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造血系統癌症診療指引

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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：2020/4/21

本共識與上一版的差異

上一版	新版
1.AML induction C/T藥物劑量修正(p9)	→A7D3:daunorubicin 刪除60-90mg/m2 A7D3、A5I2、A5D2:Cytarabine 修改為50-100mg/m2
2.AML Consolidation C/T藥物劑量修正(p10)	→修正為Azacitidine (Vidaza) 75mg/M2 ,QD (day1-7), SC ± Venclexta 4TAB (or1-2 TAB + azole類藥物) QD →HiDAC,6 dose:Cytarabine修正為2000~3000mg/m2,on Day1.3.5 9AM/9PM →HiDAC,8 dose:Cytarabine修正為2000~3000mg/m2,Q12H (Day 1-4)
3.AML Palliative C/T藥物劑量修正(p10)	→修正為Azacitidine (Vidaza) 75mg/M2 ,QD (day1-7), SC ± Venclexta 4TAB (or1-2 TAB + azole類藥物) QD →修正為Low dose Ara-C (Cytarabine 20mg/FIX) Q12H (day1-10)± Venclexta 4-6TAB QD(or 1-3 TAB + azole類藥物)
4.AML FLT3 inhibitor (p10)	→新增FLT3 inhibitor (用於induction and consolidation chemotherapy)
5.MM primary therapy(p18-19)	→Dorison更正為Dexamethasone
6.MM regimen velcade SC or IVP修改施打途徑(p18-19)	→刪除IVP途徑
7.DCEP regimen 藥名更正(p20)	→Fytosid更改為Etoposide、Abiplatin更改為Cisplatin
8.Carfilzomib藥物劑量及施打頻次修正(p20)	→修改為Kyprolis 20-70mg/M2 IV QD Day1-2 (weekly or bi weekly)

