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Degarelix for treating advanced hormone-sensitive prostate cancer

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Review first published: Issue 8, 2021

Protocol first published: Issue 2, 2017

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
1.1 Serious adverse events	9	2750	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.62, 1.05]	
1.2 Quality of life	3	2887	Std. Mean Difference (IV, Random, 95% CI)	0.06 [-0.05, 0.18]	
1.3 Injection site pain	8	2670	Risk Ratio (M-H, Random, 95% CI)	15.68 [7.41, 33.17]	
1.4 Cardiovascular events	1	80	Risk Ratio (M-H, Random, 95% CI)	0.15 [0.04, 0.61]	
1.5 Backp	5	2102	Risk Ratio (M-H, Random, 95% CI)	0.66 [0.46, 0.96]	

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
ain					
1.6 Gynecomastia	1	25	Risk Ratio (M-H, Random, 95% CI)	0.31 [0.01, 6.94]	
1.7 Constipation	4	1112	Risk Ratio (M-H, Random, 95% CI)	0.75 [0.39, 1.46]	
1.8 Diarrhea	2	253	Risk Ratio (M-H, Random, 95% CI)	1.56 [0.47, 5.18]	
1.9 Vomiting	2	837	Risk Ratio (M-H, Random, 95% CI)	1.56 [0.79, 3.08]	
1.10 Loss of sexual interest	2	270	Risk Ratio (M-H, Random, 95% CI)	1.06 [0.35, 3.17]	
1.11 Loss	2	427	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.39, 1.69]	

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
of sexual function					
1.12 Fatigue	6	1996	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.60, 1.16]	
1.13 Hot flushes	8	2412	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.86, 1.14]	
1.14 Anemia	5	1914	Risk Ratio (M-H, Random, 95% CI)	0.31 [0.13, 0.74]	
1.15 Hepatic enzyme increase (alanine am	4	1014	Risk Ratio (M-H, Random, 95% CI)	2.15 [1.26, 3.66]	

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
in otra nsfe rase)					
1.16 Dyspnea	1	182	Risk Ratio (M-H, Random, 95% CI)	0.39 [0.02, 9.41]	
1.17 Urinary tract infection	5	1908	Risk Ratio (M-H, Random, 95% CI)	0.47 [0.25, 0.87]	
1.18 Hematuria	2	636	Risk Ratio (M-H, Random, 95% CI)	1.69 [0.58, 4.94]	
1.19 Urinary retention	5	1925	Risk Ratio (M-H, Random, 95% CI)	0.43 [0.13, 1.40]	
1.20 Mortalit	4	1821	Risk Ratio (M-H, Random, 95% CI)	0.45 [0.21, 0.97]	

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
y during study conduction (post hoc)					
1.21 Discontinuation due to adverse events (post hoc)	8	2666	Risk Ratio (M-H, Random, 95% CI)	1.11 [0.79, 1.56]	
1.22 Total no	8	2412	Risk Ratio (M-H, Random, 95% CI)	1.08 [1.01, 1.15]	

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
n-serious adverse events (post hoc)					
1.2.3 Biochemical progression	2	691	Risk Ratio (M-H, Random, 95% CI)	0.61 [0.43, 0.87]	

Comparison 2

Degarelix versus androgen suppression therapy (GnRH agonists or maximum androgen suppression therapy): subgroup analysis based on different doses

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
2.1 Serious adverse events	9	2951	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.63, 1.03]	
2.1.1 Degarelix 240mg/80mg	7	1466	Risk Ratio (M-H, Random, 95% CI)	0.66 [0.39, 1.14]	
2.1.2 Degarelix 240mg/160mg	1	403	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.51, 1.42]	
2.1.3 De	2	1082	Risk Ratio (M-H, Random, 95% CI)	0.90 [0.64, 1.26]	

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
garelix 240mg/480mg					
2.2 Quality of life	3	2887	Std. Mean Difference (IV, Random, 95% CI)	0.06 [-0.05, 0.18]	
2.2.1 Degarelix 240mg/80mg	2	2040	Std. Mean Difference (IV, Random, 95% CI)	-0.03 [-0.33, 0.28]	
2.2.2 Degarelix 240mg/480	1	847	Std. Mean Difference (IV, Random, 95% CI)	0.10 [-0.04, 0.24]	

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
mg					
2.3 Injection site pain	8	2670	Risk Ratio (M-H, Random, 95% CI)	15.68 [7.41, 33.17]	
2.3.1 Degarelix 240mg/80mg	6	1286	Risk Ratio (M-H, Random, 95% CI)	14.94 [4.48, 49.81]	
2.3.2 Degarelix 240mg/160mg	1	302	Risk Ratio (M-H, Random, 95% CI)	61.20 [3.82, 979.36]	
2.3.3 Degarelix	2	1082	Risk Ratio (M-H, Random, 95% CI)	15.24 [8.50, 27.31]	

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
240mg/480mg					

History

Protocol first published: Issue 2, 2017
Review first published: Issue 8, 2021

Sources of support

Internal sources

- No sources of support provided

External sources

- No sources of support provided

Characteristics of studies

Characteristics of included studies [ordered by study ID]

Anderson 2013 (CS28)

Study characteristics		
Methods		
Participants		
Interventions		
Outcomes		
Funding sources		
Declarations of interest		
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	**Quote from publication:** "Patients were randomised 3:1" **Comment:** insufficient information to permit judgment.
Allocation concealment (selection bias)	Unclear risk	**Quote from publication:** "Patients were randomised 3:1" **Comment:** insufficient information to permit judgment.
Blinding of participants and personnel (performan	High risk	**Quote from publication:** "open-label study"; there was no blinding (or it was not reported) **Comment:** we judge that subjective outcomes are influenced by lack of blinding.

ce bias) Subjective outcomes		
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	**Quote from publication:** “open-label study”; there was no blinding of outcome assessment (or it was not reported) **Comment:** insufficient information to permit judgment.
Incomplete outcome data (attrition bias) Biochemical progression	Unclear risk	**Comment:** the study did not address this outcome.
Incomplete outcome data (attrition bias) Adverse events	Low risk	**Comment:** two of 42 randomized participants (4.8%) were excluded from analysis because they were never treated. The proportion of missing outcomes is not enough to have a clinically relevant impact on the intervention effect estimate.
Incomplete outcome data (attrition bias) Quality of life	Unclear risk	**Comment:** quality of life assessment was not included because data were not relevant to this review (scale used: IPSS).
Selective reporting (reporting bias)	Low risk	**Comment:** the study protocol is available, and all outcomes of interest have been reported.
Other bias	Low risk	**Comment:** we did not identify other sources of bias.

Axcrona 2012 (CS31)

Study characteristics		
Methods		
Participants		
Interventions		
Outcomes		
Funding sources		
Declarations of interest		
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	**Quote from publication:** “patients were randomized” **Comment:** insufficient information to permit judgment.
Allocation concealment (selection bias)	Unclear risk	**Quote from publication:** “patients were randomized” **Comment:** insufficient information to permit judgment.
Blinding of participants and personnel (performance bias) Subjective outcomes	High risk	**Quote from publication:** “open-label trial”; there was no blinding (or it was not reported) **Comment:** we judge that subjective outcomes are influenced by lack of blinding.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	**Quote from publication:** “open-label trial”; there was no blinding of outcome assessment (or it was not reported) **Comment:** insufficient information to permit judgment.
Incomplete outcome data (attrition bias) Biochemical progression	Unclear risk	**Comment:** the study did not address this outcome.
Incomplete outcome data (attrition bias) Adverse events	Low risk	**Comment:** no missing outcome data.
Incomplete outcome data (attrition bias) Quality of life	Unclear risk	**Comment:** quality of life assessment was not included because data were not relevant to this review (scale used: BPHII).
Selective reporting (reporting bias)	Low risk	**Comment:** the study protocol is available, and all outcomes that are of interest have been reported.
Other bias	Low risk	**Comment:** we did not identify other sources of bias.

Crawford 2013 (CS37)

Study characteristics		
Methods		
Participants		
Interventions		
Outcomes		
Funding sources		
Declarations of interest		
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	**Quote from publication:** “men were randomized” **Comment:** insufficient information to permit judgment.
Allocation concealment (selection bias)	Unclear risk	**Quote from publication:** “men were randomized” **Comment:** insufficient information to permit judgment.

