Original article

CED
Clinical and Experimental Dermatology

First-line treatment in lymphomatoid papulosis: a retrospective multicentre study

R. Fernández-de-Misa,[1] B. Hernández-Machín,[2] O. Servitje,[3] F. Valentí-Medina,[3] L. Maroñas-Jiménez,[4] P. L. Ortiz-Romero,[4] J. Sánchez Schmidt,[5] R. M. Pujol,[5] F. Gallardo,[5] I. Pau-Charles,[6] M. P. García Muret,[7] S. Pérez Gala,[8] C. Román,[9] J. Cañueto,[9] L. Blanch Rius,[10] R. Izu,[10] A. Ortiz-Brugués,[11] R. M. Martí,[11] M. Blanes,[12] M. Morillo,[13] P. Sánchez,[14] Y. Peñate,[15] J. Bastida,[16] A. Pérez Gil,[17] I. Lopez-Lerma,[18] C. Muniesa[3] and T. Estrach[6]

[1]*Department of Dermatology and Research Unit, Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain;* [2]*Department of Dermatology, Clínica Buenaderma, Las Palmas de Gran Canaria, Spain;* [3]*Department of Dermatology, Hospital Universitari de Bellvitge, IDIBELL, Barcelona, Spain;* [4]*Department of Dermatology, Hospital Universitario 12 de Octubre, i+12 Research Institute, Universidad Complutense Madrid, Madrid, Spain;* [5]*Department of Dermatology, Hospital del Mar, Universitat Autónoma de Barcelona, Barcelona, Spain;* [6]*Department of Dermatology, Hospital Clínico, University of Barcelona, IDIBAPS, Barcelona, Spain;* [7]*Department of Dermatology, Hospital Santa Creu i Sant Pau, UAB, Barcelona, Spain;* [8]*Department of Dermatology, Hospital Universitario Ramón y Cajal, Madrid, Spain;* [9]*Department of Dermatology, Hospital Universitario de Salamanca, Salamanca, Spain;* [10]*Department of Dermatology, Hospital de Basurto, Bilbao, Spain;* [11]*Department of Dermatology, IRBLleida, Hospital Universitari Arnau de Vilanova, Lleida, Spain;* [12]*Department of Dermatology, Hospital General Universitario de Alicante, Alicante, Spain;* [13]*Department of Dermatology, Hospital Universitario Virgen del Rocío, Sevilla, Spain;* [14]*Department of Dermatology, Hospital de León, León, Spain;* [15]*Department of Dermatology, Complejo Hospitalario Universitario Insular Materno-Infantil, Gran Canaria, Las Palmas de Gran Canaria, Spain;* [16]*Department of Dermatology, Hospital Universitario Dr. Negrín, Las Palmas de Gran Canaria, Spain;* [17]*Department of Dermatology, Hospital Virgen de Valme, Sevilla, Spain; and* [18]*Department of Dermatology, Hospital Universitari Vall d'Hebron, Barcelona, Spain*

doi:10.1111/ced.13256

Summary

Background. Data regarding response to treatment in lymphomatoid papulosis (LyP) are scarce.

Aim. To assess the daily clinical practice approach to LyP and the response to first-line treatments.

Methods. This was a retrospective study enrolling 252 patients with LyP.

Results. Topical steroids, methotrexate and phototherapy were the most common first-line treatments, prescribed for 35%, 20% and 14% of the patients, respectively. Complete response (CR) was achieved in 48% of treated patients. Eczematous lesions significantly increased relative risk (RR) of not achieving CR (RR = 1.76; 95% CI 1.16–2.11). Overall median time to CR was 10 months (95% CI 6–13 months), and 78% of complete responders showed cutaneous relapse; both results were similar for all treatment groups ($P > 0.05$). Overall estimated median disease-free survival (DFS) was 11 months (95% CI 9–13 months) but DFS for patients treated with phototherapy was 23 months (95% CI 10–36 months; $P < 0.03$). Having the Type A LyP variant (RR = 2.04; 95% CI 0.96–4.30) and receiving a first-line treatment other than phototherapy (RR = 5.33; 95% CI 0.84–33.89) were significantly associated with cutaneous early relapse. Of the 252 patients, 31 (13%) had associated mycosis fungoides unrelated to therapeutic approach, type of LyP or T-cell receptor clonality.

