Taipei Veterans General Hospital Practices Guidelines Oncology

Bone Cancer

Version 1.2021

Proofing at Bone and Sarcoma MDT Conference on 2021-10-26

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更新日期：2021/05/15		

Principles for Guideline Revision

- **This guideline will be conformed to evidence-based medicine and/or complied with the currently consented practices.**
- **This guideline will be systemically reviewed in an annual guideline revision meeting within the bone and sarcoma multidisciplinary conference.**
- **This guideline is based on consensus of the authors regarding the current evidence for appropriate approaches to workup and treatment.**
- **Any physician consulting this guideline is expected to use independent medical judgment of individual clinical circumstances to determine and apply optimal customized treatment for the cancer patient.**

Summary of Guidelines Updates

- 2013-11-26 Draft of the guideline: Discussed and revised
- 2014-08-29 Draft of the guideline: Discussed and revised
- 2014-09-12 Version 1
- 2014-11-25 Version 2, add criteria of reduced ifosfamide post-operatively in osteosarcoma protocols; change TVGH OGS M2 protocol to M2r protocol; add Ewing sarcoma protocols.
- 2016-7-26 Version 3, the OGS 2008 protocol was revised to become non-stratified post-operatively; the OGS M2r protocol was shortened
- 2016-8-10 Version 4, shift to 2 new protocols (TVGH OGS 2016 and TVGH OGS M3 protocols), revising the panel members, and add new publications
- 2017-8-9 Version 5, renamed TVGH protocols to TPOG OS-2017, ES-2017, and BC-2017, revising the panel members
- 2018-7-31 Version 6, revised according to NCCN guidelines v2.2018 updates
- 2019-11-26 Version 2019, revised according to NCCN guidelines v1.2020 updates. 2020-9-29 Version 2020, emphasized again about the major changes in NCCN guidelines v1.2020 updates.
- 2021-10-26 Version 2021, the main updates includes comprehensive genomic profiling (CGP) and testing for IDH1 mutation.

NCCN Updates in Version 1.2022 from Version 1.2021 include:

TEAM-1
- *Palliative care physician* has been added to "Specialists Critical in Certain Cases"

BONE-1
Workup
- "Age" added to <40 and ≥40.

CHON-1
Chondrosarcoma
- Deleted dedifferentiated arm "(Treat as osteosarcoma [category 2B])" and added a link to CHON-4.

CHON-4
Metastatic Chondrosarcoma
- Added the following footnote to the title: *Consider comprehensive genomic profiling (CGP) with a validated and/or FDA-approved assay to determine targeted therapy opportunities.* (Also for CHOR-3, EW-3, OSTEO-3,).
- "May consider treating as osteosarcoma (category 2B)" text moved from CHON-1 corresponding to "dedifferentiated."
- "See OSTEO-1" deleted.
- Modified footnote "k": Consider testing for tumor mutational burden (TMB) "*and MMR/MSI*" as determined by a validated and/or FDA-approved assay to inform the use of pembrolizumab. (Also for CHOR-3, EW-3, OSTEO-3).

CHOR-1
Chordoma
- Bullet 3, modified: Adequate imaging of primary site (eg, x-ray, ~~CT +/- MRI~~ *MRI ± CT*) and screening MRI of spinal axis (~~CT/MRI~~ *MRI/CT* with contrast).

CHOR-3
- Bullet 2, modified: Imaging of surgical site, timing, and modality, as clinically indicated (eg, x-ray, *MRI* ~~CT~~ with contrast ± ~~MRI~~ *CT* with contrast) for up to 10 y

EW-1
Ewing Sarcoma
- *Consider CGP or other fusion panel for Ewing sarcoma to identify translocations if pathologic workup of targeted PCR, FISH, or cytogenetics is negative,* is a new footnote corresponding to Ewing sarcoma.
- The following reference updated: *Campbell KM, et al. Pediatr Blood Cancer 2021;68:e28807.*

EW-2
Progressive Disease/Relapse
- *Relapse* in place of "~~Early relapse~~" and "~~Late relapse~~"
- RT "± surgery"
- Deleted the following footnote: ~~For late relapse, consider re-treatment with previously effective regimen.~~

GCTB-1
Giant Cell Tumor of Bone
Workup
- Bullet 2, modified: Imaging of primary site as clinically indicated (eg, x-ray *and MRI* with contrast ± *CT*) ~~CT ± MRI with contrast~~

GCTB-2
- *Consider consultation with dentist prior to initial therapy,* is a new footnote corresponding to denosumab.