Blinding of participants and personnel (performance bias) Subjective outcomes	High risk	**Quote from ClinicalTrials.gov:** "This was an open-label, randomized, parallel-arm, multicenter study" **Comment:** we judge that subjective outcomes are influenced by lack of blinding.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	**Quote from publication:** "open-label trial"; there was no blinding of outcome assessment (or it was not reported) **Comment:** insufficient information to permit judgment.
Incomplete outcome data (attrition bias) Biochemical progression	Unclear risk	**Comment:** the study did not address this outcome.
Incomplete outcome data (attrition bias) Adverse events	Low risk	**Comment:** no missing outcome data.
Incomplete outcome data (attrition bias) Quality of life	Low risk	**Comment:** missing outcome data balanced in numbers across intervention groups (Group 2 18.0% vs Group 3 15.7%).
Selective reporting (reporting bias)	Unclear risk	**Comment:** the study protocol is available, but we did not identify full-text publications.
Other bias	Low risk	**Comment:** we did not identify other sources of bias.

Klotz 2008 (CS21)

Study characteristics		
Methods		
Participants		
Interventions		
Outcomes		
Funding sources		
Declarations of interest		
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	**Quote from publication:** "Randomization lists were prepared centrally (...), using validated computer program" **Comment:** randomization was adequately performed.
Allocation concealment (selection bias)	Low risk	**Quote from publication:** "Central allocation" **Comment:** adequate allocation concealment.
Blinding of participants and personnel (performance bias) Subjective outcomes	High risk	**Quote from publication:** "open-label study" **Comment:** we judge that subjective outcomes are influenced by lack of blinding.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	**Quote from publication:** "Open-label study"; "personnel were unaware of blood values" **Comment:** insufficient information to permit judgment. The "personnel were unaware of blood values," but it remained unclear if outcome assessment was blinded to PSA values for evaluation of biochemical progression, and there was no information for assessment of adverse events.
Incomplete outcome data (attrition bias) Biochemical progression	Low risk	**Comment:** no relevant missing outcome data.
Incomplete outcome data (attrition bias) Adverse events	Low risk	**Comment:** no missing outcome data.
Incomplete outcome data (attrition bias) Quality of life	Low risk	**Comment:** the return rate of questionnaires used in the study was minimum 90.6%. Plausible effect size among missing outcomes not enough to have a clinically relevant impact on observed effect size.
Selective reporting (reporting bias)	Low risk	**Comment:** the study protocol is available, and all outcomes of interest have been reported.
Other bias	Low risk	**Comment:** we did not identify other sources of bias.

Margel 2019 (0102-15-RMC)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	
Funding sources	
Declarations of interest	
Notes	
Risk of bias	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote from publication:** “Randomization was done by minimization using MINIM software” **Comment:** we assume that randomization was adequately performed.
Allocation concealment (selection bias)	Low risk	**Quote from publication:** “The allocation sequence was created and coordinated at the study central office” **Comment:** adequate allocation concealment.
Blinding of participants and personnel (performance bias) Subjective outcomes	High risk	**Quote from publication:** “open-label study” **Comment:** we judge that subjective outcomes are influenced by lack of blinding.
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	**Quote from publication:** “A cardiologist blinded to treatment assignment reviewed all medical records and categorized all cardiac events” **Comment:** adequate outcome assessment.
Incomplete outcome data (attrition bias) Biochemical progression	Unclear risk	**Comment**: the study did not address this outcome.
Incomplete outcome data (attrition bias) Adverse events	Low risk	**Comment**: no missing outcome data
Incomplete outcome data (attrition bias) Quality of life	Unclear risk	**Comment**: the study did not address this outcome.
Selective reporting (reporting bias)	High risk	**Comment:** the study protocol is available. Quality of life is prespecified in the protocol but not reported in the results.
Other bias	Low risk	**Comment:** we did not identify other sources of bias.

Mason 2013 (CS30)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	
Funding sources	
Declarations of interest	
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Quote from publication:** “patients were randomised in a 3:1 ratio” **Comment:** insufficient information to permit judgment.
Allocation concealment (selection bias)	Unclear risk	**Quote from publication:** “patients were randomised in a 3:1 ratio” **Comment:** insufficient information to permit judgment.
Blinding of participants and personnel (performance bias) Subjective outcomes	High risk	**Quote from publication:** “open-label trial”; there was no blinding (or it was not reported) **Comment:** we judge that subjective outcomes are influenced by lack of blinding.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	**Quote from publication:** “open-label trial”; there was no blinding of outcome assessment (or it was not reported) **Comment:** insufficient information to permit judgment.
Incomplete outcome data (attrition bias) Biochemical progression	Unclear risk	**Comment**: the study did not address this outcome.
Incomplete outcome data (attrition bias) Adverse events	Low risk	**Comment:** no missing outcome data.
Incomplete outcome data (attrition bias) Quality of life	Unclear risk	**Comment:** quality of life assessment was not included because data were not relevant to this review (scale used: IPSS).
Selective reporting (reporting bias)	Low risk	**Comment:** the study protocol is available, and all outcomes of interest have been reported.
Other bias	Low risk	**Comment:** we did not identify other sources of bias.

Ozono 2018 (3550-CL-0010)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	
Funding sources	

Declarations of interest	
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote from publication:** "subjects were randomly allocated into a degarelix or goserelin group using a minimization method of adjusting age, cancer stage, pretreatment, and serum PSA" **Comment:** we assume that randomization was adequately performed.
Allocation concealment (selection bias)	Unclear risk	**Quote from publication:** "subjects were randomly allocated into a degarelix or goserelin group using a minimization method of adjusting age, cancer stage, pretreatment, and serum PSA" **Comment:** insufficient information to permit judgment.
Blinding of participants and personnel (performance bias) Subjective outcomes	High risk	**Quote from publication:** "open-label, parallel-arm study", "For the safety analysis, the incidence of AEs, SAEs, and ADRs were collected and graded according to Common Terminology Criteria for Adverse Events version 4.0." **Comment:** we judge that subjective outcomes are influenced by lack of blinding.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	**Quote from publication:** "open-label trial"; there was no blinding of outcome assessment (or it was not reported) **Comment:** insufficient information to permit judgment.
Incomplete outcome data (attrition bias) Biochemical progression	Unclear risk	**Comment**: the study did not address this outcome.
Incomplete outcome data (attrition bias) Adverse events	Low risk	**Quote from publication:** "degarelix group: withdrawals 19/117 (=16.2 %); goserelin group: withdrawals 23/117 (=19.7 %)" **Comment:** missing outcome data are balanced in numbers across intervention groups with similar reasons for missing data across groups.
Incomplete outcome data (attrition bias) Quality of life	Unclear risk	**Comment:** the study did not address this outcome.
Selective reporting (reporting bias)	Low risk	**Comment:** the study protocol is available, and all outcomes of interest have been reported.
Other bias	Low risk	**Comment:** we did not identify other sources of bias.

Sawazaki 2019

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	
Funding sources	
Declarations of interest	
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Quote from publication:** "prospective randomized, parallel-arm, open-label, single-center trial" **Comment:** insufficient information to permit judgment.
Allocation concealment (selection bias)	Unclear risk	**Quote from publication:** "prospective randomized, parallel-arm, open-label, single-center trial" **Comment:** insufficient information to permit judgment.
Blinding of participants and personnel (performance bias) Subjective outcomes	High risk	**Quote from publication:** "Open-label study" **Comment:** none of the reported outcomes were relevant to this review, therefore none were included in the review. Evaluation of adverse events could have been expected, and we judge that subjective outcomes are influenced by lack of blinding.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	**Quote from publication:** "open-label study"; there was no blinding of outcome assessment (or it was not reported) **Comment:** insufficient information to permit judgment.
Incomplete outcome data (attrition bias) Biochemical progression	Unclear risk	**Comment**: the study did not address this outcome.
Incomplete outcome data (attrition bias) Adverse events	Unclear risk	**Comment**: the study did not address this outcome.
Incomplete outcome data (attrition bias) Quality of life	Unclear risk	**Comment**: the study did not address this outcome.
Selective reporting (reporting bias)	High risk	**Comment:** adverse events were not reported, although evaluation of this outcome could have been expected.

Other bias	Low risk	**Comment:** we did not identify other sources of bias.

