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造血系統癌症診療指引

2020年04月21日第一版

血液暨淋巴癌醫療團隊擬訂

注意事項：這個診療原則主要作為醫師和其他保健專家診療癌症病人參考之用。假如你是一個癌症病人，直接引用這個診療原則並不恰當，只有你的醫師才能決定給你最恰當的治療。

會議討論

上次會議：無

本共識與上一版的差異

上一版	新版
無	審視最新版NCCN guidelines，並新制定本院造血系統(AML及Multiple myeloma)癌症指引。

PROTOCOLS FOR TREATMENT OF AML

Version 1. 2020

Acute Myeloid Leukemia

Version 1. 2020

Evaluation and diagnosis:

- History taking (including previous chemotherapy and radiation therapy) and physical examination
- Complete blood count (CBC), platelets, differential count, biochemistry profile
- Prothrombin time (PT), partial thromboplastin time (PTT), fibrinogen
- Immunophenotyping or cytochemistry of bone marrow or peripheral blood
- Bone marrow with cytogenetics (karyotype +/- FISH) and molecular analyses
- Check HBsAg, anti-HBcAb and anti-HCV Ab:
  (1) HBsAg (-), may check anti-HBs Ab (optional); HBsAg (+), check HBeAg, anti-HBeAb, HBVDNA
  (2) HCV Ab (+) with liver function impairment, check HCV-RNA (optional)
- Chest X ray, EKG
- Cardiac scan if previous heart disease or prior anthracycline use, age 60 y/o or clinical symptoms which would rise concern about cardiac function
- Central venous access of choice: Port A or PICC
- CT / MRI if neurological symptoms
- PET/CT if clinical suspecion of extramedullary disease
- Lumbar puncture (LP), if symptomatic (screening LP should be considered at first remission for patients with M4, M5 morphology or WBC count > 40,000/ul at diagnosis)
- HLA typing (in patients considered potential candidate for stem cell transplantation)

WHO classification of AML Version 1. 2020

AML with certain genetic abnormalities (gene or chromosome changes)
AML with a translocation between chromosomes 8 and 21 [t(8;21)]
AML with a translocation or inversion in chromosome 16 [t(16;16) or inv(16)]
APL with the *PML-RARA* fusion gene
AML with a translocation between chromosomes 9 and 11 [t(9;11)]
AML with a translocation between chromosomes 6 and 9 [t(6:9)]
AML with a translocation or inversion in chromosome 3 [t(3;3) or inv(3)]
AML (megakaryoblastic) with a translocation between chromosomes 1 and 22 [t(1:22)]
AML with the *BCR-ABL1* (*BCR-ABL*) fusion gene*
AML with mutated *NPM1* gene
AML with biallelic mutations of the *CEBPA* gene (that is, mutations in both copies of the gene)
AML with mutated *RUNX1* gene*

* This is still a "provisional entity," meaning it's not yet clear if there's enough evidence that it's a unique group.

WHO classification of AML Version 1. 2020

AML with myelodysplasia-related changes
AML related to previous chemotherapy or radiation
AML not otherwise specified
● AML with minimal differentiation (FAB M0)
● AML without maturation (FAB M1)
● AML with maturation (FAB M2)
● Acute myelomonocytic leukemia (FAB M4)
● Acute monoblastic/monocytic leukemia (FAB M5)
● Pure erythroid leukemia (FAB M6)
● Acute megakaryoblastic leukemia (FAB M7)
● Acute basophilic leukemia
● Acute panmyelosis with fibrosis
Myeloid sarcoma
Myeloid proliferations related to Down syndrome

