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Glymbaxi: A New Drug Designed to Assist Type 2 Diabetes Patients with Glycemic Control

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Title: Glyxambi a new drug designed to assist type 2 diabetes patients with glycemic control

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CHEM 205

Eli Lilly and Boehringer Ingleheim Pharmaceuticals

A Randomized, Open-Label, Crossover Study to Evaluate the Pharmacokinetics of Empagliflozin and Linagliptin After Coadministration in Healthy Male Volunteers

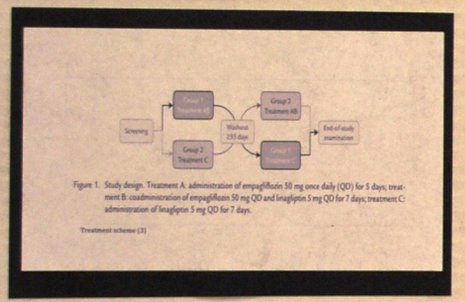


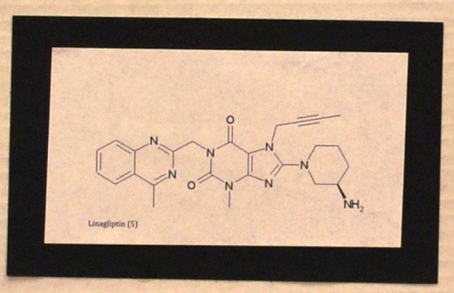
Figure 1. Study design. Treatment A: administration of empagliflozin 50 mg once daily (QD) for 5 days; treatment B: coadministration of empagliflozin 50 mg QD and linagliptin 5 mg QD for 7 days; treatment C: administration of linagliptin 5 mg QD for 7 days.

Treatment scheme (3)

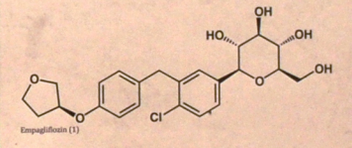
Glyxambi®
(EMPAGLIFLOZIN/LINAGLIPTIN) TABLETS

Glyxambi (2)

- First drug companies to design a drug that combined the mechanisms of SGLT2 and DPP-4 inhibitors to improve glycemic control (6)
- Just recently approved by the FDA
- Has not yet been studied in patients with a history of pancreatitis (6)
- Empagliflozin predominant transporter that's responsible for reabsorption of glucose from the glomerular filtrate back to circulation (2)
- Linagliptin inhibits DPP-4 an enzyme that degrades incretin hormones and increases the concentrations of active incretin hormones and stimulates the release of insulin (2)
- Incretin hormones are involved in the regulation of glucose homeostasis, they are secreted at low levels throughout the day and rise immediately after meals (2).



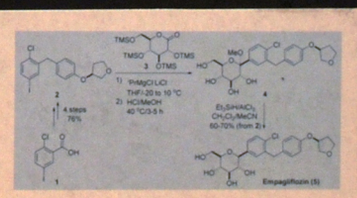
Linagliptin (5)



Empagliflozin (1)

- 16 male volunteer test subjects
- Randomized multiple dose crossover
- Treatment A empagliflozin 50 mg- 5days
- Treatment B empagliflozin 50 mg and linagliptin 5 mg- 7 days
- Treatment C linagliptin 5 mg – 7days
- Treatments done in sequence AB then C or C then AB
- Subjects did not see very many adverse side affects (3)
- Conlcusion- co-adminstration had an effect on glycemic control
- Results were in the norm for previous clinical trials (3)

- Glyxambi is not synthesized from either of the drugs used to make it.
- Researchers performed a diastereoselective synthesis of β- anomers of C-glycosides utilizing an α-face hydride reduction of an anomerically stabilized carbenium intermediate (7).
- Scientists used an acid 1,2-chloroiodobenzoic acid and replaced the alcohol group using (COCl)2 in DMF then a Friedal Crafts reaction was performed to add a fluorine phenyl group to the carbonyl. Aromatic substitution was performed using (S)-3-hydroxytetrahydrofuran and BuOK in THF (7).



Synthesis of empagliflozin (7)

Conclusion:

Glyxambi was a drug designed from empagliflozin and linagliptin two well known and used antidiabetic drugs used to treat type 2 diabetes. This newly designed drug combines the two mechanisms of these drugs to co-administer simultaneous glycemic control on all fronts to provide a more effective and efficient treatment for patients diagnosed with type 2 diabetes. Glyxambi was created by combining appropriate dosages of emagliflozin and linagliptin into a single tablet for once daily use. This drug is now available for physicians to administer to their patients because companies such as BIPI and Eli Lilly have pooled their resources to provide more effective treatment options for this disease. This new drug glyxambi is the first of its kind, but drug companies will continue to research and design better and more effective drugs for all diseases to provide a better quality of care and life for those suffering with diseases such as type 2 diabetes.

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