PLENARY SESSION 3: Immunological approach to personalized medicine

O3.1

No abstract available

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The Complex Challenges of Stratifying Patients for Immunotherapy

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With an increasing focus on the delivery of precision medicine, biomarkers for patient stratification play a critical role in both immunotherapy drug development and the subsequent diagnostic testing of patient specimens. In the area of immunotherapy, a variety of cell, tissue and genomic based biomarkers are currently used for purposes ranging from exploratory assessments to patient stratification during the various stages of the drug development process. Recent examples include as PD-L1 status which is considered a companion diagnostic for certain therapeutic approaches and clinical indications; tumor mutation burden; neo-antigen burden; genomic instability; and cytokine/chemokine expression patterns. The use of biomarkers in trial design for individual immunotherapeutic approaches, as well as combination therapies, is increasingly relevant in this very complex and competitive area of drug development. The topics covered in this presentation will include a review of relevant biomarkers for immunotherapies; the impact of biomarkers on trial design and execution; and the role of companion diagnostics in the development and commercialization of specific immunotherapies.

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No abstract available

O3.5 Patient-specific peptide vaccination

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Therapeutic cancer vaccination trials reaching phase 3 until very recently were either complete failures or showed only marginal benefit. In contrast, there is a large number of phase II or earlier clinical trials, and case reports, reporting therapeutic vaccination with tumor antigens, viral, mutated, tumor-associated or tissue-specific, leading to antigen specific T cell responses associated with clinical benefit, especially when efficient adjuvants had been used. Since analysis of T cell responses of melanoma patients responding to checkpoint inhibition indicated neoantigens as targets of such therapeutically effective T cells, efforts are now concentrating on developing vaccination strategies against such antigens. Based on various sources, it can now be estimated that only between 0.1 and 1 percent of exome mutations can be detected as neoantigens.

However, tumors regularly present non-mutated tumor associated peptides with highly tumor specific expression. For both categories, the approach needs to be personalized with few exceptions, since both mutated as well as non-mutated tumor specific HLA ligands are different in every patient. Analyzing the entire detectable landscape of HLA ligands on tumor samples, consisting of 1000 through 5000 non-mutated peptides per sample, we do find dozens to hundreds of peptides in germline sequence with apparently tumor specific expression, based on the absence of these peptides on adjacent autologous benign tissue and absence on a large number of normal tissue samples from all organs and tissue types available for analysis, all, of course, within the sensitivity limits of our technology, tandem mass spectrometry. The population of these tumor peptides is highly different between patients. Many of these apparently tumor specific peptides are immunogenic, as tested by in vitro priming experiments with human T cells from healthy donors. We suggest that germline sequence HLA ligands with tumor specific expression should be efficient as targets for personalized antigen specific immunotherapy, combined with neoantigens, if one finds them. Critical will be the use of efficient vaccine delivery, powerful adjuvants, and combination with checkpoint inhibition or other immunomodulation.