

Metastatic Melanoma treatment

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Metastatic melanoma

- Usual sites: distant skin, subcutaneous nodules, L/nodes
Lung/liver/other visceral organs/brain

Prognosis

- Very poor
- Median survival 6 – 9 mnths with lung/
L/node/ skin only may be up to 15 mnths
- Surgical treatment should always be
considered

Chemotherapy

- Melanoma is generally resistant to chemotherapy
- Dacarbazine - is FDA approved
 - Response rate of 7% but other clinical trial have reported higher RR of up to 15%
 - OS - 8 mnths

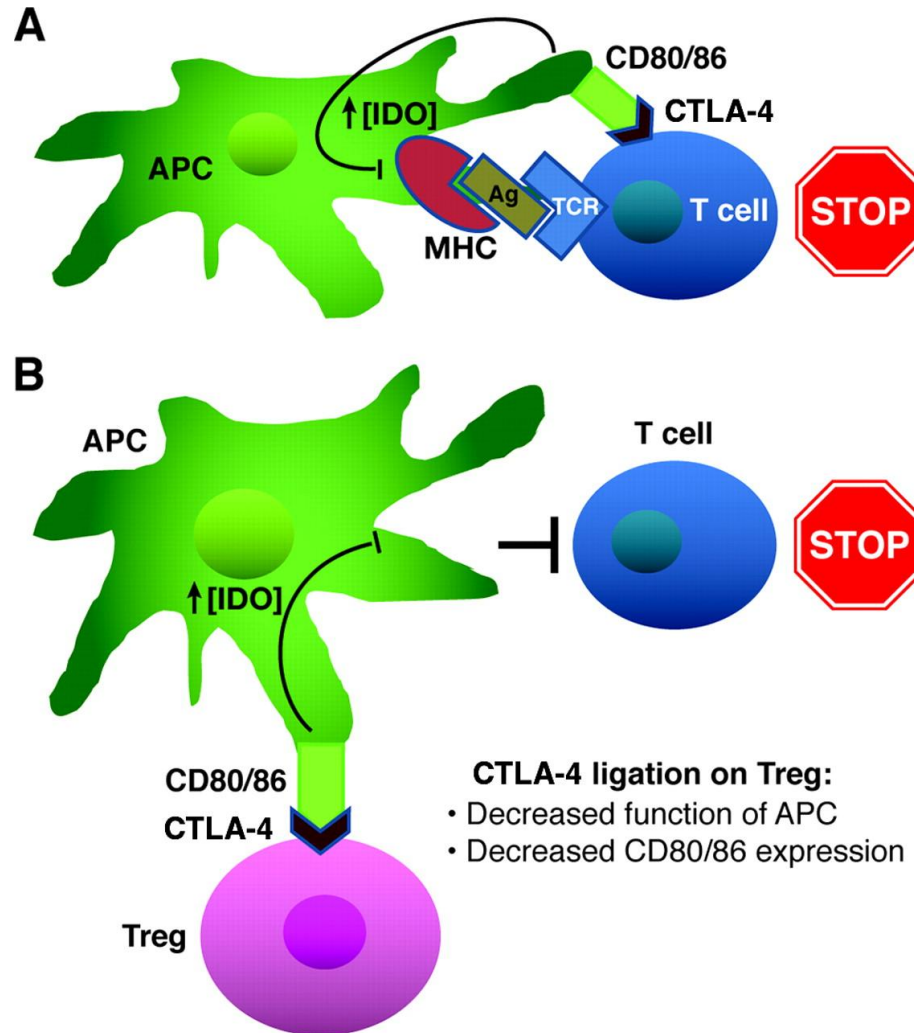
Immunotherapy

- Interleukin-2: - FDA approved
 - RR of 6 – 9%
 - Atkins et al, in 199 published in JCO – HD IL-2 data
 - 720 000iu/kg iv bolus
 - OOR - 15,5%
 - Brain mets were excluded

