PBI-4050 Reduces Key Cardiorenal Biomarkers and Urinary Microparticles in Type 2 Diabetes Patients with Metabolic Syndrome

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Introduction and Aim

PBI-4050 is an orally active drug candidate with antifibrotic efficacy in multiple preclinical models of fibrosis in kidney, liver, lung, heart and pancreas. Phase I studies in normal volunteers, and Phase Ib studies in patients with advanced nephropathy associated with type 2 diabetes (T2D) have been successfully completed.

Open label, single arm phase II study (NCT02562573) of oral administration of PBI-4050, 160 mg once daily for 12 or 24 weeks was conducted in T2DM subjects with metabolic syndrome with suboptimal glycemic control despite oral anti-hyperglycemic medications.

Study Design

Only fasting blood glucose monitored- Weekly phone calls and 4-point profile.

Objectives

Safety and tolerability

- Very well tolerated, no drug related SAEs
- Excellent safety profile even when added to cocktail of drugs to treat diabetes, hypertension, etc.

Primary Endpoints:

- Safety/adverse events
- Hypoglycemia

Secondary Endpoints:

- Change in glycemic control (HbA1c, FPG, 7 point profile)
- Change in metabolic parameters (HOMA-B, HOMA-IS)
- Need for rescue therapy

Secondary Endpoints:

- Change in inflammatory biomarkers
- Need for rescue therapy

Inclusion Criteria:

- Adults with Type 2 diabetes and metabolic syndrome (WHO)
- Treatment with oral agents
- HbA1c > 7.10% despite treatment > 3 months
- BMI > 27 kg/m²

Exclusion Criteria:

- History of severe hypoglycemia
- Significant cardiovascular disease
- Active infection or inflammation
- Active in infection or inflammation
- Need for rescue therapy
- Hypoglycemia risk
- Hypoglycemia risk
- Weight gain – overall reduction, waist circumference reduction
- Pharmacokinetic
- PK in patients with CKD was the same as healthy volunteers

Biomarkers

- Positive effects on pro-inflammatory biomarkers associated with higher risk of cardiovascular events, and renal events

Conclusions

- Advantages, potential reduction of complications – disease progression/fibrosis in heart, kidney, pancreas and liver

Results

- HbA1c reduction in patients with baseline HbA1c > 7.5% (p=0.007)
- HbA1c reduction in patients with baseline HbA1c > 8% (p=0.0004)

Biomarkers associated with kidney injury

- % change of HbA1c between baseline, week 12 and 24
- For patients opting to continue after 12 weeks

- IL-18 0.69 (p=0.017)
- Calbindin 0.69 (p=0.042)
- Pentraxin 0.69 (p=0.017)
- TFF3 0.85 (p=0.036)

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