Effectiveness of prandial insulin therapy for patients with type 2 diabetes – clinical results of PHAZIT®

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Background:

Providing short-acting insulin at mealtimes is an increasingly common therapy for patients with type 2 diabetes, despite a lack of information regarding the cost-effectiveness of prandial use of insulin. The PHAZIT® study has been designed to compare the prandial use of a short-acting insulin analogue (insulin aspart; ASP) with human soluble insulin (HI) – both in combination with metformin (MET) – with regard to metabolic control, dose requirement, weight and incurred treatment costs.

Material and Methods:

- Combined clinical and economic study[1]
- National, prospective, non-randomised, non-interventional observational study to compare results of treatment change under outpatient real-life conditions (post-marketing survey [PMS][2])
- Participating 51 outpatient diabetes clinics
- Inclusion criteria:
  - Type 2 diabetes mellitus
  - Previous therapy with two oral hypoglycaemic agents, including MET
  - Insufficient metabolic control at time of treatment change (HbA_{1c} between 7.0% and 12.0%)
  - Patients switched to a combination of MET either with the short-acting insulin analogue ASP or an HI

Therapy

- Short-acting insulin analogue ASP in combination with MET (ASP/MET: n=312) or HI in combination with MET (HI/MET: n=292)
- Observation period: 24 weeks
- Points of observation: baseline, after 12 weeks and 24 weeks of therapy

Primary outcome parameter was change of HbA_{1c} after 24 weeks of therapy compared with baseline. Secondary parameters were change of weight, safety, insulin dosage and costs. Preliminary data from 604 patients with type 2 diabetes are presented

Quality assurance

- Signed study protocol defined the study design and statistical methods for all analyses
- Measurement of HbA_{1c} in a central laboratory to ensure comparability of measured values
- Performed external monitoring to assure quality of data

Study population

- Number of patients included: 745 (ASP/MET: 392, HI/MET: 353)
- Present preliminary data show results of 604 patients (intention-to-treat population) from 51 participating study centres with at least two documented observation points

Patients in both groups were very similar regarding age, duration of diabetes, gender, co-morbidities and risk factors (Tab. 1)

Table 1.

Parameter (mean +/– SD)	ASP/MET	HI/MET
Number of patients	312	292
Gender	female 48.1% male 51.9%	female 49.7% male 50.3%
Age (years)	61.1* (+/–9.4)	63.0* (+/–9.5)
Duration of diabetes (years)	9.7 (+/–6.2)	9.7 (+/–6.8)
Hypertension (%)	73.6	73.3
Dyslipidaemia (%)	61.6	55.6
HbA_{1c} at baseline	8.77% (+/–1.09)	8.77% (+/–1.13)
Bodyweight (kg) (baseline)	89.9 (+/–17.95)	89.8 (+/–17.48)
BMI (kg/m²) (baseline)	31.4 (5.69)	31.6 (5.43)
Dose of insulin/day (baseline)	24.0* U (+/–13.1)	26.9* U (+/–14.9)
Dose of insulin/day (24 weeks)	29.7** U (+/–16.3)	35.3** U (+/–17.3)

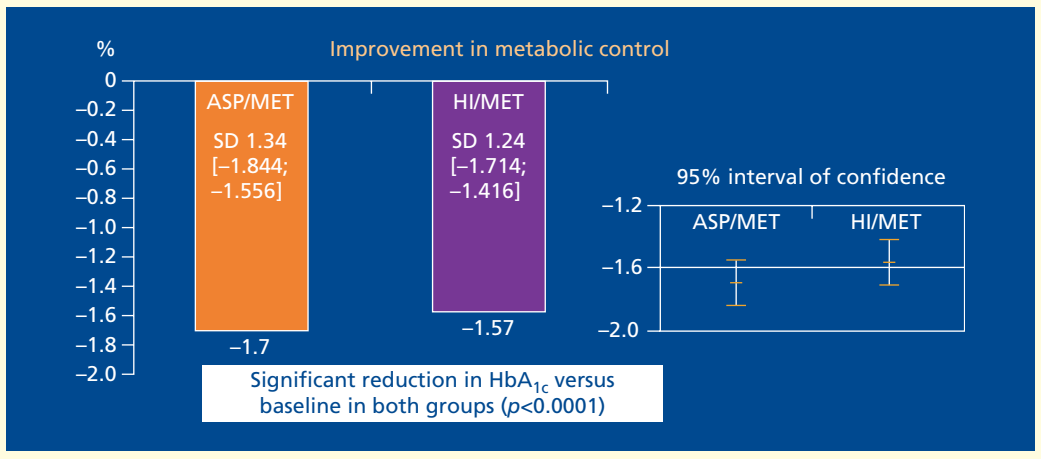
SD = standard deviation; U = units; **p<0.01; *p<0.05

Results:

Primary endpoint HbA_{1c}

- Mean HbA_{1c} at baseline was nearly identical in both groups (Tab. 1)
- Significant (p<0.0001) reduction in HbA_{1c} after 24 weeks of therapy versus baseline in both groups (Fig. 1)
- Slightly greater reduction in HbA_{1c} after 24 weeks of therapy in the ASP/MET group compared with the HI/MET group (Fig. 1)

