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| Leukemia Program Clinical Practice Guidelines |
| Chemotherapy Regimens |

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**Table of Contents**

1. 7+3+ HD Daunorubicin
2. 7+3+GO
3. 7+3+Midostaurin
4. DAC
5. CPX-351
6. CLAG
7. G-CLAC
8. 7+3+GO Consolidation
9. CLAG Consolidation
10. G-CLAC Consolidation
11. HiDAC Consolidation
12. Azacitidine
13. Azacitidine + Venetoclax
14. Azacitidine + Sorafenib
15. Inotuzumab Ozogamicin
16. ATRA/ATO
17. ARTA/ATO/Idarubicin
18. Modified AALL0232 High dose Methotrexate
19. GRAAPH 2005
20. Dasatinib+Prednisone
21. HyperCVAD (R-HyperCVAD) age <60 +/- Dasatinib
22. HyperCVAD (R-HyperCVAD) age >60 +/- Dasatinib
23. Mini-HyperCVD
24. Blinatumomab
25. CCG 1941
26. CALGB10403

(Not Covered:CAR-T; Decitabine)

**7+3+HD Daunorubicin**

**Leukemia Type: AML, favorable/intermediate risk, age <65 yo, good performance status**

**Regimen: Cycle length D1-7, though recovery takes 3-6 weeks from day 1, longer if reinduction given (**Löwenberg B, et al. High-dose daunorubicin in older patients with acute myeloid leukemia. N Engl J Med. 2009 Sep 24;361(13):1235-48**)**

 **Cytarabine 100 mg/m2 IV Days 1 to 7**

 **Daunorubicin 90 mg/m2 IV Days 1, 2, 3**

*D14 Reinduction* **(Cellularity >20% and Blasts >5 % on BMBx)**

 **Cytarabine 100 mg/m2 IV Days 1 – 5**

 **Daunorubicin 45 mg/m2 IV Days 1 –2**

**Consolidation: HiDAC (estimated length of stay 5-6 days)**

**Antiemetics**:

           Dexamethasone 8mg every 24 hours x3 doses

Zofran 24mg every 24 hours x 7 doses

Compazine 10 mg IV/PO every 6 hours PRN

**Antimicrobial prophylaxis**: Valtrex 500 mg daily; Once ANC <0.5, Levaquin 500 mg daily, posaconazole 300 mg daily

           Posaconazole started after completing anthracycline

**TLS prophylaxis**: Yes

**GCSF**: No

**Interim lab checks**: per inpatient indications

**Response BMBx:** D14; Recovery (typically at steady state blood counts ANC >1.0, platelets >100 and typically as outpatient; if such recovery is not achieved by day 42, bone marrow biopsy should be done at that time)

**CNS prophylaxis**: Yes, if WBC >40,000, Monocytic differentiation, mixed phenotype, extramedullary disease per (NCCN guidelines) at time of diagnosis (should be timed to coincide with no circulating blasts if patient asymptomatic, and at a time when platelet transfusion needs are reasonable—day 21 thru discharge. Intrathecal cytarabine 100 mg with hydrocortisone 50 mg)

**Central access**: Yes. TLC IJ on admission

 Single lumen port or Hickman ordered for outpatient placement prior to discharge based on SCT status

**Can we give outpatient**: No

**Regimen specific:**

           -Pre-treatment ECHO required

-Major side effects: highly emetogenic; myelosuppression/infection/death; heart failure (anthacycline); mucositis

-Fertility counseling for all reproductive age patients

**7+3+GO Cytarabine, Daunorubicin and Gemtuzumab ozogamicin\***

**Leukemia Type: AML, CD33 positive, age 50-70 yo , favorable or intermiate risk cytogenetics**

**Regimen: Cycle length D1-7 (**Castaigne S, et al. Effect of gemtuzumab ozogamicin on survival of adult patients with de-novo acute myeloid leukaemia (ALFA-0701): a randomised, open-label, phase 3 study. Lancet. 2012 Apr 21;379(9825):1508-16**)**

 **Cytarabine 200 mg/m2 IV Days 1 - 7**

 **Daunorubicin 60 mg/m2 IV Days 1 – 3**

 **Gemtuzumab ozogamicin 3 mg/m2 (Max dose 4.5 mg) IV Days 1, 4, 7,**

*D15 Reinduction* **(Cellularity >20% and Blasts >5 % on BMBx)**

**Cytarabine 1 g/m2 IV Q12 x 6 doses**

**Daunorubicin 60 mg/m2 IV Q24 hours x 2 doses**

**Consolidation: 7+3+GO Consolidation**

**Antiemetics**:

           Dexamethasone 8mg every 24 hours, starting S+1, x2 doses

Zofran 24mg every 24 hours x 7 doses

Compazine 10 mg IV/PO every 6 hours PRN

**Antimicrobial prophylaxis**: Valtrex 500 mg daily; Once ANC <0.5, Levaquin 500 mg daily, posaconazole 300 mg daily with loading dose

           Posaconazole started after completing gemtuzumab ozogamicin

**TLS prophylaxis**: Yes

**GCSF**: No

**Interim lab checks**: Daily CBC with differential with daily CMP while on chemotherapy, after chemotherapy, daily CBC with differential, daily BMP, Q72 hour LFTs

**Response BMBx: D15; recovery**

**CNS prophylaxis**: Yes, if WBC >40,000, Monocytic differentiation, mixed phenotype, extramedullary disease per (NCCN guidelines) at time of diagnosis

**Central access**: Yes. TLC IJ on admission

 Single lumen port or Hickman ordered for outpatient placement prior to discharge based on SCT status

**Can we give outpatient**: No

**Regimen specific:**

           - Pre-treatment ECHO required

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

- Fertility counseling for all reproductive age patients

- Caution if pre-existing liver disease (risk of VOD). Dose modifications for elevated AST/ALT/bilirubin of gemtuzumab ozogamicin in prescribing information

**7+3+Midostaurin**

**Leukemia Type: AML**

**Regimen: Cycle length D1-7 (**Stone RM, et al. Midostaurin plus Chemotherapy for Acute Myeloid Leukemia with a FLT3 Mutation. N Engl J Med. 2017 Aug 3;377(5):454-464**)**

 **Cytarabine 200 mg/m2 IV Days 1 - 7**

 **Daunorubicin 60 mg/m2 IV Days 1 – 3**

 **Midostaurin 50 mg PO, D8-21**

*Reinduction D21 (***Cellularity >20% and Blasts >5 % on BMBx)**

 **Cytarabine 200 mg/m2 IV Days 1 - 7**

 **Daunorubicin 60 mg/m2 IV Days 1 – 3**

 **Midostaurin 50 mg PO, D8-21**

**Consolidation: HiDAC +Midostaurin (length of stay 5-6 days)**

**Antiemetics**:

           Dexamethasone 8mg every 24 hours x3 doses

Zofran 24mg every 24 hours x 7 doses

Compazine 10 mg IV/PO every 6 hours PRN

**Antimicrobial prophylaxis**: Valtrex 500 mg daily. Start once ANC <0.5; Levaquin 500 mg daily, Micafungin 50 mcg

**TLS prophylaxis**: Yes

**GCSF**: No

**Interim lab checks**: per inpatient indications

**Response BMBx**: D21; recovery

**CNS prophylaxis**: Yes, if WBC >40,000, Monocytic differentiation, mixed phenotype, extramedullary disease per (NCCN guidelines) at time of diagnosis

**Central access**: Yes. TLC IJ on admission

 Single lumen port or Hickman ordered for outpatient placement prior to discharge based on SCT status

