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# EPAC-Lung

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# TRANSLATIONAL RESEARCH

#### 210 EPAC-Lung: Pooled analysis of circulating tumor cells in advanced nonsmall cell lung cancer

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**Background:** We assessed the clinical validity of circulating tumor cell (CTC) quantification for prognostication of patients with advanced non-small cell lung cancer (NSCLC) by undertaking a European pooled analysis of individual patient data. This is the largest study of its kind and the first to examine between-centre heterogeneity of CTC identification in NSCLC.

Methods: Nine European NSCLC CTC centers were asked to provide reported/unreported anonymised data for patients with advanced NSCLC who participated in CellSearch CTC studies from January 2003 - March 2017. We used Cox regression models, stratified by centre, to establish the association between CTC count and survival. We assessed the added value of CTCs to prognostic clinico-pathological models using likelihood ratio (LR) statistics and c-indices.

**Results:** Seven out of nine eligible centers provided data for 550 eligible patients, including 209 patients whose prognostic information was previously unpublished. CTC counts of  $\ge 2$  and  $\ge 5$  per 7.5 mL were associated with reduced progression-free survival ( $\ge 2$  CTCs: HR 1.72, p < 0.001;  $\ge 5$  CTCs: HR 2.13, p < 0.001;  $\ge 5$  CTCs: HR 2.75, p < 0.001) and overall survival ( $\ge 2$  CTCs: HR 2.18, p < 0.001;  $\ge 5$  CTCs: HR 2.75, p < 0.001), respectively. Survival prediction was significantly improved by addition of baseline CTC count to LR clinico-pathological models (log-transformed CTCs p < 0.0001;  $\ge 2$  CTCs p < 0.0001), while more moderate improvements were observed with the use of c-index models. There was minor evidence of between-center heterogeneity in the effect on PFS, but not OS.No difference in CTC profile was observed between key NSCLC molecular subsets such as EGFR, ALK, and KRAS.

**Conclusions:** These data confirm CTCs as an independent prognostic indicator of progression-free survival and overall survival in advanced NSCLC. CTC count improves prognostication when added to full clinico-pathological predictive models.  $\geq$ 2 CTCs is an appropriate cutoff to move towards establishing clinical utility.

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