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Ocular Oncology Symposium

Phase 2 Trial of Belzupacap Sarotalocan (Bel-Sar, AU-011), aTargeted Therapy for Choroidal Melanoma via Suprachoroidal Administration

- Amy Schefler, MD FACS FASRS

Objective: The primary objective is to assess safety and efficacy of bel-sar via suprachoroidal (SC) administration to treat primary indeterminate lesions and small choroidal melanomas (ILs/CMs).
Purpose: Many ILs/CMs are monitored initially and then treated with radiotherapy, which may cause severe and irreversible vision loss. Bel-sar is an investigational virus-like drug conjugate with potential to be a vision-preserving therapy for the early treatment of ILs/CMs. The purpose of the ongoing Phase 2 trial is to evaluate safety and efficacy of bel-sar given via SC administration followed by near-infrared light activation in ILs/earlyCMs.
Methods: This Phase 2 multicenter trial (NCT04417530), is being conducted at 22 U.S. sites. The prospective, non-randomized, open-label design included 6 single- and multiple-dose escalation cohorts. Included subjects must have had a diagnosis of primary IL or small CM, no evidence of metastatic disease confirmed by imaging, and be treatment naïve for IL/CM. Exclusion criteria were known contraindications or sensitivities to the study drug or laser and active ocular disease. Adult subjects received up to 3 cycles of bel-sar treatment via SC administration with a maximum dose of 80 µg with 2 laser applications. Each cycle consisted of bel-sar administration followed by 2 laser applications the same day, once a week, for 3 consecutive weeks. All treated subjects were evaluated for safety and efficacy, including visual acuity failure (loss of ≥15 ETDRS letters) and tumor progression.
Results: Preliminary results include 20 subjects in all dose escalation cohorts. Early outcomes showed a high tumor control rate (89%) with median of 4.9 months and mean of 6 months follow up in subjects in the highest dose regimen cohorts, and a statistically significant reduction of tumor growth rate (p=0.0007). There were no dose-limiting toxicities and no treatment-related serious or grade 3/4 AEs, severe vision loss, or vitritis. A visual acuity preservation rate of 89% was observed in subjects in the highest dose regimens (n=9), and 87% in subjects with tumors close to the fovea or optic disc across all dose cohorts (n=15).

Conclusion: Preliminary results indicate bel-sar via SC administration to be safe, effective and vision-preserving, supporting its potential to be a targeted therapy for the first-line treatment of ILs/CMs.

IRB APPROVAL Yes

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Ocular Oncology Symposium

Validated Approach to Estimating Choroidal Lesion Thickness Using 2D Ultra-Widefield Optomap Images With Implications for High-Risk Lesion Detection

- Prithvi Mruthyunjaya, MD, MHS
- Michael Heiferman, MD
- Aneesha Ahluwalia
- Gina Yu, MD
- Edward Korot, MD
- Michael Yu

Objective: Can two dimentional ultrawide field image of a melanocytic choroidal lesion be used to accurately estimate thickness and thus provide three dimentional information?
Purpose: Tumor thickness is a well-established risk factor for transformation of choroidal nevus (CN) into choroidal melanoma (CM) and thus plays an important role in risk stratification of melanocytic choroidal lesions (MCL). Herein, we describe a novel technique for rapid extraction of tumor thickness data from 2D ultra-widefield (UWF) dual-wavelength scanning laser ophthalmoscope Optomap images (Optos PLC, Dunfermline, Fife, Scotland, UK).

Methods: A consecutive series of patients seen by the Ocular Oncology Service at the Byers Eye Institute (Stanford University, Palo Alto, CA) with clinically diagnosed MCL underwent complete clinical examination, UWF imaging, and standardized B-scan ultrasonography (Eye Cubed, Ellex Medical, Adelaide, Australia). The UWF images were post-processed to isolate the green-wavelength-only image. Using Image J (National Institutes of Health, Bethesda, MD, USA), average pixel intensities within the lesion and of the adjacent retina were obtained, and the difference between both values calculated ("pixel intensity difference"; average lesion intensity minus average adjacent retina intensity). The pixel intensity difference was then plotted against the reference standard for tumor thickness as measured by standardized B-scan ultrasonography. The significance of the relationship between both variables was assessed by linear regression analysis. To internally validate the approach, thickness estimation and thickness thresholding ($\geq$2.0 mm) was then performed on a set of representative lesions ("validation set") excluded from any prior analyses.

