

Submitted by: Chief Medical Officer
Name: Johnathan Lancaster, MD, PhD
Company/Organization: Myriad Genetic Laboratories, Inc.
Address: 320 Wakara Way, Salt Lake City, UT 84108
Phone: 801-505-5090
Email: jlancaster@myriad.com
Date of request: August 21, 2015
NCCN Guidelines Panel: Pancreatic Adenocarcinoma

Specific Changes: 1) Incorporate recommendation for familial/genetic risk assessment currently appearing on page MS-5 in the discussion section of the current guidelines into treatment flowcharts (i.e. page PANC-1), and 2) recommend consideration of genetic testing for all newly diagnosed patients with pancreatic cancer utilizing a panel including all genes with a known association to pancreatic cancer risk.

FDA Clearance: Not applicable.

Rationale: These guidelines already contain language recognizing the importance of familial/genetic risk assessment to both guide chemotherapy choices and provide risk information to relatives for screening and prevention of pancreatic and other cancers. Positioning familial genetic risk assessment as an essential element of the diagnosis and treatment plan would increase the likelihood that it will be accomplished in the relatively small time window available for pancreatic cancer patients. Genetic testing for many, if not all, newly diagnosed pancreatic cancer patients is supported by recent studies demonstrating that 3.8% to 21.9% of pancreatic cancer patients carry clinically significant germline pathogenic variants in inherited cancer genes, with the higher percentages in those with a family history of pancreatic (8.0%), breast (10.7%), colorectal cancer (11.1%), or Ashkenazi Jewish ancestry (4.6% to 19.2%).

The following articles are submitted in support of this proposed change. We would like to acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors of some of these publications.

Germline mutation prevalence studies:

1. Ferrone CR, et al. BRCA germline mutations in Jewish patients with pancreatic adenocarcinoma. *J Clin Oncol*. 2009 Jan 20;27:433-8. Epub 2008 Dec 8. PMID: 19064968.
2. Grant RC, et al. Prevalence of germline mutations in cancer predisposition genes in patients with pancreatic cancer. *Gastroenterology*. 2015;148:556-64. Epub 2014 Dec 2. PMID: 25479140.
3. Holter S, et al. Germline BRCA Mutations in a Large Clinic-Based Cohort of Patients With Pancreatic Adenocarcinoma. *J Clin Oncol*. 2015 May 4. [Epub ahead of print] PMID: 25940717.

4. Lucas AL, et al. BRCA1 and BRCA2 germline mutations are frequently demonstrated in both high-risk pancreatic cancer screening and pancreatic cancer cohorts. *Cancer*. 2014 Jul 1;120:1960-7. Epub 2014 Apr 15. PMID: 24737347.
5. Zhen DB, et al. BRCA1, BRCA2, PALB2, and CDKN2A mutations in familial pancreatic cancer: a PACGENE study. *Genet Med*. 2015;17:569-77. Epub 2014 Nov 20. PMID:25356972.

Genetic/Familial Risk and Treatment Studies:

1. Chapman JS, et al. Clinical Sequencing Contributes to a BRCA-Associated Cancer Rediagnosis That Guides an Effective Therapeutic Course. *J Natl Compr Canc Netw*. 2015 Jul;13:835-45. PMID: 26150578.
2. Golan T, et al. Overall survival and clinical characteristics of pancreatic cancer in BRCA mutation carriers. *Br J Cancer*. 2014 Sep 9;111:1132-8. Epub 2014 Jul 29. PMID: 25072261.
3. Lohse I, et al. BRCA1 and BRCA2 mutations sensitize to chemotherapy in patient-derived pancreatic cancer xenografts. *Br J Cancer*. 2015 Jul 28;113:425-32. Epub 2015 Jul 16. PMID: 26180923.
4. Lowery MA, et al. An emerging entity: pancreatic adenocarcinoma associated with a known BRCA mutation: clinical descriptors, treatment implications, and future directions. *Oncologist*. 2011;16:1397-402. Epub 2011 Sep 20. PMID: 21934105.
5. Oliver GR, et al. Family history of cancer and sensitivity to platinum chemotherapy in pancreatic adendocarcinoma [abstract]. *Gastrointestinal Cancers Symposium* 2010:180. Available at <http://meetinglibrary.asco.org/content/2395-72>.

Sincerely,

A handwritten signature in black ink, appearing to be 'J. Lancaster', with a large, stylized loop at the beginning.

Johnathan Lancaster, MD, PhD
Chief Medical Officer, Myriad Genetic Laboratories Inc.