**Can we give outpatient**: No

**Regimen specific:**

           - Pre-treatment ECHO required

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

- Fertility counseling for all reproductive age patients

- May require pre-medication Zofran prior Midostaurin doses (if not tolerated)

- Midostaruin access (include signature waiver) for consolidation should be investigated prior to discharge

- Weekly EKGs for QTc monitoring. Dose modification based on QTcf and as in prescribing information of midostaurin

**DAC**

**Leukemia Type: AML, age <60 yo, poor risk cytogenetics, not typically including myelodysplasia related changes**

**Regimen: Cycle length D1-7 (enter reference)**

 **Cytarabine 200 mg/m2 IV Days 1 - 7**

 **Daunorubicin 60 mg/m2 IV Days 1 – 3**

 **Cladribine 5 mg/m2 IV Days 1 – 5**

**Consolidation: HiDAC Consolidation**

**Antiemetics**:

           Dexamethasone 8mg every 24 hours x5 doses

Zofran 24mg every 24 hours x 7 doses

Compazine 10 mg IV/PO every 6 hours PRN

**Antimicrobial prophylaxis**: Valtrex 500 mg daily; Once ANC <0.5, Levaquin 500 mg daily, posaconazole 300 mg daily with loading dose

           Posaconazole started after completing anthracycline

**TLS prophylaxis**: Yes

**GCSF**: No

**Interim lab checks**: per inpatient indications

**Response BMBx**: Recovery

**CNS prophylaxis**: Yes, if WBC >40,000, Monocytic differentiation, mixed phenotype, extramedullary disease per (NCCN guidelines) at time of diagnosis

**Central access**: Yes. TLC IJ on admission

 Single lumen port or Hickman ordered for outpatient placement prior to discharge based on SCT status

**Can we give outpatient**: No

**Regimen specific:**

           - Pre-treatment ECHO required

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

- Fertility counseling for all reproductive age patients

- Daily neuro exam while receiving Cladribine

**CPX-351 (Vyxeos, liposomal daunorubicin and cytarabine)\***

**Leukemia Type: AML newly diagnosed for therapy-related AML [t-AML] or AML with myelodysplasia-related changes [AML-MRC], per WHO criteria**

**Regimen: Cycle length D1-5** (Lancet JE, et al. J Clin Oncol. CPX-351 (cytarabine and daunorubicin) Liposome for Injection Versus Conventional Cytarabine Plus Daunorubicin in Older Patients With Newly Diagnosed Secondary Acute Myeloid Leukemia. 2018 Sep 10;36(26):2684-2692). Median length of stay 35 days for one cycle (longer than standard induction and beyond this estimate if 2 cycles given)

**Daunorubicin 44 mg/m2 and cytarabine 100 mg/m2 (liposomal) on days 1, 3, and 5**

*D14 Re-Induction* (**Cellularity >20% and Blasts >5 % on BMBx)**

**Daunorubicin 44 mg/m2 and cytarabine 100 mg/m2 (liposomal) on days 1 and 3**; the second induction cycle may be administered 2 to 5 weeks after the first induction cycle (if no unacceptable toxicity with previous cycle).

**Antiemetics**:

           Dexamethasone 8mg days 1,3,5,

Zofran 24mg days 1,3,5,

Compazine 10 mg IV/PO every 6 hours PRN

**Antimicrobial prophylaxis**: Valtrex 500 mg daily; Once ANC <0.5, Levaquin 500 mg daily, posaconazole 300 mg daily with loading dose

           Posaconazole started after completing anthracycline

**TLS prophylaxis**: Yes

**GCSF**: No

**Interim lab checks**: per inpatient indications

**Response BMBx**: D14 (up to day 21); recovery

**CNS prophylaxis**: Yes, if WBC >40,000, Monocytic differentiation, mixed phenotype, extramedullary disease per (NCCN guidelines) at time of diagnosis

**Central access**: Yes. TLC IJ on admission

 Single lumen port or Hickman ordered for outpatient placement prior to discharge based on SCT status

**Can we give outpatient**: No

**Regimen specific:**

           - Pre-treatment ECHO required

- Major side effects: highly emetogenic; prolonged myelosuppression (Median time D35) ; heart failure (anthracycline);

- Less mucoitis and no hair loss compared to 7+3

- Fertility counseling for all reproductive age patients

- Outpatient use most be authorized prior to inpatient initiation (expensive)

- Notify pharmacy of infusional issues or need for retiming (product stable for only 4 hours)

**CLAG Salvage therapy**

**Leukemia Type: Relapsed/Refractory AML (standand salvage regimen)**

**Regimen: Cycle length D1-5 (**Robak T, et al. Combination regimen of cladribine (2-chlorodeoxyadenosine), cytarabine and G-CSF (CLAG) as induction therapy for patients with relapsed or refractory acute myeloid leukemia. Leuk Lymphoma. 2000 Sep;39(1-2):121-9.**)**

 **Tbo-filgrastim (Granix) 300 mcg SQ every 24 hours x5 doses (if WBC <20K give D0 Granix for a total of 6 doses)**

 **Cladribine 5 mg/m2 IV Days 1 – 5**

 **Cytarabine 2g/m2 IV Days 1 – 5**

**Consolidation: CLAG consolidation**

**Antiemetics**:

           Dexamethasone 8mg every 24 hours, starting Days 1 - 5 doses

Zofran 24mg every 24 hours, starting D1- 5 doses

Compazine 10 mg IV/PO every 6 hours PRN

**Supportive Care:** Prednisolone acetate 1% eye drops, 2 drops, both eyes, every 6 hours starting Days 1- 12

**Antimicrobial prophylaxis**: Valtrex 500 mg daily; Once ANC <0.5, Levaquin 500 mg daily, posaconazole 300 mg daily with loading dose

           Posaconazole started after completing anthracycline

**TLS prophylaxis**: Yes, cycle 1 only

**GCSF**: within regimen

**Interim lab checks**: per inpatient indications during induction

**Response BMBx**: Recovery

**CNS prophylaxis**: Yes, if WBC >40,000, Monocytic differentiation, mixed phenotype, extramedullary disease per (NCCN guidelines) at time of diagnosis

**Central access**: Yes. TLC IJ on admission

 Single lumen port or Hickman ordered for outpatient placement prior to discharge based on SCT status

**Can we give outpatient**: No

**Regimen specific:**

- Major side effects: highly emetogenic; myelosuppression;

- Fertility counseling for all reproductive age patients

- Consult pharmacy if CrCl less than 60

**G-CLAC Salvage therapy or Initial induction for secondary leukemia or patients with exclusions for anthracyclines**

**Leukemia Type: AML, non- anthracylcine induction, salvage**

**Regimen: Cycle length D1-5**

**Relapsed/Refractory (**Becker PS, et al. Clofarabine with high dose cytarabine and granulocyte colony-stimulating factor (G-CSF) priming for relapsed and refractory acute myeloid leukaemia. Br J Haematol. 2011 Oct;155(2):182-9**)**

**Tbo-filgrastim (Granix) 5mcg/kg SQ, begin day 0 until ANC is 2 for at least 2 consecutive days**

 **Clofarabine 25 mg/m2 IV Days 1 – 5**

 **Cytarabine 2 g/m2 IV Days 1 – 5**

**Newly diagnosed: (**Becker PS, et al. G-CSF priming, clofarabine, and high dose cytarabine (GCLAC) for upfront treatment of acute myeloid leukemia, advanced myelodysplastic syndrome or advanced myeloproliferative neoplasm. Am J Hematol. 2015 Apr;90(4):295-300. doi: 10.1002/ajh.23927. Epub 2015 Jan 30)

