Primary cutaneous CD30+ anaplastic large cell lymphomas (pc-ALCL) belong to the group of rare, non-mycosis fungoides T-cell lymphomas (1). Similar to lymphomatoid papulosis the characteristic immunohistochemical finding of pc-ALCL is CD30-positivity of infiltrating neoplastic T cells. To date, only limited data is available on the treatment of pc-ALCL and current recommendations are largely based on case reports and small cohort studies (2). Surgical excision and/or radiotherapy are usually performed in limited disease. In cases of disseminated disease, multi-agent chemotherapy has shown good effects, but is accompanied with high toxicity and high recurrence rates. Herein, we report a case of refractory, widespread pc-ALCL that was successfully treated with brentuximab vedotin.

CASE REPORT
A 56-year-old Caucasian man was initially referred to our department with a solid erythematos nodule 4 cm in diameter located in the left popliteal region. The patient’s further medical history included coronary heart disease, peripheral arterial disease, and hyperuricemia. Histopathological analysis of the lesions showed secondary scar as well as palpable, enlarged lymph nodes in the left inguinal region. Histological analysis of the lesions showed secondary infiltration of the CD30+ pc-ALCL (the histological evaluation of 5 out of 8 removed lymph nodes showed loss of normal lymph node architecture as well as large amounts of tumour infiltrates consisting of large, anaplastic, proliferating, CD30+ lymphoid cells. Complete computed tomography (CT) scan and bone marrow biopsy were unremarkable. We decided to initiate radiation therapy of the popliteal and inguinal area as well as low-dose therapy with methotrexate (15 mg/week). However, new skin lesions and lymph node metastases developed within a few weeks. Subsequent inguinal lymphadenectomy, a second course of radiation therapy, low-dose interferon alpha, bexarotene, and 6 cycles of monochemotherapy with gemcitabine did not result in any substantial clinical improvement of the disease. Actually, new skin lesions occurred with rapid ulceration and secondary superinfection (Fig. 2a). Facing the aggressive course of the disease, lack of efficacy of the previously performed conventional therapy, and the patient’s comorbidities we decided to initiate treatment with brentuximab vedotin (1.8 mg/kg every 3 weeks). Four weeks after initiation of therapy, all cutaneous nodules had significantly decreased in size. After a total of 8 cycles of therapy with brentuximab vedotin, a complete clearance of all lesions was observed (Fig. 2b). There was no sign for residual lymph node involvement. Side effects during therapy were moderate and included grade 3 neutropenia, which necessitated antibiotic and antimycotic prophylaxis as well as treatment with granulocyte colony-stimulating factor.

DISCUSSION
Brentuximab vedotin is a novel antineoplastic agent licensed for systemic CD30+ lymphomas that have relapsed or are resistant against first and/or second line therapies. It is an antibody-drug conjugate in which the antimitotic agent monomethyl auristatin E is bound to monoclonal antibodies against the cell membrane protein CD30 (3). In this respect it is supposed to have a highly targeted antineoplastic effect against CD30+ cells. After binding to the extracellular domain of CD30, brentuximab vedotin enters the cell. Intracellular released monomethyl auristatin E induces growth arrest and apoptosis of CD30+ cells. Thereafter, monomethyl auristatin E diffuses into the surrounding microenvironment and induces further cytotoxic effects on CD30+ lymphoma cells (bystander

Fig. 1. (a) Dense lymphocytic infiltrates of predominantly large, partially anaplastic cells with nuclear polymorphism. (b) The immunohistochemical staining showed CD30-positivity in more than 70% of the infiltrating cells.
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Fig. 2. (a) Multiple, confluent, partly ulcerated nodes on the left thigh. (b) Clearance of all skin lesions with residuals after 6 months of treatment with brentuximab vedotin.

The authors therefore suggest brentuximab vedotin as an effective new treatment option in patients with large tumours in cosmetically sensitive areas, especially if radiation or operative therapies are contraindicated.

The patient presented herein differs from previous case reports due to the widespread involvement of the lower extremities with additional regional lymph node infiltration by tumour cells, factors that predict a worse prognosis in comparison to pc-ALCL with skin involvement only (10). This might explain the delayed response and the higher cumulative dosage of brentuximab vedotin that was necessary to achieve a complete remission in our patient compared to the previously published case reports (6–9). Future controlled studies are necessary to fully determine the role of brentuximab vedotin in the treatment of cutaneous CD30+ lymphomas. Such studies are currently ongoing.

The authors declare no conflict of interest.

REFERENCES