Result Summary

This study included 18 eyes of 18 patients diagnosed with CRVO. Eligible patients were randomly allocated into two equal treatment groups. **Group A** comprised nine eyes that received intravitreal **ziv-aflibercept** at a dose of 2 mg/0.08 mL, whereas **Group B** comprised nine eyes that received intravitreal **ranibizumab** at a dose of 0.5 mg/0.05 mL.

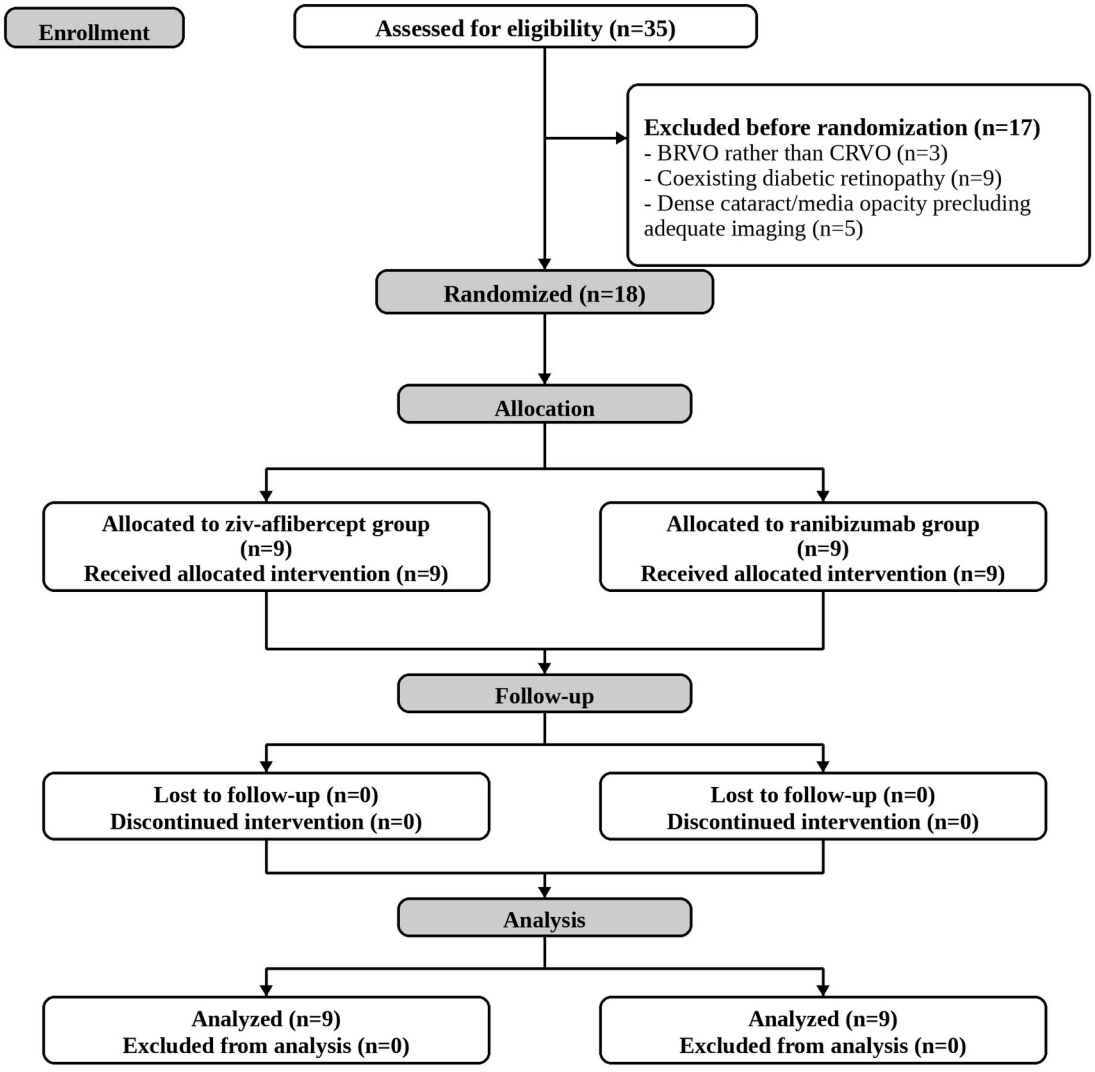


Figure. CONSORT flow diagram showing patient assessment for eligibility, exclusion before randomization, allocation to treatment groups, follow-up, and final analysis.

Baseline demographic and clinical characteristics

Table 1. Comparison between the studied groups regarding baseline characteristics.

