| SPHN-PHRT Symposium | Zurich | 28.08.25 |

SPO-NDS: Fueling Precision Oncology in Switzerland

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Strategic Focus Area
Personalized Health and Related Technologies

SPHN Swiss Personalized Health Network

Swiss Personalized Oncology

Introduction: precision oncology, a new paradigm

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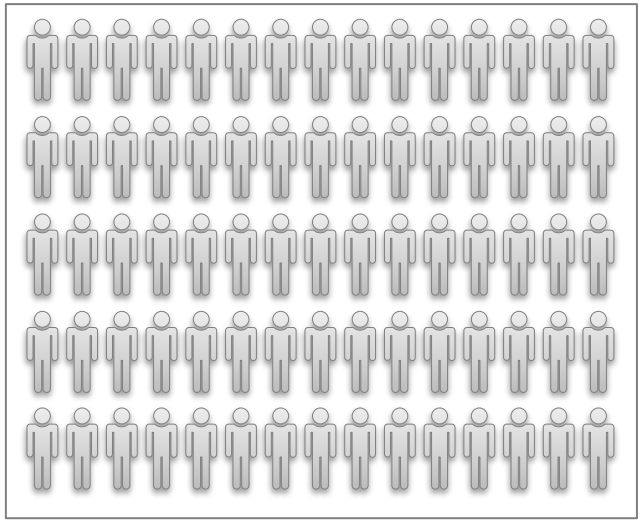
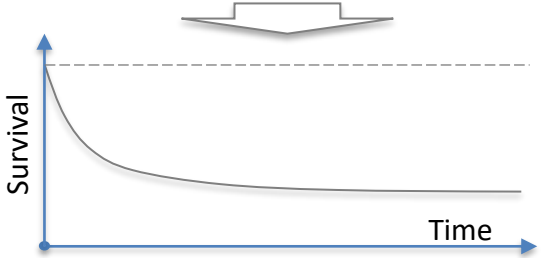
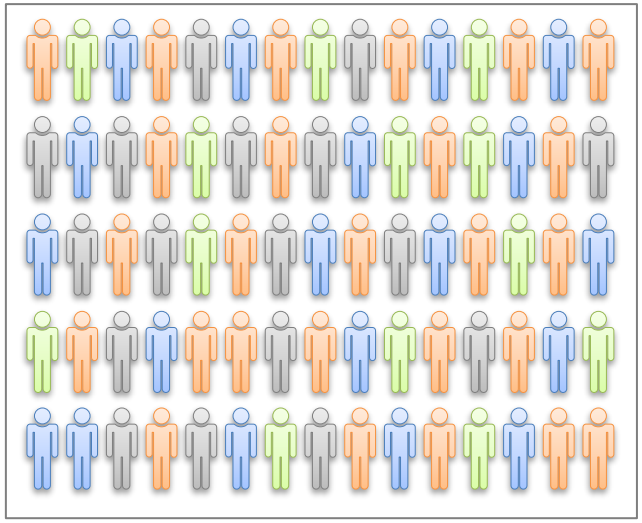
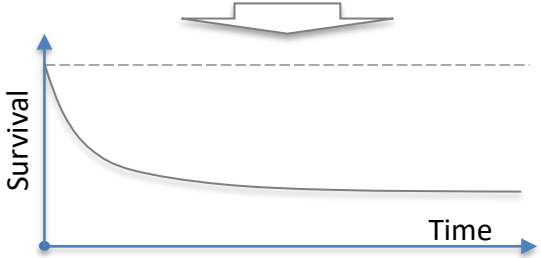
Personalization





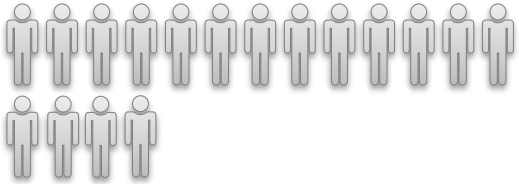
Personalization



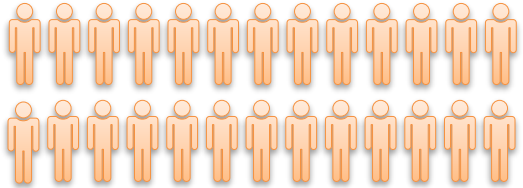


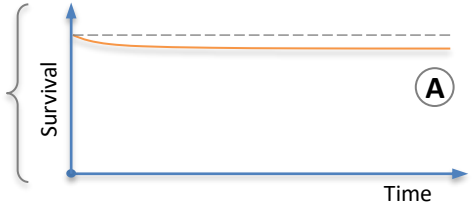
Personalization

No treatment!

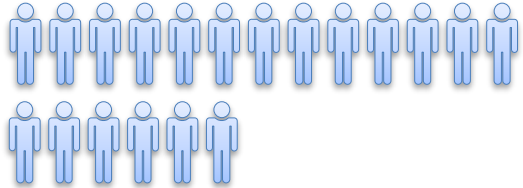


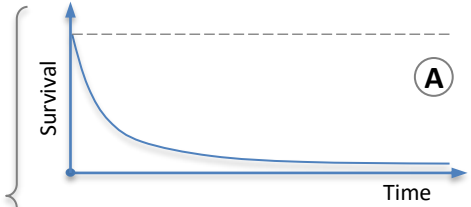
Treatment A



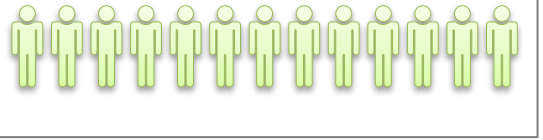


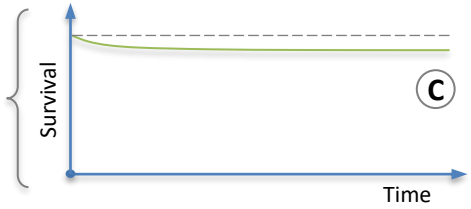
Treatment B



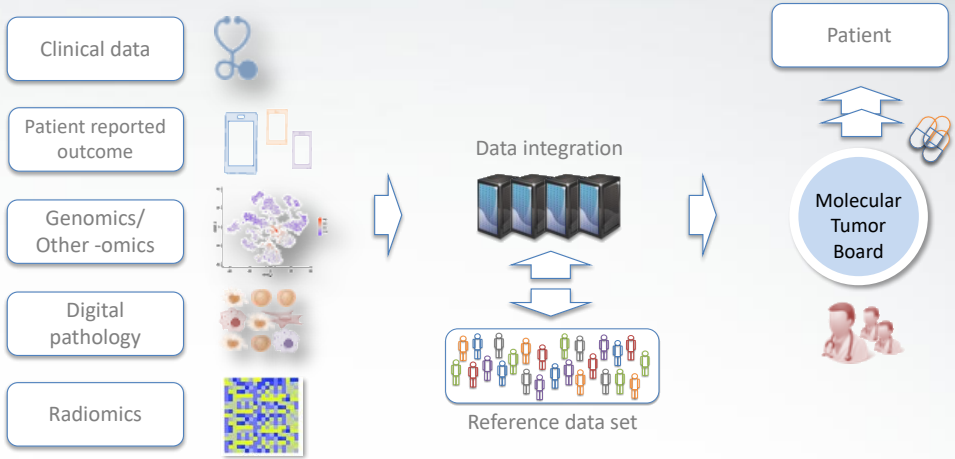


Treatment C





Key data streams in precision oncology



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Personalized Health and Related Technologies

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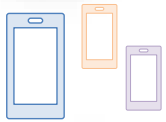
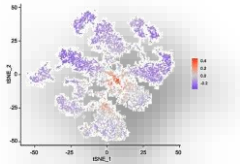
Precision oncology: integrating multiple data streams

