Immunotherapy in Cancer

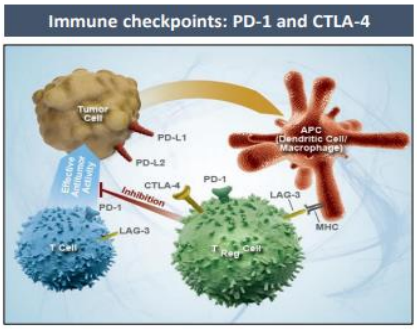
Pharmacology 3
Dr. Rawan Abudalo

Department of Clinical Pharmacy and Pharmacy Practice
Faculty of Pharmaceutical Sciences
Hashemite University

المفروض ال immune system في خلايا بتلعب دور كبير to invade the cancer cell لكن للأسف most of cancer cell or tumor cell may to try to inactivate the T cell or immune cell once its activation this is mean that the cancer cell or immune cell that will be incapable to recognize the cancer cell

Targeting the Immune Checkpoint Pathway on the Immune System

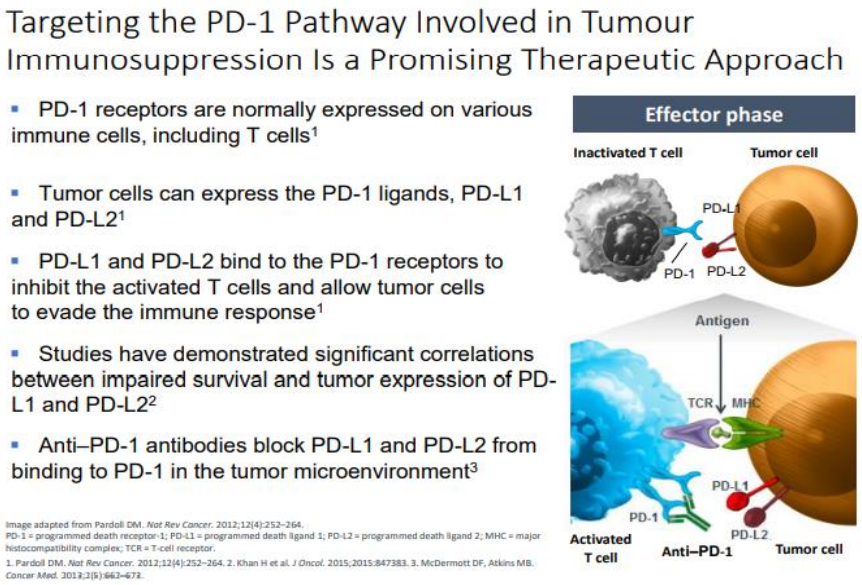
- The immune checkpoint pathway is an elaborate series of cellular interactions that prevent excessive T-cell effector activity[1]
- Inhibitory receptors, such as CTLA-4 and PD-1, downregulate T-cell activity[2]
- Monoclonal antibodies that block CTLA-4 or PD-1 pathway components have been developed[2]



APC = antigen-presenting cell; CTLA-4 = cytotoxic T lymphocyte associated protein-4; LAG-3 = lymphocyte-activation gene 3; MHC = major histocompatibility complex; PD-1 = programmed death receptor-1; PD-L1 = programmed death ligand 1; PD-L2 = programmed death ligand 2; Treg = regulatory T cell.

1. Ott PA. *Clin Cancer Res.* 2013;19(19):5300–5309. 2. Pardoll DM. *Nat Rev Cancer.* 2012;12(4):252–264.

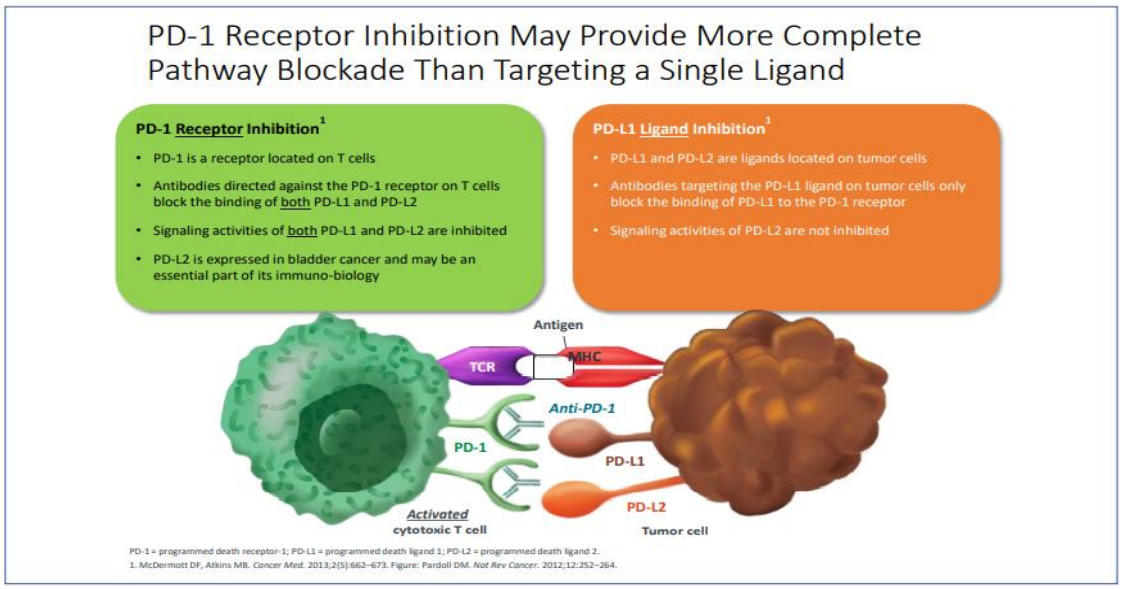
في عنا اشي اسمه checkpoint اللي بصير اللي هوه الوضع الطبيعي في عنا cascade of reaction (complex reaction) الخلايا السرطانية في عندها على سطح الخلايا مستقبلات pd-l1 and pd-l2 المفروض ال t cell تعمل recognize the cancer cell from these receptor mean wile في عنا ال apc also replay a rule (هاي ما بتهمني كتير) المهم انه ال t cell المفروض can recognize the cancer cell من خلال ال T ring عنا في مشكلة بتصير اذا صار في عنا complex في ال t cell and tumor cell قبل ما يصير أي recognition انا صار عندي inhibition or downe regulation for t cell activity this is mean that Mack the immune cell incapable to recognize cancer cell المفروض انا عندي interaction between t cell and cancer cell so we can enhance this interaction



