Author contributions
LH took pictures and wrote the manuscript under the guidance of JZ and ZY. JZ organized the follow-up. All authors cared for the patient.

Conflict of interest
The authors state no conflict of interest.

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Reply to “Psoriasis exacerbation after COVID-19 vaccination: report of 14 cases from a single centre” by Sotiriou E et al.

Dear Editor,
We have read with great interest the article recently published by Sotiriou et al. who reported 14 patients with psoriasis worsening after COVID-19 vaccination suggesting the possibility of the association between COVID-19 vaccines and psoriasis flares, especially in patients who do not receive any treatment for their psoriasis.

In our experience at the Dermatology Centre of the University of Naples Federico II, we observed 11 cases (8 male 72.7%, mean age 54.5 ± 8.9 years) of psoriasis exacerbation after COVID-19 vaccination with Pfizer mRNA-BNT162b2, Moderna mRNA-1273 or AstraZeneca-Oxford AZD1222 from February 2021 to July 2021 (Table 1). In line with Sotiriou et al., psoriasis flares were observed within 14 days from the vaccination (mean 8.5 ± 2.8 days) and mainly after the 2nd dose (81.8%). According to Sotiriou et al., plaque form is the most frequent clinical presentation (10/11, 90.9%). Moreover, psoriasis flare possibility does not seem to be linked to the type of COVID-19 vaccine (72.7% with mRNA technology vaccines and 27.3% with adenovirus vaccine).

Concerning the Psoriasis Area Severity Index (PASI) at the moment of clinical examination, our results are similar to Sotiriou et al. (10.4 ± 4.7 vs 9.8 ± 3.5). However, we believe that patients who experienced a less severe psoriasis flare after COVID-19 vaccination tend to self-medicate and do not seek medical attention. A comparison between Sotiriou et al.’s data and ours are reported in Table 2.

Interestingly, differing from Sotiriou et al., we observed 6 cases (54.5%) of psoriasis flares due to COVID-19 vaccine in subjects under biologic treatment. Among these, topical calcipotriol/betamethasone combination and/or phototherapy were added to current biologic treatment in 4 cases, while switching biologic agent was necessary in the remaining 2 patients. Although literature reported that COVID-19 vaccine does not seem to induce psoriasis flare in patients under biologics, we observed a small percentage of subjects that experienced this flare nevertheless being under biologic treatment. To note, we want to highlight that they represent a very limited number of patients considering that more than 1200 psoriatic patients attending our Department are being treated with biologics for psoriasis and that currently about 60% of Italian population is vaccinated.

As regards the treatment of the 5 remaining patients, biologic therapy or methotrexate was prescribed to 4 and 1 subjects after COVID-19 vaccine induced psoriasis worsening respectively.

Our results show a highly percentage of psoriatic flare in male patients (8/11, 72.7%) suggesting male sex as a potential predictive risk factor. However, these data may be influenced by the fact that the majority of psoriasis patients attending our centre is male (68.9%).

Previous concerns about the infectious risk of more severe COVID-19 infection in psoriatic subjects have been solved, and the safety and effectiveness of COVID-19 vaccines has been showed, also for these patients. In the literature, there are only few cases reporting the worsening of psoriasis after COVID-19 vaccine. In our opinion, systemic treatment may reduce the risk of psoriasis flares after COVID-19 vaccination by the protection against the inflammatory process, which can cause the worsening of the disease. Hence, patients undergoing topical treatment for psoriasis have...
a higher risk of psoriatic flares compared with patients treated with systemic drugs. However, our experience showed that psoriasis exacerbation after COVID-19 vaccination may also develop in patients undergoing biologic treatment, even if the risk is reduced and limited. In conclusion, clinicians must keep in mind the possibility of psoriasis worsening after COVID-19 vaccine, regardless the mechanism of action of vaccines, advising patients to self-control their disease, especially within 14 days after vaccination, and to refer to clinicians if a worsening of the condition is noted. Being on biologic for psoriasis seems to strongly reduce but not to completely undo this risk.

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The patients in this manuscript have given written informed consent to publication of their case details.

Conflict of interest
None.

