PNH: Understanding Your Disease and Treatment Options

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PNH: What's in a Name

- It is not paroxysmal[1]
  - Even in the absence of symptoms, destructive progression of hemolysis is ongoing
- It is not nocturnal[1]
  - Hemolysis in PNH is subtle and constant, 24 hours a day
- Hemoglobinuria is a less commonly seen complication
  - ¾ patients present without hemoglobinuria[2]

1. Rother R *et al. Nature Biotechnology* 2007;25,11:1256–1264;
2. International PNH Interest Group. *Blood.* 2005;106:3699–3709.

The Defect in PNH

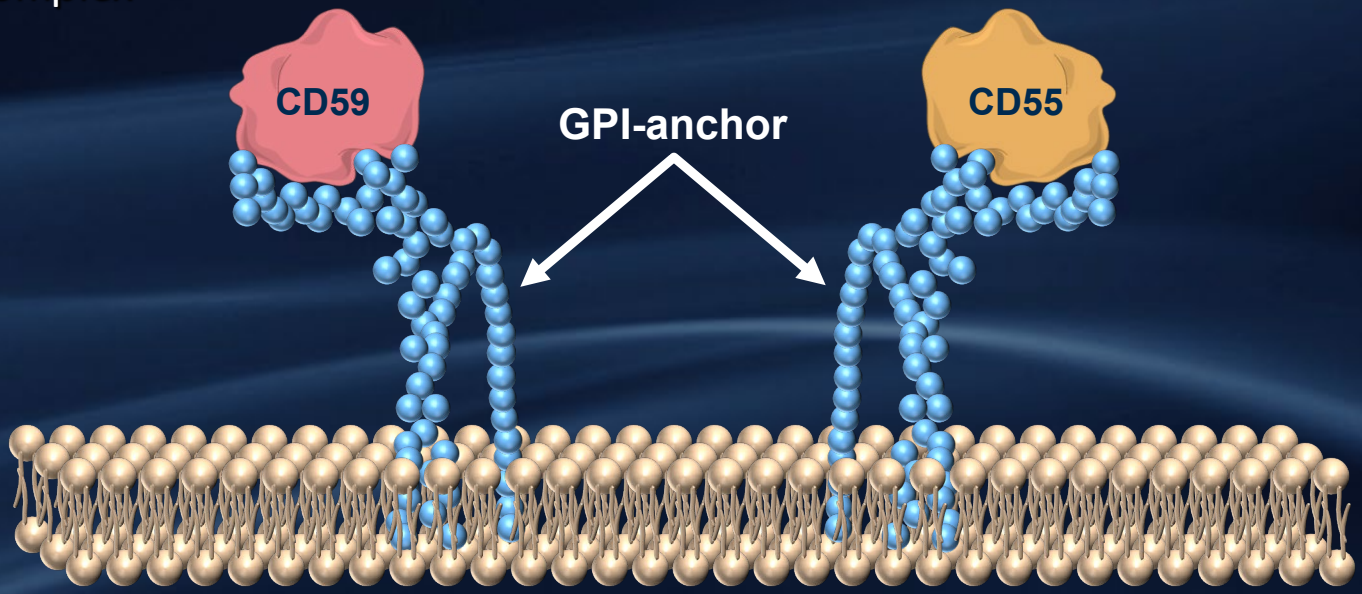
PNH clones are defined as PNH cells with a deficiency of proteins that require a GPI anchor for attachment to the cell membrane[1]

CD59 (MIRL)

- Forms a defensive shield for red blood cells (RBCs) from complement-mediated lysis
- Inhibits the assembly of the membrane attack complex

CD55 (DAF)

- Prevents formation and augments instability of the C3 convertases, attenuating the complement cascade



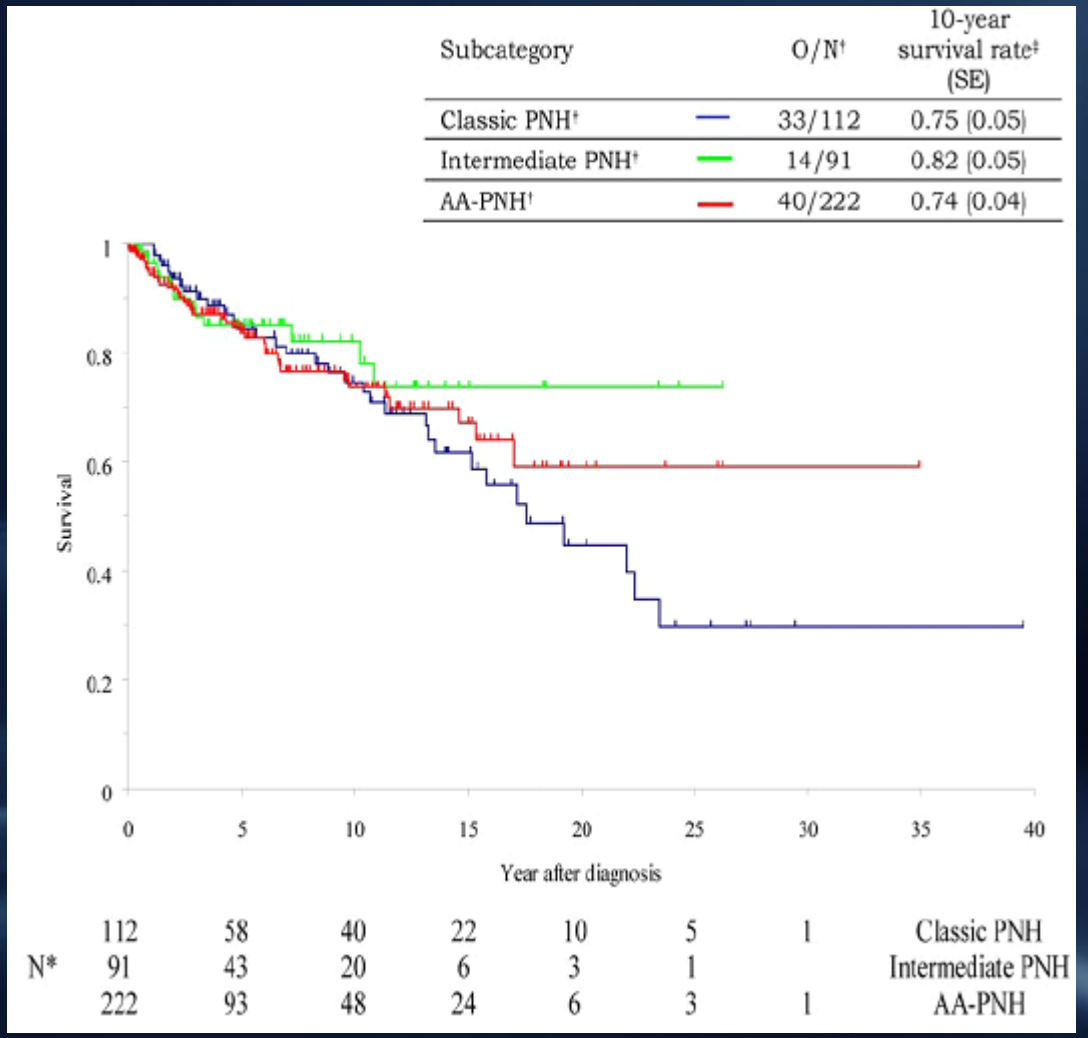
GPI = glycerophosphatidylinositol; MIRL=membrane inhibitor of reactive lysis; DAF=decay accelerating factor.

1. Borowitz MJ *et al. Cytometry B Clin Cytom* 2010;78:211–230.

Adapted from: Johnson RJ *et al. J Clin Pathol: Mol Pathol* 2002;55:145–152; Brodsky R. Paroxysmal nocturnal hemoglobinuria. In: R Hoffman *et al,* eds. *Hematology - Basic Principles and Practices*. 4th ed. Philadelphia, PA: Elsevier Churchill Livingstone; 2005;419–427.

PNH Classification

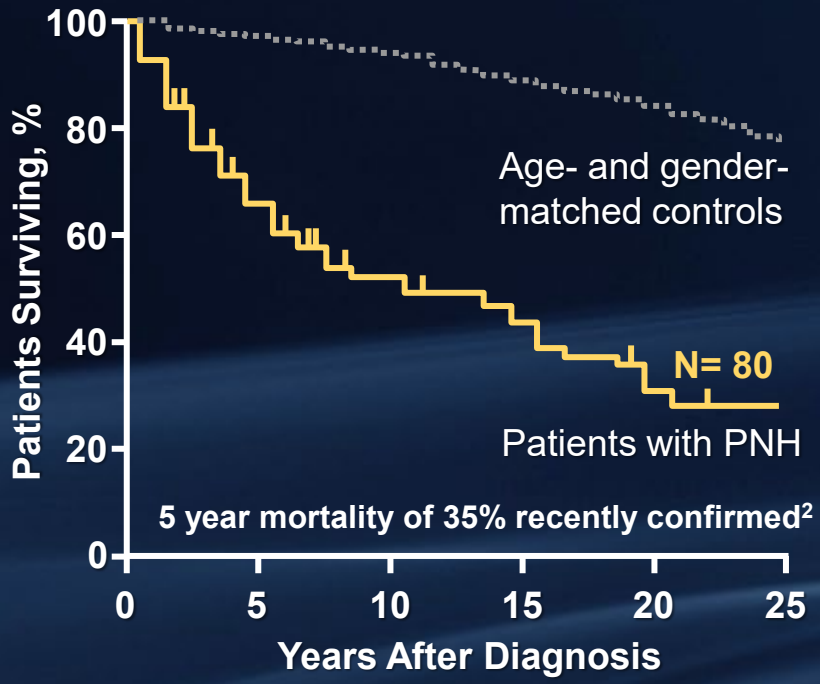
- **Classic PNH**
  - Intravascular hemolysis
    - Reticulocytosis
    - Increased LDH
    - Increased indirect bilirubin
    - Low haptoglobin
- **PNH + Bone Marrow Disorder**
  - Intravascular hemolysis + AA/MDS/Myelofibrosis
- **Subclinical PNH**
  - No clinical/lab evidence of hemolysis
  - Detected by very sensitive flow cytometric analysis
  - In association with AA/MDS



Parker et al. *Blood* 2005;106:3699-3709
de Latour et al. *Blood* 2008;112:3099-3106

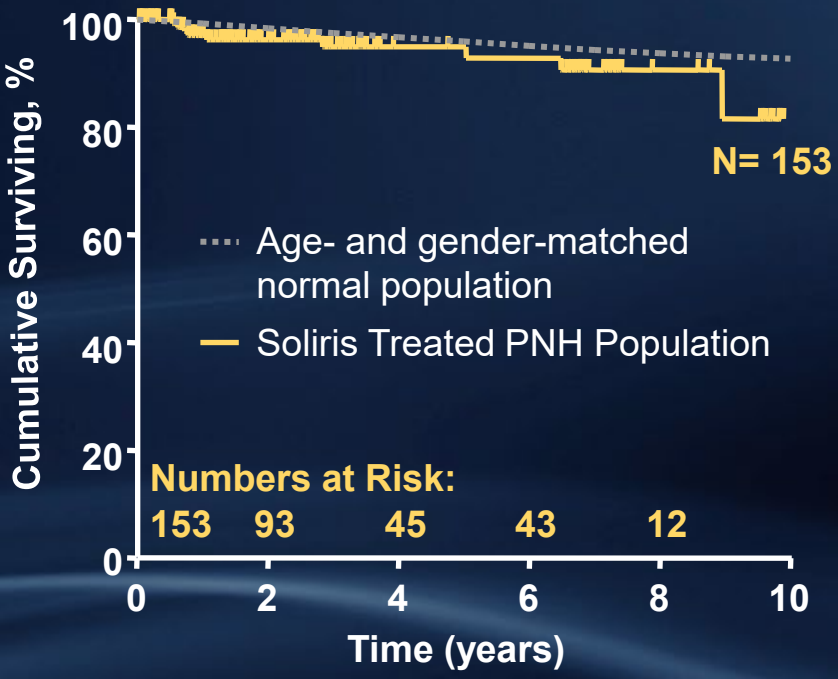
Paroxysmal Nocturnal Hemoglobinuria:
Compelling Long Term Clinical Benefits in PNH Patients

Pre-Soliris from Time of Diagnosis in 80 Patients With PNH[1,2]



- Despite best supportive care - 5 year mortality: 35%[1]

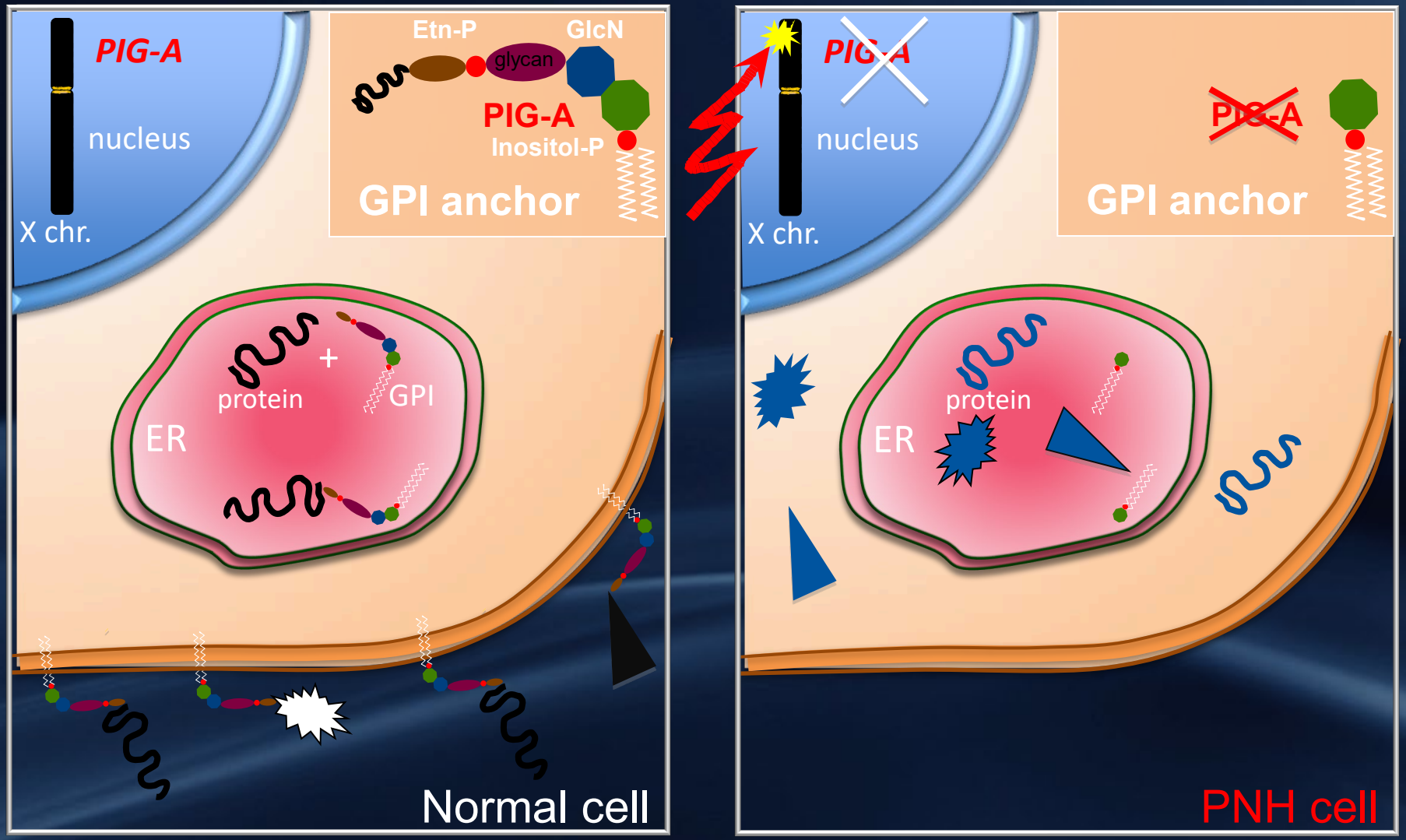
Survival of PNH Patients Treated With Soliris Compared With the Normal UK Population[3]



1. Hillmen P et al. *N Engl J Med.* 1995;333:1253-1258. 2. Kelly RJ et al. *Blood.* 2011;117:6786-6792 3. Hillmen et al. *Br Jnl Haematol*. 2013;162:62-73

