UNIVERSITÄT BAYREUTH

LMV LEHRSTUHL FÜR MEDIZINMANAGEMENT UND VERSORGUNGSFORSCHUNG

Use of liquid biopsy in non-squamous NSCLC – A model-based assessment of clinical and health economic performance in German clinical care setting

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Introduction and Objective

Background

- Lung cancer is one of the leading cancer deaths worldwide with non-small cell lung cancer (NSCLC) accounts for more than 80 % of all lung cancer cases.
- Steadily growing insights into molecular tumour biology has allowed the development of molecular targeted therapies prolonging the PFS as compared to conventionally used cytotoxic agents.
- To initiate a targeted therapy, a molecular pathological examination is inevitable via tissue (gold standard) or liquid biopsy.

Relevant alterations NSCLC[1]:

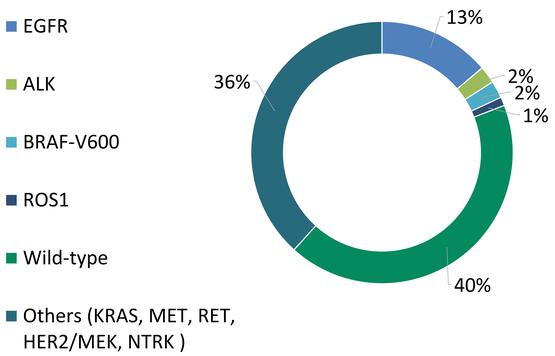

Figure 1 Therapy-relevant gene alterations in non-squamous NSCLC

Tissue biopsy[2]

- Site specific
- Relatively high specificity and sensitivity; however, in some cases difficult to capture all clones
- Invasive
- Applications: Tissue architecture and histology for initial diagnosis, staging and PD-L1 expression, rebiopsy enables detection of emerging genetic alterations and response to therapy
- Additional costs for e.g. bronchoscopy

Liquid biopsy[2]

- May better reflect spatial tumour heterogeneity and enhances comprehensive monitoring of clonal evolution in the course of the disease.
- Moderate sensitivity (depends on concentration of tumour-derived DNA in the plasma), high specificity
- Minimally invasive character, laboratory technology subject to ongoing optimization
- Applications: molecular differential diagnosis, clinical decision making, prognosis, monitoring of tumour evolution and disease burden and response to therapy

→ Yet liquid biopsy used as an add-on if no tumour tissue is available or if the tissue is insufficient for molecular analysis.

However, in Germany liquid biopsy is neither part of the standard care processes nor does an appropriate reimbursement policy support timely and comprehensive access for patients.

Objective

To evaluate the cost-effectiveness (incremental cost-effectiveness ratio, ICER) of liquid biopsy application (ctDNA detection) in the German care pathway for metastatic non-squamous NSCLC patients as an add-on to tissue biopsy

Methods

Cost-effectiveness analysis

The parameters used for modelling were obtained by evidence synthesis and pooling of relevant international RCT results and published national CRISP[3]-register data. Model input data, and where required, model related assumptions were validated with clinical experts.

- Model: Decision tree (microsimulation 10,000 trials)
- Population: non-squamous NSCLC metastatic stage (four subgroups: EGFR, ALK, BRAF-V600, ROS1)
- Intervention: Care pathway with liquid biopsy
- Comparator: Care pathway without liquid biopsy (only tissue biopsy can be performed for molecular profiling)
- Perspective: Public health insurer
- Outcomes: Direct medical cost (drugs, pathological examination, tissue biopsy) and progression-free survival (PFS)
- ICER = $\frac{\text{Cost Intervention – Cost Comparator}}{\text{PFS Intervention – PFS Comparator}}$

