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Standardizing Genomic Testing of Pancreatic Cancer in a Community Oncology Practice

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Abstract

Problem. Ordering genomic testing for patients with pancreatic cancer can discover germline or somatic mutations that may allow for targeted therapy. There are some difficulties in obtaining genomic tests, such as which test to order, and optimal timing of ordering. In addition, interpreting results and maintaining easy access to the report in the electronic medical record can be difficult. Delays in ordering genomic testing can delay the discovery of an actionable mutation for treatment.

Methods. A descriptive comparison project was developed comparing rates and timing of ordering of genomic testing for patients with pancreatic cancer who established care with a medical oncology practice between December 2019 and April 2020, and December 2020 and April 2021. Between the two data collection periods, medical oncologists began ordering genomic testing of pancreatic cancer patients upon initial consultation.

Previously, there was no standard process of ordering genomic testing. The sample included adult patients at a Midwestern community medical oncology practice.

Results. The mean number of days from tissue diagnosis of pancreatic cancer to ordering of genomic testing decreased from 56.7 days in the first group ($n=6$) to 13 days in the second group ($n=5$). No actionable mutations were found in either group.

Implications for Practice. Early genomic testing of pancreatic cancer can lead to earlier discovery of genetic mutations and opportunities for matched targeted therapy, which could improve outcomes for patients with pancreatic cancer.

Standardizing Genomic Testing of Pancreatic Cancer in a Community Oncology Practice

Pancreatic cancer is a malignancy with a poor prognosis. As this disease generally does not exhibit early symptoms, it may not be discovered until it is at an advanced stage, and it is currently the fourth leading cause of cancer death in the United States (Siegel, Miller, & Jemal, 2020). Over the next decade, pancreatic cancer is expected to rise to the second leading cause of cancer death (Pishvaian et al., 2020). For those diagnosed with locally advanced disease, median survival is 15-months, and for those diagnosed with metastatic disease, median survival decreases to only three- to six-months (Dai et al., 2019). The foundation of treatment is chemotherapy, typically in regimens of combined medications, which can be given as neoadjuvant treatment before surgery, adjuvant treatment after surgery, or alone when given for metastatic disease (Krepline et al., 2020). In recent years, the development of precision medicine has attempted to change the treatment landscape for many malignancies, including pancreatic cancer.

Precision medicine uses an individual patient's genetic information to find targeted therapy to match genetic alterations, both somatic and germline. Matched targeted therapy has the potential to provide successful treatment with lower toxicity to the patient, which has been demonstrated in studies for lung cancer and breast cancer (Singhi et al., 2019). Though a variety of mutations may be found using the standard tests of fluorescence in situ hybridization (FISH) and immunohistochemistry (IHC), genetic testing is often done through molecular next generation sequencing (NGS) technology (Levit et al., 2019). Studies have shown that actionable somatic mutations exist in about 25% of pancreatic cancers. Actionable mutations have an approved medication targeted

for that mutation specifically. Some of these mutations include mismatch repair (MMR) deficiency, *ROS1*, *NTRK1*, *NTRK2*, *NTRK3*, and *BRAF*. In addition, pancreatic cancer patients with germline *BRCA1* and *BRCA2* mutations have recently had targeted therapy approved (Pishvaian, 2020). These targeted therapies can potentially improve the outcome for those with pancreatic cancer significantly. However, obtaining NGS molecular profiles can be difficult, with multiple barriers to obtaining the tests and difficulty interpreting and maintaining the tests once they are completed.