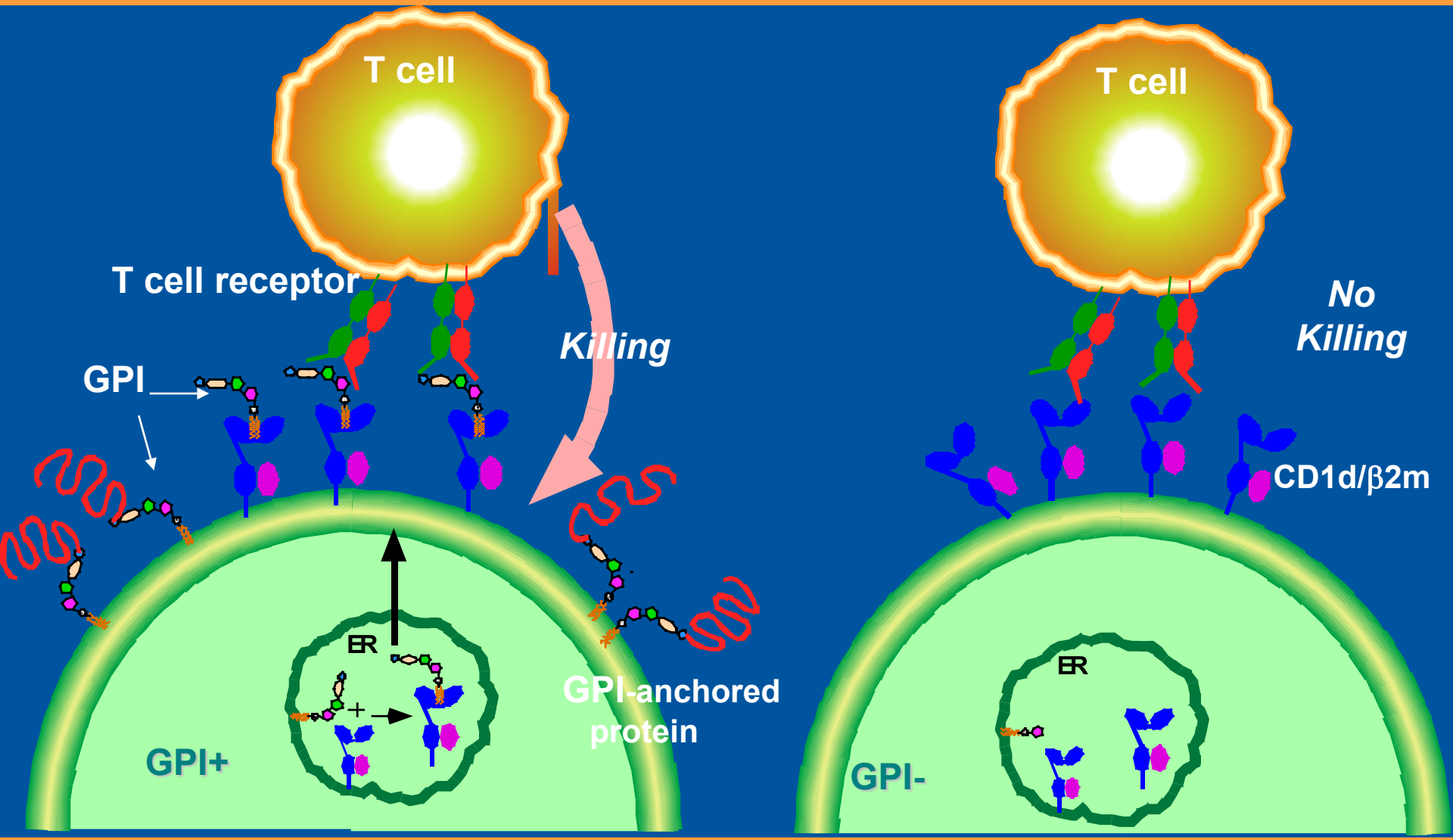
Paroxysmal Nocturnal Hemoglobinuria

Pathogenesis



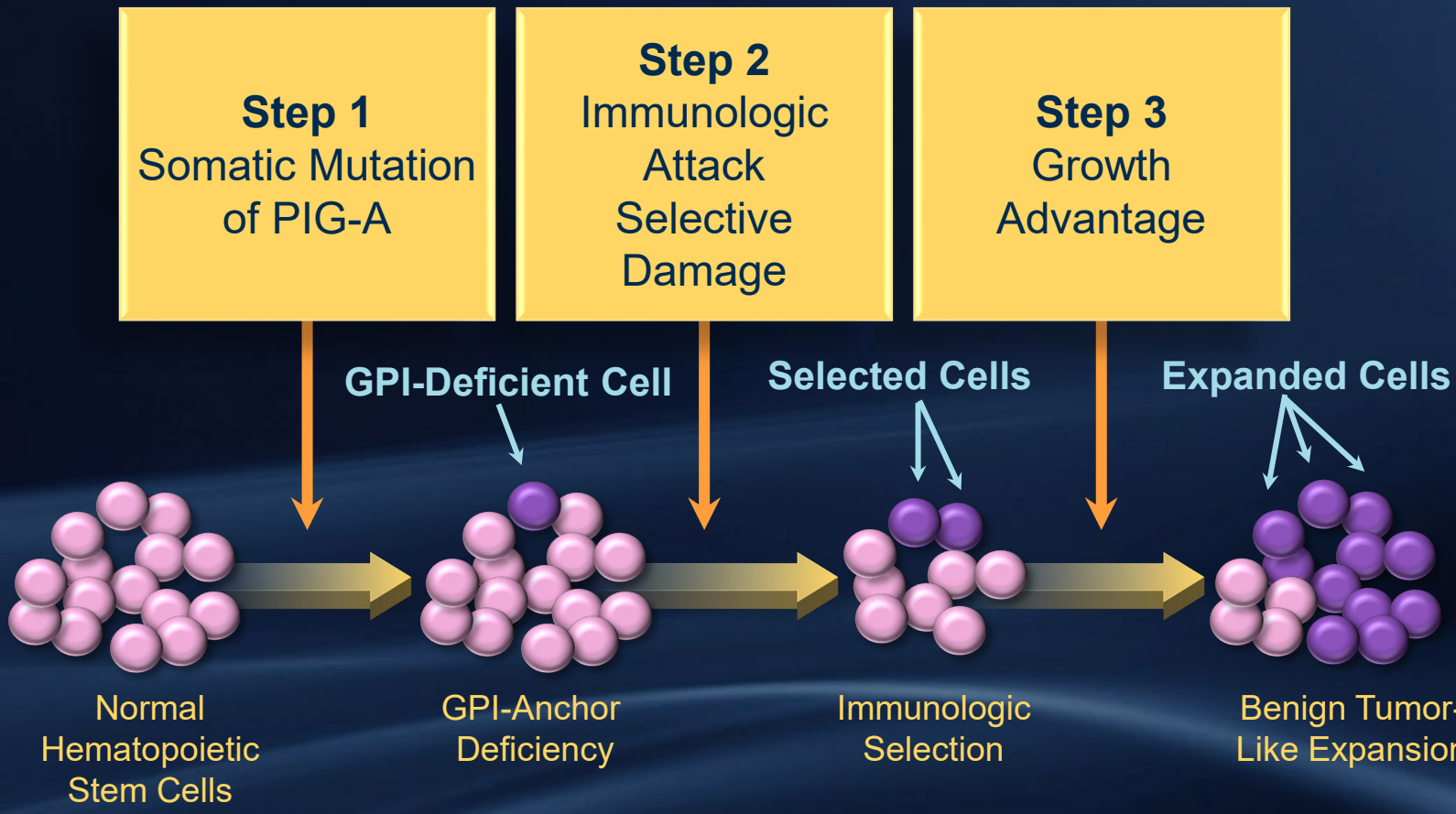
Hematopoietic Stem Cells

Hypothesis: GPI-specific, CD1d-restricted T cells responsible for selection of PNH cells



Karadimitris and Luzzatto, *Leukemia* 2001

Expansion of the PNH Clone Is Necessary to Result in Clinical PNH

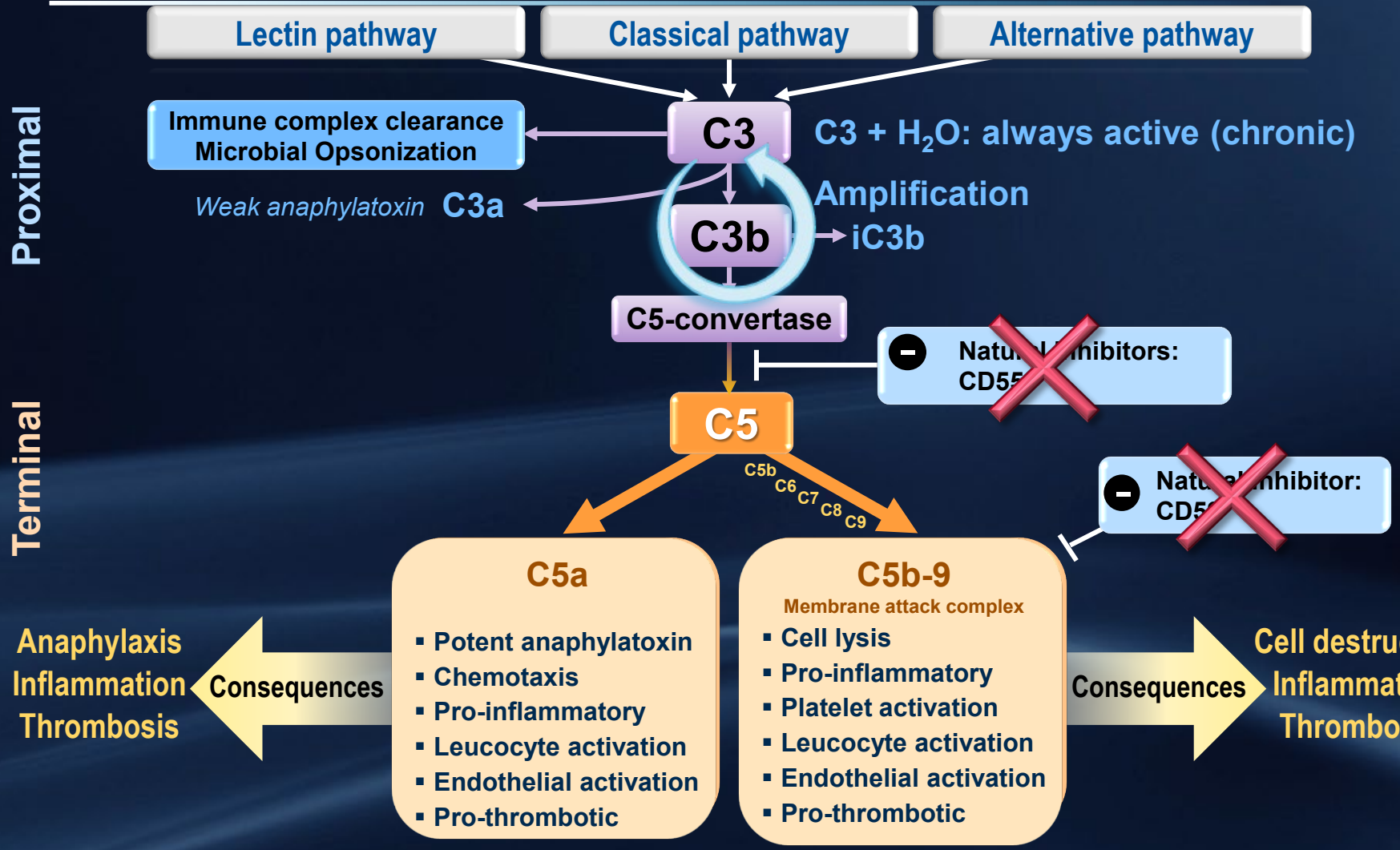


- Expansion may be due to another somatic mutation
- The need for both selection and expansion may explain the rarity of PNH

Adapted from: Inoue N *et al. Int J Hematol* 2003;77:107.

The Role of Complement

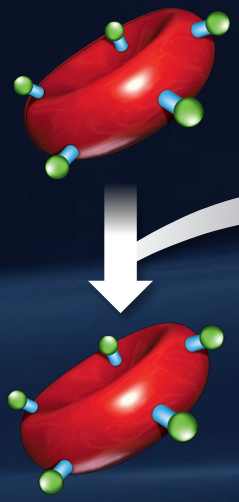
Chronic Uncontrolled Complement Activation Leads to Devastating Consequences in PNH



1. Zipfel PF et al. *Vaccine*. 2008;26(Suppl 8):I67-74; 2. Figueroa JE, Densen P. *Clin Microbiol Rev*. 1991;4:359-95; 3. Walport MJ. *N Engl J Med*. 2001;344:1058-66;
4. Rother RP et al. *Nat Biotechnol*. 2007;25:1256-64; 5. Meyers G et al. *Blood*. 2007;110:abs 3683; 6. Hill A et al. *Br J Haematol*. 2010;149:414-25; 7. Hillmen P et al. *Am J Hematol*. 2010;85:553-9;
8. Parker C et al. *Blood*. 2005;106:3699-709; 9. Hillmen P et al. *N Engl J Med*. 1995;333:1253-8; 10. Nishimura J et al. *Medicine (Baltimore)*. 2004;83:193-207; 11. Caprioli J et al. *Blood*. 2006;108:1267-79;
12. Noris M et al. *Clin J Am Soc Nephrol*. 2010;5:1844-59; 13. George JN. *Blood*. 2010;116:4060-9; 14. Loirat C et al. *Pediatr Nephrol*. 2008;23:1957-72;
15. Ståhl AL et al. *Blood*. 2008;111:5307-15; 16. Hosler GA et al. *Arch Pathol Lab Med*. 2003;127;834-9; 17. Ariceta G et al. *Pediatr Nephrol*. 2009;24:687-96.

Historically Viewed as a Hemolytic Anemia

Normal red blood cells (RBCs) are protected from complement attack by a shield of terminal complement inhibitors

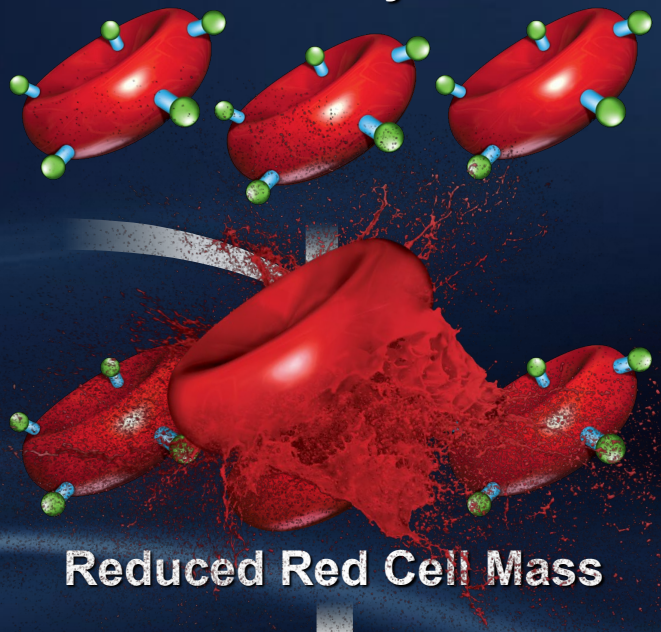


Intact RBC

Complement Activation

Lack of Bound CD55, CD59 Leads to Uncontrolled Complement Activation

Without this protective complement inhibitor shield, PNH RBCs are destroyed

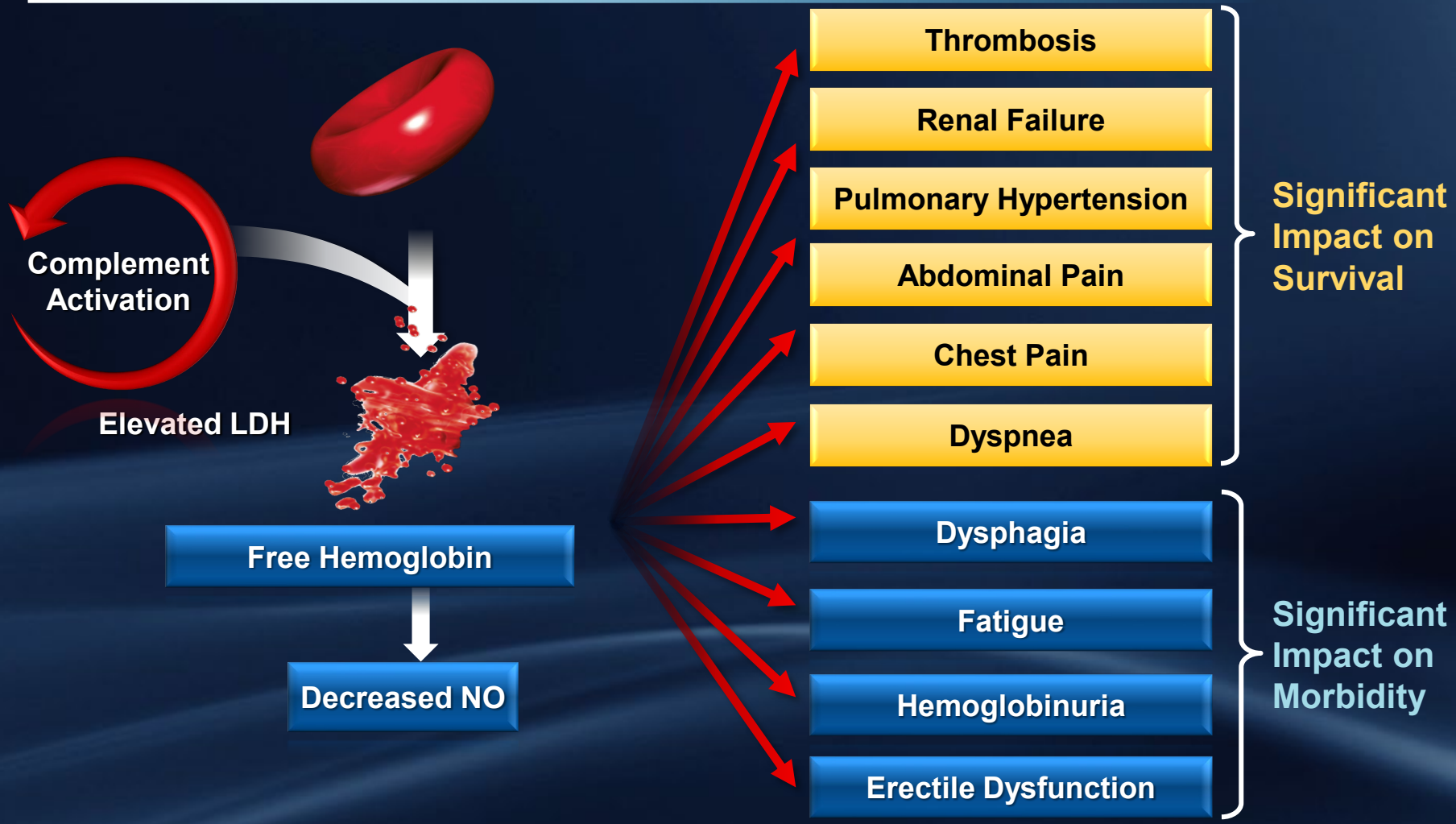


Reduced Red Cell Mass

Free Hemoglobin

1. International PNH Interest Group. *Blood* 2005;106:3699–3709. 2. Brodsky R Paroxysmal Nocturnal Hemoglobinuria. In: *Hematology - Basic Principles and Practices*. 4th ed. R Hoffman; EJ Benz; S Shattil *et al.* eds. Philadelphia, PA: Elsevier Churchill Livingstone;2005;419–427. 3. Rother RP *et al. JAMA* 2005;293:1653–1662. 4. Socie G *et al. Lancet* 1996;348:573–577. 5. Hill A *et al. Br J Haematol* 2007;137:181–192.

Chronic Uncontrolled Complement Activation Leads to Devastating Consequences



LDH = lactate dehydrogenase.

1. International PNH Interest Group. *Blood* 2005;106:3699–3709; 2. Brodsky R. Paroxysmal nocturnal hemoglobinuria. In: R Hoffman *et al,* eds. *Hematology - Basic Principles and Practices*. 4th ed. Philadelphia, PA: Elsevier Churchill Livingstone; 2005;419–427; 3. Rother RP *et al. JAMA.* 2005;293:1653–1662; 4. Socie G *et al. Lancet* 1996;348:573–577; 5. Hill A *et al. Br J Haematol* 2007;137:181–192; 6. Lee JW *et al. Hematologica* 2010;95(s2): Abstracts 505 and 506; 7. Hill A *et al. Br J Haematol* 2010;149:414–425; 8. Hillmen P *et al. Am J Hematol* 2010;85:553–559.

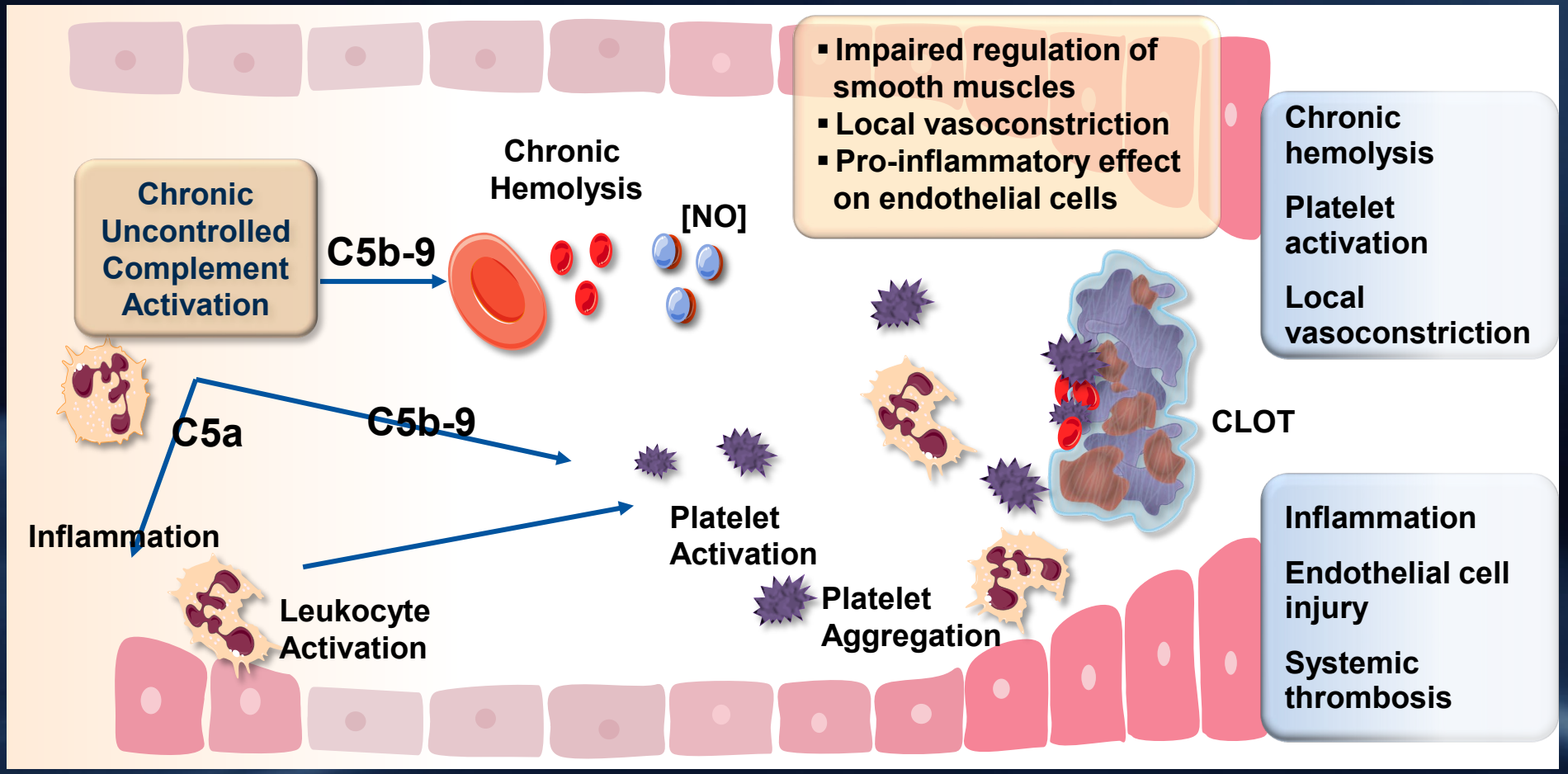
Morbidities and Mortality in PNH

Thrombosis Is the Leading Cause of Death in PNH[1]

