Rigshospitalet
Department of Oncology

UNIVERSITY OF COPENHAGEN

REGION

Precision medicine: The Danish Research Environment (Oncology)

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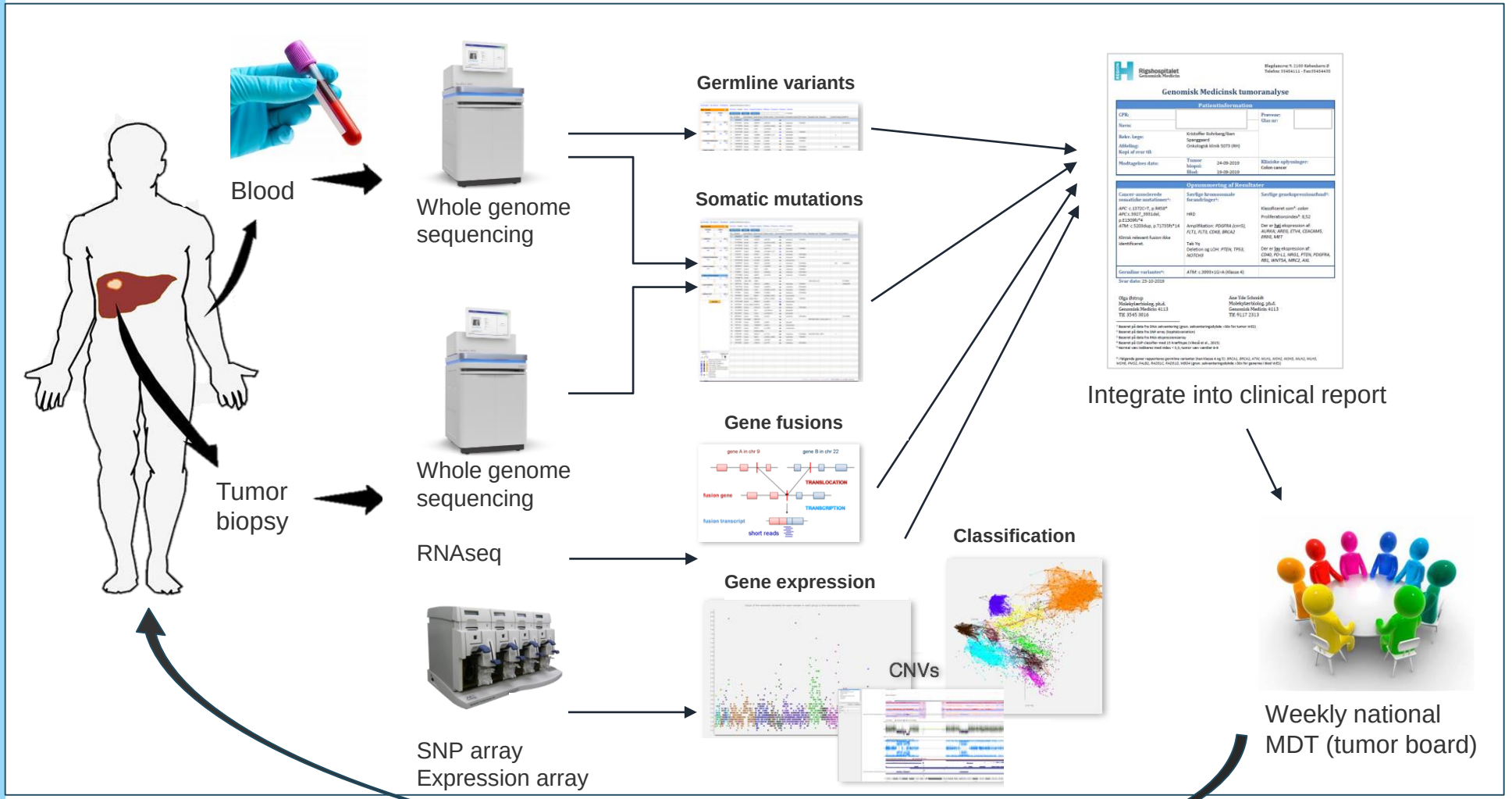
Disclosures

- Advisory roles: Bayer, Pfizer, Novartis
- Research grants: BMS, Roche, Pfizer and GSK
- Stocks: none
- Others: none

Setup for genomic profiling of cancer



Which patients?
Patients with exhausted options:

