NCG GUIDELINES- 2019
Adult Hematolymphoid Malignancies Management Guidelines

Categories of the guidelines

a) Essential
b) Optimal
c) Optional

**Herewith essential will be referred as (a), optimal as (b) and optional as (c)*

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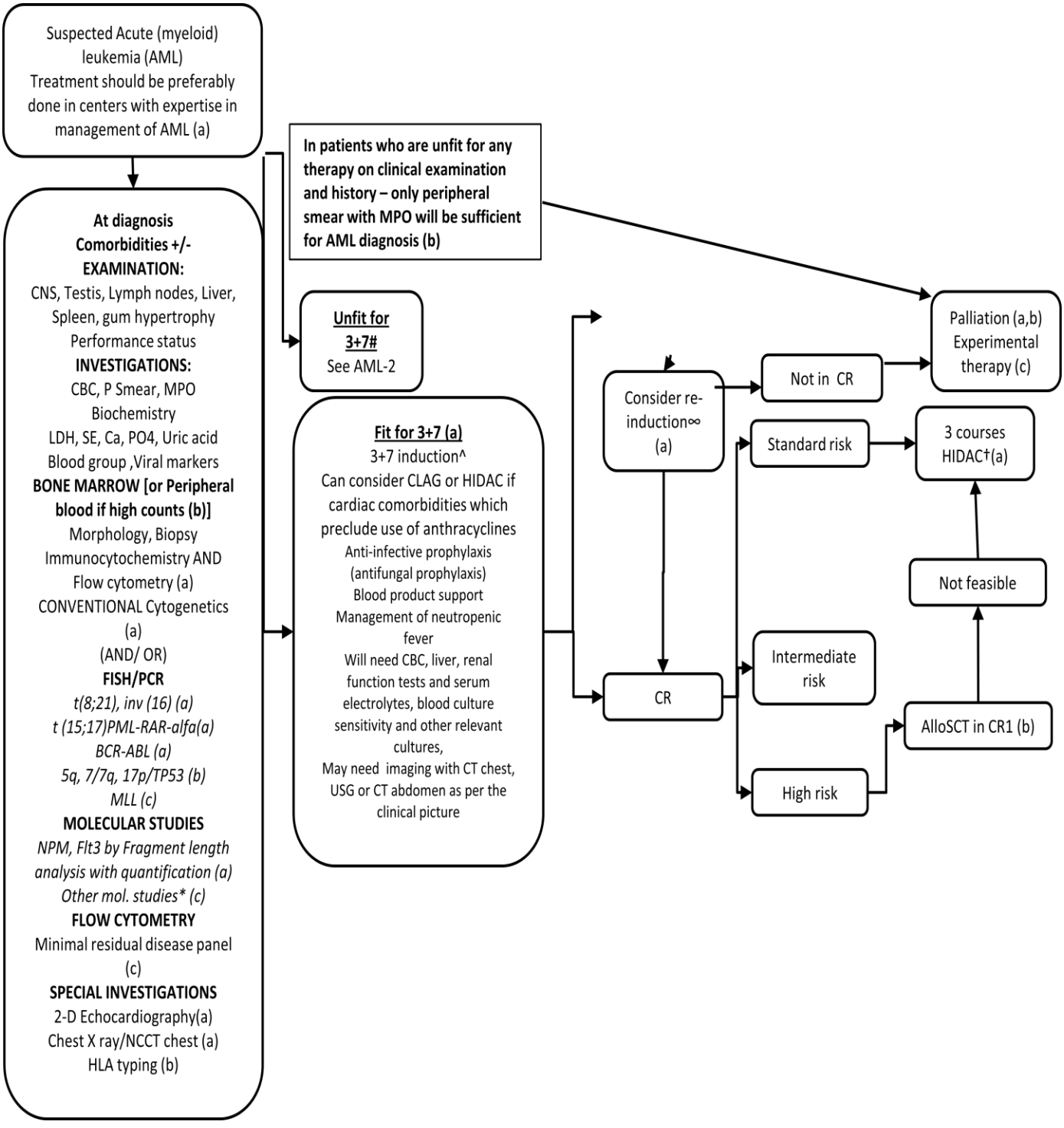
AML-1 (NON APML)



Favorable risk	Intermediate risk	Poor risk
Inv 16, t (8;21), Normal cytogenetics with isolated NPM_1 mutation/ biallelic CEBPA	Normal cytogenetics c-KIT mutation in patients with t(8;21) and inv 16	Complex (≥3 abnormalities) -5, -7, 5q-, 7q-, Inversion 3, Abnormalities of 11q23 except t(9;11)
	+ 8 only. t(9;11) Other abnormalities not listed as standard or poor risk	t(3;3), t(6;9), t(9;22) Normal cytogenetics with isolated FLT3 mutations, high allelic ratio Any patient not in CR after 1 course of induction

* Other molecular studies *CEBP alfa, kit mutations, IDH mutation, RUNX1, MLL*

^ 3+7: cytarabine (100mg/m2/day CIV X 7 days, Daunorubicin 60 mg/m2 IV over 15-20 min D1-D3)

∞re-induction with either repeat 3+7 with daunomycin 45 mg/m2 or with HIDAC or with FLAG-Ida type protocols may be considered if patient is fit for 2nd induction

Fitness for intensive therapy 3+7 in AML is a complex clinical decision using the following parameters: age, performance status, organ functions, baseline organ infection/sepsis, comorbidities, patient willingness, and individual institutional protocols.

†Dose of HIDAC: 1.5-3 grams/m2 per dose over 2 hours twice a day X 3 days – total 6 doses (9-18 gram/m2 total dose per course, either on D1,2,3 or Day 1,3 5)

AML-1 (non APML)

3 + 7 INDUCTION

Inj GRANISET 3mg IV Day 1 – day 7

Inj CYTARABINE 100mg/m2 in 500ml NS iv over 24hrs Day 1-Day 7 through PICC

Inj DAUNORUBICIN 60mg/m2 in 100 ml NS iv over 15mins Day 1 –day 3 Through PICC

OR

Inj IDARUBICIN 12mg/m2 in 100ml NS iv over 15mins Day 1 –day 3 Through PICC

IF CARDIAC COMORBIDITIES WHICH PRECLUDE USE OF ANTHRACYCLINES

CLAG PROTOCOL for AML(Relapse / refractory or high risk Denovo / secondary AML/MDS-AML)

Inj.GRANISET 1 mg Day2 –Day6

Inj. G-CSF 300mcg SC Day 1 – Day 6 (if TLC is>20,000/mm3 then start concurrently with chemotherapy)

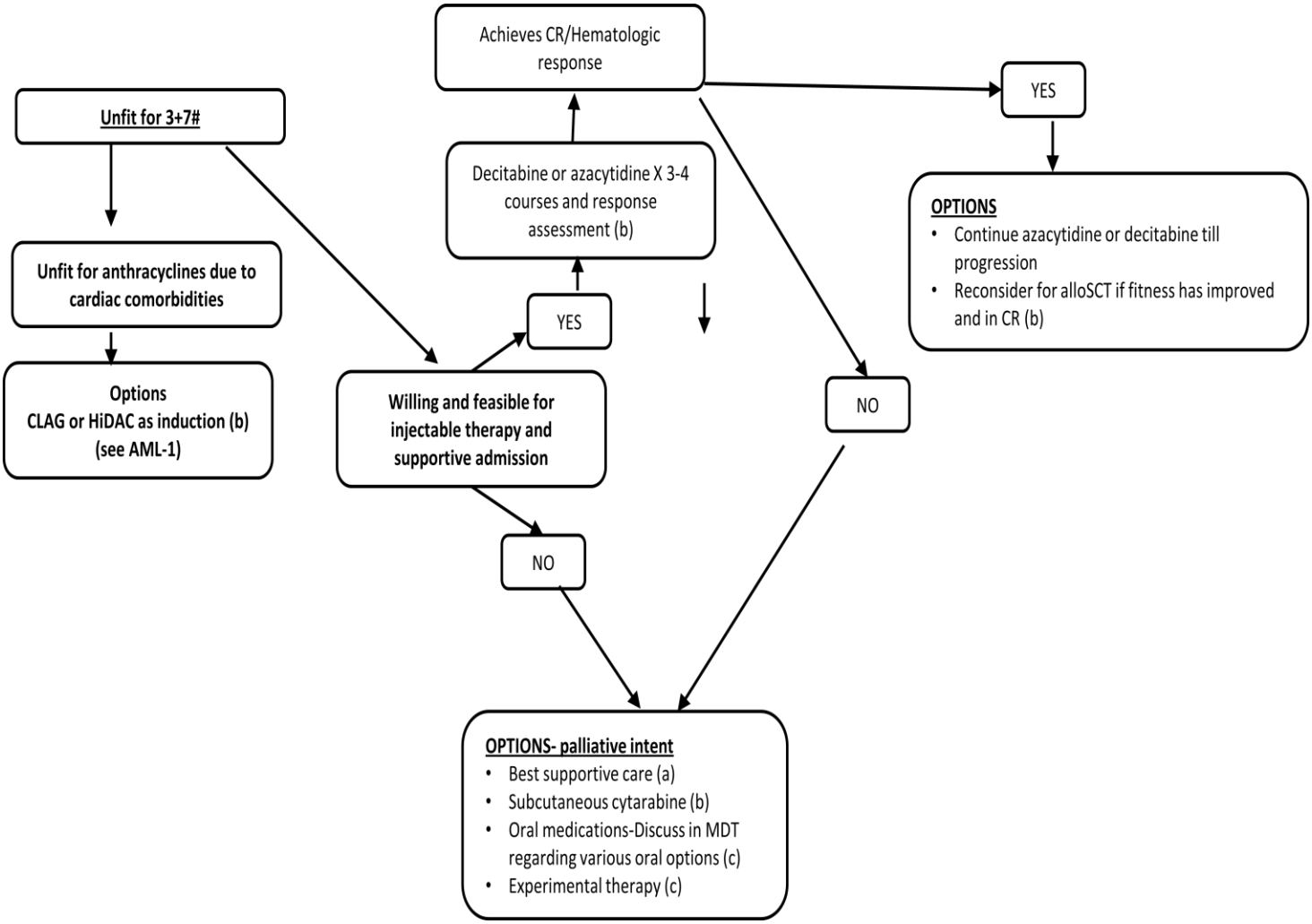
Inj.CLADRIBINE 5mg/m2 in 500ml NS iv over2hours Day 2 – Day6

Inj.CYTARABINE 2gm/m2 in 500ml NS iv over4hours to be started 2hoursafter cladribine infusion Day 2 – Day6

OR HIDAC

Inj CYTARABINE 12gm/m2 / 9 gm/m2 in 6 divided doses 12hrly on Day 1, Day 3, Day 5 every 21 days x 3 cycles

AML-2 (non- APML)- Unfit for aggressive Rx



#IF UNFIT FOR 3 + 7 INDUCTION

Tab ONDANSETRON / GRANISETRON PO 1 hour before

Inj. AZACITIDINE 75mg/M2 Sc/Iv D 1-7 q 28days

OR

Inj. DECITABINE 20 mg / m2 iv infusion over 1 hr on days 1 to 5 every 4 weeks

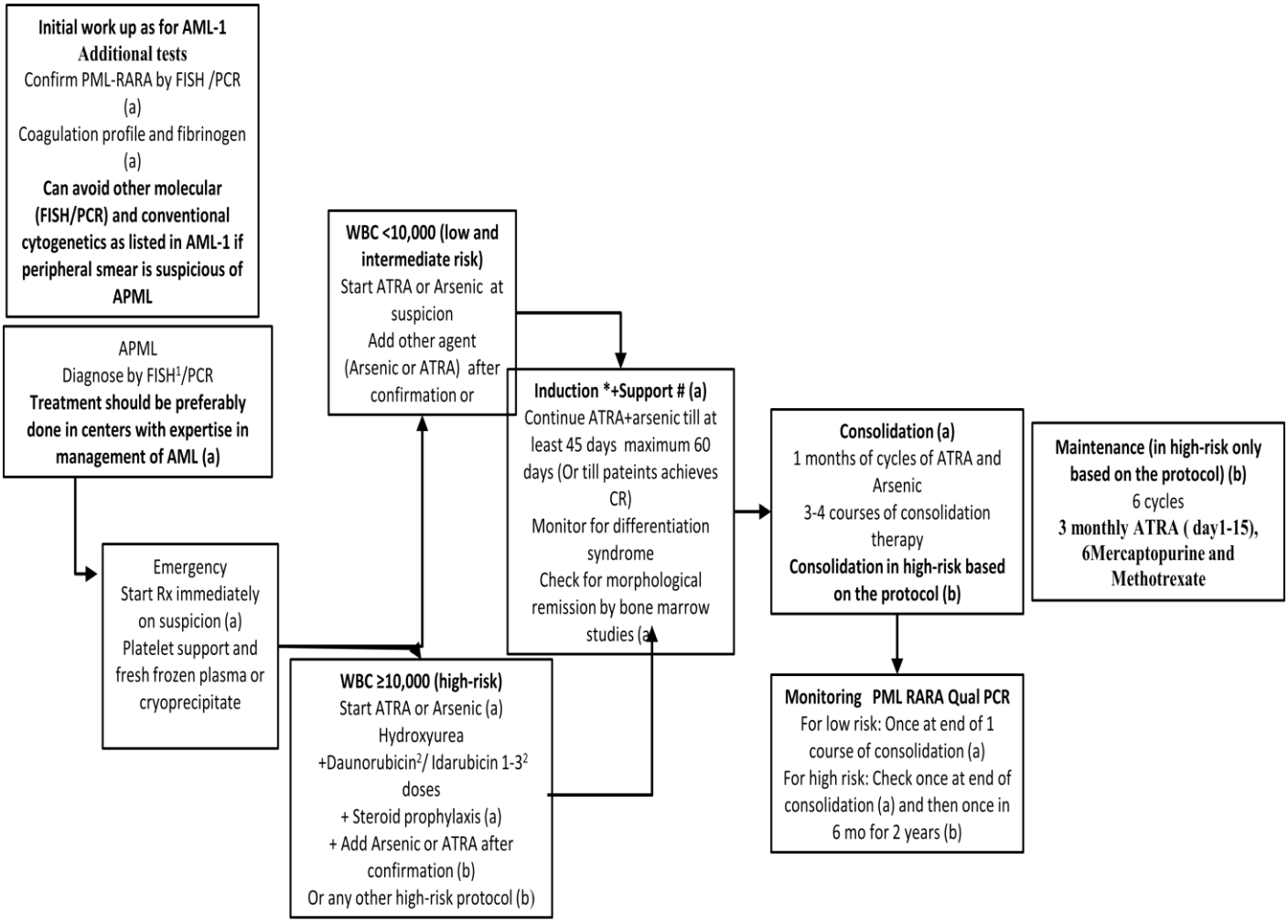
OR

Inj. DECITABINE 15 mg / m2 iv infusion over 3 hrs q8h for day 1 to day 3 every 6 weeks

OR

Inj. DECITABINE 20 mg/m2 iv infusion over 1 hr on days 1 -10 every 4 weeks

AML-3 (APML)



#Supportive care

- Platelet transfusion to keep platelets > 50,000/cmm
- FFP or cryoprecipitate transfusion to keep fibrinogen >150mg/dL

*** Management of Sudden increase in WBC/ differentiation syndrome (DS)**

- Start Hydroxyurea/ Daunorubicin for controlling counts
- Steroids if not started already- dexa 8 mg BD till counts drop below less than 10,000/cumm and no evidence of differentiation
- For severe DS, hold ATRA/ Arsenic temporarily
- Management for febrile neutropenia as per high risk guidelines

1. Ideally breakapart probe to be used to identify variant translocations

2.To check whether anthracyclines required based on cytoreduction achieved by hydroxyurea or based on the protocol for high risk APML

AML3 (APML)

Induction (a)-ATO-0.15mg/kg in 250ml 5% Dextrose iv over 3 hours D1-D45 for max 60 days

Cap. ATRA 45mg/m2/day in two divided doses for 45 days till max 60 days

Consolidation-(a)(b)

ATO 0.15mg/kg in 250ml 5% Dextrose iv over 3 hours 5 days/week for 4weeks on and 4weeks off for 4 cycles

Cap. ATRA 45mg/m2/day in two divided doses 2weeks on and 2weeks off for 7 cycles

For high risk (b):

Induction (b): Daunorubicin 30mg/m2 or Idarubicin 12mg/m2 IV or or Mitoxantrone 12mg/m2 IV 1-3 doses during induction along with

ATO-0.15mg/kg in 250ml 5% Dextrose iv over 3 hours D1-D45 for max 60days

Cap. ATRA 45mg/m2/day in two divided doses for 45 days till max 60 days

Dexamethasone(b) 10mg/m2 twice a day

If Anthracycline and ATRA consolidation is used-

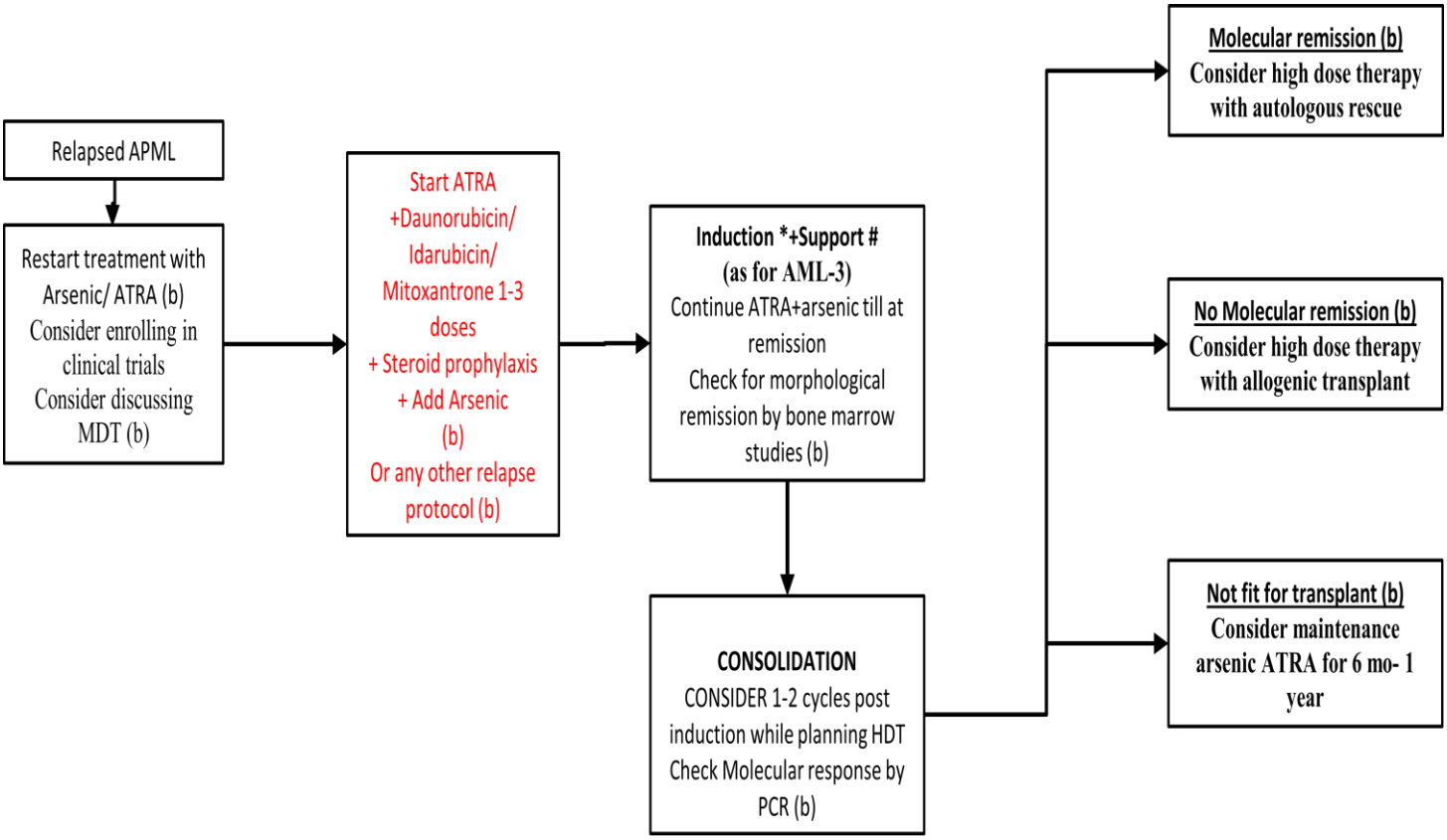
Maintenance-

ATRA 45mg/m2 day in two divided doses D1-D15

6-MP 50mg/m2/day, MTX 15mg/m2/week from Day 16 to Day 90

For total 8 cycles (2 years)

AML-4 (RELAPSED APML)



AML3 (APML)

Induction (a)-ATO-0.15mg/kg in 250ml 5% Dextrose iv over 3 hours D1-D45 for max 60days
Cap. ATRA 45mg/m2/day in two divided doses for 45 days till max 60 days

Consolidation-(a)(b)

ATO 0.15mg/kg in 250ml 5% Dextrose iv over 3 hours 5 days/week for 4weeks on and 4weeks off for 4 cycles
Cap. ATRA 45mg/m2/day in two divided doses 2weeks on and 2weeks off for 7 cycles

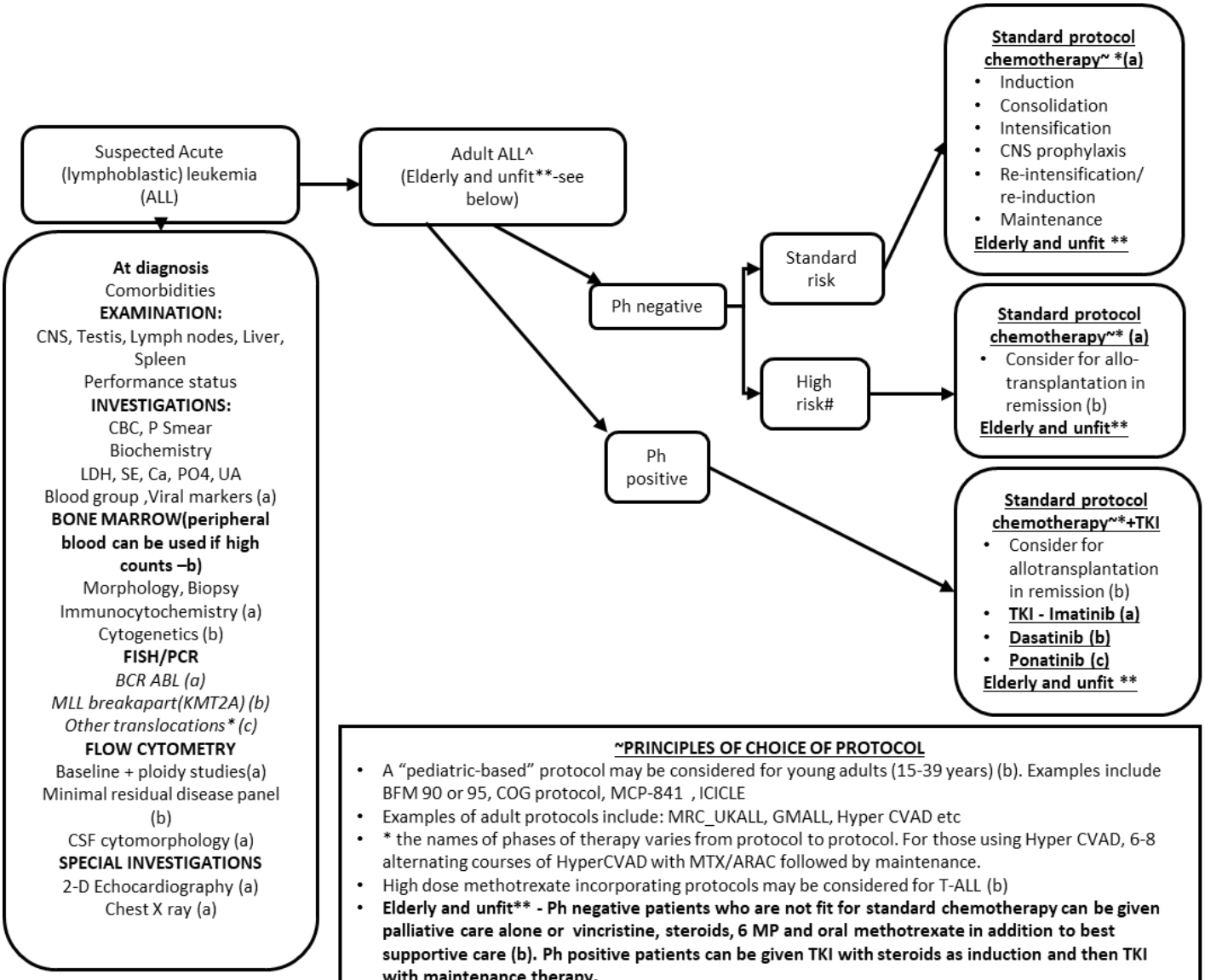
For high risk (b):

Induction (b): Daunorubicin 30mg/m2 or Idarubicin 12mg/m2 IV or Mitoxantrone 12mg/m2 IV 1-3 doses during induction along with
ATO-0.15mg/kg in 250ml 5% Dextrose iv over 3 hours D1-D45 for max 60days
Cap. ATRA 45mg/m2/day in two divided doses for 45 days till max 60 days
Dexamethasone(b) 10mg/m2 twice a day

If Anthracycline and ATRA consolidation is used-

Maintenance-
ATRA 45mg/m2 day in two divided doses D1-D15
6-MP 50mg/m2/day, MTX 15mg/m2/week from Day 16 to Day 90
For total 8 cycles (2 years)

ALL-1



~PRINCIPLES OF CHOICE OF PROTOCOL

- A "pediatric-based" protocol may be considered for young adults (15-39 years) (b). Examples include BFM 90 or 95, COG protocol, MCP-841 , ICICLE
- Examples of adult protocols include: MRC_UKALL, GMALL, Hyper CVAD etc
- * the names of phases of therapy varies from protocol to protocol. For those using Hyper CVAD, 6-8 alternating courses of HyperCVAD with MTX/ARAC followed by maintenance.
- High dose methotrexate incorporating protocols may be considered for T-ALL (b)
- **Elderly and unfit** - Ph negative patients who are not fit for standard chemotherapy can be given palliative care alone or vincristine, steroids, 6 MP and oral methotrexate in addition to best supportive care (b). Ph positive patients can be given TKI with steroids as induction and then TKI with maintenance therapy.**