ال pd-1 receptor موجودة في ال t cell وال pd-l receptor موجودة في الخلايا السرطانية اللي بصير انه الخلايا السرطانية في الوضع الطبيعي الخلايا السرطانية PD-L1or pd-l2 بتيجي الخلية السرطانية تتحد مع ال t cells وبتعمللها inactive وبالتالي other t cell will not be activated انا بدي أحاول امنع هذا الارتباط اما بعطي anti pd-1 (t cell become free and stay active and farther activation of other immune cell to recognize the cancer cell) or anti pd-l1 يعني اما بتعمل block of receptor on cancer cell or block of receptor on t cell من ناحية انك تمنع

الارتباط او ال complex formation between t cell and cancer cell لأنه اذا صار هذا الارتباط بصير كانه الخلايا السرطانية بتحول ال t cell to inactive cell

انا بدي ال t cell تضل فعالة من خلال منع هذا الارتباط



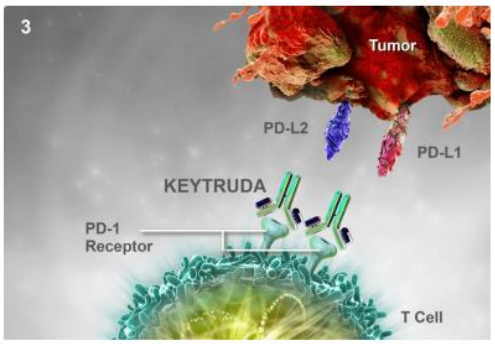
they are targeted to increasing the activity or the t cell وهذا بالتالي allowing the t cell to be incapable to invade the cancer cell وهذا هوه مبدا عملها

حسب نوع السرطان بقروا البروتوكول للعلاج

من الأمثلة انه ال pd-l1 will found in bladder cancer so we will try to suppress this effect

PD-1 Receptor Blockade With KEYTRUDA® (Pembrolizumab)

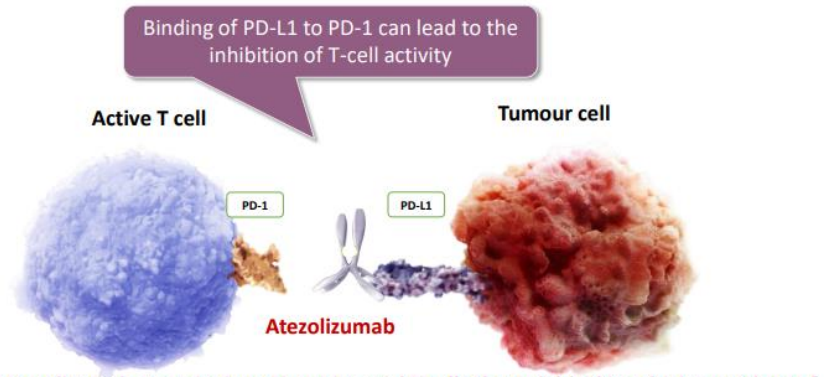
By inhibiting the PD-1 receptor from binding to its ligands, **Pembrolizumab** reactivates tumor-specific cytotoxic T lymphocytes in the tumor microenvironment and reactivates antitumor immunity.



برضه هوه monoclonal antibody

حكت الدكتورة لازم نحفظ الامثلة

Atezolizumab can reactivate suppressed T cells in the tumour microenvironment



Atezolizumab can reinvigorate suppressed T cells through blocking the interactions of PD-L1 (on tumour cells with PD-1 (on T cells) in the tumour microenvironment

Deemah sartawi