

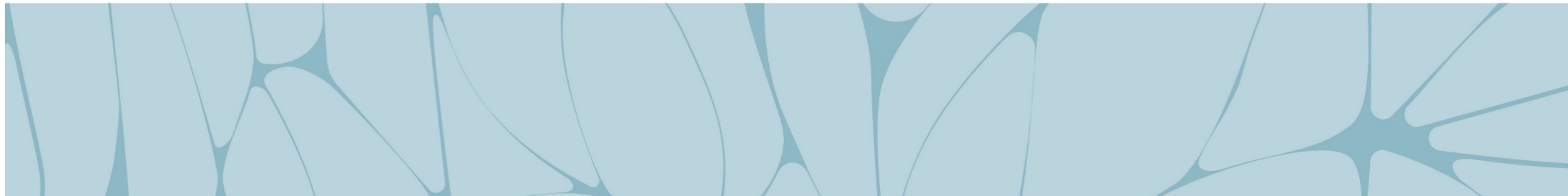
Precision Oncology – Standards and challenges for personalized, evidence-based and translational cancer therapy in clinical routine

Damian Rieke

*Department of Hematology, Oncology and Cancer Immunology, Campus Benjamin Franklin, Charité –
Universitätsmedizin Berlin*

Comprehensive Cancer Center, Charité – Universitätsmedizin Berlin

Hasso-Plattner-Institut, 01.12.2022



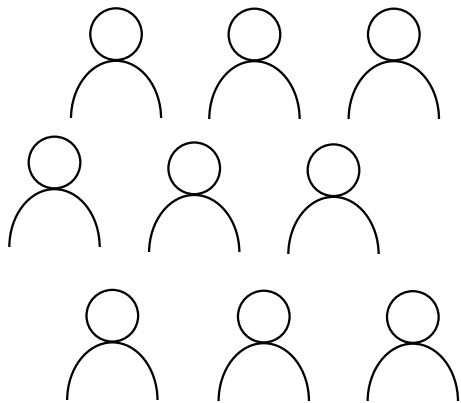
CONTENT

1. Background
2. Standards
3. Challenges
4. Summary

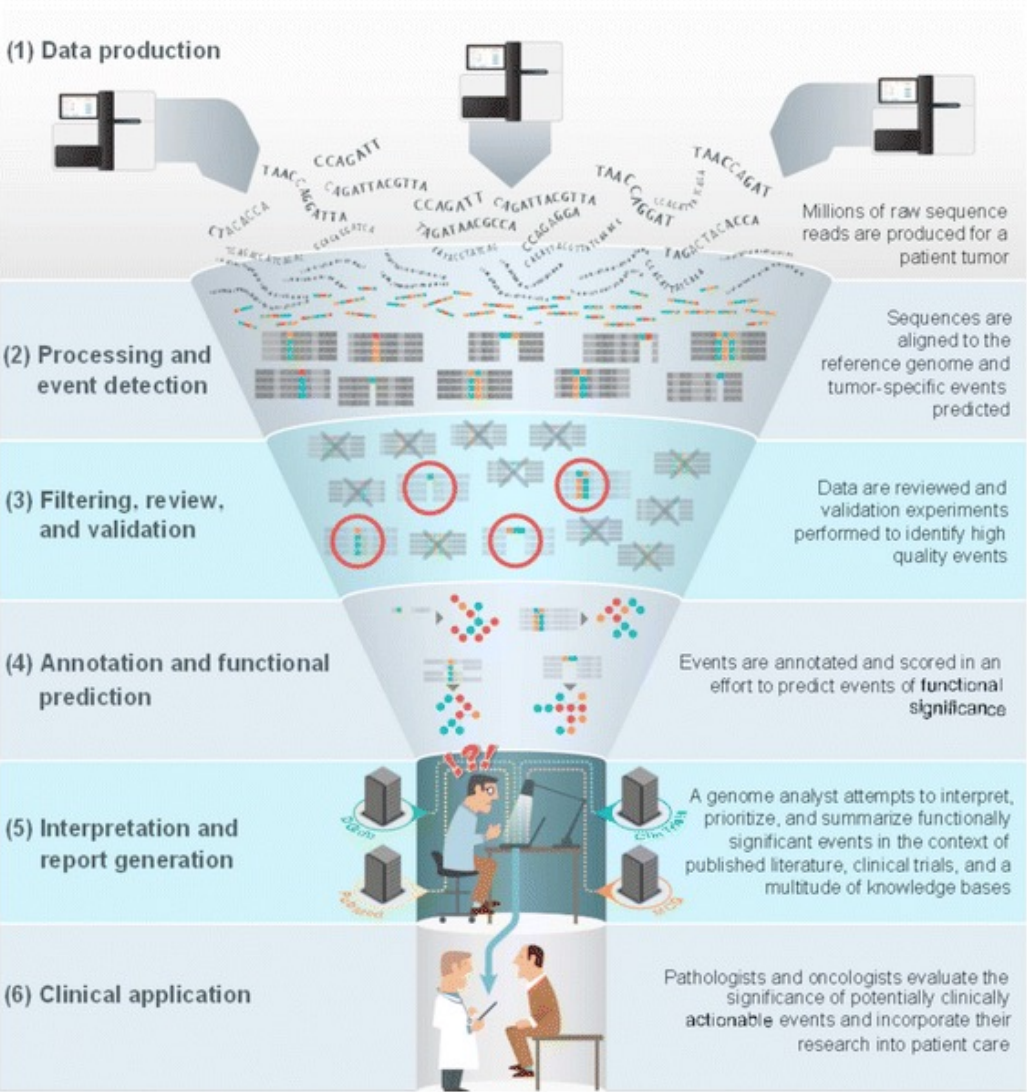
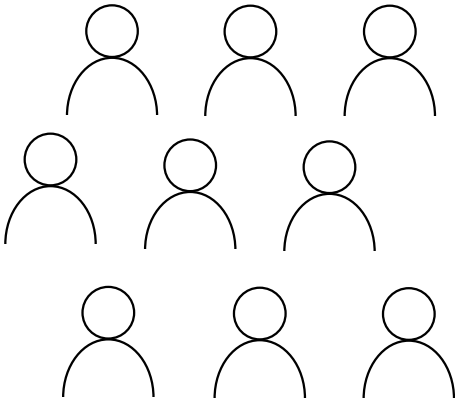
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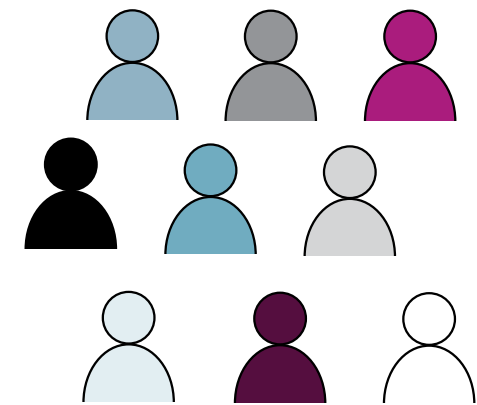
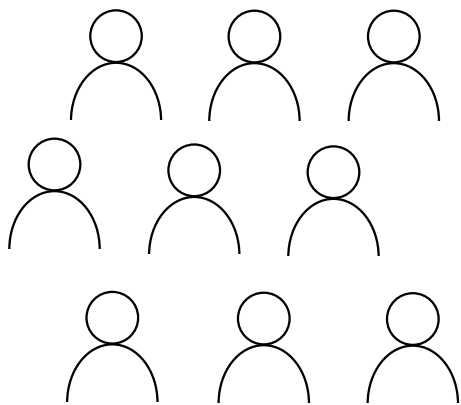
Background



