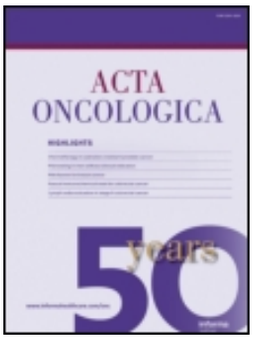

Acta Oncologica

ISSN: 0284-186X (Print) 1651-226X (Online) Journal homepage: informahealthcare.com/journals/ionc20

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To cite this article: Fabio Stagno, Paolo Vigneri, Vittorio Del Fabro, Stefania Stella, Nunzio Restuccia, Cesarina Giallongo, Michele Massimino, Salvatore Berretta, Maria Stella Pennisi, Daniele Tibullo, Elena Tirrò, Calogero Buscarino, Angelo Messina & Francesco Di Raimondo (2010) Concomitant and feasible treatment with dasatinib and the anti-EGFR antibody cetuximab plus radiotherapy in a CML patient with multiple squamous neoplasias, Acta Oncologica, 49:1, 111-112, DOI: 10.3109/02841860903302913

To link to this article: https://doi.org/10.3109/02841860903302913

Acta Oncologica, 2010; 49: 109–110

informa
healthcare

LETTER TO THE EDITOR

Concomitant and feasible treatment with dasatinib and the anti-EGFR antibody cetuximab plus radiotherapy in a CML patient with multiple squamous neoplasias

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To the Editor,

The advent of biological targeted therapies has changed the prognosis of several hematologic and solid malignancies including Chronic Myeloid Leukemia (CML), breast, colo-rectal (CRC) and head and neck squamous cell carcinomas (HNSCC) [1].

Dasatinib (DAS) is a multitarget inhibitor of the ABL and SRC tyrosine kinases, currently approved for CML patients resistant or intolerant to imatinib (IM) [2]. Cetuximab (CTX) is an anti-EGFR antibody employed for the treatment of metastatic CRC or, in association with external beam radiation therapy (EBRT), for locally advanced HNSCCs [3,4]. We report the case of a CML patient who developed both benign and malignant squamous lesions during the course of his hematologic disease and was treated concomitantly with DAS and the association of EBRT and CTX.

In 1991, a 54-year-old Caucasian male was diagnosed with Chronic Phase CML (low Sokal risk; BCR-ABL-transcript: e13a2). The patient started α-interferon (9 MUI/daily) obtaining a complete hematological remission (CHR) that he maintained until February 1996 when he was switched to Hydroxyurea (HU) since he lost his CHR. In May 1996, the patient developed a scalp spinocellular epithelioma that was surgically removed. Four years later, still on HU, he was diagnosed with a keratoacanthoma of the left ear that was also excised. In January 2001, he began conventional IM therapy (400 mg/daily), achieving a CHR without any cytogenetic response (CyR) after 12 months of therapy. He was therefore considered resistant to conventional IM dosage and escalated to 800 mg/daily but had to return to 400 mg because of the repeated occurrence of grade 3/4 thrombocytopenia. In November 2006, he lost his CHR and was placed on DAS (140 mg/daily). At that time, his BCR-ABL/ABL ratio was 106.838^{IS} and sequencing of the BCR-ABL kinase domain demonstrated the presence of low levels of mutations (P230H, T231N). After the first month of treatment, DAS was reduced to 100 mg/daily because of persistent headaches unresponsive to medical treatment. He quickly regained his CHR but never obtained more than a minor CyR. In November 2007, the patient developed a vocal cord squamous carcinoma that was removed by laser resection. Six months later, he presented an ulcerated squamous carcinoma of the tongue. He refused a further surgical excision and began EBRT (44 Gy on the neck and the oral cavity with a 22 Gy boost on the tongue) with CTX (400 mg/sm as a loading dose followed by weekly infusions at 250 mg/sm) obtaining a partial remission of the disease, that was confirmed at the last follow-up in April 2009. As a precautionary measure, DAS was administered at 50 mg/daily during the first week of EBRT and CTX and brought back to 100 mg for the remainder of the EBRT and CTX

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(Received 25 August 2009; 1 September 2009)

ISSN 0284-186X print/ISSN 1651-226X online
DOI: 10.3109/02841860903302913

treatment. Overall, the patient well tolerated the concomitant treatment with DAS and CTX + EBRT, with the exception of leukopenia and thrombocytopenia (grade 2/3) and mucositis (grade 2/3) as main adverse events. Further, the addition of CTX to DAS did not show neither synergic nor additive therapeutic effects on CML disease (BCR-ABL/ABL ratio 83.310^{IS}).

Radical improvements in the long-term survival of CML patients pose novel medical challenges, as treating physicians will often have to manage several simultaneous chronic illnesses in an aging population [5] as well as second tumors. To the best of our knowledge, this is the first case reporting the concomitant use of a tyrosine kinase inhibitor with EBRT and CTX. Our experience suggests that EBRT and CTX may be safely administered to CML patients placed on DAS therapy because of resistance or intolerance to IM.

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