Media Backgrounder:

Canagliflozin Phase 3 Clinical Trial Programme

Overview

The global phase 3 programme evaluated the safety and efficacy of anti-hyperglycaemic agent canagliflozin, a selective sodium glucose co-transporter 2 (SGLT2) inhibitor. The programme enrolled 10,285 patients in nine studies.

The trials assessed the safety and efficacy of canagliflozin dosed at 100mg or 300mg once daily, when used as monotherapy, and in combination with oral anti-hyperglycaemic agents, and in combination with insulin with or without oral anti-hyperglycaemic agents.

Understanding the canagliflozin Phase 3 clinical trial programme

The comprehensive global Phase 3 clinical trial programme[1-9] is one of the largest late-stage development programmes for a pharmacological product for the treatment of type 2 diabetes submitted to health authorities to date.

The trials were randomised and double-blind and were either placebo-controlled or active comparator-controlled.

Three studies compared canagliflozin to current standard treatments[1-3]; two of which compared canagliflozin to sitagliptin[1,2] and the other to glimepiride.[3]

The Phase 3 programme also included three large studies in special populations: patients over 55 with type 2 diabetes[4], patients with type 2 diabetes who had moderate renal impairment[5], and patients with type 2 diabetes who were considered to be at high risk for cardiovascular disease.[6]

Results from the programme showed that both the 100mg and the 300mg doses of canagliflozin improved glycaemic control, compared to baseline, both as monotherapy and as add-on therapy with other anti-hyperglycaemic medicinal products.[10]

A secondary study endpoint showed that there was body weight reduction in the canagliflozin groups compared to those on placebo or an active comparator.[10]

Phase 3 results showed that canagliflozin was generally well-tolerated. Adverse drug reactions due to SGLT2 inhibition and associated with canagliflozin included; genital mycotic infections, urinary tract infections (UTIs), osmotic diuresis (such as urinary frequency, thirst or constipation), reduced intravascular volume (such as postural dizziness). Canagliflozin was also associated with a low incidence of rash or urticaria.[10]

The frequency of hypoglycaemia was low when canagliflozin was used as a monotherapy, or as an add-on to metformin or in combination with other agents with a low risk of hypoglycaemia.[10]

Janssen
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Media Backgrounder:

Canagliflozin Phase 3 Clinical Trial Programme

Phase 3 Clinical Development Programme:

10,285 patients in nine studies

Canagliflozin as a monotherapy[7]

- 26 weeks with 26 week extension
- 587 patients (randomised)
- 3 treatment arms:
- canagliflozin 100mg
- canagliflozin 300mg
- and placebo

Canagliflozin as dual therapy[1,3]

Combination with metformin[1]
- 26 weeks with 26 week extension
- 1284 patients (randomised)

4 treatment arms:
- canagliflozin 100mg
- canagliflozin 300mg
- sitagliptin 100mg
- placebo

Combination with metformin vs glimepiride[3]

52/52 weeks

1450 patients (randomised)

3 treatment arms:
- canagliflozin 100mg
- canagliflozin 300mg
- glimepiride (titrated up to 6-8 mg)

Canagliflozin as triple therapy[2,8,9]

Combination with metformin/ sulfonylurea vs. sitagliptin[2]
- 52 weeks
- 756 patients (randomised)

2 treatment arms:
- canagliflozin 300mg
- sitagliptin 100mg

Combination with metformin/ sulfonylurea[8]
- 26/26 weeks
- 469 patients (randomised)

3 treatment arms:
- canagliflozin 100mg
- canagliflozin 300mg
- placebo

Combination with metformin/ pioglitazone[9]
- 26/26 weeks
- 342 patients (randomised)

3 treatment arms:
- canagliflozin 100mg
- canagliflozin 300mg
- placebo

Canagliflozin in special populations[5,6,4]

Moderate renal impairment[5]
- 26/26 weeks
- 269 patients (randomised)

3 treatments arms:
- canagliflozin 100mg
- canagliflozin 300mg
- placebo

CV outcome study in people with, or at high risk of cardiovascular disease[6]
- Event-driven, up to 9 years in duration
- 4330 patients (randomised)

3 treatment arms:
- canagliflozin 100mg
- canagliflozin 300mg
- placebo

Older subjects[4]
- 26/78 weeks
- 716 patients (randomised)

3 treatment arms:
- canagliflozin 100mg
- canagliflozin 300mg
- placebo

References

1. Lavalle-González FJ et al. Efficacy and safety of canagliflozin compared with placebo and sitagliptin in patients with type 2 diabetes on background metformin monotherapy: a randomised trial. Diabetologia. 2013;56(12):2582-92
2. Schernthaner G et al. Canagliflozin compared with sitagliptin for patients with type 2 diabetes who do not have adequate glycemic control with metformin plus sulfonylurea: a 52-week randomized trial. Diabetes Care. 2013; 36(9):2508-15
3. Cefalu WT et al. Efficacy and safety of canagliflozin versus glimepiride in patients with type 2 diabetes inadequately controlled with metformin (CANTATA-SU): 52 week results from a randomised, double-blind, phase 3 non-inferiority trial. Lancet. 2013; 382(9896):941-50.
4. Bode B et al. Efficacy and safety of canagliflozin treatment in older subjects with type 2 diabetes mellitus: a randomized trial. Hosp Pract. 2013;41(2):72-84.
5. Yale JF et al. Efficacy and safety of canagliflozin in subjects with type 2 diabetes and chronic kidney disease. Diabetes Obes Metab. 2013;15(5):463-73.
6. Neal B, Perkovic V, et al. (2013). Rationale, design, and baseline characteristics of the Canagliflozin Cardiovascular Assessment Study (CANVAS)—A randomized placebo-controlled trial. American Heart Journal; 166(2): 217-223
7. Stenlof et al. Efficacy and safety of canagliflozin monotherapy in subjects with type 2 diabetes mellitus inadequately controlled with diet and exercise. Diabetes Obes Metab. 2013;15(4):372-82.
8. Wilding JP et al. Efficacy and safety of canagliflozin in patients with type 2 diabetes mellitus inadequately controlled with metformin and sulphonylurea: a randomised trial. Int J Clin Pract. 2013;67(12):1267-82
9. Forst T et al. Efficacy and Safety of Canagliflozin in subjects with Type 2 Diabetes on Metformin and Pioglitazone. Poster presented at the 4th World Congress on Controversies to Consensus in Diabetes, Obesity and Hypertension (CODHy), 2012;Nov.8-11; Barcelona, Spain, (P64).
10. INVOKANA SmPC. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002649/WC500156456.pdf Last accessed April 2014

Janssen
PHARMACEUTICAL COMPANIES OF Johnson & Johnson