
**Efficacy and safety profile of
intravitreal dexamethasone implant
versus antivascular endothelial growth
factor treatment: a systematic review
and meta-analysis**

(Supplemental Materials)

Supplemental Material

Supplemental Material 1. Search strategy

Supplemental Material 2. Funnel plot of BCVA change

Supplemental Material 3. Funnel plot of CRT change

Supplemental Material 4. Funnel plot of IOP change

Supplemental Material 5. Funnel plot of SAE occurrence

Supplemental Material 6. BCVA change – subgroup analysis of nonresistant DME patients

Supplemental Material 7. BCVA change – meta-regression

Supplemental Material 8. CRT change – subgroup analysis of nonresistant DME patients

Supplemental Material 9. CRT change – meta-regression

Supplemental Material 10. Forest plot of IOP change and subgroup analysis of nonresistant DME patients

Supplemental Material 11. IOP change – meta-regression

Supplemental Material 12. Severe ocular adverse events and subgroup analysis of nonresistant DME patients

Supplemental Material 13. Risk of bias assessment (ROB)

Supplemental Material 14. Risk of bias assessment ROBINS-1 (BCVA)

Supplemental Material 15. Subgroup analysis - type of Anti-vegf - BCVA change

Supplemental Material 16. Subgroup analysis - type of Anti-vegf - CRT decrease

Supplemental Material 17. Subgroup analysis - study design - BCVA change

Supplemental Material 18. Subgroup analysis - study design - CRT decrease

Supplemental Material 19. Summary of OCT biomarker

Supplemental Material 1
Search strategy

Supplemental Material 1

Search strategy

Primary search steps:

- #1 anti- vascular endothelial growth factors
- #2 anti-VEGF
- #3 ranibizumab
- #4 lucentis
- #5 aflibercept
- #6 eylea
- #7 bevacizumab
- #8 avastin
- #9 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
- #10 ozurdex
- #11 intravitreal dexamethasone implant
- #12 dexamethasone
- #13 #10 OR #11 OR #12
- #14 diabetic retinopathy
- #15 diabetic macular edema
- #16 DME
- #17 DMO
- #18 cystoid macular edema
- #19 CME
- #20 #16 OR #17 OR #18 OR #19
- #21 #9 AND #13 AND #20

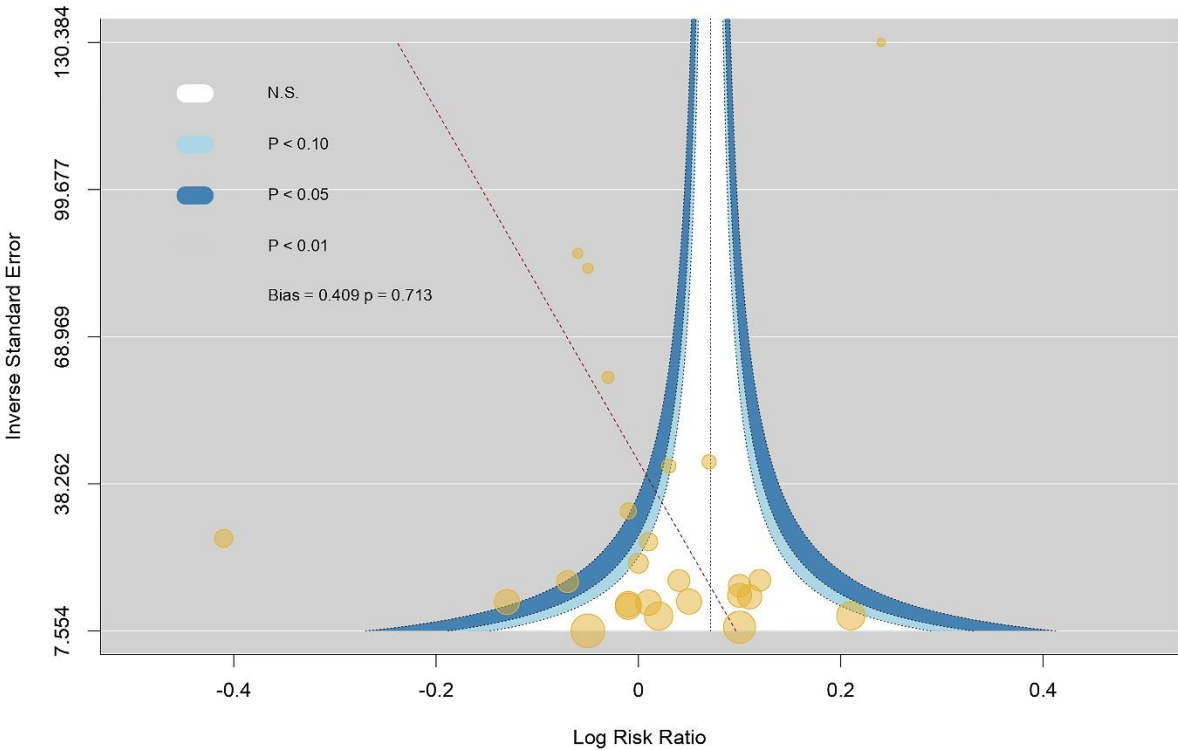
Final syntax in PubMed (an example):

(((((((((anti- vascular endothelial growth factors) OR (anti-VEGF)) OR (ranibizumab)) OR (lucentis)) OR (aflibercept)) OR (eylea)) OR (bevacizumab)) OR (avastin)) AND (((ozurdex) OR (intravitreal dexamethasone implant)) OR (dexamethasone))) AND (((DME) OR (DMO)) OR (cystoid macular edema)) OR (CME)) Sort by: Publication Date