GCTB-3
Surveillance
- Bullet 3, modified: Chest imaging every 6–*12* mo for ~~2~~ *4* y then annually thereafter.

BONE-A
Principles of Bone Cancer Management
- Biopsy
  - Bullet 8, modified: Appropriate communication between the surgeon, musculoskeletal *or interventional* radiologist, and bone pathologist is critical.

BONE-B (1 of 5)
~~Bone Cancer Systemic Therapy Agents~~
- *Testing for IDH1 mutation can be performed by next-generation sequencing (NGS) or targeted exon sequencing,* is a new footnote corresponding to ivosidenib.
- *Consider (CGP with a validated and/or FDA-approved assay to determine targeted therapy opportunities.* TMB-H for patients with unresectable or metastatic tumors who have progressed following prior treatment and who have no satisfactory alternative treatment options. Not for Giant Cell Tumor of Bone.

這些改變將在以下slides中說明

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2022
Bone Cancer

NCCN Guidelines Index
Table of Contents
Discussion

NCCN Categories of Evidence and Consensus	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

All recommendations are category 2A unless otherwise indicated.

NCCN Categories of Preference	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for selected patient populations (defined with recommendation).

All recommendations are considered appropriate.

Palliative care physician對某些病患來說很重要

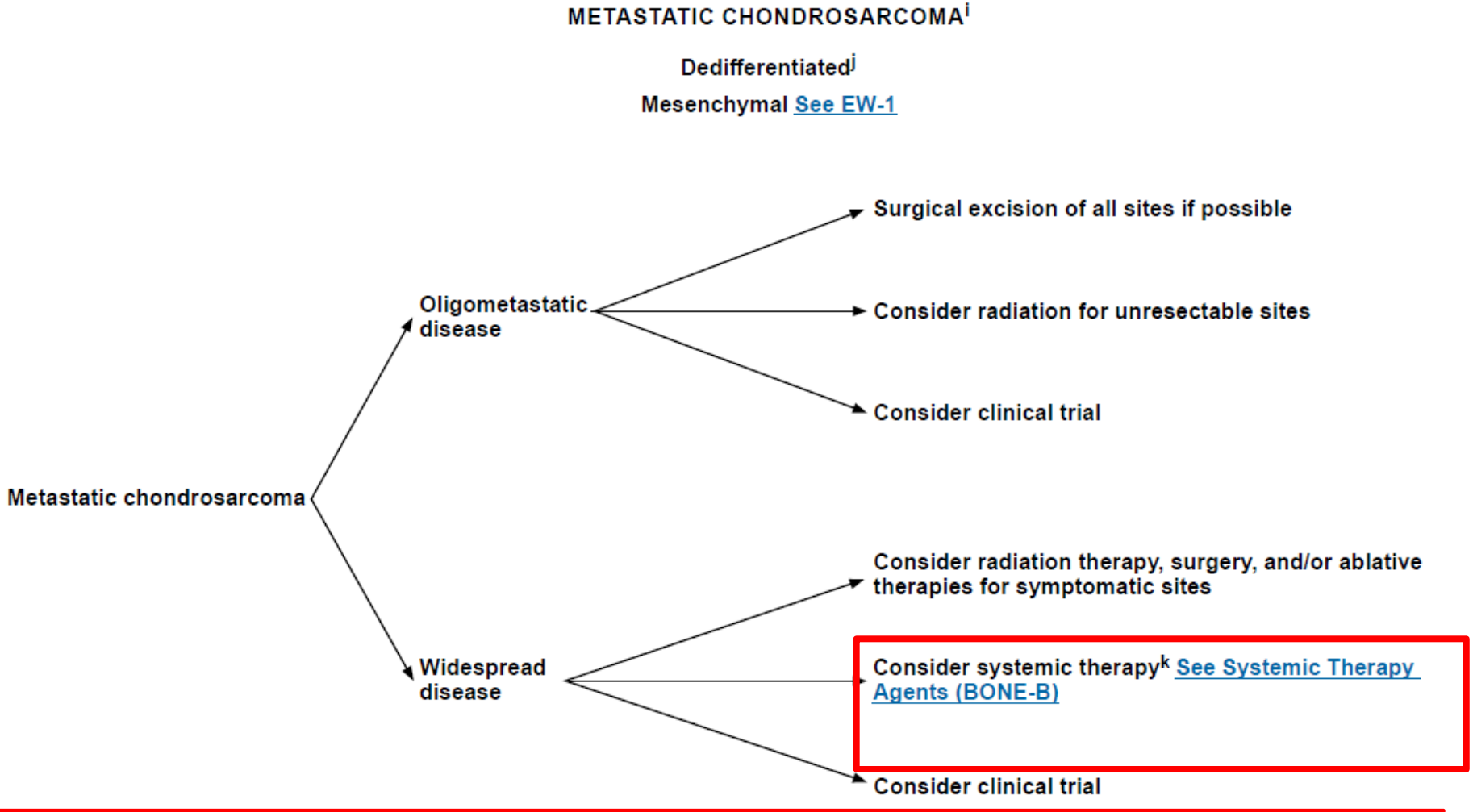
MULTIDISCIPLINARY TEAM

Primary bone tumors and selected metastatic tumors should be evaluated and treated by a multidisciplinary team with expertise in the management of these tumors. The team should meet on a regular basis and should include:

