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Germline Genetic Testing in Unselected Pancreatic Ductal Adenocarcinoma (PDAC) Patients.

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Abstract Text:

Background: The aim of this study is to assess the prevalence of known heritable germline mutations in unselected PDAC patients and to determine how well current guidelines for genetic testing identify mutation carriers.
Methods: Consecutive, unselected patients with recently diagnosed PDAC from three centers were enrolled from May to December 2016 in an ongoing prospective study. A three-generation pedigree was obtained. Germline mutations in 12 genes associated with PDAC risk (*APC, ATM, BRCA1, BRCA2, CDKN2A, EPCAM, MLH1, MSH2, PALB2, PMS2, STK11, TP53*) and in 19 genes related to other cancer risks were screened for by NGS. American College of Gastroenterology and NCCN criteria for genetic testing for *BRCA1/2*, Lynch syndrome, and Familial Pancreatic Cancer (FPC) were assessed. **Results:** Among 183 patients, 46% are female, 79% are Caucasian and 10% are Ashkenazi Jewish, with median (IQR) age 68 (62,75) years at diagnosis. 41% of patients met ³1 criteria for genetic testing (35.5% *BRCA1/2*, 2.7% Lynch, 9.3% FPC). Twenty patients (11%) were found to have a total of 21 pathogenic mutations (table). Mutation status was not associated with age at diagnosis, sex, or personal history of cancer (all p > 0.05). Six mutation carriers (30% of positives) did not meet current criteria for genetic testing.
Conclusions: Preliminary results show that 6.6% of unselected PDAC patients carry a germline mutation in a gene known to increase PDAC risk and 4.3% have a mutation in genes not previously linked to PDAC. Existing testing criteria did not identify 30% of carriers. Continued refinement of guidelines is necessary to align genetic testing with inherited PDAC risk.

Patient	Gene	Mutation	Testing Criteria Met		
			BRCA1/2	Lynch	FPC
1	*ATM*	c.1027_1030delGAAA	**Y**	N	N
2	*ATM*	c.1564_1565delGA	**Y**	N	N
3	*ATM*	c.3245_3247delATCinsTGAT	N	N	N
4	*ATM*	c.5932G > T	N	N	N
5	*ATM*	c.6027C > G	N	N	**Y**
	RAD50	c.1052-2A > C			
6	*ATM*	c.7630-2A > C	N	N	**Y**

7	*BRCA1*	c.68_69delAG	**Y**	N	N
8	*BRCA1*	c.181T > G	**Y**	N	N
9	*BRCA1*	c.5266dupC	**Y**	N	N
10	*BRCA2*	c.1237delC	**Y**	N	N
11*	*CDKN2A*	c.-34G > T	N	N	N
12	*CHEK2*	c.470T > C	**Y**	N	N
13	*CHEK2*	c.470T > C	N	N	N
14	*CHEK2*	c.470T > C	**Y**	N	**Y**
15	*CHEK2*	c.470T > C	**Y**	**Y**	N
16	*CHEK2*	c.1116dupC	**Y**	N	N
17	*CHEK2*	c.1283C > T	**Y**	N	**Y**
18	*CHEK2*	EX8_9del	N	N	N
19	*MSH6*	c.2230dupG	N	N	N
20	*NF1*	c.663G > A	N	N	**Y**

*No personal or family history of melanoma or other PDAC

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CV_Jan 17_2 page.doc (68.0KB) - Curriculum Vitae

Title:
Germline Genetic Testing in Unselected Pancreatic Ductal Adenocarcinoma (PDAC) Patients.

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Is this a late-breaking data submission?
No

Is this abstract a clinical trial?
Yes

Is this clinical trial registered?
Yes

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Would like to be considered for a Merit Award:
Yes

Have the data in this abstract been presented at another major medical meeting?
Yes

Meeting:
DDW 2017

Updates to Data:
Early results from the study, focusing on prevalence of mutations, were submitted to DDW. That analysis included 128 patients and described the mutation pattern found among a subset of those patients. The current abstract is expanded to 182 patients with genetic testing results, and covers their eligibility for genetic testing based on national guidelines in addition to prevalence.

Has this research been submitted for publication in a medical journal?
No

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Biomarker
Research Category:
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Continued Trial Accrual:
Yes
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