* Other molecular studies *ETV6-RUNX1, TCF3-PBX1 (1;19), Ph-like abnormalities, iAMP21, 3 centromeric probes for 7 and 10*
^ MPAL (mixed phenotype ALL) is usually treated like a high risk adult ALL
# High risk: Any of the following: Ph or BCR-ABL positive, MLL rearrangements, poor prednisolone responders , MRD positivity post consolidation >.0.01%), ETP-ALL, Ph –like genotype, Age >35 years, WBC >30,000/cumm if B-cell ALL, >100,000/cumm if T-cell ALL, CNS positive
Elderly **- Age >60 years , comorbidities, poor performance status (age alone should not be considered in deciding the fitness for therapy)

BFM-90: Rajendra A, Jain H, Bonda VNA, et al (2021) Outcomes and prognostic factors in adolescents and young adults with ALL treated with a modified BFM-90 protocol. Blood Advances 5:1178–1193

BFM-95: Möricke A, Reiter A, Zimmermann M, et al. Risk-adjusted therapy of acute lymphoblastic leukemia can decrease treatment burden and improve survival: treatment results of 2169 unselected pediatric and adolescent patients enrolled in the trial ALL-BFM 95 [published correction appears in Blood. 2009 Apr 30;113(18):4478. Dosage error in article text]. *Blood*. 2008;111(9):4477-4489. doi:10.1182/blood-2007-09-112920

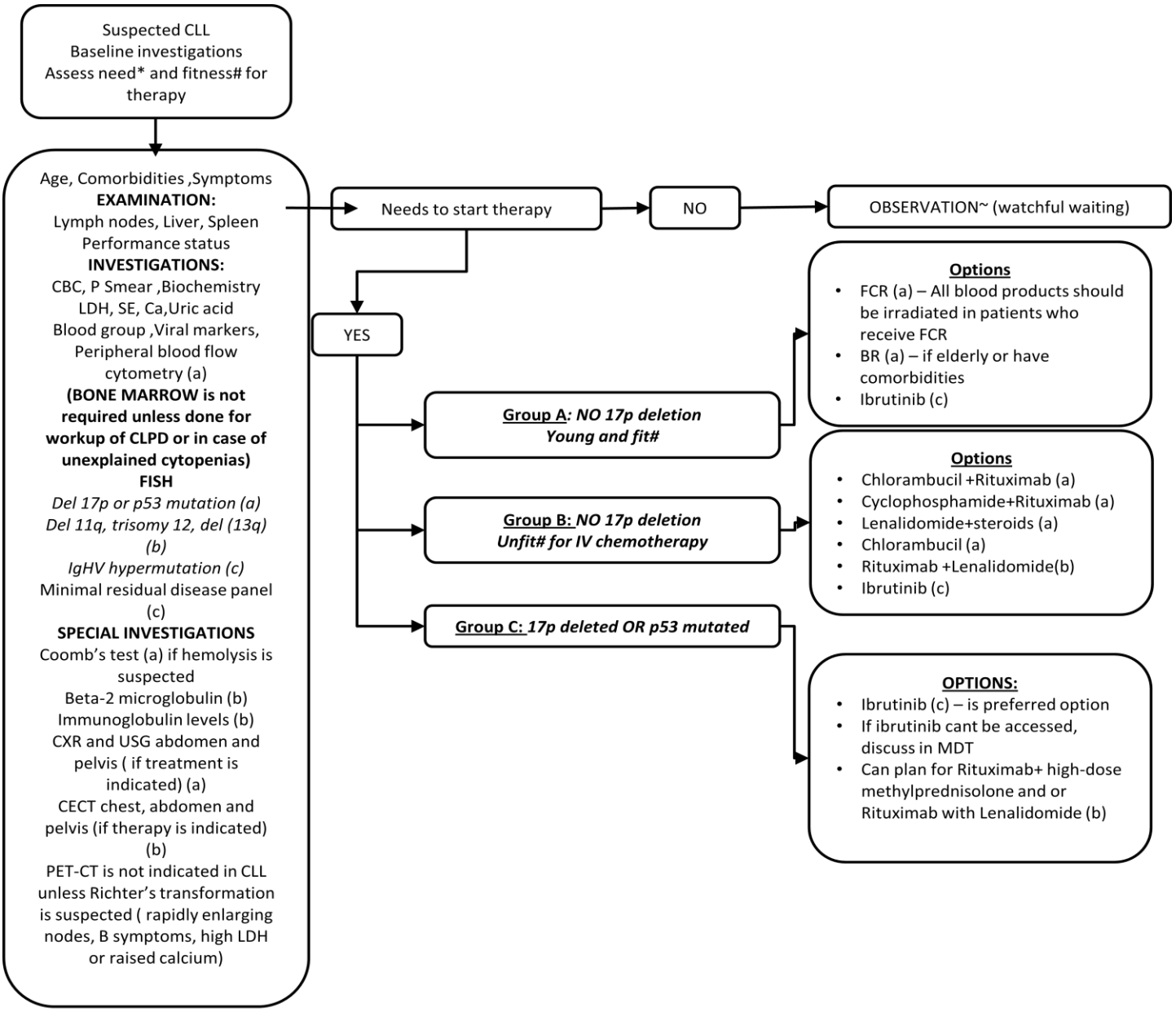
COG: Larsen EC,Devidas M,Chen S,et al.Dexamethasone and high-dose methotrexate improve outcome for children and young adults with high-risk B-acute lymphoblastic leukemia: a report from Children's Oncology Group Study AALL0232.*J Clin Oncol*.2016;34(20):2380-2388.

MCP-841: Advani S, Pai S, Venzon D, et al (1999) Acute lymphoblastic leukemia in India: An analysis of prognostic factors using a single treatment regimen. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO 10:167–76

MRC-UK-ALL: 3. Hough R, Rowntree C, Goulden N, Mitchell C, Moorman A, Wade R, Vora A (2016) Efficacy and toxicity of a paediatric protocol in teenagers and young adults with Philadelphia chromosome negative acute lymphoblastic leukaemia: results from UKALL 2003. British Journal of Haematology 172:439–451

GMALL: Bajel A, George B, Mathews V, Viswabandya A, Kavitha ML, Srivastava A, Chandy M (2007) Adult ALL: treatment outcome and prognostic factors in an Indian population using a modified German ALL (GMALL) protocol. Leukemia 21:2230–2233
Hyper-CVAD: 5. Kantarjian H, Thomas D, O'Brien S, et al (2004) Long-term follow-up results of hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone (Hyper-CVAD), a dose-intensive regimen, in adult acute lymphocytic leukemia. Cancer 101:2788–2801

CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)



*NEED for therapy in CLL: Presence of B symptoms/end organ dysfunction due to CLL/progressive bulky disease (spleen.6cm, LNs >10cm) anemia (not hemolytic anemia or hemolytic anemia non-responsive to steroids and rituximab)/thrombocytopenia, lymphocyte doubling in less than 6 months
#FITNESS for therapy in CLL: age>70 years, multiple comorbidities, performance status 2 or more (frail elderly)
~OBSERVATION in CLL: Review once in 3 months with physical examination, history and complete blood counts. The frequency can be made once in 6 months or longer based on the disease kinetics (if stable blood counts, asymptomatic and no increase in nodes or organomegaly) on initial follow up

CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)

Needs to start therapy – No
OBSERVATION

GROUP A: NO 17P DELETION YOUNG AND FIT#

FCR
RITUXIMAB 375 mg/m2 in Cycle 1 f/b 500mg/m2 in Cycle 2-6 IV infusion* DAY 1 ONLY
FLUDARABINE 25 mg/m2 IV infusion NS/500ml/30 min DAY1 – DAY3
CYCLOPHOSPHAMIDE 250 mg/m2 IV infusion NS/100 ml/30 min DAY1 TO DAY3

FOR ELDERLY OR HAVING CO MORBIDITIES

BR (Bendamustine Rituximab)
RITUXIMAB 375 mg/m2 IV D1
BENDAMUSTINE 70 mg/ IV Infusion NS/ 500ml /1 hr Day1 – Day2
Or
IBRUTINIB 420 MG (Dose/BSA) 140 mg capsules x 3 P.O 30 min before or 2 hrs after food

GROUP B: NO 17p DELETION UNFIT# FOR IV CHEMOTHERAPY

CHLORAMBUCIL + RITUXIMAB
CHLORAMBUCIL 10mg/m2POOnce a day for 7days (multiples of 2 mg)

RITUXIMAB 375 mg/m2 IV Infusion Dissolve 100 mg in 100ml of N Saline Start at 25 ml/hour –if no reaction in 20 minutes ↑↑ infusion to 50 ml/hr. if no reaction Dissolve the remaining dose in 500ml of N Saline increase by 25 ml/hour every 20 minutes Day 1 ONLY of each cycle

CYCLOPHOSPHAMIDE + RITUXIMAB
CYCLOPHOSPHAMIDE 250 mg/m2 IV infusion NS/100 ml/30 min DAY1 TO DAY3
RITUXIMAB 375 mg/m2 IV Day 1 ONLY of each cycle

LENALIDOMIDE + STEROIDS
LENALIDOMIDE 25 mg daily DAY 1-21 HS PO
PREDNISOLONE 100 mg PO after Breakfast Day 1 to 5

CHLORAMBUCIL
CHLORAMBUCIL 10mg/m2 PO Once a day for 7days (multiples of 2 mg)

RITUXIMAB + LENALIDOMIDE
RITUXIMAB 375 mg/m2 IV Infusion on Day 1 ONLY

LENALIDOMIDE 25 mg daily DAY 1-21 HS PO

IBRUTINIB
IBRUTINIB 420 MG (Dose/BSA) 140 mg capsules x 3 P.O 30 min before or 2 hrs after food

GROUP C: 17p DELETED OR p53 MUTATED

IBRUTINIB
IBRUTINIB 420 MG (Dose/BSA) 140 mg capsules x 3 P.O 30 min before or 2 hrs after food

RITUXIMAB + HIGH DOSE METHYL PREDNISOLONE

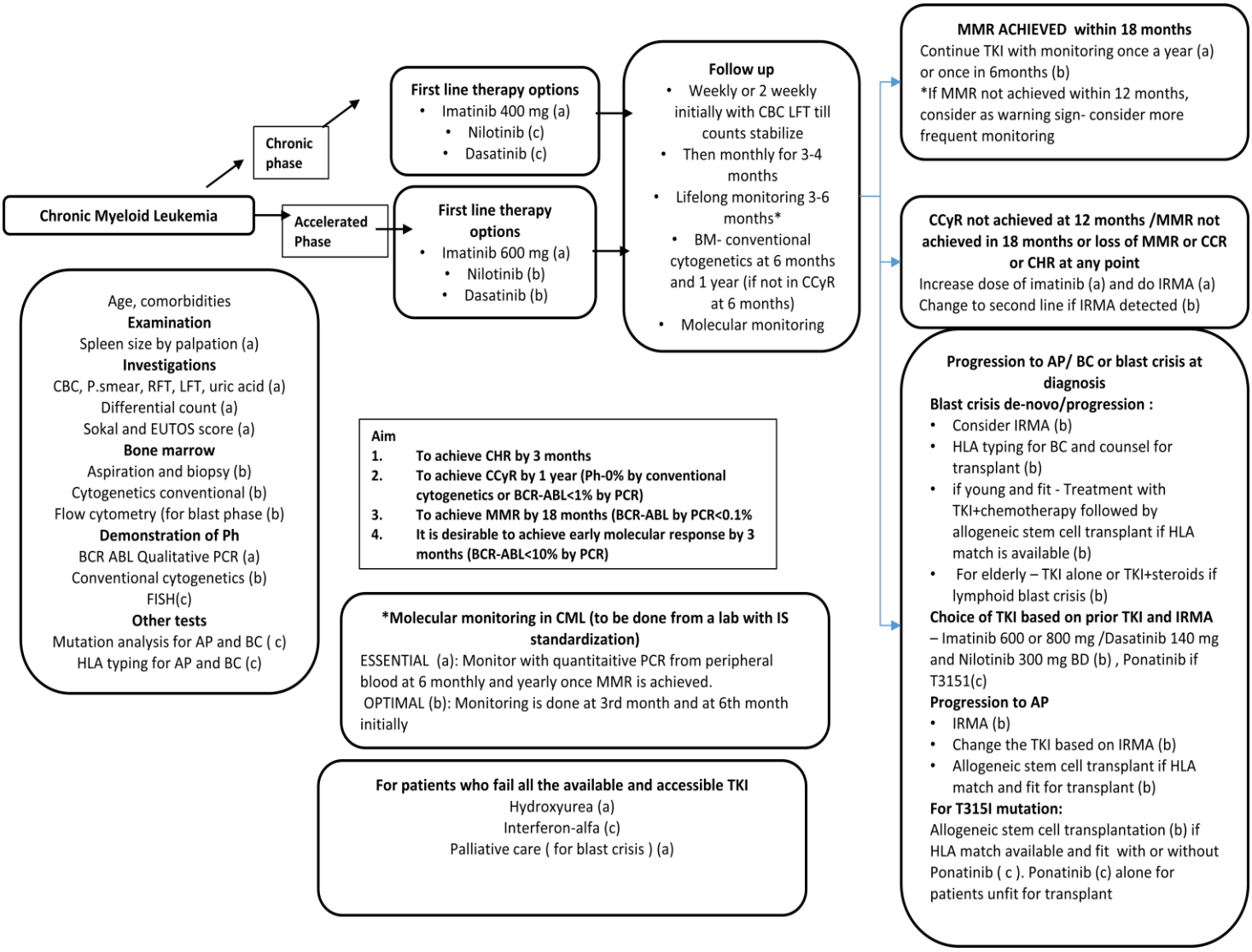
Inj METHYL PREDNISOLONE 1000mg IV 1 hour before Rituximab
RITUXIMAB 375 mg/m2 IV Infusion on Day 1 ONLY of each cycle

AND / OR

RITUXIMAB + LENALIDOMIDE

RITUXIMAB 375 mg/m2 IV Infusion on Day 1 ONLY of each cycle
LENALIDOMIDE 25 mg daily DAY 1-21 HS PO

CHRONIC MYELOID LEUKEMIA (CML)

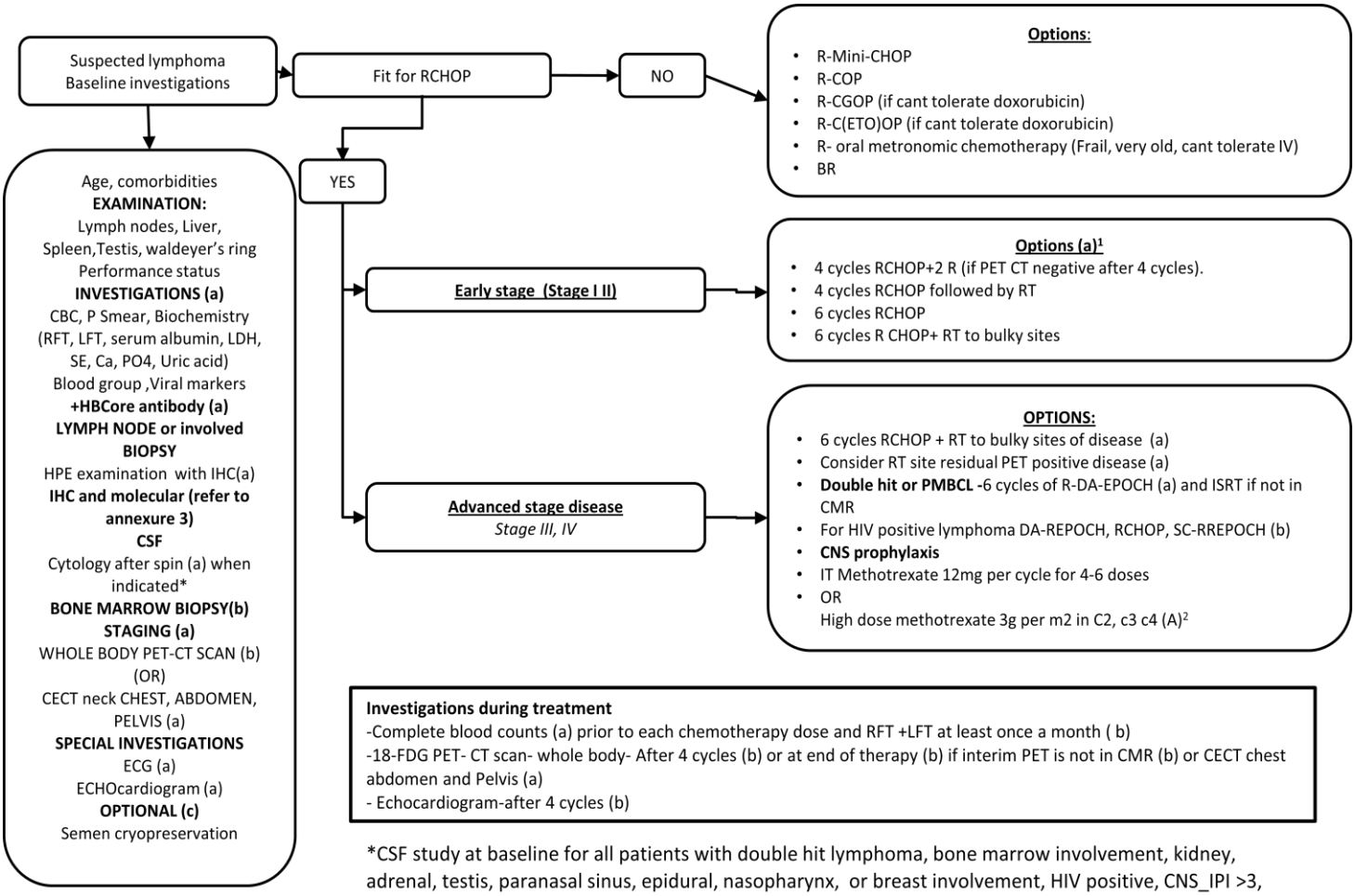


CHRONIC MYELOID LEUKEMIA (CML)

CML – CP
Tab IMATINIB 400 mg OD Per Oral
Tab NILOTINIB 300 mg BD Per Oral
Tab DASATINIB 100 mg OD Per Oral
Tab BOSUTINIB 400mg OD Per Oral

CML-AP/BC
Tab IMATINIB 600 mg OD Per Oral
Tab NILOTINIB 400 mg BD Per Oral
Tab DASATINIB 140 mg OD Per Oral
Tab BOSUTINIB 500mg OD Per Oral

DIFFUSE LARGE B CELL LYMPHOMA (DLBCL-1)-NEWLY DIAGNOSED (systemic)



Investigations during treatment
-Complete blood counts (a) prior to each chemotherapy dose and RFT +LFT at least once a month (b)
-18-FDG PET- CT scan- whole body- After 4 cycles (b) or at end of therapy (b) if interim PET is not in CMR (b) or CECT chest abdomen and Pelvis (a)
- Echocardiogram-after 4 cycles (b)

*CSF study at baseline for all patients with double hit lymphoma, bone marrow involvement, kidney, adrenal, testis, paranasal sinus, epidural, nasopharynx, or breast involvement, HIV positive, CNS_IPI >3, two or more extranodal sites with raised LDH

1. To be discussed in MDT for tailoring of therapy. RT must be considered for bulky disease (>7 cm)
2. Requirements for HDMTx- Creatinine clearance >60 ml/min, no third space collection, facilities to monitor methotrexate level, in-patient beds

DIFFUSE LARGE B CELL LYMPHOMA (DLBCL-1)- NEWLY DIAGNOSED (systemic)

EARLY STAGE (I& II)

4 # RCHOP + # 2 RITUXIMAB (If PET CT Negative after 4 cycles)

OR

4 # RCHOP FOLLOWED BY RADIATION

OR

6 # RCHOP
OR
6 # RCHOP FOLLOWED BY RADIATION to BULKY SITE

RCHOP
Inj AVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab
RITUXIMAB 375 mg/m2 IV Infusion on Day 1
CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

ADVANCED STAGE DISEASE (III, IV)
6 # RCHOP FOLLOWED BY RADIATION TO BULKY SITE

RCHOP
Inj AVIL I AMP IV + Tab CROCIN 750 MG PO 30 min Before RITUXIMAB
RITUXIMAB 375 MG/M2 IV Infusion on Day 1
CYCLOPHOSPHAMIDE 750MG/M2 IV Infusion NS/500ML/20 min on Day 1
ADRIAMYCIN 50 MG/M2 IV Infusion NS/250ML /20 min on Day 1
VINCRISTINE 1.4 MG/M2 (2MG MAX) IV Push on Day 1
PREDNISOLONE 100 MG PO After Breakfast Day 1 TO 5

FOR RESIDUAL PET POSITIVE DISEASE SITE
Radiation

DOUBLE HIT OR PMBCL
6 # R-DA-EPOCH and ISRT if not in CMR
Inj RITUXIMAB (D1) 375mg/m2 IV (Omit if CD20 Negative)
Inj. ETOPOSIDE (D1-4) 50 mg/m2/day CIV
Inj. ADRIAMYCIN (D1-4) 10 mg/m2/day CIV
Inj. VCR (D1-4) 0.4mg/m2/d CIV
Inj. ENDOXAN (D 5) 750mg/m2/d Over 1 hour
FOR HIV POSITIVE LYMPHOMA
DA-REPOCH
Inj. RITUXIMAB (D1) 375mg/m2 IV (Omit if CD20 Negative)
Inj. ETOPOSIDE (D1-4) 50 mg/m2/day CIV
Inj. ADRIAMYCIN (D1-4) 10 mg/m2/day CIV
Inj. VCR (D1-4) 0.4mg/m2/d CIV
Inj ENDOXAN (D 5) 750mg/m2/d Over 1 hour

Dose escalation -

Dose-Adjustment Paradigm

- Dose adjustments above starting dose level (level 1) apply to etoposide, doxorubicin and cyclophosphamide
- Dose adjustments below starting dose level (level 1) apply to cyclophosphamide only.
- Drug Doses based on previous cycle ANC nadir:

  - If Nadir ANC ≥ 500/µl on all measurements: ↑ 1 dose level above last cycle
  - If Nadir ANC < 500/µl on 1 or 2 measurements: Same dose level as last cycle
  - If Nadir ANC < 500/µl ≥ 3 measurements: ↓ 1 dose level below last cycle

  Or

  - If nadir platelet < 25,000/µl** on 1 measurement: ↓ 1 dose level below last cycle.

- If ANC ≥ 1000/µl and platelets ≥ 100,000/µl on day 21, begin treatment.
- If ANC < 1000/µl or platelets < 100,000/µl** on day 21, delay up to 1 week. G-CSF may be started for ANC < 1000/µl and stopped 24 hours before treatment. If counts still low after 1 week delay, ↓ 1 dose level below last cycle.

- **Important: Measurement of ANC nadir based on twice weekly CBC only (3 days apart). Only use twice weekly CBC for dose-adjustment, even if additional CBC's are obtained.**

- ****Please Note: This does not apply to patients who have low platelets at baseline due to lymphoma or immune-mediated mechanism caused by lymphoma. In those cases, no delay or dose reduction is required. The dose adjustments for these patients will be based solely on the ANC nadir and the PI or designee's clinical judgment.**

6.2 Table of doses per level for adjusted agents:

Drugs	Drug Doses per Dose Levels							
	-2	-1	1	2	3	4	5	6
Doxorubicin (mg/m^2/day)	10	10	10	12	14.4	17.3	20.7	24.8
Etoposide (mg/m^2/day)	50	50	50	60	72	86.4	103.7	124.4
Cyclophosphamide (mg/m^2/day)	480	600	750	900	1080	1296	1555	1866

OR

RCHOP

InjAVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab
Inj. RITUXIMAB 375 mg/m2 IV Infusion on Day 1
Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Inj. VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

OR

SC-RREPOCH

Inj AVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab
InjRITUXIMAB 375 mg/m2 IV Infusion on Day 1
Inj ETOPOSIDE 50mg/m2/day CIV DAY 1- 4
Inj ADRIAMYCIN 10mg/m2/day CIV DAY 1- 4
Inj VCR 0.4mg/m2/day CIV DAY 1- 4
Inj ENDOXAN 750mg/m2 DAY 5
Inj RITUXIMAB* 375mg/m2 DAY5
PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

Response assessment for SC-RREPCOH

PET-CT after 2#-if CR-Then 1 more Cycle
After 2# if PET-CT -positive repeat PET-CT after 2 additional cycles until negative for a maximum of 6 cycles.

Dose adjustment for SC-RREPOCH:

Cyclophosphamide dose is reduced by 25% for a nadir ANC <500/mm3 or Platelet count <25000/mm3 lasting 2-4 days and 50% if the nadir ANC <500/mm3 or Platelet count <25000/mm3 lasting for 5 or more days, based on twice weekly blood counts.