Correspondence: Dr Ricardo Fernández-de-Misa, Department of Dermatology and Research Unit, Hospital Universitario Nuestra Señora de Candelaria, Carretera del Rosario, 145, 38010 Santa Cruz de Tenerife, Spain
E-mail: rfdezdemisa@me.com

Conflict of interest: the authors declare that they have no conflicts of interest.

Accepted for publication 29 December 2016

© 2017 British Association of Dermatologists

Conclusions. Current epidemiological, clinical and pathological data support previous results. Topical steroids, phototherapy and methotrexate are the most frequently prescribed first-line treatments. Although CR and cutaneous relapse rates do not differ between them, phototherapy achieves a longer DFS. Presence of Type A LyP and use of topical steroid or methotrexate were associated with an increased risk of early relapse.

Introduction

Lymphomatoid papulosis (LyP)[1] is considered the least aggressive member of the group of primary cutaneous CD30 lymphoproliferative disorders.[2–4] LyP usually runs a chronic course from years to decades, with recurrent crops of papules or nodules that may crust and ulcerate, then resolve. However, the clinical course seems to vary from patient to patient, with most patients developing flares over decades, and a significant percentage of patients developing associated lymphomas.[5] Overall, large published series focusing on LyP are scarce, and precise treatment and follow-up data are difficult to assess.[3,6–10] Topical steroids, psoralen ultraviolet A (PUVA) phototherapy and low-dose methotrexate are the best-documented treatments,[5] but series are short and often do not provide data on dosage or follow-up. Treatments may be followed by long-term complications,[5] and do not seem to alter the natural course of LyP, with active disease expected at follow-up in up to 62%[3] of patients.

Methods

The study was approved by the local ethics committee. Informed consent was obtained from each participant.

Patients

Using the convenience sampling method, the Spanish Cutaneous Lymphoma Task Force retrospectively analysed the clinical records of patients with LyP treated in 17 university hospitals in Spain between May 1986 and March 2014. All patients fulfilled the diagnostic criteria of the World Health Organization (WHO) and European Organisation for Research and Treatment of Cancer classifications for LyP.[2] The following data were recorded for each patient: sex, age at diagnosis, interval to diagnosis, lesion location, clinical appearance and extent,[3] histopathological type of LyP, T-cell receptor (TCR) clonality, first-line therapy outcome, and follow-up data. Patients were treated as per physician's choice. Response was graded as complete response (CR) (complete disappearance of all the lesions), partial response (PR) (> 50% reduction in skin involvement), or no response (NR) (< 50% reduction in skin involvement, no change in disease or worsening of disease). Cutaneous relapse was defined as the development of any new lesion after CR.[5] For patients achieving CR, the following end points were computed: time to CR, disease-free survival (DFS) and cutaneous relapse rate. Early relapse and late relapse were defined as the development of new lesions within 6 months and after 12 months, respectively, following declaration of CR.

Statistical analysis

Statistical calculations were performed using SPSS software (v19.0; IBM SPSS, Armonk, NY, USA). Summary results for continuous variables are expressed as medians, means and interquartile ranges (IQR). Qualitative variables are expressed as percentages. Intergroup differences were analysed using the Mann–Whitney *U*-test or Kruskal–Wallis test for continuous variables, and the χ^2 or Fisher exact test for dichotomous variables. Kaplan–Meier estimates of time to CR and DFS were compared using the log-rank test. The 95% CIs were calculated. Sample size was not planned. All P values shown are two-tailed, with alpha of 5%, hence significance was set at $P < 0.05$.

Results

Patient demographics

In total, 252 patients (140 men and 112 women) were included. Median age at diagnosis was 48 years (range 1–80 years). There was no significant difference in LyP course in the different age groups. Median interval to diagnosis was 6 months (range 1–280 months), and median follow-up was 52 months (range 1–277 months).

Disease

There was no predominant anatomical site of involvement; 83% of the patients showed generalized cutaneous disease and none had nodal or visceral

 © 2017 British Association of Dermatologists

involvement.[5] The Type A LyP variant, characterized by a wedge-shaped dense dermal perivascular lymphoid infiltrate composed of small lymphocytes and large atypical CD30+ cells with Reed–Sternberg appearance, was seen in 70% of patients.[2] Monoclonal rearrangement of TCR was detected in 47% of patients. A papular eruption was present in 90% of the 252 patients at diagnosis, whereas only 30% had ulcerated papules. Table 1 lists the main clinical features of the included patients.

