Case study

- A 37 year old man was referred to the hematology clinic for evaluation and management of MDS
- He had anemia for 7 years, and was treated with iron supplements, epo, and had a bone marrow biopsy eventually which showed low risk MDS, and absent iron stores.
- He had been evaluated for hematuria and was evaluated by a urologist who performed 2 cystoscopies, which were not revealing.

Case study

- At the time of his clinic visit, he complained of fatigue, and episodes of back pain
- He also described episodes of dark urine
- His iron studies were consistent with iron deficiency anemia
- A flow cytometry of the peripheral blood was sent for RBC/Granulocytes testing to detect a possible PNH clone.
Paroxysmal Nocturnal Hemoglobinuria: A Chronic Disabling and Life-Threatening Disease

- PNH is an acquired disorder of the hematopoietic stem cell
- Estimated 4,000–6,000 patients in U.S.
- 5 year mortality: 35%
- Diagnosed at all ages; median age early 30s

The Defect in PNH

The Somatic Mutation of the X-chromosome PIG A Gene Prevents All GPI Anchored Proteins from Binding to Cell Surface

Overview of Complement

Complement Cascade
Classification of PNH

1. Classical PNH: Manifests with florid intravascular hemolysis and episodes of visible hemoglobinuria.
2. PNH in the setting of another BM failure state: This entity is characterized by mild hemolysis and a small clone size
3. Subclinical PNH: With <1% clone, and no clinical or biochemical evidence of intravascular hemolysis

PNH Clonal Expansion in an AA Representative Population

<table>
<thead>
<tr>
<th>Translational pattern</th>
<th>n (%)</th>
<th>Classic PNH</th>
<th>Expansion</th>
<th>Persistent</th>
<th>Newly developed</th>
<th>Disappearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>(119/124) 119 (11%)</td>
<td>119 (11%)</td>
<td>119 (11%)</td>
<td>119 (11%)</td>
<td>119 (11%)</td>
<td>119 (11%)</td>
<td>119 (11%)</td>
</tr>
</tbody>
</table>

PNH+ Patients 119 / 124

PNH- Patients 109 / 124
Peripheral Blood Abnormalities at Presentation

<table>
<thead>
<tr>
<th></th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia alone</td>
<td>22.8</td>
</tr>
<tr>
<td>Anemia and Thrombocytopenia</td>
<td>25.3</td>
</tr>
<tr>
<td>Anemia and Neutropenia</td>
<td>4.0</td>
</tr>
<tr>
<td>Pancytopenia</td>
<td>39.1</td>
</tr>
</tbody>
</table>

Paroxysmal Nocturnal Hemoglobinuria
Clinical manifestations

- Hemolytic anemia
  - paroxysmal
  - Even in the absence of symptoms, destructive progression of hemolysis is ongoing
  - nocturnal
  - Hemolysis in PNH is subtle and constant, 24 hours a day
  - Hemoglobinuria is a less commonly seen complication
  - ¾ patients present without hemoglobinuria
- Bone marrow failure/pancytopenia
- Thrombophilia/ Propensity for clots

Factors Determining Hemolysis

- Proportion of abnormal cells
- Abnormality – type III vs type II
- Activation of complement
Definition of PNH type RBCs

**Type I cells**
- Normal RBC's with normal CD59 expression
- Circulating survival: 90-120 days\(^1,2\)

**Type II cells**
- PNH clone with complete CD59 deficiency
- Circulating survival: 20 days\(^1,2\)

**Type III cells**
- PNH clone with complete deficiency (Type II cells) and partial CD59 deficiency
- Circulating survival: 45 days\(^1,2\)

---

Things That Activate Complement *in vivo*

- "Tick-over" spontaneous activation –
  - Alternative pathway
    - Chronic hemolysis
- Exposure to endotoxin from GI tract leads to increased risk of massive hemolysis
- Other infections, surgery, trauma, pregnancy

---

Common Symptoms in Patients With PNH

- Dysphagia: 41%
- Pulmonary Hypertension: 47%
- Dyspnea: 66%
- Abdominal Pains: 57%
- Chronic Renal Insufficiency: 47%
- Erectile dysfunction: 47%
- Hemoglobinuria: 26%
- Thrombosis: 89%
- Anemia: 96%
- Fatigue, Impaired QoL: 41%

---

**PNH and Hemolysis**

Normal red blood cells are protected from complement attack by a shield of terminal complement inhibitors.

