RMD Open
Rheumatic & Musculoskeletal Diseases

SHORT REPORT

Secukinumab does not impair the immunogenic response to the influenza vaccine in patients

Patricia Richi,[1,2] María Dolores Martín,[3] Fernando de Ory,[4] Rosa Gutiérrez-Larraya,[2] Inmaculada Casas,[5] Ana María Jiménez-Díaz,[1] Fernando Cava,[6] Santiago Muñoz-Fernandez[1,2]

To cite: Richi P, Martín MD, de Ory F, *et al*. Secukinumab does not impair the immunogenic response to the influenza vaccine in patients. *RMD Open* 2019;**5**:e001018. doi:10.1136/rmdopen-2019-001018

Received 23 May 2019
Revised 21 July 2019
Accepted 17 August 2019

[1]Rheumatology Department, Infanta Sofía University Hospital, San Sebastian de los Reyes, Spain
[2]School of Medicine, European University of Madrid, Madrid, Spain
[3]Bactereology Department, BR Salud Laboratories, San Sebastian de los Reyes, Spain
[4]National Microbiology Centre, CIBER-ESP, Instituto de Salud Carlos III, Majadahonda, Spain
[5]National Microbiology Centre, Instituto de Salud Carlos III Campus de Majadahonda, Majadahonda, Spain
[6]BR Salud Laboratories, San Sebastian de los Reyes, Spain

Correspondence to
Dr Patricia Richi;
patricia.richi@salud.madrid.org

ABSTRACT

Objective To evaluate whether immunological response to influenza vaccination is impaired in patients who are receiving secukinumab.

Patients and methods Subjects suffering from psoriatic arthritis or ankylosing spondylitis who were receiving treatment with secukinumab and healthy volunteers were included.

All participants received seasonal inactivated trivalent influenza vaccine recommended by the WHO in the 2017–2018 northern hemisphere influenza season, which contained an A/Michigan/45/2015 (H1N1)pdm09-like virus, an A/Hong Kong/4801/2014 (H3N2)-like virus and a B/Brisbane/60/2008-like virus.

Haemagglutination inhibition was used to evaluate basal antibody (Ab) titres against the three influenza vaccine virus strains just before vaccination and at least 4 weeks after the vaccine administration. Response to vaccine was considered as >4-fold increases in Ab titre.

Results Thirty subjects, 17 patients and 13 healthy controls, with a follow-up duration of 33±8 days, were analysed. There were no demographic differences between groups. Patients and controls achieved a median of 4.6-fold and 4.0-fold increases, respectively, for anti H1N1 and almost 4.0 (3.7) for patients and 5.3 for controls for anti-B Ab. Both groups presented a poor response against H3N2, with <1.5-fold increase. Seroconversion rates were similar in both groups. Secukinumab did not influence the response to the influenza vaccine (relative risk: 1.09 (95% CI 0.58 to 2.07) for H1N1, RR: 1.53 (95% CI 0.15 to 15.0) for H3N2 and RR: 0.72 (95% CI 0.32 to 1.83) for B strain).

Conclusion In our study, secukinumab has no effect on the immunogenic response to the influenza vaccine.

Key messages

What is already known about this subject?

- Seasonal influenza vaccination is recommended for patients who undergo biological therapy.
- Secukinumab does not affect the immune response to the influenza vaccine in healthy volunteers.

What does this study add?

- Secukinumab does not impair the immune response to the influenza vaccine in patients.

How might this impact on clinical practice?

- Physicians should be concerned about their patients on secukinumab seasonal influenza immunisation.

We present a pilot study designed in order to acertain if secukinumab impairs the immunogenic response to the influenza vaccine in patients with inflammatory arthropathies.

Secukinumab is a fully human anti-interleukin-17A IgG1κ monoclonal antibody (Ab) approved for the treatment of psoriasis, psoriatic arthritis (PsA) and ankylosing spondylitis (AS).

Secukinumab has a good safety profile, with infection rates similar to etanercept and consisting mainly of non-serious nasopharyngitis and upper respiratory tract infections.[1]

Patients with autoimmune inflammatory rheumatic disease (AIIRD) have a higher risk of infections than healthy people. There are no specific immunisation recommendations for patients on secukinumab, but taking into account they suffer an AIIRD, we follow the vaccination guidelines established for this population that includes annual influenza vaccination.[2] We designed a pilot study in order to assess the efficacy of influenza vaccine in patients with arthropathies who were on treatment with secukinumab.

After the approval of the local ethics committees, we enrolled 17 patients suffering from PsA or AS and 13 controls, each of whom provided a signed written informed consent. There were no demographic differences between groups. Patients had been receiving secukinumab during 8.9±5.8 months. Ten patients (58.82%) were also receiving concomitant treatment with synthetic disease-modifying antirheumatic drugs, five

Table 1 Geometric means HI titres against each of the three virus strains before vaccination and at least 4 weeks later

	H1N1 baseline	H1N1 final	H3N2 baseline	H3N2 final	B baseline	B final
Patients on secukinumab, n=17	60	276	65	91	20	74
Healthy controls, n=13	107	428	85	86	32	171

of them were on leflunomide, four on methotrexate and one on sulfasalazine.