Supplemental Material 2
Funnel plot of BCVA change

Supplemental Material 2

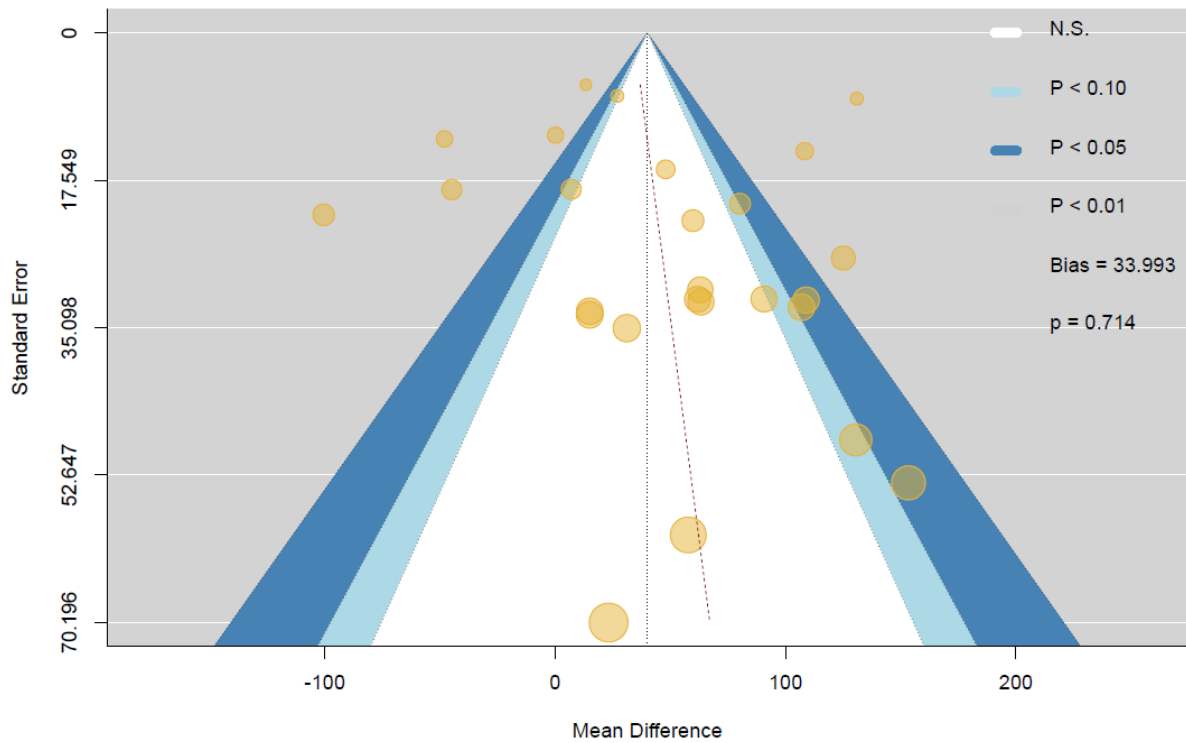
Funnel plot of BCVA change



Supplemental Material 3
Funnel plot of CRT change

Supplemental Material 3

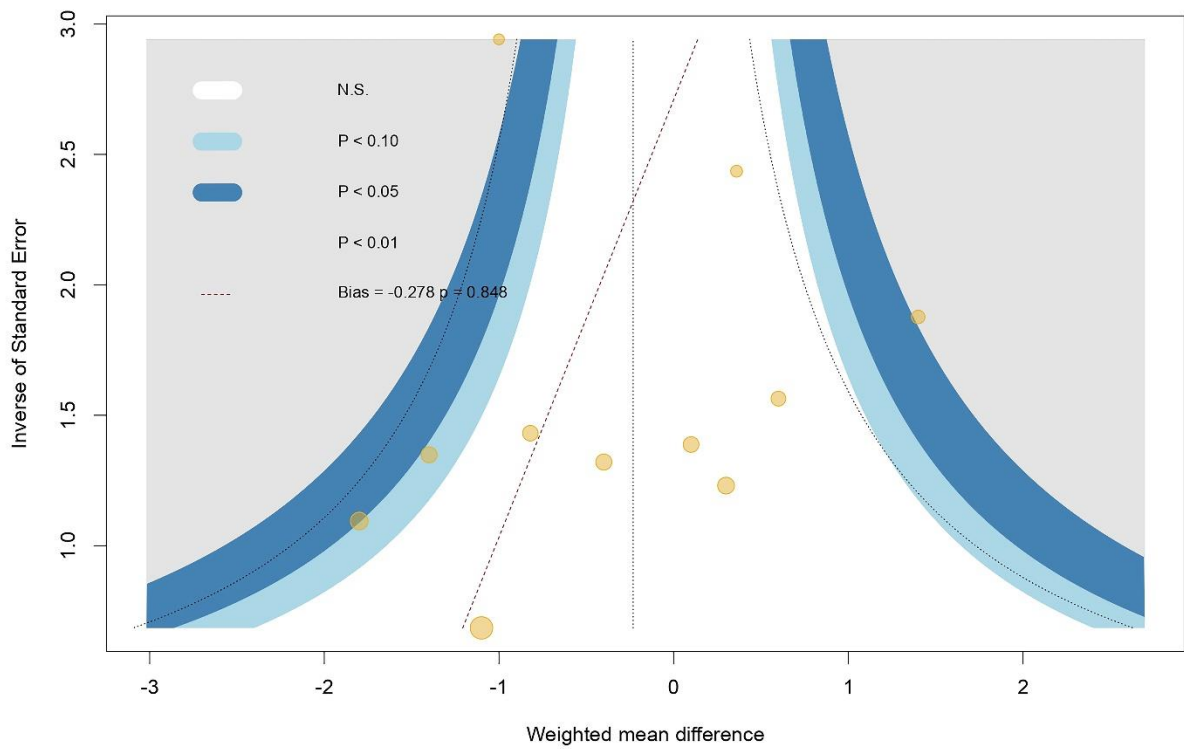
Funnel plot of CRT change



Supplemental Material 4
Funnel plot of IOP change

Supplemental Material 4

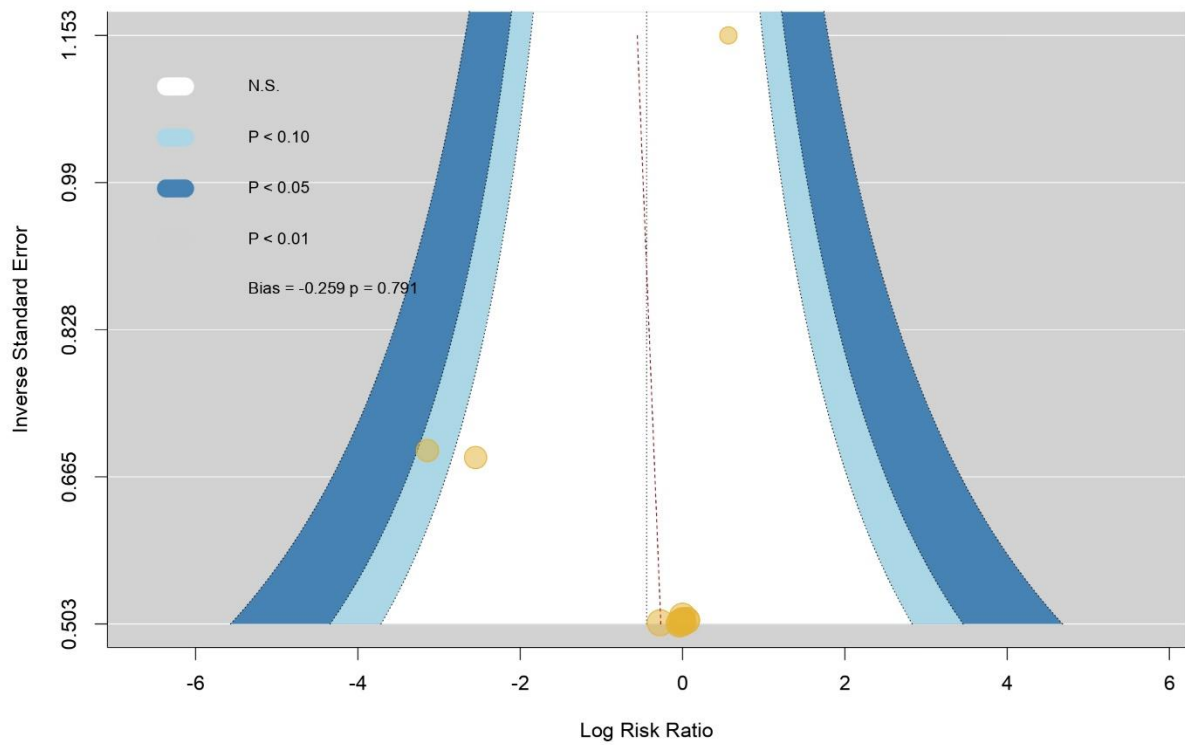