PROTOCOLS FOR TREATMENT OF AML

Version 1. 2021

Acute Myeloid Leukemia

Version 1. 2021

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. 2021

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. 2021

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

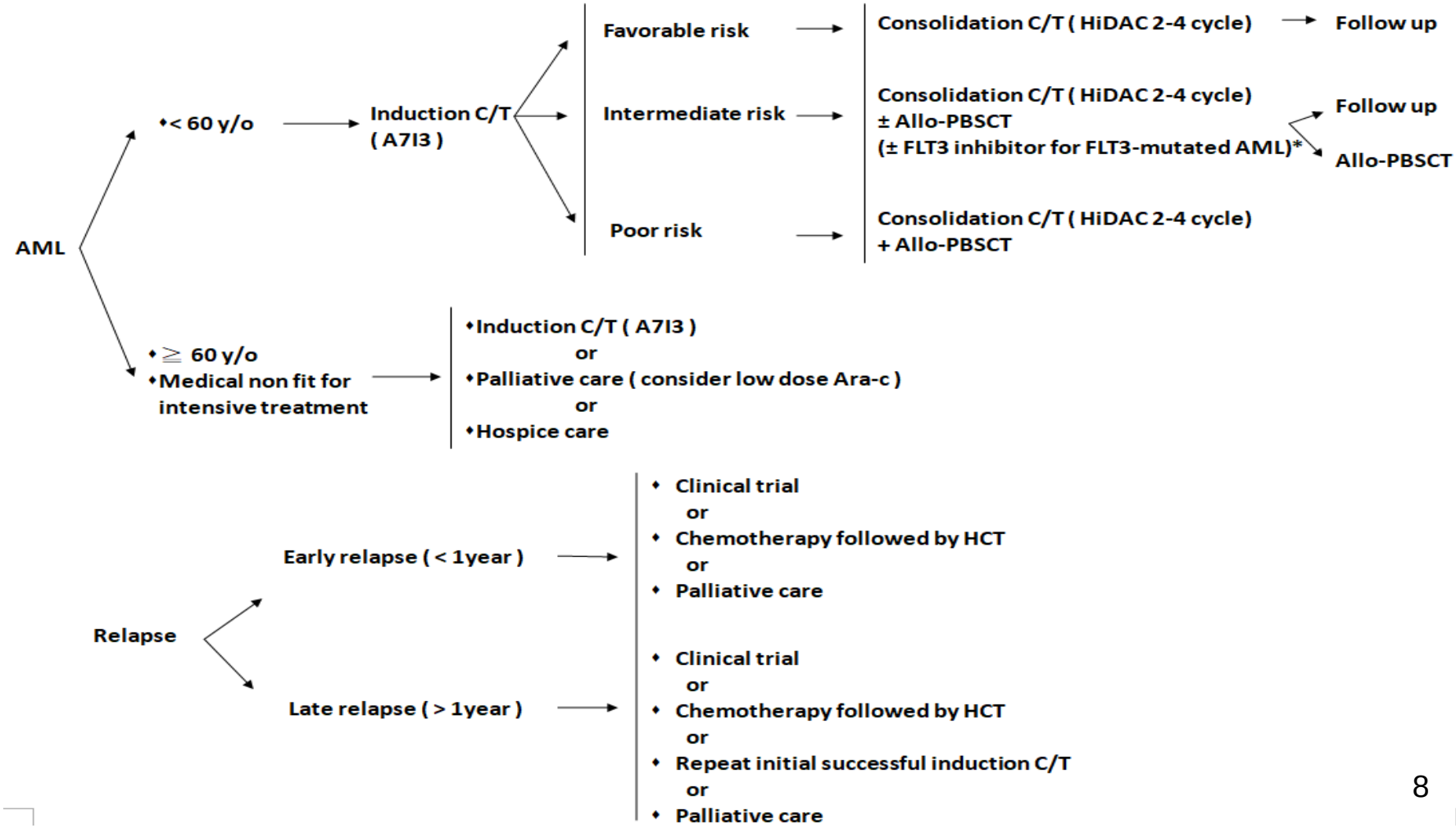
Version 1. 2021

- 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. 2021

Treatment protocol in AML



Acute Myeloid Leukemia Version 1.2021

➢ 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)
適用於年紀大患者	
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 ± Venclexta 4-6TAB (or 1-3 TAB + azole類藥物) QD	

Acute Myeloid Leukemia Version 1.2021

➢ 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
Low dose Ara-C (Cytarabine 20mg/FIX) Q12H(Day1-10) ,SC ± 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)

Acute Myeloid Leukemia Version 1.2021

- **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 1.2021

- **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. 2021

Multiple myeloma

Version 1.2021

➢ 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 1.2021

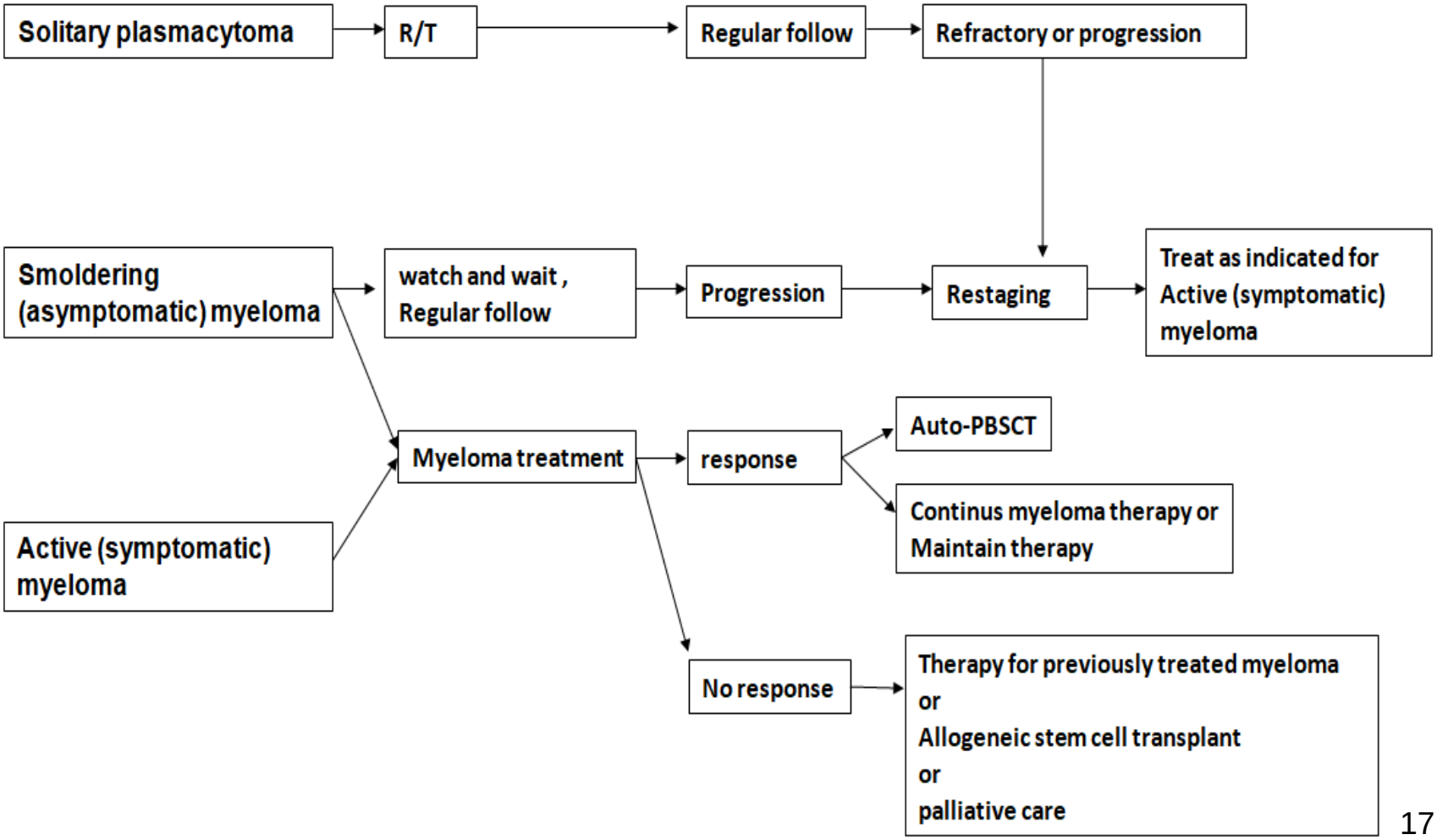
➢ **Staging systems for multiple myeloma**

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 1.2021

➢ Clinical Presentation



Multiple myeloma

Version 1.2021

➢ 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 1.2021

➢ 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 1.2021

➢ 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)

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