

Exploring the latest in cancer therapy

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Medical Center



Nebraska
Medicine



Disclosures

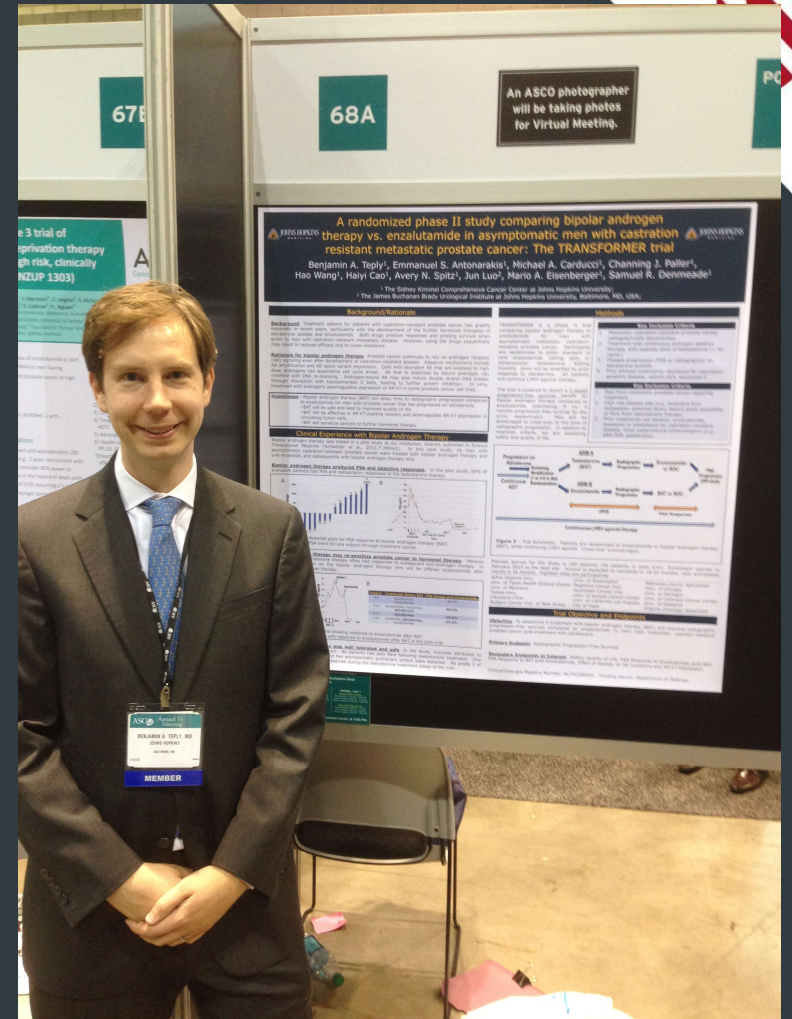
Institutional Principal Investigator for studies funded by Bristol Myers Squibb, Bellicum Pharmaceuticals, Seagen, Merck. Paid consultant for Exelixis. Teaching fees for Clinical Care Options / National Comprehensive Cancer Network.



Learning Objectives:

- Recognize the different types of cancer therapies (e.g., chemotherapy, immunotherapy, targeted therapies, gene therapy, and personalized medicine).
- Gain an understanding of how newer therapies work and how they are evolving to treat various cancers more effectively.
- Learn about breakthrough therapies that have shown significant promise in clinical trials or recent FDA approvals.
- Provide a look into the future of cancer care and how these advances may shape the prognosis for cancer patients.

2016... completing fellowship





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Tiebreaker!

- This is the number of FDA new drug approvals for use in oncology [chemo, biologics, diagnostics, supportive care] since July 1, 2013 to June 1, 2016

- | | | |
|--------------------------------------|--|-------------------------------------|
| 1. Afatinib (7/12/13) | 12. Pembrolizumab (9/4/14) | 23. Osimertinib (11/13/15) |
| 2. Ibrutinib (10/25/13) | 13. Blinatumomab (12/3/14) | 24. Ixazomib (11/20/15) |
| 3. Obinutuzumab (11/1/13) | 14. Nivolumab (12/22/14) | 25. Alectinib (12/11/15) |
| 4. Ceritinib (4/29/14) | 15. Palbociclib (2/3/15) | 26. Dinutuximab (3/10/15) |
| 5. Belinostat (7/3/14) | 16. Lenvatinib (2/13/15) | 27. Daratumumab (11/16/15) |
| 6. Idelalisib (7/7/14) | 17. Panobinostat (2/23/15) | 28. Necitumumab (11/24/15) |
| 7. Netupitant/Palonesetron (8/19/14) | 18. Sonidegib (7/24/15) | 29. Elotuzumab (11/30/15) |
| 8. Olaparib (12/19/14) | 19. Rolapitant (9/1/15) | 30. Defibrotide (3/30/16) |
| 9. Ramucirumab (4/21/14) | 20. Trifluridine and tipiracil (9/22/15) | 31. Venetoclax (4/11/16) |
| 10. Siltuximab (4/23/14) | 21. Trabectedin (10/23/15) | 32. Atezolizumab (5/18/16) |
| 11. Pembrolizumab (9/4/14) | 22. Cobimetinib (11/10/15) | 33. fluciclovine F 18 (5/27/16) |
| | | 34. gallium Ga 68 dotatate (6/1/16) |

- What is 34!



