Strategic Focus Area
Personalized Health
and Related Technologies

Non-small cell lung cancer without targetable biomarkers: proposal of a patient-first approach to personalize treatment decision

Fresh ideas for cancer care 2.0

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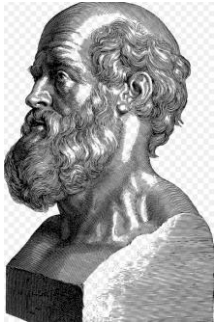
Aim of the challenge

How can we support **treatment decisions** in non-small cell lung cancer (NSCLC) patients based on **available and potential cancer-specific biomarkers**?

We propose a **patient-first** approach to enable clinicians to **personalize treatment decisions** for each patient

Precision Medicine



"*it is far more important to know what person the disease has than what disease the person has*"

Hippocrates

- Identification of the right treatment for every patient
- precision oncology uses **morphological**, **molecular** and **functional** characteristics of the patient's tumor (biomarkers) to tailor cancer-specific treatment

Precision Medicine: the most famous example

The New England
Journal of Medicine

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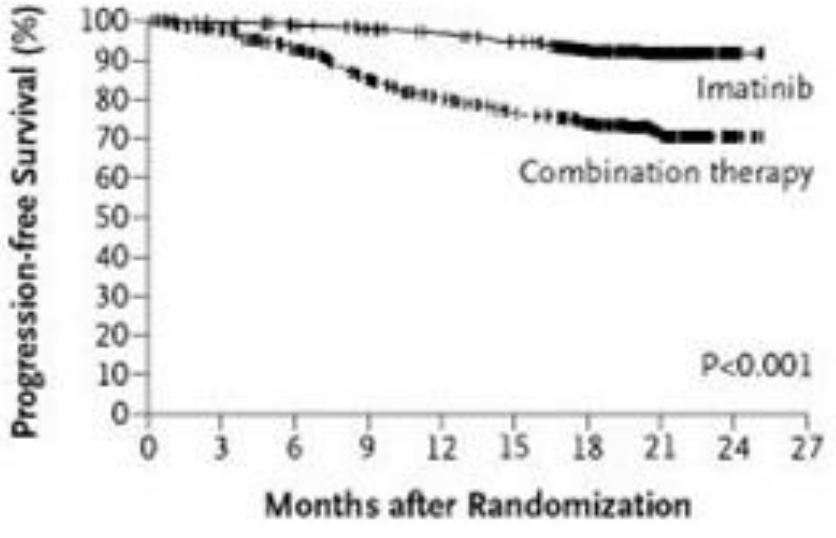
EFFICACY AND SAFETY OF A SPECIFIC INHIBITOR OF THE BCR-ABL TYROSINE KINASE IN CHRONIC MYELOID LEUKEMIA

BRIAN J. DRUKER, M.D., MOSHE TALPAZ, M.D., DEBRA J. RESTA, R.N., BIN PENG, PH.D., ELISABETH BUCHDUNGER, PH.D., JOHN M. FORD, M.D., NICHOLAS B. LYDON, PH.D., HAGOP KANTARJIAN, M.D., RENAUD CAPDEVILLE, M.D., SAYURI OHNO-JONES, B.S., AND CHARLES L. SAWYERS, M.D.



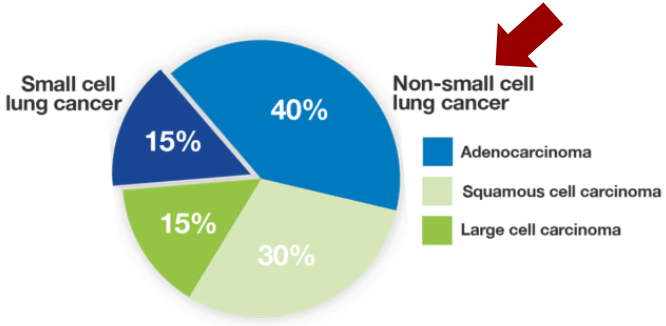
O'Brien, S. et al. N Engl J Med 2003;348:994-1004

