

Prolonged Intraocular Residence of a Fourth Generation Compstatin Complement C3 Inhibitor Supports Its Clinical Development for Geographic Atrophy

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Financial Disclosures

- B.J.K. Consultant: Synergy Research Inc., Allergan
- J.D.L. is the founder of Amyndas Pharmaceuticals, which is developing complement inhibitors (including AMY-106), and inventor of patents or patent applications that describe the use of complement inhibitors for therapeutic purposes, some of which are developed by Amyndas Pharmaceuticals. J.D.L. is also the inventor of the compstatin technology licensed to Apellis Pharmaceuticals (4(1MeW)7W, also known as POT-4 and APL-1) and PEGylated derivatives such as APL-2.



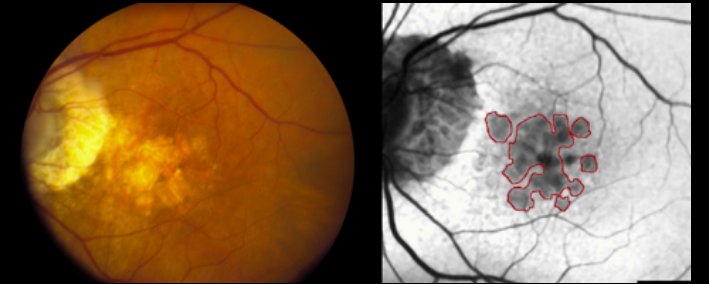
Summary

- Finding a treatment for geographic atrophy remains a top priority.
- Complement inhibition is currently the most promising approach in clinical trials for geographic atrophy.
- A fourth generation compstatin Complement C3 inhibitor (Cp40-KKK, AMY-106) can block C3 for at least 3 months with a single intravitreal injection.
- Cp40-KKK localizes primarily to the choriocapillaris and Bruch's membrane.
- A Phase I trial for Cp40-KKK is being developed.



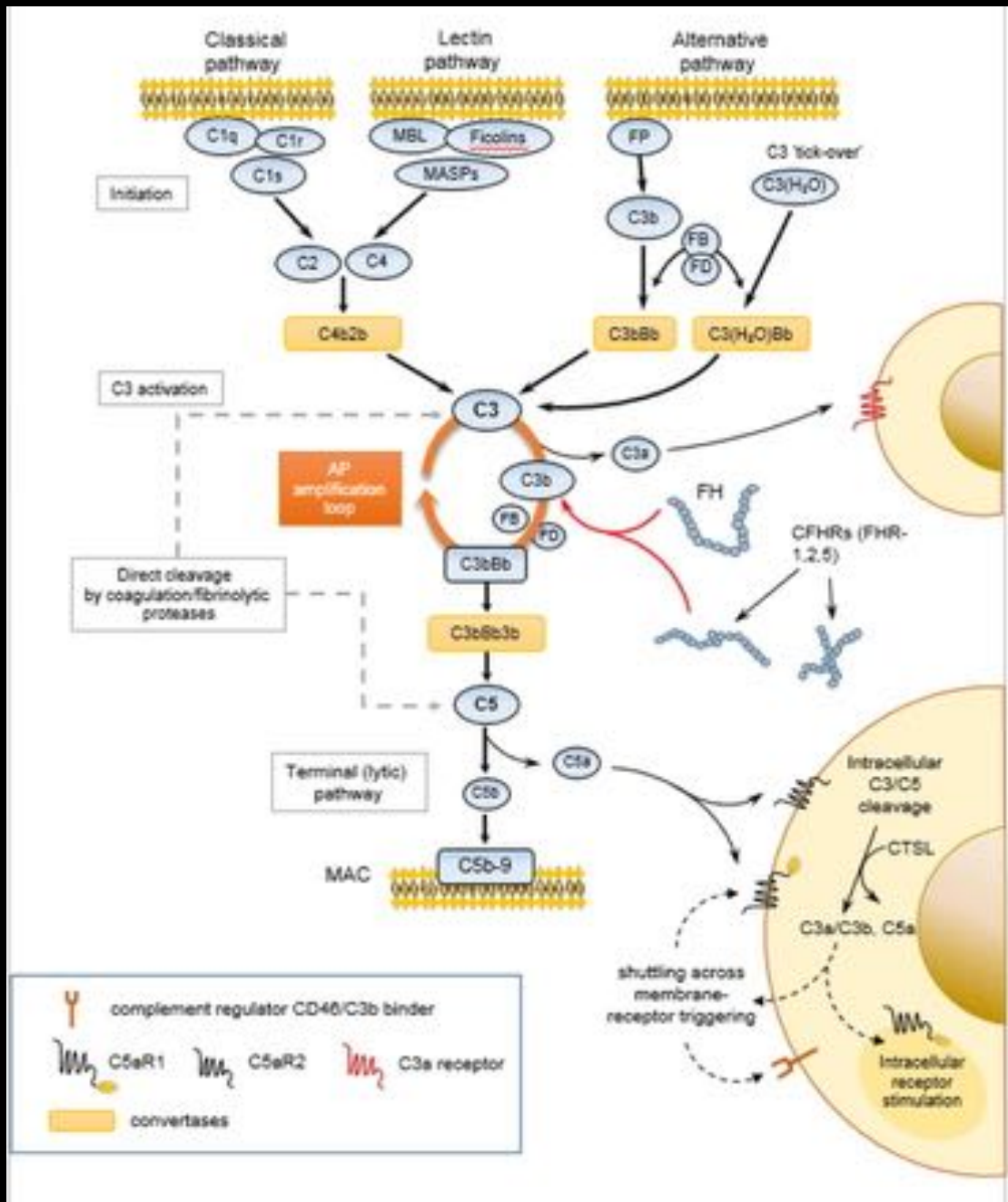
Geographic atrophy (GA) is estimated to affect over 8 million people worldwide.