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Author contributions
Matteo Megna: conceptualization, validation, visualization, writing – original draft preparation, writing – review and editing. Luca Potestio: data curation, formal analysis, investigation, visualization, writing – original draft preparation. Lucia Gallo: data curation, investigation, methodology, visualization, writing – original draft preparation. Giuseppina Caiazzo: data curation, formal analysis, validation. Angelo Ruggiero: data curation, validation, visualization, writing – review and editing, supervision. All authors read and approved the final version of the manuscript.

Table 1 Psoriasis flares after COVID-19 vaccine

| Sex | Age | Vaccine/dose | Days | PASI | Type of psoriasis flare | Previous treatment | New treatment |
|-----|-----|--------------|------|------|-------------------------|-------------------|---------------|
| M   | 55  | mRNABNT162b2 / 2 | 5    | 14.8 | Plaque                  | None              | Methotrexate   |
| M   | 49  | mRNABNT162b2 / 2 | 6    | 17.3 | Plaque                  | None              | Adalimumab    |
| M   | 45  | AZD1222 / 1     | 10   | 9.9  | Plaque                  | Secukinumab       | Secukinumab†  |
| M   | 61  | mRNABNT162b2 / 2 | 12   | 11.9 | Plaque                  | Adalimumab        | Ixekizumab†   |
| M   | 62  | mRNA-1273 / 2   | 8    | 15.9 | Plaque                  | None              | Brodalumab    |
| M   | 47  | mRNABNT162b2 / 2 | 9    | 4.3  | Guttate                 | Ixekizumab        | Ixekizumab†   |
| M   | 70  | mRNABNT162b2 / 2 | 8    | 7.6  | Plaque                  | Calpica/betam     | Adalimumab    |
| F   | 39  | AZD1222 / 2     | 7    | 5.2  | Plaque                  | Gusekumab         | Gusekumab†    |
| M   | 58  | mRNABNT162b2 / 2 | 5    | 4.3  | Plaque                  | Secukinumab       | Secukinumab†  |
| F   | 55  | AZD1222 / 2     | 10   | 13.9 | Plaque                  | Nb-UVB            | Risankizumab  |
| M   | 59  | mRNA-1273 / 1   | 14   | 9.2  | Plaque                  | Etanercept        | Ixekizumab    |

M, male; F, female; AZD1222, AstraZeneca-Oxford AZD1222; mRNA-1273, Moderna mRNA-1273; mRNABNT162b2, Pfizer mRNA-162b2. Dose, number of doses after which psoriasis flare occurred; PASI, Psoriasis Area and Severity Index score at presentation in our department following the psoriasis flare. Calpica/betam, topical calcipotriol/betamethasone combination; nbUVB, narrowband ultraviolet B.
†Biologic treatment associated with topical calcipotriol/betamethasone combination and/or phototherapy.

Table 2 Comparison between Sotiriou et al.’s population and ours

|                        | Our data (n = 11) | Sotiriou et al. (n = 14) |
|------------------------|------------------|--------------------------|
| Demographic features   |                  |                          |
| Sex, M (%)             | 8 (72.7%)        | 5 (35.7%)                |
| Mean age (years)       | 54.5 ± 8.9       | 66 ± 9.7                 |
| Vaccine type           |                  |                          |
| AZD1222                | 3 (27.3%)        | 7 (50.0%)                |
| 1st dose               | 1 (9.1%)         | 2 (14.3%)                |
| 2nd dose               | 2 (18.2%)        | 5 (35.7%)                |
| mRNA-1273              | 1 (9.1%)         | 1 (7.1%)                 |
| 1st dose               | 0 (0%)           | 0 (0%)                   |
| 2nd dose               | 1 (9.1%)         | 1 (7.1%)                 |
| mRNABNT162b2           | 7 (63.6%)        | 6 (42.9%)                |
| 1st dose               | 1 (9.1%)         | 0 (0%)                   |
| 2nd dose               | 6 (54.5%)        | 6 (42.9%)                |
| Days after psoriasis flare | 8.5 ± 2.8 | 10.4 ± 7.7               |
| PASI                   | 10.4 ± 4.7       | 9.8 ± 3.5                |
| Type of psoriasis      |                  |                          |
| Plaque                 | 10 (90.9%)       | 13 (92.9%)               |
| Guttate                | 1 (9.1%)         | 1 (7.1%)                 |
| Ongoing treatment during vaccination | | |
| Biologic treatment     | 6 (54.5%)        | 0 (0%)                   |
| Topical treatment and/or Phototherapy | 2 (18.2%) | 5 (35.7%)               |
| No treatment           | 3 (27.3%)        | 9 (64.3%)                |
| Treatment after psoriasis exacerbation | | |
| Biologic treatment     | 10 (90.9%)       | 3 (21.4%)                |
| Small molecules        | 0 (0%)           | 1 (7.1%)                 |
| Immunosuppressant agents | 1 (9.1%)      | 1 (7.1%)                 |
| Topical treatment and/or phototherapy | 41 (36.4%) | 9 (64.3%)               |

