



KELLOGG EYE CENTER
MICHIGAN MEDICINE

“Treatment of Choroidal Metastasis with Combined PDT and Bevacizumab Leads to Faster Recovery of Visual Acuity and Better Tumor Control than PDT Alone”

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Background

- **Choroidal metastases** are secondary to systemic cancer usually with multiple system involvement and has a poor prognosis with a short **average survival time of 17 months**.¹
- Systemic therapies such as chemotherapy or local therapies such as brachytherapy, photodynamic therapy (PDT), and intravitreal antivascular endothelial growth factor (anti-VEGF) injection have been used in the management of choroidal metastasis.²
- A meta-analysis reported **tumor regression in 82% of eyes treated with PDT, and either improvement or stability of vision in 78% of the eyes**.³

Objective

- **To evaluate the treatment of choroidal metastasis with combined PDT and intravitreal bevacizumab (IVB) and compare it to PDT alone.**

Methods

- Consecutive patients diagnosed with choroidal metastasis and treated with PDT alone or combined PDT and IVB in Kellogg eye center, university of Michigan, between **2011-2023** were retrospectively included.
- Best corrected visual acuity (BCVA), tumor basal diameter and thickness, and tumor control rate evaluated before treatment, at the **6-week, and last visits**.
- **Tumor control** was defined as **the simultaneous complete resolution SRF and a decrease in tumor thickness**, as measured by OCT or USG.

Results

- Total 41 choroidal metastasis (21 patients).
- **PDT and IVB** in 19 choroidal metastatic tumors (in 13 patients).
- **PDT alone** in 22 choroidal metastatic tumors (in 8 patients).

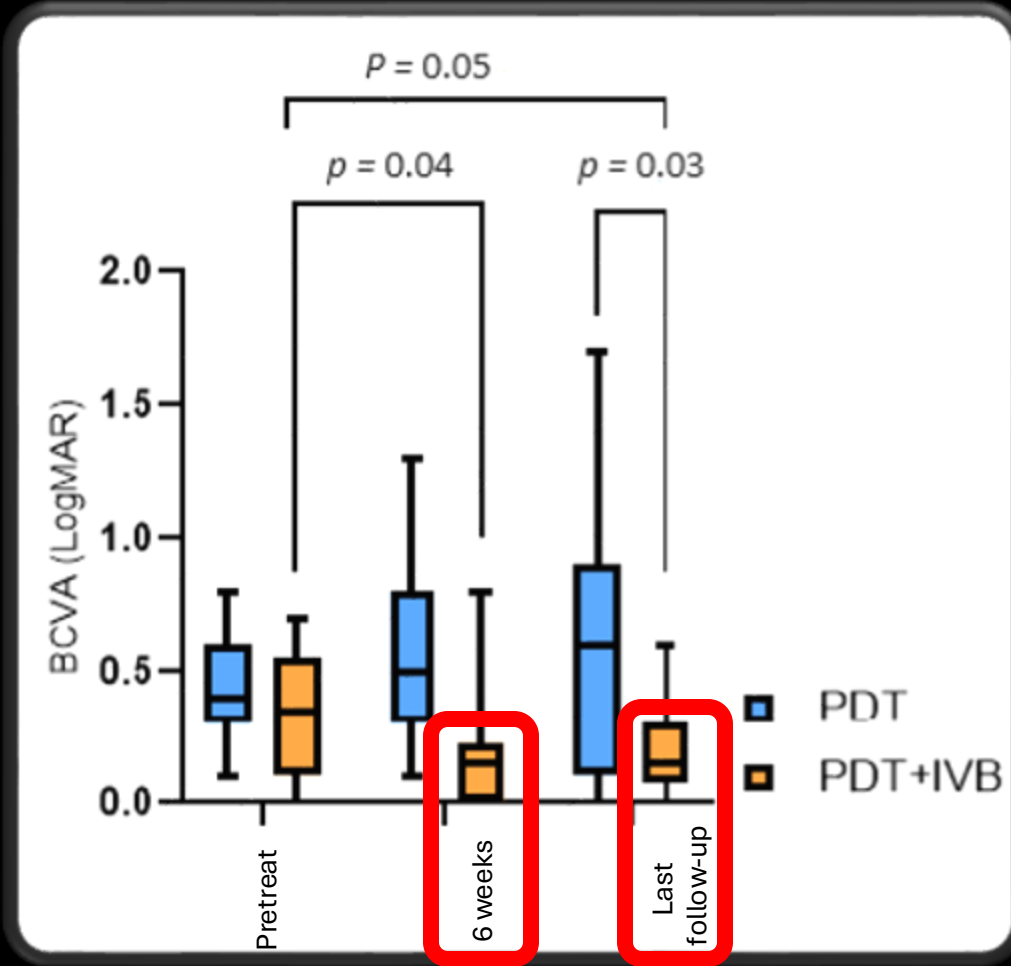
Demographics, tumor characteristics, and baseline