 **Tbo-filgrastim (Granix) 5mcg/kg SQ, begin day 0 until ANC is 2 for at least 2 consecutive days**

 **Clofarabine 30 mg/m2 IV Days 1 – 5**

 **Cytarabine 2 g/m2 IV Days 1 – 5**

**D21 Reinduction:**

 **Relapsed/Refractory:**

**Tbo-filgrastim (Granix) 5mcg/kg SQ, begin day 0 until ANC is 2 for at least 2 consecutive days**

 **Clofarabine 25 mg/m2 IV Days 1 – 5**

 **Cytarabine 2 g/m2 IV Days 1 – 5**

 **New Diagnosed:**

**Tbo-filgrastim (Granix) 5mcg/kg SQ, D1 - 4**

 **Clofarabine 25 mg/m2 IV Days 1 – 4**

 **Cytarabine 2 g/m2 IV Days 1 – 4**

**Consolidation: G-CLAC Consolidation**

**Antiemetics**:

           Dexamethasone 8mg every 24 hours x5 doses

Zofran 24mg every 24 hours x 5 doses

Compazine 10 mg IV/PO every 6 hours PRN

**Supportive Care:** Prednisolone acetate 1% eye drops, 2 drops, both eyes, every 6 hours Days 1-12

**Antimicrobial prophylaxis**: Valtrex 500 mg daily; Once ANC <0.5, Levaquin 500 mg daily, posaconazole 300 mg daily with loading dose

           Posaconazole started after completing anthracycline

**TLS prophylaxis**: Yes

**GCSF**: within regimen

**Interim lab checks**: per inpatient indications

**Response BMBx**: D21; recovery

**CNS prophylaxis**: Yes, if WBC >40,000, Monocytic differentiation, mixed phenotype, extramedullary disease per (NCCN guidelines) at time of diagnosis

**Central access**: Yes. TLC IJ on admission

 Single lumen port or Hickman ordered for outpatient placement prior to discharge based on SCT status

**Can we give outpatient**: No

**Regimen specific:**

- Major side effects: highly emetogenic; myelosuppression; skin rash;

- Fertility counseling for all reproductive age patients

- Consult pharmacy if CrCl less than 60

**7+3+GO Consolidation**

**Leukemia Type: AML, consolidation following 7+3+GO**

**induction**

**Regimen: Cycle length 28 days or dependent on hematologic recovery (**Castaigne S, et al. Effect of gemtuzumab ozogamicin on survival of adult patients with de-novo acute myeloid leukaemia (ALFA-0701): a randomised, open-label, phase 3 study. Lancet. 2012 Apr 21;379(9825):1508-16**)**

 **Cycle 1:**

 **Outpatient D1: Daunorubicin 60 mg/m2 x1 dose, Gemtuzumab 3 mg/m2 x 1 dose, Cytarabine 1 g/m2 x1 dose**

 **Inpatient D2 thru 5: Cytarabine 1 g/m2 every 12 hours for 7 doses**

 **Cycle 2:**

 **Outpatient D1: Daunorubicin 60 mg/m2 x1 dose, Gemtuzumab 3 mg/m2 x 1 dose, Cytarabine 1 g/m2 x1 dose**

 **Inpatient D2 thru 5: Daunorubicin 60 mg/m2 x1 dose, Cytarabine 1 g/m2 every 12 hours x 7 doses**

**Antiemetics**:

           Dexamethasone 8mg every 48 hours x3 doses

Zofran 24mg every 48 hours x 3 doses

Compazine 10 mg IV/PO every 6 hours PRN

**Supportive Care:** Prednisolone acetate 1% eye drops, 2 drops, both eyes, every 6 hours Day 1- 12

**Antimicrobial prophylaxis**: Valtrex 500 mg daily;

On Discharge: Levaquin 500 mg daily, Fluconazole 400 mg daily (unless on treatment antifungal)

**TLS prophylaxis**: No

**GCSF**: Yes, Udenyca (or equivalent) 24-72 hours after completion of chemotherapy

**Interim lab checks**: Yes, 3x weekly labs (CBC with Diff and CMP) with transfusion support

**Response BMBx**: Recovery

**CNS prophylaxis**: No

**Central access**: Yes. Port (single lumen) or Hickman – should be placed prior to admission

**Can we give outpatient**: Hybrid inpatient-outpatient (see above)

**Regimen specific:**

- Major side effects: highly emetogenic; myelosuppression; skin rash; neurotoxicity

- Consult pharmacy if CrCl less than 60

-Gemtuzumb ozogamicin during consolidation omitted if platelets <100,000 by day 45 of induction therapy

**CLAG Consolidation**

**Leukemia Type: AML, consolidation following CLAG induction**

**Regimen: Cycle length 28 days or dependent on rate of hematologic recovery (**Robak T, et al. Combination regimen of cladribine (2-chlorodeoxyadenosine), cytarabine and G-CSF (CLAG) as induction therapy for patients with relapsed or refractory acute myeloid leukemia. Leuk Lymphoma. 2000 Sep;39(1-2):121-9.**)**

 **Tbo-filgrastim (Granix) 300 mcg SQ every 24 hours x5 doses (if WBC <20K give D0 Granix for a total of 6 doses)**

 **Cladribine 5 mg/m2 IV Days 1 – 5**

 **Cytarabine 2g/m2 IV Days 1 – 5**

**Antiemetics**:

           Dexamethasone 8mg every 48 hours x3 doses

Zofran 24mg every 48 hours x 3 doses

Compazine 10 mg IV/PO every 6 hours PRN

**Supportive Care:** Prednisolone acetate 1% eye drops, 2 drops, both eyes, every 6 hours Day 1- 12

**Antimicrobial prophylaxis**: Valtrex 500 mg daily;

On Discharge: Levaquin 500 mg daily, Fluconazole 400 mg daily (unless on treatment antifungal)

**TLS prophylaxis**: No

**GCSF**: Yes, Udenyca (or equivalent) 24-72 hours after completion of chemotherapy

**Interim lab checks**: Yes, 3x weekly labs (CBC with Diff and CMP) with transfusion support

**Response BMBx**: Recovery

**CNS prophylaxis**: No

**Central access**: Yes. Port (single lumen) – should be placed prior to admission

**Can we give outpatient**: Yes

**Regimen specific:**

- Major side effects: highly emetogenic; myelosuppression; skin rash; neurotoxicity

- Consult pharmacy if CrCl less than 60

**G-CLAC Consolidation**

**Leukemia Type: AML, consolidation – following G-CLAG induction**

**Regimen: Cycle length 28 days**

**Tbo-filgrastim (Granix) 5mcg/kg SQ, begin day 0 until ANC is 2 for at least 2 consecutive days**

 **Clofarabine 20 mg/m2 IV Days 1 – 5**

 **Cytarabine 1 g/m2 IV Days 1 – 5**

**Antiemetics**:

           Dexamethasone 8mg every 48 hours x3 doses

Zofran 24mg every 48 hours x 3 doses

Compazine 10 mg IV/PO every 6 hours PRN

**Supportive Care:** Prednisolone acetate 1% eye drops, 2 drops, both eyes, every 6 hours Day 1- 12

**Antimicrobial prophylaxis**: Valtrex 500 mg daily;

On Discharge: Levaquin 500 mg daily, Fluconazole 400 mg daily (unless on treatment antifungal)