Non small cell lung cancer (NSCLC)

Lung cancer:

- 2nd most common cancer & leading cause for cancer-related death

- 5-year survival rate:
  - **non-small cell lung cancer (NSCLC) 26 %**
  - small cell lung cancer (SCLC) 7 %

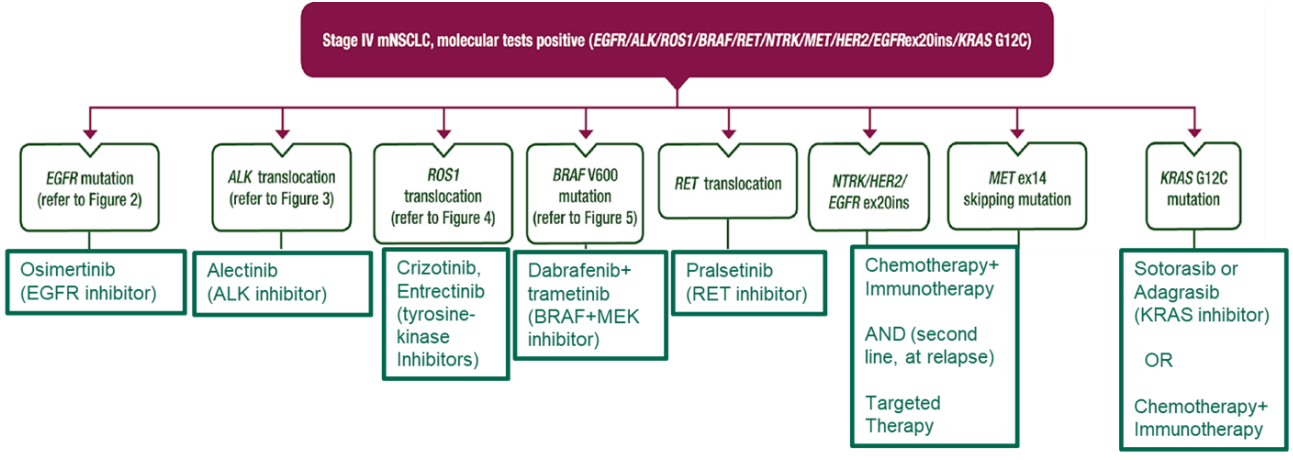


- **High number of potential targetable biomarkers -> NSCLC is a paradigm for precision oncology**

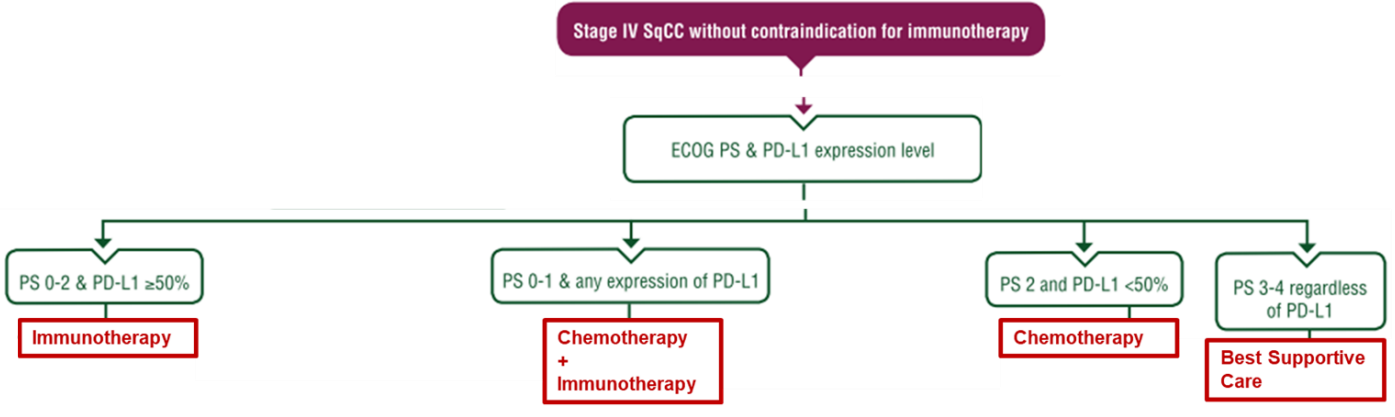
what if no targetable biomarkers is available?

