ADA Analyst Presentation
Saturday 9th June

Carlo Russo

Senior Vice-President & Albiglutide Team Leader, GSK

Agenda

Welcome & introduction to the Harmony Clinical Programme	Carlo Russo Senior Vice-President, Albiglutide Team Leader
Results from Harmony 6 & Harmony 7	Dr Richard E. Pratley Director, Florida Hospital Diabetes Institute, USA
The Evolution of Type 2 Diabetes Treatment	Professor Philip Home Professor of Diabetes Medicine, Newcastle University, UK
Q&A discussion	
Refreshments	

The HARMONY Programme: Ongoing Phase III Studies

Study	Background Therapy	Comparators	No. of Patients Randomized	Primary Endpoint	Estimated LPLV
H2H vs liraglutide HARMONY 7	Metformin, pioglitazone, glimepiride, or combination	Liraglutide	841	32 weeks	COMPLETED Presented at ADA 2012
Add-on to insulin glargine HARMONY 6	Basal insulin glargine	Prandial insulin	586	6 months	COMPLETED Presented at ADA 2012
Renal impairment HARMONY 8	Metformin, pioglitazone, glimepiride, or combination	Sitagliptin	507	6 months	Jul 2012
Monotherapy HARMONY 2	Diet & exercise (treatment-naïve patients)	Placebo	309	1 year	Jan 2013
Add-on to pioglitazone HARMONY 1	Pioglitazone ± metformin	Placebo	310	1 year	Jan 2013
Add-on to metformin + SU HARMONY 5	Metformin + glimepiride	Pioglitazone or placebo	685	1 year	Mar 2013
H2H vs insulin glargine HARMONY 4	Metformin or metformin + SU	Insulin glargine	779	1 year	Feb 2013
Add-on to metformin HARMONY 3	Metformin	Sitagliptin, glimepiride, or placebo	1049	2 years	Feb 2013

Harmony 6 Results

Add-on to Insulin Glargine vs prandial Lispro Insulin in Subjects With Type 2 Diabetes Mellitus

Richard Pratley MD
Director, Florida Hospital Diabetes Institute & Diabetes Professor, Sanford Burnham Medical Research Institute, Florida, US

Harmony 6 Study Design

Insulin glargine
≥20 units per day
N = 500
HbA1c: 7-10.5%

Albiglutide 30 → 50 mg weekly
n = 250

Prandial lispro
N = 250

Primary Endpoints:
- Non-inferiority vs lispro
    - Superiority vs lispro, if non-inferiority met

Other Endpoints:
- Time to, and % requiring rescue
- Weight
- Hypoglycemia
- QoL
- FP

Study Design
- Randomized, open-label active controlled, parallel group study
- Optional up-titration of albiglutide 30→50 mg weekly, starting at Week 8
- Titration of basal and pre-prandial insulin, to meet pre-specified protocol criteria
- Primary Endpoint: 26 weeks
- Study Duration: 52 weeks
- 586 randomized; 566 received treatment

Overall Conclusions

- Efficacy
  - Both albiglutide and lispro produced clinically significant reductions in HbA1c from baseline (-0.82 % vs -0.66%, respectively)
  - Albiglutide met the non-inferiority endpoint for HbA1c vs. lispro ($p<0.0001$) at 26 weeks, and only just missed showing superiority ($p=0.0533$)
  - The FPG trend mirrored the HbA1c curve, with greater reduction in the albiglutide treatment arm than the pre-prandial Lispro arm
  - The observed weight change at Week 26 in the albiglutide arm was statistically greater than the pre-prandial insulin arm (-0.73 kg vs +0.81 kg)
  - No meaningful difference between treatment groups when viewed by subgroup (background OAD, gender, race, etc)
  - Efficacy and weight loss in the albiglutide arm were maintained through 52 weeks

Overall Conclusions

- Safety
  - The 52 week nausea/vomiting rates for albiglutide were consistent with Harmony 7. Rates were higher in the albiglutide arm compared to Lispro:
      - Nausea: 13.0% with albiglutide and 2.1% with Lispro
      - Vomiting: 7.0% with albiglutide and 1.4% with Lispro
    - Hypoglycemia at week 52: 32.6% with albiglutide and 49.8% with Lispro
      - Three events of severe hypoglycemia in the pre-prandial Lispro arm vs zero in the albiglutide arm
  - Rates of events of special interest at Week 52 with albiglutide were consistent between this study and Harmony 7:
    - Injection site reactions: 9.5% with albiglutide and 5.3% with Lispro
    - Acute pancreatitis: Zero events with both albiglutide and Lispro
    - Thyroid nodules/neoplasm: one subject who received one dose of albiglutide with calcitonin elevated at baseline & subsequently determined to be MEN positive, and no subjects with Lispro

Harmony 7 Results

A Randomized, Open-Label, Parallel-Group, Multicenter Study to Determine the Efficacy and Safety of Albiglutide as Compared With Liraglutide in Subjects With Type 2 Diabetes Mellitus

Harmony 7 Study Design

Inadequate control on Met, TZD, SU, or combination
N = 800
HbA_{1c}: 7%-10%

Albiglutide
n = 400

Liraglutide
n = 400

Primary endpoints
- Noninferiority (≥ superiority) vs liraglutide

Other endpoints
- FPG
- Time to rescue
- Weight
- Hypoglycemia
- QoL

Study Design

- Randomized, double-blind, active-controlled, parallel-group study
- Titration protocol of albiglutide 30 → 50 mg QW and liraglutide (1.2 → 1.8 mg QD)
- Study duration: 32 weeks
- Primary endpoint: Change in HbA_{1c} from baseline as compared with liraglutide

Overall conclusions

- Liraglutide (once daily) and albiglutide (once weekly) clinically and statistically reduced HbA1c from baseline. (−0.78% 0.99 with ALBI and −0.99% 1.02 with LIRA [treatment difference: 0.21% $P < .001$])
- The treatment difference did not meet non-inferiority criteria. (95% CI: 0.08–0.34%).
- Albiglutide was generally well tolerated and had a better GI tolerability than liraglutide
- Both agents showed reductions in weight loss, but this was better with liraglutide (LIRA [−2.19 kg] greater than ALBI [−0.64 kg])

Type II diabetes: An evolving treatment landscape

Professor Philip Home

Professor of Diabetes Medicine, Newcastle University, UK

Q&A