Without this protective complement inhibitor shield, PNH red blood cells are destroyed.

**Consequences of Chronic Hemolysis and Free Hemoglobin**

- Intact RBC
- Free Hemoglobin

- Thrombosis
- Renal Failure
- Pulmonary Hypertension
- Abdominal Pain
- Dyspnea
- Dysphagia
- Fatigue
- Hemoglobinuria
- Erectile Dysfunction

**Thrombosis in PNH:**

- 40% of patients experience clinical thrombotic events
- Leading cause of death
  - Accounts for 40-67% of deaths
  - First thrombotic event can be fatal
  - Median time to TE was 2.1-2.3 years from diagnosis
  - First TE increases risk for death 5-10-fold
Common Sites of Thrombosis Occur Frequently in PNH

<table>
<thead>
<tr>
<th>TE Type</th>
<th>Hillmen P et al. 1995 (N=80)</th>
<th>Hillmen P et al. 2007 (N=185)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT or PE</td>
<td>33%</td>
<td>40%</td>
</tr>
<tr>
<td>CVA/MI</td>
<td>16%</td>
<td>15%</td>
</tr>
<tr>
<td>Typical VTE</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Atypical VTE</td>
<td>√</td>
<td>√</td>
</tr>
</tbody>
</table>

Higher proportion of PE and/or DVT sites of thrombosis consistently found in PNH patients – Socie et al. 1996 (29%) and Nishimura and Rosse. 2004 (27%).


Clinical Symptoms Predictive of TE

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Pain</td>
<td>4.0</td>
</tr>
<tr>
<td>Chest Pain</td>
<td>3.84</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>3.1</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>2.92</td>
</tr>
</tbody>
</table>

Potential Assessments to Identify Thrombosis Risk in PNH

<table>
<thead>
<tr>
<th>Baseline Platelet Count</th>
<th>Proportion with History of TE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenic &lt;100,000 X 10^9/L</td>
<td>45%</td>
</tr>
<tr>
<td>Non-Thrombocytopenic ≥100,000 X 10^9/L</td>
<td>27%</td>
</tr>
</tbody>
</table>

- Patients with thrombocytopenia have elevated incidence of TE
  - Evidence of platelet consumption in PNH
  - Platelet consumption may result from microthrombi
  - D-dimer and other markers of elevated inflammatory response
  - 61% and 82% of PNH patients in French and US studies demonstrated an elevated risk for TE as indicated by increased D-dimer levels
  - Chronic terminal complement activation leads to systemic inflammatory and hypercoagulable state in PNH

Kidney Pathology in PNH

- Chronic hemolysis and cell-free plasma hemoglobin lead to chronic kidney disease in PNH\(^1\).\(^2\)
- Repetitive exposure of tissue to cell-free hemoglobin may lead to renal damage in PNH\(^3\).\(^4\)
- 80% of PNH patients (median age of 31.5 years) had MRI evidence of significant renal hemosiderosis\(^1\).\(^5\)
  - 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
- Autopsy and biopsy often show interstitial nephritis and fibrosis\(^3\).\(^4\)


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

![Graph showing the proportion of patients with CKD stages](image)

53% of patients with minimal (0-1) transfusion history had CKD (n=22)

Impact of PNH on Quality of Life

-75% of Patients Reported Symptoms as Moderate to Very Severe

59% patients were transfusion-free for at least 12 mo or had never been transfused
76% were forced to modify their daily activities to manage their PNH
17% were unemployed due to PNH