Table 1 Main clinical and pathological findings and follow-up data.

Total (N = 252)		Male n = 140	Female n = 112	P
Age at diagnosis, years				
Median	48	51	46	0.18*
IQR (25th–75th percentile)	35–61	37–62	34–61	
Range	1–80	1–79	2–80	
Time to diagnosis, months				
Median	6	7	4	0.53*
IQR (25th–75th percentile)	1–25	2–28	1–21	
Range	1–280	1–250	1–280	
Follow-up, months				
Median	52	48	52	0.79*
IQR (25th–75th percentile)	17–101	11–105	23–99	
Range	1–277	1–263	1–277	
Extent of skin lesions % (n)				
Generalized	83 (210)	83 (116)	84 (94)	
Regional	17 (42)	17 (24)	16 (18)	0.48†
T-cell receptor rearrangement % (n)				
Monoclonal	47 (44)	40 (24)	59 (20)	> 0.05†
Polyclonal	47 (44)	55 (33)	32 (11)	
Oligoclonal	6 (6)	5 (3)	9 (3)	
Pathological variant % (n)				
A	70 (133)	69 (73)	72 (60)	> 0.05†
B	24 (45)	22 (24)	25 (21)	
C	1 (3)	1 (1)	2 (2)	
D	2 (4)	4 (4)	–	
E	3 (5)	4 (4)	1 (1)	
Type of lesion % (n)				
Papules	90 (227)	89 (124)	92 (103)	> 0.05†
Nodules	20 (50)	27 (38)	11 (12)	0.001†
Plaques	12 (29)	11 (16)	12 (13)	
Tumours	7 (17)	9 (12)	5 (5)	
Eczematous	5 (12)	7 (10)	2 (2)	
Location of lesions % (n)				
Limbs	92 (225)	90 (124)	94 (101)	
Trunk	58 (142)	58 (80)	58 (62)	
Head/neck	25 (60)	27 (37)	22 (23)	> 0.05†
Mucosa	3 (8)	3 (4)	4 (4)	
Disease-related survival, years, %				
5	100	100	100	0.98‡
10	100	100	100	
Lymphoma-related survival, years, %				
5	98	96	100	0.16‡
10	98	96	100	
Overall survival, years, %				
5	96	96	96	0.98‡
10	96	96	96	
Association with lymphoma % (n)				
Mycosis fungoides	13 (31)	16 (22)	9 (10)	0.08†
Overall	14 (36)	18 (25)	9 (10)	

IQR, interquartile range. *Mann-Whitney U-test; †χ^2 or Fisher test; ‡Wilcoxon test.

© 2017 British Association of Dermatologists

Treatment

In total, 87 patients (35%) were initially treated with topical steroids, while 51 (20%) received systemic methotrexate (≤ 20 mg weekly), 36 (14%) underwent phototherapy [PUVA for 30 patients and ultraviolet (UV)B for 6 patients] and 19 (6%) received other treatments (topical and systemic antibiotics, dapsone, antihistamines or oral steroids). The remaining 59 patients (23%) did not receive any treatment. First-line therapies did not differ between men and women ($P > 0.05$), or between patients with regional and those with generalized lesions ($P > 0.05$).

Response

Clinical response to first-line treatment is shown in Table 2. Of the 193 patients treated, 86 (48%) achieved CR. No significant difference was detected for any treatment with regard to patient sex or cutaneous disease extent, but having lesions with an eczematous morphology conferred a significantly increased relative risk (RR) of not achieving CR ($P < 0.03$) (RR = 1.76; 95% CI 1.16–2.11) (supplementary Table S1). Overall estimated median time to CR was 10 months (95% CI 6–13 months), and there was no significant difference between the analysed treatments ($P = 0.09$). Of the 86 patients who achieved CR, 67 (78%) developed cutaneous relapse, and this rate was similar for all investigated treatments ($P = 0.24$) (Table 2).