- Accounts for 40–67% of deaths[2]
  - First thrombotic event (TE) can be fatal[2,3]
  - First TE increases risk for death 5- to 10-fold[2]
- Up to 44% of patients experience clinical thrombotic events[2]
- Occurs in typical and atypical sites[4]
- Is not adequately managed with anticoagulation[2]
- All patients with PNH are at risk for thrombosis[2]

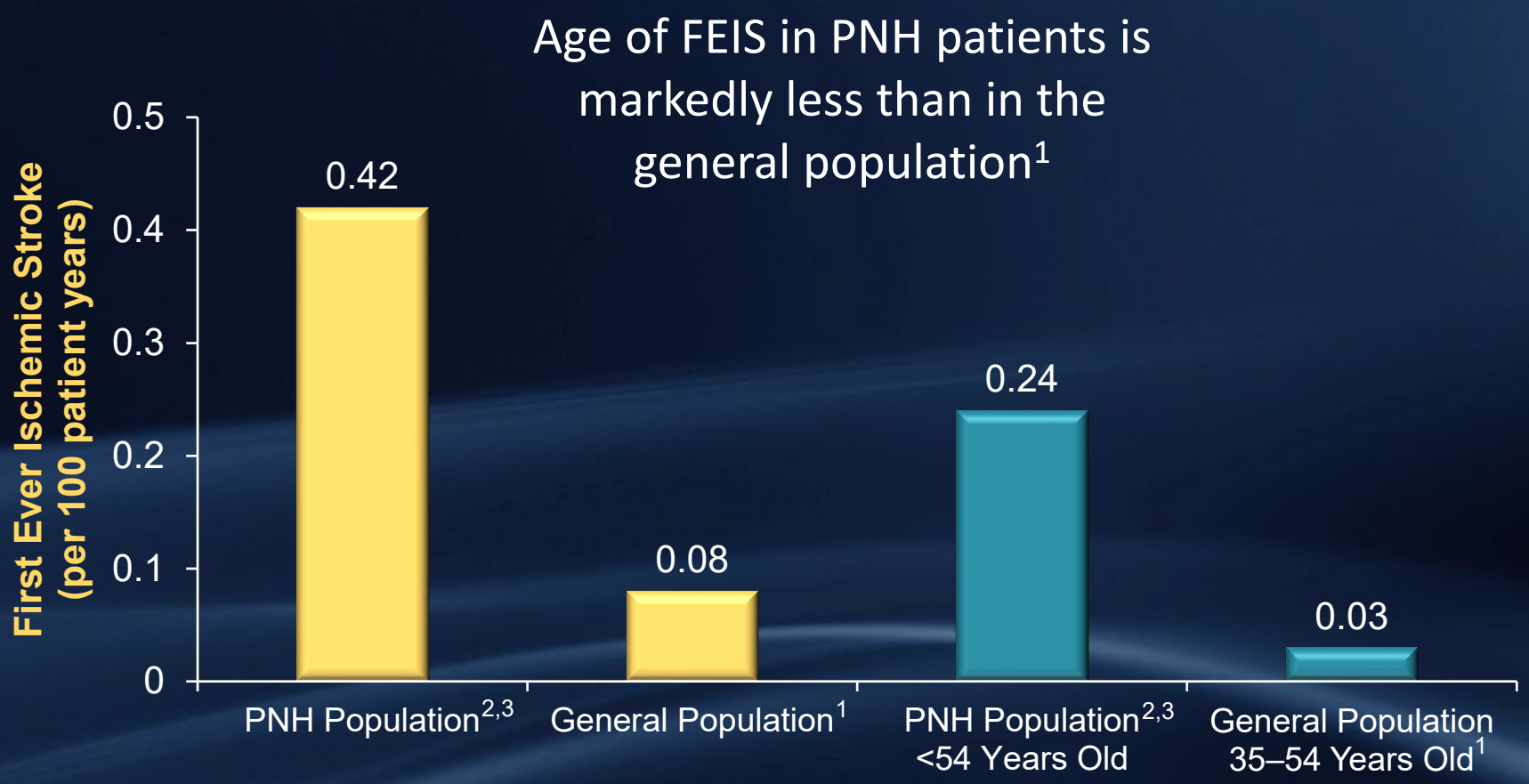
1. International PNH Group *et al. Blood* 2005;106:3699–3709; 2. Hillmen *et al. Blood* 2007;110:4123–4128;
3. Audebert HJ *et al. J Neurol* 2005;252:1379–1386; 4. Lee JW *et al. Hematologica* 2010;95(s2): Abstract 506.

Chronic Uncontrolled Complement Activation Leads to Vasoconstriction and Thrombosis



Adapted from: Gladwin MT *et al. Free Rad Biol & Med* 2004;36:707–717; Rother RP *et al. JAMA* 2005;293:1653–1662.

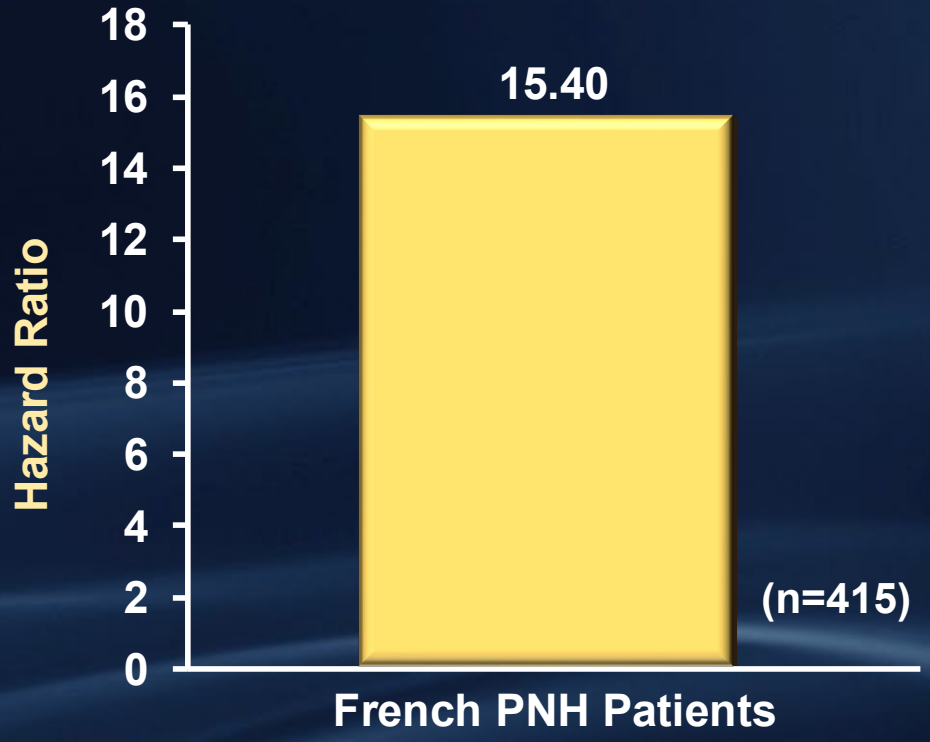
Risk of First Ever Ischemic Stroke (FEIS) Elevated in PNH



1. Gostynski M *et al. J Neurol* 2006;253:86–91; 2.Hillmen P *et al*. *Blood* 2007;110:4123–4281; 3. Data on file. Alexion Pharmaceuticals, Inc.

Thrombosis is Associated With Risk of Early Mortality

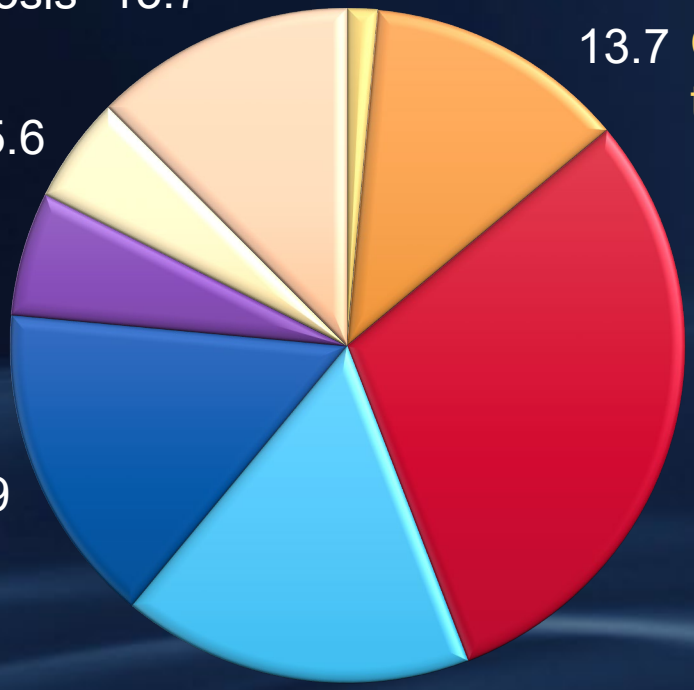
TE increases risk of death 15-fold over patients with no TE



- TE was an independent prognostic factor related to poor survival (HR 15.4; 95% CI 9.3–25.4; *P*<0.001) in a large cohort of French PNH patients

de Latour RP *et al. Blood* 2008;112:3099–3106.

Thrombosis Occurs in Both Typical and Atypical Sites*

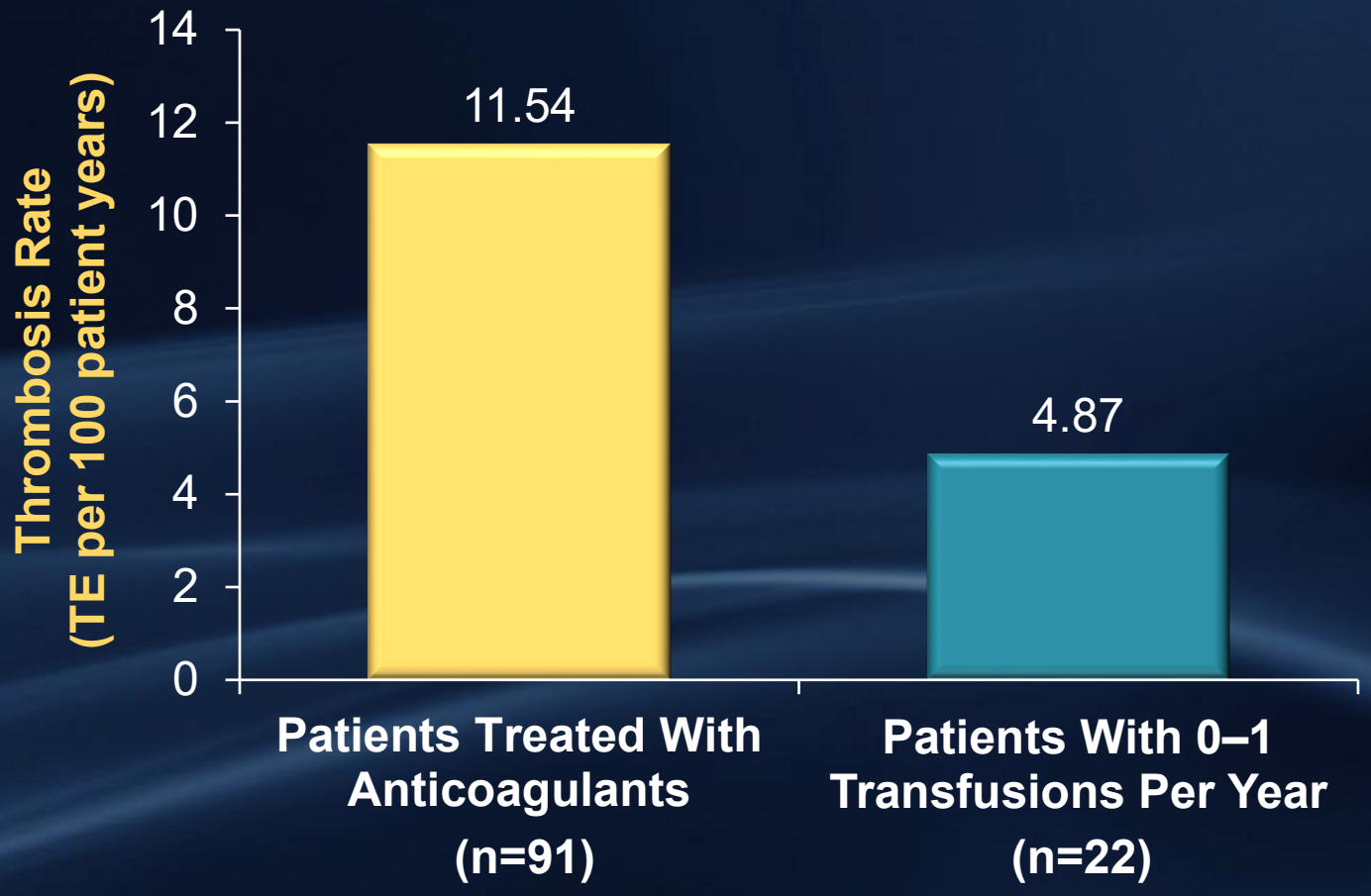


*124 events, 63 patients

*Includes 18.5% lower extremity and 14.5% other (inferior vena cava, bilateral lower extremity, pelvic, ureter, axillary, subclavian, and brachiocephalic veins).

Hillmen P *et al. Blood* 2007;110:4123–4128.

PNH Patients are at Risk of Thrombosis Despite Anticoagulation or Minimal Transfusion Requirements



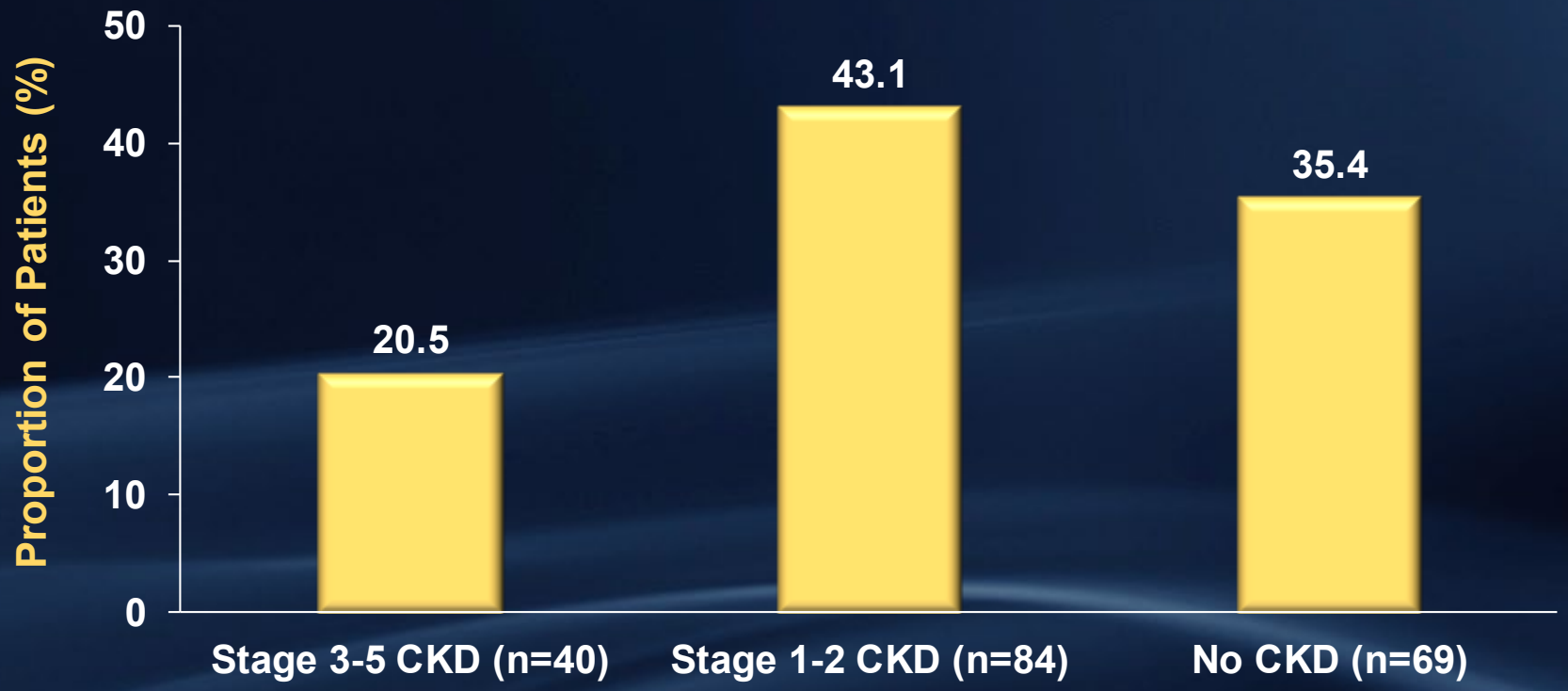
Hillmen P *et al. Blood* 2007;110:4123–4128.

Chronic Kidney Disease: Morbidity and Mortality in PNH

- Kidney failure is the cause of 8–18% of PNH-related deaths[1]
- 80% of PNH patients (median age of 31.5 years) had MRI evidence of significant renal hemosiderosis[2,3]
  - Marked hemosiderin deposits in the proximal renal tubule are a common feature in all autopsy and biopsy reports dealing with PNH
  - Demonstrable by MRI even when no overt hemoglobinuria is seen

1. Hillmen P, et al. *Am J Hematol* 2010;85:553–559; 2. Brodsky R. Hematology: Paroxysmal nocturnal hemoglobinuria. In: R Hoffman et al, eds. *Hematology - Basic Principles and Practices*. 4th ed. Philadelphia, PA: Elsevier Churchill Livingstone 2005;419–427. 3. Hill A. et al. *Blood* 2006;108: Abstract 979.

64% of PNH Patients Exhibit Clinical Chronic Kidney Disease (CKD)



1. Hillmen P *et al. Am J Hematol* 2010;85:553–559.

Kidney Disease in PNH: Conclusions

- Kidney failure is the cause of 8–18% of PNH-related deaths[1]
- Kidney disease in PNH is caused by complement-mediated hemolysis[2,3]
- 64% of patients with PNH exhibit chronic kidney disease at any one time[4]
- Kidney disease is underappreciated in PNH[4]

1. Nishimura JI *et al. Medicine* 2004;83:193–207; 2. Clark DA *et al. Blood* 1981;57:83–89; 3. McKeage K. *Drugs* 2011;71:2327–2345; 4. Hillmen P *et al. Am J Hematol* 2010;85:553–559; 5. Kim JS *et al. Hematologica* 2011;96(s2): Abstract 271.

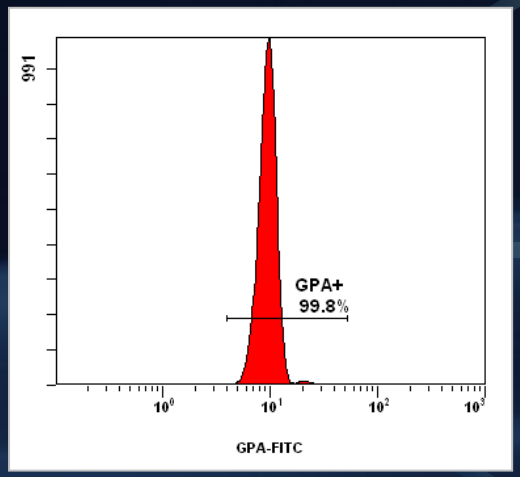
How Do You Test for PNH?

Standard Diagnostic Test for PNH

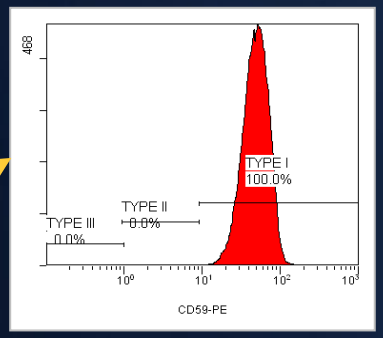
- Flow cytometry performed on peripheral blood
- Granulocytes and at least one additional cell line should be evaluated
  - RBCs
  - Monocytes
- Quantitative results
  - Optimal–high sensitivity analysis: ≥0.01%
  - Routine analysis: ≥1%
- Easy to understand PNH reports
- Use more than one reagent against GPI-anchored proteins

Borowitz MJ *et al.;* Clinical Cytometry Society. *Cytom B Clin Cytom* 2010;78B:211–230.