| Features | PDT alone | Combined PDT with IVB | P value |
|-------------------------------------------------------------------------|-----------------|-----------------------|---------|
| Age (years), | | | 0.38 |
| Median (min-max) | 64 (41-77) | 65.50 (58-80) | |
| Mean ± SD | 61.08 ± 11.83 | 66.38 ± 7.35 | |
| Gender, n (%) | | | 1.00 |
| Female | 7 (53.8%) | 4 (50.0%) | |
| Male | 6 (46.2%) | 4 (50.0%) | |
| Follow-up (months) | | | 0.46 |
| Median(min-max) | 6 (3-84) | 9.5 (3-25) | |
| Mean± SD | 12.25± 22.2 | 10.23±8.53 | |
| Time between primary cancer diagnosis and choroidal metastasis (months) | | | 0.34 |
| Median (min-max) | 50 (0-194) | 84 (1-148) | |
| Mean ± SD | 64.31 ± 59.76 | 83.86 ± 49.74 | |
| Number of patients with systemic metastasis other than eye | | | 1.00 |
| n(%) | 12 (92.3%) | 8 (100%) | |
| Bilaterality, n (%) | | | 0.63 |
| Unilateral | 9 (75%) | 5 (62.5%) | |
| Bilateral | 3 (25%) | 3 (37.5%) | |
| Tumor location, n(%) | | | 0.23 |
| Macula | 10 (45.4%) | 8 (42.1%) | |
| Juxtapapillary | 6 (27.2%) | 3 (15.8%) | |
| Macula to equator | 6 (27.3%) | 8 (42.1%) | |
| Basal tumor diameter(mm), | | | 0.049 * |
| Median (min-max) | 8.50 (3-17) | 6.0 (1.5-17) | |
| Mean ± SD | 8.68 ± 3.64 | 1.42 ± 0.61 | |
| Tumor thickness (mm), | | | 0.33 |
| Median (min-max) | 1.5 (0.41-2.90) | 1.15(0.4-3.8) | |
| Mean ± SD | 1.45 ± 0.73 | 1.23 ± 0.95 | |
| Number of PDT sessions, | | | 0.26 |
| Median (min-max) | 2 (1-3) | 1 (1-3) | |
| Mean ± SD | 1.64 ± 0.66 | 1.42 ± 0.61 | |
| Baseline BCVA (LogMAR), | | | 0.29 |
| Median (min-max) | 0.4 (0.1-0.8) | 0.3 (0.0-0.7) | |
| Mean ± SD | 0.43 ± 0.23 | 0.33 ± 0.24 | |
| CMT(μm) | | | 0.87 |
| Median(min-max) | 521 (246-986) | 440.5 (260-1000) | |
| Mean ± SD | 525.5 ± 246.6 | 528.1 ± 253.2 | |

PDT = photodynamic therapy; IVB = intravitreal bevacizumab; SD = standard deviation; BCVA = best corrected visual acuity; LogMAR = logarithm of the minimum angle of resolution; CMT = central macular thickness; p* significant.

