Immunotherapy for head and neck squamous cell carcinoma

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Disclosure
Immunotherapy for HNSCC

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The following potential conflict of interest relationships are germane to my presentation.

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Status of FDA devices used for the material being presented
NA/Non-Clinical

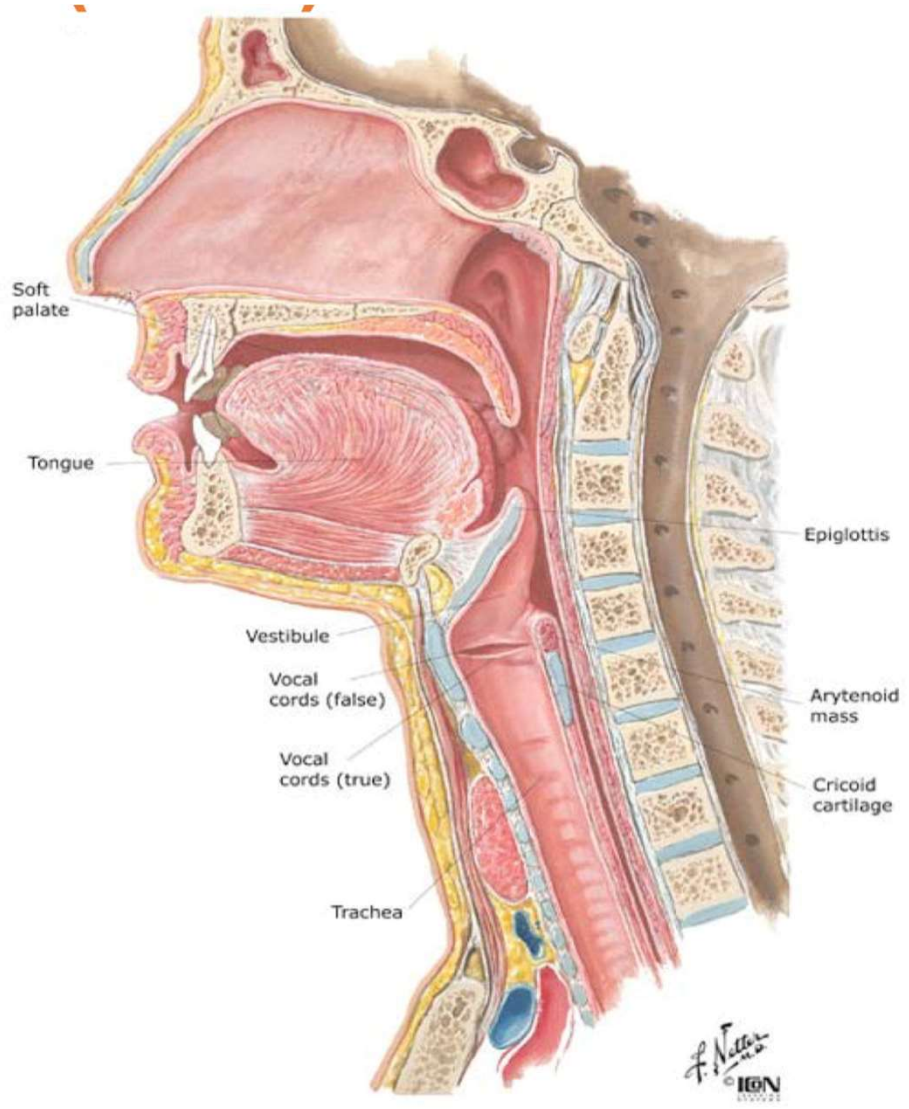
Status of off-label use of devices, drugs or other materials that constitute the subject of this presentation
NA/Non-Clinical

Head & Neck SCC

- Head and neck squamous cell carcinoma (HNSCC) is the sixth most common malignancy worldwide, with 60,000 new cases per year in the United States
- Alcohol consumption and tobacco use are the predominant risk factors for HNSCC
- Other risk factor may include genetic disorder or virus such as human papilloma virus (HPV) and Epstein–Barr virus (EBV) infections

