報告一個接著一個新的院內或是出院患者感染，看著剛出院患者被隔離到樓上的病房的病歷紀錄，出院病摘都還沒完成，心裡正想著家屬會怎樣的抱怨在病房內染病的，當下即在 Line 群組嘀咕著難道院方出院前沒有可以再驗一次新冠的 PCR 嗎？ Google 一下就可以看到英國 NHS 的流程，人家 Leeds 這麼大的一間醫學中心，上面確實是有出院前48小時再次 PCR 的檢測，自己當天晚上就開始用通訊軟體敲打朋友群問看看世界其他醫院的作法，在疫情趨緩的日本從北海道大學、福島大學、順天堂大學的附設醫院以及德國都只有維持在住院前的時候作一次 PCR。

好吧，當然也有被網友吐槽自己院內的感控要做好才不會一直院內感染，科群組內也是繼續貼著院方的提醒，提醒何時可以做 PCR 的時機，沒有可以給所有人出院前免費 PCR 的資源。在面對眾多共病的風濕科以及長患有間質性肺炎的病患，長期住院的情況下出院前不能確定 COVID status 真的是個風險，科內最終討論的結果是和病人討論出院前自己做快篩，不然病房也沒有多餘的病房空間讓所有出院病患都能做 PCR 的同時還要有足夠空間讓患者可以等待結果。

結論就是，新冠感染也應該視同需要預防的病原體，也是要規則篩檢才能避免可能併發症的發生。未來 MDA5快速進展型間質性肺炎或是其它所有有關的風濕病患者也都要注意新冠感染，是未來也該被納入風險管理的一環。

四、 建議（包括改進作法）

1. 過去本科對於類風濕性關節炎的治療透過對肺結核與 B 肝的風險管理，能有效降低這兩個感染症的發病發生率並且提高類風濕性關節炎患者治療達標的比率，並獲得 SNQ 國家品質標章銅牌。我參考本科做法針對本科死亡率最高的快速進展型間質性肺炎的治療上，對於常碰到的感染併發症像是巨細胞病毒感染以及肺囊蟲感染的預防，讓我們在採取新的治療選擇的時候像是使用捷抑炎的治療可以避免這些感染造成不可挽回的敗血症與休克。會議參加後更確信未來可以在科內對這些快速進展型間質性肺炎應該廣泛性的使用預防性抗生素治療或是更密切且規則的檢測有無巨細胞病毒或是肺囊蟲的感染。未來會希望把研究擴大並仿照過去風險管理的方式，找出這類併發症的風險因子，提供科內參考變成治療標準。
2. 而且更應該考慮除了快速進展型間質性肺炎以外應該外推到像是其它類似的狀況包括間質性肺病已經面臨呼吸衰竭風險或是即將接受肺部移植治療時等等。
3. 面臨到不可避免的需要與新冠病毒共存，目前疫情期間應該要更主動一點的在出院前應針對風險高的患者進行 COVID 檢驗，儘管非現階段建議的適應症，但是對於高風險的患者在轉換病人照護環境的時候應該仿照轉介到護理照護機構前的檢查一樣，除了在體制內我們可以建議病人自行快篩以外，可否與病房團隊討論建請院方提供資源與空間讓病人能夠安心出院或是下轉，並納入未來快速進展型間質性肺炎也須考慮到的風險。
4. 建議科內針對風濕病患者成立染疫後的登錄資料庫，應開始長期追蹤這些染疫後的患者，再向學會建請成立全國資料庫。
5. 透過論文發表爭取曝光並填好履歷參與 IMACS membership，如果能夠成功參與，更要鼓勵更多年輕對發炎性肌炎有興趣醫師一同加入。

五、 附錄

1. 2012風濕病醫學會風險管理計畫公告 http://www.rheumatology.org.tw/news/News_Info.asp?/171.html
2. IMACS 新聞以及網站 https://www.niehs.nih.gov/research/resources/imacs/index.cfm
3. 本人發表論文摘要及詳細內容在 DOI: 10.1136/annrheumdis-2022-eular.3428