Variable	Group A (n=9)	Group B (n=9)	Test	p-value
Age (years)				
Mean ± SD	57.44 ± 8.44	63.44 ± 5.43	t	0.092
Sex				
Female	2 (22.2%)	1 (11.1%)	Fisher	>0.999
Male	7 (77.8%)	8 (88.9%)		
Ocular laterality				
Left	5 (55.6%)	5 (55.6%)	Fisher	>0.999
Right	4 (44.4%)	4 (44.4%)		
Comorbidity				
Hypertension	9 (100.0%)	9 (100.0%)	-	-
Diabetes mellitus	2 (22.2%)	6 (66.7%)	Fisher	0.153
Perfusion status				
Ischemic	2 (22.2%)	3 (33.3%)	Fisher	>0.999
Non-ischemic	7 (77.8%)	6 (66.7%)		

Fisher: Fisher's exact test; t: independent-samples t-test.

As shown in **Table 1**, no statistically significant differences were observed between the two groups regarding age, sex distribution, affected eye, perfusion status, or comorbidities. These findings indicate that the two groups were comparable at baseline.

Best-Corrected Visual Acuity (BCVA)

Table 2. Comparison between the studied groups regarding BCVA before and after injection.

BCVA (logMAR)	Group A (n=9) Mean ± SD	Group B (n=9) Mean ± SD	t	p-value
Baseline	1.32 ± 0.36	1.26 ± 0.22	0.403	0.692

4 weeks	0.92 ± 0.31	1.19 ± 0.35	-1.723	0.104
8 weeks	0.96 ± 0.30	1.04 ± 0.31	-0.552	0.588
12 weeks	0.89 ± 0.26	0.95 ± 0.26	-0.497	0.626
24 weeks	0.85 ± 0.29	1.02 ± 0.31	-1.201	0.247
p (ANOVA)	0.019*	0.007*		

*t: independent-samples t-test; ANOVA: repeated-measures analysis of variance; *p < 0.05 is statistically significant; **p ≤ 0.001 is highly statistically significant.*

As shown in **Table 2**, no statistically significant difference was observed between the two groups regarding BCVA at baseline or at 4, 8, 12, and 24 weeks after intravitreal injection. However, repeated-measures analysis showed a statistically significant improvement in BCVA over the 24-week follow-up period within both groups.

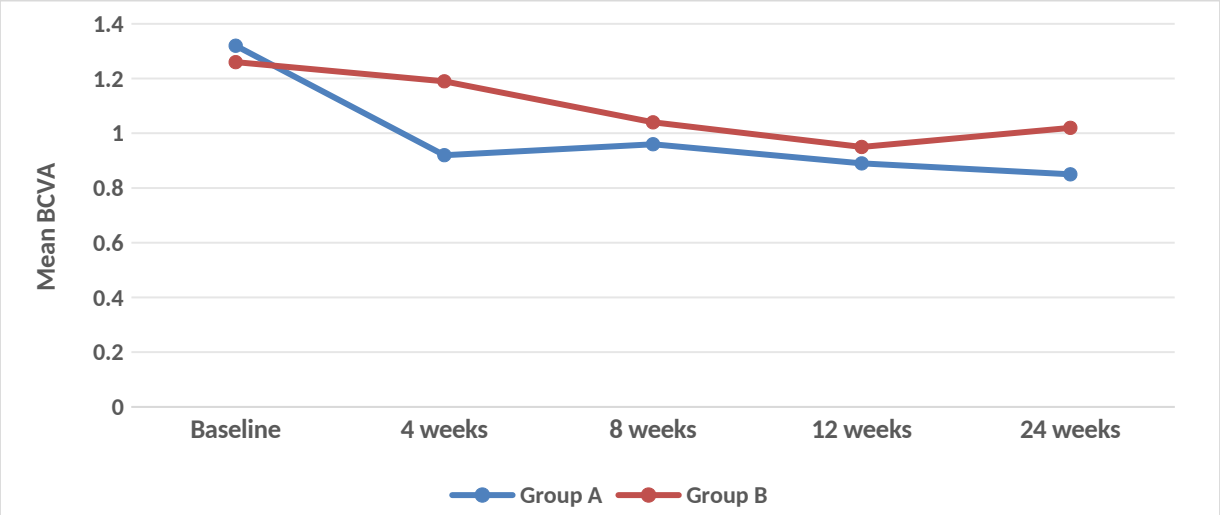


Figure 3-1. Multiple line chart showing comparison between the studied groups regarding BCVA.

Table 3. Comparison regarding BCVA before and after injection during each follow-up period within Group A.

