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Volumetric Fluid Assessment Comparing High-Dose Aflibercept to Standard Dose Aflibercept in Neovascular Age-Related Macular Degeneration in the CANDELA Phase 2 Trial

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Purpose

To evaluate the impact of aflibercept (IAI) 2 mg and IAI High Dose (IAI-HD) 8 mg on volumetric fluid dynamics in neovascular age-related macular degeneration (nAMD) in the CANDELA Phase 2 clinical trial.

Methods

- The CANDELA clinical trial is a phase II randomized, double-masked, active-controlled study comparing the impact of dosage of IAI in fluid volume in eyes with nAMD.
- Subjects were randomized 1:1 between treatment groups (IAI 2 mg and IAI-HD 8 mg).
- Following 3 monthly loading doses, IAI and IAI-HD groups were extended to q12 week dosing with as needed dosing in between intervals.
- Macular cube scans were analyzed in a machine learning enhanced retinal segmentation/ feature extraction platform for evaluation of intraretinal fluid (IRF) and subretinal fluid (SRF) volumetric assessment.
- Following automated segmentation, a certified reader reviewed every B-scan for segmentation accuracy.
- Quantification of fluid features were analyzed and compared between treatment groups.

Results

IAI (2 mg)

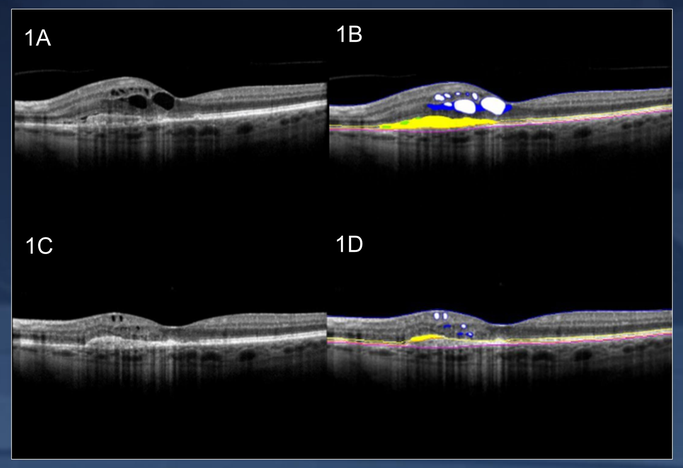


Figure 1: Foveal slice of IAI patient. 1A: Raw baseline, 1B: Fluid overlay baseline, 1C: Raw w16, 1D: Fluid overlay w16.

IAI-HD (8 mg)

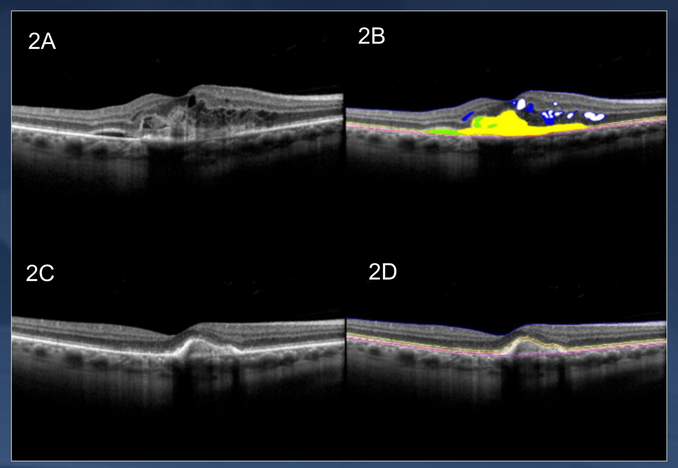
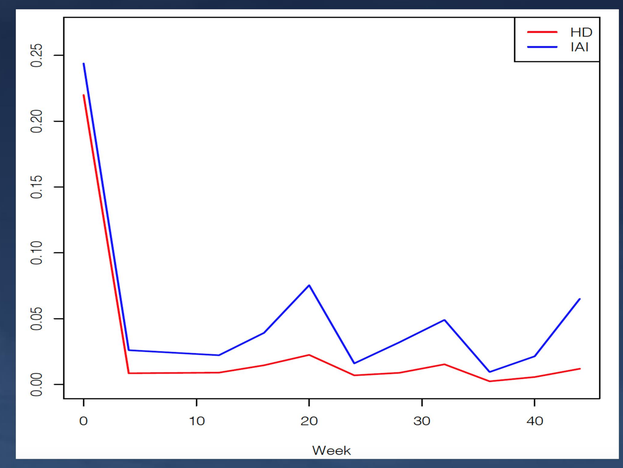


Figure 2: Foveal slice of IAI patient. 2A: Raw baseline, 2B: Fluid overlay baseline, 2C: Raw w16, 2D: Fluid overlay w16.

IRF Volume



- 104 eyes were included in the volumetric fluid analysis (51 IAI, 53 IAI-HD).
- At baseline, volumetric fluid metrics were similar between both groups.
- At week 44, both groups demonstrated significant fluid reduction.
  - IAI: 73% reduction in IRF, 85% reduction in SRF vs IAI-HD: 95% reduction in IRF, 87% reduction

Treatment Group	Baseline Mean IRF volume	Baseline Mean SRF volume	W44 IRF Mean volume	W44 SRF Mean volume
IAI (2 mg)	0.243mm^3	0.443mm^3	0.065mm^3	0.067mm^3
IAI-HD (8 mg)	0.220 mm^3	0.450mm^3	0.012mm^3	0.059mm^3

Conclusions

- Both IAI and IAI-HD demonstrated dramatic reductions in IRF and SRF volumes in nAMD in the CANDELA trial that were maintained through week 44 with an extended dosing interval.
- IAI-HD demonstrated a particularly dramatic (95%) dramatic reduction in IRF with an apparent greater stability of fluid reduction reflected by lower amplitude oscillations of fluid volume

Disclosures

- **JM:** None; **RA**: None; **KM**: None; **AI**: None; **LDV**: None; **MB**: None; **AT**: None; **YC**: None; **HC**: None; **CT**: None; **DB**: None; **EF**: None; **JB**: None; **RV**: None; **KZ**: None; **VW**: None; **JR**: None; **SKS**: Bausch and Lomb, Adverum, Novartis, Regeneron (C), Leica (P), Regeneron, Allergan, Gilead (F); **JPE**: Zeiss, Leica/Bioptigen, Alcon, Beyeonics. Allergan, Allegro, Adverum, Regeneron, Roche, Genentech, RegenxBIO, Iveric Bio, Boehringer Ingelheim, Apellis, Novartis, Boehringer Ingelheim, Stealth Biotherapeutics, Perceive Biotherapeutics, Exegenesis, Ophthalytics, Eyepoint, Abbvie, Bayer, BVI, Alexion, Ocular Therapeutix (C) Regeneron, Genentech, Oxurion/Thrombogenics, Alcon, Aerpio, Allergan, Roche, Iveric Bio, Boehringer Ingelheim, Adverum, Novartis, Zeiss, Stealth Biotherapeutics, Perceive Biotherapeutics, Alexion, Beyeonics, Ocular Therapeutix (F) Bioptigen/Leica (P)

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