Clinical data

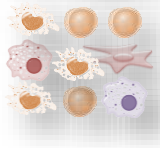
Patient reported outcome



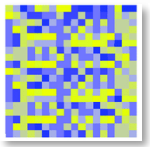
Multi -omics, Spatial -omics



Digital pathology



Radiomics



Interoperable Data integration

Reference data set

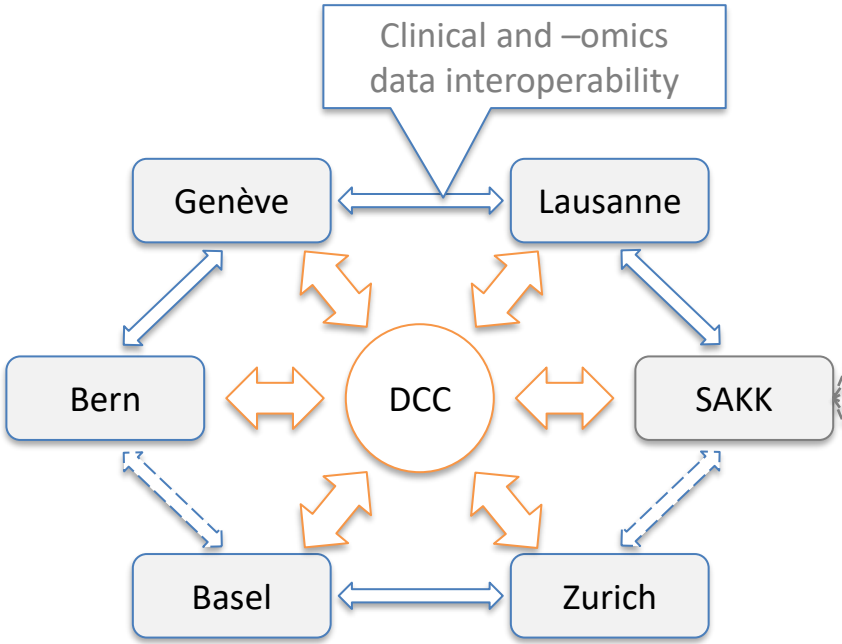
SPO Driver 2018-2021

Patient

Molecular Tumor Board

SPO NDS 2022-2025

The Swiss Personalized Oncology (SPO) network



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EPFL

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and Related Technologies

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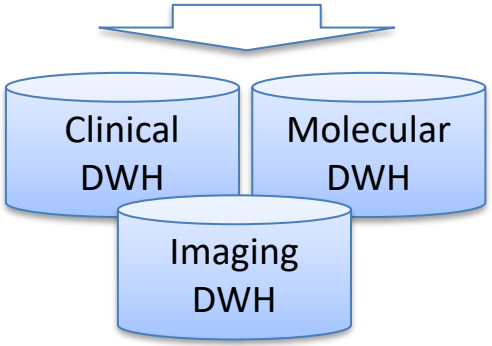
Swiss Personalized Oncology

Data strategy for SPHN SPO-Driver and SPO-NDS

Electronic Patient Reccord



#	Group	Data Category	Required Single Data Point
1	DEMOGRAPHIC	Demographic	Year of birth
2			Gender
3	1st DIAGNOSIS	Classification	First date of diagnosis (Biopsy or Main Tumor)
4			CIM 10
5			ICD-O3 / Morphology
6			ICD-O3 / Topography
7			Free text diagnosis
8		Staging	TNM classification
9			TNM Version
10			Stage
11			Staging system
12			Grade
13			Grading system
14	TREATMENT	Therapy	Type of treatment
15			Date of treatment
16			Treatment specification
17	RESPONSE	Outcome	Method of assessment
18			Date of assessment
19			Results from the assessment (RECIST 1.1)
20			Updated stage
21			Staging system
22	SURVIVAL	PFS	Follow-up event
23			Date of follow-up event
24		OS	Date of event
25			Event type

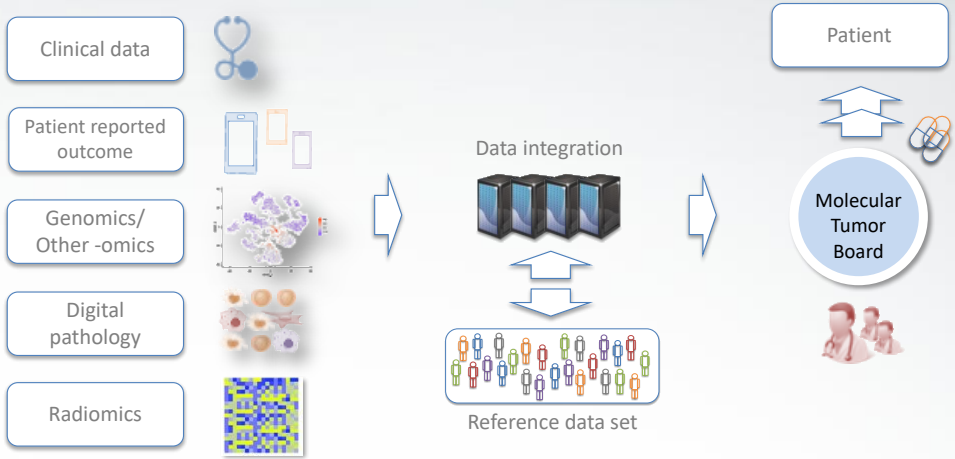
Swiss Personalized Health Network

Local infrastructure @ Hospital X: heterogeneous

Standardised dataset @ Hospital X: fully interoperable

Centralisation & mutualisation: SPHN

SPO Driver: exploiting clinical data



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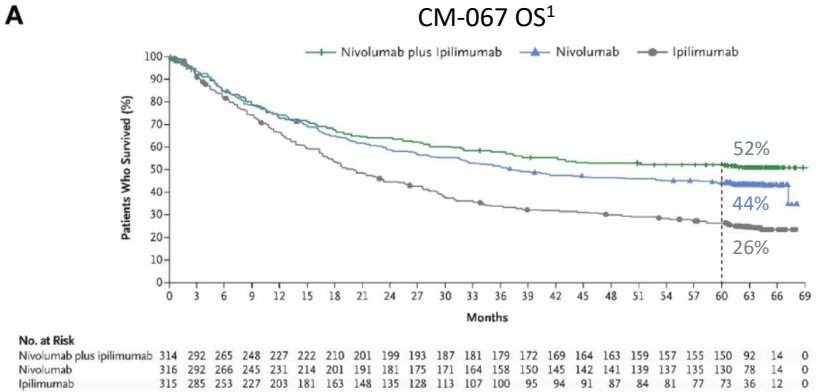
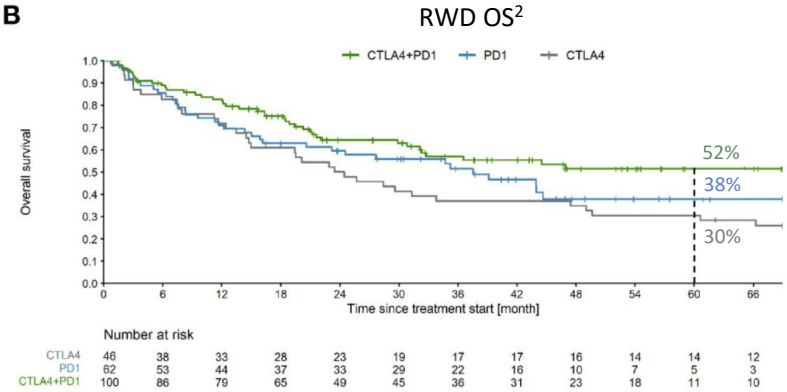
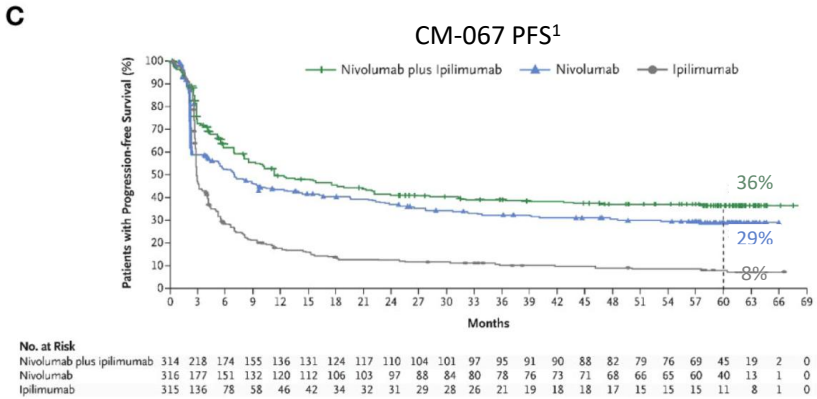
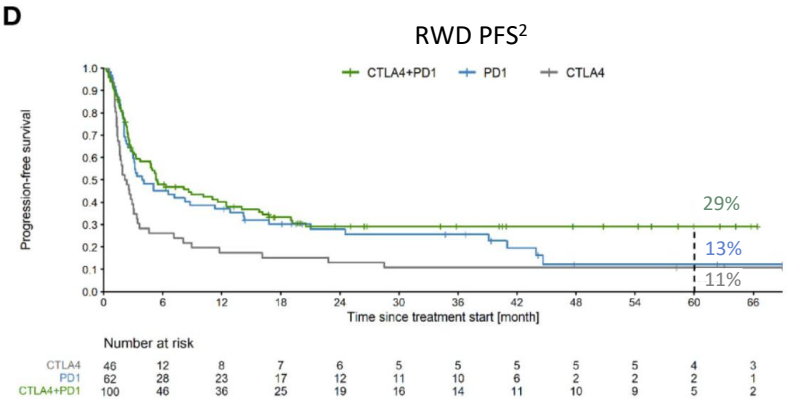
Clinical data: real-world data vs Checkmate-067 – 1st line