Core Group
- Orthopedic oncologist
- Bone pathologist
- Medical/pediatric oncologist
- Radiation oncologist
- Musculoskeletal radiologist

Specialists Critical in Certain Cases
- Thoracic surgeon
- Plastic surgeon
- Interventional radiologist
- Physiatrist
- Vascular/general surgeon
- Neurosurgeon/orthopedic spine surgeon
- Palliative care physician
- Additional surgical subspecialties as clinically indicated

Chondrosarcoma強調CGP與*IDH1* testing



[i] Consider comprehensive genomic profiling (CGP) with a validated and/or FDA-approved assay to determine targeted therapy opportunities.
[j] May consider treating as osteosarcoma (category 2B).
[k] Consider testing for tumor mutational burden (TMB) and MMR/MSI as determined by a validated and/or FDA-approved assay to inform the use of pembrolizumab.

SYSTEMIC THERAPY AGENTS

MSI-H/dMMR Tumors
Preferred Regimen • Pembrolizumab[1,2,a]
TMB-H (≥10 mutations/megabase) Tumors
Useful in Certain Circumstances • Pembrolizumab[3,4,b]

Chondrosarcoma強調*IDH1* testing
IDH1 mutation者可用ivosidenib

Chondrosarcoma	
Metastatic and widespread disease	Other Recommended Regimens • Dasatinib[5,6] • Pazopanib[7]
Conventional (Grades 1–3)	Preferred Regimens • No known standard chemotherapy options Useful in Certain Circumstances • Ivosidenib[8,c] (for susceptible *IDH1* mutations)
Dedifferentiated	Preferred Regimens • Follow osteosarcoma regimens (category 2B) Useful in Certain Circumstances • Ivosidenib[8,c] (for susceptible *IDH1* mutations)
Mesenchymal	Preferred Regimens • Follow Ewing sarcoma regimens (category 2B)