Overall estimated DFS (median) since CR was 11 months (95% CI 9–13 months), but DFS for patients treated with phototherapy was significantly longer ($P < 0.03$) (23 months; 95% CI 10–36 months) (Fig. 1). Overall estimated median DFS since first-line treatment withdrawal was 5 months (95% CI 1–10 months) but again, this was significantly ($P < 0.02$) better (23 months; 95% CI 1–50 months) for phototherapy-treated patients (Fig. 2).

Relapse

The Type A morphological variant was significantly ($P = 0.04$) more prevalent in patients who had early relapse compared with those who had late relapse (RR = 2.04; 95% CI 0.96–4.30). Use of a first-line treatment other than phototherapy was recorded more frequently in patients with early relapse than in those with late relapse ($P < 0.02$) (RR = 5.33; 95% CI 0.84–33.89) (supplementary Table S2).

Mortality and comorbidities

Four patients died of unrelated diseases and three patients died due to associated lymphomas: mycosis fungoides (MF), Sézary syndrome and CD30 anaplastic lymphoma kinase-negative anaplastic large cell lymphoma (ALCL). Table 1 lists survival data. An associated lymphoma was seen in 36 patients (14%), of whom 31 (13%) had MF (21 men and 10 women; χ^2 test; $P = 0.15$). MF developed after LyP (median gap 42 months; range 2–92 months) in 15 patients, of whom 5 received initial methotrexate treatment for LyP, 5 were treated with topical steroids and 5 underwent phototherapy. MF development showed no significant association with any type of LyP or with TCR status ($P > 0.05$).

Discussion

LyP mainly develops between 45 and 52 years of age,[3,10] although several cases have been diagnosed in young patients.[11] Classic reports of LyP describe recurrent crops of reddish-brown papules and/or nodules that frequently crust or ulcerate and then resolve, often leaving atrophic scars,[1,2] but in our study, we observed this pattern in only one-third of cases. We found that 90% of patients developed a papular eruption at diagnosis, and 20% had nodules; the latter percentage is higher than the 3–4%[3,7] previously reported. A recently proposed accurate definition of

Table 2 Response to first-line active treatment.

Rates of:	Overall	Topical steroids	Methotrexate	Photo-therapy	Others	*P*
CR, % (*n*)	48 (86)	44 (34)	52 (25)	61 (20)	37 (7)	> 0.05†
PR	37 (65)	33 (26)	44 (21)	30 (10)	42 (8)	
NR	15 (26)	23 (18)	4 (2)	9 (3)	21 (4)	
Cutaneous relapse*	78 (67)	71 (24)	92 (23)	75 (15)	71 (5)	0.24†

CR, complete response; PR, partial response; NR, no response. *Only for patients who achieved CR; †χ^2 test or Fisher exact test.

© 2017 British Association of Dermatologists

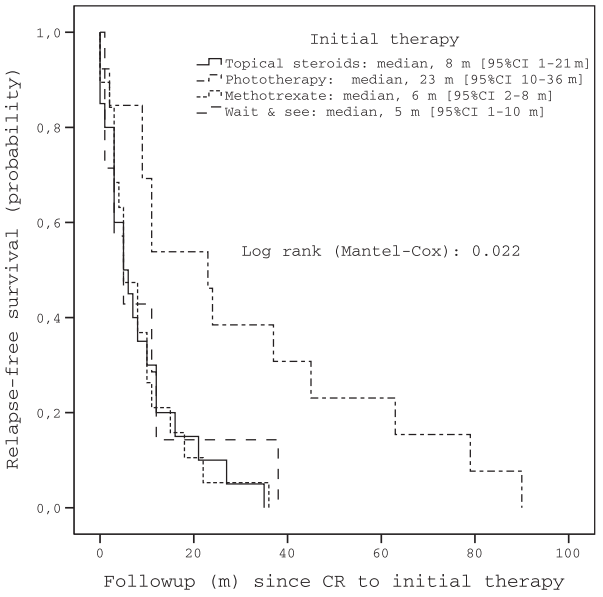

Figure 1 Disease-free survival since complete remission following initial therapy.