Results: A total of 153 MCL (28 CM and 125 CN) of 153 patients were initially evaluated. Mean ultrasonographic thickness was 1.2 mm (median: 0.9, range: 0.5-5.5). Mean pixel intensity difference was 2.8 (median: 3.8, range: -11.1 – 39.6). The linear correlation coefficient for tumor thickness to intensity difference was 0.918 (p<0.001), indicating a strong positive correlation between tumor thickness and tumor brightness on green-wavelength imaging (Figure 1). Coefficient of determination (R^2) was 0.843. Separately, PID was calculated for a validation set comprising 25 additional representative MCL (mean ultrasonographic thickness: 1.94 mm) excluded from prior analyses. For lesions $\leq$2.0 mm, the mean absolute difference (actual ultrasonographic minus estimated) was 0.29 $\pm$ 0.19 mm. A threshold of PID $\geq$5 conferred 100% sensitivity and 89% specificity in detecting lesions $\geq$2.0 mm.

Conclusion: Lesion hyperintensity (brightness) on UWF green-channel images correlates with tumor thickness. Choroidal tumor thickness can be rapidly and reliably estimated using 2D UWF images. With additional validation, this method could augment future high-throughput screening, referral, and risk stratification of MCL with UWF images alone.

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Ocular Oncology Symposium

Innovations in Brachytherapy: Brachytherapy Plaque Quick-Release Stitch Saves Time and Money

- Colin McCannel, MD
- Tara McCannel, MD, PhD

Objective: Can the brachytherapy plaque quick release stitch save time or money?
Purpose: To investigate the rate at which brachytherapy plaques could be removed outside of the operating room (OR) environment utilizing the brachytherapy plaque quick release stitch, and associated cost and time savings. The brachytherapy plaque quick release stitch allows for removal of the brachytherapy plaque by releasing the plaque without cutting sutures, and then pulling it out with a "pull handle" suture (Figure 1). No tissue retraction or exploration is necessary.
Methods: One hundred consecutive cases of brachytherapy plaque removals were assessed for the rate of in-OR versus in-clinic removal. There were no exclusion criteria. Room and procedure time for in-OR removal, and OR charges for plaque removal were ascertained.
Results: 75 of the 100 brachytherapy plaques were removed in in clinic, the remainder were removed in OR. Overall, 57% were male patients, and the mean age was 65 years old. For plaques removed in the OR, 44% were male patients, with an overall mean age of 59 years old. For plaques removed in clinic, 61% were male patients, with an overall mean age was 67 years old. Mean OR room time for plaque removal was 27.4 minutes (min) (range 10-71, median 29 min), and mean procedure time was 12.7 min (range 3-46, median 11 min). There was no record keeping for time spent in clinic removing plaques, but anecdotally it took less then 10 minutes of physician time. The charges generated for each plaque removal in the OR, excluding professional fees, consisted of pre-opertive charge $890 (flat fee), operating room (level 2) charge (30 min) $5700, Anesthesia technical charge (30 min) $340, and recovery charge (15 min) $200, for a total of $7130. When plaques are removed in the clinic there was no specific utilization fee of the clinic room.
Conclusion: The brachytherapy plaque quick release stitch facilitates removal of brachytherapy plaques, and allows removal in a non-operating room environment (clinic) three quarters of the time. Substantial cost savings, avoiding $7130 in OR charges, and time savings, by the clinician not having to go to the operating room, were achieved.

