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| Lymphoma Program Clinical Practice Guidelines |
| Chemotherapy Regimens  |

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**ABVD**

**Lymphoma Type: Classical Hodgkin, NLPHL (with rituximab)**

**Regimen: Cycle length Q28 days (Bonadonna G et al, Cancer, 1975; Canellos GP et al, NEJM, 1992)**

 **Adriamycin 25mg/m2 IV D1 and D15**

 **Bleomycin 10units/m2 IV D1 and D15**

 **Vinblastine 6mg/m2 IV D1 and D15**

 **Dacarbazine 375mg/m2 IV D1 and D15**

**Antiemetics**:

Early:

           Dexamethasone 20mg

Zofran 24mg

           Delayed (standing unless otherwise noted):

           Olanzapine 10mg nightly for 4 days

 Zofran 8 mg TID D2-5, then PRN

Compazine 10mg q6H PRN (start after olanzapine is completed)

           Refractory:

           Dexamethasone 4mg BID

           Fosaprepitant 150mg x1

**Antimicrobial prophylaxis**: None (mucositis: 4%; FN: 8%)

           If Rituximab is given (e.g. R-ABVD for NLPHL): For HBsAg+ or HBsAg-/HBcAb+: Entecavir 0.5mg PO daily x1yr

**TLS prophylaxis**: No (can add if very high tumor burden)

**GCSF**: No (increases risk of bleomycin lung toxicity: Martin et al, JCO, 2005)

**Interim lab checks**: D15 Labs

**CNS prophylaxis**: No

**Port**: Yes, single lumen

**Can we give outpatient**: Yes

**Regimen specific:**

           -Pre-treatment ECHO required

           -Pre-treatment PFTs required\*

-Major side effects: highly emetogenic; myelosuppression; heart failure (doxorubicin); lung toxicity (bleo); neuropathy

-**No dose reductions or treatment delays with ABVD** (regardless of ANC). This can be done safely per several studies: Evens et al, BJH, 2007; Boleti & Mead, Ann Onc, 2007.

-Fertility counseling for all reproductive age patients receiving ABVD (although majority will recover fertility)

\*PFTs: Strongly consider eliminating bleomycin if DLCO <60%. If DLCO between 60% and 80% will recheck after 2 cycles. If DLCO drops after 2 cycles, will recheck after 4 cycles. If it drops below 60% at any time will stop Bleo. If patients are symptomatic or if positive exam will order CXR. If patients have history of mediastinal radiation, smoking, renal failure or age >40, we will consider repeating PFTs after 2 cycles regardless of initial testing.

**BV-AVD**

**Lymphoma Type: Frontline classical Hodgkin Lymphoma**

**Regimen: Cycle length Q28 days (Connors, ASH, 2017; Younes, Lancet Oncol, 2013; Connors, Blood, 2017)**

**Adriamycin 25mg/m2 IV D1 and D15**

 **Vinblastine 6mg/m2 IV D1 and D15**

 **Dacarbazine 375mg/m2 IV D1 and D15**

 **Brentuximab vedotin 1.2 mg/kg IV D1 and D15**

**Antiemetics**:

Early:

           Dexamethasone 20mg

Zofran 24mg

           Delayed (standing unless otherwise noted):

           Olanzapine 10 mg nightly for 4 days (do not use concurrently with compazine)

 Zofran 8 mg TID D2-5, then PRN

Compazine 10mg q6H PRN (start after olanzapine is completed)

           Refractory:

           Dexamethasone 4mg BID

           Fosaprepitant 150mg x1

**Antimicrobial prophylaxis**: None

**TLS prophylaxis**: No (can add if very high tumor burden)

**GCSF**: Yes, Neulasta OBI; alternative, if prohibitively expensive, 5 days of filgrastim

**Interim lab checks**: No

**CNS prophylaxis**: No

**Port**: Yes, single lumen

**Can we give outpatient**: Yes

**Regimen specific:**

 -Note: In large RCT (ECHELON-1), BV-AVD was compared to ABVD and showed improved PFS. Long-term data are still pending, so ABVD is still SOC, but have very low threshold to use BV-AVD if bleomycin not tolerated.

 -Pre-treatment ECHO required

 -Monitor for *neuropathies* closely with vinblastine and brentuximab

-Major side effects: highly emetogenic; myelosuppression; heart failure (doxorubicin); neuropathy

-Fertility counseling for all reproductive age patients receiving BV-AVD (although majority will recover fertility)

**R-CHOP**

**Lymphoma Types: DLBCL, MCL, FL, MZL, PTCL (w/o rituximab)**

**Regimen:** **Cycle Length Q21 days (or Q14 day) (RCHOP v CHOP:** **Coiffier, Blood, 2010)**

 **Rituximab 375mg/m2 IV D1**

 **Cyclophosphamide 750mg/m2 IV D1**

 **Doxorubicin 50mg/m2 IV D1**

 **Vincristine 1.4mg/m2 IV D1 (cap at 2mg)**

 **Prednisone 100mg PO D1-5**

**Antiemetics**:

         Early:

         Prednisone 100 mg q24 days 1-5 (included in “CHOP”)

    Zofran 24mg PO x1

Delayed (standing unless otherwise noted):

 Olanzapine 10mg nightly for four nights

Zofran 8mg q8h PRN

Compazine 10mgh q6 PRN (start after olanzapine is completed)

Refractory:

        Dexamethasone 4mg BID

Fosaprepitant 150mg

**Antimicrobial prophylaxis**: None (variable mucositis/FN)

           For HBsAg+ or HBsAg-/HBcAb+: Entecavir 0.5mg PO daily x1yr (If viral load is positive – check ALT and consult hepatology. As long as liver function is normal, it is still okay to give rituximab (Kim, EJC, 2013; Kusumoto, ASH, 2014)).

**TLS prophylaxis**: Allopurinol 300mg BID x7days: yes (for the first cycle’s first week)

**GCSF**: yes, Neulasta Onpro On-Body Injector (OBI), for patients aged >65, HIV+, consider for patients with prior chemotherapy/radiation, persistent neutropenia, marrow involvement, recent surgery/wounds, liver dysfunction (bili >2), renal dysfunction (CrCl <50)

**Interim lab checks**: No; however, consider one-time nadir visit for patients aged >65

**CNS prophylaxis**: Yes, for high-risk (see Lymphoma Management SOP, Approach to CNS Prophylaxis)

 -High Dose MTX vs. IT Triple Therapy (Cytarabine 40mg IT, MTX 15mg IT, Hydrocortisone 50mg IT; Lee, JCO, 2001)

**Port**: Yes, single lumen

**Can we give outpatient:** Yes

**Regimen Specific**:

 -Major side effects: highly emetogenic; myelosuppression; heart failure (doxorubicin); neuropathy

 -**R-miniCHOP** (50% dose reductions) after prephase of prednisone 60mg/m2 x7d for age >80 (Pfeundschuh, Blood, 2010).

**Other Comments:**

 -Pre-treatment ECHO required

 -Make sure HBV and HIV serologies have been checked

 -Fertility counseling for all reproductive age patients.

**R-CHOP + HD-MTX**

**Lymphoma Types: High CNS Risk DLBCL; Concurrent CNS and Systemic DLBCL**

**Regimen: Cycle Length Q21 days (Abramson, Cancer, 2010; NCCN 2017)**

 **Rituximab 375mg/m2 IV D1**

 **Cyclophosphamide 750mg/m2 IV D1**

 **Doxorubicin 50mg/m2 IV D1**

 **Vincristine 1.4mg/m2 IV D1 (cap at 2mg)**

 **Prednisone 100mg PO D1-5**

 **Methotrexate 3.5g/m2 IV D15 (C2, 4, 6)**

**Antiemetics**:

         Early:

         Prednisone 100 mg q24 days 1-5 (included in “CHOP”)

    Zofran 24mg PO x1

Delayed (standing unless otherwise noted):

 Olanzapine 10mg nightly for four nights

Zofran 8mg q8h PRN

Compazine 10mgh q6 PRN (start after olanzapine is completed)

Refractory:

        Dexamethasone 4mg BID

Fosaprepitant 150mg

**Antimicrobial prophylaxis**: None (variable mucositis/FN)

           For HBsAg+ or HBsAg-/HBcAb+: Entecavir 0.5mg PO daily x1yr (If viral load is positive – check ALT and consult hepatology. As long as liver function is normal, it is still okay to give rituximab (Kim, EJC, 2013; Kusumoto, ASH, 2014)).