Sayyid 2017 (DEG_PRE-OP)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	
Funding sources	
Declarations of interest	
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	**Quote from publication:** "patients were block-randomized 1:1:1" **Quote from correspondence:** "This study followed block randomization and was stratified by study site using a computer-generated list of random numbers." **Comment:** adequate random sequence generation.
Allocation concealment (selection bias)	Low risk	**Quote from publication:** not reported **Quote from correspondence:** "The allocation sequence was created and coordinated centrally, through the University Health Network Uro-Oncology Research Unit in Toronto. Participant enrolment and assignment to intervention was performed at each site utilizing prefilled sequential randomisation envelopes which contained a 4-digit code (2-digit centre code followed by a 2-digit patient code plus the treatment assignment listed as Arm A, B, or C). This 4-digit randomisation number was recorded in the site enrolment log, the subject's eCRF and on the study medication page." **Comment:** adequate allocation concealment.
Blinding of participants and personnel (performance bias) Subjective outcomes	High risk	**Quote from publication:** "Open-label study" **Quote from correspondence:** "This was an open label randomized study; therefore all study investigators, participants and research coordination staff were unblinded to the treatment allocation for the duration of the study." **Comment:** we judge that subjective outcomes are influenced by lack of blinding.
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	**Quote from correspondence:** "Tissue and data handlers and analysts were blinded to the treatment allocation." **Comment:** adequate outcome assessment.
Incomplete outcome data (attrition bias) Biochemical progression	Unclear risk	**Comment**: the study did not address this outcome.
Incomplete outcome data (attrition bias) Adverse events	Low risk	**Comment:** no missing outcome data.
Incomplete outcome data (attrition bias) Quality of life	Unclear risk	**Comment**: the study did not address this outcome.
Selective reporting (reporting bias)	Unclear risk	**Quote from correspondence:** "While safety was not pre-specified as an outcome, toxicity of study treatments was monitored throughout the study, with regular reporting..." **Comment:** insufficient information to permit judgment.
Other bias	Low risk	**Comment:** we did not identify other sources of bias.

Shore 2012 (CS35)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	
Funding sources	
Declarations of interest	

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Quote from publication:** "open-label, randomised study" **Comment:** insufficient information to permit judgment.
Allocation concealment (selection bias)	Unclear risk	**Quote from publication:** "open-label, randomised study" **Comment:** insufficient information to permit judgment.
Blinding of participants and personnel (performance bias) Subjective outcomes	High risk	**Quote from publication:** "open-label study"; there was no blinding (or it was not reported) **Comment:** we judge that subjective outcomes are influenced by lack of blinding.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	**Quote from publication:** "open-label study"; there was no blinding of outcome assessment (or it was not reported) **Comment:** insufficient information to permit judgment.
Incomplete outcome data (attrition bias) Biochemical progression	Unclear risk	**Comment**: the study did not address this outcome.
Incomplete outcome data (attrition bias) Adverse events	Low risk	**Comment:** no missing outcome data.
Incomplete outcome data (attrition bias) Quality of life	Low risk	**Comment:** exclusion rate 1 of 848 (0.1%).
Selective reporting (reporting bias)	Unclear risk	**Comment:** the study protocol is available, but we did not identify full-text publications.
Other bias	Low risk	**Comment:** we did not identify other sources of bias.

Xie 2016 (PANDA)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	
Funding sources	
Declarations of interest	
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote from correspondence:** "Computer-generated randomisation lists allocating patients to one of the two treatments in a 1:1 ratio per stratum. The randomisation lists were stratified into groups of patients having had previous therapy with 5-alpha reductase inhibitors within the last year, and those patients that did not." **Comment:** adequate random sequence generation.
Allocation concealment (selection bias)	Unclear risk	**Quote from correspondence:** "The treatment allocation was open-label." **Comment:** insufficient information to permit judgment.
Blinding of participants and personnel (performance bias) Subjective outcomes	High risk	**Quote from correspondence:** "An open-label design was chosen as blinding was not feasible due to the formulation differences between degarelix and goserelin." **Comment:** we judge that subjective outcomes are influenced by lack of blinding.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	**Quote from correspondence:** "Testosterone and PSA levels (with the exception of the screening samples) were masked for Sponsor personnel directly involved in the trial." **Comment:** blood values are not likely to being influenced by lack of blinding, but insufficient reporting regarding outcome assessment of adverse events.
Incomplete outcome data (attrition bias) Biochemical progression	Low risk	**Comment**: no relevant missing outcome data.
Incomplete outcome data (attrition bias) Adverse events	Low risk	**Quote from correspondence:** "There were two patients withdrawing consent after randomisation and before first trial product administration ('first dose'); otherwise no exclusions were made." **Comment:** the proportion of missing outcomes is not enough to have a clinically relevant impact on the intervention effect estimate.
Incomplete outcome data (attrition bias) Quality of life	Unclear risk	**Comment:** the study did not address this outcome.
Selective reporting (reporting bias)	Unclear risk	**Comment:** no study protocol is available.

Other bias	Low risk	**Comment:** we did not identify other sources of bias.

References

References to studies included in this review

Anderson 2013 (CS28) {published data only}

Axcrona 2012 (CS31) {published data only}

Crawford 2013 (CS37) {published data only}

Klotz 2008 (CS21) {published data only}

Margel 2019 (0102-15-RMC) {published data only}

Mason 2013 (CS30) {published data only}

Ozono 2018 (3550-CL-0010) {published data only}

Sawazaki 2019 {published data only}

Sayyid 2017 (DEG_PRE-OP) {published data only}

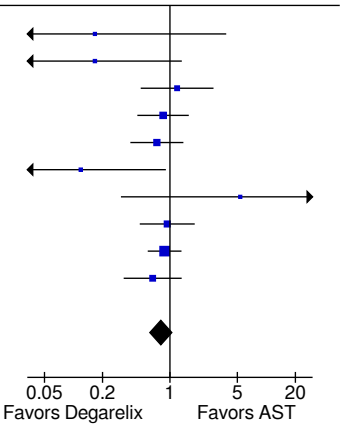
Shore 2012 (CS35) {published data only}

Xie 2016 (PANDA) {published data only}

Analysis 1.1

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Anderson 2013 (CS28)	0	27	1	13	0.7%	0.17 [0.01 , 3.83]
Axcrona 2012 (CS31)	1	84	7	98	1.6%	0.17 [0.02 , 1.33]
Crawford 2013 (CS37)	6	50	18	178	8.4%	1.19 [0.50 , 2.83]
Klotz 2008 (CS21)[a]	24	202	14	100	15.5%	0.85 [0.46 , 1.57]
Klotz 2008 (CS21)[b]	21	207	14	101	14.7%	0.73 [0.39 , 1.38]
Margel 2019 (0102-15-RMC)[c]	1	41	8	39	1.6%	0.12 [0.02 , 0.91]
Mason 2013 (CS30)	7	181	0	64	0.8%	5.36 [0.31 , 92.49]
Ozono 2018 (3550-CL-0010)[d]	15	117	16	117	13.8%	0.94 [0.49 , 1.81]
Shore 2012 (CS35)[e]	58	565	33	283	30.2%	0.88 [0.59 , 1.32]
Xie 2016 (PANDA)	12	142	18	141	12.6%	0.66 [0.33 , 1.32]
Total (Wald[f])		**1616**		**1134**	**100.0%**	**0.80 [0.62 , 1.05]**
Total events:	145		129			

Test for overall effect: Z = 1.63 (P = 0.10)



Heterogeneity: Tau² (DL[g]) = 0.02; Chi² = 9.93, df = 9 (P = 0.36); I² = 9%

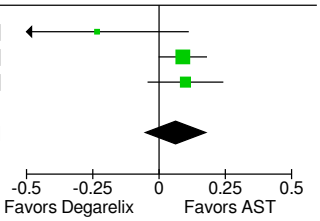
Footnotes

[a]Degarelix 240 mg induction dose/160 mg maintenance dose s.c.
[b]Degarelix 240 mg induction dose/80 mg maintenance dose s.c.
[c]Major cardiovascular and cerebrovascular events
[d]Degarelix 240 mg induction dose/480 mg maintenance dose every 3 months s.c.
[e]Degarelix 240 mg induction dose/480 mg maintenance dose every 3 month s.c.
[f]CI calculated by Wald-type method.
[g]Tau² calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 1: Serious adverse events

Analysis 1.2

Study or Subgroup	Degarelix Mean	Degarelix SD	Degarelix Total	AST Mean	AST SD	AST Total	Weight	Std. Mean Difference IV, Random, 95% CI
Crawford 2013 (CS37)[a]	-4.28	11.34	41	-1.65	11.15	150	9.6%	-0.23 [-0.58 , 0.11]
Klotz 2008 (CS21)[b]	0.871	0.11	935	0.861	0.113	914	54.4%	0.09 [-0.00 , 0.18]
Shore 2012 (CS35)[c]	0.18	10.9	565	-0.87	9.76	282	36.0%	0.10 [-0.04 , 0.24]
Total (Wald[d])			**1541**			**1346**	**100.0%**	**0.06 [-0.05 , 0.18]**