Current treatment decision guidelines from the European Society of Medical Oncology (ESMO)

When **targetable mutations are present:** targeted therapy is recommended



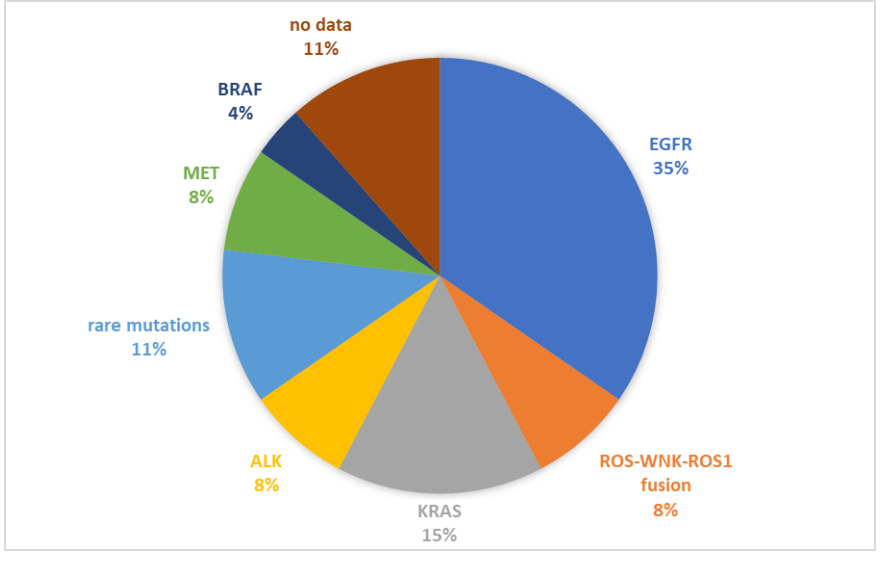
In the **absence of targetable mutations**, therapy recommendations are solely based on PD-L1 expression and on the ECOG performance score



adapted from Hendriks et al. 2023

Cohort overview – population of patients that have no treatment options

Preselected patient cases: not a representative cohort



in **large hospitals**: discussion of the individual patient case in **tumor boards**

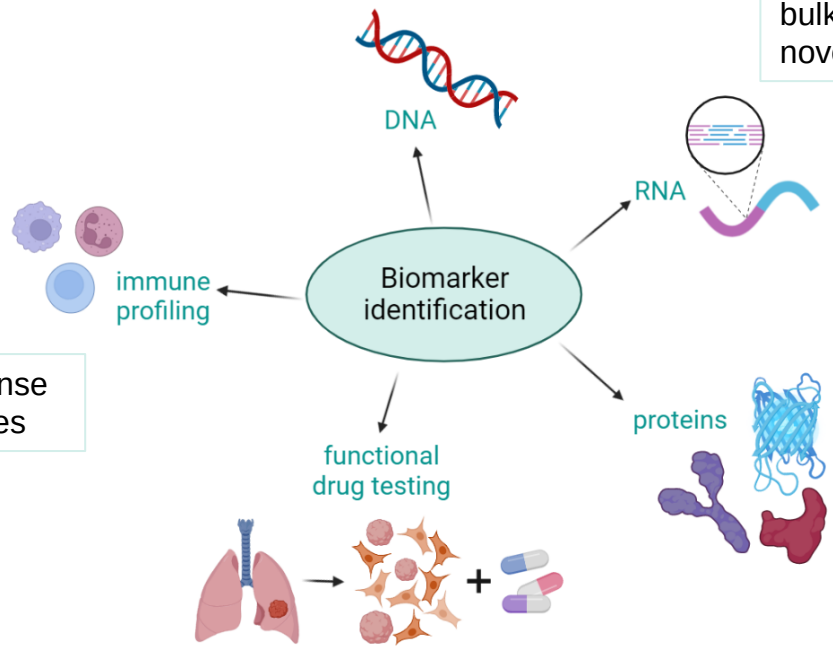
difficulty in **smaller clinics** with little resources

