

The Future



Treating C3 Glomerulopathy

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C3 Glomerulopathy Family Support Group – October 2022

Disclosures

The following includes a list of current (within the last 24 months) affiliations:

| Affiliation / Financial Interest | Organization |
|-----------------------------------|--|
| Associate Director | Molecular Otolaryngology and Renal Research Laboratory |
| NIH | 1R01DK110023-01A1 |
| Site Investigator | ChemoCentryx |
| Site Investigator | Alexion Pharmaceuticals |
| Site Investigator, Advisory Board | Novartis |
| Site Investigator | Retrophin |
| Site Investigator, Advisory Board | BioCryst |
| Site Investigator, Advisory Board | Apellis |
| Data Safety Monitoring Board | Kira |
| Author Royalties | UpToDate |

My conflicts are managed by a University of Iowa mandatory conflict plan.
Both prior and current relationships are on record at the University of Iowa's Conflict in Research Office:

<https://coi.research.uiowa.edu/>

Objectives

- Quickly review how to find a clinical trial
- Understand inclusion and exclusion criteria for trials
- Understand the features of a given trial
- Quickly review published data on current trial agents

How to find a trial

– No complement drugs in last 6 months



• Sample exclusions

- Age (most are 12 and older)
- Not all accept transplant
- Urine protein too low
- Too much scarring
- eGFR below 30

<https://clinicaltrials.gov/>

NIH U.S. National Library of Medicine

ClinicalTrials.gov

Find Studies ▾ About Studies ▾ Submit Studies ▾ Resources ▾ About Site ▾ PRS Login

ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.

Explore 430,425 research studies in all 50 states and in 221 countries.

See [listed clinical studies related to the coronavirus disease \(COVID-19\)](#)

ClinicalTrials.gov is a resource provided by the U.S. National Library of Medicine.

IMPORTANT: Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our [disclaimer](#) for details.

Before participating in a study, talk to your health care provider and learn about the [risks and potential benefits](#).

Find a study (all fields optional)

Status ⓘ

- Recruiting and not yet recruiting studies
- All studies

Condition or disease ⓘ (For example: breast cancer)

C3 Glomerulopathy X

Other terms ⓘ (For example: NCT number, drug name, investigator name)

X

Country ⓘ

X

| | | | | | | |
|---|--------------------------|------------|---|---------------------------|---|--|
| 1 | <input type="checkbox"/> | Completed | Controlled Trial Evaluating Avacopan in C3 Glomerulopathy | • C3 Glomerulopathy (C3G) | • Drug: Avacopan • Drug: Avacopan Matching Placebo | • Clinical Site Palo Alto, California, United States • Clinical Site Chicago, Illinois, United States • Clinical Site Iowa City, Iowa, United States • (and 38 more...) |
| 2 | <input type="checkbox"/> | Recruiting | OL Extension Study of LNP023 in C3G | • C3 Glomerulopathy | • Drug: LNP023 | • Novartis Investigative Site Iowa City, Iowa, United States • Novartis Investigative Site Montpellier, France • Novartis Investigative Site Paris, France • (and 6 more...) |

How to find a trial: <https://clinicaltrials.gov/>

Eligibility Criteria

Information from the National Library of Medicine



Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, [Learn About Clinical Studies](#).

Ages Eligible for Study: 12 Years and older (Child, Adult, Older Adult)
Sexes Eligible for Study: All
Accepts Healthy Volunteers: No

| | | | | | | |
|---|--------------------------|------------|---|---|--|--|
| 1 | <input type="checkbox"/> | Completed | Controlled Trial Evaluating Avacopan in C3 Glomerulopathy | <ul style="list-style-type: none">• C3 Glomerulopathy (C3G) | <ul style="list-style-type: none">• Drug: Avacopan• Drug: Avacopan Matching Placebo | <ul style="list-style-type: none">• Clinical Site Palo Alto, California, United States• Clinical Site Chicago, Illinois, United States• Clinical Site Iowa City, Iowa, United States• (and 38 more...) |
| 2 | <input type="checkbox"/> | Recruiting | OL Extension Study of LNP023 in C3G | <ul style="list-style-type: none">• C3 Glomerulopathy | <ul style="list-style-type: none">• Drug: LNP023 | <ul style="list-style-type: none">• Novartis Investigative Site Iowa City, Iowa, United States• Novartis Investigative Site Montpellier, France• Novartis Investigative Site Paris, France• (and 6 more...) |