[a] Pembrolizumab is a systemic treatment option for adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options. Additional dosing recommendations follow: 200 mg IV Day 1, repeat every 3 weeks or 400 mg IV Day 1, repeat every 6 weeks until disease progression, unacceptable toxicity, or up to 24 months for treatment of patients with MSI-H bone cancer. Not for Giant Cell Tumor of Bone or Chordoma.
[b] Consider CGP with a validated and/or FDA-approved assay to determine targeted therapy opportunities. TMB-H for patients with unresectable or metastatic tumors who have progressed following prior treatment and who have no satisfactory alternative treatment options. Not for Giant Cell Tumor of Bone.
[c] Testing for *IDH1* mutation can be performed by next-generation sequencing (NGS) or targeted exon sequencing.

Ivosidenib: IDH1抑制劑

- 2018年6月，基石藥業與 Agios 宣佈就 TIBSOVO 在中國大陸、香港、澳門及台灣地區（「大中華區」）的臨床開發與商業化達成獨家合作與授權許可協議。
- 關於TIBSOVO（ivosidenib）: TIBSOVO（ivosidenib）是一種異檸檬酸脫氫酶-1（IDH1）抑制劑，在美國適用於治療經檢測攜帶易感IDH1突變的
  - 年齡>=75歲或因為其它合併症無法使用強化化療的新診斷 AML 成人患者
  - 復發或難治性 AML 的成人患者

  有關更多信息，請訪問TIBSOVO.com。
- 關於基石藥業: 基石藥業（HKEX: 2616）是一家生物製藥公司，專注於開發及商業化創新腫瘤免疫治療及精準治療藥物，以滿足中國和全球癌症患者的殷切醫療需求。成立於2015年底，基石藥業已集結了一支在新藥研發、臨床研究以及商業化方面擁有豐富經驗的世界級管理團隊。公司以聯合療法為核心，建立了一條包括15種腫瘤候選藥物組成的強大腫瘤藥物管線。目前五款後期候選藥物正處於或接近關鍵性試驗。憑借經驗豐富的團隊、豐富的管線、強大的臨床開發驅動的業務模式和充裕資金，基石藥業的願景是通過為全球癌症患者帶來創新腫瘤療法，成為全球知名的領先中國生物製藥公司。
- 欲瞭解更多，請瀏覽www.cstonepharma.com

Osteosarcoma第一線與第二線藥物

Osteosarcoma			
First-line therapy (primary/ neoadjuvant/adjuvant therapy or metastatic disease)	Preferred Regimens • Cisplatin and doxorubicin[44-46] (category 1) • MAP (high-dose methotrexate, cisplatin, and doxorubicin)[46-49] (category 1)[g]	Other Recommended Regimens • Doxorubicin, cisplatin, ifosfamide, and high-dose methotrexate[50,g]	
Second-line therapy (relapsed/ refractory or metastatic disease)	Preferred Regimens • Ifosfamide (high dose) ± etoposide[35,51] • Regorafenib[52] (category 1) • Sorafenib[53]	Other Recommended Regimens • Cabozantinib[36] • Cyclophosphamide and topotecan[24] • Docetaxel and gemcitabine[37] • Gemcitabine[55] • Sorafenib + everolimus (category 2B)[54]	Useful in Certain Circumstances • Cyclophosphamide and etoposide[56] • Ifosfamide, carboplatin, and etoposide[38] • High-dose methotrexate[g] • High-dose methotrexate, etoposide, and ifosfamide[57,g] • Sm^{153}-EDTMP for relapsed or refractory disease beyond second-line therapy[58]

High-Grade Undifferentiated Pleomorphic Sarcoma (UPS)
Follow osteosarcoma regimens (category 2B)

