Kurzzusammenfassung: Drug resistance is currently an inevitable consequence of drug therapy for solid cancers and greater understanding of underlying resistance mechanisms using novel tools that can be translated into the clinical setting to guide treatment selection is critical to improve clinical cancer outcomes. I will describe the impact of an important compensatory/drug resistance mechanism we have termed therapy-induced ErbB/HER/Met receptor tyrosine kinase (RTK) rewiring; whereby tumors evolve, under treatment pressure, a conformational alteration in ErbB/HER receptor(s) favouring the formation of increased oncogenic ErbB dimer which can now be measured in circulating exosomes in cancer patients.

Tissue and circulating exosome based ErbB assays have been combined successfully with the use of clinical imaging to predict the efficacy of cancer treatment, especially in the context of human epidermal growth factor receptor (HER) targeted treatments. We have recently shown in a Phase II head and neck anti-HER cancer therapy trial, that exosomal HER receptor measurements, which present a new way of following this receptor rewiring mechanism, can contribute significantly to the prediction of treatment response/resistance as measured by CT (RECIST) (ASCO, 2018). Furthermore, we have demonstrated in preclinical models and breast cancer patients that exosomal PD-L1 is part of a tightly regulated immune surveillance mechanism linking exosomal measurements in the blood to direct cell-cell immunosuppressive interactions. These new blood multianalytes are of value to contribute towards developing a biologically based & translationally oriented Imaging-Omic combination approach for clinical studies.

Learning objectives:
State of the art exosome and immunological assays that can be combined with medical imaging in targeted therapies and conventional chemotherapy studies.

Lernziele: The ability to monitor non-invasively these biological/immunological mechanisms may facilitate novel design of stratified and sequential treatment study combining targeted therapies and conventional chemotherapy and immunotherapeutics.
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