<table>
<thead>
<tr>
<th>Symptom</th>
<th>% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Pain</td>
<td>37</td>
</tr>
<tr>
<td>Shortness of Breath*</td>
<td>46</td>
</tr>
<tr>
<td>Ophthalmia</td>
<td>41</td>
</tr>
<tr>
<td>Erectile Dysfunction</td>
<td>47</td>
</tr>
<tr>
<td>Fatigue</td>
<td>56</td>
</tr>
</tbody>
</table>
Two Independent International Groups Recommend Testing High Risk Patient for PNH

Guidelines for the diagnosis and monitoring of paroxysmal nocturnal hemoglobinuria and related disorders by flow cytometry


Standard Diagnostic Test for PNH

- Flow cytometry performed on peripheral blood
- Granulocytes and at least one additional cell line should be evaluated
  - Red blood cells (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

Testing for PNH in Red Blood Cells

Normal RBCs with normal CD59 expression: Type I cells

PNH clone with complete CD59 deficiency: Type III cells

PNH clone with partial CD59 deficiency: Type II cells

Gating on GPA+ RBCs
Testing for PNH: RBC’s and Granulocytes

Data Source: Dahl - Chase Diagnostic Services.

CD24 - Granulocytes
FLAER - GPI Anchor Binding Marker
CD59 - GPI Anchored Protein

80.1% of Granulocytes lack GPI proteins
31.4% RBCs are Type III PNH cells

Historical Management of PNH

- Transfusions
  - Risk of iron overload
  - Transient treatment of anemia
- Anticoagulants
  - Risk of hemorrhage
  - Ineffective in many patients
- Red cell supplements
  - ESAs may expand clones and elevate hemolysis
  - Folic acid, iron, erythropoiesis-stimulating agents
- Steroids/androgen hormones
  - No controlled clinical trials
  - AE's

Pennsylvania State University

PNH Bone Marrow Transplant

- BMT is the only potentially curative therapy for PNH
- Indications for transplant include
  1. uncontrollable hemolysis
  2. thrombosis
  3. Bone marrow failure state
- There is considerable morbidity and mortality associated with BMT for PNH
- Patient selection and timing of transplant are important variables in making the decision.
Bone Marrow Transplant

- In a recent retrospective study in France examining PNH patients, 54% had GVHD.
- In another study examining PNH patients (n=23), 50% chronic GVHD; 42% acute GVHD.
- BMT has a significant impact on quality of life post transplant.
- Allogeneic BMT recommended for PNH patients with life-threatening cytopenias or possibly the rare patient with disabling hemolysis or thrombosis not controlled with existing therapy.