CNS PROPHYLAXIS

IT METHOTREXATE 12mg per cycle for 4-6 doses

OR

High Dose METHOTREXATE 3g per m2 in C2, C3,C4

IF NOT FIT FOR RCHOP

R-Mini-CHOP
Inj. AVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab
Inj. RITUXIMAB 375 mg/m2 IV Infusion on Day 1
Inj. CYCLOPHOSPHAMIDE 400mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 25 mg/m2 IV infusion NS/250ml /20 min on Day 1
Inj. VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
Tab PREDNISOLONE 40mg/m2 PO After Breakfast DAY 1 to 5

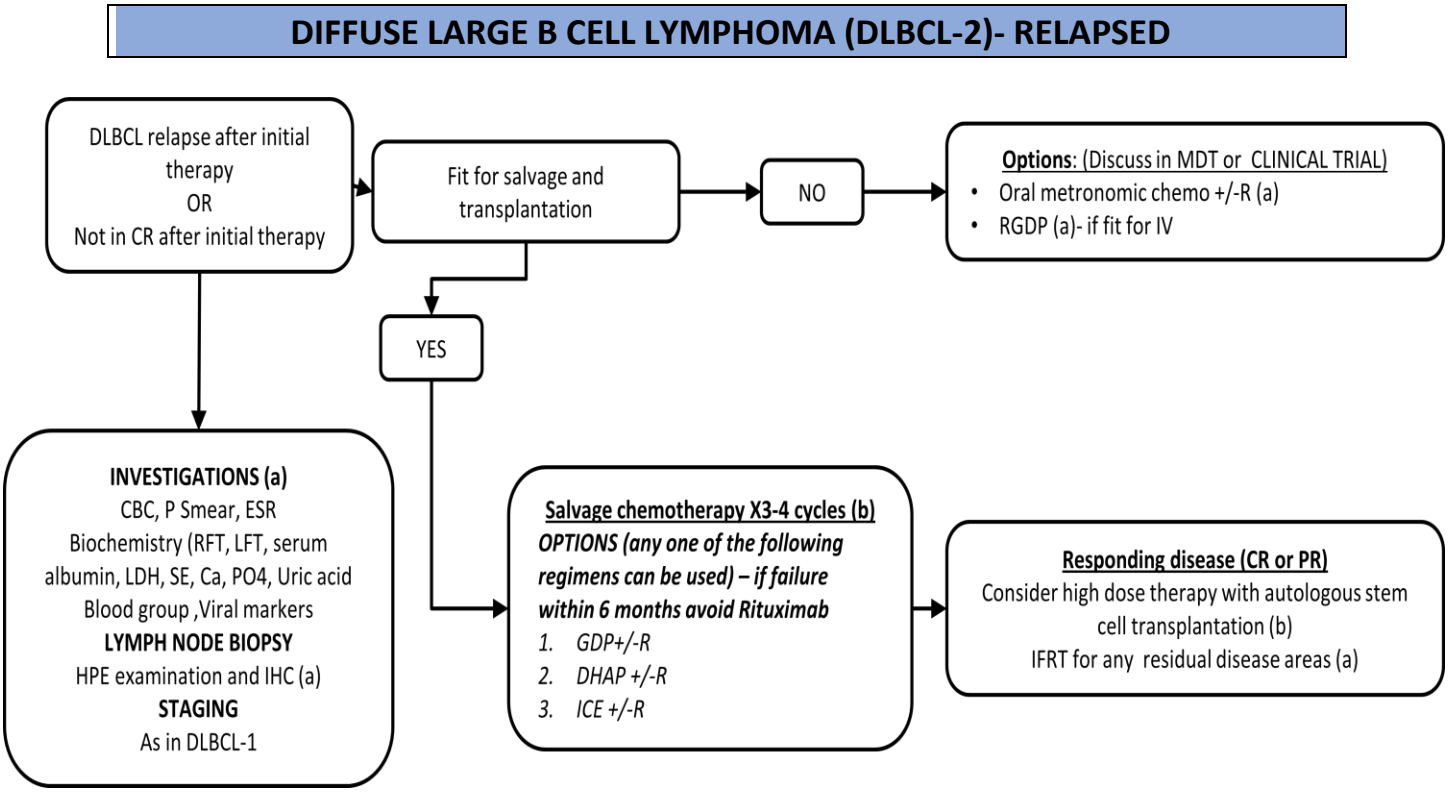
OR
R-COP
Inj. AVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab
Inj. RITUXIMAB 375 mg/m2 IV Infusion on Day 1
Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

OR
R-C(ETO)OP (IF CAN'T TOLERATE DOXORUBICIN)
Inj. AVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab
Inj. RITUXIMAB 375 mg/m2 IV Infusion on Day 1
Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
CAP ETOPOSIDE 65 MG/ M2 PO OD D1 TO 3
Inj. VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5
OR

FOR PATIENTS WHO ARE FRAIL, VERY OLD OR CAN'T TOLERATE IV
R- ORAL METRONOMIC CHEMOTHERAPY (PEP-C)
Inj. AVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab
Inj. RITUXIMAB 375 mg/m2 IV Infusion on Day 1
PREDNISOLONE 20MG PO OD
ETOPOSIDE 50MG PO OD
PROCARBAZINE 50MG PO OD
Induction (1 cycle): Once daily until WBC less than 3 x 109 /L then hold cyclophosphamide, etoposide and procarbazine until Maintenance begins Maintenance starts at count recovery (until disease progression or unacceptable toxicity): Cycle length determined by blood counts predniSONE starts with Induction and is taken continuously throughout

OR

BR
RITUXIMAB 375 mg/m2 IV on Day 1 ONLY
BENDAMUSTINE 70 mg/ IV Infusion NS/ 500ml /1 hr Day1 – Day2



DIFFUSE LARGE B CELL LYMPHOMA (DLBCL -2)- RELAPSED

FIT FOR SALVAGE AND TRANSPLANTATION

GDP+/-R - Frequency Q 21 Days; Max Cycles -6

GEMCITABINE 1 gm/m2 Yes/No IV infusion NS/500 ml/30 min DAY 1 and 8

Tab DEXAMETHASONE 40 mg Yes/No PO OD after breakfast Day 1 to Day 4

CISPLATIN 75 mg/m2 Yes/No Continuous IV infusion over 2 hours NS/1000 ml/ Day1 ONLY OR

CARBOPLATIN AUC-5 IN 250ML 5% DEXTROSE IV OVER 30MINS Day1 OF EACH CYCLE (IN CISPLATIN INELIGIBLE)

+ / -

RITUXIMAB 375 mg/m2 IV infusion on DAY 1 ONLY

OR

DHAP +/-R Frequency once every 21 days Cycles -6 (maximum) 2

OR

ICE +/-R Cycle 3 weekly schedule

GRANISETRON 3 MG DAY 2- DAY 4
DEXAMETHASONE 8 MG DAY 2- DAY 4
ETOPOSIDE 100 MG/M2 DAY 2- DAY 4
CARBOPLATIN AUC-5 DAY 3
IFOSFAMIDE WITH MESNA 5000 MG/M2 (Both drip should run simultaneously through a three way) DAY 3 OR IFOSFAMIDE WITH MESNA 1800MG/M2 ON D1-D3 OF EACH CYCLE (DAY CARE)

+/-

TAB CROCIN AND INJ AVIL AS PREMEDICATION 30 MIN PRIOR TO RITUXIMAB DAY 1
TAB CROCIN 500 MG INJ AVIL 10 MG IV
RITUXIMAB 375 MG/M2 Watch for hypersensitivity reaction and inform doctor if required day 1
I.V FLUIDS 1.5L/M2

IF NOT FIT FOR SALVAGE AND TRANSPLANTATION

ORAL METRONOMIC CHEMO +/-R

(PEP-C)+/-R
Inj. AVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab
Inj. RITUXIMAB 375 mg/m2 IV Infusion on Day 1
PREDNISOLONE 20MG PO OD
ETOPOSIDE 50MG PO OD
PROCARBAZINE 50MG PO OD
Induction (1 cycle): Once daily until WBC less than 3 x 109 /L then hold cyclophosphamide, etoposide and procarbazine until Maintenance begins Maintenance starts at count recovery (until disease progression or unacceptable toxicity): Cycle length determined by blood counts predniSONE starts with Induction and is taken continuously throughout

OR

IF FIT FOR IV

RGDP - Frequency Q 21 Days; Max Cycles -6
RITUXIMAB 375 mg/m2 IV infusion on DAY 1 ONLY
GEMCITABINE 1 gm/m2 Yes/No IV infusion NS/500 ml/30 min DAY 1 and 8
Tab DEXAMETHASONE 40 mg Yes/No PO OD after breakfast Day 1 to Day 4
CISPLATIN 75 mg/m2 Yes/No Continuous IV infusion over 2 hours NS/1000 ml/ Day1 Only
CARBOPLATIN AUC-5 IN 250ML 5% DEXTROSE IV OVER 30MINS Day1 Only OF EACH CYCLE (IN CISPLATIN INELIGIBLE)

FOLLICULAR LYMPHOMA (FL-1)- NEWLY DIAGNOSED

FL Grade I, 2, 3A
Baseline investigations
(3b to be managed as DLBCL)

Age, Comorbidities, B symptoms
EXAMINATION:
Lymph nodes, Liver, Spleen
Performance status
INVESTIGATIONS (a)
CBC, P Smear,
Biochemistry (RFT, LFT, serum albumin, LDH, SE, Ca, PO4, Uric acid)
Blood group ,Viral markers
Hepatitis B core Antibody Ig G
LYMPH NODE BIOPSY
HPE examination (a)
IHC and molecular
AS per Annexure 2 and 3
Flow cytometry on peripheral blood presenting with lymphocytosis (a). In this case biopsy of representative node will be needed to determine the grade of FL.
BONE MARROW BIOPSY
FOR ALL PATIENTS except if peripheral blood is involved (a)
STAGING (a)
WHOLE BODY PET-CT SCAN (b)
(OR)
CECT CHEST, ABDOMEN, PELVIS WITH BONE MARROW (a)
SPECIAL INVESTIGATIONS
ECG (a)
ECHOcardiogram (a) –if planned for RCHOP
Beta 2-microglobulin
OPTIONAL (c)
Semen cryopreservation

Early stage (Stage I II)

Options (a)
- **Encompassable in RT field**
  - IFRT (a)
- **Not encompassable in RT field**
  - Treat as in advanced stage (a)
  - Observation maybe an option to be discussed (b)

Advanced stage disease
Stage III, IV

OPTIONS:
- **Treatment not required as listed in Indications**
  - Observation (a)
- **Treatment required, low volume disease**
  - 4 doses of rituximab (weekly X 4) and follow up (c)
- **Treatment required, high risk and high disease load**
  - BRX6 –preferred (a)
  - RCHOPX6 (b)
- **Maintenance**
  - FOLLOWING RCHOP in patients who achieve CR/PR FOR 2 YEARS (c)
- **Unfit for IV chemotherapy (age, comorbidities, poor PS)**
  - Single agent rituximab (b)
  - Rituximab+Lenalidomide (b)
  - Rituximab+oral metronomic chemotherapy (c)
  - Oral chemotherapy alone (b)

Investigations during treatment
-Complete blood counts (a) prior to each chemotherapy dose and RFT +LFT at least once a month (b)
-18-FDG PET- CT scan- whole body- After 4 cycles (b) or at end of therapy (b) or CECT chest, abdomen and Pelvis (a)
- Echocardiogram-after 4 cycles (b) for patients planned for 6 RCHOP

Indications for therapy
B symptoms, bulky nodes (>7 cms), symptomatic splenomegaly, organ dysfunction, bone lesions, effusions, cytopenias, progressive lymphocytosis, transformation
Observation or watchful waiting:
Monitoring with clinical examination, symptoms and CBC, LFT, RFT every 3-6 months for any indication of therapy. In case of abdominal nodes USG abdomen and Pelvis can be done once in 6-12 months

FOLLICULAR LYMPHOMA (FL-1)- NEWLY DIAGNOSED

EARLY STAGE (STAGE I II)
ENCOMPASSABLE IN RT FIELD
IFRT
NOT ENCOMPASSABLE IN RT FIELD
TREATMENT REQUIRED, LOW VOLUME DISEASE
SINGLE AGENT
RITUXIMAB 375 mg/m2 IV infusion Weekly (Weekly X 4 Cycles)
TREATMENT REQUIRED, HIGH RISK AND HIGH DISEASE LOAD
BR x 6 Cycles
RITUXIMAB 375 mg/m2 IV on Day 1 ONLY
BENDAMUSTINE 70 mg/ IV Infusion NS/ 500ml /1 hr Day1 – Day2
OR
RCHOP X 6 Cycles
Inj AVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab
Inj. RITUXIMAB 375 mg/m2 IV Infusion on Day 1
Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Inj. VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5
UNFIT FOR IV CHEMOTHERAPY (DUE TO AGE, COMORBIDITIES, POOR PS)
SINGLE AGENT
Inj. RITUXIMAB 375 mg/m2 IV
OR
RITUXIMAB + LENALIDOMIDE
RITUXIMAB 375 mg/m2 IV on Weekly for 4 doses in CYCLE1 and Day1 of each cycle from C2-C6
LENALIDOMIDE 25 mg daily DAY 2-21 HS PO
OR
Inj. RITUXIMAB + ORAL METRONOMIC CHEMOTHERAPY
(PEP-C)+R
Inj. AVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab
Inj. RITUXIMAB 375 mg/m2 IV Infusion on Day 1
PREDNISOLONE 20MG PO OD
ETOPOSIDE 50MG PO OD
PROCARBAZINE 50MG PO OD
Induction (1 cycle): Once daily until WBC less than 3 x 109 /L then hold cyclophosphamide, etoposide and procarbazine until Maintenance begins Maintenance starts at count recovery (until disease progression or unacceptable toxicity): Cycle length determined by blood counts predniSONE starts with Induction and is taken continuously throughout

OR

ORAL CHEMOTHERAPY ALONE (PEP-C)
PREDNISOLONE 20MG PO OD
ETOPOSIDE 50MG PO OD
PROCARBAZINE 50MG PO OD
Induction (1 cycle): Once daily until WBC less than 3 x 109 /L then hold cyclophosphamide, etoposide and procarbazine until Maintenance begins Maintenance starts at count recovery (until disease progression or unacceptable toxicity): Cycle length determined by blood counts predniSONE starts with Induction and is taken continuously throughout

OR
OBSERVATION MAYBE AN OPTION TO BE DISCUSSED

ADVANCED STAGE DISEASE (III, IV)
TREATMENT NOT REQUIRED AS LISTED IN INDICATIONS
OBSERVATION
TREATMENT REQUIRED, LOW VOLUME DISEASE
SINGLE AGENT
RITUXIMAB 375 mg/m2 IV infusion Weekly (Weekly X 4 Cycles)
TREATMENT REQUIRED, HIGH RISK AND HIGH DISEASE LOAD
BR x 6 Cycles
RITUXIMAB 375 mg/m2 IV on Day 1 ONLY
BENDAMUSTINE 70 mg/ IV Infusion NS/ 500ml /1 hr Day1 – Day2
OR
RCHOP X 6 Cycles
Inj. AVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab
Inj. RITUXIMAB 375 mg/m2 IV Infusion on Day 1
Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Inj. VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

MAINTENANCE RITUXIMAB FOLLOWING RCHOP IN PATIENTS WHO ACHIEVE CR/PR FOR 2 YEARS (c)
TREATMENT REQUIRED, LOW VOLUME DISEASE
SINGLE AGENT
RITUXIMAB 375 mg/m2 IV infusion Weekly (Weekly X 4 Cycles)
TREATMENT REQUIRED, HIGH RISK AND HIGH DISEASE LOAD
BR x 6 Cycles
RITUXIMAB 375 mg/m2 IV on Day 1 ONLY
BENDAMUSTINE 70 mg/ IV Infusion NS/ 500ml /1 hr Day1 – Day2
OR
RCHOP X 6 Cycles
Inj. AVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab

Inj. RITUXIMAB 375 mg/m2 IV Infusion on Day 1
Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Inj. VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

UNFIT FOR IV CHEMOTHERAPY (Due to age, comorbidities, poor PS)

SINGLE AGENT

Inj. RITUXIMAB 375 mg/m2 IV

OR

RITUXIMAB + LENALIDOMIDE

RITUXIMAB 375 mg/m2IV day 1 Weekly for 4 doses in CYCLE1 and Day1 of each cycle from C2-C6
LENALIDOMIDE 25 mg daily DAY 1-21 HS PO

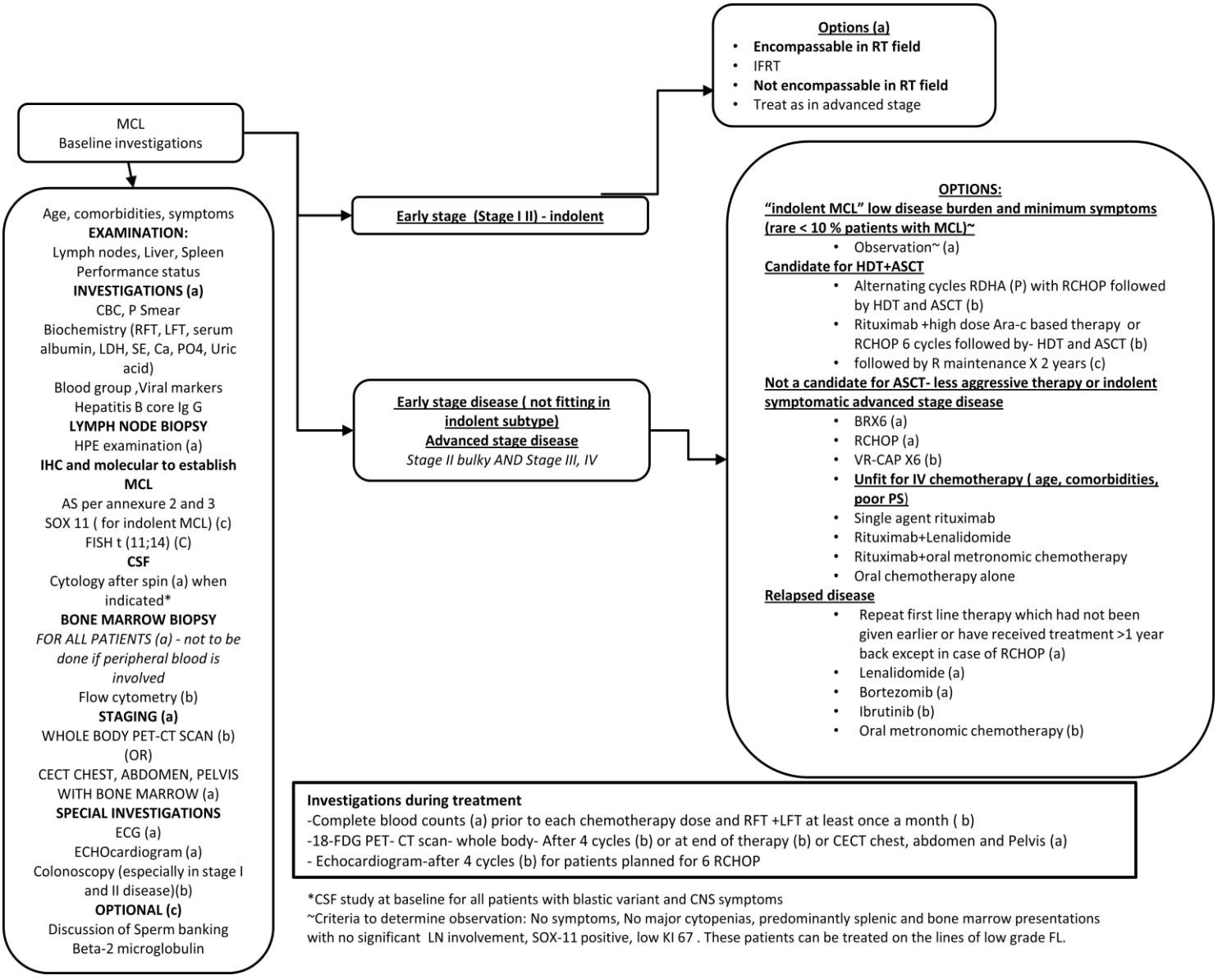
OR

Inj. RITUXIMAB + ORAL METRONOMIC CHEMOTHERAPY(PEP-C)
Inj. AVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab
Inj. RITUXIMAB 375 mg/m2 IV Infusion on Day 1
PREDNISOLONE 20MG PO OD
ETOPOSIDE 50MG PO OD
PROCARBAZINE 50MG PO OD
Induction (1 cycle): Once daily until WBC less than 3 x 109 /L then hold cyclophosphamide, etoposide and procarbazine until Maintenance begins Maintenance starts at count recovery (until disease progression or unacceptable toxicity): Cycle length determined by blood counts predniSONE starts with Induction and is taken continuously throughout

OR

Oral chemotherapy alone (PEP-C)
PREDNISOLONE 20MG PO OD
ETOPOSIDE 50MG PO OD
PROCARBAZINE 50MG PO OD
Induction (1 cycle): Once daily until WBC less than 3 x 109 /L then hold cyclophosphamide, etoposide and procarbazine until Maintenance begins Maintenance starts at count recovery (until disease progression or unacceptable toxicity): Cycle length determined by blood counts predniSONE starts with Induction and is taken continuously throughout

MANTLE CELL LYMPHOMA (MCL)



Investigations during treatment
-Complete blood counts (a) prior to each chemotherapy dose and RFT +LFT at least once a month (b)
-18-FDG PET- CT scan- whole body- After 4 cycles (b) or at end of therapy (b) or CECT chest, abdomen and Pelvis (a)
- Echocardiogram-after 4 cycles (b) for patients planned for 6 RCHOP

*CSF study at baseline for all patients with blastic variant and CNS symptoms
~Criteria to determine observation: No symptoms, No major cytopenias, predominantly splenic and bone marrow presentations with no significant LN involvement, SOX-11 positive, low KI 67 . These patients can be treated on the lines of low grade FL.

MANTLE CELL LYMPHOMA (MCL)

EARLY STAGE (STAGE I II) - INDOLENT

ENCOMPASSABLE IN RT FIELD

IFRT

NOT ENCOMPASSABLE IN RT FIELD

Treat as in advanced stage

EARLY STAGE DISEASE (NOT FITTING IN INDOLENT SUBTYPE)

ADVANCED STAGE DISEASE STAGE II BULKY AND STAGE III, IV

"INDOLENT MCL" low disease burden and minimum symptoms (Rare < 10 % patients with MCL)~

Observation

CANDIDATE FOR HDT+ASCT

Alternating Cycles RDHA (P) with RCHOP followed by HDT and ASCT

R-DHA(P)

Inj ONDANSETRON 16 mg IV Push Day1 to Day 2
Inj FOSAPREPITANT 150mg IV in 150ml NS over 20mins, 30mins prior to Cisplatin
Tab DEXAMETHASONE 40 mg Yes/No PO OD after breakfast Day 1 to Day 4
CISPLATIN 100 mg/m2 Yes/No CIV infusion NS/1000 ml/24 hours Day1 ONLY OR CARBOPLATIN AUC-5 IN 250ML 5% DEXTROSE IV OVER 30MINS Day1 OF EACH CYCLE (IN CISPLATIN INELIGIBLE)
CYTARABINE (two doses 12 hrs apart) 2gm/m2 Yes/No IV infusion NS/500 ml/3 hour BD on Day2
+ / -

RITUXIMAB 375 mg/m2 IV infusion on DAY 1 ONLY

R-CHOP

Inj. AVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab
Inj. RITUXIMAB 375 mg/m2 IV Infusion on Day 1
Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Inj. VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

RITUXIMAB +HIGH DOSE ARA-C BASED therapy OR RCHOP 6 cycles followed by- HDT and ASCT

R-BAC EVERY 28DAYS CYCLE FOR MAXIUMUM 6 CYCLES

Inj AVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab

Inj. RITUXIMAB 375 mg/m2 IV Infusion on Day 1

INJ. BENDABUSTINE 70MG/M2 D2-D3

INJ. CYTARABINE 500MG/M2 D2-D4

Followed by R maintenance x 2 years

R-MAINTENANCE-EVERY 2MONTHLY

Inj AVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab

Inj. RITUXIMAB 375 mg/m2 IV Infusion on Day 1

NOT A CANDIDATE FOR ASCT- LESS AGGRESSIVE THERAPY OR INDOLENT SYMPTOMATIC

ADVANCED STAGE DISEASE

BR x 6 Cycles

RITUXIMAB 375 mg/m2 IV on Day 1 Only
BENDAMUSTINE 70 mg/ IV Infusion NS/ 500ml /1 hr Day1 – Day2

OR

RCHOP X 6 Cycles

Inj AVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab
Inj. RITUXIMAB 375 mg/m2 IV Infusion on Day 1
Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Inj. VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

OR

VR-CAP X6

Inj AVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab
Inj. RITUXIMAB 375 mg/m2 IV Infusion on Day 1
Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Inj. Bortezomib 1.3mg/m2 S/C D1,4,8,11 of each cycle
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

UNFIT FOR IV CHEMOTHERAPY (DUE TO AGE, COMORBIDITIES, POOR PS)

SINGLE AGENT
RITUXIMAB 375 mg/m2 IV

OR

RITUXIMAB + LENALIDOMIDE

RITUXIMAB 375 mg/m2 IV Infusion Dissolve 100 mg in 100ml of N Saline Start at 25 ml/hour –if no reaction in 20 minutes ↑↑ infusion to 50 ml/hr. if no reaction Dissolve the remaining dose in 500ml of N Saline increase by 25 ml/hour every 20 minutes Day 1 ONLY of each cycle
LENALIDOMIDE 25 mg daily DAY 1-21 HS PO
OR

RITUXIMAB+ORAL METRONOMIC CHEMOTHERAPY (PEP-C)

RITUXIMAB 375 mg/m2 IV Infusion Day 1 ONLY of each cycle
Oral chemotherapy alone (PEP-C)
PREDNISOLONE 20MG PO OD
ETOPOSIDE 50MG PO OD
PROCARBAZINE 50MG PO OD
Induction (1 cycle): Once daily until WBC less than 3 x 109 /L then hold cyclophosphamide, etoposide and procarbazine until Maintenance begins Maintenance starts at count recovery (until disease progression or unacceptable toxicity): Cycle length determined by blood counts predniSONE starts with Induction and is taken continuously throughout

OR

Oral chemotherapy alone (PEP-C)
PREDNISOLONE 20MG PO OD
ETOPOSIDE 50MG PO OD
PROCARBAZINE 50MG PO OD
Induction (1 cycle): Once daily until WBC less than 3 x 109 /L then hold cyclophosphamide, etoposide and procarbazine until Maintenance begins Maintenance starts at count recovery (until disease progression or unacceptable toxicity): Cycle length determined by blood counts predniSONE starts with Induction and is taken continuously throughout

RELAPSED DISEASE

REPEAT FIRST LINE THERAPY WHICH HAD NOT BEEN GIVEN EARLIER OR HAVE RECEIVED
TREATMENT >1 YEAR BACK EXCEPT IN CASE OF RCHOP
LENALIDOMIDE 25 mg daily DAY 1-21 HS PO
OR
BORTEZOMIB1.3 mg/m2 on days 1, 8, 15, 22 of each cycle IV push over 3-5 seconds or subcutaneous
OR
IBRUTINIB 420 MG (Dose/BSA) 140 mg capsules x 3 P.O 30 min before or 2 hrs after food
OR
Oral metronomic chemotherapy

MARGINAL ZONE LYMPHOMA (MZL)

MZL
Baseline investigations

C
EXAMINATION:
Lymph nodes, Liver, Spleen
Evaluation of extranodal sites
Performance status
INVESTIGATIONS (a)
CBC, P Smear,Biochemistry (RFT, LFT, serum albumin, LDH, SE, Ca, PO4, Uric acid)
Blood group ,Viral markers
LYMPH NODE BIOPSY or the disease site biopsy (extranodal site)
HPE examination (a)
IHC and molecular
As per Annexure 2,3
MYD88 mutation study (b)
PCR for 11:18 (c)
H pylori staining on gastric biopsy (for gastric MZL) (a)
In patients with SMZL – Peripheral blood flow cytometry or bone marrow examination will be diagnostic
BONE MARROW BIOPSY
FOR ALL PATIENTS (a) except if peripheral blood is involved
STAGING (a)
CECT CHEST, ABDOMEN, PELVIS WITH BONE MARROW (a)
SPECIAL INVESTIGATIONS
ECG (a)
ECHOcardiogram (a)- if planned for RCHOP
UGI endoscopy (b)
Thyroid function tests (b)
Head and neck evaluation (b)
Anti Ro/Anti La (b) if salivary glandinvolvement
Anti-TPO (b) if thyroid involved
OPTIONAL (c)
Discussion of Sperm banking
Serum protein electrophoresis

Options (a)

Gastric marginal zone (all stages)

- **H**.Pylori positive - Anti-H. Pylori therapy – one course – reassess after 3 months if responding then observe (UGI scopy with biopsy and documentation of H.Pylori eradication). If H.Pylori is present or no response give a second course of H.Pylori therapy and reassess after 3 months
- In responding patients - follow up with UGI scpoy every 6 months for 2 years (a).
- H.Pylori negative – One course– reassess after 3 months if responding then observe
- IFRT if early stage - for non-responding patients

Early stage - Other extranodal MALTOMA

- RT alone
- observation or treatment like advanced stage if can not be included in one RT field

In HCV positive patients – anti-HCV therapy should be given to assess response

All MZL and H.Pylori therapy non responsive Gastric MZL –advanced stage

OPTIONS:

Treatment not required ~

- Observation~

Treatment required, low risk disease

- 4 doses of rituximab (weekly X 4) and follow up- Nodal MZLand other EMZL(b)
- Weekly X6 Riuximab for SMZL or Splenectomy for SMZL (b)

Treatment required, high risk and high disease load (B symptoms, bulky nodes)

- BRX6 (a) - preferred
- RCOP X6 (a)

Unfit for IV chemotherapy (age, comorbidities, poor PS)

- Single agent rituximab (a)
- Rituximab+Lenalidomide (b)
- Rituximab+oral metronomic chemotherapy (c)
- Oral chemotherapy alone (b)

In HCV positive patients – anti-HCV therapy should be given to assess response

Investigations during treatment
-Complete blood counts (a) prior to each chemotherapy dose and RFT +LFT at least once a month (b)
CECT chest +abdomen and Pelvis – post cycle 4 and cycle 6 (for MZL other than SMZL, In SMZL imaging for assessment is needed in patients with significant lymphadenopathy)

~Criteria to determine observation: No symptoms, No significant cytopenias, non-bulky disease

- Must take precautions like vaccinations for encapsulated bacteria prior to splenectomy

MARGINAL ZONE LYMPHOMA (MZL)

GASTRIC MARGINAL ZONE (ALL STAGES)

H.PYLORI Positive - Anti-H. PYLORI therapy – one course – reassess after 3 months if responding then observe (UGI scopy with biopsy and documentation of H.Pylori eradication). If H.PYLORI is present or no response give a second course of H.Pylori therapy and reassess after 3 months

in responding patients - follow up with UGI scopy every 6 months for 2 years (a).