Ewing sarcoma第一線與第二線藥物

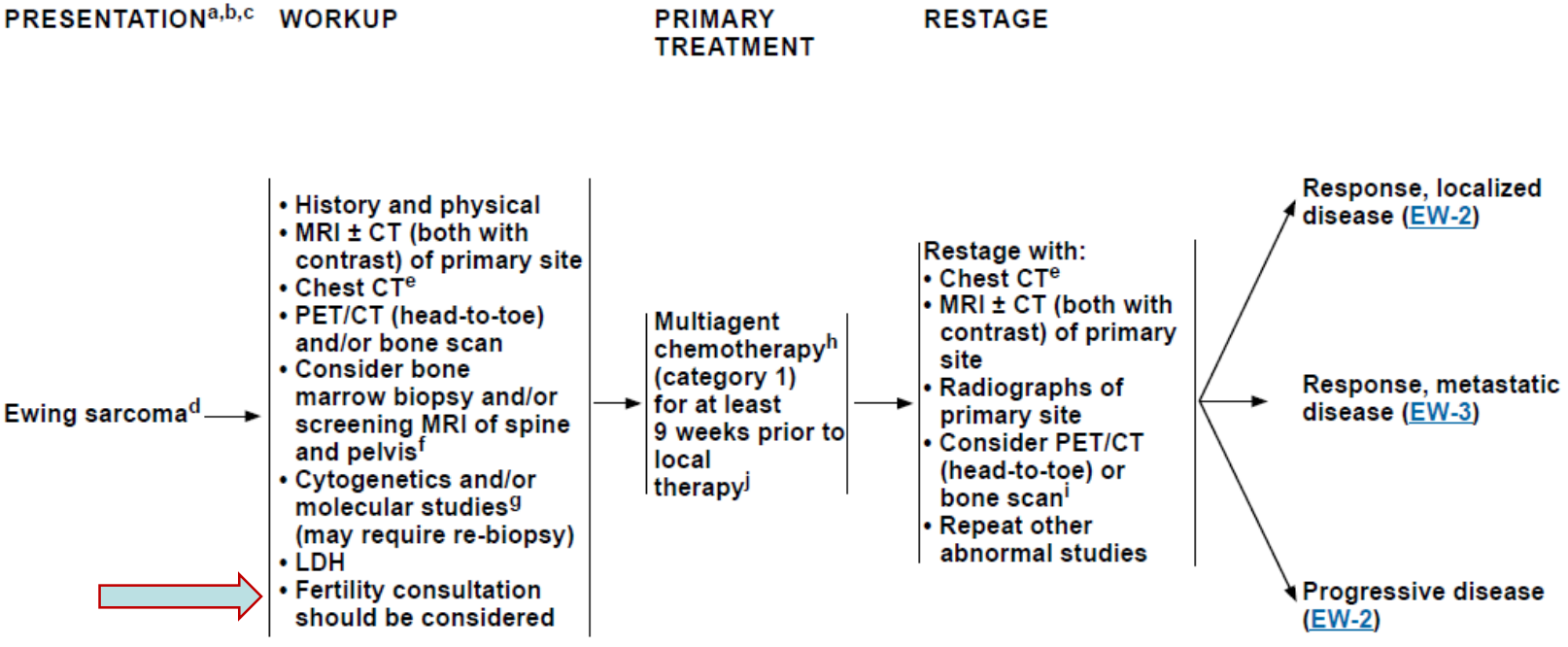
SYSTEMIC THERAPY AGENTS

Chordoma
Other Recommended Regimens • Imatinib[9,10,11] • Dasatinib[5,6] • Sunitinib[12]
Useful in Certain Circumstances • Imatinib with cisplatin[13] or sirolimus[14] • Erlotinib[15] • Lapatinib for EGFR-positive chordomas[16] • Sorafenib[17,18]