Test for overall effect: Z = 1.07 (P = 0.28)

Heterogeneity: Tau² (DL[e]) = 0.00; Chi² = 3.27, df = 2 (P = 0.19); I² = 39%

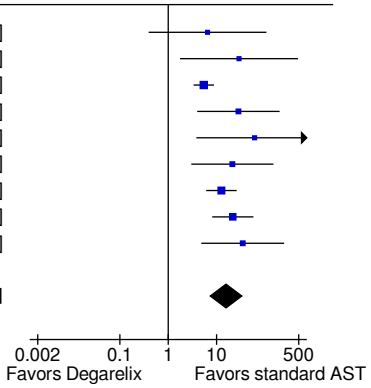
Footnotes

[a]Functional Assessment of Cancer Therapy – Prostate (FACT-P)
[b]EORTC QLQ-C30 mapped to EORTC-8D; degarelix 240 mg induction dose/80 mg maintenance dose every 4 weeks
[c]Short-Form-36 (SF-36); degarelix 240 mg induction dose/480 mg maintenance dose every 3 months s.c.
[d]CI calculated by Wald-type method.
[e]Tau² calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 2: Quality of life

Analysis 1.3

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Anderson 2013 (CS28)	6	27	0	13	5.5%	6.50 [0.39 , 107.32]
Axcrona 2012 (CS31)	12	84	0	98	5.4%	29.12 [1.75 , 484.51]
Crawford 2013 (CS37)	29	50	19	178	21.1%	5.43 [3.34 , 8.83]
Klotz 2008 (CS21)	58	207	1	101	9.0%	28.30 [3.98 , 201.39]
Klotz 2008 (CS21)[a]	61	202	0	100	5.6%	61.20 [3.82 , 979.36]
Mason 2013 (CS30)	60	181	1	64	9.0%	21.22 [3.00 , 149.95]
Ozono 2018 (3550-CL-0010)[b]	88	117	7	117	19.0%	12.57 [6.08 , 25.98]
Shore 2012 (CS35)[b]	173	565	4	283	16.6%	21.66 [8.12 , 57.77]
Xie 2016 (PANDA)	35	142	1	141	8.9%	34.75 [4.83 , 250.22]
Total (Wald[c])		**1575**		**1095**	**100.0%**	**15.68 [7.41 , 33.17]**
Total events:	522		33			



Test for overall effect: Z = 7.20 (P < 0.00001)

Heterogeneity: Tau² (DL[d]) = 0.63; Chi² = 21.56, df = 8 (P = 0.006); I² = 63%

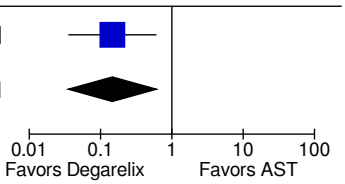
Footnotes

[a]Degarelix 240 mg induction dose/160 mg maintenance dose s.c.
[b]Degarelix 240 mg induction dose/480 mg maintenance dose every 3 months s.c.
[c]CI calculated by Wald-type method.
[d]Tau² calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 3: Injection site pain

Analysis 1.4

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Margel 2019 (0102-15-RMC)	2	41	13	39	100.0%	0.15 [0.04 , 0.61]
Total		**41**		**39**	**100.0%**	**0.15 [0.04 , 0.61]**
Total events:	2		13			



Test for overall effect: Z = 2.65 (P = 0.008)

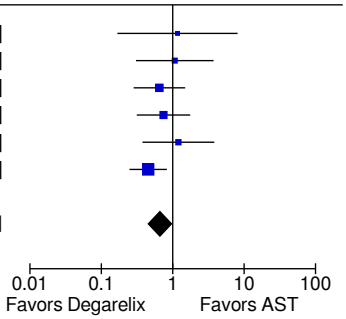
Heterogeneity: Not applicable

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 4: Cardiovascular events

Analysis 1.5

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Axcrona 2012 (CS31)	2	84	2	98	3.7%	1.17 [0.17 , 8.10]
Crawford 2013 (CS37)	3	50	10	178	8.9%	1.07 [0.31 , 3.73]
Klotz 2008 (CS21)	12	207	9	101	20.2%	0.65 [0.28 , 1.49]
Klotz 2008 (CS21)[a]	12	202	8	100	18.7%	0.74 [0.31 , 1.76]
Ozono 2018 (3550-CL-0010)[b]	6	117	5	117	10.4%	1.20 [0.38 , 3.82]
Shore 2012 (CS35)[c]	19	565	21	283	38.2%	0.45 [0.25 , 0.83]
Total (Wald[d])		**1225**		**877**	**100.0%**	**0.66 [0.46 , 0.96]**
Total events:	54		55			

Test for overall effect: Z = 2.17 (P = 0.03)



Heterogeneity: Tau² (DL[e]) = 0.00; Chi² = 3.49, df = 5 (P = 0.63); I² = 0%

Footnotes

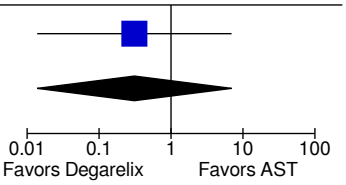
[a]Degarelix 240 mg induction dose/160 mg maintenance dose every 4 weeks s.c.
[b]Degarelix 240 mg induction dose/480 mg maintenance dose every 3 months s.c.
[c]Degarelix 240 mg induction dose/480 mg maintenance dose every 3 month s.c.
[d]CI calculated by Wald-type method.
[e]Tau² calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 5: Back pain

Analysis 1.6

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Sayyid 2017 (DEG_PRE-OP)	0	13	1	12	100.0%	0.31 [0.01 , 6.94]
Total		**13**		**12**	**100.0%**	**0.31 [0.01 , 6.94]**
Total events:	0		1			

Test for overall effect: Z = 0.74 (P = 0.46)



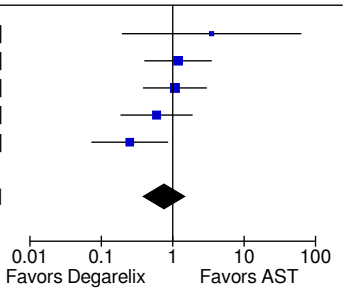
Heterogeneity: Not applicable

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 6: Gynecomastia

Analysis 1.7

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Anderson 2013 (CS28)	3	27	0	13	4.9%	3.50 [0.19 , 63.16]
Crawford 2013 (CS37)	4	50	12	178	24.9%	1.19 [0.40 , 3.52]
Klotz 2008 (CS21)	11	207	5	101	26.8%	1.07 [0.38 , 3.01]
Klotz 2008 (CS21)[a]	6	202	5	100	22.7%	0.59 [0.19 , 1.90]
Ozono 2018 (3550-CL-0010)[b]	3	117	12	117	20.7%	0.25 [0.07 , 0.86]
Total (Wald[c])		**603**		**509**	**100.0%**	**0.75 [0.39 , 1.46]**
Total events:	27		34			

Test for overall effect: Z = 0.84 (P = 0.40)



Heterogeneity: Tau² (DL[d]) = 0.15; Chi² = 5.43, df = 4 (P = 0.25); I² = 26%

Footnotes

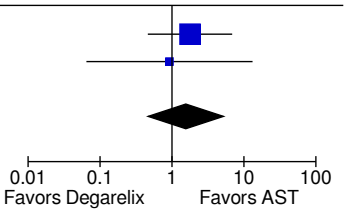
[a]Degarelix 240 mg induction dose/160 mg maintenance dose every 4 weeks s.c.
[b]Degarelix 240 mg induction dose/480 mg maintenance dose every 3 months s.c.
[c]CI calculated by Wald-type method.
[d]Tau² calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 7: Constipation

Analysis 1.8

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Crawford 2013 (CS37)	3	50	6	178	79.5%	1.78 [0.46 , 6.87]
Sayyid 2017 (DEG_PRE-OP)	1	13	1	12	20.5%	0.92 [0.06 , 13.18]
Total (Wald[a])		**63**		**190**	**100.0%**	**1.56 [0.47 , 5.18]**
Total events:	4		7			

Test for overall effect: Z = 0.72 (P = 0.47)



Heterogeneity: Tau² (DL[b]) = 0.00; Chi² = 0.19, df = 1 (P = 0.67); I² = 0%

Footnotes

[a]CI calculated by Wald-type method.

