Supplemental Table S2. Risk of Bias Assessment

Study	Risk of bias	Author judgement
Chacra et al. (2017) [6]		
Random sequence generation (selection bias)	Low risk	Randomized, placebo-controlled, parallel-group study. Patients were stratified according to their renal, cardiovascular, and insulin-treatment status.
Allocation concealment (selection bias)	Unclear risk	The authors did not mention methods of randomization.
Blinding of participants & personnel (performance bias)	Low risk	Double-blinded RCT
Blinding of outcome assessment (detection bias)	Low risk	Double-blinded RCT
Incomplete outcome data (attrition bias)	Low risk	Of the 213 subjects randomized (107 in the omarigliptin group and 106 in the placebo group), 195 (91.5%) completed study phase A on study medication, and 170 (79.8%) completed phase B. Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes are reported.
Other biases	High risk	Funding for this study was provided by Merck & Co. Inc., Kenilworth, NJ, USA. Authors are employees of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co. Inc., who may own stock and/or hold stock options in the company. Antonio Chacra lists no conflict of interest.
Gantz et al. (2017a) [7]		
Random sequence generation (selection bias)	Low risk	Randomized controlled trial. Patients were stratified according to their background oral anti-diabetic drugs.
Allocation concealment (selection bias)	Low risk	The study subjects were randomized in a 2:1 ratio to omarigliptin 25 mg q.w. or matching placebo using a sponsor-generated allocation schedule and an interactive voice response or integrated Web response system.
Blinding of participants & personnel (performance bias)	Low risk	Double-blind RCT
Blinding of outcome assessment (detection bias)	Low risk	Double-blind RCT. Outcomes were evaluated in a blinded manner by external clinical adjudication committees.
Incomplete outcome data (attrition bias)	Low risk	380 of 389 in the omarigliptin group and 191 of 196 in the placebo group completed phase A. Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes are reported.
Other biases	High risk	Funded by Merck & Co. Inc. All of the authors are company employees.
Gantz et al. (2017b) [8]		
Random sequence generation (selection bias)	Low risk	Randomized, placebo- and sitagliptin-controlled, parallel-group trial. Randomization was stratified according to the use of baseline OHA.
Allocation concealment (selection bias)	Low risk	Patients were randomized using a double-dummy design in a 2:2:1 ratio by an interactive voice response or integrated web response system was used for randomization.
Blinding of participants & personnel (performance bias)	Low risk	Double-blind RCT
Blinding of outcome assessment (detection bias)	Low risk	Double-blind RCT
Incomplete outcome data (attrition bias)	Low risk	Of the 414 randomized patients, 400 (96.6%) completed the 24-week double-blind period and 365 (88.2%) completed the 28-week open-label period. Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes are reported.
Other biases	High risk	Funded by Merck & Co. Inc. All of the authors are company employee.

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Supplemental Table S2. Continued

Study	Risk of bias	Author judgement
Gantz et al. (2017c) [9]		
Random sequence generation (selection bias)	Low risk	Randomized, placebo-controlled, parallel-group phase 3 trial
Allocation concealment (selection bias)	Low risk	Patients were randomly assigned in a 1:1 ratio to omarigliptin 25 mg q.w. or placebo using an interactive voice response system.
Blinding of participants & personnel (performance bias)	Low risk	Double-blind RCT
Blinding of outcome assessment (detection bias)	Low risk	Double-blind RCT. External committees assessed safety outcome data.
Incomplete outcome data (attrition bias)	Low risk	Only 8 patients randomized to the omarigliptin group and 2 randomized to the placebo group did not take any study medication and were not included in any safety or efficacy analyses.
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes are reported.
Other biases	High risk	Funding for this trial was provided by Merck & Co. Inc. All authors are employees of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co. Inc., who may own stock and/or hold stock options in the company.
Gantz et al. (2017d) [10]		
Random sequence generation (selection bias)	Low risk	Randomized, placebo-controlled, parallel-group trial
Allocation concealment (selection bias)	Low risk	The study subjects were randomized (1:1) using an interactive voice response system to omarigliptin and placebo groups.
Blinding of participants & personnel (performance bias)	Low risk	Double-blind RCT
Blinding of outcome assessment (detection bias)	Low risk	Double-blind RCT
Incomplete outcome data (attrition bias)	Low risk	Of the 203 randomized patients, 186 (91.6%) completed the study on trial medication. 8 of 102 in omarigliptin group and 9 of 101 in placebo group discontinued. Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes are reported.
Other biases	High risk	Funding for this trial was provided by Merck & Co. Inc. All the authors are employees of the pharma company.
Goldenberg et al. (2017) [11]		
Random sequence generation (selection bias)	Low risk	Randomized, double-dummy, active-controlled, non-inferiority trial
Allocation concealment (selection bias)	Low risk	Double-dummy design, patients were randomized centrally, using an interactive voice response system, in 1:1 ratio to omarigliptin 25 mg once-weekly (and placebo matching sitagliptin, dosed once-daily) or sitagliptin 100 mg once-daily (and placebo matching omarigliptin, dosed once-weekly).
Blinding of participants & personnel (performance bias)	Low risk	Double-blind RCT
Blinding of outcome assessment (detection bias)	Low risk	Double-blind RCT. Safety endpoints were evaluated in a blinded manner by external clinical adjudication committees.
Incomplete outcome data (attrition bias)	Low risk	Of the 642 randomized patients, 588 (91.6%) completed the study on study medication. Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes are reported.
Other biases	High risk	The first author has received research payments from Merck & Co. Inc. as an investigator. The other authors are employees of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co. Inc., who may own stock and/or hold stock options in the company.

