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ORIGINAL RESEARCH

Ethnic Differences in Efficacy and Safety of Alogliptin: A Systematic Review and Meta-Analysis

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ABSTRACT

Introduction: Alogliptin is a highly selective, potent, and orally available dipeptidyl peptidase-4 (DPP-4) inhibitor. This study compared the glucose-lowering efficacy and safety of alogliptin between Asian and non-Asian patients with type 2 diabetes.

Methods: We systematically searched MEDLINE, EMBASE, Cochrane Library, and ISI Web of Science databases for articles published June 2017 and earlier in English. We identified randomized controlled trials (RCTs) of adults with type 2 diabetes that compared alogliptin with placebo as either monotherapy or add-on therapy. We divided subgroups by ethnicity, and compared the results of alogliptin use in Asian and non-Asian-dominant studies.

Results: A total of 15 RCTs with 4456 patients with type 2 diabetes were included in this study. Alogliptin lowered glycated hemoglobin (HbA1c) to a much greater extent in Asian-dominant studies [− 0.75% (95% CI − 0.84 to − 0.65)] than in non-Asian-dominant studies [− 0.61% (95% CI − 0.68 to − 0.54)] ($P = 0.02$). The risk ratio of achieving HbA1c goal was larger in Asian-dominant studies [2.88 (95% CI 2.15–3.87)] than in non-Asian-dominant studies [1.93 (95% CI 1.55–2.41)] ($P = 0.03$). The postprandial blood glucose-lowering efficacy was higher in Asian-dominant studies [− 2.42 mmol/l (95% CI − 2.99 to − 1.85)] than in non-Asian-dominant studies [− 0.60 mmol/l (95% CI − 1.60 to 0.40)] ($P = 0.002$), while the fasting blood glucose and body weight changes were similar between the two subgroups. The incidence of adverse events, including hypoglycemia, nasopharyngitis, upper respiratory tract infection, headache, and diarrhea, were comparable between the two groups.

Conclusions: Alogliptin is more effective in improving glycemic levels in Asians than in other ethnic populations. Future studies are required to explore the potential mechanisms.

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Keywords: Alogliptin; Asian; Meta-analysis; Type 2 diabetes

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is becoming a worldwide disease, especially, in Asia; it is expected that by 2025, 380 million Asian people will have type 2 diabetes [1]. Compared to other races, Asian patients with type 2 diabetes are physiologically characterized by lower β-cell function and less obesity [2]. The increase in prevalence of type 2 diabetes in the Asian population may be linked to the strong gene–environment interaction associated with lifestyle changes due by modernization [3].

To date, dipeptidyl peptidase-4 (DPP-4) inhibitors and glucagon-like peptide-1 (GLP-1) analogues are increasingly popular in clinical use. Interestingly, several meta-analyses compared the glycated hemoglobin (HbA1c)-lowering effect of DPP-4 inhibitors and GLP-1 analogues in Asian-dominant studies ($\geq$ 50% Asian population) against those in non-Asian-dominant studies ($<$ 50% Asian population) [4–6]. Both DPP-4 inhibitors and GLP-1 analogues include many different kinds of agents. For example, alogliptin, sitagliptin, and vildagliptin are DPP-4 inhibitors; liraglutide and exenatide are GLP-1 analogues. Actually, it is still not clear whether the glucose-lowering efficacy of any single incretin-based drug differs by ethnic groups. Thus, we carried out a systematic review and meta-analysis to explore the efficacy as well as safety of alogliptin in Asians and other ethnic populations.

METHODS

Literature Search

We systematically searched MEDLINE, EMBASE, Cochrane Library, and ISI Web of Science databases for articles published up until June 2017 in English. Relevant articles were identified using generic and brand names of "alogliptin" and "type 2 diabetes" as keyword search terms. We supplemented this search by a manual search of the reference list of relevant articles.

Inclusion Criteria

Inclusion criteria were as follows: (1) all subjects were non-pregnant adults with T2DM; (2) $\geq$ 12 weeks' duration; (3) studies involved randomized controlled trials (RCTs); (4) methodologies compared alogliptin with placebo; (5) HbA1c levels were reported as one of the outcomes; and (6) in the case of duplicate publications, only the population with larger sample size or that containing more useful data was included. Exclusion criteria were trials enrolling patients (1) with type 1 diabetes; (2) health or pregnant; (3) with hepatic or renal impairment.