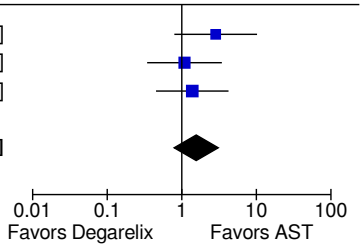
[b]Tau² calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 8: Diarrhea

Analysis 1.9

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Crawford 2013 (CS37)	4	50	5	178	28.4%	2.85 [0.79 , 10.21]
Klotz 2008 (CS21)	9	207	4	100	34.7%	1.09 [0.34 , 3.44]
Klotz 2008 (CS21)[a]	11	201	4	101	36.9%	1.38 [0.45 , 4.23]
Total (Wald[b])		**458**		**379**	**100.0%**	**1.56 [0.79 , 3.08]**
Total events:	24		13			

Test for overall effect: Z = 1.28 (P = 0.20)



Heterogeneity: Tau² (DL[c]) = 0.00; Chi² = 1.29, df = 2 (P = 0.53); I² = 0%

Footnotes

[a]Degarelix 240 mg induction dose/160 mg maintenance dose every 4 weeks s.c.

[b]CI calculated by Wald-type method.

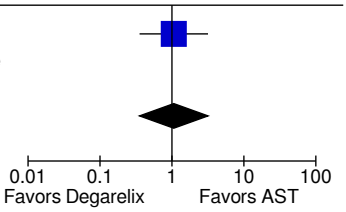
[c]Tau² calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 9: Vomiting

Analysis 1.10

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Mason 2013 (CS30)	12	181	4	64	100.0%	1.06 [0.35 , 3.17]
Sayyid 2017 (DEG_PRE-OP)	0	13	0	12		Not estimable
Total		**194**		**76**	**100.0%**	**1.06 [0.35 , 3.17]**
Total events:	12		4			

Test for overall effect: Z = 0.11 (P = 0.92)



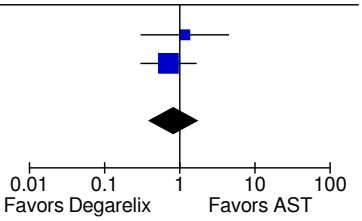
Heterogeneity: Not applicable

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 10: Loss of sexual interest

Analysis 1.11

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Axcrona 2012 (CS31)	4	84	4	98	28.8%	1.17 [0.30 , 4.52]
Mason 2013 (CS30)	14	181	7	64	71.2%	0.71 [0.30 , 1.67]
Total (Wald[a])		**265**		**162**	**100.0%**	**0.82 [0.39 , 1.69]**
Total events:	18		11			

Test for overall effect: Z = 0.55 (P = 0.59)



Heterogeneity: Tau² (DL[b]) = 0.00; Chi² = 0.37, df = 1 (P = 0.54); I² = 0%

Footnotes

[a]CI calculated by Wald-type method.

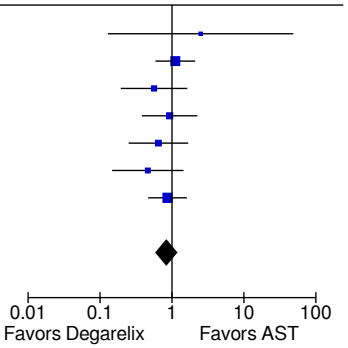
[b]Tau² calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 11: Loss of sexual function

Analysis 1.12

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Anderson 2013 (CS28)	2	27	0	13	1.2%	2.50 [0.13 , 48.62]
Crawford 2013 (CS37)	10	50	32	178	26.8%	1.11 [0.59 , 2.10]
Klotz 2008 (CS21)	7	207	6	100	9.6%	0.56 [0.19 , 1.63]
Klotz 2008 (CS21)[a]	13	202	7	101	13.8%	0.93 [0.38 , 2.25]
Mason 2013 (CS30)	11	181	6	64	12.0%	0.65 [0.25 , 1.68]
Sayyid 2017 (DEG_PRE-OP)	3	13	6	12	8.3%	0.46 [0.15 , 1.45]
Shore 2012 (CS35)[b]	26	565	15	283	28.3%	0.87 [0.47 , 1.61]
Total (Wald[c])		**1245**		**751**	**100.0%**	**0.83 [0.60 , 1.16]**
Total events:	72		72			

Test for overall effect: Z = 1.08 (P = 0.28)



Heterogeneity: Tau^2 (DL^d) = 0.00; Chi^2 = 3.21, df = 6 (P = 0.78); I^2 = 0%

Footnotes

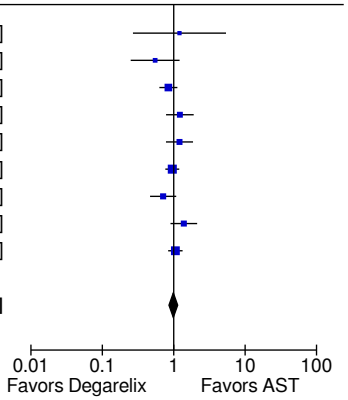
[a]Degarelix 240 mg induction dose/160 mg maintenance dose every 4 weeks s.c.
[b]Degarelix 240 mg induction dose/480 mg maintenance dose every 3 months s.c.
[c]CI calculated by Wald-type method.
[d]Tau^2 calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 12: Fatigue

Analysis 1.13

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Anderson 2013 (CS28)	5	27	2	13	0.9%	1.20 [0.27 , 5.40]
Axcrona 2012 (CS31)	8	84	17	98	3.0%	0.55 [0.25 , 1.21]
Crawford 2013 (CS37)	26	50	110	178	16.4%	0.84 [0.63 , 1.12]
Klotz 2008 (CS21)	53	207	21	100	8.4%	1.22 [0.78 , 1.90]
Klotz 2008 (CS21)[a]	53	202	22	101	8.7%	1.20 [0.78 , 1.86]
Mason 2013 (CS30)	108	181	40	64	22.8%	0.95 [0.76 , 1.19]
Ozono 2018 (3550-CL-0010)[b]	27	117	38	117	9.2%	0.71 [0.47 , 1.08]
Sayyid 2017 (DEG_PRE-OP)	12	13	8	12	8.9%	1.38 [0.90 , 2.13]
Shore 2012 (CS35)[b]	160	565	76	283	21.8%	1.05 [0.84 , 1.33]
Total (Wald[c])		**1446**		**966**	**100.0%**	**0.99 [0.86 , 1.14]**
Total events:	452		334			

Test for overall effect: Z = 0.18 (P = 0.85)



Heterogeneity: Tau^2 (DL^d) = 0.01; Chi^2 = 10.15, df = 8 (P = 0.25); I^2 = 21%

Footnotes

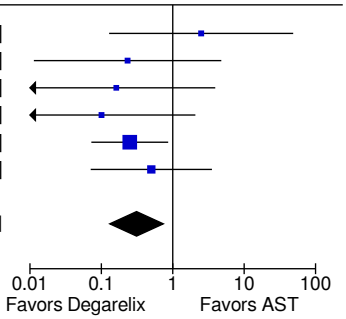
[a]Degarelix 240 mg induction dose/160 mg maintenance dose every 4 weeks s.c.
[b]Degarelix 240 mg induction dose/480 mg maintenance dose every 3 months s.c.
[c]CI calculated by Wald-type method.
[d]Tau^2 calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 13: Hot flushes

Analysis 1.14

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Anderson 2013 (CS28)	2	27	0	13	8.5%	2.50 [0.13 , 48.62]
Axcrona 2012 (CS31)	0	84	2	98	8.1%	0.23 [0.01 , 4.79]
Klotz 2008 (CS21)	0	207	1	100	7.3%	0.16 [0.01 , 3.94]
Klotz 2008 (CS21)[a]	0	202	2	101	8.1%	0.10 [0.00 , 2.07]
Ozono 2018 (3550-CL-0010)[b]	3	117	12	117	48.5%	0.25 [0.07 , 0.86]
Shore 2012 (CS35)[b]	2	565	2	283	19.5%	0.50 [0.07 , 3.54]
Total (Wald[c])		**1202**		**712**	**100.0%**	**0.31 [0.13 , 0.74]**
Total events:	7		19			

Test for overall effect: Z = 2.65 (P = 0.008)



Heterogeneity: Tau² (DL[d]) = 0.00; Chi² = 2.97, df = 5 (P = 0.70); I² = 0%

Footnotes

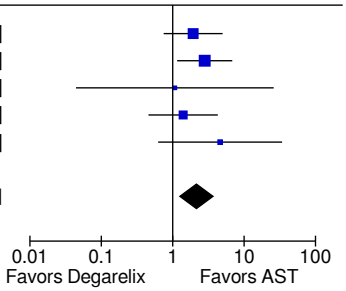
[a]Degarelix 240 mg induction dose/160 mg maintenance dose every 4 weeks s.c.
[b]Degarelix 240 mg induction dose/480 mg maintenance dose every 3 months s.c.
[c]CI calculated by Wald-type method.
[d]Tau² calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 14: Anemia