Results : VA

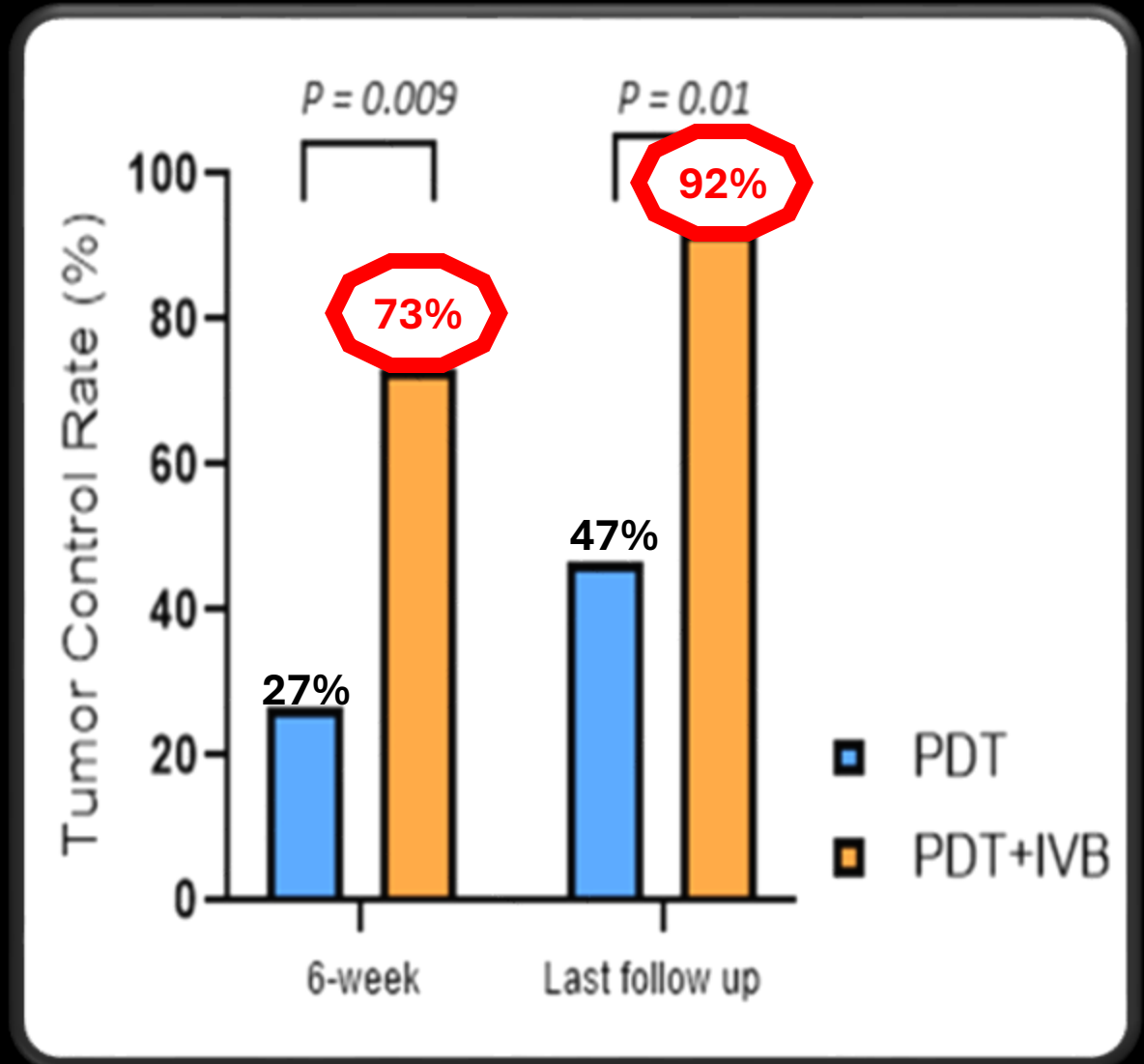
Visual Acuity Changes with Treatment



The BCVA in both the 6-week and last follow-up visits was **significantly better in the combined PDT and IVB group** compared with the PDT alone group ($p=0.02$ for both visits).

