

高雄榮民總醫院 造血系統癌症診療指引

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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：2021/4/21

本共識與上一版的差異

上一版	新版
<p>1. AML induction C/T藥物新增(p10)</p> <p>2. AML induction C/T藥物劑量及途徑修正(p10) Azacitidine (Vidaza) 75mg/M2 , QD , SC ± Venclexta 4TAB (or 1-2 TAB + azole類藥物) QD Low dose Ara-C (Cytarabine 20mg/FIX) Q12H,SC ± Venclexta 4-6TAB (or 1-3 TAB + azole類藥物) QD</p> <p>3. AML Palliative C/T藥物新增(p11)</p> <p>4. AML Palliative C/T藥物劑量及途徑修正(p11) Low dose Ara-C (Cytarabine 20mg/FIX) Q12H(Day1-10) ,SC</p> <p>5. Multiple Myeloma Relapse or progressive therapy 新增藥物(p21)</p>	<p>→新增Decitabine 10-20mg/m2 IVA, QD*5 ±Venclexta 4tab po QD*28days</p> <p>→Azacitidine (Vidaza) 75mg/M2 , QD (Day1-7) , SC ± Venclexta 4TAB (or 1-2 TAB + azole類藥物) QD*28days</p> <p>→Low dose Ara-C (Cytarabine 20mg) Q12H(Day1-10),SC / IVA ± Venclexta 4-6TAB (or 1-3 TAB + azole類藥物) QD*28days</p> <p>→新增Decitabine 10-20mg/m2 IVA, QD*5 ±Venclexta 4tab po QD*28days</p> <p>→Low dose Ara-C (Cytarabine 20mg) Q12H(Day1-10) ,SC / IVA</p> <p>→新增Ninlaro(3mg/4mg) 1Cap PO QW (D1, 8, 15 of a 28-day)</p>

PROTOCOLS FOR TREATMENT OF AML

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Acute Myeloid Leukemia

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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 suspicion 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

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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. 2022