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Supplemental Table S2. Continued

Study	Risk of bias	Author judgement
Handelsman et al. (2017) [12]		
Random sequence generation (selection bias)	Low risk	Randomized, active-controlled, non-inferiority study trial
Allocation concealment (selection bias)	Low risk	Double-dummy design, randomized centrally, using an interactive voice response system, in a 1:1 ratio to omarigliptin 25 mg q.w. and placebo matching glimepiride q.d. or glimepiride q.d. and placebo matching omarigliptin q.w.
Blinding of participants & personnel (performance bias)	Low risk	Double-blind RCT
Blinding of outcome assessment (detection bias)	Low risk	Double-blind RCT. Safety endpoints were evaluated in a blinded manner by external clinical adjudication committees.
Incomplete outcome data (attrition bias)	Low risk	Of the 751 randomized patients, 574 (76.4%) completed the study on study medication. Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes are reported.
Other biases	High risk	Merck & Co. Inc., provided financial support for the conduct of the study. Most of the authors, except the first author, are employees of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co. Inc., who may own stock and/or hold stock options in the company.
Hattori (2020) [13]		
Random sequence generation (selection bias)	Low risk	Randomized controlled trial
Allocation concealment (selection bias)	Low risk	The patients were allocated in a 1:2 ratio using numbered containers.
Blinding of participants & personnel (performance bias)	High risk	Open-label study
Blinding of outcome assessment (detection bias)	High risk	Open-label study
Incomplete outcome data (attrition bias)	Low risk	No missing outcome data.
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes are reported.
Other biases	Low risk	The study was not funded. The author declares no COI.
Home et al. (2018) [14]		
Random sequence generation (selection bias)	Low risk	Randomized controlled trial
Allocation concealment (selection bias)	Unclear risk	The process of allocation was not described by the authors.
Blinding of participants & personnel (performance bias)	Low risk	Double-blind study
Blinding of outcome assessment (detection bias)	Low risk	Double-blind study. Outcomes were evaluated in a blinded manner by external clinical adjudication committees.
Incomplete outcome data (attrition bias)	Low risk	Of the 165 participants in the omarigliptin group, 89.1% (147/165) completed phase A on trial medication, 88.5% (146/165) entered phase B, 87.3% (144/165) completed the trial through 54 weeks, and 73.3% (121/165) completed on trial medication. Of the 164 participants in the placebo group, 92.1% (151/164) completed phase A on trial medication and entered phase B; 83.5% (137/164) completed the trial through 54 weeks, and 77.4% (127/164) completed on trial medication. Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes are reported.
Other biases	High risk	Funding for this study was provided by Merck Sharp and Dohme Corp., a subsidiary of Merck & Co. Inc. Most of the authors are employees of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co. Inc., and may own stock and/or hold stock options in the company.

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Supplemental Table S2. Continued

Study	Risk of bias	Author judgement
Ishii et al. (2023) [15]		
Random sequence generation (selection bias)	Low risk	Randomized controlled trial
Allocation concealment (selection bias)	Low risk	Randomization was performed using a computer-based dynamic allocation method with a minimization procedure to balance the two allocation factors (HbA1c level and age) across the groups.
Blinding of participants & personnel (performance bias)	High risk	Open-label study
Blinding of outcome assessment (detection bias)	High risk	Open-label study. Outcome data, including DTBQ scores, were assessed by the investigators.
Incomplete outcome data (attrition bias)	Low risk	212 of 216 completed the study. Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes are reported.
Other biases	High risk	This study and the study publication expenses were financially supported by Kissei Pharmaceutical Co. Ltd.
Kadowaki et al. (2021) [16]		
Random sequence generation (selection bias)	Low risk	Randomized, placebo-controlled trial. Randomization was stratified based on a participant's use of an OHA at screening.
Allocation concealment (selection bias)	Low risk	Participants were randomized centrally, using an interactive internet-based response system, in a 2:1 ratio to receive either omarigliptin 25 mg weekly or placebo matching omarigliptin.
Blinding of participants & personnel (performance bias)	Low risk	Double-blind study
Blinding of outcome assessment (detection bias)	Low risk	Double-blind study
Incomplete outcome data (attrition bias)	Low risk	184 were randomized (123 to omarigliptin and 61 to placebo), 99.2% (n=122) of those treated with omarigliptin, and 95.1% (n=58) of those treated with placebo, completed the double-blind portion of the study (through week 16). Reasons for missing data provided.
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes are reported.
Other biases	High risk	The study was funded and conducted by MSD K.K., Tokyo, Japan, a subsidiary of Merck & Co. Inc. Some of the authors are current employees of MSD K.K., or Merck Sharp & Dohme Corp., subsidiaries of Merck & Co. Inc., and may own stock/stock options in Merck & Co. Inc.
Lee et al. (2017) [17]		
Random sequence generation (selection bias)	Low risk	Randomized controlled trial. Randomization was stratified based on sulfonylurea status at screening.
Allocation concealment (selection bias)	Low risk	Patients were randomized centrally, using an interactive voice response system, in a 1:1 ratio to omarigliptin 25 mg q.w. or matching placebo.
Blinding of participants & personnel (performance bias)	Low risk	Double-blind study
Blinding of outcome assessment (detection bias)	Low risk	Double-blind study. Outcomes were evaluated in a blinded manner by external clinical adjudication committees.
Incomplete outcome data (attrition bias)	Low risk	Of the 307 randomized patients, 256 (83.4%) completed the study on study medication. Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes are reported.
Other biases	High risk	Funding for this study was provided by Merck Sharp and Dohme Corp., a subsidiary of Merck & Co. Inc. Most of the authors are employees of Merck & Co. Inc.

