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Oral Presentation  
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### **Molecular Test May Predict Patient Response to Anemia Drug**

*Summary contains updated data not in the abstract*

Researchers have shown that testing levels of erythropoietin receptor (EpoR) messenger RNA (mRNA) in tumor tissue from patients with head and neck cancer may predict whether patients will experience tumor progression after taking the anemia drug erythropoietin. Anemia (low red blood cell count) is a very common side effect of cancer treatment, and erythropoietin (a drug that boosts red blood cell count) is commonly prescribed to anemic patients to reverse this condition and enable cancer patients to better tolerate their treatments without the need for blood transfusions. Recently concerns have emerged about erythropoietin and risk of tumor progression in certain cancers, including head and neck cancer.

Using retrieved pathological specimens, researchers measured EpoR mRNA levels in 101 tumors from patients who had enrolled in the ENHANCE trial, a Phase III clinical trial of erythropoietin in patients receiving radiation therapy for head and neck cancer. For the subset of patients treated with radiation therapy alone, without prior surgery, they found that tumors with high levels of EpoR mRNA progressed faster in patients who received erythropoietin compared with patients who received a placebo. They found a similar effect for patients having tumors with high mRNA levels of Janus Kinase 2 (Jak2), which is the primary transmitter of EpoR signals in red blood cells. They emphasized that their findings should be considered preliminary until they are validated by retrieving and testing tumor specimens from patients in other phase III clinical trials of erythropoietin.

#### **Abstract #11007**

##### **Predictive testing for erythropoietin induced tumor progression in head and neck cancer**

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**Background:** Although anemia is an independent poor prognostic factor in cancer, its correction using erythropoietin (Epo) may promote cancer progression and reduce survival, as suggested by several recent Phase III trials. We tested whether measuring Epo receptor (EpoR) mRNA levels in head and neck cancer could identify patients susceptible to Epo induced tumor growth. We also examined whether endogenous Epo might stimulate tumor growth.

**Methods:** We measured EpoR mRNA levels in tumors from a previously reported Phase III trial in which 351 patients irradiated for head and neck cancer were randomized to Epo or placebo (Henke et al., *Lancet* 2003). 154 of these tumors had been evaluated previously with a polyclonal antibody raised against the human EpoR (C20) (Henke et al., *J Clin Oncol* 2006), but which also cross reacts with non-EpoR proteins (Elliott et al., *Blood* 2006). EpoR mRNA levels were measured in 106 tumors. We examined the relationship between EpoR mRNA level and locoregional progression free survival (LPFS), the primary study endpoint, in subjects assigned to Epo versus placebo. For patients enrolled in the placebo arm we also compared baseline serum Epo levels, C20 status, EpoR mRNA levels, and LPFS.

**Results:** Epo-treated patients with unresected tumors that expressed above-median EpoR mRNA levels experienced a reduction in LPFS compared to the placebo group ( $p=0.02$ ,  $n=14$ ). This effect was not observed in patients with unresected tumors that expressed below-median EpoR mRNA levels ( $p=0.80$ ,  $n=14$ ). EpoR mRNA levels had no effect in patients with completely resected or partially resected tumors. In placebo patients with unresected or incompletely resected tumors, increased Epo levels were associated with impaired LPFS if their tumors were C20 positive ( $p=0.02$ ,  $n=22$ ), and improved LPFS if their tumors were C20 negative ( $p=0.09$ ,  $n=15$ ). C20 status and EpoR mRNA levels did not correlate ( $r=-0.11$ ).

**Conclusion:** Adverse effects of Epo on tumor progression may depend on tumor EpoR expression. Whether a relationship exists between other C20 targets and Epo induced tumor progression deserves further exploration. Our findings present clear hypotheses that should be tested in archival tumors from other Phase III trials.

**Disclosures for research team:** Consultant or advisory role for Hoffman-La Roche.