Molecularly-Matched Therapies (Tx) Improve OS/PFS in Pancreatic Cancer

Real-World Data from the Know Your Tumor® Program

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Summary

- Initial results[1] from the KYT program demonstrated a significant improvement in progression-free survival (PFS) for molecularly-matched therapies that align to highly actionable molecular alterations (e.g. MSI-high, NTRK fusions, BRCA mutations, etc)
- Here, we report a significant improvement in overall survival (OS) in patients with highly actionable alterations that received a molecularly-matched therapy versus patients with highly actionable alterations that only received unmatched therapies.
- Real-world outcomes analyses include OS comparisons from the onset of advanced disease and from initiation of 2nd line (matched therapies were typically given in 2nd line or later)

Multi-Omic & Real-World Data

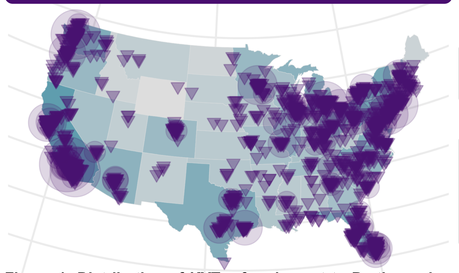


Figure 1: Distribution of KYT referrals sent to Perthera via PanCAN Patient Central, partnering hospitals/institutions, and physician practices. Informed consent was obtained to collect medical records and to coordinate molecular profiling via CLIA/CAP labs (>90% samples tested at Foundation Medicine).

Patient Demographics

Table 1: Pancreatic Cancer Analysis Cohort Summary

Patient Baseline Characteristics (% Reporting)	Pancreatic Cancer Analysis Cohort (n=677)	Highly Actionable Findings (n=189)		No Highly Actionable Findings (n=488)
		Molecularly-Matched Therapy (n=46)	Only Unmatched Therapies (n=143)	
Sex (100%)				
Male	359 (53.0%)	20 (43.5%)	63 (55.9%)	259 (53.1%)
Female	318 (47.0%)	26 (56.5%)	80 (44.1%)	229 (46.9%)
Age (100%)				
28-59 at Diagnosis	267 (39.4%)	23 (50.0%)	66 (46.2%)	178 (36.5%)
60-90 at Diagnosis	410 (60.6%)	23 (50.0%)	77 (54.8%)	310 (63.5%)
Ethnicity/Race (46%)				
White, non-Hispanic	312 (85.0%)	19 (86.4%)	159 (83.2%)	236 (86.8%)
White, Hispanic	12 (5.4%)	1 (4.5%)	6 (8.2%)	5 (1.8%)
Black	11 (3.0%)	0 (0.0%)	3 (4.1%)	8 (2.9%)
Asian	20 (3.3%)	0 (0.0%)	6 (8.2%)	14 (5.2%)
Other	12 (3.3%)	2 (9.1%)	1 (1.4%)	9 (3.3%)
Not Reported	310 (N/A)	24 (N/A)	70 (N/A)	216 (N/A)

Know Your Tumor (KYT) Program

1856 KYT Referrals *(all pancreatic cancer subtypes)*

9 in process

1594 Patients Consented *(86% of referrals to Perthera)*

- **253 Closed Pre-Consent**
  - 93 unable to contact
  - 43 patient unsupportive
  - 28 doctor unsupportive
  - 14 unable to biopsy
  - 12 cost/insurance
  - 18 health concerns
  - 20 deceased

35 in process

1223 Patients Biopsied *(77% of consented patients)*

- **336 Closed Pre-Biopsy**
  - 66 unable to contact
  - 34 patient unsupportive
  - 41 doctor unsupportive
  - 43 unable to biopsy
  - 3 cost/insurance
  - 21 health concerns
  - 99 deceased

46 in testing

1082 Perthera Reports *(88% of biopsied patients)*

- **95 Closed Pre-Report**
  - 15 unable to contact
  - 5 patient unsupportive
  - 2 doctor unsupportive
  - 15 unable to re-biopsy
  - 8 health concerns
  - 49 deceased

Pancreatic Adenocarcinoma: 1005
Adenosquamous Carcinoma: 11
Acinar Cell Carcinoma: 12
*Neuroendocrine Tumor: 35
*Other Pancreaticobiliary: 19

**Omitted from OS/PFS Analysis Cohort*

Highly Actionable Molecular Findings

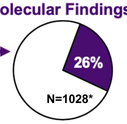


Figure 2: Operational summary of the KYT program. To promote the implementation of precision oncology, Perthera coordinates molecular testing and delivers molecularly-tailored treatment recommendations intended for patients and their treating oncologists. Perthera's patient registry includes an optional consent to collect real-world outcomes longitudinally for research. Multi-omic molecular results included genomic profiling by NGS and protein/phosphoprotein expression by IHC.