The initial barrier to obtaining NGS begins with which test to order. Many companies provide NGS molecular profiling, with panels ranging from a targeted group of genes to whole genome sequencing. The type of tissue needed also varies and can be performed on tissue directly from the tumor or from circulating tumor cells found in the blood (Malone, Oliva, Sabatini, Stockley, & Siu, 2020). Once testing has been ordered and resulted, the report itself can be complex and difficult to interpret. In addition to reporting mutations that may have an associated targeted therapy, variations of unknown significance are often found. Clinicians may not have the understanding or time to fully interpret the findings of these complicated reports. Many of these tests are done by commercial laboratories outside of health systems, and the reports can be difficult to store in the electronic health record (EHR) for easy retrieval in the future (Levit et al., 2019). Optimal timing of when to order molecular profiling is also not well documented, as they are generally not done unless cancer is metastatic. However, studies are in progress to determine if targeted therapy may have a role in the adjuvant setting following neoadjuvant chemotherapy and surgical resection in pancreatic cancer (Krepline et al., 2020).

In a Midwestern suburban community oncology clinic, there had previously been no consistent process for molecular profiling of pancreatic cancer patients. However, over the last 12 months, somatic and germline testing for pancreatic cancer was being ordered upon establishing care with the medical oncologist. Previously, although genomic testing was being ordered for pancreatic cancer patients, there was no standard practice of when to order them. The aim of this project is to determine the impact of early molecular profiling of pancreatic cancer patients as compared to previous way of ordering. The goal is to have molecular profiling performed within two-months of tissue diagnosis in 90% of adult patients diagnosed with pancreatic cancer of any stage. The primary outcome measure of interest is molecular profiling rates with secondary outcome measures including the time from diagnosis and the number of actionable mutations found. The question of study is in adult patients in a Midwestern community medical oncology practice, what is the impact of early molecular profiling? The Iowa Model of Evidence-Based Practice was the framework used to guide this project.

Literature Review

The literature search for this project began with three search engines: MEDLINE, PubMed, and Cumulative Index of Nursing and Allied Health Literature (CINAHL). The key search terms used were “pancreatic cancer” AND “molecular profiling”, “pancreatic cancer patient” AND “molecular profiling”, and “pancreatic cancer” AND “precision medicine”. The total number of all articles found with the above search terms was 109,784. The search was further refined with inclusion and exclusion criteria. Inclusion criteria included adult studies, articles published since 2015, and those that were peer-reviewed. Pediatric patients were excluded from the search. After applying inclusion and

exclusion criteria, the search generated 69,155 articles, with most of the articles returned from the PubMed search engine. Ultimately, 10 articles were selected for this literature review to include the various aspects concerning genomic testing. The evidence table for these articles can be found in Appendix A. The articles were selected to obtain evidence supporting the use of molecular profiling for pancreatic cancer, and to find evidence of the current practice of molecular profiling across the globe.

The use of NGS was discussed in most of the chosen articles. NGS may be performed by in-house or commercial laboratories, and though no study reported benefit of one test over another, multiple options exist. Kim et al. (2017) reported using CancerSCAN, a custom-made genomic panel for their medical center, which can evaluate up to 381 cancer-related genes. Other studies using an institutional laboratory were from Sholl et al. (2016), who performed molecular profiling with their tests, OncoMap and OncoPanel, and the study from Mitri et al. (2018) who utilized GeneTrails, a 124 gene test. The commercial laboratories Caris Life Sciences and Foundation Medicine were used in multiple studies (Krepline et al., 2020; Pishvaian et al., 2020; Wheler et al, 2016). Caris testing included two panels: a 53 gene test, as well as Caris Molecular Intelligence, a 472 gene test. Foundation Medicine provided a 472 gene panel test, Foundation One. Sunami et al. (2019) used an NGS panel of 114 genes with the National Cancer Center Oncopanel Test. The Know Your Tumor trial utilized a variety of laboratories, with the majority (97%) from the commercial laboratories of Foundation Medicine or Caris Life Sciences, and the remaining 3% from either in-house pathology or other commercial companies (Pishvaian et al., 2020).

The acquisition of specimens for NGS testing varied in the studies reviewed.

