clinical outcome. These data are consistent with previous studies showing hypoxia to be of predictive value in head/neck cancer patients.

Conclusions: These results support previous studies showing that detailed analysis of EF5 binding is predictive of head and neck cancer progression. However, this analysis requires consideration of EF5 binding patterns. Previous studies have reported binding of nitroimidazole agents to terminally differentiated cells in tumors as well as normal tissue such as skin. Our data suggests that this binding in terminally differentiated cells, although hypoxia-mediated, may not be clinically relevant for patient outcome. Using the analysis paradigm of excluding such binding, low stage tumors had minimal EF5 binding, a finding which is consistent with our data across tumor types. There is substantial inter- and intratumoral heterogeneity in the binding of high grade tumors, a finding that is also consistent with previous studies in head/neck cancer and other tumor sites. The data presented herein emphasizes the complexity of hypoxia measurements in SCC.

Grant support: NIH RO175285 (SM Evans).

2420 Comparison of Darbepoetin Alfa and Epoetin Alfa for Radiotherapy(RT) or Chemoradiotherapy(CT/RT)-Induced Anemia

P. Samper, C. Vallejo, C. Lopez-Carrizosa, A. Rodriguez, J. Saez, J. Delgado

Radiation Oncology, Hospital Central de la Defensa, Madrid, Spain

Purpose/Objective: A large European Survey has shown that more than 38% of the cancer patients treated with RT were anemic (Hb$<$12.0g/dL) at least once during the survey. This figure reached 60–70% when patients were treated with both CT and RT[1]. Correction of anemia may have a positive impact on radiotherapy (RT) or chemoradiotherapy (CT/RT) treatment outcomes[2,3]. Both darbepoetin alpha and epoetin alpha effectively correct CT-induced anemia, but data comparing both drugs are scarce, especially on the RT setting. Objective: To compare darbepoetin alpha and epoetin alpha administered once weekly (qw) for RT-induced anemia.

Materials/Methods: This is a prospective, single-institution study. Cancer patients with anemia (Hb$<$13g/dL men or $<$12g/dL women) treated with RT in our institution between 03/03 and 03/04 where consecutively assigned to receive darbepoetin alpha 150mcg/qw SC (group 1) or epoetin alpha 40.000IU/qw SC (group 2). Oral iron was administered to all patients. The dose of erythropoietic proteins (EP) was increased to 300mcg/qw (darbepoetin alpha) or 60.000IU (40.000IU + 20.000IU)/qw (epoetin alpha) in non-responders (Hb rise$<$1g/dL after 4 weeks). The treatment was withheld if either Hb$\geq$15g/dL during the RT treatment or $\geq$14g/dl after RT. Maximum treatment duration was 16 weeks(w).

Results: 125 patients (group 1, n=62; group 2, n=63) were enrolled. 81 patients received RT and 44 CT/RT. Age (mean (SD)) was 67.4(11.3)years. 67% of the patients where men. 54% were on stage III/IV. No major differences were observed between the two groups regarding tumor type, stage, previous treatments, treatment intention, or baseline Hb (mean (SD):12.1(1.3)g/dl darbepoetin alpha, 11.9 (1.3)g/dL epoetin alpha). Treatment duration was also similar for both the EP therapy (mean(SD)) (6.5(4.1)w darbepoetin alpha, 6.5(4.3)w epoetin alpha) and RT (7.1(2.1)w darbepoetin alpha, 7.1(2.6)w epoetin alpha). Comparing both groups on an intention-to-treat (ITT) basis: 64.5% of the patients in the darbepoetin alpha group and 47.6% in the epoetin alpha group reached an Hb increase$\geq$1g/dL at 4week, but only 19.4% of darbepoetin alpha patients and 23.8% of epoetin alpha patients increased the dose. 3.2% in each group required blood transfusions. 2 patients, both in the epoetin alpha group, required to restore EP treatment after withholding it, due to reoccurrence of anemia. At the end of the treatment, the proportion of responders (Hb increase $\geq$2g/dl without transfusions) was 72.5% darbepoetin alpha and 66.7% epoetin alpha. The Hb rise by one month after the last EP administration was(mean(SD): 2.2(1.3)g/dL darbepoetin alpha and 2.5(1.5)g/dL epoetin alpha. 4 patients experienced cardiovascular events (2 in each group: 2 myocardial infarctions, 1 thrombophlebitis, 1 aortic aneurysm break).

Conclusions: Darbepoetin alpha 150mcg/qw and epoetin alpha 40.000UI/qw are both efficacious in RT-induced anemia. At these doses, the proportion of patients achieving $\geq$1g/dL at 4w seems higher with darbepoetin alpha, without reaching statistical significance, therefore more studies are needed. Recently, the EORTC recommended to initiate the treatment with EP at an Hb level of 9-11g/dL based on anemia-related symptoms and the target Hb concentration was fixed in 12–13g/dL[4]. We have already adjusted our actual clinical practice to these guidelines.

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2421 BRCA1 and BRCA2 Deficient Cells Are Sensitive to Etoposide-induced DNA Double Strand Breaks via Topoisomerase II

A. Treszezamsky,[1] Z. Feng,[1] Z. Junran,[1] C. Tokadjian,[1] L.A. Kachnic,[1] S.N. Powell[1,2]

[1]Radiation Oncology, Massachusetts General Hospital, Boston, MA, [2]Radiation Oncology, Washington University School of Medicine, St. Louis, MO

Purpose/Objective: Mutations in the breast cancer susceptibility genes (BRCA1 and BRCA2) account for the majority of hereditary breast and ovarian cancers. BRCA-deficient tumors have been shown to be sensitive to drugs inducing DNA interstrand crosslinks, such as mitomycin C, secondary to a defect in DNA repair by homologous recombination. Accumulating evidence now suggests that BRCA-deficient tumors may be hypersensitive to a broader range of chemotherapeutic agents. Understanding the nature of this cytotoxicity should ultimately become an important component of planning therapy for BRCA-related cancers. Etoposide binds to topoisomerase II (topo II), an enzyme that decatenates DNA by introducing a transient double strand break (DSB), followed by passage of the unbroken DNA molecule through the break. The enzyme then re-ligates the DNA break and releases both DNA molecules. Etoposide prevents this re-ligation step by covalently binding to