Head & Neck SCC

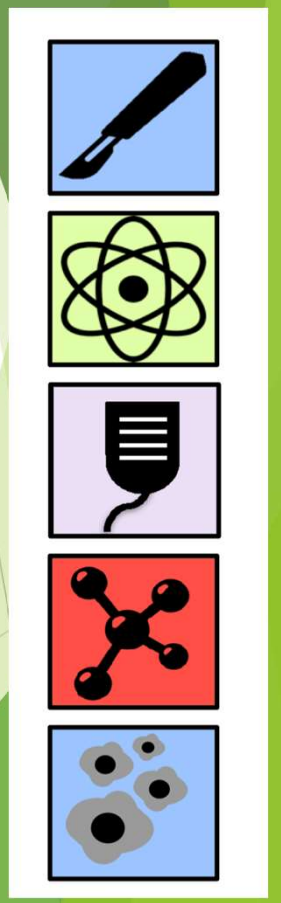
- HNSCCis a heterogeneous disease occurring in various sites, including the oral cavity, nasopharynx, oropharynx, and hypopharynx



Head & Neck SCC Treatment

- The current treatments for HNSCC patients include:

Surgery	Local/Regional
Radiation therapy	
Chemotherapy	Advanced / Metastatic
Targeted Therapy	



Head & Neck SCC Treatment

- Treatment is based on the primary tumor site, stage of the disease, patient's status, and prior therapies.
- Treatment failure and locoregional recurrence are common and account for the majority of deaths

Head & Neck SCC Treatment

T1-2

Head & Neck SCC Treatment

T3-4

Head & Neck SCC Treatment

- The conventional treatments are associated with severe long-term side effects.

- **Disfigurement**
- **Loss of function**
- **Toxicity**
- **Dysphagia**
- **Neutropenia**
- **Anemia**
- **Thrombocytopenia**
- **Hyponatremia**

Head & Neck SCC Treatment

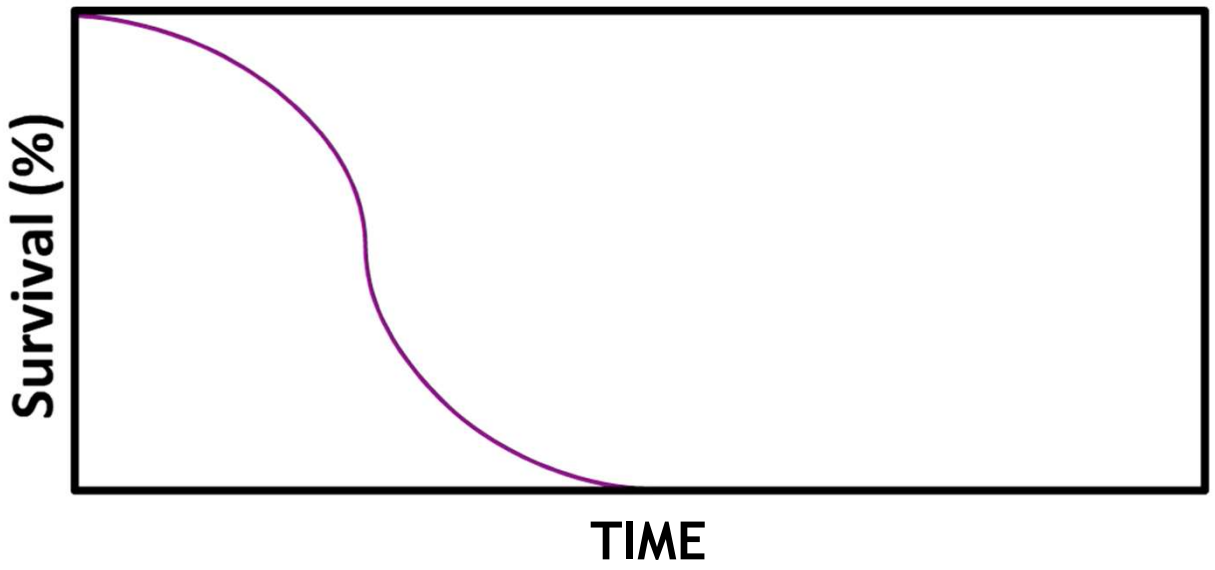
- the 5-year overall survival (OS) rate has remained 40–50% over the last four to five decades despite recent advances in the treatment of patients with HNSCC, such as transoral robotic surgery, precise intensity-modulated radiotherapy (IMRT), multiagent chemotherapy regimens, and the development of targeted therapies.

- Therefore, there is a need for novel treatment strategies that are less toxic and able to extend survival rates and improve patient quality of life.