Funnel plot of IOP change



Supplemental Material 5
Funnel plot of SAE occurrence

Supplemental Material 5

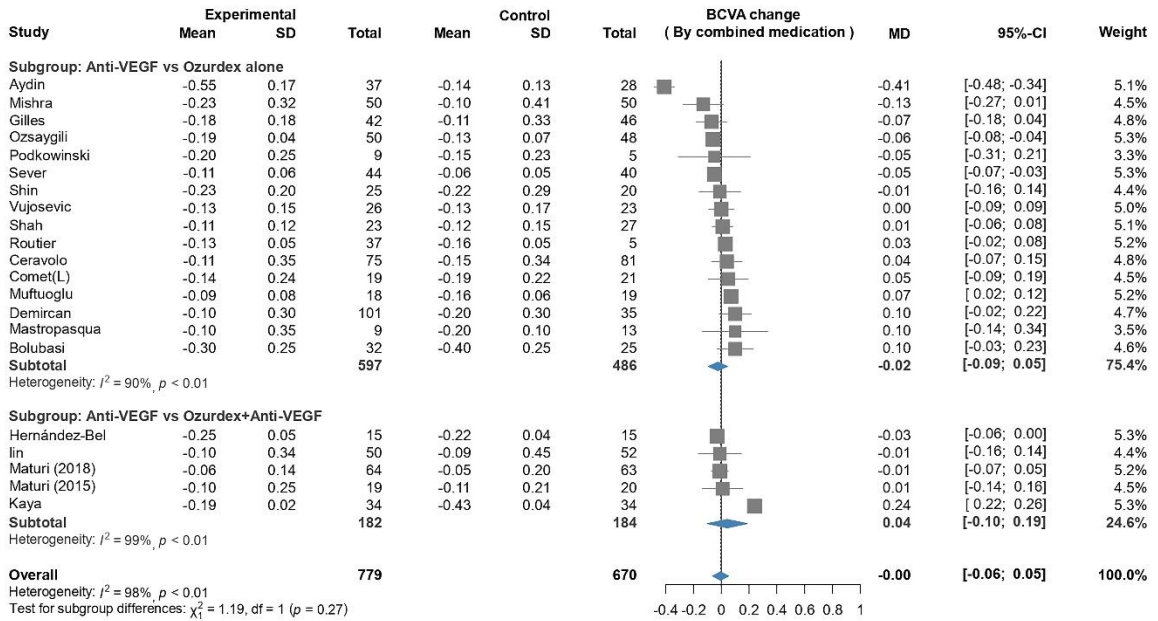
Funnel plot of SAE occurrence



Supplemental Material 6
BCVA change –
subgroup analysis of nonresistant DME patients

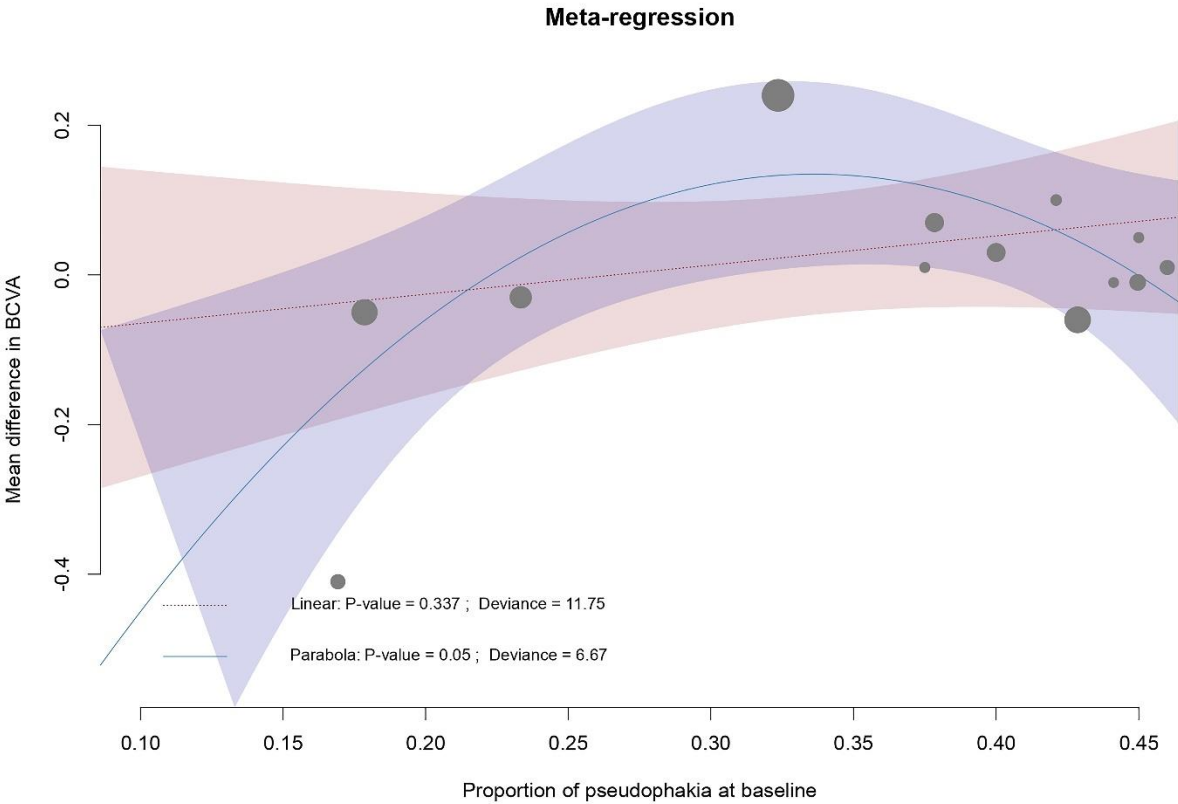
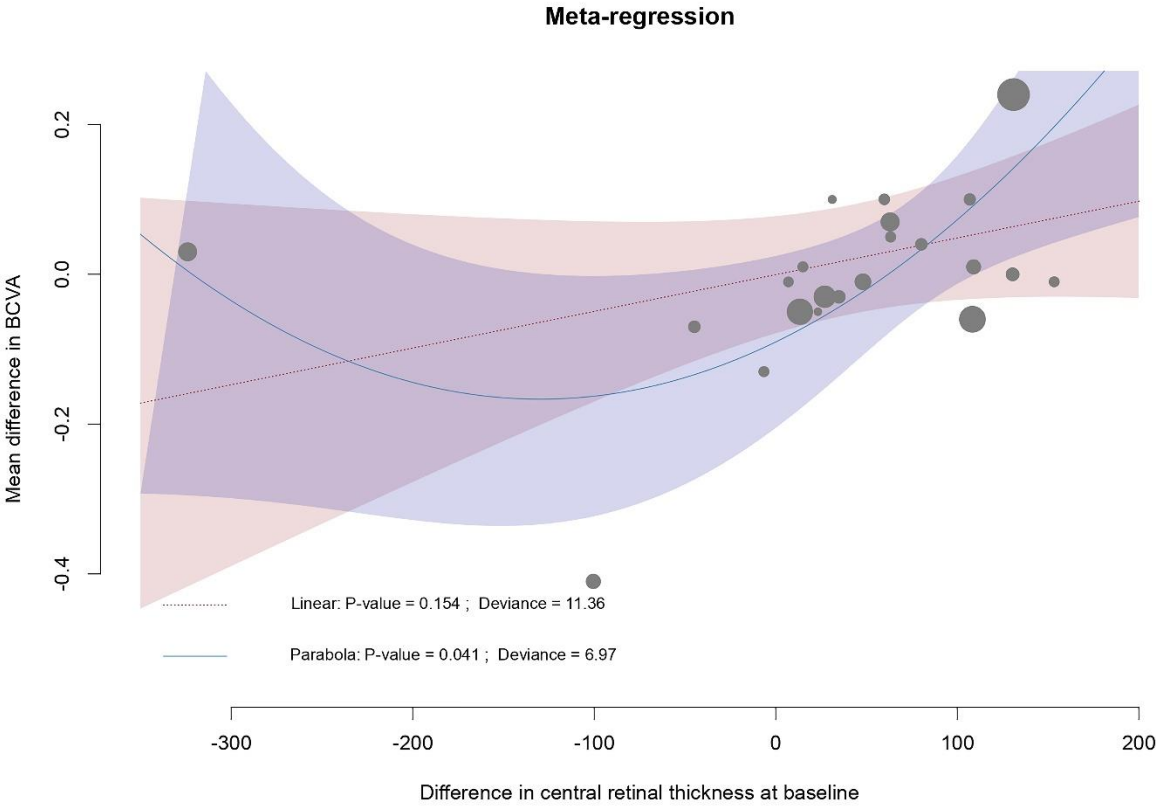
Supplemental Material 6