Data Extraction

We extracted data using the methods described in previous work [7]. The properties extracted from each selected article were as follows: (1) study characteristics, including first author name, year of publication, study design, and sample size; (2) participants' baseline characteristics, including age, sex, ethnicity, baseline HbA1c, and body weight; and (3) outcomes of efficacy in terms of change of HbA1c and body weight from baseline, and the proportion of patients achieving the glycemic goal; (4) safety outcomes, as derived from the percentage of participants experiencing adverse events in each group, such as hypoglycemic event, nasopharyngitis, or upper respiratory tract infection.

Quality Assessment

Study quality was assessed according to the Cochrane Collaboration's risk of bias tool [8], which is widely used to evaluate the quality of RCTs. The criteria were (1) random sequence generation, (2) allocation concealment, (3) blinding of participants and personnel, (4) incomplete outcome data, and (5) selective reporting. We evaluated each report for overall risk of bias of using these five criteria. Risk was deemed high if any domain presented high bias, low if all key domains (except random sequence

generation and allocation concealment) were of low bias, and unclear in all other cases.

Statistical Analysis

Consistent with previous studies, we categorized the studies into Asian-dominant studies if the percentage of Asian participants was at least 50%; otherwise, the study was deemed a non-Asian-dominant study. Statistical analyses were performed using the Cochrane Collaboration RevMan 5.2 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012) and STATA 12.0 (Stata Corporation, College Station, TX, USA). For continuous data, weighted mean difference (WMD) and 95% confidence interval (CI) were calculated to assess the difference between intervention group and control group. If a paper did not report a standard deviation, we calculated this according the sample size and standard error or 95% CI. Dichotomous outcomes were expressed as risk ratios and 95% CI. χ^2-test-based Q statistic test and I^2 were used to assess heterogeneity among studies. If $P > 0.05$ in Q test or $I^2 < 50\%$, the fixed effect model was selected [9], or else the random effect model was used [10].

Compliance with Ethics Guidelines

This article is based on previously conducted studies and does not involve any new studies of human or animal subjects performed by any of the authors.

RESULTS

Search Results

The search strategy retrieved 359 potentially relevant references. On the basis of the inclusion criteria, 15 RCTs [11–25] were included in the following meta-analysis and 344 papers were excluded. The selection process is shown in Fig. 1.

