VIRTUAL R&D DAY

March 22, 2021

Forward-looking Statements:

BioCryst's presentation may contain forward-looking statements, including statements regarding future results, unaudited and forward-looking financial information and company performance or achievements. These statements are subject to known and unknown risks and uncertainties which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied in this presentation. You should not place undue reliance on the forward-looking statements. For additional information, including important risk factors that could affect the forward-looking statements contained in this presentation, please refer to BioCryst's documents filed with the SEC and located at ir.biocryst.com/financial-information/sec-filings

Today's Agenda

9:00-9:05	Welcome	John Bluth, Chief Communications Officer
9:05-9:35	BioCryst's Approach to R&D	Jon Stonehouse, President and Chief Executive Officer Yarlagadda Babu, Ph.D., Chief Discovery Officer Dr. Bill Sheridan, Chief Medical Officer Helen Thackray, M.D., Chief Research and Development Officer
9:35-9:40	Overview of PNH	Austin Kulasekararaj, M.D., Consultant Hematologist King's College Hospital, London
9:40-9:55	BCX9930 Data Presentation	Dr. Bill Sheridan, Chief Medical Officer
9:55-10:10	Expert Panel Discussion	Barry Katsof, PNH Patient Founder and President, PNH Patient's Association of Canada Founder, PNH Global Alliance Brad H. Rovin, M.D., Professor of Medicine and Pathology Division of Nephrology The Ohio State University Wexner Medical Center
10:10-10:30	PNH Patient Market Research	Charlie Gayer, Chief Commercial Officer Jinky Rosselli, Vice President, Global Business Analysis & Operations
10:30-11:00	Q&A	

VIRTUAL R&D DAY

March 22, 2021

Overview of PNH

Austin Kulasekararaj, M.D.

Consultant Hematologist

King’s College Hospital, London

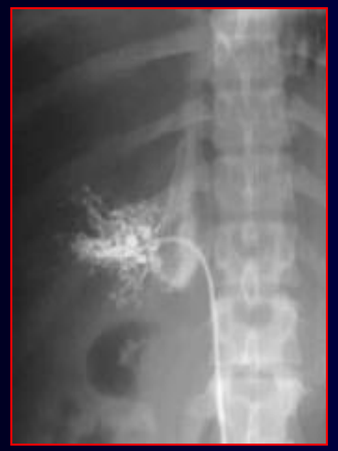
THE CLINICAL TRIAD OF PNH

EPIDEMIOLOGY: rare disease (0.3-1per million/year)

Prevelance « 14/million

1. Chronic haemolytic anaemia with paroxysmal attacks

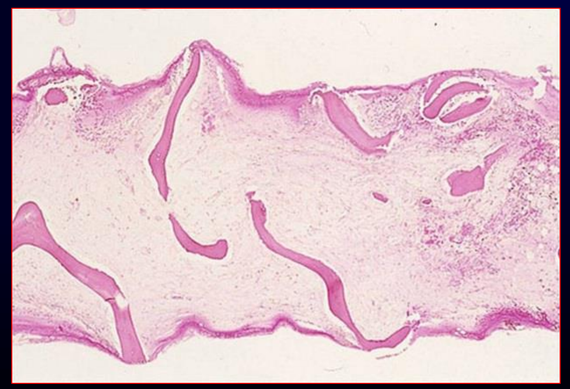
Intravascular haemolysis, complement mediated



2. Propensity to thromboembolisms

Often at unusual site, especially veins (cerebral veins, hepatic veins, splenic vein)

30-40% of all PNH patients



3. Variable cytopenia

Stigmata of marrow failure

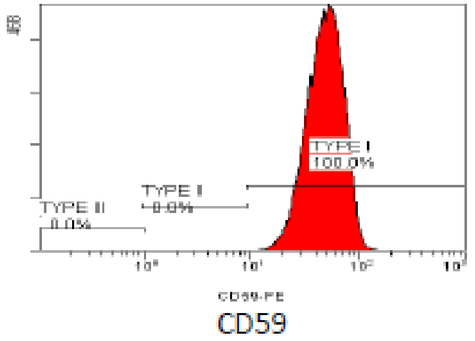
overlapping with aplastic anaemia (AA/PNH)

Life span of red cells

Cell Type[1]	Type I	Type II	Type III
CD59 Expression[1]	Normal	Partial deficiency	Complete deficiency
Approximate Lifespan[3,4]	90-120 days	30-40 days	8-10 days

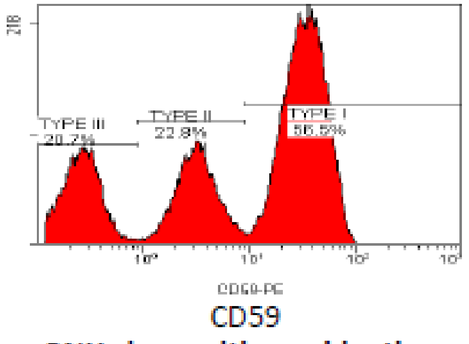
2.4 million new erythrocytes are produced per second in human adults

84% of the cells in the human body are 20–30 trillion red blood cells



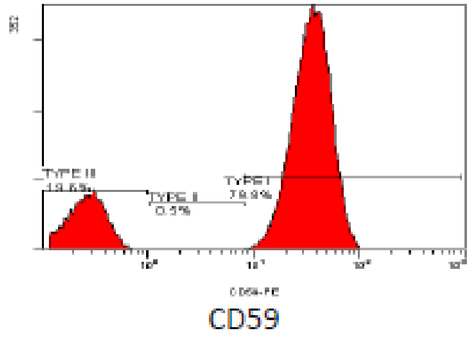
CD59

Normal RBCs: Type I cells[2]



CD59

PNH clone with combination of Type II and Type III cells[2]



CD59

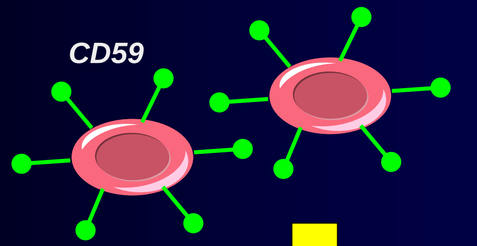
PNH clone with Type III cells[2]

1. Borowitz MJ, et al; Clinical Cytometry Society. *Cytometry B Clin Cytom*. 2010;78(4):211-230.
2. Data source: Dahl-Chase Diagnostic Services.
3. Rosse WF. *Blood*. 1971;37(5):556-562.
4. Rachidi S, et al. *Eur J Intern Med*. 2010;21(4):260-267.

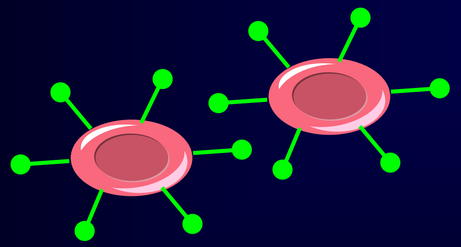
PATHOPHYSIOLOGY OF HAEMOLYSIS IN PNH

Normal

Terminal complement inhibitors protect RBC from complement attack



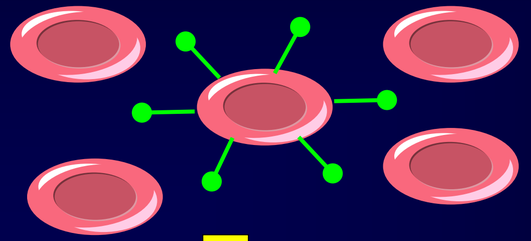
Complement activation



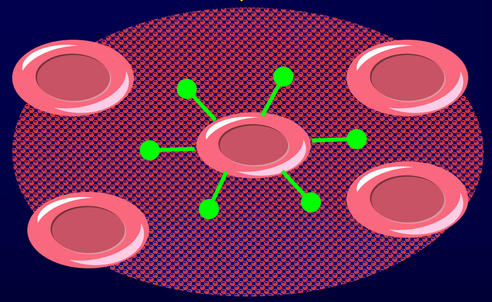
Intact RBC

PNH

Without complement inhibitors PNH RBC are susceptible to complement attack



Complement activation



Haemolysis of PNH RBC

Anaemia, free haemoglobin, haemoglobinuria, painful swallowing, abdominal pain, thrombosis