New in 2024

1. Tislelizumab-jsgr (3/13/24) – Esophageal Cancer
2. Danicopan (3/29/24) – Paroxysmal Nocturnal Hemoglobinuria
3. Pegulicianine (4/17/24) – Cancer Detection
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16!

<https://www.fda.gov/drugs/novel-drug-approvals-fda/novel-drug-approvals-2024>



Pillars of Cancer Treatment

1. Surgery

2. Radiotherapy

3. Chemotherapy

4. Targeted Therapy

5. Immunotherapy

Roles for Chemotherapy



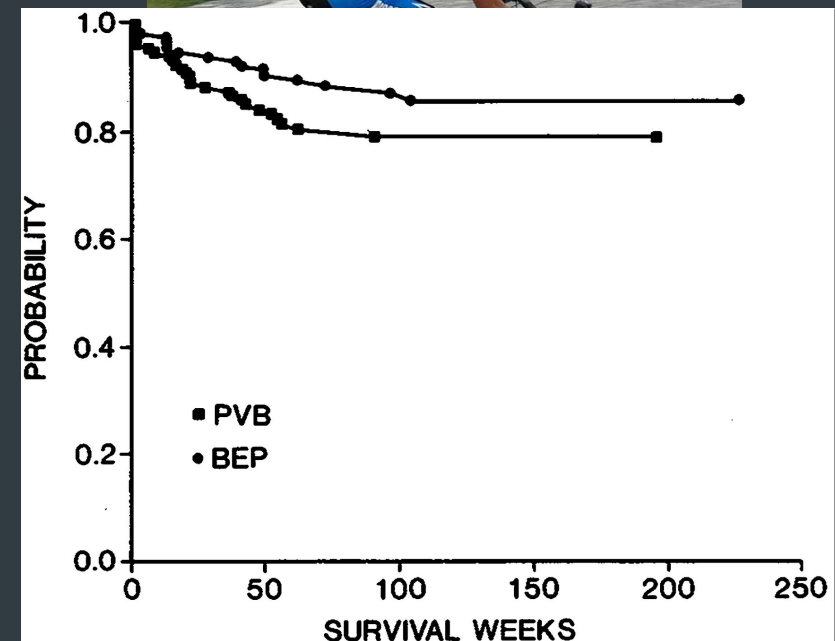
- Palliative therapy in metastatic disease
- Curative intent therapy
 - Peri-operatively / adjuvant
 - Concurrent with radiotherapy
 - Primary therapy for metastatic disease (uncommon)

Curative Chemotherapy



Case: A patient is diagnosed with metastatic nonseminomatous germ cell tumor (testicular Ca) with bulky lung and lymph node masses.

- **Combination chemotherapy with cisplatin-etoposide-bleomycin is administered**
- **Long term cure is expected!**



NEJM 1987 Jun; 316: 1435-40.

Targeted Therapy



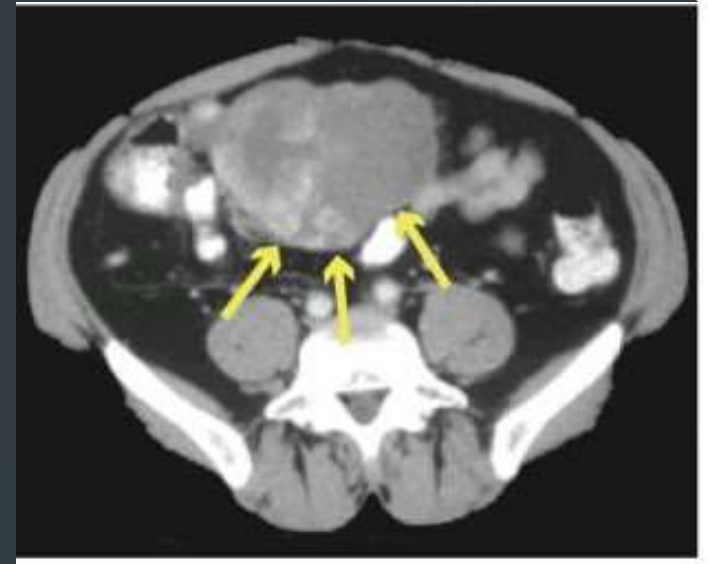
Inhibiting proteins in pathways that are principal drivers of growth and survival in a tumor

- **HER2/neu amplification in breast cancer**
- **Androgen receptor (AR) in prostate cancer**
- **EGFR mutation or ALK Translocation in non-small cell lung cancer**
- **BRAF V600E mutation in melanoma**
- **VEGF overexpression in kidney cancer**