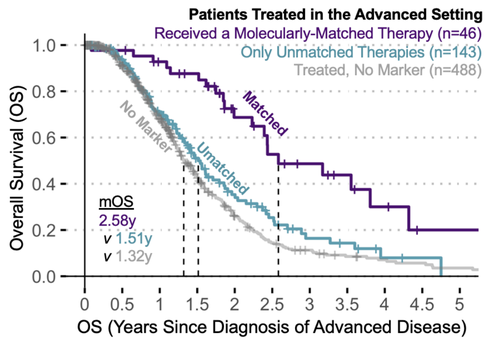
Table 2: Actionability summary as assessed by Perthera's Molecular Tumor Board

Highly Actionable Molecular Findings

Immunotherapy for
Microsatellite Instability: 8
PARP inhibitors for
HR-DDR Deficiencies: 121
ALK/ROS1/TRK inhibitors for
ALK/ROS1/NTRK Oncogenic Fusions: 4
BRAF/MEK/ERK inhibitors for
BRAF Oncogenic Mutations/Fusions: 18
PI3K/AKT/mTOR inhibitors for
PI3K/AKT/mTOR Pathway Alterations: 45
CDK4/6 inhibitors for
CDK4/6 Amplifications: 14
mult-targeted TKIs for
FGFR/RET Activating Alterations: 4
HER2 antibody combinations for
HER2 Amplified/Overexpression: 6
EGFR inhibitors for
EGFR Mutations (RASwt): 2
Other (IDH1/2, NOTCH): 5

N=227

1-Year OS Benefit with Matched Tx



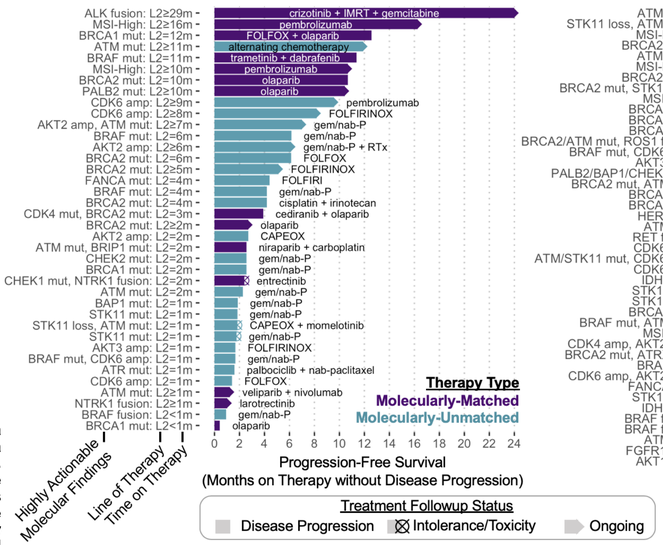
Molecularly-Matched *vs* Only Unmatched History (Highly Actionable)
p-value = 0.000388, HR = **0.42** [0.26-0.68]
Molecularly-Matched *vs* Patients without Highly Actionable Findings
p-value = 0.00000229, HR = **0.34** [0.22-0.53]

Figure 3 (Above): Patients with highly actionable alterations who received a molecularly-matched therapy lived longer than patients who did not receive a molecularly-matched therapy (with or without highly actionable findings). Kaplan-Meier curves highlight real-world outcomes from patients starting from the time when the patient was diagnosed with advanced disease. Relative to patients who received a molecularly-matched therapy that aligned to highly actionable findings (**Matched**), OS was significantly shorter in patients that did not receive any molecularly-matched therapies (**Unmatched**) as well as patients whose tumors did not demonstrate any highly actionable findings (**No Marker**).