**TLS prophylaxis**: No

**GCSF**: Yes, Udenyca (or equivalent) 24-72 hours after completion of chemotherapy

**Interim lab checks**: Yes, 3x weekly labs (CBC with Diff and CMP) with transfusion support

**Response BMBx**: Recovery

**CNS prophylaxis**: No

**Central access**: Yes. Port (single lumen) – should be placed prior to admission

**Can we give outpatient**: Yes

**Regimen specific:**

- Major side effects: highly emetogenic; myelosuppression; skin rash; neurotoxicity

- Consult pharmacy if CrCl less than 60
**HiDAC Consolidation**

**Leukemia Type: AML, consolidation**

**Regimen: Cycle length 28 days or according to hematologic recovery, may be given up to 4 cycles (**Mayer RJ, et al. Intensive postremission chemotherapy in adults with acute myeloid leukemia. Cancer and Leukemia Group B. N Engl J Med. 1994 Oct 6;331(14):896-903**)**

 **Age <60: Cytarabine 3 g/m2 IV every 12 hours Days 1, 3, 5**

**Age >60: Cytarabine 1.5 g/m2 IV every 12 hours Days 1, 3, 5**

**Antiemetics**:

           Dexamethasone 8mg every 48 hours x3 doses

Zofran 24mg every 48 hours x 3 doses

Compazine 10 mg IV/PO every 6 hours PRN

**Supportive Care:** Prednisolone acetate 1% eye drops, 2 drops, both eyes, every 6 hours Day 1- 12

**Antimicrobial prophylaxis**: Valtrex 500 mg daily;

On Discharge: Levaquin 500 mg daily, Fluconazole 400 mg daily (unless on treatment antifungal)

**TLS prophylaxis**: No

**GCSF**: Yes, Udenyca (or equivalent) 24-72 hours after completion of chemotherapy

**Interim lab checks**: Yes, 3x weekly labs (CBC with Diff and CMP) with transfusion support

**Response BMBx**: None

**CNS prophylaxis**: No

**Central access**: Yes. Port (single lumen) – should be placed prior to admission

**Can we give outpatient**: No

**Regimen specific:**

- Major side effects: highly emetogenic; myelosuppression; skin rash; neurotoxicity (cerebellar), chemical conjunctivitis

- Consult pharmacy if CrCl less than 60

**Azacitadine**

**Leukemia Type: MDS, AML**

**Regimen: Cycle length 28 days (**Fenaux P, et al. Azacitidine Prolongs Overall Survival Compared With Conventional Care Regimens in Elderly Patients With Low Bone Marrow Blast Count Acute Myeloid Leukemia. J Clin Oncol 2009;28:562-569**)**

 **Azacitadine 75 mg/m2 SQ (or IV) daily Day 1-7**

**Antiemetics**:

Zofran 16 mg q24h D1-7

Compazine 10 mg PO every 6 hours PRN

**Supportive Care:** None

**Antimicrobial prophylaxis**: Yes, when neutropenic

Valtrex 500 mg daily, Levaquin 500 mg daily, Fluconazole 400 mg daily

           Posaconazole if antifungal treatment indicated

**TLS prophylaxis**: No

**GCSF**: No

**Interim lab checks**: Yes, 3x weekly labs (CBC with Diff and CMP) with transfusion support (based on transfusion needs)

**Response BMBx: may be discussed with continuity leukemia clinic team**

**CNS prophylaxis**: No

**Central access**: No. Usually will use PIV for transfusion. Azacitidine usually SQ but can be given through PIV.

**Can we give outpatient**: Yes

**Regimen specific:**

-Major side effects: myelosuppression, injection site reaction

**Azacitadine and Venetoclax\***
**Leukemia Type: Newly diagnosed AML not fit for induction, Refractory AML**

**Regimen: Cycle length Q28 days (**DiNardo CD, et al. Venetoclax combined with decitabine or azacitidine in treatment-naive, elderly patients with acute myeloid leukemia. Blood. 2018 Oct 25. pii: blood-2018-08-868752**)**

 **Azacitidine 75 mg/m2 SQ (or IV) on days 1-7**

Venetoclax Ramp up – NOT on CYP3A4 inhibitor

 **Venetoclax 100 mg, PO, once daily Week 1; Day 1**

 **Venetoclax 200 mg, PO, once daily Week 1; Days 2**

 **Venetoclax 400 mg, PO, once daily Week 1; Days 3 and beyond**

Venetoclax Ramp up – Already on strong CYP3A4 inhibitor (voriconazole/posaconazole/ritonavir) that may not be discontinued for medical reasons. Avoid when possible. (CLL “starter pack” needed when doses under 100 mg used)

 **Venetoclax 10 mg, PO, once daily Week 1; Day 1**

 **Venetoclax 20 mg, PO, once daily Week 1; Day 2**

 **Venetoclax 50 mg, PO, once daily Week 1; Day 3**

 **Venetoclax 70 mg, PO, once daily Week 1; Day 4**

 **Venetoclax 100 mg, PO, once daily Week 1; Day 5 and beyond**

Venetoclax Ramp up – Already on Moderate CYP3A4 inhibitor that cannot be discontinued for medical reasons (isavuconazole/fluconazole/diltiazem). Avoid when possible.

 **Venetoclax 100 mg, PO, once daily Week 1; Day 1-2**

 **Venetoclax 200 mg, PO, once daily Week 1; Days 3 and beyond**

**Antiemetics**:
 Zofran 16mg daily Days 1-7

**Antimicrobial prophylaxis**: Yes, when neutropenic

 Levaquin 500 mg PO daily

 Valtrex 500 mg PO daily

 Posaconazole 300 mg PO daily (no loading dose) starting Day 8. Reduce venetoclax to 100 mg daily starting Day 8.

**TLS prophylaxis**: Yes, Allopurinol 300mg daily, starting 3 days prior to venetoclax until remission status is known

**GCSF**: No

**Interim lab checks**: Yes, CBC (w/ diff) 3 times weekly with transfusion support; CMP weekly

**Response BMBx: Prior to cycle 2 (around D28)**

**CNS prophylaxis**: same as for intensive induction (use language as in induction)

**Central line** No. Usually will use PIV for transfusion. Azacitidine usually SQ but can be given through PIV.

**Can we give outpatient**: Yes

**Regimen specific:**

-Major side effects: monitor for TLS (cycle 1), myelosuppression, injection site reaction

**Other Comments:** Educate patient to drink plenty of water

**Azacitidine and Sorafenib\***
**Leukemia Type: AML w/FLT3-ITD mutation**

**Regimen: Cycle length Q28 days (**Ravandi F, et al. Phase 2 study of azacytidine plus sorafenib in patients with acute myeloid leukemia and FLT-3 internal tandem duplication mutation. Blood. 2013 Jun 6;121(23):4655-62)

 **AzaCITIDine 75 mg/m2 SQ/IV on days 1 to 7**

**SORAfenib 400 mg PO twice a day**

**Antiemetics**:

           Zofran 16 mg PO every daily x 7 doses

 Compazine 10 mg every 6 hours PRN

**Supportive Care:** n/a

**Antimicrobial prophylaxis**: Yes, when neutropenic

 Levaquin 500 mg PO daily

 Valtrex 500 mg PO daily

 Posaconazole 300 mg PO daily

**TLS prophylaxis**: Yes, allopurinol 300 mg daily, starting 3 days prior to treatment

**GCSF**: No

**Interim lab checks**: Yes, CBC (w/ diff) 3 times weekly with transfusion support, CMP weekly

**Response BMBx**: Prior to C2 (round D28)

**CNS prophylaxis**: No

**Central access**: No. Usually will use PIV for transfusion. Azacitidine usually SQ but can be given through PIV.

**Can we give outpatient**: Yes

**Regimen specific:**

* Monitor QTc
* hand foot syndrome
* Monitor for hypertension and VTE

**Inotuzumab Ozogamicin\***
**Leukemia Type: Relapse/refractory AML**

**Regimen: Cycle length C1:21 days, C2 and beyond: 28 days (**As per BESPONSA (inotuzumab ozogamicin) package insert)

 **inotuzumab ozogamicin 0.8 mg/m2 IV on day 1, then 0.5 mg/m2 IV on days 8, 15 on cycle 1**. Dosing regimen for subsequent cycles depending on response to treatment.