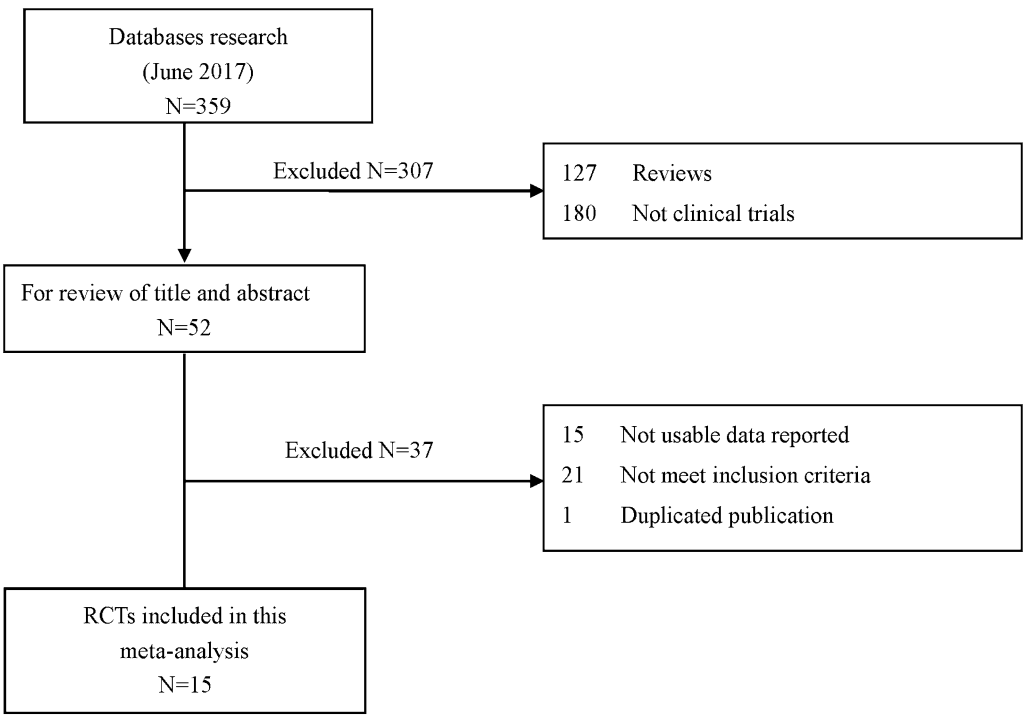

Fig. 1 Study flow diagram

Table 1 Characteristics of included studies

Study	Sample size	Age (years)	Female (%)	Ethnicity	Duration of study (weeks)	Baseline HbA1c (%)	Diabetes duration (years)	Alogliptin	Comparator	Background therapy
DeFronzo [12]	195	53.4	46.8	White 66.9% Other 33.1%	26	7.9	NR	25 mg/day	Placebo	None
DeFronzo [11]	518	53.1–56.1	47.7–61.2	White 62–82.3% Asian 3.8–11.6% African-American 1.5–6.2% Other 12.3–22.5%	26	8.5–8.6	5.6–7.6	25 mg/day	Placebo	Pioglitazone 15 mg/day + metformin (≥ 1500 mg/day) Pioglitazone 30 mg/day + metformin (≥ 1500 mg/day) Metformin (≥ 1500 mg/day)
Kaku [14]	179	62.7	45.8	Japanese	12 + 40	8.43	14.9	25 mg/day	Placebo	Insulin
Kaku [13]	228	59.3–60.8	37.2	Japanese	12 + 40	7.89–7.92	6.51–6.8	25 mg/day	Placebo	Pioglitazone 15–30 mg/day
Nauck [15]	314	55	45.7–52.6	White 76–80% Asian 6–9% African American 2–7% Other 9–11%	26	7.9–8.0	6	25 mg/day	Placebo	Metformin ≥ 1500 mg/day
Pan [16]	505	51.6–53.2	45–72	Chinese	16	7.86–8.04	1.9–5.8	25 mg/day	Placebo	None/ metformin/pioglitazone

Table 1 continued

Study	Sample size	Age (years)	Female (%)	Ethnicity	Duration of study (weeks)	Baseline HbA1c (%)	Diabetes duration (years)	Alogliptin	Comparator	Background therapy
Pratley [17]	784	53.5	52.3	White 71.6% Asian 18.2% Black or African American 4.7% Other 5.5%	26	8.45	4.0	25 mg/day	Placebo	Metformin 1000–2000 mg/day or none
Pratley [19]	296	55.4	41.8	White 72.6–76.4% Asian 9.1–12.1% Black or African American 6.5–11.2% Other 5.0–7.1%	26	8.0–8.1	7.6	25 mg/day	Placebo	Pioglitazone 30–45 mg/day ± metformin/sulfonylurea
Pratley [18]	297	57	45.3–50	White 69.5–72.7% Asian 10.3–13.1% Black/African American 3.0–5.6% Other 11.1–16.3%	26	8.1	8	25 mg/day	Placebo	Glyburide ≥ 5 mg/day

Table 1 continued

Study	Sample size	Age (years)	Female (%)	Ethnicity	Duration of study (weeks)	Baseline HbA1c (%)	Diabetes duration (years)	Alogliptin	Comparator	Background therapy
Van Raalte [25]	49	58.7–59.1	30	Caucasian	16	6.6–6.8	5.5–6.4	25 mg/day	Placebo	Metformin/ sulfonylurea/glinide
Rosenstock [21]	259	55–55.9	52–66	White 62–69% Asian 12% Black/African American 12–15% Other 8–12%	26	9.3	12.1–13.4	25 mg/day	Placebo	Insulin (15–100 units) ± metformin
Rosenstock [20]	327	53	51.1	Caucasian 80.3%	26	8.8	3	25 mg/day	Placebo	Pioglitazone 30 mg/day
Seino [22]	154	61.0–62.9	36–42	Japanese	12 + 40	7.91–8.12	7.28–8.44	25 mg/day	Placebo	Voglibose 0.2 mg tid
Seino [23]	155	58.7–59.5	21.3–29.8	Japanese	12 + 40	7.85–7.99	5.94–6.98	25 mg/day	Placebo	None
Seino [24]	196	52.6	31.3	Japanese	12 + 40	7.97	6.33	25 mg/day	Placebo	Metformin 500–750 mg/day

NR not reported

Study and Patient Characteristics

A total of 15 RCTs compared alogliptin with placebo as monotherapy or add-on therapy. Add-on therapy included metformin, pioglitazone, glipizide, voglibose, and insulin. All studies were multicenter trials, nine were international [11, 12, 15, 17–21, 25], five studies were conducted in Japan [13, 14, 22–24], and one study was carried out in China [16]. All trials used parallel study design with 2–12 arms; however, we excluded some arms of the included studies because several doses seemed unlikely to be used in clinical practice. In that way, we extracted only a dose of 25 mg administered once daily. The studies under consideration were of 12–52 weeks' duration. We excluded the extensive study of four trials [13, 14, 22, 23], since the studies switched to open-label and had no control group in the extension. All RCTs were sponsored by Takeda Pharmaceutical Company.