Mitri et al. (2018) performed new biopsies specifically for genomic testing, though many studies performed NGS on previously obtained tissue. Kaderbhai et al. (2016) used previously biopsied samples from 2012-2014. Krepline et al. (2019) used specimens from biopsies of pancreatic cancer patients from those who completed neoadjuvant chemotherapy and surgery between 2013 and 2018. An international cohort of archived pancreatic cancer specimens was used to test NGS in a study by Singhi et al. (2019). Archived tissue was also used by Sunami et al. (2019). Either fresh biopsy or archived tissue were utilized by Wheler et al. (2016) and Kim et al. (2017). A significant limitation to all the above studies was that NGS was performed on tissue specimens only, and none included the use of blood-based tests.

The number of patients with mutations found using NGS was another theme reported throughout many of the articles. However, many articles discussed the use of NGS in a variety of solid tumor malignancies, not just pancreatic cancer. Many studies found most patients tested had at least one somatic genetic mutation, as high as 93% of participants in one study (Kaderbhai et al., 2016; Mitri et al., 2018; Sunami et al., 2019; Tsimberidou et al., 2017; Wheler et al., 2016). However, the rate of actionable mutations was generally much smaller than the number of total mutations found. The IMPACT trial found that 82.1% of patients had at least one genetic mutation, but only 54% had an actionable mutation (Tsimberidou et al., 2017). A study from Kim et al. (2017) of solid tumors found that only 44.7% of 418 patients had an actionable mutation. Despite the presence of actionable mutations, targeted therapy is not always available, as demonstrated by Sholl et al. (2016). They found 73% of their patients had an actionable mutation, but only 19% with a currently approved medication. Two studies reported data

specifically for pancreatic cancer and had a lower incidence of actionable mutations as compared to solid tumors in general. Pishvaian et al. (2020) found that 26% of 1,082 samples of those with pancreatic cancer had an actionable mutation. Singhi et al. (2019) reported that 17% of 3,594 pancreatic ductal carcinoma specimens had a mutation with a currently available targeted medication and found that 88% of all specimens had a *KRAS* mutation, of which there is no current approved targeted therapy. This certainly represents an area of future research and drug development.

Though many NGS panels are ordered, it was discovered through the various studies that there were often patients who were unable to have successful NGS profiling completed. The SHIVA trial had test rate success of only 69.2%. The reasons for not having complete profiling were that many biopsies did not contain tumor cells, had insufficient cellularity, insufficient DNA, or experienced run failures (Le Tourneau et al., 2015). Low DNA yield and/or low tissue cellularity was also found to be an issue for Sunami et al. (2019), Sholl et al. (2016), and Kim et al. (2017).

Molecular tumor boards were utilized in two of the studies reviewed. A molecular tumor board is a meeting attended by medical oncologists, advanced practice providers, pathologists, molecular biologists, and geneticists who review NGS reports for individual patients and make suggestions for therapy. Suggested therapies included clinical trial enrollment, approved targeted therapy, or targeted therapy in an off-label manor in the paper by Kaderbhai et al. (2016). Sunami et al. (2019) used a molecular tumor board which met twice a month to review cases and make treatment suggestions. This panel then provided their recommendations to the treating physician for decision making.

As previously stated, matched targeted therapy has the potential to provide

successful treatment with lower toxicity to the patient, with multiple studies reporting improvement in stable disease, increased time to treatment failure, and improved overall survival with matched targeted therapy (Tsimberidou, 2017; Wheler et al., 2016).

Interestingly, the SHIVA trial, a phase II trial evaluating targeted molecular therapy versus physician choice in patients with metastatic solid tumor malignancies, found that there was no statistical significance in progression free survival in patients on targeted therapy. The one exception was those with *RAF/MEK* mutations, as they had slight improvement in progression-free survival. It was suggested that the negative result was due to certain medications given for genetic mutations which were later found to be ineffective (Le Tourneau et al., 2015). Specifically, regarding pancreatic cancer, the Know Your Tumor trial found that patients with matched therapy had significantly longer overall survival compared to those who did not receive matched therapy (2.58 years versus 1.51 years). Progression free survival was also significantly longer in matched versus unmatched therapy (10.93 months versus 4.53 months) (Pishvaian et al., 2020).

