PUBLICATIONS

ORAL ONCOLOGY
The Head and Neck Cancer Journal

Non-invasive Real-time Chemoresistance Profiling of Circulating Tumor Associated Cells in Head and Neck Cancers.

Authors
Stefan Schuster, Dadasaheb Akolkar, Darshana Patil, Vineet Datta, Sanket Patil, Vishakha Mhase, Sachin Apurwa, Sushant Pawar, Ajay Srinivasan, Rajan Datar.

ABSTRACT

Background

Standard of Care (SoC) systemic treatment approaches for SCCHN include taxanes (paclitaxel, docetaxel), platins (cisplatin, carboplatin) and antimetabolites (5-fluorouracil, methotrexate, gemcitabine). However innate and acquired resistance to these agents are frequently encountered in SCCHN and are largely undetected until disease progression. There are presently no means for real-time chemoresistance monitoring in SCCHN. We describe chemoresistance profiling (CRP) in SCCHN using peripheral blood Circulating-Tumor Associated Cells (C-TACs), which are EpCAM+, panCK+ and CD45 cells of tumorigenic origin.

Method

Peripheral blood was collected from 252 SCCHN patients, among whom 156 were therapy naïve and 96 were pretreated. C-TACs were enriched and harvested from Peripheral blood mononuclear cells (PBMCs) using an epigenetically activating media that is cytotoxic towards normal (non-tumorigenic) cells but confers survival privilege on apoptosis resistant C-TACs (of tumorigenic origin). C-TACs were confirmed by immune-fluorescent (IF) staining for EpCAM, pan-CK and CD45. C-TACs were treated in vitro with anticancer agents used in SCCHN and the surviving fraction estimated to determine resistance.

Results

Innate chemoresistance was observed in 40.7 % of therapy naïve patients' samples, which included resistance towards platins in 44.2% cases, taxanes in 37.7% cases and antimetabolites in 40.9% cases. Acquired chemoresistance was observed in 91.1% pretreated patients' samples, which included resistance towards platins in 90.5% cases, taxanes in 90.5% cases and antimetabolites in 93.8% cases.

Conclusion

Chemoresistance profiling (CRP) of C-TACs is a viable strategy to determine innate and acquired chemoresistance in SCCHN. Higher chemoresistance in C-TACs from pretreated patients, as compared to C-TACs from therapy naïve patients indicates that C-TACs are resistance-educated by previous treatments.

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