A total of 4456 patients with T2DM were included in the present meta-analysis and systematic review. The mean age of the participants in the studies ranged from 51.6 to 69.9 years, female proportion ranged from 21.3% to 72%, and the mean baseline HbA1c ranged from 6.6% to 9.3%. Table 1 summarizes the main characteristics of included studies.

Risk of Bias Within Studies

According to the Cochrane Collaboration's risk of bias tool, overall risk of bias was judged for the primary outcomes was low in four [13, 16, 22, 23], unclear in ten [11, 12, 14, 15, 17–21, 24], and high in one report [25], mainly due to lack information on the random sequence generation. The average quality of the RCTs was acceptable (Table 2).

HbA1c

Figure 2a shows the meta-analysis of the change in HbA1c from baseline for the alogliptin in comparison with placebo. It can be seen that a total of 14 trials [11, 13–25] fulfilled inclusion criteria. Overall, the meta-analysis found that alogliptin resulted in lowering HbA1c much greater than the placebo (WMD = − 0.68%, 95% CI − 0.74 to − 0.61, $P < 0.00001$; $I^2 = 57\%$). In the Asian-dominant studies, HbA1c changed by − 0.75% (95% CI − 0.84 to − 0.65; $I^2 = 59\%$). In the non-Asian studies, HbA1c decreased − 0.61% (95% CI − 0.68 to − 0.54; $I^2 = 19\%$). The difference between two subgroups was statistically significant ($P = 0.02$).

Percentage of Patients Achieving HbA1c Target

Twelve studies [12–20, 22–24] explored the proportion of participants achieving HbA1c targets. Seven trials [12, 15–20] determined HbA1c ≤ 7% as the treatment target according to the American Diabetes Association (ADA) [26], while five trials [13, 14, 22–24] performed in Japan set HbA1c < 6.9% as the goal based on the Japanese Diabetes Society and the European Association for the Diabetes [27]. As expected, the percentage of patients achieving HbA1c target was significantly larger with alogliptin [risk ratio (RR) = 2.38, 95% CI 1.96–2.91, $P < 0.0001$; $I^2 = 59\%$] (Fig. 2b). The RR was numerically greater in the Asian-dominant studies than Non-Asian-dominant studies [2.88 (95% CI 2.15–3.87) versus 1.93 (95% CI 1.55–2.41), $P = 0.03$].

Fasting Blood Glucose

A total of 14 trials [11–23, 25] explored the fasting blood glucose (FBG) level changes after using alogliptin or placebo. Overall, FBG decreased more significantly in alogliptin group (WMD = − 1.12 mmol/l, 95% CI − 1.28 to − 0.97, $P < 0.00001$; $I^2 = 55\%$). There was no difference ($P = 0.53$) between Asian-dominant studies [− 1.07 mmol/l (95% CI − 1.28 to − 0.85); $I^2 = 44\%$] and Non-Asian-dominant studies [− 1.16 mmol/l (95% CI − 1.37 to − 0.96); $I^2 = 47\%$] (Fig. 2c).

Postprandial Blood Glucose

Only four trials [13, 17, 23, 24] explored postprandial blood glucose (PBG) level changes. The

Table 2 Summary of risk of bias assessment

Study ID	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Incomplete outcome data	Selective reporting	Overall risk of bias
DeFronzo [12]	U	U	L	L	L	U
DeFronzo [11]	U	U	L	L	L	U
Kaku [13]	L	L	L	L	L	L
Kaku [14]	U	L	L	L	L	U
Nauck [15]	L	U	L	L	L	U
Pan [16]	L	L	L	L	L	L
Pratley [17]	U	U	L	L	L	U
Pratley [18]	L	U	L	L	L	U
Pratley [19]	L	U	L	L	L	U
Van Raalte [25]	H	U	L	L	L	H
Rosenstock [21]	L	U	L	L	L	U
Rosenstock [20]	U	U	L	L	L	U
Seino [22]	L	L	L	L	L	L
Seino [23]	L	L	L	L	L	L
Seino [24]	L	U	L	L	L	U

U unclear, *L* low, *H* high

overall PBG changed from baseline was 2.04 mmol/l (95% CI − 2.85 to − 1.23; $P < 0.00001$; $I^2 = 81\%$). Alogliptin proved to be much more effective in the Asian-dominant studies [− 2.42 mmol/l (95% CI − 2.99 to − 1.85); $I^2 = 59\%$] than in non-Asian-dominant studies [− 0.60 mmol/l (95% CI − 1.60 to 0.40)] ($P = 0.002$) (Fig. 2d).