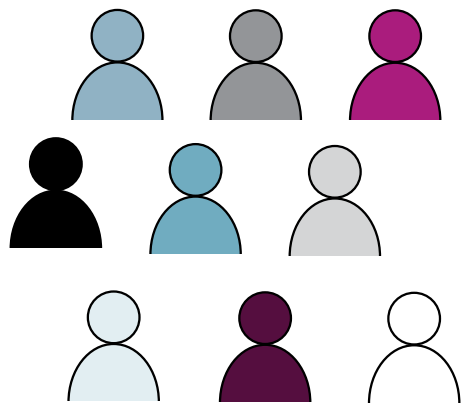
Background



Background



Background



CONTENT

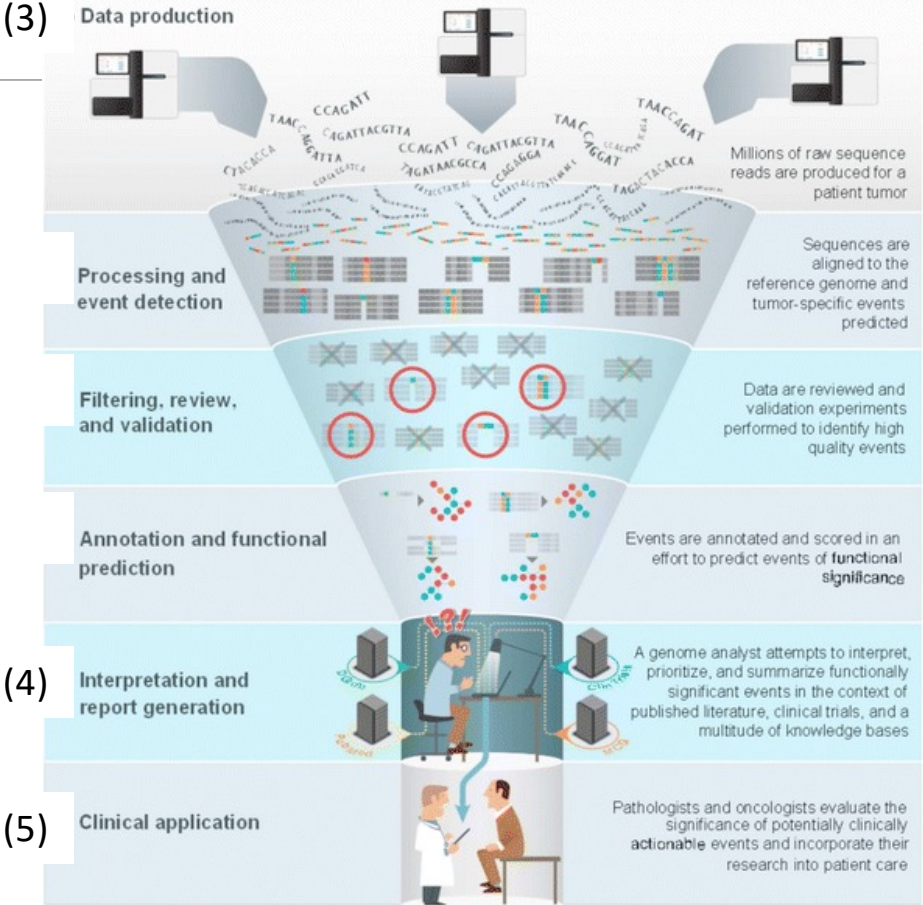
1. Background
2. Standards
3. Challenges
4. Summary

Standards

- (1) Sample selection
- (2) Technology selection

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- (6) Follow-up/Trial infrastructure

Standards

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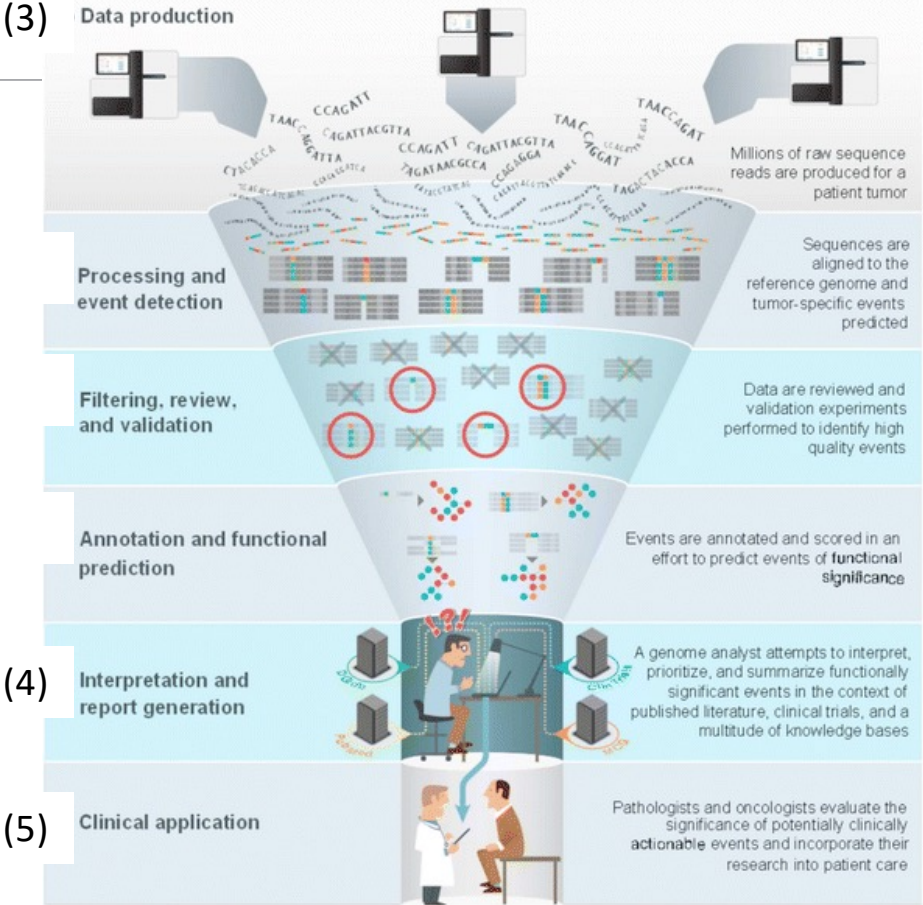
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Pat. *1975

Met. Colon Cancer 2020

Standards

- (1) Sample selection
- (2) Technology selection



(6) Follow-up/Trial infrastructure



Leistungen



zurück

**Präzisionsonkologische
Sprechstunde**

Für Patientinnen, Patienten
& Interessierte



Für Ärztinnen, Ärzte &
medizinisches Personal

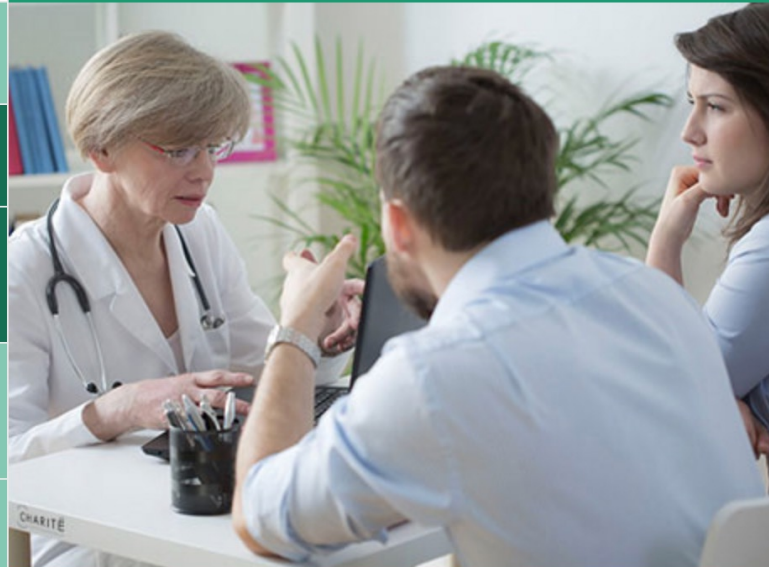


Für Wissenschaftlerinnen
& Wissenschaftler

Forschung



Karriere



Präzisionsonkologische Sprechstunde

Die präzisionsonkologische Sprechstunde am Charité Comprehensive Cancer Center bietet die Möglichkeit einer additiven Diagnostik für Patient:innen der Charité, für Betroffene aus externen Kliniken sowie onkologischen Praxen.

Durchsuchen Sie diese Website



[Startseite](#) > [Leistungen](#) > [Plattform für personalisierte Krebsmedizin der Charité \(PPK-C\)](#) >
[Präzisionsonkologische Sprechstunde](#)

Präzisionsonkologische Sprechstunde - Reevaluation und unabhängige Beratung bei soliden Tumoren

Standards

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Met. Colon Cancer 2021

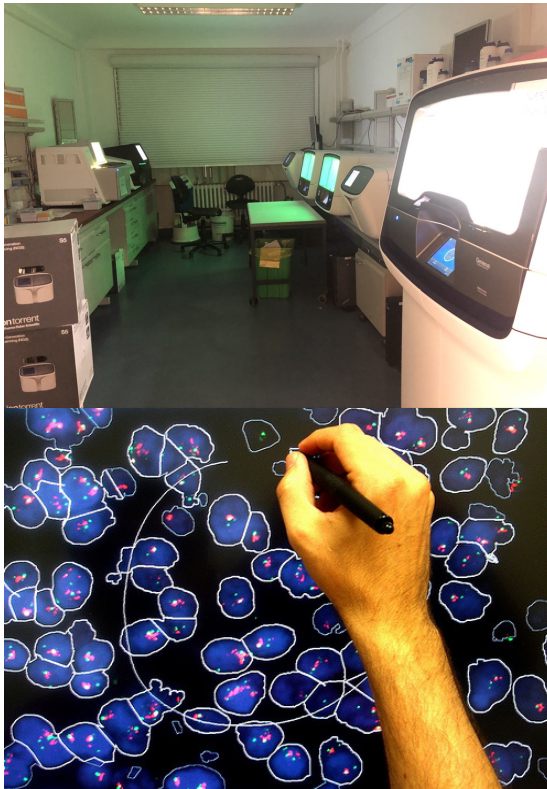
Molecular Pathology (KRAS-Test): KRAS/NRAS wt

Met. Spread: pulm, hep, local

01/2021	Diagnosis of met. CRC Resection
03/21-10/21	FOLFOX/Beva
11/21	pulmonary/hepatic metastases
12/21	14x FOLFIRI/Beva
06/22-09/22	Bevacizumab monotherapy
09/22	Surgery, local tumor progression

Standards

Portfolio Molecular Diagnostics Pathology, Charité



NGS (accredited/validated)

