10/11/2021 3:35PM

A Phase 2 Safety and Efficacy Trial of AU-011, a Virus-Like Drug Conjugate, With Dose Escalation and Randomized Masked Expansion in Uveal Melanoma

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OBJECTIVE To evaluate safety and efficacy with recommended pivotal dose/regimen of AU-011 via suprachoroidal (SC) administration for treating primary indeterminate lesions and small choroidal melanoma (IL/CM)

PURPOSE Many IL and small CMs are monitored closely and subsequently treated with radiotherapy which is associated with adverse effects including irreversible vision loss. AU-011, an investigational novel, targeted VDC is being evaluated in a Phase 2 trial. Trial design using SC administration, interim safetyand the maximum tolerated dose from the open-label dose escalation phase will be presented.

METHODS Clinically diagnosed subjects with IL/CM with tumor thickness from 0.5 - 3.0 mm and largest basal diameter ≤13 mm received SC administration of AU-011 at doses of 20µg or 40µg followed by application of Near Infrared light with a laser at a fluence of 50 J/cm2. Regimens consisting of 1, 2 or 3 weekly treatments (one cycle) with AU-011 each followed by 1 or 2 laser applications have been evaluated in 5 dose escalation cohorts with the last cohort to receive up to two cycles of treatment. The randomized, masked expansion phase plans to enroll 40 subjects in a 2:1:2 ratio to receive up to 2 cycles of 40µg AU-011,

20µg AU-011 or sham treatment, and will serve as the first pivotal trial.

RESULTS 12 subjects have been enrolled in the dose escalation phase of the trial with single and repeat doses up to one cycle for Cohorts 1 through 5, and with two cycles planned for Cohort 5. No serious adverse events, dose limiting toxicities or severe (grade 3) adverse events have been reported to date. Key treatment-related adverse events included two reports of mild anterior chamber inflammation in Cohorts 2 & 5 and one report of moderate anterior scleritis in Cohort 3. These events were treated with standard of care therapy, were transient and resolved without sequelae, indicating AU-011 was generally well-tolerated for this route of administration. The maximum treatment regimen anticipated for the randomized phase is two cycles of three weekly treatments of AU-011 at a dose of 40µg with 2 laser administrations.

CONCLUSION Preliminary results of the trial indicate a positive tolerability profile for AU-011 via suprachoroidal administration with all treatment regimens assessed to date. The randomized phase of the trial is planned to begin later in 2021 in subjects with documented growth to establish the safety and efficacy of AU-011 and serve as the first pivotal trial for the treatment of IL/CM.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.

10/11/2021 3:47PM

Comparison of Tumor Size at Presentation and Genomics in Uveal Melanoma Patients Before and After the COVID-19 Pandemic

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- Bin Teh, MD

OBJECTIVE The objective of this study is to examine the difference in the time at presentation of uveal melanoma before and after the onset of the COVID-19 pandemic.

PURPOSE Studies in general medical oncology have demonstrated that one of the devastating effects of the COVID-19 pandemic has been a later presentation of patients with many cancer types. The purpose of this study was to analyze the size at presentation and genomics of uveal melanoma tumors before and after the COVID-19 pandemic.

METHODS This is a retrospective single center matched cohort study examining 40 patients diagnosed with uveal melanoma and treated in 2019 before the pandemic versus 40 patients treated from April-September 2020 after the pandemic began. Clinical and genomic variables examined to assess disease stage at presentation included: thickness and largest base diameter of tumor at presentation; AJCC Class and COMS size, GEP class; Prame status; and presence of prognostic driver mutations.

RESULTS Among pre-pandemic patients, median tumor thickness was 3.2mm (range 1.4-10.6), and median largest basal diameter was 11.5mm (range 5.5-21), compared to a similar 2.9mm (range 1.2-15) and 11.5mm (range 4-20.5) among post-pandemic patients (P=.719 and .834, respectively). AJCC staging was also similar for the pre/post pandemic cohorts with 44/44% Stage I, followed by 23/26% IIA, 15/15% IIB, 10/8% IIIA, 8/5% IIIB, and 0 presenting at Stages IIIC and IV in either group (P=.984). Pre-pandemic COMS size distribution was 41% small, 36% medium, and 23% large, versus 38% small, 44% medium,

and 18% large tumors in the post-pandemic group (P=.751). At presentation before the pandemic, most patients (69%) were GEP Class 1A, followed by 8% Class 1B and 23% Class 2, and 28% were PRAME positive. Genomics were similar after the start of the pandemic (P=.520), with 61% Class 1A, 16% Class 1B, and 24% Class 2, while 32% were PRAME positive.

CONCLUSION The current study did not identify any significant differences in uveal melanoma stage, size, and genomics at presentation among patients treated before and during the ongoing COVID-19 pandemic. Further long-term studies are needed to assess the ultimate impact of the pandemic on patient presentation with uveal melanoma.

IRB APPROVAL Not applicable — I responded “No” to previous question regarding human subjects.

10/11/2021 3:51PM

Combined MIVS/Phacoemulsification for Concomitant Management of Retinal Pathology With Cataract: 5-Year Follow-up of a Large, Consecutive Case Series

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OBJECTIVE To evaluate the long-term impact of combined MIVS/Phacoemulsification targeted to visual and anatomic improvements, along with safety, in eyes with concomitant retinal disease and cataract.

PURPOSE To evaluate a large, consecutive case series of 648 eyes undergoing MIVS combined with phacoemulsification inclusive of a minimum followup of 24 months and a mean followup of 5 years, evaluated by indication for surgery, visual and anatomic outcomes, and short/long-term complications.

METHODS IRB approved retrospective review of a consecutive case series of 648 eyes of 611 patients undergoing combined MIVS (23/25 gauge) with phacoemulsiviation/IOL implantation between December 2012 and January January 2016. Impact of ICG guided ILM peeling and intravitreal triamcinolone acetonide will be presented. Mean patient age was 66 years (29-83). 324 patients were women (53%). 343 eyes had intraocular tumor (53%), 169 eyes with erm/VMT (26%), and 136 eyes with PDRTRD (21%). All eyes were followed for resolution of retinal pathology, VA, IOP, sdOCT, and post-MIVS complications.

RESULTS Mean patient age was 66 years. Minimum followup was 36 and mean was 60 months (36 -96 months). Entry level VA was LogMAR 0.983 (20/192) and improved at all timepoints: 3 months 0.810, 6 months 0.675, 12 months 0.371 and remained stable through 36 months at 0.371 (20/46) [p<0.02]. Overall 557/648 eyes experienced 3 line VA gain (86%). OCTA CPT at entry was 467 microns and at year 3 was 301 microns, (P<0.01). All 648 eyes recieved a PCIOL without compromise. Intraoperatively 25 cases had capsular tears (3.9%), while postoperatively 21 cases had vitreous hemorrhage (3.2%), epiretinal

membrane formation (1.7%), and retinal detachment (1.8%). Post-op day 1 hypotony was seen in 4 eyes (0.06%). Predictors of best VA outcomes was better entry level vision for all subsets undergoing surgery. Predcictors for worse VA outcomes was pre-surgical ongoing anti-VEGF treatment for macular edema followed by persistent macular edema requiring anti-VEGF treatment.

CONCLUSION Combined MIVS/Phacoemulsification with IOL implantation achieves excellent visual and anatomic outcomes in this large consecutive case series with extended followup. Shifting demographics and drivers to cost containment favor a re-evaluation of combined surgery in these complex eyes.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.