Immunotherapy, Bringing It All Together: The Next Generation of Approaches & Combinations

Moderator: Axel Hoos, MD, Vice President, Oncology Research and Development, GlaxoSmithKline

Panelists:

- Neil Berinstein, MD, Affiliate Scientist, Sunnybrook Research Institute
- Paul Higham, Chief Executive Officer, Immatics
- Sara Zaknoen, MD, CMO, Polynoma, LLC
- Dennis L. Panicali, Ph.D, Vice President, Technical Operations Bavarian Nordic ImmunoTherapeutics
- Charles J. Link, Jr. MD, Chairman, Chief Executive & Scientific Officer at NewLink Genetics Corp

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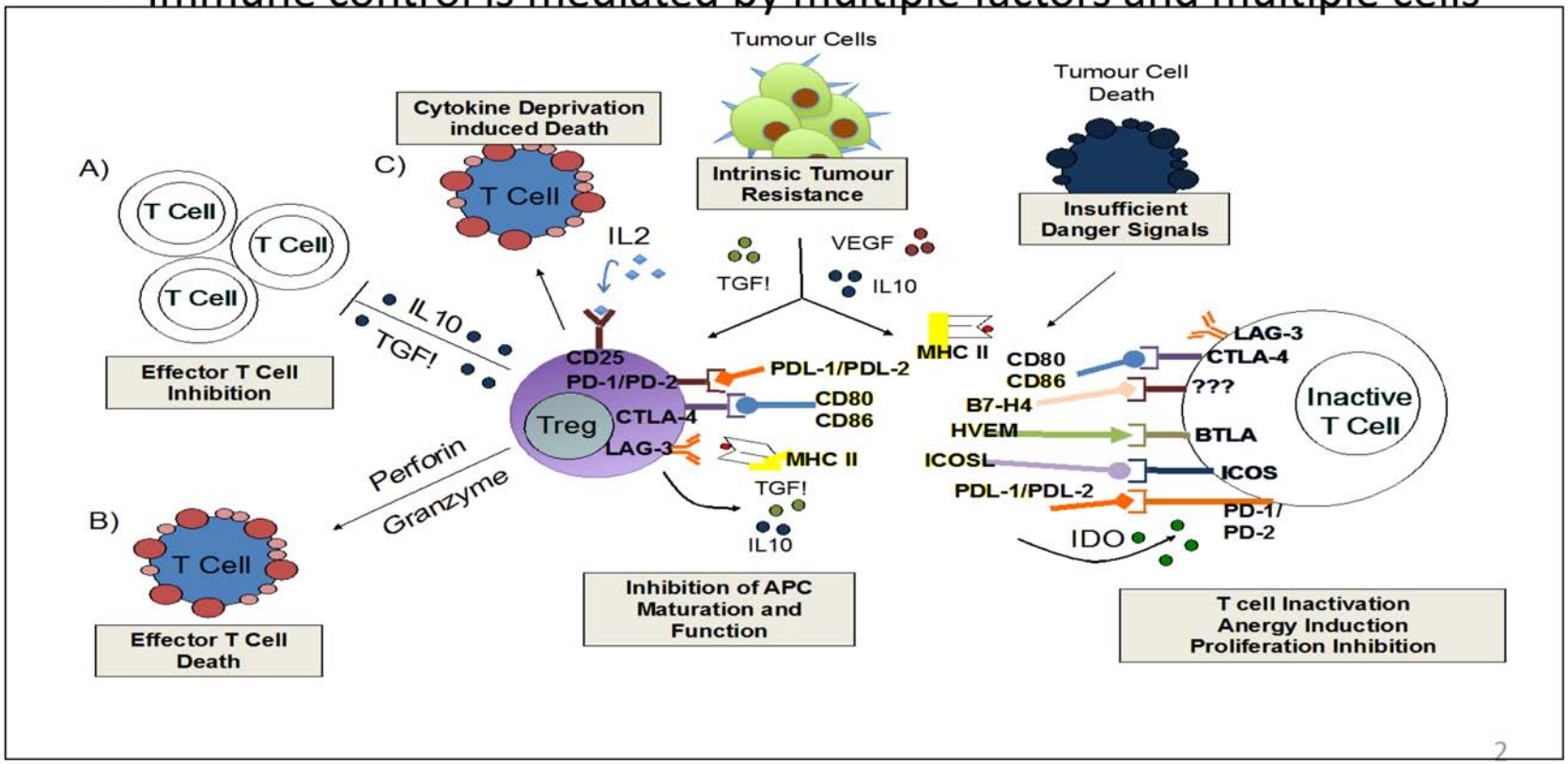
Challenges for development of cancer immunotherapies

- Cancer immunotherapy is mechanistically different than most other cancer therapeutics
  - Immune system is complex with multiple cellular players and exquisite regulation
    - Immune control is mediated by multiple factors and multiple cells

