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A Ki-67-based clinical trial assay for neoadjuvant endocrine therapy response monitoring in breast cancer

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Background: Ki-67 Proliferation marker-based neoadjuvant endocrine therapy response monitoring has been proposed for tailoring the use of adjuvant chemotherapy. We proposed the development of a standard operating procedure for Ki-67 evaluation.

Methods: Ki-67 assay assessment focused on reproducing a 2.7% Ki-67 cut point (CP) required for calculating the Preoperative Endocrine Prognostic Index (PEPI). A CP of 10% for poor responder identification within the first month of neoadjuvant endocrine treatment was also evaluated. Image analysis was assessed to increase the efficiency of the scoring process using samples from the POL and P024 trials. Clinical outcome concordance for two independent Ki-67 scores was the primary performance metric.

Results: Discordant scores led to a triage approach where cases with complex histological features that software algorithms could not resolve were flagged for visual point counting (17%). The final Ki-67 scoring approach was run on T1/2 N0 cases from the P024 and POL trials (N=58). The percent positive agreement (PPA) for the 2.7% CP was 87.5% (95% CI 61.7-98.5%); percent negative agreement (PNA) 88.9% (95% CI: 65.3-98.6%). Minor discordance did not affect the ability to predict similar relapse-free outcomes (Log Rank P=0.044 and P=0.055). The data for the 10% early triage CP in the POL trial was similar (N=66), the PPA was 100%; PNA 93.55% (95% CI: 78.58-99.21%). The independent survival predictions were concordant (Log rank P=0.0001 and P=0.01).

Conclusions: We have developed a standard operating procedure for Ki-67 evaluation that is both reliable and reproducible. NCI review considered the scoring algorithm appropriate for CTEP-sponsored studies.

Biography

Rodrigo Goncalves has completed his MD at the age of 23 years from University of Campinas, Brazil (UNICAMP). He has trained in OB/GYN and has a fellowship in Breast surgery from the same institution completed in 2011. He completed a Masters degree in Clinical investigation at Washington University in St. Louis in 2013 with one of the highest GPA's in his class. He is currently a post-doctoral research fellow in Dr. Matthew Ellis' laboratory where he has been doing research for the past 2 years. During this time, he has published 3 papers in Nature, JNCCN and Cell Reports.

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