Patient Characteristics	Number of patients (%)
Sex	
Male	10 (38%)
Female	16 (62%)
Total	26 (100%)
Age at diagnosis (years, mean)	64
Stage at diagnosis	
Metastatic disease	24 (92%)
Smoking history?	
yes	12 (46%)
no	8 (30%)
not reported	6 (24%)
Pack Years (mean)	17
Molecular markers at diagnosis	
Genetic	23 (89%)
Protein (PD-L1) expression	
>50%	6 (24%)
5 - 50 %	4 (15%)
1- 4.9 %	3 (11%)
<1 %	7 (27%)
no data	6 (24%)
Therapy at first line	
surgery	2 (8%)
targeted therapy *	9 (35%)
ICI alone	2 (8%)
Chemotherapy + ICI	9 (35%)
no data / not yet started	6 (24%)
First line response	
partial response	8
stable disease	1
progressive	1
PFS (months, mean) **	10

Opportunities for biomarker identification

- mainly used to identify targeted therapies up to this point
- main biomarkers: EGFR, KRAS, BRAD, ALK and MET

bulk or single cell RNA sequencing to identify novel biomarkers



- protein analysis reflects functional changes
- whole proteome analysis vs. targeted quantification of biomarkers

To predict patient response towards immunotherapies

- Ideally: maintain 3D growth, tumor heterogeneity, immune system, cellular crosstalk across cell types
- Organoids vs. maintaining the tumor microenvironment
- Identification of responders vs. non-responders

Our therapy-decision tree

→ to tailor personalized treatment decisions for NSCLC patients

Strengths:

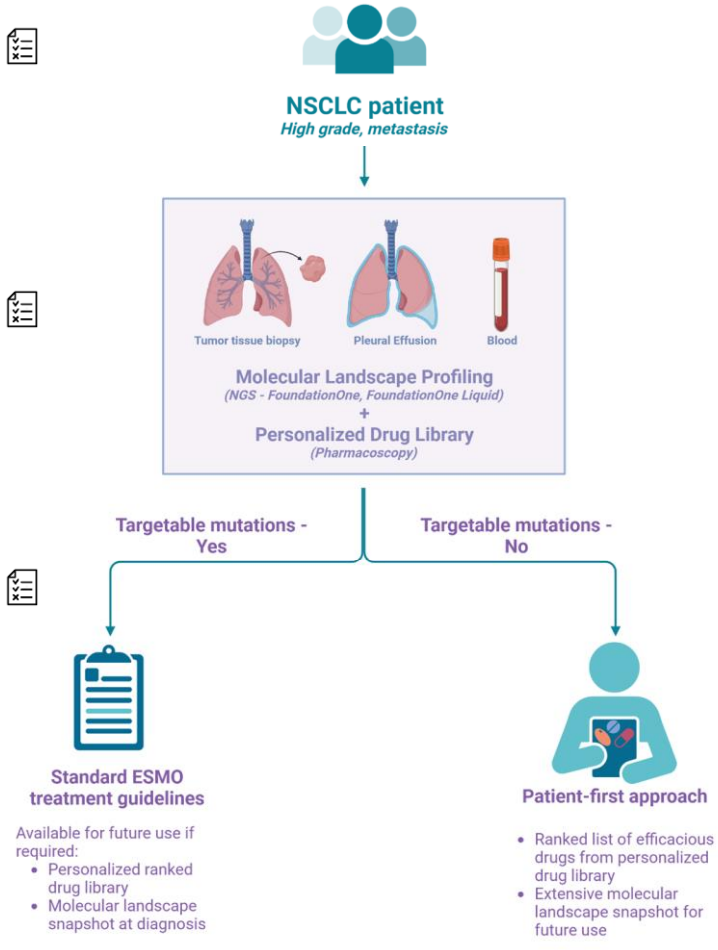
→ dynamic set-up: space for new emerging technologies

