CD44, a cancer stem cell (CSC)-related surface marker, correlates with local control after radiotherapy of early laryngeal cancer. For the first time, a CSC-related marker has been functionally validated for radiotherapy in patients. CD44 expression bears the potential to predict the outcome of radiotherapy by assessment of CSC density. *Clin Cancer Res;* 16(21); 5091–3. ©2010 AACR.
cancer cell lines were evaluated. Here, the CD44 expression correlated with in vitro plating efficiency, a marker for the percentage of clonogenic tumor cells, but not with intrinsic radiosensitivity of the clonogenic tumor cells in vitro. Although clonogenic cells in vitro do not necessarily reflect CSCs in vivo [4], these data support that CD44 correlates with the number and not with the intrinsic radiosensitivity of CSCs.

The data published by de Jong and colleagues are of great relevance for translational research in radiotherapy. For the first time, a clinical dataset on a CSC-related biomarker has become available, which is consistent with the preclinical experiments showing the importance of intertumoral heterogeneity of CSC density for local tumor control after radiotherapy. On the basis of these results, CD44 should be further evaluated in patients with early laryngeal cancer for its potential as a predictive biomarker for individualized treatments; for example, radiation dose escalation or primary use of surgery in those tumors judged as radioresistant. Such studies may also be used to address whether CD44 is a surrogate marker or measures CSCs directly. In the latter case, evaluation of CD44 together with tumor volumetry might permit estimating the absolute CSC number of tumors. Radiobiologically, a direct correlation is expected between the logarithm of CSC number and the dose necessary for tumor control. If the CSC number were available for a given tumor, in principle, this parameter could be directly integrated into dose prescription and radiation treatment planning.

Another important avenue for further research is validating the findings made in early laryngeal cancer for other HNSCC. In contrast to early laryngeal cancer, most other HNSCC treated by radiotherapy are much larger and potentially more heterogeneous in other radiobiological parameters that determine outcome. One, therefore, might speculate that CD44 may lose some of its dominance as a predictor and may assume clinically relevant potential as a biomarker only when combined with other parameters, such as a quantitative assessment of hypoxia, cellular radiosensitivity, or proliferative activity.

The last decade has seen major achievements in identification of markers that may be used for the accumulation of CSCs, thereby increasing understanding of CSC biology. The study by de Jong and colleagues intelligently combines such technologies with analysis of local tumor control, the only clinical endpoint that is specific for CSC survival after radiotherapy. This study, for the first time, functionally validates a CSC-related marker in patients, and widely opens the door for further translational research into CSC-linked biomarkers for radiotherapy.

**Disclosure of Potential Conflicts of Interest**

No potential conflicts of interest were disclosed.
References

CD44: A Cancer Stem Cell–Related Biomarker with Predictive Potential for Radiotherapy

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