

Supplementary Table 2. Rating of individual items of the Risk of Bias tool for each study.

Note: CSR: Clinical Study Report

ACTIV-3/TICO LY-CoV555 Study Group [18]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	"Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied." Information from full CSR, Blinding.
Blinding assessor	LOW	"Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied." Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	No details on selective reporting.
Other bias	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Notes	First author contacted but not able to provide additional information.	

Ahmed S et al [19]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	"Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied." Information from full CSR, Blinding.
Blinding assessor	LOW	"Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied." Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	No details on selective reporting.
Other bias	UNCLEAR	No details on other bias.
Notes	Authors contacted but no reply.	

Aman J et al [20]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	"Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied." Information from full CSR, Blinding.

Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	No details on selective reporting.
Other bias	UNCLEAR	No details on other bias.
Notes	First author contacted but not able to provide additional information.	

Biber A et al [21]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	No details on selective reporting.
Other bias	UNCLEAR	No details on other bias.
Notes	Authors contacted but no reply.	

Blum Vf et al [22]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	UNCLEAR	No details on incomplete data outcome.
Selective reporting	LOW	Outcomes listed in the CSR synopsis reported in the journal article.
Other bias	UNCLEAR	No details on other bias.
Notes	Not possible to contact authors.	

Cadegiani FA et al (a) [23]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .

Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	LOW	First author confirmed that all measures listed in the protocol are reported in the journal article.
Other bias	UNCLEAR	No details on other bias.
Notes	First author provided additional information.	

Cadegiani FA et al (b) [24]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	No details on selective reporting.
Other bias	UNCLEAR	No details on other bias.
Notes	First author informed that additional data are not available anymore.	

Caricchio R et al [25]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	No details on selective reporting.
Other bias	UNCLEAR	No details on other bias.
Notes	First author contacted but not able to provide additional information.	

Chaccour C et al [26]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from the Journal article, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	UNCLEAR	No protocol/CSR available.
Blinding assessor	UNCLEAR	No protocol/CSR available.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned were reported in the Journal article.
Selective reporting	LOW	Information provided by the manufacturer: some outcomes were not reported in the journal article (however, available from Clinicaltrials.gov.)
Other bias	UNCLEAR	No protocol/CSR available.
Notes		Manufacturer provided additional information.

Chen J et al [27]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from the Journal article, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	UNCLEAR	No protocol/CSR available.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from the Journal article, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned were reported in the Journal article.
Selective reporting	UNCLEAR	No protocol/CSR available.
Other bias	UNCLEAR	No protocol/CSR available.
Notes		First author contacted but not able to provide additional information.

Devpura G et al [28]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Incomplete data outcome	UNCLEAR	No details on incomplete data outcome.
Selective reporting	LOW	Information provided by the manufacturer: some outcomes were not reported in the journal article (however, available from Clinicaltrials.gov.)
Other bias	UNCLEAR	No details on other bias.
Notes		Authors provided additional information.

Dubee V et al [29]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	LOW	Information provided by the manufacturer: some outcomes were not reported in the journal article (however, available from Clinicaltrials.gov.)
Other bias	UNCLEAR	No details on other bias.
Notes	Authors provided additional information.	

Eom JS et al [30]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	No details on selective reporting.
Other bias	UNCLEAR	No details on other bias.
Notes	First author contacted but not able to provide additional information.	

Feld JJ et al [31]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.

Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	LOW	Primary and secondary outcomes listed in full CSR all reported in the journal article.
Other bias	UNCLEAR	No details on other bias.
Notes	Authors provided additional information.	

Gonzalez-Ochoa AG et al [32]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from the Journal article, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	HIGH	No information on how blinding was preserved.
Blinding assessor	HIGH	No information on how blinding was preserved.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned were reported in the Journal article.
Selective reporting	UNCLEAR	No protocol/CSR available.
Other bias	UNCLEAR	No protocol/CSR available.
Notes	First author contacted but not able to provide additional information.	

Gottlieb RL et al [33]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	LOW	Manufacturer confirmed that “All outcomes were reported in published papers”.
Other bias	UNCLEAR	No details on other bias.
Notes	Authors provided additional information.	

Gunst GD et al [34]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.

Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	LOW	Manufacturer confirmed that “All outcomes were reported in published papers”.
Other bias	UNCLEAR	No details on other bias.
Notes	Authors provided additional information.	