Objectives: To evaluate SSc immuno-clinical associations in the Rheumatic Diseases Portuguese Register (Reuma.pt) cohort.
Methods: Multicentre open cohort study including adult SSc patients registered in Reuma.pt up to February 2021. The associations between Ab expression and clinical data were established using Chi-Square, Fischer's Exact or Mann-Whitney U tests. The Bonferroni correction for multiple comparisons was applied to get $\alpha \leq 0.05$. Definite associations were defined by $p \leq 0.002$, and likely associations by $p \leq 0.05$.
Results: 1080 patients were included, with a mean age and disease duration of 60.2±14.6 and 12.4±10.0 years, respectively. Most were females (87.5%) and had white European ancestry (WEA, 93.2%). The most common disease subtypes were limited cutaneous (lcSSc, 57.4%), diffuse cutaneous (dcSSc, 17.7%), and very early diagnosis of SSc (VEDOSS, 12.3%). Most patients expressed antinuclear Ab (ANA, 93.4%), and the most frequent were anti-centromere (ACA, 54.6%), anti-topoisomerase I (Scl70, 21.8%), and anti-Pm/Scl Ab (PmScl, 4.7%). ACA had definite positive associations with female sex, older age at diagnosis, lcSSc, lower modified Rodnan skin score (mRSS, median 0 vs 4), and isolated sclerodactyly, and likely associations with a higher diagnosis delay, WEA and VEDOSS. ACA had definite inverse associations with flexion contractures (FC), myositis, digital ulcers (DU), and interstitial lung disease (ILD), and likely inverse associations with pitting scars (PS) and oesophageal involvement (OI).
Scl70 had definite positive associations with male sex, dcSSc, higher mRSS, FC, DU, PS, ILD, and OI, and likely associations with younger age at diagnosis, tendon friction rubs, active scleroderma pattern in capillaroscopy, and heart involvement.
PmScl had a definite association with myositis and likely associations with male sex, calcinosis, joints involvement, and ILD. Anti-U1RNP Ab had definite associations with younger age at diagnosis, MCTD and myositis, and likely associations with a lower diagnosis delay, African ancestry and joint involvement. Anti-RNA polymerase III Ab (RP3) had likely associations with higher mRSS and renal involvement. Anti-U3RNP Ab had a definite association with dcSSc and likely associations with calcinosis and renal involvement. Anti-Th/To Ab had likely associations with male sex and myositis. Anti-Ku Ab had likely associations with systemic lupus erythematosus and mixed connective tissue disease (MCTD) overlap syndromes.
Conclusion: There was a higher prevalence of ACA and PmScl compared to other cohorts, most likely due to the high proportion of WEA patients. Most immuno-clinical associations described in the literature apply, including ACA with lcSSc and Scl70 with dcSSc, DU, PS and ILD. However, Scl70+ patients did not have an increased risk of renal involvement, and ACA+ patients did not have an increased risk for calcinosis, PAH or OI, contrary to what was described in the literature. New findings included the association of PmScl with ILD and Scl70 with an active pattern in capillaroscopy. Also, anti-U3RNP+ and Th/To+ patients did not have an increased risk of ILD or PAH, contrarily to what was previously reported. These nuances may be specific to the Portuguese SSc population or signal previously reported associations as geographically specific.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.3389

AB0697 DRAMATIC REDUCTION OF MORTALITY RATE BY TOFACITINIB IN ANTI-MDA-5 ANTIBODY-POSITIVE PATIENTS WITH RAPIDLY PROGRESSIVE INTERSTITIAL LUNG DISEASE

C. W. Tseng[1,2], M. Satoh[3], Y. M. Chen[1,2,4,5,6]. [1]*Taichung Veterans General Hospital, Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, Taichung, Taiwan, Republic of China;* [2]*National Chung Hsing University, Department of Post-Baccalaureate Medicine, College of Medicine, Taichung, Taiwan, Republic of China;* [3]*University of Occupational and Environmental Health, Department of Clinical Nursing, School of Health Sciences, Kitakyushu, Fukuoka, Japan;* [4]*Taichung Veterans General Hospital, Department of Medical Research, Taichung, Taiwan, Republic of China;* [5]*National Chung Hsing University, Rong Hsing Research Center for Translational Medicine & Ph.D. Program in Translational Medicine, Taichung, Taiwan, Republic of China;* [6]*National Yang Ming Chiao Tung University, School of Medicine, College of Medicine, Taipei, Taiwan, Republic of China*

Background: Rapidly progressive interstitial lung disease (RP-ILD) is often seen in dermatomyositis patients with anti-melanoma differentiation-associated gene 5 (anti-MDA-5) antibody. They often have a poor prognosis with rapid decline in pulmonary function, leading to respiratory failure (1). Aggressive immunosuppressive therapy has been reported with improved prognosis, however; it may lead to opportunistic infections, including cytomegalovirus (CMV) or Pneumocystis pneumonia (PCP) infection (2, 3).
Objectives: This study aimed to evaluate the effectiveness of tofacitinib (TOF) in combination with CMV and PCP prophylaxis in anti-MDA-5-positive patients.
Methods: Medical records of 17 anti-MDA-5-positive RP-ILD patients enrolled during Mar 2017 to May 2021 were reviewed. RP-ILD was defined by the presence of deteriorated dyspnea, with a decrease in PaO2 levels and emerging radiographic anomalies within 4 weeks without evidence of infection (4). Chest CT was scored using Ichikado score (5). Clinical parameters including ferritin levels, white counts (WBC), Lactate dehydrogenase (LDH) levels, GAP scores (Gender, Age, and Physiology score for idiopathic pulmonary fibrosis) were recorded. Medications included cyclophosphamide (CyP), intravenous immunoglobulin (IVIG), mycophenolic acid derivatives (MPA), rituximab (RTX), and calcineurin inhibitor (CNI). Kaplan-Meier survival analysis and Log-rank test were used to evaluate one-year mortality differences (MedCalc version 19.6). The Ethics Committee approved our study (CE17038B).
Results: Six anti-MDA-5-positive RP-ILD patients were treated with tofacitinib; five had concomitant CMV prophylaxis with valganciclovir (VGCV); 4 had PCP prophylaxis with trimethoprim/sulfamethoxazole (TMP-SMX). Patients' demographic data are shown in Table 1. The median age, clinical manifestations, laboratory data, and chest CT scores were comparable between tofacitinib and non-tofacitinib groups. Prevalence of MPA use was higher in the non-TOF group. Kaplan-Meier survival analysis (Figure 1) indicated that patients with tofacitinib treatment (p=0.001), valganciclovir (p=0.003), and TMP-SMX (p=0.028) prophylaxis exhibited better 1-year survival rates compared with those without TOF therapy, VGCV, and TMP-SMX prophylaxis.