BCVA (logMAR)	Group A (n=9) Mean ± SD	p-value
Baseline	1.32 ± 0.36	
4 weeks	0.92 ± 0.31	0.001**
8 weeks	0.96 ± 0.30	0.002*
12 weeks	0.89 ± 0.26	0.001**
24 weeks	0.85 ± 0.29	0.001**

*p-values were calculated using the paired-samples t-test between baseline and each follow-up visit. *p < 0.05 is statistically significant; **p ≤ 0.001 is highly statistically significant.*

As shown in **Table 3**, BCVA improved significantly in Group A compared with baseline at 4 weeks (p = 0.001), 8 weeks (p = 0.002), 12 weeks (p = 0.001), and 24 weeks (p = 0.001).

Table 4. Comparison regarding BCVA before and after injection during each follow-up period within Group B.

BCVA (logMAR)	Group B (n=9) Mean ± SD	p-value
Baseline	1.26 ± 0.22	
4 weeks	1.19 ± 0.35	0.339
8 weeks	1.04 ± 0.31	0.003*
12 weeks	0.95 ± 0.26	0.001**
24 weeks	1.02 ± 0.31	0.001**

*p-values were calculated using the paired-samples t-test between baseline and each follow-up visit. *p < 0.05 is statistically significant; **p ≤ 0.001 is highly statistically significant.*

As shown in **Table 4**, BCVA in Group B did not show statistically significant improvement at 4 weeks compared with baseline (p = 0.339). However, statistically significant improvement was observed at 8 weeks (p = 0.003) and was maintained at 12 and 24 weeks after injection (p = 0.001).

Central Macular Thickness (CMT)

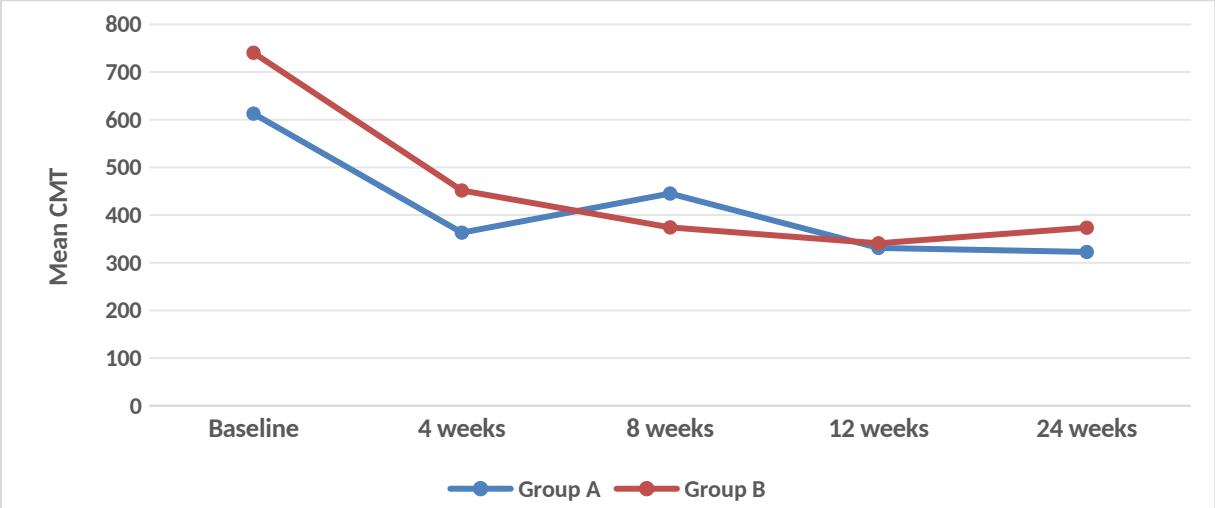
Table 5. Comparison between the studied groups regarding CMT before and after injection.

CMT (µm)	Group A (n=9) Mean ± SD	Group B (n=9) Mean ± SD	t	p-value
Baseline	612.78 ± 190.60	740.44 ± 169.35	-1.502	0.153
4 weeks	363.00 ± 79.33	451.44 ± 84.05	-2.296	0.036*
8 weeks	445.11 ± 241.37	374.00 ± 146.37	0.756	0.461
12 weeks	330.89 ± 78.05	340.67 ± 97.56	-0.235	0.817

24 weeks	322.44 ± 87.07	373.33 ± 109.52	-1.091	0.291
p (ANOVA)	0.054	0.002*		

*t: independent-samples t-test; ANOVA: repeated-measures analysis of variance; *p < 0.05 is statistically significant; **p ≤ 0.001 is highly statistically significant.*