BCVA change – subgroup analysis of nonresistant DME patients



Supplemental Material 7
BCVA change –
meta-regression

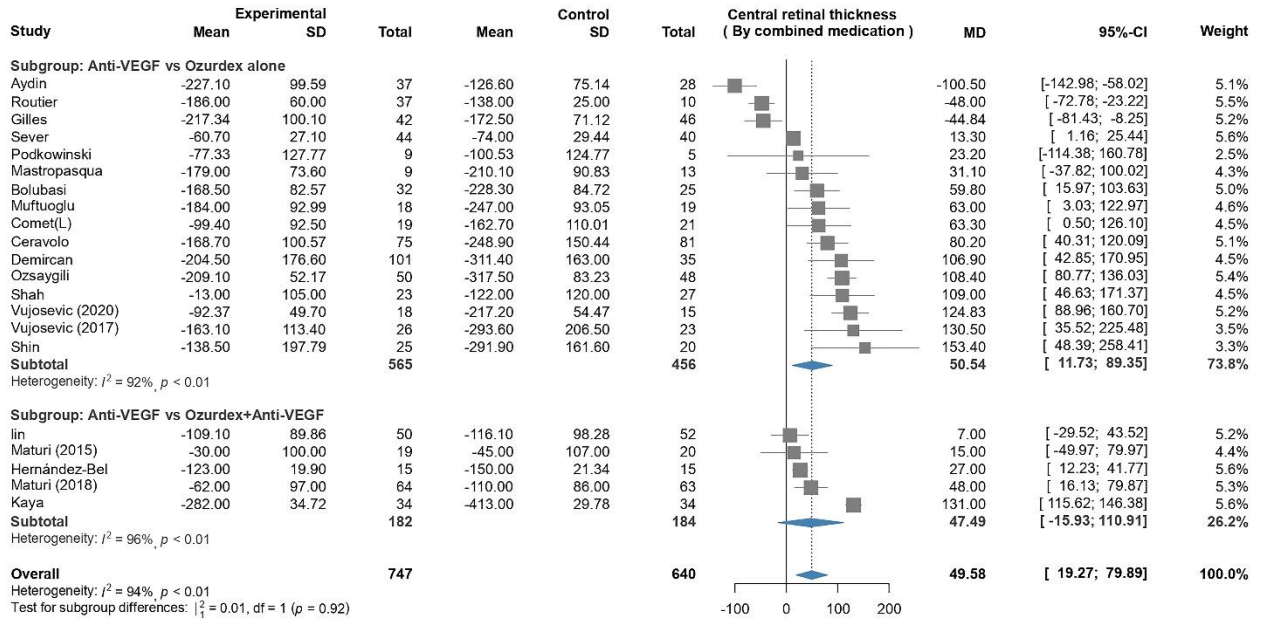
Supplemental Material 7
BCVA change - meta-regression



Supplemental Material 8
CRT change –
subgroup analysis of nonresistant DME patients

Supplemental Material 8

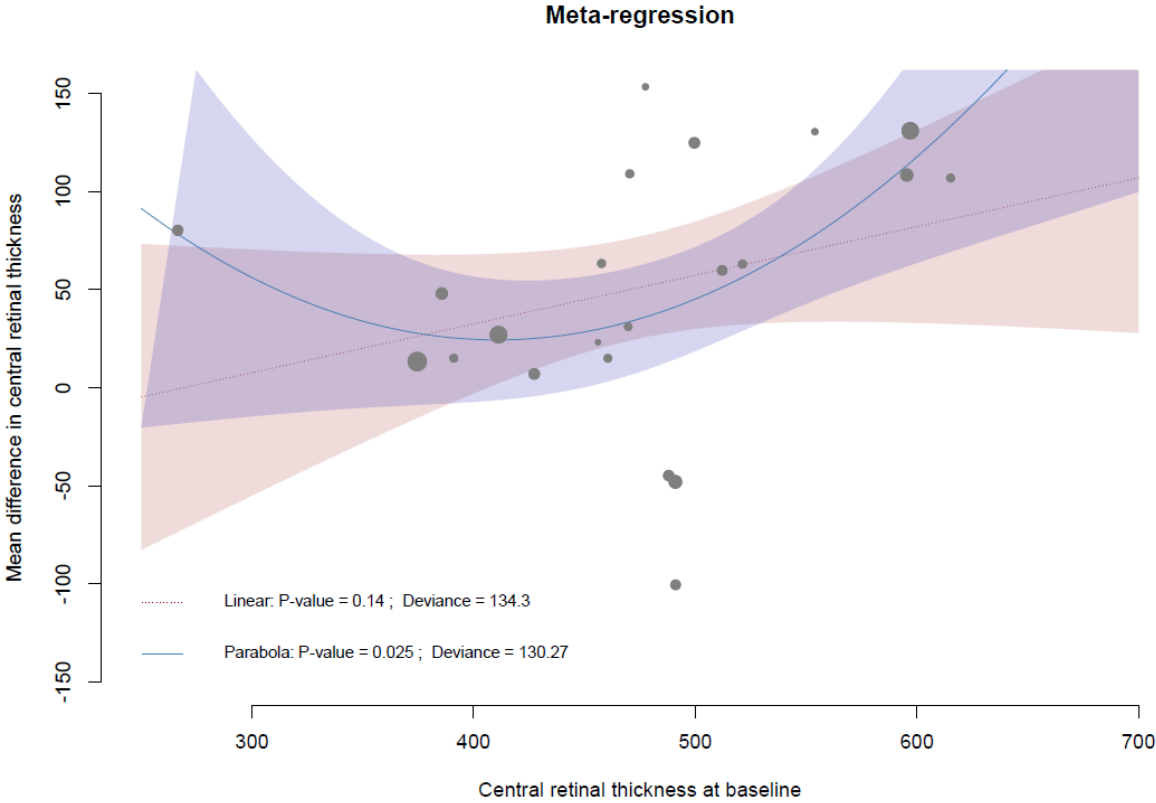
CRT change – subgroup analysis of nonresistant DME patients