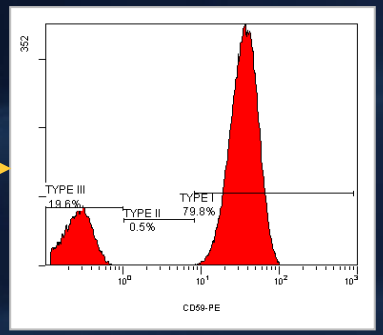
Testing for PNH in RBCs



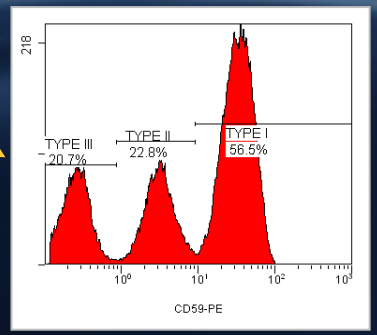
Gating on GPA+ RBCs



Patient 1:
Normal RBCs with normal CD59 expression (Type I cells)



Patient 2:
PNH clone with complete CD59 deficiency (Type III cells)



Patient 3:
PNH clone with complete CD59 deficiency (Type III cells) and partial CD59 deficiency (Type II cells)

GPA = glycophorin A.
Data Source: Dahl-Chase Diagnostic Services..

Why Look Beyond RBCs for PNH?

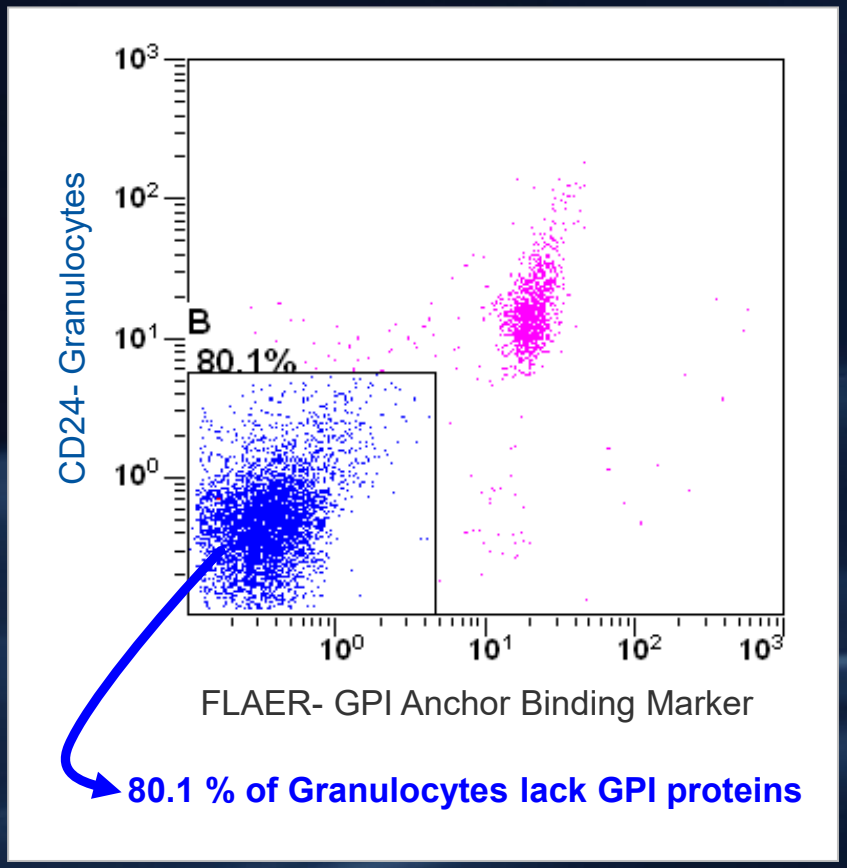
- Granulocytes provide more accurate representation of PNH clone size[1]
- Percentages of PNH RBCs may be affected by:
  - Hemolysis
  - Blood transfusion

PNH reports should provide quantitative results expressing clone size on both granulocytes and RBCs

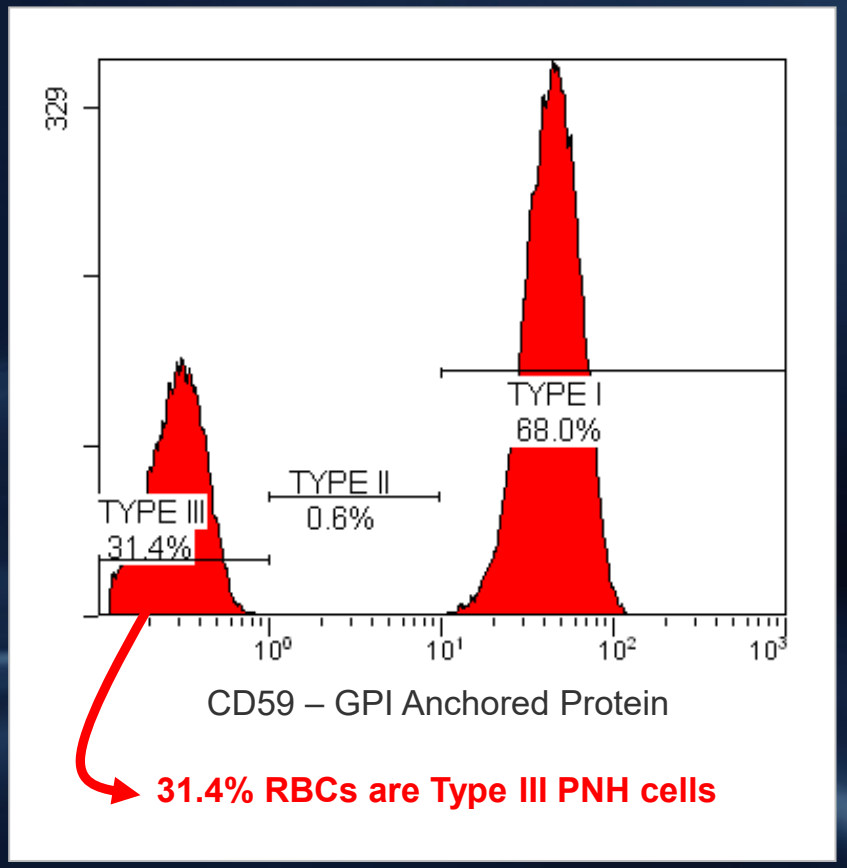
1. Borowitz MJ *et al;* Clinical Cytometry Society. *Cytom B Clin Cytom* 2010;78B:211–230.

PNH Patient With an 80% WBC Clone Size and 31% RBC Clone Size Indicating Hemolysis

WBC



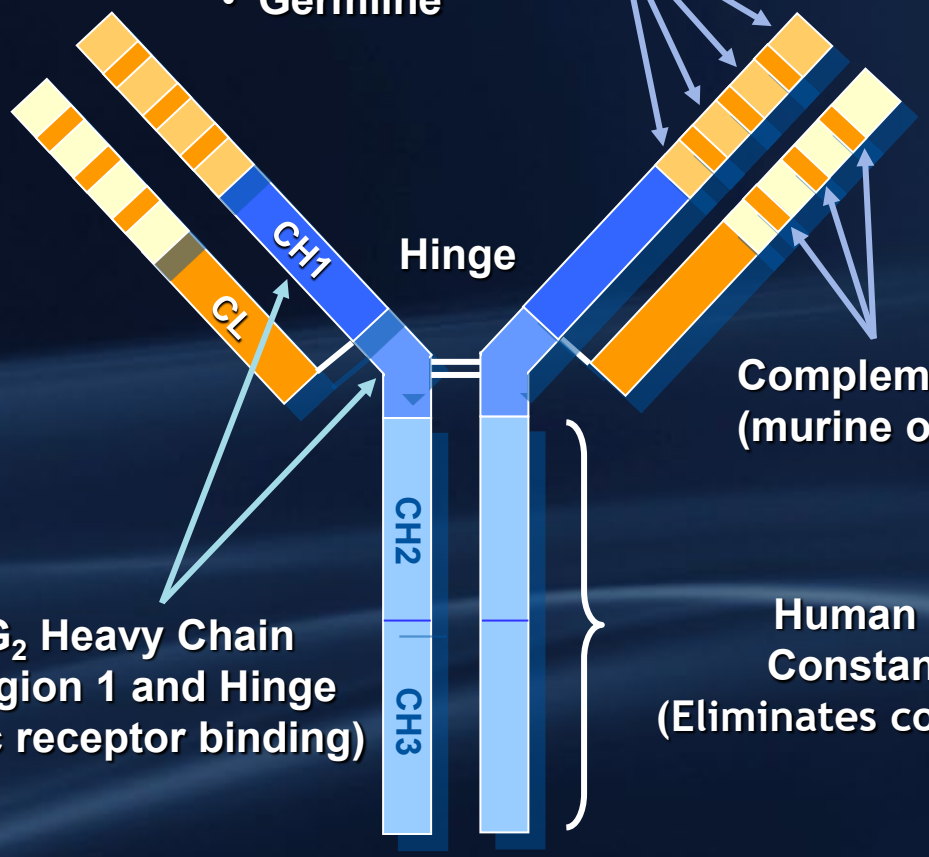
RBC



Data Source: Dahl-Chase Diagnostic Services.

Treatment of PNH with Complement Inhibitor Eculizumab

Eculizumab (Soliris) Humanized First in Class Anti - C5 Antibody

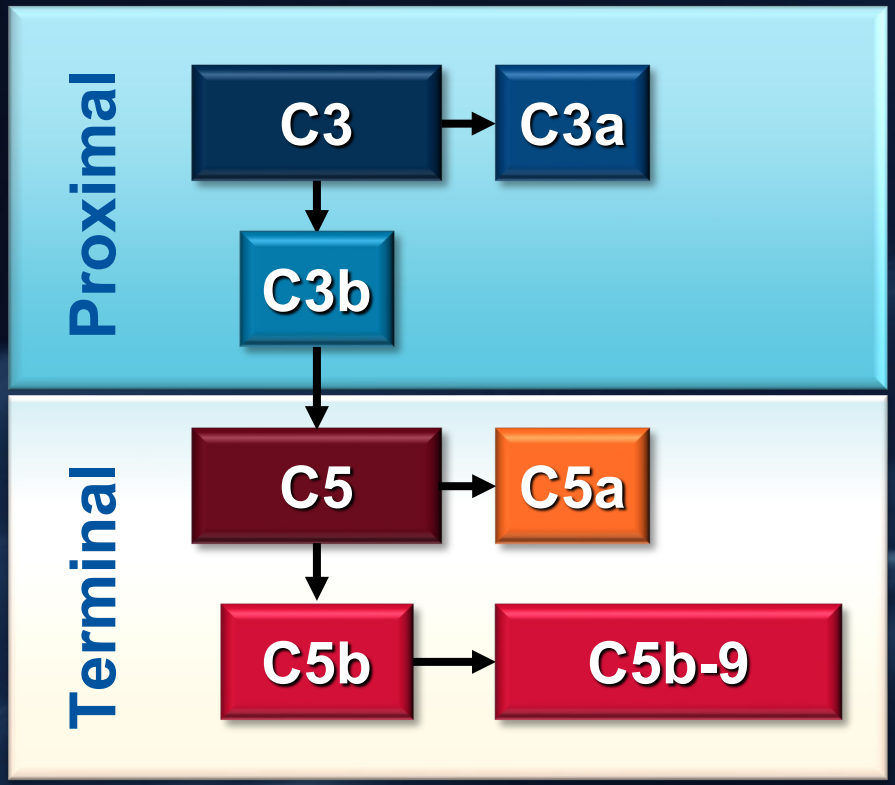


Rother R et al. Nat Biotech 2007;25:1256

Eculizumab Blocks Terminal Complement[1,2]

Eculizumab

Complement Cascade[2,3]



- Eculizumab binds with high affinity to C5[1,2]
- Terminal complement - C5a and C5b-9 formation blocked[1,2]
- Proximal functions of complement remain intact[1,2]
  - Weak anaphylatoxin[2,4]
  - Immune complex clearance[2]
  - Microbial opsonization[2]

Please see full prescribing information for Soliris® (eculizumab).

1. Soliris® (eculizumab) Summary of Product Characteristics. Alexion Europe SAS; 2012; 2. Rother RP *et al*. *Nature Biotech* 2007;25:1256–1264;
3. Walport MJ. *N Engl J Med* 2001;344:1058–1066; 4. Figueroa JE, Densen P. *Clin Microbiol Rev* 1991;4:359–395.

Clinical Trials With Eculizumab

Pilot Study – *NEJM* 2004
Phase II, Age ≥18 years, PNH+, ≥4 RBC TFN over 1 year,
Primary endpt: hemolysis
N=11

TRIUMPH – *NEJM* 2006
Phase III, Double-Blind placebo-control,
Age ≥18 years, RBC clone ≥10%, LDH ≥ 1.5X ULN
≥4 RBC TFN over 1 year, plat. Ct. ≥100K, N=87
Primary endpts: Hgb level, RBC TFN

SHEPHERD – *Blood* 2008
Phase III, Age ≥18 years, RBC clone ≥10%, LDH ≥ 1.5X ULN, ≥1 RBC TFN over 2 years, plat. ct. ≥30K,
Primary endpt: LDH
N = 97

Long-Term Extension Trial *Blood* 2007
Evaluated long-term safety, efficacy and effect on thrombosis; Placebo patients switched to eculizumab
N=187

AEGIS– *Int. Jnl. Hematol. 2013*
Japanese population, Age ≥12 years, RBC clone ≥10%, LDH ≥ 1.5X ULN, ≥1 RBC TFN over 2 years, plat. ct. ≥30K,
Primary endpt: LDH
N = 27

Please see full prescribing information for Soliris® (eculizumab).
Soliris® (eculizumab) Summary of Product Characteristics. Alexion Europe SAS; 2012.

Eculizumab is a Chronic Treatment for a Chronic Disease

Eculizumab PNH Dosing Schedule										
Pretreatment		**Induction Phase**				**Maintenance Phase**				
≥2 weeks before induction	**Week →**	1	2	3	4	5	6	7	8	9
Neisseria meningitidis vaccination	**Ecu dose, mg**	600	600	600	600	900	X	900	X	900

q14d

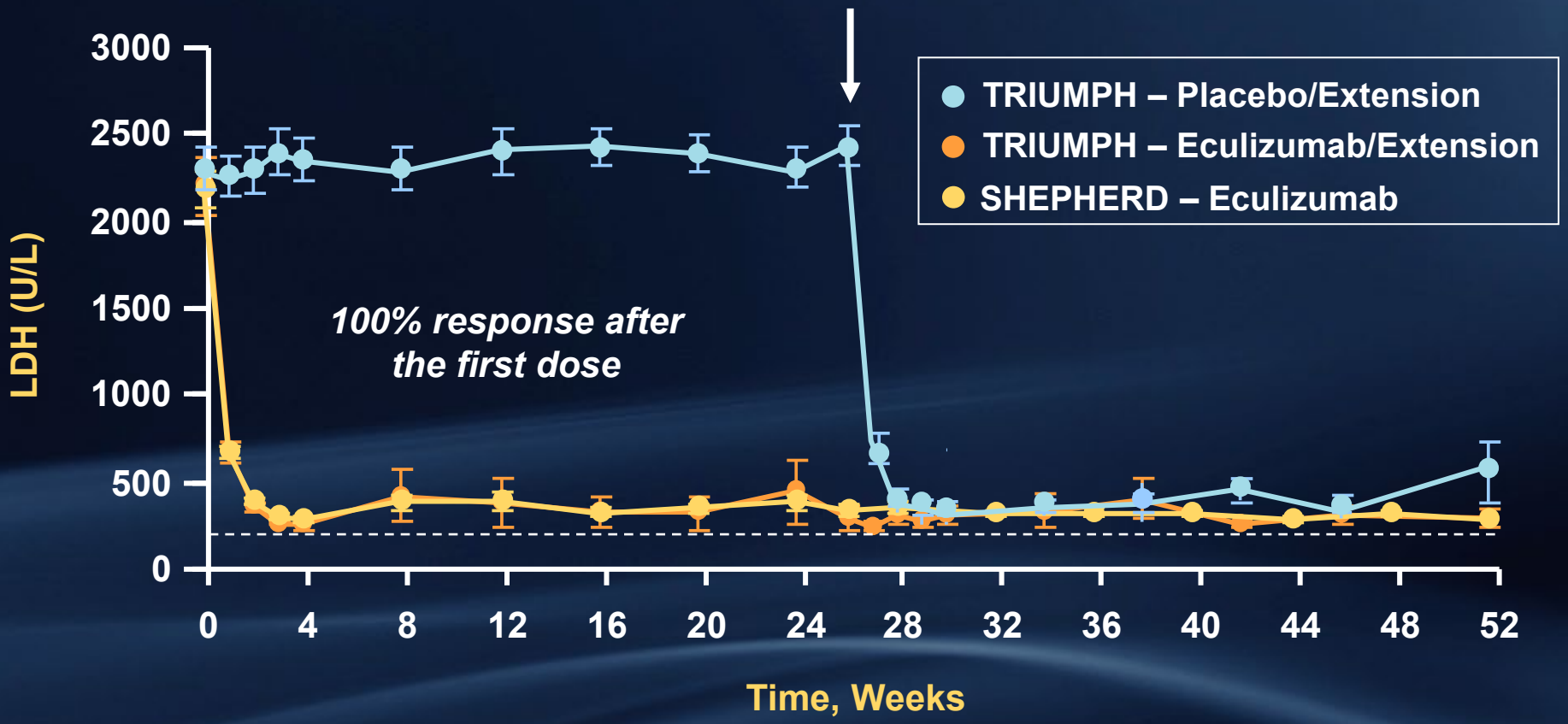
Dose within ±2 days.

- In clinical trials all patients were vaccinated against *Neisseria meningitidis*[1]
- Concomitant medications allowed:
  - Steroids, immunosuppressant drugs, anti-clotting agents and hematinics[2]
- Eculizumab should be administered via IV infusion within 25-45 minutes every 7 days during induction and every 14 days during maintenance[1]
- Eculizumab dose adjustment to every 12 days may be necessary for some patients to maintain LDH reduction[1]

Please see full prescribing information for Soliris® (eculizumab).

1. Soliris® (eculizumab) Summary of Product Characteristics. Alexion Europe SAS; 2012. 2. Hillmen P *et al. N Engl J Med* 2004;350:552–559.

86% Reduction in LDH: TRIUMPH and SHEPHERD



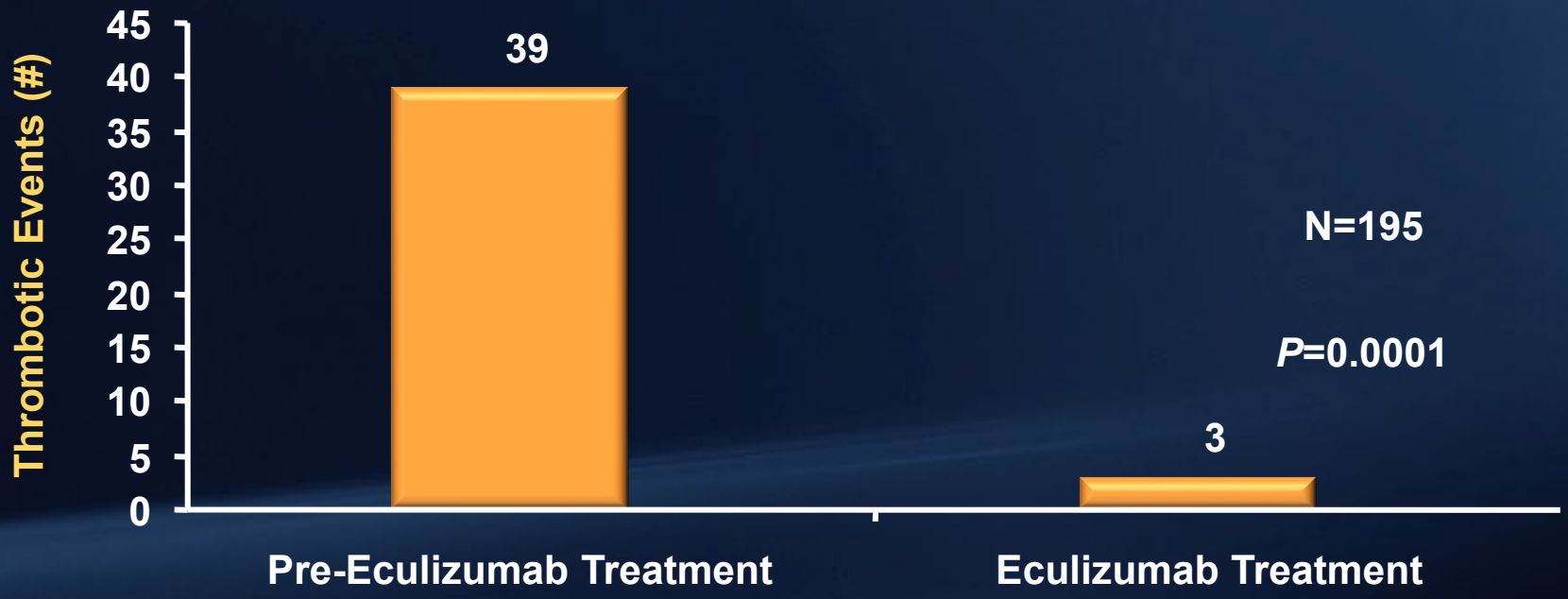
- TRIUMPH placebo patients switched to Eculizumab after Week 26
- All TRIUMPH patients entered the long-term extension study

P<0.001 at all measured time points.