Patients who have achieved a CR or CRi:

**inotuzumab ozogamicin 0.5 mg/m2 IV on days 1, 8, 15, every 28 days**

Patients who have NOT achieved a CR or CRi:

 **inotuzumab ozogamicin 0.8 mg/m2 IV on day 1, then 0.5 mg/m2 IV on days 8, 15 every 28 days**

**Antiemetics**:

 Compazine 10 mg every 6 hours PRN

**Supportive Care:**

 Prior to each dose: Methylprednisolone 125 mg, Acetaminophen 650 mg, Diphenhydramine 50 mg

Ursodiol 300 mg PO TID

**Antimicrobial prophylaxis**: Yes, when neutropenic

 Levaquin 500 mg PO daily

 Valtrex 500 mg PO daily

 Fluconazole 400 mg PO daily

**TLS prophylaxis**: Yes, allopurinol 300 mg daily

**GCSF**: No

**Interim lab checks**: Yes, CBC (w/ diff) 3 times weekly with transfusion support; CMP weekly

**Response BMBx**: Cycle 1, D21

**CNS prophylaxis**: No

**Central access**: No

**Can we give outpatient**: Yes

**Regimen specific:**

**-**liver toxicity (sinusoidal obstruction syndrome)

- QT prolongation

- myelosuppression

**ATRA/ATO**

**Leukemia Type: APL - induction for low- and intermediate-risk APL (WBC <10K)**

**Regimen: Cycle length 60 days (**Lo-Coco, F et al. Retinoic acid and arsenic trioxide for acute promyelocytic leukemia. N Engl J Med. 2013 Jul 11;369(2):111-21.**)**

**Induction:**

**Tretinoin (ATRA) 22.5 mg/m2 PO BID; days 1 to 60 or CR**

**Arsenic trioxide (ATO) 0.15 mg/kg IV once daily; days 1 to 60 or CR**

**Prednisone 0.5 mg/kg PO once daily starting day 1. Begin tapering between D14-D21 depending on clinical status/differentiation syndrome**

**Consolidation:**

ATO 5 days/week, 4 weeks on 4 weeks off, for a total of 4 courses

ATRA 2 weeks on and 2 weeks off for a total of 7 courses

**Antiemetics**:

           Ativan 1 mg PO every 4 hours PRN

**Supportive Care:**

Cardiac electorlyte repletion: Mg >2 and K>4

monitor for differentiation syndrome: Weight, fever, O2 requirement

Transfusion parameters: If fibrinogen < 150 give 2 units cryoprecipitate; PLT goal 30 thru D10, then goal 20

During treatment, if WBC 10-50: hydrea 500 mg QID; >50: 1 g QID

EKG twice weekly (e.g. Mondays/Thursdays)

**Antimicrobial prophylaxis**: Yes, Valtrex 500 mg daily; Once ANC <0.5, Levaquin 500 mg daily (or cefdinir 300 mg BID if QT prolonged), micafungin 50 mcg daily

**TLS prophylaxis**: Yes, allopurinol 300 mg daily

**GCSF**: No

**Interim lab checks**:

Induction: per inpatient indications; Triglycerides weekly

Consolidation: CBC (w/diff), CMP and triglycerides once week

**Response BMBx**: Induction: D28-35

 Consolidation

**CNS prophylaxis**: No

**Central access**: Yes, PICC DL but can be started without a central line

**Can we give outpatient**: Induction- Inpatient; Consolidation – outpatient

**Regimen specific:**

-Major side effects: DIC, Differentiation syndrome, QTc prolongation, pseudotumor cerebri, rash, hepatotoxicity. May require holding for LFTs >5x ULN

- ATRA is teratogeneic

**ATRA/ATO/Idarubicin**
**Leukemia Type: APL - induction for high risk APL (WBC >10K)**

**Regimen: Cycle length 36 days . Reference\*\*\***

**Induction:**

 **Idarubicin – Age adjusted**

12 mg/m2/d IV (ages 1-60) Days 2, 4, 6, and 8

9 mg/m2/d IV (ages 61-70)

6 mg/m2/d IV (ages \_ 70)

**Tretinoin (ATRA) 22.5 mg/m2 PO BID; days 1 to 36**

**Arsenic trioxide (ATO) 0.15 mg/kg IV once daily; days 9 to 36**

**Prednisone 1 mg/kg PO once daily; days 1 to 10 or until WBC falls below 10K or until resolution of differentiation syndrome (whichever comes first).**

**Consolidation:**

 **Consolidation cycle 1 (3-4 wks after the end of induction)**

ATRA 45 mg/m2/d PO Days 1-28

ATO 0.15 mg/kg/d IV Days 1-28

**Consolidation cycle 2 (3-4 wks after the end of consolidation cycle 1)**

ATRA 45 mg/m2/d PO Days 1-7, 15-21, 29-35

ATO 0.15 mg/kg/d IV Days 1-5, 8-12, 15-19, 22-26, 29-33

**Maintenance: 8 cycles (3-4 wks after the end of consolidation cycle 2)**

ATRA 45 mg/m2/d PO Days 1-14

MTX 5-15 mg/m2/wk PO Days 15-90

6MP 50-90 mg/m2/d PO Days 15-90

**Antiemetics**:

           Ondansetron 24 mg daily D2, 4, 6, 8

Ativan 1 mg PO every 4 hors PRN

**Supportive Care:**

Cardiac electorlyte repletion: Mg >2 and K>4

monitor for differentiation syndrome: Weight, fever, O2 requirement

Transfusion parameters: If fibrinogen < 150 give 2 units cryoprecipitate; PLT goal 30 thru D10, then goal 20

During treatment, if WBC 10-50: hydrea 500 mg QID; >50: 1 g QID

EKG twice weekly (e.g. Mondays/Thursdays)

**Antimicrobial prophylaxis**: Yes, Valtrex 500 mg daily; Once ANC <0.5, Levaquin 500 mg daily (or cefdinir 300 mg BID if QT prolonged), micafungin 50 mcg daily

**TLS prophylaxis**: Yes

**GCSF**: No

**Interim lab checks**: Induction: per inpatient indications; Triglycerides weekly; Consolidation: CBC (w/diff), CMP and triglycerides once week

**Response BMBx**: count recovery or D45

**CNS prophylaxis**: Yes , IT cytarabine 100 mg

**Central access**: Yes, DL PICC

**Can we give outpatient**: Induction- Inpatient; Consolidation – outpatient

**Regimen specific:**

**- Pre treatment ECHO required**

-Major side effects: DIC, Differentiation syndrome, QTc prolongation, pseudotumor cerebri, rash, Alopecia, mucositis, myelosuppression, body fluid discolor and hepatotoxicity. May require holding for LFTs >5x ULN