As shown in **Table 5**, no statistically significant difference was observed between the two groups regarding CMT at baseline or at 8, 12, and 24 weeks after injection. At 4 weeks, mean CMT was significantly lower in Group A than in



Group B (363.00 ± 79.33 µm versus 451.44 ± 84.05 µm; p = 0.036). Repeated-measures analysis showed that the overall change in CMT over the 24-week follow-up period reached statistical significance in Group B (p = 0.002) but not in Group A (p = 0.054). Nevertheless, pairwise comparisons with baseline in Group A demonstrated significant CMT reductions at 4, 12, and 24 weeks, whereas the reduction at 8 weeks did not reach statistical significance.

Figure 3-2. Multiple line chart showing comparison between the studied groups regarding CMT.

Table 6. Comparison regarding CMT before and after injection during each follow-up period within Group A.

CMT (µm)	Group A	p-value

	(n=9) Mean ± SD	
Baseline	612.78 ± 190.60	
4 weeks	363.00 ± 79.33	0.006*
8 weeks	445.11 ± 241.37	0.109
12 weeks	330.89 ± 78.05	0.003*
24 weeks	322.44 ± 87.07	0.002*

*p-values were calculated using the paired-samples t-test between baseline and each follow-up visit. *p < 0.05 is statistically significant; **p ≤ 0.001 is highly statistically significant.*

As shown in **Table 6**, CMT in Group A showed a statistically significant reduction from baseline at 4 weeks (p = 0.006), 12 weeks (p = 0.003), and 24 weeks after injection (p = 0.002). However, the reduction at 8 weeks was not statistically significant (p = 0.109). The lack of statistical significance at 8 weeks may be attributed to an increase in CMT of more than 20% in three patients during this follow-up visit. One of these patients developed a recurrent episode of vein occlusion, and these patients required an additional intravitreal injection after the initial three loading doses.

Table 7. Comparison regarding CMT before and after injection during each follow-up period within Group B.

CMT (µm)	Group B (n=9) Mean ± SD	p-value
Baseline	740.44 ± 169.35	

4 weeks	451.44 ± 84.05	0.001**
8 weeks	374.00 ± 146.37	0.001**
12 weeks	340.67 ± 97.56	0.001**
24 weeks	373.33 ± 109.52	0.001**

*p-values were calculated using the paired-samples t-test between baseline and each follow-up visit. *p < 0.05 is statistically significant; **p ≤ 0.001 is highly statistically significant.*

As shown in **Table 7**, CMT in Group B showed a statistically significant reduction from baseline at all follow-up visits, including 4, 8, 12, and 24 weeks after injection (p = 0.001).

Intraocular Pressure

Table 8. Comparison between the studied groups regarding IOP at baseline and during follow-up.

IOP (mmHg)	Group A (n=9) Mean ± SD	Group B (n=9) Mean ± SD	t	p-value
Baseline	15.11 ± 2.26	16.00 ± 3.16	-0.686	0.503
4 weeks	16.00 ± 2.45	15.78 ± 2.33	0.197	0.846
8 weeks	15.78 ± 3.23	16.67 ± 1.73	-0.727	0.478
12 weeks	15.33 ± 2.45	16.44 ± 3.43	-0.791	0.441
24 weeks	14.89 ± 2.26	16.00 ± 1.41	-1.250	0.229
p (ANOVA)	0.336	0.695		

