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Percentage decrease in Haemoglobin values after chemotherapy and radiation therapy as a predictive response factor to Epoetin beta

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Summary: Erythropoietin receptor agonists (ERA) are effective in the treatment of cancer-related anaemia. Their use improves haemoglobin (Hb) levels, reduces needs for transfusion, and improves quality of life. However, predictive response factors to ERA are insufficiently studied.
Objective: To evaluate the predictive value of response of Epoetin beta, the percentage decrease of Hb due to chemotherapy (CT) and radiation therapy (RT) in patients with lung cancer (LC).
Material and Methods: From May 2004, 23 patients with LC treated with CT and RT, received 30,000 IU per week of Epoetin beta for symptomatic cancer-related anaemia. Thirteen patients received RT-CT (Carbo-Taxol) concomitantly with intentions to cure, 1 patient CT and RT after pneumonectomy and 9 cases underwent diverse regimens of CT for palliative purposes. In all these patients Hb levels were measured at successive points: before oncological treatment (Vo), on initiating treatment with Epoetin beta (V1) and after 4 (V2) and 8 (V3) weeks. Response to treatment was considered as an increase of at least 1 gr/dL in Hb levels after 4 weeks. At the same time, the quality of life of patients was evaluated through questionnaires: Fatigue Symptom Inventory (FSI) and the ECOG scale.
Results: The mean levels of Hb at the successive points of measurement were V0: 12.7 g/dL; V1: 10.4 g/dL; V2: 12.3 g/dL, V3: 13.3 g/dL. The highest value of Hb in V0 and the greatest percentage reduction in Hb after treatment showed significant correlation ($p = 0.028$) after administration of Epoetin beta applying Pearson's test. Patients with concomitant CT-RT showed greater significance ($p < 0.001$). The discriminative point in the response to treatment was 10% in the reduction of Hb levels after CT-RT. Correlation between successive Hb values and scores on FSI and ECOG scales were highly significant. One patient required transfusion. No patient received Epoetin beta in doses of more than 30,000 IU per week.
Conclusions: In this group of patients with lung cancer, Hb levels before CT-RT and percentage decrease in Hb after treatment, are predictive of response o Epoetin beta. The relationship was more evident in the concomitant CT-RT group of patients treated for curative purposes. Variations between values of Hb are closely related to parameters of quality of life.

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Results of a prospective, randomised, placebo-controlled, triple-blind phase III multicenter study on the efficacy of proteolytic enzymes on radiation-induced oral mucositis

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Background: The present study was initiated to investigate the efficacy and safety of a proteolytic enzyme preparation (Wobe-Mugos®E) with regard to a reduction of oral mucositis during radiotherapy for head and neck tumours.
Materials and Methods: The study was designed as a prospective, randomised, multicenter, placebo-controlled, triple-blind phase III study with parallel groups. Sixty-nine patients with carcinomas of the oropharynx or the oral cavity were enrolled between 1996 and 2000 in 5 centers; 54 of these were recruited in Dresden. Of the 69 patients 61 (Dresden: 46) were available for analysis. Radiotherapy protocols comprised conventional fractionation with 1.8−2.0 Gy/fraction, 5x/week to total doses of 60−66 Gy/6−7 weeks, or hyperfractionation with 2×1.2 Gy/day, 5x/week to a total dose of 72 Gy/6−7 weeks. Hyperfractionation was applied in 8/36 (22%) patients in the Wobe-Mugos®E group and in 11/33 (33%) patients in the placebo group. Tumours were mainly located at tonsils (20.5%), floor of the mouth (15.7%), or tongue (margin: 15.7%, base: 12.0%, body: 8.4%), and were well balanced between the groups. All patients received a dose >40 Gy to a significant area of oral mucosa, based on the tumour localisations. The proteolytic enzymes tested (Wobe-Mugos®E) comprised papain 100 mg, trypsin 40 mg, chymotrypsin 40 mg. Primary endpoint for confirmative analysis was the maximum grade of oral mucositis during radiotherapy according to a modified RTOG/EORTC classification. Scoring was done twice per week. Average mucositis scores over weeks 1 to 6 of radiotherapy served as a secondary endpoint.
Results: The enzyme preparation was well tolerated. With regard to maximum mucositis scores during radiotherapy, no statistically significant differences were found between the placebo and the verum group. For the average mucositis scores over weeks 1−6, a significant difference in favour of the placebo arm was found. The latter was based on an earlier onset of mucositis in the group receiving proteolytic enzymes as compared to placebo.
Conclusions: In the present, randomized study, no beneficial effect of treatment with proteolytic enzymes (Wobe-Mugos®E) on radiation-induced oral mucositis was observed. Enzyme treatment resulted in an earlier onset of mucositis.