No effective therapy yet available



Complement dysregulation is a key component of GA pathophysiology
-dysfunction of complement alternative pathway
-**complement inhibition** is at the forefront of GA clinical trials





- C3 is the converging point for all 3 complement pathways

- C5 leads to the membrane attack complex (MAC) that lyses cells



Apellis Phase III trials ongoing.

- pegcetacoplan: PEGylated C3 inhibitor
- monthly or every other month injection

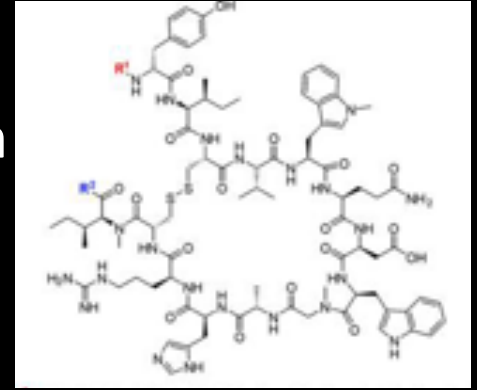
Iveric Bio Phase III trial

- avacincaptad pegol: PEGylated anti-C5 aptamer
- monthly injection

Both showed efficacy in Phase II, but with more than expected conversions to exudative AMD.



- Compstatins are a family of synthetic peptide C3 inhibitors
 - Pegcetacoplan/APL-2 is a PEGylated earlier generation compstatin



Berger N, *J Med Chem* 2018

- Cp40-KK and Cp40-KKK (Amyndas Pharmaceuticals) are 4th generation compstatins
 - Improved solubility (small molecule that is Not PEGylated)
 - Improved target affinity
 - Improved pharmacokinetic profile