Ewing Sarcoma			
First-line therapy (primary/ neoadjuvant/adjuvant therapy)[d]	**Preferred Regimens** • VDC/IE (vincristine, doxorubicin, and cyclophosphamide alternating with ifosfamide and etoposide)[19,20,e] (category 1)	**Other Recommended Regimens** • VAI (vincristine, doxorubicin, and ifosfamide)[21,22] • VIDE (vincristine, ifosfamide, doxorubicin, and etoposide)[23]	
Primary therapy for metastatic disease at initial presentation[d]	**Preferred Regimens** • VDC/IE[19] • VAI[21,22] • VIDE[23] • VDC (vincristine, doxorubicin, and cyclophosphamide)[24]		
Second-line therapy (relapsed/ refractory or metastatic disease)	**Preferred Regimens** • Cyclophosphamide and topotecan[25-28,f] • Irinotecan + temozolomide ± vincristine[29-35]	**Other Recommended Regimens** • Cabozantinib[36] • Docetaxel and gemcitabine[37,f]	**Useful in Certain Circumstances** • Ifosfamide, carboplatin, and etoposide[38,f]

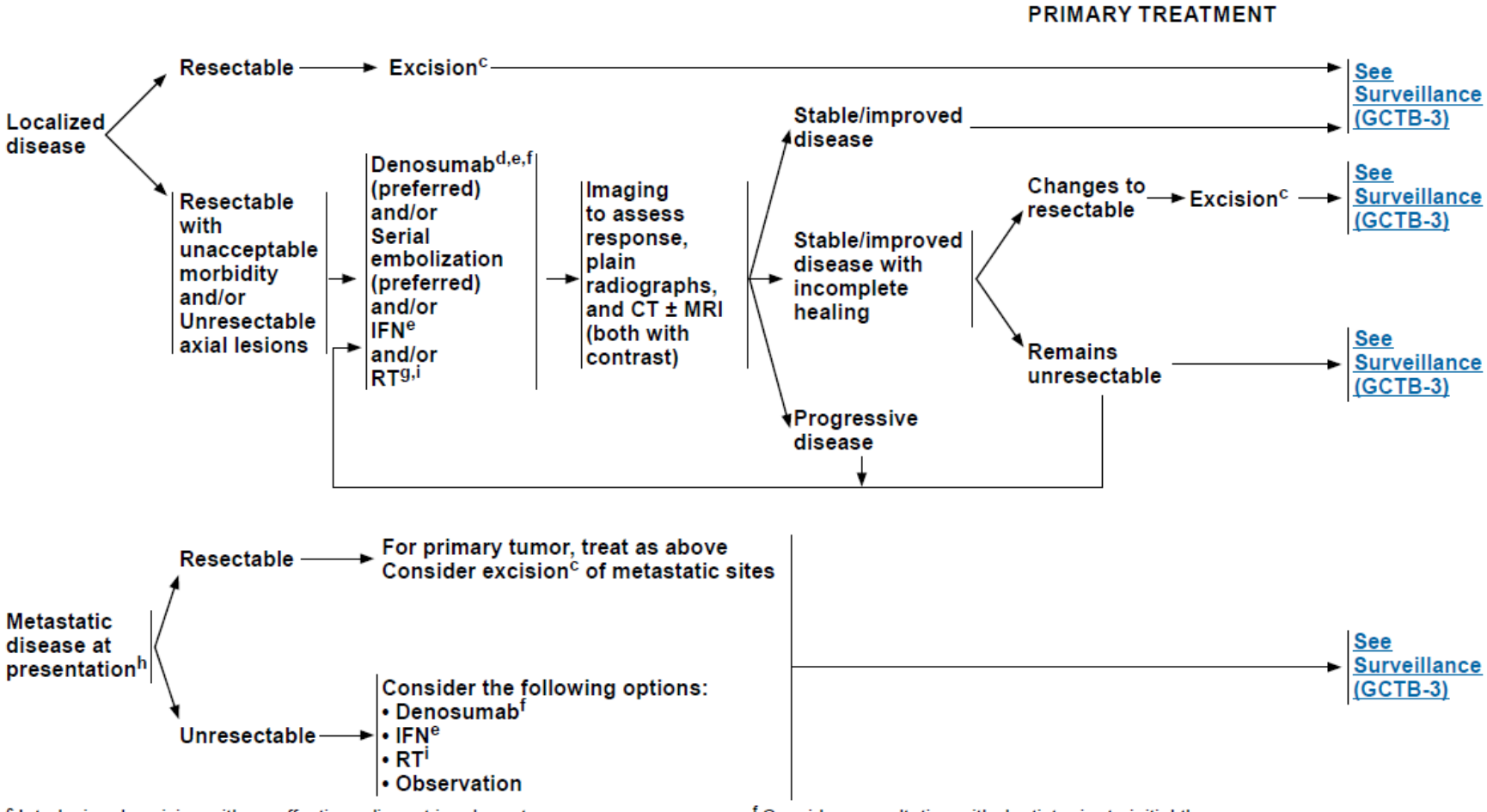
[d] Dactinomycin can be substituted for doxorubicin for concerns regarding cardiotoxicity.
[e] In patients younger than 18 y, evidence supports 2-week compressed treatment.
[f] Vincristine could be added to these regimens.