Please see full prescribing information for Soliris® (eculizumab). Soliris® (eculizumab) Summary of Product Characteristics. Alexion Europe SAS; 2012.

Hillmen P *et al. Blood* 2007;110:4123–4128.

92% Reduction in Thrombotic Events

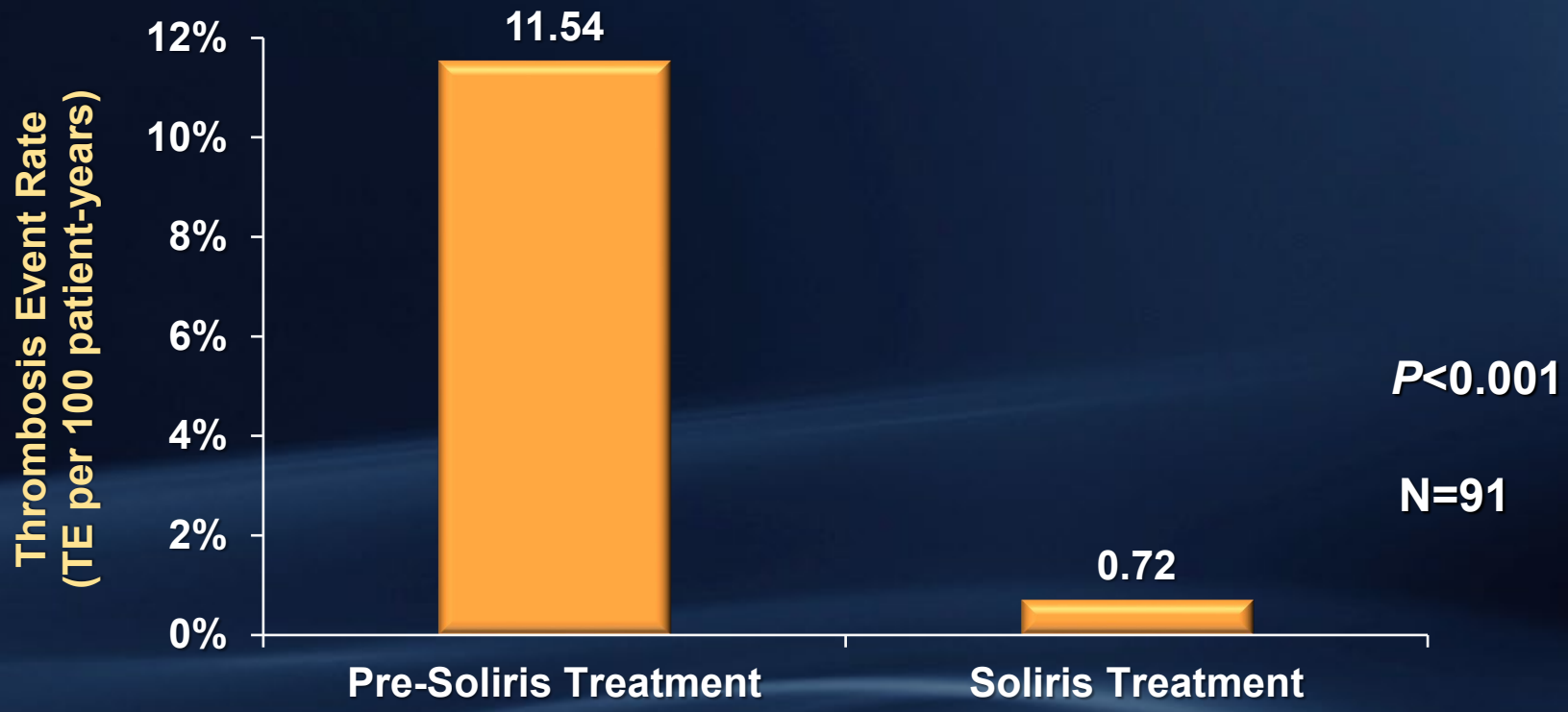


- 63% of patients received concomitant anticoagulants[1]
- The effect of anticoagulant withdrawal was not studied[2]
- Events observed in both venous and arterial sites[3]
- There were fewer thrombotic events with Eculizumab treatment than during the same period of time prior to treatment[2]

Please see full prescribing information for Soliris® (eculizumab).

1. Brodsky R *et al. Blood* 2008;111:1840–1847; 2. Soliris® (eculizumab) Summary of Product Characteristics. Alexion Europe SAS; 2012;
3. Hillmen P *et al. Blood* 2007;110:4123–4128.

Eculizumab Reduced Thrombosis in Patients Treated with Anticoagulants[1]



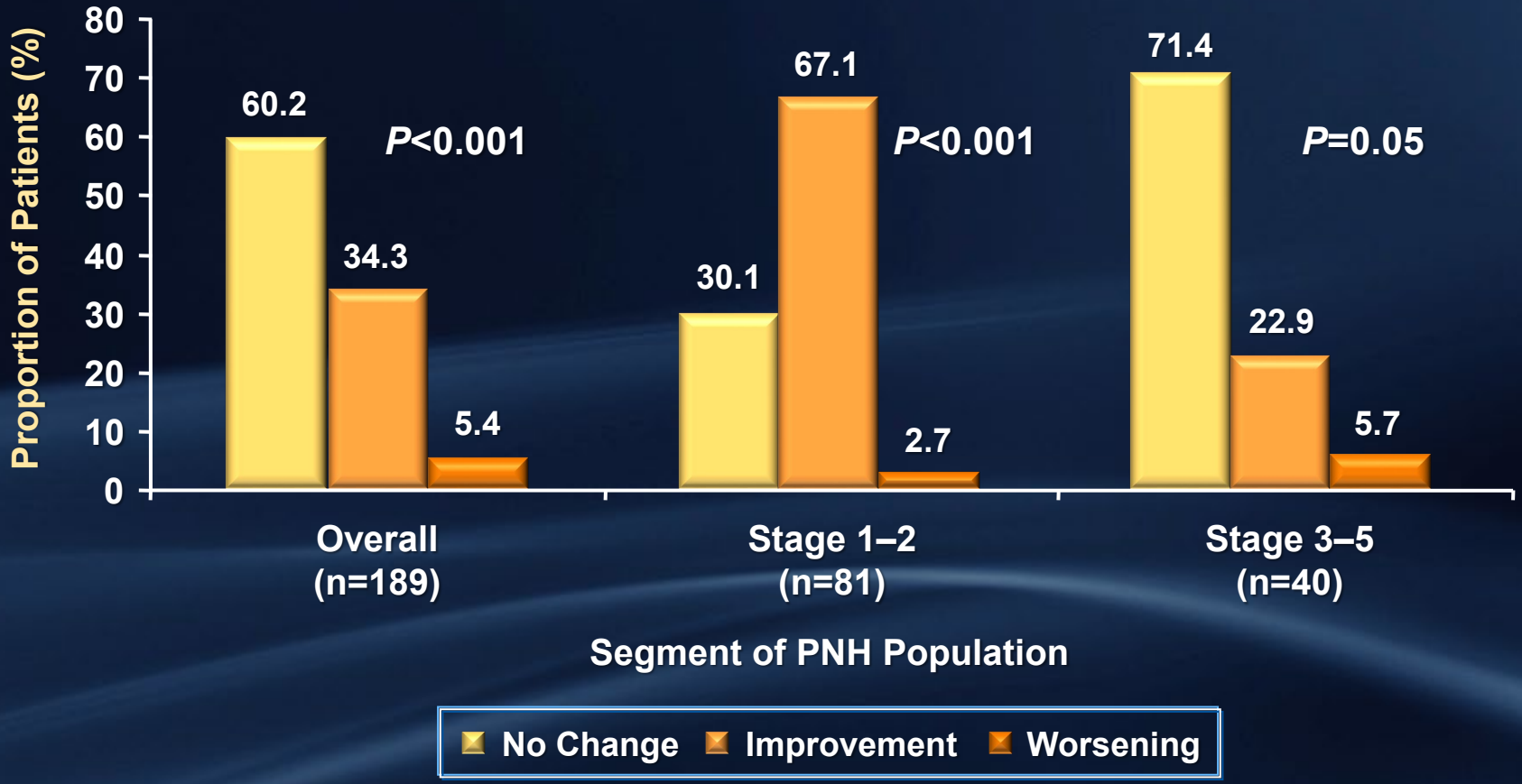
94% reduction in event rate with Eculizumab

*Excludes patients on antiplatelet agents.

Please see full prescribing information for Soliris® (eculizumab). Soliris® (eculizumab) Summary of Product Characteristics. Alexion Europe SAS; 2012.

1. Hillmen P *et al. Blood* 2007;110:4123–4128.

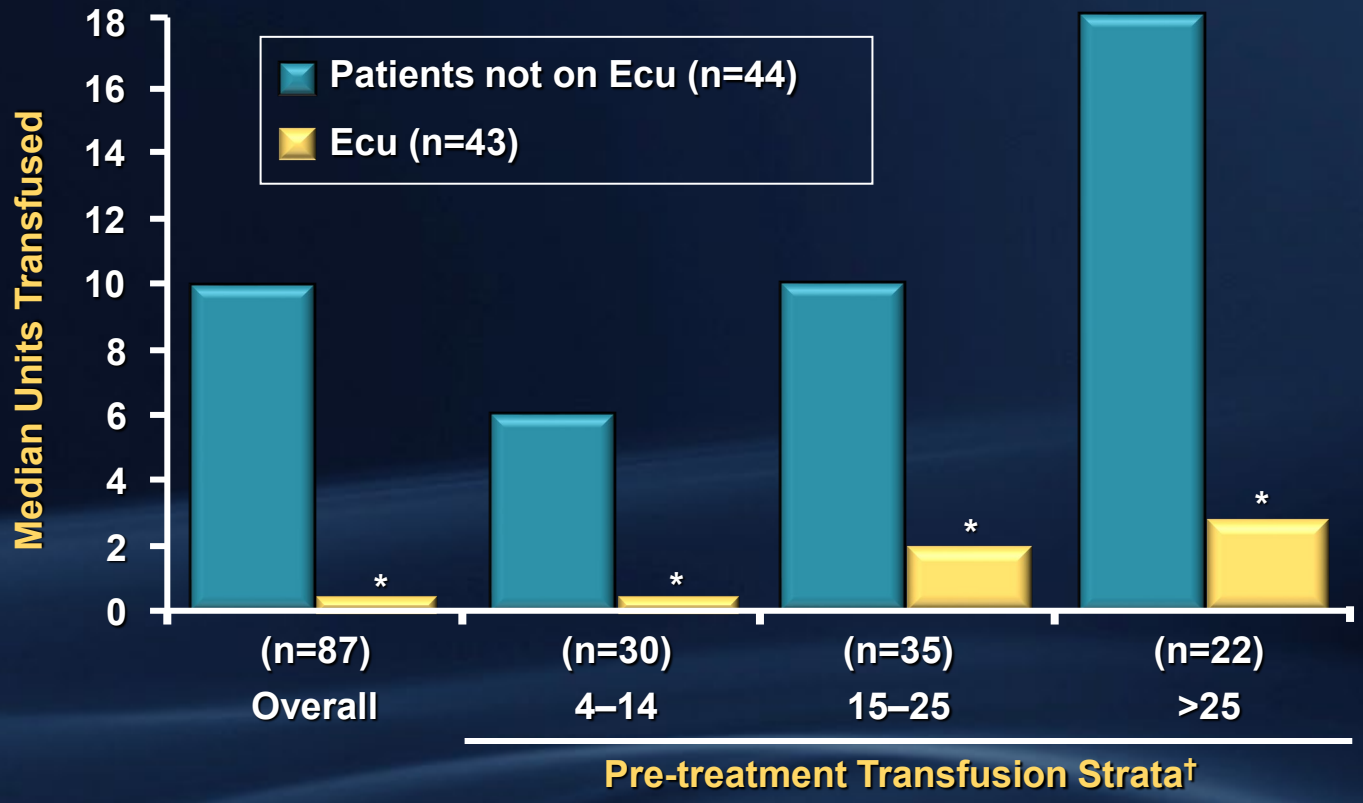
Renal Function With Eculizumab in Different Baseline PNH Populations – 18 Months[1]



Please see full prescribing information for Soliris® (eculizumab). Soliris® (eculizumab) Summary of Product Characteristics. Alexion Europe SAS; 2012.

1. Hillmen P *et al. Am J Hematol* 2010;85:553–559.

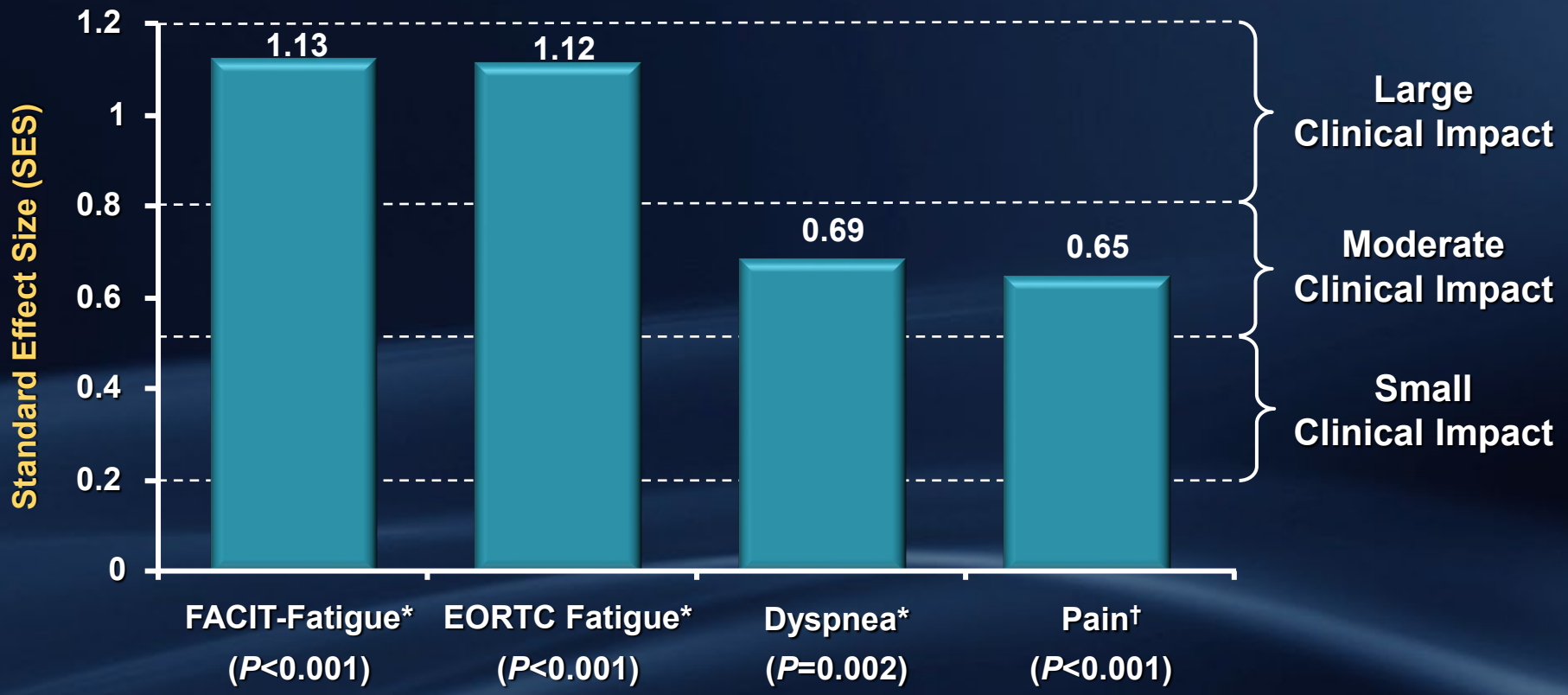
73% Reduction in Mean Units Transfused Across All Subgroups: TRIUMPH



- 51% of Ecu patients achieved transfusion independence vs 0% of patients not on Ecu[1]
- Patients with concomitant bone marrow dysfunction may continue to require transfusions[2]

*P<0.001.
†Transfusion data obtained during 12 months before treatment; values were normalized for a 6-month period.
Please see full prescribing information for Soliris® (eculizumab). Soliris® (eculizumab) Summary of Product Characteristics. Alexion Europe SAS; 2012.
1. Hillmen P *et al. N Engl J Med* 2006;355;1233–1243; 2. Schubert J. *Br J Haematol* 2008;142:263–272.

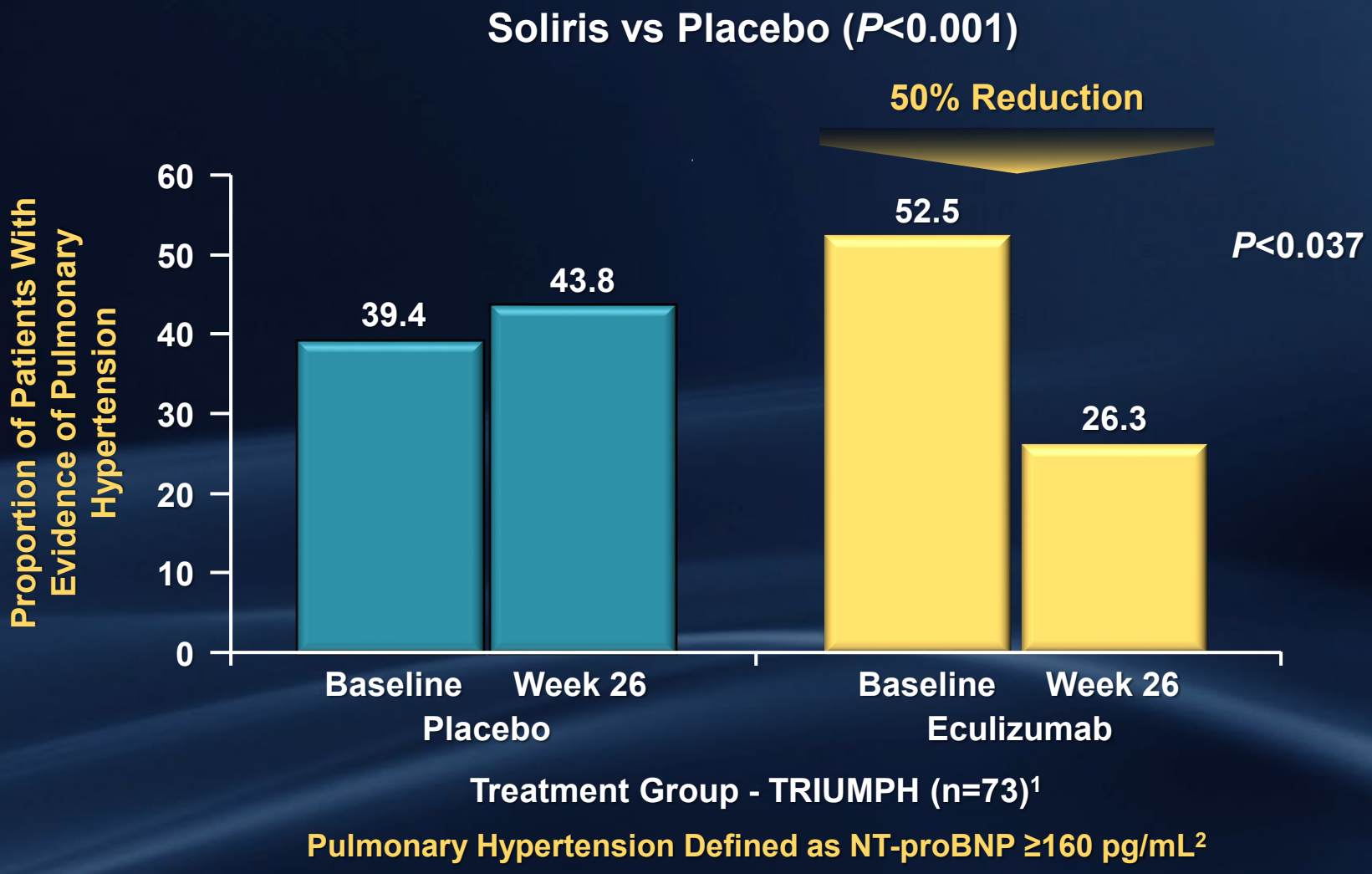
Eculizumab Treatment Results in Large and Clinically Meaningful Improvements in Patient-Reported Outcomes



Please see full prescribing information for Soliris® (eculizumab). Soliris® (eculizumab) Summary of Product Characteristics. Alexion Europe SAS; 2012.

