

Victoza® clinical development programme

Overview

The safety and efficacy of Victoza® (liraglutide) has been extensively investigated in a clinical development programme involving more than 6,500 people from 40 countries worldwide. The phase 3 clinical trials for Victoza®, called LEAD™ (Liraglutide Effect and Action in Diabetes), comprised five randomised, controlled, double-blinded trials plus one open-label trial.

The LEAD™ programme compared once-daily liraglutide (Victoza®) with three widely-used classes of diabetes therapies – glimepiride, rosiglitazone and insulin glargine, as well as a direct comparison (LEAD™ 6) between liraglutide and exenatide.

A summary of the results from the LEAD™ programme is provided below:

Results summary

Study design	Efficacy summary	Safety summary
LEAD™ 3: Liraglutide as monotherapy versus glimepiride		
<ul style="list-style-type: none"> 52-week study, followed by a 208-week open-label extension 746 patients were randomised into three groups: liraglutide 1.2 mg, liraglutide 1.8 mg or glimepiride 8 mg 	<ul style="list-style-type: none"> Treatment with liraglutide 1.2 mg and 1.8 mg resulted in superior HbA_{1c} (blood sugar) reduction compared with glimepiride monotherapy The percentage of patients reaching ADA target HbA_{1c} <7% was significantly higher with both liraglutide doses compared with glimepiride monotherapy Change in bodyweight was significant for both liraglutide dose groups compared with glimepiride Blood pressure was significantly reduced with liraglutide 1.8 mg compared with glimepiride 	<ul style="list-style-type: none"> There were no major hypoglycaemic episodes reported during the study The rate of minor hypoglycaemia was significantly lower in both liraglutide dose groups compared with the glimepiride-treated group and was not dose-dependent Most adverse events were short term and mild or moderate in severity
LEAD™ 2: Liraglutide added on to metformin versus glimepiride		
<ul style="list-style-type: none"> 26-week study 1091 patients were randomised into five groups: 0.6 mg liraglutide plus metformin, 1.2 mg liraglutide plus metformin, 1.8 mg liraglutide plus metformin, metformin monotherapy, or glimepiride plus metformin 	<ul style="list-style-type: none"> Treatment with liraglutide 0.6 mg, 1.2 mg and 1.8 mg added on to metformin resulted in superior HbA_{1c} reduction compared with metformin monotherapy. The 1.2 mg and 1.8 mg liraglutide doses were non-inferior to glimepiride/metformin combination therapy The percentage of patients reaching ADA target HbA_{1c} <7% was significantly higher with all liraglutide doses compared with metformin monotherapy Change in body weight in all the liraglutide dose groups were superior to those in the glimepiride/metformin group, and changes in the 1.2 mg and 1.8 mg liraglutide groups were superior to those in the metformin monotherapy group Blood pressure was significantly reduced in the liraglutide 1.2 and 1.8 mg groups compared with the glimepiride/metformin combination therapy group 	<ul style="list-style-type: none"> There were no major hypoglycaemic episodes reported during the study The rate of minor hypoglycaemia was significantly lower in all three liraglutide dose groups compared with the glimepiride/metformin group The most frequently reported adverse events in the liraglutide groups were gastrointestinal in nature. The majority were mild and transient, decreasing over time