Copenhagen,
Since 2013:
WES+RHA seq
Since 2020: WGS + RNA
In 2021: national in DK

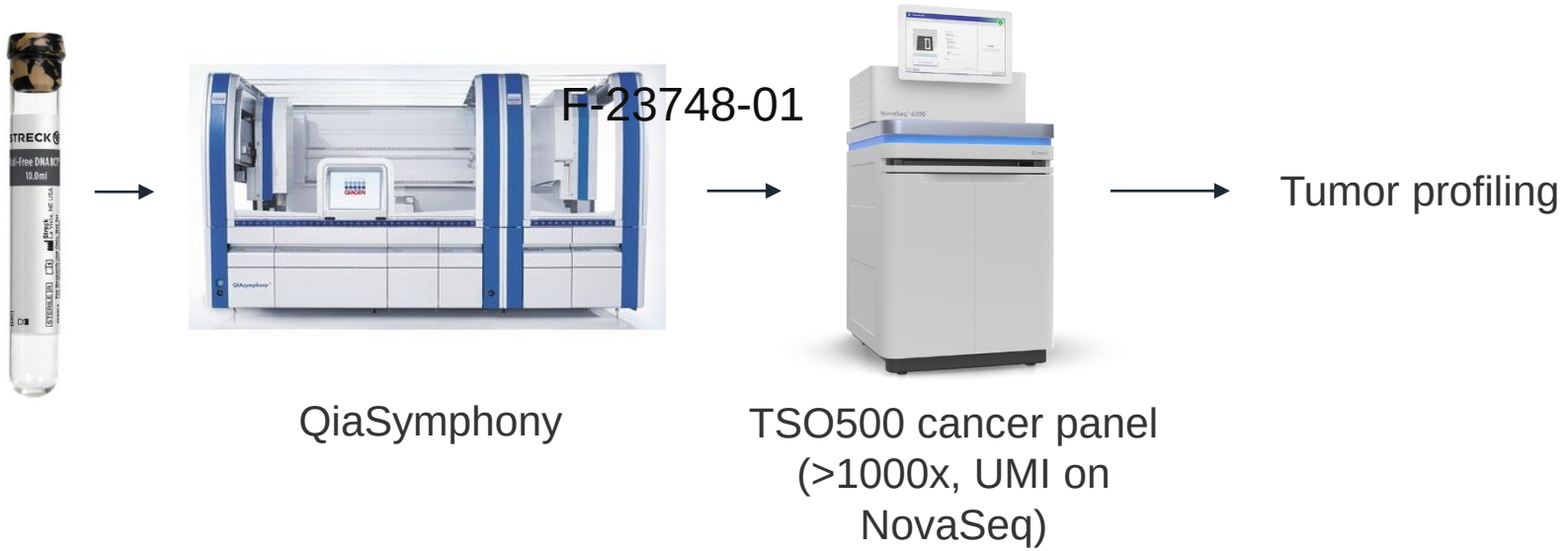
Newly diagnosed GBM
Copenhagen
Since 2016:
WES+RNA seq
Since 2020: WGS + RNA
In 2021: national in DK

In 2021-22
Newly diagnosed NSCLC*
Metastatic Breast Cancer*
Sarcoma
Pediatric and up to 30 yr.
Hematological cancer
Inherited cancer

