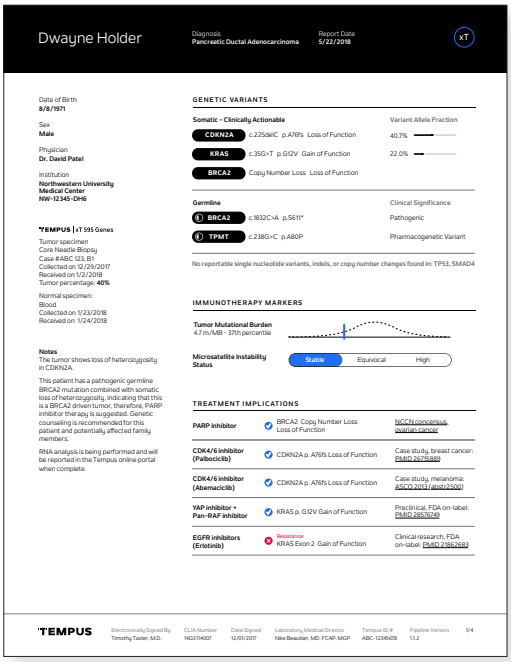
The Tempus Platform

We provide complimentary technology that allows providers safe and secure access to clinical reports and cutting-edge research applications. Powered by a rapidly growing library of clinical and genomic data, the Tempus platform is an easy and intuitive way to gain relevant insights by patient or by project.

In about two weeks, physicians receive a comprehensive report for each patient that highlights key findings, including potentially actionable treatments and immunotherapy markers that can be immediately translated into patient care.



Dwayne Holder

Diagnosis: Pancreatic Ductal Adenocarcinoma

Report Date: 5/22/2018

Date of Birth: 8/8/1971

Sex: Male

Physician: Dr. David Patel

Institution: Northwestern University Medical Center NW-12345-DH6

TEMPUS | xT 595 Genes

Tumor specimen: Core Needle Biopsy, Case # ABC 123, B1, Collected on 12/29/2017, Received on 1/2/2018, Tumor percentage: 40%

Normal specimen: Blood, Collected on 1/23/2018, Received on 1/24/2018

Notes: The tumor shows loss of heterozygosity in CDKN2A.

This patient has a pathogenic germline BRCA2 mutation combined with somatic loss of heterozygosity, indicating that this is a BRCA2 driven tumor, therefore, PARP inhibitor therapy is suggested. Genetic counseling is recommended for this patient and potentially affected family members.

RNA analysis is being performed and will be reported in the Tempus online portal when complete.

GENETIC VARIANTS

Somatic - Clinically Actionable			Variant Allele Fraction
CDKN2A	c.225delC p.A76fs	Loss of Function	40.7%
KRAS	c.35G>T p.G12V	Gain of Function	22.0%
BRCA2	Copy Number Loss	Loss of Function	

Germline		Clinical Significance
BRCA2	c.1832C>A p.S611*	Pathogenic
TPMT	c.238G>C p.A80P	Pharmacogenetic Variant

No reportable single nucleotide variants, indels, or copy number changes found in: TP53, SMAD4

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden: 4.7 m/MB - 37th percentile

Microsatellite Instability Status: Stable | Equivocal | High

TREATMENT IMPLICATIONS

PARP inhibitor	BRCA2 Copy Number Loss Loss of Function	NCCN concensus, ovarian cancer
CDK4/6 inhibitor (Palbociclib)	CDKN2A p. A76fs Loss of Function	Case study, breast cancer: PMID: 29715889
CDK4/6 inhibitor (Abemaciclib)	CDKN2A p. A76fs Loss of Function	Case study, melanoma: ASCO 2017 (abstr2500)
YAP inhibitor + Pan-RAF inhibitor	KRAS p. G12V Gain of Function	Preclinical, FDA on-label: PMID 28031749
EGFR inhibitors (Erlotinib)	Resistance: KRAS Exon 2 Gain of Function	Clinical research, FDA on-label: PMID 21862513