→ it includes periodic assessment of the **Quality of Life (QoL)** to engage the patient in the treatment decision-making process

Challenges:

→ off-label use of drugs / drug reimbursement

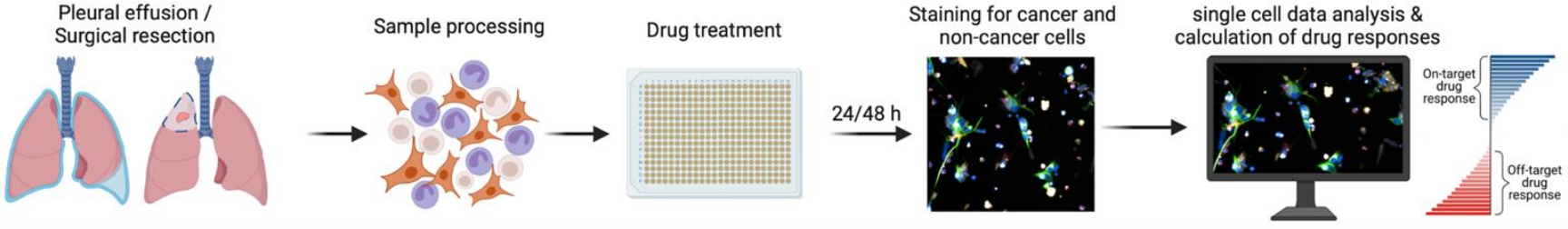
→ establish clinical trial to prove clinical predictiveness of pharmacoscopy



Patient-first approach

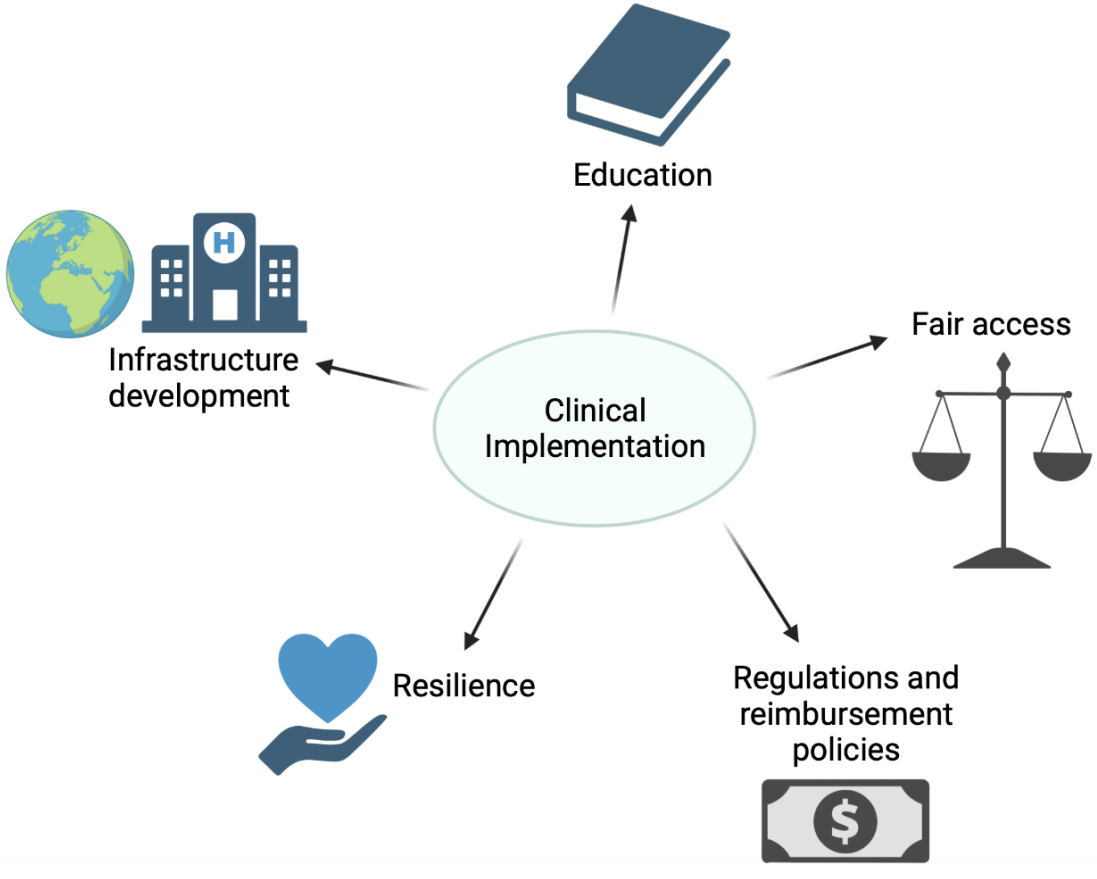
The summed up results go to a **tumor board**, that takes the **patient molecular profile**, the **clinical data** and the ***ex vivo* drug screening results** into account and decide for a specific drug treatment.