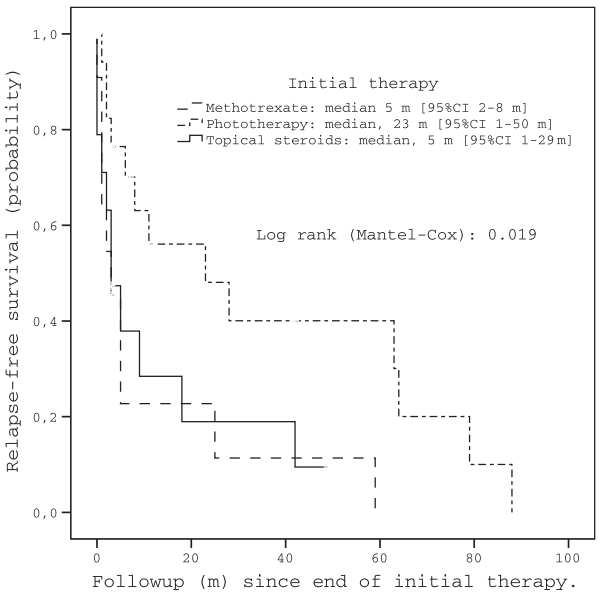

Figure 2 Disease-free survival since the end of initial therapy (only for patients with complete response).

nodular lesions will help to reduce bias.[5] Current data suggest that eczematous features of LyP lesions are significantly associated with a poorer response to treatment. Widespread cutaneous involvement prevails,[1,2,7,9] and there is no predominant anatomical site of involvement.[3] Mucosal locations have been described in up to 3% of patients.[12]

The updated WHO classification of haematological malignancies recognizes the three original variants (Types A, B and C) of LyP, as well as the more recently described type D (mimics primary cutaneous aggressive epidermotropic CD8 cytotoxic T-cell lymphoma), type E (angioinvasive), LyP with chromosome 6p25 rearrangement, and some even rarer variants.[13] Type A is the most common LyP variant,[2,4,5,10,14] and we observed it in 70% of cases in our study. We also found that Type A LyP was slightly but significantly associated with early relapse. The second most frequent variant was Type B LyP, which has a predominance of atypical cells with cerebriform nuclei.[2,5]

Clonally rearranged TCR genes have been detected in approximately 60–70% of LyP lesions.[15] We identified it in around 50% of our patients, but, in contrast to previous reports,[6,14] we did not find any correlation between clonality and disease behaviour (supplementary Tables S1 and S2).

Grouping the most relevant studies focusing on PUVA phototherapy,[5,10,16–19] we found useful information on response for 44 patients; CR, PR and NR rates were 13%, 62% and 25%, respectively. Phototherapy with UVA 1[20] or UVB[11] was also associated with a favourable outcome. Our study includes response data for 33 patients treated with phototherapy as first-line therapy, which showed higher CR rates in those patients, highlighting the need for controlled studies. Some authors have suggested that patients treated with phototherapy achieve a faster response,[5] but our results do not support this hypothesis. In previous studies, rapid relapse after therapy withdrawal was reported in 84% of the patients treated with PUVA.[5,10,16–19] The relapse rate in our study was similarly high (75%), but DFS was longer than previously described, and was also longer than DFS in patients who received treatments other than phototherapy.

Single-agent chemotherapy with low-dose methotrexate (15–25 mg weekly) seems to be effective in controlling LyP. Results for around 150 patients have been reported previously. In three previous large series,[10,21,22] CR and PR was achieved by 36% and 41%, respectively, of 119 patients. In our study, the rates were 52% and 44%, respectively, of 47 treated patients. Although satisfactory long-term control has been described in 87% of patients with maintenance doses,[21] a relapse rate of 67–75% after drug withdrawal has been reported.[5,9,21,22] We observed an even higher relapse rate (92%) after a short DFS (median 5 months).

Topical steroids are often used in LyP,[5,10] and in our study, they were the first-line therapy for 35% of

© 2017 British Association of Dermatologists

patients. A recent study on 151 patients[10] reported CR and PR in 8% and 38%, respectively, whereas we found higher rates (44% and 33%, repecively), similar to those achieved by the other treatments assessed.

Several additional approaches have been used in patients with LyP,[5,10] but only very limited numbers of patients have been reported, and follow-up data are often not available, thus they will be not discussed further here. To our knowledge, brentuximab vedotin[23] is the only treatment that has been prospectively evaluated in LyP, and induced CR in 5/9 patients.