Analysis 1.15

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Klotz 2008 (CS21)	20	207	5	100	31.4%	1.93 [0.75 , 5.00]
Klotz 2008 (CS21)[a]	17	102	6	101	35.9%	2.81 [1.15 , 6.83]
Mason 2013 (CS30)	1	181	0	64	2.8%	1.07 [0.04 , 25.97]
Ozono 2018 (3550-CL-0010)	7	117	5	117	22.7%	1.40 [0.46 , 4.29]
Sayyid 2017 (DEG_PRE-OP)	5	13	1	12	7.1%	4.62 [0.63 , 34.05]
Total (Wald[b])		**620**		**394**	**100.0%**	**2.15 [1.26 , 3.66]**
Total events:	50		17			

Test for overall effect: Z = 2.81 (P = 0.005)



Heterogeneity: Tau² (DL[c]) = 0.00; Chi² = 1.70, df = 4 (P = 0.79); I² = 0%

Footnotes

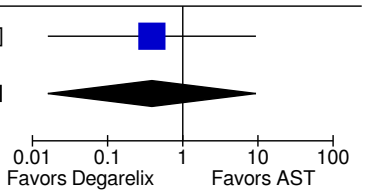
[a]Degarelix 240 mg induction dose/160 mg maintenance dose every 4 weeks s.c.
[b]CI calculated by Wald-type method.
[c]Tau² calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 15: Hepatic enzyme increase (alanine aminotransferase)

Analysis 1.16

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Axcrona 2012 (CS31)	0	84	1	98	100.0%	0.39 [0.02 , 9.41]
Total		**84**		**98**	**100.0%**	**0.39 [0.02 , 9.41]**
Total events:	0		1			

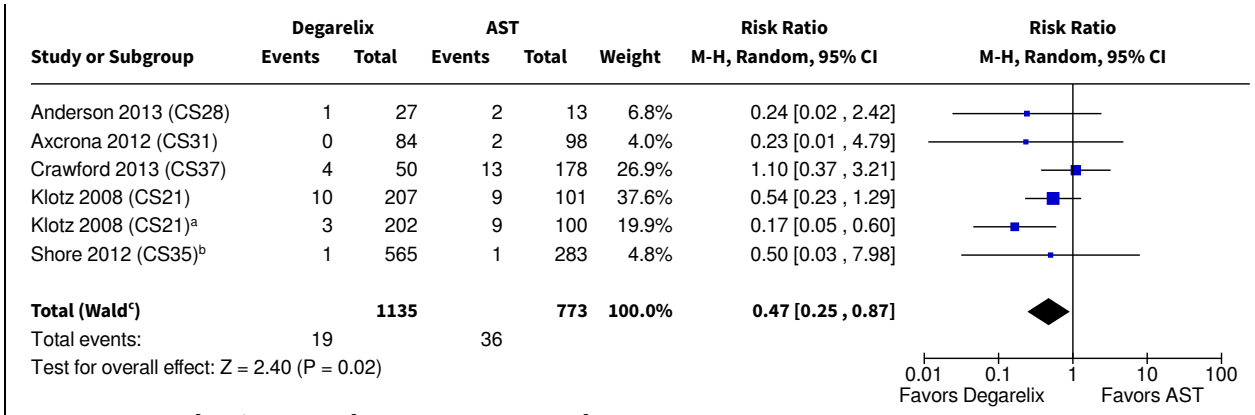
Test for overall effect: Z = 0.58 (P = 0.56)



Heterogeneity: Not applicable

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 16: Dyspnea

Analysis 1.17



Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Anderson 2013 (CS28)	1	27	2	13	6.8%	0.24 [0.02 , 2.42]
Axcrona 2012 (CS31)	0	84	2	98	4.0%	0.23 [0.01 , 4.79]
Crawford 2013 (CS37)	4	50	13	178	26.9%	1.10 [0.37 , 3.21]
Klotz 2008 (CS21)	10	207	9	101	37.6%	0.54 [0.23 , 1.29]
Klotz 2008 (CS21)[a]	3	202	9	100	19.9%	0.17 [0.05 , 0.60]
Shore 2012 (CS35)[b]	1	565	1	283	4.8%	0.50 [0.03 , 7.98]
Total (Wald[c])		**1135**		**773**	**100.0%**	**0.47 [0.25 , 0.87]**
Total events:	19		36			

Test for overall effect: Z = 2.40 (P = 0.02)

Heterogeneity: Tau² (DL[d]) = 0.07; Chi² = 5.58, df = 5 (P = 0.35); I² = 10%

Footnotes

[a]Degarelix 240 mg induction dose/160 mg maintenance dose every 4 weeks s.c.

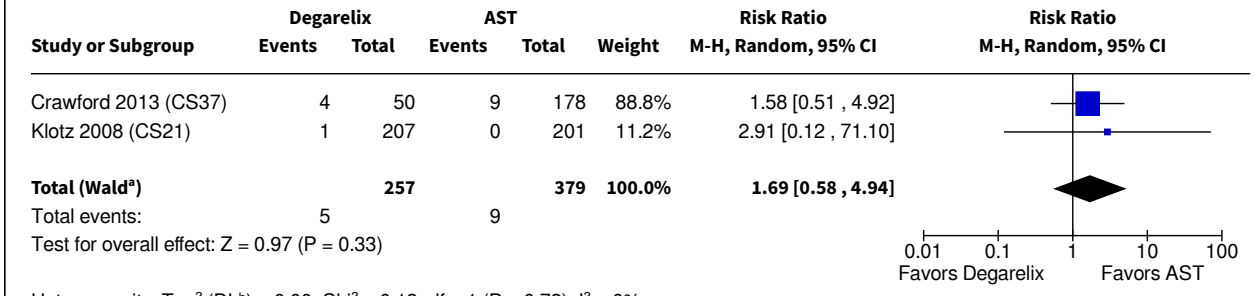
[b]Degarelix 240 mg induction dose/480 mg maintenance dose every 3 months s.c.

[c]CI calculated by Wald-type method.

[d]Tau² calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 17: Urinary tract infection

Analysis 1.18



Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Crawford 2013 (CS37)	4	50	9	178	88.8%	1.58 [0.51 , 4.92]
Klotz 2008 (CS21)	1	207	0	201	11.2%	2.91 [0.12 , 71.10]
Total (Wald[a])		**257**		**379**	**100.0%**	**1.69 [0.58 , 4.94]**
Total events:	5		9			

Test for overall effect: Z = 0.97 (P = 0.33)

Heterogeneity: Tau² (DL[b]) = 0.00; Chi² = 0.13, df = 1 (P = 0.72); I² = 0%

Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 18: Hematuria

Analysis 1.19

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Anderson 2013 (CS28)	0	27	1	13	14.3%	0.17 [0.01 , 3.83]
Axcrona 2012 (CS31)	0	84	2	98	15.3%	0.23 [0.01 , 4.79]
Klotz 2008 (CS21)	0	207	1	101	13.8%	0.16 [0.01 , 3.98]
Klotz 2008 (CS21)[a]	2	202	1	100	24.6%	0.99 [0.09 , 10.79]
Mason 2013 (CS30)	1	181	0	64	13.8%	1.07 [0.04 , 25.97]
Shore 2012 (CS35)[b]	1	565	1	283	18.3%	0.50 [0.03 , 7.98]
Total (Wald[c])		**1266**		**659**	**100.0%**	**0.43 [0.13 , 1.40]**
Total events:	4		6			

Test for overall effect: Z = 1.40 (P = 0.16)

Heterogeneity: Tau² (DL[d]) = 0.00; Chi² = 1.66, df = 5 (P = 0.89); I² = 0%

Footnotes

[a]Degarelix 240 mg induction dose/160 mg maintenance dose every 4 weeks s.c.

[b]Degarelix 240 mg induction dose/480 mg maintenance dose every 3 months s.c.

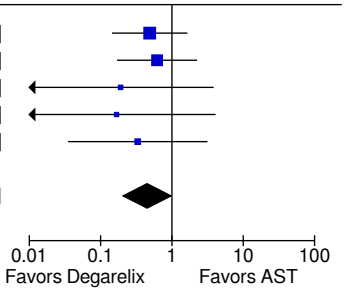
[c]CI calculated by Wald-type method.