- **Pharmacoscopy**: *ex vivo* drug screening on **pleural effusions or tissue**



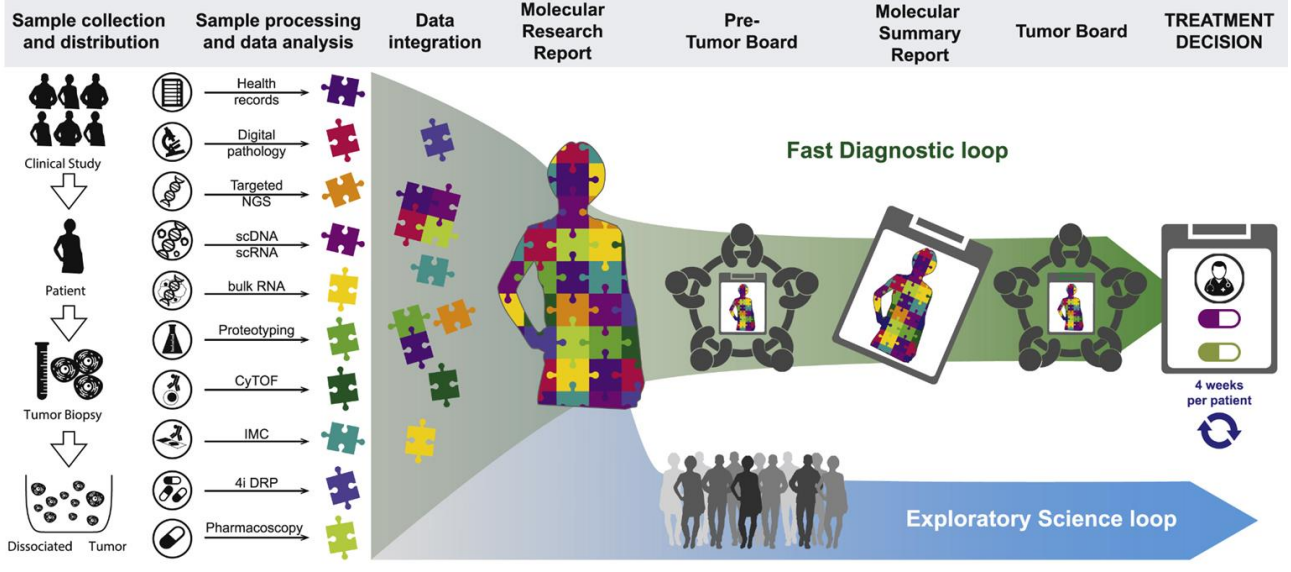
- The **drug library** will include:
- targeted drugs that are recommended by the ESMO guidelines
- drugs currently included in clinical trials
- possible combinatory treatments

Considerations for clinical implementation



Personalized medicine in the future

- Use of databases for patient matching to clinical trials
- Integration of data from multiple disciplines



Identification of:

- biomarkers
- predictive tools
- association of collected parameters

"The Tumor Profiler Study: integrated, multi-omic, functional tumor profiling for clinical decision support", Irmisch et al. Cancer Cell, 2021.

Thanks to our mentors !

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