Gupta A et al [35]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	LOW	Outcomes relevant for the present meta-analysis mentioned in the CSR were reported in the Journal article.
Other bias	UNCLEAR	No details on other bias.
Notes	First author provided additional information.	

Gutierrez-Castrellon P et al [36]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	No details on selective reporting.
Other bias	UNCLEAR	No details on other bias.
Notes	Author contacted but no reply.	

Humeniuk R et al [37]

ITEM	RATING	SUPPORT
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Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	No details on selective reporting.
Other bias	UNCLEAR	No details on other bias.
Notes	Author contacted but no reply.	

Jagannathan P et al [38]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from the Journal article, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	UNCLEAR	No protocol/CSR available.
Blinding assessor	UNCLEAR	No protocol/CSR available.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned were reported in the Journal article.
Selective reporting	UNCLEAR	No protocol/CSR available.
Other bias	UNCLEAR	No protocol/CSR available.
Notes	First author contacted but not able to provide additional information.	

Jeronimo CMP et al [39]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	UNCLEAR	No details on incomplete data outcome.
Selective reporting	UNCLEAR	No details on selective reporting.
Other bias	UNCLEAR	No details on other bias.
Notes	Author contacted but no reply.	

Lenze EJ et al [40]

ITEM	RATING	SUPPORT
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Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	No details on selective reporting.
Other bias	UNCLEAR	No details on other bias.
Notes	Corresponding author contacted but not able to provide additional information.	

López-Medina E et al [41]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	UNCLEAR	No details on incomplete data outcome.
Selective reporting	UNCLEAR	No details on selective reporting.
Other bias	UNCLEAR	No details on other bias.
Notes	First author provided additional information.	

Marconi VC et al [42]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	LOW	Outcomes pertinent to the present meta-analysis identified in the full CSR reported.
Other bias	UNCLEAR	No details on other bias.

Notes	Corresponding author contacted but no reply.
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McCoy J et al [43]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Incomplete data outcome	UNCLEAR	No details on incomplete data outcome.
Selective reporting	UNCLEAR	No details on selective reporting.
Other bias	UNCLEAR	No details on other bias.
Notes	First author provided additional information.	

Mohan A et al [44]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Incomplete data outcome	UNCLEAR	No details on incomplete data outcome.
Selective reporting	UNCLEAR	No details on selective reporting.
Other bias	UNCLEAR	No details on other bias.
Notes	First author contacted but not able to provide additional information.	

Monk PD et al [45]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.

Selective reporting	UNCLEAR	No details on selective reporting.
Other bias	UNCLEAR	No details on other bias.
Notes	First author contacted but not able to provide additional information.	

Omrani AS et al [46]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full article, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	HIGH	No details on who was blinded and how blinding was preserved.
Blinding assessor	UNCLEAR	No protocol/CSR available.
Incomplete data outcome	UNCLEAR	No protocol/CSR available.
Selective reporting	UNCLEAR	No protocol/CSR available.
Other bias	HIGH	No protocol/CSR available.
Notes	Corresponding author not able to provide additional details.	

Patel O et al [47]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	UNCLEAR	Not specified.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	LOW	All outcomes of relevance reported in published journal article.
Other bias	UNCLEAR	Not specified.
Notes	First author provided additional information.	

Puskarich MA et al [48]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.

Selective reporting	LOW	All outcomes of relevance reported in published journal article.
Other bias	UNCLEAR	Not specified.
Notes	First author contacted but not able to provide additional information.	

Rastogi A et al [49]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from journal article, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	UNCLEAR	No protocol/CSR available.
Blinding assessor	UNCLEAR	No protocol/CSR available.
Incomplete data outcome	UNCLEAR	No protocol/CSR available.
Selective reporting	LOW	All outcomes of relevance reported in published journal article.
Other bias	UNCLEAR	No protocol/CSR available.
Notes	First author unable to provide additional details.	

Ravikirti et al [50]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full article, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	UNCLEAR	No protocol/CSR available.
Blinding assessor	UNCLEAR	No protocol/CSR available.
Incomplete data outcome	UNCLEAR	No protocol/CSR available.
Selective reporting	LOW	All outcomes of relevance reported in published journal article.
Other bias	UNCLEAR	No protocol/CSR available.
Notes	First author contacted but not able to provide additional information.	

Reis G et al [51]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	HIGH	No details on who was blinded and how blinding was preserved.
Blinding assessor	HIGH	No details on who was blinded and how blinding was preserved.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	Not specified.
Other bias	LOW	All reported in published papers.

