Utility of gross tumor palpability or tumor size as a measure of drug efficacy for cancer prevention

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Introduction

- The options to prevent breast cancer development are limited. Only endocrine agents have proven efficacy of reducing the risk of ER+ breast cancer by about 50%.
- No agents are available to reduce the risk of non-ER+ breast cancers
- Multiple other agents, such as lapatinib, rexinoid, and arzoxifene have shown preventative efficacy in preclinical studies, but not for clinical studies.
- Potential reasons for this discrepancy include inherent differences between preclinical models and human subjects, as well as the inconsistent endpoints chosen for assessment of efficacy in preclinical studies
- Preclinical efficacy studies typically use tumor size as endpoints, as measured by gross examination of the mammary lesions
- Another measure of tumor development which is commonly used in patients but not so much in preclinical cancer prevention studies is histological grading
- The concordance between the histologic and gross diagnosis of tumor has not been well described

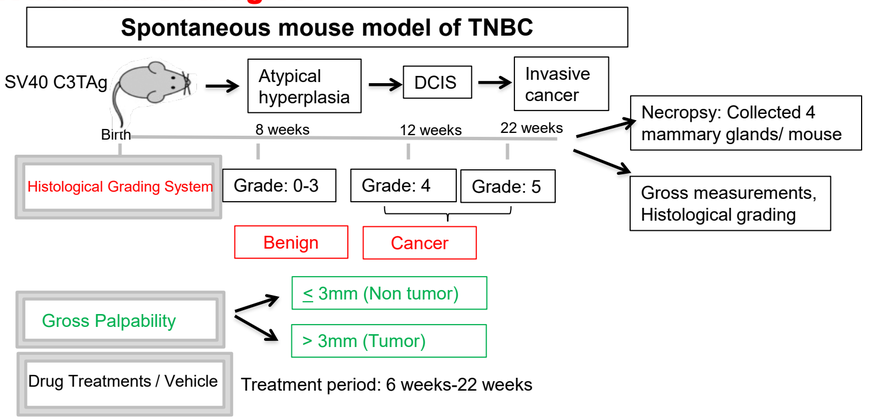
Objective

The objective of this study was to assess the concordance between histological grading and gross tumor assessment in determining the presence or absence of cancer in preclinical models.

Hypothesis

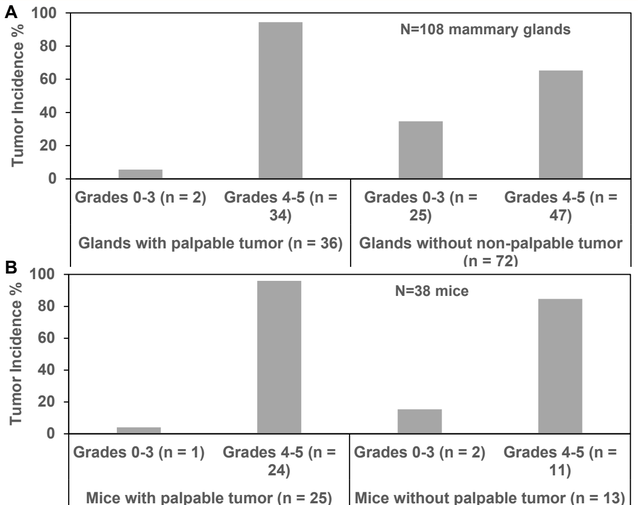
We hypothesized that concordance between gross palpability or histological grading, for measuring tumor development and drug efficacy, will be poor in non-palpable tumors.

Models and strategies



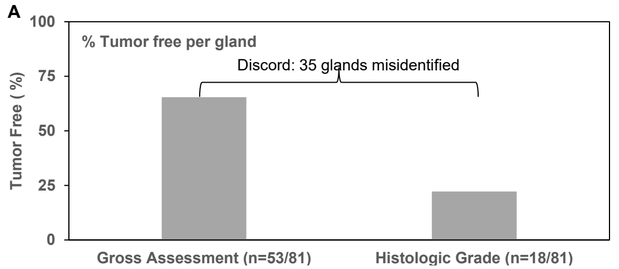
Results

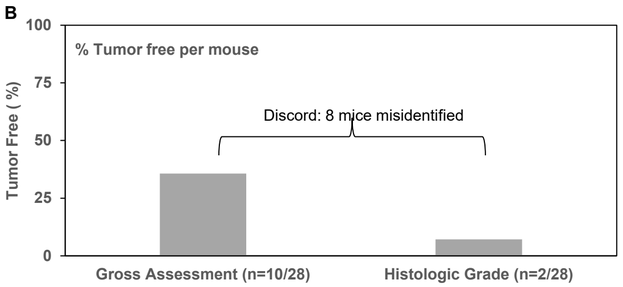
There is high concordance between tumor palpability and a higher histological grading for palpable tumors, but poor concordance in nonpalpable glands



Tumor incidence measured by two different methods. (A) shows this relationship for each mammary gland sample, and (B) shows this for each mice.

Drug efficacy studies show significant discord between the two systems of measuring tumor development. Histological grading is a better measure of tumor development and drug efficacy





Drug efficacy as measured by two different methods. (A) shows this relationship for each mammary gland, and (B) shows this for each mice.

Summary

1. Concordance is high (>90 %) between the two assessment methods for palpable tumors
2. Concordance is poor (< 40 %) between the two assessment methods for non-palpable glands, with many of these glands harboring tumors histologically
3. Response to drug treatment is overestimated when using gross assessment of the mammary gland as the study endpoint

Conclusion

Due to the lack of consistency between the two differing methods of identifying tumor development, the use of tumor palpability as the sole endpoint measure in chemoprevention studies should be reconsidered.