Primary cutaneous B-cell lymphomas (PCBCL) are a distinct group of primary cutaneous lymphomas with few and controversial reports on their treatment and prognostic factors. The aim of this retrospective study of a large international series of PCBCL patients was to analyze the patient and lymphoma characteristics as well as treatment-related variables associated with clinical outcome. From 1980 to 2006, 507 patients were referred to 19 cancer centers of 6 countries all over the world. The median age was 55 years (range, 16-92 years) and the M/F ratio was 1.4. According to the WHO-EORTC classification indolent lymphomas included 341 FCL and 122 MZL, while aggressive NHL were represented by DLBCL, leg type (n=44). Sixty patients (12%) had stage II. The majority of cases was diagnosed in trunk/arms (52%), while in 29% in head/neck and in 13% in the legs; 7% of patients had a generalized disease (>1 site). The maximal lesion diameter was >4 cm in 21% of cases and >2 lesions were recorded in 39%. The prevailing type of lesions were nodules (74%), while only a minority of patients (6%) were affected by tumors. Few patients had B symptoms (5%), poor ECOG-PS (9%) or elevated LDH (7%). Two hundred eighty-four out of 446 patients (64%) were treated only with surgery (n=86) or chemotherapy (n=95), mostly consisting of a short course of anthracyclin containing regimens, or radiotherapy (30-50 Gy) (n=103). One hundred sixty two cases (36%) received combined therapy, mostly including surgery or chemotherapy, followed by radiotherapy. A small subgroup of 35 patients were given rituximab alone (n=19) or in combination with other treatments. The remaining 26 patients did not receive any therapy. The response rate of 446 patients was the following: 402 achieved CR (86%), 38 PR and 6 were in SD. Neither histology nor treatment significantly influenced CR rate. Among 402 responders, 128 (32%) eventually relapsed, 86% in the skin, 10% in extracutaneous sites and 4% in both. The relapse rate varied according to histology, ranging from 52% in DLBCL leg-type to 29% in MZL and 28% in FL. Moreover, combined treatments significantly reduced relapse rate (24% vs. 37%; p=0.008). The achievement and maintenance of CR significantly influenced the long-term disease specific survival (at 20 year 99 % vs. 45%; p=0.0001). The CR rate of subgroup of 35 patients treated with rituximab, was 74%, while the relapse rate was 35%. These results were not influenced by the addition of other therapies to rituximab. After a median follow-up of 53 months (range, 2-333 months), 5 and 10-year estimate of OS, disease-specific survival, PFS and DFS were 91%, 92%, 61%, 65% and 82%, 88%, 49% and 56%, respectively. Cox multivariate analysis, stratified for age with a stepwise selection of the significant variables, identified DLBCL, leg-type histology, elevated LDH, type of lesion (nodules and tumors), B symptoms and female gender, as significant predictors of a poor OS.

In conclusion this retrospective analysis confirms, on a large series of cases, that patients with PCBCL belong to different risk categories requiring a tailored treatment approach. These data can be usefully taken into account for an adequate management strategy of PCBCL patients.