BCX9930 Data

Dr. Bill Sheridan

Chief Medical Officer

Oral Monotherapy w/BCX9930 Offers Advantage of Controlling Both Intravascular (IVH) and Extravascular (EVH) Hemolysis

Goal of Total Hemolytic Control

IVH Control

↓ LDH

+

EVH Control

↓ Opsonized RBCs

Hemolytic Control

↑ RBC/Granulocyte Clone Size

Patient Outcomes from Controlled Hemolysis over Time

Relieve Anemia

↑ Hemoglobin

Reduce PNH Clinical Symptoms

↓ Appearance of Symptoms

Avoid Transfusions

↓ Transfusions

A. M. Risitano *et al.*, *Front Immunol* **10**, 1157 (2019)

PNH Proof of Concept Study Design
Study Goals and Patient Eligibility Criteria

Key Study Goals

- Evaluate safety and tolerability
- Identify therapeutically active dose regimen
- Characterize PD on clinical outcomes & biomarkers
- Characterize PK

Key Eligibility Criteria at Screening:

All Patients:

- PNH clone size > 10%
- Platelet count > 30,000/µL
- Reticulocyte count > 100,000/µL

Naïve Criteria:

- No C5 Inhibitor
- Hb < 10 g/dL or blood transfusion within the last 12 months
- LDH ≥ 2 x ULN

Inadequate Responders Criteria:

- Stable C5 Inhibitor for 6 months
- Hb < 10 g/dL or blood transfusion within the last 3 months

PNH Proof of Concept Study Design

Patients Enrolled

Cohort	Naive	Inadequate Responders
1	4	--
2	4	2
3	2	4
Clinical Site Locations	*South Africa*	*United Kingdom Austria*

Dose Escalation per Cohort

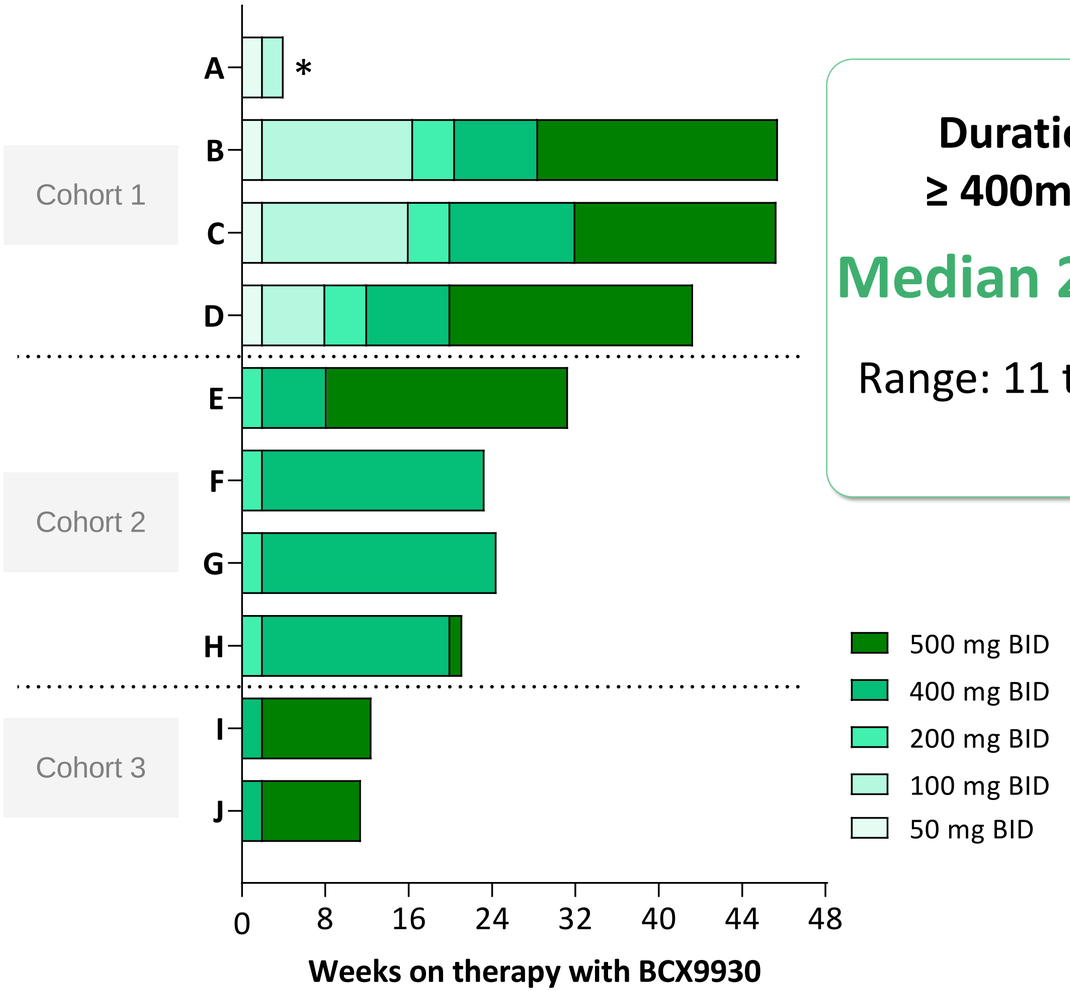
Days 1 - 14	Days 15 - 28	Extension > 28 days
50 mg BID	100 mg BID	Patients **benefitting on treatment may continue** on BCX9930 and **dose-escalate** at physicians' discretion
200 mg BID	400 mg BID	
400 mg BID	500 mg BID	

- 10 Naïve patients enrolled w/ BCX9930 monotherapy treatment
- 6 Inadequate Response patients enrolled w/ BCX9930 + C5-inhibitor treatment

Naïve Patients Enrolled had Severe Disease Prior to Treatment

9 naive patients remain in study with average overall treatment duration of 6 months

Parameter @ Baseline	N = 9 *
Age	29.2 years
Duration since Diagnosis	3.2 years
Gender	8 (89%) Male
Race: African Caucasian Other	 5 (56%) 3 (33%) 1 (11%)
Bone Marrow Failure	4 (44%)
RBC transfusion-dependent (prior 12 months)	7 (78%)
RBC transfusions in prior 12 months, mean	7.6 units
Hb, mean g/dL (range)	8.3 (6 – 11)
Reticulocyte count, mean $10^3/\mu L$ (range)	176 (104 – 305)
LDH, mean x ULN (range)	7.5 (3.7 – 13.1)
AST, mean x ULN (range)	2.1 (0.8 – 3.8)



Duration on ≥ 400mg BID:

