News from the 87th Annual Meeting of the Endocrine Society

San Diego, California, US June 2005

Pioglitazone: good performer long-term

Long-term treatment with pioglitazone as a first-line monotherapy for type 2 diabetes mellitus is as effective as glibenclamide, according to the results of a multicentre study.[1] This double-blind 56-week study included 502 treatment-naive patients who had diabetes for < 2 years and an HbA_{1c} of 7.5–11.5%. Patients were randomised to receive pioglitazone 15mg (n = 251) or glibenclamide 5mg; doses were up-titrated every 4 weeks for the first 16 weeks to achieve fasting plasma glucose levels of 70–140 mg/dL.

At week 56, there were no significant differences between the two treatment groups in the mean reductions from baseline in fasting plasma glucose levels and HbA_{1c} values [*see table 1*]. However, patients receiving pioglitazone had significantly greater reductions from baseline in postprandial plasma glucose levels, compared with patients receiving glibenclamide. Significantly fewer patients in the pioglitazone group, compared with glibenclamide recipients withdrew from the study due to lack of efficacy or adverse events (12.8% vs 20.8%).

Table 1. Long-term effects on glycaemic control in patients with diabetes, according to therapy

	Glibenclamide	Pioglitazone
Mean change from baseline at week 56:		
HbA_{1c} (%)	−2.02	−2.07
Fasting plasma glucose (mg/dL)	−38.8	−40.5
Postprandial plasma glucose (mg/dL)	−49.5	−66.5*

* $p < 0.05$ vs glibenclamide

Octreotide first-line therapy for acromegaly

Sustained-release octreotide [Sandostatin LAR] is effective in the first-line treatment of acromegaly, according to the results of a multicentre study.[2] Of the 98 patients involved in the study, 79 patients completed 48 weeks of treatment with octreotide and were included in the analysis. Patients received four IM injections of sustained-release octreotide 20mg, followed by doses of 10mg, 20mg or 30mg every 4 weeks thereafter. The majority of patients (n = 70) had macroadenomas and the rest had microadenomas.

Table 2. Effects of octreotide in patients with acromegaly

	Patients with microadenoma (n = 9)	Patients with macroadenoma (n = 70)
Mean 2-hour growth hormone profile (μg/L):		
Baseline	5.44	34.85
Week 48	1.71	9.87
Mean insulin-like growth factor-I level (μg/L):		
Baseline	562.2	702.0
Week 48	218.4	435.6
Reduction from baseline in tumour volume (% of patients):		
> 20%	100.0	69.8
≥ 30%	87.5	54.0
≥ 40%	87.5	41.3
≥ 50%	75.0	27.0
≥ 60%	75.0	12.7

After 48 weeks, patients had a reduction from baseline in the incidence and severity of acromegaly symptoms; the mean composite symptom score was reduced from baseline by 70%. Patients with macroadenomas and those with microadenomas had reductions from baseline in mean 2-hour growth hormone profiles and serum insulin-like growth factor (IGF)-I levels [*see table 2*]. Furthermore, the majority of patients (73.2%) had a reduction from baseline in tumour volume of > 20%; a reduction in tumour volume of ≥ 60% was observed in 19.7% of patients.

Metformin superior to clomifene

In a randomised study, metformin was more effective than clomifene in the treatment of anovulatory infertility in women with polycystic ovary syndrome (PCOS).[3] The study included 100 such patients who received metformin 850mg twice daily and were followed for 221 cycles, or clomifene 150mg once daily for 5 days commencing on day 3 of progesterone withdrawal bleeding and were followed for 205 cycles.

There were no significant differences between the metformin and clomifene groups in the ovulation rate [*see table 3*]. However, the pregnancy rate was significantly higher in patients receiving metformin, compared with patients receiving clomifene. After six cycles of treatment, patients in the metformin group had a significantly greater cumulative pregnancy rate than clomifene recipients. Compared with patients in the clomifene group, metformin recipients had a significantly lower incidence of abortion and a non-significant trend towards a higher live birth rate.