- Durability of CR is the hallmark of IL-2 therapy
- 80% of complete responders are likely cured
- Toxicity: very toxic –e.g capillary leak syndrome
- Need ICU

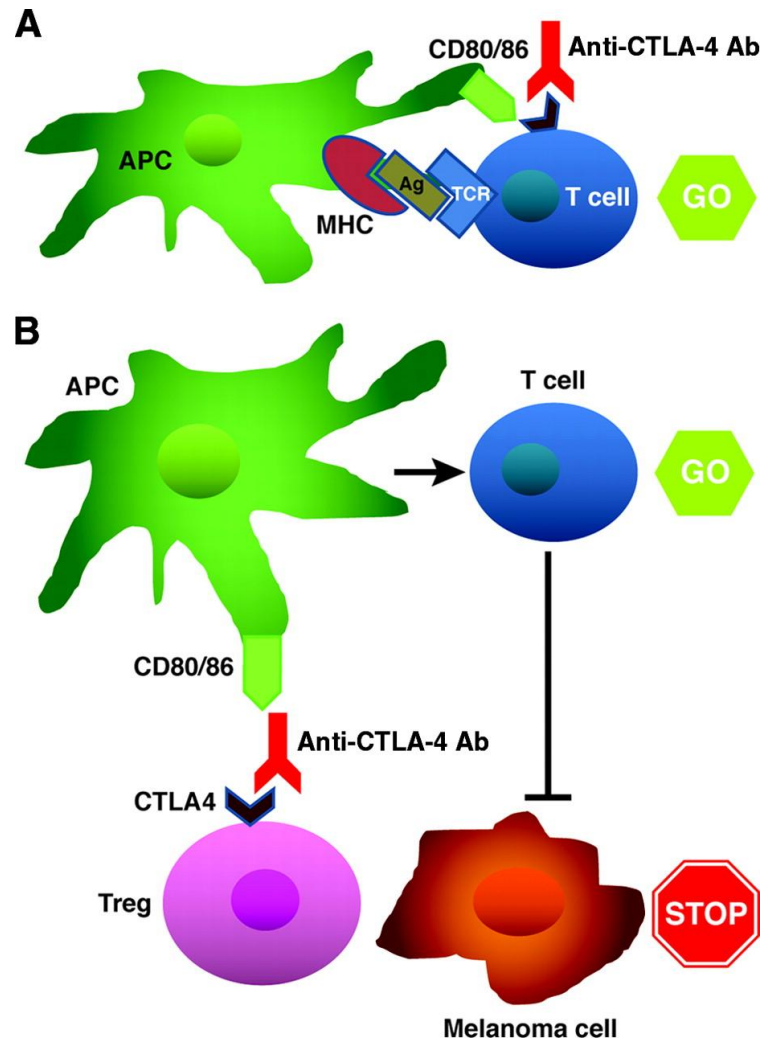
- IPILIMUMAB

CTLA-4 blockade prevents downregulation of T cells.



Robert C , Ghiringhelli F The Oncologist 2009;14:848-861

Antitumor effects of CTLA-4 blockade.