*Copenhagen only

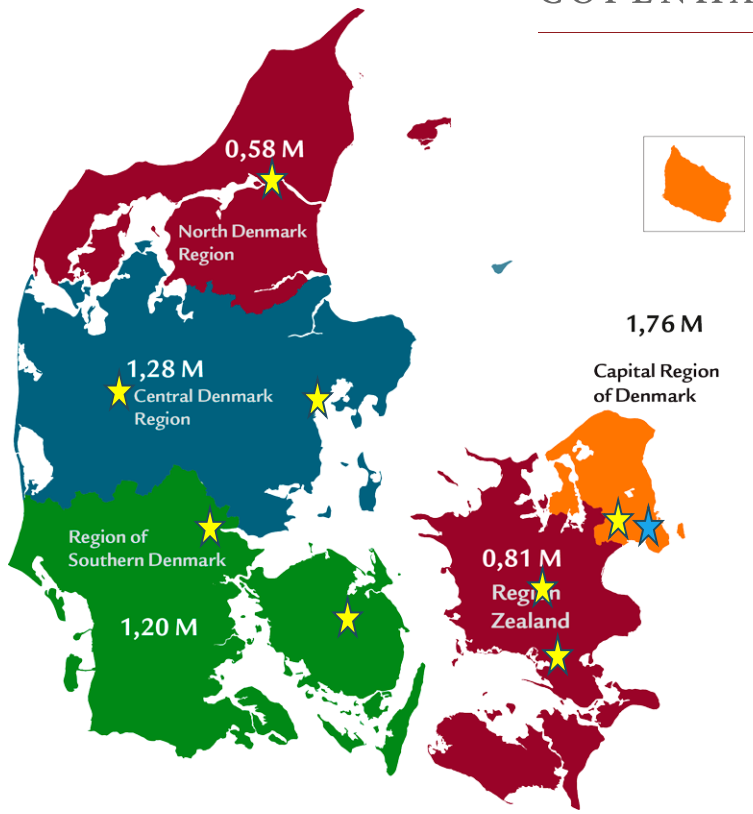
Circulating tumor DNA

- When biopsy is not possible
- When biopsy contained normal tissue

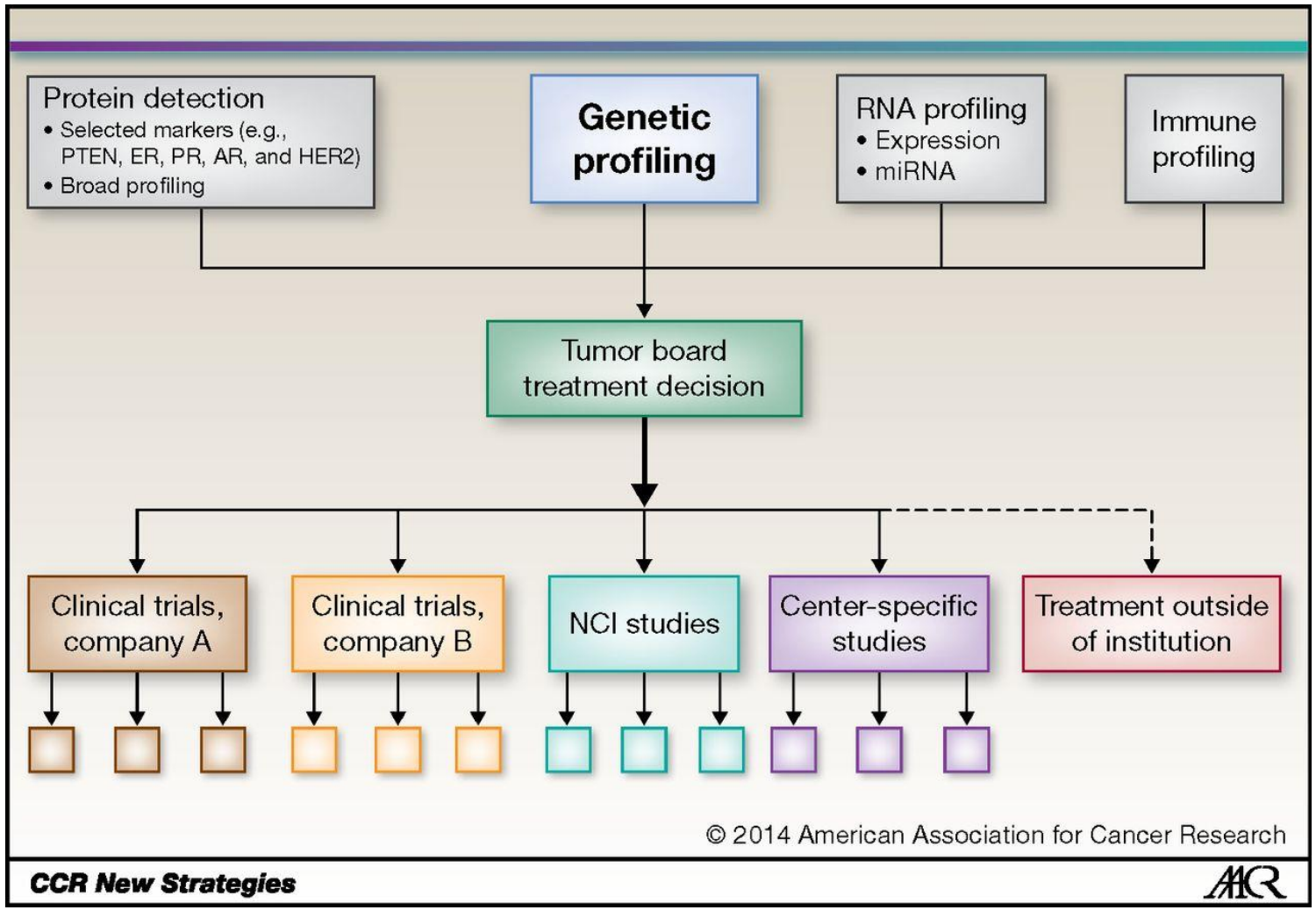


National Tumor Board

- ✓ Meeting every week (virtual meeting)
- ✓ Experts in: Clinical Oncology, Molecular Biology, Genomics, Clinical Genetics, Bioinformatics and Pathology