Acute Myeloid Leukemia

Version 1. 2020

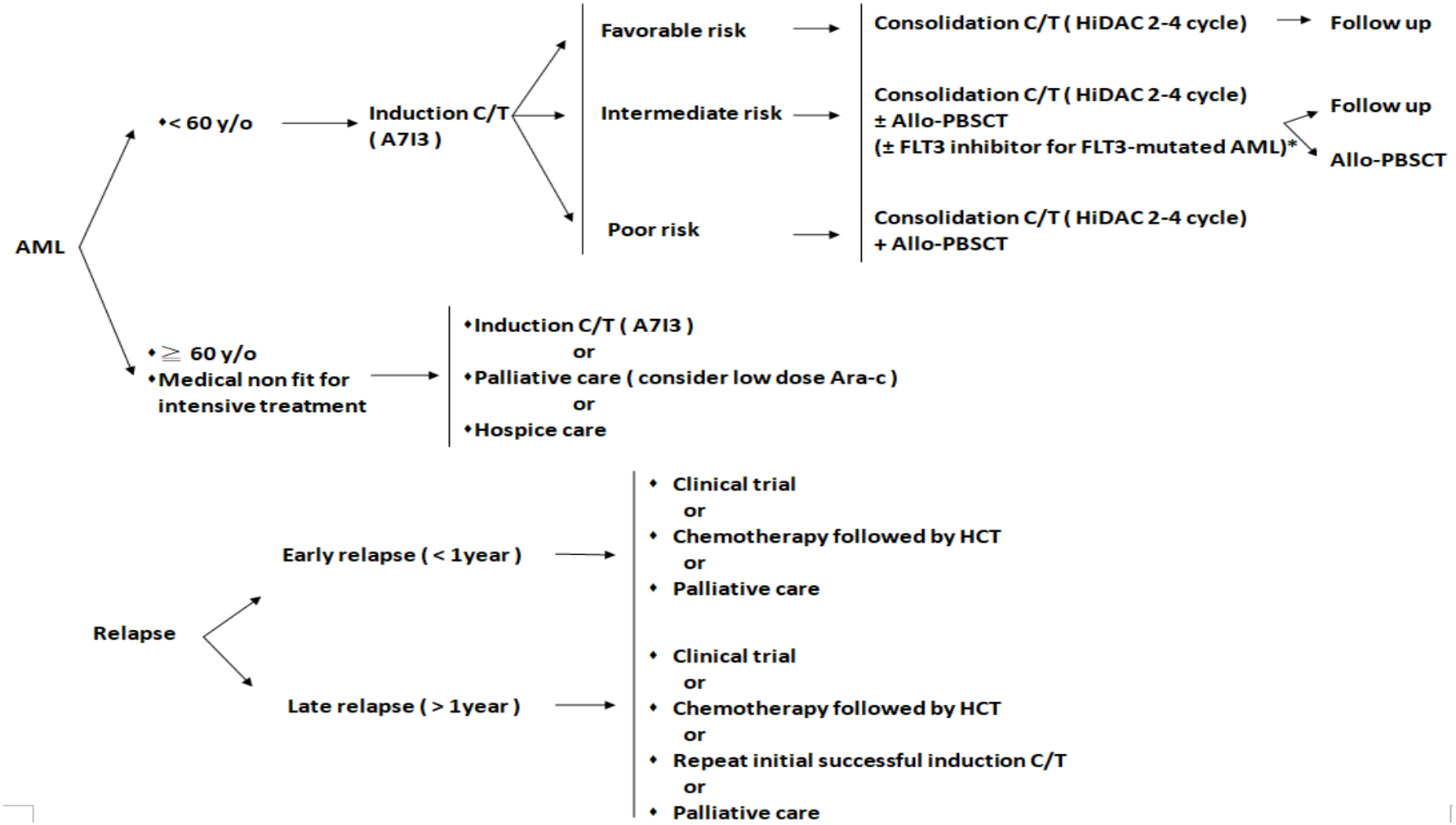
- Risk stratification by genetcis in non-APL AML