[1]Larkin, NEJM 2019;
[2]Wicky, *Frontiers* 2023

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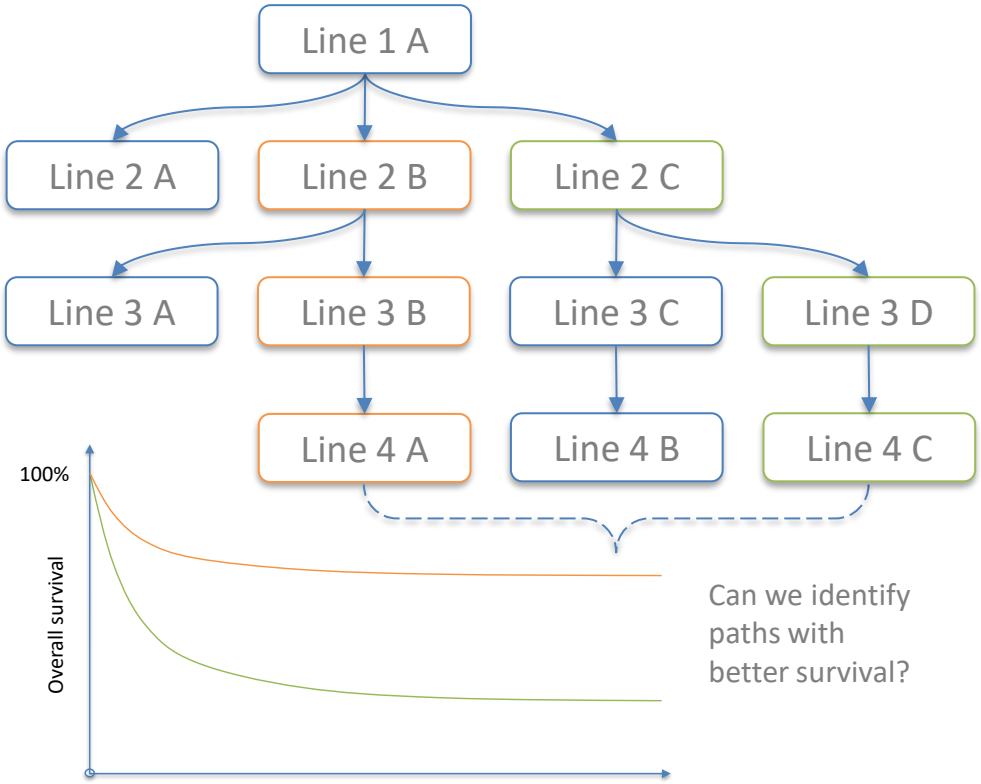
Swiss Personalized Oncology

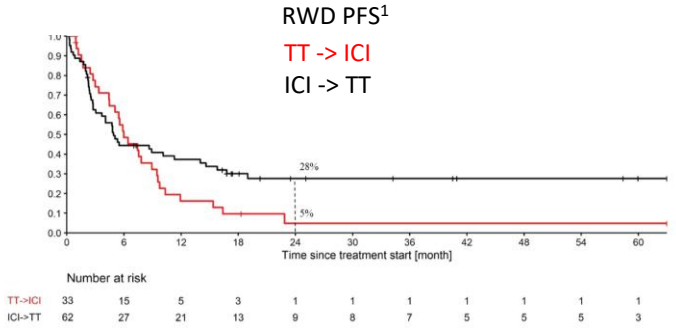
Analyzing sequence of events: Process mining

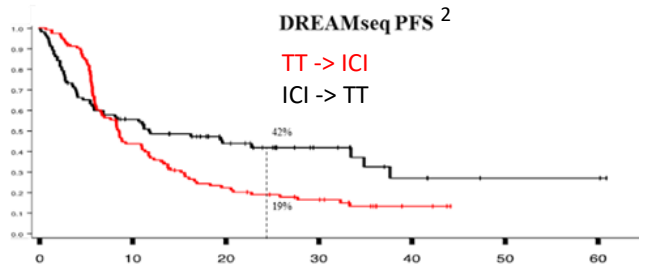
- Clinical data -> sequence of events:
  - Treatments
  - Evaluation Scanners
  - …
- SPO can capture all these events as data extraction originates from the hospital data warehouses (DWH)

- Process mining approaches can be used to detect preferred therapeutic pathways as well as outliers
- Important information can be projected onto these pathways, including PFS or OS



Melanoma real-world data analysis using process mining[1]





[1]Wicky, *Frontiers* 2023

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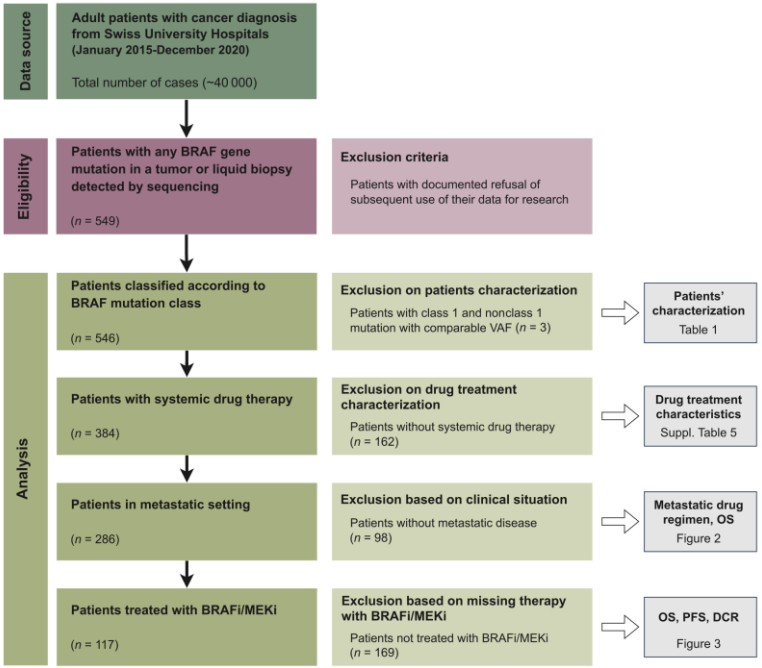
SPO: Example of nation-wide data extraction – BRAF mutations

- The first nation-wide studies are now being conducted[1]



ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

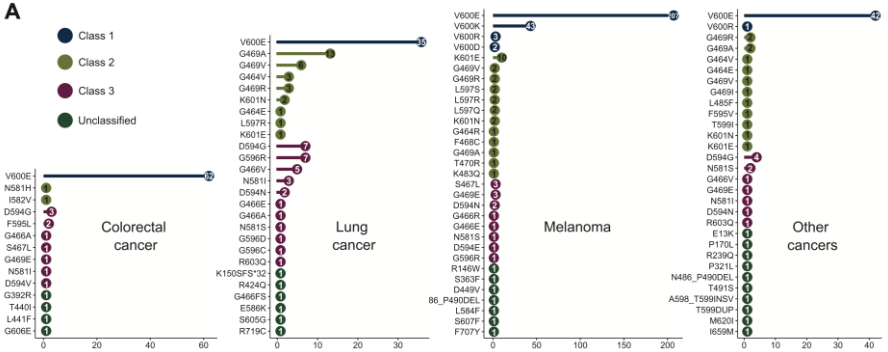
ESMO REAL WORLD DATA AND DIGITAL ONCOLOGY

ORIGINAL ARTICLE

Real-world occurrence, therapy, and outcome of patients with class 2 or 3 BRAF compared with class 1 BRAF-mutated cancers

S. Pradervand[1], N. Freundler[1], B. Gosztonyi[2], L. Roncoroni[2], R. Achermann[3], T. Schwenk[4], G. de Fraipont[5], J. Garessus[1], S. Haefliger[6], A. B. Leichtle[7], M. K. Kiessling[2], T. Mueller-Focke[2], F. S. Krebs[8], V. Zoete[8,9], P. Tsantoulis[5], O. Michielin[5†], C. Britschgi[2,10†‡] & A. Wicki[2*‡]