1. Ewing sarcoma無轉移者，可做PET/CT就好，省略BMBA
2. CIC-DUX4者可以考慮使用其他治療方式



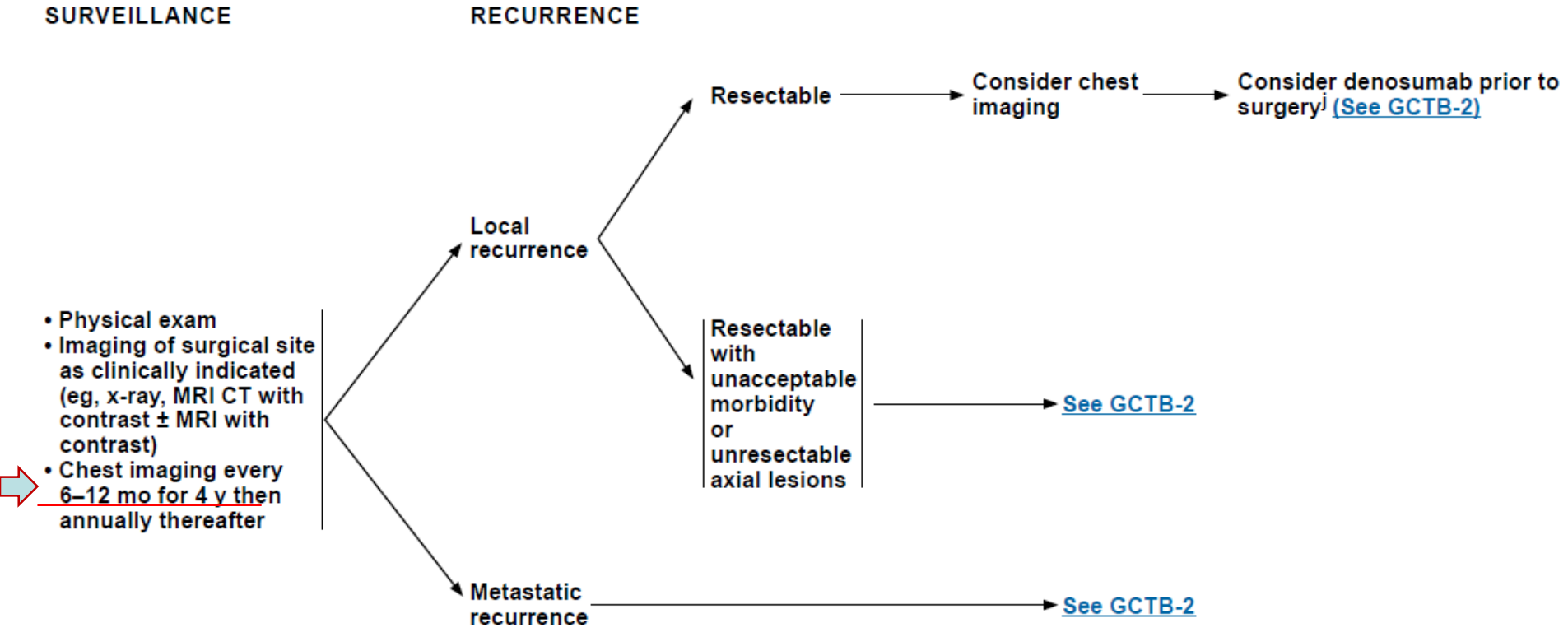
[a] See Multidisciplinary Team (TEAM-1).
[b] See Principles of Bone Cancer Management (BONE-A).
[c] Ewing sarcoma can be treated using this algorithm, including primitive neuroectodermal tumor of bone, Askin tumor, and extraosseous Ewing sarcoma.
[d] Consider CGP or other fusion panel for Ewing sarcoma to identify translocations if pathologic workup of targeted PCR, FISH, or cytogenetics is negative.
[e] Chest CT with or without contrast as clinically indicated.
[f] Campbell KM, et al. Pediatr Blood Cancer 2021;68:e28807.
[g] Ninety percent of Ewing sarcoma will have one of four specific cytogenetic translocations. For patients with Ewing-like sarcoma (eg, CIC-DUX4) an alternate treatment paradigm can be considered. For those who are negative, additional molecular testing is recommended.
[h] See Bone Cancer Systemic Therapy Agents (BONE-B).
[i] Use the same imaging technique that was performed in the initial workup.
[j] Longer treatment prior to local control therapy can be considered in patients with metastatic disease based on response.