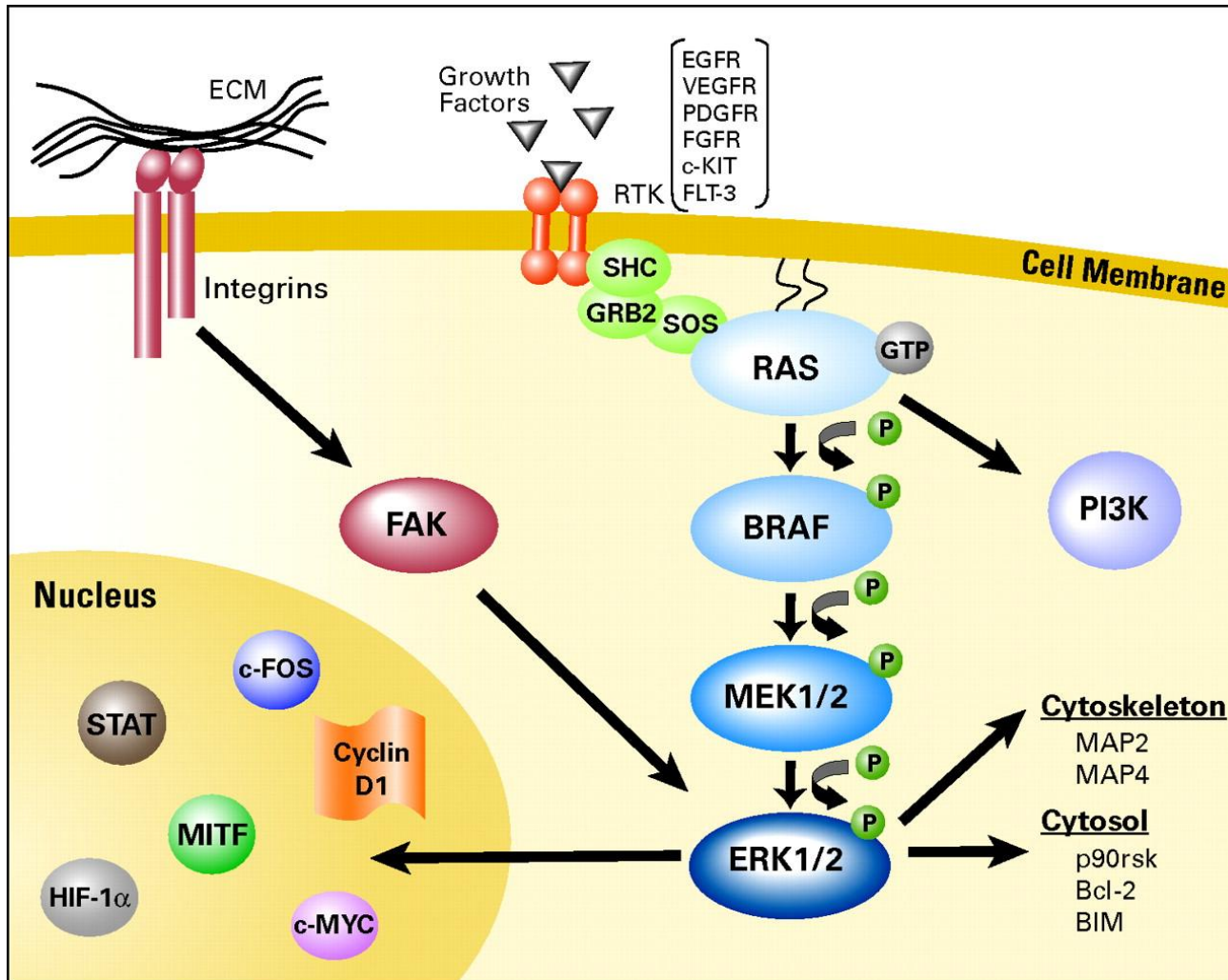


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- Ipilimumab: FDA approved
Anti-CTLA-4 Monoclonal
antibody
ORR 10 – 15%
Disease control rate of 30%
Toxicity is manageable
Induce long-term responses in
minority of pts

VEMURAFENIB

The mitogen-activated protein kinase (MAPK) signaling cascade.



Fecher L A et al. JCO 2007;25:1606-1620

- Vemurafenib: TKI, BRAF inhibitor

BRAF activating mutation is found in approx 40-60% of melanoma pts

Response is seen within 2 wks but PD of disease is notice at 6 months

- Vemurafenib: Important mutation is V600E

Combination Chemotherapy

- Only in Clinical trials
- None has shown better results

- Immunotherapy plus targeted therapies?

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THANK YOU

References

- To be added later