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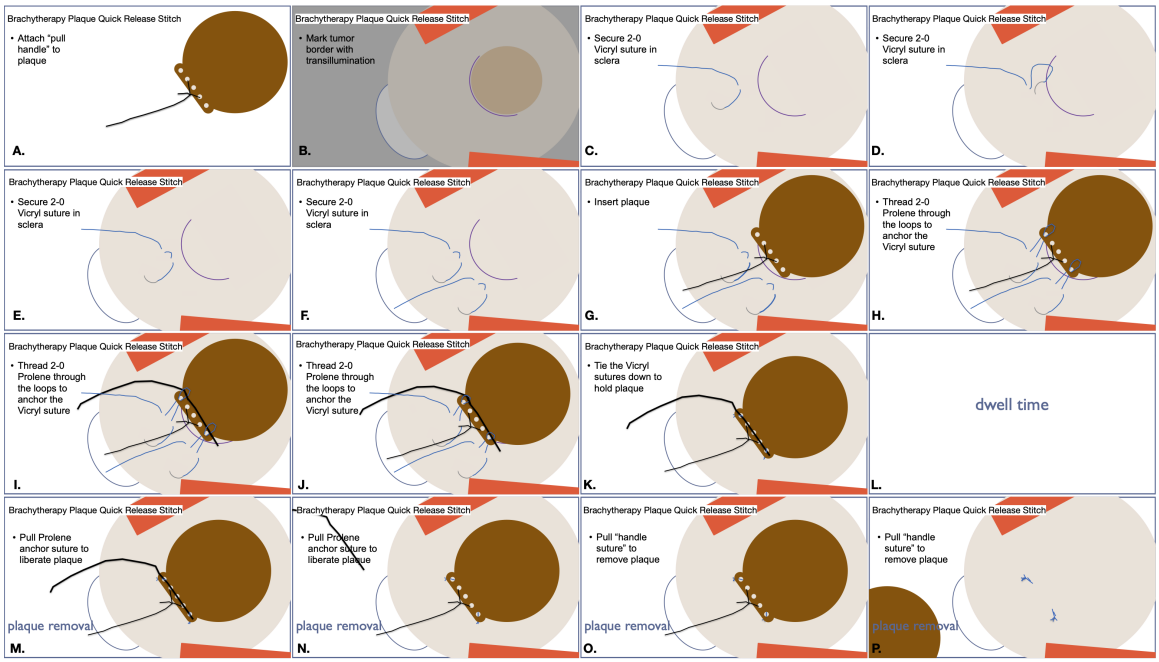

Brachytherapy Plaque Quick Release Stitch

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Ocular Oncology Symposium

Impact of Confirmatory Cytopathology on the Predictive Value of Gene Expression Profiling in Uveal Melanoma

- Ivana Kim, MD
- Caleb Hartley
- Disorn Suwajanakorn, MD
- Ashley Go
- Mary Aronow, MD
- Frances Wu, MD
- Evangelos Gragoudas, MD
- Anne Marie Lane, MPH

Objective: To determine if a commercial gene expression profiling assay has similar prognostic accuracy in samples with and without confirmatory cytopathology.
Purpose: To compare rates of metastasis in patients with uveal melanoma (UM) who underwent gene expression profiling (GEP) [DecisionDx-UM, Castle Biosciences] and confirmatory cytopathology (CP) to patients who had GEP alone.
Methods: A retrospective review identified patients diagnosed with UM at Mass Eye and Ear who underwent fine needle aspiration biopsy prior to proton therapy between 2013-2020. Patients were divided by CP status: those with CP results confirming or suspicious for UM along with GEP (GEP+CP group), and those who had no CP or non-diagnostic CP results (GEP group). Patient age, baseline tumor dimensions, development of metastatic disease, and time to metastatic disease were assessed.

Results: One hundred and forty patients had GEP results, 98 (70%) with CP and 42 (30%) without CP. Patients in the GEP+CP group were older (median age: 62.8 v. 55.0 years, P=0.02) with larger tumors (median tumor thickness 5.0 v. 3.1 mm, P=0.0001; largest basal diameter 14 v. 13.8 mm, P=0.69) than those in the GEP group. Median follow-up was 3.6 v. 4.3 years in the GEP+CP and GEP groups, respectively (P=0.21). In the GEP+CP group, 24 (24.5%) patients were diagnosed with metastasis versus 7 (16.7%) in the GEP group (P=0.38). GEP class for the GEP+CP and GEP groups, respectively, were as follows: 1A: 38 (38.8%) v. 20 (47.6%); 1B: 20 (20.4%) v. 15 (35.7%); 2: 40 (40.8%) v. 7 (16.7%) [P=0.01]. In those with class 1A tumors, 3 v. 2 patients developed metastasis in the GEP+CP and GEP groups (7.9% v. 10.0%, P=1.0). Three class 1B patients in the GEP+ CP group v. 1 class 1B patient in the GEP group developed metastasis (15.0% v. 6.7%, P=0.62). Among patients with class 2 tumors, 18 (45.0%) developed metastasis in the GEP+CP group compared to 4 (57.1%) in the GEP group (P=0.69). The 5-year rate of metastasis in patients with class 2 tumors was 49.7% (95% CI: 32.5-70.0) in the GEP+CP group and 57.1% (95% CI: 26.6-90.0) in the GEP group (P=0.77). Median time from UM diagnosis to metastasis in the GEP+CP and GEP groups, respectively, was 24.5 v. 21.1 months in patients with class 1A tumors (P=0.80), 37.8 v. 68.6 months in class 1B tumors (P=1), and 19.0 v. 21.5 months in class 2 tumors (P=0.85).