- Oncomine Focus/Precision DNA Assay
- Oncomine Focus/Precision RNA Assay
- ColonLung Panel V2
- Cancer Hotspot Panel
- Myeloid Panel (Custom)
- (B-cell) Lymphoma Panel
- Oncomine cfDNA (Liquid Biopsies)
- Breast cfDNA Panel (Liquid Biopsies)
- BRCA1/2 Panel
- Tumor Mutational Burden (1.7 Mbases)
- Molecular Health 600+ Panel (3 Mbases); NextSeq
- Oncomine Comprehensive Assay V4 (500+) Panel
- TSO500 (DNA/RNA) Panel
- Ig/TCR Clonality Panel
- Archer RNA Panel

IHC/FISH

- nTRK screening
- TMB
- Other Targets (e.g. HER2, AR...)
- Fusion Gene validation

Other

- e.g. EPIC (Methylom)

DKTK MASTER

- WES/WGS
- RNASeq

ExLiquid

- ctDNA

Functional Analyses

Standards

- (1) Sample selection
- (2) Technology selection

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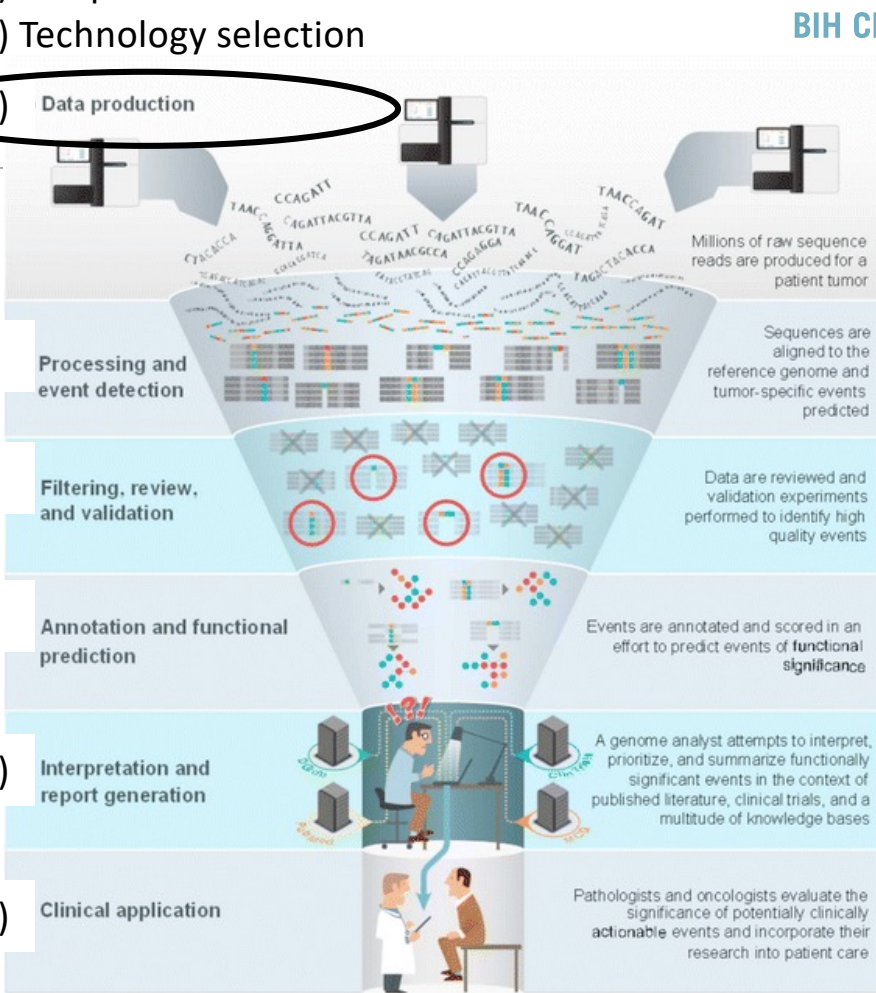
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	NGS (accredited/validated)	IHC/FISH
Pat. *1975	<ul style="list-style-type: none">• Molecular Health 600+ Panel (3 Mbases); NextSeq• Archer RNA Panel	<ul style="list-style-type: none">• HER2• MMR
Met. Colon Cancer 2021		
Molecular Pathology (KRAS-Test): KRAS/NRAS wt		
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Standards

- (1) Sample selection
- (2) Technology selection

(3) Data production



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(6) Follow-up/Trial infrastructure



Special Article

Standards for the classification of pathogenicity of somatic variants in cancer (oncogenicity): Joint recommendations of Clinical Genome Resource (ClinGen), Cancer Genomics Consortium (CGC), and Variant Interpretation for Cancer Consortium (VICC)

Peter Horak ¹  , Malachi Griffith ², Arpad M. Danos ², Beth A. Pitel ³, Subha Madhavan ⁴, Xuelu Liu ⁵, Cynthia Chow ⁶, Heather Williams ⁷, Leigh Carmody ⁸, Lisa Barrow-Laing ⁹, Damian Rieke ¹⁰, Simon Kreuzfeldt ¹, Albrecht Stenzinger ¹¹, David Tamborero ¹², Manuela Benary ¹⁰, Padma Sheila Rajagopal ¹³, Cristiane M. Ida ³, Harry Lesmana ¹⁴, Laveniya Satgunaseelan ¹⁵, Jason D. Merker ¹⁶ ...Dmitriy Sonkin ³⁵  

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Met. Colon Cancer ED 2020

Molecular Pathology (KRAS-Test): KRAS/NRAS wt

Met. Spread: pulm, local

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06/22-09/22	Bevacizumab monotherapy
09/22	Surgery, local tumor progression

Local Resection 09/2022

TMB 3.86 Mut/Mb

HER2 0

pMMR

PD-L1 CPS 15

NTRK negative

BRAF p.V600E (AF 14%)

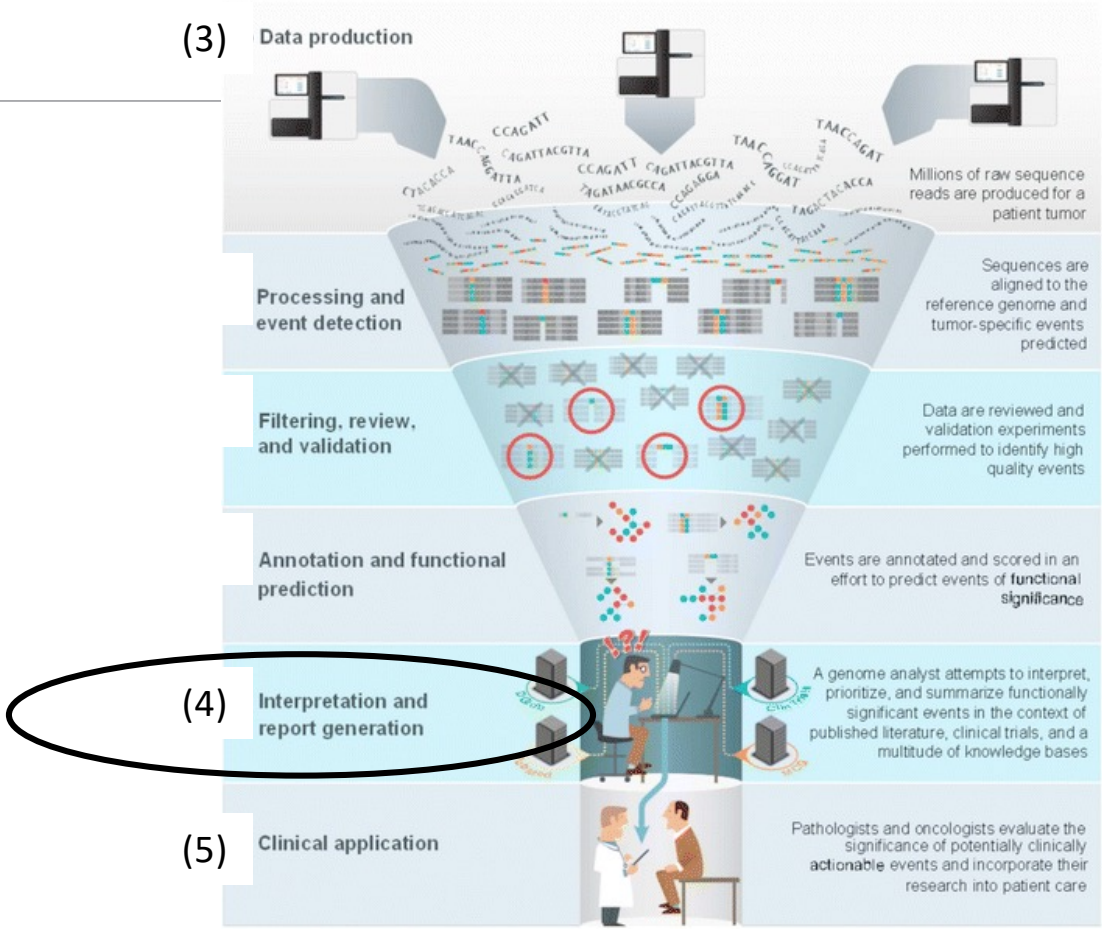
TP53 p.C182* (AF 39%)

