Rituximab Use in the Acute Setting
A Medication Use Evaluation

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Background

- Rituximab is a monoclonal antibody directed against the CD20 antigen on the surface of B-lymphocytes

- FDA-approved indications
  - Chronic lymphocytic leukemia (CLL)
  - Non-Hodgkin lymphoma (NHL)
  - Granulomatosis with polyangitis (GPA; Wegener’s)
  - Microscopic polyangitis (MPA)
  - Rheumatoid arthritis
## Off-Label Indications

<table>
<thead>
<tr>
<th>Category</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oncology</strong></td>
<td>Burkitt and CNS lymphoma</td>
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<td></td>
<td>Hodgkin lymphoma, nodular lymphocyte-predominant</td>
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<td></td>
<td>Mucosa-associated lymphoid tissue lymphoma (gastric)- advanced</td>
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<td>Splenic marginal zone lymphoma</td>
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<td><strong>Rheumatology</strong></td>
<td>Autoimmune hemolytic anemia- refractory</td>
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<td></td>
<td>Advanced idiopathic membranous nephropathy- resistant</td>
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<td></td>
<td>Immune thrombocytopenia (ITP)- refractory</td>
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<td></td>
<td>Lupus nephritis- refractory</td>
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<td></td>
<td>Pemphigus vulgaris</td>
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<td></td>
<td>Thrombotic thrombocytopenic purpura (acquired) (TTP)</td>
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<td></td>
<td>Waldenström macroglobulinemia</td>
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<tr>
<td><strong>Transplant</strong></td>
<td>Antibody-mediated rejection in cardiac transplantation</td>
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<td></td>
<td>Graft-versus-host disease (GVHD), chronic- refractory</td>
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<td></td>
<td>Refractory posttransplant lymphoproliferative disorder (PTLD)</td>
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</tbody>
</table>
Adverse Reactions

- **Black Box Warning**
  - Infusion reactions
  - Hepatitis B virus reactivation
  - Severe mucocutaneous reactions
  - Progressive multifocal leukoencephalopathy

- **Additional warnings and precautions**
  - Tumor lysis syndrome
  - Arrhythmias
  - Infections
  - Bowel obstruction and perforation
  - Cytopenias
Background

- At MUSC, certain chemotherapy regimens require a hospital admission for administration
  - R-EPOCH, R-ICE, R-HyperCVAD, R-DHAP, R-CODOX-M
    - Some institutions give some of these regimens outpatient
    - Rituximab is given on Day 1
  - HD MTX and rituximab or R-MPV
    - Require admission for monitoring of high-dose methotrexate
  - Rubenstein induction
    - Requires admission for monitoring of high-dose methotrexate
    - Rituximab is given on Day 3
Rationale

- Rituximab is a high-cost medication
  - In the top 15 drugs by expenditures overall (2014)

- MUSC Health vs. 10 comparator Vizient institutions
  - $150,000 more per year
  - 25 more patients per year
Rationale

- **Cost: Inpatient vs. Outpatient Acquisition**
  - Per 100-mg vial: $500 difference in cost
  - Per 500-mg vial: $2,500 difference in cost

- **Reimbursement**
  - Inpatient: reimbursement as DRG lump sum payment for admission
  - Outpatient: reimbursement by Medicare and private payers
The aim of this project was to evaluate the use of rituximab in the inpatient setting.

- **Primary objective**
  - Characterize indications for which rituximab is used within inpatient adult patients in our institution.

- **Secondary objective**
  - Measure appropriateness of use.
  - Develop recommendations to improve appropriate use.
What is appropriate use?

- Hard to delineate for rituximab

**Definition**

- Appropriate use of rituximab in the inpatient setting must meet one of these criteria:
  - Part of chemotherapy regimen currently given inpatient at MUSC
  - First cycle for outpatient chemotherapy regimens
  - First dose for non-oncology indications (eg, rheumatology)

- Appropriate use of rituximab in general defined as rituximab given for an indication located on Palmetto GBA Local Coverage Determination (LCD)
Methods

- **Inclusion criteria**
  - Patients > 18 years of age
  - Received at least 1 dose of rituximab while hospitalized
  - Ordered between 7/1/15 and 6/30/16

- **Exclusion criteria**
  - Ordered dose not administered to patient

- **Retrospective chart review**
Results

- 179 orders
- 87 patients
  - Mean 56.2 ± 16.7 years
  - 38 female, 49 male
- 162 admissions
  - Median LOS 5.1 days
  - IQR: 4.1 days to 8.1 days
  - Range: 1.9 days to 189.7 days

Distribution of Payers (n = 87)

- Private Payer 30, 34%
- Medicare 25, 29%
- Medicaid 14, 16%
- Military 10, 12%
- Self-Pay 8, 9%
- Self-Pay 8, 9%
Results

- **87 patients**
  - 64 receiving chemotherapy

- **Regimens**
  - R-CHOP
  - R-EPOCH
  - R-HyperCVAD
  - R-ICE
  - Rubenstein induction

Distribution of Indications (n = 87)

- Diffuse Large B-cell Lymphoma: 43, 49%
- Other Lymphoma: 10, 12%
- CNS Lymphoma: 7, 8%
- Connective Tissue Disorder: 13, 15%
- Leukemia: 4, 5%
- Other: 10, 11%
Results

- Pre-medications
  - 95.5% of orders preceded by diphenhydramine and acetaminophen
  - Administered median 49 min prior to infusion
    - IQR: 37 min to 67 min
    - Range: 2 min to 16.6 hr

- For 52.5% of orders (n=179), premedications were given 30-60 min before infusion
Results

- **Safety**
  - Minimal adverse effects related to rituximab infusion

<table>
<thead>
<tr>
<th>Adverse Effects Associated with Rituximab Infusion (n = 87)</th>
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<tbody>
<tr>
<td>Infusion Reaction, n (%)</td>
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<tr>
<td>Death at time of data collection, n (%)</td>
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<td><strong>Within 24 hours after end of infusion</strong></td>
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<tr>
<td>Tumor Lysis Syndrome, n (%)</td>
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<tr>
<td>Arrhythmia, n (%)</td>
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<tr>
<td>Death, n (%)</td>
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</tbody>
</table>
Conclusions

- Generally use is for appropriate indications
  - 87.7% appropriately used inpatient based on current policies
  - 90.5% on South Carolina LCD list

- Can make improvements to premedication administration
  - 95.5% of orders preceded by diphenhydramine and acetaminophen
  - 52.5% of orders had premedications given 30-60 min before infusion

- Predominantly used as part of chemotherapy regimens
  - R-EPOCH and R-CHOP regimens account for 29% and 15% of all orders
Recommendations

- Shift rituximab doses as part of chemotherapy outpatient
  - Chemotherapy regimens with rituximab on Day 1
  - Allow first cycle to be administered inpatient
  - Get PHS pricing for eligible patients if outpatient

- Potential cost savings associated with this strategy
  - Eliminate 70/179 doses (39.1% of orders)
  - Approximately $400,000 annual savings
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