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A prospective observation study of treatment of chemotherapy-induced anaemia with darbepoetin alfa every 3 weeks: the OASIS (Observational Aranesp® Survey to Investigate the q3w Schedule) study

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Introduction: Darbepoetin alfa (DA) can be administered 500μg every 3 weeks (Q3W) to treat chemotherapy-induced anemia (CIA), allowing synchronisation with Q3W chemotherapy (CTX). This study examines pattern of use of DA Q3W in daily practice in Belgium and Luxembourg, and adherence to erythropoiesis-stimulating agent (ESA) treatment guidelines.
Methods: OASIS was a nationwide, prospective observation study of DA use in 41 oncology centres between April 2005 and January 2006. Adult patients (pts) with non-myeloid malignancies receiving DA for CIA were included. Specific data, described below, were prospectively defined and collected. Pts were followed: begin when DA started, until 1 week after last DA dose, for a maximum of 16 weeks.
Results: 293 pts were included: mean age, 63 yrs (range 25−89); 51% men; mean weight, 68 kg. 263 pts had a solid tumor (NSCLC n = 91; breast cancer n = 64; and SCLC n = 32; others n = 76) and 30 had hematologic malignancies. 57% of pts had platinum (plat)-containing CTX (almost 63% lung cancer pts). 50.9% and 31.1% of pts had baseline Hb of 10−11 g/dL and 9−10 g/dL, respectively. DA was started with the first (21.8%), second (29.4%) and third (24.6%) courses of CTX; median number of administrations was 3. Use of iron supplementation was marginal (8.5% of pts). In an analysis correcting for transfusions (TFN) (disregarding Hb values 28 days after any TFN), the crude hematopoietic response rate was 53.8% in plat-treated pts versus 54.0% in non-plat treated pts. 72% of pts (both plat and non-plat) had Hb $\geqslant$11 g/dL. TFN rate was 26.6%, similar in plat or non-plat treated pts. 63.4% of pts experienced a very good to satisfactory improvement of anemia related symptoms. Most pts (69.6%) were treated in a Q3W CTX schedule (with mostly 6 cycles planned). The DA Q3W interval could be maintained in a 66.7% of pts. The most common reason for not respecting the Q3W DA interval was practical (mainly remain synchronized with CTX). There were no unexpected safety concerns, with only 7 adverse and 3 serious adverse events.
Conclusion: This prospective observation study confirms the phase 3 study efficacy and safety findings of Canon J et al. (2006) in a broader community setting. Adherence to guidelines was good, as ESA therapy was started at a Hb between 9 and 11 g/dL in more than 80% of pts. The synchronisation of Q3W CTX and DA therapy could be maintained in a 76% of pts.

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High dose palonosetron does not alter ECG parameters including QTc interval in healthy subjects: results of a dose-response, double blind, randomized, parallel E14 study of palonosetron vs. moxifloxacin or placebo

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Background: New chemical entities in several drug classes must demonstrate cardiac safety with particular attention to changes in ventricular repolarization assessed by the QTc interval duration (ICH E14). With 5HT3