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

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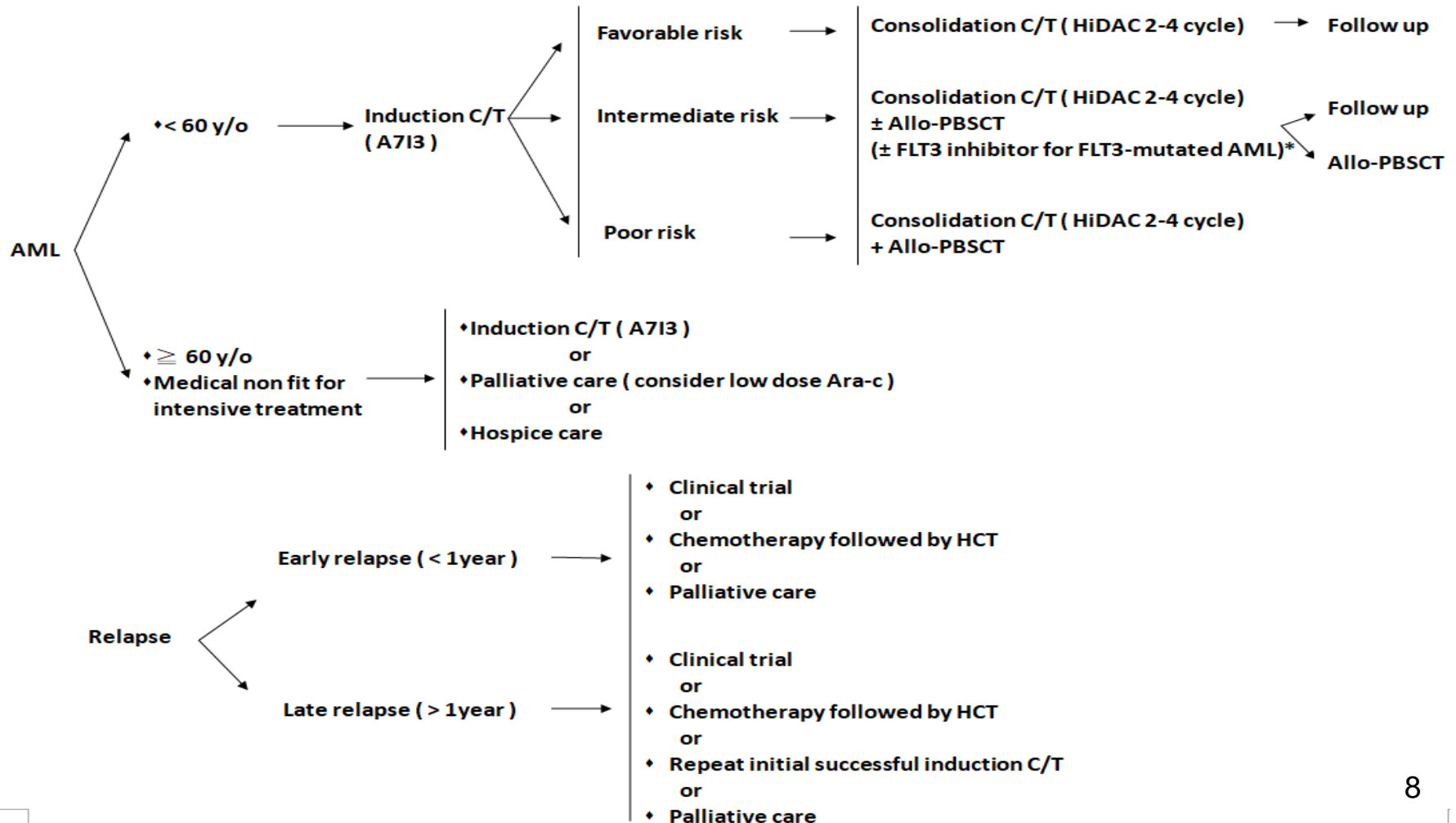
➤ Risk stratification by genetics in non-APL AML

Risk Category*	Genetic Abnormality
Favorable	t(8;21)(q22;q22.1); <i>RUNX1-RUNX1T1</i> inv(16)(p13.1;q22) or t(16;16)(p13.1;q22); <i>CBFB-MYH11</i> Biallelic mutated <i>CEBPA</i> Mutated <i>NPM1</i> without <i>FLT3-ITD</i> or with <i>FLT3-ITD</i> ^{low†}
Intermediate	Mutated <i>NPM1</i> and <i>FLT3-ITD</i> ^{high†} Wild-type <i>NPM1</i> without <i>FLT3-ITD</i> or with <i>FLT3-ITD</i> ^{low†} (without adverse-risk genetic lesions) t(9;11)(p21.3;q23.3); <i>MLL3-KMT2A</i> ‡ Cytogenetic abnormalities not classified as favorable or adverse
Poor/Adverse	t(6;9)(p23;q34.1); <i>DEK-NUP214</i> t(v;11q23.3); <i>KMT2A</i> rearranged t(9;22)(q34.1;q11.2); <i>BCR-ABL1</i> inv(3)(q21.3;q26.2) or t(3;3)(q21.3;q26.2); <i>GATA2,MECOM(EVI1)</i> -5 or del(5q); -7; -17/abn(17p) Complex karyotype,§ monosomal karyotype Wild-type <i>NPM1</i> and <i>FLT3-ITD</i> ^{high†} Mutated <i>RUNX1</i> ¶ Mutated <i>ASXL1</i> ¶ Mutated <i>TP53</i> #