1. Brodsky R *et al. Blood* 2006;108: Abstract 3770; 2. Data on file. Alexion Pharmaceuticals. 3. Weitz I, et al. *Internal Medicine Journal* 2012. Accepted Article; doi: 10.1111/j.1445-5994.2012.02924.x

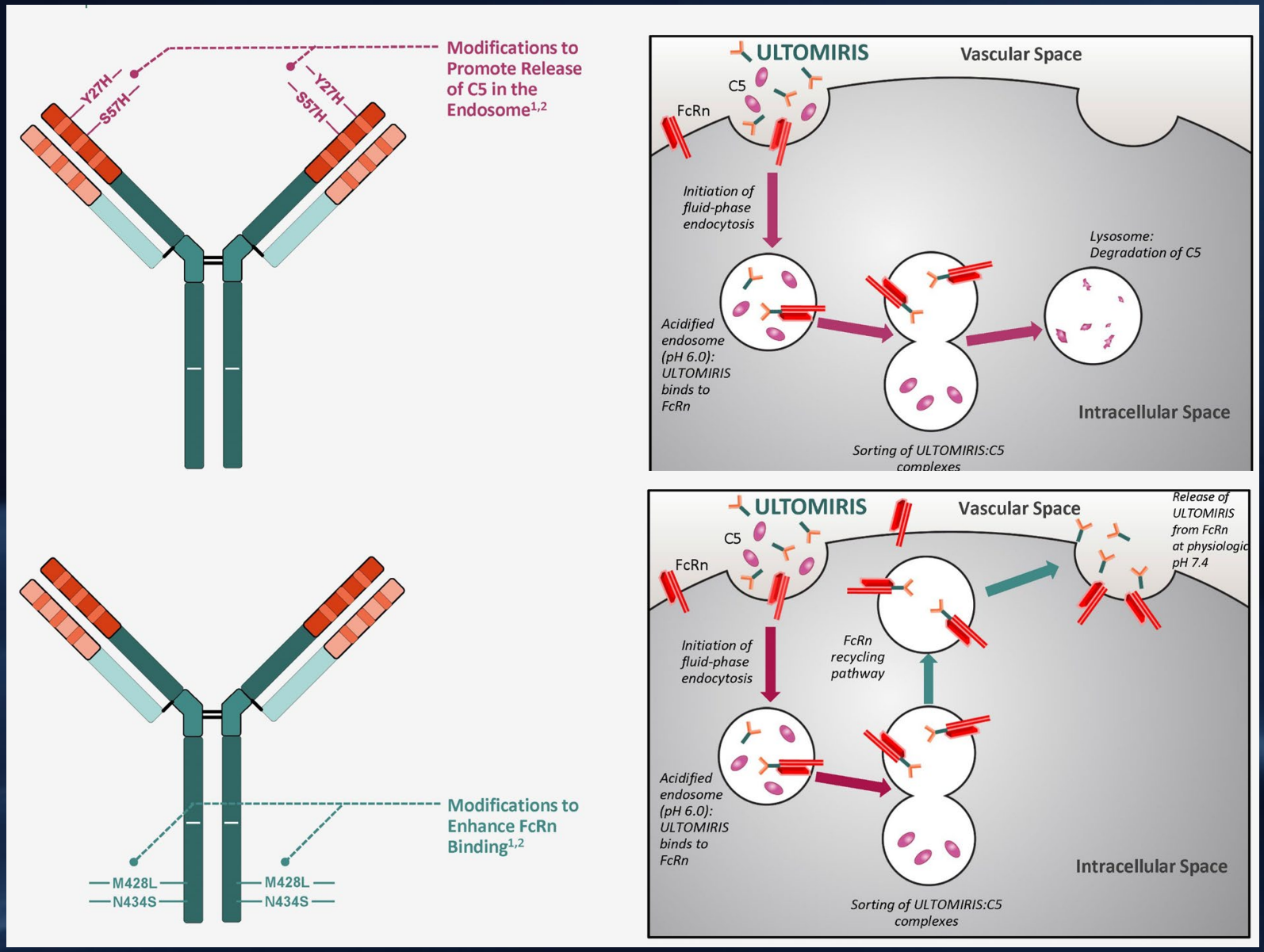
Reduction of Pulmonary Hypertension With Eculizumab as Measured by NT-ProBNP



Please see full prescribing information for Soliris® (eculizumab). Soliris® (eculizumab) Summary of Product Characteristics. Alexion Europe SAS; 2012.

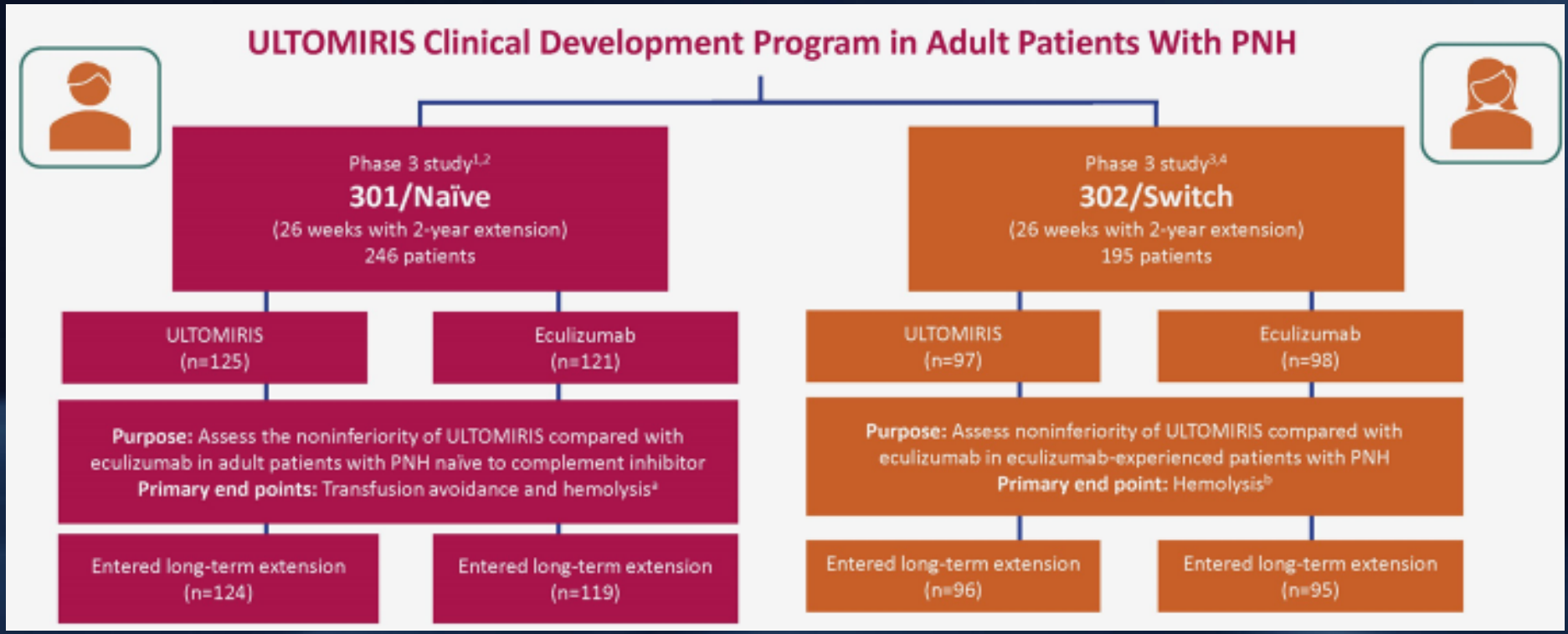
1. Hill A *et al. Br J Haematol* 2012;158:409–414. 2. Machada *et al. JAMA*. 2006.

Development of Ravulizumab (Ultomiris)



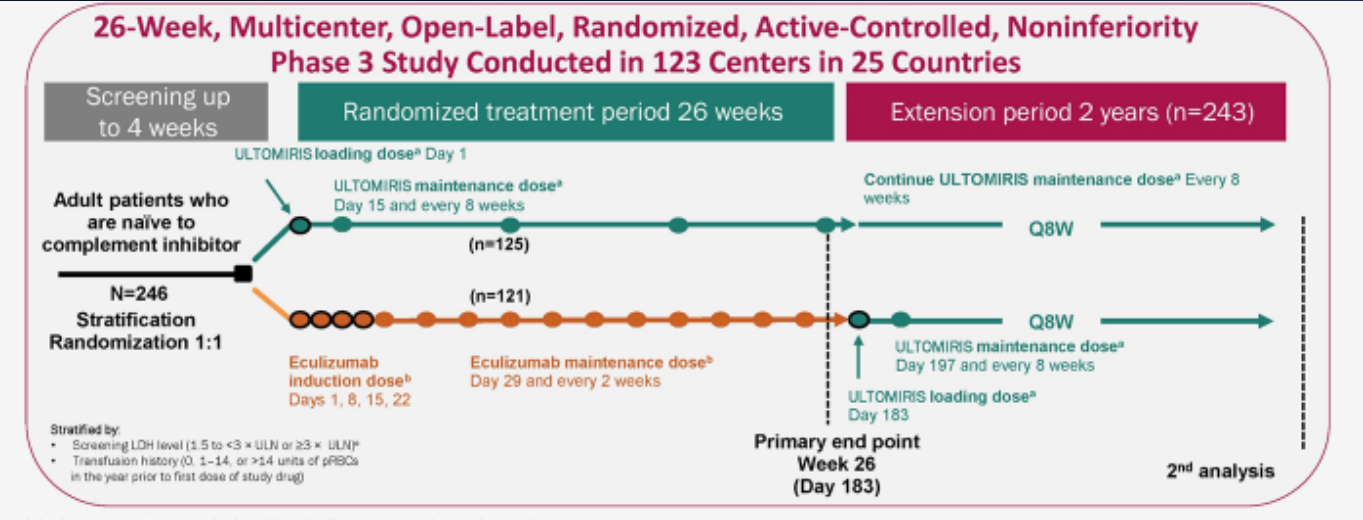
Röth et al. Blood Advances 2018;2:2176-2185

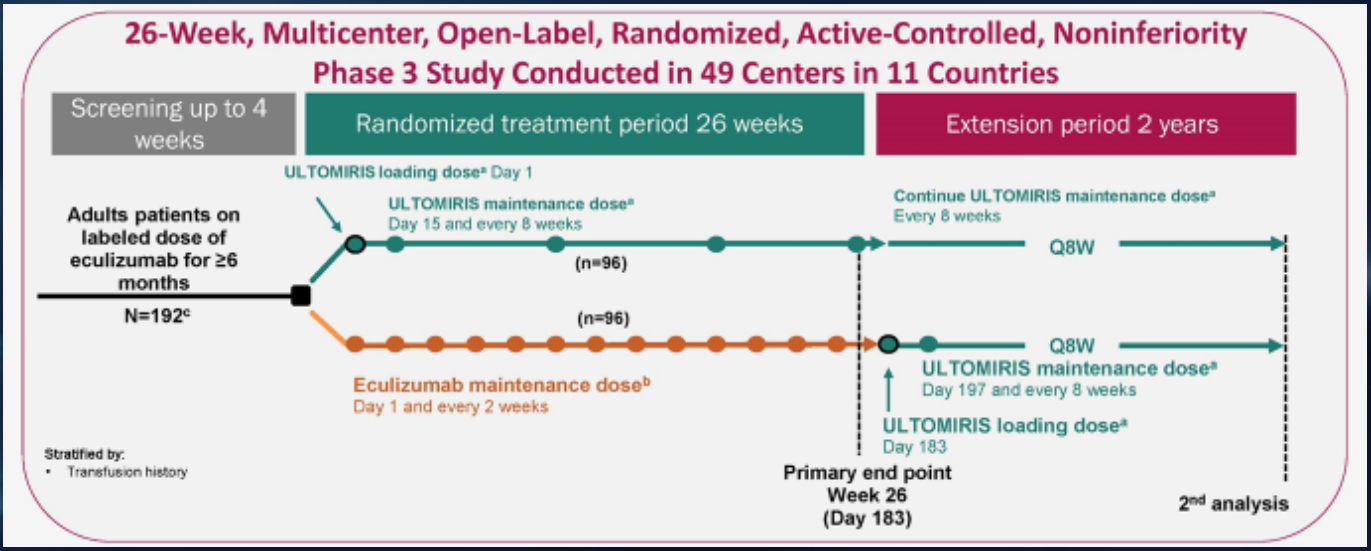
Ravulizumab: 2 Randomized Non-inferiority Trials