Median 22 weeks

Range: 11 to 31 weeks

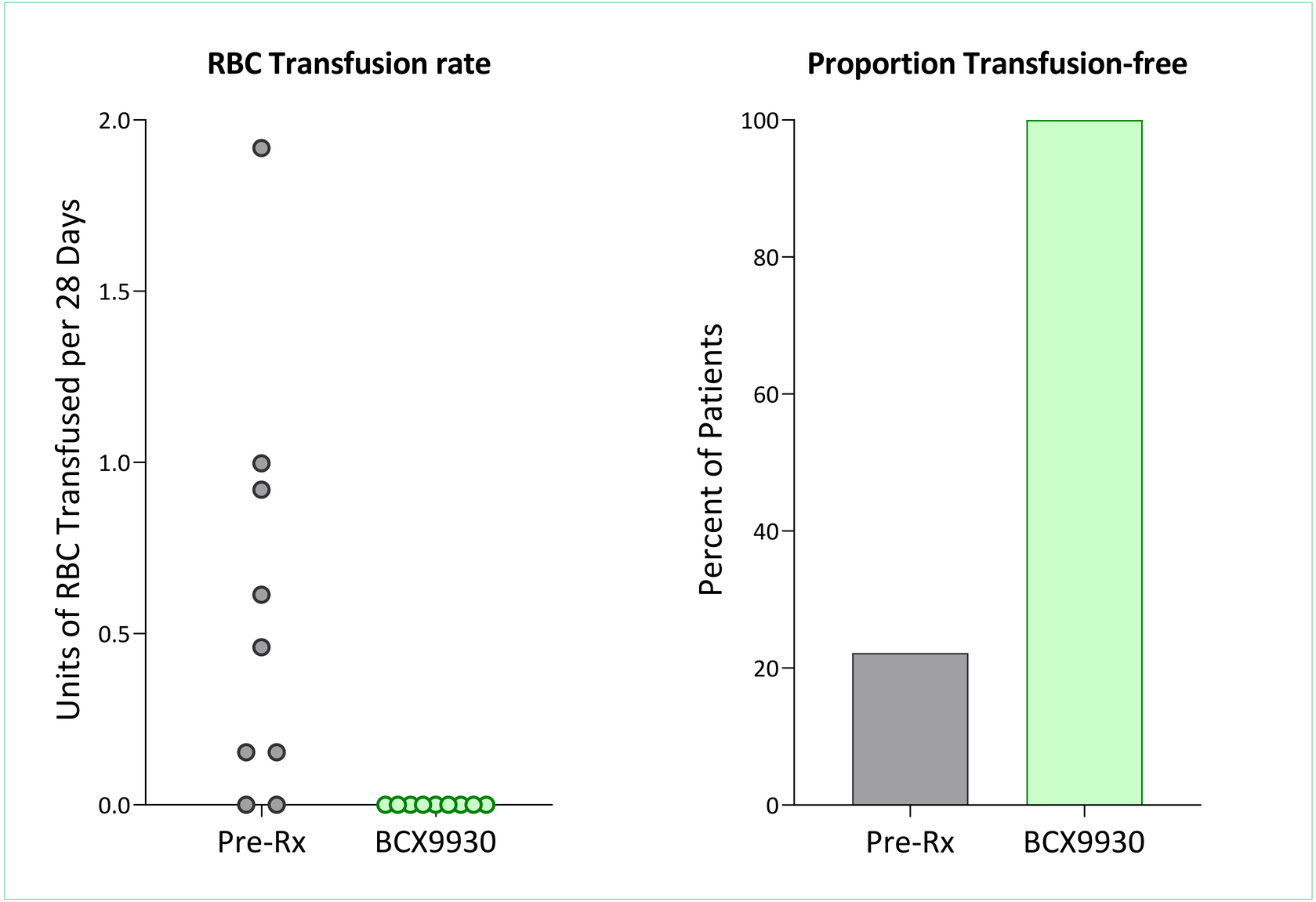
∗ *As disclosed in May 2020, Patient A discontinued due to an unrelated SAE.*

C5-inhibitor Naïve Patients had Significant Increase in Hemoglobin as a Result of Control of Hemolysis, with Reductions in Reticulocytes, LDH, Bilirubin, and AST

Response Parameter	Baseline N = 9	Last visit* N = 9	Change from Baseline
Hemoglobin g/dL, mean (SEM)	8.3 (0.6)	11.8 (0.6)	+3.5 (0.6)
Hemoglobin > 12 g/dL, n (%)	0	5 (56%)	+5 (56%)
Hemoglobin > 10 g/dL, n (%)	2 (22%)	7 (78%)	+5 (56%)
RBC clone size %, mean (SEM)	47% (5)	86% (4.2)	+40% (4.7)
Reticulocytes 10^3/µL, mean (SEM)	176 (21)	115 (8.5)	-60 (21)
Patients with reticulocytes ≤ 150,000/µL, n (%)	4 (44%)	8 (89%)	+4 (44%)
LDH U/L, mean (SEM)	1721 (264)	544 (104)	-1177 (281)
LDH xULN, mean (SEM)	7.5 (1.2)	2.0 (0.3)	-5.5 (1.1)
Total bilirubin mg/dL, mean (SEM)	1.24 (0.19)	0.59 (0.05)	-0.66 (0.19)
AST U/L, mean (SEM)	86 (14)	22 (4.8)	-64 (14)

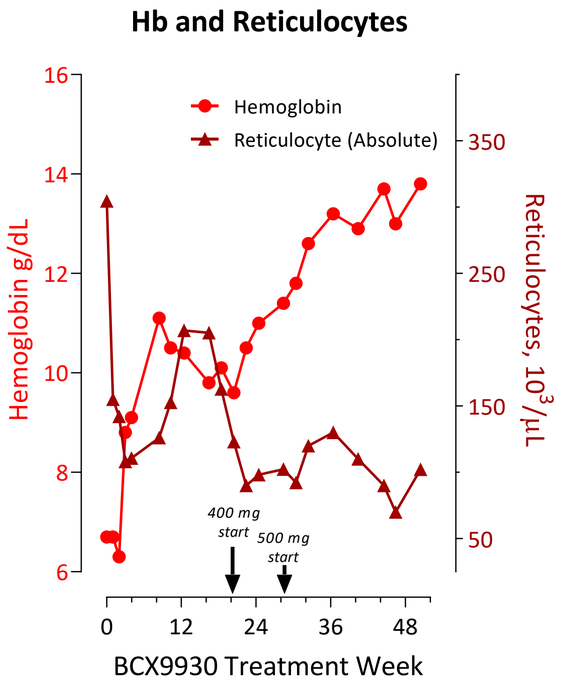
Last treatment visit at 400mg or 500mg BID

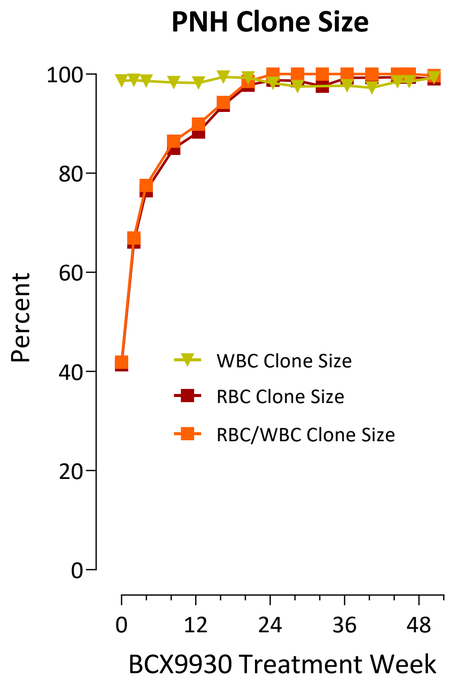
Transfusion Burden in C5-inhibitor Naïve Subjects was Reduced to Zero at Doses of 400 mg or 500 mg BID – 100% of Patients were Free of Transfusions

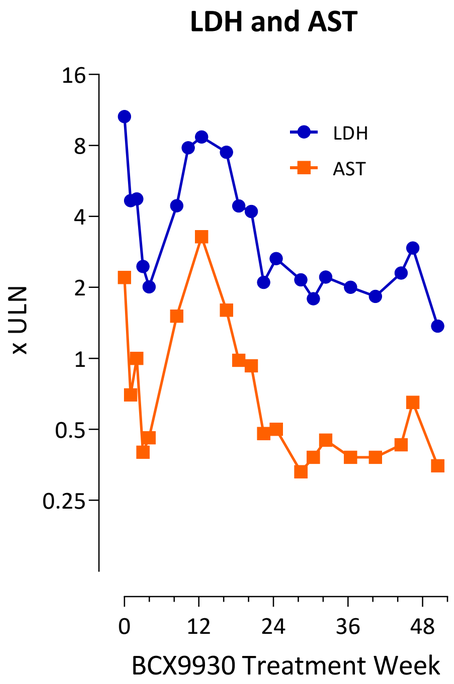


Example of C5-inhibitor Naïve Subject with Dose Escalated to 500 mg BID at Week 28