**TLS prophylaxis**: Allopurinol 300mg BID x7days: yes (for the first cycle’s first week)

**GCSF**: Yes, Neulasta Onpro On-Body Injector (OBI), for all patients on C2D1, C4D1, C6D1 (HD-MTX cycles). Patients with any of following should receive Neulasta with every cycle: aged >65, HIV+, consider for patients with prior chemotherapy/radiation, persistent neutropenia, marrow involvement, recent surgery/wounds, liver dysfunction (bili >2), renal dysfunction (CrCl <50)

**Interim lab checks**: All patients will receive labs on D15 of HD-MTX cycles. Otherwise, can consider one-time nadir visit for patients aged >65.

**CNS prophylaxis**: Yes, this regimen is for high CNS-risk patients or patients with active CNS and systemic DLBCL

**Port**: Yes, single lumen

**Can we give outpatient:** R-CHOP: Yes; HD-MTX: No

**Regimen Specific**:

 -Major side effects R-CHOP: highly emetogenic; myelosuppression; heart failure (doxorubicin); neuropathy

 -Major side effects HD-MTX: Renal toxicity; mucositis

 -Methotrexate: **No PPIs**, NSAIDs, anti-fungals, Bactrim

 -For patients >80, consider another approach (no MTX, or dose-reduced MTX)

**Other Comments:**

 -Pre-treatment ECHO required

 -Make sure HBV and HIV serologies have been checked

 -Fertility counseling for all reproductive age patients

-To expedite High Dose Methotrexate start: Sodium Bicarbonate 650 mg PO tab. Take 3 tablets the night before methotrexate. Then take 3 tablets when you wake up and every 4 hours until methotrexate admission.

**R-CEOP**

**Lymphoma Types: DLBCL w/ poor cardiac function, cardiac transplant, prior anthracycline exposure, or older patients**

**Regimen: Cycle Length Q21D (****Moccia, Blood, 2009; Rashidi, Leuk & Lymph, 2016)**

 **Rituximab 375mg/m2 IV D1**

 **Cyclophosphamide 750mg/m2 IV D1**

 **Etoposide 50mg/m2 IV D1; 100mg/m2 PO D2-3**

 **Vincristine 1.4mg/m2 IV D1 (cap at 2mg)**

 **Prednisone 100mg PO D1-5**

**Antiemetics**:

         Early:

Zofran 24 mg D1-D3

 Olanzapine 5mg D1-D3

Delayed (standing unless otherwise noted):

 Olanzapine 10mg nightly D4 and D5

Zofran 8mg q8h PRN

Compazine 10mgh q6 PRN (start after olanzapine is completed)

Refractory:

           Fosaprepitant 150mg

Dexamethasone 4mg BID

**Antimicrobial prophylaxis**: None

 For HBsAg+ or HBsAg-/HBcAb+: Entecavir 0.5mg PO daily x1yr (If viral load is positive – check ALT and consult hepatology. As long as liver function is normal, it is still okay to give rituximab (Kim, EJC, 2013; Kusumoto, ASH, 2014)).

**TLS prophylaxis**: Allopurinol 300mg BID x7days: yes (for the first cycle’s first week)

**GCSF**: yes, Neulasta OBI on D3, for patients aged >65, consider for patients with prior chemotherapy/radiation, persistent neutropenia, marrow involvement, recent surgery/wounds, liver dysfunction (bili >2), renal dysfunction (creatinine clearance <50)

**Interim lab checks**: No; however, one-time nadir visit for patients aged >65 or clinically indicated

**CNS prophylaxis**: Yes, for high-risk (see Lymphoma Management SOP, Approach to CNS Prophylaxis)

 -High Dose MTX vs. IT Triple Therapy (Cytarabine 40mg IT, MTX 15mg IT, Hydrocortisone 50mg IT; Lee, JCO, 2001)

**Port**: Yes, single lumen

**Regimen Specific**:

 -Major side effects: highly emetogenic; myelosuppression; neuropathy

**Other Comments:**

 -Echo will have already been performed (regimen is for those with cardiac dysfunction)

 -Make sure HBV and HIV serologies have been checked

 -Fertility counseling for all reproductive age patients.

**BV-CHP**

**Lymphoma Types: CD30-Expressing T-Cell Lymphomas (study included >10% CD30 expression; label is for any expression)**

**Regimen: Cycle Length Q21 days (Horwitz, Lancet, 2018)**

 **Brentuximab vedotin 1.8mg/kg IV D1**

 **Cyclophosphamide 750mg/m2 IV D1**

 **Doxorubicin 50mg/m2 IV D1**

 **Prednisone 100mg PO D1-5**

**Antiemetics**:

         Early:

         Prednisone 100 mg q24 days 1-5 (included in “CHP”)

    Zofran 24mg PO x1

Delayed (standing unless otherwise noted):

 Olanzapine 10mg nightly for four nights

Zofran 8mg q8h PRN

Compazine 10mgh q6 PRN (start after olanzapine is completed)

Refractory:

Fosaprepitant 150mg

Dexamethasone 4mg BID

**Antimicrobial prophylaxis**: None (FN=18%)

**TLS prophylaxis**: Allopurinol 300mg BID x7days: yes (for most patients on initiation of therapy – x1 week)

**GCSF**: Yes, FN rate is 18%. Neulasta Onpro On-Body Injector (OBI) for all patients.

**Interim lab checks**: Not routine, but can order for elderly or poor PS patients.

**CNS prophylaxis**: Not standard. Can consider for certain high-risk groups (see Lymphoma Management SOP, Approach to CNS Prophylaxis).

**Port**: Yes, single lumen

**Can we give outpatient:** Yes

**Regimen Specific**:

 -Major side effects: highly emetogenic; myelosuppression; heart failure (doxorubicin); neuropathy; febrile neutropenia, **diarrhea**

**Other Comments:**

 -Pre-treatment ECHO required

 -Viral serologies

 - Fertility counseling for reproductive age patients

 - Counsel: loperamide OTC for diarrhea

**VR-CAP**

**Lymphoma Types: MCL**

**Regimen: Cycle Length Q21 days (Robak, NEJM, 2015)**

 **Velcade 1.3mg/m2 SC D1, 4, 8, 11 (was IV in study)**

 **Rituximab 375mg/m2 IV D1**

 **Cyclophosphamide 750mg/m2 IV D1**

 **Doxorubicin 50mg/m2 IV D1**

 **Prednisone 100mg PO D1-5**

**Antiemetics**:

         Early:

         Prednisone 100 mg q24 days 1-5 (included in “CAP”)

    Zofran 24mg PO x1

Delayed (standing unless otherwise noted):

 Olanzapine 10mg nightly for four nights

Zofran 8mg q8h PRN

Compazine 10mgh q6 PRN (start after olanzapine is completed)

Refractory:

        Dexamethasone 4mg BID

Fosaprepitant 150mg

**Antimicrobial prophylaxis**: Yes, valacyclovir 500mg PO daily (for velcade); no other prophylaxis (15% FN)

           For HBsAg+ or HBsAg-/HBcAb+: Entecavir 0.5mg PO daily x1yr (If viral load is positive – check ALT and consult hepatology. As long as liver function is normal, it is still okay to give rituximab (Kim, EJC, 2013; Kusumoto, ASH, 2014)).

**TLS prophylaxis**: Consider Allopurinol 300mg BID x7days (for the first cycle’s first week)

**GCSF**: yes, Neulasta OBI (D1), for patients aged >65, consider for patients with prior chemotherapy/radiation, persistent neutropenia, marrow involvement, recent surgery/wounds, liver dysfunction (bili >2), renal dysfunction (CrCl <50) (extrapolated from R-CHOP)

**Interim lab checks**: Yes, CBC/CMP on D8 for velcade dosing

**CNS prophylaxis**: Yes, for high-risk: Blastoid or ki67>30% (see Lymphoma Management SOP, Approach to CNS Prophylaxis)

 -IT Triple Therapy (Cytarabine 40mg IT, MTX 15mg IT, Hydrocortisone 50mg IT; Lee, JCO, 2001)

 -Unclear impact of HD MTX with velcade dosing

**Port**: Yes, single lumen

**Can we give outpatient:** Yes

**Regimen Specific**:

 -Major side effects: highly emetogenic; myelosuppression (particularly thrombocytopenia); heart failure (doxorubicin); neuropathy (particularly important)

 -Dosing:

 Cytopenias: plates<25,000; ANC<750: withhold D8 and recheck D11. If low on D11 then hold until next cycle. If still low at next cycle, lower dose to 1mg/m2, then 0.7mg/m2.

 Neuropathy: Grade 1 w/ pain or grade 2: 1mg/m2; grade 2 w/ pain or grade 3: 0.7mg/m2; grade 4: stop

**Other Comments:**

 -Pre-treatment ECHO required

 -Make sure HBV and HIV serologies have been checked

 -Fertility counseling for AYA patients.