Supplemental Material 9
CRT change –
meta-regression

Supplemental Material 9

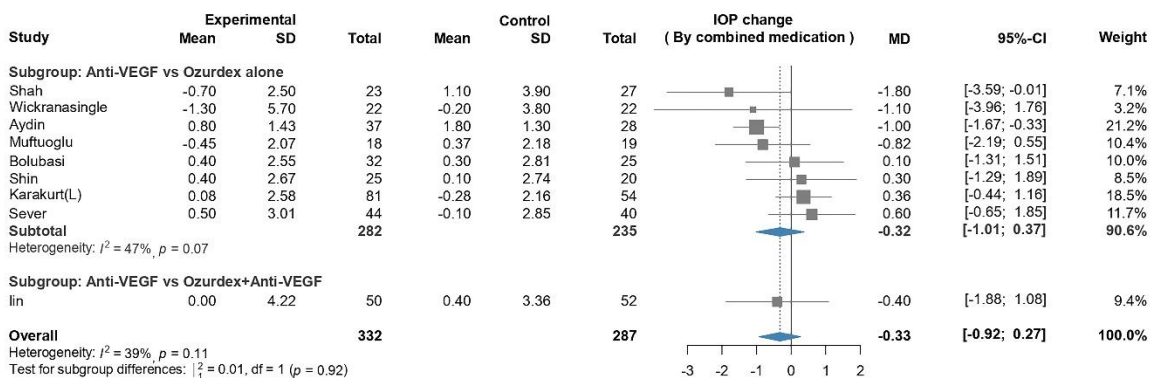
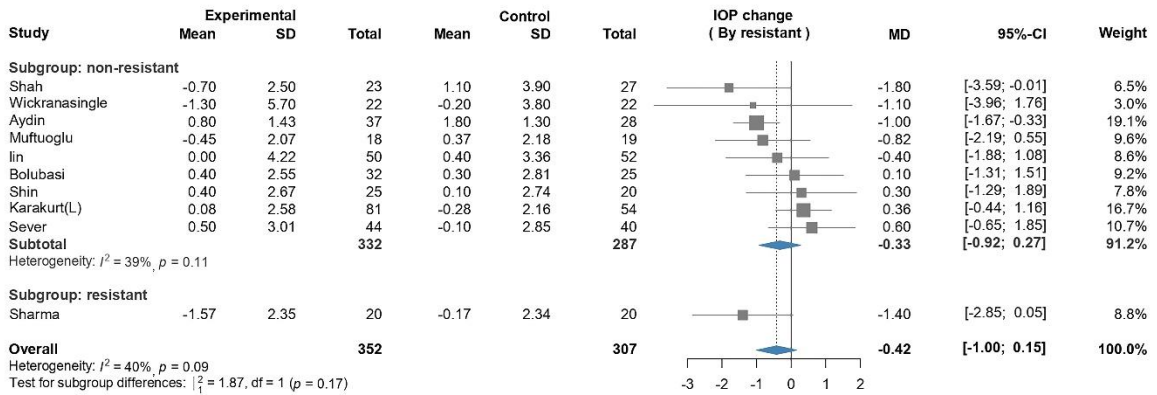
CRT change – meta-regression



Supplemental Material 10
Forest plot of of IOP change and
subgroup analysis of nonresistant DME patients

Supplemental Material 10

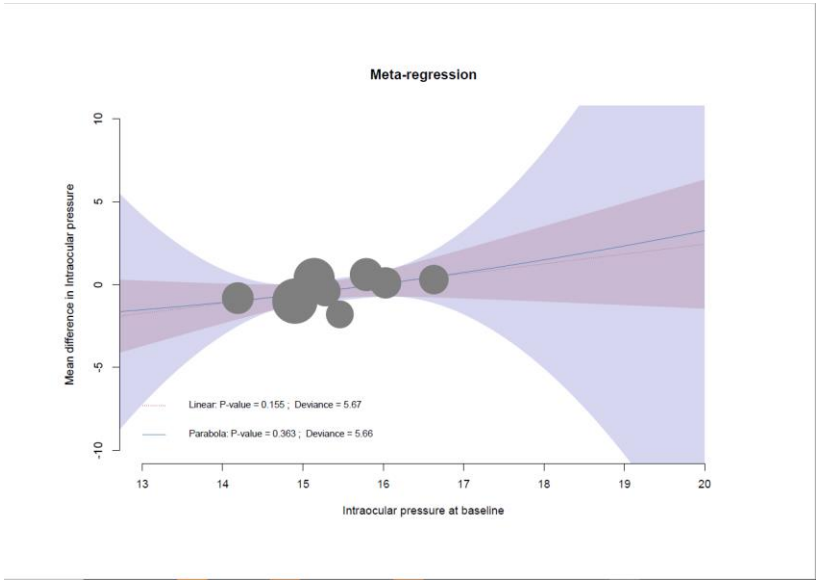
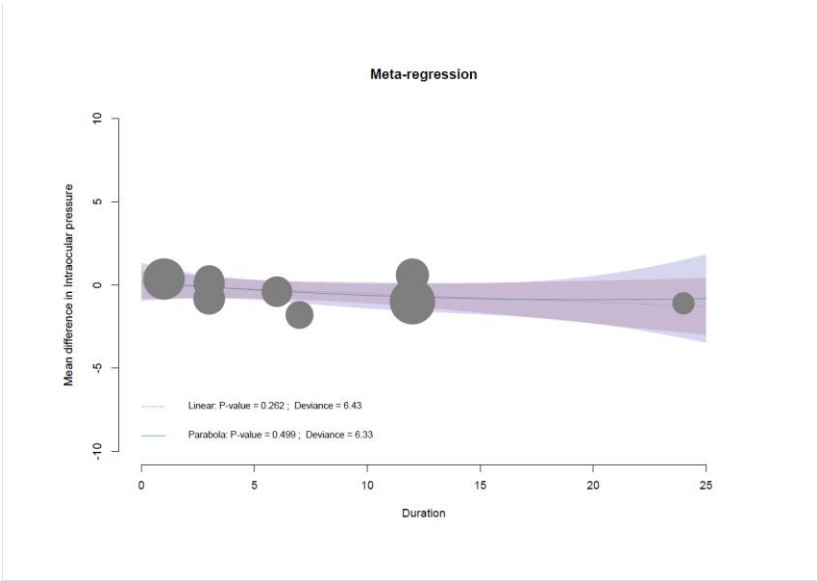
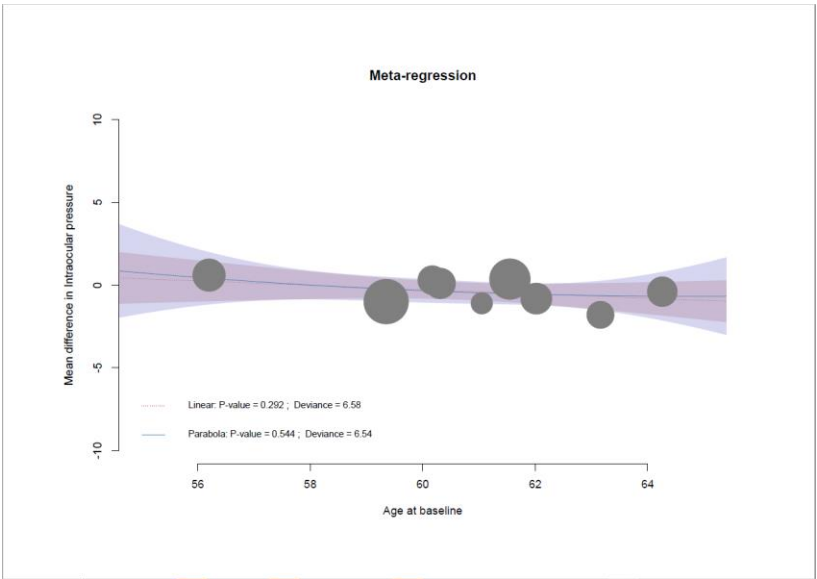
Forest plot of IOP change and subgroup analysis of nonresistant DME patients