Patient B – 2 weeks Rx at 50 mg BID then escalating in steps to 500 mg BID







Prior to study, patient received 13 units of RBCs in prior 12 months

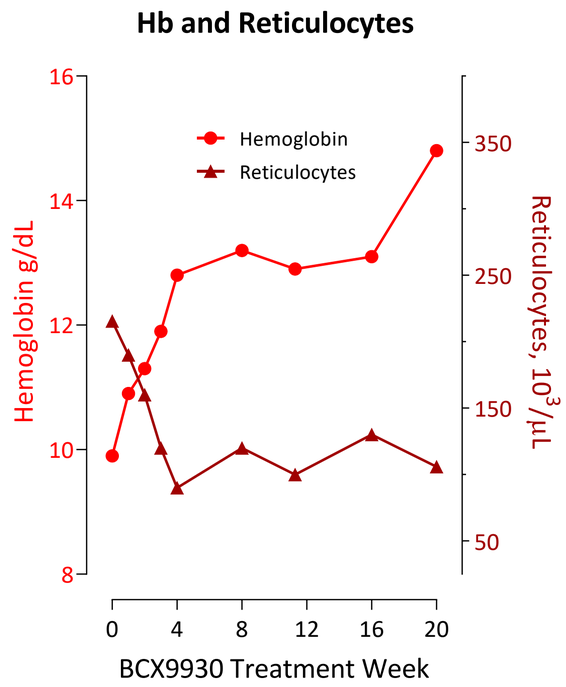
- 2 unit RBC transfusion on study day 15 after 2 weeks of 50 mg BID BCX9930
- Hb rose steadily from 6.7 to 13.8 g/dL over 50 weeks
- Reticulocytes normalized, falling from 305 to 102 x10^3/µL
- RBC/WBC clone size rose from 41.9% to 99.7%
- LDH fell from 10.6 x ULN to 1.4 x ULN at week 50
- AST fell from 2.2 x ULN to 0.35 x ULN
- Tonsillitis was noted in week 46, associated with asymptomatic increase in LDH (<50%) and fall in Hb (<1g/dL)

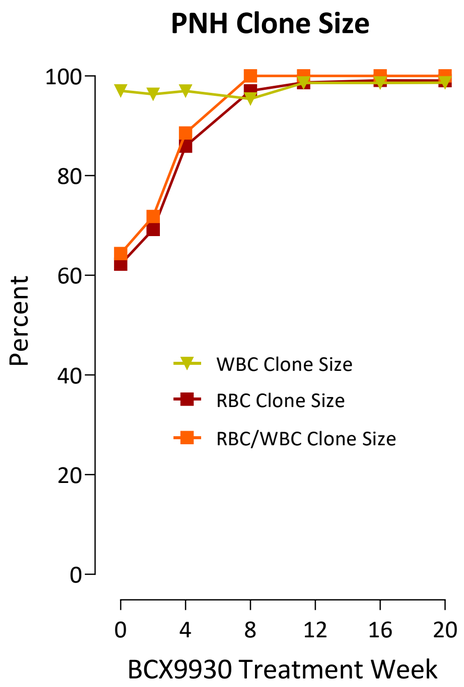
- *Updated from last September with longer follow up, almost a year of treatment*
- *At suboptimal doses, hemolysis was not controlled*
- *Relative RBC clone size reached >99% – maximum control, then LDH stabilized*
- *Fluctuations in biomarkers occur, for example due to infection – not clinically significant*

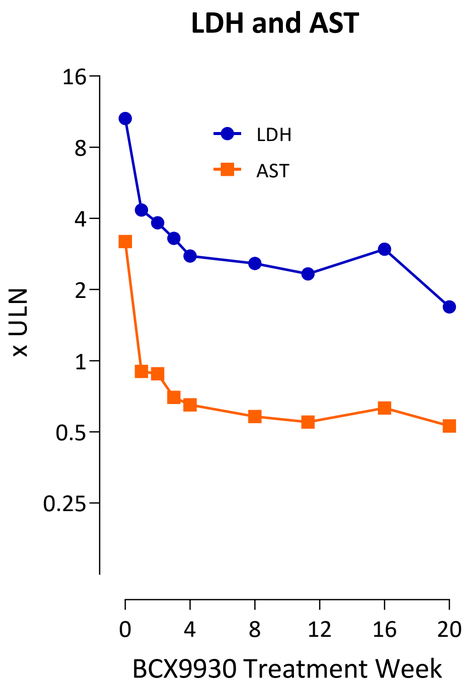
Preliminary data

Example of C5-inhibitor Naïve Subject Response Over Time

Patient H – 2 weeks Rx at 200 mg BID then 400 mg BID through week 20







Prior to study, patient received 8 units of RBCs in previous 12 months

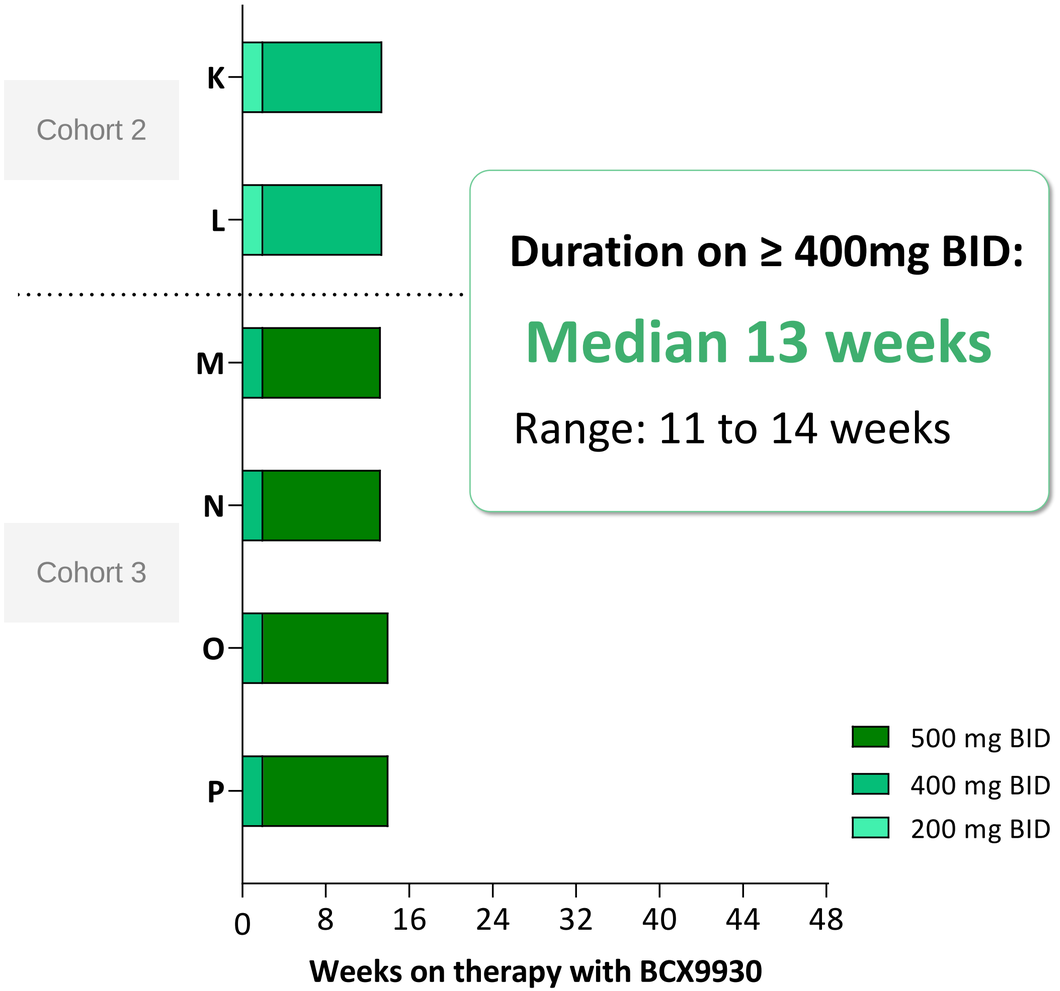
- No RBC transfusions on study
- Hb rose from 9.9 to 14.8 g/dL over 20 weeks
- Reticulocytes normalized, falling from 215 to 106 x 10^3/µL
- RBC/WBC clone size rose from 64% to 100%
- LDH fell from 10.6 x ULN to 1.7 x ULN
- AST fell from 3.2 x ULN to 0.5 x ULN