AZD1222, AstraZeneca-Oxford AZD1222; mRNA-1273, Moderna mRNA-1273; mRNABNT162b2, Pfizer mRNA-162b2; PASI, Psoriasis Area and Severity Index score at presentation in our department following the psoriasis flare.
†Topical treatment and/or phototherapy added to biologic therapy.
Euthal approval
Not required.

Data availability statement
Data are reported in the current study.

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A case of bullous pemphigoid after the SARS-CoV-2 mRNA vaccine

Dear Editor,
A 68-year-old, otherwise healthy, man presented to our dermatology department in late April 2021 with a history of a blistering eruption which commenced 3 days after his first dose of the Pfizer BioNTech COVID-19 vaccine (2 March 2021) and worsened after the second dose given three weeks later. The blisters first appeared over the sternal area and were accompanied by intense, generalized pruritus which started a day before the blisters appeared. His family doctor prescribed acyclovir for a presumed diagnosis of herpes zoster with no improvement and later desloratadine and a 5-day course of 20-mg oral prednisolone. However, the blisters continued to increase in number and erupted over the right side of the chest and upper back particularly after the patient received the second dose of the Pfizer vaccine.

At presentation to dermatology, the patient had several healing crusted areas scattered over the right chest and back but no intact blisters and was prescribed clobetasol propionate ointment and an emollient cream. Routine blood tests, epidermal basal membrane antibodies and prickle cell desmosomes antibodies were normal and negative respectively.

At follow-up, 2 weeks later, there was a recently ruptured blister arising in an area of urticated erythema over his back (Fig 1a, b) and an ulcer situated on the left buccal mucosa (Fig 1c). A biopsy taken from one of the truncal lesions revealed subepidermal blistering associated with a superficial dermal inflammatory infiltrate composed of eosinophils and hemosiderophages. The roof of the bulla consisted of thinned, viable epidermis whilst within the bulla, erythrocytes and scattered inflammatory cells including eosinophils were seen (Fig 1d). Direct immunofluorescence showed linear basal deposition of IgG and C3 (Fig 1e, f). All these findings were in keeping with a diagnosis of bullous pemphigoid (BP). He was advised to continue the previously prescribed topical treatment, and at follow-up 3 months after the first dose of COVID-19 vaccine, he was found to be completely asymptomatic with no new blisters present and only residual post-inflammatory hyperpigmentation present at previously affected sites.

This case is intriguing since to our knowledge it is the first reported case of BP related to the SARS-CoV-2 mRNA vaccine. We acknowledge that a possible differential diagnosis for this case would be epidermolysis bullosa acquisita (EBA). However, the histological features, particularly the eosinophilic-predominant infiltrate, are not typical of EBA and are more in keeping with BP. A large number of cases of BP have been reported following other vaccines including the pneumococcal vaccine and influenza vaccine. However, the pathogenesis is not clear. It has been hypothesized that vaccine-induced inflammation could lead to disruption of the basement membrane architecture with subsequent generation of anti-basement membrane-specific antibodies, and such vaccines may also increase the antigenicity of BP antigens. However, there are no known similarities between the basement membrane protein and the implicated vaccines; therefore, it is unlikely that the vaccine coupled with its respective antibody response is the sole cause of this phenomenon. In fact, it has also been postulated that these vaccines...