Title: New strategies to improve drug development in carcinoid tumors (Alliance A021202)

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Background/Significance: Numerous factors inhibit efficient drug development for carcinoid (CARC). No “actionable” mutations effectively stratify patients into empiric-risk or biology-based cohorts. Conventional imaging poorly monitors this slow-growing disease; “active drugs” are typically only cytostatic and/or cause toxicity. We propose to leverage data from A021202, a randomized phase II trial of oral VEGF inhibitor pazopanib v placebo in CARC to identify better methods of assessing treatment response. A021202 results showed pazopanib improves mPFS compared to placebo (11.8 vs. 7.6 mo; p= 0.0004, HR 0.53 (0.41-0.67)), but potential benefits are undermined by increased toxicity.
Materials and Methods/Experimental Approach: Serial blood samples and radiographic images were banked throughout A021202 (N=171 patients enrolled). We propose to 1) characterize radiologic features of tumor growth and treatment response by assessing changes in CT images over time, including total tumor volume and validated “radiomic” features, 2) evaluate candidate predictive and pharmacodynamic circulating plasma biomarkers of pazopanib effect, and 3) integrate these data into computational models of CARC growth in placebo-treated patients and inhibition of growth by pazopanib to develop new clinical trial designs (ideally requiring fewer patients and shorter observation periods).
Results: Pending.
Conclusions/Next Steps: Our ultimate goal is identification of superior endpoints to RECIST PFS and improved detection of clinically meaningful treatment effects that facilitate testing the next generation of therapeutic agents in NETs. This should identify patients most likely to benefit from a given drug, while minimizing drug exposure and toxicity for patients unlikely to benefit.

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