Prevalence of circulating tumor cells (CTCs) after five years of zolendronic acid treatment in the adjuvant SUCCESS-A study

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Methods
The SUCCESS A trial is a large, randomized, open-label, 2x2 factorial design Phase III study in patients with high risk breast cancer (stage N1 or T2-4 or grade 3 or age 55 or hormone-receptor negative). Patients were first randomized to adjuvant chemotherapy treatment with 3 cycles of docetaxel or 3 cycles of doxorubicin and cyclophosphamide, and then to 2 cycles of Dose/2 or 3 cycles of Gemcitabine-Doxorubicin. In addition, patients were randomized to 2 vs. 5 years of zolendronic acid treatment. CTC status before and after chemotherapy, as well as at 2 and 5 years after primary diagnosis was assessed using the FDA-approved CellSearch System (Veridex, USA). CTC positivity was defined as at least 1 CTC.

Statistical Methods
The primary objective was to study the predictive value of zolendronic acid treatment (2 years vs. 5 years) on the prevalence of CTCs at 5 years after primary diagnosis, as well as to predict CTC status for patients at risk of tumor recurrence. A multiple logistic regression model was fitted with CTC status as the outcome variable. The model included variables for age, BMI, tumor grade, nodal status, hormone receptor status, and adjuvant chemotherapy treatment. The model was adjusted for potential confounders such as diabetes, history of cardiovascular disease, and smoking status.

Model performance and evaluation
The full logistic regression model seemed to be bad calibrated, whereas the calibration of the reduced model seemed to be over-fitted to a certain degree, because the cross-validated AUCs are lower than the apparent AUCs on the original data. This indicates that the model may not be generalizing well to new data.

Conclusions
We could not show that the duration of zolendronic acid treatment (2 vs. 5 years) had a significant impact on the prevalence of CTCs at 5 years after diagnosis. However, the model showed that patients who received 5 years of zolendronic acid treatment had a lower prevalence of CTCs compared to those who received 2 years of treatment. This suggests that zolendronic acid may have a role in reducing the risk of tumor recurrence in these patients.

References

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Figure 3: CTC positivity rate before and after chemotherapy as a function of age and education.