[1]Centre Hospitalier Universitaire Vaudois — CHUV, Department of Oncology, Lausanne; [2]Department of Medical Oncology and Hematology, University Hospital Zurich, University of Zurich; [3]Department of Medical Informatics, Universitätsspital Basel — USB, Basel; [4]Oncology, Hematology and Transfusion Medicine, Kantonsspital Aarau, Aarau; [5]Geneva University Hospitals — HUG, Geneva; [6]Department of Medical Oncology, Inselspital, Bern University Hospital, University of Bern; [7]Department of Clinical Chemistry, Inselspital — Bern University Hospital and Center for Artificial Intelligence, University of Bern, Bern; [8]Computer-Aided Molecular Engineering Group, Department of Oncology UNIL-CHUV, Ludwig Institute for Cancer Research Lausanne, Lausanne; [9]Molecular Modelling Group, Swiss Institute of Bioinformatics, Lausanne; [10]Swiss Group for Clinical Cancer Research (SAKK), Bern, Switzerland



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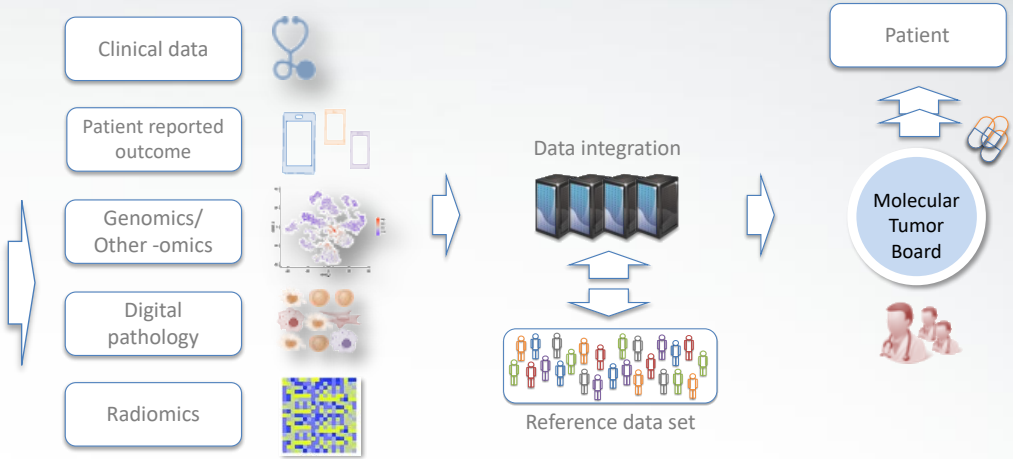
[1]Pradervand, *ESMO Open* 2024

Precision oncology: omics & spatial -omics



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Spatiomics as a new way to design predictive biomarkers

npj | precision oncology

Review article

Published in partnership with The Hormel Institute, University of Minnesota

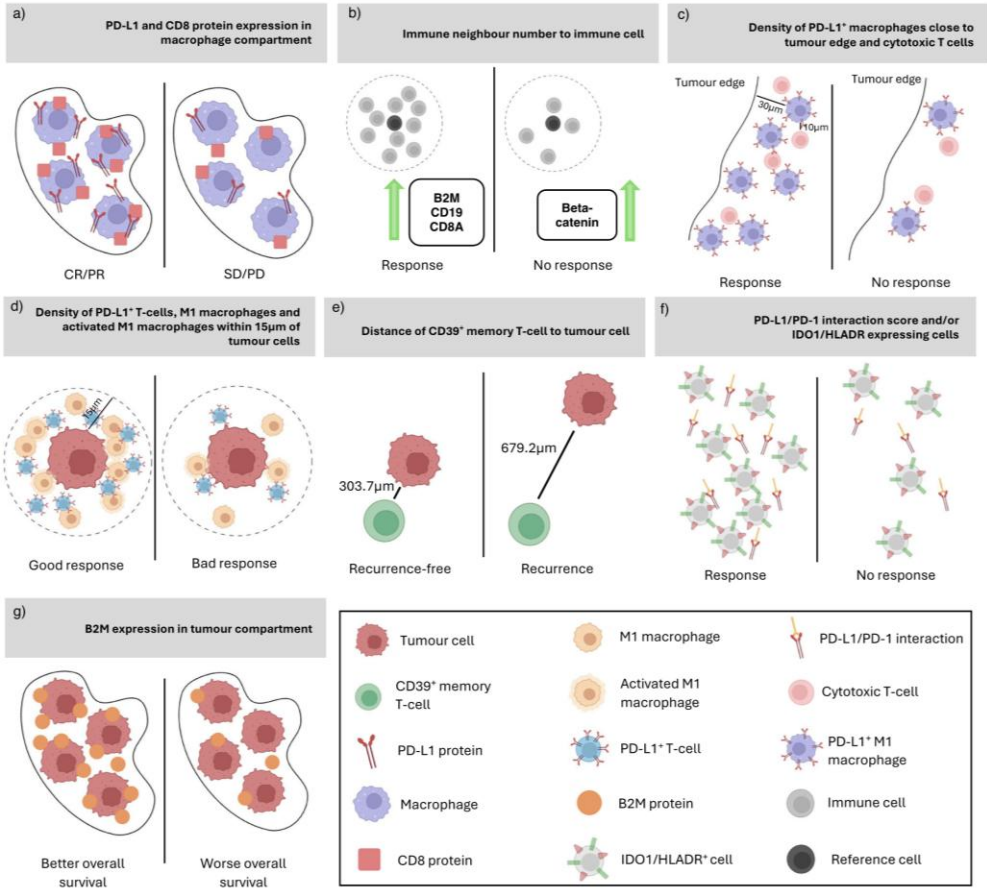
https://doi.org/10.1038/s41698-024-00671-1

The current landscape of spatial biomarkers for prediction of response to immune checkpoint inhibition