The Iowa Model was chosen for the evidence-based practice framework for this project. This model identifies the clinical problem that clinicians find important, which is called a trigger. The trigger in this project was the complexity of ordering NGS molecular profiling in current medical oncology practice. This model uses frequent feedback loops to continually evaluate the effectiveness of the intervention and uses a team approach in developing practice change (Melnyk & Fineout-Overholt, 2019). This model is valuable as the project required collaboration with multiple individuals including physicians, nurse practitioners, nurses, patients, and NGS laboratories to ensure patients with pancreatic cancer receive appropriate testing in a timely manner to provide the best potential

outcome.

In summary, pancreatic cancer is a malignancy with poor long-term survival, with less than nine percent 5-year survival rate (Singhi et al., 2019). The use of NGS testing in solid tumor malignancies to uncover targetable genetic mutations has increased in recent years. For those with pancreatic cancer, treatment with matched targeted therapy can improve survival outcomes, and studies have shown that actionable mutations exist in about 25% of pancreatic cancers. (Pishvaian et al., 2020). However, the process of obtaining NGS testing can be cumbersome, and is not always successful. While research is promising regarding the benefits of NGS, additional research is needed to evaluate successful genomic sequencing using blood-based specimens versus tissue-based samples, as this may influence the success rate of NGS sample testing. The results of NGS may also continue to lead researchers to the development of new, targeted medications. Developing this practice protocol for NGS testing may lead to finding actionable mutations to improve outcomes for pancreatic cancer patients in the Midwest.

Method

Design

The design of this project is a descriptive comparison, comparing the rates and timing of NGS testing of pancreatic cancer patients establishing care with a medical oncology practice between December 2019 and April 2020 to pancreatic cancer patients establishing care between December 2020 and April 2021. Retrospective chart review was utilized.

Setting

A Midwestern suburban community oncology clinic was the setting for this

project. The practice employs two full-time medical oncologists as well as two full-time nurse practitioners as part of a large multi-state health system. Over the previous three years this practice has averaged 785 new patients annually, with an average of 32 new adult pancreatic cancer patients annually.

Sample

A purposeful sample was taken to include all adult pancreatic cancer patients of any stage. Pediatric patients were excluded.

Approval Processes

Approval of this project was required and granted from the University of Missouri- St. Louis IRB as well as the health system IRB. Approval from the practice site was also granted.

Data Collection/Analysis

Data that was collected included age, gender, stage of pancreatic cancer, date of tissue diagnosis, date of ordering of NGS testing, the presence of any actionable mutation, and the availability of matched targeted therapy. The data collection tool is found in Appendix B. Data was collected on newly established pancreatic cancer patients from December 2019 to April 2020, and again from December 2020 to April 2021 through retrospective chart review. An independent sample t-test was used to compare the differences in NGS testing between the previous way of ordering and after NGS testing was ordered on the first visit. Data was deidentified by using numbers in place of patient name. No date of birth or other patient identification was used.

Procedures

Using the data collection tool, retrospective chart review and data collection was

completed on subjects diagnosed with any stage of pancreatic cancer from December 2019 to April 2020. Subjects were identified through a review of providers' schedules in the given time frame in the Epic electronic health record. This process was repeated in May 2021, when retrospective chart review was done on subjects with pancreatic cancer establishing care with medical oncology between December 2020 to April 2021. Data was analyzed following the second data collection period.

