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Editorial

New challenges for laboratory diagnostics in non-small cell lung cancer

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Lung cancer is still one of the challenges in medicine with major impact on society. With an estimated incidence of 1.35 million new cases worldwide each year it accounts for one of the most frequent cancer diseases. With an estimated mortality of 1.18 million deaths per year, it constitutes one of the most deadly cancer entities [1,2]. The tremendous influence of tobacco smoking is widely recognized which has led to various national anti-smoking campaigns [3–5]. During recent years, mortality rates among men could be reduced considerably after a huge increase during the post-war decades while it reached a plateau phase in women. In the latter group, the dramatic increase occured with some delay, starting in the 1970ies [1,4]. Concerning histological subtyping, non-small cell lung cancer (NSCLC) is the more frequent variant (about 80% of all lung cancers). Unfortunately it is often only detected in late stages of disease (about 80%) when tumor has already spread locally or systemically and cannot be cured by surgical means anymore [6,7]. Screening programs by imaging and biochemical methods have tried to increase the detection rates of early stage cancers, however, they have lacked medical and / or economical efficiency so far [3,8].

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Being confronted with rather poor one-year survival rates of 20% in NSCLC stage IIIb and 5% in stage IV disease, efforts to improve efficacy of systemic therapies have been little successful for many years. However, some moderate progress has been achieved during the recent decade by identifying new radiochemotherapeutic strategies and introducing new biological drugs enabling second and third-line treatments in due course [8–10]. Those developments created new challenges for lung cancer diagnostics for both the imaging and the biochemical part, respectively.

As circulating biomarkers are abundantly released by lung cancer disease, potentially indicate cancer growth at an early time point, can predominantly be assessed by non-invasive means and therefore lend themselves for serial measurements, and are economic as compared to other diagnostic approaches, they are promising tools which might be helpful for supporting an effective diagnosis, estimating of prognosis and therapy monitoring of patients suffering from lung cancer.

Although the course of disease in patients with NSCLC is often quite limited, there are plenty of indications circulating biomarkers can be used for (FIGURE): Supporting the diagnosis would be relevant in case of suspicious symptoms or findings in medical imaging. However, there are also many attempts to apply markers in the non-symptomatic stage for screening purposes. At time of diagnosis, further information is needed concerning the histological subtyping and the estimation of prognosis which are highly relevant for

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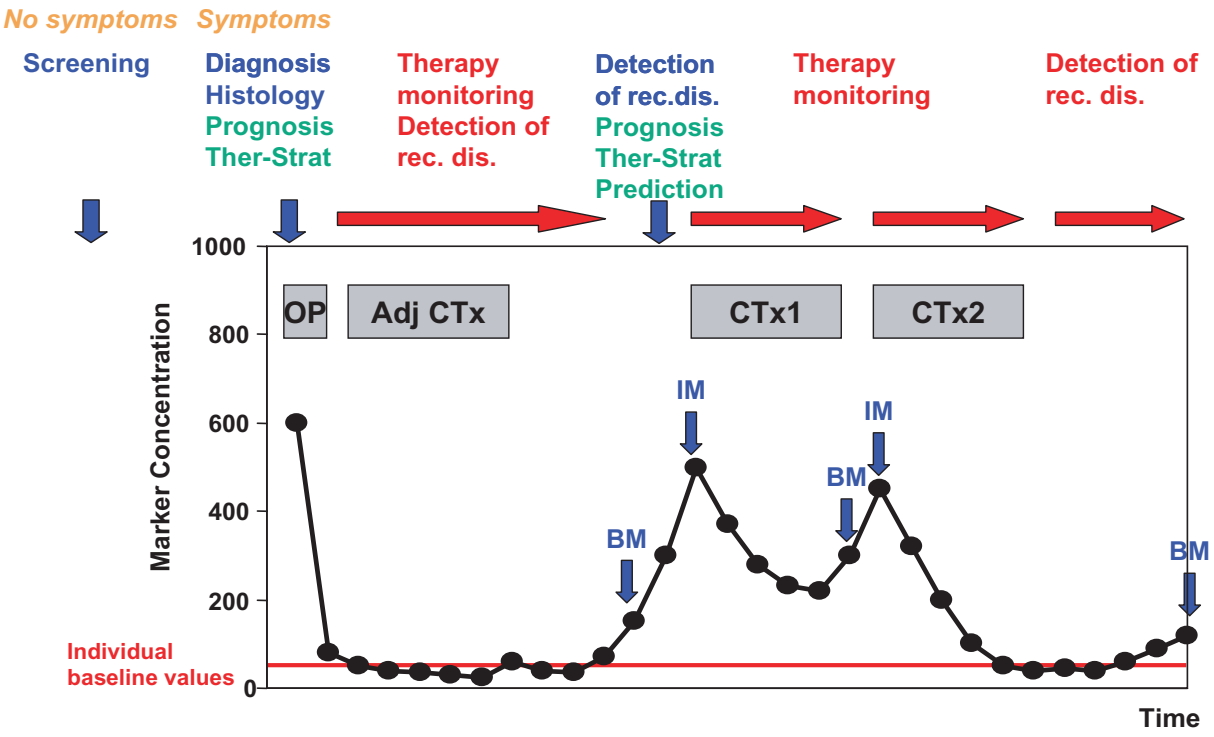