Conclusion: Within each GEP tumor class, we did not find significant differences in rates of metastasis between patients with and without confirmatory CP. Such findings suggest GEP is adequate for risk prediction even without cytologic confirmation of biopsy specimens. Additional analyses of the a larger cohort to validate these findings will be beneficial.

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Ocular Oncology Symposium

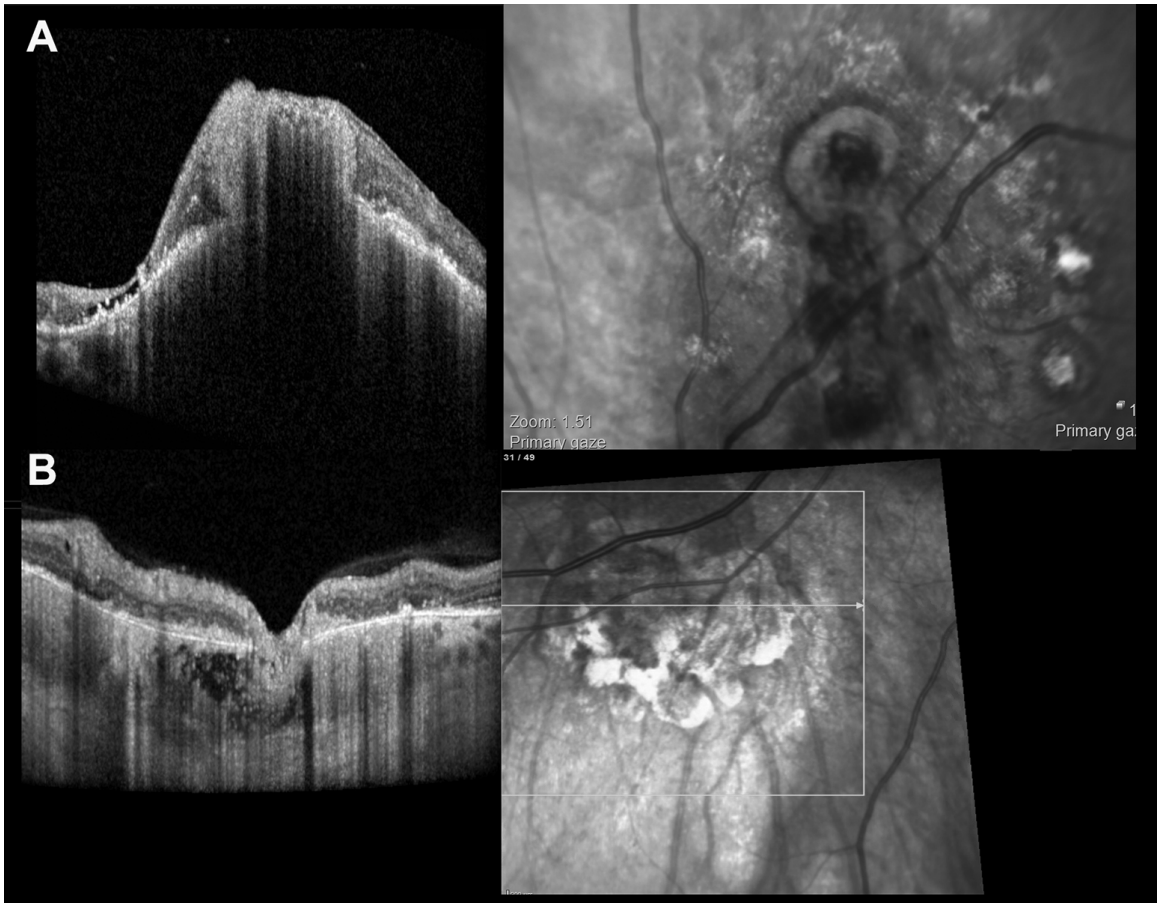
OCT Evaluation of Morphologic Changes at FNAB Site After Transvitreal Approach for Melanocytic Choroidal Tumors