Results

Upon completion of data collection, a total of six subjects ($n=6$) were diagnosed with pancreatic cancer in the first group between December 2019 and April 2020. Four of the subjects were female (67%), and two of the subjects were male (33%). The age of the subjects ranged from 55-years-old to 85-years-old, with a mean average age of 72 years. Three subjects (50%) were diagnosed with stage II pancreatic cancer, and three subjects (50%) were diagnosed with stage IV disease. Regarding days from tissue diagnosis to ordering of genomic testing there was a range of nine days to 133 days, with a mean of 56.7 days. No actionable mutations were found in this group, and thus no matched targeted therapy was available.

Five subjects ($n=5$) were diagnosed with pancreatic cancer in the second group between December 2020 and April 2021. Three of the subjects were male (60%) and two subjects (40%) were female. The age of the subjects ranged from 60-years-old to 85-years-old with a mean age of 70.6 years. One subject (20%) was diagnosed with stage II disease, three subjects (60%) were diagnosed with stage III disease, and one subject (20%) was diagnosed with stage IV disease. The range of days from tissue diagnosis to ordering of genomic testing in the second group had a range of six days to 17 days, with a

mean of 13 days. No actionable mutations were found in this group, and therefore no matched targeted therapy was available.

Analysis of the data using an independent samples t-test for days from diagnosis to ordering of genetic testing between the groups did not demonstrate statistical significance ($t(9) = 1.77, p = 0.111$). There was also no statistical significance found between the age of the subjects in either group ($t(9) = 0.20, p = 0.846$). Using Chi-square analysis for gender ($\chi^2 = 0.782, df = 1, p = 0.376$) and cancer stage ($\chi^2 = 4.95, df = 2, p = 0.084$), no statistical significance was found between the two groups (Tables 2 and 3).

Discussion

The purpose of this project was to determine the impact of early molecular profiling of pancreatic cancer patients, with a goal of 90% having molecular profiling ordered within two-months of tissue diagnosis. This goal was met with the second group having molecular profiling ordered less than one month from tissue diagnosis. Although this was not statistically significant as compared to the first group, there is definite clinical significance, as the mean days of testing was 56.7 days in the first group and only 13 days in the second group. Decreased days to genomic testing could potentially uncover an actionable mutation with matched targeted therapy quickly, though this was not demonstrated in this sample.

No actionable mutations were found in any of the subjects of either the first or second group. These findings from this sample were not consistent with the national average of approximately 25% of pancreatic cancer patients with an actionable mutation (Pishvaian, 2020).

Limitations

There were several limitations to this project, with the most significant being a small sample size. A larger sample size may have improved statistical significance as well as potentially finding the presence of actionable mutations and matched targeted therapy.

Another limitation was having an open data collection period of four months. As cancer diagnosis is unpredictable, there may potentially have been a number of subjects that were unable to be included due to this limitation. The location of this project averages 32 new pancreatic cancer patients annually, however, they may not be evenly distributed throughout the 12 months of the year. Having a longer time for data collection would possibly capture more subjects appropriate for inclusion.

A barrier found during this project was the data collection method. Due to administrative barriers of searching for patients in the EMR by cancer diagnosis, considerable time was spent in reviewing physician and nurse practitioner clinic schedules to search for patients with a new diagnosis of pancreatic cancer. This method of searching can lead to the potential of missed subjects who may have not been easily discovered in the search.

Conclusion

Studies have demonstrated the potential for improvement of patient outcomes with the adoption of precision medicine and matched targeted therapy in pancreatic cancer. This project demonstrated that though there was not statistical significance in this sample, it did demonstrate clinical significance. As early identification of genetic mutations may lead to better treatment outcomes for patients, this descriptive comparison project demonstrated a clinically significant decrease in the mean number of days of

genomic testing of pancreatic cancer patients.

Adopting a model of ordering of both germline and somatic genetic testing for pancreatic cancer patients upon initial consultation with the medical oncology team has shown that time to ordering genetic testing decreased from a mean of 56.7 days to a mean of 13 days. The benefits of ordering genomic testing upon consultation with pancreatic cancer patients can be easily disseminated to other medical oncology providers in the health system. This could result in genetic mutations being found more quickly, allowing for matched targeted therapy when available. These findings can also be relevant to the nursing and other support staff in the medical oncology practice, as often these groups are involved in the logistics of ordering genomic testing.