Notes	First author unable to provide additional details.
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Rocco PRM et al [52]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from the full article, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from the full article, Blinding.
Blinding assessor	UNCLEAR	No protocol/CSR available.
Incomplete data outcome	UNCLEAR	No protocol/CSR available.
Selective reporting	LOW	All outcomes of relevance reported in published journal article.
Other bias	LOW	All reported in published papers.
Notes	First author unable to provide additional details.	

Salama C et al [53]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from the full article, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from the full article, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from the full article, Blinding.
Incomplete data outcome	UNCLEAR	No protocol/CSR available.
Selective reporting	UNCLEAR	No protocol/CSR available.
Other bias	UNCLEAR	No protocol/CSR available.
Notes	First author unable to provide additional details.	

Silva M et al [54]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from the full article, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from the full article, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from the full article, Blinding.
Incomplete data outcome	UNCLEAR	No protocol/CSR available.
Selective reporting	UNCLEAR	No protocol/CSR available.
Other bias	UNCLEAR	No protocol/CSR available.

Notes	First author contacted but not able to provide additional information.
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Sivapalan P et al [55]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Incomplete data outcome	UNCLEAR	Not specified.
Selective reporting	HIGH	Unbalanced reasons for selective reporting.
Other bias	LOW	No protocol/CSR available.
Notes	First author contacted but not able to provide additional information.	

Skipper CP et al [56]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	Not specified.
Other bias	LOW	All information listed in clinicaltrial.gov was reported in the journal article.
Notes	Authors provided additional information.	

Stone JH et al [57]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Incomplete data outcome	UNCLEAR	Not specified.

Selective reporting	LOW	All outcomes listed in clinicaltrials.gov were reported in the journal article (which included additional outcomes)
Other bias	UNCLEAR	Not specified.
Notes	Authors provided additional information.	

Tardif JC et al [58]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	LOW	All outcomes listed in clinicaltrials.gov were reported in the journal article (which included additional outcomes)
Other bias	UNCLEAR	Not specified.
Notes	Authors provided additional information.	

Tornling G et al [59]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	UNCLEAR	Not specified.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	Not specified.
Other bias	LOW	All information listed in clinicaltrials.gov was reported in the journal article.
Notes	First author contacted but not able to provide additional information.	

Ulrich RJ et al [60]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.

Blinding assessor	LOW	Throughout, a pharmacy prepared, distributed and tracked all the drugs, separately from raters and subjects in order to maintain double-blind conditions.
Incomplete data outcome	UNCLEAR	Not specified.
Selective reporting	LOW	All outcomes listed in clinaltrial.gov were reported in the journal article (which included additional outcomes)
Other bias	UNCLEAR	Not specified.
Notes	Authors provided additional information.	

Vallejos J et al [61]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	Throughout, a pharmacy prepared, distributed and tracked all the drugs, separately from raters and subjects in order to maintain double-blind conditions.
Incomplete data outcome	UNCLEAR	Not specified.
Selective reporting	UNCLEAR	Not specified.
Other bias	LOW	All information listed in clinaltrial.gov was reported in the journal article.
Notes	Authors provided additional information.	

Wang Y et al [62]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	Throughout, a pharmacy prepared, distributed and tracked all the drugs, separately from raters and subjects in order to maintain double-blind conditions.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	LOW	All outcomes listed in clinaltrial.gov were reported in the journal article (which included additional outcomes)
Other bias	UNCLEAR	Not specified.
Notes	First author contacted but not able to provide additional information.	

Weinreich DM et al [63]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.

Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Blinding assessor	LOW	Throughout, a pharmacy prepared, distributed and tracked all the drugs, separately from raters and subjects in order to maintain double-blind conditions.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	Not specified.
Other bias	UNCLEAR	Not specified.
Notes	Authors not able to provide additional information.	

CaoY et al [64]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	HIGH	No details on who was blinded and how blinding was preserved.
Blinding assessor	HIGH	No details on who was blinded and how blinding was preserved.
Incomplete data outcome	UNCLEAR	Not specified.
Selective reporting	LOW	All outcomes listed in clinicaltrial.gov were reported in the journal article (which included additional outcomes)
Other bias	UNCLEAR	Not specified.
Notes	First author contacted but not able to provide additional information.	