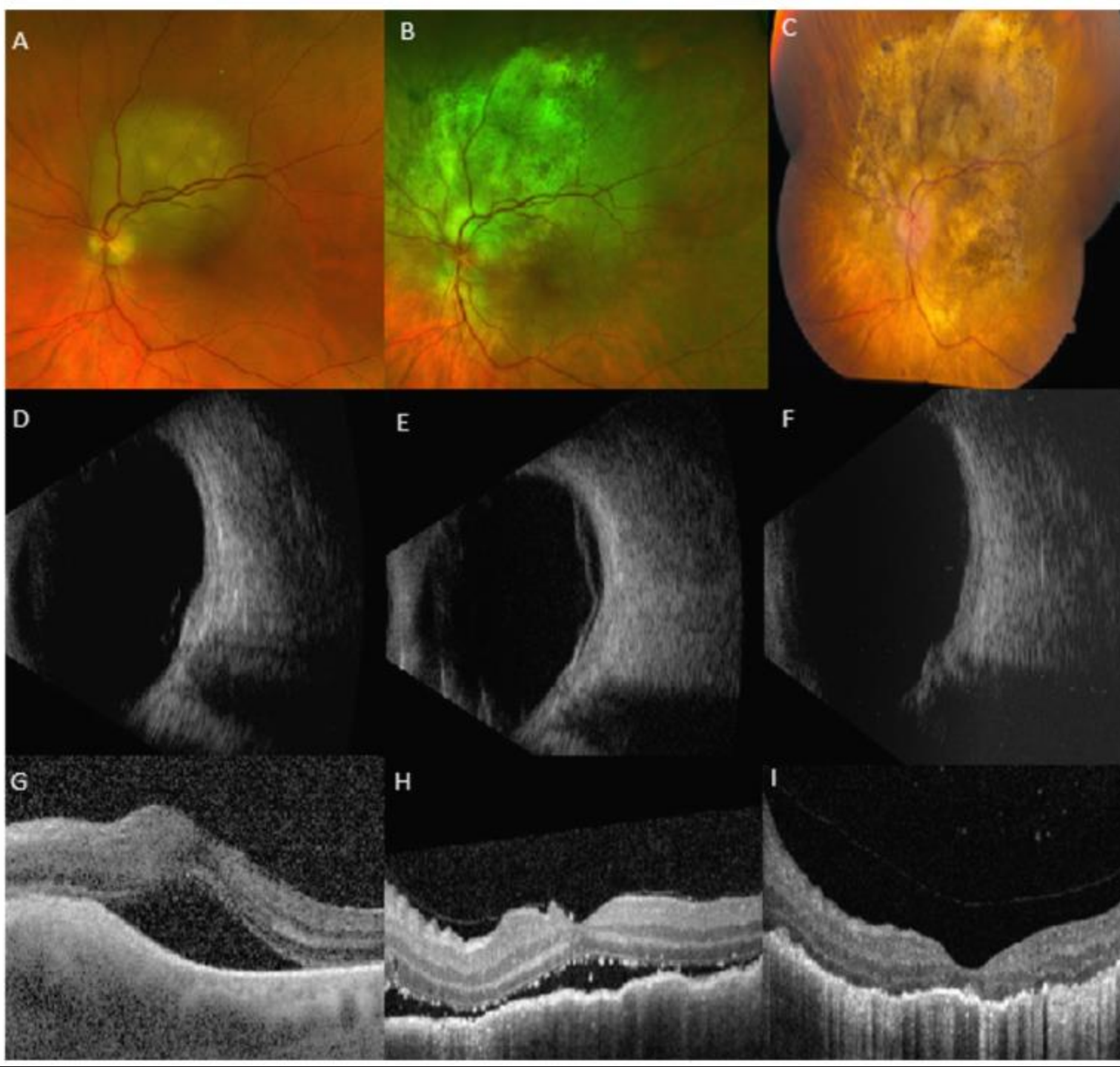
Results: tumor control rates

- At the **6-week** visit, the PDT+IVB group demonstrated a significantly higher rate of **tumor control with a rate of 73.3%**, compared to **26.6%** in the PDT alone group ($p = 0.009$).
- In the **last visit**, the **tumor control rate was 92%** in the combined group and **47%** in the PDT alone group. There was a significant difference between two treatment groups ($p = 0.01$).