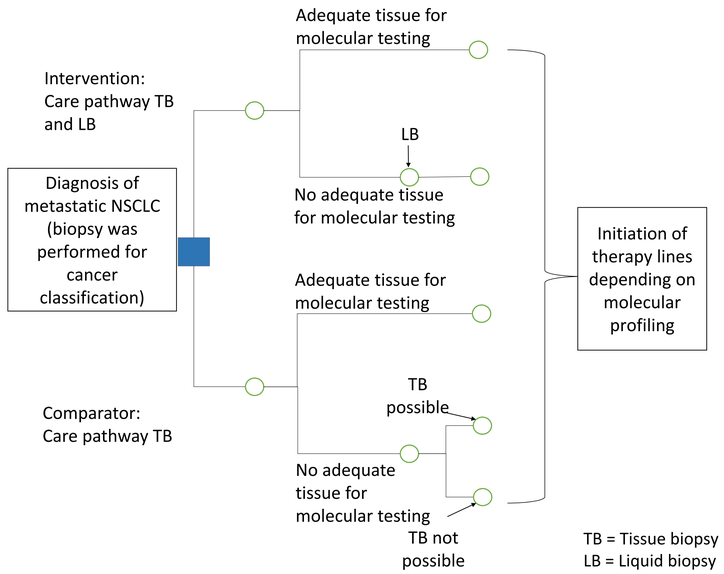

Figure 2 Model structure – Care pathways for modelling

Results

- The results of the microsimulation demonstrated that the use of a liquid biopsy as an add-on was associated with an extended PFS2 in all subgroups.
- A care pathway with liquid biopsy as an add-on to tissue biopsy showed a moderate cost-effectiveness with an incremental cost-effectiveness ratio of €-2,784.
- The care pathway with liquid biopsy showed an ICER of €-3,423 in patients with an activated mutation in the EGFR gene and dominates the pathway without liquid biopsy.

Table 1 ICER of the competing care pathways for different subgroups

ALK	BRAF-V600	EGFR	ROS1	Known alterations	Known and unknown alterations
€2,513	€7,579	€-3,423	€2,241	€-1,170	€-2,784

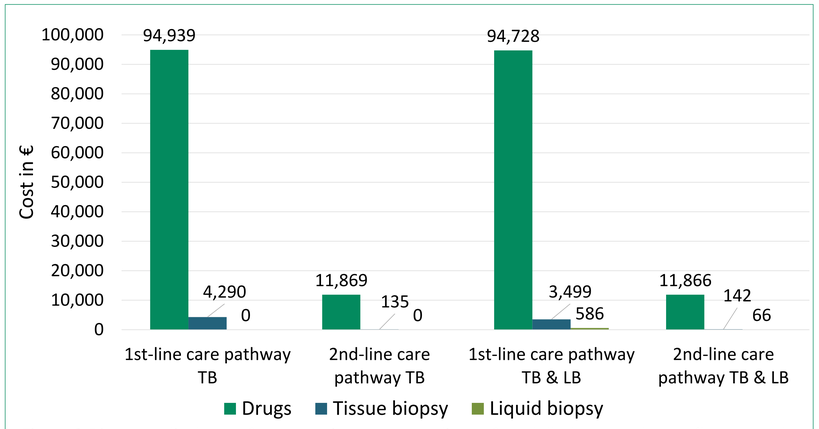

Figure 3 Direct medical costs for respective treatment lines of modelled care pathways (known and unknown alterations)

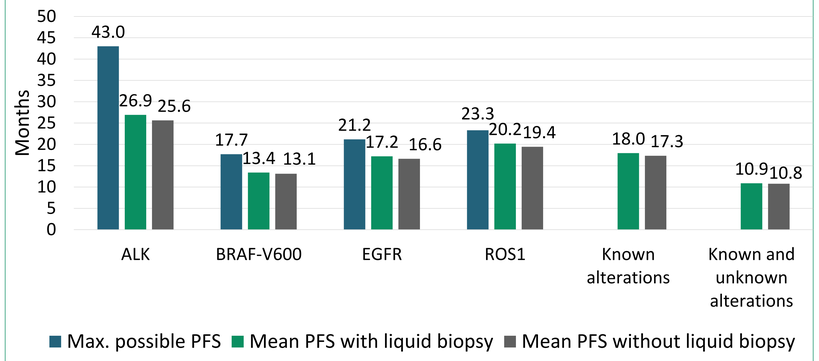

Figure 4 Progression-free survival derived from the respective therapy lines of the corresponding care pathways

Discussion

- Including liquid biopsy as an add-on into the care pathway of metastatic NSCLC had positive clinical effects in terms of PFS and a moderate cost effectiveness, depending on the genetic alteration (highly cost-effective for EGFR mutated patients).
- Liquid biopsy use also appears to be promising for patients with ALK translocations since resistance mechanisms are also well understood with further targeted therapies available and approved.
- The initiation of targeted therapies based on liquid biopsy derived information is linked to a higher response rate than chemotherapy-dominated treatment algorithms.[4,5]
- However, patient access to both molecular differential diagnosis and targeted NSCLC therapies across the course of the disease in Germany is limited and can be traced back to not fully established and inconsistent reimbursement policies which finally control access and translation into care practice.

Literature

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