LDL Lowring Agents

(1) Bempedoic acid

Citrate ⟶ acytelcholine ⟶ cholesterol

↳ stop here by inhibit ATp-citrate Lyase

↓cholesterol ⟹ ↑LDL-receptors to get more cholesterol from any part

↑HDL-receptors to get back another cholesterol from foam cells towards the liver

↑deudenoum absorption we use ezetimibe drug

of cholesterole

ردة فعل جاولوا يفزعوا لنقص الكوليسترول

- Maximum efficacy 3ol, used as combination with Statins

Side effects

- Increase ↳ blood urea nitrogen
  ↳ Creatinine
  ↳ uric acid cause Gout
- ↓hemoglobin ⟶ anemia
- hyperglycemia not very much
- muscle pain — unknown mechanisme

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(2) PCSK9 inhibitors by monoclonal antibodies

(A)

first PCSK9 is enzyme produce in the liver that cause degredation of LDL receptors ⟶ No LDL receptors for LDL لا اعتصاص كافي

increase LDL plasma concentrations

لذلك هذه الأدوية تثبط الإنزيم حتى يبقى مستقبلات كافية ويجن اعتصاص للكوليسترول من البدرا

↓PCSK9 ⟶ ↑LDLR ⟶ ↓Plasma LDL-C Levels

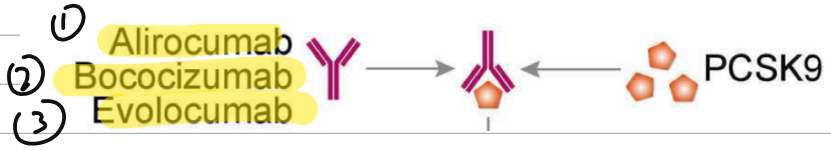
It is jop done without interacting with synthesis of cholesterol and without having hyperuricemia or myopatny or rabdomyolsis

Insted we just inhibiting PCSK9 — inhibition of lysosomal degeneration

Normally No side effects if their is it will be flulike symptoms

drugs are

1. Alirocumab
2. Bococizumab
3. Evolocumab



(B) pcsk9 inhibition by RNA silencing

Inclisiran it is a synthetic a small interfering RNA

عشان في تركيبه جزء اسمه GAINAc بيساعدني توجيهه إلى الكبد

- It binds to RNA molecules involved in producing pcsk9 and triggers their degredation and you will not get the pcsk9 enzyme hence you will get more LDL receptors because their is no lyzozomal degredation for them

↓ pcsk9 -> ↑ LDLR -> ↓ plasma LDL-C levels

- both (A) and (B) have same toryet but (A) by directly binding to the enzyme while (B) uses RNA interference

- No side effects, canbe cumbinate with statin

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(3) Apo C-III inhibitors

ApoC-III -> TAG يحكم, LPL يحكم

ApoC-III inhibitors -> help revarse ApoC-III affects

- Lipoprotein lypase is enzyme breakdown TAGs, ApoC-III stop Lpl from working -> No TAGs break down will be high tryglycerones so this ApoC-III inhibitors will help Lpl

- The idea of this drug -> It was found that loss-of-function mutations in the Apo3 gene are associated with 40% lower plasma TG levels and 40% lower risk of CVD
  ↳ espacially if the cause by VLDL

ApoC-III inhibitor: Volanesoren

- it is an antisence oligonucleotide ASO targeting apoC3 gene, it is a small interference RNA like Inclisiran
- used for patients with FCS and hypertriglyceridemia
- Adverse events:- thrombocytopenia rare, small incidence
  - Injection-Site reactions

(4) ANGPTL3 inhibitor

ANGPTL3 cause ⟶ ↓LPL ↓EL this will increase TG, LDL-C and HDL-C plasma levels

inhibitors will preserve the function of LPL and EL and will be most significant in decreasing TGs

LDL will not be affected

- therapies targeting ANGPTL3 were developed by two mechanisms:

1. **Evinacumab** a monoclonal antibody neutralizing levels in the serum

Side effect: It has an Influenza like effect was observed in 11%

1. **Vupanorsen** an antisense oligonucleotide (an siRNA) inhibiting production in hepatocytes

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