



Management of Diabetes and Hyperglycemia in the Patient with Cancer

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Diabetes and cancer are diagnosed within the same individual more frequently than would be expected by chance, even adjusted by age. Patients with cancer and diabetes have higher mortality rate than those who don't have cancer.

Shared Characteristics

- Aging
- Increased adiposity
- Diet
- Inactivity
- Chronic inflammation
- Hyperinsulinemia
- Insulin resistance
- Hyperlipidemia
- Insulin-like growth factor-1
- Adipokines
- Cytokines
- Gut microbiome

Cancer Cell Characteristics

- Grows without signals or excessive growth signals
- No scheduled apoptosis
- Can proliferated/metastasize
- Can cause blood vessel formation

Type 2 Diabetes: increased risk for:

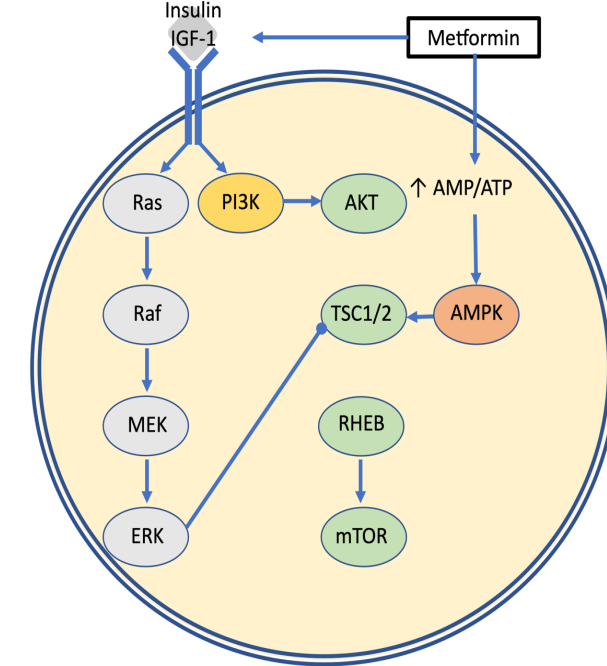
- Pancreatic
- Liver
- Endometrial /Ovarian / breast
- Non-Hodgkin lymphoma
- Leukemia
- Stomach
- Colon / rectum
- Thyroid
- Kidney
- Bladder / gallbladder

Type 1 Diabetes: increased risk for:

- Pancreatic
- Ovarian
- Liver
- Stomach
- Lung
- Kidney
- Decreased risk for breast

Metformin and Cancer

- Reduced incidence of cancer
- Reduces mortality from cancer
- Improves response to radio/ chemotherapy
- Improves tumor reduction
- Reduces relapse
- ↓bad effects of inandrogen derivatives
- Can be use with many cancer treatments