Risk Category*	Genetic Abnormality
Favorable	t(8;21)(q22;q22.1); *RUNX1-RUNX1T1* inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11* Biallelic mutated *CEBPA* Mutated *NPM1* without *FLT3*-ITD or with *FLT3*-ITD^{low}†
Intermediate	Mutated *NPM1* and *FLT3*-ITD^{high}† Wild-type *NPM1* without *FLT3*-ITD or with *FLT3*-ITD^{low}† (without adverse-risk genetic lesions) t(9;11)(p21.3;q23.3); *MLLT3-KMT2A*‡ Cytogenetic abnormalities not classified as favorable or adverse
Poor/Adverse	t(6;9)(p23;q34.1); *DEK-NUP214* t(v;11q23.3); *KMT2A* rearranged t(9;22)(q34.1;q11.2); *BCR-ABL1* inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2,MECOM(EVI1)* -5 or del(5q); -7; -17/abn(17p) Complex karyotype,§ monosomal karyotype‖ Wild-type *NPM1* and *FLT3*-ITD^{high}† Mutated *RUNX1*¶ Mutated *ASXL1*¶ Mutated *TP53*#

Acute Myeloid Leukemia

Version 1.2020

Treatment protocol in AML



Acute Myeloid Leukemia Version 1.2020

➢ Induction C/T

A7I3	Cytarabine 50~100mg/M2 Q12H (Day 1-7)
	Idarubicin 10~12mg/M2 (Day 1-3)
A7D3	Cytarabine 100mg/M2 Q12H (Day 1-7)
	daunorubicin 45~60(60-90)mg/M2 (Day 1-3)
A5I2	Cytarabine 100mg/M2 Q12H (Day 1-5)
	Idarubicin 10mg/M2 (Day 1-2)
A5D2	Cytarabine 100mg/M2 Q12H (Day 1-5)
	daunorubicin 45mg/M2 (Day 1-2)
適用於年紀大患者	
Azacitidine (Vidaza) 75mg/M2 , QD , SC ± Venclexta 1TAB QD	
Low dose Ara-C (Cytarabine 20mg/FIX) Q12H ± Venclexta 1TAB QD	

Acute Myeloid Leukemia Version 1.2020

➢ Consolidation C/T

HiDAC,6 dose (Day 1,3,5)	Cytarabine 3000mg/M2 , QOD(9AM/9PM)
HiDAC,8 dose (Day 1-4)	Cytarabine 3000mg/M2 , QD(Day 1-4)

➢ Palliative C/T

Azacitidine (Vidaza) 75mg/M2 , QD , SC ± Venclexta 1TAB QD
Low dose Ara-C (Cytarabine 20mg/FIX) Q12H ± Venclexta 1TAB QD

➢ FLT3 inhibitor for FLT3-mutated AML

Rydapt	Rydapt(Midostaurin) 2 CAP , Q12H , D8-21(共14天)

Acute Myeloid Leukemia Version 1.2020

- **Aggressive C/T for relapsed or refractory disease**

FLAG	G-CSF 300mcg SC (Day1-6)
	Fludarabine 30mg/M2 IV (Day 2-6)
	Cytarabine 2000mg/M2 IV (Day 2-6)
FLAG-Ida	G-CSF 300mcg SC (Day1-6)
	Idarubicin 8mg/M2 (Day 2-4)
	Fludarabine 30mg/M2 IV (Day 2-6)
	Cytarabine 2000mg/M2 IV (Day 2-6)
HiDAC/Daunorubicin	Cytarabine 3000mg/M2 IV (Day 1-3)
	Daunorubicin 45mg/M2 (Day 1-3)
HiDAC/Idarubicin	Cytarabine 3000mg/M2 IV (Day 1-3)
	Idarubicin 10mg/M2 (Day 1-3)
HiDAC/Mitoxantrone	Cytarabine 3000mg/M2 IV (Day 1-3)
	Mitoxantrone 10mg/M2 IV (Day 1-3)

Acute Myeloid Leukemia Version 1.2020

- **Aggressive C/T for relapsed or refractory disease**

MEC	Mitoxantrone 8mg/M2 IV (Day 1-5)
	Etoposide 100mg/M2 IV (Day 1-5)
	Cytarabine 1000mg/M2 IV (Day 1-5)
VP-16 + Mitoxantrone	Mitoxantrone 10mg/M2 IV (Day 1-5)
	Etoposide 100mg/M2 IV (Day 1-5)

Acute Myeloid Leukemia Version 1.2020

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PROTOCOLS FOR TREATMENT OF Multiple myeloma