**CHOEP**

**Lymphoma Types: PTCL-NOS, AITL, ALCL (ALK+/-), EATL; pts <60 (w/ or w/o autoSCT consolidation)**

**Regimen: Cycle length q21D (or q14D) (written as q21D in EPIC) (d’Amore, JCO, 2012; Wunderlich, Ann Oncol, 2003)**

 **Cyclophosphamide 750mg/m2 IV D1**

 **Doxorubicin 50mg/m2 IV D1**

 **Vincristine 1.4mg/m2 IV D1 (cap at 2mg)**

 **Etoposide 100mg/m2 IV D1-3 (****Can substitute 200mg/m2 PO D2-3; Kroschinsky, Cancer Chemo Pharm, 2008)**

 **Prednisone 100mg PO D1-5**

**Antiemetics**:

         Early:

Zofran 24 mg D1-D3

 Olanzapine 5mg D1-D3

Delayed (standing unless otherwise noted):

 Olanzapine 10mg nightly D4 and D5

Zofran 8mg q8h PRN

Compazine 10mgh q6 PRN (start after olanzapine is completed)

Refractory:

           Dexamethasone 4mg BID

 Fosaprepitant 150mg

**Antimicrobial prophylaxis**: None (mucositis: 3%; FN 12.2%)

**TLS prophylaxis**: Allopurinol 300mg BID x7days: yes (for the first cycle’s first week)

**GCSF**: Only with RF for q21d regimen (Neulasta OBI on D3/Pegfilgrastim D4 if RFs). For q14d regimen: All get Neupogen on D4-11

 -Risk factors: patients aged >65, consider for patients with prior chemotherapy/radiation, persistent neutropenia, marrow involvement, recent surgery/wounds, liver dysfunction (bili >2), renal dysfunction (creatinine clearance <50) (from R-CHOP)

**Interim lab checks**: No, not standard; reassess clinically throughout treatment

**CNS prophylaxis**: Yes, for high-risk (see Lymphoma Management SOP, Approach to CNS Prophylaxis)

 -IT Triple Therapy (Cytarabine 40mg IT, MTX 15mg IT, Hydrocortisone 50mg IT; Lee, JCO, 2001)

 -Unclear impact of HD MTX with CHOEP

**Port**: Yes, single lumen

**Regimen Specific**:

 -Major side effects: highly emetogenic; myelosuppression; heart failure (doxorubicin); neuropathy

 **Other Comments:**

 -Pre-treatment ECHO required

 -Make sure HBV and HIV serologies have been checked

 -Fertility counseling for all patients.

**R-EPOCH**
**Lymphoma Type: DLBCL, Burkitt, DHL, DEL, HIV-Lymphomas, PMBCL, GZL, PTCL (w/o rituximab), PBL (w/ velcade)**

**Regimen: Cycle length Q21 days (DLBCL: Wilson, Blood, 2002; Burkitt: Dunleavy, NEJM, 2013; DEL: Aggarwal, Blood, 2016; DHL:** **Petrich, Blood, 2014)**

 **Rituximab^ 375mg/m2 IV D1 (may be moved to D5 or D6)**

 **Etoposide 50mg/m2 IV per day D1-4 (96hr continuous infusion)**

 **Vincristine 0.4mg/m2 IV per day D1-4 (96hr continuous infusion)**

 **Doxorubicin 10mg/m2 IV per day D1-4 (96hr continuous infusion)**

 **Prednisone^ 60mg/m2 PO BID D1-5 (*Daily* D1-5 in HIV)**

 **Cyclophosphamide^ 750mg/m2 IV D5 (consider mesna for >1.5g/m2 – DL5/6)**

\*dose adjustment occurs after the first cycle based on nadir ANC and plats and continues throughout treatment (labs 2x/wk)

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| Drug Level    | -2    | -1    | 1    | 2    | 3    | 4    | 5    | 6    |
| Doxo mg/m2/day    | 10    | 10    | 10    | 12    | 14.4    | 17.3    | 20.7    | 24.8    |
| Etop mg/m2/day    | 50    | 50    | 50    | 60    | 72    | 86.4    | 103.7    | 124.4    |
| Cytox mg/m2/day    | 480    | 600    | 750    | 900    | 1080    | 1296    | 1555    | 1866    |

* + If ANC nadir is > 0.5 --> Increase by 1 dose level
	+ If ANC nadir is < 0.5 --> No change in dose
	+ If ANC nadir is < 0.5 x 3 --> Dec by 1 dose level
	+ If Plt nadir is <25, decrease by 1 dose level

**Antiemetics**:

 Early:
 Zofran 24mg daily days 1-5

 Olanzapine 10 mg qhs D-4

 Prednisone 60mg/m2 PO BID D1-5

           Delayed (standing unless otherwise noted):

           Zofran 8 mg q8h D6-8, then PRN

Compazine 10mg q6H PRN

Add Fosaprepitant 150mg x1 on day 5 for DL5 or higher

         Refractory:

           Olanzapine 10mg nightly (extend to D1-8)

           Dexamethasone 4mg BID

           Fosaprepitant 150mg x1

**Antimicrobial prophylaxis**: Yes (mucositis Gr 3: 6%; FN: 22%)

           Non-HIV or HIV w/ CD4>200:

 - Levaquin 500mg PO daily

  For HIV w/ CD4<200:

 - Levaquin 500mg PO daily

 -Fluconazole 400mg PO daily (do NOT prescribe with ibrutinib, i.e. AMC-101 pts)

 -Bactrim DS tablet Sat/Sun (stop after C4>200 x 3 months)

 For HBsAg+ or HBsAg-/HBcAb+: Entecavir 0.5mg PO daily x1yr (If viral load is positive – check ALT and consult hepatology. As long as liver function is normal, it is still okay to give rituximab (Kim, EJC, 2013; Kusumoto, ASH, 2014)).

**TLS prophylaxis**: Yes, Allopurinol 300mg BID x7days: yes (just for cycle 1)

**GCSF**: yes, Neulasta for all pts

**Interim lab checks**: Yes, CBC (w/ diff) twice weekly until next cycle.

**CNS prophylaxis**: Yes, for most patients receiving R-EPOCH (see Lymphoma Management SOP, Approach to CNS Prophylaxis)

 -IT Triple Therapy (Cytarabine 40mg IT, MTX 15mg IT, Hydrocortisone 50mg IT; Lee, JCO, 2001)

 -Of note: 8 treatments with 2 treatments per cycle, cycles 1-4 was used in original study.

 -Use of HD-MTX with R-EPOCH has been studied, but remains difficult to administer (Chihara, BJH, 2016)

**Port**: Yes, double lumen

**Can we give outpatient?** Yes (Cytoxan, rituximab and neulasta on-body injector on day 5)

**Regimen specific:**

           -Major side effects: highly emetogenic; myelosuppression; heart failure (doxorubicin – less than R-CHOP); neuropathy

^For HIV (Sparano, Blood, 2010): start cyclophosphamide at 187mg/m2 if CD4<100 or 375mg/m2 if CD4>100. Only dose-adjust the cyclophosphamide – can increase in increments of 187mg/m2 if nadir ANC>500 and plats>25,000. Hold rituximab if CD4<50.

-Fertility counseling for all patients.

**Other Comments:** Pre-treatment ECHO required; Make sure HBV and HIV serologies have been checked. Consider dose reductions age >80

**V-EPOCH**
**Lymphoma Type: Plasmablastic lymphoma, primary effusion lymphoma**

**Regimen: Cycle length Q21 days (DLBCL: Wilson, Blood, 2002; PBL: Castillo, BJH, 2015; Dunleavy, Blood, 2009)**

 **Velcade 1.3 mg/m2 subcutaneous on D1, D4, D7, D10**

 **Etoposide 50mg/m2 IV per day D1-4 (96hr continuous infusion)**

 **Vincristine 0.4mg/m2 IV per day D1-4 (96hr continuous infusion)**

 **Doxorubicin 10mg/m2 IV per day D1-4 (96hr continuous infusion)**

 **Prednisone^ 60mg/m2 PO BID D1-5 (*Daily* D1-5 in HIV)**

 **Cyclophosphamide^ 750mg/m2 IV D5 (consider mesna for >1.5g/m2 – DL5/6)**

\*dose adjustment occurs after the first cycle based on nadir ANC and plats and continues throughout treatment (labs 2x/wk)

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Drug Level    | -2    | -1    | 1    | 2    | 3    | 4    | 5    | 6    |
| Doxo mg/m2/day    | 10    | 10    | 10    | 12    | 14.4    | 17.3    | 20.7    | 24.8    |
| Etop mg/m2/day    | 50    | 50    | 50    | 60    | 72    | 86.4    | 103.7    | 124.4    |
| Cytox mg/m2/day    | 480    | 600    | 750    | 900    | 1080    | 1296    | 1555    | 1866    |

* + If ANC nadir is > 0.5 --> Increase by 1 dose level
	+ If ANC nadir is < 0.5 --> No change in dose
	+ If ANC nadir is < 0.5 x 3 --> Dec by 1 dose level
	+ If Plt nadir is <25, decrease by 1 dose level

**Antiemetics**:

 Early:
 Zofran 24mg daily days 1-5

 Prednisone 60mg/m2 PO BID D1-5

           Delayed (standing unless otherwise noted):

           Zofran 8 mg q8h for days 6-8

Compazine 10mg q6H PRN

Add Fosaprepitant 150mg x1 on day 5 for DL5 or higher.