H. PYLORI negative – one course– reassess after 3 months if responding then observe

ifrt if early stage - for non-responding patients

EARLY STAGE - OTHER EXTRANODAL MALTOMA

Radiation alone
OR
Observation
OR
TREATMENT LIKE ADVANCED STAGE IF CAN NOT BE INCLUDED IN ONE RT FIELD
In HCV positive patients – Anti-HCV therapy should be given to assess response

All MZL and H. PYLORI THERAPY NON RESPONSIVE GASTRIC MZL –ADVANCED STAGE

TREATMENT NOT REQUIRED ~

Observation

Treatment Required, Low Risk Disease

4 DOSES OF RITUXIMAB (WEEKLY X 4) AND FOLLOW UP- NODAL MZL AND OTHER EMZL

RITUXIMAB 375 mg/m2 IV Infusion Weekly x 4 cycles
OR

WEEKLY X6 RIUXIMAB FOR SMZL

RITUXIMAB 375 mg/m2 IV Weekly x 6 cycles
OR

SPLENECTOMY FOR SMZL

TREATMENT REQUIRED, HIGH RISK AND HIGH DISEASE LOAD (B SYMPTOMS, BULKY NODES)

BR X 6 CYCLES

RITUXIMAB 375 mg/m2 IV on Day 1 ONLY
BENDAMUSTINE 70 mg/ IV Infusion NS/ 500ml /1 hr Day1 – Day2

OR

RCOP X6

Inj. AVIL I AMP IV + Tab CROCIN 750 mg PO 30 min before Rituximab
Inj. RITUXIMAB 375 mg/m2 IV Infusion on Day 1
Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

UNFIT FOR IV CHEMOTHERAPY (DUE TO AGE, COMORBIDITIES, POOR PS)

SINGLE AGENT RITUXIMAB

RITUXIMAB 375 mg/m2 IV Infusion
OR

RITUXIMAB + LENALIDOMIDE

RITUXIMAB 375 mg/m2 IV DAY1 of each cycle
LENALIDOMIDE 25 mg daily DAY 1-21 HS PO
OR

RITUXIMAB+ORAL METRONOMIC CHEMOTHERAPY

RITUXIMAB 375 mg/m2 IV Infusion
OR

ORAL CHEMOTHERAPY ALONE

In HCV POSITIVE Patients – ANTI-HCV THERAPY should be given to assess response

BURKITT'S LYMPHOMA (BL-1)

Suspected BL
Baseline investigations

Highly curable cancer but complex treatment
Treatment should be preferably done in centers with expertise in management of BL (a)

Age , Comorbidities, symptoms
INVESTIGATIONS (a)
CBC, P Smear
Biochemistry (RFT, LFT, serum albumin, LDH, SE, Ca, PO4, Uric acid)
Blood group ,Viral markers
Hepatitis B core Ig G
LYMPH NODE BIOPSY
HPE examination (a)
IHC and molecular
As per annexure 2,3(a)
FISH for 8;14 (c)
CSF
Cytology after spin (a)
BONE MARROW BIOPSY
BMA and biopsy (a) except in patients with peripheral blood involvement
FCM FOR PHENOTYPING (b)
STAGING (a)
WHOLE BODY PET-CT SCAN (b)
(OR)
CECT CHEST, ABDOMEN, PELVIS WITH BONE MARROW (a)
SPECIAL INVESTIGATIONS
ECG (a)
ECHOcardiogram (a)
FISH BCL2 and BCL6 rearrangements on tissue biopsy (c)
OPTIONAL (c)
Semen cryopreservation

Options: (a)

- R GMAL NHL 2002 protocol, 6 cycles (8 Rituximab) in stage III/IV and 4 cycles(6 Rituximab) in stage I/II disease
- R DA EPOCH regimen 6 cycles(for low risk disease* 3 cycles if CR 1 more cycle) with Intrathecal methotrexate with each cycle)
- R-CODOX-M/IVAC- 2 cycles each, For low risk disease-3# R-CODOX-M alone
- R-Hyper CVAD/MA regimen- Total 8 cycles

HDMTX based protocols are preferred in high-risk disease and young fit patients
DA-REPOCH can be used in elderly and HIV positive patients

Investigations during treatment
-Complete blood counts (a) prior to each chemotherapy dose and RFT +LFT at least once a month (b)
-18-FDG PET- CT scan- whole body- After 2 cycles (b) or at end of therapy (b) or CECT chest , abdomen and Pelvis (a)
Bone marrow should be done after 2 cycles if involved at baseline or in patients with peripheral blood involvement
- Echocardiogram-after 4 cycles (b)

*Low-risk- Single site <10cm and normal LDH, stage I, completely resected

BURKITT'S LYMPHOMA (BL-1)

R GMAL NHL 2002 PROTOCOL,

IN STAGE III/IV

6 CYCLES (8 RITUXIMAB)

IN STAGE I/II DISEASE

4 CYCLES (6 RITUXIMAB)

R DA EPOCH 6 CYCLES (FOR LOW RISK DISEASE 3 CYCLES IF CR 1 MORE CYCLE) WITH INTRATHECAL METHOTREXATE WITH EACH CYCLE - CYCLE FREQUENCY ONCE EVERY 21 DAYS

Inj RITUXIMAB (D1) 375MG/M2 IV (OMIT IF CD20 NEGATIVE)
Inj ETOPOSIDE (D1-4) 50 MG/M2/DAY CIV
Inj ADRIAMYCIN (D1-4) 10 MG/M2/DAY CIV
Inj VCR (D1-4) 0.4MG/M2/D CIV
Inj ENDOXAN (D 5) 750MG/M2/D OVER 1 HOUR

OR

R-CODOX-M/IVAC- 2 CYCLES EACH, FOR LOW RISK DISEASE-3# R-CODOX-M ALONE

R-CODOX-M

Inj RITUXIMAB (D1) 375MG/M2 IV D8
CYCLOPHOSPHAMIDE 800MG/M2 IV D1,D2
DOXORUBICIN 50MG/M2 IV D1
VINCRISTINE 1.4MG/M2 IV D1, D8
METHOTREXATE 3000MG/M2 IV 24 HOURS INFUSION DAY 10
LEUCOVORIN RESCUE 36 HOURS FROM START OF METHOTREXATE EVERY 6 HRLY UNTILL MTX LEVEL <0.1 UMOL/L
IT CYTARABINE 50MG ON D1, D3
INJ. G-CSF 300MCG S/C FROM DAY 13

IVAC-R
IFOSFAMIDE 1500MG/M2 IV OVER 2HRS INFUSION D1-D5
CYTARABINE 2000MG/M2 IV ON D1,D2
MESNA 375MG/M2 IV PUSH D1-D5
ETOPOSIDE 60MG/M2 D1-D5
Inj RITUXIMAB (D1) 375MG/M2 IV D4
IT MTX 12MG ON DAY 6
INJ. G-CSF 300MCG S/C FROM DAY 7

OR

R-HYPER CVAD/MA REGIMEN- TOTAL 8 CYCLES

CYCLOPHOSPHAMIDE 300MG/M2 OVER 3HRS IV D1-D3

DOXORUBICIN 25MG/M2 24HRS INFUSION TO BEGIN 12HRS AFTER LAST DOSE OF CYCLOPHOSPHAMIDE ON D4 AND D5
VINCRISTINE 1.4MG/M2 IV PUSH ON D4 AND D11
DEXAMETHASONE 40MG ON D1-D4 AND D11-D14

ALTERNATE EVERY 21 DAY CYCLE WITH

METHOTREXATE 1GM/M2 IV OVER 24 HRS INFUSION D1
CYTARABINE 3GM/M2 OVER 2HOURS 12HRLY D2-D3
METHOTREXATE 50MG PO AT THE END OF MTX INFUSION FOLLOWED BY 25MG PO OD EVERY 6 HOURLY TILL MTX LEVEL <0.03

OR
HDMTX BASED PROTOCOLS ARE PREFERRED IN HIGH-RISK DISEASE AND YOUNG FIT PATIENTS
GMALL NHL 2002: Hoelzer D, Walewski J, Döhner H, et al. Improved outcome of adult Burkitt lymphoma/leukemia with rituximab and chemotherapy: report of a large prospective multicenter trial. *Blood*. 2014;124(26):3870-3879. doi:10.1182/blood-2014-03-563627

OR
DA-REPOCH CAN BE USED IN ELDERLY AND HIV POSITIVE PATIENTS
Inj RITUXIMAB (D1) 375MG/M2 IV (OMIT IF CD20 NEGATIVE)
Inj ETOPOSIDE (D1-4) 50 MG/M2/DAY CIV
Inj ADRIAMYCIN (D1-4) 10 MG/M2/DAY CIV
Inj VCR (D1-4) 0.4MG/M2/D CIV
Inj ENDOXAN (D 5) 750MG/M2/D OVER 1 HOUR

Dose-Adjustment Paradigm

- Dose adjustments above starting dose level (level 1) apply to etoposide, doxorubicin and cyclophosphamide
- Dose adjustments below starting dose level (level 1) apply to cyclophosphamide only.
- Drug Doses based on previous cycle ANC nadir:

  - If Nadir ANC ≥ 500/µl on all measurements: ↑ 1 dose level above last cycle
  - If Nadir ANC < 500/µl on 1 or 2 measurements: Same dose level as last cycle
  - If Nadir ANC < 500/µl ≥ 3 measurements: ↓ 1 dose level below last cycle

  Or

  - If nadir platelet < 25,000/µl** on 1 measurement: ↓ 1 dose level below last cycle.

- If ANC ≥ 1000/µl and platelets ≥ 100,000/µl on day 21, begin treatment.
- If ANC < 1000/µl or platelets < 100,000/µl** on day 21, delay up to 1 week. G-CSF may be started for ANC < 1000/µl and stopped 24 hours before treatment. If counts still low after 1 week delay, ↓ 1 dose level below last cycle.

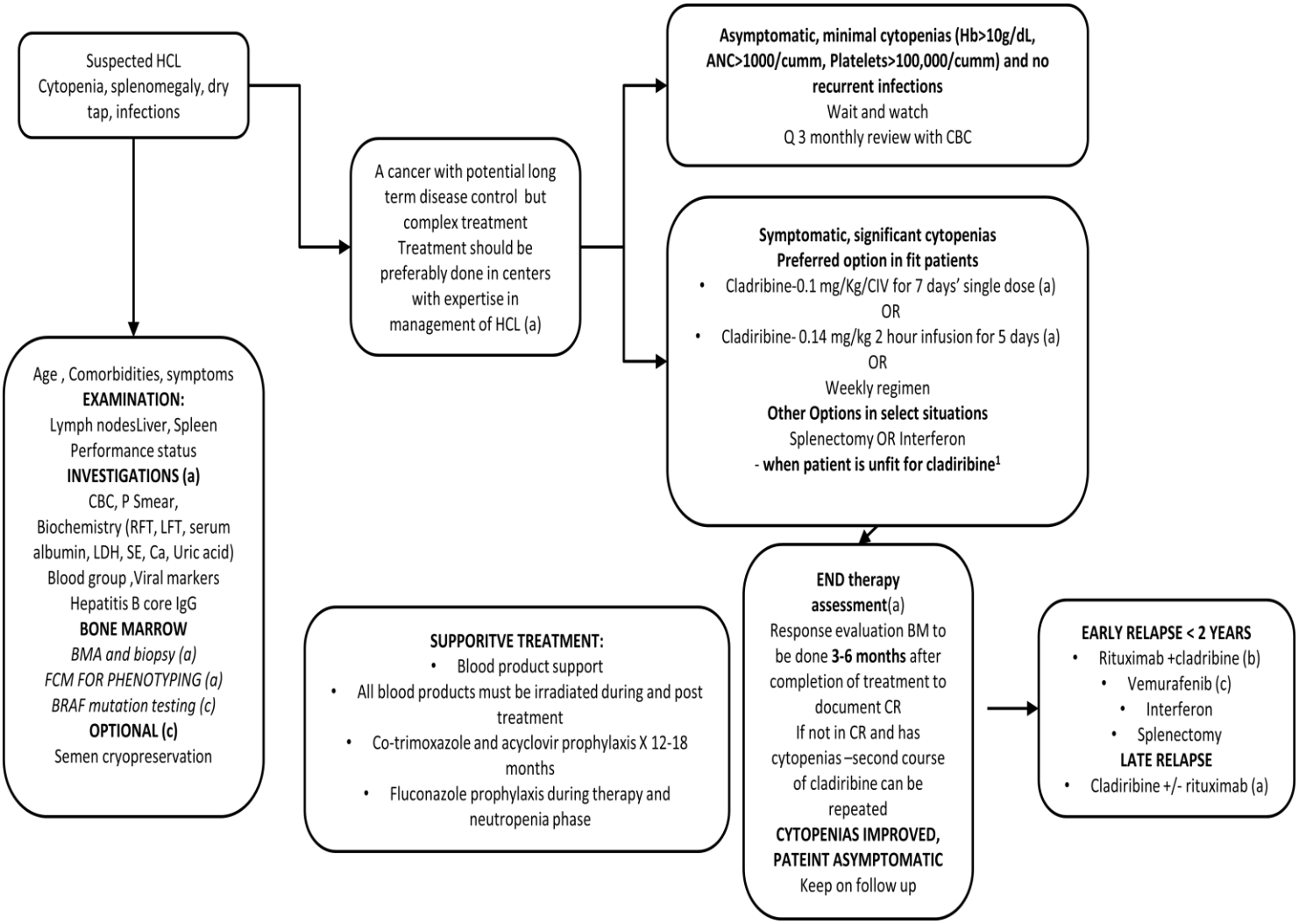
- **Important: Measurement of ANC nadir based on twice weekly CBC only (3 days apart). Only use twice weekly CBC for dose-adjustment, even if additional CBC's are obtained.**

- ****Please Note: This does not apply to patients who have low platelets at baseline due to lymphoma or immune-mediated mechanism caused by lymphoma. In those cases, no delay or dose reduction is required. The dose adjustments for these patients will be based solely on the ANC nadir and the PI or designee's clinical judgment.**

6.2 Table of doses per level for adjusted agents:

Drugs	Drug Doses per Dose Levels							
	-2	-1	1	2	3	4	5	6
Doxorubicin (mg/m^2/day)	10	10	10	12	14.4	17.3	20.7	24.8
Etoposide (mg/m^2/day)	50	50	50	60	72	86.4	103.7	124.4
Cyclophosphamide (mg/m^2/day)	480	600	750	900	1080	1296	1555	1866

HAIRY CELL LEUKEMIA (HCL-1)



HAIRY CELL LEUKEMIA (HCL-1)

SYMPTOMATIC, SIGNIFICANT CYTOPENIAS

PREFERRED OPTION IN FIT PATIENTS

CLADRIBINE-0.1 MG/KG/CIV FOR 7 DAYS' single dose

OR

CLADIRIBINE- 0.14 MG/KG 2 hour infusion for 5 days

OR

WEEKLY REGIMEN

OTHER OPTIONS IN SELECT SITUATIONS

SPLENECTOMY OR INTERFERON

WHEN PATIENT IS UNFIT FOR CLADIRIBINE[1]

EARLY RELAPSE < 2 YEARS

RITUXIMAB +CLADRIBINE

RITUXIMAB 375 mg/m2 IV Infusion Day 1 ONLY of each cycle
+ CLADRIBINE-0.1 MG/KG/CIV FOR 7 DAYS' single dose

OR
CLADIRIBINE- 0.14 MG/KG 2 HOUR infusion for 5 days
OR
VEMURAFENIB
OR
INTERFERON ALPHA 2MU/M2 IM/SC 3 TIMES A WEEK FOR UPTO 6MONTHS
OR
SPLENECTOMY
LATE RELAPSE
CLADIRIBINE +/- RITUXIMAB
CLADRIBINE-0.1 MG/KG/CIV FOR 7 DAYS' single dose
OR
CLADIRIBINE- 0.14 MG/KG 2 HOUR infusion for 5 days
+/-

RITUXIMAB 375 mg/m2 IV Infusion Day 1 ONLY of each cycle

WALDENSTROMS MACROGLOBULINEMIA (WM)/ LYMPHOPLASMACYTIC LYMPHOMA (LPL)

WM
B symptoms, Hyperviscosity, adenopathy, hepatosplenomegaly, cryoglobulinemia, vasculitis, amyloidosis.

Asymptomatic → **Observation**

Age , Comorbidities, symptoms
INVESTIGATIONS (a)
CBC, P Smear,
Biochemistry (RFT, LFT, serum albumin, LDH, SE, Ca, PO4, Uric acid)
Blood group ,Viral markers
Hepatitis B core Ig G
Coomb's test
LYMPH NODE BIOPSY (IF LN PRESENT and no other site involved like BM)
HPE examination (a)
IHC and molecular
As per annexure 2,3 (a)
MONOCLONAL PROTEIN
Serum electropheroresis (A)
Serum IFE (a)
Quantitative immunoglobulins (a)
BONE MARROW BIOPSY
FOR ALL PATIENTS (a)
STAGING (a)
CECT CHEST, ABDOMEN, PELVIS WITH BONE MARROW (a)
SPECIAL INVESTIGATIONS
ECG (a)
ECHOcardiogram (a)
OPTIONAL (c)
Beta-2 macroglobulin
MYD88 mutation study
Cold agglutinin titers
Viscosity

Symptomatic
Cytopenias, hyperviscosity, Bulky lymphadenopathy, Symptomatic organomegaly,Peripheral neuropathy Cold agglutinin anemia, hemolytic anemia, symptomatic cryoglobulinemia, cytopenias(Hb<10 g/dL, Platelets<100,000/cumm), B symptoms, Amyloidosis, recurrent infections, nephropathy

→ Immediate control required due to Bulky disease or cytopenias with significant IgM (risk of flare)- R-Bendamustine* (a)/ BDR (Bortezomib/Dexamethasone/Rituximab) (a)/ Ibrutinib-Rituximab regimen. (c)
Peripheral neuropathy – DRC (a), BR (a)
Immediate control not required- DRC(a), BDR (a) BR (a)
Plasmapheresis(b) -if Ig M flare
Ibrutinib-Rituximab regimen. (c)

Investigations during treatment
-Complete blood counts (a) prior to each chemotherapy dose and RFT +LFT at least once a month (b)
-CECT ABDOMEN AND PELVIS AFTER 4-6 CYCLES –if bulky Lymphadenopathy
- MEASUREMENT OF SERUM M PROTEIN AFTER 4 TO 6 CYCLES

-FLARE REACTION: *For patients with significantly raised viscosity, rituximab may cause a transient rise in the paraprotein (and therefore viscosity) and / or a flare of paraprotein-associated symptoms such as neuropathy. In these patients, consider plasma exchange immediately before giving first cycle (or using DC initially, adding in the rituximab once the paraprotein is reducing/total IgM < 4).

Anti-HCV therapy is helpful in patients with HCV infection

WALDENSTROMS MACROGLOBULINEMIA (WM)/ LYMPHOPLASMACYTIC LYMPHOMA (LPL)

IMMEDIATE CONTROL REQUIRED DUE TO BULKY DISEASE OR CYTOPENIAS WITH SIGNIFICANT IGM (RISK OF FLARE)- BR

RITUXIMAB 375 mg/m2 IV on Day 1 ONLY
BENDAMUSTINE 70 mg/ IV Infusion NS/ 500ml /1 hr Day1 – Day2

OR

BDR (BORTEZOMIB/DEXAMETHASONE/RITUXIMAB)

BORTEZOMIB (CYCLE 1- ONLY BZ) 1.3 MG/M2 (= MG) ON DAY 1, 4, 8, 11. 21- DAYS CYCLE SUBCUTANEOUS* /IV
CYCLE 2 ONWARDS
INJ AVIL 1 AMP IV + TAB CROCIN 750 MG PO 30 MIN BEFORE RITUXIMAB
BORTEZOMIB (CYCLE 2- CYCLE 5) 1.6 MG/M2 ON DAYS 1, 8, 15, 22 SUBCUTANEOUS* /IV
RITUXIMAB (CYCLE 2 AND 5) 375 MG/M2/DAY ON DAYS 1, 8, 15, 22*
DEXAMETHASONE (CYCLE 2 AND 5) 40 MG ON DAYS 1, 8, 15, 22 INTRAVENOUS IN 100 ML NS OVER 20 MIN
OR

IBRUTINIB-RITUXIMAB REGIMEN.