The implications of NGS testing for pancreatic cancer patients upon consultation with medical oncology could improve the rates of these tests ever being ordered, especially in community oncology practices, as studies have demonstrated that community practices order less genomic testing for their patients as compared to academic centers. Improving the rates of genetic testing has the opportunity to improve patient outcomes for not only pancreatic cancer patients but all cancer patients, especially in rural areas as well as other underserved areas generally served by community oncology practices (Ball et al., 2020).

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Appendix A

Literature Matrix

Citation (in APA)/ Purpose	Design/ Method	Setting/ Sample	Major Variables	Outcome Measures	Statistical Analysis	Findings	Strengths/Limitations / Recommendations
<p>Kaderbhai, C., Boidot, R., Beltjens, F., Chevrier, S., Arnould, L., Favier, L... Ghiringhelli, F. (2016). Use of dedicated gene panel sequencing using next generation sequencing to improve the personalized care of lung cancer. <i>Oncotarget</i>, 7 (17), 24860-24870.</p> <p>Use of dedicated NGS test and how it would affect treatment vs routine molecular testing</p>	Single center, observational	50 lung tumor specimens were tested with NGS. All were from French cancer centers	Type of lung cancer, mutations found, Targeted treatment	Number of mutations found in lung cancer with NGS vs standard testing	Not reported	48% had mutation found with standard molecular test, NGS found mutations in all but one patient	<p>Limits: only lung cancer, only small number of patients received targeted therapy (9/29), tested only advanced cancer</p> <p>Strengths: molecular tumor board was able to help match treatments to mutation. Was fairly easily adapted into practice</p> <p>Recommendations: Need to have more standardized approach of when to test</p>
<p>Krepline, A., Bliss, L., Geurts, J., Akinola, I., Christians, K., George, B... Tsai, S. (2019). Role of molecular profiling of pancreatic cancer after neoadjuvant therapy: does it change practice? <i>Journal of Gastrointestinal Surgery</i>, 24, 235-242. https://doi.org/10.1007/s11605-019-04423-6</p> <p>Determine frequency of actionable test results of pancreatic cancer patients who received neoadjuvant therapy with commercially available NGS</p>	Single center, Non-randomized	Medical College of Wisconsin, 236 patients with pancreatic cancer who completed neoadjuvant chemotherapy from 2013-2018. Foundation One testing or Caris testing was used as well as IHC	Neoadjuvant chemotherapy regimen given, NGS testing used	Number of potentially actionable mutations found	Specific alteration frequency, Continuous variable compared using Wilcoxon rank-sum, SS p value <0.05	94% had at least one variant (KRAS most common mutation). Some were found to have results on IHC which would show favorable response to adjuvant 5-FU and/or gemcitabine therapy	<p>Limits: multiple NGS tests used, multiple neoadjuvant chemotherapy regimens given, discordant results in some tests</p> <p>Strength: some had germline testing as well, first study to look at this population</p> <p>Recommendations: Look further into specific genomic testing and see what results show vs having multiple NGS tests used in one study.</p>
<p>Determine if use of molecularly targeted therapy improves outcomes for solid tumor malignancy compared to physician's choice</p>	Multi-center, randomized phase II trial	8 French academic centers, adults with metastatic solid tumors progressed on standard of care	Matched treatment group (experimentally) vs physician choice (control) in those with	Progression free survival, safety, objective response	Log-rank test, presented in Kaplan-Meier curves, stratified Cox proportion	No statistical significance between experimental and control group	<p>Limitations: Most of these patients were heavily pretreated. A large variety of solid tumors participated in the trial, not just pancreatic cancer. This trial didn't show improvement in</p>

