downregulated PTEN expression, cooperating with TP53, is a characteristic of activated synovial fibroblast of RA patients displaying a significant role in inflammation and immune response by modulating various cytokines production and T-cell lineage [2]. This aspect of RA pathogenesis makes the article even more interesting because the association of long-term ADT and risk of RA could be due to not only to immunosuppressive action of testosterone, as the authors discussed, but also to PTEN alterations, an early frequent event in prostate carcinogenesis. Genomic studies on tumor tissue from patients developing RA in this work are warranted to better understand RA pathogenesis and potential prognostic-therapeutic implications.

Beyond genomic alterations, the autoimmune-inflammatory response in RA may require, in most cases, a second hit leading to immune-complex formation and complement activation, to induce or increase cytokine production and synovial vascular leakage. Similar events have been extensively described in several chronic inflammatory disorders due to different etiologies. For example, HCV chronic infection sustains B cells clonal expansion and autoantibodies production (i.e. IgM molecules with rheumatoid factor activity), characterizing mixed cryoglobulinemia, a model of autoimmunity, involving immune complexes formation, cytokines and complement activation [3]. Consequently, the knowledge of baseline features as potential triggers of autoimmunity, would have been useful to better characterize the onset and activity of RA, likely also correlated with progression of damage and disability.

Lastly, current findings established a significant relationship among chronic inflammation, metabolic syndrome and prostate cancer [4, 5]. Yang et al. [1] could evaluate the impact of RA development on clinical outcome and probably the detection of autoimmune disease during cancer history might provide a proper management of prostate cancer patients in both early and late disease stages. Recently, our group showed that pre-treatment metabolic syndrome/inflammation status had a negative impact on progression-free/overall survival (PFS/OS) [5]. A subanalysis showed that 23 of 551 (4.2%) castration-resistant prostate cancer patients treated with abiraterone or enzalutamide had an autoimmune condition, of whom 8 (1.5%) was affected by RA. Pre-therapy metabolic/inflammatory alterations were observed in 17 out of these 23 (73.9%) patients ($P = 0.045$) who had a shorter PFS/OS [hazard ratio (HR) = 3.7, 95% confidence interval (CI) 2.9–5.9, $P < 0.0001$ and HR = 5.8, 95% CI 4.0–14.3, $P < 0.0001$, respectively). These evidences confirm the importance of identifying autoimmune disease during ADT not only in localized disease but also in all steps of prostate cancer, especially for the growing number and increasingly early use of new hormonal prolonging-life drugs.

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Treatment of the myeloid/lymphoid neoplasm with *FGFR1* rearrangement with FGFR1 inhibitor

To the Editor,

Myeloid/lymphoid neoplasm with *FGFR1* rearrangement [1] is a rare aggressive disease characterized by myeloid hyperplasia, marked eosinophilia, tendency to rapidly progress to an acute leukemia (AML) and high refractoriness to chemotherapy [2].

The molecular pathogenesis results from a chromosomal translocation involving the *FGFR1* gene at the 8p11 locus with various partner genes causing a constitutive activation of the FGFR1 tyrosine kinase, impacting cell proliferation and survival [3].

Recently, a phase I/II study evaluating a novel, highly selective FGFR kinase inhibitor, INCB054828, in patients with refractory advanced malignancies (ClinicalTrials.gov: NCT02393248) has been initiated [4]. Herein, we present a patient who achieved a complete remission on this highly selective inhibitor.

A 50-year-old male presented with a 5-month history of leukocytosis, fatigue and anorexia. He was found to have leukocytosis with an absolute eosinophilia, anemia, and thrombocytopenia, and bone marrow biopsy revealed hypercellular marrow with eosinophilia consistent with a myeloproliferative neoplasm. Further studies involving conventional cytogenetics, fluorescent in situ hybridization, reverse transcriptase polymerase chain reaction, and Sanger sequencing confirmed t(8; 9)(p11.2; q33) with an *FGFR1* rearrangement leading to an abnormal *CEP110-FGFR1* fusion transcript (breakpoints at exon 38 and 9, respectively) (Figure 1).

After signing informed consent, the patient was enrolled into the clinical trial with INCB054828, 9 mg orally once daily on a 2 weeks-on/1 week-off schedule, in 21 day cycles. The patient achieved rapid response on therapy with complete resolution of