Supplemental Material 11
IOP change – meta-regression

Supplemental Material 11

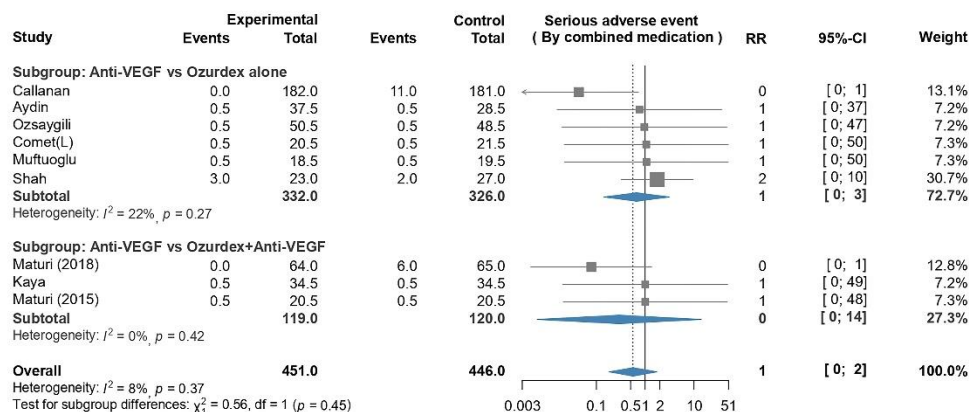
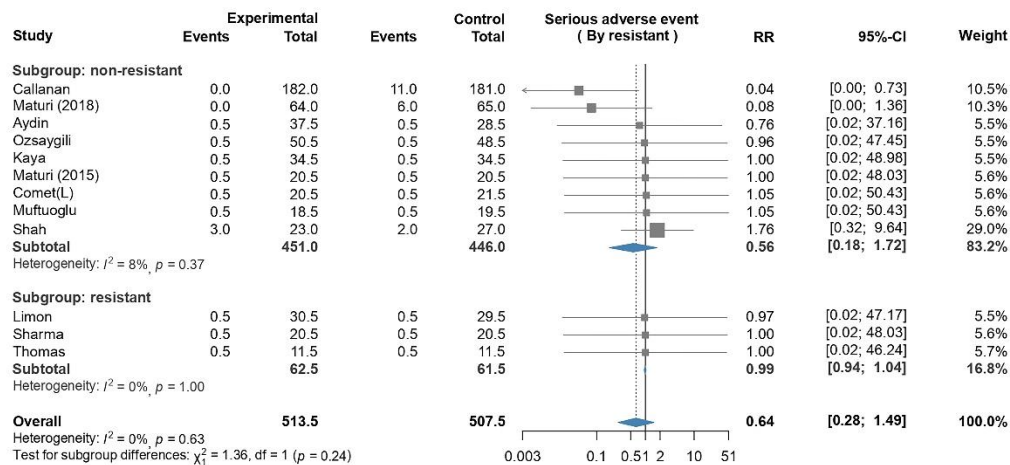
IOP change – meta-regression



Supplemental Material 12
**Severe ocular adverse events and
subgroup analysis of nonresistant DME patients**

Supplemental Material 12

Severe ocular adverse events and subgroup analysis of nonresistant DME patients



Supplemental Material 13
Risk of bias assessment
ROB

Supplemental Material 13

Risk of bias assessment (ROB)

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Callanan 2017	+	+	-	+	+	-	○
Kaya 2021	○	○	-	○	+	+	○
Maturi 2015	○	○	○	○	+	+	○
Maturi 2018	+	+	-	+	+	+	+
Mishira 2021	○	○	○	○	+	+	○
Ozsaygili 2020	+	○	-	+	+	+	○
Podkowinski 2019	○	○	○	○	-	+	○
shah 2016	+	+	○	○	+	+	○
Sharma 2019	+	○	-	-	○	+	○

Supplemental Material 14
Risk of bias assessment
ROBINS-1 (BCVA)