[d]Tau² calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 19: Urinary retention

Analysis 1.20

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Klotz 2008 (CS21)	5	207	5	101	40.2%	0.49 [0.14 , 1.65]
Klotz 2008 (CS21)[a]	5	202	4	100	35.6%	0.62 [0.17 , 2.25]
Margel 2019 (0102-15-RMC)	0	41	2	39	6.6%	0.19 [0.01 , 3.85]
Shore 2012 (CS35)[b]	0	565	1	283	5.8%	0.17 [0.01 , 4.09]
Xie 2016 (PANDA)	1	142	3	141	11.7%	0.33 [0.03 , 3.14]
Total (Wald[c])		**1157**		**664**	**100.0%**	**0.45 [0.21 , 0.97]**
Total events:	11		15			
Test for overall effect: Z = 2.04 (P = 0.04)						



Heterogeneity: Tau² (DL[d]) = 0.00; Chi² = 1.02, df = 4 (P = 0.91); I² = 0%

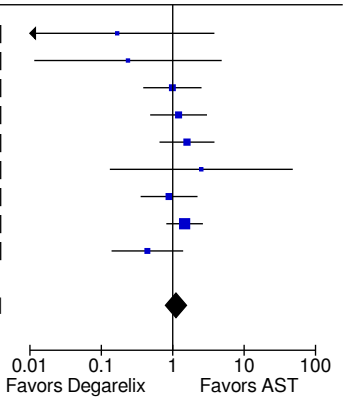
Footnotes

[a]Degarelix 240 mg induction dose/160 mg maintenance dose every 4 weeks s.c.
[b]Degarelix 240 mg induction dose/480 mg maintenance dose every 3 months s.c.
[c]CI calculated by Wald-type method.
[d]Tau² calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 20: Mortality during study conduction (post hoc)

Analysis 1.21

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Anderson 2013 (CS28)	0	27	1	13	1.2%	0.17 [0.01 , 3.83]
Axcrona 2012 (CS31)	0	82	2	97	1.3%	0.24 [0.01 , 4.85]
Crawford 2013 (CS37)	5	50	18	178	13.0%	0.99 [0.39 , 2.53]
Klotz 2008 (CS21)	15	207	6	100	13.6%	1.21 [0.48 , 3.02]
Klotz 2008 (CS21)[a]	19	202	6	101	14.6%	1.58 [0.65 , 3.84]
Mason 2013 (CS30)	3	180	0	64	1.3%	2.51 [0.13 , 48.01]
Ozono 2018 (3550-CL-0010)	8	117	9	117	13.6%	0.89 [0.36 , 2.22]
Shore 2012 (CS35)[b]	41	565	14	283	32.9%	1.47 [0.81 , 2.65]
Xie 2016 (PANDA)	4	142	9	141	8.6%	0.44 [0.14 , 1.40]
Total (Wald[c])		**1572**		**1094**	**100.0%**	**1.11 [0.79 , 1.56]**
Total events:	95		65			
Test for overall effect: Z = 0.60 (P = 0.55)						



Heterogeneity: Tau² (DL[d]) = 0.00; Chi² = 6.95, df = 8 (P = 0.54); I² = 0%

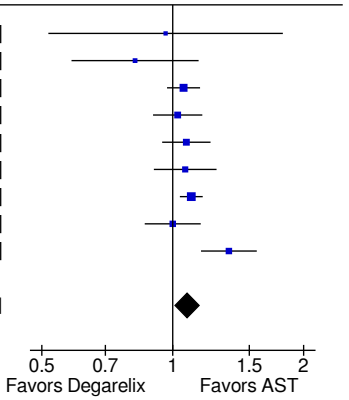
Footnotes

[a]Degarelix 240 mg induction dose/160 mg maintenance dose every 4 weeks s.c.
[b]Degarelix 240 mg induction dose/480 mg maintenance dose every 3 months s.c.
[c]CI calculated by Wald-type method.
[d]Tau² calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 21: Discontinuation due to adverse events (post hoc)

Analysis 1.22

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Anderson 2013 (CS28)	14	27	7	13	1.0%	0.96 [0.52 , 1.79]
Axcrona 2012 (CS31)	33	84	47	98	3.1%	0.82 [0.59 , 1.15]
Crawford 2013 (CS37)	47	50	158	178	17.8%	1.06 [0.97 , 1.16]
Klotz 2008 (CS21)	162	207	77	101	12.5%	1.03 [0.90 , 1.17]
Klotz 2008 (CS21)[a]	165	202	76	100	12.8%	1.07 [0.95 , 1.22]
Mason 2013 (CS30)	142	181	47	64	9.4%	1.07 [0.90 , 1.26]
Ozono 2018 (3550-CL-0010)[b]	117	117	106	117	21.6%	1.10 [1.04 , 1.17]
Sayyid 2017 (DEG_PRE-OP)	13	13	12	12	10.9%	1.00 [0.86 , 1.16]
Shore 2012 (CS35)[b]	336	565	125	283	10.9%	1.35 [1.16 , 1.56]
Total (Wald[c])		**1446**		**966**	**100.0%**	**1.08 [1.01 , 1.15]**
Total events:	1029		655			
Test for overall effect: Z = 2.35 (P = 0.02)						



Heterogeneity: Tau² (DL[d]) = 0.00; Chi² = 15.56, df = 8 (P = 0.05); I² = 49%

Footnotes

[a]Degarelix 240 mg induction dose/160 mg maintenance dose every 4 weeks s.c.

[b]Degarelix 240 mg induction dose/480 mg maintenance dose every 3 months s.c.

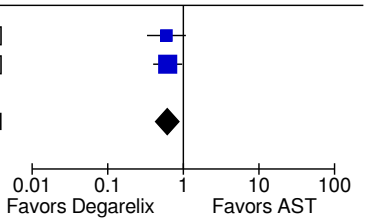
[c]CI calculated by Wald-type method.

[d]Tau² calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 22: Total non-serious adverse events (post hoc)

Analysis 1.23

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
Klotz 2008 (CS21)	16	207	26	201	35.8%	0.60 [0.33 , 1.08]
Xie 2016 (PANDA)	25	142	40	141	64.2%	0.62 [0.40 , 0.97]
Total (Wald[a])		**349**		**342**	**100.0%**	**0.61 [0.43 , 0.87]**
Total events:	41		66			
Test for overall effect: Z = 2.72 (P = 0.007)						



Heterogeneity: Tau² (DL[b]) = 0.00; Chi² = 0.01, df = 1 (P = 0.92); I² = 0%

Footnotes

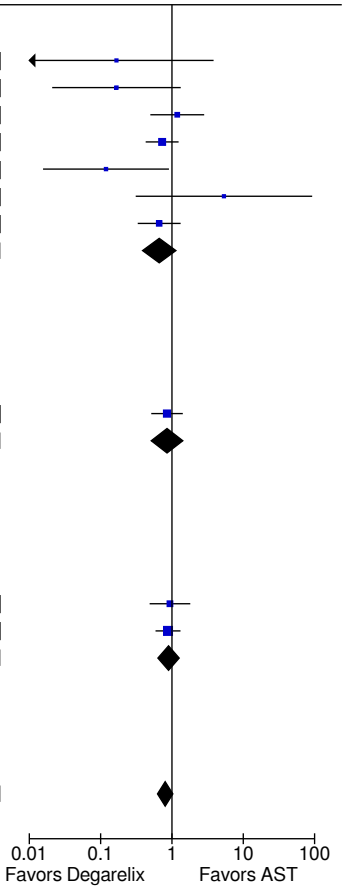
[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Comparison 1: Degarelix versus standard androgen suppression therapy, Outcome 23: Biochemical progression