- ATRA is teratogenic,

**Modified AALL0232 High dose Methotrexate**

**Leukemia Type: ALL**

**Regimen: Cycle length Q14 days (**)

 **Mercaptopurine 25 mg/m2 PO nightly D1-56**

 **Vincristine 1.5 mg/m2 (max 2 mg ) IV once D1, 15, 29, 43**

 **Methotrexate 5 g/m2 IV D1, 15, 29, 43**

**Antiemetics**:

           Zofran 24 mg PO once on D1, 15, 29, 43

 Dexamethasone 8 mg PO once on D1, 15, 29, 43

**Supportive Care:**

Sodium Bicarbonate 150 mEq in 1 L D5W or SWFI at 250 ml/hr (may reduce for volume overload)

Leucovorin 15 mg/m2 PO every 6 hours beginning at hour 42, then every 6 hours until MTX less than 0.05 uM

**Antimicrobial prophylaxis**: Valtrex, bactrim (stop 2 days prior to MTX); LVQ & fluc if ANC <0.5 & LFTs ok

\*\*No bactrim or PPIs while clearing MTX

**TLS prophylaxis**: No

**GCSF**: No

**Interim lab checks**: Yes, inpatient specific.

 MTX level a 24, 36 (if elevated at hour 24), 42, 48 hours, then daily thereafter until MTX less than 0.05 uM

**Response BMBx**: No

**CNS prophylaxis**: Yes, IT MTX D1 and D29

**Central access**: Yes, ideally at least 2 lumens

**Can we give outpatient**: No

**Regimen specific:**

* Urine pH >7 prior to start of MTX
* HOLD chemo if ANC <0.8 and platelets <75,000
* HOLD Bactrim, PPI, NSAIDs, folic acid and aminoglycosides with MTX
* Consider CXR prior to MTX infusion to assess for pleural effusion

**GRAAPH 2005**

**Leukemia Type: newly diagnosed Ph (+) ALL, fit for induction**

**Regimen: Cycle length 28 days for 1 cycle (**)

 **Vincristine 2 mg Days 1, 8, 15 and 22**

**Dexamethasone 40 mg Days 1-2, 8-9, 15-16, and 22-23**

**Dasatinib 140 mg po daily Days 1-28**

**Cycles 2-8 refer to hyperCVAD**

**Antiemetics**: None

**Supportive Care:**  None

**Antimicrobial prophylaxis**: Levo,flu 200 when neutrop , Valtrex, PCP on discharge (Bactrim pref – HOLD prior to cycle 2 HyperCVAD)

AVOID posaconazole/Voriconazole (strong CYP3A4 inhi)

**TLS prophylaxis**: Yes, allopurinol

**GCSF**: No

**Interim lab checks**: Induction: per inpatient indications; Consolidation: N/A

**Response BMBx**: D28, no sooner (inpatient or outpatient)

**CNS prophylaxis**: Yes Triple IT on D2, 9 and 16 (adjust timing for logi conv)

**Central access**: Yes, TLC IJ while inpatinet. Hickman vs Double port (based on SCT status)

**Can we give outpatient**: Initiated inpatient but can be continued outpatient pending count recovery and clinical status

**Regimen specific:**

Monitor for Constipation and neuropathy while on Vincristine

Dasatinib – pleural effusion. NO PPI or H2RA (e.g PEPcid) (reduces dasatinib absorption). Antacids (e.g. Tums) Ok if separated by 2 hours from dasatinib.

**Dasatinib + Prednisone**

**Leukemia Type: Ph (+) ALL, frail**

**Regimen: Cycle length (**Ottmann O, et al. Dasatinib induces rapid hematologic and cytogenetic responses in adult patients with Philadelphia chromosome positive acute lymphoblastic leukemia with resistance or intolerance to imatinib: interim results of a phase 2 study. Blood. 2007 Oct 1;110(7):2309-15)

 Dasatinib 140 mg PO daily x 84 doses

 Prednisone 60 mg/m2 (Max 120 mg) PO daily x 24 doses then taperd over 7-9 days

**Antiemetics**: None

**Supportive Care:**  None

**Antimicrobial prophylaxis**: Yes, Levo,flu 200 when neutrop , Valtrex, PCP on discharge (Bactrim pefer)

**TLS prophylaxis**: Yes, allopurinol

**GCSF**: No

**Interim lab checks**: weekly CMP while on Dasatinib, 3x weekly with transfusions (adjust based on transf needs)

**Response BMBx**: Remission assessment on count recovery

**CNS prophylaxis**: IT MTX D22 and D43 (adjust for logist)

**Central access**: No

**Can we give outpatient**: Yes, based on transfusion needs

**Regimen specific**

Dasatinib – pleural effusion

NO PPI or H2RA (e.g PEPcid) (reduces dasatinib absorption). Antacids (e.g. Tums) Ok if separated by 2 hours from dasatinib.

**HyperCVAD +/- Rituximab +/- Dasatinib Age <60**

**Leukemia Type: ALL, age <60 yo**

**Regimen: Cycle length Q21 days (**If patient is Philadelphia chromosome positive (Ph +) Benjamini O, et al. Phase II trial of hyper CVAD and dasatinib in patients with relapsed Philadelphia chromosome positive acute lymphoblastic leukemia or blast phase chronic myeloid leukemia. Am J Hematol. 2014 Mar;89(3):282-7.

If patient is Philadelphia chromosome negative (Ph -) Thomas DA, et al. Chemoimmunotherapy with hyper-CVAD plus rituximab for the treatment of adult Burkitt and Burkitt-type lymphoma or acute lymphoblastic leukemia. Cancer. 2006 Apr 1;106(7):1569-80.)

**Odd**

 **Dexamethasone 40 mg PO daily Days 1-4**

 **Dexamethasone 40 mg PO daily Days 11-14**

 **Cyclophosphamide 300 mg/m2 IV every 12 hours Days 1-3**

 **Vincristine 2 mg IV once D4, D11**

 **Doxorubicin 50 mg/m2 IV once on D4**

**Even**

 **Methotrexate 1g mg/m2 IV over 24 hours D1 (200 mg/m2 over 2 hours then 800 mg/m2 over 22 hours)**

 **Cytarabine 3 g/m2 IV every 12 hours D2-3**

**If +CD20: Rituxiumab 375 mg/m2 once per cycle (may be given outpatient on same day as G-CSF)**

Check Hep B serologies (Hepatitis/HIV screening panel (non-acute);

If Hep B Core positive OR If Hep B surface antigen positive, consider Entecavir 0.5 mg PO daily – discuss with attending

**If Ph+ Disease**: Refer to GRAAPH 2005 for cycle 1

 Cycle 2-8: Dasatinib 70 mg PO daily continuous

**Antiemetics**:

Odd:

Zofran 24 mg PO daily x 4 doses

Zyprexa 10 mg PO daily x 4 doses

           Even:

Zofran 24 mg PO daily x 3 doses

           Solu-Medrol 50 mg IV every 12 hours D3 x 4 doses

**Supportive Care:**

Odd cycle : Mesna 600 mg/m2 IV continuous Days 1-3

Even cycle : Leucovorin 50 mg IV once D3 – 12 hours after end of MTX infusion

 Leucovorin 25 mg PO every 6 hours, starting 6 hours after IV dose until MTX level less than 0.05 uM

 Prednisonlone acetate 1% ophthalmic suspension 2 drops, both eyes, every 6 hours starting D2 until 7 days after last dose of cytarabine

Daily UA while on Cyclophos (monitor gross hematuria)

**Antimicrobial prophylaxis**: Levo,flu 200 when neutrop , Valtrex, PCP on discharge (Bactrim pref – HOLD prior to MTX cycles)

AVOID posaconazole/Voriconazole (strong CYP3A4 inhi)

**TLS prophylaxis**: Yes, induction cycle only

**GCSF**: Yes, Tbo-Filgra during induction cycle then pegfilg thereafter

**Interim lab checks**: Twice weekly labs (CBC with diff, CMP)

**Response BMBx**: Yes, induction cycle following count recovery

**CNS prophylaxis**: Yes, 2 IT chemos per cycle (alternating MTX and Cytarabine)

**Central access**: Yes, TLC IJ during first cycle, Hickman vs Double lumen Port based on SCT status

**Can we give outpatient**: No

**Regimen specific:**

Pre treatment ECHO required

Monitor for constipation and neuropathy with Vincristine

Monitor for Constipation and neuropathy while on Vincristine

Dasatinib – pleural effusion. NO PPI or H2RA (e.g PEPcid) (reduces dasatinib absorption). Antacids (e.g. Tums) Ok if separated by 2 hours from dasatinib.

