



UNIVERSITÀ
DEGLI STUDI
FIRENZE

FLORE

Repository istituzionale dell'Università degli Studi di Firenze

Comment on "Association of bullous pemphigoid with malignancy: A systematic review and meta-analysis".

Questa è la Versione finale referata (Post print/Accepted manuscript) della seguente pubblicazione:

Original Citation:

Comment on "Association of bullous pemphigoid with malignancy: A systematic review and meta-analysis" / Maglie R, Antiga E, Caproni M. - In: JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY. - ISSN 0190-9622. - ELETTRONICO. - (2021), pp. ...

Availability:

The webpage <https://hdl.handle.net/2158/1114067> of the repository was last updated on 2022-10-02T15:58:38Z

Terms of use:

Open Access

La pubblicazione è resa disponibile sotto le norme e i termini della licenza di deposito, secondo quanto stabilito dalla Policy per l'accesso aperto dell'Università degli Studi di Firenze (<https://www.sba.unifi.it/upload/policy-oa-2016-1.pdf>)

Publisher copyright claim:

La data sopra indicata si riferisce all'ultimo aggiornamento della scheda del Repository FloRe - The above-mentioned date refers to the last update of the record in the Institutional Repository FloRe

(Article begins on next page)

Accepted Manuscript

Comment on “Association of bullous pemphigoid with malignancy: A systematic review and meta-analysis”

Maglie Roberto, MD, Antiga Emiliano, MD, PhD, Caproni Marzia, MD, PhD



PII: S0190-9622(17)32812-8

DOI: [10.1016/j.jaad.2017.10.053](https://doi.org/10.1016/j.jaad.2017.10.053)

Reference: YMJD 12172

To appear in: *Journal of American Dermatology*

Received Date: 29 October 2017

Accepted Date: 30 October 2017

Please cite this article as: Roberto M, Emiliano A, Marzia C, Comment on “Association of bullous pemphigoid with malignancy: A systematic review and meta-analysis”, *Journal of American Dermatology* (2018), doi: 10.1016/j.jaad.2017.10.053.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

1 **Article type: NOTES & COMMENTS**

2

3 **Title:** Comment on “Association of bullous pemphigoid with malignancy: A systematic review and meta-
4 analysis”.

5

6 Maglie Roberto, MD¹, Antiga Emiliano, MD, PhD¹, Caproni Marzia, MD, PhD¹.

7

8 ¹Department of Surgery and Translational Medicine, Section of Dermatology, University of Florence,
9 Florence, Italy.

10

11 **Corresponding author:**

12

13 Maglie Roberto, MD

14 Viale Michelangiolo 41

15 Florence (Italy), 50100

16 Telephone: +39 055 6939627

17 Fax: 055-6939598

18 Email: robertomaglie.med@libero.it

19

20 **Funding sources:** None

21

22

23 **Conflicts of Interest:** None declared.

24

25 **Reprint requests:** Maglie Roberto

26

27 **Manuscript word count:** 389 words [excluding references]

28 **References:** 5

29 **Figures:** 0

30 Supplementary figures: 0

31 **Tables:** 0

32 Supplementary tables: 0

33

34 **Keywords:** cutaneous immunopathology, bullous pemphigoid, eosinophilic dermtoses of hematologic
35 malignancies.

36

37

38

39

40

41

42

43

44 **To the Editor.** We read with interest the manuscript published by Atzmony et al, concerning the
45 association between bullous pemphigoid (BP) and malignancies.¹ As known, numerous studies have
46 tried to investigate the link between BP and cancer. Besides the temporal association, some clinical
47 evidences such as skin lesions improvement while on cancer-targeting procedures and the lack of
48 recurrence after tumour excision are thought to support this relationship. Conversely, experimental
49 studies providing plausible explanations about cancer-induced production of anti-basement membrane
50 zone autoantibodies are still lacking. Moreover, revision studies have yielded contrasting results,
51 because devoid of systematic approach.¹ Thus, the issue remains open to speculation as yet.

52 Interestingly, analysing the data of one cohort and four cross-sectional studies, Atzmony et al found a
53 possible association between BP and hematoproliferative diseases, but not with overall malignancies.¹

54 It is our opinion that the results by Atzmony et al might be influenced by an overestimated incidence of
55 BP in hematologic patients, due to its clinico-pathologic, and sometimes immunopathologic, overlap
56 with eosinophilic dermatoses of haematologic malignancies (EDHM). The latter refer to a heterogeneous
57 spectrum of cutaneous manifestations occurring in patients with underlying hematologic cancer, mostly
58 B-cells chronic lymphocytic leukaemia (B-CLL). Clinically, EDHM may present with urticarial papules,
59 plaques, or nodules mimicking the pre-bullous phase of BP. Even blistering eruptions have been often
60 reported.^{2,3,4} Histopathologically, dermo-epidermal detachment and eosinophil-rich dermal
61 inflammatory infiltrates are classically detected in both diseases.⁴ Finally, EDHM may show confounding
62 immunopathologic features, as reported in a study by Bottoni et al, in which six B-CLL patients with
63 insect bite-like reactions had positive anti-BP180 antibodies on immunoblotting test,⁵ and in a case by
64 our group, in which a B-CLL patient with EDHM had linear deposition of Immunoglobulin M and C3 at
65 direct immunofluorescence test.⁴ Indeed, EDHM and BP appear challenging to distinguish, leading to
66 potential diagnostic pitfalls. However, their distinction is crucial for many reasons: i) patients with
67 idiopathic eosinophilic dermatoses has to be closely monitored because of the further risk of developing

68 hematologic malignancies, compared to idiopathic BP; ii) EDHM follow a waxing and waning behaviour
69 despite both dermatologic and hematologic treatments; iii) the treatment of the two conditions is
70 different.

71 To conclude, although BP may occur as a paraneoplastic event in patients with hematoproliferative
72 diseases, clinicians should keep in mind EDHM in the diagnostic work-up of hematologic patients
73 experiencing BP-like blistering eruptions.

74

75

76

77

78

79

80

81

82

83

84

85

86

87

88

89

90

91

92 **References**

- 93 1. Atzmony L, Mimouni I, Reiter O, et al. Association of bullous pemphigoid with malignancy: A
94 systematic review and meta-analysis. *J Am Acad Dermatol.* 2017;77:691-699.
- 95 2. Bairey O, Goldschmidt N, Ruchlemer R et al. Insect-bite-like reaction in patients with chronic
96 lymphocytic leukemia: a study from the Israeli Chronic Lymphocytic Leukemia Study Group. *Eur*
97 *J Haematol.* 2012;89:491–6.
- 98 3. Rosen LB, Frank BL, Rywlin AM. A characteristic vesiculo-bullous eruption in patients with
99 chronic lymphocytic leukemia. *J Am Acad Dermatol.* 1986;15:943–50.
- 100 4. Maglie R, Antiga E, Vannucchi M, et al. Bullous eruption in a patient with B-cells chronic
101 lymphocytic leukaemia: a diagnostic challenge. *Int J Dermatol.* DOI: 10.1111/ijd.13807
- 102 5. Bottoni U, Mauro FR, Cozzani E, Innocenzi D. Bullous lesions in chronic lymphocytic leukaemia:
103 pemphigoid or insect bites? *Acta Derm Venereol.* 2006;86:74-6.

104

105

106

107

108

109

110

111

112

113

114

115

116 **ABBREVIATIONS**

117 Bullous pemphigoid: BP.

118 Eosinophilic dermatoses of hematologic malignancies: EDHM.

119 B-cells chronic lymphocytic leukemia: B-CLL.

ACCEPTED MANUSCRIPT