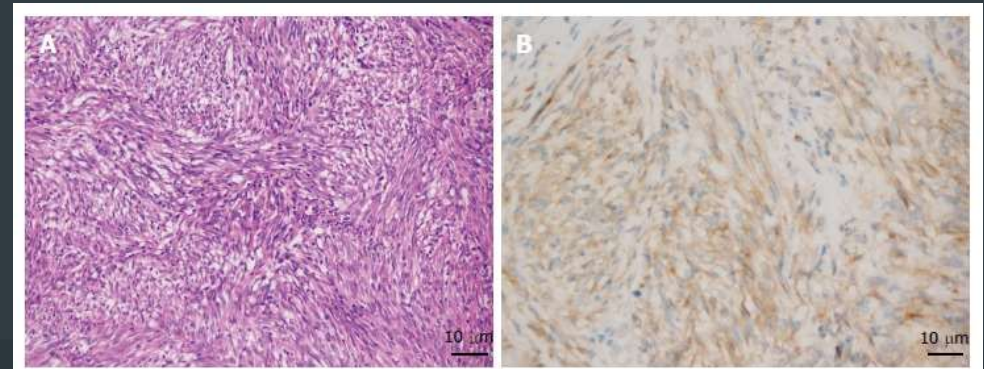
Targeted Therapy



Case: A patient undergoes CT of the abdomen which shows a large mass. It is deemed unresectable.



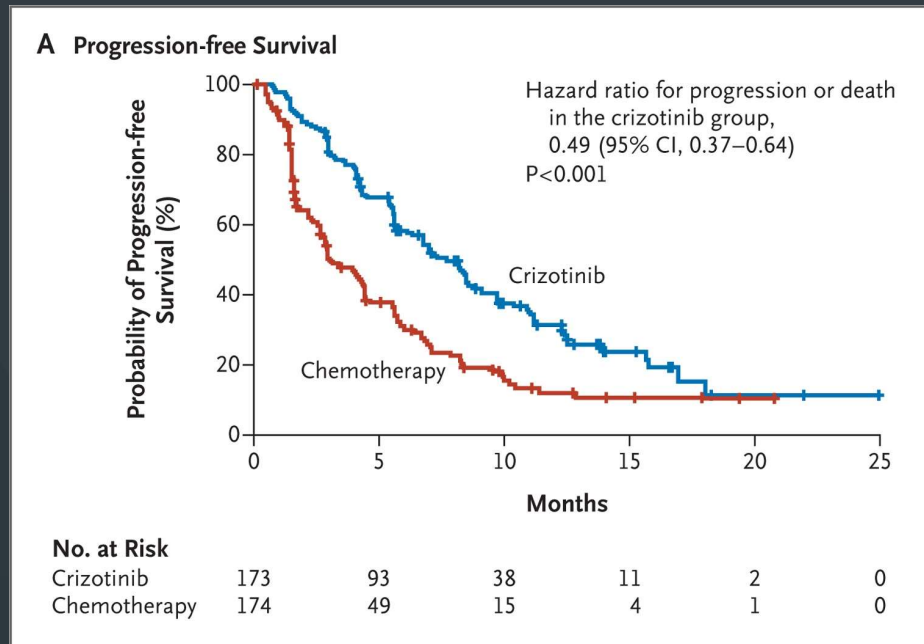
- Tumor is identified as a sarcoma (Gastrointestinal Stromal Tumor) with CD117+. Further molecular characterization: KIT exon 11 mutation
- Imatinib is administered



Targeted Therapy



Example: targeting ALK translocation vs chemotherapy in lung cancer



Targeted Therapy



- Inhibition of molecular pathways that are driving cancer growth
- Most solid tumors have 0 or 1 (currently) targetable driver mutations.
- Resistance is a hurdle to long-term efficacy of targeted therapy



Immunotherapy

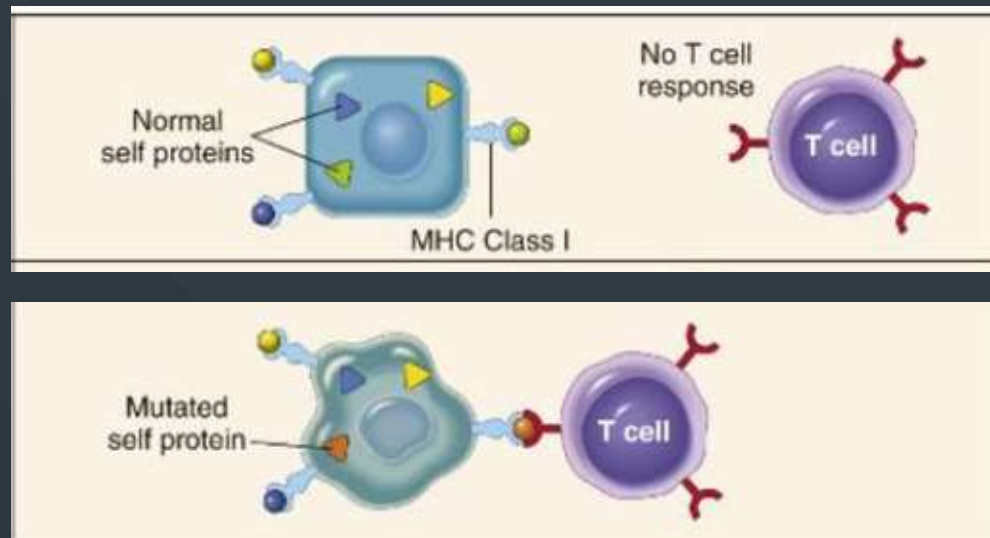
Therapy to augment or engender an immune response for anticancer effect.

