and safety of the addition of bevacizumab to carboplatin plus paclitaxel (CPB) chemotherapy [3]. Although the study did not achieve progression free survival (PFS) advantage as the primary end point, adding bevacizumab to carboplatin plus paclitaxel (CP) showed 3-month OS advantage over the to CP arm. In a multicenter, single-arm, open-label phase II study, bevacizumab plus fotemustine as first-line treatment in metastatic melanoma patients, PFS and OS were 8.3 and 20.5 months, respectively [4]. Grignol et al. reported that administration of bevacizumab with interferon alpha led to a clinical response in 24% of patients with stage IV melanoma and stabilization of disease in another 20% of patients with median PFS and OS of 4.8 and 17 months, respectively [5]. Bevacizumab with erlotinib and bevacizumab with everolimus combinations have synergistic activity against melanoma and can be novel treatment regimens for metastatic melanoma, but no well-designed trials exist to prove therapeutic activity of erlotinib and everolimus as first-line treatment in metastatic melanoma.

In the first-line treatment of metastatic melanoma, dacarbazine/temozolomide, ipilimumab±dacarbazine and vemurafenib in BRAF600E mutation-bearing patients can be used safely due to the more or less clear data of these regimens, but there is no well-designed randomized clinical trial of CP to use in untreated metastatic melanoma as first-line.

CP combination is not standard choice of treatment for metastatic melanoma and the optimal combination dose is not known. In phase II-III studies CP combination was generally used and accepted as second-line treatment [3].

In the absence of data from randomized clinical trials, it is unclear which chemotherapeutic schedule is better to be combined with bevacizumab. As a result, larger phase III studies are needed to observe benefit of bevacizumab, if any. Hence, it is not possible to state bevacizumab is a new a treatment approach in metastatic melanoma. Also, the results of ongoing studies of adding bevacizumab to dacarbazine or to ipilimumab in patients with unresectable/metastatic melanoma are eagerly awaited.

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Rituximab-related cryptogenic organizing pneumonia and late onset neutropenia in a patient with non-Hodgkin lymphoma: Report of two rare complications and review of the literature

Dear Editor,

Rituximab is a chimeric anti-CD20 monoclonal antibody and it has been used for the treatment of lymphomas either alone or combined with chemotherapy. Rituximab is a well tolerated agent, except allergic reactions which are usually associated with the first infusion. Late onset neutropenia (LON) and cryptogenic organizing pneumonia (COP) are rare complications of rituximab.

A 53-year-old male patient with diffuse large B cell lymphoma limited to the right iliac bone (stage IE) was admitted to our clinic in October 2007. Eight cycles of R-CHOP were administered (day 1: rituximab 375 mg/m^2, cyclophosphamide 750 mg/m^2, vincristine 1.4 mg/m^2 [maximum 2 mg], doxorubicin 50 mg/m^2 and methylprednisolone 100 mg/day for 5 days) and involved field radiotherapy (RT) was delivered after chemotherapy. Two months after the last dose of rituximab the patient was admitted to our clinic with dyspnea. Physical examination revealed bilateral rales in the lungs. Erythrocyte sedimentation rate and CRP were 96 mm/hour and 15.24 mg/dl, respectively. In thoracic CT patchy, ground-glass appearance and consolidation areas were seen in both lungs. Fiberoptic bronchoscopic examination showed normal bronchial mucosa. Bronchoalveolar lavage (BAL) was negative for acid-fast stain. Cytological examination of BAL showed spumy macrophages and rare polymorphonuclear leukocytes were seen, while viral inclusions were not detected. Empirical antibiotic treatment with ceftriaxone and clarithromycin was started but the patient's clinical course didn't improve. The diagnosis of interstitial pneumonia and COP were made, so 1 mg/kg prednisolone i.v. was started. Significant clinical improvement was achieved with corticosteroid therapy. The patient was admitted to our clinic for reevaluation 4 weeks later. He had no significant symptoms and his general health status was good. Lung infiltration was almost completely resolved in chest X-ray (Figure 1)and CT. Laboratory examinations were as follows: hemoglobin 11.7 g/dl, white blood cell 3.700/mm^3, neutrophils 400/mm^3, lymphocytes 2100/mm^3, and platelets 184,000 /mm^3. Bone marrow biopsy showed hypocellularity without any specific changes or lymphoma involvement. In flow cytometric analysis, decreased levels of B lymphocytes and significantly increased levels of active T lymphocytes were detected. Restaging including imaging procedures showed that the patient was still in complete remission for non-Hodgkin's lymphoma. Laboratory and clinical findings known to cause neutropenia could not be

