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Trial in Progress- Genetic Predisposition Testing Program for Pancreatic Neuroendocrine Neoplasms (PanNENs)

Bryan Khuong Le[1], Adrienne Wakeling[2], Farhana Moon[1], Li Zhang[3], Elaina Li[4], Shadera Slatter[1], Paige Steiding[1], Alan Paciorek[3], Amie Blanco[2], Emily Bergsland[1,5].

[1]Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA; [2]Cancer Genetics and Prevention Program, University of California San Francisco, San Francisco, CA; [3]Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, CA; [4]San Mateo High School, San Mateo, CA; [5]Department of Medicine, Division of Hematology/Oncology, University of California San Francisco, San Francisco, CA.

BACKGROUND

The incidence of PanNENs is rising and varies by race/ethnicity, but the impact of genetic predisposition has not been fully elucidated. Preliminary studies suggest 17% of patients with well-differentiated pancreatic tumors harbor pathogenic germline alterations. Despite this, reflex germline testing is not routine. The consequences of a positive test remain controversial and the impact of patient and tumor characteristics is uncertain. This pilot study aims to further explore the rates of germline mutations in a diverse population of patients with PanNENs.

METHODS

This ongoing prospective multicenter study (IRB#22-37899) involves University of California medical centers in San Francisco (UCSF), Los Angeles (UCLA), and San Diego (UCSD) which serve a diverse (majority minority) population in the state; 300 evaluable patients will be enrolled (N=100 each center). Eligibility includes age≥18, histologically/cytologically confirmed PanNEN, regardless of family history or prior germline testing, histologic grade, or stage. Exclusions include a primary language unsupported by our genetics department, active hematologic malignancy, or history of allogeneic bone marrow or stem cell transplant. UCSF Expanded Hereditary Cancer Panel is offered to those without prior large panel (N≥80 genes) germline testing. Primary endpoint is rate of pathogenic/likely pathogenic germline mutations (PGM) in PanNENs. Secondary endpoints include: 1) Rates of different PGM overall and by race/ethnicity and other clinical variables (age, stage, grade, sex, campus); 2) Rates of different variants of unknown significance (VUS), overall and by race/ethnicity and other clinical variables; 3) Rate of declination for patients offered testing; 4) Rate of completion of testing for those who agree to testing. Exploratory endpoints include assessing the relationship between PGM/ somatic mutations and the consequences of a PGM (e.g. second cancers, cascade testing in family members).

RESULTS

Enrollment is complete at UCSF (4/2023-6/2024) and ongoing at the other centers. UCSF includes 102 patients, median age 52.5 years, 50% female, 65% non-Hispanic ethnicity, 64% White, 22% Asian, and 17% other race/unknown. Prior testing had been performed in 67% (68/102): 83% (57/68) with a large panel, thus 44% (45/102) were offered prospective testing

CONCLUSIONS

The impact of, race, ethnicity and sex on the rates of germline pathogenicity in panNENs is largely unknown. This ongoing multicenter pilot study aims to examine the rates of PGM and VUS in a diverse population of patients with PanNENs, while also exploring the attitudes of patients about genetic testing, and the consequences of a positive test.

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