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Supplemental Table S2. Continued

Study	Risk of bias	Author judgement
Ohara et al. (2021) [18]		
Random sequence generation (selection bias)	Low risk	Randomized controlled trial. Permuted-block randomization was used.
Allocation concealment (selection bias)	Low risk	Participants were randomly assigned to either the daily group or the weekly group with 1:1 allocation via permuted-block randomization using an Excel-based allocation system with stratification.
Blinding of participants & personnel (performance bias)	High risk	Open-label study
Blinding of outcome assessment (detection bias)	High risk	Open-label study. Outcome assessment, including assessment of treatment satisfaction using a validated self-administered questionnaire, the DTSQs, was unblinded.
Incomplete outcome data (attrition bias)	Low risk	36 of 47 participants completed a 24-week follow-up. Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes are reported.
Other biases	Low risk	The authors have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. The study was funded by Ministry of Education, Culture, Sports, Science and Technology, Tokyo, Japan (to S.Y.).
Shankar et al. (2017) [19]		
Random sequence generation (selection bias)	Low risk	Randomized, placebo-controlled trial
Allocation concealment (selection bias)	Unclear risk	The process of allocation was not described by the authors.
Blinding of participants & personnel (performance bias)	Low risk	Double-blind study
Blinding of outcome assessment (detection bias)	Low risk	Double-blind study. Outcomes were evaluated blind to randomized treatments by external clinical adjudication committees.
Incomplete outcome data (attrition bias)	Low risk	Of the 402 subjects randomized (201 each in the omarigliptin and placebo groups), 361 (89.8%) completed phase A on trial medication, and 265 (65.9%) completed phase B. Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes are reported.
Other biases	High risk	Funding for this trial was provided by Merck & Co. Inc. One author has served as a consultant to Merck. Most of the authors are employees of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co. Inc., and may hold stock or stock options in the company.
Sheu et al. (2015) [20]		
Random sequence generation (selection bias)	Low risk	Randomized controlled trial. At randomization, subjects were stratified according to their use of oral AHAs at screening and region location (Japan or not Japan).
Allocation concealment (selection bias)	Unclear risk	The authors did not describe the process of allocation.
Blinding of participants & personnel (performance bias)	Low risk	Double-blind study
Blinding of outcome assessment (detection bias)	Low risk	Double-blind study
Incomplete outcome data (attrition bias)	Low risk	Of the 685 randomized subjects, 93.4% completed the base study. No reasons for missing data were provided.
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes are reported.
Other biases	High risk	This study received support from Merck & Co. Inc. The first author received speaker honorarium and served as a scientific advisor board member for Merck Sharp & Dohme. Most of the authors are current or former employees of Merck Sharp & Dohme, a subsidiary of Merck & Co. Inc., and may own stock or stock options in the company.

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Supplemental Table S2. Continued

Study	Risk of bias	Author judgement
Yoshizawa et al. (2021) [21]		
Random sequence generation (selection bias)	Low risk	Randomized controlled trial. Randomization was done using block randomization.
Allocation concealment (selection bias)	Low risk	The random sequence of envelope allocations was generated using block randomization. The block sequence was determined on the basis of random numbers generated in Excel. A controller outside the trial administration center performed the randomization process and created the sealed envelopes.
Blinding of participants & personnel (performance bias)	High risk	Open-label study
Blinding of outcome assessment (detection bias)	High risk	Open-label study. Blinding of outcome assessment was not done.
Incomplete outcome data (attrition bias)	Low risk	30 of 33 completed the 24 weeks of trial period.
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes are reported.
Other biases	Low risk	No funding or sponsorship was received for this study. The journal's Rapid Service Fee was paid by Niigata University. Some of the authors have received lecture fees from the manufacturer, MSD K.K.

RCT, randomized controlled trial; q.w., once-weekly; OHA, oral hypoglycemic agent; q.d., once a day; COI, conflicts of interest; HbA1c, hemoglobin A1c; DTBQ, diabetic treatment burden questionnaire; DTSQ, diabetes treatment satisfaction questionnaire; AHA, antihyperglycemic agent.