Acute Myeloid Leukemia

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Treatment protocol in AML



Acute Myeloid Leukemia

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➤ Induction C/T

A7I3	Cytarabine 50~100mg/M2 Q12H (Day 1-7)
	Idarubicin 10~12mg/M2 (Day 1-3)
A7D3	Cytarabine 50~100mg/M2 Q12H (Day 1-7)
	daunorubicin 45~60mg/M2 (Day 1-3)
A5I2	Cytarabine 50~100mg/M2 Q12H (Day 1-5)
	Idarubicin 10mg/M2 (Day 1-2)
A5D2	Cytarabine 50~100mg/M2 Q12H (Day 1-5)
	daunorubicin 45~60mg/M2 (Day 1-2)

Acute Myeloid Leukemia

Version 1.2022

➤ Induction C/T

適用於年紀大患者

Azacitidine (Vidaza) 75mg/M2 , QD (Day1-7) , SC
± Venclexta 4TAB (or 1-2 TAB + azole類藥物) QD*28days

Decitabine 10-20mg/M2 , IVA QD*5
± Venclexta 4TAB (or 1-2 TAB + azole類藥物) QD*28days

Low dose Ara-C (Cytarabine 20mg/FIX) Q12H(Day1-10),SC / IVA
± Venclexta 4-6TAB (or 1-3 TAB + azole類藥物) QD*28days

Acute Myeloid Leukemia

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➤ Consolidation C/T

HiDAC,6 dose	Cytarabine 2000~3000mg/M2 , on Day 1,3,5 9AM/9PM
HiDAC,8 dose	Cytarabine 2000~3000mg/M2 , Q12H(Day 1-4)

➤ Palliative C/T

Azacitidine (Vidaza) 75mg/M2 , QD (Day1-7), SC ± Venclexta 4TAB(or 1-2 TAB + azole類藥物) QD*28days
Decitabine 10-20mg/M2 , IVA QD*5 ± Venclexta 4TAB (or 1-2 TAB + azole類藥物) QD*28days
Low dose Ara-C (Cytarabine 20mg/FIX) Q12H(Day1-10) , SC / IVA ± Venclexta 4-6TAB(or 1-3 TAB + azole類藥物) QD*28days

➤ FLT3 inhibitor for FLT3-mutated AML

(用於induction and consolidation chemotherapy)

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

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➤ 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 1.2022

➤ 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)

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PROTOCOLS FOR TREATMENT OF Multiple myeloma