- Zelia Correa, MD, PhD
- J. William Harbour, MD
- James Augsburger, MD

Objective: What are the morphological changes occurring in the retina post transvitreal FNAB of choroidal melanocytic tumors?
Purpose: Transvitreal FNAB (fine needle aspiration biopsy) of choroidal melanocytic tumors for diagnostic and prognostic purposes are becoming the standart of care for these tumors. There is no consensus on the optimal surgical technique. There is a lot of debate around the need for laser and even tamponade to avoid vitreous hemorrhage or rhegmatogenous retinal detachment after transvitreal FNAB. The purpose of this stury is to describe the morphological features of the FNAB puncture site after transvitreal approach through the retina performed without vitrectomy, vitreous tamponade and retinopexy.
Methods: Retrospective review of consecutive patients evaluated by diagnostic or prognostic FNAB for their choroidal melanocytic tumor over a two-year period. Inclusion criteria were patients sequentially evaluated by OCT pre and post FNAB with sufficient quality to assess the puncture site.

Results: Of 155 patients undergoing transretinal tumor biopsies during the study period, 88 of them were transvitreal, and of those, 56 fulfilled the inclusion criteria. None of the patients developed a retinal detachment or tumor seeding. Preoperative findings on OCT included PVD (31%), intraretinal fluid (30%), and subretinal fluid (89%). At 3 months, a PVD was present in 36%, vitreous plugging of the biopsy site could be seen in 45%, and herniated tumor through the puncture site was present in 5%. At 6 months, two distinct morphological patterns could be observed – a plugging of the retinal defect with subretinal/choroidal tissue in 45% and a flat, open hole with attached edges in 55%. One- and 2-years post FNAB, these wound healing patterns persisted. In the group with open holes, some patients presented a covering of the defect with atrophic retina, but no retinal tissue could be seen within the hole in the choroidal plug group.
Conclusion: Our results suggest that transvitreal FNAB for choroidal tumors performed without vitrectomy, tamponade or retinopexy is able to provide a stable outcome and satisfactory healing of the retina puncture site.

IRB APPROVAL No - exempt



A- choroidal plug presentation and, B- atrophic hole presentation post-FNAB

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Ocular Oncology Symposium

Management of Complex Retinal Detachment in the Setting of Conservatively Treated Uveal Melanoma

- Timothy Murray, MD, MBA, FASRS
- Aaron Gold, OD
- Azeema Latiff, RN, BSN, MBA

Objective: This study documents the relative rarity of complex retinal detachments in eyes with definitively treated uveal melanoma, documents the approach to surgery, and establishes the outcome for these patients.
Purpose: To report the presenting signs, surgical management, and outcomes for complex retinal detachment in the setting of treated uveal melanoma with confirmed GEP obtained via fine needle aspiration biopsy.

Methods: IRB approved consecutive case series of 372 patients with confirmed GEP obtained via fine needle aspiration biopsy in the setting of treated uveal melanoma. Uveal melanoma patients with Rhegmatogenous retinal detachment developing after treatment were identified. All patients were followed from biopsy treatment with serially evaluation including ocular oncology comprehensive evaluation utilizing widefield imaging, sdOCT, and quantitative a/b scan ultrasound to confirm ocular tumor stability and to direct targeted anti- VEGF treatment for tumor related maculopathy. Targeted medical oncology evaluation was based on GEP status per NCCN guidelines. For patients developing Rhegmatogenous retinal detachment, surgical repair was performed using 23 gauge valved micro-incisional vitrectomy with direct surgical repair followed by 1000 centistoke silicone oil tamponade.

Results: 7/372 patients developed complex retinal detachment in this cohort of all treated patients with GEP classification. Mean interval to retinal detachment progression was 8.2 months. Each eye had PVR present with the detachment. 7/7 eyes were macular off. Pre-operative VA was a mean of 20/400. All 7 patients underwent surgical repair with silicone oil placement. All patients were successfully repaired with a mean VA 0f 20/63. No tumor exhibited tumor control failure. All 7 patients are alive and well at a mean follow-up of 53 months (range 6- 120 months). No patient required enucleation. All eyes developed retinopathy and have received anti-VEGF treatment.

Conclusion: Treated uveal melanoma patients undergoing gene expression profiling by fine needle aspiration biopsy have an infrequent development of complex retinal detachment (1.9%, 7/372 eyes). Post-treatment uveal melanoma eyes are amenable to advanced vitreoretinal surgical repair and recover anatomic stability, visual improvement while avoiding enucleation.

IRB APPROVAL Yes