Head & Neck SCC Treatment

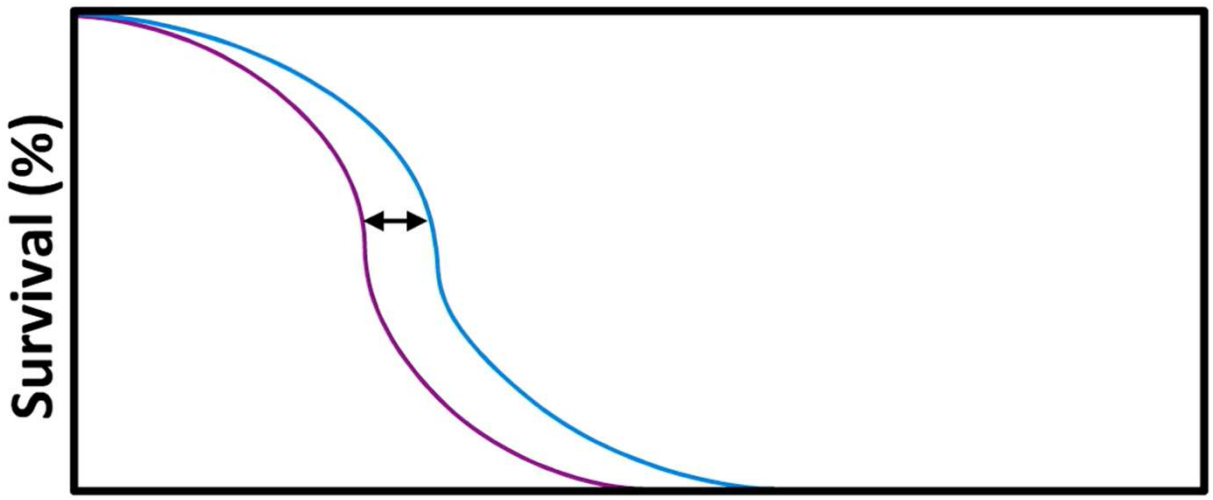
- The immune system plays a major role in the development and progression of HNSCC with numerous immunological alterations occur that allow the tumors to escape immunosurveillance.

- Various immunological strategies have been proposed in recent years in order to restore the function of the host's immune system and induce anti-tumor immune responses in HNSCC.