Version 1. 2020

Multiple myeloma

Version 1.2020

➢ Diagnostic Workup

1. History and physical examination
2. CBC/DC
3. BUN, Cr, Ca, P, uric acid, albumin, total protein, AST, ALT, Alk-p, Bil-T, Na, K, sugar(AC)
4. Beta2-microglobulin and LDH
5. Serum PEP and IFE, IgG, IgA, IgM, IgD, 24h urine PEP and IFE
6. Serum free light chain assay
7. Bone marrow aspiration and biopsy
8. HBsAg, anti-HCV antibody
9. Dental department consultation before bisphosphonate therapy
10. Skeletal survey : Whole body MRI / Whole body low-dose CT scan (Avoid contrast as possible) / PET/CT scan
11. Tissue biopsy to diagnose a solitary osseous or extraosseous plasmacytoma
12. Evaluate for light chain amyloidosis, if appropriate
13. FISH [del 17p13, t(4;14), t(14;16), t(11;14),1q21 amplification, t(14;20)] (all these are poor risk except t(11;14); the first three used in R-ISS staging)

Multiple myeloma

Version 1.2020

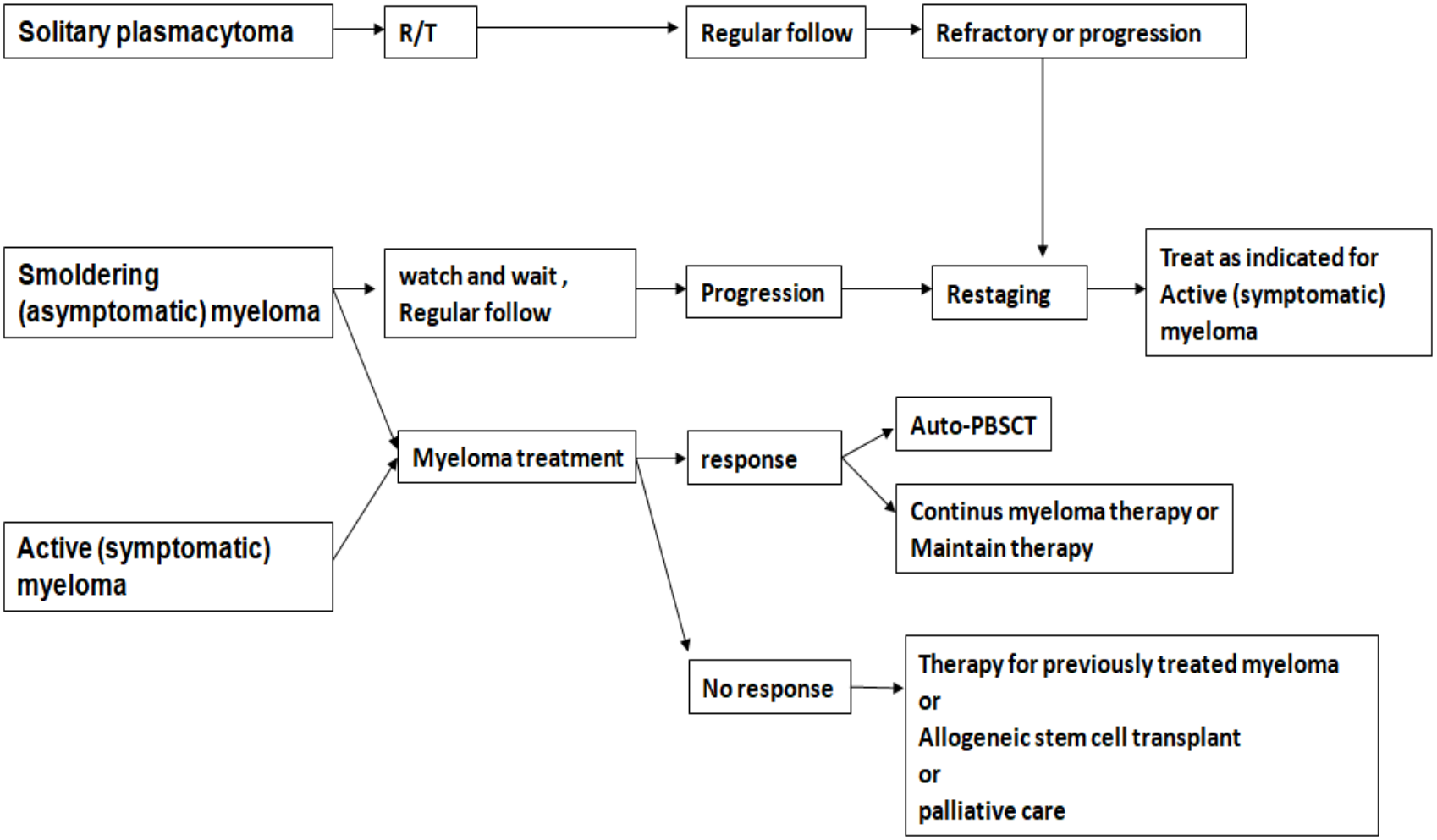
- **Staging systems for multiple myeloma**