Body Weight

As shown in Fig. 2e, results on the outcome of body weight were available from eight studies [12–14, 18, 20–23]. Although participants taking alogliptin showed a slightly greater weight gain than those on placebo in the context of overall treatment (WMD = 0.24 kg, 95% CI 0.06–0.41, $P = 0.007$; $I^2 = 47\%$), there was no difference ($P = 0.47$) between Asian-dominant studies [0.20 kg (95% CI 0.00–0.40); $I^2 = 24\%$] and non-Asian-dominant studies [0.35 kg (95% CI 0.00–0.70); $I^2 = 66\%$] as regards to weight gain.

Safety

Hypoglycemia

As shown in Fig. 3c, data on hypoglycemic episodes were retrieved in 12 trials [11, 13–15, 17–19, 21–25]. In general, no

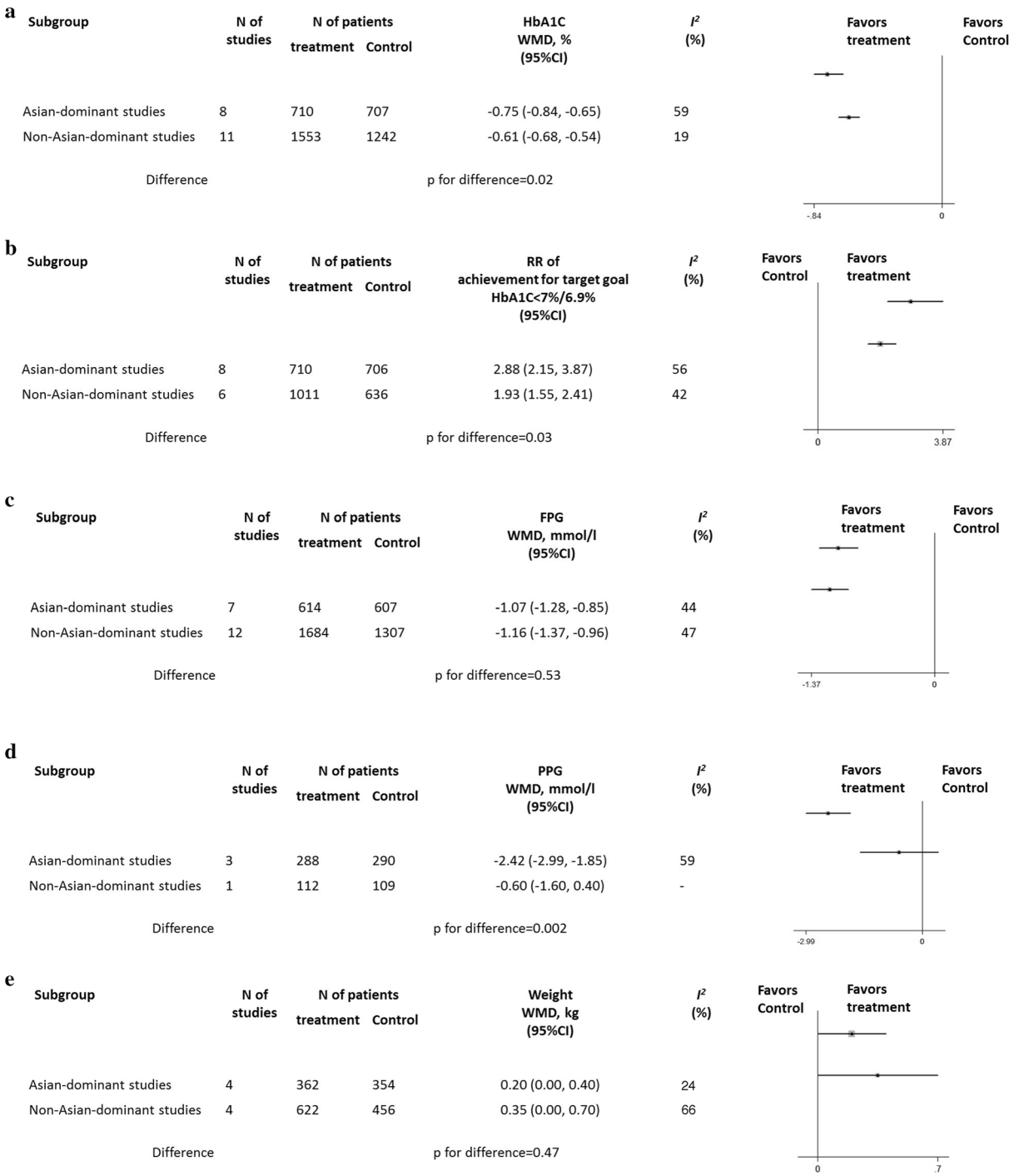

Fig. 2 Difference between Asian-dominant studies and non-Asian-dominant studies in **a** HbA1c, **b** relative risk of achievement for target goal HbA1c < 7.0%/6.9%, **c** FPG, **d** PPG, **e** weight. CI confidence interval, FPG fasting plasma glucose, PPG postprandial plasma glucose, N number, RR risk ratio, WMD weighted mean difference