- ✓ Defines the actionable target
- ✓ Suggest treatment
- ★ ✓ Clinical Trial Units (TrialNation)
- ★ ✓ Dedicated Phase 1 Unit (TrialNation)



The academic medical center precision medicine tumor board model.



Jürgensmeier J M et al. Clin Cancer Res 2014;20:4425-4435

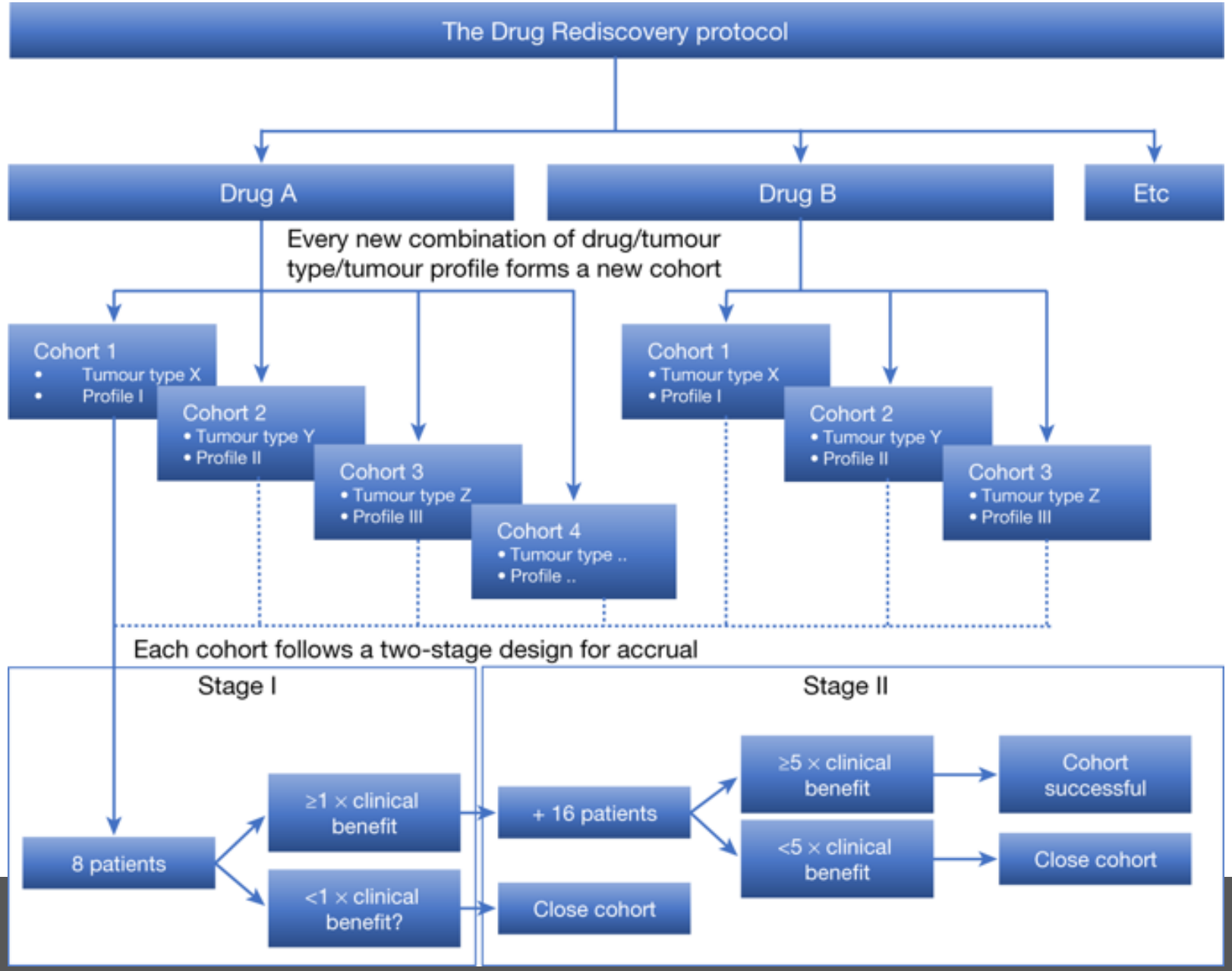
Expression profiles are refined according to actionable targets