- Cytokine Therapy
- Cellular Therapy
- Vaccines
- Immune checkpoint blockade



Immunotherapy

Immune surveillance – immune system recognition of abnormal antigens



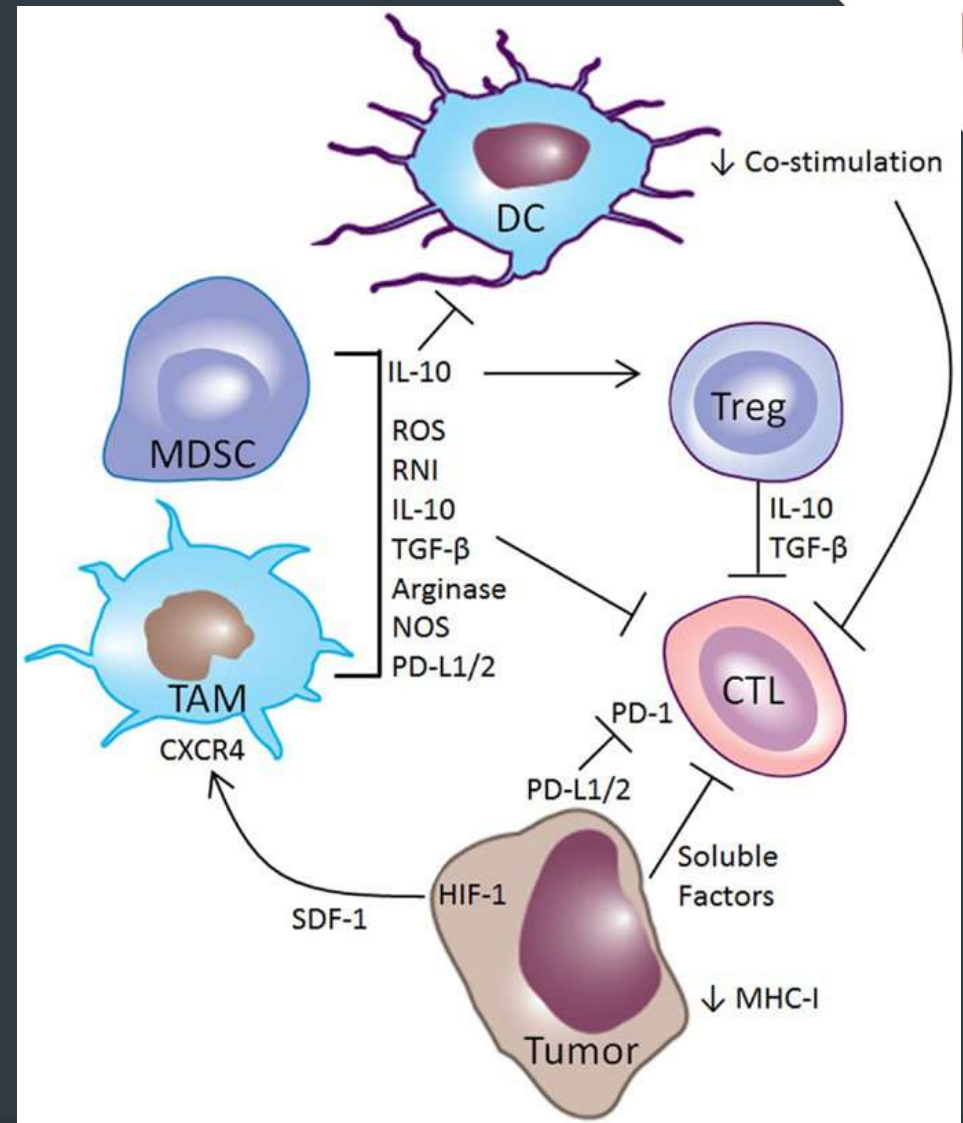


Immunotherapy

Basic Principles

Carcinogenesis--

- Weak antigens
- Immune evasion



Immunotherapy

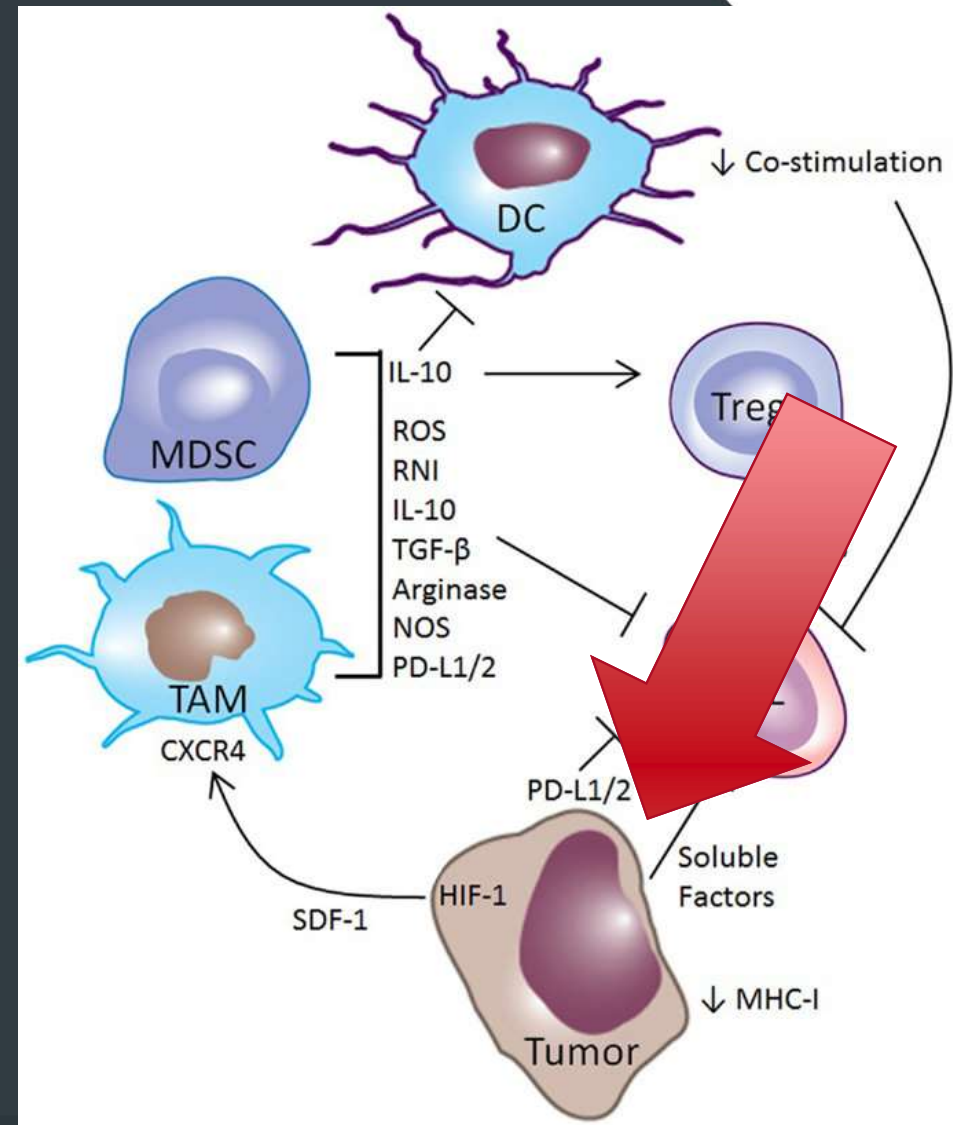
Cellular Therapy

Introduce non-tolerant immune cells (or system)