         Refractory:

           Olanzapine 10mg nightly (do not use concurrently with compazine)

           Dexamethasone 4mg BID

           Fosaprepitant 150mg x1

**Antimicrobial prophylaxis**: Yes (Velcade: HZV 6-11%; HSV: 1-3%)

 Non-HIV or HIV w/ CD4>200:

 -Valtrex 500mg PO daily while getting velcade

 - Levaquin 500mg PO daily

  For HIV w/ CD4<200:

 -Valtrex 500mg PO daily while getting velcade

 - Levaquin 500mg PO daily

 -Fluconazole 400mg PO daily (do NOT prescribe with ibrutinib)

 -Bactrim DS tablet Sat/Sun (stop after C4>200 x 3 months)

**TLS prophylaxis**: Yes, Allopurinol 300mg BID x7days: yes (just for cycle 1)

**GCSF**: Yes, Neulasta for all pts

**Interim lab checks**: Yes, CBC (w/ diff) twice weekly until next cycle. CMP on D10 for velcade dosing.

**CNS prophylaxis**: Yes, for all patients receiving V-EPOCH (see Lymphoma Management SOP, Approach to CNS Prophylaxis)

 -IT Triple Therapy (Cytarabine 40mg IT, MTX 15mg IT, Hydrocortisone 50mg IT; Lee, JCO, 2001)

 -Use of HD-MTX with R-EPOCH has been studied, but remains difficult to administer (Chihara, BJH, 2016)

**Port**: Yes, double lumen

**Can we give outpatient?** Yes; we should move forward with this for patients who live locally

 \*Cytoxan, rituximab and neulasta on-body injector on day 5

**Regimen specific:**

           -Major side effects: highly emetogenic; myelosuppression; heart failure (doxorubicin – less than R-CHOP); neuropathy

^For HIV (Sparano, Blood, 2010): start cyclophosphamide at 187mg/m2 if CD4<100 or 375mg/m2 if CD4>100. Only dose-adjust the cyclophosphamide – can increase in increments of 187mg/m2 if nadir ANC>500 and plats>25,000. Hold rituximab if CD4<50.

-Fertility counseling for all patients.

**Other Comments:** Pre-treatment ECHO required; Make sure HBV and HIV serologies have been checked. Consider dose reductions age >80

**Modified Magrath (CODOX-M/IVAC)**
**Lymphoma Type: Burkitt lymphoma with CNS involvement**

**Regimen is given in 4 alternating cycles of regimen A and B (LaCasce, Leukemia & Lymphoma, 2004; Noy, Blood, 2015)**

**Regimen A (Odd Cycles): CODOX**

 **Rituximab 375 mg/m2 on D1**

 **Cyclophosphamide 800 mg/m2 on D1 and D2**

 **Vincristine 1.4 mg/m2 on D1 and D8**

 **Doxorubicin 50 mg/m2 on D1**

 **Methotrexate 3000 mg/m2 on D15**

 **C1D1: IT triple therapy, D3 IT cytarabine 50 mg (Depocyte no longer available)**

**C3: D2 IT triple therapy, D4 IT cytarabine 50 mg**

**Regimen B (Even Cycles): IVAC**

 **Rituximab 375 mg/m2 on D1**

 **Ifosfamide 1500 mg/m2 continous infusion on D1-D5**

 **Mesna 1500 mg/m2 on continuous infusion on D1-D5**

 **Etoposide 60 mg/m2 on D1-D5 (split into two 30 mg/m2 bags q12h due to stability)**

 **Cytarabine 2000 mg/m2 q12h on D1 and D2**

 **C2 and C4: D2 and D5 methotrexate IT with cycles 2 and 4**

**Antiemetics (regimen A, CODOX)**

 Early:
 Zofran 24mg daily on D1 and D2

 Dexamethasone 20 mg IV on day 1

Delayed (standing unless otherwise noted):

Zofran 8mg q8h D3-5, then PRN

 Olanzapine 10mg nightly for four nights

Compazine 10mgh q6 PRN (start after olanzapine is completed)

Refractory:

Dexamethasone 4mg BID

Fosaprepitant 150mg

**Antiemetics (regimen B, IVAC)**

 Early:
 Zofran 24mg daily on D1-5

 Dexamethasone 8mg on D1-5

Delayed (standing unless otherwise noted):

Zofran 8mg q8h D6-8, then PRN

 Olanzapine 10mg nightly for five nights (IP)

Compazine 10mgh q6 PRN (start after olanzapine is completed)

Refractory:

Dexamethasone 4mg BID

Fosaprepitant 150mg

**Antimicrobial prophylaxis (both regimens):** Yes (mucositis: 7%; FN 24%/17%)

           Non-HIV or HIV w/ CD4>200:

 - Levaquin 500mg PO daily

  For HIV w/ CD4<200:

 - Levaquin 500mg PO daily

 -Fluconazole 400mg PO daily (do NOT prescribe with ibrutinib)

 -Bactrim DS tablet Sat/Sun (stop after C4>200 x 3 months)

 For HBsAg+ or HBsAg-/HBcAb+: Entecavir 0.5mg PO daily x1yr (If viral load is positive – check ALT and consult hepatology. As long as liver function is normal, it is still okay to give rituximab (Kim, EJC, 2013; Kusumoto, ASH, 2014)).

**TLS prophylaxis**: Yes, Allopurinol 300mg BID x7days: yes (just for cycle 1)

**GCSF (both regimens)**: yes, Neulasta after CODOX and IVAC, and Neupogen after the methotrexate

**Interim lab checks**:

CODOX: Pts are here frequently enough to receive regular labs in clinic; IVAC: Weekly

**Port**: Yes, double lumen

**Can we give outpatient?** Yes for CODOX (except D15 methotrexate must be inpatient); no for IVAC

**Regimen specific:** CD4 counts for HIV+ patients

**Other Comments:** Pre-treatment ECHO required; Make sure HBV and HIV serologies have been checked.

**CNS prophylaxis**: Yes, see schedule above in Regimen Section

**R-ICE**
**Lymphoma Type: Any aggressive relapsed (usually pre-autoSCT)**

**Regimen: Cycle Length Q14 or Q21 days (Kewalramani, Blood, 2004; Gisselbrecht, JCO, 2010)**

 **Rituximab 375mg/m2 IV D1 or D3 (or Obinutuzumab 1000mg IV D1 or D3)**

 **Ifosfamide 5000mg/m2 IV D2 (24hr continuous infusion w/ Mesna 5000mg/m2)**

 **Carboplatin AUC 5mg/mL IV D2**

 **Etoposide 100mg/m2 IV D1-3**

 \*if performing outpatient, need to have infusion appointment in the first slot on each day

**Antiemetics**:

Early:

Zofran 24mg daily

Dexamethasone 8mg daily

Delayed (standing unless otherwise noted):

Zofran 8mg q8h D4-5, then PRN

Olanzapine 10mg nightly for four nights (starting on D2)

Refractory:

Dexamethasone 4mg BID

Fosaprepitant 150mg

**Antimicrobial prophylaxis**: None (FN: 17%)

           For HBsAg+ or HBsAg-/HBcAb+: Entecavir 0.5mg PO daily x1yr (If viral load is positive – check ALT and consult hepatology. As long as liver function is normal, it is still okay to give rituximab (Kim, EJC, 2013; Kusumoto, ASH, 2014)).

**TLS prophylaxis**:Yes: Allopurinol 300mg BID x7days

**GCSF**: Yes: q2weeks Neupogen; q3weeks Neulasta

**Interim lab checks**: Weekly until RTC

**CNS prophylaxis**: No

**Port**: Yes, double-lumen

**Can we give outpatient:** Yes

**Regimen Specific:**

-Urinalysis if symptomatic

**Other Comments:**

 -Consider pre-treatment ECHO, especially for transplant candidates

 -Make sure HBV and HIV serologies have been checked within 1 year

 -Consider dose reductions age >80

 -Major side effects: highly emetogenic; myelosuppression; hemorrhagic cystitis; ifosfamide toxicity

 -Fertility counseling for all patients.