Table 3. Comparison of fertility rates in patients with polycystic ovary syndrome, according to therapy

	Clomifene	Metformin
Incidence of events (% of patients):		
Ovulation	67.0	62.9
Pregnancy	7.2	15.1*
Cumulative pregnancy	34.0	68.9**
Abortion	37.5	9.5†
Live births	56.3	83.9

* $p < 0.01$ vs clomifene
** $p < 0.001$ vs clomifene
† $p < 0.05$ vs clomifene

Sustained-release somatropin effective

Weekly injections of sustained-release somatropin [LB 03002] were shown to be as effective as standard release somatropin in children with growth hormone deficiency in a phase II study.[4] This randomised, open-label, 6-month study included 42 prepubertal children who received sustained-release somatropin 0.3 mg/kg (n = 13) or 0.5 mg/kg (14) once weekly, or standard release somatropin 0.3 mg/kg/week administered as daily injections six times a week. At baseline, the three treatment groups had mean annualised height velocities of 3.1, 3.9 and 3.0 cm/year, respectively.

At 6 months, patients receiving sustained-release somatropin 0.3 mg/kg and 0.5 mg/kg had significant improvements from baseline in mean annualised height velocity, which were comparable with the improvement observed in patients receiving standard release somatropin (9.3, 10.2 and 11.1 cm/year, respectively). The mean levels of IGF-I and IGF binding protein (IGFBP)-3 were significantly increased from baseline in all three treatment groups; the between-group differences were not statistically significant. There were no significant differences between the treatment groups in the Height Standard Deviation Scores for Chronological Age.

There were no clinically relevant adverse events during the study period and no clinically significant changes from baseline in laboratory parameters. The most frequent study drug related adverse events were injection site reactions which were generally mild-to-moderate and transient.

Risedronic acid preserves BMD

Results of a 4-year study showed that risedronic acid increases bone mineral density (BMD) and prevents loss of BMD associated with discontinuation of HRT in patients with osteoporosis or osteopenia.[5] This open-label included 201 patients who received risedronic acid 30mg or 35mg, once weekly for 4 years. Of the 25 patients who discontinued HRT during the study, 15 patients commenced risedronic acid prior to discontinuation, whilst the other 10 patients started risedronic acid therapy a few days after HRT was withdrawn.

After 4 years, patients had significant and progressive increases from baseline in BMD of the lumbar spine L1-L4, femoral neck and total hip (5.1%, 4.0% and 4.7%, respectively). Among the 25 patients receiving HRT, there were no significant reductions in lumbar spine, femoral neck and total hip BMD after a mean follow-up period of 14.4 months after HRT discontinuation.

1. Kupfer S, et al. 56-Week glycemic effects of pioglitazone vs glyburide in subjects with recently diagnosed type 2 diabetes. 87th Annual Meeting of the Endocrine Society (Poster Abstr.): 263, 4 Jun 2005.
2. Mercado M, et al. A prospective, multicenter study to investigate the efficacy, safety and tolerability of Sandostatin (Rm) LAR (Rm) in the primary therapy of patients with newly diagnosed acromegaly. 87th Annual Meeting of the Endocrine Society : 296-297, 4 Jun 2005.
3. Palomba S, et al. Clomiphene citrate versus metformin cloridrate as first-line treatment for ovulation induction in non-obese anovulatory PCOS women. 87th Annual Meeting of the Endocrine Society : 258, 4 Jun 2005.
4. Kim DH, et al. A sustained release human growth hormone (LB03002): efficacy and safety following six-month treatment in children with growth hormone deficiency. 87th Annual Meeting of the Endocrine Society : 122 (plus oral) abstr. OR33-2, 4 Jun 2005.
5. Gordon MS, et al. Once-weekly risedronate prevents loss of bone mineral density associated with discontinuation of hormone replacement therapy and increases bone mineral density for up to four years. 87th Annual Meeting of the Endocrine Society : 637 (plus poster) abstr. P3-388, 4 Jun 2005.

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