| | | | | |
|---|---|---|---|---|
| 1 | <input checked="" type="checkbox"/> Recruiting OL Extension Study of LNP023 in C3G | <ul style="list-style-type: none"> • C3 Glomerulopathy | <ul style="list-style-type: none"> • Drug: LNP023 | <ul style="list-style-type: none"> • Novartis Investigative Site Iowa City, Iowa, United States • Novartis Investigative Site Montpellier, France • Novartis Investigative Site Paris, France • (and 6 more...) |
| 2 | <input checked="" type="checkbox"/> Recruiting Evaluation of a Renin Inhibitor, Aliskiren, Compared to Enalapril, in C3 Glomerulopathy | <ul style="list-style-type: none"> • C3 Glomerulopathy • Membranoproliferative Glomerulonephritis • Complement Abnormality • (and 2 more...) | <ul style="list-style-type: none"> • Drug: Aliskiren • Drug: Enalapril | <ul style="list-style-type: none"> • Sahlgrenska Hospital Gothenburg, Sweden • Region Skåne Skåne Universitetssjukhus Lund, Sweden • Karolinska Hospital Stockholm, Sweden • Akademiska sjukhuset Uppsala, Sweden |
| 3 | <input checked="" type="checkbox"/> Recruiting Phase III Study Assessing the Efficacy and Safety of Pegcetacoplan in Patients With C3 Glomerulopathy or Immune-Complex Membranoproliferative Glomerulonephritis | <ul style="list-style-type: none"> • C3G • IC-MPGN • C3 Glomerulopathy • (and 9 more...) | <ul style="list-style-type: none"> • Drug: Pegcetacoplan • Other: Placebo | <ul style="list-style-type: none"> • University of Alabama at Birmingham Birmingham, Alabama, United States • Academic Medical Research Institute Los Angeles, California, United States • UCI Center for Clinical Research Orange, California, United States • (and 25 more...) |
| 4 | <input checked="" type="checkbox"/> Recruiting Study of ARO-C3 in Adult Healthy Volunteers and Patients With Paroxysmal Nocturnal Hemoglobinuria and Complement-Mediated Renal Disease | <ul style="list-style-type: none"> • Paroxysmal Nocturnal Hemoglobinuria • C3 Glomerulopathy • IgA Nephropathy | <ul style="list-style-type: none"> • Drug: ARO-C3 • Drug: Placebo | <ul style="list-style-type: none"> • Research Site 1 Camperdown, New South Wales, Australia • Research Site 2 Clayton, Victoria, Australia • Research Site 3 Clayton, Victoria, Australia • (and 17 more...) |
| 5 | <input checked="" type="checkbox"/> Recruiting Study of Efficacy and Safety of Iptacopan in Patients With C3 Glomerulopathy. | <ul style="list-style-type: none"> • C3G | <ul style="list-style-type: none"> • Drug: Placebo • Drug: iptacopan | <ul style="list-style-type: none"> • Novartis Investigative Site Aurora, Colorado, United States • Novartis Investigative Site Lawrenceville, Georgia, United States • Novartis Investigative Site Iowa City, Iowa, United States • (and 54 more...) |
| 6 | <input checked="" type="checkbox"/> Recruiting Study Assessing the Safety and Efficacy of Pegcetacoplan in Post-Transplant Recurrence of C3G or IC-MPGN | <ul style="list-style-type: none"> • C3G • IC-MPGN • Renal Transplant • (and 9 more...) | <ul style="list-style-type: none"> • Drug: Pegcetacoplan | <ul style="list-style-type: none"> • Keck School of Medicine, University of Southern California Los Angeles, California, United States • Children's Hospital Colorado Aurora, Colorado, United States • Washington University, St.Louis Saint Louis, Missouri, United States • (and 19 more...) |