Fig. 1. Indications for the use of circulating biomarkers during the course of cancer disease. During the course of cancer disease, circulating biomarkers are relevant for establishing primary diagnosis, histological subtyping, and prognosis which enables stratification for individual treatment strategies. In the further follow up, they play a role in therapy monitoring during primary (OP = surgery) and adjuvant therapy as well as during systemic cytotoxic therapies (CTx). For detection of recurrent disease, interpretation of relative changes from individual baseline values is required. Often biomarkers (BM) reveal recurrences earlier than imaging techniques (IM) with a lead time of several weeks or months. In the advanced setting, biomarkers provide clinically relevant information concerning prognosis the prediction of respone to therapy.

the selection of the appropriate primary treatment strategy as well as for potential adjuvant therapies. Currently the differentiation between small and non-small cell lung cancer is crucial to stratify the patients for systemic or potentially surgical approaches. Further differentiations between adenocellular and squamous cellular cancers might be relevant in future for the stratification to some biological therapies [8–10]. After primary therapy, circulating biomarkers are important for the early detection of recurrent disease. Thereby the kinetics of marker concentrations interpreted rather by the relative changes from the individual baseline values than crossing any reference values will be of highest relevance and often reveal recurrent disease earlier (BM) with a lead time of several weeks or months as compared to imaging techniques (IM; 11). In the advanced setting, biomarkers should provide information concerning the biology of the tumor, the prediction of respone to therapy, the prognosis and, when measured during the follow up of the treatment applied, the monitoring of the actual therapy efficacy (FIGURE).

In this special edition on circulating biomarkers in NSCLC, we first introduce into the clinical situation of the disease from the view of a thoracic oncologist [12] and demonstrate the potential relevance of biomarkers in occupational medicine for screening purposes, particularly in silicosis patients with high risks of developing lung cancer [13,14]. A further contribution highlights the role of circulating biomarkers for the diagnosis and differential diagnosis in lung cancer patients suggesting a rationale and effective procedure in case of specific symptoms or suspicious findings [15]. The utility of biomarkers for the estimation of prognosis is then discussed for the early and the advanced stages of NSCLC [16]. A special focus is spotted on the use of circulating biomarkers on the therapy monitoring during local and systemic therapy as well as on the follow up after therapy in order to early detect recurrences of the cancer disease [17]. The potential of apoptotic biomarkers as well as of circulating nucleic acids in plasma and serum (CNAPS) which currently are under investigation and might open some views on possible

future diagnosics are presented in the following contributions [18,19]. Finally, the current recommendations on the sensible use of lung biomarkers reflected by international guidelines [20] are demonstrated [21].

We hope to have assembled a broad picture of the relevance of circulating biomarkers in NSCLC disease mirroring the present knowledge in this field and suggest practical procedures for the modern laboratory diagnostics of patients suffering from NSCLC.

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