Cremer PC et al [65]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	UNCLEAR	Not specified.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Blinding assessor	LOW	Throughout, a pharmacy prepared, distributed and tracked all the drugs, separately from raters and subjects in order to maintain double-blind conditions.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	LOW	All outcomes listed in clinicaltrial.gov were reported in the journal article (which included additional outcomes)
Other bias	UNCLEAR	Not specified.
Notes	Authors not able to provide additional information.	

de Alencar JCG et al [66]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .

Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Blinding assessor	LOW	Throughout, a pharmacy prepared, distributed and tracked all the drugs, separately from raters and subjects in order to maintain double-blind conditions.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	Not specified.
Other bias	UNCLEAR	Not specified.
Notes	First author contacted but not able to provide additional information.	

Dequin PF et al [67]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	Throughout, a pharmacy prepared, distributed and tracked all the drugs, separately from raters and subjects in order to maintain double-blind conditions.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Incomplete data outcome	UNCLEAR	Not specified.
Selective reporting	UNCLEAR	Not specified.
Other bias	UNCLEAR	Not specified.
Notes	Manufacturer provided additional information.	

Gharebaghi N et al [68]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	Throughout, a pharmacy prepared, distributed and tracked all the drugs, separately from raters and subjects in order to maintain double-blind conditions.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.“ Information from full CSR, Blinding.
Incomplete data outcome	UNCLEAR	Not specified.
Selective reporting	LOW	All outcomes listed in clinaltrial.gov were reported in the journal article (which included additional outcomes)
Other bias	UNCLEAR	Not specified.
Notes	First author contacted but not able to provide additional information.	

Lescure FX et al [69]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	LOW	All outcomes listed in clinicaltrials.gov were reported in the journal article (which included additional outcomes)
Other bias	UNCLEAR	Not specified.
Notes	Authors not able to provide additional information.	

Libster R et al [70]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	UNCLEAR	Not specified.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	Not specified.
Other bias	UNCLEAR	Not specified.
Notes	Contacted author but not valid e-mail; no other e-mail addresses found.	

Munch MW et al [71]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	Not specified.

Other bias	LOW	All information listed in clinicaltrial.gov was reported in the journal article.
Notes	Contacted author but not valid e-mail; no other e-mail addresses found.	

Rosas IO et al [72]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	LOW	Outcomes listed in short CSR reported in the journal article.
Other bias	UNCLEAR	Not specified.
Notes	E-mail address for corresponding author not valid; no other email addresses found.	

Sehgal IS et al [73]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	UNCLEAR	Not specified.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	Not specified.
Other bias	UNCLEAR	Not specified.
Notes	First author contacted but not able to provide additional information.	

Shi L et al [74]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	UNCLEAR	Not specified.

Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	LOW	Outcomes listed in short CSR reported in the journal article.
Other bias	UNCLEAR	Not specified.
Notes	Manufacturer provided additional information.	

Simonovich VA et al [75]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	UNCLEAR	Not specified.
Blinding assessor	UNCLEAR	Not specified.
Incomplete data outcome	UNCLEAR	Not specified.
Selective reporting	LOW	Outcomes listed in short CSR reported in the journal article.
Other bias	UNCLEAR	Not specified.
Notes	First author contacted but not able to provide additional information.	

Sivapalasingam S et al [76]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	Not specified.
Other bias	UNCLEAR	Not specified.
Notes	Authors not able to provide additional information.	

Temesgen Z et al [77]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.

Blinding assessor	LOW	“Investigator and the patient were blinded to treatment. To maintain blinding, all investigational products were supplied.” Information from full CSR, Blinding.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	UNCLEAR	Not specified.
Other bias	UNCLEAR	Not specified.
Notes	First author contacted but not able to provide additional information.	

Zhong M et al [78]

ITEM	RATING	SUPPORT
Random sequence generation	LOW	Received medications and placebo in a random order, double-blind .
Allocation concealment	LOW	Information from full CSR, Method of Assigning Subjects to Treatment Groups.
Blinding participants/personnel	UNCLEAR	Not specified.
Blinding assessor	UNCLEAR	Not specified.
Incomplete data outcome	LOW	Outcomes relevant for the present meta-analysis mentioned in the full CSR were reported in the Journal article.
Selective reporting	LOW	Outcomes listed in short CSR reported in the journal article.
Other bias	UNCLEAR	Not specified.
Notes	Authors not able to provide additional information.	