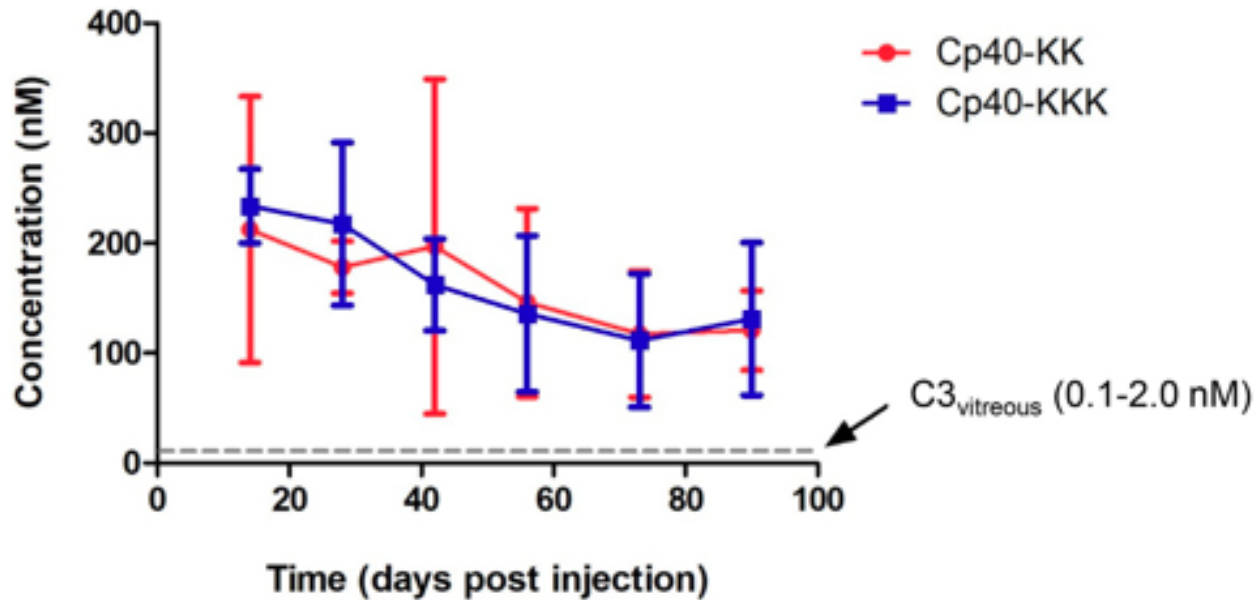
- We evaluated the intraocular pharmacokinetic profile and location of Cp40-KK and CP40-KKK
- Methods:
 - Monkeys given intravitreal injection of 500 μg of Cp40-KK or Cp40-KKK. Fifty μl of vitreous sampled at multiple time points out to 90 days.
 - Monkeys given intravitreal injection of Cp40-KKK, euthanized after 1 month, immunohistochemistry performed to evaluate retinal tissue distribution of Cp40-KKK and C3.



A single IVT injection of the Fourth-Generation Compstatin Cp40-KKK Saturates C3 For 3 Months