LEAD™ 1: Liraglutide added on to glimepiride versus rosiglitazone		
<ul style="list-style-type: none"> • 26-week study • 1041 patients were randomised into five groups: 0.6 mg liraglutide plus glimepiride, 1.2 mg liraglutide plus glimepiride, 1.8 mg liraglutide plus glimepiride, glimepiride monotherapy, or glimepiride plus rosiglitazone 	<ul style="list-style-type: none"> • Treatment with liraglutide 0.6 mg, 1.2 mg and 1.8 mg added on to glimepiride resulted in superior blood sugar control compared with glimepiride monotherapy • The 1.2 mg and 1.8 mg liraglutide doses resulted in superior blood sugar control compared with glimepiride/rosiglitazone • Change in body weight significantly favoured all three doses of liraglutide compared with rosiglitazone 	<ul style="list-style-type: none"> • One patient treated with liraglutide 1.8 mg plus glimepiride experienced a major hypoglycaemic episode • Most adverse events were mild or moderate, and the majority were gastrointestinal in nature. Gastrointestinal adverse events were more common among patients treated with liraglutide, but were transient in nature
LEAD™ 4: Liraglutide added on to metformin + rosiglitazone versus placebo		
<ul style="list-style-type: none"> • 26-week study • 533 patients were randomised into three groups: 1.2 mg liraglutide plus metformin and rosiglitazone, 1.8 mg liraglutide plus metformin and rosiglitazone, or metformin and rosiglitazone plus liraglutide placebo 	<ul style="list-style-type: none"> • Treatment with liraglutide 1.2 mg and 1.8 mg added on to metformin and rosiglitazone resulted in statistically significant mean reductions in HbA_{1c} compared with metformin and rosiglitazone alone • The percentage of patients reaching ADA target HbA_{1c} <7% was significantly higher in both liraglutide dose groups compared with metformin and rosiglitazone alone • Change in body weight significantly favoured both liraglutide dose groups compared with metformin and rosiglitazone alone • Blood pressure was significantly reduced in both liraglutide groups compared with metformin/rosiglitazone 	<ul style="list-style-type: none"> • There were no major hypoglycaemic episodes reported during the study • The frequency of minor hypoglycaemia was low with both liraglutide doses. The rate of minor hypoglycaemic events was, however, significantly higher with 1.8 mg liraglutide compared with metformin/rosiglitazone alone • Nausea and diarrhoea were the most common adverse events in the liraglutide groups. Most adverse events with liraglutide were mild in severity
LEAD™ 5: Liraglutide added on to metformin + glimepiride versus placebo insulin glargine		
<ul style="list-style-type: none"> • 26-week study • 581 patients were randomised into three groups: 1.8 mg liraglutide, liraglutide placebo or once-daily insulin glargine, each added to glimepiride/metformin combination therapy 	<ul style="list-style-type: none"> • The addition of liraglutide 1.8 mg to glimepiride/metformin combination therapy resulted in superior HbA_{1c} reduction compared with glimepiride/metformin therapy alone and glimepiride/metformin plus insulin glargine therapy • The percentage of patients reaching ADA target HbA_{1c} <7% was significantly higher among Liraglutide-treated patients compared with patients treated with insulin glargine or glimepiride/metformin • Mean weight loss was significantly greater in the liraglutide group compared with the other groups. Weight increased by 1.6 kg in the insulin glargine group • Blood pressure was significantly reduced in patients treated with liraglutide compared with those in the insulin glargine group 	<ul style="list-style-type: none"> • Six major hypoglycaemic episodes occurred in five subjects, all in the liraglutide group • Rates of minor hypoglycaemic episodes were similar in the groups that received liraglutide, insulin glargine and glimepiride plus metformin alone • The rate of nocturnal minor hypoglycaemic episodes appeared to be lower in the liraglutide treated group • Diarrhoea and nausea were the most common adverse events in the liraglutide group. Most of these adverse events were mild, decreasing over time
LEAD™ 6: Liraglutide added on to metformin + and/or glimepiride versus exenatide		
<ul style="list-style-type: none"> • 26-week study • 464 patients were randomised to receive 1.8 mg once-daily liraglutide or 10 µg twice-daily exenatide, both added to ongoing OAD treatment (SU [sulphonylurea] 10%, metformin 30%, SU + metformin 60%) 	<ul style="list-style-type: none"> • Mean HbA_{1c} reduction was significantly greater with liraglutide treatment than with exenatide • Changes in body weight were comparable between the two treatment groups, and clinically meaningful (-3.24 kg with liraglutide treatment and -2.87 kg with exenatide) 	<ul style="list-style-type: none"> • No major cases of hypoglycaemia occurred with liraglutide treatment; two episodes occurred in the exenatide group • Minor hypoglycaemia was significantly less frequent with liraglutide treatment than with exenatide • The rate of nocturnal minor hypoglycaemic episodes appeared to be lower in the liraglutide treated group • Nausea was the most frequently reported adverse event with liraglutide and exenatide, however the percentage of patients with nausea decreased more rapidly with liraglutide treatment

References

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