**R-DHAP (R-DHAX)**

**Lymphoma Type: Any aggressive relapsed (better than R-ICE in GC-DLBCL) (usually pre-autoSCT); Frontline MCL (Le Gouill, NEJM, 2017).**

**Regimen: Cycle length Q21 days (Gisselbrecht, JCO, 2010; Divided dosing of cisplatin: Lisenko, BMC Cancer, 2016)**

 **Rituximab 375mg/m2 IV D1 or D4 (or Obinutuzumab 1000mg IV D1 or D4)**

**Dexamethasone 40mg IV D1-4**

 **Cytarabine 2g/m2 IV q10-12hrs x2 doses on D2**

 **Cisplatin 25mg/m2 IV D1-4 (original dosing is 100mg/m2 IV D1)**

 **\*Can replace cisplatin with oxaliplatin 100mg/m2 IV D1 (R-DHAX) if renal impairment (Lignon, Clin L,M,L, 2010)**

**Antiemetics**:

            Early:

 Fosaprepitant 150mg D1 (DHAP only, not necessary with DHAX)

 Olanzapine 10 mg D1-4 (DHAP only, not necessary for DHAX)

 Dexamethasone 40mg daily days1-4

 Zofran 24mg daily

            Delayed (standing unless otherwise noted):

 Fosaprepitant and olanzapine (DHAP only, both early and delayed)

 Zofran 8mg q8h PRN

 Compazine 10 mg q6h PRN

            Refractory:

 Olanzapine 10mg daily (do not use concurrently with compazine)

**Antimicrobial prophylaxis**: FN 16%.

            For HBsAg+ or HBsAg-/HBcAb+: Entecavir 0.5mg PO daily x1yr (If viral load is positive – check ALT and consult hepatology. As long as liver function is normal, it is still okay to give rituximab (Kim, EJC, 2013; Kusumoto, ASH, 2014)).

**TLS prophylaxis**: Yes (build in but add as a hard stop): Allopurinol 300mg BID x7days

**GCSF**: Yes, Neulasta

**Interim lab checks**: Yes, weekly

**CNS prophylaxis**: No

**Port**: Yes, double-lumen preferred, but single lumen adequate

**Can we give outpatient?** Yes

**Agent Specific**:

 -Neuro checks by nursing staff baseline day 1
 -Monitor renal function
 -1L NS IV daily during infusion with cisplatin
 -Consider audiology assessment for ototoxicity r/t cisplatin
 -Prednisolone eye drops q6h
 -Consider dose reductions age >80

**Other Comments:**

 -Pre-treatment ECHO: Consider if going

 -Make sure HBV and HIV serologies have been checked within 1 year

 -Major side effects: highly emetogenic; myelosuppression; renal failure; hearing toxicity; cerebellar/ocular toxicity

 -Fertility counseling for all patients.

**R-GDP**

**Lymphoma Types: Any aggressive relapsed (DLBCL, PTCL, ALCL, PMBCL, cHL included in studies)**

**Regimen: Cycle Length Q21 Days (Crump, JCO, 2014; Crump, Cancer, 2004; Gopal, Leuk&Lymph, 2010)**

 **Gemcitabine 1000 mg/m2 IV on D1 and D8**

 **Cisplatin 75 mg/m2 IV on D1**

 **Dexamethasone 40 mg IV or PO D1-4**

 **Rituximab 375mg/m2 IV D1 (or obinutuzumab 1000mg on D1)**

**Antiemetics**:

         Early:

D1-4:

Fosaprepitant 150mg

         Dexamethasone 40 mg daily D 1-4

 Zofran 24 mg

D8:

Zofran 24 mg

Delayed (standing unless otherwise noted):

Fosaprepitant 150mg on D1

Zofran 8mg q8h PRN

Compazine 10mgh q6 PRN

Refractory:

           Olanzapine to 10mg (do not use concurrently with compazine)

**Antimicrobial prophylaxis**:

           For HBsAg+ or HBsAg-/HBcAb+: Entecavir 0.5mg PO daily x1yr (If viral load is positive – check ALT and consult hepatology. As long as liver function is normal, it is still okay to give rituximab (Kim, EJC, 2013; Kusumoto, ASH, 2014)).

**TLS prophylaxis**: No, not standard

**GCSF**: Yes potentially; days 2-6 and 9-13 neupogen

**Interim lab checks**: No note necessary; labs being checked on D8 with gemcitabine

**CNS prophylaxis**: No

**Port**: Yes, either double (going to autoSCT) or single lumen (not going to autoSCT)

**Can we give outpatient:** Yes

**Regimen Specific**:

 -Renal toxicity (give prophylactic fluids with D1 cisplatin)

-Check CBC/CMP on D8 to include liver function parameters for gemcitabine

-D1 <75 platelets, ANC <1, delay by a week and recheck; notify provider if CrCl <40, bili > 1.8

 -D8 <75 platelets, ANC<1, decrease dose level 25% or give neupogen; platelets <50 decrease dose by 25% regardless

**Other Comments: None.**

**R-GEMOX**

**Lymphoma Types: Any Aggressive Relapsed**

**Regimen: Cycle Length Q14 days (Gnaoui et al, Ann Oncol, 2007; Mounier et al, Haematologica, 2013)**

 **Rituximab 375mg/m2 IV D1**

 **Gemcitabine 1000mg/m2 IV D1**

 **Oxaliplatin 100 mg/m2 IV D1**

**Antiemetics**:

         Early:

    Zofran 24mg PO

 Dexamethasone 8 mg PO

Delayed (standing unless otherwise noted):

Zofran 8mg q8h D2-5, then PRN

Compazine 10mgh q6 PRN (if patient is on olanzapine, start after olanzapine is completed)

Refractory:

 Olanzapine 10 mg nightly for four days

 Fosaprepitant 150 mg IV

**Antimicrobial prophylaxis**:

 For HBsAg+ or HBsAg-/HBcAb+: Entecavir 0.5mg PO daily x1yr (If viral load is positive – check ALT and consult hepatology. As long as liver function is normal, it is still okay to give rituximab (Kim, EJC, 2013; Kusumoto, ASH, 2014)).

**TLS prophylaxis**: No, not standard.

**GCSF**: Not standard for first cycle; initial approach to delay therapy one week for count recovery. Use of Neulasta recommended for patients who have experienced neutropenic fever, in which case would utilize OBI, or Neulasta subq on D2.

**Interim lab checks**: No

**CNS prophylaxis**: No

**Port**: Not necessary, but will likely have access from previous regimen

**Can we give outpatient:** Yes

**Regimen Specific**:

 -Paralaryngeal dysesthesia: duration of infusion extend from 2 hours to 6 hours

**Other Comments:**

 -Notify provider for ANC <1000 and platelets less than 75,000

 -Notify provider if bilirubin >1.6 (consider dose-reduction); if mid-treatment consider cutting 50% or holding gemcitabine

 -Notify provider if AST/ALT/Alk Phos >3x upper limit of normal

**R-MPV (rdWBRT and High-Dose Cytarabine Consolidation)**

**Lymphoma Type: Primary CNSL, Secondary CNSL (brain only), possible CNS MCL**

**Regimen: Cycle Length Q14 days x5-7 cycles (Morris PG, et al, JCO, 2013; Omuro A, et al, Blood, 2015)**

 **Rituximab 500mg/m2 IV D1**

 **Methotrexate 3.5g/m2 IV D2**

 **Procarbazine 100mg/m2 PO D1-7 (odd cycles only)**

 **Vincristine 1.4mg/m2 IV D2 (cap at 2.8mg)**

 **Radiation: if CR: rdWBRT (23.4Gy); if PR: standard WBRT (45Gy)**

 **High-Dose Cytarabine 3g/m2 q24 D1-D2 q28days x2 cycles**

**Antiemetics**:

            Early:

 Zofran 24mg once day 1

 Dexamethasone 12mg once day 1

Delayed:

Zofran 8 mg daily for days 2-7 on cycles 1/3/5

            Refractory:

 Compazine 10mg 6h prn

 Dexamethasone 4mg BID for five days

**Antimicrobial prophylaxis**: None.

 For HBsAg+ or HBsAg-/HBcAb+: Entecavir 0.5mg PO daily x1yr (If viral load is positive – check ALT and consult hepatology. As long as liver function is normal, it is still okay to give rituximab (Kim, EJC, 2013; Kusumoto, ASH, 2014)).