		therapy, alteration in one of 3 molecular pathways, 496 patients enrolled but only 195 made it to randomization	alterations in PI3K/AKT/mTOR, RAF/MEK, or HR pathways		al hazards model, all tests were two sided		matched treatment group (surprising). Strengths: If matched treatment was available, it could be given off label. There was an adequate # enrolled in the trial. Recommendations: Repeat study with single tumor types specifically. Could look more into off-label use of medications for specific mutations by malignancy.
Mitri, Z., Parmar, S., Johnson, B., Kolodzie, A., Keck, J., Morris, M...Bergan, R. (2018). Implementing a comprehensive translational oncology platform: from molecular testing to actionability. <i>Journal of Translational Medicine</i> , 16 (1). http://dx.doi.org/10.1186/s12967-018-1733-y Implement a precision medicine oncology platform	quantitative	Oregon Health outpatient oncology setting with advanced solid tumor malignancy. Initially started with 38 patients, only 28 participated in trial	Enrollment in MM-TERT program, number of patients with actionable mutations	The existence of potentially actionable genetic mutations in metastatic or locally advanced unresectable cancers	n/a	88% of tumors that were biopsied had potentially actionable mutations	Strengths: Strong genetic testing platform, ability to biopsy as needed. Limitations: Small sample size, limitation of cancers tested, one location of study, exclusion of two molecular markers as actionable. Recommendations: Use these results to continue to develop treatments based on presence of actionable mutations, develop molecular tumor board to assist in managing these patients
Pishvaian, M., Blais, E., Brody, J., Lyons, E., DeArbeloa, P., Hendifar, A...Petricoin, E. (2020). Overall survival in patients with pancreatic cancer receiving matched therapies following molecular profiling: a retrospective analysis of the Know Your Tumor registry trial. <i>Lancet Oncology</i> , 21 (4), 508-518. To see if patients with matched molecular therapy had longer median OS than patients who didn't	Observational, retrospective	Adults with pancreatic cancer of any stage, enrolled in the Know Your Tumor program, 1856 patients	Patients with matched molecular therapy, patients without	Overall survival	Post-hoc analysis, multivariate Cox regression model, Cox proportional hazards model, significance set at p <0.05	Patients with actionable mutation who received matched therapy had significantly longer OS 1.51 years (2.58 years vs than those without matched therapy	Strengths: large sample size, sample came from all over the United States, had positive results Limitations: sometimes matched therapy was combined with chemotherapy, patients were enrolled at various points in their treatment and may have been heavily pretreated Recommendation: This will serve as foundation for future clinical trials looking into best options for targeted therapy