### BMT In PNH

<table>
<thead>
<tr>
<th>Year</th>
<th>Pub</th>
<th>N</th>
<th>Age Median (range)</th>
<th>Study Population</th>
<th>Mortality</th>
<th>GVHD Cause of Death</th>
<th>Risk of Death or GVHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>Santarone et al.</td>
<td>26</td>
<td>33 (20-59)</td>
<td>PNH patients; 23 HLA matched (22 identical sib), 3 unmatched</td>
<td>42% overall [34% at 6 mo. (from abstract)]</td>
<td>n=10 of 20 evaluable patients (50%) cGVHD, N=11 aGVHD (42%)</td>
<td>At least 42%</td>
</tr>
<tr>
<td>2009</td>
<td>De Latour et al.</td>
<td>185</td>
<td>30 (23-38)</td>
<td>N=83 (54%) BMF; N=69 (45%) PNH 31% treated vs. 17% controls at 5 years</td>
<td>N=100 (54%)</td>
<td>N=53 deaths - 28 from infections, 13 from GVHD</td>
<td>At least 31%</td>
</tr>
<tr>
<td>2009</td>
<td>Ruggeri et al.</td>
<td>58</td>
<td>12</td>
<td>SAA 7 PNH 53% 2 years (projected) 28 +/-6% aGVHD</td>
<td>N=14 of 44 at risk (32%) cGVHD</td>
<td>NA</td>
<td>At least ~28%</td>
</tr>
<tr>
<td>2009</td>
<td>de Latour et al.</td>
<td>52</td>
<td>42% (n=22)</td>
<td>NA</td>
<td>NA</td>
<td>42% (death)</td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td>Witherspoon et al.</td>
<td>14</td>
<td>32 (19-42)</td>
<td>Hemolytic PNH 43% &lt; 6 months</td>
<td>N=6: GVHD n=2, infections n=2, other n=2</td>
<td>NA</td>
<td>At least 43%</td>
</tr>
<tr>
<td>2007</td>
<td>Parker</td>
<td>121</td>
<td>30</td>
<td>PNH Patients</td>
<td>44% (10 yr)</td>
<td>NA</td>
<td>44% (death)</td>
</tr>
<tr>
<td>2003</td>
<td>Hegenbart et al.</td>
<td>7</td>
<td>34 (25-49)</td>
<td>Hemolytic PNH; 2 BMF</td>
<td>43% n=5 (71%)</td>
<td>n=3: Infection n=1; GVHD n=1; Organ failure n=1</td>
<td>At least 43%</td>
</tr>
<tr>
<td>1999</td>
<td>Saso et al.</td>
<td>57</td>
<td>28 (10-47)</td>
<td>32% SAA 44% at 2 yr</td>
<td>n=16 (34%) aGVHD 21d engraftment; n=13/39 cGVHD with 90d engraftment</td>
<td>• 19/48 (40%) died in HLA identical cohort • GVHD (n=3)</td>
<td>At least 33%</td>
</tr>
</tbody>
</table>

### Considerations for Managing the PNH/AA Patient

- PNH with hemolysis
- PNH Intermediate + hemolysis
- Eculizumab
- Moderate AA without thrombosis
- IST
- Prophylactic Anticoagulation
- BMT
- Moderate AA without hemolysis
- Severe AA without therapy
- Eculizumab
- IST
- BMT
Eculizumab (Soliris)

Complement Cascade

- SOLIRIS® binds with high affinity to C5
- Terminal complement C5a and C5b-9 activity blocked
- Proximal functions of complement remain intact
  - Weak anaphylatoxin
  - Immune complex clearance
  - Microbial opsonization

3. SOLIRIS® (eculizumab) [package insert]. Alexion Pharmaceuticals; 2009.

Eculizumab Clinical Trials in PNH

Pilot Study – NEJM. 2004
N = 11
Primary endpoint: reduction of hemolysis

TRIUMPH – NEJM. 2006
Pivotal Phase III, Double-Blind, Placebo-Controlled Trial, N = 87

SHEPHERD – Blood. 2008
Broader patient population, including those receiving minimal transfusions or with thrombocytopenia, N = 97

Long-Term Extension Trial
Hillmon; Blood. 2003
Evaluated long-term safety, efficacy and effect on thrombosis; Placebo patients switched to SOLIRIS®
N = 107

Dosing Schedule

<table>
<thead>
<tr>
<th>Pretreatment</th>
<th>Induction Phase</th>
<th>Maintenance Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>~2 weeks before induction</td>
<td>Week 1</td>
<td>1</td>
</tr>
<tr>
<td>Neisseria meningitidis vaccination</td>
<td>SOLIRIS® dose, mg</td>
<td>600</td>
</tr>
</tbody>
</table>

- In clinical trials all patients received a meningococcal vaccination
- SOLIRIS® should be administered via IV infusion over 35 minutes every 7 days during induction and every 14 days during maintenance
- SOLIRIS® dose adjustment to every 12 days may be necessary for some patients to maintain LDH reduction
- Concomitant medications allowed
  - Steroids, immunosuppressant drugs, anti-clotting agents and hematins

SOLIRIS® (eculizumab) [package insert]. Alexion Pharmaceuticals; 2009.
Hillmon Trial; Blood. 2003.
TRIUMPH and SHEPHERD: Response

**Response**

P <0.001 at all measured time points.