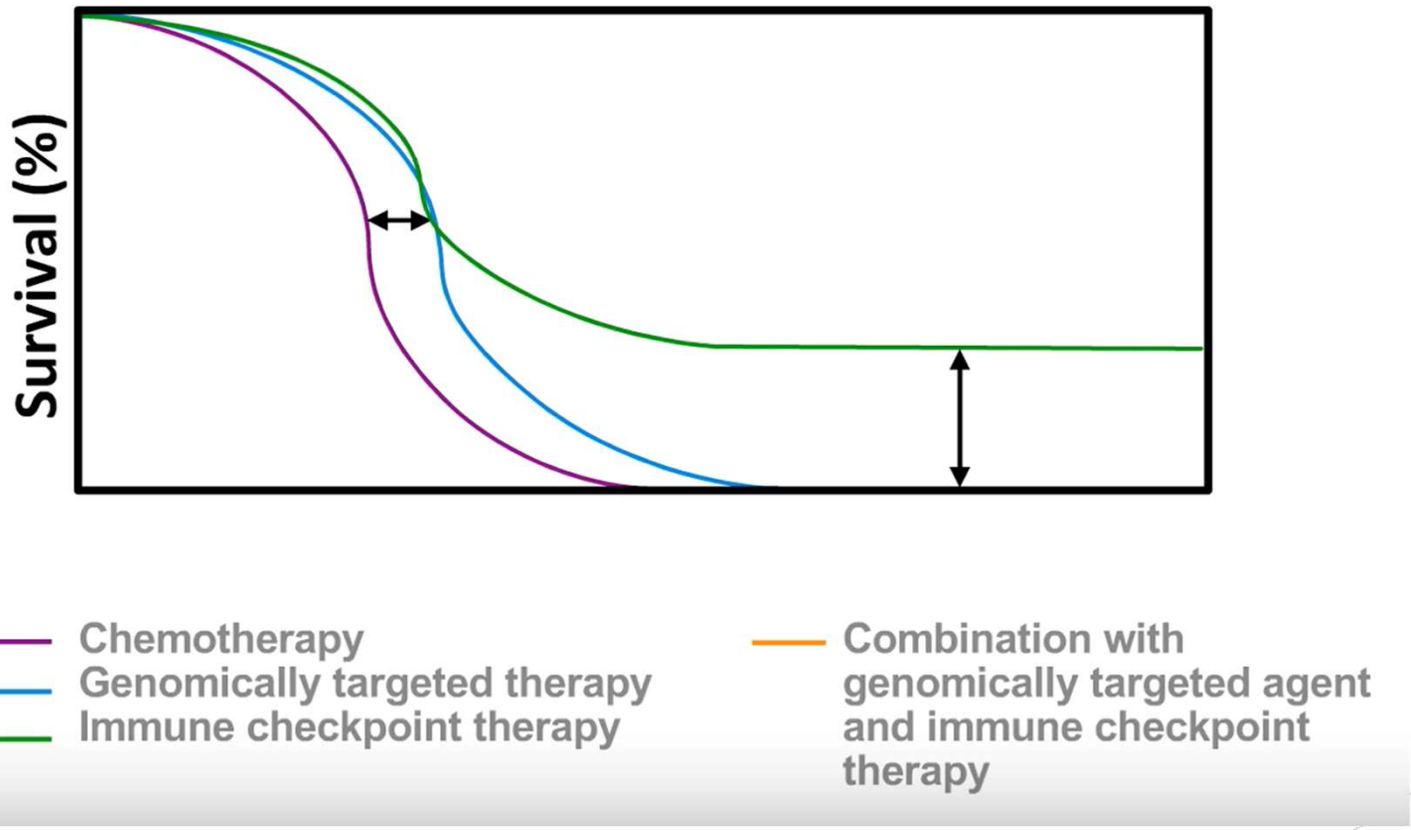
Head & Neck SCC Treatment

Sharma P & Allison JP. Cell 2015

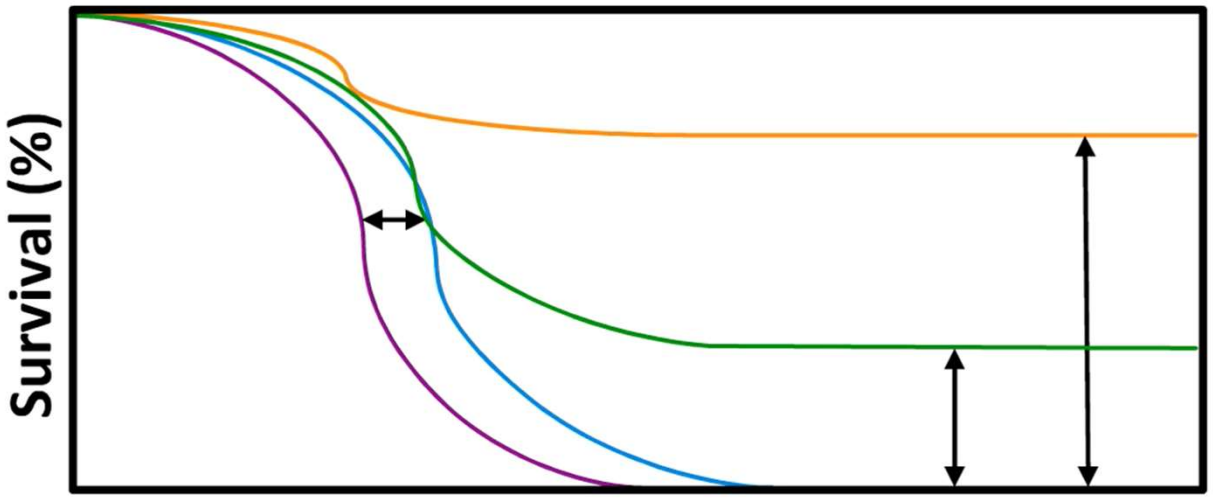


Chemotherapy
Genomically targeted therapy
Immune checkpoint therapy
Combination with genomically targeted agent and immune checkpoint therapy