Supplemental Material 14

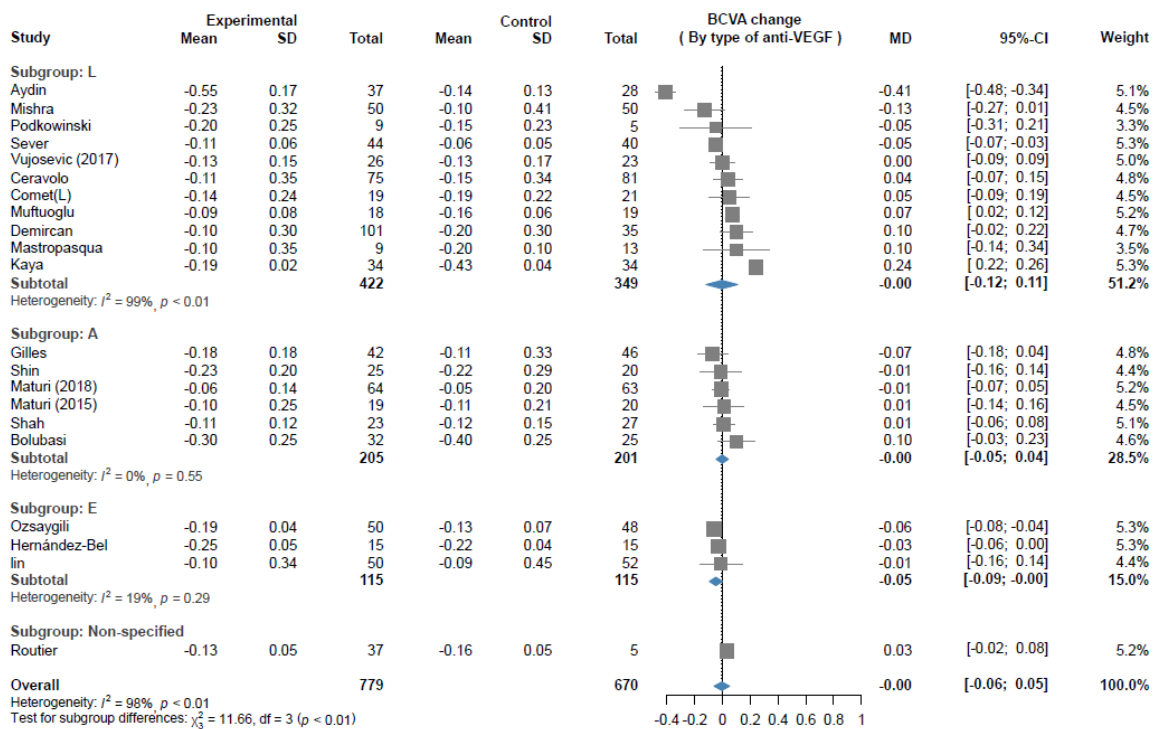
Risk of bias assessment ROBINS-1 (BCVA)

Study	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall Bias
AKSOY 2020	Serious	Low	Low	NI	Low	Moderate	Moderate	Serious
Aydin 2020	Low	Low	Low	NI	Low	Moderate	Low	Moderate
Bolubasi 2019	Serious	Low	Low	NI	Low	Moderate	Low	Serious
Busch 2019	Moderate	Low	Low	NI	Low	Low	Low	Moderate
Ceravolo 2020	Low	Low	Low	NI	Low	Moderate	Low	Moderate
Comet 2020	Low	Low	Low	Moderate	Low	Moderate	Low	Moderate
Demircan 2018	Serious	Low	Low	NI	Low	Moderate	Low	Serious
Hernández-Bel 2019	Low	Low	Low	NI	Low	Moderate	Low	Moderate
Limon 2021	Low	Low	Low	Low	Low	Moderate	Low	Moderate
Lin 2021	Serious	Low	Low	NI	Low	Moderate	Low	Serious
Mastropasqua 2019	Low	Low	Low	NI	Moderate	Moderate	Low	Moderate
Muftuogluet 2021	Low	Low	Low	Low	Low	Moderate	Low	Moderate
Routier 2021	Serious	Low	Low	NI	Low	Low	Low	Serious
Rijbsam 2021	Serious	Low	Low	NI	Low	Low	Low	Serious
Sever 2017	Serious	Low	Low	NI	Low	Moderate	Low	Serious
Shin 2017	Serious	Low	Low	NI	Moderate	Low	Low	Serious
Thomas 2016	Low	Low	Low	NI	Low	Moderate	Low	Moderate
Vujosevic 2017	Serious	Low	Low	Low	Low	Moderate	Low	Serious

