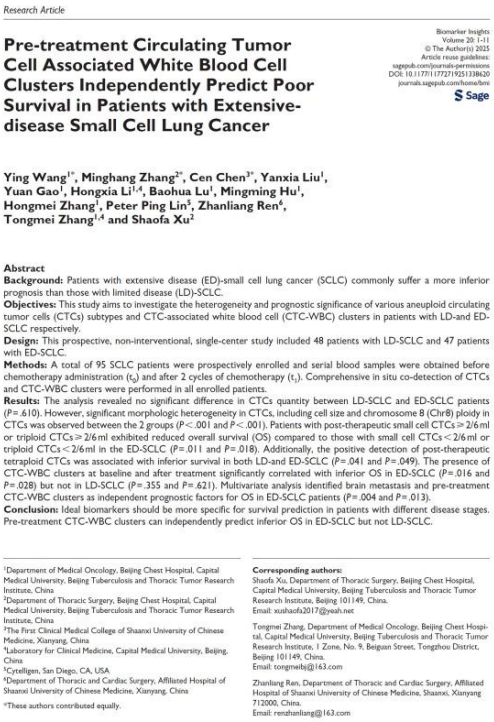
广泛期小细胞肺癌 (ED-SCLC) 治疗前的基线 CTC-WBC 细胞团与较差预后密切相关

分为局限期 (LD) 和广泛期 (ED) 两大类的小细胞肺癌 (SCLC)是致死率最高的肺癌类别。与局限期相比，广泛期小细胞肺癌 (ED-SCLC) 预后更差。为了寻找更有效的判别 SCLC 预后的独立风险因素，北京胸科医院与赛特生物密切合作，在一项非干预性临床研究中针对前瞻性入组的 95 例 SCLC 患者 (包括 48 例 LD 及 47 例 ED) 于化疗前 (t_0) 和二程化疗后 (t_1) 开展了 SE-i•FISH 检测。获得的一系列新发现刚得到发表 (Wang et al. 2025 Biomarker Insights 20:1)。



Research Article

Pre-treatment Circulating Tumor Cell Associated White Blood Cell Clusters Independently Predict Poor Survival in Patients with Extensive-disease Small Cell Lung Cancer

Biomarker Insights
Volume 20: 1-11
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DOI: 10.1177/11772719251338620
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Abstract

Background: Patients with extensive disease (ED)-small cell lung cancer (SCLC) commonly suffer a more inferior prognosis than those with limited disease (LD)-SCLC.

Objectives: This study aims to investigate the heterogeneity and prognostic significance of various aneuploid circulating tumor cells (CTCs) subtypes and CTC-associated white blood cell (CTC-WBC) clusters in patients with LD-and ED-SCLC respectively.

Design: This prospective, non-interventional, single-center study included 48 patients with LD-SCLC and 47 patients with ED-SCLC.

Methods: A total of 95 SCLC patients were prospectively enrolled and serial blood samples were obtained before chemotherapy administration (t_0) and after 2 cycles of chemotherapy (t_1). Comprehensive in situ co-detection of CTCs and CTC-WBC clusters were performed in all enrolled patients.

Results: The analysis revealed no significant difference in CTCs quantity between LD-SCLC and ED-SCLC patients ($P = .610$). However, significant morphologic heterogeneity in CTCs, including cell size and chromosome 8 (Chr8) ploidy in CTCs was observed between the 2 groups ($P < .001$ and $P < .001$). Patients with post-therapeutic small cell CTCs ≥ 2/6 ml or triploid CTCs ≥ 2/6 ml exhibited reduced overall survival (OS) compared to those with small cell CTCs < 2/6 ml or triploid CTCs < 2/6 ml in the ED-SCLC ($P = .011$ and $P = .018$). Additionally, the positive detection of post-therapeutic tetraploid CTCs was associated with inferior survival in both LD-and ED-SCLC ($P = .041$ and $P = .049$). The presence of CTC-WBC clusters at baseline and after treatment significantly correlated with inferior OS in ED-SCLC ($P = .016$ and $P = .028$) but not in LD-SCLC ($P = .355$ and $P = .621$). Multivariate analysis identified brain metastasis and pre-treatment CTC-WBC clusters as independent prognostic factors for OS in ED-SCLC patients ($P = .004$ and $P = .013$).