Tumor Control Rates

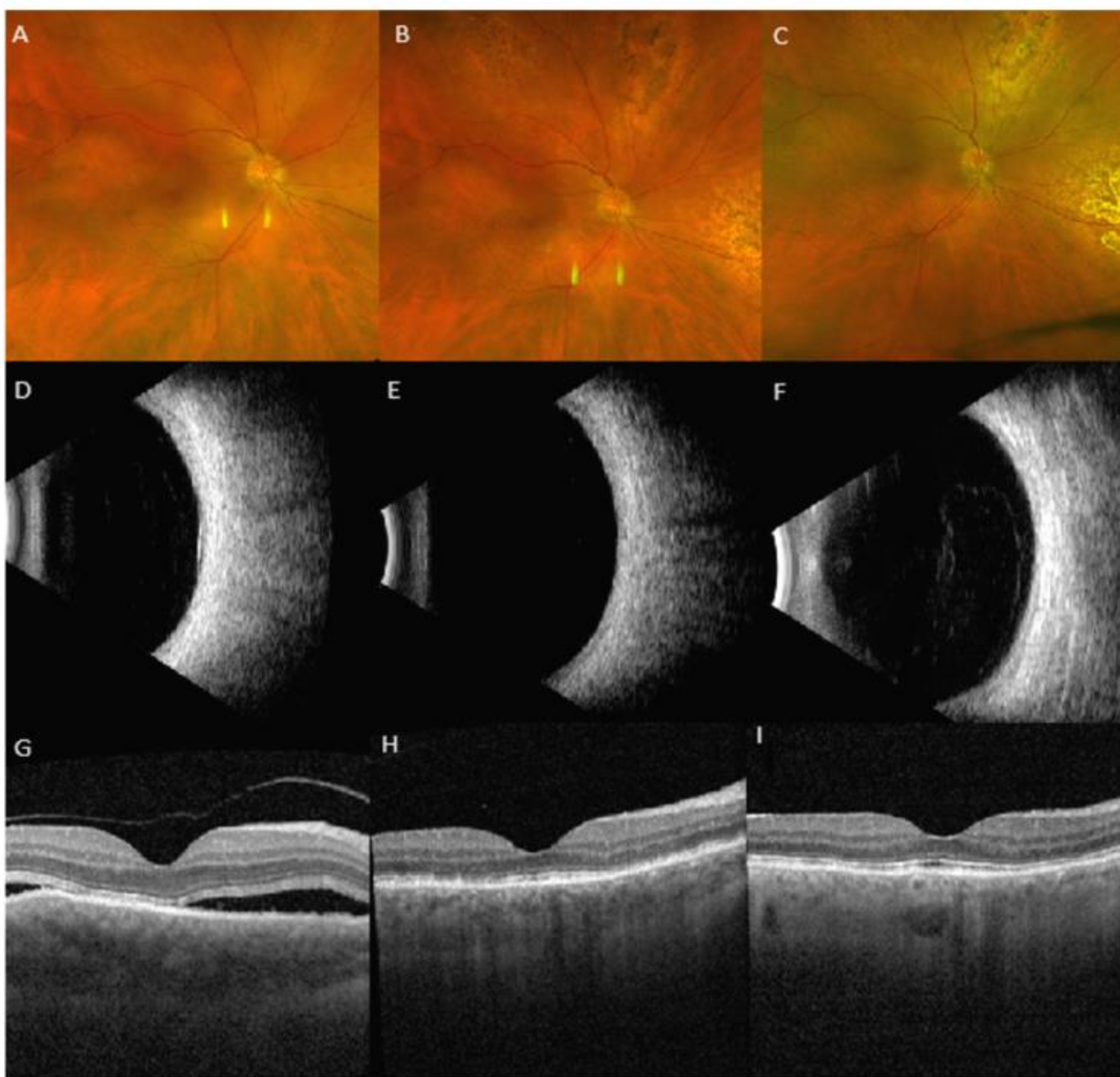
Multimodal imaging findings



Pancreatic choroidal metastasis treated with Photodynamic Therapy (PDT) alone

- 6 weeks after PDT, tumor thickness decreased on USG however **exudative detachment along the macula increased.**
- last follow-up, SRF was resolved under **the macula with ellipsoid zone disruption**

Multimodal imaging findings



Adenocarcinoma of lung
choroidal metastasis treated
with Photodynamic Therapy
(PDT) and intravitreal
bevacizumab (IVB),

- At 6 weeks after PDT and IVB, choroidal lesions were partially regressed with retinal pigment epithelium (RPE) changes and ellipsoid zone (EZ) disruption sparing the fovea.
- last visit, there was no SRF under the macula with RPE and EZ healing

Discussion

- **PDT controls tumor growth by destroying functional vasculature**
However, **the inflammatory responses** induced by hypoxia after PDT can reduce treatment efficacy by promoting signaling cascades for an enhanced environment for tumor recurrence.⁴ **IVB may play a role in minimizing this angiogenic environment after PDT.**⁵
- Previous studies have primarily focused on evaluating the final visual outcomes, and there is **limited data on the earlier visual changes** following treatment. In **our study**, we evaluated BCVA at an earlier time (6-week follow-up), and **found a significant improvement in the combined PDT and IVB group** compared to the PDT alone group.