In our study, 78% of the patients who achieved CR after first-line active treatment relapsed, and even higher rates have been published[3,6,7,9,24] with longer follow-up. Our study provides new data regarding time to CR and DFS; median time to CR was 10 months without significant differences between treatments, while median DFS after CR was 11 months, but a significantly longer DFS was found for patients who received phototherapy compared with those managed with topical steroids, methotrexate or no treatment (Fig. 1), even after treatment withdrawal (Fig. 2). Accordingly, first-line treatments other than phototherapy carry a significantly increased risk of early relapse.

Association with lymphoma has been reported in up to 62% of patients with LyP, but wide variability exists between series.[3–7,9,10] Our results agree with those of a previous large series,[3] in which 19% of patients had an associated lymphoma. Referral bias and the convenience sampling method may partially explain the variability between studies.[7,10,25] Development of the second lymphoma may be delayed as long as 36 years,[6] making life-long follow-up of patients with LyP essential.[5] Mycosis fungoides is the most common associated malignancy,[5,6,9,10,25] followed by ALCL and Hodgkin disease.[3,10] There is not enough evidence supporting a decreased risk of lymphoma in treated patients,[9,10] and in our study, all subsequent lymphomas developed in treated patients.

Conclusion

In summary, the present study supports previous clinical, pathological and epidemiological findings, based upon a large number of patients. It also enhances knowledge about the routine initial therapeutic approach to patients with LyP, chiefly concerning response rates, time to response, DFS and risk factors for relapse. However, LyP is difficult to assess by retrospective studies, and the commonly used convenience sampling method carries generalizability limitations. The consensus proposal by Kempf *et al.*[5] is crucial for reproducibility of future studies. They recommend that there should be better definitions for clinical morphology, recording of potentially useful variables and development of a global response score. Prospective and controlled studies are mandatory to address the natural course of LyP, response to treatments and prognostic biomarkers.

Learning points

- The current study reports the largest series of patients with LyP published to date.
- The clinical, pathological and epidemiological data support previous results.
- Topical steroids, phototherapy and methotrexate are the most commonly prescribed first-line treatments.
- CR and cutaneous relapse rates do not differ between these treatments, but phototherapy achieves a longer DFS time.
- Early relapse is associated with having the Type A variant and receiving first-line treatment other than phototherapy.

References

1 Macaulay WL. Lymphomatoid papulosis. A continuing self-healing eruption, clinically benign—histologically malignant. *Arch Dermatol* 1968; **97**: 23–30.
2 Willemze R, Jaffe ES, Burg G *et al.* WHO-EORTC classification for cutaneous lymphomas. *Blood* 2005; **105**: 3768–85.
3 Bekkenk MW, Geelen FA, van Voorst Vader PC *et al.* Primary and secondary cutaneous CD30(+) lymphoproliferative disorders: a report from the Dutch Cutaneous Lymphoma Group on the long-term follow-up data of 219 patients and guidelines for diagnosis and treatment. *Blood* 2000; **95**: 3653–61.
4 Kempf W. Cutaneous CD30-positive lymphoproliferative disorders. *Surg Pathol Clin* 2014; **7**: 203–28.
5 Kempf W, Pfaltz K, Vermeer MH *et al.* EORTC, ISCL, and USCLC consensus recommendations for the treatment of primary cutaneous CD30-positive lymphoproliferative disorders: lymphomatoid papulosis and primary cutaneous anaplastic large-cell lymphoma. *Blood* 2011; **118**: 4024–35.
6 el-Azhary RA, Gibson LE, Kurtin PJ *et al.* Lymphomatoid papulosis: a clinical and histopathologic review of 53 cases with leukocyte immunophenotyping, DNA flow cytometry, and T-cell receptor gene