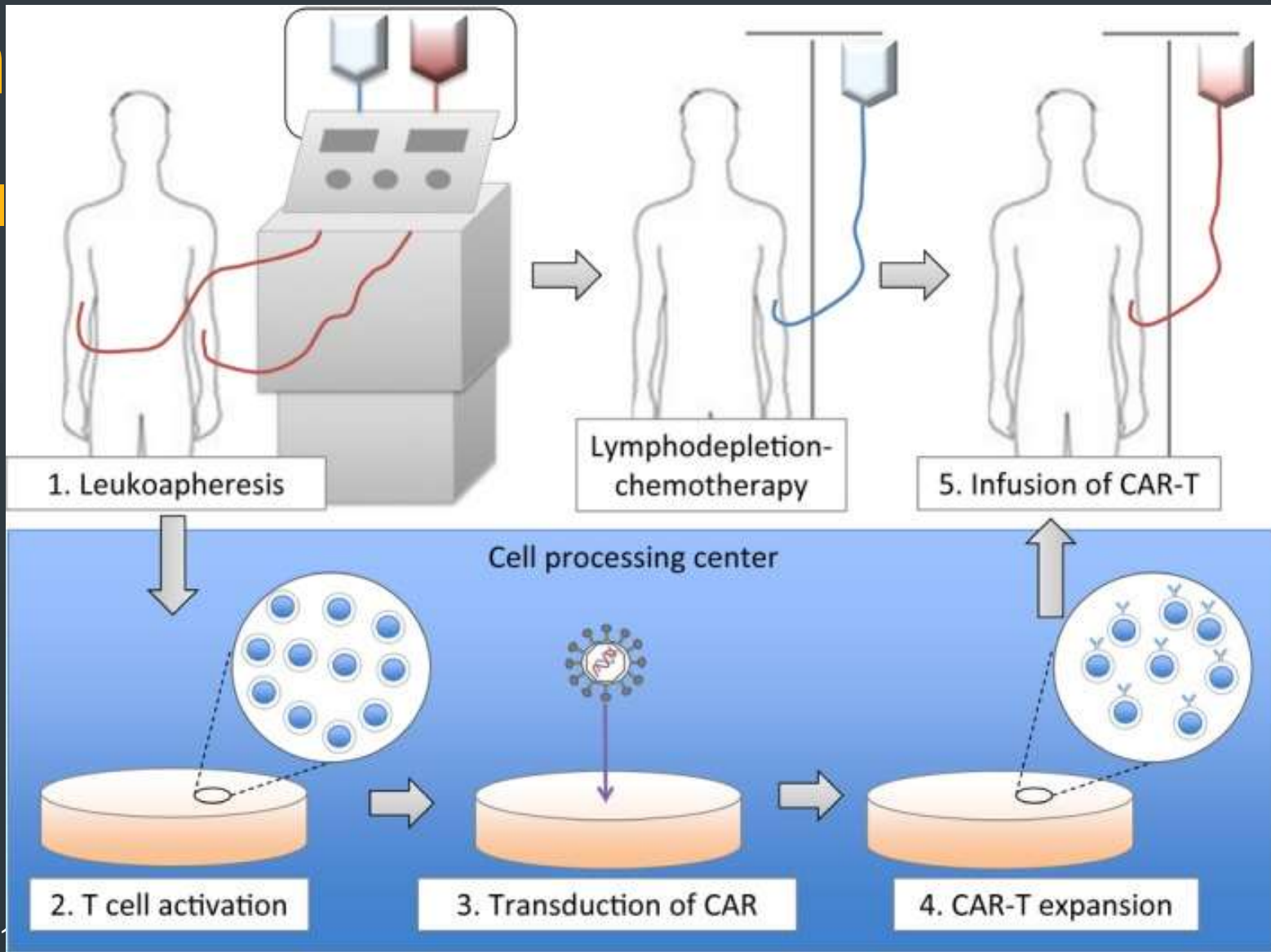
- Allogeneic bone marrow transplantation