Version 1. 2022

➤ 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 1.2022

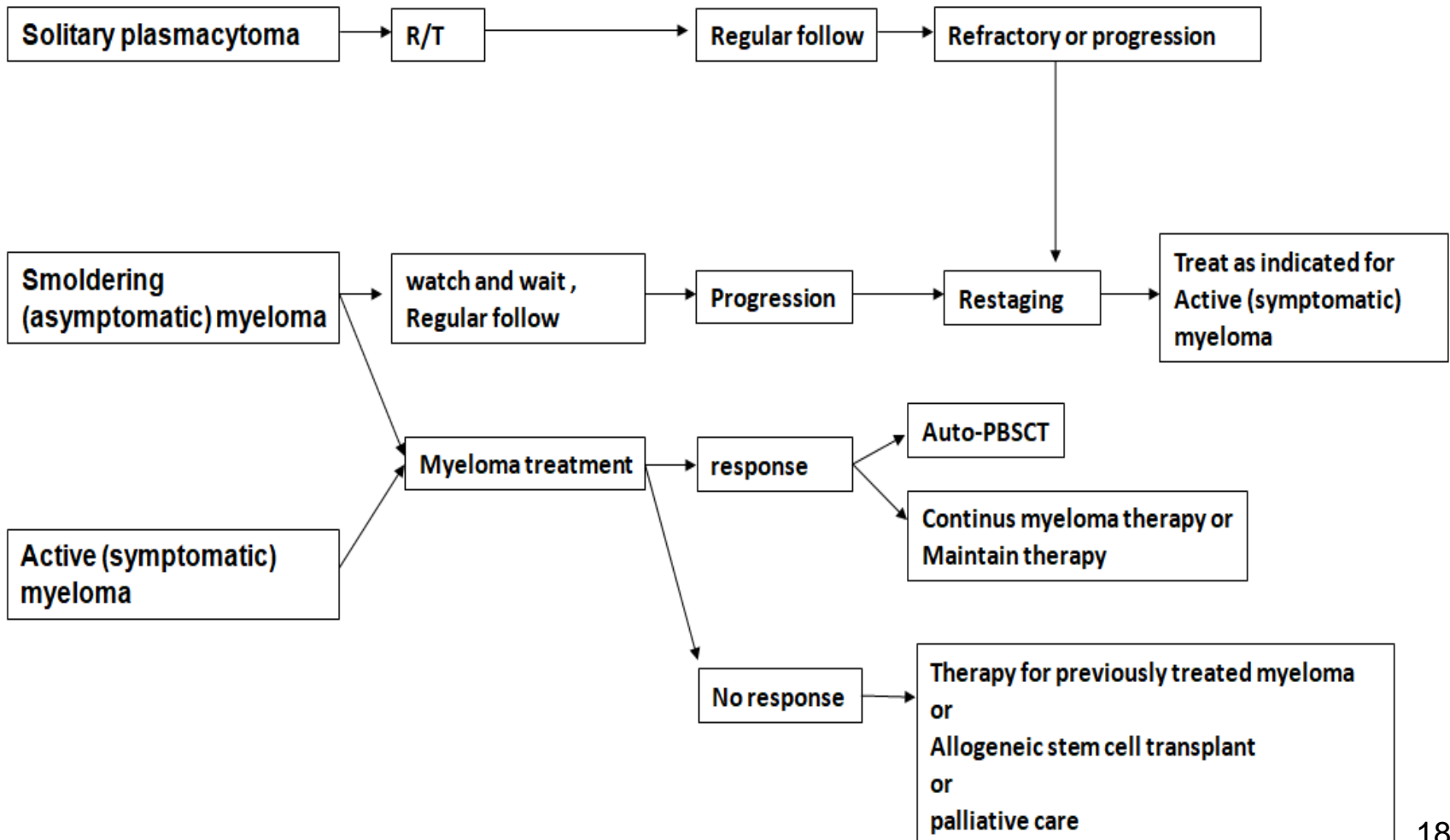
➤ Staging systems for multiple myeloma

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 1.2022

➤ Clinical Presentation



Multiple myeloma

Version 1.2022

➤ Primary therapy

VCD weekly	Velcade 1.3mg/M2 SC
	Dexamethasone 40mg PO or IV weekly
	Cyclophosphamide 300mg/M2 weekly PO or IV
VCD Biweekly	Velcade 1.3mg/M2 SC Day 1、4
	Dexamethasone 40mg PO or IV weekly
	Cyclophosphamide 300mg/M2 weekly PO or IV
Velcade BIW	Velcade 1.3mg/M2 SC Day 1、4
Velcade	Velcade 1.3mg/M2 SC Day 1、4、8、11
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 1.2022

➤ Primary therapy

DVD	Dexamethasone 20mg 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
	Dexamethasone 40mg PO weekly
	Revlimid (25mg) 1CAP PO QD Day1-21

Multiple myeloma

Version 1.2022

➤ Primary therapy

DCEP	Dexamethasone 40MG IV QD Day1-4
	Cyclophosphamide 400mg/M2 IV QD Day1-4
	Etoposide 40mg/M2 IV QD Day1-4
	Cisplatin 15mg/M2 IV QD Day1-4

➤ Relapse or progressive therapy

Lenalidomide	Revlimid (25mg) 1CAP PO QD Day1-21
Pomalidomide	Pomalyst (3mg) 1CAP PO QD Day1-21
Daratumumab	Darzalex 16mg/Kg IV
Carfilzomib	Kyprolis 20-70mg/M2 IV QD Day1-2 (weekly or bi weekly)
Ixazomib	Ninlaro(3mg/4mg) 1Cap PO QW (D1, 8, 15 of a 28-day)

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