Conclusion

- This is the **first study** to investigate the efficacy of combined PDT and IVB in treating choroidal metastases.
- Our findings suggest that the **combined PDT and IVB approach** provides **superior visual recovery and tumor control** compared to **PDT alone**, both at early and last follow-up visits.
- Studies with a larger number of patients are needed to confirm these results.

References

1. Shields, C. L., Shields, J. A., Gross, N. E., Schwartz, G. P., & Lally, S. E. (1997). Survey of 520 eyes with uveal metastases. *Ophthalmology*, 104(8), 1265-1276. doi:10.1016/s0161-6420(97)30148-1
2. Arepalli S, Kaliki S, Shields CL. Choroidal metastases: origin, features, and therapy. *Indian journal of ophthalmology*. 2015;63(2):122-127.
3. Nguyen MT, Stacey AW. PHOTODYNAMIC THERAPY FOR THE TREATMENT OF CHOROIDDAL METASTASES: A Case Series and Meta-analysis. *Retina (Philadelphia, Pa)*. 2022;42(6):1176-1183.
4. Olivo M, Bhuvanewari R, Lucky SS, Dendukuri N, Soo-Ping Thong P. Targeted Therapy of Cancer Using Photodynamic Therapy in Combination with Multi-faceted Anti-Tumor Modalities. *Pharmaceuticals (Basel, Switzerland)*. 2010;3(5):1507-1529.
5. Bhuvanewari R, Gan YY, Soo KC, Olivo M. The effect of photodynamic therapy on tumor angiogenesis. *Cellular and molecular life sciences : CMLS*. 2009;66(14):2275-2283.



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Thank you...



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