Supplemental Material 15
Subgroup analysis
type of Anti-vegf
BCVA change

Supplemental Material 15

Subgroup analysis type of Anti-vegf BCVA change



*

Subgroup L= Ranibizumab (Lucentis) group

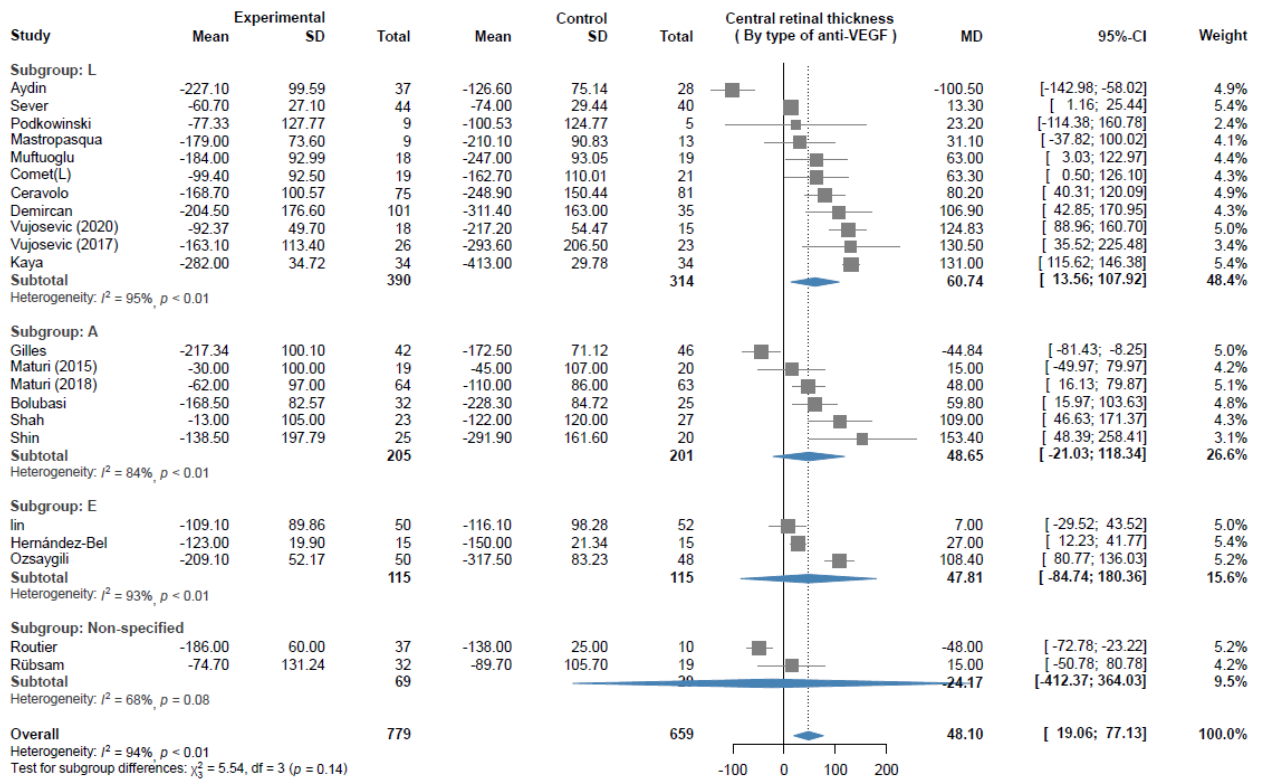
Subgroup A= Bevacizumab (Avastin) group

Subgroup E= Aflibercept (Eylea) group

Supplemental Material 16
Subgroup analysis
type of Anti-vegf
CRT decrease

Supplemental Material 16

Subgroup analysis type of Anti-vegf CRT decrease



Subgroup L= Ranibizumab (Lucentis) group

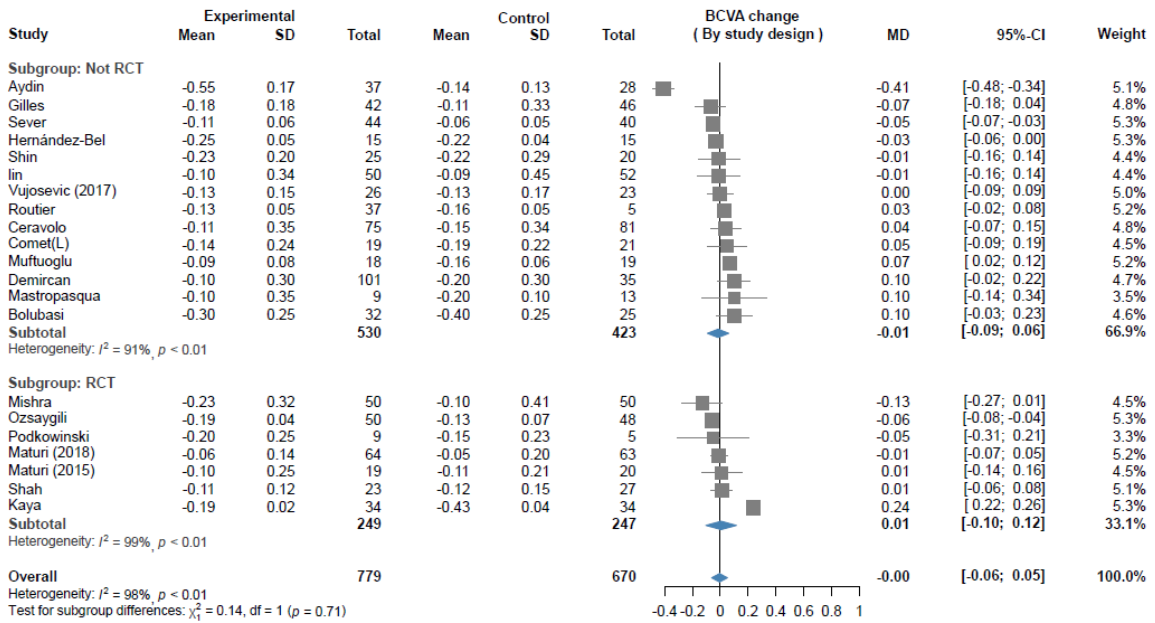
Subgroup A= Bevacizumab (Avastin) group

Subgroup E= Aflibercept (Eylea) group

Supplemental Material 17
Subgroup analysis
study design
BCVA change

Supplemental Material 17

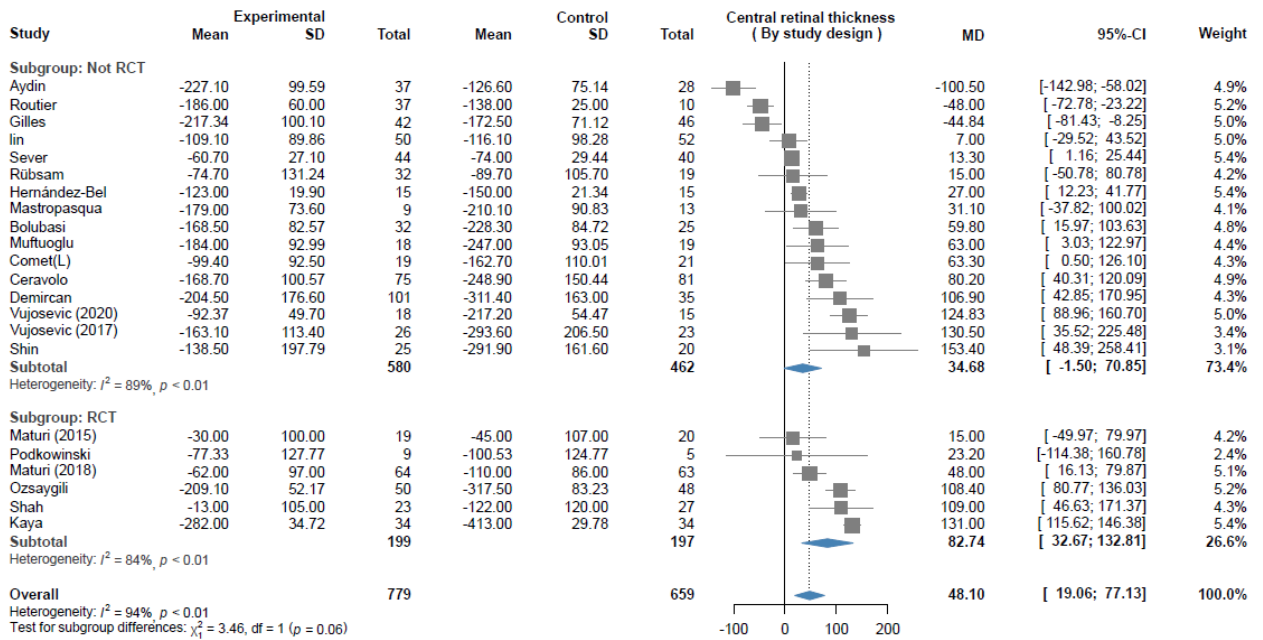
Subgroup analysis study design BCVA change



Supplemental Material 18
Subgroup analysis
study design
CRT decrease

Supplemental Material 18

Subgroup analysis study design CRT decrease



Supplemental Material 19
Summary of OCT biomarker

Supplemental Material 19

Summary of OCT biomarker

Study	Treatment	Hyperreflective dots (HRD) change (numbers)	Hyperreflective dots (HRD) yes/no, after treatment(eye)	Subfoveal serous retinal detachment (SRD) change (um)	Change of choroidal thickness change (um)	disorganization of inner retinal layers (DRIL) (um)
Aksoy et al	1. Aflibercept				-92.94	
	2. Ozurdex				-94.58	
Bolubasi et al	1. Bevacizumab			-110.69		
	2. Ozurdex			-162.66*		
Ceravolo et al	1. Ranibizumab	-6.7		-37.4	-1.9	
	2. Ozurdex	-13.22*		-89.3*	-28.6	
Demircan et al	1. Ranibizumab			-133.6		
	2. Ozurdex			-133.6		
Hernández-Bel et al	1. Aflibercept		10/5	5/10 (resolution after tx)		
	2. Ozurdex+		7/8	7/6 (resolution after tx)		
	Aflibercept					
Vujosevic et al 2017	1. Ranibizumab	-28		5/10 (resolution after tx)	-9.3%	
	2.Ozurdex	-32.4		7/6 (resolution after tx)	-11.3%	
Vujosevic et al 2020	1. Ranibizumab	-5.94		-96.7%		-80.52
	2.Ozurdex	-21.38*		-86.8%		-394.65

* Ozurdex group had significant change comparing with Anti-VEGF group