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Oral glucose lowering with linagliptin plus metformin is a viable initial treatment strategy in patients with newly diagnosed type 2 diabetes and marked hyperglycaemia

Author Block: B. Gallwitz[1], S.A. Ross[2], A.E. Caballero[3], S. Del Prato[4], D. Lewis-D'Agostino[5], Z. Bailes[6], S. Thiemann[7], S. Patel[6], H.-J. Woerle[7], M. von Eynatten[5];
[1]Dept. Medicine IV, Universitätsklinikum Tübingen, Tübingen, Germany, [2]LMC Endocrinology Centres, University of Calgary, Calgary, AB, Canada, [3]Joslin Diabetes Center and Harvard Medical School, Boston, MA, USA, [4]Department of Endocrinology and Metabolism, Section of Diabetes, University of Pisa, Pisa, Italy, [5]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA, [6]Boehringer Ingelheim Ltd, Bracknell, UK, [7]Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany.

Abstract:
Background and aims: Newly diagnosed type 2 diabetes (T2D) patients commonly present with marked hyperglycaemia. This condition has rarely been studied for novel oral diabetes drugs and insulin is often proposed as the preferred starting therapy.

Materials and methods: We explored oral glucose-lowering combination therapy in newly diagnosed (≤12 months) T2D patients with marked hyperglycaemia (n=316) utilising prespecified exploratory subgroup analyses from a randomised double-blind study of initial combination of linagliptin+metformin versus linagliptin. Baseline mean±SD age and HbA1c was 48.8±11.0 years and 9.8±1.1%, respectively. The primary endpoint was HbA1c change from baseline to week 24.

Results: Mean±SE HbA1c reduction was -3.4±0.2% versus -2.5±0.2% with linagliptin+metformin and linagliptin, respectively, in patients with baseline HbA1c ≥9.5%, and -2.1±0.2% versus -1.4±0.2% in patients with baseline HbA1c <9.5%. Similar HbA1c reductions occurred in all subgroups of age, body-mass index (BMI), renal function, race, and ethnicity (table). Hypoglycaemia was rare (1.9% and 3.2% of patients, respectively) with no severe episodes.

Conclusion: In our analysis of newly diagnosed T2D patients presenting with marked hyperglycaemia, initial linagliptin+metformin elicited consistent HbA1c reductions across different subgroups. Oral glucose-lowering combination therapy may be a viable initial

Table. Adjusted* mean HbA1c (%) change from baseline at week 24 (per protocol completers cohort, last observation carried forward; n=245)**

	Linagliptin 5 mg qd + metformin bid†		Linagliptin 5 mg qd		Treatment difference (linagliptin + metformin minus linagliptin)	
	n	Mean±SE	n	Mean±SE	Mean±SE	95% CI
Baseline HbA1c						
<9.5%	56	−2.1±0.2	52	−1.4±0.2	−0.7±0.3	−1.2, −0.2
≥9.5%	76	−3.4±0.2	61	−2.5±0.2	−0.8±0.3	−1.3, −0.4
Age						
<35 years	12	−2.5±0.4	13	−2.2±0.4	−0.2±0.5	−1.3, 0.8
35–<50 years	47	−3.0±0.2	35	−2.3±0.2	−0.7±0.3	−1.3, −0.1
50–<65 years	66	−2.7±0.2	58	−1.9±0.2	−0.8±0.2	−1.2, −0.3
≥65 years	7	−3.5±0.5	7	−1.1±0.5	−2.4±0.7	−3.8, −1.0
Renal function‡						
Normal	102	−2.7±0.1	89	−2.0±0.1	−0.7±0.2	−1.1, −0.3
Impaired	30	−3.1±0.2	24	−2.0±0.3	−1.0±0.4	−1.8, −0.3
BMI, kg/m^2						
<25	28	−3.0±0.3	18	−2.0±0.3	−1.0±0.4	−1.8, −0.2
25–<30	46	−2.9±0.2	40	−1.9±0.2	−1.0±0.3	−1.6, −0.4
30–<35	31	−2.7±0.2	34	−2.0±0.2	−0.6±0.3	−1.3, 0.1
≥35	27	−2.7±0.3	21	−2.2±0.3	−0.4±0.4	−1.2, 0.4
Race						
White	83	−2.7±0.2	65	−2.1±0.2	−0.6±0.2	−1.1, −0.2
Black	3	−2.3±0.8	4	−1.2±0.7	−1.1±1.0	−3.1, 1.0
Asian	46	−3.0±0.2	44	−2.0±0.2	−1.1±0.3	−1.6, −0.5
Ethnicity						
Not Hispanic/Latino	104	−2.8±0.1	89	−1.8±0.1	−1.0±0.2	−1.4, −0.6
Hispanic/Latino	28	−3.0±0.3	24	−3.0±0.3	−0.1±0.4	−0.8, 0.7

*ANCOVA model with terms for treatment, continuous baseline HbA1c, subgroup, subgroup by treatment interaction; for analyses of baseline HbA1c subgroups, the term for continuous baseline HbA1c was replaced by the categorical baseline HbA1c.
**Randomised patients who received ≥1 dose of study drug and a baseline HbA1c measurement, with no important protocol violations, who completed 24 weeks of treatment without glycaemic rescue, and had an HbA1c measurement at week 24
†Metformin was uptitrated in the first 6 weeks to a maximal dose of 2000 mg/day
‡Estimated creatinine clearance by the Cockcroft-Gault equation: normal renal function is ≥90 mL/min; impaired renal function is <90 mL/min.

alternative to insulin for effective treatment of these patients.

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Tel: +49-211-758 469 0 - Fax: +49-211-758 469 29
Web: http://www.easd.org
E-mail: abstracts@easd.org