IBRUTINIB 420 MG (Dose/BSA) 140 mg capsules x 3 P.O 30 min before or 2 hrs after food

RITUXIMAB 375 mg/m2 IV Infusion

PERIPHERAL NEUROPATHY –

DRC-3WEEKLY CYCLE FOR MAX 8 CYCLES

CYCLE-1

CYCLOPHOSPHAMIDE 100MG/M2 TWICE A DAY D1-D5 ORALLY

DEXAMETHASONE 2OMG ONCE A DAY IV /ORAL D1

RITUXIMAB 375 mg/m2 IV on Day 1 , 325MG/M2 IV D2 (OMIT RITUXIMAB IF GIM >4GM)

CYCLE-2 TO CYCLE-8

CYCLOPHOSPHAMIDE 100MG/M2 TWICE A DAY D1-D5 ORALLY

DEXAMETHASONE 2OMG ONCE A DAY IV /ORAL D1

RITUXIMAB 375 mg/m2 IV on Day 1 , 325MG/M2 IV D2 (OMIT RITUXIMAB IF GIM >4GM)

OR

BENDAMUSTINERITUXIMAB

RITUXIMAB 375 mg/m2 IV on Day 1 ONLY
BENDAMUSTINE 70 mg/ IV Infusion NS/ 500ml /1 hr Day1 – Day2

IMMEDIATE CONTROL NOT REQUIRED

DRC 3WEEKLY CYCLE FOR MAX 8 CYCLES

CYCLE-1

CYCLOPHOSPHAMIDE 100MG/M2 TWICE A DAY D1-D5 ORALLY

DEXAMETHASONE 2OMG ONCE A DAY IV /ORAL D1

RITUXIMAB 375 mg/m2 IV on Day 1 , 325MG/M2 IV D2 (OMIT RITUXIMAB IF GIM >4GM)

CYCLE-2 TO CYCLE-8

CYCLOPHOSPHAMIDE 100MG/M2 TWICE A DAY D1-D5 ORALLY

DEXAMETHASONE 2OMG ONCE A DAY IV /ORAL D1

RITUXIMAB 375 mg/m2 IV on Day 1 , 325MG/M2 IV D2 (OMIT RITUXIMAB IF GIM >4GM)

OR

BDR (BORTEZOMIB/DEXAMETHASONE/RITUXIMAB)

BORTEZOMIB (CYCLE 1- ONLY BZ) 1.3 MG/M2 (= MG) ON DAYS 1,4,8,11. 21- DAYS CYCLE SUBCUTANEOUS* /IV
CYCLE 2 ONWARDS
INJ AVIL 1 AMP IV + TAB CROCIN 750 MG PO 30 MIN BEFORE RITUXIMAB
BORTEZOMIB (CYCLE 2- CYCLE 5) 1.6 MG/M2 ON DAYS 1, 8, 15, 22 SUBCUTANEOUS* /IV
RITUXIMAB (CYCLE 2 AND 5) 375 MG/M2/DAY ON DAYS 1, 8, 15, 22*
DEXAMETHASONE (CYCLE 2 AND 5) 40 MG ON DAYS 1, 8, 15, 22 INTRAVENOUS IN 100 ML NS OVER 20 MIN
OR

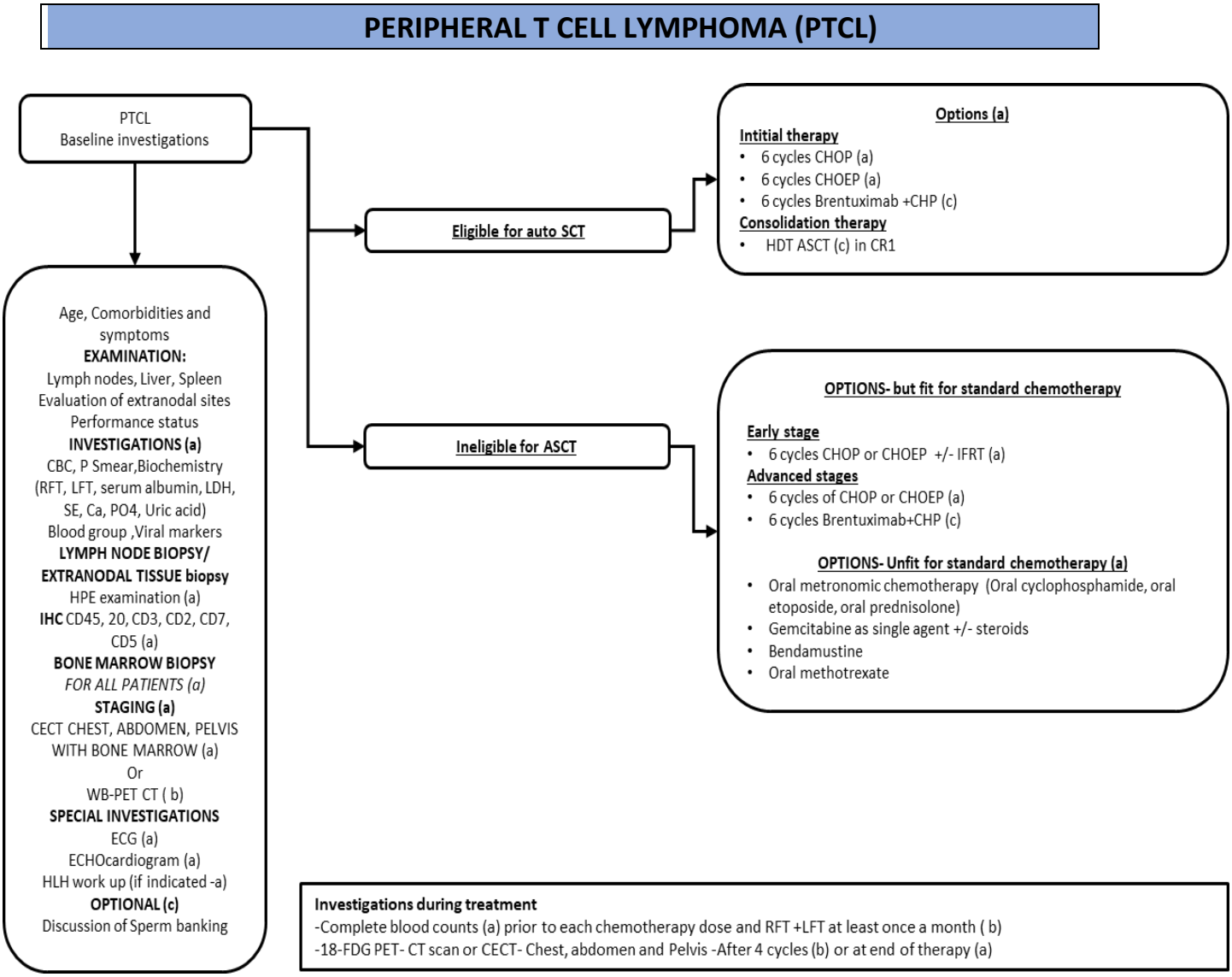
BENDAMUSTINERITUXIMAB

RITUXIMAB 375 mg/m2 IV on Day 1 ONLY
BENDAMUSTINE 70 mg/ IV Infusion NS/ 500ml /1 hr Day1 – Day2

PLASMAPHERESIS -IF IG M FLARE

IBRUTINIB-RITUXIMAB REGIMEN

IBRUTINIB 420 MG (Dose/BSA) 140 mg capsules x 3 P.O 30 min before or 2 hrs after food
RITUXIMAB 375 mg/m2 IV Infusion on Day 1



PERIPHERAL T CELL LYMPHOMA (PTCL)

ELIGIBLE FOR AUTO SCT

INTITIAL THERAPY

CHOP X 6

Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Inj. VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5
OR

CHOEP 6 CYCLES

CYCLOPHOSPHAMIDE 750MG/M2 IV INFUSION NS/100ML/20 MIN D 1
ADRIAMYCIN 50 MG/M2IV INFUSION NS/250 ML/20 MIN D1
VINCRISTINE 1.4 MG/M2 (2 MG MAX) IV INFUSION D1
CAP ETOPOSIDE 65 MG/ M2 PO OD D1 TO 3
TAB. PREDNISOLONE 100 MG PO AFTER BREAKFAST D 1 TO 5
OR

BRENTUXIMAB +CHP # 6

BRENTUXIMAB 1.8 MG/KG IN 150 ML SODIUM CHLORIDE 0.9% (FINAL CONCENTRATION 0.4-1.2 MG/ML) IV INFUSION OVER 30 MINUTES (MAXIMUM DOSE: 180 MG)
+

CHP

Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

CONSOLIDATION THERAPY

HDT ASCT in CR1

INELIGIBLE FOR ASCT

EARLY STAGE

CHOP X 6

Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Inj. VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5
OR

CHOEP

CYCLOPHOSPHAMIDE 750MG/M2 IV INFUSION NS/100ML/20 MIN D 1
ADRIAMYCIN 50 MG/M2IV INFUSION NS/250 ML/20 MIN D1
VINCRISTINE 1.4 MG/M2 (2 MG MAX) IV INFUSION D1
CAP ETOPOSIDE 65 MG/ M2 PO OD D1 TO 3
TAB. PREDNISOLONE 100 MG PO AFTER BREAKFAST D 1 TO 5
+/- IFRT

ADVANCED STAGES

CHOP X 6

INJ. CYCLOPHOSPHAMIDE 750MG/M2 IV INFUSION NS/500ML/20 MIN ON DAY 1
INJ. ADRIAMYCIN 50 MG/M2 IV INFUSION NS/250ML /20 MIN ON DAY 1
INJ. VINCRISTINE 1.4 MG/M2 (2MG MAX) IV PUSH ON DAY 1
TAB PREDNISOLONE 100 MG PO AFTER BREAKFAST DAY 1 TO 5
OR

CHOEP

CYCLOPHOSPHAMIDE 750MG/M2 IV INFUSION IN 100ML NS OVER 20 MIN D 1
ADRIAMYCIN 50 MG/M2 IV INFUSION 250 ML NS OVER 20 MIN D 1
VINCRISTINE 1.4 MG/M2 (2 MG MAX) IV INFUSION D1
CAP ETOPOSIDE 65 MG/ M2 PO OD D1 TO 3
TAB. PREDNISOLONE 100 MG PO AFTER BREAKFAST D 1 TO 5

OR

BRENTUXIMAB+CHP x 6 Cycles

BRENTUXIMAB 1.8 MG/KG IN 150 ML SODIUM CHLORIDE 0.9% (FINAL CONCENTRATION 0.4-1.2 MG/ML) IV INFUSION OVER 30 MINUTES (MAXIMUM DOSE: 180 MG)
+

CHP

Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

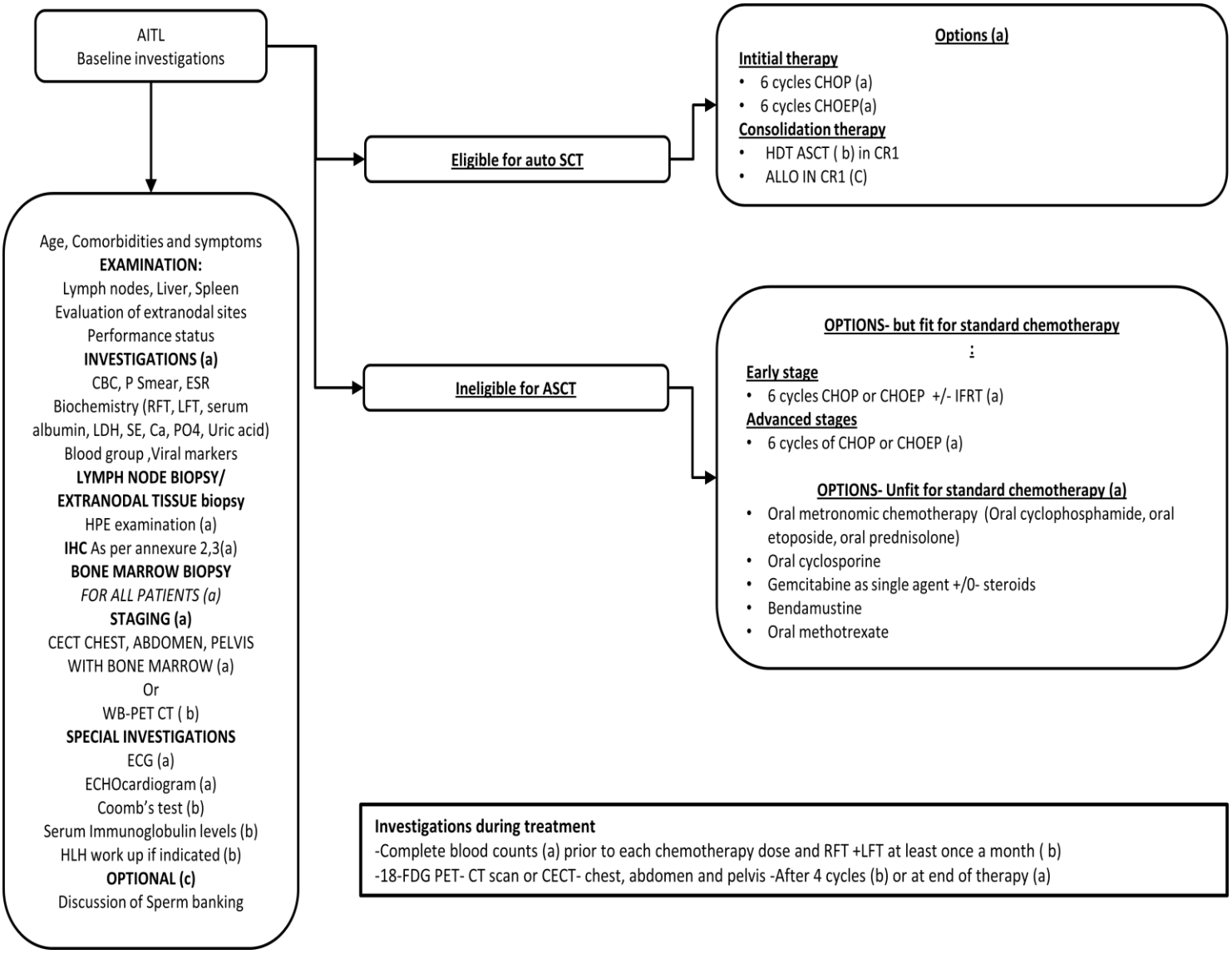
UNFIT FOR STANDARD CHEMOTHERAPY

ORAL METRONOMIC CHEMOTHERAPY (ORAL CYCLOPHOSPHAMIDE, ORAL ETOPOSIDE, ORAL PREDNISOLONE)
OR

GEMCITABINE AS SINGLE AGENT +/- STEROIDS
GEMCITABINE 1 GM/M2 IV INFUSION NS/500 ML/30 MIN DAY 1 AND 8
+/- STEROIDS
TAB DEXAMETHASONE 40 MG PO OD AFTER BREAKFAST DAY 1 TO DAY 4

OR
BENDAMUSTINE
BENDAMUSTINE 70 mg/ IV Infusion NS/ 500ml /1 hr Day1 – Day2
OR
ORAL METHOTREXATE

ANGIOIMMUNOBLASTIC T CELL LYMPHOMA (AITL)



ANGIOIMMUNOBLASTIC T CELL LYMPHOMA (AITL)

ELIGIBLE FOR AUTO SCT

INTITIAL THERAPY

CHOP X 6

Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Inj. VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5
OR

CHOEP 6 CYCLES

CYCLOPHOSPHAMIDE 750MG/M2 IV INFUSION NS/100ML/20 MIN D 1
ADRIAMYCIN 50 MG/M2IV INFUSION NS/250 ML/20 MIN D1
VINCRISTINE 1.4 MG/M2 (2 MG MAX) IV INFUSION D1
CAP ETOPOSIDE 65 MG/ M2 PO OD D1 TO 3
TAB. PREDNISOLONE 100 MG PO AFTER BREAKFAST D 1 TO 5
OR

BRENTUXIMAB +CHP # 6

BRENTUXIMAB 1.8 MG/KG IN 150 ML SODIUM CHLORIDE 0.9% (FINAL CONCENTRATION 0.4-1.2 MG/ML) IV INFUSION OVER 30 MINUTES (MAXIMUM DOSE: 180 MG)
+

CHP

Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

CONSOLIDATION THERAPY

HDT ASCT in CR1

INELIGIBLE FOR ASCT

EARLY STAGE

CHOP X 6

Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Inj. VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

OR

CHOEP

CYCLOPHOSPHAMIDE 750MG/M2 IV INFUSION NS/100ML/20 MIN D 1
ADRIAMYCIN 50 MG/M2IV INFUSION NS/250 ML/20 MIN D1
VINCRISTINE 1.4 MG/M2 (2 MG MAX) IV INFUSION D1
CAP ETOPOSIDE 65 MG/ M2 PO OD D1 TO 3
TAB. PREDNISOLONE 100 MG PO AFTER BREAKFAST D 1 TO 5

+/- IFRT

ADVANCED STAGES

CHOP X 6

INJ. CYCLOPHOSPHAMIDE 750MG/M2 IV INFUSION NS/500ML/20 MIN ON DAY 1
INJ. ADRIAMYCIN 50 MG/M2 IV INFUSION NS/250ML /20 MIN ON DAY 1
INJ. VINCRISTINE 1.4 MG/M2 (2MG MAX) IV PUSH ON DAY 1
TAB PREDNISOLONE 100 MG PO AFTER BREAKFAST DAY 1 TO 5
OR

CHOEP

CYCLOPHOSPHAMIDE 750MG/M2 IV INFUSION IN 100ML NS OVER 20 MIN D 1
ADRIAMYCIN 50 MG/M2 IV INFUSION 250 ML NS OVER 20 MIN D 1
VINCRISTINE 1.4 MG/M2 (2 MG MAX) IV INFUSION D1
CAP ETOPOSIDE 65 MG/ M2 PO OD D1 TO 3
TAB. PREDNISOLONE 100 MG PO AFTER BREAKFAST D 1 TO 5

OR

BRENTUXIMAB+CHP x 6 Cycles

BRENTUXIMAB 1.8 MG/KG IN 150 ML SODIUM CHLORIDE 0.9% (FINAL CONCENTRATION 0.4-1.2 MG/ML) IV INFUSION OVER 30 MINUTES (MAXIMUM DOSE: 180 MG)
+

CHP

Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

UNFIT FOR STANDARD CHEMOTHERAPY

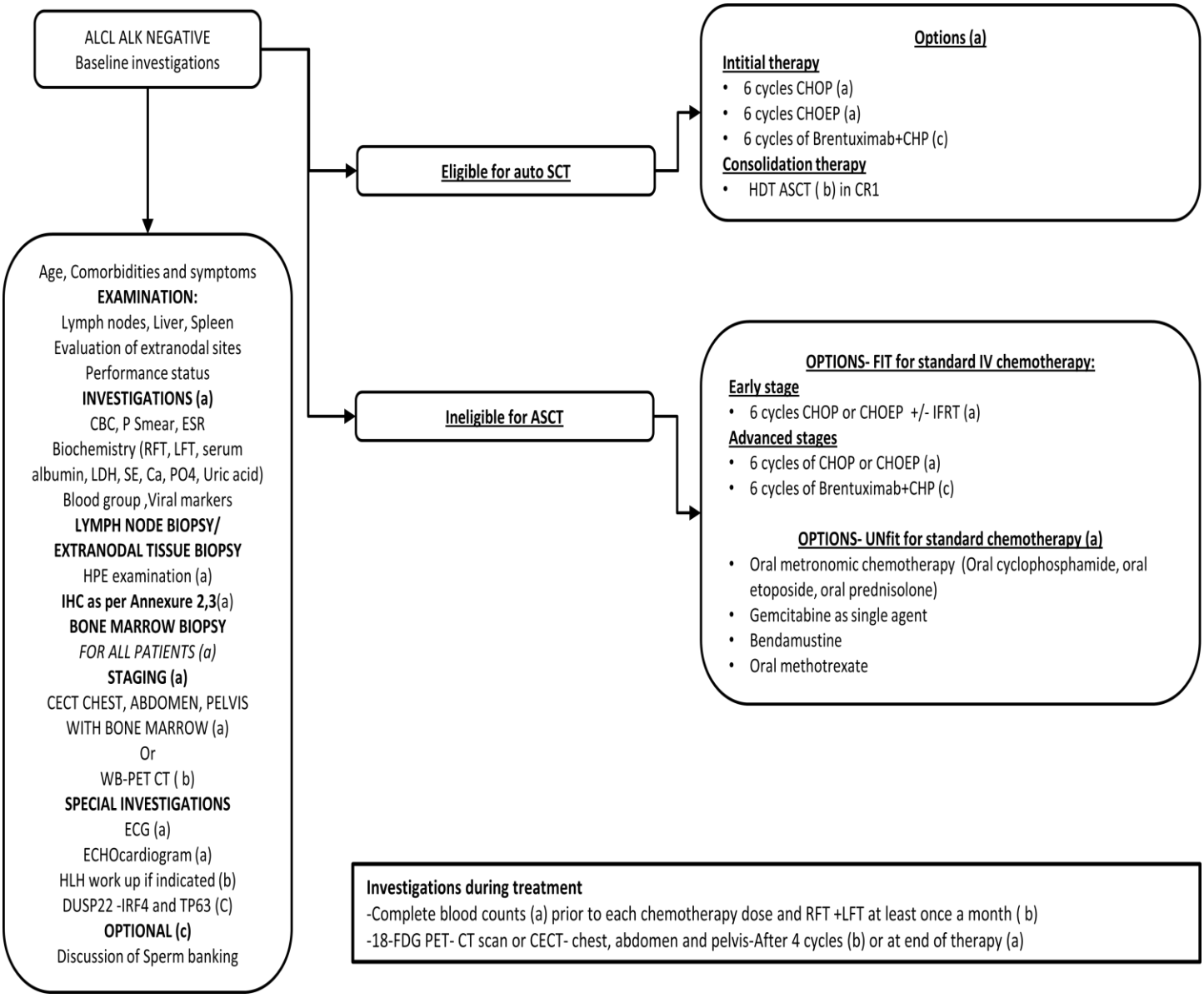
ORAL METRONOMIC CHEMOTHERAPY (ORAL CYCLOPHOSPHAMIDE, ORAL ETOPOSIDE, ORAL PREDNISOLONE)
OR

GEMCITABINE AS SINGLE AGENT +/- STEROIDS
GEMCITABINE 1 GM/M2 IV INFUSION NS/500 ML/30 MIN DAY 1 AND 8
+/- STEROIDS
TAB DEXAMETHASONE 40 MG PO OD AFTER BREAKFAST DAY 1 TO DAY 4

OR
BENDAMUSTINE
BENDAMUSTINE 70 mg/ IV Infusion NS/ 500ml /1 hr Day1 – Day2

OR
ORAL METHOTREXATE

ANAPLASTIC LARGE CELL LYMPHOMA ALK –VE (ALCL-1)



Investigations during treatment

-Complete blood counts (a) prior to each chemotherapy dose and RFT +LFT at least once a month (b)

-18-FDG PET- CT scan or CECT- chest, abdomen and pelvis-After 4 cycles (b) or at end of therapy (a)

ANAPLASTIC LARGE CELL LYMPHOMA ALK –VE (ALCL-1)

ELIGIBLE FOR AUTO SCT

INTITIAL THERAPY

CHOP X 6

Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Inj. VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5
OR

CHOEP 6 CYCLES

CYCLOPHOSPHAMIDE 750MG/M2 IV INFUSION NS/100ML/20 MIN D 1
ADRIAMYCIN 50 MG/M2IV INFUSION NS/250 ML/20 MIN D1
VINCRISTINE 1.4 MG/M2 (2 MG MAX) IV INFUSION D1
CAP ETOPOSIDE 65 MG/ M2 PO OD D1 TO 3
TAB. PREDNISOLONE 100 MG PO AFTER BREAKFAST D 1 TO 5
OR

BRENTUXIMAB +CHP # 6

BRENTUXIMAB 1.8 MG/KG IN 150 ML SODIUM CHLORIDE 0.9% (FINAL CONCENTRATION 0.4-1.2 MG/ML) IV INFUSION OVER 30 MINUTES (MAXIMUM DOSE: 180 MG)
+

CHP

Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

CONSOLIDATION THERAPY

HDT ASCT in CR1

INELIGIBLE FOR ASCT

EARLY STAGE

CHOP X 6

Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Inj. VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

OR

CHOEP

CYCLOPHOSPHAMIDE 750MG/M2 IV INFUSION NS/100ML/20 MIN D 1
ADRIAMYCIN 50 MG/M2IV INFUSION NS/250 ML/20 MIN D1
VINCRISTINE 1.4 MG/M2 (2 MG MAX) IV INFUSION D1
CAP ETOPOSIDE 65 MG/ M2 PO OD D1 TO 3
TAB. PREDNISOLONE 100 MG PO AFTER BREAKFAST D 1 TO 5

+/- IFRT

ADVANCED STAGES

CHOP X 6

INJ. CYCLOPHOSPHAMIDE 750MG/M2 IV INFUSION NS/500ML/20 MIN ON DAY 1
INJ. ADRIAMYCIN 50 MG/M2 IV INFUSION NS/250ML /20 MIN ON DAY 1
INJ. VINCRISTINE 1.4 MG/M2 (2MG MAX) IV PUSH ON DAY 1
TAB PREDNISOLONE 100 MG PO AFTER BREAKFAST DAY 1 TO 5
OR

CHOEP

CYCLOPHOSPHAMIDE 750MG/M2 IV INFUSION IN 100ML NS OVER 20 MIN D 1
ADRIAMYCIN 50 MG/M2 IV INFUSION 250 ML NS OVER 20 MIN D 1
VINCRISTINE 1.4 MG/M2 (2 MG MAX) IV INFUSION D1
CAP ETOPOSIDE 65 MG/ M2 PO OD D1 TO 3
TAB. PREDNISOLONE 100 MG PO AFTER BREAKFAST D 1 TO 5

OR

BRENTUXIMAB+CHP x 6 Cycles

BRENTUXIMAB 1.8 MG/KG IN 150 ML SODIUM CHLORIDE 0.9% (FINAL CONCENTRATION 0.4-1.2 MG/ML) IV INFUSION OVER 30 MINUTES (MAXIMUM DOSE: 180 MG)
+

CHP

Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

UNFIT FOR STANDARD CHEMOTHERAPY

ORAL METRONOMIC CHEMOTHERAPY (ORAL CYCLOPHOSPHAMIDE, ORAL ETOPOSIDE, ORAL PREDNISOLONE)
OR

GEMCITABINE AS SINGLE AGENT +/- STEROIDS
GEMCITABINE 1 GM/M2 IV INFUSION NS/500 ML/30 MIN DAY 1 AND 8
+/- STEROIDS
TAB DEXAMETHASONE 40 MG PO OD AFTER BREAKFAST DAY 1 TO DAY 4

OR
BENDAMUSTINE
BENDAMUSTINE 70 mg/ IV Infusion NS/ 500ml /1 hr Day1 – Day2

OR
ORAL METHOTREXATE

ANAPLASTIC LARGE CELL LYMPHOMA ALK +VE(ALCL-2)

ALCL ALK POSITIVE
Baseline investigations

Age, Comorbidities and symptoms
EXAMINATION:
Lymph nodes, Liver, Spleen
Evaluation of extranodal sites
Performance status
INVESTIGATIONS (a)
CBC, P Smear,Biochemistry (RFT, LFT, serum albumin, LDH, SE, Ca, PO4, Uric acid)
Blood group ,Viral markers
LYMPH NODE BIOPSY/ EXTRANODAL TISSUE BIOSPY
HPE examination (a)
IHC CD45, 20, CD3, CD2, CD7, CD5. ALK, CD30 (a)
BONE MARROW BIOPSY
FOR ALL PATIENTS (a)
STAGING (a)
CECT CHEST, ABDOMEN, PELVIS WITH BONE MARROW (a)
Or
WB-PET CT (b)
SPECIAL INVESTIGATIONS
ECG (a)
HLH work up if indicated (b)
OPTIONAL (c)
Discussion of Sperm banking

Early stage I, II

Options (a)

Intitial therapy
- 6 cycles CHOP (a)
- 6 cycles CHOEP (a)

Advanced stage III, IV

Options (a)

Advanced stages
- 6 cycles of CHOP or CHOEP (a)
- 6 cycles of Brentuximab+CHP (c)

OPTIONS- Unfit for standard chemotherapy
- Oral metronomic chemotherapy (Oral cyclophosphamide, oral etoposide, oral prednisolone) (a)
- Oral cyclosporine (a)
- Gemcitabine (a)
- Bendamustine (a)
- Oral methotrexate (a)
- ALK inhibitors: Crizotinib or ceritiinib (c)

Investigations during treatment
-Complete blood counts (a) prior to each chemotherapy dose and RFT +LFT at least once a month (b)
-18-FDG PET- CT scan or CECT- chest, abdomen and pelvis -After 4 cycles (b) or at end of therapy (a)

ANAPLASTIC LARGE CELL LYMPHOMA ALK +VE(ALCL-2)

EARLY STAGE I, II

CHOP X 6

Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Inj. VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5
OR

CHOEP 6 CYCLES

CYCLOPHOSPHAMIDE 750MG/M2 IV INFUSION NS/100ML/20 MIN D 1
ADRIAMYCIN 50 MG/M2IV INFUSION NS/250 ML/20 MIN D1
VINCRISTINE 1.4 MG/M2 (2 MG MAX) IV INFUSION D1
CAP ETOPOSIDE 65 MG/ M2 PO OD D1 TO 3
TAB. PREDNISOLONE 100 MG PO AFTER BREAKFAST D 1 TO 5

ADVANCED STAGE III, IV

CHOP X 6

Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Inj. VINCRISTINE 1.4 mg/m2 (2mg max) IV push on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

OR

CHOEP

CYCLOPHOSPHAMIDE 750MG/M2 IV INFUSION NS/100ML/20 MIN D 1
ADRIAMYCIN 50 MG/M2IV INFUSION NS/250 ML/20 MIN D1
VINCRISTINE 1.4 MG/M2 (2 MG MAX) IV INFUSION D1
CAP ETOPOSIDE 65 MG/ M2 PO OD D1 TO 3
TAB. PREDNISOLONE 100 MG PO AFTER BREAKFAST D 1 TO 5

OR

6 CYCLES OF BRENTUXIMAB+CHP

BRENTUXIMAB 1.8 MG/KG IN 150 ML SODIUM CHLORIDE 0.9% (FINAL CONCENTRATION 0.4-1.2 MG/ML) IV INFUSION OVER 30 MINUTES (MAXIMUM DOSE: 180 MG)
+

CHP

Inj. CYCLOPHOSPHAMIDE 750mg/m2 IV infusion NS/500ml/20 min on Day 1
Inj. ADRIAMYCIN 50 mg/m2 IV infusion NS/250ml /20 min on Day 1
Tab PREDNISOLONE 100 mg PO After Breakfast DAY 1 to 5

UNFIT FOR STANDARD CHEMOTHERAPY

ORAL METRONOMIC CHEMOTHERAPY (PEP-C)
PREDNISOLONE 20MG PO OD
ETOPOSIDE 50MG PO OD
PROCARBAZINE 50MG PO OD
Induction (1 cycle): Once daily until WBC less than 3 x 109 /L then hold cyclophosphamide, etoposide and procarbazine until Maintenance begins Maintenance starts at count recovery (until disease progression or unacceptable toxicity): Cycle length determined by blood counts predniSONE starts with Induction and is taken continuously throughout

OR

ORAL CYCLOSPORINE 75MG PO ONCE A DAY STARTING DOSE TO ESCALATE DOSE IF NO RESPONSE

OR

GEMCITABINE

GEMCITABINE 1 GM/M2 IV INFUSION NS/500 ML/30 MIN DAY 1 AND 8
OR

BENDAMUSTINE

BENDAMUSTINE 70 mg/ IV Infusion NS/ 500ml /1 hr Day1 – Day2

OR

ORAL METHOTREXATE

OR

ALK INHIBITORS: CRIZOTINIB 280MG/M2 TWICE DAILY OR CERITIINIB 750MG/DAY

NK T CELL LYMPHOMA (NKT-1)

NKT cell lymphoma
Nasal mass , epistaxis , nasal blockage , headache , Hearing loss , facial pain , fever, night sweats, weight loss, lymphadenopathy, altered bowel habits , soft tissue masses , skin lesions.