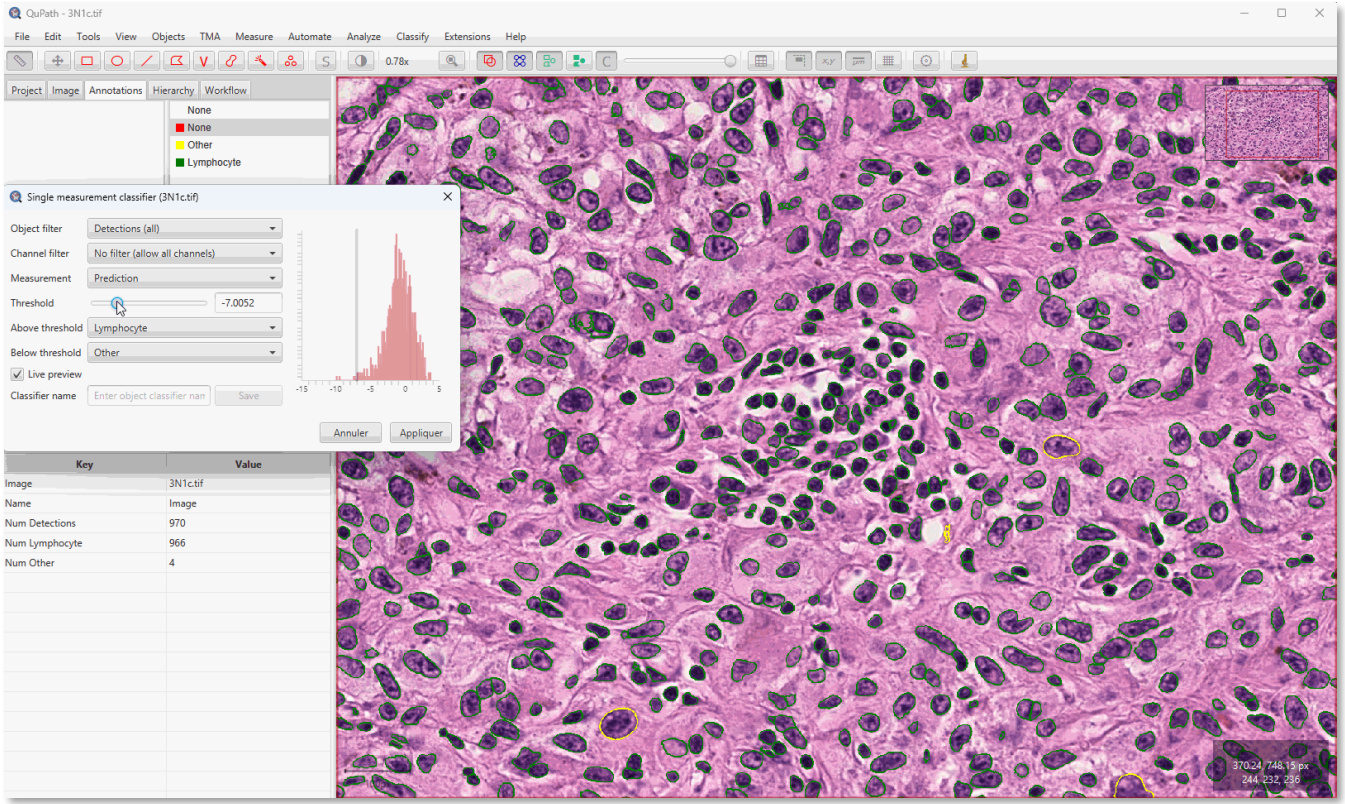
Check for updates

Hannah L. Williams[1,7], Ana Leni Frei[1,2,7], Thibaud Koessler[3,4,5], Martin D. Berger[6], Heather Dawson[1], Olivier Michielin[3,4,5] & Inti Zlobec[1]

- **Spatial information** provided by spatial proteomics and/or spatial transcriptomics can be leveraged to **build predictive biomarkers**
- This work has started in many IO sensitive tumor types including melanoma and lung cancer
- Our national program plans to make **extensive use of these technologies** and data to develop predictive biomarkers for precision oncology



Digital pathology: decoding spatial properties of lymphocytes



Visualization with different classification thresholds on a ROI in QuPath (lymphocytes in green, other cells in yellow)

Andrew Janowczyk,
Petros Liakopoulos,
Michel Cuendet,
Doron Merkler
HUG & UNIGE

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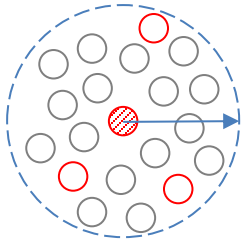
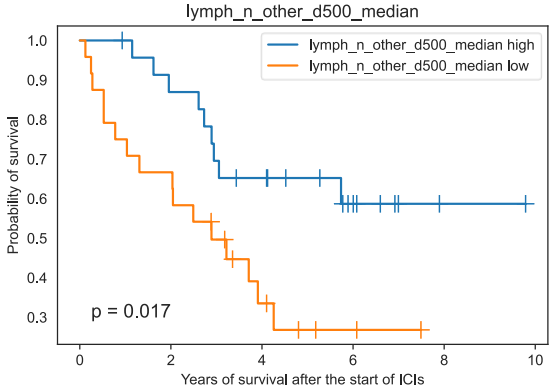
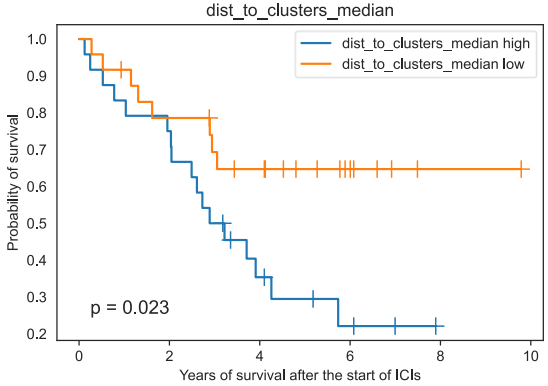
Example of abstract features

- We can stratify PD-1 benefit with sophisticated higher-order features, available only via computational pathology
- Multiple features are promising, 2 examples:
  - Median number of non-lymphocyte cells within 500 pixels of each lymphocyte (lymph_notherd500_median)
  - Median distance between each non-lymphocyte cell to the nearest lymphocyte cluster (dist_to_clusters_median)



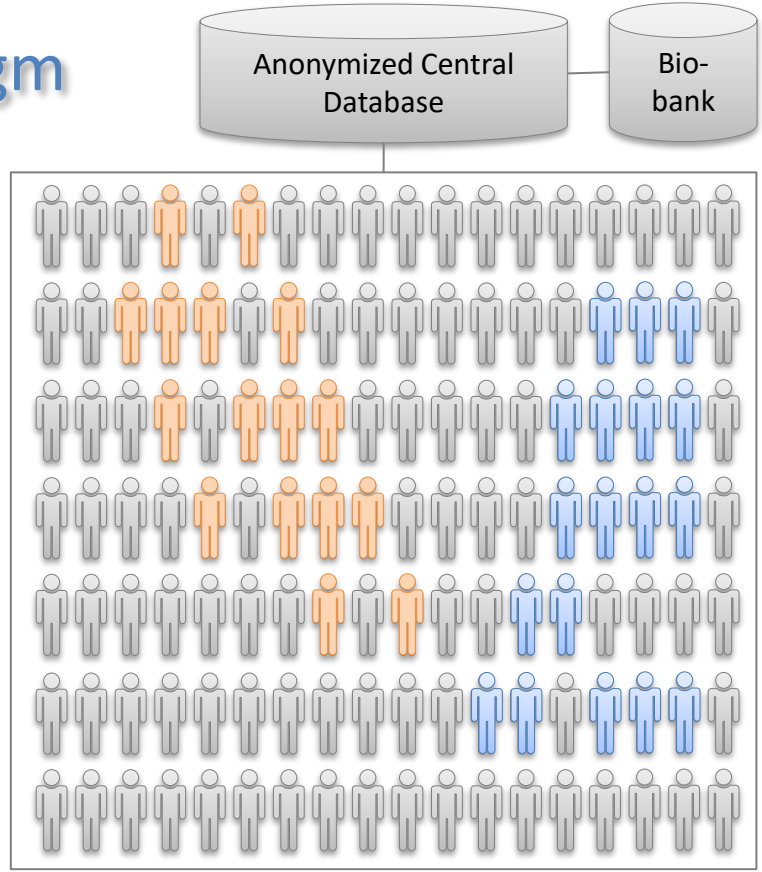
Lymphocyte
Non-Lymphocyte

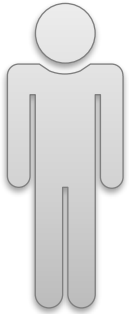




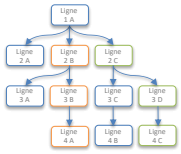
- Importantly: neither of these features are visually discernable in routine practice and require computer aided approaches!

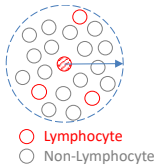
N=1 paradigm





Patient with clinical, molecular, imaging, and omics data



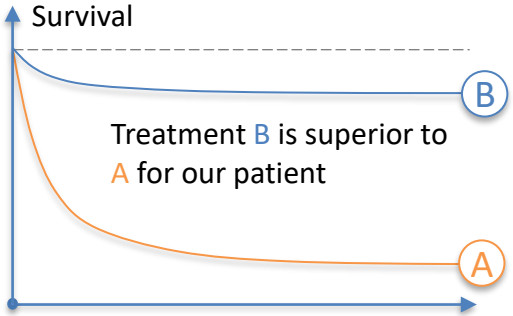


"Similar" patient with treatment A

"Similar" patient with treatment B

Treatment Recommendation

Molecular tumor board



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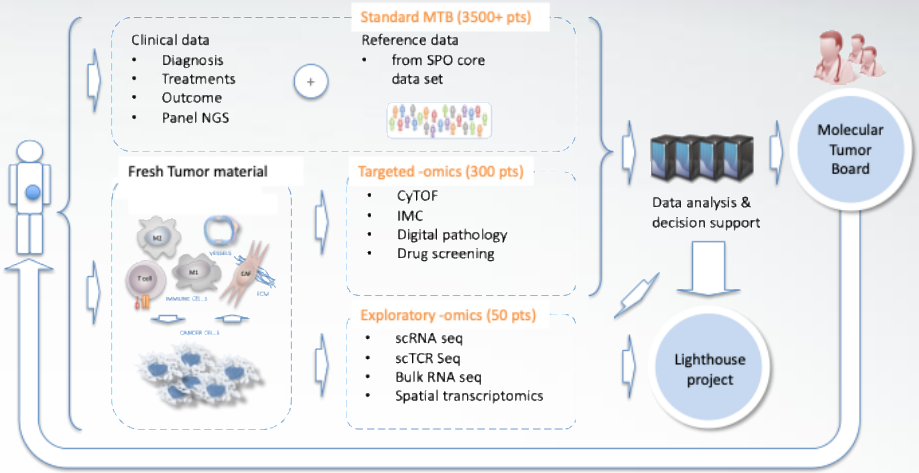
Prospective multi-omics: SPO - NDS