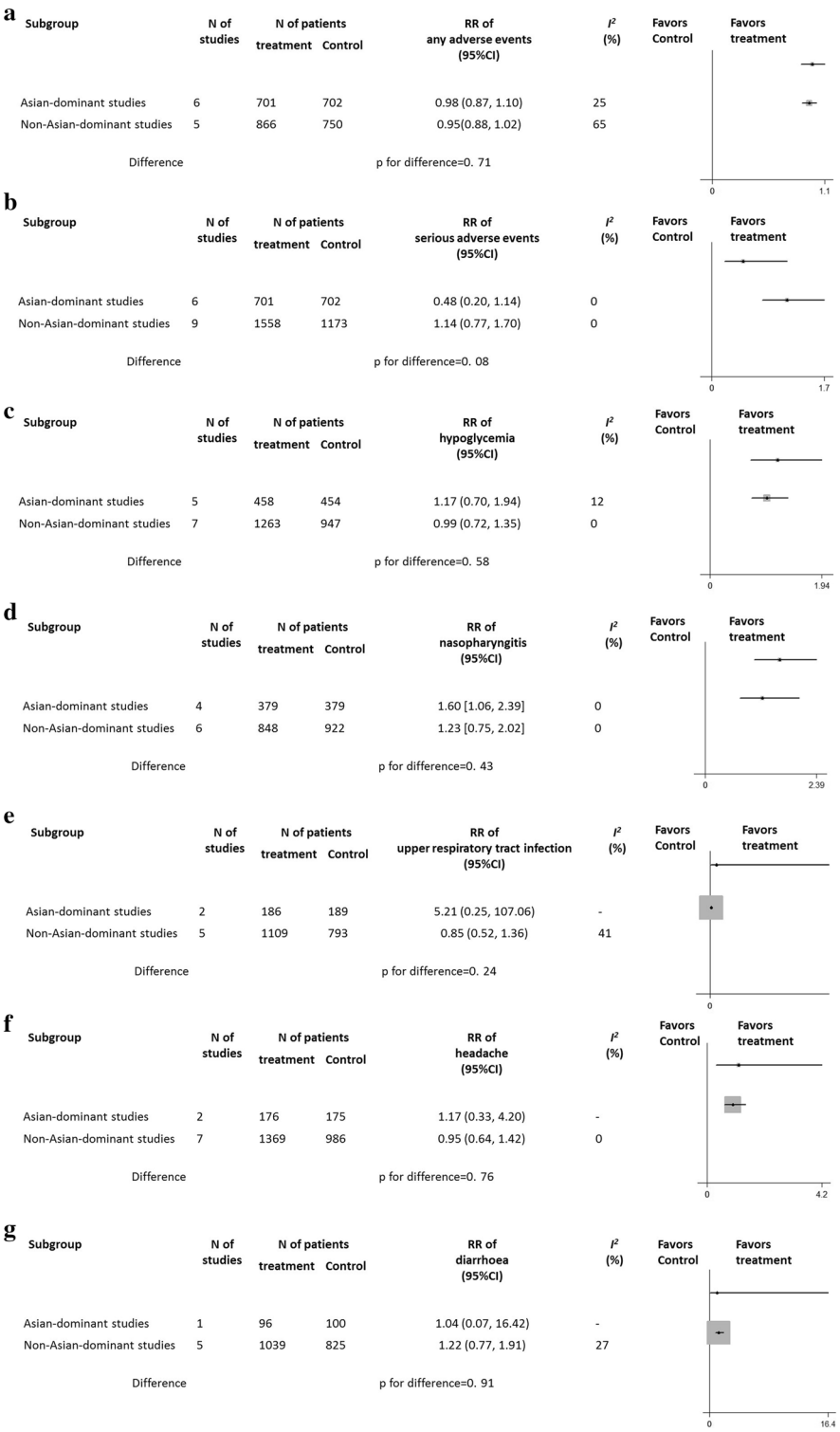

Fig. 3 Difference between Asian-dominant studies and non-Asian-dominant studies in **a** any adverse events, **b** serious adverse events, **c** hypoglycemia, **d** nasopharyngitis, **e** upper respiratory tract infection, **f** headache, **g** diarrhea. CI confidence interval, N number, RR risk ratio

significant difference ($P = 0.58$) was found between Asian-dominant studies [RR = 1.17 (95% CI 0.70–1.94); $I^2 = 12\%$] and non-Asian-dominant studies [RR = 0.99 (95% CI 0.72–1.35); $I^2 = 0\%$].

Other Adverse Events

Figure 3 shows the meta-analysis results for other adverse events. The RR of any adverse events did not indicate statistically significant difference ($P = 0.71$) between Asian-dominant studies [0.98 (95% CI 0.87–1.10); $I^2 = 25\%$] and non-Asian-dominant studies [0.95 (95% CI 0.88–1.02); $I^2 = 65\%$]. Also, there was no significant difference between two subgroups as regards to serious adverse events [RR = 0.48 (95% CI 0.20–1.14) versus RR = 1.14 (95% CI 0.77–1.70), $P = 0.08$]. The most commonly reported adverse events were nasopharyngitis, upper respiratory tract infection, headache, and diarrhea. In addition, there was no significant difference between Asian-dominant studies and non-Asian-dominant studies as regards to nasopharyngitis [RR = 1.60 (95% CI 1.06–2.39) versus RR = 1.23 (95% CI 0.75–2.02) ($P = 0.43$)], upper respiratory tract infection [RR = 5.21 (95% CI 0.25–107.06) versus 0.85 (95% CI 0.52–1.36) ($P = 0.24$)], headache [RR = 1.17 (95% CI 0.33–4.20) versus 0.95 (95% CI 0.64–1.42) ($P = 0.76$)], and diarrhea [RR = 1.04 (95% CI 0.07–16.42) versus 1.22 (95% CI 0.77–1.91) ($P = 0.91$)].

DISCUSSION

This systematic review and meta-analysis involved 15 RCTs focused on alogliptin, a highly selective, potent, and orally available DPP-4 inhibitor [28]. We found that the HbA1c-lowering efficacy of alogliptin as well as the percentage of patients achieving HbA1c target was greater in Asian-dominant studies than in