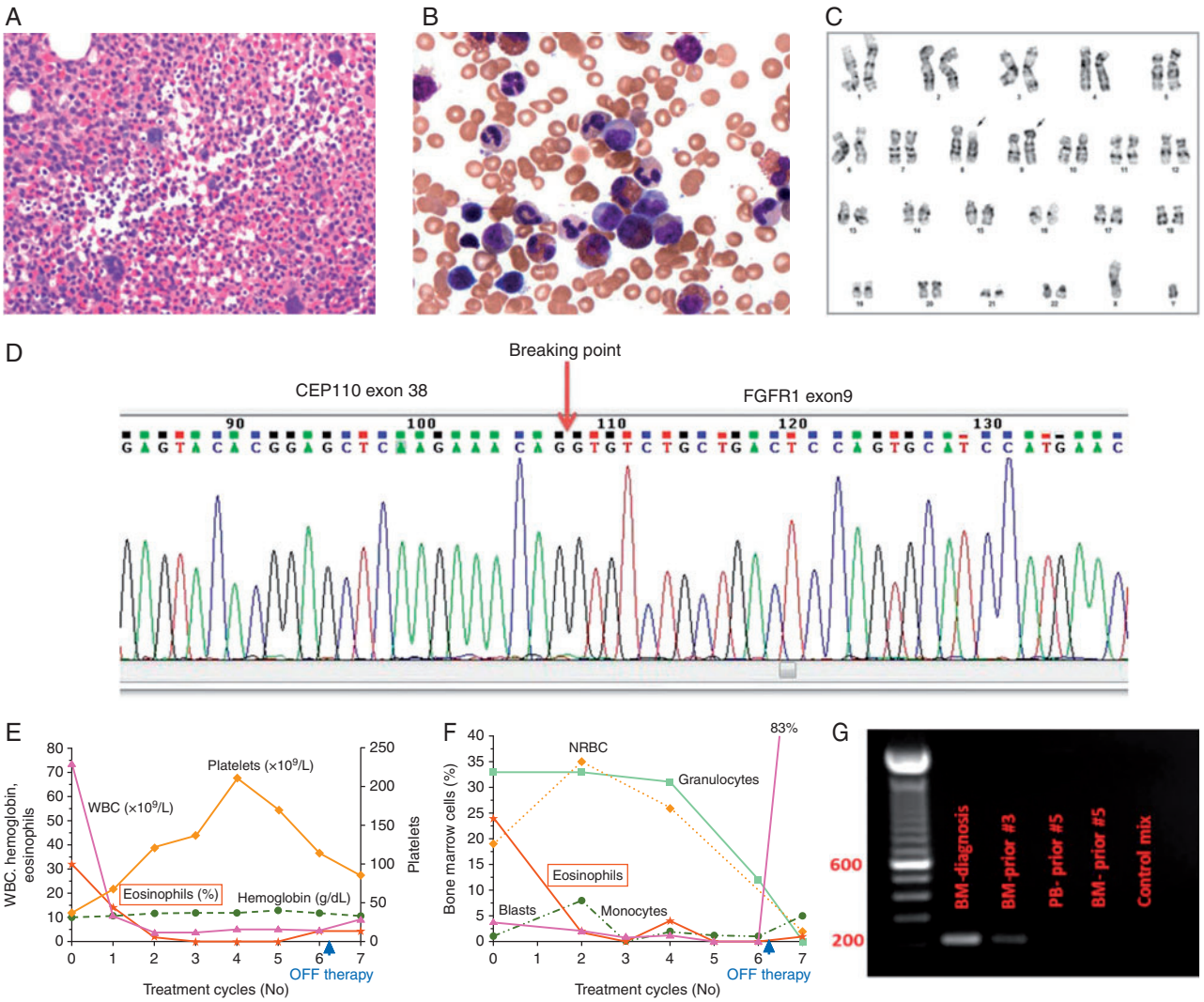

Figure 1. Diagnostic findings. (A) Hypercellular bone marrow with granulocytic hyperplasia (H&E, ×400). (B) Bone marrow with granulocytic hyperplasia and eosinophilia (Wright Giemsa, ×500). (C) Chromosomal analysis showing t(8; 9) (p11; q33) (black arrows). (D) Sanger sequencing of the *CEP110-FGFR1* fused PCR product shows breaking points at exon 38 of the *CEP110* gene and at exon 9 of the *FGFR1* gene. (E) Peripheral blood counts and (F) bone marrow findings at diagnosis and over time on during therapy with INCB054828 (*x*-axis = treatment cycles 1–6, cycle 7 was not administered). (G) RT-PCR demonstrating *CEP110–FGFR1* fusion at diagnosis and over time: electrophoresis on a 1.5% agarose gel; PCR product of 212 bp was amplified from bone marrow cells (lanes 2, 3, 5—BM) and peripheral blood (lane 4, PB): lane 2 at initial diagnosis; lanes 3–5 during therapy; and control sample (lane 6). Before cycle 5, the patient was in remission, therefore no signal was detected.

eosinophilia, complete hematologic and cytogenetic remission, and complete molecular remission with undetectable *CEP110-FGFR1* fusion transcript after the second, third, and fourth cycles, respectively (Figure 1E–G). Overall tolerance was excellent without any treatment interruptions, or requirement of blood product transfusion.