Phase 1

Tests drug on healthy individuals

Tests for safety, dosage and side effects



Phase 2

Tests on larger group of effected individuals

Tests for efficacy and side effects



Phase 3

Tests on new and wider demographic

Tests for long term effectiveness and comparisons with other medications



FDA approval

Treatment determined effective and safe for public use

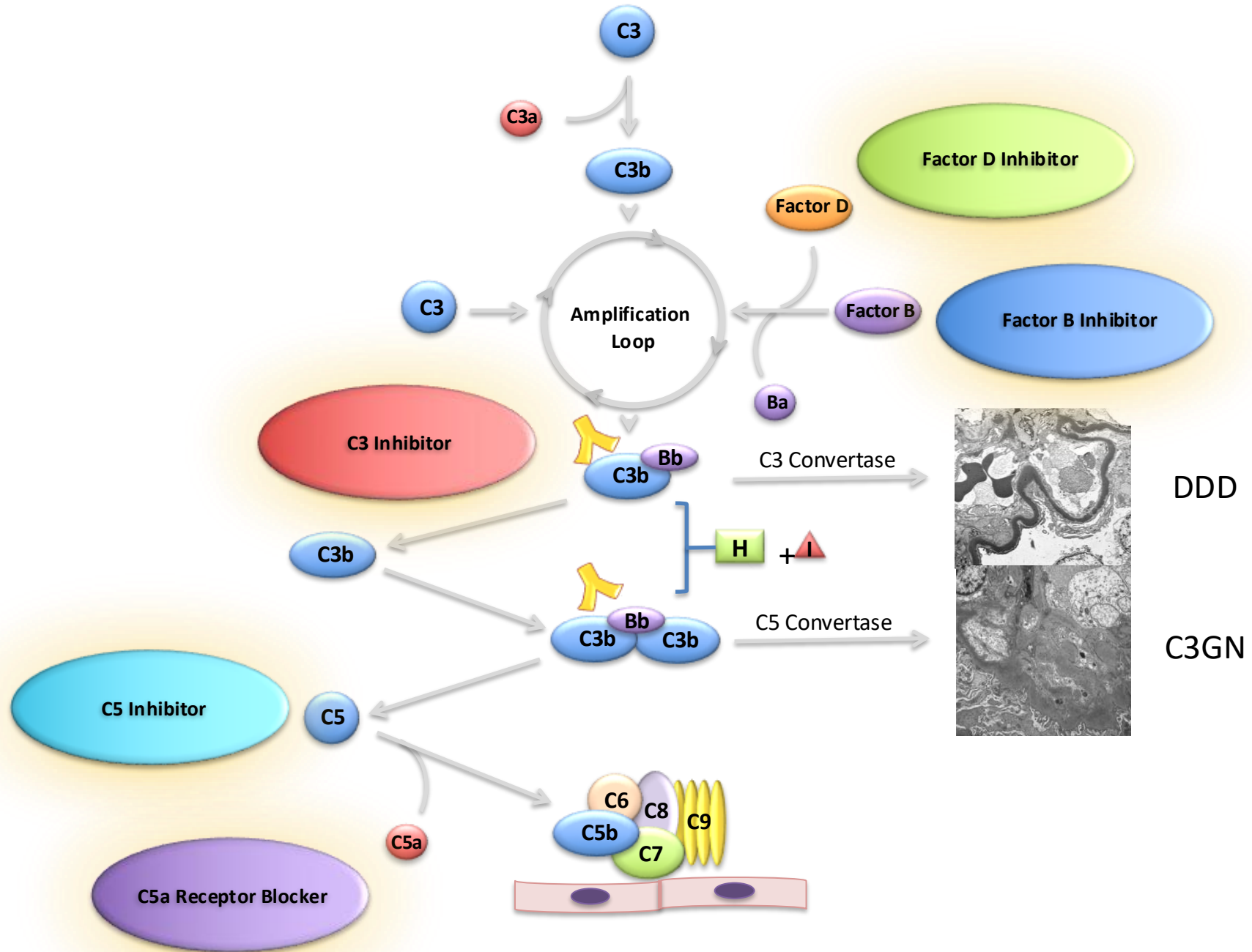


Phase 4

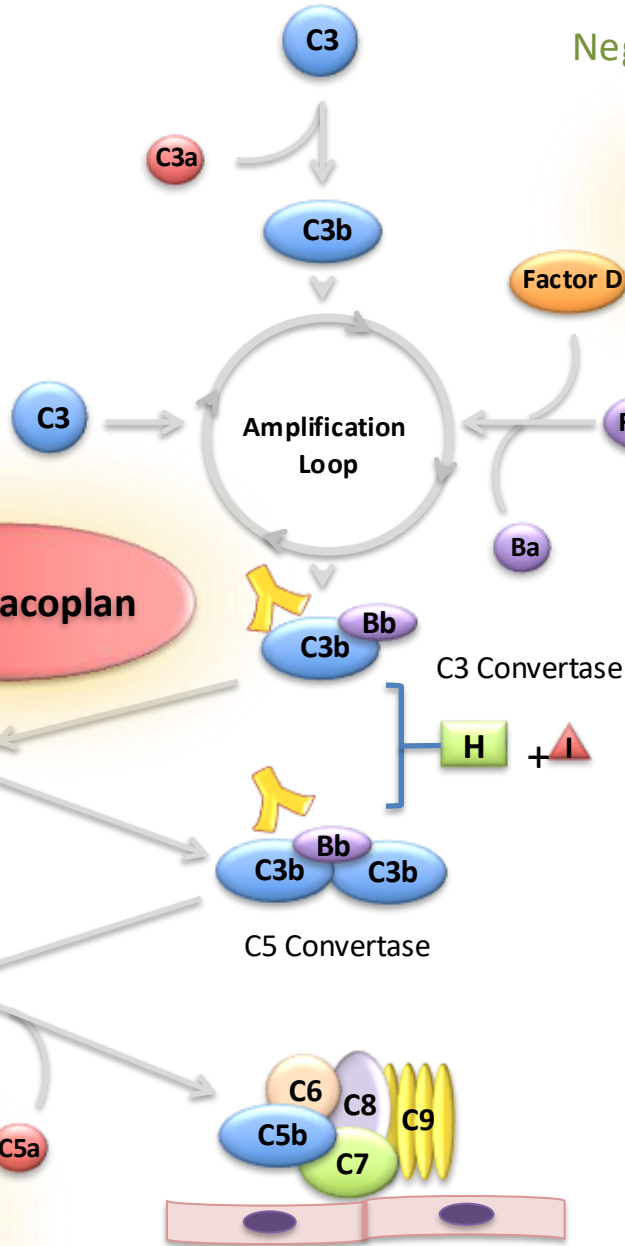
Continues to test for effectiveness and safety

Can be taken off the market if necessary

Alternative Pathway



Alternative Pathway



Negative Trial – Soon to be published in AJN

Danicopan

BCX9930

Iptacopan

Pegcetacoplan

Avacopan

Single Arm – 5 Patients
 1. 74% UPCR reduction at 48 w
 2. Significant increases in serum albumin and serum C3

ASN 2020

Placebo Controlled (26 and 26)
 Main outcome: Change in -disease activity in a second kidney biopsy at 26 w

Results:

1. No significant change in activity
2. Significant improvement in eGFR
3. Significant decrease of UPCR and urinary MCP-1
4. Significantly less progression of chronicity lesions

EDTA 2021

Single Arm

Cohort A (n=16) Native kidneys: Proteinuria reduction at 12w.