Stage	International Staging System (ISS)	Revised-ISS (R-ISS)
I	Serum beta-2 microglobulin <3.5 mg/L, Serum albumin ≥3.5 g/dL	ISS stage I and standard-risk chromosomal abnormalities by FISH[b] and Serum LDH ≤ the upper limit of normal
II	Not ISS stage I or III	Not R-ISS stage I or III
III	Serum beta-2 microglobulin ≥5.5 mg/L	ISS stage III and either high-risk chromosomal abnormalities by FISH[b] or Serum LDH > the upper limit of normal

Multiple myeloma

Version 1.2020

➢ Clinical Presentation



Multiple myeloma

Version 1.2020

- Primary therapy

VCD weekly	Velcade 1.3mg/M2 SC
	Dorison 40mg PO or IV weekly
	Cyclophosphamide 300mg/M2 weekly PO or IV
VCD Biweekly	Velcade 1.3mg/M2 SC Day 1、4
	Dorison 40mg PO or IV weekly
	Cyclophosphamide 300mg/M2 weekly PO or IV
Velcade BIW	Velcade 1.3mg/M2 SC or IVP Day 1、4
Velcade (D1or4or8or11)	Velcade 1.3mg/M2 SC or IVP Day 1、4
VMP	Velcade 1.3mg/M2 SC Day 1、4
	Melphalan 0.075TAB/Kg PO QD Day1-7
	Prednisolone 4TAB PO TID Day1-7

Multiple myeloma

Version 1.2020

- Primary therapy

DVD	Dorison 5TAB PO BID Day1-4
	Vincristine 2mg IV Day1
	Lipo-Dox 20mg 40mg/M2 IV Day1
VED	Dexamethasone 20MG IV BID Day1-4
	Vincristine 0.4mg/M2 IV Day1-4
	Epirubicin 13.5mg/M2 IV Day1-4
VDT (D1,15)	Dexamethasone 10MG IV STAT Day1
	Velcade 1.3mg/M2 SC BIW Day7
	Lipo-Dox 20mg 20mg/M2 IV STAT Day1
	Thado 200mg PO HS Day1-14
VRD	Velcade 1.3mg/M2 SC
	Dorison 40mg PO weekly
	Revlimid (25mg) 1CAP PO QD Day1-21

Multiple myeloma

Version 1.2020

- Primary therapy

DCEP	Dexamethasone 40MG IV QD Day1-4
	Cyclophosphamide 400mg/M2 IV QD Day1-4
	Fytosid 40mg/M2 IV QD Day1-4
	Abiplatin 15mg/M2 IV QD Day1-4

- Relapse or progressive therapy

Lenalidomide	Revlimid (25mg) 1CAP PO QD Day1-21
Pomalidomide	Pomalyst (4mg) 1CAP PO QD Day1-21
Daratumumab	400mg Darzalex 16mg/Kg IV STAT
Carfilzomib	Kyprolis 20mg/M2 IV QD Day1-2

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