Melanoma, Metastasis, and Ipilimumab

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Melanoma: Stages of Growth
- Sixth leading type of cancer in the U.S.
- Melanocytes grow out of control – Between epidermis and dermis
  1. Radial growth phase (tumor less than 1mm thick)
  2. Invasive radial growth phase (tumor less than 1mm thick)
  3. Vertical growth phase (tumor more than 1mm thick)
    - Host elicits immunological reaction
  4. Regression

Diagnosis and Classification
- “ABCDE”
  - A: asymmetrical skin lesion
  - B: borders of the lesion are irregular
  - C: color (multiple)
  - D: diameter greater than 6mm
  - E: Enlarging or evolving
- Various categories of classification:
  - Superficial spreading, mucosal, nodular, soft tissue

Therapy Options
- Surgery
  - Standard: complete surgical excision, assessment of detectable metastatic disease, followup
- Radiation therapy
  - After surgical excision for patients with locally or regionally advanced disease or for patients with unresectable melanoma
- Adjuvant therapy
  - Chemotherapy: dacarbazine (DTIC)
  - Immunotherapy: Interleukin-2, interferon

Ipilimumab (Yervoy)
- FDA approved monoclonal antibody developed by Bristol-Myers Squibb
  - Approved in March 2011 to treat patients with late-stage melanoma that has spread or cannot be removed by surgery
- Adverse effects due to T cell activation and proliferation
  - Mostly associated with GI tract
- Mode of action...

CTLA-4 is a critical immunoregulatory molecule. Anti-CTLA-4 antibodies can reverse immunoregulation.
M.D. Anderson Study

- "Chart review" through patient database
- Data collected:
  - Prior systemic treatment: Y/N
  - Prior IL-2 treatment: Y/N
  - Lesions/Metastases
    - Soft tissue, lymph nodes, lungs, liver, bone, brain/meninges
  - Cancer stage
  - Serum LDH
  - Brain mets: Y/N
  - Date of brain mets/recurrence
  - PD in brain: Y/N
  - Brain response to IPI: Y/N
  - Overall survival from treatment

Disclaimer!

Other Results

- Technical difficulties...
- Median time to PD in patients who developed brain mets = 0.21 years, 95% CI = 0.17-0.24 years
- Nearly 42% of the treated patients had disease progression/recurrence on IPI treatment.

Conclusions

- Based on current study, metastases to brain did not significantly affect OS in melanoma patients
- Ipilimumab did not appear to prevent recurrence or disease progression in the brain
  - Is Ipilimumab more effective than chemotherapy?
Future Directions

• Completing data analysis
  – Data of patients not on ipilimumab to compare with our patient group
    • e.g. OS and PD in patients using IPI vs. not using IPI
  • As is fairly recently approved, further studies to compare effectiveness to other available treatment protocols.

References