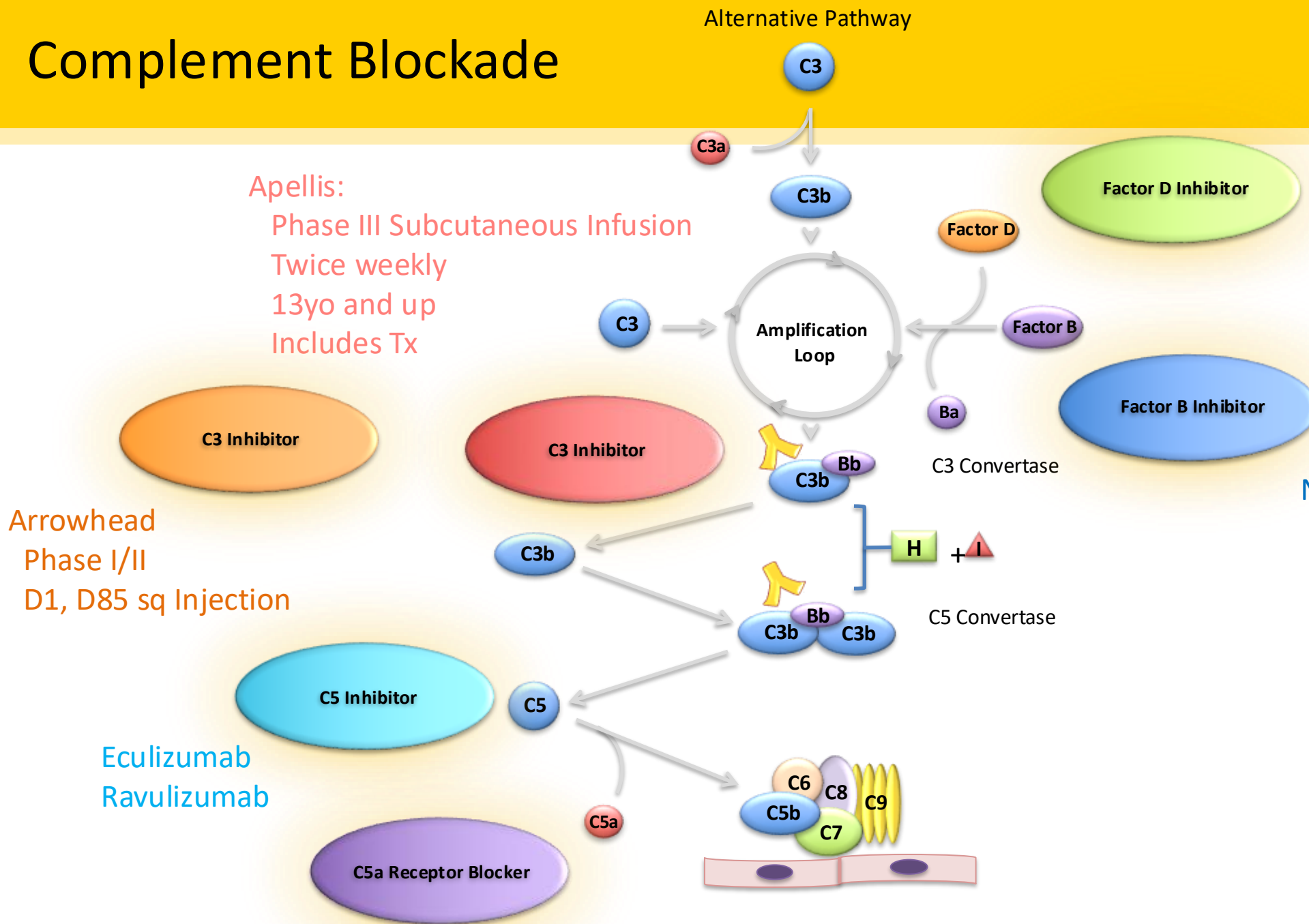
Cohort b (n=11) Transplant: Change in C3 IF at 12 w

Results:

1. 45% proteinuria reduction in Cohort A
2. Significant decrease of C3 deposit score in Cohort B

ASN 2021

Complement Blockade



Apellis:
Phase III Subcutaneous Infusion
Twice weekly
13yo and up
Includes Tx

BioCryst:
Phase II/III? open
in Europe
Oral
Twice daily
18yo and up

Arrowhead
Phase I/II
D1, D85 sq Injection

Novartis:
Phase III
Oral
Twice daily
18yo and up

Eculizumab
Ravulizumab

C5a Receptor Blocker

Thank You

Good Health To All!