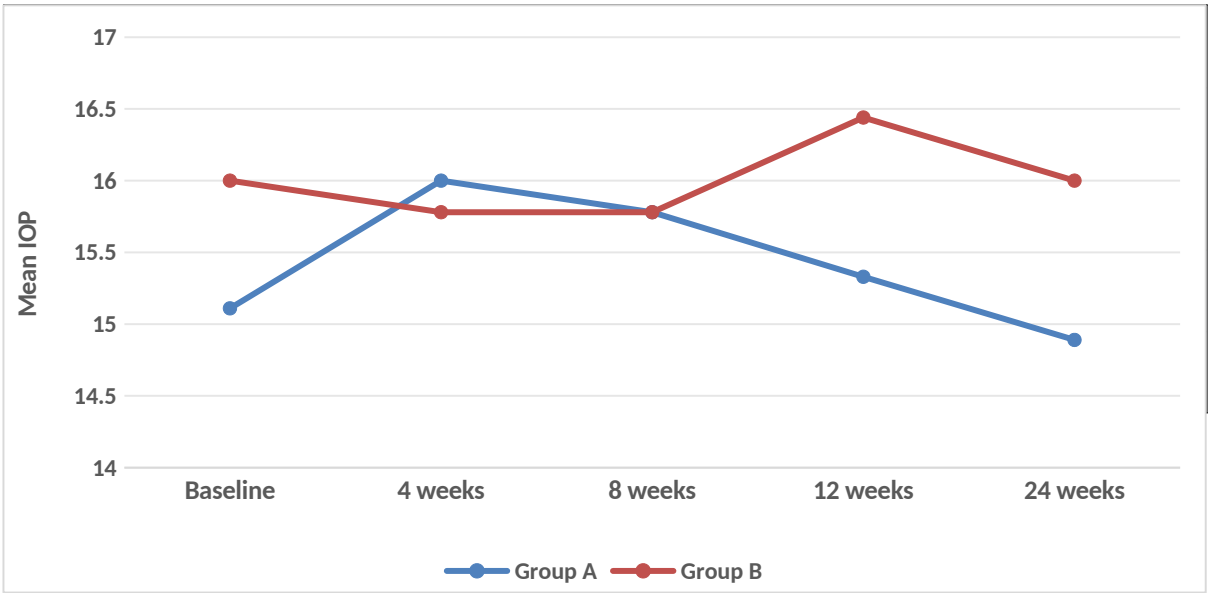
t: independent-samples t-test; ANOVA: repeated-measures analysis of variance.

As shown in **Table 8**, no statistically significant difference was observed between the two groups regarding intraocular pressure (IOP) at baseline or at any follow-up visit. Repeated-measures analysis also showed no statistically significant change in IOP over the 24-week follow-up period within either group.

Figure 3-3. Multiple line chart showing comparison between the studied groups regarding IOP.

Table 9. Comparison regarding IOP before and after injection during each follow-up period within Group A.

IOP (mmHg)	Group A (n=9) Mean ± SD	p-value



*p-values were calculated using the paired-samples t-test between baseline and each follow-up visit. *p < 0.05 is statistically significant; **p ≤ 0.001 is highly statistically significant.*

As shown in **Table 9**, no statistically significant change in IOP was observed in Group A at 4 weeks (p = 0.169), 8 weeks (p = 0.397), 12 weeks (p = 0.729), or 24 weeks (p = 0.594) compared with baseline.

Table 10. Comparison regarding IOP before and after injection during each follow-up period within Group B.

IOP (mmHg)	Group B (n=9) Mean ± SD	p-value
Baseline	16.00 ± 3.16	
4 weeks	15.78 ± 2.33	0.760
8 weeks	16.67 ± 1.73	0.347
12 weeks	16.44 ± 3.43	0.559
24 weeks	16.00 ± 1.41	0.999

*p-values were calculated using the paired-samples t-test between baseline and each follow-up visit. *p < 0.05 is statistically significant; **p ≤ 0.001 is highly statistically significant.*

As shown in **Table 10**, no statistically significant change in IOP was observed in Group B at 4 weeks (p = 0.760), 8 weeks (p = 0.347), 12 weeks (p = 0.559), or 24 weeks (p = 0.999) compared with baseline.

Percentage Change in Outcome Parameters

Table 11. Comparison between the studied groups regarding percentage change in outcome parameters.

Parameter	Group A (n=9) Median (IQR)	Group B (n=9) Median (IQR)	Z	p-value
BCVA	-39.5 (-45.1, -25.5)	-17.7 (-25.6, -14.5)	-2.304	0.021*
CMT	-45.5 (-53.9, -36.9)	-51.6 (-59.7, -39.9)	0.927	0.354
IOP	0.0 (-6.3, 0.0)	0.0 (-5.6, 15.5)	-0.707	0.437

Z: standardized test statistic for the Mann–Whitney U test; p < 0.05 is statistically significant.

As shown in **Table 11**, there was a statistically significant difference between the two groups regarding the percentage change in BCVA, favoring Group A. The median percentage change in BCVA was -39.5% in Group A compared with -17.7% in Group B. However, no statistically significant difference was observed between the two groups regarding the percentage change in CMT or IOP.