non-Asian-dominant studies, which implied that alogliptin was more effective in Asian patients with type 2 diabetes than other ethnic groups. Previous meta-analyses, performed by Kim et al., revealed that DPP-4 inhibitors and GLP-1 analogues both exhibit greater glucose-lowering efficacy in Asian patients than in non-Asian patients with type 2 diabetes [4, 5]. Zhang et al. [29], however, found the improvement of DPP-4 inhibitors in HbA1c was similar between Asian and non-Asian patients. The current meta-analysis is the first to identify the efficacy and safety of alogliptin in Asians and non-Asians.

It was believed that BMI value was a main contributor to the differential glycemic effect of DPP-4 inhibitors [4]. The Asian-dominant studies were conducted on lower-BMI groups, whereas non-Asian dominant studies belonged to higher BMI groups. According to the meta-regression analysis by Kim et al. [4], when average BMI was less than 30 kg/m^2, the BMI was significantly correlated with HbA1c-lowering efficacy in patients with DPP-4 inhibitors. In a 12-month study, Yagi et al. [30] discovered that DPP-4 inhibitors were more effective in patients with low BMI. Several Japanese studies also found a significant correlation between baseline BMI and HbA1c-lowering effect in patients with sitagliptin treatment [31–33]. The ethnic difference in the glucose-lowering response of alogliptin, therefore, could be largely ascribed to the difference in BMIs.

DPP-4 was proven to be an adipokine, which was substantially expressed in the visceral fat of obese people, and augmented release into circulation [34]. Also, the activity of DPP-4 is higher in obese people [34, 35]. Since both circulating DPP-4 level and activity are increased in obese subjects, the efficacy of DPP-4 inhibitors in non-Asian patients with high BMI should be lower than in Asian patients. So alogliptin was more effective in the Asian group with lower BMI. This may partly explain the difference in effects of alogliptin by ethnicity.