- *Rapid response was seen*
- *The response was durable and improved over time*
- *Relative RBC clone size reached 100% – this means maximum complement inhibition effect*
- *LDH took time to stabilize once effect on clone size was achieved*

Preliminary data

Patients with Inadequate Response Represented a Severely Ill Patient Group with Persistent Anemia and Transfusion Dependence Despite Optimized C5 Inhibitor Treatment

Parameter @ Baseline	N = 6
Age /Years since Diagnosis	40.3 yrs / 12.5 yrs
Gender	4 (67%) Female
Race: African Caucasian Asian	2 (33%) 3 (50%) 1 (17%)
Bone Marrow Failure	3 (50%)
Thrombosis	3 (50%)
RBC Transfusion-dependent (prior 12 months)	5 (83%)
RBC Transfusions in prior 12 months, mean	13.7 units
Hb, mean g/dL* (range)	8.9 (7.5 – 10.2)
Reticulocyte count, mean $10^3/\mu L$ (range)	184 (125 – 235)
RBC C3 Opsonization, mean % (range)	15% (1% – 31%)
Total Bilirubin, mean mg/dL (range)	2.6 (0.8 – 5.3)
LDH x ULN (range)	0.9 (0.6 – 1.1)



Duration on ≥ 400mg BID:

Median 13 weeks

Range: 11 to 14 weeks

** Note, Hb data for one C5-INH-IR patient receiving transfusions was censored*

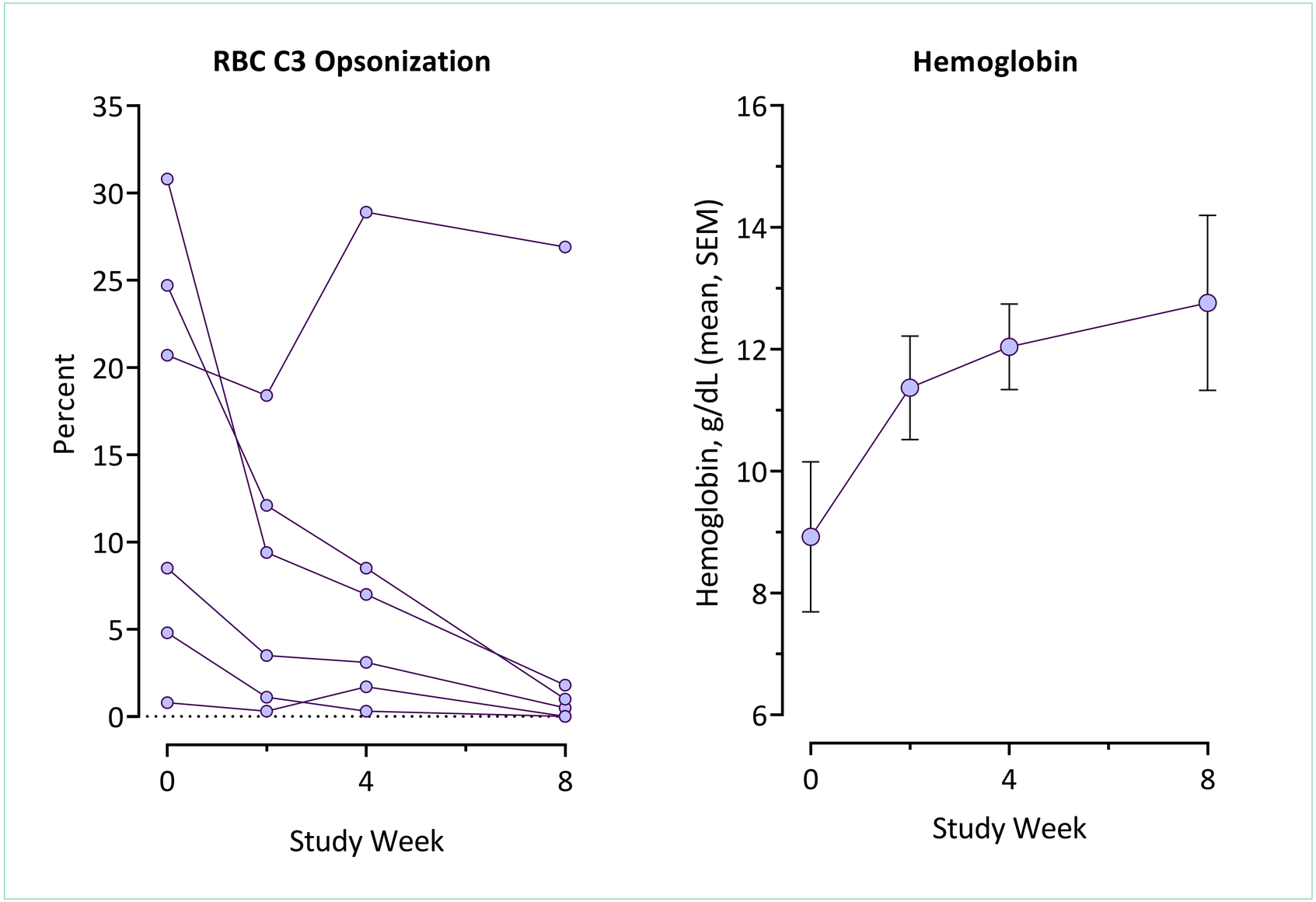
C5-inhibitor Inadequate Response Patients Experienced Significant Increase in Hemoglobin as a Result of Control of Hemolysis, with Reductions in C3 Opsonization, Bilirubin, and Reticulocytes

Response Parameter	Baseline N = 6	Last visit** N = 6	Change from Baseline
Hemoglobin g/dL, mean (SEM)*	8.9 (0.5)	12.2 (1.0)	+3.2 (0.6)
Hemoglobin > 12 g/dL, n (%)	0	3 (50%)	+3 (60%)
Hemoglobin > 10 g/dL, n (%)	2 (40%)	4 (80%)	+2 (40%)
RBC clone size %, mean (SEM)	48 (6)	77 (8)	+30 (7)
Reticulocytes 10^3/µL, mean (SEM)	184 (16)	139 (23)	-45 (18)
Patients with Reticulocytes ≤ 150,000/µL, n (%)	1 (17%)	4 (67%)	+3 (50%)
Total Bilirubin mg/dL, mean (SEM)	2.6 (0.7)	1.3 (0.3)	-1.3 (0.4)
RBC C3 Opsonization %, mean (SEM)	15 (4.9)	5 (4.4)	-10 (14)