Introduce activated immune cells

- Autologous cellular vaccines
- Chimeric antigen receptor (CAR) T-Cells



Imm Cel

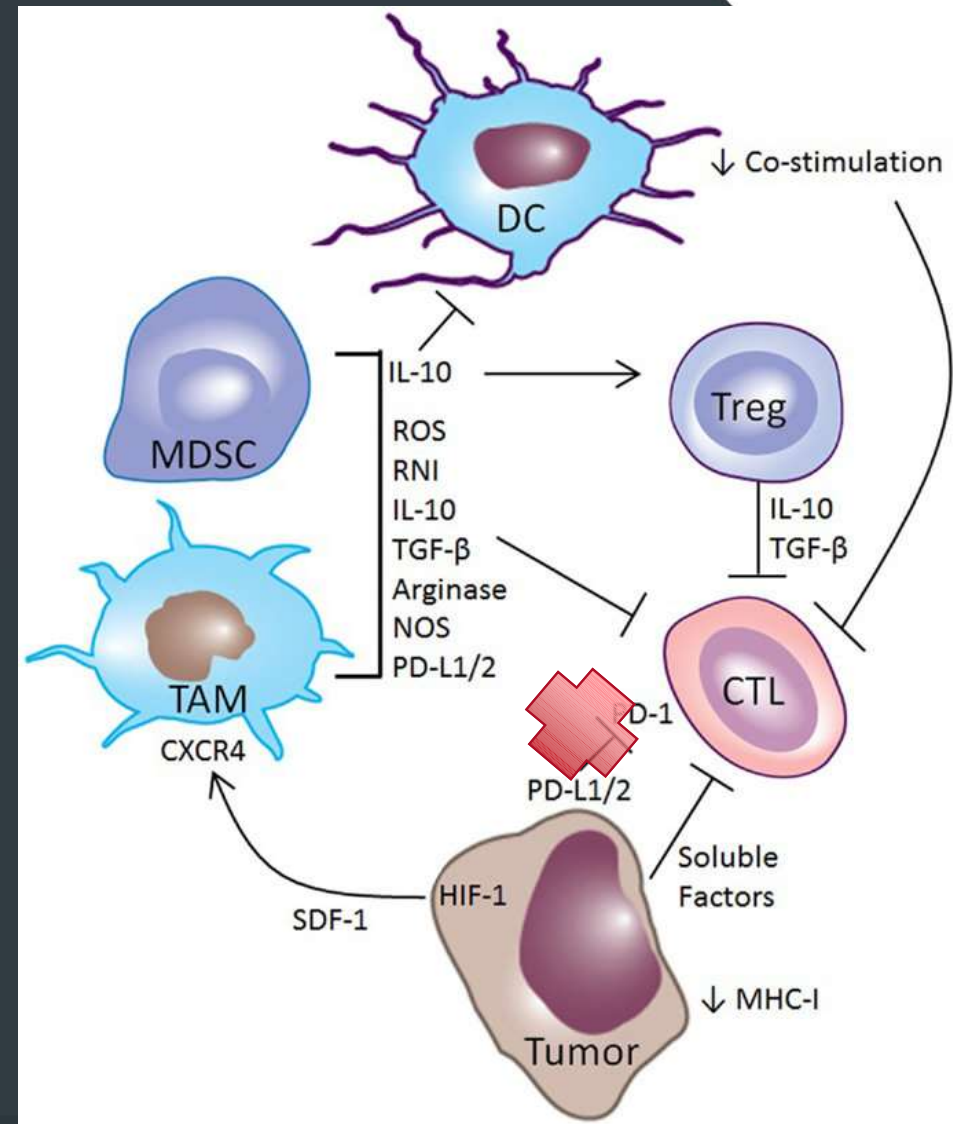


Immunotherapy

Immune Checkpoint Blockade