All participants received seasonal inactivated trivalent influenza vaccine recommended by the WHO in the 2017–2018 Northern hemisphere influenza season, which contained an A/Michigan/45/2015 (H1N1) pdm09-like virus, an A/Hong Kong/4801/2014 (H3N2)-like virus and a B/Brisbane/60/2008-like virus. Blood samples were taken just before vaccination and 33±8 days afterwards, and the haemagglutination inhibition test was used to evaluate Ab titres against the three vaccine virus strains. Participants with >4-fold increases in the Ab titre were considered responders.

Patients and controls achieved a median of 4.6-fold and 4.0-fold increases, respectively, for anti-H1N1 and almost 4.0 (3.7) for patients and 5.3 for controls for anti-B Ab. Both groups presented a poor response against H3N2, with a <1.5-fold increase. Geometric median titres against each of the three virus strains are shown in table 1.

We found no significant differences in the proportion of patients who responded to the vaccine. (table 2).

Although not significant, there was a higher proportion of healthy controls that achieved seroconversion against the influenza B virus. Thus, we calculated the sample size needed to identify possible significant differences between both cohorts. We found that it would be possible to identify differences, with better results in the control group, if a sample of 312 participants were enrolled (statistical power 80%, 95% CI). To include such a number of subjects, a multicenter study should be conducted that would confirm or not the different responses to the influenza B virus in healthy people and in patients on secukinumab.

In our study, secukinumab did not influence the response to the influenza vaccine (RR: 1.09 (95% CI 0.58 to 2.07) for H1N1, RR: 1.53 (95% CI 0.15 to 15.0) for H3N2 and RR: 0.72 (95% CI 0.32 to 1.83) for B strain).

As far as we know, this is the first study published that investigates if secukinumab impairs the immunogenic response to the influenza vaccination in patients. Seroconversion rates were low but in line with the vaccine effectiveness rates reported for the 2017–2018 season.[3] Our results corroborate those communicated by Elkayam *et al* (available as abstract), who, during the 2017 season, found similar rates of seroprotection after the vaccine in patients with PsA treated with secukinumab and in healthy controls.[4] Chioato *et al* described an immunogenic response of around 90% 4 weeks after the influenza vaccination in healthy volunteers treated with secukinumab.[5] Although seroconversion rates were lower in our series, neither study found worse responses in subjects taking secukinumab.

In summary, in our pilot study, we found that secukinumab has no effect on the immunogenic response to the influenza vaccine. Larger studies are needed to ratify this finding.

Table 2 Responders against each of the three virus strains

	Patients on secukinumab, n=17 (%)	Healthy controls, n=13 (%)	P value
H1N1	10 (58.82)	7 (53.85)	0.999
H3N2	2 (11.69)	1 (7.69)	1.011
B	6 (35.29)	6 (46.15)	0.821

Acknowledgements The authors acknowledge Dr Jesús Llorente for coordinating the influenza vaccine supply and Dr Beatriz Paredes for carrying out the processes to obtain de institutional permissions.

Collaborators Jesús Llorente. Beatriz Paredes.

Contributors PR conceived and designed the work, contributed to the acquisition and interpretation of data, and wrote the paper. MDM contributed substantially to the acquisition and analysis of data and drafting of the work. FdO contributed substantially to the acquisition and analysis of data. RG-L contributed substantially to the acquisition and analysis of data and drafting of the paper. IC contributed substantially to the acquisition and analysis of data. AMJ-D contributed substantially to the acquisition of data. FC contributed substantially to the acquisition of data. SM-F contributed substantially to the conception of the work and analysis of data. All authors revised critically the work, approved the final version and agreed on all aspects of the work.

Funding The study was approved by La Paz University Hospital Ethic Committee. Approval ID: PI-3076. Data not published is available on request to the corresponding author, Dr PR.

Competing interests SM-F declares he has received grants for conference attendance and educational programmes, as well as consultancy payments from Novartis, during the conduct of the study.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement The data that support the findings of this study are available on request from the corresponding author, PR.

REFERENCES

1. van de Kerkhof PCM, Griffiths CEM, Reich K, *et al*. Secukinumab long-term safety experience: a pooled analysis of 10 phase II and III clinical studies in patients with moderate to severe plaque psoriasis. *J Am Acad Dermatol* 2016;75:83–98.
2. van Assen S, Agmon-Levin N, Elkayam O, *et al*. EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases. *Ann Rheum Dis* 2011;70:414–22.

3. Centers for Disease Control and Prevention. Summary of the 2017-2018 influenza season. Available: https://www.cdc.gov/flu/about/season/flu-season-2017-2018.htm [Accessed Mar 2019].
4. Elkayam O, Zisman D, Kaufman I, *et al*. The effect of Secukinumab on the immunogenicity of influenza vaccine in patients with psoriatic arthritis (Abstract). *Arthritis Rheumatol* 2018;70:2917–8.
5. Chioato A, Noseda E, Stevens M, *et al*. Treatment with the interleukin-17A-blocking antibody secukinumab does not interfere with the efficacy of influenza and meningococcal vaccinations in healthy subjects: results of an open-label, parallel-group, randomized single-center study. *Clin Vaccine Immunol* 2012;19:1597–602.