Hold PPIs 48 hours prior to high dose IV methotrexate

Mucositis

**HyperCVAD +/- Dasatinib Age >60**

**Leukemia Type: ALL, age >60 yo**

**Regimen: Cycle length Q21 days (**If patient is Philadelphia chromosome positive (Ph +)
1. Benjamini O, et al. Phase II trial of hyper CVAD and dasatinib in patients with relapsed Philadelphia chromosome positive acute lymphoblastic leukemia or blast phase chronic myeloid leukemia. Am J Hematol. 2014 Mar;89(3):282-7.

If patient is Philadelphia chromosome negative (Ph -)
1. Thomas DA, et al. Chemoimmunotherapy with hyper-CVAD plus rituximab for the treatment of adult Burkitt and Burkitt-type lymphoma or acute lymphoblastic leukemia. Cancer. 2006 Apr 1;106(7):1569-80.)

**Odd**

 **Dexamethasone 40 mg PO daily Days 1-4**

 **Dexamethasone 40 mg PO daily Days 11-14**

 **Cyclophosphamide 300 mg/m2 IV every 12 hours Days 1-3**

 **Vincristine 2 mg IV once D4, D11**

 **Doxorubicin 50 mg/m2 IV once on D4**

**Even**

 **Methotrexate 1g mg/m2 IV over 24 hours D1 (200 mg/m2 over 2 hours then 800 mg/m2 over 22 hours)**

 **Cytarabine 1 g/m2 IV every 12 hours D2-3**

**If +CD20: Rituxiumab 375 mg/m2 once per cycle (may be given outpatient on same day as G-CSF)**

Check Hep B serologies (Hepatitis/HIV screening panel (non-acute);

If Hep B Core positive OR If Hep B surface antigen positive, consider Entecavir 0.5 mg PO daily – discuss with attending

**If Ph+ Disease**: Refer to GRAAPH 2005 for cycle 1

 Cycle 2-8: Dasatinib 70 mg PO daily continuous

**Antiemetics**:

Odd:

Zofran 24 mg PO daily x 4 doses

Zyprexa 10 mg PO daily x 4 doses

           Even:

Zofran 24 mg PO daily x 3 doses

           Solu-Medrol 50 mg IV every 12 hours D3 x 4 doses

**Supportive Care:**

Odd cycle : Mesna 600 mg/m2 IV continuous Days 1-3

Even cycle : Leucovorin 50 mg IV once D3 – 12 hours after end of MTX infusion

 Leucovorin 25 mg PO every 6 hours, starting 6 hours after IV dose until MTX level less than 0.05 uM

 Prednisonlone acetate 1% ophthalmic suspension 2 drops, both eyes, every 6 hours starting D2 until 7 days after last dose of cytarabine

Daily UA while on Cyclophos (monitor gross hematuria)

**Antimicrobial prophylaxis**: Levo,flu 200 when neutrop , Valtrex, PCP on discharge (Bactrim pref – HOLD prior to MTX cycles)

AVOID posaconazole/Voriconazole (strong CYP3A4 inhi)

**TLS prophylaxis**: Yes, induction cycle only

**GCSF**: Yes, Tbo-Filgra during induction cycle then pegfilg thereafter

**Interim lab checks**: Twice weekly labs (CBC with diff, CMP)

**Response BMBx**: Yes, induction cycle following count recovery

**CNS prophylaxis**: Yes, 2 IT chemos per cycle (alternating MTX and Cytarabine)

**Central access**: Yes, TLC IJ during first cycle, Hickman vs Double lumen Port based on SCT status

**Can we give outpatient**: No

**Regimen specific:**

Pre treatment ECHO required

Monitor for constipation and neuropathy with Vincristine

Monitor for Constipation and neuropathy while on Vincristine

Dasatinib – pleural effusion. NO PPI or H2RA (e.g PEPcid) (reduces dasatinib absorption). Antacids (e.g. Tums) Ok if separated by 2 hours from dasatinib.

Hold PPIs 48 hours prior to high dose IV methotrexate

Mucositis

**Mini-HyperCVAD – discuss with Leukemia group**

**Leukemia Type: ALL, age <60 yo**

**Regimen: Cycle length Q21 days (**If patient is Philadelphia chromosome positive (Ph +) Benjamini O, et al. Phase II trial of hyper CVAD and dasatinib in patients with relapsed Philadelphia chromosome positive acute lymphoblastic leukemia or blast phase chronic myeloid leukemia. Am J Hematol. 2014 Mar;89(3):282-7.

If patient is Philadelphia chromosome negative (Ph -) Thomas DA, et al. Chemoimmunotherapy with hyper-CVAD plus rituximab for the treatment of adult Burkitt and Burkitt-type lymphoma or acute lymphoblastic leukemia. Cancer. 2006 Apr 1;106(7):1569-80.)

**Odd**

 **Dexamethasone 40 mg PO daily Days 1-4**

 **Dexamethasone 40 mg PO daily Days 11-14**

 **Cyclophosphamide 300 mg/m2 IV every 12 hours Days 1-3**

 **Vincristine 2 mg IV once D4, D11**

 **Doxorubicin 50 mg/m2 IV once on D4**

**Even**

 **Methotrexate 1g mg/m2 IV over 24 hours D1 (200 mg/m2 over 2 hours then 800 mg/m2 over 22 hours)**

 **Cytarabine 3 g/m2 IV every 12 hours D2-3**

**If +CD20: Rituxiumab 375 mg/m2 once per cycle (may be given outpatient on same day as G-CSF)**

Check Hep B serologies (Hepatitis/HIV screening panel (non-acute);

If Hep B Core positive OR If Hep B surface antigen positive, consider Entecavir 0.5 mg PO daily – discuss with attending

**If Ph+ Disease**: Refer to GRAAPH 2005 for cycle 1

 Cycle 2-8: Dasatinib 70 mg PO daily continuous

**Antiemetics**:

Odd:

Zofran 24 mg PO daily x 4 doses

Zyprexa 10 mg PO daily x 4 doses

           Even:

Zofran 24 mg PO daily x 3 doses

           Solu-Medrol 50 mg IV every 12 hours D3 x 4 doses

**Supportive Care:**

Odd cycle : Mesna 600 mg/m2 IV continuous Days 1-3

Even cycle : Leucovorin 50 mg IV once D3 – 12 hours after end of MTX infusion

 Leucovorin 25 mg PO every 6 hours, starting 6 hours after IV dose until MTX level less than 0.05 uM

 Prednisonlone acetate 1% ophthalmic suspension 2 drops, both eyes, every 6 hours starting D2 until 7 days after last dose of cytarabine

Daily UA while on Cyclophos (monitor gross hematuria)

**Antimicrobial prophylaxis**: Levo,flu 200 when neutrop , Valtrex, PCP on discharge (Bactrim pref – HOLD prior to MTX cycles)

AVOID posaconazole/Voriconazole (strong CYP3A4 inhi)

**TLS prophylaxis**: Yes, induction cycle only

**GCSF**: Yes, Tbo-Filgra during induction cycle then pegfilg thereafter

**Interim lab checks**: Twice weekly labs (CBC with diff, CMP)

**Response BMBx**: Yes, induction cycle following count recovery

**CNS prophylaxis**: Yes, 2 IT chemos per cycle (alternating MTX and Cytarabine)

**Central access**: Yes, TLC IJ during first cycle, Hickman vs Double lumen Port based on SCT status

**Can we give outpatient**: No

**Regimen specific:**

Pre treatment ECHO required

Monitor for constipation and neuropathy with Vincristine

Monitor for Constipation and neuropathy while on Vincristine

Dasatinib – pleural effusion. NO PPI or H2RA (e.g PEPcid) (reduces dasatinib absorption). Antacids (e.g. Tums) Ok if separated by 2 hours from dasatinib.