Block immunosuppressive second signals to restore immune response

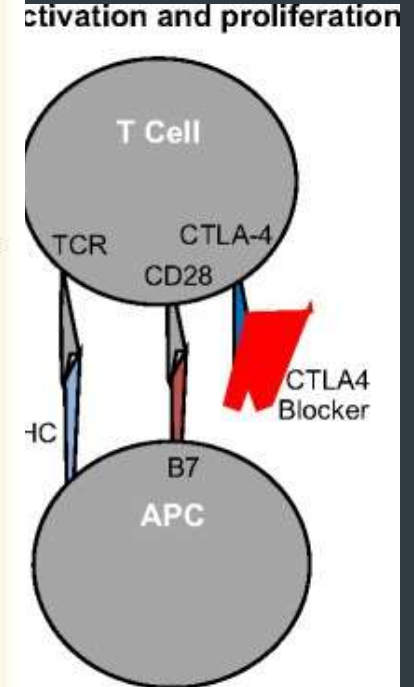
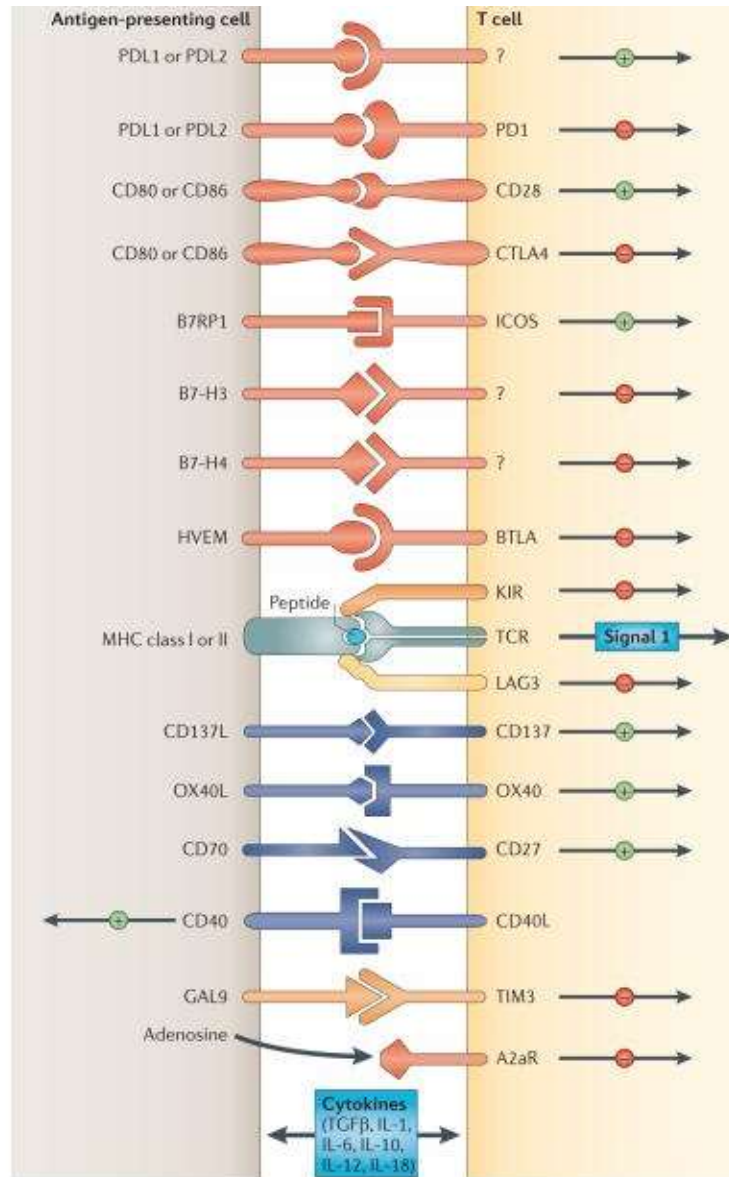
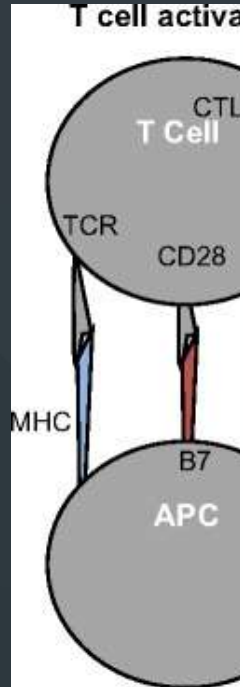
- Anti-CTLA4
- Anti-PD1
- Anti-PD-L1/L2
- Anti-Lag-3