SPO-NDS

Melanoma cohort:
- PD-1 resistance setting

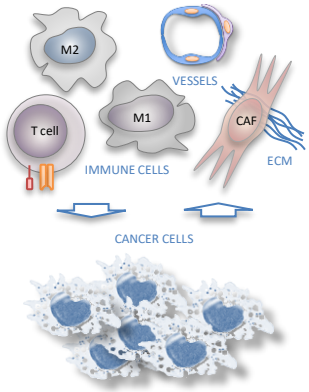
Standard MTB (3500+ pts)

Clinical data
- Diagnosis
- Treatments
- Outcome
- Panel NGS

+

Reference data
- from SPO core data set

Fresh Tumor material



Targeted -omics (300 pts)
- CyTOF
- IMC
- Digital pathology
- Drug screening

Exploratory -omics (50 pts)
- scRNA seq
- scTCR Seq
- Bulk RNA seq
- Spatial transcriptomics

Data analysis & decision support

Molecular Tumor Board

Lighthouse project

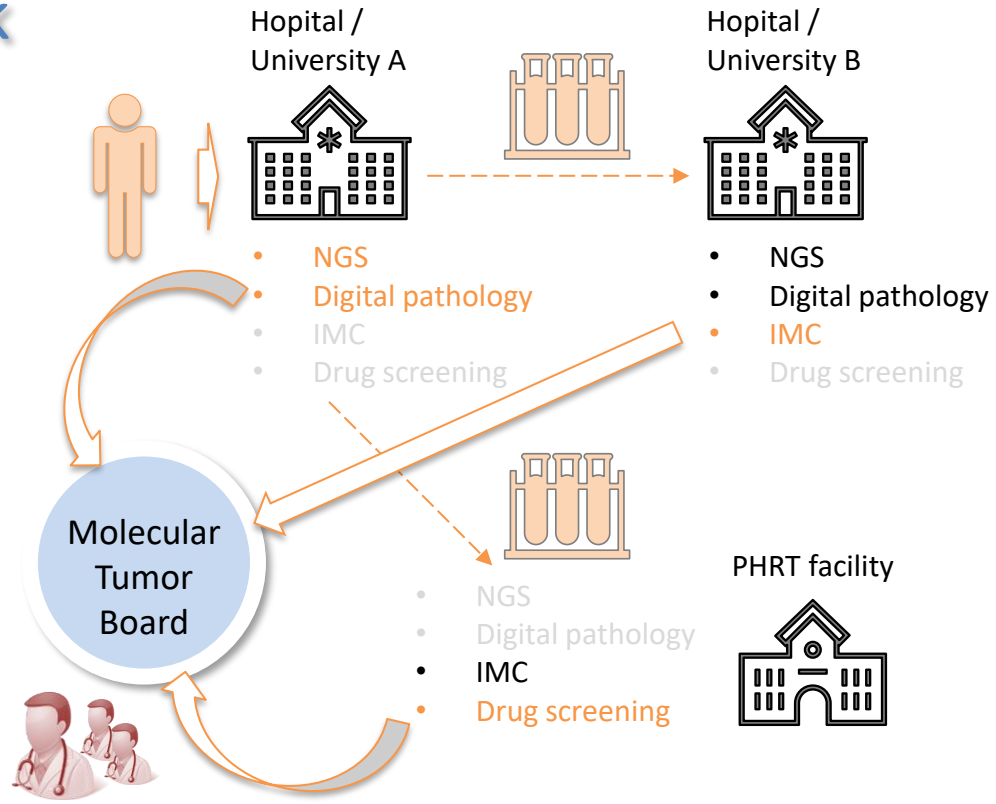
First patient in: 02-2024

Innovative therapeutic options

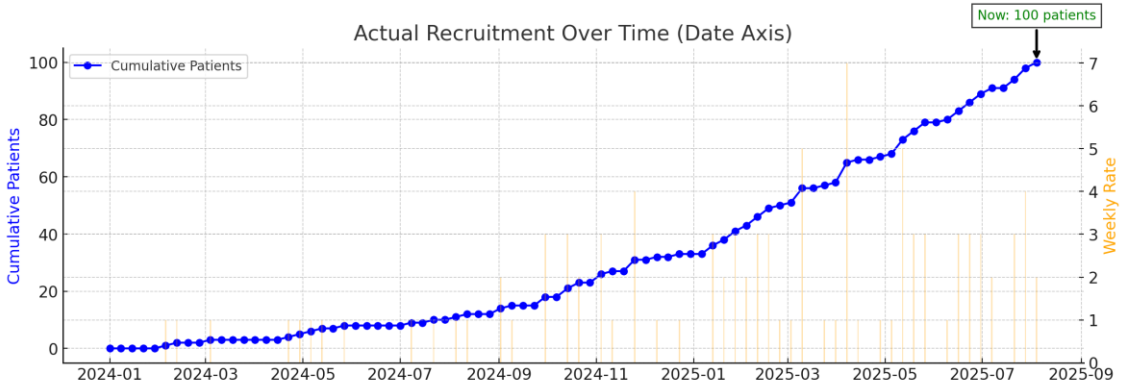
PI O. Michielin & Bernd Bodenmiller

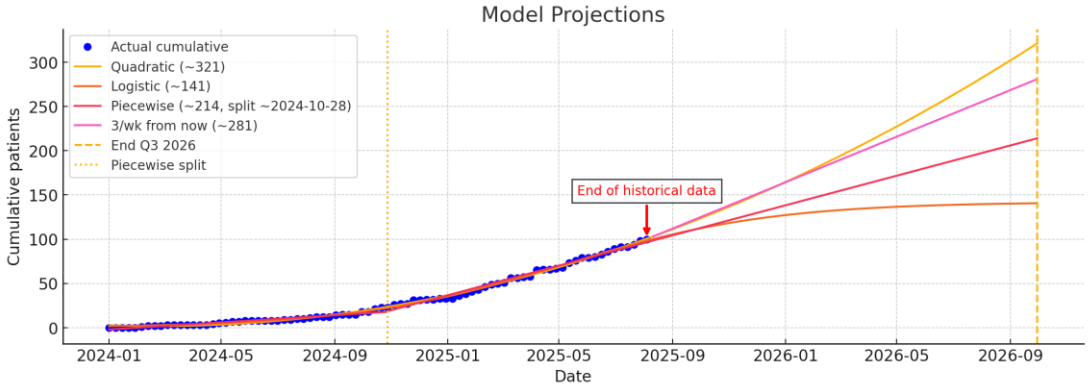
National –omics network

- We have built a decentralized program that allows recruitment of patients at all sites, multi-omics analyses in specific locations, yet central data integration
- New sites can be onboarded if they develop one of the multi-omics technology locally
- The multi-omics platforms are tumor specific (different anti-body panels, normalization, …)
- QC programs are in place within the –omics facilities



SPO-NDS: current recruitment rates





Upper panel:
Cumulative recruitment (blue circles) and weekly inclusion rate (orange bars) are shown from February 2024 to present (top).

Lower panel:
Model-based projections to 30 September 2026 are shown (bottom) using four approaches: quadratic, logistic, piecewise linear (change point ~28 Oct 2024), and fixed rate (3 patients/week).

Projected totals on 30 Sept 2026 are shown in the legend.

Current recruitement rate:
3-5 patients / week!