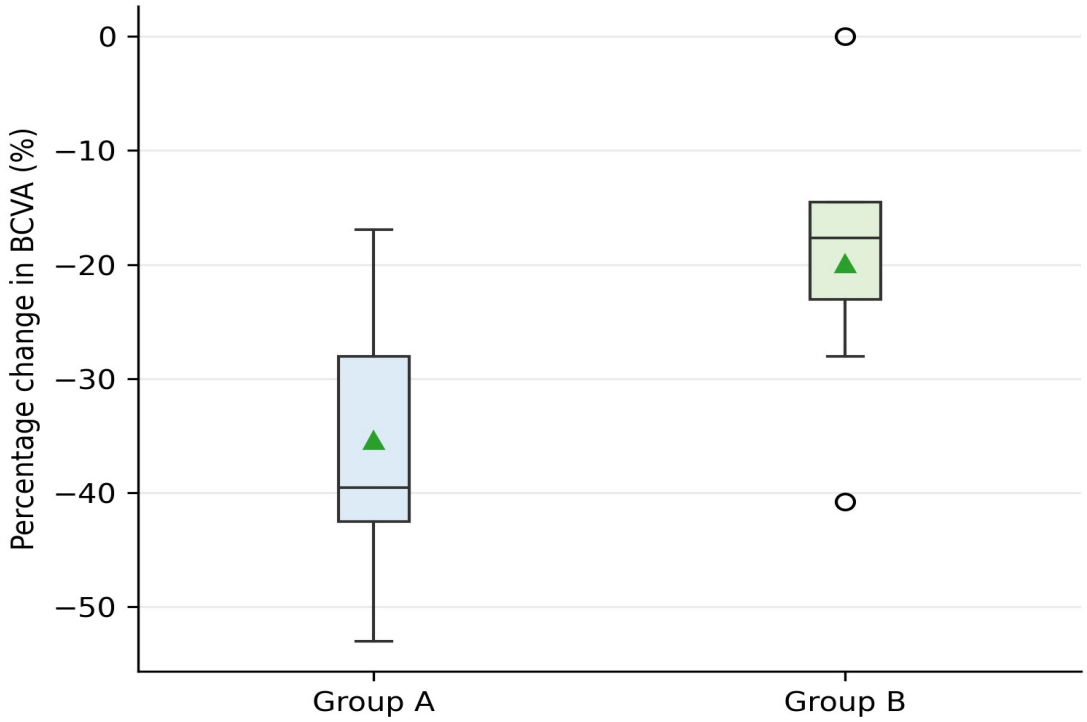


Figure 3-4. Box-and-whisker plot showing the percentage change in BCVA in Group A and Group B. The horizontal line inside each box represents the median, the box represents the interquartile range, the whiskers represent the range of non-outlier values, the green triangle represents the mean, and the circles represent outliers.

As shown in **Figure 3-4**, the box-and-whisker plot demonstrates the distribution of percentage change in BCVA in both study groups. Group A

showed a greater negative percentage change compared with Group B, indicating a more pronounced improvement in BCVA. The median percentage change was lower in Group A than in Group B, while the mean values showed a similar trend. However, Group A demonstrated wider variability in treatment response, as reflected by the larger interquartile range and longer whiskers. In contrast, Group B showed a more compact distribution, although two outlying values were observed.