Age, Comorbidities and symptoms
EXAMINATION:
Lymph nodes, Liver, Spleen
Evaluation of extranodal sites, nasal endoscopy
Performance status
INVESTIGATIONS (a)
CBC, P Smear, Biochemistry (RFT, LFT, serum albumin, LDH, SE, Ca, PO4, Uric acid)
Blood group ,Viral markers, Hepatitis B –core Ig G
LYMPH NODE BIOPSY/ EXTRANODAL TISSUE Biopsy
HPE examination (a)
IHC CD45, 20, CD3, CD2, CD7, CD5. ALK, CD30 (a)
BONE MARROW BIOPSY
FOR ALL PATIENTS (a)
STAGING (a)
CECT NECK, CHEST, ABDOMEN, PELVIS WITH BONE MARROW (a)
Or
WB-PET CT (b)
SPECIAL INVESTIGATIONS
ECG (a)
ECHOcardiogram (a)
HLH work up if indicated (b)
EBER ISH on tissue or BM biopsy (c)
EBV DNA (c)
OPTIONAL (c)
Discussion of Sperm banking

Early stage I, II

Options (a)
Intitial therapy
- 4# SMILE followed by RT (a)
- DEVIC regimen or VIPD regimen with RT (a)

Advanced stage III, IV

Options (a)
6# SMILE +/- RT

Ineligible for HDMTX and SMILE

OPTIONS-
- 6# DDGP (a)
- 6# GEL OX (a)
- 2# LVP followed by RT followed by 4# LVP (a)

Investigations during treatment
-Complete blood counts (a) prior to each chemotherapy dose and RFT +LFT at least once a month (b)
-18-FDG PET- CT scan or CECT- chest , abdomen and pelvis After 4 cycles (b) or at end of therapy (a)
EBV DNA PCR post cycle 4 and 6 (c)

NK T CELL LYMPHOMA (NKT-1)

EARLY STAGE I, II

INTITIAL THERAPY

4# SMILE FOLLOWED BY RT

INJ PALANOSETRON 0.25 MG SLOW IV PUSH ON DAY -1
CAP APREPITANT 125 MG PO ON DAY 1 AND 80 MG PO ON D2 AND D3
INJ METHOTREXATE 2GM/M2IN 500 ML NS OVER 6 HRS ON D1 ONLY HYDRATION AT 3 L/M2/DAY FROM DAY 0 TILL DAY 4.
INJ LEUCOVORIN 15MG/M2 Q6H STARTING AT 24 HOUR FROM START OF METHOTREXATE TILL SERUM MTX < 0.25MMOL/L
INJ IFOSFAMIDE 1.5GM/M2 IN 500 ML NS OVER 2 HRS ON D2-D4
INJ MESNA 600MG/M2 0, 4, 8 HOURS OF IFOSFAMIDE ON D2-D4
INJ ETOPOSIDE 100MG/M2IN 500 ML NS OVER 1 HR ON D2-D4 , START AFTER 1 HR OF IFOSFAMIDE
INJ LEUNASE 6000 UNITS/M2DEEP IM ON D8/D10/D12/D14/D16/D18/D20
TAB DEXAMETHASONE 40MG PO OD ON D1-D4
INJ GCSF 5 MG/KG SC OD FROM D-6 ONWARDS TILL WBC > 5000 /ML.
+

RADIATION

DEVIC REGIMEN OR VIPD REGIMEN WITH RT

2/3 DEVIC

DEXAMETHASONE 40MG IV/PO DAY 1-3

ETOPOSIDE 67MG/2 IV DAY1-3

CISPLATIN 33MG/M2 IV DAY1-3

CARBOPLATIN 200MG/M2 IV DAY1

VIDP

ETOPOSIDE 100MG/M2 D1-D3

IFOSFOMIDE 1200MG/M2 IV DAY1-3

CISPLATIN 33MG/M2 IV DAY1-3

DEXAMETHASONE 40MG IV/PO DAY 1-3

ADVANCED STAGE III, IV

6# SMILE

INJ PALANOSETRON 0.25 MG SLOW IV PUSH ON DAY -1
CAP APREPITANT 125 MG PO ON DAY 1 AND 80 MG PO ON D2 AND D3
INJ METHOTREXATE 2GM/M2IN 500 ML NS OVER 6 HRS ON D1 ONLY HYDRATION AT 3 L/M2/DAY FROM DAY 0 TILL DAY 4.
INJ LEUCOVORIN 15MG/M2 Q6H STARTING AT 24 HOUR FROM START OF METHOTREXATE TILL SERUM MTX < 0.25MMOL/L
INJ IFOSFAMIDE 1.5GM/M2 IN 500 ML NS OVER 2 HRS ON D2-D4
INJ MESNA 600MG/M2 0, 4, 8 HOURS OF IFOSFAMIDE ON D2-D4
INJ ETOPOSIDE 100MG/M2IN 500 ML NS OVER 1 HR ON D2-D4 , START AFTER 1 HR OF IFOSFAMIDE
INJ LEUNASE 6000 UNITS/M2DEEP IM ON D8/D10/D12/D14/D16/D18/D20
TAB DEXAMETHASONE 40MG PO OD ON D1-D4
INJ GCSF 5 MG/KG SC OD FROM D-6 ONWARDS TILL WBC > 5000 /ML.
+ / -

RADIATION

INELIGIBLE FOR HDMTX AND SMILE

6# DDGP 3WEEKLY

DEXAMETHASONE 15MG/M2 IV/PO D1-D5

CISPLATIN 20MG/M2 IV DAY`1-4

GEMCITABINE 800 MG/M2 IV INFUSION NS/500 ML/30 MIN DAYS 1 AND 8
PEGASPARAGINASE 2500IU/M2 DAY 1

OR

GEL OX # 6

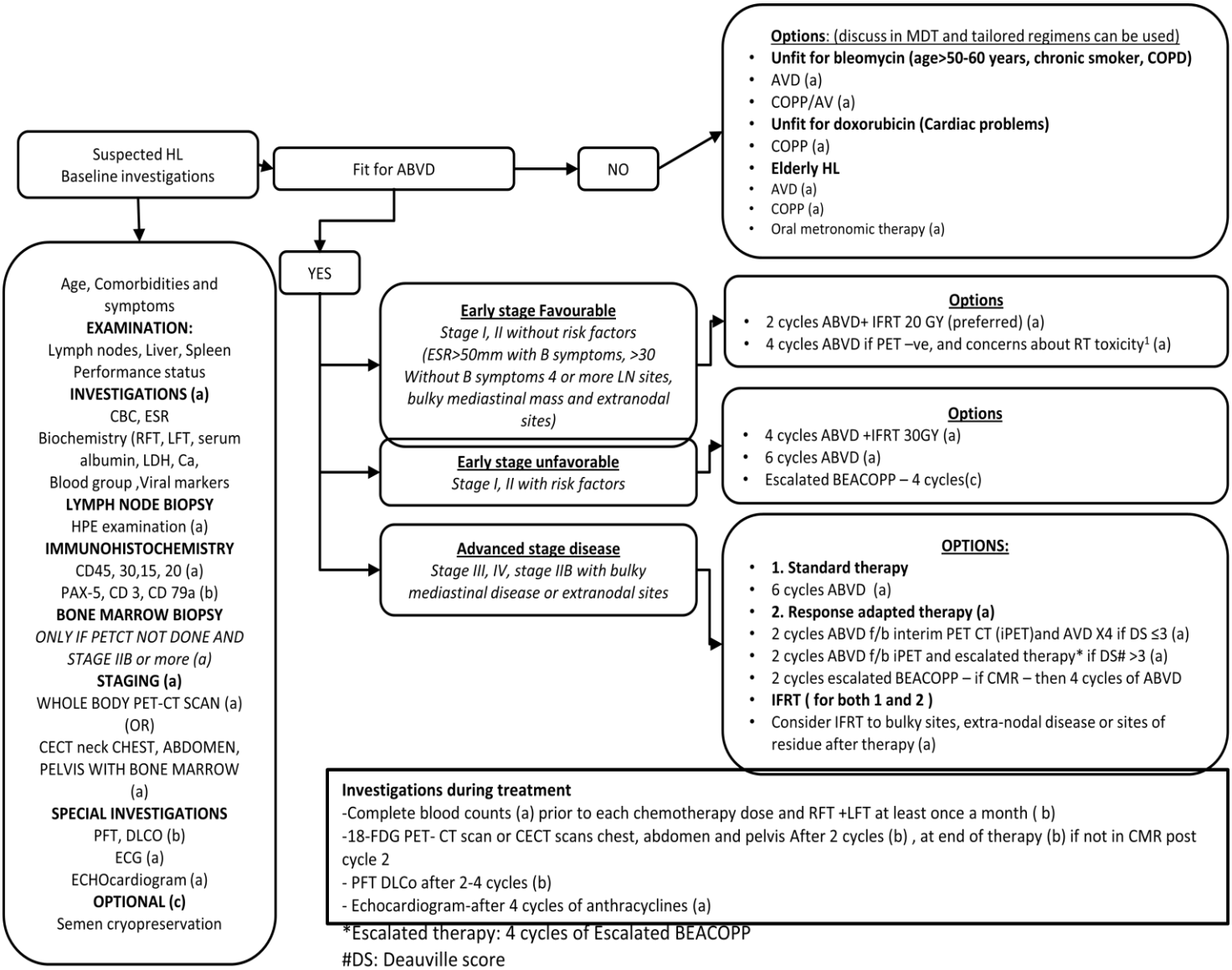
GEMCITABINE 1000 MG/M2 IV INFUSION NS/500 ML/30 MIN DAYS 1 AND 8
L-ASPARAGINASE 6000 U/M2 IM ON DAY 1 TO DAY-7
OXALIPLATIN 130 MG/M2 CONTINUOUS IV INFUSION 5% DW/500 ML/1 HOURS DAY1 ONLY
OR

2# LVP FOLLOWED BY RT FOLLOWED BY 4# LVP

LVP

L-ASPARAGINASE 6000 U/M2 IM ON DAY 1 TO DAY-5
VINCRISTINE 1.4MG/M2 DAY1
PREDNISOLONE 100MG PO OD DAY1-DAY5

HODGKIN'S LYMPHOMA (HL-1)- NEWLY DIAGNOSED HL



Investigations during treatment

-Complete blood counts (a) prior to each chemotherapy dose and RFT +LFT at least once a month (b)

-18-FDG PET- CT scan or CECT scans chest, abdomen and pelvis After 2 cycles (b) , at end of therapy (b) if not in CMR post cycle 2

- PFT DLCo after 2-4 cycles (b)
- Echocardiogram-after 4 cycles of anthracyclines (a)

*Escalated therapy: 4 cycles of Escalated BEACOPP

#DS: Deauville score

1. Eg. Mediastinal mass in a female- concerns about RT exposure to breast

HODGKIN'S LYMPHOMA (HL-1)- NEWLY DIAGNOSED HL

FIT FOR ABVD

EARLY STAGE FAVOURABLE STAGE I, II WITHOUT RISK FACTORS

(ESR>50MM WITH B SYMPTOMS, >30 WITHOUT B SYMPTOMS 4 OR MORE LN SITES, BULKY MEDIASTINAL MASS AND EXTRANODAL SITES)

ABVD X 2 CYCLES

ADRIAMYCIN 25mg/m2 IV infusion NS/100ml/10 min Day1,15
BLEOMYCIN 10 U/m2 IV Push Day1,15
VINBLASTINE 6 mg/m2 IV push Day1,15
DACARBAZINE 375 mg/m2 IV infusion NS/500ml/30 min Day1,15
+

IFRT 20 GY

OR

4 CYCLES ABVD IF PET –VE, AND CONCERNS ABOUT RT TOXICITY

ADRIAMYCIN 25mg/m2 IV infusion NS/100ml/10 min Day1,15
BLEOMYCIN 10 U/m2 IV Push Day1,15
VINBLASTINE 6 mg/m2 IV push Day1,15
DACARBAZINE 375 mg/m2 IV infusion NS/500ml/30 min Day1,15

EARLY STAGE UNFAVORABLE STAGE I, II WITH RISK FACTORS

ABVD X 4 CYCLES

ADRIAMYCIN 25mg/m2 IV infusion NS/100ml/10 min Day1,15
BLEOMYCIN 10 U/m2 IV Push Day1,15
VINBLASTINE 6 mg/m2 IV push Day1,15
DACARBAZINE 375 mg/m2 IV infusion NS/500ml/30 min Day1,15
+

IFRT 30GY

OR

ABVD X 6 CYCLES

ADRIAMYCIN 25mg/m2 IV infusion NS/100ml/10 min Day1,15
BLEOMYCIN 10 U/m2 IV Push Day1,15
VINBLASTINE 6 mg/m2 IV push Day1,15
DACARBAZINE 375 mg/m2 IV infusion NS/500ml/30 min Day1,15

OR

ESCALATED BEACOPP – 4 CYCLES

INJ PALONOSETRON 0.2MG IV D1 BEFORE CHEMOTHERAPY
INJ FOSAPREPITANT 150MG IV D1 BEFOR CHEMOTHERAPY
ETOPOSIDE 200MG/M2 IN 1L NS IV OVER 1 HOUR D1-D3
DOXORUBICIN 35MG/M2 IN 100ML NS IV OVER 30MIN D1
ENDOXAN 1250MG/M2 IN 500ML NS IV OVER 1 HOUR D1
MESNA 600MG/M2 IV AT 0, 3 HRS D1
CAP PROCARBAZINE 100MG/M2 ORALLY(ROUND DOSE TO NEAREST 50MG) D1-D7
TAB PREDNISOLONE 40MG/M2 ORALLY AFTER FOOD IN THE MORNING D1-D14
BLEOMYCIN 10MG/M2 IV IN 100ML NS OVER 1H D8
VINCRISTINE1.4MG/M2 (MAX 2MG) IV PUSH D8

ADVANCED STAGE DISEASE

STAGE III, IV, STAGE IIB WITH BULKY MEDIASTINAL DISEASE OR EXTRANODAL SITES

1. STANDARD THERAPY

ABVD 6 CYCLES

ADRIAMYCIN 25mg/m2 IV infusion NS/100ml/10 min Day1,15
BLEOMYCIN 10 U/m2 IV Push Day1,15
VINBLASTINE 6 mg/m2 IV push Day1,15
DACARBAZINE 375 mg/m2 IV infusion NS/500ml/30 min Day1,15

OR

RESPONSE ADAPTED THERAPY

OR

2 CYCLES ABVD F/B INTERIM PET CT (IPET) AND AVD X4 IF DS ≤3

ADRIAMYCIN 25mg/m2 IV infusion NS/100ml/10 min Day1,15
BLEOMYCIN 10 U/m2 IV Push Day1,15
VINBLASTINE 6 mg/m2 IV push Day1,15
DACARBAZINE 375 mg/m2 IV infusion NS/500ml/30 min Day1,15

OR

2 CYCLES ABVD F/B IPET AND ESCALATED THERAPY* IF DS# >3

ADRIAMYCIN 25mg/m2 IV infusion NS/100ml/10 min Day1,15
BLEOMYCIN 10 U/m2 IV Push Day1,15
VINBLASTINE 6 mg/m2 IV push Day1,15
DACARBAZINE 375 mg/m2 IV infusion NS/500ml/30 min Day1,15

OR

2 CYCLES ESCALATED BEACOPP – IF CMR – THEN 4 CYCLES OF ABVD

INJ PALONOSETRON 0.2MG IV D1 BEFORE CHEMOTHERAPY
INJ FOSAPREPITANT 150MG IV D1 BEFOR CHEMOTHERAPY
ETOPOSIDE 200MG/M2 IN 1L NS IV OVER 1 HOUR D1-D3
DOXORUBICIN 35MG/M2 IN 100ML NS IV OVER 30MIN D1
ENDOXAN 1250MG/M2 IN 500ML NS IV OVER 1 HOUR D1
MESNA 600MG/M2 IV AT 0, 3 HRS D1
CAP PROCARBAZINE 100MG/M2 ORALLY(ROUND DOSE TO NEAREST 50MG) D1-D7
TAB PREDNISOLONE 40MG/M2 ORALLY AFTER FOOD IN THE MORNING D1-D14
BLEOMYCIN 10MG/M2 IV IN 100ML NS OVER 1H D8
VINCRISTINE1.4MG/M2 (MAX 2MG) IV PUSH D8

OR

IFRT (FOR BOTH 1 AND 2)

Consider IFRT to bulky sites, extra-nodal disease or sites of residue after therapy

IF NOT FIT FOR ABVD

(DISCUSS IN MDT AND TAILORED REGIMENS CAN BE USED)

UNFIT FOR BLEOMYCIN (AGE>50-60 YEARS, CHRONIC SMOKER, COPD)

AVD

ADRIAMYCIN 25mg/m2 IV infusion NS/100ml/10 min Day1,15
VINBLASTINE 6 mg/m2 IV push Day1,15
DACARBAZINE 375 mg/m2 IV infusion NS/500ml/30 min Day1,15

COPP/AV

CYCLOPHOSPHAMIDE 600MG/M2 IV INFUSION NS/100ML/10 MIN DAY 1, 8
VINBLASTINE 6 MG/M2 IV PUSH DAY 1, 8
CAP PROCARBAZINE 100 MG/ M2 PO OD DAY 1 TO DAY14 (MULTIPLES OF 50 MG)
TAB PREDNISOLONE 45 MG/M2 PO AFTER BREAKFAST DAY 1 TO DAY14 (IN MULTIPLE OF 20 MG)

OR

ADRIAMYCIN 25mg/m2 IV infusion NS/100ml/10 min Day1,15
VINBLASTINE 6 mg/m2 IV push Day1,15

UNFIT FOR DOXORUBICIN (CARDIAC PROBLEMS)

COPP

CYCLOPHOSPHAMIDE 600MG/M2 IV INFUSION NS/100ML/10 MIN DAY 1, 8
VINBLASTINE 6 MG/M2 IV PUSH DAY 1, 8
CAP PROCARBAZINE 100 MG/ M2 PO OD DAY 1 TO DAY14 (MULTIPLES OF 50 MG)
TAB PREDNISOLONE 45 MG/M2 PO AFTER BREAKFAST DAY 1 TO DAY14 (IN MULTIPLE OF 20 MG)

ELDERLY HL

AVD

ADRIAMYCIN 25mg/m2 IV infusion NS/100ml/10 min Day1,15
VINBLASTINE 6 mg/m2 IV push Day1,15
DACARBAZINE 375 mg/m2 IV infusion NS/500ml/30 min Day1,15

OR

COPP

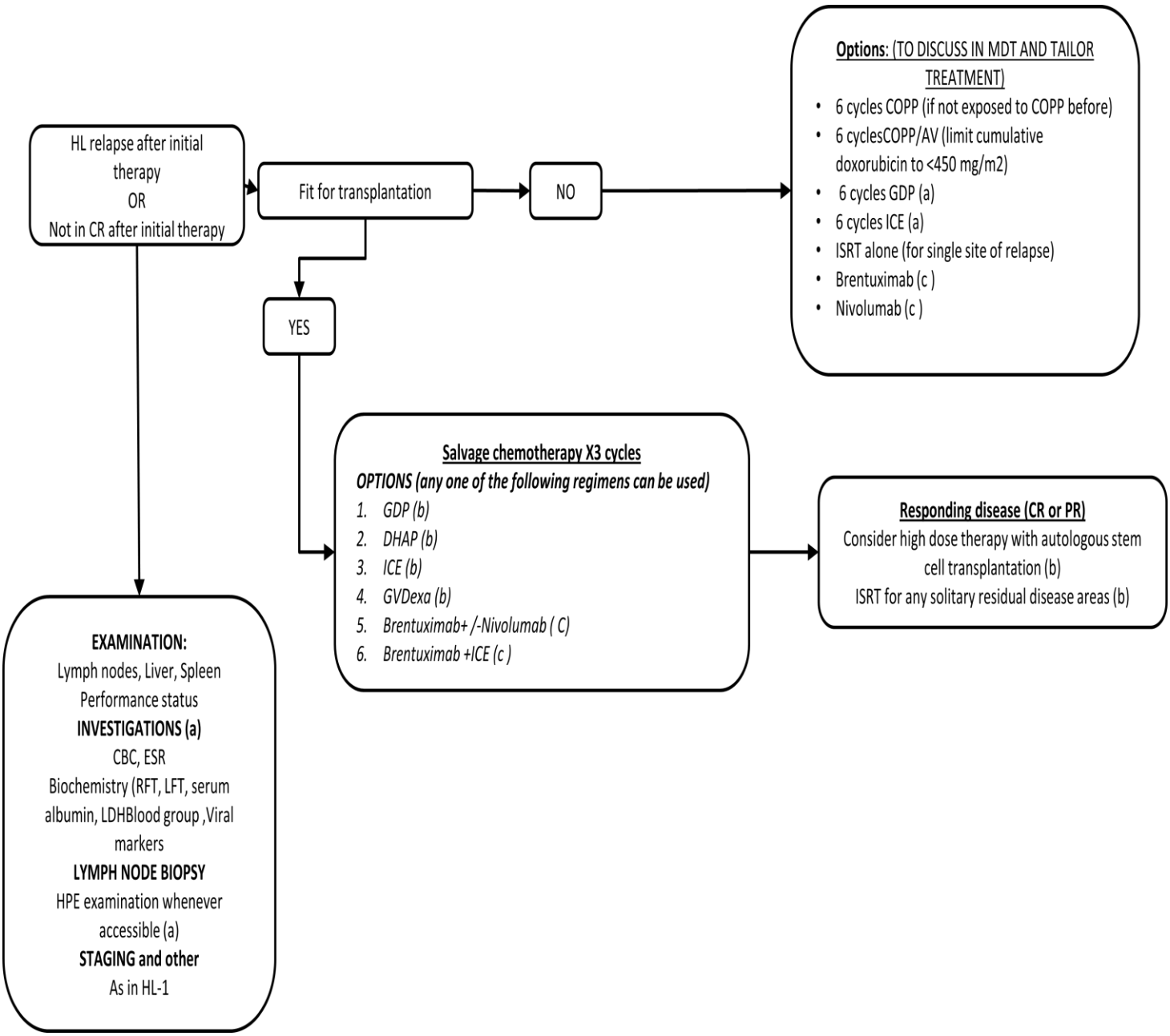
CYCLOPHOSPHAMIDE 600MG/M2 IV INFUSION NS/100ML/10 MIN DAY 1, 8
VINBLASTINE 6 MG/M2 IV PUSH DAY 1, 8
CAP PROCARBAZINE 100 MG/ M2 PO OD DAY 1 TO DAY14 (MULTIPLES OF 50 MG)
TAB PREDNISOLONE 45 MG/M2 PO AFTER BREAKFAST DAY 1 TO DAY14 (IN MULTIPLE OF 20 MG)

OR

ORAL METRONOMIC THERAPY (PEP-C)

PREDNISOLONE 20MG PO OD
ETOPOSIDE 50MG PO OD
PROCARBAZINE 50MG PO OD
Induction (1 cycle): Once daily until WBC less than 3 x 109 /L then hold cyclophosphamide, etoposide and procarbazine until Maintenance begins Maintenance starts at count recovery (until disease progression or unacceptable toxicity): Cycle length determined by blood counts predniSONE starts with Induction and is taken continuously throughout

HODGKIN'S LYMPHOMA (HL-2)- RELAPSED



HODGKIN'S LYMPHOMA (HL-2)- RELAPSED

IF FIT FOR TRANSPLANTATION

SALVAGE CHEMOTHERAPY X3 CYCLES

GDP Frequency Q 21 Days; Max Cycles -6

GEMCITABINE 1 gm/m2 IV infusion NS/500 ml/30 min DAY 1 and 8
TAB DEXAMETHASONE 40 mg PO OD after breakfast Day 1 to Day 4
CISPLATIN 75 mg/m2 Continuous IV infusion over 2 hours NS/1000 ml/ Day1 ONLY