Lee et al. Blood 2019;133:530-539
Kulasekararaj et al. Blood 2019;133:54-549

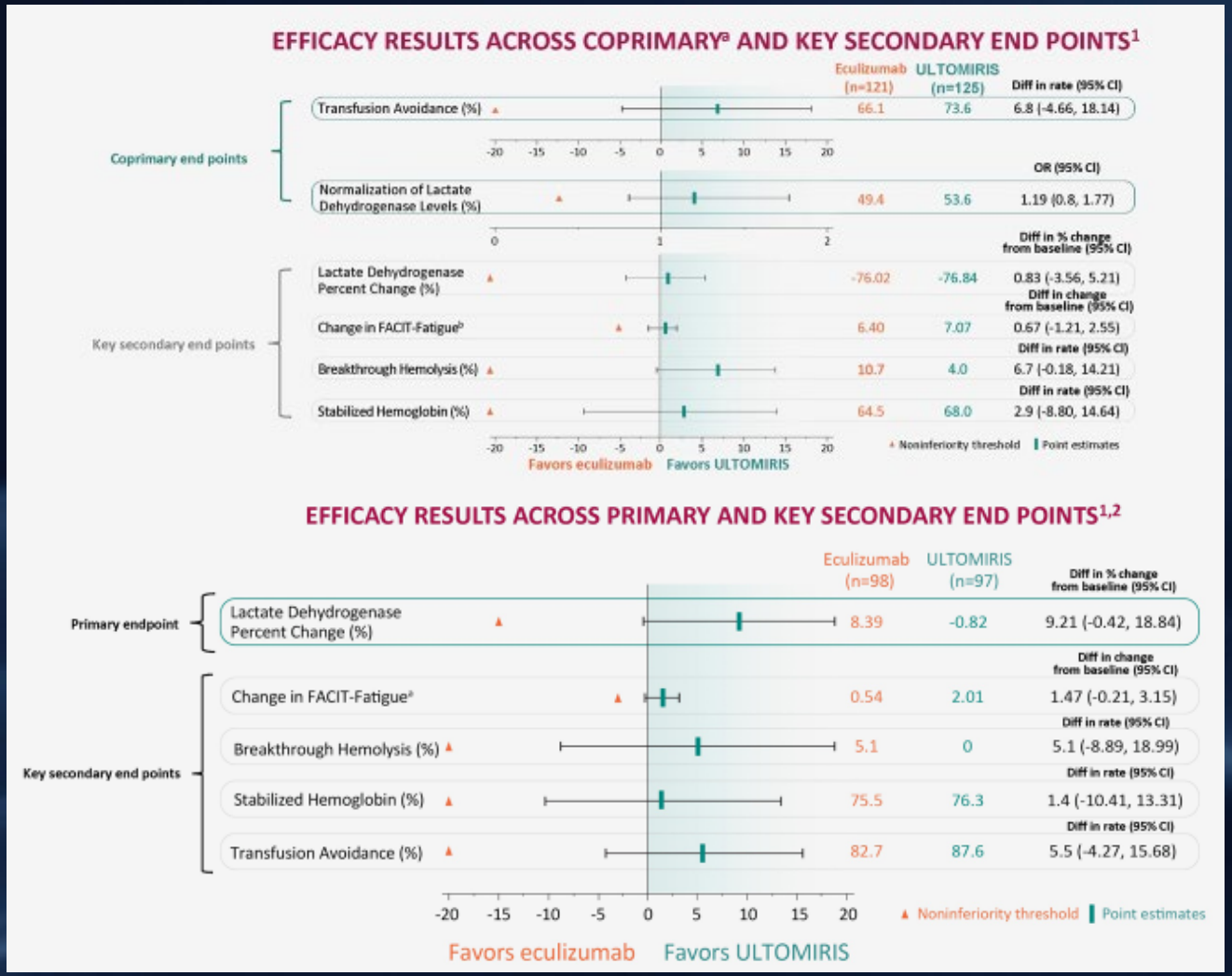
Ravulizumab: Naïve and Switch Trials





Lee et al. Blood 2019;133:530-539
Kulasekararaj et al. Blood 2019;133:54-549

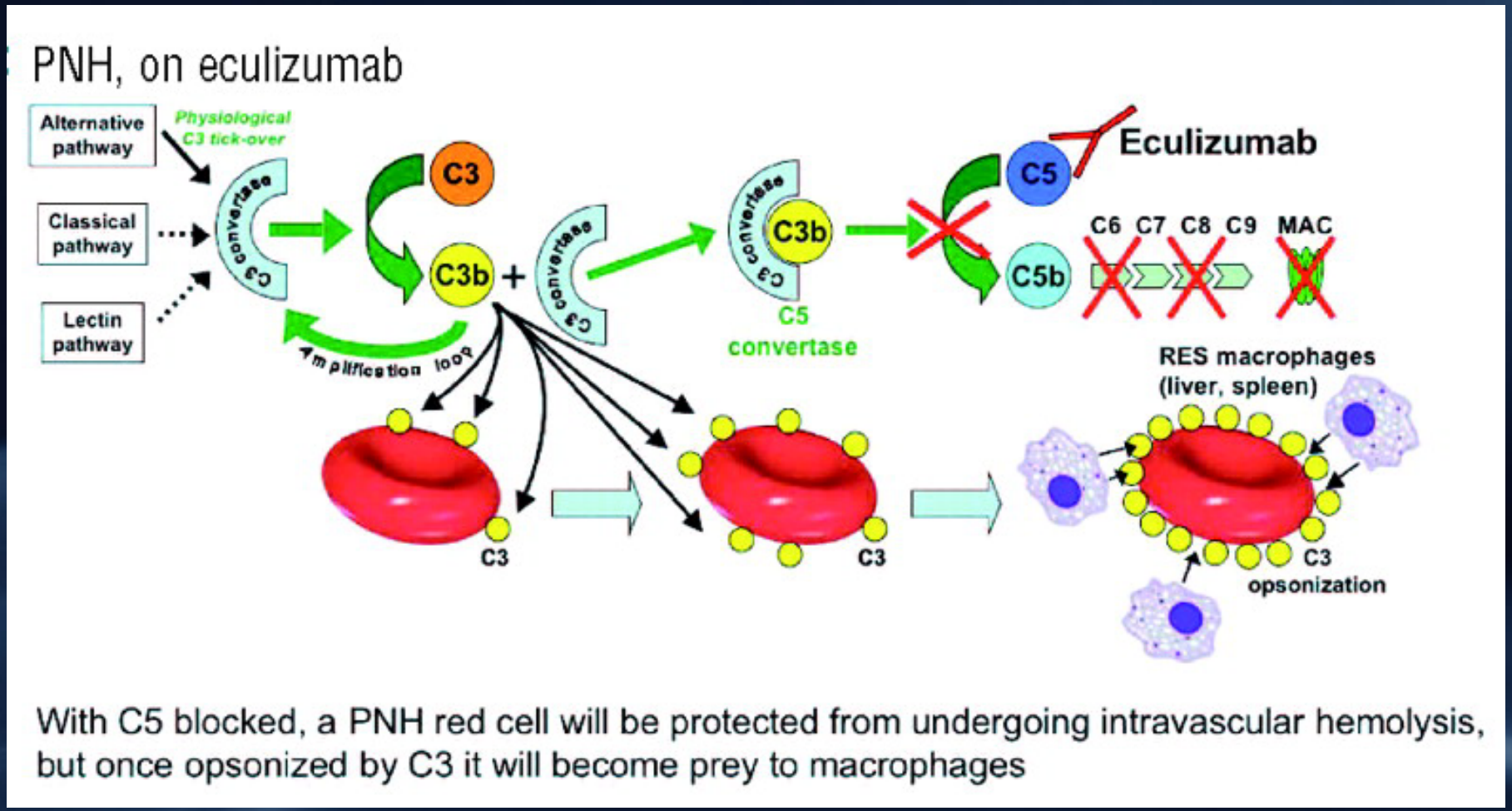
Ravulizumab vs. Eculizumab 301 and 302



Lee et al. Blood 2019;133:530-539
Kulasekararaj et al. Blood 2019;133:54-549

Role of Complement 3 in Continued Extravascular Hemolysis

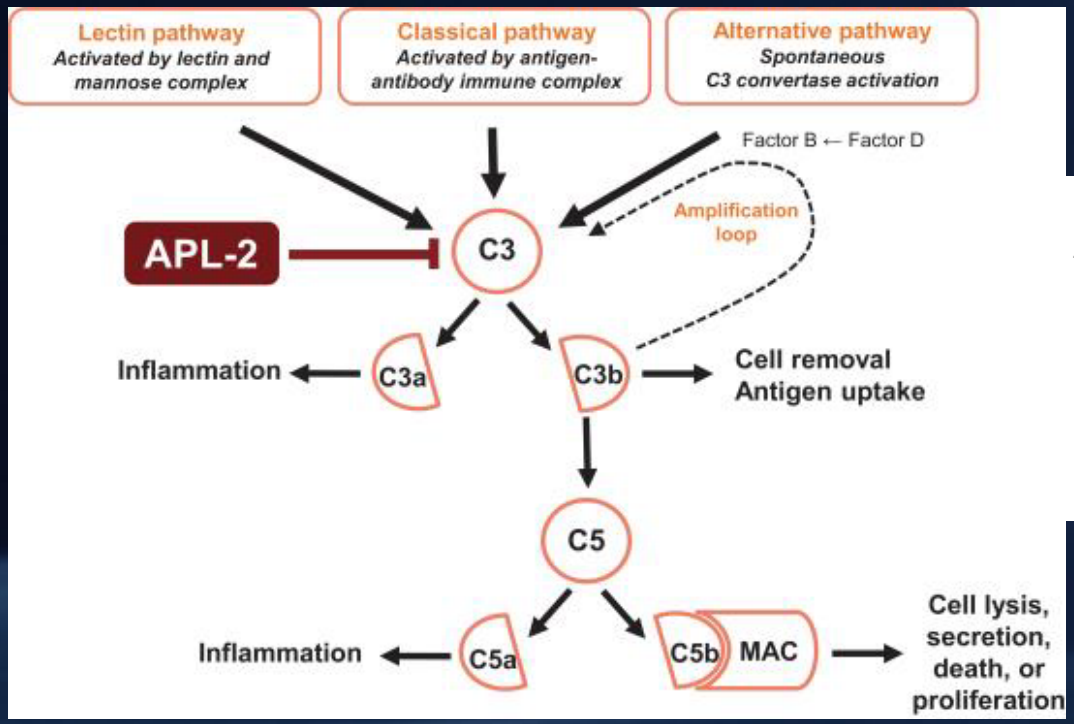
Complement Cascade Regulation and Erythrocytes

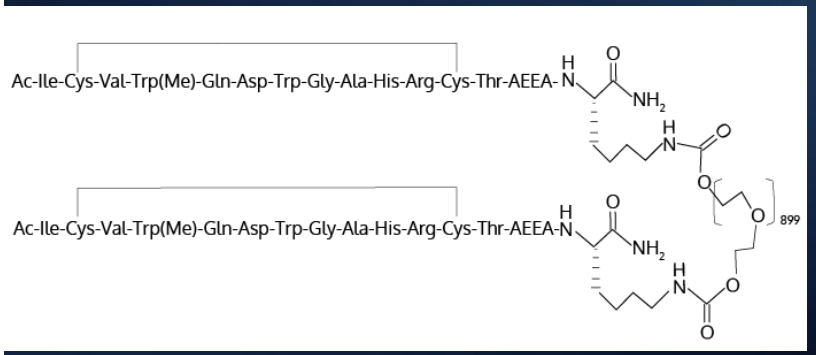


With C5 blocked, a PNH red cell will be protected from undergoing intravascular hemolysis, but once opsonized by C3 it will become prey to macrophages

Lucio Luzzatto et al. Haematologica 2010;95:523-526

PEGCETACOPLAN (EMPAVELI)

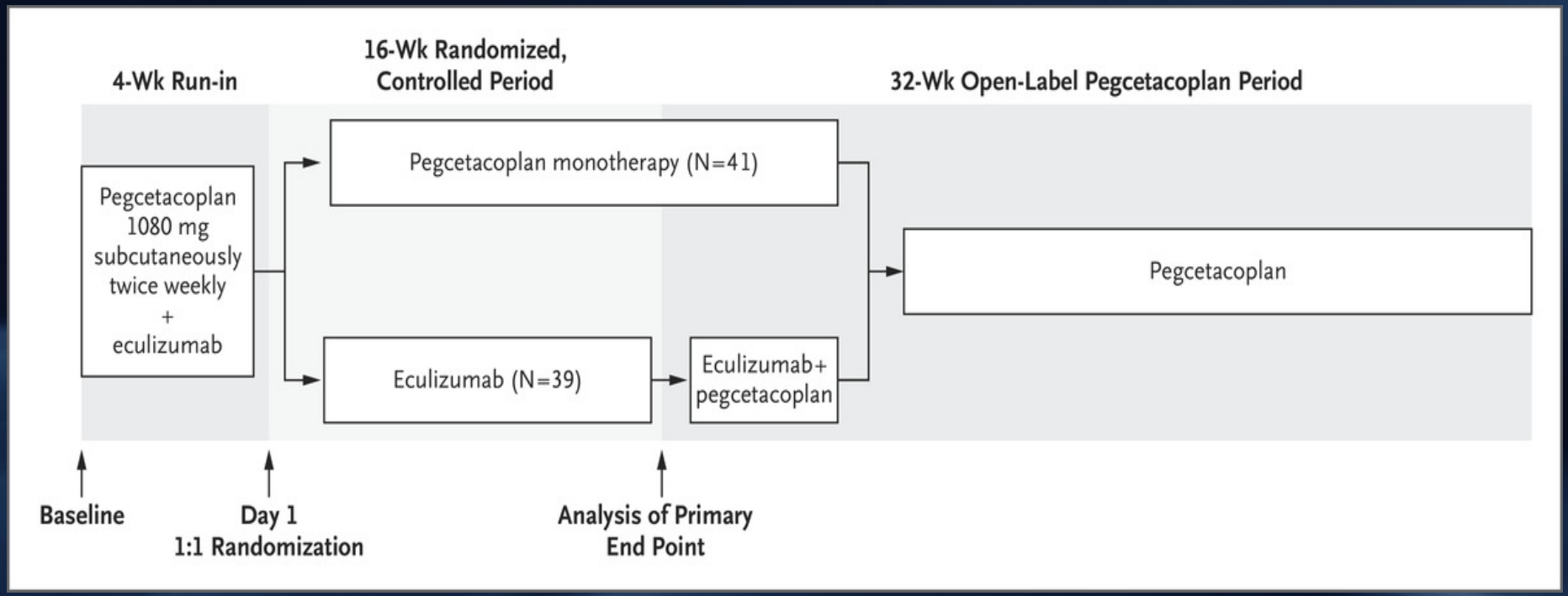




Pegylated peptide binds to C3
1080 mg/20ml SQ infusion twice weekly increase to 3/wk if LDH elevated
Meningitis, HIB, Srep vaccine required 2 weeks prior to starting
Self-infusion at home, infusion time 30 min with 2 sites or 60 min with 1 site

PEGASUS—RCT Pegcetacoplan

EC: stable dose of Ecu for 3 months, at least 1 TFN within 12 months, Hgb <10.5, ANC >500, plat >30K, abs retic >1.5

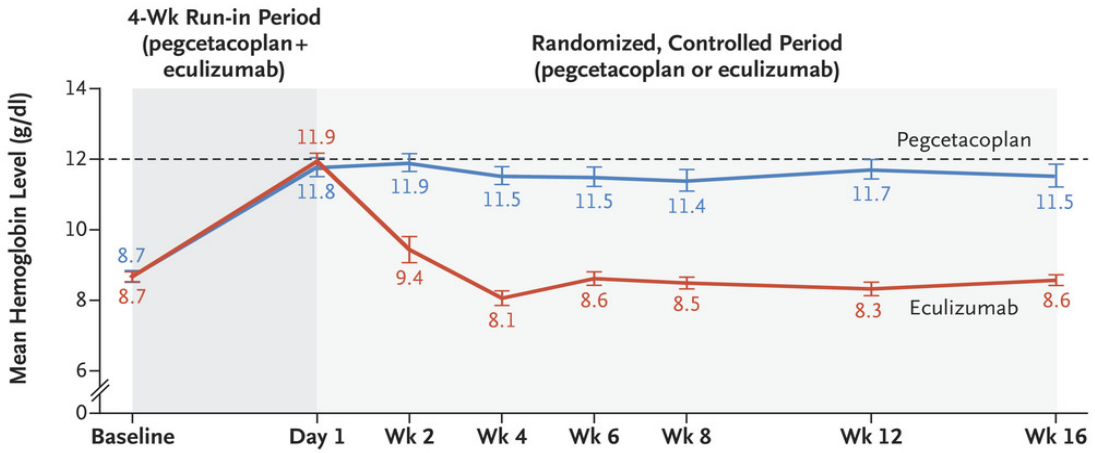


Primary endpoint: average change from baseline Hgb from week 4 to week 16

Hillmen et al. New Eng Jnl. 2021;384:1028-1037

PEGASUS—Primary Endpoint

A



No. with Available Data								
Pegcetacoplan	41	40	40	40	39	37	38	37
Eculizumab	39	37	38	39	36	39	39	38

B

Subgroup	No. of Patients		Adjusted Change in LS Mean Hemoglobin		Difference (95% CI)
	Pegcetacoplan	Eculizumab	Pegcetacoplan	Eculizumab	
			g/dl ± SE		
Censored for transfusion events, all values after intercurrent events set to missing	41	39	2.37±0.36	−1.47±0.67	3.84 (2.33–5.34)
All available data, regardless of tranfusion events	41	39	2.66±0.25	−0.03±0.26	2.69 (1.99–3.38)
No. of transfusions in previous 12 mo					
<4	20	16	2.97±0.36	−0.01±0.49	2.98 (1.73–4.23)
≥4	21	23	2.11±0.60	−4.02±2.40	6.13 (0.79–11.48)

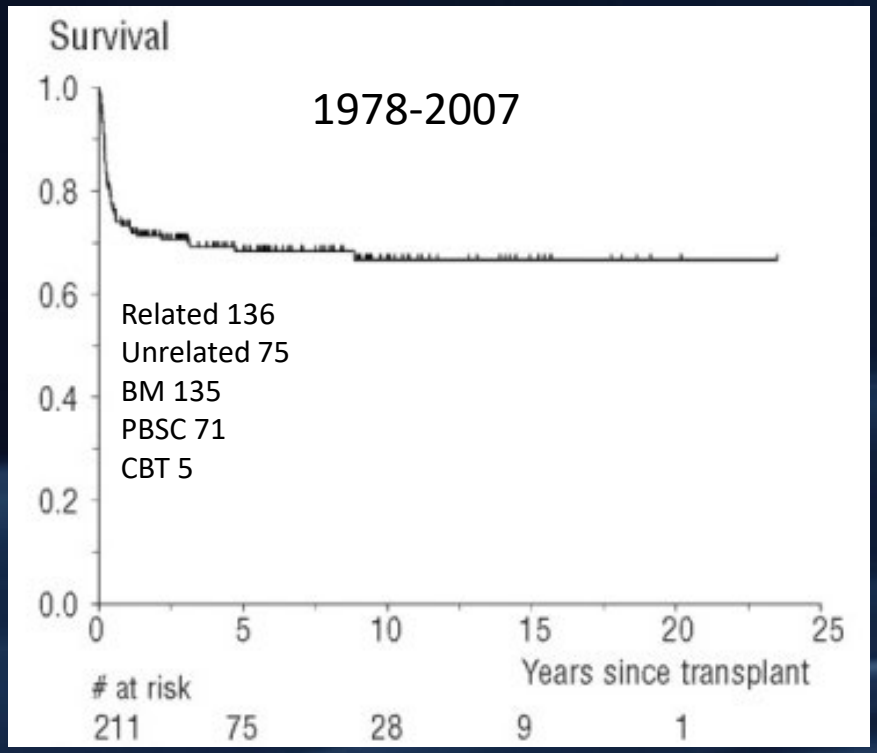
Hillmen et al. New Eng Jnl. 2021;384:1028-1037

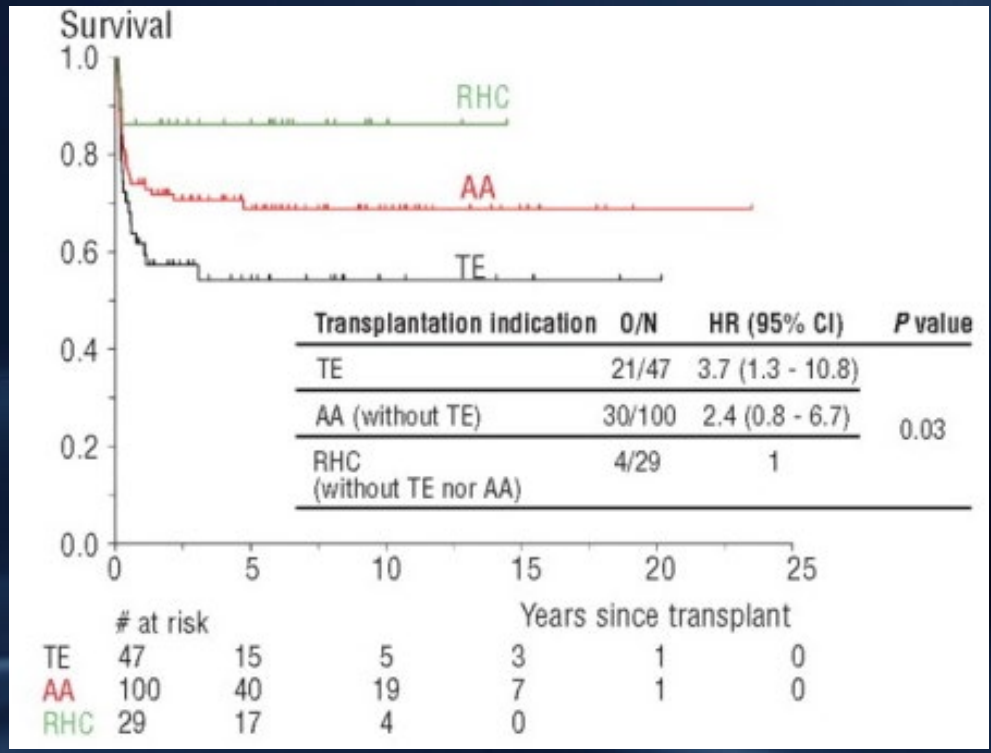
Summary

- PNH chronic life threatening complement mediated disease
  - Thrombosis is major cause of death
- Aquired and associated with BMF disorders
- Three FDA approved treatments
  - Eculizumab-tx of PNH patients to reduce hemolysis March 19, 2007
  - Ravulizumab-tx of adult and ped 1 mos or older with PNH December 21, 2018
  - Pegcetacoplan-tx of adult patients with PNH May 14, 2021
- No superiority studies for upfront treatment
- LDH should be followed
- EVH is an important component of PNH

Transplantation for PNH

HCT for PNH

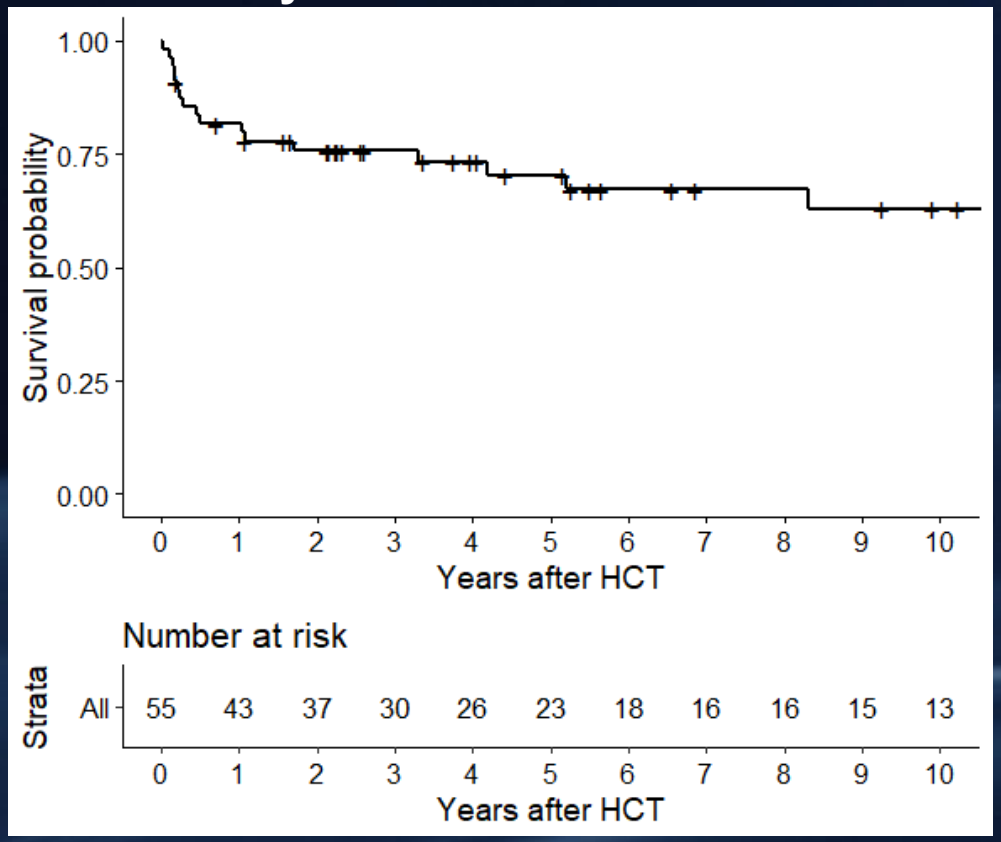




De Latour Haematologica 2012;97:1666-1673

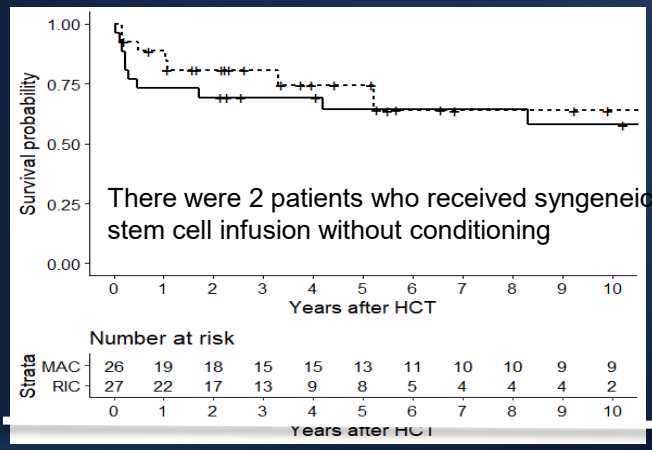
FHCRC Outcomes on HCT in PNH

5-year OS estimated at 70%

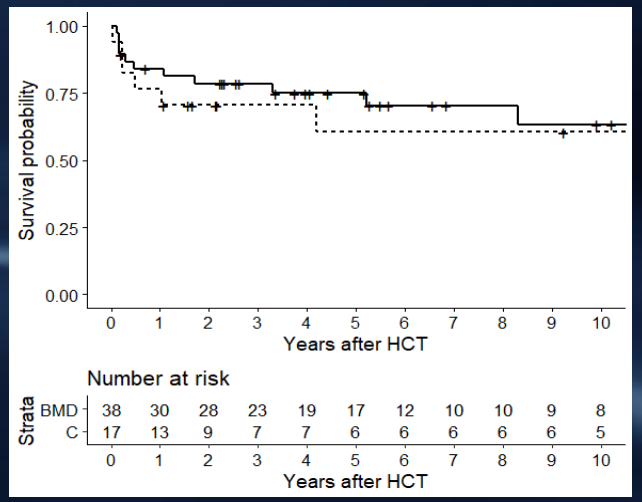


17 classical PNH
38 associated BMF
- AA 26
- MDS 9
- MPN 2
- AML 1

MAC vs. RIC



Classical vs. Marrow disorder



Cooper et al. Biol. Blood Marrow Transplant 2019;7:1331-1339

Agents in Development

- LNP 023 (Iptacopan): oral factor B inhibitor
  - Phase 2 trial as add on with ecu was positive
  - single arm open label trial oral 200 mg BID naïve patients
- BCX9930: oral factor D inhibitor
  - Phase 1 testing
- ALXN2050 and (ACH-0145228) (Danicopan): oral factor D inhibitor
  - Phase 2 trial as add on with ecu was positive 100-200 mg TID
  - Phase 2 single arm study currently enrolling for both naïve and patient with inadequate response to Ecu
- RO7112689 or SKY59 (Crovalimab): IV loading dose and then subq anti-C5
  - COMPOSER trial completed, 680 mg SQ once every 4 weeks effective at controlling C5 activation