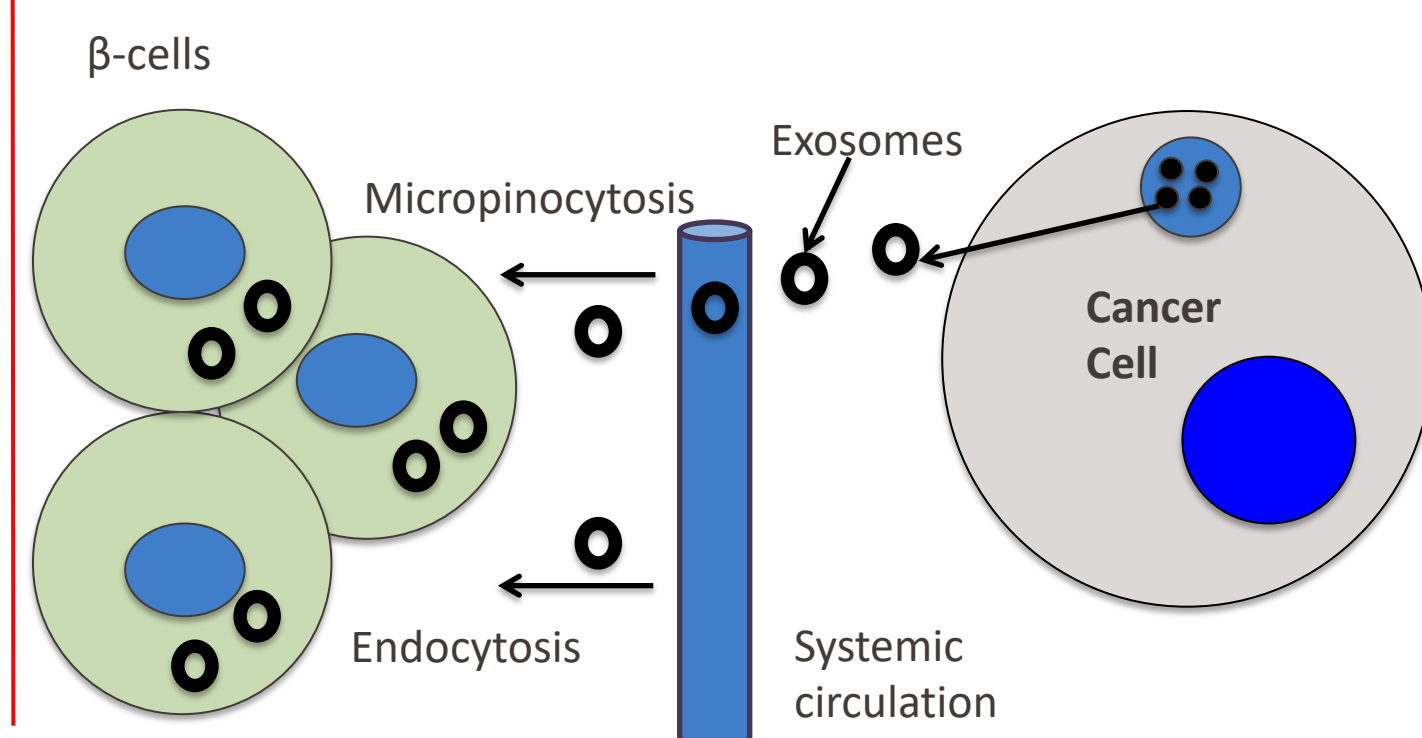


Thiazolidinedione (TZD) and Cancer

- Increased risk bladder cancer associated with duration of TZD
- Has antitumor effect via:
 - Induces cell apoptosis
 - May induce cell growth arrest
 - May prevent cell differentiation