OR

DHAP

Inj ONDANSETRON 16 mg IV Push Day1 to Day 2
Inj FOSAPREPITANT 150mg IV in 150ml NS over 20mins, 30mins prior to Cisplatin
Tab DEXAMETHASONE 40 mg Yes/No PO OD after breakfast Day 1 to Day 4
CISPLATIN 100 mg/m2 Yes/No CIV infusion NS/1000 ml/24 hours Day1 ONLY
CYTARABINE (two doses 12 hrs apart) 2gm/m2 Yes/No IV infusion NS/500 ml/3 hour BD on Day2
OR

ICE

GRANISETRON 3 MG DAY 2- DAY 4
DEXAMETHASONE 8 MG DAY 2- DAY 4
ETOPOSIDE 100 MG/M2 DAY 2- DAY 4
CARBOPLATIN AUC-5 DAY 3
IFOSFAMIDE WITH MESNA 5000 MG/M2 (BOTH DRIP SHOULD RUN SIMULTANEOUSLY THROUGH A THREE WAY) DAY 3 OR IFOSFAMIDE WITH MESNA 1800MG/M2 ON D1-D3 OF EACH CYCLE (DAY CARE)

OR

GVDEXA -3WEEKLY CYCLE

GEMCITABINE 1 gm/m2 IV infusion NS/500 ml/30 min DAY 1 and 8
TAB DEXAMETHASONE 40 mg PO OD after breakfast Day 1 to Day 4
VINBLASTINE 25MG/M2 IV PUSH ON D1, D8

OR

BRENTUXIMAB+ /-NIVOLUMAB

BRENTUXIMAB 1.8 mg/kg IV infusion in 150 mL sodium chloride 0.9% (final concentration 0.4-1.2 mg/mL) IV infusion over 30 minutes (maximum dose: 180 mg)
+ /-

NIVOLUMAB

Inj. NIVOLUMAB (3mg/kg) IV IN 100 ml Non DHEP NS (via codon set) over 1 hour
Or
Inj .NIVOLUMAB 240mg IV in 100ml NS Non DHEP codon set over 1 hour (2weekly) x 12 doses

OR

BRENTUXIMAB +ICE

BRENTUXIMAB 1.8 mg/kg IV infusion in 150 mL sodium chloride 0.9% (final concentration 0.4-1.2 mg/mL) IV infusion over 30 minutes (maximum dose: 180 mg)
+
GRANISETRON 3 MG DAY 2- DAY 4
DEXAMETHASONE 8 MG DAY 2- DAY 4
ETOPOSIDE 100 MG/M2 DAY 2- DAY 4
CARBOPLATIN AUC-5 DAY 3
IFOSFAMIDE WITH MESNA 5000 MG/M2 (BOTH DRIP SHOULD RUN SIMULTANEOUSLY THROUGH A THREE WAY) DAY 3 OR IFOSFAMIDE WITH MESNA 1800MG/M2 ON D1-D3 OF EACH CYCLE (DAY CARE)

IF NOT FIT FOR TRANSPLANTATION

TO DISCUSS IN MDT AND TAILOR TREATMENT

6 CYCLES COPP (IF NOT EXPOSED TO COPP BEFORE)

CYCLOPHOSPHAMIDE 600MG/M2 IV INFUSION NS/100ML/10 MIN DAY 1, 8
VINBLASTINE 6 MG/M2 IV PUSH DAY 1, 8
CAP PROCARBAZINE 100 MG/ M2 PO OD DAY 1 TO DAY14 (MULTIPLES OF 50 MG)
TAB PREDNISOLONE 45 MG/M2 PO AFTER BREAKFAST DAY 1 TO DAY14 (IN MULTIPLE OF 20 MG)

OR

6 CYCLES COPP/AV (LIMIT CUMULATIVE DOXORUBICIN TO <450 MG/M2)

CYCLOPHOSPHAMIDE 600MG/M2 IV INFUSION NS/100ML/10 MIN DAY 1, 8
VINBLASTINE 6 MG/M2 IV PUSH DAY 1, 8
CAP PROCARBAZINE 100 MG/ M2 PO OD DAY 1 TO DAY14 (MULTIPLES OF 50 MG)
TAB PREDNISOLONE 45 MG/M2 PO AFTER BREAKFAST DAY 1 TO DAY14 (IN MULTIPLE OF 20 MG)

OR

GDP Frequency Q 21 Days; Cycles -6

GEMCITABINE 1 gm/m2 IV infusion NS/500 ml/30 min DAY 1 and 8
TAB DEXAMETHASONE 40 mg PO OD after breakfast Day 1 to Day 4
CISPLATIN 75 mg/m2 Continuous IV infusion over 2 hours NS/1000 ml/ Day1 ONLY

OR

ICE 6 CYCLES

GRANISETRON 3 MG DAY 2- DAY 4
DEXAMETHASONE 8 MG DAY 2- DAY 4
ETOPOSIDE 100 MG/M2 DAY 2- DAY 4
CARBOPLATIN AUC-5 DAY 3
IFOSFAMIDE WITH MESNA 5000 MG/M2 (Both drip should run simultaneously through a three way) DAY 3 OR IFOSFAMIDE WITH MESNA 1800MG/M2 ON D1-D3 OF EACH CYCLE (DAY CARE)

FOR SINGLE SITE OF RELAPSE

ISRT ALONE

OR

BRENTUXIMAB

BRENTUXIMAB 1.8 MG/KG IV INFUSION IN 150 ML SODIUM CHLORIDE 0.9% (FINAL CONCENTRATION 0.4-1.2 MG/ML) IV INFUSION OVER 30 MINUTES (MAXIMUM DOSE: 180 MG)

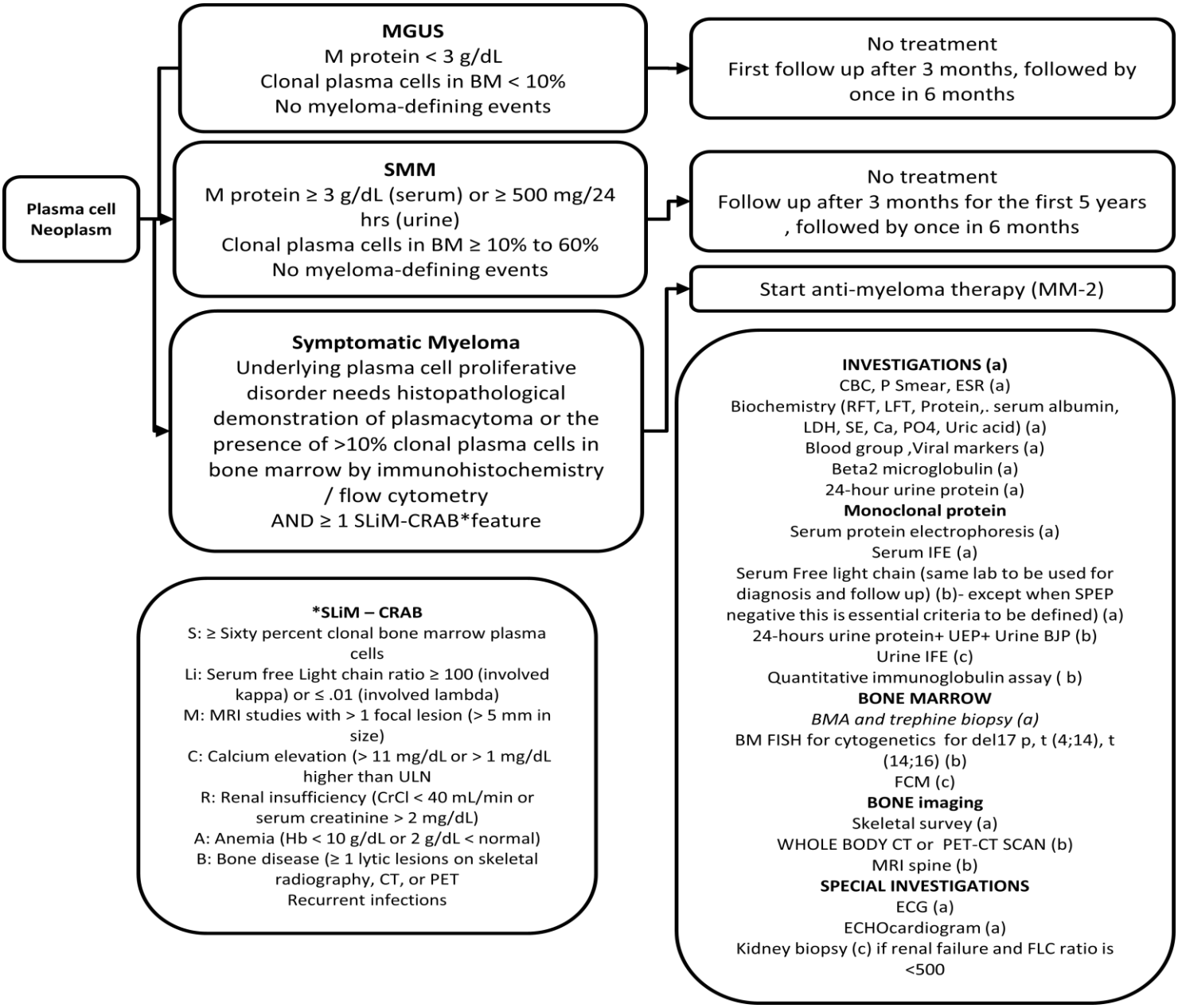
OR

NIVOLUMAB

INJ. NIVOLUMAB (3MG/KG) IV IN 100 ML NON DHEP NS (VIA CODON SET) OVER 1 HOUR
OR
INJ. NIVOLUMAB 240MG IV IN 100ML NS NON DHEP CODON SET OVER 1 HOUR (2WEEKLY) X 12

DOSES

MULTIPLE MYELOMA (MM-1-DIAGNOSIS AND INITIAL WORK UP)



MULTIPLE MYELOMA (MM-2)

SYMPTOMATIC MYELOMA TRANSPLANT ELIGIBLE
Novel agent based triplet induction 4-6 cycles
OPTIONS (a)

- Bortezomib-Lenalidomide- Dexamethasone
- Bortezomib-Cyclophosphamide-Dexamethasone
- Bortezomib-Thalidomide- Dexamethasone
- Cyclophosphamide-Thalidomide-Dexamethasone

ASCT WITH HIGH DOSE MELPHALAN (a)
Dose of Melphalan
200mg/m2 if CrCl >60
140mg/m2 if CrCl <60 or if age >65 yrs. irrespective of creatinine
Patients on renal replacement therapy
Mel 70mg/m2 on day -2, -1,
Stem cell infusion
12 hrs after HD Mel if CrCl >60
24 hrs after HD Mel if CrCl <60
For patients on renal replacement therapy , Dialysis to be done 24 hrs after 2nd Mel followed by stem cell infusion

SYMPTOMATIC MYELOMA TRANSPLANT INELIGIBLE
Novel agent based triplet induction 912 cycles TILL RESPONSE PLATEAUE
OPTIONS (a)

- Bortezomib-Lenalidomide- Dexamethasone
- Bortezomib-Cyclophosphamide-Dexamethasone
- Bortezomib-Thalidomide- Dexamethasone
- Cyclophosphamide-Thalidomide-Dexamethasone
- Melphalan – Prednisolone – Thalidomide
- Lenalidomide- Dexamethasone
- Dara VMP (c)

MAINTENANCE
Post transplant (a)
Non transplant (c)
(Till progression or till tolerated)
Lenalidomide is the drug of choice
Dose 5-15mg for 21 days in a 28 day cycle
Bortezomib 1.3 mg/m2mg s/c once in 2 weeks
if - patient has renal failure, t(4;14)
Dual Maintenance
Bortezomib – Lenalidomide if del 17p/ tp53 positive

Supportive care in Myeloma
Acyclovir prophylaxis in patients on Bortezomib (till 6 weeks from last dose of Bortezomib)
Bone protection - Zoledronate 4mg monthly for 1st 1 yr followed by 3 monthly for 2nd year with calcium and vitamin D supplement (a)
- Denosumab 120mg s/c once a month (in patients with renal failure) (C)
Ecosprin in all patients on lenalidomide or thalidomide Analgesics (to avoid NSAIDS)
Orthopedics/ spine surgery consult for impeding or actual long bone fractures/ spinal cord compression
Palliative radiation for pain relief and cord compression

Response assessment
SPEP every 3rd cycle
S. FLC assay – if no M band – every 3rd cycle
BJP – if no serum M band and FLC assay is not available

MULTIPLE MYELOMA (MM-1- DIAGNOSIS AND INITIAL WORK UP)

BORTEZOMIB-LENALIDOMIDE- DEXAMETHASONE

BORTEZOMIB 1.3 MG/M2 ON DAYS 1, 8, 15, 22 OF EACH CYCLE IV PUSH OVER 3-5 SECONDS OR SUBCUTANEOUS
LENALIDOMIDE 25 MG DAY 1 TO 21 PO
DEXAMETHASONE (TAB/INJ) 40 MG / 20MG ON DAYS 1, 8, 15, 22 IV / PO (ALONG WITH FOOD)

OR

BORTEZOMIB-CYCLOPHOSPHAMIDE-DEXAMETHASONE

BORTEZOMIB (CHECK DILUTION AND VOLUME AT THE END OF PROTOCOL) 1.3 MG/M2 ON DAYS 1, 8, 15, 22 OF EACH CYCLE IV PUSH OVER 3-5 SECONDS OR SUBCUTANEOUS
CYCLOPHOSPHAMIDE 100 mg DAY 1-14 OD PO Or 300mg/m2 I.V ON DAY1,8,15,22 OF EACH CYCLE
DEXAMETHASONE (INJ) 20MG ON DAYS 1, 8, 15, 22 IV

OR

BORTEZOMIB-THALIDOMIDE- DEXAMETHASONE

BORTEZOMIB (CHECK DILUTION AND VOLUME AT THE END OF PROTOCOL) 1.3 MG/M2 ON DAYS 1, 8, 15, 22 OF EACH CYCLE IV PUSH OVER 3-5 SECONDS OR SUBCUTANEOUS
THALIDOMIDE 100 mg daily DAY1-28 HS PO
DEXAMETHASONE (INJ) 20MG ON DAYS 1, 8, 15, 22 IV

OR

CYCLOPHOSPHAMIDE-THALIDOMIDE-DEXAMETHASONE

CYCLOPHOSPHAMIDE 100 mg DAY 1-14 OD PO Or 300mg/m2 IV ON DAY1,8,15,22 OF EACH CYCLE
THALIDOMIDE 100 mg daily DAY1-28 HS PO
DEXAMETHASONE 40 mg /20mg* Day1.,8,15,22 OD after breakfast PO

OR

ASCT WITH HIGH DOSE MELPHALAN

DOSE OF MELPHALAN

200MG/M2 IF CRCL >60

140MG/M2 IF CRCL <60 OR IF AGE >65 YRS. IRRESPECTIVE OF CREATININE

PATIENTS ON RENAL REPLACEMENT THERAPY

MEL 70MG/M2 ON DAY -2, -1,

STEM CELL INFUSION

12 HRS AFTER HD MEL IF CRCL >60

24 HRS AFTER HD MEL IF CRCL <60

FOR PATIENTS ON RENAL REPLACEMENT THERAPY, DIALYSIS TO BE DONE 24 HRS AFTER 2ND MEL

FOLLOWED BY STEM CELL INFUSION

SYMPTOMATIC MYELOMA TRANSPLANT INELIGIBLE

NOVEL AGENT BASED TRIPLET INDUCTION 9-12 CYCLES TILL RESPONSE PLATEAUE

BORTEZOMIB-LENALIDOMIDE- DEXAMETHASONE

BORTEZOMIB (CHECK DILUTION AND VOLUME AT THE END OF PROTOCOL) 1.3 MG/M2 ON DAYS 1, 8, 15, 22 OF EACH CYCLE IV PUSH OVER 3-5 SECONDS OR SUBCUTANEOUS
DEXAMETHASONE (INJ) 20MG ON DAYS 1, 8, 15, 22 IV

OR

BORTEZOMIB-CYCLOPHOSPHAMIDE-DEXAMETHASONE

CYCLOPHOSPHAMIDE 100 mg DAY 1-14 OD PO Or 300mg/m2 ON DAY1,8,15,22 OF EACH CYCLE
BORTEZOMIB (CHECK DILUTION AND VOLUME AT THE END OF PROTOCOL) 1.3 MG/M2 ON DAYS 1, 8, 15, 22 OF EACH CYCLE IV PUSH OVER 3-5 SECONDS OR SUBCUTANEOUS
DEXAMETHASONE (INJ) 20MG ON DAYS 1, 8, 15, 22 IV

OR

BORTEZOMIB-THALIDOMIDE- DEXAMETHASONE

BORTEZOMIB 1.3 MG/M2 ON DAYS 1, 8, 15, 22 OF EACH CYCLE IV PUSH OVER 3-5 SECONDS OR SUBCUTANEOUS
THALIDOMIDE 100 mg daily DAY1-28 HS PO
DEXAMETHASONE 40 mg /20mg* Day1.,8,15,22 OD after breakfast PO

OR

CYCLOPHOSPHAMIDE-THALIDOMIDE-DEXAMETHASONE

CYCLOPHOSPHAMIDE 100 mg DAY 1-14 OD PO Or 300mg/m2 IV ON DAY1,8,15,22 OF EACH CYCLE
THALIDOMIDE 100 mg daily DAY1-28 HS PO
DEXAMETHASONE 40 mg /20mg* Day1.,8,15,22 OD after breakfast PO

OR

MELPHALAN – PREDNISOLONE – THALIDOMIDE

MELPHALAN 4MG/M2 ROUND OFF THE TOTAL DOSE TO THE MULTIPLE OF 2MG DAY 1-4 OD PO
PREDNISOLONE 40 MG/M2 NB: DOSE OF PREDNISOLONE MAY BE REDUCED IN THE VERY ELDERLY OR IF SIGNIFICANT TOXICITY OCCURS DAY1-5 OD AFTER BREAKFAST PO
THALIDOMIDE 100MG/DAY USUALLY START WITH 50MG/DAY FOR FIRST CYCLE DAY 1-28 OD PO
OR

LENALIDOMIDE- DEXAMETHASONE

LENALIDOMIDE 25 mg day 1 to 21 PO
DEXAMETHASONE (Tab/Inj) 40 mg / 20mg on days 1, 8, 15, 22 IV / PO (along with food)
OR

DARA VMP 42 DAY CYCLE FOR MAX 9 CYCLES.

DARATUMUMAB 16MG/KG IV WITH DEXA 20MG ORAL/IV ONCE WEEKLY IN CYCLE 1 , EVERY

3WEEKLY FROM CYCLE 2 TO CYCLE 9

BORTEZOMIB 1.3MG S/C TWICE WEEKLY ON WEEK 1, 2, 4, 5 OF CYCLE 1 AND ONCE WEEKLY ON

WEEK 1, 2, 4, 5 FROM CYCLE 2-9

ORAL MELPHALAN 9MG/M2 ONCE A DAY ON DAY 1 TO DAY 4 OF EACH CYCLE

ORAL PREDNISOLONE 60MG/M2 DAILY ON DAY 1 TO DAY4 OF EACH CYCLE

MAINTENANCE

POST TRANSPLANT

NON TRANSPLANT

(TILL PROGRESSION OR TILL TOLERATED)

LENALIDOMIDE DOSE 5-15MG FOR 21 DAYS IN A 28 DAY CYCLE

OR

BORTEZOMIB 1.3 MG/M2MG S/C ONCE IN 2 WEEKS

IF - PATIENT HAS RENAL FAILURE, T(4;14)

DUAL MAINTENANCE

BORTEZOMIB – LENALIDOMIDE IF DEL 17P/ TP53

BORTEZOMIB (CHECK DILUTION AND VOLUME AT THE END OF PROTOCOL) 1.3 MG/M2 EVERY 2WEEKS SUBCUTANEOUS
LENALIDOMIDE 5-15 MG DAY 1 TO 21 PO EVERY 28 DAY CYCLE

AL AMYLOIDOSIS

SUSPECTED AL AMYLODOSIS

a.non-diabetic nephrotic syndrome;

b.non ischemic cardiomyopathy with "hypertrophy" on echocardiography;

c.hepatomegaly or increased alkaline phosphatase value with no imaging abnormalities of the liver;

d.chronic inflammatory demyelinating polyneuropathy with a monoclonal protein

e.presence of a monoclonal gammopathy in a patient with unexplained fatigue, edema, weight loss, or paraesthesia

LOW RISK- all criteria met

NT Pro BNP <5000 pg/mL
Trop T <60
Age <65
ECOG PS 0-2
Normal renal function
NYHA <III
Normal cardiac function
SBP >100mm Hg
DLCO >90
BMPC <10%

BMPC >10%
Or
Any adverse factor present

CyBOR DX 4-6
OR
CTD X 4-6

- Autologous stem cell transplant with Melphalan 200mg/sq.m
- Consider maintenance therapy with Bortezomib-Dexamethasone if response is <CR after autologous stem cell transplantation (b)

Transplant ineligible

CyBOR DX 4-6 (a)
Bortezomib Mel Dexamethasone 4-6# (a)
Melphalan Dexamethasone (c)

Maintenance options

- Bortezomib + Dexamethasone
- thalidomide

Diagnostic tests for AL Amyloidosis

1.Complete blood counts, serum chemistries – creatinine, Ca, Ph, LDH, LFT, PT , APTT

2.Biopsy with Congo red staining with apple green birefringence on polarizing microscopy and/or thioflavin T , confirming the diagnosis of amyloidosis from organs – abdominal fat pad, rectal etc. In all cases an immunohistochemistry for light chain restriction is advised though interpretation is difficult because of background staining.

3.Bone marrow aspiration, biopsy and FISH after plasma cell sorting.

4.Serum free light chain assay, quantitative immunoglobulin assay, and 24 hr. urine protein assessment

5.Skeletal survey as in myeloma.

6.ECG, echocardiogram, serum NT-Pro BNP, serum troponin T levels

7.In case there is an associated multiple myeloma, a full myeloma work up needs to be done as per the diagnostic evaluation given under myeloma.

SUPPROTIVE CARE

- Bortezomib is preferably given as intravenous in patients who are fluid overloaded where there is a concern about the adequacy of absorption with subcutaneous administration
- 1. Salt restriction
- 2. Diuretics (Be cautious as aggressive diuresis can lead to intravascular fluid depletion and this can worsen cardiac function as cardiac function is preload dependent).
- 3. Patients at high risk of venous thromboembolism should be considered for prophylactic heparin and low risk for Ecospirin.
- 4. Patients with gastrointestinal symptoms should receive nutritional support.

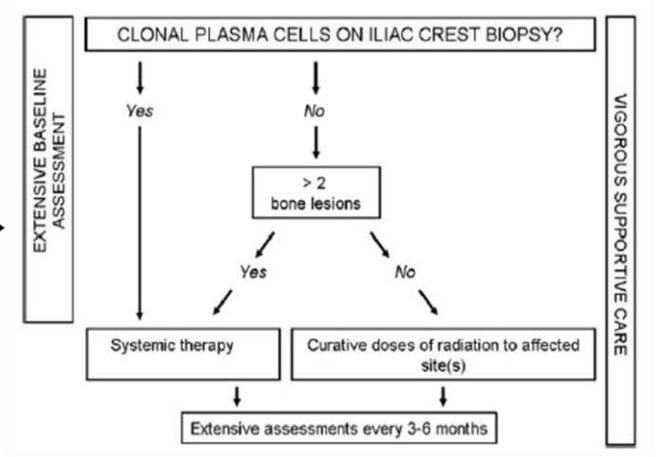
AL AMYLOIDOSIS
FOR LOW RISK- ALL CRITERIA MET
CYBOR DX 4-6
CYCLOPHOSPHAMIDE 100 mg DAY 1-14 OD PO Or 300mg/m2 IV ON DAY1,8,15,22 OF EACH CYCLE
BORTEZOMIB 1.3 MG/M2 ON DAYS 1, 8, 15, 22 OF EACH CYCLE IV PUSH OVER 3-5 SECONDS OR SUBCUTANEOUS
DEXAMETHASONE 40 mg /20mg* Day1.,8,15,22 OD after breakfast PO
OR
CTD X 4-6
CYCLOPHOSPHAMIDE 100 mg DAY 1-14 OD PO or 300mg/m2 I.V D1,D8,D15,D22 OF EACH CYCLE
THALIDOMIDE 100 mg daily DAY1-28 HS PO
DEXAMETHASONE 40 mg /20mg* Day1.,8,15,22 OD after breakfast PO
FOR TRANSPLANT INELIGIBLE
CYBOR DX 4-6 (A)
OR
BORTEZOMIB MEL DEXAMETHASONE 4-6#
BORTEZOMIB 1.3 MG/M2 ON DAYS 1, 8, 15, 22 OF EACH CYCLE IV PUSH OVER 3-5 SECONDS OR SUBCUTANEOUS
MELPHALAN 10mg/m2 Round off the total dose to the multiple of 2mg DAY 1-4 OD PO
DEXAMETHASONE 40 mg Day1-4 OD after breakfast PO
OR
MELPHALAN DEXAMETHASONE
MELPHALAN 10mg/m2 Round off the total dose to the multiple of 2mg DAY 1-4 OD PO
DEXAMETHASONE 40 mg Day1-4 OD after breakfast PO
OR
MAINTENANCE OPTIONS
OR
BORTEZOMIB + DEXAMETHASONE
BORTEZOMIB 1.3 MG/M2 ON DAYS 1, 8, 15, 22 OF EACH CYCLE IV PUSH OVER 3-5 SECONDS OR SUBCUTANEOUS
DEXAMETHASONE 40 mg /20mg* Day1.,8,15,22 OD after breakfast PO
OR
THALIDOMIDE
THALIDOMIDE 100 mg daily DAY1-28 HS PO

POEM SYNDROME

POEM SYNDROME

FULFILS DIAGNOSTIC CRITERIA

A diagnosis of POEM syndrome is confirmed when **both of the mandatory criteria, one of the three major criteria, and one of the six minor criteria are present.**



Investigations at diagnosis

Complete blood counts, S. Creatinine, S. Calcium, Total protein/ Albumin
Serum protein electrophoresis, Serum Free light chain, Immunofixation
Bone marrow aspiration and trephine biopsy
Skeletal survey by x rays
OR
Whole body low dose CT/ PET CT.(a)
Hormonal profile- Testosterone, oestradiol, FBS, HbA1C, TSH, PTH, prolactin, 8am Sr. Cortisol levels, luteinizing hormone (b)
NCV studies (a)
Plasma VEGF levels (c)

Optional regimens in POEMS

- Cyclophosphamide – Bortezomib- Dexamethasone (c)
- Lenalidomide – Dexamethasone (a)
- Bortezomib – Dexamethasone (c)

Mandatory (Both needed)	1.	Polyneuropathy (Typically demyelinating) – seen in all patients (peripheral, ascending, symmetrical, and affecting both sensation and motor function should be elicited)
	2.	Monoclonal plasma cell proliferative disorder(almost always λ)
Major (1/3 needed)	1.	Castleman disease [a]
	2.	Sclerotic bone disease
	3.	Elevated VEGF levels
Minor (1/6 needed)	1.	Organomegaly (Hepatomegaly, Splenomegaly, lymphadenopathy)
	2.	Extravascular fluid overload (edema, pleural effusion, ascites)
	3.	Endocrinopathy [b] (adrenal, thyroid, pituitary, gonadal, parathyroid, and pancreatic)
	4.	Skin changes (Hyperpigmentation, hypertrichosis, glomeruloid haemangiomata, plethora, acrocyanosis, flushing, and white nails)
	5.	Papilledema (seen in 1/3 of patients)
	6.	Thrombocytosis/polycythaemia
	a.	There is a Castleman disease variant of POEMS syndrome that occurs without evidence of a clonal PCD that is not accounted for in this table. This entity should be considered separately.
	b.	Because of the high prevalence of diabetes mellitus and thyroid abnormalities, this diagnosis alone is not sufficient to meet this minor criterion.