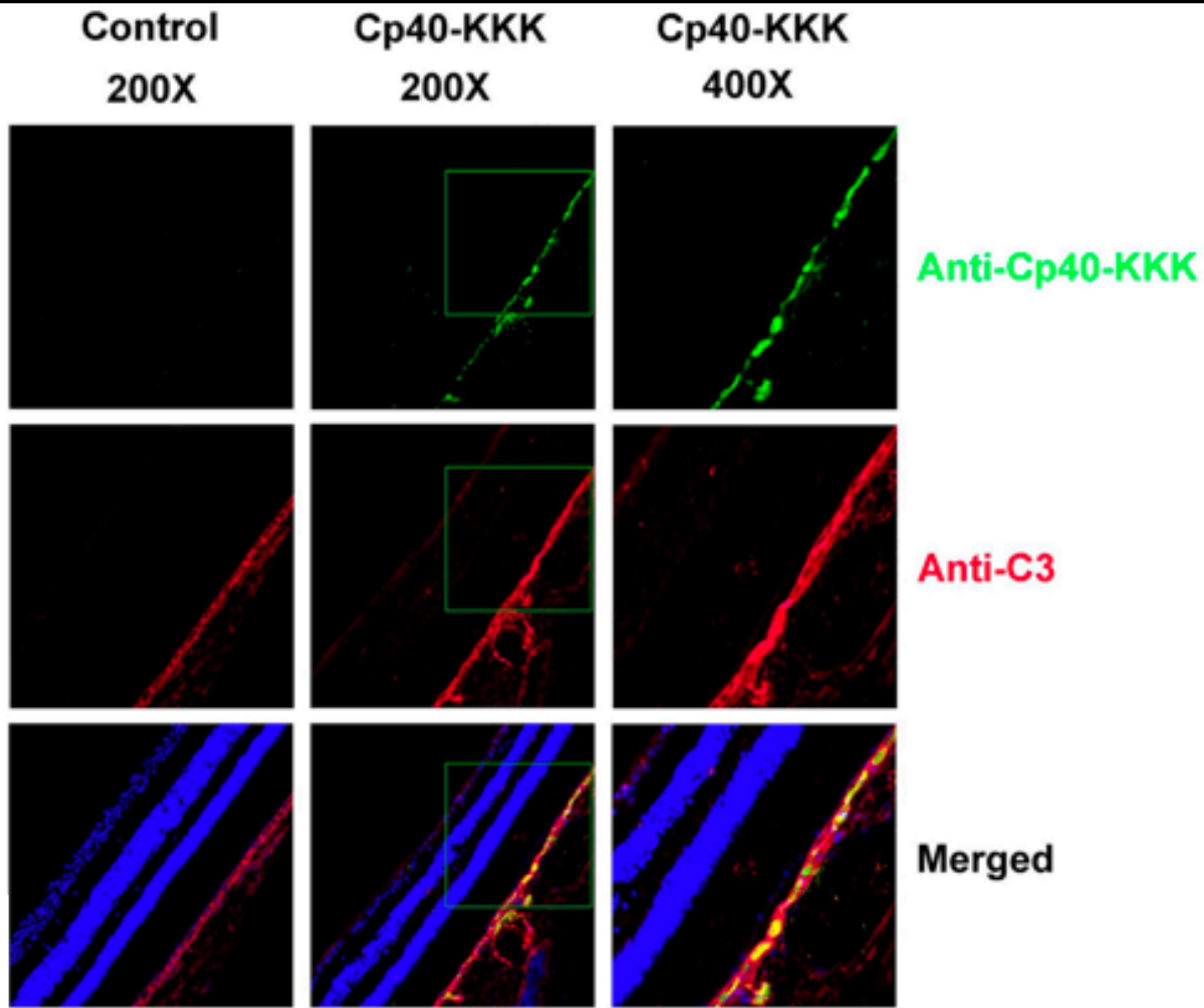


Intravitreal injection:
0.5 mg C3 inhibitor/eye



- Both 4th generation compstatins Cp40-KK and Cp40-KKK were detectable at 90 days and remained at concentrations that exceeded the average local concentration of C3 by about 100 fold.
- The two compstatin analogs not only exhibited prolonged intraocular residence but were fully active in binding to C3.





- C3 target driven distribution profile.
- Localized predominantly to the choriocapillaris and Bruch's membrane.
- Demonstrates retina and RPE penetration.



- These data support the clinical development of Cp40-KKK (AMY-106) as a treatment for GA.
 - Significant benefit for less frequent injections for GA.
 - > 3 month injection intervals may be possible
- Data evaluating > 3 months inhibition of C3 is pending.
- Phase I trial is in development



Thanks for your attention!

For additional information:

- Hughes S, Gumas J, Lee R, Romano M, Berger N, Gautam AK, Sfyroera G, Chan AL, Gnanaguru G, Connor KM, Kim BJ, Dunaief JL, Ricklin D, Hji shengallis G, Yancopoulou D, Reis ES, Mastellos DC, Lambris JD. Prolonged intraocular residence and retinal tissue distribution of a fourth generation compstatin-based C3 inhibitor in non-human primates. *Clinical Immunology*, 2020