- FGFR-pathway
- Notch pathway
- RAS-RAF-MEK-ERK pathway
- PTEN/PI3K/AKT/mTOR
- ALK, ROS1, RET and NTRK-fusions
- EGFR, HER2, HER3, and HER4
- C-met and IDH1
- BRCA and HRD
- Protein and ligand expression
  - in relationen to Mab in development: CEA, TF, mesothelin, EGFR, HER2, FAP, LAMP1
- Immunoscore: MSI, mutational load, PD-L1

REGION H

In general, there are no structured clinical data collections of the outcome of off-label use

- In the Netherlands, this approach has been incorporated into a ‘Drug Rediscovery Protocol’ (acronym DRUP) study (ClinicalTrials.gov Identifier: NCT02925234).
- DRUP serves as a platform where patients can be treated with off-label targeted agents whilst collecting all relevant outcome data.
- This approach improves access to these off-label drugs, diminishing inequalities in care, ensures robust review of target and treatment selection, and prospectively collects outcome data to be shared with industry, payers and regulatory bodies.
- Several countries are using similar protocols [e.g. TAPUR (NCT02693535) and CAPTUR (NCT03297606)] which specifically allow data sharing.



Van der Velden et al. Nature 2019

ProTarget: A Danish Nationwide Clinical Trial on Targeted Anti-Cancer Treatment based on Genomic Profiling

Study Objectives:

- To describe in different types of population the anti-tumor activity of commercially available, targeted anti-cancer drugs used for treatment of patients with a genomic variant known (i) to be a target of an EMA-approved anti-cancer drug or (ii) to predict sensitivity to an EMA-approved anti-cancer drug.

- To record the site investigator determination treatment-related adverse events experienced by patients receiving treatment with commercially available, targeted anti-cancer drugs.

- To perform refined biomarker analyses, including (but not limited to) whole genome sequencing, on a fresh tumor biopsy specimen at baseline and at progression.

- To study mechanisms of resistance by the use of serial fresh tumor biopsies for WGS and liquid biopsies.

ClinicalTrials.gov Identifier: NCT04341181

Inclusion criteria

- Patient (age≥ 18 years) with a histologically-proven locally advanced or metastatic malignant disease who is no longer benefitting from standard anti-cancer treatment or for whom, in the opinion of the investigator, no such treatment is available or indicated.

- ECOG performance status 0-2
- Patients must have acceptable organ function as defined below. However, as noted above, drug-specific inclusion/exclusion criteria specified for each agent will take precedence for this and all inclusion criteria

- Patients must have measurable or evaluable disease (per RECIST v1.1)

Agents: so far…supported free of charge from pharma (Roche, Pfizer and GSK)

- Cotellic (cobimetinib)
- Zelboraf (vemurafenib)
- Herceptin (trastuzumab)
- Perjeta (pertuzumab)
- Tarceva (erlotinib)
- Alecensa (alectinib)
- Erivedge (vismodigib)
- Tecentriq (atezolizumab
- Kadcyla (Trastuzumab emtansin)
- Bavencio (avelumab)
- Inlyta (axitinib)
- Zejula (niraparip)