Standards

- (1) Sample selection
- (2) Technology selection
- (3) Data production
- (4) Interpretation and report generation
- (5) Clinical application
- (6) Follow-up/Trial infrastructure

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Standards

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Met. Colon Cancer ED 2021

Molecular Pathology (KRAS-Test): KRAS/NRAS wt

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Local Resection 08/2022

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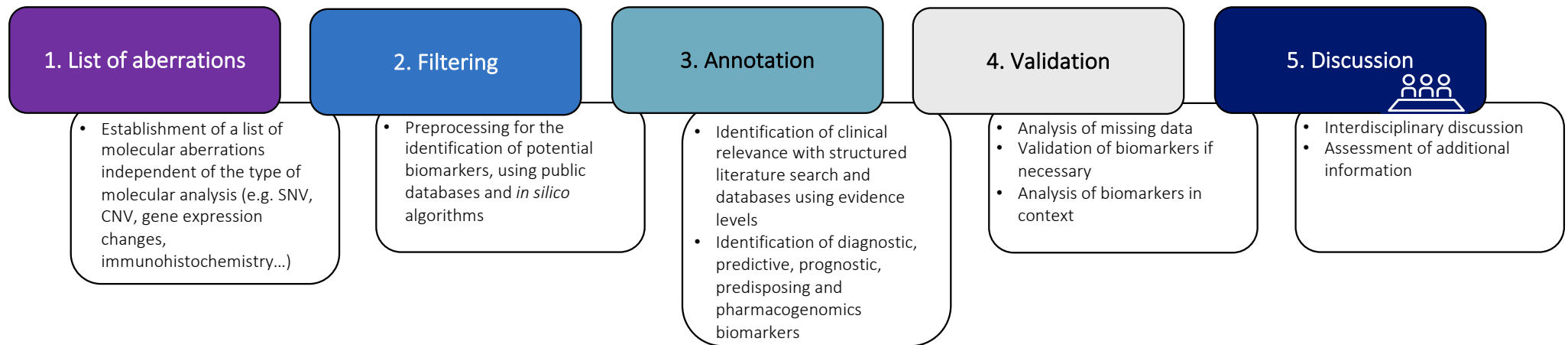
PD-L1 CPS 15

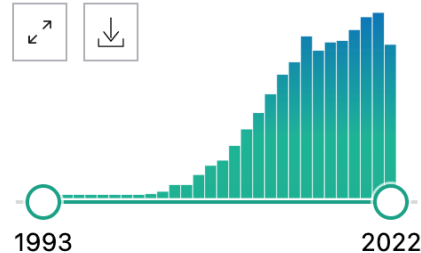
NTRK negative

BRAF p.V600E (AF 14%)

TP53 p.C182* (AF 39%)

Standards





Diagnosis and Treatment of Metastatic Colorectal Cancer: A Review.

1 Biller LH, Schrag D.

Cite JAMA. 2021 Feb 16;325(7):669-685. doi: 10.1001/jama.2021.0106.

PMID: 33591350 Review.

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IMPORTANCE: **Colorectal cancer** (CRC) is the third most common cause of **cancer** mortality worldwide with more than 1.85 million cases and 850 000 deaths annually. ...OBSERVATIONS:


Colorectal cancer is the third most common cause of **cancer** mo ...

Griffith et al., Nat Genet. 2017
 Krysiak et al., Nat Cancer. 2022
 Krysiak et al., Nucleic Acids Res. 2022

Standards

The screenshot shows the CIViC website interface. At the top left is the CIViC logo (Clinical Interpretation of Variants in Cancer). A search bar is located at the top center. Navigation links for Home, About CIViC, and Help are on the right. A user profile for Damian Rieke is visible in the top right corner. A left sidebar contains a 'KNOWLEDGEBASE' menu with categories like Assertions, Evidence, Genes, Variants, Variant Groups, Clinical Trials, Diseases, Drugs, Phenotypes, Sources, and Variant Types. Below this is a 'CURATION' section with Activity and Queues, and a 'COMMUNITY' section with Contributors and Organizations. At the bottom of the sidebar is a 'RESOURCES' section with Data Releases. The main content area features a large purple banner with the text 'Discover supported clinical interpretations of mutations related to cancer.' Below the banner is a 'Knowledgebase Statistics' section with a table of metrics and filters (Total, Weekly, Monthly, Yearly). The table includes: Total Assertions (55), Total Evidence (9,402), Total Genes (479), Total Variants (3,362), Total Contributors (333), Total Diseases (341), Total Drugs (498), Total Sources (3,287), Total Revisions (34,230), and Total Comments (61,999). Below the statistics are two sections: 'News & Events' featuring a news item about CIViC winning an award, and 'Live Curation Activity' showing recent user actions like submitting evidence items and adding comments.

Standards



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KNOWLEDGEBASE

- [Assertions](#)
- [Evidence](#)
- [Genes](#)
- [Variants](#)
- [Variant Groups](#)
- [Clinical Trials](#)
- [Diseases](#)
- [Drugs](#)
- [Phenotypes](#)
- [Sources](#)
- [Variant Types](#)

CURATION

- [Activity](#)
- [Queues](#)

COMMUNITY

- [Contributors](#)
- [Organizations](#)

RESOURCES

BRAF — Aliases: B-RAF1, BRAF1, B-raf, BRAF, BRAF-1

BRAF - AKAP9::BRAF — Gene: BRAF
Aliases: AKAP9-BRAF

BRAF - AGK::BRAF — Gene: BRAF
Aliases: AGK-BRAF

BRAF - TRIM24::BRAF — Gene: BRAF
Aliases: TRIM24-BRAF

BRAF - PPFIBP2::BRAF — Gene: BRAF
Aliases: PPFIBP2-BRAF

Sources

PubMed: Li et al., 2009, Oncol. Rep.

PubMed: Pakneshan et al., 2013, Pathology

PubMed: Yao et al., 2017, Nature

Aliases

B-RAF1 B-raf BRAF BRAF-1 BRAF1 NS7 RAFB1

Resources

[DGIdb](#) [ProteinPaint](#)

MyGeneInfo

[Overview](#) Summary Protein Domains (10) Pathways (144)

Entrez Symbol: BRAF (ID: 673) **UniProtKB ID:** P15056

Chromosome: 7 **Strand:** -1 **Start:** 140419125 **Stop:** 140624564

Aliases: B-RAF1, B-raf, BRAF1, NS7, RAFB1

Protein Domains: Diacylglycerol/phorbol-ester binding, Protein kinase C-like, phorbol ester/diacylglycerol-binding domain, Protein kinase domain, Protein kinase, ATP binding site, Protein kinase-like domain, Raf-like Ras-binding, Serine-threonine/tyrosine-protein kinase catalytic domain, Serine/threonine-protein kinase, active site, Serine/threonine/dual specificity protein kinase...

Pathways: EGFR1, Neurotransmitter Receptor Binding And Downstream Transmission In The Postsynaptic Cell, Transmission across Chemical Synapses, Neuronal System, IRS-mediated signalling, SOS-mediated signalling, Signaling by ERBB2, Signaling by ERBB4, SHC1 events in ERBB2 signaling, SHC1 events in ERBB4 signaling, Developmental Biology, Cytokine Signaling in I...

BRAF Variants 111 Total (50 displayed)

Filter: Order By: Show:


A598V A728V AGK::BRAF AKAP9::BRAF Amplification BRAF::CUL1 CUX1::BRAF Class 2 Mutations Class 3 Mutations D594 D594A

D594E D594G D594H D594K D594N D594V DEL 485-490 DELNV TAP E585K Exon 15 Mutation F247L F594L F595L

FAM131B::BRAF FAM73A::BRAF Fusion or Mutation G463E G463V G464V G465A G466A G466E G466V G468A G469 G469A

G469E G469R G469S G469V G496A G593D G596 G596C G596R G596V G606E I462S K439Q

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- Assertions
- Evidence
- Genes
- Variants
- Variant Groups
- Clinical Trials
- Diseases
- Drugs
- Phenotypes
- Sources
- Variant Types

CURATION

- Activity
- Queues

COMMUNITY

- Contributors
- Organizations

RESOURCES

- Data Releases

Aliases:

Variant Type:

HGVS:

Descriptions:

[Overview](#) [ClinVar](#) [gnomAD \(2.1.1\)](#) [EXAC \(0.3.1\)](#) [CADD](#) [EGL](#) [Effect S](#) ...