 © 2017 British Association of Dermatologists

rearrangement studies. *J Am Acad Dermatol* 1994; **30**: 210–18.
7 Liu HL, Hoppe RT, Kohler S *et al.* CD30+ cutaneous lymphoproliferative disorders: the Stanford experience in lymphomatoid papulosis and primary cutaneous anaplastic large cell lymphoma. *J Am Acad Dermatol* 2003; **49**: 1049–58.
8 Tomaszewski MM, Lupton GP, Krishnan J, May DL. A comparison of clinical, morphological and immunohistochemical features of lymphomatoid papulosis and primary cutaneous CD30(Ki-1)-positive anaplastic large cell lymphoma. *J Cutan Pathol* 1995; **22**: 310–18.
9 Christensen HK, Thomsen K, Vejlsgaard GL. Lymphomatoid papulosis: a follow-up study of 41 patients. *Semin Dermatol* 1994; **13**: 197–201.
10 Wieser I, Oh CW, Talpur R, Duvic M. Lymphomatoid papulosis: treatment response and associated lymphomas in a study of 180 patients. *J Am Acad Dermatol* 2016; **74**: 59–67.
11 de Souza A, Camilleri MJ, Wada DA *et al.* Clinical, histopathologic, and immunophenotypic features of lymphomatoid papulosis with CD8 predominance in 14 pediatric patients. *J Am Acad Dermatol* 2009; **61**: 993–1000.
12 de-Misa RF, Garcia M, Dorta S *et al.* Solitary oral ulceration as the first appearance of lymphomatoid papulosis: a diagnostic challenge. *Clin Exp Dermatol* 2010; **35**: 165–8.
13 Swerdlow SH, Campo E, Pileri SA *et al.* The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood* 2016; **127**: 2375–90.
14 de Souza A, el-Azhary RA, Camilleri MJ *et al.* In search of prognostic indicators for lymphomatoid papulosis: a retrospective study of 123 patients. *J Am Acad Dermatol* 2012; **66**: 928–37.
15 Weiss LM, Wood GS, Trela M *et al.* Clonal T-cell populations in lymphomatoid papulosis. Evidence of a lymphoproliferative origin for a clinically benign disease. *N Engl J Med* 1986; **315**: 475–9.
16 Hoetzenecker W, Guenova E, Hoetzenecker K *et al.* Successful treatment of recalcitrant lymphomatoid papulosis in a child with PUVA-bath photochemotherapy. *Eur J Dermatol* 2009; **19**: 646–7.
17 Volkenandt M, Kerscher M, Sander C *et al.* PUVA-bath photochemotherapy resulting in rapid clearance of lymphomatoid papulosis in a child. *Arch Dermatol* 1995; **131**: 1094.
18 Gambichler T, Maushagen E, Menzel S. Foil bath PUVA in lymphomatoid papulosis. *J Eur Acad Dermatol Venereol* 1999; **13**: 63–5.
19 Perna AG, Jones DM, Duvic M. Lymphomatoid papulosis from childhood with anaplastic large-cell lymphoma of the small bowel. *Clin Lymphoma* 2004; **5**: 190–3.
20 Calzavara-Pinton P, Venturini M, Sala R. Medium-dose UVA1 therapy of lymphomatoid papulosis. *J Am Acad Dermatol* 2005; **52**: 530–2.
21 Vonderheid EC, Sajjadian A, Kadin ME. Methotrexate is effective therapy for lymphomatoid papulosis and other primary cutaneous CD30-positive lymphoproliferative disorders. *J Am Acad Dermatol* 1996; **34**: 470–81.
22 Newland KM, McCormack CJ, Twigger R *et al.* The efficacy of methotrexate for lymphomatoid papulosis. *J Am Acad Dermatol* 2015; **72**: 1088–90.
23 Duvic M, Tetzlaff MT, Gangar P *et al.* Results of a Phase II trial of brentuximab vedotin for cd30+ cutaneous T-cell lymphoma and lymphomatoid papulosis. *J Clin Oncol* 2015; **33**: 3759–65.
24 Paulli M, Berti E, Rosso R *et al.* CD30/Ki-1-positive lymphoproliferative disorders of the skin—clinicopathologic correlation and statistical analysis of 86 cases: a multicentric study from the European Organization for Research and Treatment of Cancer Cutaneous Lymphoma Project Group. *J Clin Oncol* 1995; **13**: 1343–54.
25 Kunishige JH, McDonald H, Alvarez G *et al.* Lymphomatoid papulosis and associated lymphomas: a retrospective case series of 84 patients. *Clin Exp Dermatol* 2009; **34**: 576–81.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Predictive variables for complete response with first line therapy.

Table S2. Predictive variables for early (< 6 months) vs. late (> 12 months) cutaneous relapse in patients who achieved CR with initial therapy.

© 2017 British Association of Dermatologists