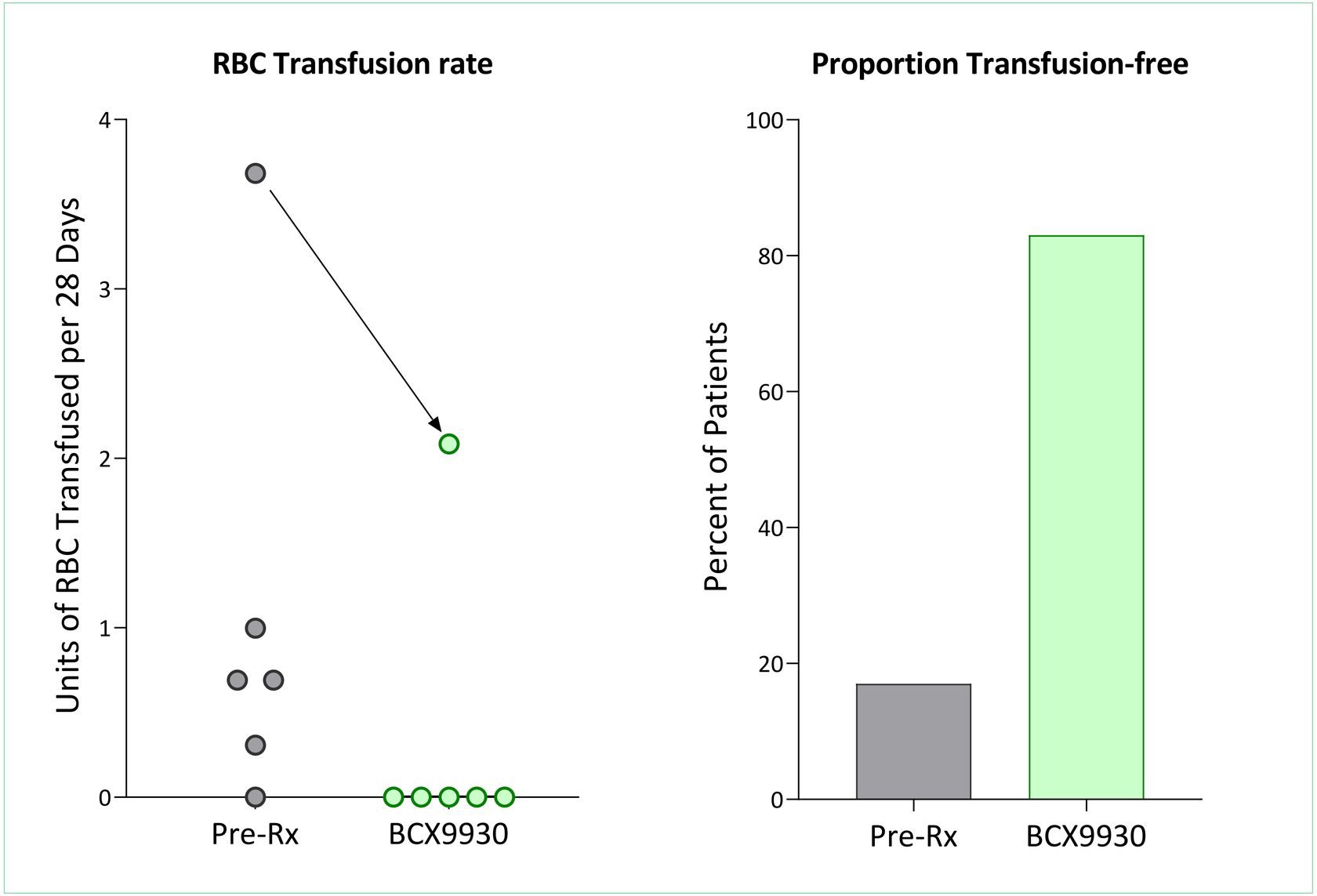
** Note, Hb data for one C5-INH-IR patient receiving transfusions was censored*

***Last treatment visit at 400mg or 500 mg BID*

RBC C3 Opsonization Showed a Pattern of Early Response in 5 of 6 Patients, and Hemoglobin also Responded Within Weeks

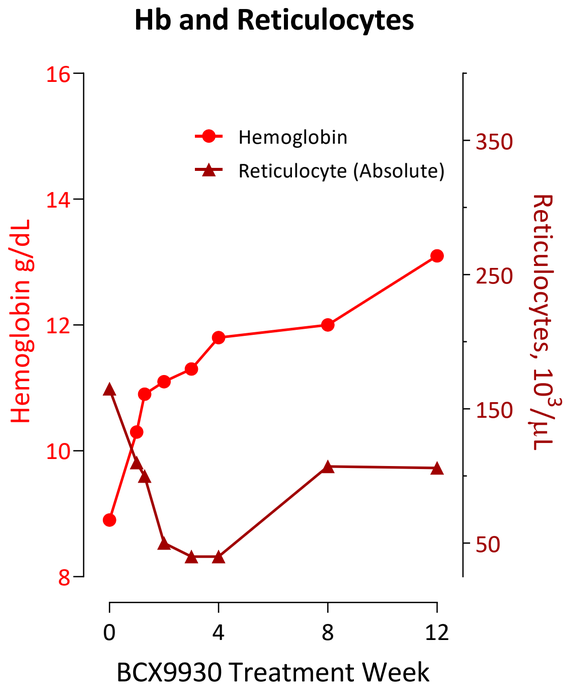


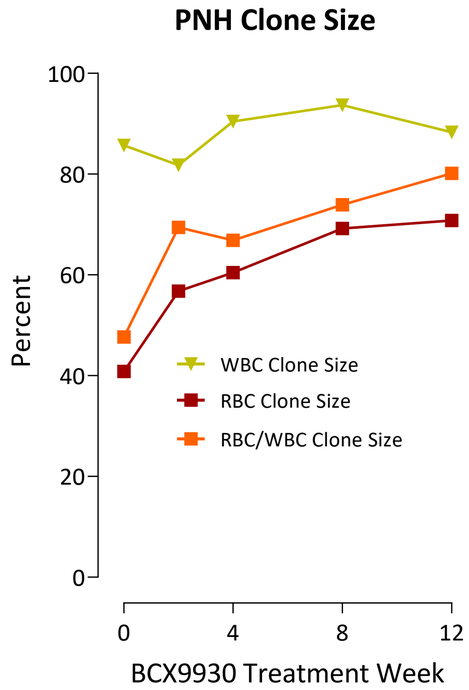
Transfusion Burden in C5-inhibitor Inadequate Response Subjects was Reduced to Zero in 5 of 6 Subjects – 83% of Patients were Free of Transfusions

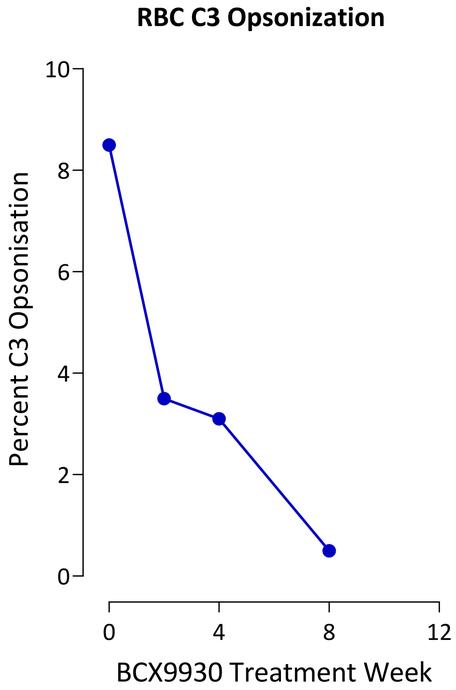


Example of C5-inhibitor Inadequate Responder Subject Response over the First 12 Weeks of Treatment with BCX9930

Patient N – 2 weeks Rx at 400 mg BID then 500 mg BID through week 12







Patient treated with eculizumab 1200 mg IV every two weeks for 3.8 years

- No RBC transfusions in 12 months before or on study
- Hb rose from 8.9 to 13.1 g/dL over 12 weeks
- Reticulocytes normalized, falling from 165 to 106 x 10^3/µL
- RBC/WBC clone size rose from 48% to 80%
- RBC C3 opsonization fell from 8.5% to 0.5%

Preliminary data

BCX9930 has been Safe and Well Tolerated in PNH Patients

Overall Safety

- No safety signals in routine monitoring of adverse events, vital signs, ECGs, or laboratory evaluations of hematology, clinical chemistry, coagulation, or urinalysis
- Treatment-emergent AEs of hemolysis occurred in 2/16, without changes to dosing
- No discontinuations or interruptions of dosing due to BCX9930-related treatment-emergent AEs

Related Adverse Events

- The most common BCX9930-related TEAE was mild-moderate headache in 8/10 C5-inhibitor naïve subjects and 2/6 C5-inhibitor inadequate response subjects, lasting 1-3 days, onset generally soon after commencing dosing – typical complement inhibition effect in PNH patients
- Mild or moderate drug rash observed in 6/16 subjects, onset generally in second week of dosing, lasting median of 10 days; all resolved without treatment interruption

BCX9930 Dose-ranging Proof-of-Concept Study in PNH: Conclusions

Overall outcomes seen in PNH patients on study at doses of 400 mg BID or 500 mg BID

- Hemoglobin increased, with relief of anemia
- Transfusions were avoided
- Intravascular and extravascular hemolysis were brought under control
- Consistent hematologic outcomes in both C5-inhibitor naïve and C5-inhibitor inadequate response patients

PK and PD profile

- Drug exposure and PD effects on complement activity in PNH patients were similar to that seen in healthy subjects