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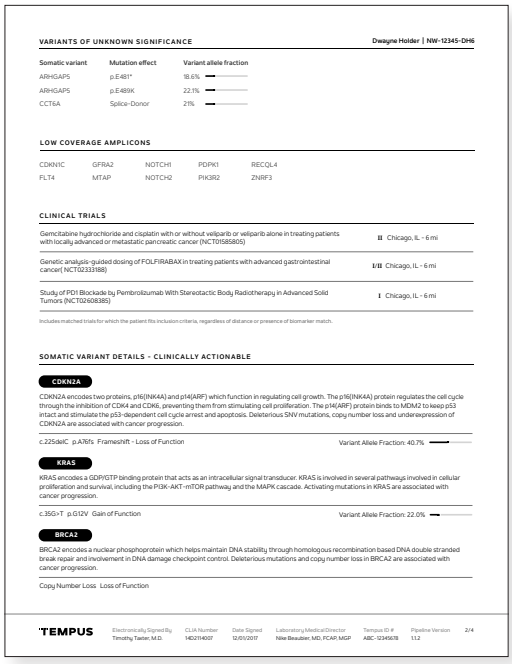

VARIANTS OF UNKNOWN SIGNIFICANCE — Dwayne Holder | NW-12345-DH6

Somatic variant	Mutation effect	Variant allele fraction
ARHGAP5	p.E481*	18.6%
ARHGAP5	p.E489K	22.1%
CCT6A	Splice-Donor	21%

LOW COVERAGE AMPLICONS

CDKN1C	GFRA2	NOTCH1	PDPK1	RECQL4
FLT4	MTAP	NOTCH2	PIK3R2	ZNRF3

CLINICAL TRIALS

Gemcitabine hydrochloride and cisplatin with or without veliparib or veliparib alone in treating patients with locally advanced or metastatic pancreatic cancer (NCT01585805)	II	Chicago, IL - 6 mi
Genetic analysis-guided dosing of FOLFIRABAX in treating patients with advanced gastrointestinal cancer(NCT02331188)	I/II	Chicago, IL - 6 mi
Study of PD1 Blockade by Pembrolizumab With Stereotactic Body Radiotherapy in Advanced Solid Tumors (NCT02608385)	I	Chicago, IL - 6 mi

Includes matched trials for which the patient fits inclusion criteria, regardless of distance or presence of biomarker match.

SOMATIC VARIANT DETAILS - CLINICALLY ACTIONABLE

CDKN2A

CDKN2A encodes two proteins, p16(INK4A) and p14(ARF) which function in regulating cell growth. The p16(INK4A) protein regulates the cell cycle through the inhibition of CDK4 and CDK6, preventing them from stimulating cell proliferation. The p14(ARF) protein binds to MDM2 to keep p53 intact and stimulate the p53-dependent cell cycle arrest and apoptosis. Deleterious SNV mutations, copy number loss and underexpression of CDKN2A are associated with cancer progression.

c.225delC p.A76fs Frameshift - Loss of Function — Variant Allele Fraction: 40.7%

KRAS

KRAS encodes a GDP/GTP binding protein that acts as an intracellular signal transducer. KRAS is involved in several pathways involved in cellular proliferation and survival, including the PI3K-AKT-mTOR pathway and the MAPK cascade. Activating mutations in KRAS are associated with cancer progression.

c.35G>T p.G12V Gain of Function — Variant Allele Fraction: 22.0%

BRCA2

BRCA2 encodes a nuclear phosphoprotein which helps maintain DNA stability through homologous recombination based DNA double-stranded break repair and involvement in DNA damage checkpoint control. Deleterious mutations and copy number loss in BRCA2 are associated with cancer progression.

Copy Number Loss Loss of Function

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Clinical Report Key Features:

1 Genomic Alterations

An intuitive and concise presentation of clinically actionable somatic alterations, clinically significant germline variants, and pertinent negatives.

2 Immunotherapy Markers

Key decision drivers for immunotherapy including microsatellite instability (MSI), tumor mutational burden (TMB), and PD-L1 and MMR IHC when ordered.