Conclusion: Ideal biomarkers should be more specific for survival prediction in patients with different disease stages. Pre-treatment CTC-WBC clusters can independently predict inferior OS in ED-SCLC but not LD-SCLC.

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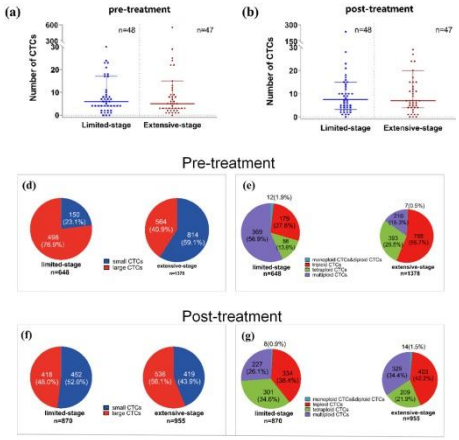
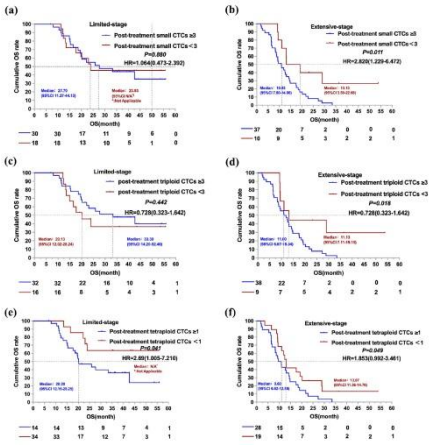
本文要点：

1. 无论治疗前、后，LD 和 ED 两组间的 CTC 数目无显著差别，但 8 号染色体倍体和细胞形态则有显著差别。其中，治疗前 LD 和 ED 分别以大细胞 (76.9%) 和小细胞 (59.1%) 为主；治疗后，比例变为相反，分别以小细胞 (52.0%) 和大细胞 (56.1%) 为主。倍体分析显示，治疗前 LD 和 ED 分别以多倍体 (56.9%) 和三倍体 (55.7%) 为主；治疗后 LD 无特定占优势倍体，ED 仍以三倍体为主 (42.2%).

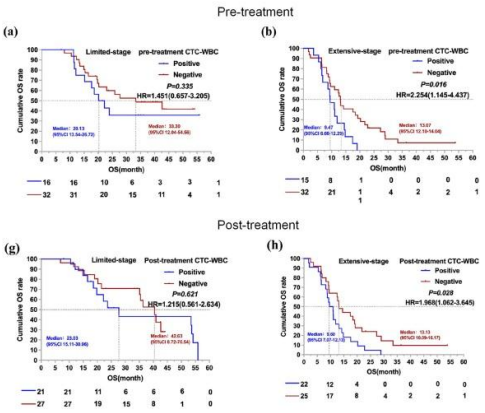


2. 对于接受治疗的 ED-SCLC (t_1)，检测出 ≥ 3 小细胞或三倍体 CTC/6 ml 血液，患者总生存期 (OS) 显著降低，与 < 3 患者相比，差异有统计学意义。对于接受治疗的 LD 和 ED 患者，无论治疗前、后检测

出任何数目的四倍体 CTC，则患者预后较差。



3. 对于 ED-SCLC，治疗前或治疗开始后检测出 CTC-WBC 细胞团，则患者预后较差，OS 显著降低。



结论：

统计学多元分析显示，ED-SCLC 患者治疗前存在 CTC-WBC 或发生脑转移是不良预后 (OS 显著降低) 的有效独立风险因素指标。