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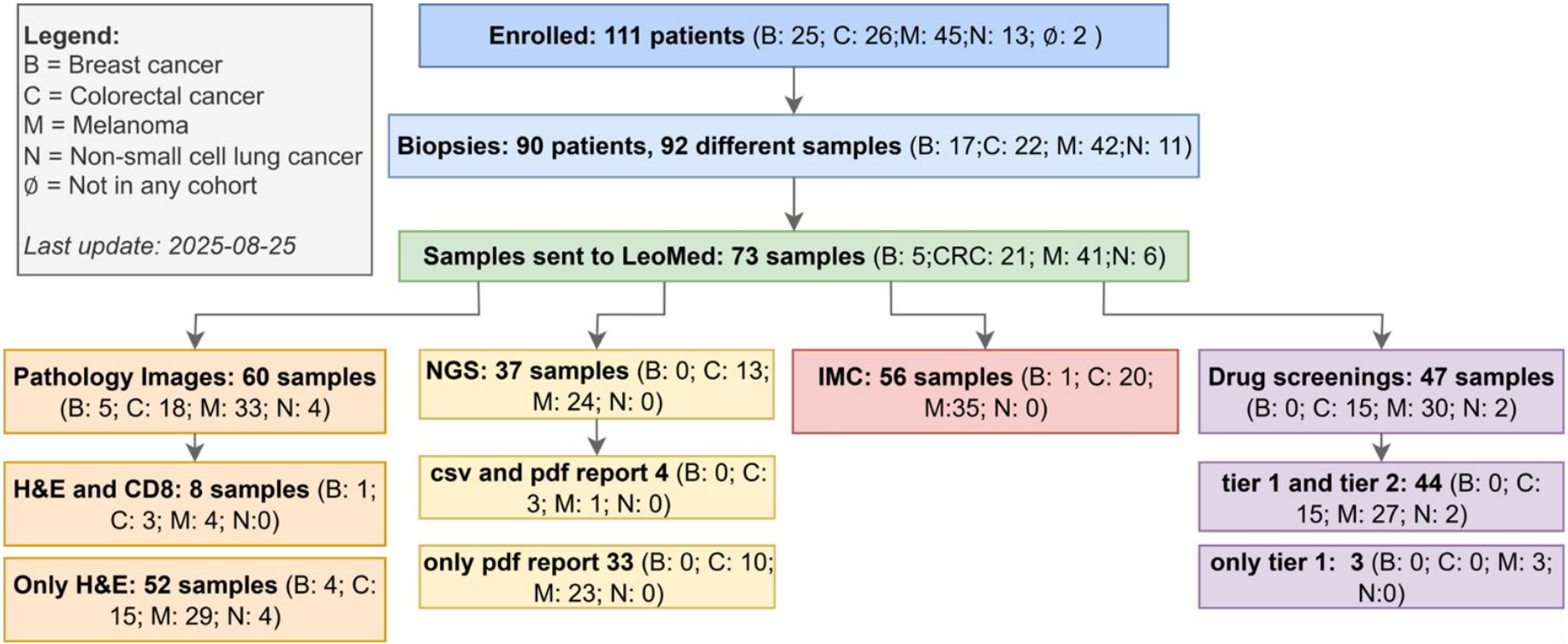
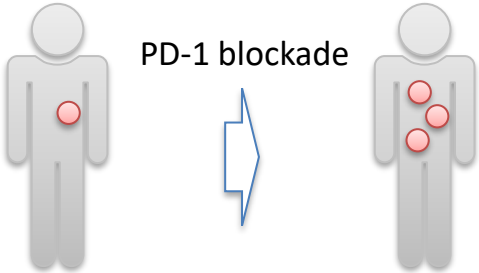
SPO-NDS: Prospective study data collection

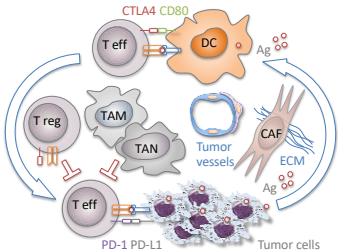


SPO-NDS: melanoma cohort – resistance to PD-1



PD-1 blockade

Deep characterization of immune resistance mechanism



Biomarker 1 → PD-1 + CTLA-4

Biomarker 2 → PD-1 + LAG-3

Biomarker 3 → PD-1 + CD40

Biomarker 4 → PD-1 + RP-1

Biomarker 5 → TIL therapy

Biomarker n → PD-1 + X?

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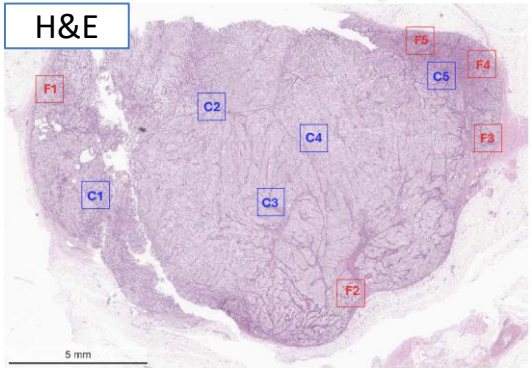
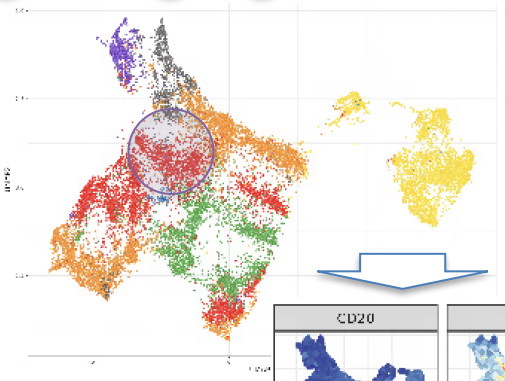
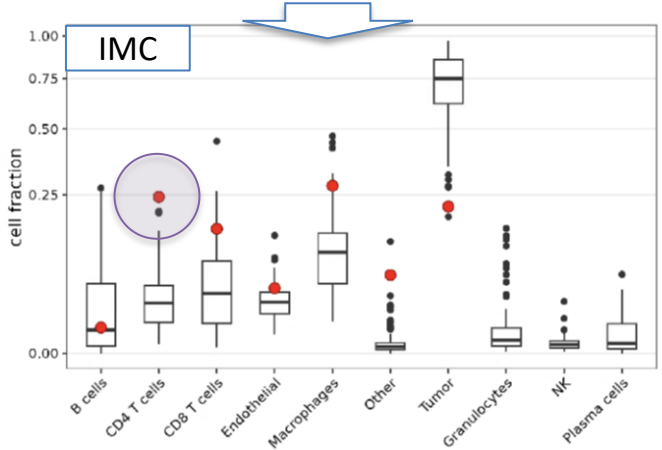
SPO-NDS: empowering imaging mass cytometry data

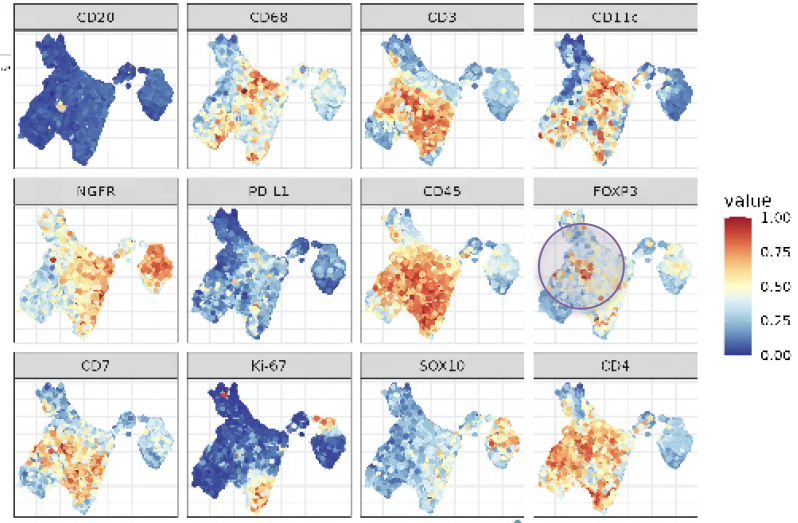




High Treg infiltrate
Possible proposition:
botensilimab
(2nd generation αCLTA-4)



IMC: cellular compositio n compared to reference samples (TuPro)