Fourteen days after starting the sixth cycle, the patient had treatment interrupted for an unrelated issue, and his disease progressed rapidly to AML. The patient was subsequently taken off study, and underwent treatment with intensive chemotherapy followed by allogeneic stem-cell transplantation (SCT). Twenty-four months from the original diagnosis, the patient continues to be in complete remission.

To the best of our knowledge, this report marks the first demonstration of a deep complete remission in a patient with myeloid/lymphoid neoplasm with *FGFR1* rearrangement achieved with a targeted therapy, a highly selective FGFR kinase inhibitor, INCB054828. Up until now, molecular remissions in this disease have only been attainable with SCT. The use of a targeted inhibitor of a pathway clearly implicated in disease pathogenesis may offer more effective therapy with the possibility of 'functional cure', as first noted in chronic myeloid leukemia treated with tyrosine kinase inhibitors. INCB054828 not only represents a 'bridge' to SCT, but might also be an important treatment option for patients not eligible for an SCT. Based on this one patient experience, a phase II trial of INCB054828 in patients with

myeloid/lymphoid neoplasms with *FGFR1* rearrangement (NCT03011372) [5] has been initiated and is recruiting patients.

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Six cycles of R-CHOP-21 are not inferior to eight cycles for treatment of diffuse large B-cell lymphoma: a Nordic Lymphoma Group Population-based Study

The majority of randomised clinical trials that have established R-CHOP-21 as the current standard treatment of adult patients with diffuse large B-cell lymphoma (DLBCL) have applied eight cycles of chemotherapy [1–3]. Despite a lack of solid evidence to support the use of six instead of eight cycles of R-CHOP-21, six cycles are commonly assigned in clinical routine and endorsed in guidelines.

No randomised trial has demonstrated superiority of eight compared with six cycles of R-CHOP-21. Therefore, we examined whether the use of six versus eight cycles of R-CHOP-21 had impact on survival probability, using data from the Danish and Swedish lymphoma registries, as previously described [4].

This study includes 1170 adult patients diagnosed with DLBCL 2007–2014 in Sweden and Denmark, who received treatment with six or eight cycles of R-CHOP-21. Of these, 1013 (87%) were administered six cycles and 157 (13%) received eight cycles. Median follow-up time was 5.0 years (range 1.2–9.4).

Reflecting the population-based setting, patient characteristics in the two treatment groups slightly differed and were marginally inferior in the cohort treated with eight cycles of R-CHOP-21. In survival estimates, crude 5-year overall survival (OS) rates were similar for patients treated with six and eight cycles of R-CHOP-21; 74% (95% CI: 71% to 77%) and 72% (95% CI: 63% to 79%), respectively (Figure 1). Furthermore, in a multivariate Cox model adjusting for IPI variables and gender, eight cycles of R-CHOP-21 was not associated with better outcome than six cycles [hazard ratio (HR): 0.92; 95% CI: 0.66–1.29; $P = 0.63$].

To further adjust for imbalances in prognostic factors, a matched sample analysis was carried out. Here, the 157 patients who received 8 cycles were compared with 157 patients who received 6 cycles of chemotherapy, matched according to IPI variables and bulky disease. Similar 5-year OS of 72% (95% CI: 63% to 79%) and 76% (95% CI: 67% to 83%) were observed in the

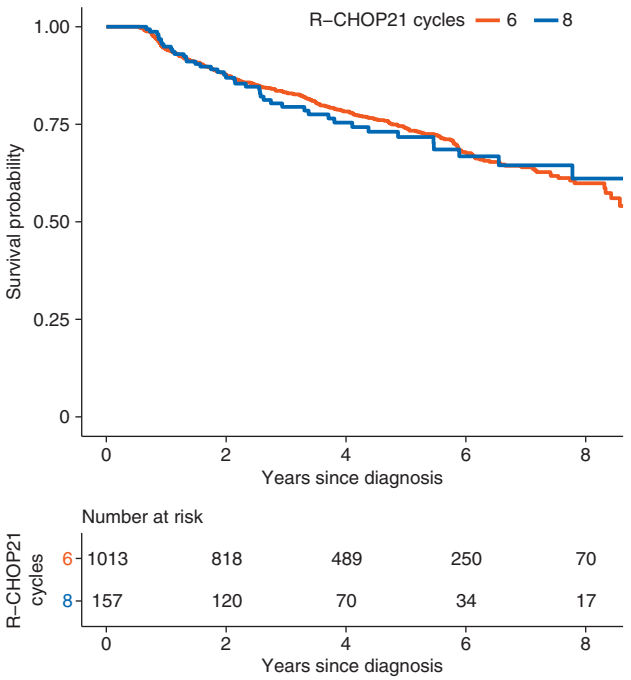

Figure 1. Overall survival for patients treated with six (orange line) and eight (blue line) cycles of R-CHOP-21.