**TLS prophylaxis**: No

**GCSF**: For R-MPV: Yes, Neupogen x4 days (order 2 cycles at a time); For Cytarabine: Neulasta OBI D2

**Interim lab checks**: Not necessary unless there is a patient-specific concern

**CNS prophylaxis:** Do an LP with cycle 1 give cytarabine 100 mg and hydrocortisone 50 mg; if positive once-per-cycle IT cytarabine on day 1

**Port**: Yes, double-lumen

**Can we give outpatient?** No, R-MPV. Yes, cytarabine consolidation.

**Regimen Specific**:

 -Methotrexate: **No PPIs**, NSAIDs, anti-fungals, Bactrim

 -Check liver and kidney function

 -Leucovorin rescue to prevent mucositis

 -Major side effects: highly emetogenic (C1,3,5); myelosuppression; renal toxicity; neuropathy

**Other comments**:

 -Baseline Echo

 -check HBV and HIV serologies

          -consider dose reductions age >80

 -Fertility counseling for all patients.

**MATRix**

**Lymphoma Type: Primary CNSL, Secondary CNSL (brain only), possible CNS MCL**

**Regimen: Cycle Length Q21 x4C with iMRI with C3 (Ferreri, Lancet Haematol, 2016; Ferreri, Lancet Haematol, 2017)**

 **Rituximab 375mg/m2 IV D0 (admit next day during week)**

 **Methotrexate 3.5g/m2 IV D1**

 **Cytarabine 2g/m2 q12 D2/D3**

 **Thiotepa 30mg/m2 IV D4**

 **\*Bicarbonate 1950mg (3 tabs 650mg) q6 hours until admission #48**

**Antiemetics**:

            Early:

 Zofran 24mg PO D1-4

 Dexamethasone 12mg PO D1-3

Delayed:

Zofran 8 mg q8 prn D5-7

Compazine 10mg PO prn D5-7

            Refractory:

 Fosaprepitant

 Olanzapine 10mg

**Antimicrobial prophylaxis**: None.

 For HBsAg+ or HBsAg-/HBcAb+: Entecavir 0.5mg PO daily x1yr (If viral load is positive – check ALT and consult hepatology. As long as liver function is normal, it is still okay to give rituximab (Kim, EJC, 2013; Kusumoto, ASH, 2014)).

**TLS prophylaxis**: No

**GCSF**: Neulasta OBI for high-risk of febrile neutropenia (risk 25%>60yrs 13%<60)

**Interim lab checks**: Not necessary unless there is a patient-specific concern

**CNS prophylaxis:** Perform an LP with cycle 1 and give cytarabine 100 mg and hydrocortisone 50 mg. If CSF flow is negative – no further IT treatments; if CSF flow positive – once-per-cycle IT cytarabine on day 1 for all cycles.

**Port**: Yes, double-lumen

**Can we give outpatient?** No

**Regimen Specific**:

 -Methotrexate: **No PPIs**, NSAIDs, azoles interact with LFTs

 -Bactrim DS SAT/SUN if HIV PCNSL or if on long course of steroids (hold 48 hrs prior to MTX)

 -Check liver and kidney function

 -Leucovorin rescue to prevent mucositis

 -Cytarabine: cerebellar toxicity

 -Cytopenias

**Other comments**:

 -check HBV and HIV serologies

 -Fertility counseling

 -Consider dose reductions if >80 yrs

**BR**

**Lymphoma Type: FL, MZL, MCL, LPL/WM, CLL/SLL, NLPHL-maybe**

**Regimen: Cycle Length Q28 days (Rummel MJ, et al, Lancet, 2013)**

 **Bendamustine 90mg/m2 IV D1-2**

 **Rituximab 375mg/m2 IV D1**

**Antiemetics**:

Early:

Zofran 24mg

 Dexamethasone 8mg

Delayed (standing/prn):

Zofran 8mg q8h PRN

Compazine 10mg q6h PRN

Refractory (options):

Zofran 8mg TID

Olanzapine 10mg nightly (do not use concurrently with compazine)

Dexamethasone 4mg BID

Fosaprepitant 150mg (IV)

**Antimicrobial prophylaxis**:

 Initial studies: low risk for any infection w/ bendamustine: 37%; Sepsis<1%.

 Later studies are showing risk of VZV and PJP w/ Benda (Hiddemann, JCO, 2018; NCCN, 5/2018, Follicular Lymphoma).

 Based on newer studies, will add: **Valtrex 500mg daily and Bactrim DS BID on Sat/Sun for 1 year**

 For HBsAg+ or HBsAg-/HBcAb+: Entecavir 0.5mg PO daily x1yr (If viral load is positive – check ALT and consult hepatology. As long as liver function is normal, it is still okay to give rituximab (Kim, EJC, 2013; Kusumoto, ASH, 2014)).

**TLS prophylaxis**: No but consider for high-risk disease (Allopurinol 300mg BID x7days)

**GCSF**: No but consider if complications arise in treatment

**Interim lab checks**:  No but consider for elderly patients

**CNS prophylaxis**: No

**Port**: No

**Can we give outpatient?** Yes

**Regimen Specific**:

 -Consider dose reductions vs. delaying x1 week for LFT abnormalities

 -Major Side Effects: mild-mod emetogenic; myelosuppression; No hair loss with this regimen.

**Other comments**:

 -Make sure HBV and HIV serologies have been checked within 1 year

 -Consider dose reductions for >80

 -Fertility counseling for all patients.

**R-BAC**

**Lymphoma Type: MCL**

**Regimen: Cycle Length Q28 days (Visco C et al, JCO, 2013)**

 **Rituximab 375mg/m2 IV D3**

 **Bendamustine 70mg/m2 IV D1-2**

 **Cytarabine 800mg/m2 IV D1-3 (or 500mg/m2 IV D1-3: Visco, Lancet Haemat, 2017)**

**Antiemetics**:

            Early:

 Zofran 24mg

 Dexamethasone 8mg

            Delayed (standing/prn):

 Zofran 8mg TID D4-5, then PRN

 Compazine 10mg q6h PRN

            Refractory (options):

Fosaprepitant 150mg on Day 1 of subsequent

Olanzapine 10mg nightly (do not use concurrently with compazine)

 Dexamethasone 4mg BID

**Antimicrobial prophylaxis**:

 Initial studies: low risk for any infection with bendamustine

 Later studies are showing risk of VZV and PJP w/ Benda (Hiddemann, JCO, 2018; NCCN, 5/2018, Follicular Lymphoma).

 Based on newer studies, will add: **Valtrex 500mg daily and Bactrim DS BID on Sat/Sun for 1 year**

            For HBsAg+ or HBsAg-/HBcAb+: Entecavir 0.5mg PO daily x1yr (If viral load is positive – check ALT and consult hepatology. As long as liver function is normal, it is still okay to give rituximab (Kim, EJC, 2013; Kusumoto, ASH, 2014)).

**TLS prophylaxis**: Not standard but build in and d/c if not needed (Allopurinol 300mg BID x7days)

**GCSF**: Yes, D3 Neulasta OBI

**Interim lab checks**: Yes, once-weekly

**CNS prophylaxis**: No

**Port**: Yes, single-lumen if no transplant, double-lumen if transplant

**Can we give outpatient?** Yes

**Regimen Specific**:

 **-**Major Side Effects: Highly emetogenic;myelosuppression; severe neutropenia

 **-Note: Dose is below threshold for high dose cytarabine precautions (eye drops and cerebellar checks)**

**Other comments**:

 -Make sure HBV and HIV serologies have been checked within 1 year

 -Fertility counseling for all patients.

**SMILE**

**Lymphoma Type: Extranodal NK/T-cell Lymphoma, Nasal Type**

**Regimen: Cycle Length Q28 days x2C followed by autoSCT (Yamaguchi M et al, JCO, 2011)**

 **Methotrexate 2g/m2 IV D1 (w/ leucovorin rescue)**

 **Ifosfamide 1500mg/m2 IV D2-4 (w/ mesna)**

 **Etoposide 100mg/m2 IV D2-4**

 **Dexamethasone 40mg D2-4**

 **Pegaspargase 3750 units IV D8**

 \*we will be giving pegaspargase x1 instead of L-asparaginase x7

**Antiemetics**:

            Early

 Dexamethasone 40mg daily days 2-4

 Zofran 24mg daily days 1-4

 Olanzapine 10mg nightly days 2-5

            Delayed (standing unless otherwise noted):

             Zofran 8mg TID D5-6, then PRN

 Compazine 10mg q6h PRN (start after olanzapine is completed)

            Refractory:

Fosaprepitant 150mg x1

**Antimicrobial prophylaxis**: Yes (mucositis: 13%; FN: 45%)

 For all patients:

 -Valtrex 500mg PO daily during chemotherapy

 -Levaquin 500mg PO daily during chemotherapy

 -Bactrim DS BID on Saturday and Sunday

**TLS prophylaxis**: Allopurinol 300mg BID x7days: yes

**GCSF**: yes; day 6 Neulasta

**Interim lab checks**: Yes.

 -2x weekly: CBC w/diff, CMP, coags, DIC, ATIII

 -1x weekly: lipase and triglycerides

 \*if fibrinogen <100 give cryo

 \*ATIII <60 give thrombate

**CNS prophylaxis**: Not standard (already receiving high-dose methotrexate)

**Port**: Yes; double-lumen

**Can we give outpatient?** Not the entire regimen: D1-4 inpatient; D8 outpatient pegaspargase

**Agent Specific**:

 -This is an anthracycline-resistant lymphoma; therefore, standard CHOP-like regimens are ineffective.

