EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Type 2 Diabetes PIP Overview

Janina Karres, PhD

Paediatric Medicines, EMA

Number of PIPs: 16

Number of studies per PIP

One Pivotal Study and **one** PK/PD: 12/16

One Pivotal including PK sub-study: 2/16

Two Pivotals, one including PK sub-study: 2/16

-> 18 pivotal studies

-> 13 separate PK/PD studies

Type of Studies – Patient Population (Pivotal)

Monotherapy: 2/18

Add-on to Metformin: 6/18

Add-on to Metformin +/- Insulin: 1/18

Mixed population (Monotherapy and Add-on to Metformin): 7/18

Mixed population (Monotherapy and Add-on to Metformin or SU): 1/18

Mixed population (Monotherapy and Add-on to Insulin): 1/18

Type of Studies- Patient Population (PK/PD- single studies only)

Monotherapy: 5/13

Add-on to Metformin: 2/13

Mixed population (Monotherapy and Add-on to Metformin): 6/13

Type of studies (pivotal)

2-arm study (Placebo and New Drug): 16/18

3-arm study (Placebo and New Drug and Metformin): 2/18

Parallel study arms: 18/18

Cross-over studies: 0/18

(Cross-over PK/PD studies: 2/12)

Patient Population (Pivotal Studies)

HbA1c values

Monotherapy:
HbA1c from **6.5% to 7%** up to **10%**

Add-on:
(to metformin or insulin or metformin + insulin)
HbA1c from **6.5% to 7%** up to **10%**

Mixed Population:
(monotherapy plus add-on to metformin or insulin or SU)
HbA1c from **6.5% to 7%** up to **10% to 11%**

Patient Population (Pivotal Studies)

Allow previous glucose lowering agent:

Insulin for less than **1w / 4w / 5w / 6w / 10w** within

the **3 months** prior to screening.

Trail Duration (Pivotal Studies)

Placebo controlled treatment phase

3 months: 5/18

4 months: 7/18

6 months: 5/18

12 months: 1/18

One year exposure data for safety for all pivotal studies

Endpoints (Pivotal Studies)

Primary endpoint:

Mean change in HbA1c levels from baseline to 12/16/26 weeks, active versus placebo

Secondary endpoints:

Percentage of patients achieving HbA1c of <6.5% and <7%
Change in fasting plasma glucose
Body weight and BMI SDS (age and gender adjusted)
Incidence of rescue treatment
Lipid profile

Endpoints (PIPs)

Secondary endpoint:

Beta- Cell Function: 11/16

5 Gliptins

4 GLP1 analogue

1 Sodium glucose co-transporter 2 inhibitor

1 G-protein coupled receptor 40 agonist

Method: - mostly C peptide levels (after standard meal)

Number of patients per PIP (PK or PK/PD and Pivotal Studies)

Total number of paediatric patients in all PIPs: **3588**

Total number of patients in all PK or PK/PD Studies: **504**
Average per PK or PK/PD Study: **32** (range: **12 – 100**)

Total number of patients in all Pivotal Studies: **3196**
Average per Pivotal Study: **178** (range: **90 – 300**)

Main differences amongst PIPs

Patient population within studies (Mono-, Add-on, Mixed population)

2-arm study vs 3-arm study (pivotal)

Previous glucose lowering agents

Duration of placebo controlled treatment phase/
Timepoint of primary endpoint evaluation

Large range of patients in PK/PD studies