Head & Neck SCC Treatment



Head & Neck SCC Treatment



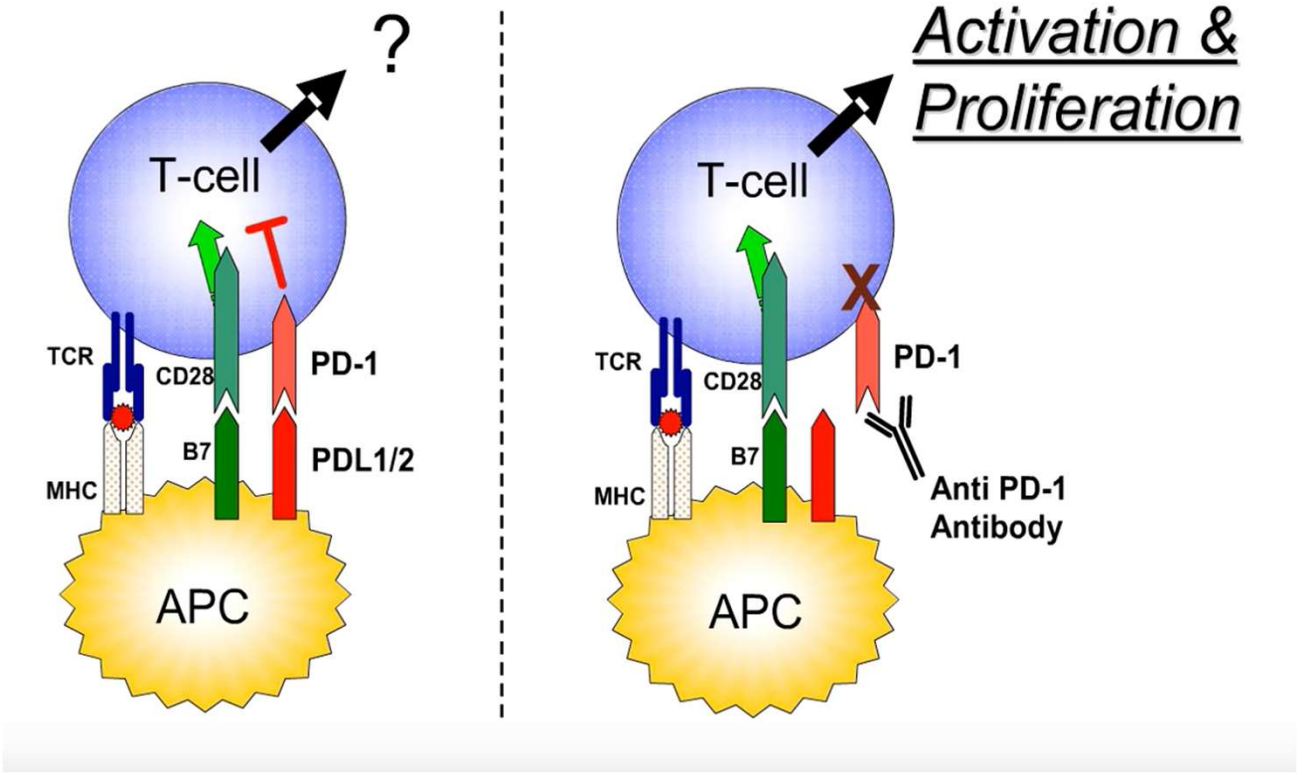
Chemotherapy
Genomically targeted therapy
Immune checkpoint therapy
Combination with genomically targeted agent and immune checkpoint therapy