TRIUMPH placebo patients switched to SOLIRIS® after week 26. All TRIUMPH patients entered the long-term extension study.

TRIUMPH – Placebo/Extension
TRIUMPH – SOLIRIS®/Extension
SHEPHERD – SOLIRIS®

Lactate Dehydrogenase (U/L)

<table>
<thead>
<tr>
<th>Time, Weeks</th>
<th>0</th>
<th>4</th>
<th>8</th>
<th>12</th>
<th>16</th>
<th>20</th>
<th>24</th>
<th>28</th>
<th>32</th>
<th>36</th>
<th>40</th>
<th>44</th>
<th>48</th>
<th>52</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>500</td>
<td>1000</td>
<td>1500</td>
<td>2000</td>
<td>2500</td>
<td>3000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

Patients not on SOLIRIS® (n=44)
SOLIRIS® (n=43)

- % of SOLIRIS patients achieved transfusion independence vs % of patients not on SOLIRIS®
- Patients with concomitant bone marrow dysfunction may continue to require minimal transfusions


Patients Report Rapid and Sustained Improvement Across Broad Range of Measures

EORTC Functioning
EORTC Symptoms
FACIT-Fatigue
Global Health
Physical Role
Cognitive
Dyspnea
Pain
Insomnia
Constipation
Nausea
Diarrhea
Eculizumab therapy and Thrombotic Events

63% of patients received concomitant anticoagulants.

The effect of anticoagulant withdrawal was not studied.

Events observed in both venous and arterial sites.

There were fewer thrombotic events with SOLIRIS treatment than during the same period of time prior to treatment.

2. SOLIRIS® (eculizumab) [package insert]. Alexion Pharmaceuticals; 2009.

Renal Function change with eculizumab* At 6 Months

<table>
<thead>
<tr>
<th>Segment of PNH Population</th>
<th>No Change</th>
<th>Improvement</th>
<th>Worsening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall (n=189)</td>
<td>66.3%</td>
<td>31.7%</td>
<td>2.0%</td>
</tr>
<tr>
<td>Stage 1 (n=81)</td>
<td>79.2%</td>
<td>16.7%</td>
<td>4.1%</td>
</tr>
<tr>
<td>Stage 3 (n=40)</td>
<td>75.0%</td>
<td>20.0%</td>
<td>5.0%</td>
</tr>
</tbody>
</table>

* P < 0.001

Eculizumab has a Major Impact on Survival in PNH

Survival is comparable to age and sex matched control population.

• There was no difference in mortality between patients on eculizumab and the normal population (P=0.46).
• 2 patients over 70 years of age had worse survival (P=0.0042). No patients under the age of 50 years died.
Warning

WARNING: SERIOUS MENINGOCOCCAL INFECTION

- SOLIRIS® increases the risk of meningococcal infections. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early.
  - Vaccinate patients with a meningococcal vaccine at least 2 weeks prior to receiving the first dose of SOLIRIS®
  - Revaccinate according to current medical guidelines for vaccine use
  - Monitor patients for early signs of meningococcal infections, evaluate immediately if infection is suspected, and treat with antibiotics if necessary

Safety: Warnings and Precautions

- The effect of withdrawal of anticoagulant therapy during SOLIRIS® treatment has not been established. Therefore, treatment with SOLIRIS should not alter anticoagulant management.
- Patients who discontinue SOLIRIS must be monitored closely for signs of serious hemolysis
  - If serious hemolysis occurs after SOLIRIS discontinuation, consider the following procedures/treatments: blood transfusion (packed RBCs), or exchange transfusion if the PNH RBCs are >50% of the total RBCs by flow cytometry; anticoagulation; corticosteroids; or reinstitution of SOLIRIS
  - In clinical trials, 16 of 196 PNH patients discontinued SOLIRIS treatment; no serious hemolysis was observed