Sholl, L, Shivdasani, P., Cerami, E., Dubuc, A., Kuo, F., Garcia, E...MacConaill (2016). Institutional implementation of clinical tumor profiling on an unselected cancer population. <i>JCI Insight</i> , 1 (19), e87062 https://doi.org/10.1172/jci.insight.87062 Diagnostic clarification and new predictors of response to targeted therapy, identify challenges and barriers	Systematic analysis of profile initiative	3700 reports of molecular profiled which was available to any cancer patient at DFCI, Brigham and Women's and Boston Children's Hospital	n/a	Genomic panel testing, patients with actionable mutations	Chi square test with Bonferroni correction . P<0.05 was statistically significant	Genomic profiling is feasible, useful for research, can be valuable for clinical trials	Limitations: anecdotal analysis as it is not a clinical trial Strengths: They looked at reports from multiple institutions Recommendations: Using information collected to see if whole genome sequencing vs targeted gene panels may be more cost effective and appropriate for certain malignancies
Singhi, A., George, B., Greenbowe, J., Chung, J., Suh, J., Maitra, A...Bahary, N. (2019). Real-time targeted genome profile analysis of pancreatic ductal adenocarcinomas identifies genetic alterations that might be targeted with existing drugs or used as biomarkers. <i>Gastroenterology</i> , 156 (8), 2242-2253.	Retrospective, observational	3738 pancreatic ductal adenocarcinoma (PDAC) specimens, international cohort and targeted genomic profile analysis was performed	PDAC specimens, genomic test	PDAC, genomic test	Variables reported as frequencies and percentages, Fisher exact or	17% of the specimens had genomic alteration, discovered genes that could contribute with IPMN transforming to cancer	Limitations: retrospective Strengths: large number studied. Data shows that this is a feasible program Recommendations: Use results to look further into IPMN transformation and how to prevent it from becoming pancreatic cancer
Sunami, K., Ichikawa, H., Kubo, T., Kato, M., Fujiwara, Y., Shimomura, A...Kohno, T. (2019). Feasibility and utility of a panel testing for 114 cancer-associated genes in a clinical setting: a hospital-based study. <i>Cancer Science</i> , 110, 1480-1490. Investigate feasibility and utility of NGS analysis of 114 genes	Prospective cohort study	230 cases of patients >16 years old, any tumor type	Gene profiling	Number of gene profilings completed, actionable mutations found	Not reported	81.3% were able to have gene profiling done. 83% with gene profiling had at least one mutation, 59% had actionable mutation	Strengths: multiple cancer types Limitations: did not look at response rate of actionable mutations/matched treatment, some had cross contamination Recommendations: Use of this data to assist in the development of targeted drugs for various mutations found in solid tumor malignancies
Tsimberidou, A., Hong, D., Ye, Y., Cartwright, C., Wheler, J., Falchook, G., Naing,	Retrospective/non-randomized	Patients with advanced cancer with tumor genetic sequencing,	Patients with ability for matched targeted therapy, patients	Response and survival outcomes for those treated with matched therapy	RECIST guidelines to assess CR, PR, SD, FFS, OS	Patients with matched targeted therapy had higher	Limits: retrospective study, patients were heavily pretreated Strengths: large number of study

<p>A...Kurzrock, R. (2017). Initiative for molecular profiling and advanced cancer therapy (IMPACT): An MD Anderson precision medicine study. <i>JCO Precision Oncology</i>, doi: 10.1200/PO.17.00002</p> <p>Determine response and survival outcomes for matched targeted therapy in a phase one trial</p>		<p>treated with matched therapy if available. Total of 1436 patients. Out of 1436 patients, 1179 had one or more alteration, 914 of those had a targetable mutation, 277 did not participate for various reasons, so overall 637 had at least one targetable mutation and received treatment for that</p>	<p>without matched targeted therapy</p>		<p>Log-rank test</p>	<p>rates of CR and PR, longer FFS, longer OS 61% of initial N received matched targeted therapy</p>	<p>participants, variety of solid tumor malignancies</p> <p>Recommendations: Use these results to help develop a testing program outside of academic center. Could also further test by individual malignancy</p>
<p>Wheler, J., Janku, F., Naing, A., Li, Y., Stephen, B., Zinner, R...Kurzrock, R. (2016). Cancer therapy directed by comprehensive genomic profiling: a single center study. <i>Cancer Research</i>, 76 (13), 3690-3701.</p> <p>Determine feasibility and response rate of NGS in phase one study</p>	<p>Navigational trial, single-arm, nonrandomized</p>	<p>500 patients with advanced malignancies</p>	<p>Comprehensive genomic profiled matched patients</p>	<p>Rate of SD, TTF, OS, matching score</p>	<p>Univariate analysis, multivariate analysis</p>	<p>93% had at least one actionable mutation though some were off label</p>	<p>Limitations: only phase 1 drugs given, physicians could choose therapy, many died before getting treated, not randomized</p> <p>Strengths: Large sample size, multiple tumor types, was done as it would be done in a regular practice vs trial</p> <p>Recommendations: Can be used to develop program for matched therapy in clinical practice</p>