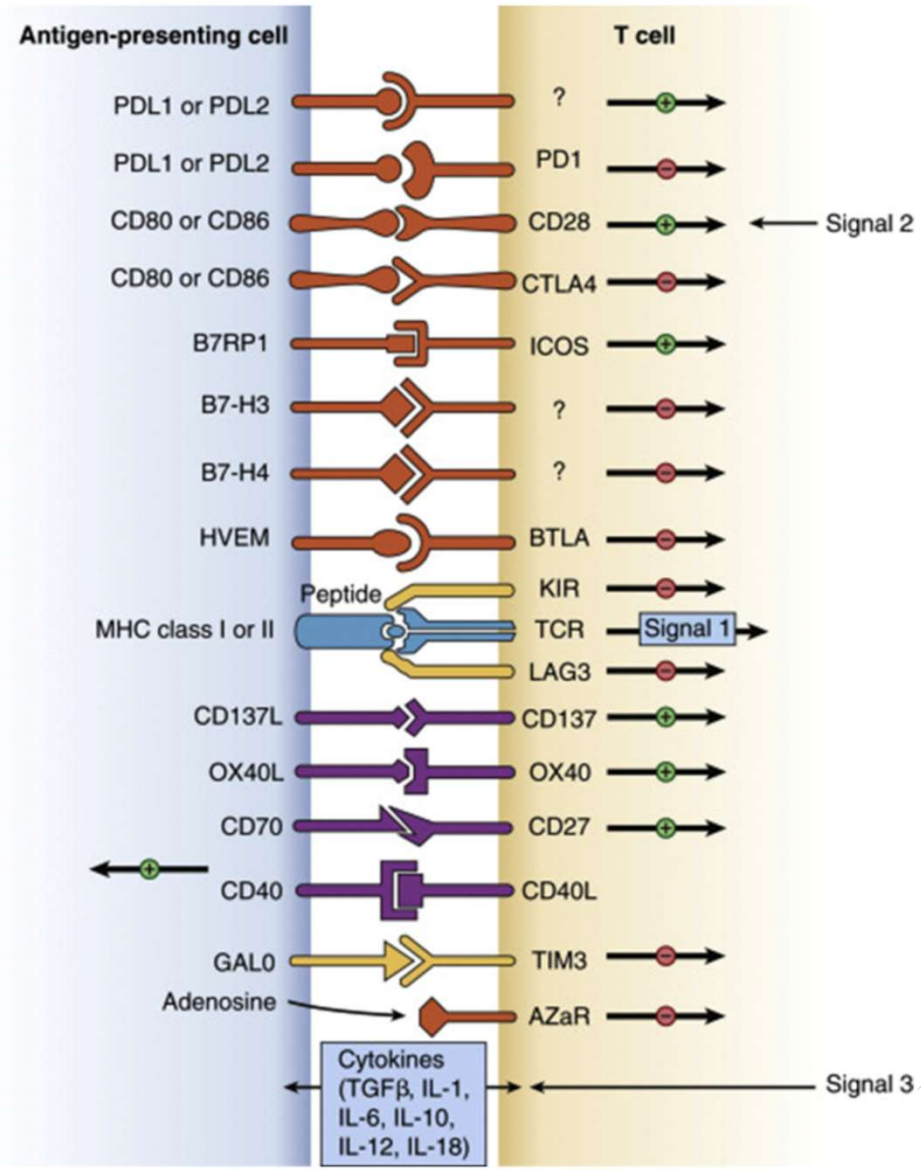
Head & Neck SCC Treatment

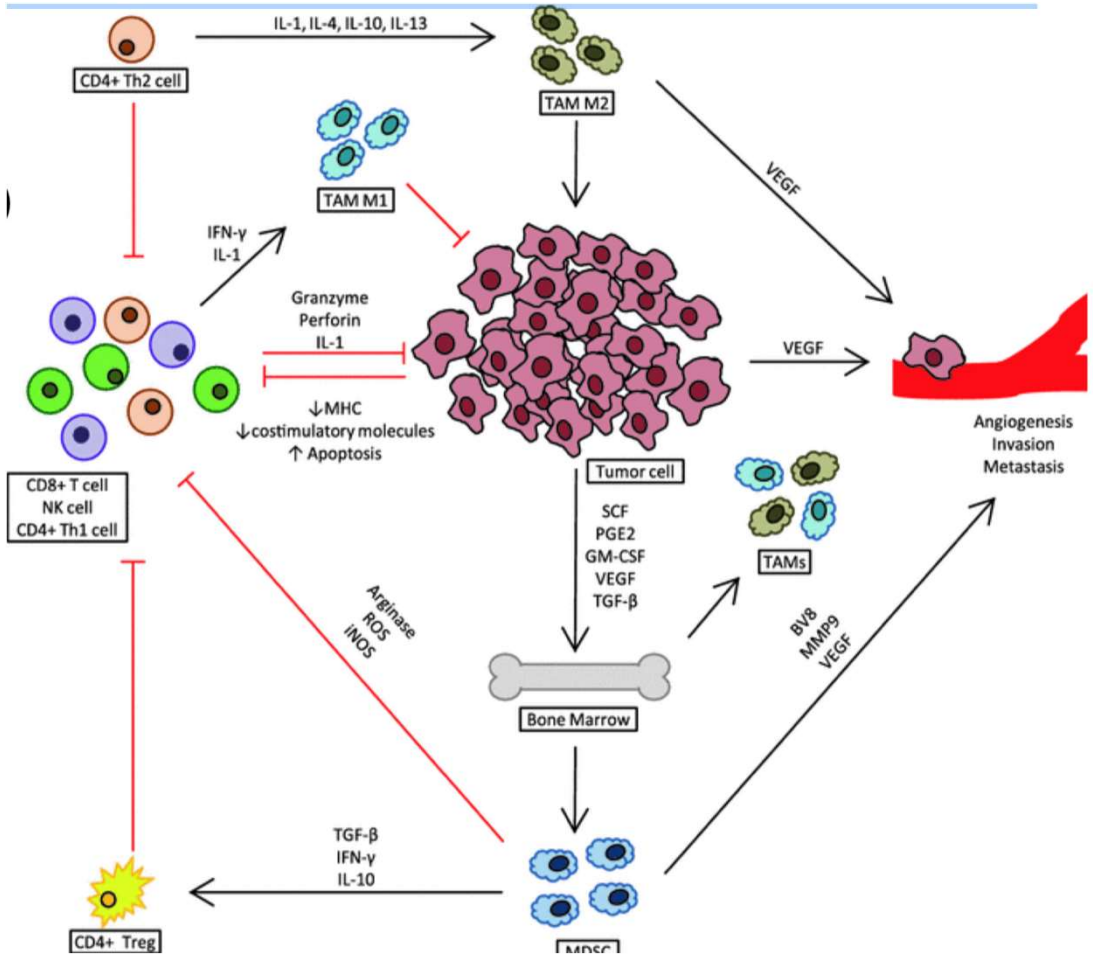
Immunotherapy for HDSCC

Immunosurveillance of cancer is a coordinated process involving both the innate and adaptive immune system.

Identifying tumor antigen-specific T cells from patients with cancer has important implications for immunotherapy diagnostics and therapeutics.


?
T-cell
TCR
CD28
PD-1
B7
PDL1/2
MHC
APC
Activation &
Proliferation
T-cell
TCR
CD28
PD-1
B7
MHC
Anti PD-1
Antibody
APC


Antigen-presenting cell
T cell
PDL1 or PDL2
?
PDL1 or PDL2
PD1
CD80 or CD86
CD28
Signal 2
CD80 or CD86
CTLA4
B7RP1
ICOS
B7-H3
?
B7-H4
?
HVEM
BTLA
Peptide
KIR
MHC class I or II
TCR
Signal 1
LAG3
CD137L
CD137
OX40L
OX40
CD70
CD27
CD40
CD40L
GAL0
TIM3
Adenosine
AZaR
Cytokines (TGFβ, IL-1, IL-6, IL-10, IL-12, IL-18)
Signal 3


IL-1, IL-4, IL-10, IL-13
CD4+ Th2 cell
TAM M2
TAM M1
VEGF
IFN-γ
IL-1
Granzyme
Perforin
IL-1
VEGF
↓MHC
↓costimulatory molecules
↑ Apoptosis
Angiogenesis
Invasion
Metastasis
CD8+ T cell
NK cell
CD4+ Th1 cell
Tumor cell
SCF
PGE2
GM-CSF
VEGF
TGF-β
TAMs
Arginase
ROS
iNOS
BV8
MMP9
VEGF
Bone Marrow
TGF-β
IFN-γ
IL-10
CD4+ Treg
MDSC

AS1

Immune checkpoint (inhibitors PD-1 inhibitors)

- Nivolumab and pembrolizumab, were shown to improve OS in patients with recurrent, metastatic HNSCC and were approved by the US Food and Drug Administration (FDA) for use in the second-line setting with disease progression on or after a platinum-based CT.
- But still response rates to PD-1/PD-L1 inhibitors in HNSCC range from 13% to 20%, whereas survival is improved in just 1 of 10 patients treated.

Slide 20

AS1 Alzahrani, Shadi, 6/18/2019

Conclusion

- The tumor microenvironment plays an important role in cancer development and progression and may be associated with systemic inflammation
- HNSCC has been found to be one of the most immune-infiltrated cancer types suggesting there are other mechanisms underlying the immunosuppressive microenvironment generated by the tumor.
- The upregulation of PD-L1 can occur in tumor cells and allows cancer cells to escape from host immune systems by functionally inactivating T-cell immune surveillance
- The inhibition of this interaction can enhance T-cell response and mediate clinical anti-tumor activity

Summary

- Immune checkpoint inhibitors have demonstrated durable improvements in patient outcomes in HNSCC

- PD-L1 was reported to be associated with resistance to anticancer therapies, but combined immunotherapy with other treatment modalities decrease the resistance of disease

I’M DONE

Officially
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