3 Smart Treatment Implications

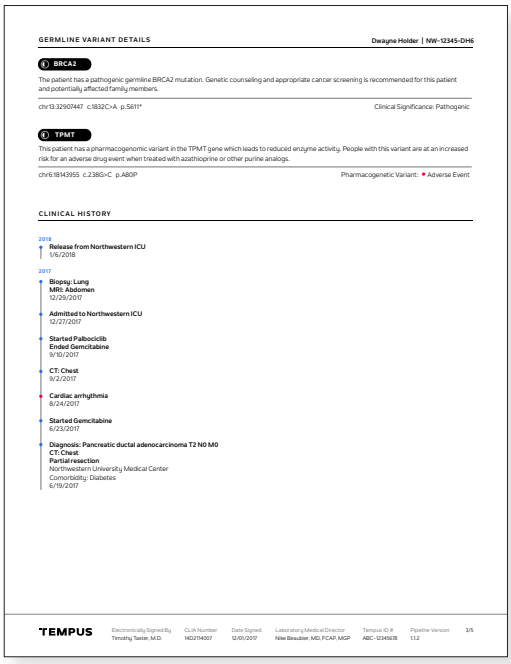
Genome-driven therapies organized by level of clinical evidence from FDA-approved to preclinical. Tempus also reports previously prescribed therapies based on the clinical documents we receive and have abstracted.

4 Tempus Insights

Patient-specific insights derived from our aggregated database of real-world evidence and genomic results that provide additional context to empower physicians to make data-driven treatment decisions. Insights are delivered when data is available to support these personalized findings.

5 Clinical Trials

Relevant clinical trials based on the patient's molecular profile and the provided clinical information that is pertinent to trial inclusion/exclusion criteria.



GERMLINE VARIANT DETAILS — Dwayne Holder | NW-12345-DH6

BRCA2

The patient has a pathogenic germline BRCA2 mutation. Genetic counseling and appropriate cancer screening is recommended for this patient and potentially affected family members.

chr13:32907447 c.1832C>A p.S611* — Clinical Significance: Pathogenic

TPMT

This patient has a pharmacogenomic variant in the TPMT gene which leads to reduced enzyme activity. People with this variant are at an increased risk for an adverse drug event when treated with azathioprine or other purine analogs.

chr6:18143955 c.238G>C p.A80P — Pharmacogenetic Variant: Adverse Event

CLINICAL HISTORY

2018
- Release from Northwestern ICU — 1/6/2018

2017
- Biopsy: Lung; MRI: Abdomen — 12/29/2017
- Admitted to Northwestern ICU — 12/27/2017
- Started Palbociclib; Ended Gemcitabine — 9/10/2017
- CT: Chest — 9/2/2017
- Cardiac arrhythmia — 8/24/2017
- Started Gemcitabine — 6/23/2017
- Diagnosis: Pancreatic ductal adenocarcinoma T2 N0 M0; CT: Chest; Partial resection; Northwestern University Medical Center; Comorbidity: Diabetes — 6/19/2017

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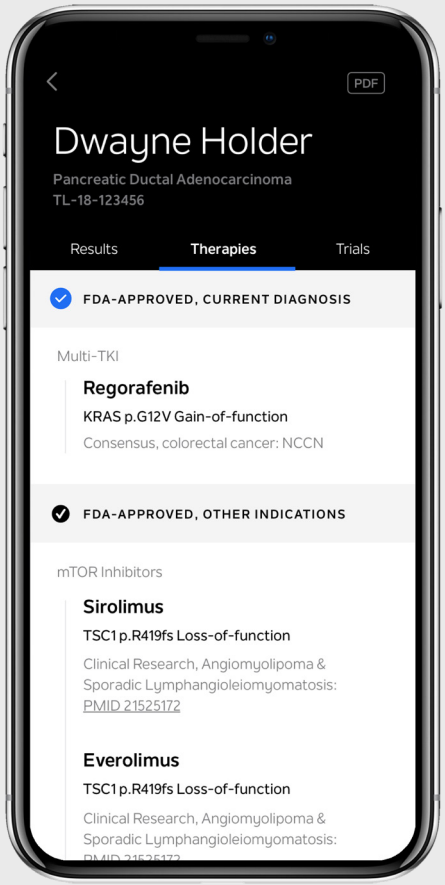
6 Gene Descriptions

Additional clinical context for all reported variants.

7 Clinical History

Patient's clinical history organized into a sequential timeline including past procedures and treatments, informing reported smart therapy implications.



Mobile Accessibility

We're focused on providing accessible and useful insights, so we deliver your results however you prefer — emailed PDF, interactive Tempus Hub, and mobile app. Our app gives you an interactive and in-depth view of your patient's molecular and clinical data whenever convenient, not just when you have the PDF or printed report on hand.

1. **Sortable and filterable list of patients and report statuses**
2. **Therapies sorted by level of evidence and matched clinical trials**
3. **In-depth gene descriptions and clinical timeline for each patient**
4. **Easy and secure access from anywhere**