MyVariant.info ID: chr7:g.140453136A>T **ClinVar ID:**

dbSNP RSID: **COSMIC ID (v68):**

SNPEff Effect: missense_variant

SNPEff Impact: MODERATE

V600E Evidence 174 total, showing 60

EID	Disease	Drugs	DIT	DESC	EL	ET	ED	CS	VO	R
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	All	All	All	All	All	All
<input type="text" value="EID6178"/>	<input type="text" value="Melanoma"/>	<input type="text" value="Dabrafenib"/> <input type="text" value="Trametinib"/>	<input type="text"/>	<input type="text"/>	B	👁	👍	❤	...	5★
<input type="text" value="EID6938"/>	<input type="text" value="Melanoma"/>	<input type="text" value="Dabrafenib"/> <input type="text" value="Trametinib"/>	<input type="text"/>	<input type="text"/>	B	👁	👍	❤	...	5★
<input type="text" value="EID7612"/>	<input type="text" value="Colorectal Cancer"/>	<input type="text" value="Encorafenib"/> <input type="text" value="Binimetinib"/> <input type="text" value="Cetuximab"/>	<input type="text"/>	<input type="text"/>	B	👁	👍	❤	...	5★
<input type="text" value="EID816"/>	<input type="text" value="Colorectal Cancer"/>	<input type="text" value="Cetuximab"/> <input type="text" value="Panitumumab"/>	<input type="text"/>	<input type="text"/>	B	👁	👍	🚫	...	4★
<input type="text" value="EID1127"/>	<input type="text" value="Hairy Cell Leukemia"/>	N/A	N/A	<input type="text"/>	B	🔍	👍	+	...	4★
<input type="text" value="EID1405"/>	<input type="text" value="Colorectal Cancer"/>	<input type="text" value="Vemurafenib"/>	N/A	<input type="text"/>	B	👁	👍	❤	...	4★
<input type="text" value="EID1421"/>	<input type="text" value="Melanoma"/>	<input type="text" value="Vemurafenib"/> <input type="text" value="Cobimetinib"/>	<input type="text"/>	<input type="text"/>	B	👁	👍	❤	...	4★

V600E Assertions 4 total, showing 4

AID	Gene	Variant	Disease	Drugs	DIT	SUM	Count
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text" value="AID20"/>	<input type="text" value="BRAF"/>	<input type="text" value="V600E"/>	<input type="text" value="Colorectal Cancer"/>	N/A	N/A	<input type="text"/>	6
<input type="text" value="AID7"/>	<input type="text" value="BRAF"/>	<input type="text" value="V600E"/>	<input type="text" value="Melanoma"/>	<input type="text" value="Trametinib"/> <input type="text" value="Dabrafenib"/>	<input type="text"/>	<input type="text"/>	4
<input type="text" value="AID10"/>	<input type="text" value="BRAF"/>	<input type="text" value="V600E"/>	<input type="text" value="Melanoma"/>	<input type="text" value="Vemurafenib"/> <input type="text" value="Cobimetinib"/>	<input type="text"/>	<input type="text"/>	3
<input type="text" value="AID23"/>	<input type="text" value="BRAF"/>	<input type="text" value="V600E"/>	<input type="text" value="Colorectal Cancer"/>	<input type="text" value="Cetuximab"/> <input type="text" value="Encorafenib"/> <input type="text" value="Binimetinib"/>	<input type="text"/>	<input type="text"/>	1

Standards



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KNOWLEDGEBASE

- 🔍 Assertions
- ⊕ Evidence**
- 🧬 Genes
- 📄 Variants
- 📁 Variant Groups
- 🏥 Clinical Trials
- 📄 Diseases
- 💊 Drugs
- 👤 Phenotypes
- 📄 Sources
- 🔗 Variant Types

CURATION

- 📄 Activity
- 📄 Queues

COMMUNITY

- 👤 Contributors

Evidence / EID7612 / Summary

EID7612 Parents: 🔵 BRAF 🟢 V600E

⊕ EID7612

- [📄 Summary](#)
[💬 Comments](#)
[🔄 Revisions](#)
[🚩 Flags](#)
[📅 Events](#)

Curators: Editors:

Description

665 patients with BRAF V600E-mutated metastatic CRC were enrolled in this open-label, phase 3 trial. Patients were randomly assigned in a 1:1:1 ratio to receive encorafenib, binimetinib, and cetuximab (triplet-therapy group); encorafenib and cetuximab (doublet-therapy group); or the investigators' choice of either cetuximab and irinotecan or cetuximab and FOLFIRI. The median overall survival was 9.0 months in the triplet-therapy group and 5.4 months in the control group (hazard ratio for death, 0.52; 95% confidence interval [CI], 0.39 to 0.70; P<0.001). The confirmed response rate was 26% (95% CI, 18 to 35) in the triplet-therapy group and 2% (95% CI, 0 to 7) in the control group (triplet group vs. control P<0.001). The median progression-free survival in the triplet-therapy group was 4.3 months (95% CI, 4.1 to 5.2) and 1.5 months (95% CI, 1.5 to 1.7) in the control group (hazard ratio for disease progression or death, 0.38; 95% CI, 0.29 to 0.49; P<0.001).

Type	👁 Predictive	Direction	👍 Supports
Clinical Significance	♥ Sensitivity / Response	Variant Origin	⋮ Somatic
Level	B	Rating	★★★★★

Source	📄 PubMed: Kopetz et al., 2019, N. Engl. J. Med.
Clinical Trial	📄 NCT02928224

Status	Submitted (Oct 2, 2019)	Accepted (Nov 19, 2021)
✅ Accepted	by 👤 DamianRieke	by 👤 CamGrisdale
Gene	🔵 BRAF	
Variant	🟢 V600E	
Disease	📄 Colorectal Cancer	
Phenotype	None Specified	
Drugs	👤 Encorafenib 👤 Binimetinib 👤 Cetuximab	
Drug Interaction Type	Combination	

Standards

evidence assigning their level of [clinical actionability](#).

If you notice any mistakes or omissions, please reach out to us. ✉

Search ...

Level ▾	Alterations	Level-associated cancer types ⓘ	Drugs	Citations
1	V600	Erdheim-Chester Disease	Vemurafenib	2
1	V600	Melanoma	Vemurafenib + Cobimetinib + Atezolizumab	1
1	V600E	All Solid Tumors (excluding Colorectal Cancer)	Dabrafenib + Trametinib	7
1	V600E	Anaplastic Thyroid Cancer	Dabrafenib + Trametinib	1
1	V600E	Biliary Tract Cancer, NOS	Dabrafenib + Trametinib	7
1	V600E	Colorectal Cancer	Encorafenib + Cetuximab	1
1	V600E	Melanoma	Dabrafenib	3
1	V600E	Melanoma	Dabrafenib + Trametinib	10
1	V600E	Melanoma	Encorafenib + Binimetinib	1
1	V600E	Melanoma	Trametinib	4
1	V600E	Melanoma	Vemurafenib	3
1	V600E	Melanoma	Vemurafenib + Cobimetinib	3
1	V600E	Non-Small Cell Lung Cancer	Dabrafenib + Trametinib	2
1	V600K	Melanoma	Dabrafenib + Trametinib	10

Standards

https://ckb.jax.org/geneVariant/show?geneVariantId=49							
						V600E-positive metastatic melanoma, with estimated OS rates of 56%, 30%, 21%, and 17% at 1, 2, 3, and 4 years, respectively (PMID: 28961848, PMID: 21639808; NCT01006980), and BRAF V600E is included on the companion diagnostic (FDA.gov).	detail... 21639808
BRAF V600E	melanoma	sensitive	Dabrafenib + Trametinib	FDA approved - On Companion Diagnostic	Actionable	In a Phase III trial (COMBI-v) that supported FDA approval, the combination of Tafinlar (dabrafenib) and Mekinist (trametinib) resulted in an improved overall survival rate at 12 months (72% vs 65%, HR=0.69, p=0.005), median progression-free survival (11.4 vs 7.3 months, HR=0.56, p<0.001), and objective response rate (64% vs 51%, p<0.001) compared to Zelboraf (vemurafenib) in melanoma patients harboring BRAF V600E or V600K (PMID: 25399551; NCT01597908).	detail... detail... 25399551
BRAF V600E	colorectal cancer	sensitive	Cetuximab + Encorafenib	FDA approved - On Companion Diagnostic	Actionable	In a Phase III (BEACON CRC) trial that supported FDA approval, Braftovi (encorafenib) and Erbitux (cetuximab) combination treatment (n=113) resulted in improved median overall survival (8.4 vs 5.4 months, HR=0.60, p<0.001), confirmed response rate (20% vs 2%, p<0.001), and median progression-free survival (4.2 vs 1.5 months, HR=0.40, p<0.001) compared to control (n=107) in patients with metastatic colorectal cancer harboring BRAF V600E (PMID: 31566309; NCT02928224).	detail... 31566309

ZPM Standard, according to

<https://pct.mdanderson.org/pctService/resources/imageManager/image/loe>

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Gleiche Tumorentität	m1A	In der gleichen Tumorentität wurde der prädiktive Wert des Biomarkers oder die klinische Wirksamkeit in einer Biomarker-stratifizierten Kohorte einer adäquat gepowerten prospektiven Studie oder Metaanalyse gezeigt.
	m1B	In der gleichen Tumorentität wurde der prädiktive Wert des Biomarkers oder die klinische Wirksamkeit in einer retrospektiven Kohorte oder Fall-Kontroll-Studie gezeigt.
	m1C	Ein oder mehrere Fallberichte in der gleichen Tumorentität .
Andere Tumorentität	m2A	In einer anderen Tumorentität wurde der prädiktive Wert des Biomarkers oder die klinische Wirksamkeit in einer Biomarker-stratifizierten Kohorte einer adäquat gepowerten prospektiven Studie oder Metaanalyse gezeigt.
	m2B	In einer anderen Tumorentität wurde der prädiktive Wert des Biomarkers oder die klinische Wirksamkeit in einer retrospektiven Kohorte oder Fall-Kontroll-Studie gezeigt.
	m2C	Unabhängig von der Tumorentität wurde beim Vorliegen des Biomarkers eine klinische Wirksamkeit in einem oder mehreren Fallberichten gezeigt.
In vitro oder Tiermodell	m3	Präklinische Daten (<i>in vitro</i> -/in vivo-Modelle, funktionelle Untersuchungen) zeigen eine Assoziation des Biomarkers mit der Wirksamkeit der Medikation, welche durch eine wissenschaftliche Rationale gestützt wird.
Biologische Rationale	m4	Eine wissenschaftliche, biologische Rationale legt eine Assoziation des Biomarkers mit der Wirksamkeit der Medikation nahe, welche bisher nicht durch (prä)klinische Daten gestützt wird.