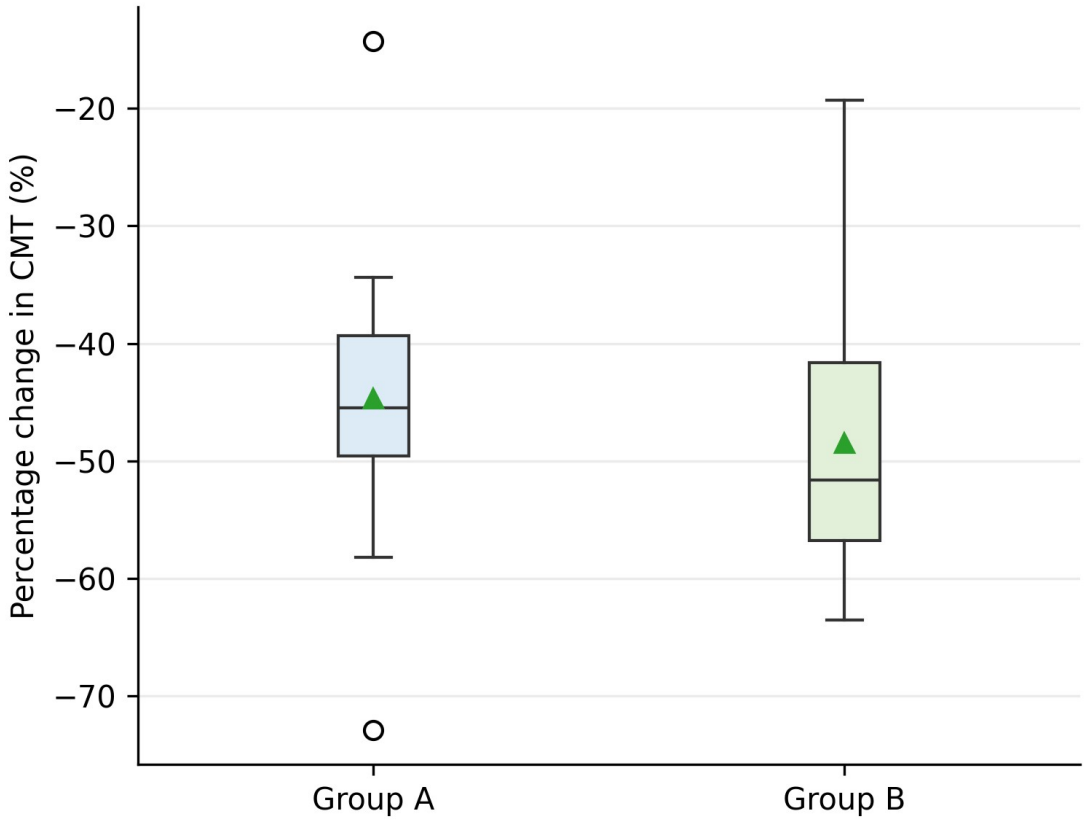


Figure 3-5. Box-and-whisker plot showing the percentage change in central macular thickness (CMT) in Group A and Group B. The horizontal line within each box represents the median, the box represents the interquartile range, the whiskers represent the non-outlier range, the green triangle represents the mean, and the circles represent outliers.

As shown in **Figure 3-5**, the box-and-whisker plot demonstrates the distribution of percentage change in CMT in both study groups. Both groups

showed a negative percentage change, indicating a reduction in CMT after treatment. Group B demonstrated a slightly greater median reduction in CMT compared with Group A. However, the distribution in Group B was wider, indicating greater variability in anatomical response. Group A showed a relatively more compact interquartile range, although two outlying values were observed.

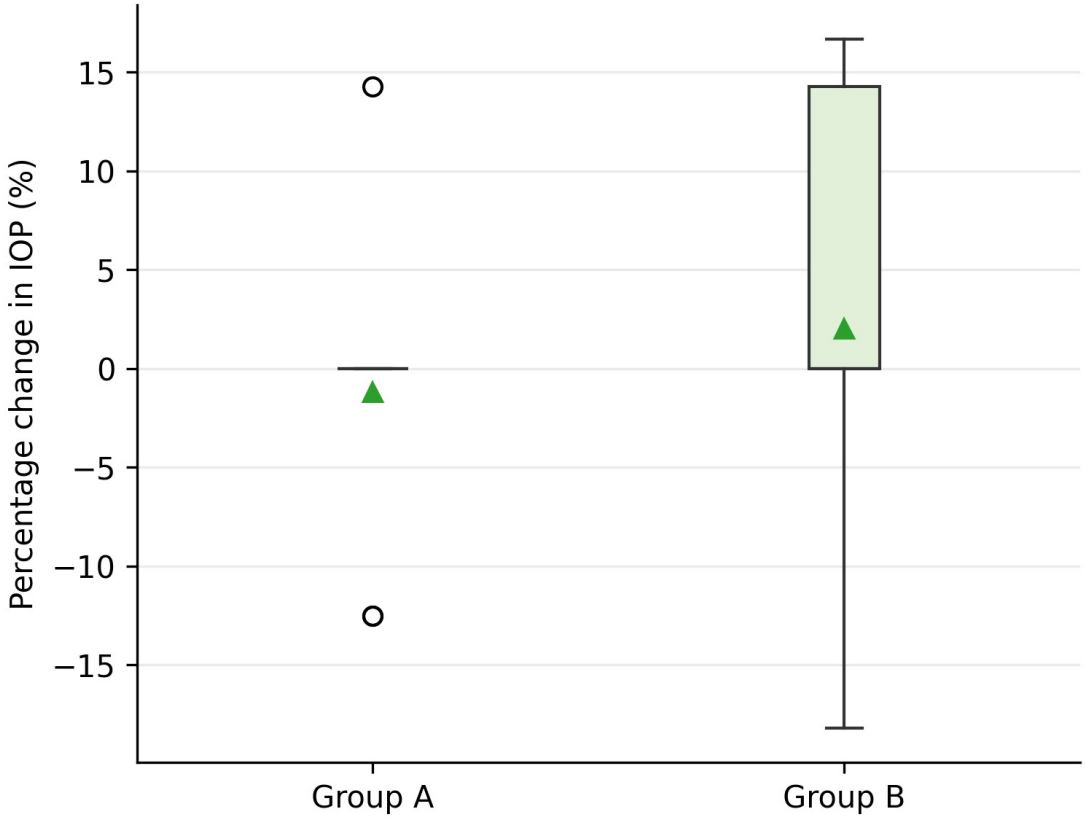


Figure 3-6. Box-and-whisker plot showing the percentage change in intraocular pressure (IOP) in Group A and Group B. The horizontal line within each box represents the median, the box represents the interquartile range, the whiskers represent the non-outlier range, the green triangle represents the mean, and the circles represent outliers.