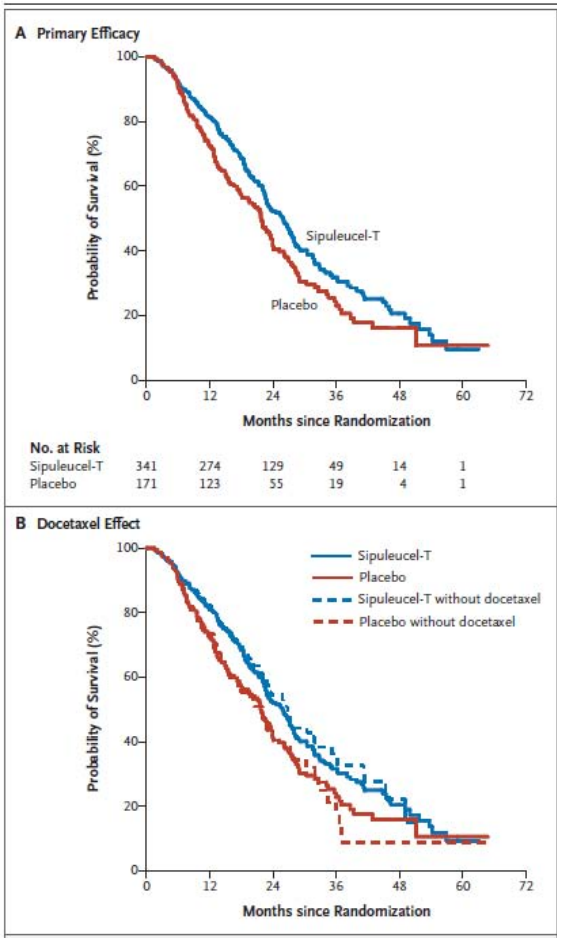


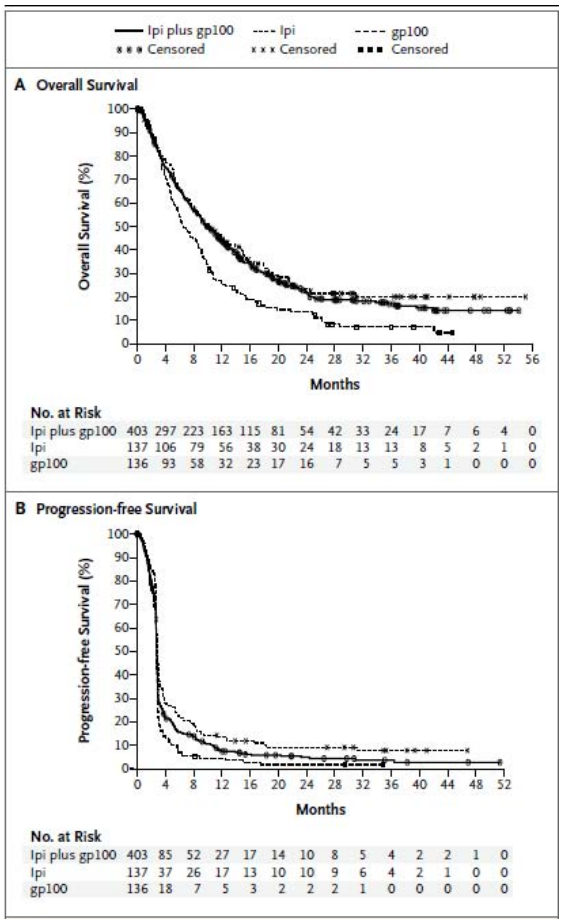
Challenges for development of cancer immunotherapies

- Immune response is suppressed in cancer with greater suppression as cancers progress
  - Suppression may be greatest in the tumour microenvironment
  - Elimination, Equilibrium, Escape (R. Schreiber)
- High levels of tolerance to most common Tumour Associated Antigens (required to minimize autoimmunity)

Challenges for development of cancer immunotherapies

– Immune response takes time to fully develop





Challenges for development of cancer immunotherapies

- Immune activation monitoring is not yet fully validated in the clinic
- Difficult to measure/monitor the specific details of human response to cancer in other species-antigens, cytokines, immune cells are species-specific
- Standard therapies for cancer may have distinct effects on immune function
- Many immunotherapies are best at controlling low volume or microscopic disease and preventing progression/metastases rather than shrinking primary tumour masses
    - Thus must use different paradigms in designing, monitoring and developing immunotherapeutics

Immunotherapy Challenges are dependent on the phase of clinical development

Preclinical	Phase I	Phase II	Phase III

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Predictive animal models			
Models of tolerance with human reagents			
Representative toxicology models			
Species differences			

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Preclinical	Phase I	Phase II	Phase III
Predictive animal models	Patient population for initial trials		
Models of tolerance with human reagents	Validated immune response assays		
Representative toxicology models	Assessment of immune response in tumour tissue		
Species differences			

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Preclinical	Phase I	Phase II	Phase III
Predictive animal models	Patient population for initial trials	Documenting clinical activity	
Models of tolerance with human reagents	Validated immune response assays	Combination therapies-standard care, immune modulation	
Representative toxicology models	Assessment of immune response in tumour tissue	Incorporating scientific improvements	
Species differences			

Immunotherapy Challenges are dependent on the phase of clinical development

Preclinical	Phase I	Phase II	Phase III
Predictive animal models	Patient population for initial trials	Documenting clinical activity	Biomarkers for better assessment of those who may benefit most
Models of tolerance with human reagents	Validated immune response assays	Combination therapies-standard care, immune modulation	Time and size of trials
Representative toxicology models	Assessment of immune response in tumour tissue	Incorporating scientific improvements	Changing standard of care
Species differences			

Challenges for all Phases

Preclinical	Phase I	Phase II	Phase III

- Cost
- Time
- Access to other immunomodulatory/therapeutic reagents
- Regulatory
  - establishing infrastructure to meet clinical and manufacturing regulatory requirements
- Commercial structure
  - Biotechnology companies are usually technology champions and technology experts
    - Need partners to complete clinical development/drug registration
  - Partners can bring resources, reagents, clinical, regulatory and marketing expertise
  - Achieving effective/ideal partnership not easy

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