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Prognostic role of exosome in patients with stage IIIA(N2) non-small cell lung cancer treated with perioperative durvalumab in addition to neoadjuvant chemotherapy in the trial SAKK 16/14

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Background

In the trial SAKK 16/14 perioperative durvalumab showed favorable outcomes for patients (pts) with resectable stage IIIA(N2) non-small cell lung cancer (NSCLC). Exosomes are extracellular vesicles (EV) released by cancer cells, holding promise as prognostic biomarkers and for therapeutic monitoring.

Methods

In this phase II trial 68 pts with stage IIIA(N2) NSCLC were treated with perioperative durvalumab in addition to neoadjuvant chemotherapy with cisplatin/docetaxel, followed by surgery. For each patient, blood serum samples were acquired at baseline (timepoint 1, TP1), post neoadjuvant chemotherapy (TP2), post neoadjuvant durvalumab (TP3) and after four cycles of adjuvant durvalumab (TP4) and at the end of adjuvant durvalumab (TP5). This study examines exosomal dynamics in 20 serum samples from this trial. A recently developed galectin-based exosome isolation bead technique was used. Bead-based flow cytometry was used to assess five exosomal markers (PD-L1, PanEV, PanCK, EpCAM, and CD45) at five defined time points. Successful exosome isolation was confirmed by nanoparticle tracking analysis and electron microscopy.

Results

There was a trend toward decreasing extracellular vesicle (EV) mean fluorescence intensity (MFI) values at TP2. Notably, smoking status influenced exosomal profiles, with current smokers exhibiting significantly lower PanEV levels. The area under the receiver operating characteristic curve (AUC) for PD-L1$^+$ PanEV$^+$ EV-bead complexes at TP4 was 0.875. Prognostic analysis and AUC evaluation revealed a significant negative correlation between post-therapy (TP4) PanEV$^+$ PanCK$^+$ EV-bead complexes and both overall survival (OS) and event-free survival (EFS) ($p = 0.0067$, AUC = 0.838; $p = 0.0003$, AUC = 0.789, respectively). A similar trend was observed for PanEV$^+$/PanCK$^+$ levels at TP1 and for EpCAM$^+$/PanEV$^+$ exosomes at TP4.

Conclusions

These findings emphasize the feasibility of assessing exosomes in NSCLC and highlight their prognostic potential. Elevated post-treatment PanEV/PanCK levels were associated with significant shorter EFS and OS, highlighting the potential of exosome-based liquid biopsies.

Clinical trial identification

NCT02572843.

Legal entity responsible for the study

Swiss Group for Clinical Cancer Research (SAKK).

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Disclosure

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