RESPONSE ASSESSMENT IN POEMS SYNDROME

Hematologic response:

- Complete response (CRH) – Negative bone marrow and negative immunofixation of the serum and urine. Patients are not required to have a repeat bone marrow aspirate if the baseline bone marrow was negative.
- Very good partial response (VGPRH) – A 90 percent reduction in the M-protein or immunofixation positive only as long as M-protein was at least 0.5 g/dL at baseline.
- Partial response (PRH) – A 50 percent reduction in M-protein or immunofixation positive as long as baseline M-protein was at least 1.0 g/dL.
- No response – Less than a PRH.

VEGF response:

- Complete response (CRV) – Normalization of VEGF (<87 pg/mL).
- Partial response (PRV) – Decrease of ≥50 percent (baseline must be ≥200 pg/mL).
- No response (NRV) – Less than a PRV.

Radiologic response by FDG-PET:

- Complete radiologic response (CRR) – Initial FDG avidity on a baseline PET scan that disappears.
- Partial radiologic response (PRR) – Initial FDG avidity that was 50 percent improved.
- No radiologic response – Not meeting CRR or PRR.

Clinical response: A clinical response assessment incorporates information regarding peripheral neuropathy, organomegaly, papilledema, erythrocytosis, thrombocytosis, endocrinopathy, extravascular fluid overload (ascites, effusions, edema), and abnormal pulmonary function tests. There are four clinical response categories, which include clinical improvement (IC), clinical progression (PC), mixed clinical response (MC), and clinical stability (SC).

POEM SYNDROME

CYCLOPHOSPHAMIDE – BORTEZOMIB- DEXAMETHASONE

CYCLOPHOSPHAMIDE 100 mg DAY 1-14 OD PO or 300mg/m2 I.V D1,D8,D15,D22
BORTEZOMIB 1.3 MG/M2 ON DAYS 1, 8, 15, 22 OF EACH CYCLE IV PUSH OVER 3-5 SECONDS OR SUBCUTANEOUS
DEXAMETHASONE 40 mg /20mg* Day1.,8,15,22 OD after breakfast PO

OR

LENALIDOMIDE – DEXAMETHASONE

LENALIDOMIDE 25 mg day 1 to 21 PO
DEXAMETHASONE (Tab/Inj) 40 mg / 20mg on days 1, 8, 15, 22 IV / PO (along with food)

OR

BORTEZOMIB – DEXAMETHASONE

BORTEZOMIB 1.3 MG/M2 ON DAYS 1, 8, 15, 22 OF EACH CYCLE IV PUSH OVER 3-5 SECONDS OR SUBCUTANEOUS
DEXAMETHASONE (INJ) 20MG ON DAYS 1, 8, 15, 22 IV

ANNEXURE -1. RADIOLOGY SYNOPTIC REPORTING FORMATS

Myeloma MRI

Template for reporting of Multiple Myeloma.

WHOLE BODY MRI EXAMINATION.

Indication: work up for multiple myeloma / response assessment

Technique: Myeloma protocol – whole spine T1 T2 and STIR, whole body axial or coronal T1 gradient Dixon (5mm), whole body axial diffusion, whole body axial T2 5mm (c), additional sequences for regional assessment (c)

Comparison:

Findings:

Evaluation of bones: Spine and then head to thigh in descending order.

Measurement of up to 5 focal lesions and pattern of marrow infiltration: Normal / focal/ focal on diffuse/ diffuse/ micronodular

Paramedullary or extramedullary sites: Site with measurement

Vertebral fractures: Document presence and benign / malignant

Response assessment Categories (RAC) for each anatomic region: Cervical / thoracic / lumbar spine, pelvis, long bones, skull, ribs.

Posterior iliac crest: Is trephine likely to be representative?

Incidental findings:

Conclusion:

Summary statement, RAC score according to anatomical regions, heterogeneity, recommendations including for investigation of equivocal findings.

State level of concern regarding incidental findings.

MY-RADS response assessment categories

Response assessment category (RAC) description:

1: Highly likely to be responding

Return of normal fat containing marrow in areas previously infiltrated by focal or diffuse myelomatous infiltration

Unequivocal decrease in number or size of focal lesions

Conversion of a packed bone marrow infiltrate into discrete nodules, with unequivocal decrease in tumour load in the respective bone marrow space

Decreasing soft tissue associated with bone disease

Emergence of intra-or peritumoral fat within/ around focal lesions (fat.dot or halo signs)

Previously evident lesion shows increase ADC in from <= 1400 micron square /sec to >1400 micron square /sec

>= 40% increase in ADC from baseline with corresponding decrease in normalized high b value signal intensity; morphologic findings consistent with stable or corresponding disease

For soft tissue disease, RECIST version 1.1 criteria for PR/CORONA RADIATA

2: Likely to be responding

Evidence of improvement but not enough to fulfil criteria for RAC 1. For example:
Slight decrease in number / size of focal lesions
Previously evident lesions showing increase in ADC from <= 1000 micron square /sec to <1400 micron square /sec
>25% but <40% increase in ADC from baseline with corresponding decrease in high b value signal intensity:
Morphologic findings consistent with stable or responding disease
For soft tissue disease, RECIST version 1.1 not meeting requirement for PR
3: Stable
No observable change
4: Likely to be progressing
Evidence of worsening disease, but not enough to fulfil criteria for RAC 5
Equivocal appearance of new lesion (s)
No change in size but increasing signal intensity on high b value (with ADC values <1400 micron square /sec) consistent with possible disease progression
Relapsed disease: reemergence of lesion (s) that previously disappeared or enlargement of lesion (s) that had partially regressed / stabilized with prior treatments.
Soft tissue in the spinal canal causing narrowing noted associated with neurological findings and not requiring radiation therapy
For soft tissue disease, RECIST version 1.1 not meeting requirement for PD
5: Highly likely to be progressing
New critical fracture(s) / cord compression requiring radiation / surgical intervention ; only if confirmed as malignant with MRI signal characteristics
Unequivocal new focal (> 5 to 10mm) / diffuse area (s) of infiltration to regions of previously normal marrow
Unequivocal increase in number/ size of focal lesions
Evaluation of focal lesion to diffuse neoplastic pattern
Appearance / increasing soft tissue associated with bone disease
New lesions / region of high signal intensity on high b-value images with ADC value between 600-1000 micron square /sec

Reference:

Christina Messiou, Jens Hillengass, Stefan Delorme, et al. Guidelines for acquisition, interpretation, and reporting of whole-body MRI in myeloma: Myeloma response assessment and diagnosis system (MY-RADS) Radiology 2019;291(1):5-13.

Myeloma Whole body CT

Whole body low dose CT for multiple myeloma assessment.

Technique:

A few details about the technique used should be given, including number of detectors, slice thickness, anatomy scanned (e.g., skull to proximal tibial metaphyses), and whether MPRs were performed. If prominent artifacts degrade significantly the image quality in certain parts of the anatomy, this should be specifically stated- eg

Recommended technical parameters.

Whole body low dose plain CT should be performed from the cranial vault to at least proximal metaphysis of the tibia on a multi-detector scanner with 16 detector rows or more, using kv 120 and 50 to 70 mAs. The collimation must be set between 0.5 and 1.5 mm and images are reconstructed in bone and soft tissue algorithm. Sagittal MPRs of the bone algorithm images of the whole spine and additional MPRs reconstructed parallel to the long axis of the femora and humeri are performed.

Table for technical parameters:

Number of detector rows	16 or more
Scan coverage	Cranial vault to proximal tibial metaphysis (includehumeri in the field of view)
Tube voltage(kV)/time-current product (mAs)	120/50–70a
Collimation	0.5–1.5 mm
Reconstruction convolution kernel	Sharp, high-frequency (bone) and smooth (soft tissue). Alternatively, one middle-frequency kernel for all images
Iterative reconstruction algorithms	Yes (to reduce image noise and streak artifacts)
Thickness/increment of axial slices	2/1 mm or 3/1.5 mm
Multiplanar Reconstructions (MPRs)	Yes (sagittal, coronal and parallel to long axis of proximal limbs).

Different tube parameters (e.g., 140/14–25 or a low voltage approach) are acceptable as long as they produce images of diagnostic quality with low effective patient dose

Indication : work up

Clinical information/Prior imaging studies

Findings:

Skull:

Spine: Cervical –

Thoracic-
Lumbar-
Sacral-
Upper limbs-
Ribs-
Stermun:
Scapula:
Pelvic bones-:
Lower limbs:
Visceral assessment:
Extramedullary disease:
Other findings:

Bones should be commented upon for-

- Osteolytic lesion - presence / absence, size of main lesions
-Focal and/or diffuse intramedullary hyperdensities of the femora and humeri - present / absent, if present the location, size, density and presence/absence of significant endosteal scalloping
-Extraosseous soft tissue with spinal compromise if any
-Increased fracture risk due to the presence of extensive osteolysis, especially in weight-bearing bones such as those of the lower spine and lower limbs should be mentioned.
-Fractures and associated complications

Conclusion

A clear summary statement should highlight the most important findings regarding overall disease status. It should include number and distribution of osteolyses, presence/absence of extra-osseous soft tissue masses, likelihood of cord/nerve root compression, number of focal medullary deposits in the appendicular skeleton, presence/absence of diffuse medullary disease in the appendicular skeleton and a comment on vertebral compression fractures and/or vertebral fracture risk. Appropriate recommendations.

Reference:

Recommendations for acquisition, interpretation and reporting of whole body low dose CT in patients with multiple myeloma and other plasma cell disorders: a report of the IMWG Bone Working Group
LA Moulopoulos, VassilisKoutoulidis et al.
Blood Cancer Journal **volume 8**, Article number: 95 (2018)

Myeloma – skeletal survey

Skeletal Survey
Frontal and lateral views of the skull, cervical, thoracic and lumbar spine, bilateral oblique views of the ribs, and frontal views of the upper and lower extremities.
Clinical information
Comparison
Findings
Skull:
Cervical spine:
Thoracic spine:
Lumbar spine:
Bilateral oblique views of the ribs:
Right upper extremity:
Left upper extremity:
Right lower extremity:
Left lower extremity:
Bones are described in relation to :
Lytic lesions – present or absent (if present location)
Fractures / Bone density / associated soft tissue
Impression
Communication of findings:

Lymphoma- CT scan

CT template for lymphoma assessment:
CT SCAN OF NECK, CHEST, ABDOMEN AND PELVIS
Post contrast CT scan of neck, chest abdomen and pelvis has been performed from skull base to ischial tuberosity.
Indication: Staging / response assessment of lymphoma.
Comparison:
Findings:
Neck
Nodes: present / absent
If present – laterality / level/ longest dimension of the largest node
Pharynx and larynx:
Oral cavity and tonsils:
Salivary glands:
Thyroid:
Vessels and carotid space:
Thorax
Lungs:
Mediastinal and hilar nodes: Absent / present

If present: location / size of nodal mass in maximum dimension or transverse diameter of nodal mass excluding the normal structures/ extension to adjacent structures
Trachea and bronchi:
Pleural spaces:
Heart and pericardium:
Vessels: Thrombus present / absent
Oesophagus:
Chest wall:
Axillary nodes:
Abdomen and Pelvis
Nodes: retroperitoneal / mesenteric/ iliac / inguinal nodes - Site/ size of largest node or nodal mass in maximum dimension
Liver: normal / enlarged in size.
attenuation- normal / fatty
focal lesion - present / absent
vessels- normal / periportal infiltration
Spleen: normal/ enlarged; if enlarged size
focal lesion- present/ absent
Gall bladder:
Adrenals:
Pancreas:
Kidneys and ureters: normal / enlarged; hydronephrosis- present/ absent
focal lesion: present / absent
perirenal space: normal / soft tissue infiltration
Stomach and bowel: unremarkable/ wall thickening / aneurysmal dilatation
Peritoneum and omentum:
Urinary bladder:
Pelvic organs:
Ascites:
Bones: normal / lytic or sclerotic lesion
Conclusion:
Staging if primary / Response assessment
Cotswolds modified Ann Arbor Staging Classification for both Hodgkin and non-Hodgkin lymphoma
CT response assessment should be based on RECIL 2017 criteria.
Cotswold's modified Ann Arbor Staging Classification for both Hodgkin and non-Hodgkin lymphoma

- **stage I:** one nodal group or lymphoid organ (e.g. spleen or thymus)
  - **stage IE:** one extranodal site
- **stage II:** two or more nodal groups, same side of the diaphragm
  - **stage IIE:** localized extranodal site with stage II criteria, both on the same side of the diaphragm
- **stage III:** nodal groups on both sides of the diaphragm

- **stage IIIS(1):** with splenic involvement
- **stage IIIE(2):** with localized extranodal site
- **stage IIISE:** both

- **stage IV:** disseminated involvement of one or more extra lymphatic organ (e.g. lung, bone) with or without any nodal involvement

Additional sub-staging variables:

- **A:** asymptomatic
- **B:** presence of B symptoms (including fever, night sweats and weight loss of over 10% of body weight over 6 months)
- **X:** bulky nodal disease: nodal mass >1/3 of intrathoracic diameter or 10 cm in dimension

RECIL criteria for response assessment

Complete Response

- Complete disappearance of all target lesions and all nodes with a long axis < 10 mm
- ≥ 30% decrease in sum of longest diameters of target lesions (partial response) plus normalization of FDG-PET
- Normalization of FDG-PET (Deauville score 1–3)
- No bone marrow involvement
- No new lesions
- Reduction in the sum of diameters by ≤ 30% with normalization of FDG-PET uptake should not be considered a complete response unless documented by negative tissue biopsy.

Partial Response

- ≥ 30% decrease in the sum of longest diameters of target lesions but not a complete response
- Positive FDG-PET (Deauville score 4–5)
- Any bone marrow involvement
- No new lesions

Minor Response

- ≥ 10% decrease in the sum of longest diameters of target lesions but not a partial response
- Any FDG-PET findings
- Any bone marrow involvement
- No new lesions

Stable Disease

- < 10% decrease or ≤ 20% decrease in the sum of longest diameters of target lesions
- Any FDG-PET findings
- Any bone marrow involvement
- No new lesions

Progressive Disease

- > 20% increase in the sum of longest diameter of target lesions
- For small lymph nodes of < 15 mm post therapy, minimum absolute increase of 5 mm and long diameter > 15 mm
- Appearance of new lesion
- Any FDG-PET finding
- Any bone marrow involvement
- New or no new lesions

Infection assessment- HRCT chest
HRCT/ PLAIN CT SCAN OF THORAX

HRCT / Plain CT scan of thorax has been performed.
Indication: To look for infective focus.
Comparison:
Findings:
Lungs:
Consolidation- Absent/ Lobar/ segmental / sub segmental
Nodules- Absent / Discrete/ tree in bud / nodules with surrounding ground glass
Patchy ground glass density- Present /Absent: if present distribution.
Septal thickening- Present / Absent, distribution

Pleura: effusion / thickening
Heart and great vessels:
Mediastinal nodes:
Chest wall:

Visualized abdomen:

Visualized Bones:
Impression:
Chest findings if infective, if imaging is suggestive of possible etiology like bacterial or fungal
Any recommendation

ANNEXURE 2. LYMPHOMA DIAGNOSTIC AND IHC PANELS

1. Lymphoma –Pre-analytical requisites

Mandatory

- Tissue preservation (avoid frozen processing)
    - Fixative: 10% neutral buffered formalin
    - Fixation:
        - Lymph nodes/tissue thicker than 0.8 -1.0cms; should be bisected and large tissue should be serially sliced, perpendicular to the long axis.
        - Tissue ≤4 cm in greatest dimension should be processed in entirety
        - Should be put for fixation within 30 – 60 minutes of biopsy
        - Fixation volume should be at 3-4 times the volume of the tissue
        - Should not be left in the fixative for more than 48 hrs; and should be processed in 12-24 hrs time (in cases of inevitable delay; should be kept in cold temperature [refrigerator], preferably at 4 degrees centigrade)
- Routine processing and embedding
    - 3-4 micron thick sections with Hematoxylin and eosin stained slides of each paraffin block
    - Basic Immunohistochemistry set up
    - Microscopic evaluation

Optional (c) (Extended immunohistochemistry and Molecular diagnostic laboratories)

**For transportation – Either by immersing tissue in the adequate formalin in a sealed container or by paraffin blocks*

2. Lymphoma Diagnosis

Mandatory:

- Diagnosis:
    - Histological evaluation, i.e. biopsy as a method of investigation with comprehensive IHC panels.
    - Only in instances of inability of get adequate histology, a fine needle aspiration (FNA) based flow cytometric evaluation should be considered for diagnosis
- Staging
    - Bone marrow biopsy, aspirate and imprint smear (as listed in the algorithm

Optional/extended work-up:

- Diagnosis:
    - Fine needle aspiration (FNA) based flow cytometric immunophenotyping along with the biopsy
    - Only in instances of inability of get adequate histology, a fine needle aspiration (FNA) based flow cytometric evaluation should be considered for diagnosis
    - Molecular work-up
- Staging:
    - Flow cytometric immunophenotypic evaluation

3. Hodgkin lymphoma- cHL and NLPHL- requisites for diagnosis

Classic Hodgkin lymphoma (CHL)

- Mandatory:
    - CD3, CD20, CD30, CD15, Pax5, AE1/AE3*, ALK-1**
- Optimal/extended work-up:
    - LCA, CD3, CD20, CD30, CD15, Pax-5, Oct2, Bob1, EBV-LMP1/EBER, Gata 3

Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL)

- Mandatory:
    - CD20, CD3, CD30, CD15, Pax5
- Optimal/extended work-up:

- LCA, CD3, CD20, CD30, CD15, Pax-5, EBVLMP1/EBER, PD1, Oct2, Bob1, Gata3, CD4, CD8

* Where ever indicated, to rule out a possibility of EBV related benign proliferations, poorly differentiated / undifferentiated carcinoma
** In cases of younger patients, rule out a possibility of ALK+ve ALCL

4. <u>B cell NHL- requisites for diagnosis</u>

A. CD20 positive BNHL: large cell morphology

- Mandatory:
  - IHC: LCA, CD20, CD3, MIB-1
- Optimal/extended work-up:
  - IHC: CD3, CD20, MIB-1, cyclin D1, CD5, CD10, Bcl6, Mum1, cmyc, Bcl-2, CD30, EBV-LMP1/EBER
  - FISH: MYC/BCL2/BCL6 gene rearrangement
  - Gene expression/methylation studies – COO subtyping

B. **CD20 positive BNHL: non-large cell morphology**

- Mandatory:
  - IHC: LCA, CD20, CD3, MIB-1, CD5, CD23, CD10, bcl6, cyclin D1 (if blastic morphology, please add AMPO, ckit, CD10, CD19/Pax5, Tdt, CD34)
- Optimal/extended work-up :
  - IHC: Mum1, cmyc, Bcl-2, EBV-LMP1/EBER, CD43, CD138, Sox11
  - FISH: CMYC/BCL2/BCL6; IFR4 gene rearrangement
  - Sequencing: MYD88 mutation

5. **T-NHL-requisites for diagnosis**

CD3 positive NHL: large cell morphology

- Mandatory:
    - IHC: CD20, CD3, CD30, MIB-1, ALK-1, CD4
- Optimal/extended work-up :
    - IHC: CD3, CD20, CD4, CD8, CD2, CD5, CD7, MIB-1, CD56, CD30, ALK-1, CD10, Bcl6, PD1, Mum1, EBV-LMP1/EBER, CD123, Gata3, perforin, Granzyme A, TIA, CD21, CD23, CD35
    - FISH: DUSP22 gene rearrangement

CD3 positive NHL: non-large cell morphology

- Mandatory:
    - IHC: CD20, CD3, CD2, CD5, CD7, CD4, CD8, MIB-1, cyclin D1, Tdt, CD34, CD30, ALK-1
- Optimal/extended work-up :
    - IHC: CD56, CD10, Bcl6, PD1, Mum1, EBER-ISH, CD123, Gata3, CXCLl13, CXCR5, ICOS.perforin, Granzyme A, TIA,CD21, CD23, CD35
    - FISH: DUSP22 gene rearrangement

6. **CD3 and CD20 negative NHL- requisites for diagnosis**
    - IHC: LCA, CD3, CD20, CD30, CD19, Pax-5, CD138, ALK-1, CD5, CD10, Bcl6, Mum1, EBV-LMP1/EBER, CD56, CD7, CD4, CD8, CD123, MIB-1, c-kit, MPO, CD41, CD61, CD33, CD34, Tdt, CD1a, CD163, S-100 protein, EMA, CD23, CD21, kappa, lambda, MIB-1

***Important*: The laboratory without expertise in diagnosing hematolymphoid neoplasms and with inadequate IHC/Flow cytometric immunophenotyping panels should refer the sample to any specialized lab dealing with such neoplasms. There can't be any definite algorithms for diagnosing hematolymphoid neoplasms as each lesion is different and number of reagents used may vary case to case basis.**

ANNEXURE 3. FCM PANEL FOR HEMATOLYMPHOID MALIGNANCIES

1. Processing, Instrument Setup and Quality Control

Processing, Instrument Setup and Quality Control should be done as per Euroflow protocols or ICMR guidelines published in 2016. The links are given below
https://www.icmr.nic.in/sites/default/files/guidelines/Immunophenotyping%20of%20Hematolymphoid%20Neoplasms_0.pdf

https://www.euroflow.org/usr/pub/prlogin.php

2. Acute Leukemia- Essential panel

1. Smears stained with a Romanowsky stain and Myeloperoxidase or Sudan Black B
2. NSE, toluidine blue and Iron stain as required.

Note: Morphology is followed by flow cytometric immunophenotyping and other ancillary techniques including cytogenetics and molecular diagnostics. The final diagnosis is based on a combination of all these modalities.

Essential (a)		
Common markers	CD45, CD38, HLADR	
Markers of immaturity	CD34	
	Lineage associated	Lineage Specific
B-cell	CD10, CD19, CD20, surface or cytoplasmic CD22, CyCD79a	
T-cell	CD1a, CD4, CD5, CD7, CD8, TCRγδ	Surface and Cytoplasmic CD3
Myeloid	CD13, CD33, CD117	cyMPO or Cytochemical Myeloperoxidase or Sudan Black B
Monocytic	CD36, CD64	Non Specific Esterase
Megakaryoblastic	X	
NK-cell	CD56	
Plasmacytoid dendritic cells	CD123	

3. Acute leukemia- Optimal (b)

Essential and the following

Optimal – Essential and the following		
Common markers		
Markers of immaturity		
	Lineage associated	Lineage Specific
B-cell	CD73, CD86, CD25, CD304	
T-cell		
Myeloid	CD15,	
Monocytic	CD11c, CD14,	
Megakaryoblastic	CD41, CD61	
NK-cell		
Plasmacytoid dendritic cells		

4. **Acute leukemia- Optional (c)**
   Optimal with the following

Common markers	CD25, CD45RA	
Markers of immaturity	CD133, TdT	
	Lineage associated	**Lineage Specific**
B-cell	CD58, CD81, NG2, CRLF2	IgM, Kappa & Lambda light chains
T-cell	CD2, CD99, TCRαβ	
Myeloid	CD15, CD11b, CD16, CD65, CD66c	
Monocytic	CD86, CD300e	
Megakaryoblastic	CD42b	
NK-cell	CD94, CD161	
Plasmacytoid dendritic cells	CD303, CD304	
Mast cells	CD203c	
Erythroid lineage	CD49d, CD71, CD105	CD235a

5. **DNA ploidy for B-ALL**

Propidium Iodide
FxCycle Violet
DRAQ5
DAPI (4',6-Diamidino-2-phenyl Indole)

6. DNA ploidy for B-ALL

Propidium Iodide
FxCycle Violet
DRAQ5
DAPI (4',6-Diamidino-2-phenyl Indole)

7. B-ALL MRD

(a)	(b)	(c)
CD10, CD19, CD20, CD34, CD38, CD45, CD73, CD123, CD86, CD304		CD25, CD44, CD66c, CD81, CD200, CD58
Nuclear dye such as Syto13, Syto16, Syto44		

Recommendations for processing

- Use Euroflow recommended Bulk-lysis method
- Acquire minimum 10,00,000 CD45-positive events
- Minimum 8-color antibody panel
- Use the template-based analysis
- Should be done in a laboratory with workload of minimum 30 acute leukemia samples per month
- Mention the limit of detection and limit of quantitation of MRD assay
- Mentioned the number of events studied
- Control sample should be evaluated at-least once in month

8. T-ALL MRD

(b)	(c)
CD4, CD5, CD7, CD8, CD16, CD34, CD38, CD45, CD56, Surface and cytoplasmic CD3	CD1a, CD2, CD48, CD99, TdT
Nuclear dye such as Syto13, Syto16, Syto44	

9. AML MRD

	(b)	(c)
Deviation from normal	CD13, CD14, CD15, CD33, CD34, CD36, CD38, CD45, CD64, CD117, CD123, HLADR	CD11b, CD65, CD66c, CD71,
Leukemia associated Immunophenotypic markers	CD7, CD19, CD56	CD2, CD4, CD5,