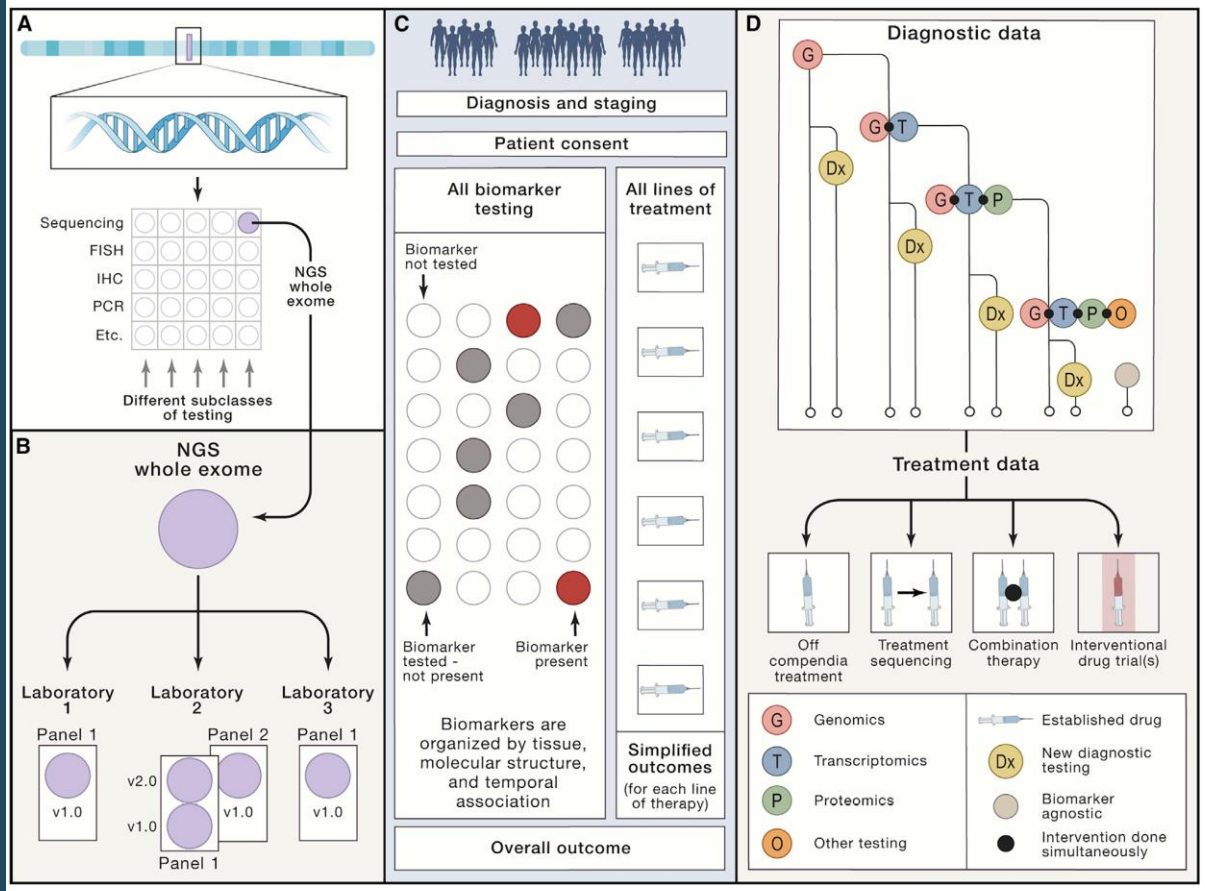
In total 12 agents so far, but more to come (hopefully)

Precision medicine is complicated

- No one group has the patient numbers and resources to collect the data necessary to fully advance the field.
- We need accessible, quality data on thousands of patients, harboring the breadth of molecular alterations in order to develop scientifically rigorous analysis.
- MOTs can fill the gap that currently exists in precision medicine but only to the degree that these are supported by community and academic practices, both nationally and internationally.
- Areas of complexity that could hinder participation include data sharing, publication rights, intellectual property, financing, and governance.
- Finding the right models that lead to formal contracts and allow for unification across institutions and borders could be challenging

[1] Dickson D et al. Cell, 2020

MASTER OBSERVATIONAL TRIAL



- Patients are broadly accepted into the trial along with diagnosis and staging (disease extent) information and informed consent.
- Biomarker testing results (both positive and negative) are collected and classified using methods shown in Figures 1A and 1B.
- High-level outcomes are collected in connection with each line of therapy.
- All of the information is tied together in a prospective observational registry using standardized reporting methods and metrics.
- (D) Interconnectivity and modularity of MOT design.
- All data collected are sorted and organized to allow for comparison and analysis of any testing or treatment method in combination or series.
- The prospective nature and precise molecular characterization allow for identification of specific subgroups of patients who can participate in interventional clinical trials that are directly related to or external to the MOT.