 -Admit on Tuesday at the earliest to allow for 48-hour window from last Bactrim dose on Sunday

 -Review lymphocyte count to be greater than 500 (not a requirement for treatment but parameter to consider)

 -Major Side Effects: highly emetogenic; myelosuppression; hemorrhagic cystitis; renal failure; mucositis

 -Pegaspargase Side Effects: hepatotoxicity (ALT/AST); hypersensitivity reaction; thrombosis; pancreatitis; hyperglycemia; coagulation disorder

**Other comments**:

 -Make sure HBV and HIV serologies have been checked within 1 year

 -Pre-treatment Echo

 -Fertility counseling for all patients.

**R2 (Revlimid+Rituximab)**
**Lymphoma Type:**

**MCL (Ruan, NEJM, 2015)**

**FL (Leonard, JCO, 2015; Fowler, Lancet Oncol, 2014)**

**MZL (Kiesewetter, Blood, 2017)**

**DLBCL (Wang, Leukemia, 2013; Zinzani, Clin Lymph, 2011); DLBCL-maintenance (Thieblemont, JCO, 2017)**

**PCNSL (Ghesquieres, ASH, 2016)**

**Regimen: Cycle Length Q28days**

 **Lenalidomide 20mg daily q21d of 28d cycle until progression or toxicity\***

 **Rituximab 375mg/m2 weekly x4 then monthly or bimonthly for 1-2 years\*\***

**Antiemetics**:

 Early:
 N/A

           Delayed (standing unless otherwise noted):

           Compazine 10mg q6H PRN

         Refractory:

           Zofran 8 mg q8h PRN

Olanzapine 10mg nightly

**Antimicrobial prophylaxis:** None.

 For HBsAg+ or HBsAg-/HBcAb+: Entecavir 0.5mg PO daily x1yr (If viral load is positive – check ALT and consult hepatology. As long as liver function is normal, it is still okay to give rituximab (Kim, EJC, 2013; Kusumoto, ASH, 2014)).

**VTE Prophylaxis:**

 No history of VTE or major risk factor: ASA 81mg PO daily

 History of VTE or other major risk factor: DOAC or enoxaparin

**TLS prophylaxis**: as needed for high-risk disease.

**GCSF**: No

**Interim lab checks**: D14 visit for CBC with pharmacist – symptoms/counts.

**CNS prophylaxis**: No

**Port**: No

**Can we give outpatient?** Yes

**Regimen specific:**

           \*Note on dosing revlimid: can generally start at 20mg unless underlying CKD. If tolerating well (stable CBC and renal function), can increase to 25mg. If cytopenias or renal dysfunction, will need to dose reduce. Can give as low as 2.5mg.

 \*\*Note on dosing rituximab: The schedule is highly variable depending on the study and the disease subtype. Many studies include a 4-week “loading dose” and then proceed with monthly or bimonthly rituximab for variable lengths of time. We feel it is appropriate to give the loading dose followed by monthly or bimonthly rituximab for 1-2yrs based on preference.

 -Thromboprophylaxis (see above)

 -Diarrhea (w/ or w/o lactose intolerance d/t capsule – can give lactaid)

 -Rash – symptom control

**Rituximab Hycela (Subcutaneous Rituximab)**

**Lymphoma Type:**

**CLL (Assouline, Br J Clin Pharmacol 2015;80:1001-9.)(Assouline, Lancet Haematol 2016;3:e128-38.)**

**FL (Salar, J Clin Oncol 2014;32:1782-91)(Davies, Lancet Haematol 2017;online)(Davies, Lancet Haematol 2014;15:343-52.)**

**DLBCL (Rummel, Ann Oncol 2017;28:836-42.)**

**Regimen: Cycle length: Same FDA indications as rituximab**

**FL/DLBCL: Administer 1400mg/23,400units subcutaneously over 5 minutes according to recommended schedule**

* **Volume 11.7ml**
* **Observe for 15 minutes following administration**

**Pre-medications**: acetaminophen and antihistamine before each dose. May consider premedication with glucocorticoids.

**Antimicrobial prophylaxis**: None.

 For HBsAg+ or HBsAg-/HBcAb+: Entecavir 0.5mg PO daily x1yr (If viral load is positive – check ALT and consult hepatology. As long as liver function is normal, it is still okay to give rituximab (Kim, EJC, 2013; Kusumoto, ASH, 2014)).

**TLS prophylaxis**: No

**GCSF**: No

**Interim lab checks**: Hepatitis B panel as per routine practice for rituximab IV

**CNS prophylaxis**: Patient-specific

**Port**: No

**Can we give outpatient**: Yes

**Regimen specific:**

Inclusion criteria:

* Regimens that employ the following dosing strategies can be substituted with rituxan hycela for patients who have no exclusion criteria for cycle 2 and beyond
	+ Rituximab 500mg/m2 IV Q4 weeks
	+ Rituximab 375mg/m2 IV Q2-3 months
	+ Rituximab 375mg/m2 IV Q3-4 weeks

Exclusion criteria:

* No approved prior authorization specifically for rituximab hycela
* BSA >/= 2.7
* Patients who have experienced any grade of hypersensitivity reaction or cytokine release syndrome (see EPIC infusion clinic nurse practitioner documentation)
* Non-malignant indications
* Patients who have not had at least one full dose of rituximab product by intravenous infusion

**Venetoclax (BCL2-Inhibitor)**

**Lymphoma Type: MCL; FL**

**Regimen: Cycle length: Continuous (Davids, JCO, 2017)**

 **Note:** foroff label use allow time for insurance approval

**MCL: Venetoclax 800mg po daily**

**FL: Venetoclax 1200mg po daily**

**Antiemetics**: No indication for up front antiemetic prophylaxis but venetoclax associated with N/V

 Refractory: Take with food. Prochlorperazine 10mg po q6h prn N/V

**Antimicrobial prophylaxis**: None.

**TLS prophylaxis: Yes. Risk stratify:**

**1) High risk TLS (LN>10cm or WBC>25,000 + LN>5cm)**

**2) Low-Intermediate risk TLS (LN<10cm)**

**Prophylaxis**: -Allopurinol 300mg po daily renally adjusted during ramp up and for one week after achieving target dose.

 -Oral hydration with 2L water per day during ramp up and for one week after achieving target dose.

**GCSF**: No. But can consider concomitant use to maintain dose intensity

**Interim lab checks**: Yes (see table for ramp up)

**CNS prophylaxis**: Patient-specific.

**Port**: No

**Can we give outpatient**: Yes.

**Regimen specific:**

**Strong inhibitor CYP3A4** (vori/posa/ritonavir): 75% dose reduction from target dose

**Moderate inhibitor CYP3A4** (isuvacon/fluc/dilt) or **Pgp inhibitor** (cyclops/tac/carvedilol): 50% dose reduction from target dose

**Induction ramp-up (see table).** May involve CPP to manage ramp up with oncologist visit PRN. Avoid ramp up with labs that fall on the weekend due to no provider available to review.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **TLS Risk** | **Schedule** | **Labwork** | **Mantle Cell Dosing** | **Follicular Dosing** |  |
| **Low-Intermediate Risk** | Week 1 | Pre-dose, 6-8h and 24h post | 50mg daily | 100mg daily |  |
| Week 2 | Pre-dose, 6-8h and 24h post | 100mg daily | 200mg daily |  |
| Week 3 | Pre-dose | 200mg daily | 400mg daily |  |
| Week 4 | Pre-dose | 400mg daily | 800mg daily |  |
| Week 5 | Pre-dose | 800mg daily | 1200mg daily |  |
| Post | 1 week later. Stop allop/hydration | - | - |  |
| **High Risk** | Week 1 | Hospital | 50mg daily | 100mg daily |  |
| Week 2 | Hospital | 100mg daily | 200mg daily |  |
| Week 3 | Pre-dose, 6-8h and 24h post | 200mg daily | 400mg daily |  |
| Week 4 | Pre-dose, 6-8h and 24h post | 400mg daily | 800mg daily |  |
| Week 5 | Pre-dose | 800mg daily | 1200mg daily |  |
| Post | 1 week later. Stop allop/hydration | - | - |  |

