G Ital Cardiol 2014;15(9):520

Cardiovascular (CV) safety of linagliptin in patients with type 2 diabetes (T2D): a pooled comprehensive analysis of prospectively adjudicated CV events in phase 3 studies
G Ital Cardiol 2014;15(2 Suppl 4):e56

In merito all'abstract P65 sopraindicato, presentato al 45° Congresso Nazionale di Cardiologia dell'ANMCO (Firenze, 29-31 maggio 2014), gli autori comunicano l'errato inserimento del testo. Si riporta integralmente l'abstract corretto:

P65

CARDIOVASCULAR (CV) SAFETY OF LINAGLIPTIN IN PATIENTS WITH TYPE 2 DIABETES (T2D): A POOLED COMPREHENSIVE ANALYSIS OF PROSPECTIVELY ADJUDICATED CV EVENTS IN PHASE 3 STUDIES

Odd Erik Johansen[1], Dietmar Neubacher[2], Thomas Sech[1], Sanjay Patel[3], Hans Juergen Woerle[1]
[1]Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany, [2]Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany, [3]Boehringer Ingelheim Ltd, Bracknell, UK

Background and aims. Incidence of cardiovascular (CV) events is increased in patients with type 2 diabetes (T2D), but the potential for CV risk modulation with glucose-lowering therapies is debated.
Materials and methods. We compared the incidence of CV events and CV mortality in patients with T2D treated with linagliptin (lina), a once-daily dipeptidyl peptidase (DPP)-4 inhibitor, with non-lina comparators (placebo or active; comp) in 19 double-blind RCTs (duration ≥12 weeks). CV events were prospectively adjudicated by a blinded independent expert committee. The primary endpoint was a composite of CV death, non-fatal stroke, non-fatal myocardial infarction, and hospitalisation for unstable angina pectoris. Other secondary and tertiary CV endpoints were also assessed.
Results. Of 9459 patients, 5847 received lina (5 mg: 5687, 10 mg: 160) and 3612 comp (placebo: 2675, glimepiride: 775, voglibose: 162). The cumulative exposure (person years) was 4421.3 for lina and 3254.7 for comp. Changes (mean ± SEM) in HbA1c and weight, for lina and comp, respectively, were -0.68±0.01%/-0.27±0.02% and -0.1±0.1/+0.4±0.1 kg, whereas there were similar changes in systolic/diastolic blood pressure and lipids. In total, 60 primary events were reported in the lina group and 62 in the comp group (36 in the placebo and 26 in the active comp group). Rates of the primary endpoint (/1000 years at risk) were lower for lina (13.4%) than for the comp group (18.9%) in line with the hazard ratio (0.78) (Table).
Conclusion. This updated pooled analysis of adjudicated CV events in a large Phase 3 programme continues to support that lina is not associated with an increased risk for CV events. Potential CV benefits with lina will be tested prospectively in more than 14,000 patients in the active-comparator (glimepiride) CAROLINA® trial (NCT01243424) and the placebo-controlled CARMELINA™ trial.

	Linagliptin (n=5847)	Comparator (n=3612)	
Characteristics of study cohort and exposure according to study arms			
Mean age (years)	58±11	59±10	
Female gender (%)	45.6	43.5	
Mean baseline HbA1c (%)	8.1±0.9	8.1±0.9	
T2D duration >5 years (%)	54.9	56.8	
Baseline BMI (kg/m^2)	29.0±5.2	29.5±5.2	
Mean (maximum) exposure (days)	276 (776)	329 (804)	
Impact on primary, secondary, and tertiary CV endpoints according to study arms	**Incidence rate/1000 pt-yr**		**Hazard ratio (Cox proportional model) (95% CI)**
Primary CV endpoint	13.4	18.9	0.78 (0.55-1.12)
Secondary CV endpoints			
CV death, stroke, or MI	9.3	14.0	0.74 (0.49-1.13)
All adjudicated CV events	21.5	29.1	0.82 (0.61-1.09)
Tertiary CV endpoints			
CV death	2.4	2.4	1.04 (0.42-2.60)
Non-fatal MI	5.1	6.1	0.86 (0.47-1.56)
Non-fatal stroke	2.0	5.8	0.34 (0.15-0.75)*
Transient ischaemic attack	0.2	2.4	0.09 (0.01-0.75)*
Hospitalisation for UAP	4.9	4.8	1.08 (0.56-2.06)

BMI, body mass index; CI, confidence interval; CV, cardiovascular; HbA1c; glycated haemoglobin; MI, myocardial infarction; T2D, type 2 diabetes; UAP, unstable angina pectoris.
*significant lower hazard ratio (upper 95% CI: <1.0).