Immunotherapy

Immune Checkpoint

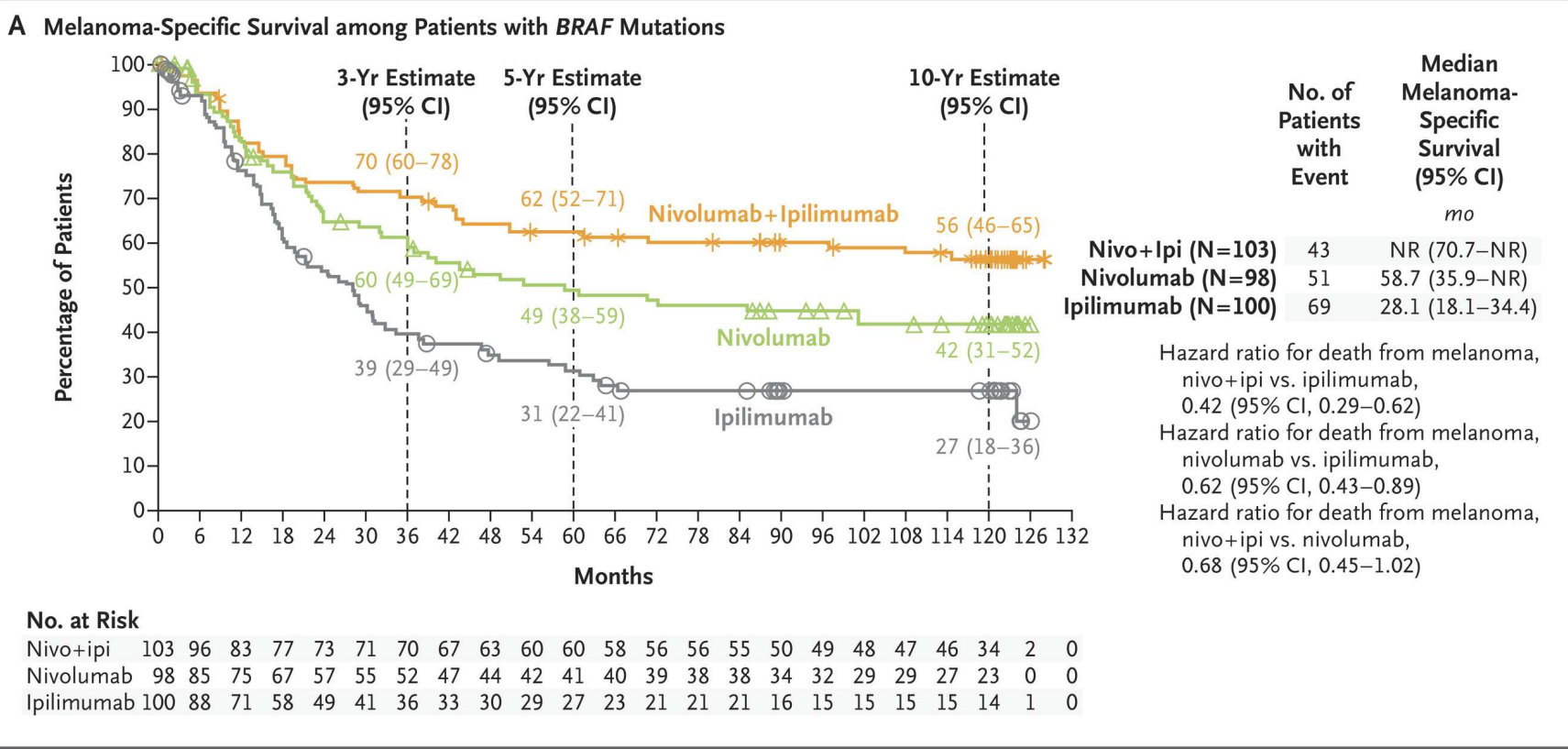
Anti-CTLA4





Immunotherapy

Melanoma Example





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Tarlatamab-dlle



Mechanism and Clinical Activity

Nogapendekin alfa inbakicept-pmIn



Mechanism and Clinical Activity

Inavolisib



Mechanism and Clinical Activity

Vorasidenib



Mechanism and Clinical Activity

Revumenib



Mechanism and Clinical Activity



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