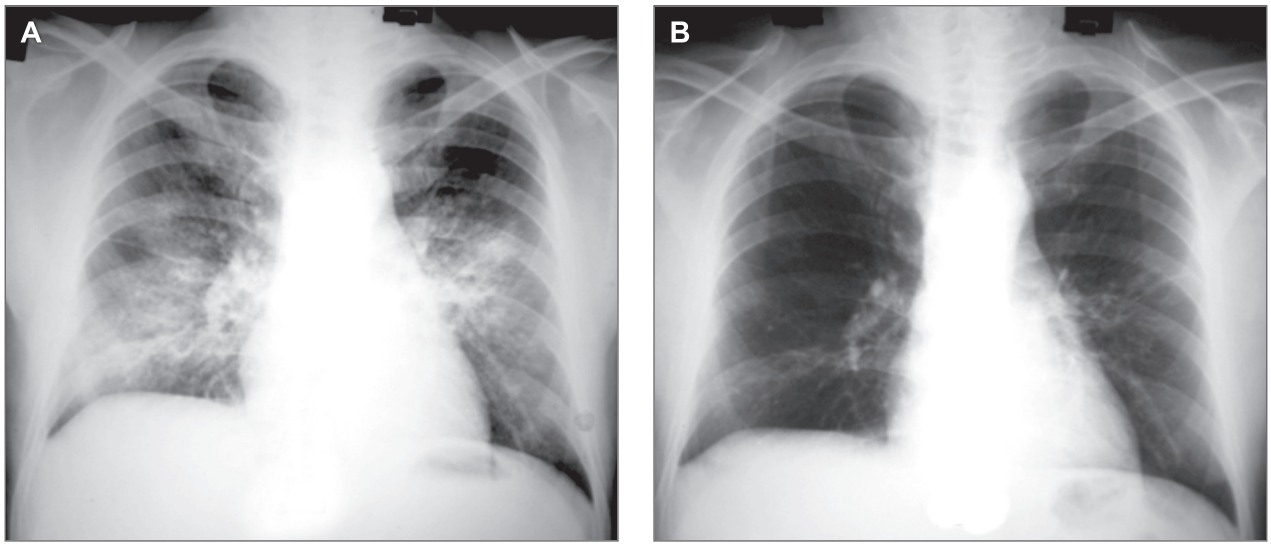

Figure 1. Patient's chest x-ray before **(A)** and after **(B)** corticosteroid treatment.

found and the patient's current situation was accepted as LON associated with rituximab. The number of neutrophils was normalized spontaneously, 6 days after admission but the depletion of B-lymphocytes continued one more year. At this time the percent of T helpers (CD4) was low and of T suppressors was high. The patient is in complete remission 32 months after the last dose of R-CHOP with no pulmonary, neurologic or hematologic toxicity except the percent of T helper cells which is still just under the normal level.

Rituximab is generally well tolerated, whether given alone or with chemotherapeutic agents. When used alone, during rituximab treatment or 30 days after treatment, various side effects are observed in 84% of patients. However, 97% of these side effects are of grade 1 or 2 and the most commonly documented adverse events are acute, infusion-related reactions which are usually observed during the first administration. Nonetheless, these side effects aren't seen in 55% of patients on subsequent administration. However, with the increasing uses of rituximab, the rare late side effects started to be reported more frequently. LON, delay in the recovery of B lymphocyte function, infections, progressive multifocal leukoencephalopathy, hepatitis B virus reactivation, interstitial pneumonitis, and COP are some of them [4,5]. Although LON and COP have been reported increasingly more often, the pathogenetic mechanisms and risk factors are unclear [4,5].

In conclusion, as rituximab is being used more widely, and for extended periods of time, it is rather certain that a greater number of late side effects are to be expected in the future. Therefore, physicians need to be aware of rituximab-related late onset toxicities.

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Case detection rates of basal cell carcinoma by gender and age in Greek population

Dear Editor,

Basal cell carcinoma (BCC) is the most common cancer in humans, deriving from non keratinizing cells that originate in the basal layer of the epidermis. If left untreated, BCC can become invasive and may result in substantial tissue damage. Metastasis is a rare event [1]. A paucity of studies from Mediterranean climates prompted us to undertake the present study.

A cross-sectional methodology was used to analyse data (1995-2002) from an outpatient setting of a dermatologic teaching clinic of a general state hospital. In Greek dermatology departments, outpatients are self-referred and ask directly for primary health care. Preoperatively, the diagnosis in obvious cases was clinical, whereas in patients with less typical lesions a histopathological confirmation was imperative.

The overall denominator and reference population consisted of 50,237 Greek dermatologic outpatients, aged 35 days to 96 years, consecutively examined by dermatologists. Males were 20,909 (41.6%) and females 29,328 (58.4%) (Table 1). The study includ-