Current Immunotherapy Strategies in the Management of Solid Tumors

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Current Immunotherapy
Strategies in the Management of Solid Tumors

• The rapid pace of cancer immunotherapy research
• Advances in technology for discovery of targets
  – On tumor whole exome sequencing (WES)
  – On immune cells
• The range of immunotherapeutic approaches available to treat cancer patients
  – Vaccine induced adoptive immunity and adoptive transfer of T-lymphocytes
  – Antibody therapies: target on tumors vs target on immune cells
  – Chimeric Antigen Receptor (CAR) T-cells
• Explanation of the molecular mechanisms of checkpoint inhibitors and other key emerging immunologic strategies
The Rapid Pace of Cancer Immunotherapy Research

From the breakthrough of year 2013 for Nature and Science to the inspiration of the moonshot project for next generation immunotherapy
Rapid and Durable Changes in Target Lesions

1 mg/kg nivolumab + 3 mg/kg ipilimumab

• A 52-year-old patient presented with extensive nodal and visceral disease

• Baseline LDH was elevated (2.3 x ULN); symptoms included nausea and vomiting

• Within 4 weeks, LDH normalized and symptoms resolved

• At 12 weeks, there was marked reduction in all areas of disease as shown

LDH, lactate dehydrogenase; ULN, upper limits of normal

Neoantigens
High mutation frequency as a likely source of neo-antigens


Mutational Load Creates Neoantigens

Current Potential Pipelines of WES for Neoantigen Discovery and Precision Oncology

Current Immunotherapy

The Range of Immunotherapeutic Approaches Available to Treat Cancer Patients

- Vaccine inducing adoptive immunity (DC-based, peptides plus adjuvants, RNA)
- Adoptive transfer of T-lymphocytes (stem cell-like TMSC their key genes transfer)
- Antibody therapies: Target on tumors (HER2, EGFR, MET, VEGF, and CD20 others) and target on immune cells (check point inhibitors and costimulations)
- CAR T-cells


TMSC, T-memory stem cells
Local Radiotherapy and Granulocyte-Macrophage Colony-Stimulating Factor to Generate Abscopal Responses in Patients With Metastatic Solid Tumors: A Proof-of-Principle Trial

Encouse B Golden, Arpit Chhabra, Abraham Chachoua, Sylvia Adams, Martin Donach, Maria Fenton-Kerimian, Kent Friedman, Fabio Ponzo, James S Babb, Judith Goldberg, Sandra Demaria, Silvia C Formenti

Talimogene Laherparepvec Improves Durable Response Rate in Patients With Advanced Melanoma

Intranodal injection with GM-CSF

Responses were observed in both injected and un-injected lesions, including a 50% decrease in size in 15% of evaluable, un-injected, measurable visceral lesions.

C. IIIB, IIIC or IVM1a

D. IVM1b or c

First-line

≥Second-line

Explantion of the Molecular Mechanisms of Checkpoint Inhibitors and Other Key Emerging Immunologic Strategies

Explanation of the Molecular Mechanisms of Checkpoint Inhibitors and Other Key Emerging Immunologic Strategies


OPTIMIZING CANCER IMMUNOTHERAPY: CHALLENGES AND OPPORTUNITIES