Table 1. Clinical characteristics of anti-MDA-5 antibody-positive patients with RP-ILD receiving tofacitinib vs non-tofacitinib treatment.

	Tofacitinib (n=6)	Non-tofacitinib (n=11)	*p* value
Age (years)	58 (42.3-77)	57 (50.0-62.0)	0.884
Female sex, n (%)	2 (33.3)	6 (54.5)	0.620
Diabetes mellitus, n (%)	0 (0)	5 (45.5)	0.102
Fever, n (%)	5 (83.3)	10 (90.9)	1.000
Mechanic's hands, n (%)	4 (66.7)	5 (45.5)	0.620
Ferritin (n=16, ng/ml))	2670.9 (719.7-4209.7)	1563.5 (967.8-3169.0)	0.635
WBC (x1000µl)	8.7 (6.5-9.9)	8.7 (6.0-12.9)	0.884
LDH (n=16, U/l)	367.0 (218.0-557.5)	433.0 (331.0-625.3)	0.313
GAP score	5 (2.5-8)	5 (2-6)	0.808
CT score	200.0 (124.2-214.2)	196.7 (153.3-273.3)	0.733
TMP-SMX, n (%)	4 (66.7)	0 (0)	0.006**
VGCV, n (%)	5 (83.3)	0 (0)	0.001**
CyP, n (%)	1 (16.7)	4 (36.4)	0.600
IVIG, n (%)	1 (16.7)	6 (54.5)	0.304
MPA, n (%)	0 (0)	7 (63.6)	0.035*
RTX, n (%)	3 (50.0)	5 (45.5)	1.000
CNI, n (%)	2 (33.3)	6 (54.5)	0.620

Continuous variables were expressed as median (inter-quartile range).*$p<0.05$, **$p<0.01$ by Mann–Whitney U test or Fisher's Exact test.

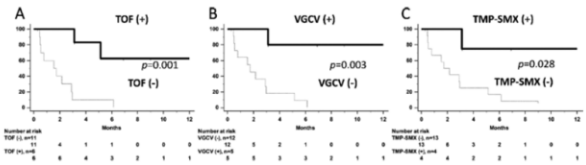

Figure 1.

Conclusion: The study demonstrated the efficacy of tofacitinib treatment in anti-MDA-5-positive RP-ILD. In addition, CMV and PCP prophylaxis appeared to improve in 1-year survival. Rheumatologists might consider TOF with prophylaxis as an option for anti-MDA-5-positive patients in daily practice.
REFERENCES:
[1] Sato S, et al. Arthritis Rheum 2009;60(7):2193-200.
[2] Sekiguchi A, et al. J Dermatol 2020;47(8):876-81.
[3] Sabbagh SE, et al. Rheumatology 2021;60(2):829-36.
[4] Kurasawa K, et al. Rheumatology 2018;57(12):2114-19.
[5] Ichikado K, et al. Radiology 2006;238(1):321-9.
Acknowledgements: We are grateful to the Biostatistics Task Force staff of Taichung Veterans General Hospital for their assistance in performing the statistical analyses and Tomoko Hasegawa for her technical assistance with the immunoassays. We also thank Dr. Wen-Nan Huang, Dr. Pin-Kuei Fu, Dr. Chia-Wei Hsieh, Dr. Yi-Hsing Chen, and Dr. Der-Yuan Chen for their help on resources and supervision.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.3428

AB0698 IMPACT OF ILOPROST WITHDRAWAL IN SCLERODERMA PATIENTS DUE TO COVID-19 PANDEMIC

L. Verardi[1], E. de Lorenzis[1,2], G. Natalello[3], L. Gigante[3], P. G. Cerasuolo[3], M. A. D'Agostino[3], S. L. Bosello[3]. [1]*Università Cattolica del Sacro Cuore, Policlinico Universitario Agostino Gemelli IRCSS, Roma, Italy., Rheumatology Department, Rome, Italy;* [2]*University of Verona-Verona, Italy., Ph.D. programme in Biomolecular Medicine-Cycle XXXV., Verona, Italy;* [3]*Università Cattolica del Sacro Cuore, Policlinico Universitario Agostino Gemelli IRCSS, Roma, Italy., Rheumatology Department, Roma, Italy*