Hold PPIs 48 hours prior to high dose IV methotrexate

Mucositis

**Blinatumomab – Relapsed/Refractory**

**Leukemia Type: relapsed/refractory ALL**

**Regimen: Cycle length Q6 weeks (Kantarjian H, Stein A, Gökbuget N, Fielding AK, Schuh AC, Ribera JM, Wei A, Dombret H, Foà R, Bassan R, Arslan Ö, Sanz MA, Bergeron J, Demirkan F, Lech-Maranda E, Rambaldi A, Thomas X, Horst HA, Brüggemann M, Klapper W, Wood BL, Fleishman A, Nagorsen D, Holland C, Zimmerman Z, Topp MS. Blinatumomab versus Chemotherapy for Advanced Acute Lymphoblastic Leukemia. N Engl J Med. 2017 Mar 2;376(9):836-847. doi: 10.1056/NEJMoa1609783. PMID: 28249141; PMCID: PMC5881572.**)

 Cycle 1: **Blinatumomab 9 mcg/day IV every 24 hours x 7 days FOLLOWED BY**

 **Blinatumomab 28 mcg/day IV every 24 hours x 21 days Followed by 14 days rest**

Cycle 2 and beyond: **Blinatumomab 28 mcg/day IV every 24 hours x 28 days followed by 14 days rest**

**Antiemetics**: None, PRN only

**Supportive Care:**  Prephase for BMBx blast >50% or peripheral blast >15K: Dexamethasone 20 mg PO daily x 3-5 day for de-bulking prior to initiation

Dexamethasone 20 mg IV 30 minutes prior to day 1 infusion and then 30 minutes prior to dose increases

**Antimicrobial prophylaxis**: Valtrex and PCP (Bactrim preferred) . No Levaquin or fluconazole 200 mg unless neutropenic at time of discharge.

**TLS prophylaxis**: Yes, induction cycle only

**GCSF**: No

**Interim lab checks**: daily CMP and CBC with diff while inpatient; CBC w diff, CMP with bag changes as outpatient

**Response BMBx**: After D28, prior to cycle 2

**CNS prophylaxis**: Per Primary oncologist, scheduled between cycles

**Central access**: Yes, Port or triple lumen Hickman (NO PICC)

**Can we give outpatient**: Yes, Cycle 1 after day 9 or cycle 2 after day 2 (if no neurologic toxicities/CRS)

**Regimen specific:**

Evaluate Hepatitis serologies

 Full neuro exam daily while inpatient

**Blinatumomab – MRD+**

**Leukemia Type: ALL, MRD+**

**Regimen: Cycle length Q6 weeks(**Gökbuget N, Dombret H, Bonifacio M, Reichle A, Graux C, Faul C, Diedrich H, Topp MS, Brüggemann M, Horst HA, Havelange V, Stieglmaier J, Wessels H, Haddad V, Benjamin JE, Zugmaier G, Nagorsen D, Bargou RC. Blinatumomab for minimal residual disease in adults with B-cell precursor acute lymphoblastic leukemia. Blood. 2018 Apr 5;131(14):1522-1531. doi: 10.1182/blood-2017-08-798322. Epub 2018 Jan 22. Erratum in: Blood. 2019 Jun 13;133(24):2625. PMID: 29358182; PMCID: PMC6027091.)

 **Blinatumomab 28 mcg/day IV every 24 hours x 28 days followed by 14 days rest**

**Antiemetics**: None, PRN only

**Supportive Care:**  Dexamethasone 16 mg IV 30 minutes prior to day 1 infusion and then 30 minutes prior to dose increases

**Antimicrobial prophylaxis**: Valtrex and PCP (Bactrim preferred) . No Levaquin or fluconazole 200 mg unless neutropenic at time of discharge.

**TLS prophylaxis**: No

**GCSF**: No

**Interim lab checks**: daily CMP and CBC with diff while inpatient; CBC w diff, CMP with bag changes as outpatient

**Response BMBx**: After D28, prior to cycle 2

**CNS prophylaxis**: Per Primary oncologist, scheduled between cycles

**Central access**: Yes, Port or triple lumen Hickman (NO PICC)

**Can we give outpatient**: Yes, Cycle 1 after day 3 or cycle 2 after day 2 (if no neurologic toxicities/CRS)

**Regimen specific:**

Evaluate Hepatitis serologies

 Full neuro exam daily while inpatient

 Dosing and schedule remains the same even if patient is found to be MRD- in subsequent cycles

**CLAGB 10403 – remission induction**
**Leukemia Type: Ph negative B cell ALL OR T-ALL, age <40**

**Regimen: Course 1 length 28 days – subsequent courses given as an outpatient ()**

 **Prednisone 30 mg/m2 PO on days 1 to 28**

**VinCRIStine 1.5 mg/m2 IV (Max 2 mg) on days 1, 8, 15, 22**

**DAUNOrubicin 25 mg/m2 IV on days 1, 8,15, 22**

**Pegaspargase 2,500 units/m2 (Max 3,750 units) IV on day 4**

**Note the following lab values prior to treatment**:  total bilirubin greater than 2.0, AST and ALT greater than 5x upper limits of normal, amylase and lipase greater than 1.5x upper limits of normal, uric acid greater than 8.

**Antiemetics**:

           Zofran 24 mg PO every 7 days x 4 doses

 Compazine 10 mg every 6 hours PRN

**Supportive Care:**

Benadryl, tylenol, hydrocort prior to pegaspargase

**Antimicrobial prophylaxis**: Levo,flu 200 when neutrop , Valtrex, PCP on discharge (Bactrim pref – HOLD prior to MTX cycles)

AVOID posaconazole/Voriconazole (strong CYP3A4 inhi)

**TLS prophylaxis**: Yes, allopurinol 300 mg daily

**GCSF**: No

**Interim lab checks**: Lipase and triglycerides x7 days, LFTs q72 hours

**Response BMBx**: D29

**CNS prophylaxis**: Yes, Cytarabine 70 mg IT on day 1 (adjust for logistics)

Methotrexate 15 mg IT on day 8 and 29 (adjust for logistics)

**Central access**: Yes, TLC IJ while inpatient. Hickman vs single Port outpatient based on SCT status

**Can we give outpatient**: No

**Regimen specific**

 Pre-treatment ECHO

Monitor for constipation and neuropathy with Vincristine

Monitor for Constipation and neuropathy while on Vincristine

Mucositis

Aspar infusion reaction, hyperglycemia, hepatic toxicity, pancreatitis, bleeding and clotting disorders

**REFERENCE**