Verlauf: 01/2021 Multiviszzerale Resektion 03/21-10/21 Chemotherapie mit Oxaliplatin, Capecitabin, Bevacizumab 11/21 pulmonale/hepatische Metastasierung 12/21 14x Irinotecan, 5-FU, Bevacizumab 06/22 Bevacizumab-Monotherapie 09/22 Stenose, Reoperation

Ausbreitung: pulmonal, lokal

Sampling: 09/22 lokal

IHC/MoIPath: TMB 3.86 Mut/Mb. HER2 0. PD-L1 IC 20%, CPS 20. pMMR.

	Aberration evidence	Drug/s	Mechanism	EvL	PMIDs/NCT	VAF	Histology
BRAF p.V600E	p.V600E	Cetuximab/Encorafenib Irinotecan/Cetuximab/Vemurafenib	BRAF	M1a M1a	31566309 (1), 33503393 33356422 AIO FIRE-10 (aktuell noch nicht rekrutierend)	21%	CRC CRC
TP53 p.C180*						43%	

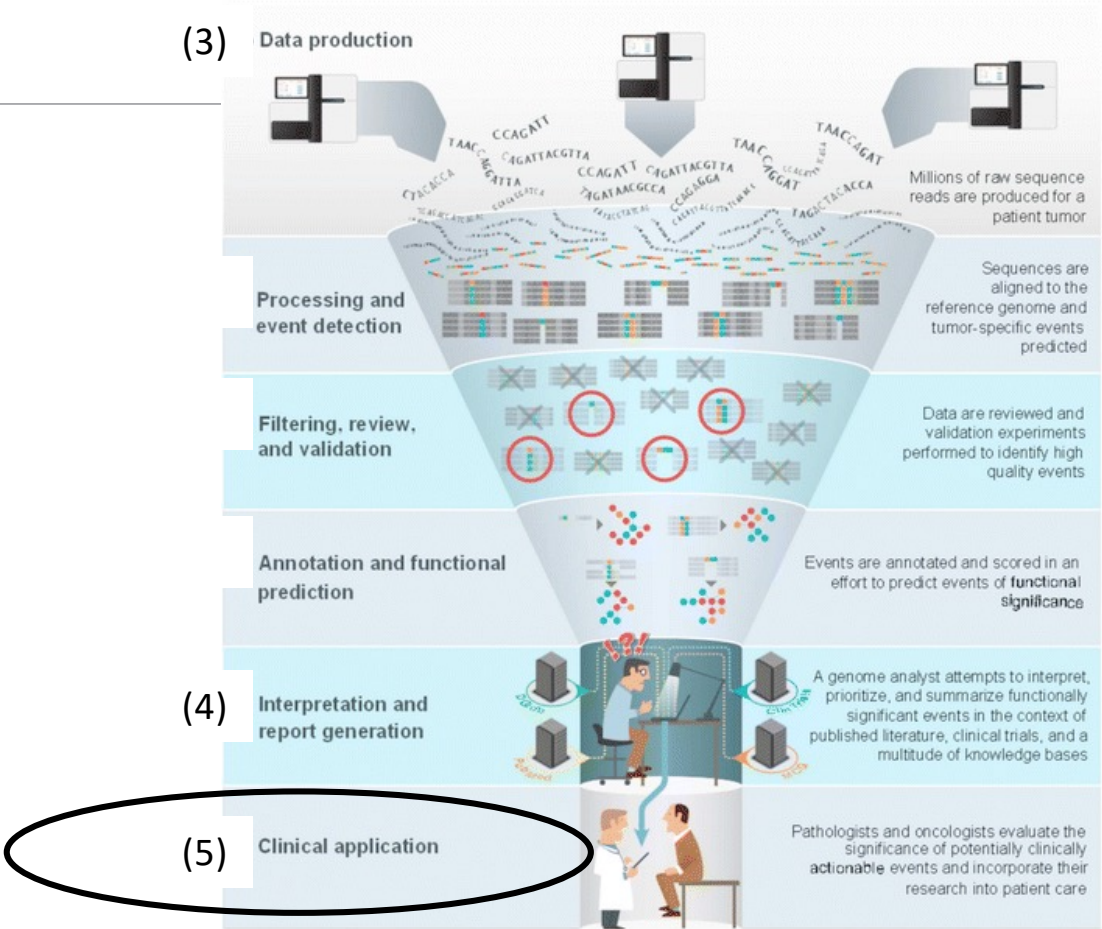
- (1) BEACON trial. 665 Patienten nach mind. 1 vorherigen Therapielinie. Encorafenib/Cetuximab/Binimetinib mit 26% ORR, OS 9 Monate. Cetuximab/Encorafenib mit OS 8.4 Monaten. Retrospektive Analyse mit äquivalentem Ergebnis Duplette
- (2) SWOG trial. 106 patients pretreated BRAF CRC. Irinotecan/Cetuximab/Vemurafenib ORR 17% vs. 4% Irinotecan/Cetuximab.

Standards

- (1) Sample selection
- (2) Technology selection
- (3) Data production
- (4) Interpretation and report generation
- (5) Clinical application
- (6) Follow-up/Trial infrastructure

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Leistungen



zurück

**Molekulare
Tumorkonferenz**

Für Patientinnen, Patienten
& Interessierte



Für Ärztinnen, Ärzte &
medizinisches Personal



Für Wissenschaftlerinnen
& Wissenschaftler

Forschung



Karriere



Molekulare Tumorkonferenz: Präzisionsonkologie in der klinischen Routine

In der molekularen Tumorkonferenz werden gemeinsam mit Forschern Gensequenzierungen in die Therapieentscheidung mit einbezogen.

Im Charité Comprehensive Cancer Center finden regelmäßig wöchentlich molekulare Tumorkonferenzen statt.

Durchsuchen Sie diese Website



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Molekulare Tumorkonferenz: Präzisionsonkologie in der klinischen Routine

Verlauf: 01/2021 Multiviszzerale Resektion 03/21-10/21 Chemotherapie mit Oxaliplatin, Capecitabin, Bevacizumab 11/21 pulmonale/hepatische Metastasierung 12/21 14x Irinotecan, 5-FU, Bevacizumab 06/22 Bevacizumab-Monotherapie 09/22 Stenose, Reoperation

Ausbreitung: pulmonal, lokal

Sampling: 09/22 lokal

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	Aberration evidence	Drug/s	Mechanism	EvL	PMIDs/NCT	VAF	Histology
BRAF p.V600E	p.V600E	Cetuximab/Encorafenib Irinotecan/Cetuximab/Vemurafenib	BRAF	M1a M1a	31566309 (1), 33503393 33356422 AIO FIRE-10 (aktuell noch nicht rekrutierend)	21%	CRC CRC
TP53 p.C180*						43%	

- (1) BEACON trial. 665 Patienten nach mind. 1 vorherigen Therapielinie. Encorafenib/Cetuximab/Binimetinib mit 26% ORR, OS 9 Monate. Cetuximab/Encorafenib mit OS 8.4 Monaten. Retrospektive Analyse mit äquivalentem Ergebnis Duplette
- (2) SWOG trial. 106 patients pretreated BRAF CRC. Irinotecan/Cetuximab/Vemurafenib ORR 17% vs. 4% Irinotecan/Cetuximab.