Fig 1: Improvement in metabolic control: HbA_{1c}



Bodyweight

- Mean bodyweight at baseline was nearly identical in both groups (Tab. 1)
- Moderate weight loss in the ASP/MET group (–0.41kg) and a moderate weight gain in the HI/MET group (+0.33 kg). This difference between the groups was significant with p<0.05 (Fig. 2)
- Weight loss or no change in weight was seen at 61.2% of the patients in the ASP/MET group while 53.3% of the patients in the HI/MET group showed weight loss or no change (Fig. 3)

Fig 2: Change of bodyweight (mean) after 24 weeks

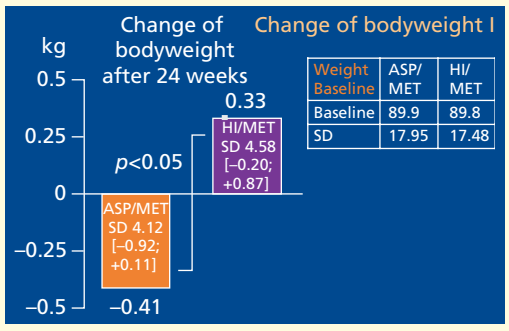
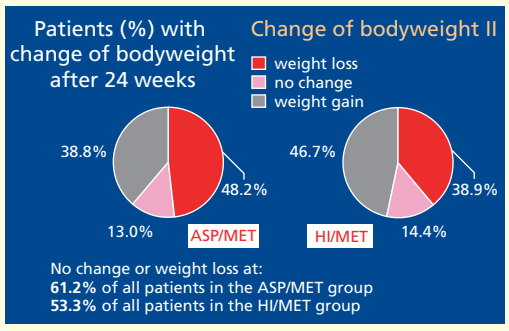


Fig. 3: Patients with weight loss, no change or weight gain



Dose requirements and therapy

- Significantly (p<0.01) less requirement for insulin in the ASP/MET group (Fig. 4) at baseline and after 24 weeks of therapy (ASP/MET 29.7 U/day; HI/MET 35.3 U/day) which corresponds to a saving of daily insulin of 16% in the ASP/MET group (Fig. 4)
- Analysing insulin dosage per kg bodyweight showed 0.34 U/kg/day in the ASP/MET group and 0.40 U/kg/day in the HI/MET group and confirmed the results

Additional benefits

- 83.6% of all patients in the ASP/MET group could use an immediate preprandial regimen, while there were only 24.9% of all patients in the HI/MET group injecting immediately before a meal (Fig. 5).

Fig. 4: Daily requirement of insulin after 24 weeks

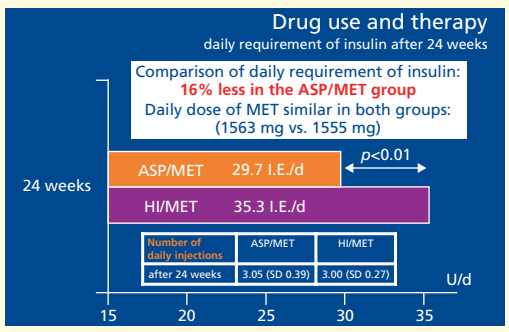
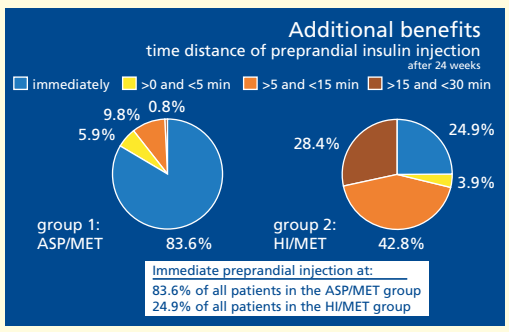


Fig. 5: Additional benefits



Summary:

- Prandial insulin therapy in combination with MET for at least 24 weeks proved to be very effective in regulating glycaemic control
- Patients in both groups were similar regarding age, duration of diabetes, gender and known co-morbidities such as hypertension and dyslipidaemia. A significant and nearly identical improvement in glycaemic control was observed in both groups, while patients in the ASP/MET group required 16% less insulin than patients in the HI/MET group (p<0.01), indicating that the usage of a short-acting insulin analogue (ASP/MET) could be more cost-effective than the use of human soluble insulin (HI/MET). The MET dose in both groups was similar
- Patients treated with ASP/MET revealed additional benefits in terms of weight loss
- Further analyses of these preliminary results will be completed, in addition to a comparison of cost-effectiveness between treatments

PHAZIT® was conducted to illustrate the use of short-acting insulin at mealtimes under real outpatient conditions. Regarding outcomes as well as data capture, extensive methods of quality assurance were used to guarantee a high degree of internal validity. Altogether, the study design of PHAZIT® follows actual recommendations for post-marketing surveys[2] as well as for pharmacoeconomic evaluation[3,4] and is appropriate to generalise results for "daily practice" under outpatient conditions (external validity)[5–9].

Through additional documentation of drug and treatment costs, PHAZIT® is a combined clinical and economic observation study conducted as a treatment comparison to analyse efficacy and costs in a real-life setting.

Literature

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