As shown in **Figure 3-6**, the box-and-whisker plot demonstrates the distribution of percentage change in IOP in both study groups. Group A showed

minimal overall change in IOP, with the median value close to zero; however, two outlying values were observed, representing one case with an increase and another with a decrease in IOP. Group B demonstrated a wider distribution of percentage change, indicating greater variability in IOP response, with values ranging from a reduction to an increase. The mean percentage change in Group B was slightly positive, suggesting a mild overall increase in IOP.

Safety Profile and Treatment Burden

Table 12. Comparison between the studied groups regarding safety profile and treatment burden.

Parameter	Group A (n=9)	Group B (n=9)	Test	p-value
Any ocular complications during follow-up	0 (0.0%)	0 (0.0%)	-	-
Any systemic complications during follow-up	0 (0.0%)	0 (0.0%)	-	-
Any overall injection-related complications	0 (0.0%)	0 (0.0%)	-	-
Additional intravitreal injections (extra IVI)	3 (33.3%)	4 (44.4%)	Fisher	1.000

Fisher: Fisher's exact test.

As shown in **Table 12**, no ocular, systemic, or overall injection-related complications were recorded in either group during the follow-up period.

Additional intravitreal injections were required in 3 eyes (33.3%) in Group A and 4 eyes (44.4%) in Group B; however, this difference was not statistically significant.

Simplified Cost-Effectiveness Analysis Based on Drug-Acquisition Cost

Table 13. Simplified comparison of drug-acquisition cost and clinical outcomes based on average same-session vial utilization during routine injection lists.

Parameter	Group A Ziv-aflibercept	Group B Ranibizumab
Price per vial (EGP)	4584.00	8167.00
Average same-session vial utilization during routine injection lists	12–15	3
Estimated drug-acquisition cost per patient dose (EGP), based on average same-session vial utilization during routine injection lists	305–382	2,722
Total number of injections over 24 weeks in the study group	30	31
Mean number of injections per patient over 24 weeks	3.33	3.44
Estimated drug-acquisition cost per patient over 24 weeks (EGP)	1,018–1,273	9,376
Mean BCVA improvement over 24 weeks (logMAR)	0.47	0.24

Estimated cost per 0.1 logMAR improvement (EGP)	216–270	3,907
Mean CMT reduction over 24 weeks (µm)	290.34	367.11
Estimated cost per 100 µm CMT reduction (EGP)	350–438	2,554

As shown in **Table 13**, this simplified cost-effectiveness comparison was based on drug-acquisition cost only and on average same-session vial utilization during routine injection lists, without storage of prepared syringes. Although a 100 mg/4 mL Zaltrap® vial can theoretically provide up to 40 aliquots of 0.1 mL, the present analysis was based on the actual average same-session utilization of approximately 12–15 patients. These routine injection lists were not limited to patients with CRVO but also included patients treated for other retinal vascular and neovascular conditions, including diabetic macular edema (DME), branch retinal vein occlusion (BRVO), and neovascular age-related macular degeneration (nAMD). In contrast, a Lucentis® vial can provide up to three same-session intravitreal doses under a standardized aseptic protocol, as described by Haider et al. (2025). Based on this average same-session utilization, the estimated drug-acquisition cost per patient dose was 305.60–382.00 EGP for ziv-aflibercept compared with 2,722.33 EGP for ranibizumab. Considering the total number of injections administered over 24 weeks, the estimated drug-acquisition cost per patient remained markedly lower in the ziv-aflibercept group. When interpreted together with BCVA and CMT outcomes, ziv-aflibercept showed a more favorable simplified cost-effectiveness profile. However, this analysis should be interpreted as an exploratory drug-acquisition cost comparison rather than a formal pharmacoeconomic evaluation.

Safety and Cost-Effectiveness Summary

Both drugs demonstrated favorable short-term safety profiles, with no documented ocular or systemic complications and no statistically significant increase in intraocular pressure during follow-up. From a simplified economic perspective based on drug-acquisition cost, ziv-aflibercept provided comparable anatomical and functional outcomes at a markedly lower cost than ranibizumab.