Analysis 2.1

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
2.1.1 Degarelix 240 mg/80 mg						
Anderson 2013 (CS28)	0	27	1	13	0.6%	0.17 [0.01 , 3.83]
Axcrona 2012 (CS31)	1	84	7	98	1.4%	0.17 [0.02 , 1.33]
Crawford 2013 (CS37)	6	50	18	178	7.5%	1.19 [0.50 , 2.83]
Klotz 2008 (CS21)	21	207	28	201	17.8%	0.73 [0.43 , 1.24]
Margel 2019 (0102-15-RMC)[a]	1	41	8	39	1.5%	0.12 [0.02 , 0.91]
Mason 2013 (CS30)	7	181	0	64	0.8%	5.36 [0.31 , 92.49]
Xie 2016 (PANDA)	12	142	18	141	11.4%	0.66 [0.33 , 1.32]
Subtotal (Wald[b])		**732**		**734**	**41.0%**	**0.66 [0.39 , 1.14]**
Total events:	48		80			
Test for overall effect: Z = 1.50 (P = 0.13)						
Heterogeneity: Tau² (DL[c]) = 0.15; Chi² = 9.05, df = 6 (P = 0.17); I² = 34%						
2.1.2 Degarelix 240 mg/160 mg						
Klotz 2008 (CS21)	24	202	28	201	19.1%	0.85 [0.51 , 1.42]
Subtotal		**202**		**201**	**19.1%**	**0.85 [0.51 , 1.42]**
Total events:	24		28			
Test for overall effect: Z = 0.61 (P = 0.54)						
Heterogeneity: Not applicable						
2.1.3 Degarelix 240 mg/480 mg						
Ozono 2018 (3550-CL-0010)	15	117	16	117	12.5%	0.94 [0.49 , 1.81]
Shore 2012 (CS35)	58	565	33	283	27.4%	0.88 [0.59 , 1.32]
Subtotal (Wald[b])		**682**		**400**	**39.9%**	**0.90 [0.64 , 1.26]**
Total events:	73		49			
Test for overall effect: Z = 0.63 (P = 0.53)						
Heterogeneity: Tau² (DL[c]) = 0.00; Chi² = 0.03, df = 1 (P = 0.87); I² = 0%						
Total (Wald[b])		**1616**		**1335**	**100.0%**	**0.80 [0.63 , 1.03]**
Total events:	145		157			
Test for overall effect: Z = 1.73 (P = 0.08)						
Test for subgroup differences: Chi² = 0.87, df = 2 (P = 0.65), I² = 0%						
Heterogeneity: Tau² (DL[c]) = 0.02; Chi² = 9.99, df = 9 (P = 0.35); I² = 10%						



Footnotes

[a]Major cardiovascular and cerebrovascular events

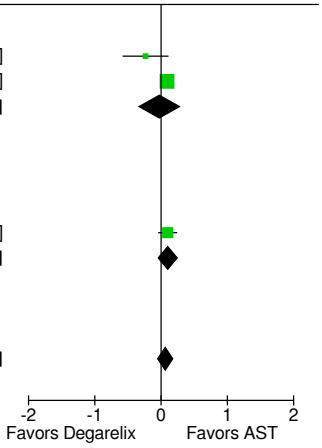
[b]CI calculated by Wald-type method.

[c]Tau² calculated by DerSimonian and Laird method.

Comparison 2: Degarelix versus androgen suppression therapy (GnRH agonists or maximum androgen suppression therapy): subgroup analysis based on different doses, Outcome 1: Serious adverse events

Analysis 2.2

Study or Subgroup	Degarelix Mean	Degarelix SD	Degarelix Total	AST Mean	AST SD	AST Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.2.1 Degarelix 240 mg/80 mg								
Crawford 2013 (CS37)[a]	-4.28	11.34	41	-1.65	11.15	150	9.6%	-0.23 [-0.58 , 0.11]
Klotz 2008 (CS21)[b]	0.871	0.11	935	0.861	0.113	914	54.4%	0.09 [-0.00 , 0.18]
Subtotal (Wald[c])			**976**			**1064**	**64.0%**	**-0.03 [-0.33 , 0.28]**
Test for overall effect: Z = 0.18 (P = 0.86)								
Heterogeneity: Tau² (DL[d]) = 0.04; Chi² = 3.14, df = 1 (P = 0.08); I² = 68%								
2.2.2 Degarelix 240 mg/480 mg								
Shore 2012 (CS35)[e]	0.18	10.9	565	-0.87	9.76	282	36.0%	0.10 [-0.04 , 0.24]
Subtotal			**565**			**282**	**36.0%**	**0.10 [-0.04 , 0.24]**
Test for overall effect: Z = 1.37 (P = 0.17)								
Heterogeneity: Not applicable								
Total (Wald[c])			**1541**			**1346**	**100.0%**	**0.06 [-0.05 , 0.18]**
Test for overall effect: Z = 1.07 (P = 0.28)								
Test for subgroup differences: Chi² = 0.55, df = 1 (P = 0.46), I² = 0%								
Heterogeneity: Tau² (DL[d]) = 0.00; Chi² = 3.27, df = 2 (P = 0.19); I² = 39%								



Footnotes

[a]Functional Assessment of Cancer Therapy – Prostate (FACT-P)

[b]EORTC QLQ-C30 mapped to EORTC-8D

[c]CI calculated by Wald-type method.

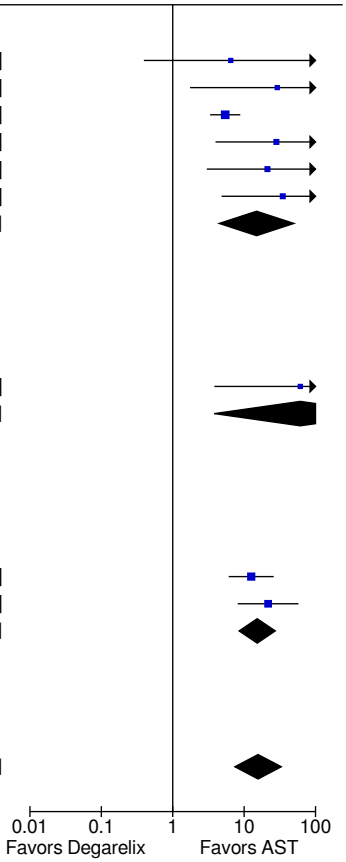
[d]Tau² calculated by DerSimonian and Laird method.

[e]Short-Form-36 (SF-36)

Comparison 2: Degarelix versus androgen suppression therapy (GnRH agonists or maximum androgen suppression therapy): subgroup analysis based on different doses, Outcome 2: Quality of life

Analysis 2.3

Study or Subgroup	Degarelix Events	Degarelix Total	AST Events	AST Total	Weight	Risk Ratio M-H, Random, 95% CI
2.3.1 Degarelix 240 mg/80 mg						
Anderson 2013 (CS28)	6	27	0	13	5.5%	6.50 [0.39 , 107.32]
Axcrona 2012 (CS31)	12	84	0	98	5.4%	29.12 [1.75 , 484.51]
Crawford 2013 (CS37)	29	50	19	178	21.1%	5.43 [3.34 , 8.83]
Klotz 2008 (CS21)	58	207	1	101	9.0%	28.30 [3.98 , 201.39]
Mason 2013 (CS30)	60	181	1	64	9.0%	21.22 [3.00 , 149.95]
Xie 2016 (PANDA)	35	142	1	141	8.9%	34.75 [4.83 , 250.22]
Subtotal (Wald[a])		**691**		**595**	**58.8%**	**14.94 [4.48 , 49.81]**
Total events:	200		22			
Test for overall effect: Z = 4.40 (P < 0.0001)						
Heterogeneity: Tau² (DL[b]) = 1.29; Chi² = 13.99, df = 5 (P = 0.02); I² = 64%						
2.3.2 Degarelix 240 mg/160 mg						
Klotz 2008 (CS21)[c]	61	202	0	100	5.6%	61.20 [3.82 , 979.36]
Subtotal		**202**		**100**	**5.6%**	**61.20 [3.82 , 979.36]**
Total events:	61		0			
Test for overall effect: Z = 2.91 (P = 0.004)						
Heterogeneity: Not applicable						
2.3.3 Degarelix 240 mg/480 mg						
Ozono 2018 (3550-CL-0010)[d]	88	117	7	117	19.0%	12.57 [6.08 , 25.98]
Shore 2012 (CS35)[d]	173	565	4	283	16.6%	21.66 [8.12 , 57.77]
Subtotal (Wald[a])		**682**		**400**	**35.6%**	**15.24 [8.50 , 27.31]**
Total events:	261		11			
Test for overall effect: Z = 9.15 (P < 0.00001)						
Heterogeneity: Tau² (DL[b]) = 0.00; Chi² = 0.84, df = 1 (P = 0.36); I² = 0%						
Total (Wald[a])		**1575**		**1095**	**100.0%**	**15.68 [7.41 , 33.17]**
Total events:	522		33			
Test for overall effect: Z = 7.20 (P < 0.00001)						
Test for subgroup differences: Chi² = 0.94, df = 2 (P = 0.63), I² = 0%						
Heterogeneity: Tau² (DL[b]) = 0.63; Chi² = 21.56, df = 8 (P = 0.006); I² = 63%						



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

[c]Degarelix 240 mg induction dose/160 mg maintenance dose every 4 weeks s.c.

[d]Degarelix 240 mg induction dose/480 mg maintenance dose every 3 months s.c.

Comparison 2: Degarelix versus androgen suppression therapy (GnRH agonists or maximum androgen suppression therapy): subgroup analysis based on different doses, Outcome 3: Injection site pain