Molekulare Tumorkonferenz:

Zusammenfassend besteht eine molekulare Rationale für

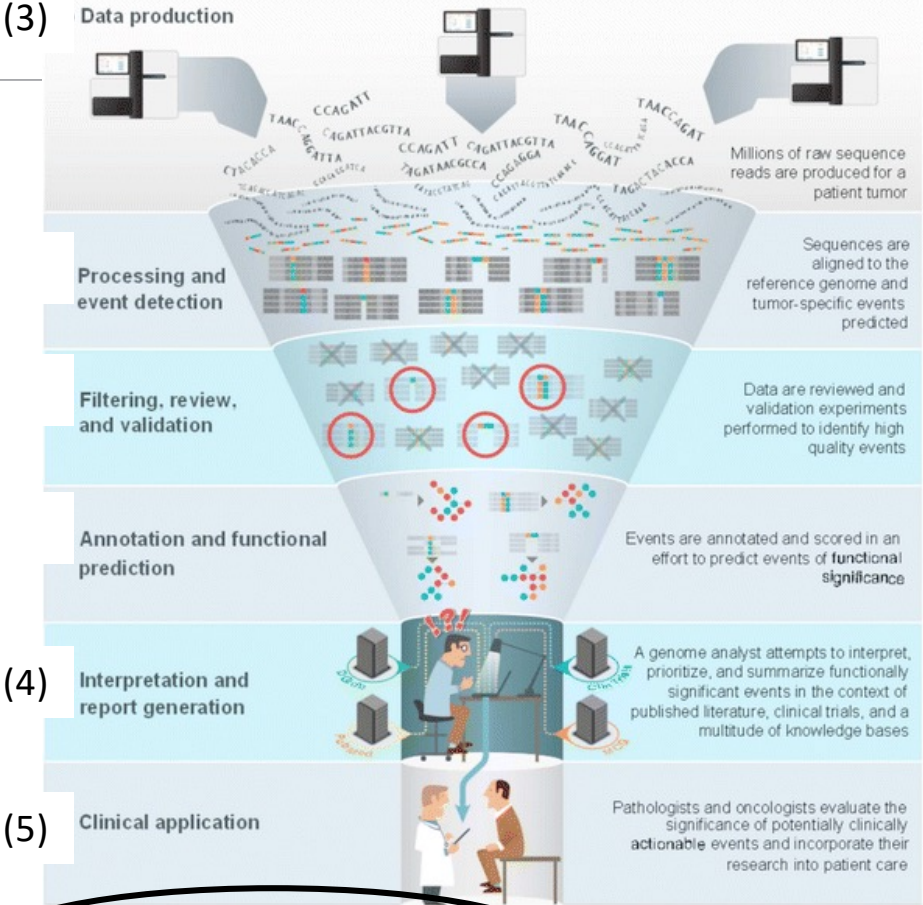
Priorität 1: Cetuximab/Encorafenib (m1a, zugelassen). Studienoption ggf. AIO FIRE-10 (aktuell noch nicht rekrutierend)

Standards

- (1) Sample selection
- (2) Technology selection

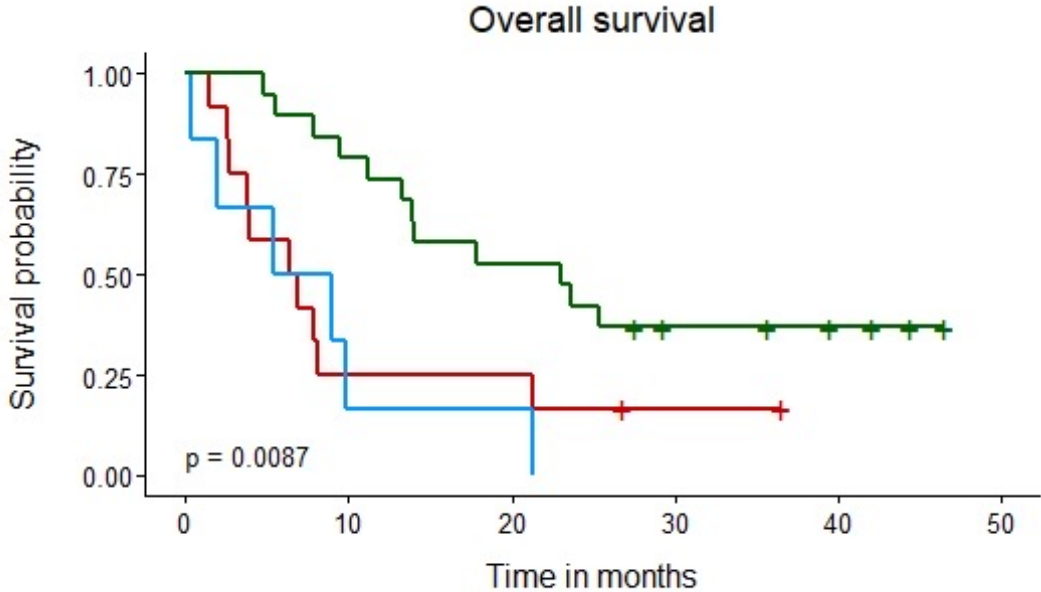
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(6) Follow-up/Trial infrastructure

Standards



Number at risk

	0	10	20	30	40	50
Doctor's choice	12	3	3	1	0	0
Differing MTB therapy	6	1	1	0	0	0
Matched MTB therapy	19	15	10	5	3	0

CONTENT

1. Background
2. Standards
3. Challenges
4. Summary

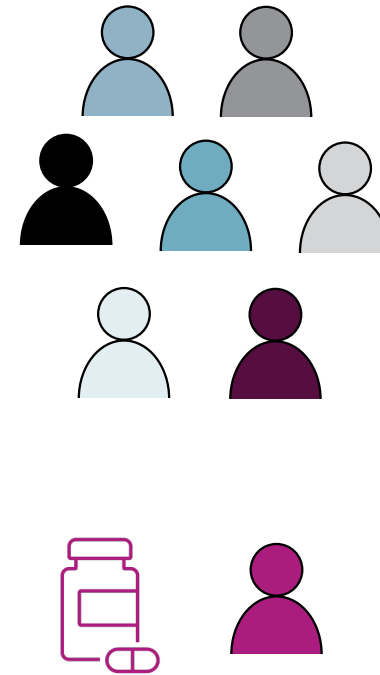
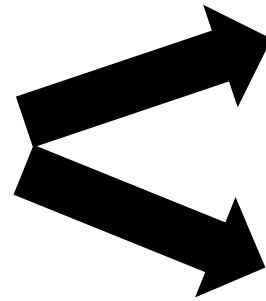
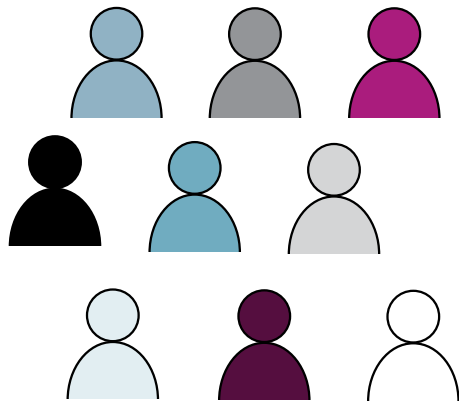
Challenges

Publication [citation]	Matched treatment ⁸	Off-label	Treated in trials	ORR ⁹	SD ⁹	PFS/TTF ⁹	OS ⁹	Other data
Zehir et al. 2017 [2]	24% (n=537)	n.r.	11% (n=527)	n.r.	n.r.	n.r.	n.r.	
Tsimberidou et al. 2014 [3]	27% (n=143)	none	100% (n=379)	12% vs. 5%	16% vs. 12%	3.9 m vs. 2.2 m	11.4 m vs. 8.6 m	
Massard et al. 2017 [4]	48% (n=199)	25% (n=50)	75% (n=149)	11%	52%	2.3 m	11.9 m	PFS2/PFS1 ≥1.3 : 33%
Burkard et al. 2017 [5]	28% (n=9)	89% (n=8)	11% (n=1)	17%	n.r.	n.r.	n.r.	
Le Tourneau et al. 2015 [6]	34% (n=99)	none	100% (n=195)	4% vs. 3%	n.r.	2.3 m vs. 2.0 m	n.r.	
Sicklick et al. 2019 [7]	49% (n=73)	none	100% (n=73)	23%	5%	3.67 m	11.8 m	PFS2/PFS1 ≥1.3: 75% vs. 36.6% in low matching score group
Rodon et al. 2019 [8]	42% (n=107)	none	100% (n=107)	11.2%	15%	2.01 m	5.9 m	PFS2/PFS >1.5: 22.4%
Tsimberidou et al. 2012 [19]	46% (n=211)	none	100% (n=352)	25% vs. 4%	23% vs. 10%	4.4 m vs. 2.3 m	11.4 m vs. 10.2 m	
Jameson et al. 2014 [20]	89% (n=29)	none	100% (n=25)	20%	32%	n.r.	7.8 m	PFS2/PFS1 ≥1.3 : 44%
Wiesweg et al. 2013 [21]	45% (n=62)	69% (n=43)	31% (n=19)	n.r.	n.r.	n.r.	n.r.	
Jones et al. 2015 [22]	n.r.	n.r.	n.r.	n.r.	n.r.	n.r.	n.r.	
Dalton et al. 2017 [23]	21% (n=28)	46% (n=11)	54% (n=13)	n.r.	n.r.	5.0 m	n.r.	
Sohal et al. 2015 [24]	22% (n=24)	38% (n=9)	50% (n=12)	n.r.	n.r.	n.r.	n.r.	
Johnson et al. 2014 [25]	21% (n=18)	39% (n=7)	61% (n=7)	22%	28%	n.r.	n.r.	
Radovich et al. 2016 [26]	100% (n=44)	none	100% (n=101)	n.r.	n.r.	2.8 m vs. 1.6 m	n.r.	PFS2/PFS1 ≥1.3 : 43.2% vs. 5.3%
Stockley et al. 2016 [27]	n.a.	none	100% (n=245)	19% vs. 9%	n.r.	n.r.	16 m vs. 13 m	any tumor shrinkage: 62% vs. 32%
Schwaederle et al. 2016 [28]	48% (n=87)	n.r.	n.r.	n.r.	n.r.	4.0 m vs. 3.0 m	12.7 m vs. 12.4 m	PFS2/PFS1 ≥1.3 : 45.3% vs. 19.3%
Von Hoff et al. 2010 [29]	79% (n=66)	n.r.	n.r.	10%	n.r.	n.r.	5 m	PFS2/PFS1 ≥1.3 : 27%
Tredan et al. 2017 [30]	11% (n=101)	n.r.	n.r.	17%	34%	2.8 m	n.r.	
Cobain et al. 2017 [31]	n.a.	n.r.	n.r.	n.r.	n.r.	n.r.	n.r.	
Hoefflin et al. 2018 [32]	32% (n=33)	67% (n=22)	6% (n=2)	33%	24%	n.r.	not reached	PFS2/PFS1 ≥1.3 (off label): 57.1%
Basse et al. 2018 [33]	10% (n=45)	n.a.	100% (n=45)	11%	n.a.	n.a.	n.a.	
median	34%	46%	100%	17%¹⁰	24%¹⁰	3.2 m¹⁰	11.4 m¹⁰	