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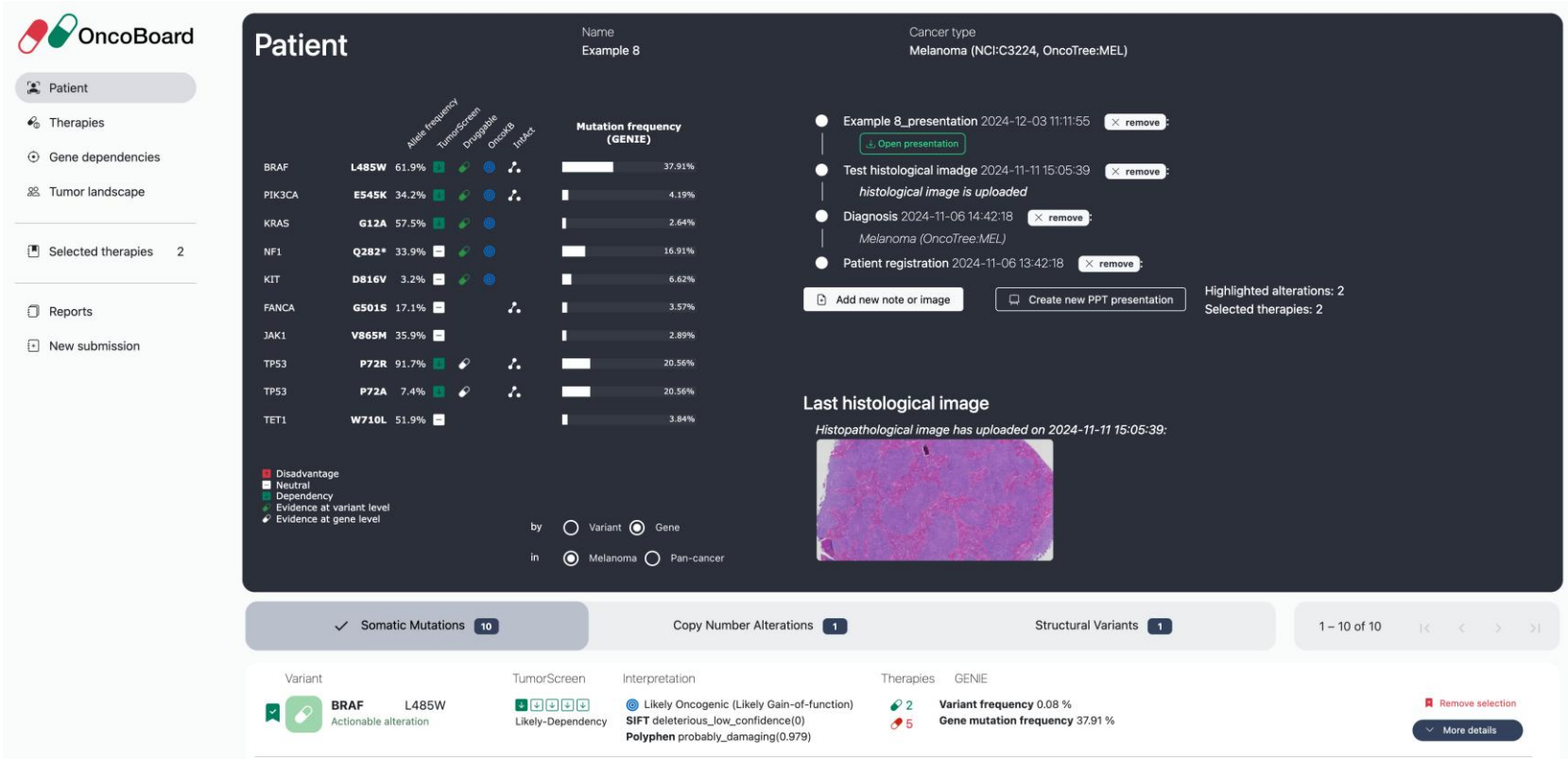
Bringing data back to the molecular tumor boards



Andras Hatos (HUG/UNIGE), Michel Cuendet (HUG/UNIGE), Giovanni Ciriello (UNIL)

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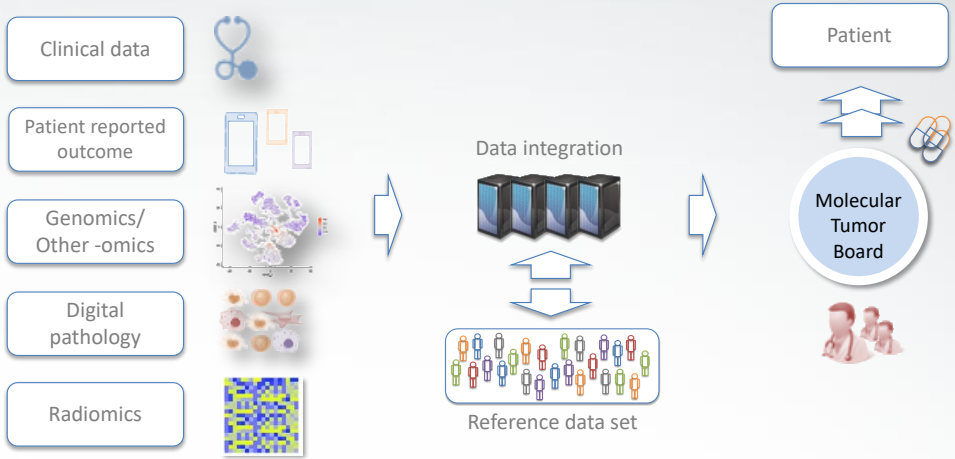
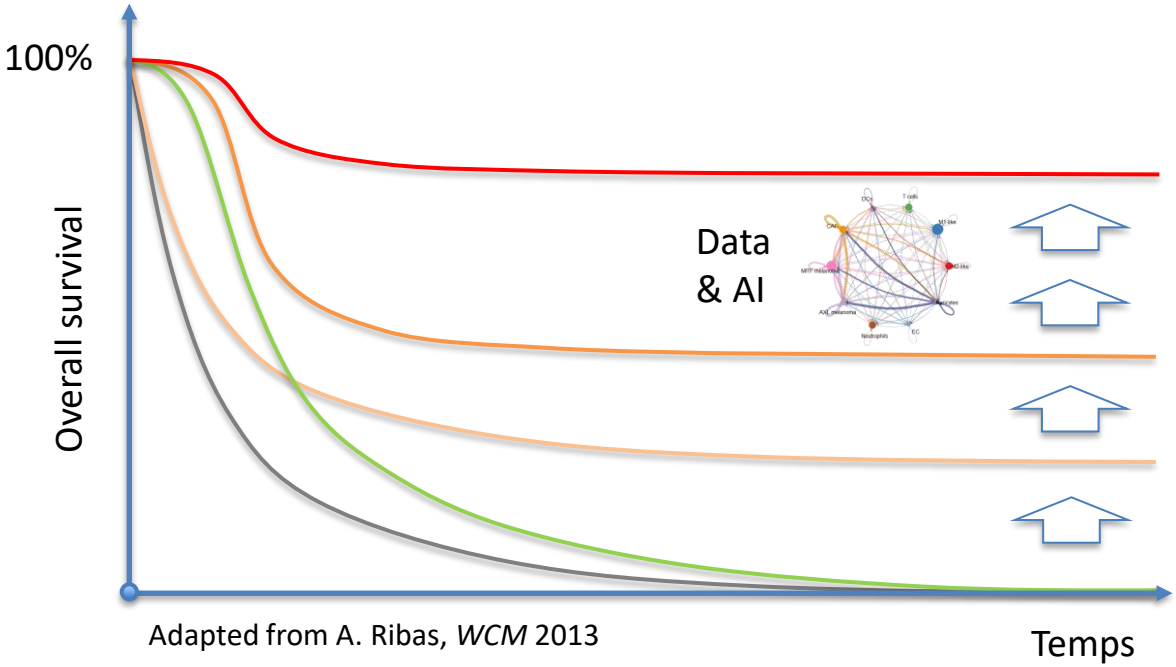
Conclusion and Outlook



Expected benefit from personalized strategies



Adapted from A. Ribas, *WCM* 2013

- Personalized therapies
- Combined therapies
- Immunotherapies
- Targeted therapies / Chemotherapies
- No treatment

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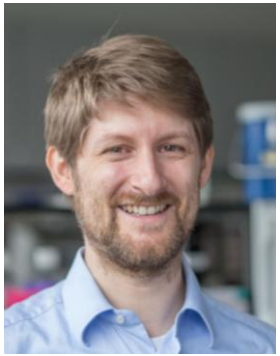
Many thanks to a fantastic team!



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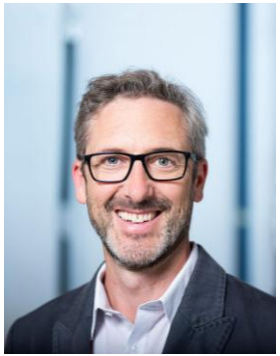
Prof. Andreas Wicki



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… and many more collaborators across CHUV, EPFL, ETHZ, HES-SO, HUG, INSEL, KISPI, KSBL, SAKK, SDSC, UNIBAS, UNIBE, UNIGE, UNIL, USB, USZ, and UZH.

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THANK YOU FOR YOUR ATTENTION!

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