Alogliptin is known to improve β-cell dysfunction and increase insulin secretion [36]. In a recent study, the authors compared the insulin action between East Asians and Northern Europeans [37]. They revealed that the effect of identical increase of insulin secretion was greater in East Asians than in Northern Europeans, as insulin sensitivity was more pronounced in East Asians than in their Northern European counterparts [37]. This difference may be a contributor to the differential efficacy of alogliptin in different ethnic groups.

As type 2 diabetes is associated with a strong gene–environmental interaction, several genetic factors were reported to affect the insulin secretion in response to incretin-based therapy. For instance, *TCF7L2* could regulate the expression of GIP and GLP-1 receptors in human pancreatic islets [38]. It is also a gene known to be associated with susceptibility of type 2 diabetes [38]. Rs7903146, the allele of the *TCF7L2* gene, was reported to confer poor glucose-lowering efficacy of a DPP-4 inhibitor in Europeans [39]. Moreover, in Europeans, the risk allele frequency of rs7903146 is almost tenfold that of East Asians [40]. This may be one of the important factors for the differential efficacy of alogliptin by ethnicity.

The reason for the higher efficacy of alogliptin in the Asian population might also be related to the dietary habit. For instance, Iwasaki and colleagues implied that differing efficacies of DPP-4 inhibitors found among different ethnic groups might be partly a result of differences in fish consumption, since they discovered that a reduction of HbA1c by DPP-4 inhibitors significantly correlates with estimated intake of fish, EPA and DHA, and serum levels of EPA and DHA [41]. In addition, several studies reported that Asian women had a higher mean daily intake of fish than Caucasians [42, 43]. Thus, dietary habit may influence the efficacy of alogliptin among different ethnicities.

It was thought that because of different body size and BMI value, the pharmacokinetics of alogliptin, which may affect the glucose-lowering efficacy, would differ between Asians and non-Asians; however, no significant difference of clinical pharmacological properties of several DPP-4 inhibitors across different ethnic groups was found [44]. A better clinical response of alogliptin in Asians, therefore, cannot be ascribed to different pharmacokinetics.

In the present meta-analysis, alogliptin reduced PBG more effectively in Asian-dominant studies than non-Asian-dominant studies, whereas the FBG-lowering efficacy across different ethnic groups was similar. Since DPP-4 inhibitors increase activity of GLP-1 and decrease glucagon levels, they are more efficient in treating post-challenge hyperglycemia than fasting hyperglycemia [45]. Interestingly, according to the diabetes epidemiological features of Asia and Europe [46, 47], the prevalence of postprandial hyperglycemia is higher in Asians than in Europeans, and more than 50% of patients in Asia experienced only isolated post-meal hyperglycemia. These analyses were consistent with our results; however, the included PBG and FBG data in this current meta-analysis were relatively limited. Further long-term RCTs are needed to define the FBG- and PBG-lowering efficacy of alogliptin among different ethnic groups.

As is well known, changes in body weight are pivotal aspects for evaluating a hypoglycemic agent. Patients with diabetes often have some comorbidities such as cardiovascular disease and obesity. Weight gain would be a great concern among these patients. Unfortunately, several antidiabetic agents, including sulfonylureas, thiazolidinediones, and insulin, are associated with enhanced risk of weight gain. The weight changes attributed to use of alogliptin in both Asian-dominant studies and non-Asian-dominant studies were minimal, and no significant difference was found between these two subgroups. Most trials reporting weight changes, however, were less than 1 year in duration, so long-term effects on weight are still unclear.

The ADA emphasizes that the prevention of hypoglycemia is crucial in the treatment of T2DM [26]. Hence, before a clinician chooses an antidiabetic agent, the drug's hypoglycemic rate should be considered carefully. The incidences of hypoglycemia and other adverse events, including nasopharyngitis, upper respiratory tract infection, headache, and diarrhea, were all very low in both Asian and non-Asian studies, which suggested that alogliptin is a relatively safe antidiabetic agent.

CONCLUSIONS

Alogliptin has been shown in 15 RCTs to confer greater glucose-lowering efficacy in Asians than in non-Asians. The difference in the treatment response could be ascribed to different BMI values, insulin action, and dietary habit, as well

as genetic factors. The present meta-analysis demonstrates that ethnic-specific guidelines are needed for alogliptin, and future studies are required to explore the potential mechanisms.

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Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not involve any new studies of human or animal subjects performed by any of the authors.

Data Availability. All data generated or analyzed during this study are included in this published article.

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