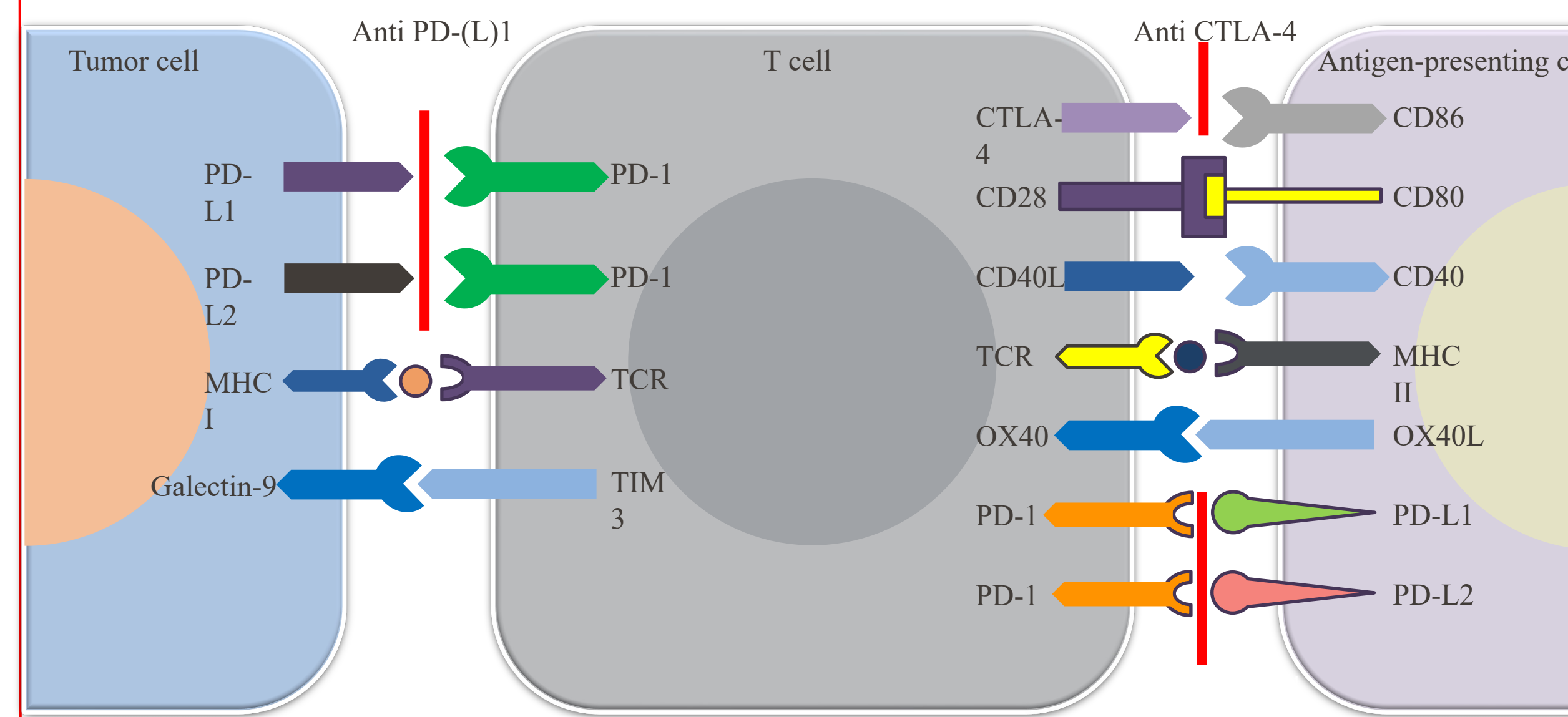
Pancreatic Related Diabetes: Type 3c

- Pancreatic cancer cells release adrenomedullin inhibiting insulin secretion
- Can cause β-cell dysfunction/death
- Often needs insulin therapy
- Avoid DPP-4i and GLP-1RA
- May need to avoid SGLT-2i
- Metformin good if no contraindications



Immune Checkpoint Inhibitors (ICI)

- Immune system attacks “foreign” cells
- Cancer cells may use checkpoint proteins to avoid attack by immune system
- ICI don't kill cancer cells but helps immune system to attack cancer
- PD-1 inhibitors
 - Pembrolizumab (Keytruda)
 - Nivolumab (Opdivo)
 - Cemiplimab (Libtayo)
- CTLA-4 inhibitors
 - Ipilimumab (Yervoy)
- PD-L1 inhibitors
 - Atezolizumab (Tecentriq)
 - Avelumab (Bavencio)
 - Durvalumab (Imfinzi)
- LAG-3 inhibitors
 - Relatlimab (Opdualag)



Immunotherapy Induced Type 1 Diabetes

- Age of onset usually older
- B-cell destruction rapid
- Unlike other ICI induced adverse effects: does not improve with steroids
- High percent with diabetic ketoacidosis at diagnosis
- Positive antibody rate lower
- HLA-DR4 in approximately 60%

PI3K Inhibitors

- Block glucose metabolism causing severe insulin resistance
- Everlimus (Affinitor)
- Alpelisib (Piqray)
- Low carbohydrate diet
- Non-insulin and/or insulin therapy if needed

Tacrolimus Induced Hyperglycemia

- ↑ insulin resistance,
- ↑ glucose absorption in the jejunum
- ↑ activity and expression of SGLT1

Steroid Induced Hyperglycemia

- ↓ insulin secretion, incretin effect glucose uptake
- ↑ glucagon, gluconeogenesis, insulin resistance
- If BG < 200 mg/dL may try non-insulin medications
- BG > 200 mg/dL: add insulin
- Effects postprandial BG more than fasting BG so may need more prandial than basal insulin

Tube Feeding Induced Hyperglycemia

- Calculate carbohydrate (CHO) grams for formula being used
- Start with 1 unit per 6-8 grams of carbohydrate
- Continuous: give 70/30 insulin every 6-8 hours
- Bolus: give Short or rapid insulin with each feeding
- May need basal insulin if needed before tube feeding

TPN Induced Hyperglycemia

- Calculate CHO grams for the bag
- Start with 1 unit Regular insulin per 10 grams CHO
- Insulin in bag should not cover basal needs
- Subcutaneous insulin should not cover TPN

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