**Management of neutropenia and thrombocytopenia**

|  |  |
| --- | --- |
|  | **Febrile neutropenia or Grade 4 neutropenia/thrombocytopenia** |
| **First occurrence** | Hold until ANC > 500/μL and/or PLT > 25 × 105/μL then restart at full dose |
| **Second occurrence** | Hold until ANC > 500/μL and/or PLT > 25 × 105/μL **and** reduce schedule to 21d on/7d off |

If the patient has recurrent cytopenias after dose attenuation, please consult with a PharmD
If the patient has active bone marrow disease, no dose adjustments are recommended

**Ibrutinib/Acalabrutinib (BTK-Inhibitor)**

**Lymphoma Type (citations for ibrutinib, unless otherwise noted):**

**MCL (Wang, NEJM, 2013) (Acalabrutinib: Wang, Lancet, 2017)**

**LPL/WM (Treon, NEJM, 2015)**

**MZL (Noy, Blood, 2017)**

**FL (Bartlett, Blood, 2017)**

**DLBCL (Wilson, Nat Med, 2015)**

**PCNSL (Grommes, ASH, 2016)**

**Regimen: Cycle length: Continuous**

 **Note:** for off label use allow time for insurance approval

**Ibrutinib 560mg po daily (4 pills/dose)**

**Acalabrutinib 100mg po Q12h (1 pill/dose)**

**Antiemetics**: N/A

**Antimicrobial prophylaxis**: None, usually.

**TLS prophylaxis**: No

**GCSF**: No

**Interim lab checks**: Yes. At 2 weeks, CBC with diff + CMP. At 4 weeks, CBC with diff + CMP. Visit + labs monthly for 6 months, then quarterly, taper PRN.

**CNS prophylaxis**: Patient-specific

**Port**: No

**Can we give outpatient**: Yes

**Regimen specific:**

 -Use ibrutinib first line when indicated.

 -Consider acalabrutinib in patients with preexisting ***atrial fibrillation*** or for those who do not tolerate ibrutinib.

 -**Bleeding risk**: grade 3 or higher (6%); Any bleeding (50%). Do not use if patient on anticoagulation or high bleeding risk

 -**Atrial fibrillation/flutter**: 6-9%, esp with cardiac RFs or with h/o atrial fibrillation.

 -**HTN**

 -**Cytopenias**

 -Check **HBV serologies** prior to initiating BTK inhibitor

 -Avoid using moderate or strong CYP3A4 inhibitors while using ibrutinib or acalabrutinib. Commonly used CYP3A4 inhibitors are:

* Strong inhibitors: Cobicistat, Indinavir, Nelfinavir, Ritonavir, Clarithromycin, Itraconazole, Ketoconazole, Nefazodone, Sequinavir, Suboxone, Telithromycin
* Moderate inhibitors: Amprenavir, Aprepitant, Atazanivir, Erythromycin, Diltiazem, Fluconazole (as well as voriconazole or posaconazole), Verapamil

**BDR**
**Lymphoma Type: LPL/WM**

**Regimen: Cycle Length Variable (see below); (Dimopoulos, Blood, 2013; Gavriatopoulou, Blood, 2017)**

 **C1 (21 days)**

 **-Bortezomib 1.3 mg/m2 on days 1, 4, 8, and 11**

 **C2 (35 days)**

 **-Bortezomib 1.6mg/m2 days 1, 8, 15, 22**

 **-Dexamethasone 20mg IV days 1, 8, 15, 22**

 **-Rituximab 375mg/m2 days 1, 8, 15, 22**

 **C3 (35 days)**

 **-Bortezomib 1.6mg/m2 days 1, 8, 15, 22**

 **C4 (35 days)**

 **-Bortezomib 1.6mg/m2 days 1, 8, 15, 22**

 **C5 (35 days)**

 **-Bortezomib 1.6mg/m2 days 1, 8, 15, 22**

 **-Dexamethasone 20mg IV days 1, 8, 15, 22**

 **-Rituximab 375mg/m2 days 1, 8, 15, 22**

**Antiemetics**:

 Early:
 N/A

           Delayed (standing unless otherwise noted):

           Compazine 10mg q6H PRN

         Refractory:

           Zofran 8 mg q8h PRN

Olanzapine 10mg nightly

**Antimicrobial prophylaxis:** Yes.

 For all patients: Valtrex 500mg PO daily during chemotherapy

 For HBsAg+ or HBsAg-/HBcAb+: Entecavir 0.5mg PO daily x1yr (If viral load is positive – check ALT and consult hepatology. As long as liver function is normal, it is still okay to give rituximab (Kim, EJC, 2013; Kusumoto, ASH, 2014)).

**TLS prophylaxis**: No

**GCSF**: No

**Interim lab checks**: Yes; for first cycle on days 1 and 8, for subsequent cycles on days 1 and 15

**CNS prophylaxis**: No

**Port**: No

**Can we give outpatient?** Yes

**Regimen specific:**

           -Major side effects: IgM flair (this is largely avoided by only giving velcade for first cycle; the flare is most associated with rituximab with elevated IgM component), neuropathies (subcutaneous velcade to decrease risk), and infusion reactions from rituximab

 -Monitor Myeloma Labs (IgM component), and serum FLC to assess treatment response.

**Brentuximab Vedotin**

**Lymphoma Types: Relapsed HL, post-auto HL; DLBCL, ALCL, CTCL, PTCL (CD30+)**

**Regimen: Cycle Length 21 days (ALCL: Pro, JCO, 2012; CTCL: Kim, JCO, 2015; HL: Younes, JCO, 2012)**

 **Brentuximab 1.8 mg/kg IV D1**

**Antiemetics**:

         Early:

         Dexamethasone 8 mg once

Delayed (standing unless otherwise noted):

Compazine 10mgh q6 PRN

Refractory:

           Zofran 8 mg q8h PRN

**Antimicrobial prophylaxis**: None.

**TLS prophylaxis**: Allopurinol 300mg BID x7days: Case-by-case (if heavy tumor burden)

**GCSF**: No

**Interim lab checks**: No

**CNS prophylaxis**: No

**Port**: No

**Regimen Specific**:

 -monitor for neuropathies as major side effect of agent

**Other Comments:**

 -dose reductions for new or worsening grade 2 neuropathies (per package insert)

**BBV (Bendamustine/Brentuximab Vedotin)**

**Lymphoma Types: Relapsed cHL**

**Regimen: Cycle Length q21 days (LaCasce Blood, 2015; Sawas Blood, 2015)**

 **Bendamustine 90mg/m2 IV D1 and D2**

 **Brentuximab vedotin 1.8mg/kg IV D1**

**Antiemetics**:

         Early:

         Dexamethasone 8 mg daily for D1 and D2

 Zofran 24 mg daily for D1 and D2

Delayed (standing unless otherwise noted):

Zofran 8mg q8h scheduled for D3-D5, then PRN

Compazine 10mgh q6 PRN

Refractory:

           Olanzapine 10 mg nightly (discontinue compazine if using)

**Antimicrobial prophylaxis**: None.

**TLS prophylaxis**: Allopurinol 300mg BID x7days: Case-by-case (if heavy tumor burden)

**GCSF**: No (can add if patient has persistent neutropenia)

**Interim lab checks**: No

**CNS prophylaxis**: No

**Port**: No

**Regimen Specific**:

 -potential occurrence of rashes with bendamustine

 -transaminase elevation possible

 -monitor neuropathies

 -Infusion reaction

**Other Comment: NA**

**Pralatrexate**

**Lymphoma Type: Peripheral T-Cell Lymphoma**

**Regimen: Cycle length: 49 days (O'connor OA, et al. J Clin Oncol. 2011;29(9):1182-1189.)**

 **Pralatrexate 30 mg/m2 IV D1, 8, 15, 22, 29, 36**

**Antiemetics**:

Early:

           Dexamethasone 8mg

Zofran 24mg

           Delayed (standing unless otherwise noted):

       Compazine 10mg q6H PRN

           Refractory:

           Dexamethasone 4mg BID

           Fosaprepitant 150mg x1

**Antimicrobial prophylaxis**: None (Mucositis: 5%; Febrile Neutropenia: 5%)

**TLS prophylaxis**: No

**GCSF**: No

**Interim lab checks**: No

**CNS prophylaxis**: No

**Port**: No

**Can we give outpatient**: Yes

**Regimen specific:**

-Pre-treatment Vitamin B12 injection and daily folic acid supplementation should be ordered (part of pre-treatment cycle in treatment plan).

-Baseline Vitamin B12 and Folate labs should be assessed on C1D1. These labs are repeated every other cycle unless they are below the lower limit of normal.