Serious Adverse Events: Clinical Trial Experience

- Meningococcal infections are the most important adverse events that may be experienced by patients receiving SOLIRIS®
- In clinical studies, 2 out of 196 patients developed serious meningococcal infections while receiving treatment with SOLIRIS
  - Both patients had been vaccinated
- In clinical studies among non-PNH patients, meningococcal meningitis occurred in one patient, who was unvaccinated
- In post-marketing experience, cases of serious or fatal meningococcal infections have been reported
Adverse Reactions Reported in ≥ 5% of SOLIRIS® Treated Patients in TRIUMPH

<table>
<thead>
<tr>
<th>Reaction</th>
<th>SOLIRIS® (n=43)</th>
<th>Placebo (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>19 (44)</td>
<td>12 (27)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>10 (23)</td>
<td>8 (18)</td>
</tr>
<tr>
<td>Back pain</td>
<td>8 (19)</td>
<td>4 (9)</td>
</tr>
<tr>
<td>Nausea</td>
<td>7 (16)</td>
<td>5 (11)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>5 (12)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Cough</td>
<td>5 (12)</td>
<td>4 (9)</td>
</tr>
<tr>
<td>Herpes simplex virus infections</td>
<td>3 (7)</td>
<td>0</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>3 (7)</td>
<td>0</td>
</tr>
<tr>
<td>Respiratory tract infection</td>
<td>3 (7)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Constipation</td>
<td>3 (7)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>3 (7)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>3 (7)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Influenza-like illness</td>
<td>2 (5)</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

SOLIRIS® (eculizumab) [package insert]. Alexion Pharmaceuticals; 2009.

Patient Safety Card
- Patients should be informed that they will be provided with a Patient Safety Card
- Patients should carry the card with them at all times
- The card describes symptoms, which if experienced, should prompt the patient to seek immediate medical attention
- Instruct patients to show the card to all health care providers involved in their care

PNH Registry Overview
The PNH Registry is an ongoing global, observational, non-interventional study collecting safety, effectiveness, clinical characteristic and quality of life data on patients with PNH irrespective of clone size or treatment.
The PNH Registry has been established in order to describe the real world outcomes of PNH, capturing a wide range of patients from all over the world.
PNH Registry Data Collection

- **Physician-Reported Data**
  - Data collected at study enrollment and every six months thereafter
  - Data entry minimally includes: demographics, medical history, PNH diagnosis, flow-cytometry results, symptoms, and clinical outcomes
  - All necessary information can be gathered from patient medical records

- **Patient Reported Outcomes**
  - Patients complete questionnaires at study enrollment and every six months thereafter
    - EORTC QLQ
    - FACIT-F-Fatigue scale
    - Overall health status
    - Symptom frequency and bother
    - Healthcare utilization
    - Work Status
      *validated quality of life instruments in other disease states

PNH Registry: Future Research Topics

- PNH and Thrombotic Events
- PNH and Renal Dysfunction
- PNH in the Pediatric Setting
- Association of Clinical & Patient Characteristics with PNH Treatment
- Evolution of PNH Clones
- Survival / Mortality
- Correlation of PNH with Laboratory Markers

PNH: Conclusions

- PNH is a rare and life threatening disease
- Delays in diagnosis range from 1 to more than 10 years
- High-risk patients should be identified and tested for PNH
- Reliable testing and reporting procedures matter
  - Granulocyte analysis in all cases
  - PNH testing on RBCs alone is not adequate
  - Adding quantitative results to report forms is essential
- With the advent of treatment options for PNH, there is a compelling reason to identify patients

References:

PNH: CONCLUSIONS

The commercial availability of Eculizumab has certainly made a positive impact on patients' quality of life, and survival.

Bone marrow transplantation is the only curative modality for bone marrow failure states.

Other therapeutic options for PNH are being currently evaluated in clinical trials (TT30).