Dose-response and selection of dose for pivotal studies

- Optimized doses are in the range of 400-500 mg BID. Final selection of dose will be based on PK-PD modeling

Safety and tolerability

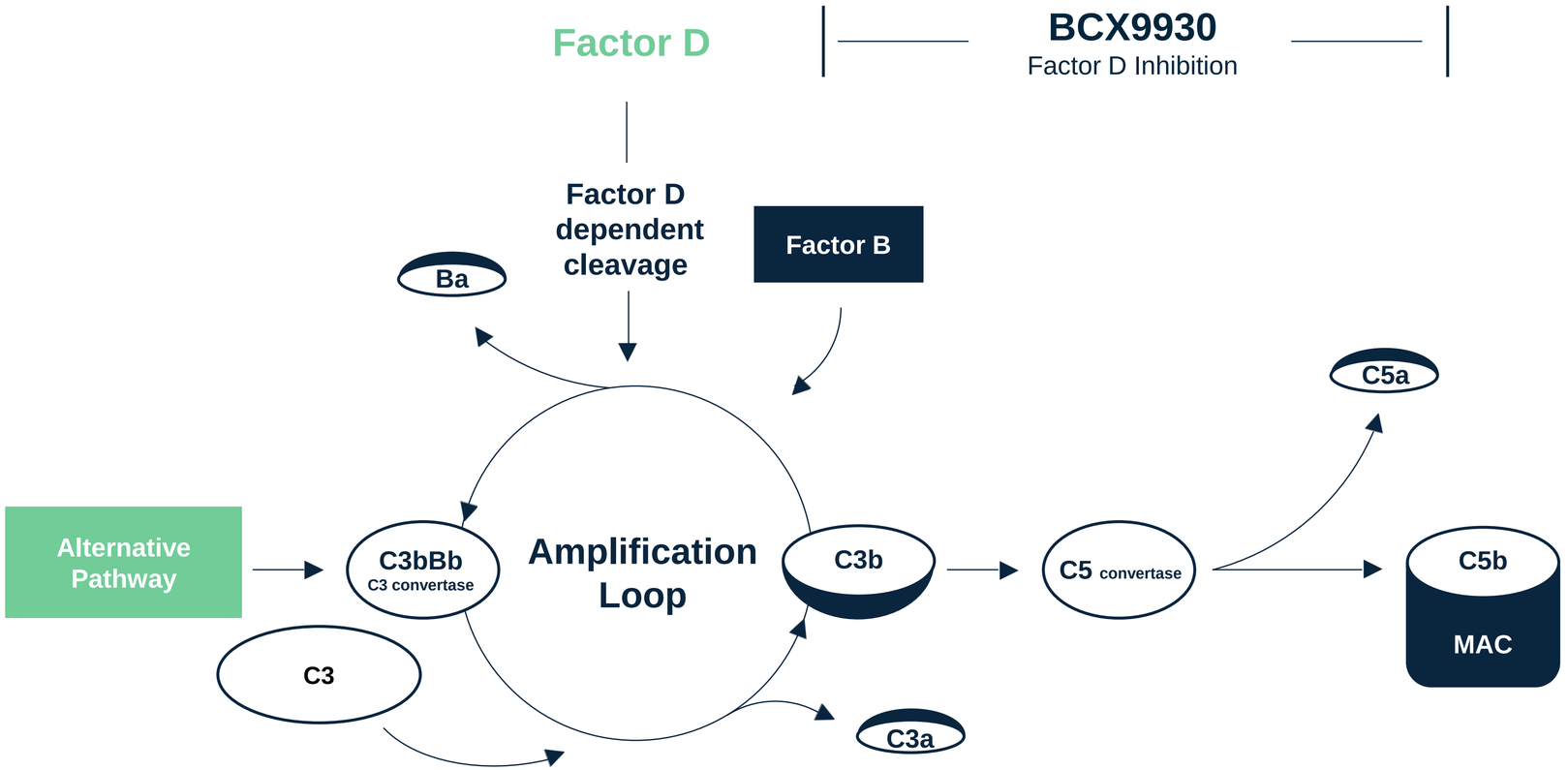
- BCX9930 dosing BID has been generally safe and well tolerated for up to over 50 weeks
- No safety signals have been seen

Conclusions and next steps

- These results support initiation of pivotal trials in PNH
- Pivotal trials in PNH are planned for start in 2H 2021

Factor D:
An Outstanding Drug Target for Complement-mediated Diseases

- Factor D is essential to initiate the Alternative Pathway
- Blocking Factor D blocks the Alternative Pathway and all downstream products



Spectrum of Alternative Pathway Dysregulation Diseases

HEMATOLOGY

PNH
paroxysmal nocturnal hemoglobinuria

aHUS
atypical hemolytic uremic syndrome

RHEUMATOLOGY

ANCA vasculitis
antineutrophil cytoplasmic antibody-associated vasculitis

Lupus nephritis

IgAN vasculitis

NEPHROLOGY

C3G
Complement component 3 glomerulonephapthy

PMN
primary membranous nephropathy

IgAN
IgA nephropathy

PNH Market Research Insights

Charlie Gayer, Chief Commercial Officer

Jinky Rosselli, VP, Global Business Analysis & Operations

Methodology

Objectives: Patient journey, current treatment satisfaction, with a focus on unmet needs and desires for future therapy

Methods: 60-minute double-blinded qualitative tele-depth interviews conducted by external research partner in Fall of 2020

US Physician Respondents (n=25)

- **All Hematologists/Oncologists and Medical Oncologists**
- **4 Key Opinion Leaders**
- **Each managing treatment for an average of 7 to 13 PNH patients**
- **Average of 16 years in practice**

US Patient Respondents (n=23)

- **All patients diagnosed with PNH and on C5-inhibitor**
  - Ultomiris: 12 patients
  - Soliris: 11 patients
- **Median Age**: 39 (25 to 76)
- **Diagnosis Length**
  - Between 1 and 2 years ago: 2 patients
  - Between 2 and 5 years ago: 3 patients
  - More than 5 years ago: 18 patients
- **Average Hemoglobin Level & Transfusion Status on Soliris/Ultomiris**
  - 9.3 g/dL (range: 7 to 12 g/dL)
  - Only 3 patients required consistent blood transfusions

Representative Patients Sharing Stories Today

Patient A

- **Age:** Late 50s
- **Initial PNH Diagnosis:** 2006
- Has been on Soliris since commercially available
- **Transfusion-dependent**
  - Experiences episodes of breakthrough hemolysis about once a month
  - 8 to 9 blood transfusions per year

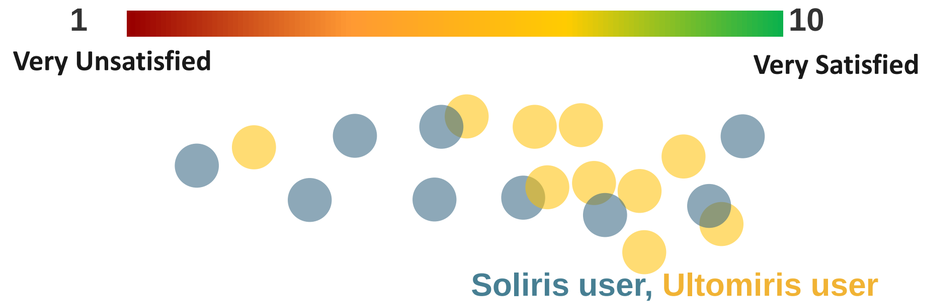
Patient B

- **Age:** Mid-30s
- **Initial Diagnosis:** 2011
- Started Soliris in 2011, switched to Ultomiris in late 2019
- **Transfusion-free**
  - Has only needed occasional transfusions when he had influenza or other severe illness

Patient Satisfaction with Soliris and Ultomiris

Patient Satisfaction with Current Treatment

n=23 patients



Key Insights

- Long journey towards diagnosis, patients are grateful for current therapy
- Generally satisfied
- Wide range of satisfaction often due to ongoing symptoms like anemia, fatigue, and transfusions

Patient A – Quote 1

- “We have a routine so right now I can function…I still have issues, but I can lead a life, I can work part time, I can get out on my bike and ride I can walk my dogs after a blood transfusion for a couple of weeks. I can travel if I need to. I have a life…that I’m okay with, it’s not what it was…but until something else comes along…right now that’s what I’ve got … So when I get a transfusion….I’m like okay; let’s go, let’s go do stuff.”