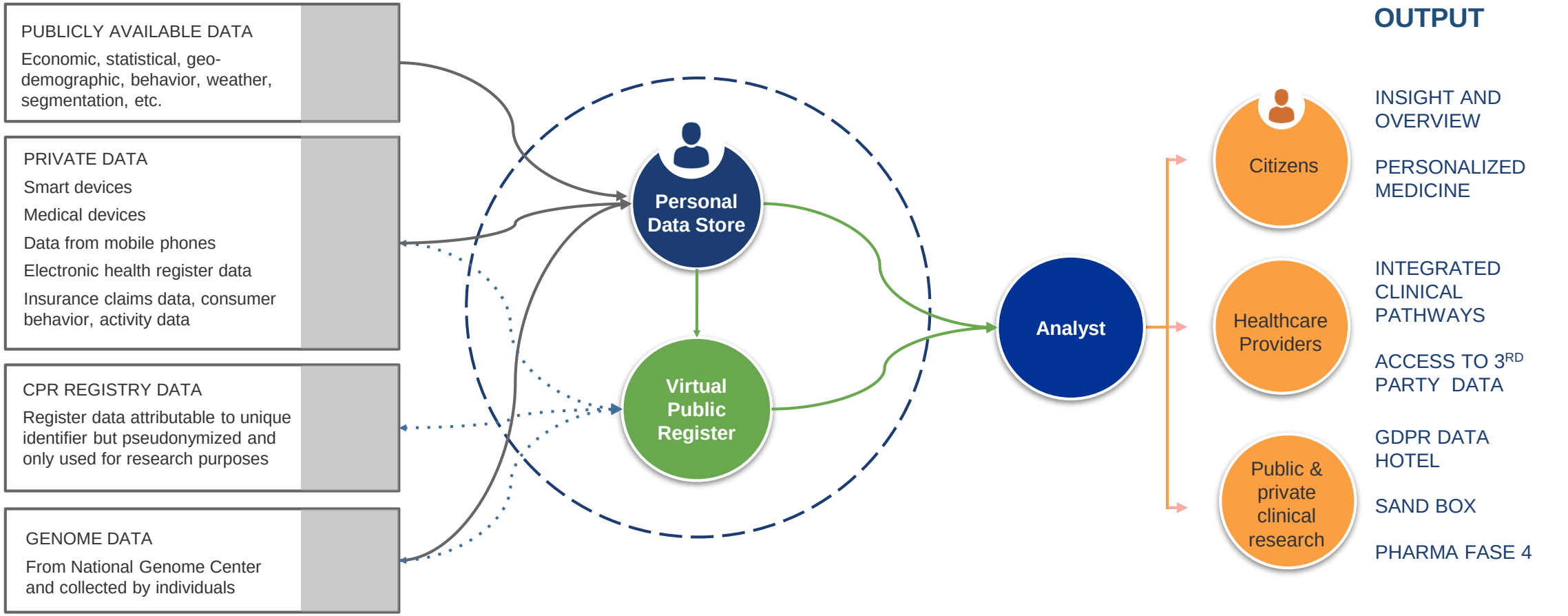
[1] **Dickson D et al. Cell, 2020**

REGION H

New Infrastructure Supports Data Sharing

Securing access to health data at the highest privacy and security levels

Enversion
Data for Good
Secata
DataFair



1. CLEAN, STRUCTURE, CONNECT & COLLECT
2. ENCRYPTED ANALYSIS
3. CLEAR TEXT ANALYSIS
4. USE

Conclusion and perspectives

- Genomic profiling with assays capable of identifying gene fusions and rare mutations should be strongly considered in patients with solid tumors of all histologies when determining systemic treatment options
- In Denmark, The National Genome Center with improved resources and infrastructure for advanced genomic profiling of more patients are paving the way for a strategy for more systematic identification of genomic aberrations
- ProTarget is a nationwide study in Denmark started in October 2020
- We are embracing the NGS technology in order to better selection and de-selection patients and study mechanisms of resistance, with weekly national MTB
- TrialNation supports the national network and facilitates fast feasibility processes

Trial Nation Center for Oncology consists of:

- Copenhagen University Hospital (Rigshospitalet), Dept. of Oncology and Dept. of Paediatrics & Adolescence
- Herlev & Gentofte Hospital, Dept. of Oncology

- Little Belt Hospital – Vejle Hospital, Dept. of Oncology
- Odense University Hospital, Dept. of Oncology

- Aarhus University Hospital, Dept. of Oncology
- Regional Hospital Unit West – Herning Hospital, Dept. of Oncology

- Zealand University Hospital, Dept. of Oncology

- Aalborg University Hospital, Dept. of Oncology

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