The Perthera Report
-Ranked Therapy Options & Clinical Trials
-Molecularly-Tailored & Clinically-Relevant
-Intended for the Patient's Treating Oncologist

Figure 4: OS analyses (right) starting from the initiation of 2nd line and PFS analyses for the best matched (if any) vs the best unmatched therapy given in 2nd line or later (one per patient).

Real-World PFS Outcomes (L2)



Real-World PFS Outcomes (L3+)

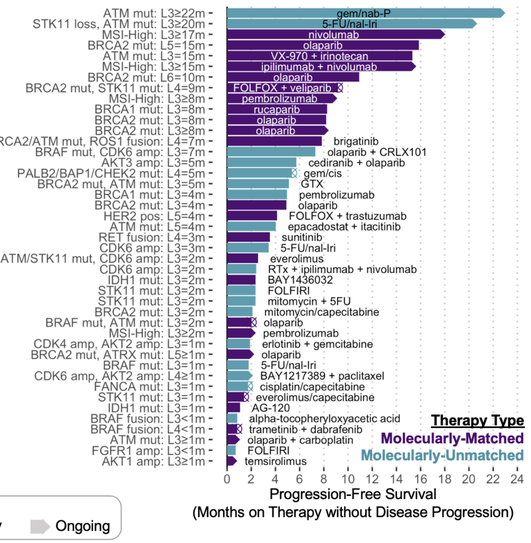
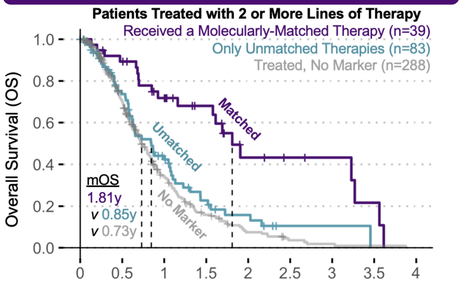


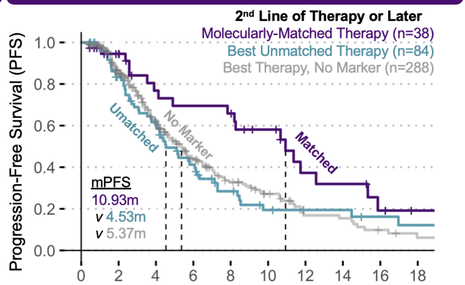
Figure 5: Highly actionable alterations alongside PFS for matched and unmatched therapies given as 2nd line (L2, left) or as later lines (L3+, right)

OS Benefit Post-2nd Line



Molecularly-Matched *vs* Only Unmatched History (Highly Actionable)
p-value = 0.000193, HR = **0.37** [0.22-0.63]
Molecularly-Matched *vs* Patients without Highly Actionable Findings
p-value = 0.00000106, HR = **0.31** [0.20-0.50]

PFS Benefit /w Matched Tx (L2+)



Molecularly-Matched *vs* Best Unmatched Therapy (Highly Actionable)
p-value = 0.0124, HR = **0.50** [0.29-0.86]
Molecularly-Matched *vs* Best Therapy (No Highly Actionable Marker)
p-value = 0.0122, HR = **0.53** [0.32-0.87]

Citations and Acknowledgments

We wish to acknowledge the patients, their families, their primary caregivers, and their cancer care teams.

1) Pishvaian, et al, Clinical Cancer Research, 24: 5018, 2018 "KYT640"

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Conflicts of Interest
Perthera is a privately-held precision oncology company.
Perthera is not a lab and did not receive financial compensation from commercial laboratories for ordering/coordinating tests.

Co-authoring clinicians have participated in Perthera's online virtual molecular tumor board platform and have referred patients to Perthera.

The Pancreatic Cancer Action Network has received support for programs unrelated to this work from companies who have or may have an interest in targeted therapies including AstraZeneca, Bristol-Myers Squibb, Celgene, Clovis Oncology, Eli Lilly & Co, Genentech, GlaxoSmithKline, Janssen Res & Dev, Johnson & Johnson, Millennium, Novartis Pharmaceuticals, Pfizer, and Takeda Pharmaceuticals.

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