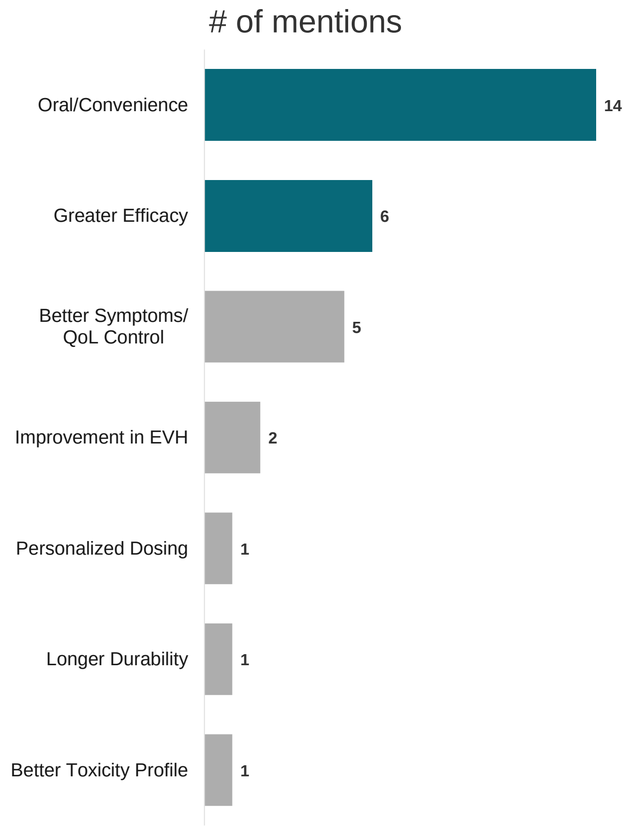
Patient B – Quote 2

- “My normal as far as my RBC counts are a lot better with Ultomiris than they were with Soliris. I used to hover between a 9 and 11, but now I’m pretty stable around 11 - 11.2; something like that. Not too bad; manageable for sure.”

Patients Want Greater Convenience and Efficacy

Patient Unaided Desires in New Treatment

n=23 patients



Key Insights

- Despite general satisfaction, the majority of patients are still looking for a therapy that is more convenient and more efficacious than their current therapies
- Primarily, these desires focus on:
  - Better overall disease control
  - Resolution of remaining symptoms, primarily fatigue
  - Reduction in burden of treatment

Patient A – Quote 3

- “Well, the back pain has improved, every now and then I’ll get walloped. It lasts for about 15 -20 minutes. I recognize the symptoms now, I can feel it coming on. The way it resolves itself is I have to lay on my stomach flat on a hard floor and it takes about 15-20 minutes and then it subsides … but I’ve learned the symptoms. It hurts like crazy, it’s pretty unbearable, but I know its gonna pass so I just have to bite my lip if you will, and just knuckle under and get through it.”

Patient B – Quote 4

- “I’d love to have my blood counts be a little higher. Absolutely. They’re pretty good. They’re better than they’ve ever been in a long time. If that could incrementally improve I’d like that. I don’t really notice fatigue that often, but if I could be less fatigued and have more energy I would take that all day too.”

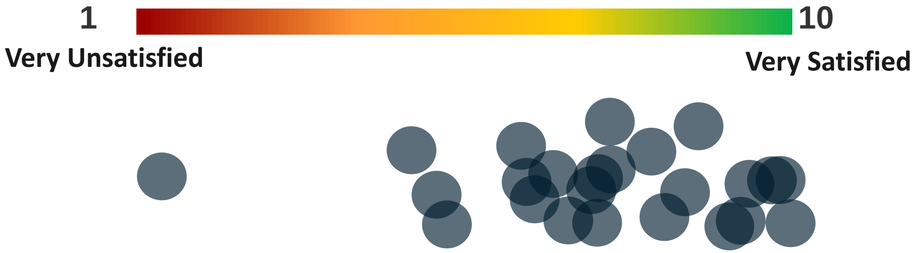
Patient B – Quote 5

- “I wish I didn’t have to do it, it didn’t take so long to administer. What I would like to see in the future is something I could do daily or…I’d rather take a pill daily than go every 8 weeks to get an infusion because I would just take it with my vitamin. I get there at 8 o’clock, and just the process of getting set up, and getting stuck, and then mixing the drug, having the right blood work done, getting the results back and then getting it. That’s cumbersome…that takes forever…I wish it wasn’t that long. I wish it was a little bit easier than that but it’s not.”

Physicians Want Greater Efficacy and Convenience

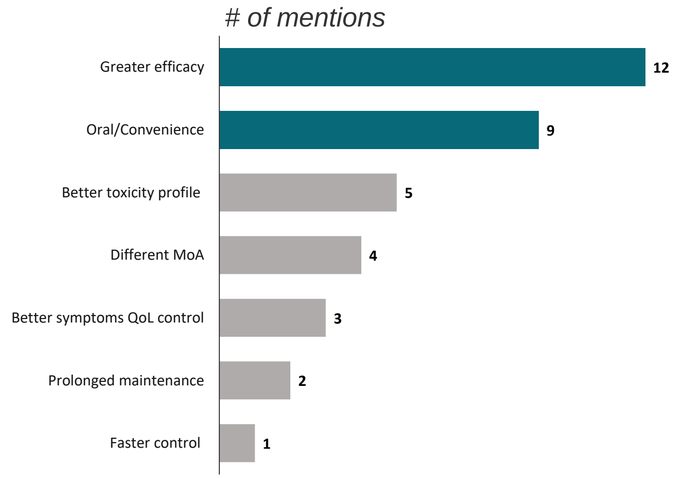
Physician Satisfaction with Treatment Options

n=25 PNH-treating physicians



Physician Unaided Desires in New Treatment

n=25 PNH-treating physicians

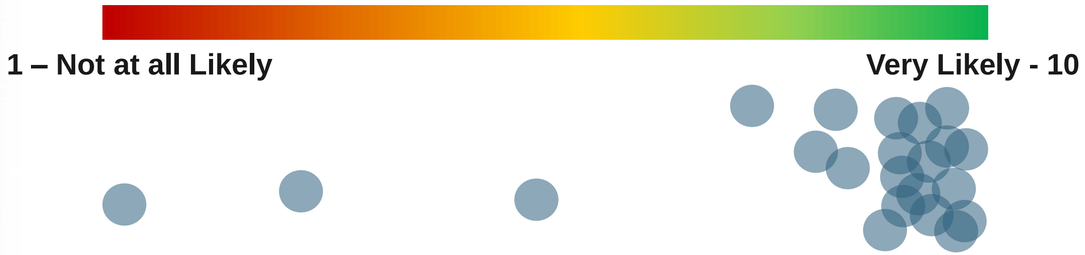


Key Insights

- Generally satisfied with C5-inhibitors as they help stabilize most patients
- Acknowledge that even stable patients have unresolved symptoms
- Recognize that most patients experience continuing burden (disease-related and/or treatment-related)

91% of Patients Surveyed Interested in Switching

Patient Desire to Switch to Product X
n=23 patients



Key Insights

- Patients describe need for greater efficacy and reduced treatment burden
- Oral treatment option, plus potential improved hemoglobin and symptom control, drive desire to switch
- Patient desire to switch to an oral factor D inhibitor is not correlated to satisfaction with current treatment

Patient B – Quote 6

- “Honestly, that’s exactly the kind of thing I’d be looking for is something like this. This would be my ‘pie-in-the-sky’ dream scenario; taking a pill twice a day rather than going and getting any kind of sticks and infusions. I would much rather do this especially if it improves my quality of life which is paramount to me…so all that stuff. This would be my dream scenario is what we are describing right here. I would switch in a heartbeat…I could take something orally like a pill every day? I’d be in so quick.”

Q&A