Challenges

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Sohal et al. 2015 [24]	22% (n=24)	38% (n=9)	50% (n=12)	n.r.	n.r.	n.r.	n.r.	
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median	34%	46%	100%	17% ¹⁰	24% ¹⁰	3.2 m ¹⁰	11.4 m ¹⁰	

Challenges







Challenges

Table 1. Sample Patients as Provided to the Molecular Tumor Boards

Patient	Clinical Information	Additional Information	Sequencing	Fusion Genes	Copy No.	Gene Expression
1. 56-year-old patient	Initial diagnosis October 2014: TTF1-positive lung adenocarcinoma T3N3M0 (UICC IIIB) with negative <i>ALK</i> / <i>ROS</i> translocation and negative <i>EGFR</i> mutation status. Definite chemoradiotherapy. Widespread metastases to the peritoneum diagnosed in Nov 2015. Progressive after platinum-based chemotherapy and PD-1 inhibition (nivolumab). ECOG 1.	Tumor specimen from diagnostic mediastinoscopy Oct 2014: 25% tumor content, 580× mean sequencing depth.	Panel sequencing: <i>KRAS</i> G13D, <i>TP53</i> A276G, <i>PTPRS</i> R238*, <i>ZFHX3</i> F2994L, <i>CDH1</i> D433N	N/A	N/A	N/A

Challenges

Table 3. Treatment Recommendations as Provided by the Respective Molecular Tumor Boards for Patient 1

Tumor Board	Recommendation	Provided Rationale	Additional Recommendation
1	Pan-Raf inhibitor 	Downstream effect <i>KRAS</i> mutation	
2	No targeted therapy		<i>MET</i> and <i>RET</i> testing
3	Clinical trial for <i>KRAS</i> mutation	<i>KRAS</i> mutation	 Genetic counseling for <i>CDH1</i> and <i>TP53</i> mutations (potential germline mutation)
4	Sorafenib clinical trial 	<i>KRAS</i> mutation	
5	Docetaxel and selumetinib	<i>KRAS</i> mutation (data from phase II clinical trial)	 Genetic counseling (<i>CDH1</i> mutation; potential germline mutation)
6	N/A because of missing information		

NOTE. Rationales were provided for only some of the recommendations and asked for if missing initially. Abbreviations: N/A, not available; RET, Ret proto-oncogene.

Challenges

Table 3. Treatment Recommendations as Provided

Tumor Board	Recommendation
1	
2	
3	
4	
5	L
6	N/ info

NOTE. Ration:
Abbreviations: N

For Immediate Release: May 28, 2021

... some of the recommendations and asked for if missing initially.
... RET, Ret proto-oncogene.

FDA Approves First Targeted Therapy for Lung Cancer Mutation Previously Considered Resistant to Drug Therapy

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... being (*CDH1* mutation;
... potential germline mutation)

Challenges

Leistungen



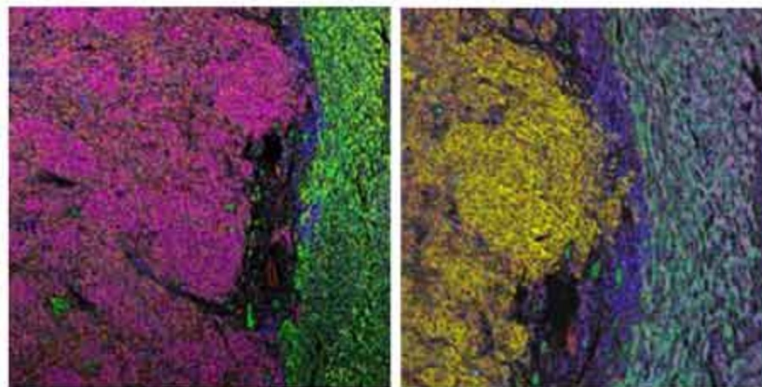
Plattform für
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Krebsmedizin der Charité
(PPK-C)



Molekulare
Tumorkonferenz

Präzisionsonkologische
Sprechstunde

AG klinische und
translationale
Präzisionsonkologie |
Research group - Clinical
and translational precision
oncology



Fotos: Prof. Klauschen
Treatzoplus program, using HYPERION technology,
Yaspo Lab at Max Planck Institute for Molecular Genetics, Berlin

Plattform für personalisierte Krebsmedizin der Charité (PPK)

Krebs ist eine Erkrankung des Erbguts und seiner Signalwege. Dabei gilt: So einzigartig wie jeder:e Patient:in ist, ist auch dessen Krebserkrankung. In der Präzisionsonkologie tragen wir diesem Umstand bestmöglich Rechnung.

Durchsuchen Sie diese Website



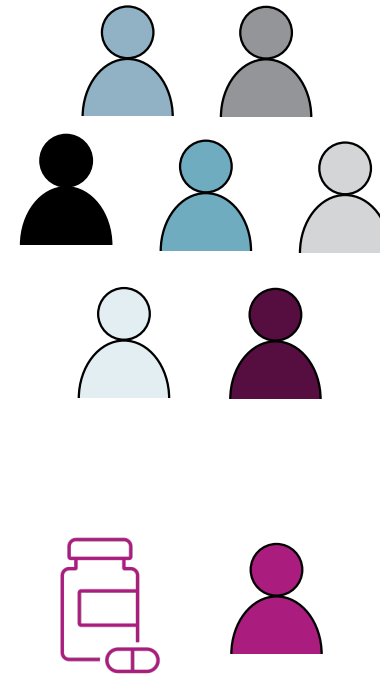
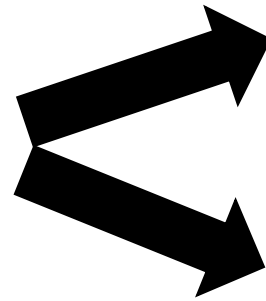
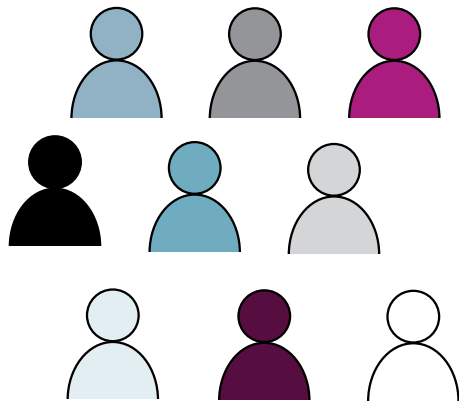
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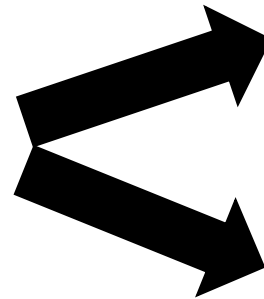
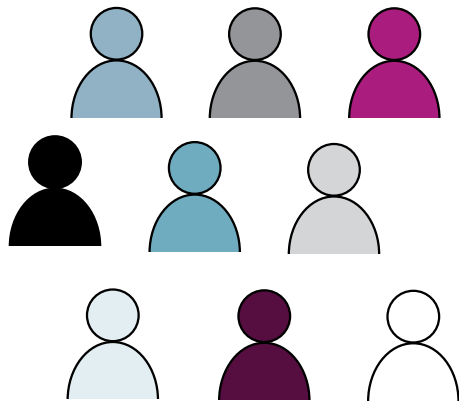
Präzisionsonkologie am Charité Comprehensive Cancer Center

Für Patientinnen, Patienten

Challenges



Challenges



Structured PO workflow
New Drugs
New Combinations
Better Understanding of Tumor Biology
Spatial/Temporal Heterogeneity



CONTENT

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2. Standards
3. Challenges
4. **Summary**

- **Multi-Step Process**
- **Integration of novel analyses, treatments, combinations**
- **Integration of complex data and multiple data layers**
- **Clinico-genomic database for research use**

Comprehensive Cancer Center

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Stefanos Bamopoulos
Manuela Benary
Elisabeth Vinis
Anna Klostermann
Yvette Jegodka
Mario Lamping
Till de Bortoli
Ivan Jelas
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THANK YOU!

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Deutsches Konsortium für translationale Krebsforschung

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