Meningitis Vaccine in PNH

Meningitis Vaccines

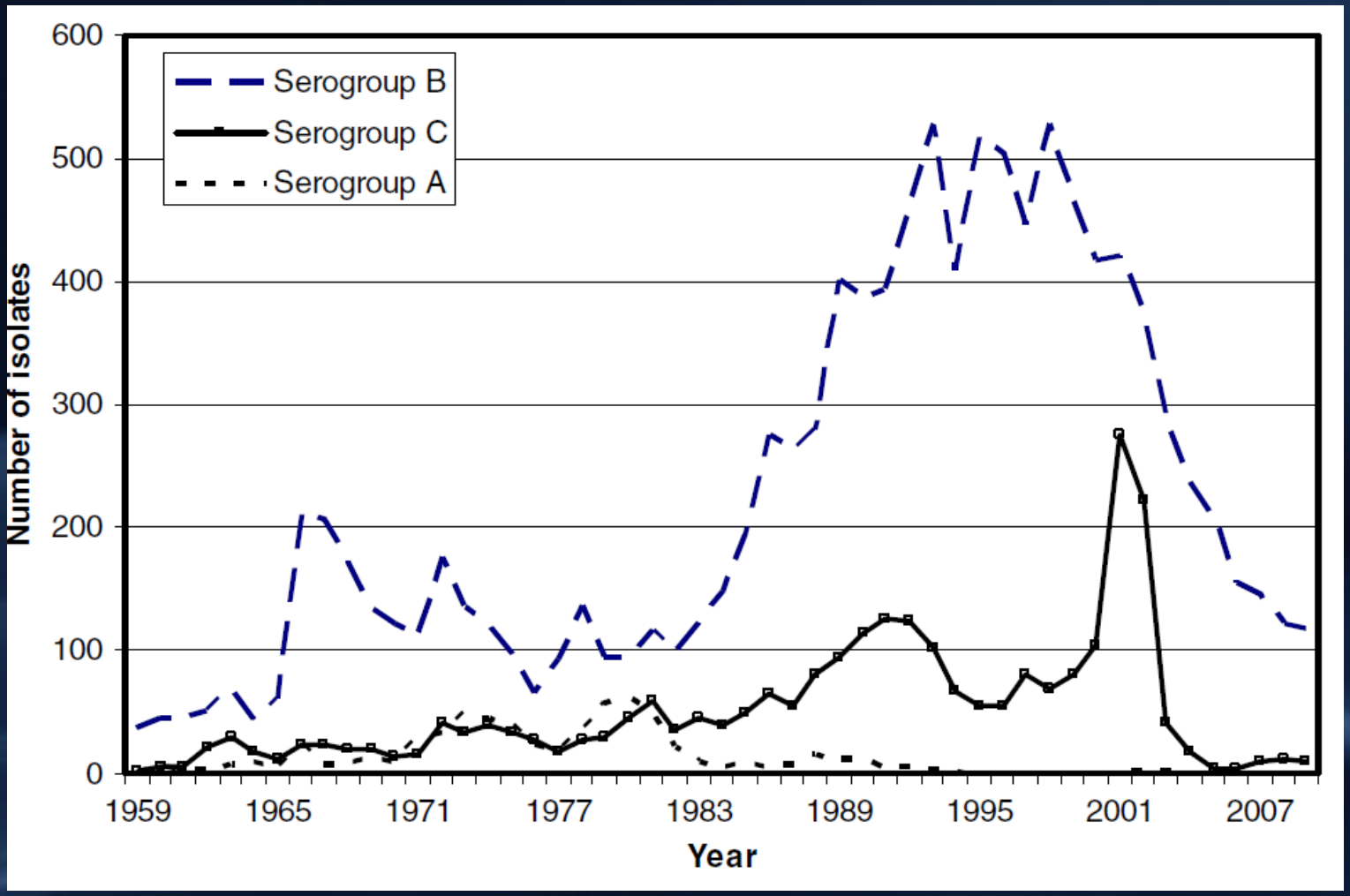
- Meningitis A, C, Y, W-135 (Quadrivalent Vaccines)
  - MenHibrix (Hib-Men CY-TT) BIVALENT children 6 weeks-18 mos
  - Menveo (Men ACWY-CRM) 2 months-55 years of age
  - Menactra (Men ACWWY-D) 9 months-55 years of age
  - Menomune (MPSV4) polysaccharide
    - allergic reactions
    - Older than 55
    - No mucosal immunity
    - Duration of immunity less than 3 years—no memory T cells

Current ACIP Recommendations for Complement Deficiencies

People with persistent complement component deficiencies[10]		
• for age 2 through 18 months	Give MCV4-CRM or Hib-MenCY at ages 2, 4, 6 and 12–15 months	Give MCV4 booster after 3 years followed by boosters every 5 years thereafter
• for children age 7 through 23 months who have not initiated a series of MCV4-CRM or Hib-MenCY	Give 2 doses, separated by 3 months, of MCV4-CRM (if age 7–23 months)[7] or MCV4-D (if age 9–23 months)	
• for ages 2 through 55 years	Give 2 doses of MCV4, 2 months apart	Boost every 5 years with MCV4[8,11]
• for age 56 years and older	Give 2 doses of MCV4, 2 months apart	Boost every 5 years with MCV4[11]

ACIP=Advisory Committee on Immunization Practices

Distribution of Meningitis Serotype in Norway



Meningitis Vaccines

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  - MenHibrix (Hib-Men CY-TT) BIVALENT children 6 weeks-18 mos
  - Menveo (Men ACWY-CRM) 2 months-55 years of age
  - Menactra (Men ACWWY-D) 9 months-55 years of age
  - Menomune (MPSV4) polysaccharide
    - allergic reactions
    - Older than 55
    - No mucosal immunity
    - Duration of immunity less than 3 years—no memory T cells
- Meningitis B
  - Bexsero (Novartis) 10-25 years of age
    - 2 dose series (0 and 1-6 months)
  - Trumenba (Pfizer) 10-25 years of age
    - 3 dose series (0,2, and 6 months)

Meningitis Vaccines

- Meningitis X
  - North America, Europe, Australia and West Africa
  - No commercially available vaccine

Laboratory Analsysis in PNH

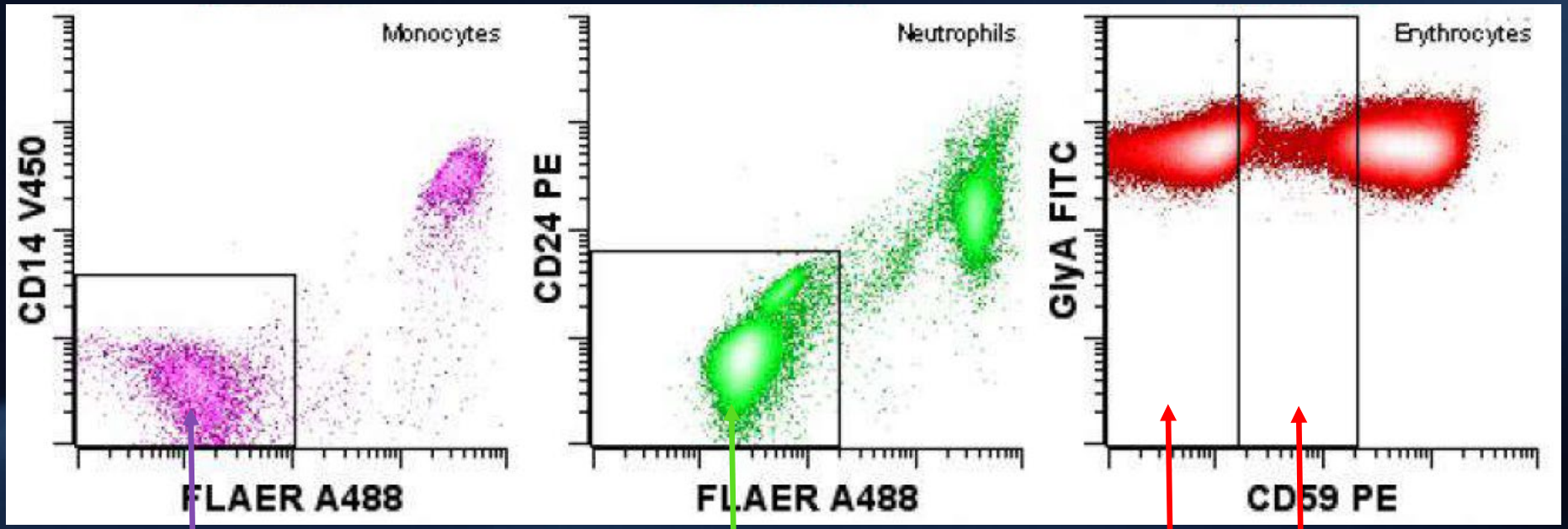
Chemistry panel in PNH

5/20/2013 11:25	Na	136	(136 - 145)
	K	3.7 (d)	(3.7 - 5.2)
	Cl	103	(98 - 108)
	CO2	30	(22 - 32)
	Anion Gap	3	(3 - 11)
	Glucose Level	96	(62 - 125)
	BUN	16	(8 - 21)
	Creatinine	1.11	(0.51 - 1.18)
	eGFR, Calculated, African American	>60	(>59 -)
	eGFR, Calculated, European American	>60	(>59 -)
	eGFR, Additional Information	Calculated GFR in mL/min/1.73 m2 by MDRD equation. Inacc...	
	Ca	9.3	(8.9 - 10.2)
	LD (Total)	2,614 (d) H	(80 - 190)
	AST (GOT)	128 H	(15 - 40)
	ALT (GPT)	38	(10 - 64)
	Alk Phos (Total)	64	(36 - 122)
	Bilirubin (Total)	2.2 H	(0.2 - 1.3)
	Protein (Total)	7.1	(6.0 - 8.2)
	Albumin	3.9	(3.5 - 5.2)
	Globulin	3.2	(2.0 - 3.9)
	Albumin/Globulin Ratio	1.2	(1.0 - 2.4)

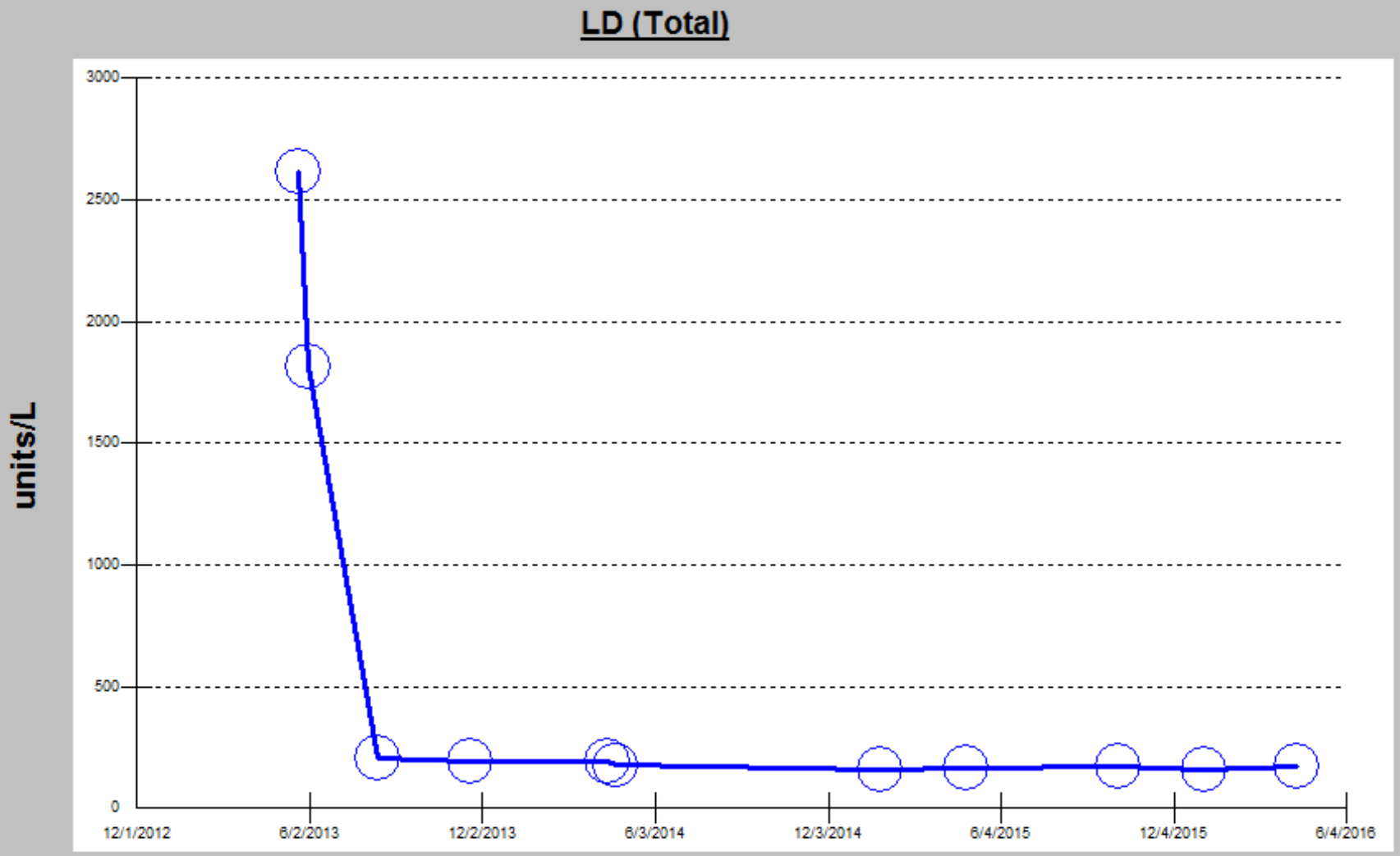
Hematology panel in PNH

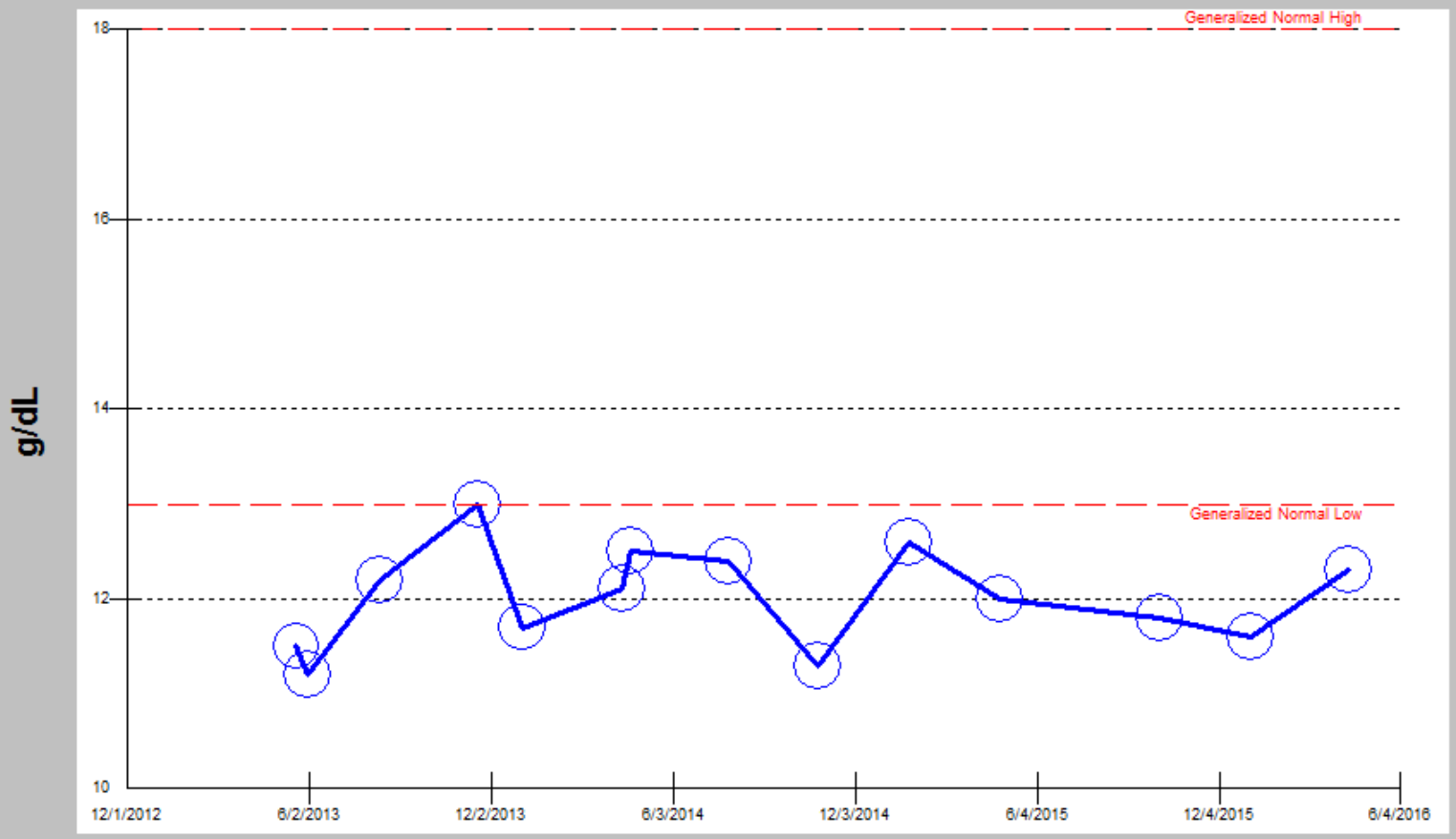
WBC	4.97	(4.3 - 10.0)
RBC	3.43 L	(4.40 - 5.60)
Hb	11.5 L	(13.0 - 18.0)
HCT	35 L	(38 - 50)
MCV	102 H	(81 - 98)
MCH	33.5	(27.3 - 33.6)
MCHC	33.0	(32.2 - 36.5)
PLT	161	(150 - 400)
RDW-CV	15.1 H	(11.6 - 14.4)
% Neutrophils	49	(34 - 71)
% Lymphocytes	37	(19 - 53)
% Monocytes	12	(5 - 13)
% Eosinophils	2	(0 - 7)
% Basophils	0	(0 - 1)
% Immature Granulocytes	0	(0 - 1)
Neutrophils	2.43	(1.80 - 7.00)
Lymphocytes	1.84	(1.00 - 4.80)
Monocytes	0.60	(0.00 - 0.80)
Eosinophils	0.10	(0.00 - 0.50)
Basophils	0.00	(0.00 - 0.20)
Immature Granulocytes	0.00	(0.00 - 0.05)
WBC Morphology	WBC Morphology	
RBC Morphology	RBC Morphology	
PLT Morphology	See PLT count	
Absolute Reticulocyte Count	346 H	(20 - 100)
Reticulocyte Count, %	10.1 H	(0.5 - 2.0)
Haptoglobin Quant	<10 L	(26 - 279)

PNH Flow Testing



LDH in PNH


LD (Total)
units/L
3000
2500
2000
1500
1000
500
0
12/1/2012
6/2/2013
12/2/2013
6/3/2014
12/3/2014
6/4/2015
12/4/2015
6/4/2016


Hb
g/dL
18
16
14
12
10
Generalized Normal High
Generalized Normal Low
12/1/2012
6/2/2013
12/2/2013
6/3/2014
12/3/2014
6/4/2015
12/4/2015
6/4/2016