Giant Cell Tumor of Bone: 使用denosumab前，先會診牙科



[c] Intralesional excision with an effective adjuvant is adequate.
[d] Denosumab should be continued until disease progression in responding disease.
[e] See Bone Cancer Systemic Therapy Agents (BONE-B).
[f] Consider consultation with dentist prior to initial therapy.
[g] RT may be associated with increased risk of malignant transformation.
[h] Treatment of primary tumor is as described for localized disease.
[i] See Principles of Radiation Therapy (BONE-C).

Giant Cell Tumor of Bone: chest imaging 每6-12月追蹤4年(原為2年)



切片前，骨科，放射科，病理科醫師要先有良好的溝通

PRINCIPLES OF BONE CANCER MANAGEMENT

Biopsy

- Prior to biopsy, consultation should be obtained with an orthopedic oncologist regarding appropriate prebiopsy imaging.
- Preoperative biopsy consultation with pediatric oncologist as appropriate is recommended for children.
- Biopsy diagnosis is necessary prior to any surgical procedure or fixation of primary site.
- Biopsy is optimally performed at a center that will do definitive management.
- Placement of biopsy is critical.
- Biopsy should be core needle or surgical biopsy.
- Technique: Apply same principles for core needle or open biopsy. Needle biopsy is not recommended for skull base tumors.
- Appropriate communication between the surgeon, musculoskeletal or interventional radiologist, and bone pathologist is critical.
- Fresh tissue may be needed for molecular studies and tissue banking.
- In general, failure to follow appropriate biopsy procedures may lead to adverse patient outcomes.

Surgery

- Wide excision should achieve histologically negative surgical margins.
- Negative surgical margins optimize local tumor control.
- Local tumor control may be achieved by either limb-sparing resection or limb amputation (individualized for a given patient).
- Limb-sparing resection is preferred to optimize function if reasonable functional expectations can be achieved.
- Final pathologic evaluation should include assessment of surgical margins, size/dimensions of tumor, and response to preoperative therapy.

Lab Studies

- Lab studies such as CBC, LDH, and ALP may have relevance in the diagnosis, prognosis, and management of bone sarcoma patients and should be done prior to definitive treatment and periodically during treatment and surveillance.

Treatment

- Fertility issues should be addressed with patients prior to commencing chemotherapy.
- See NCCN Guidelines for Adolescent and Young Adult (AYA) Oncology.
- Select patients with osteosarcoma or chondrosarcoma may benefit from a referral for genetic consultation and testing based on family history with a genetic predisposition for bone sarcomas.
- Care for patients with bone cancer should be delivered directly by physicians on the multidisciplinary team (category 1). See TEAM-1.

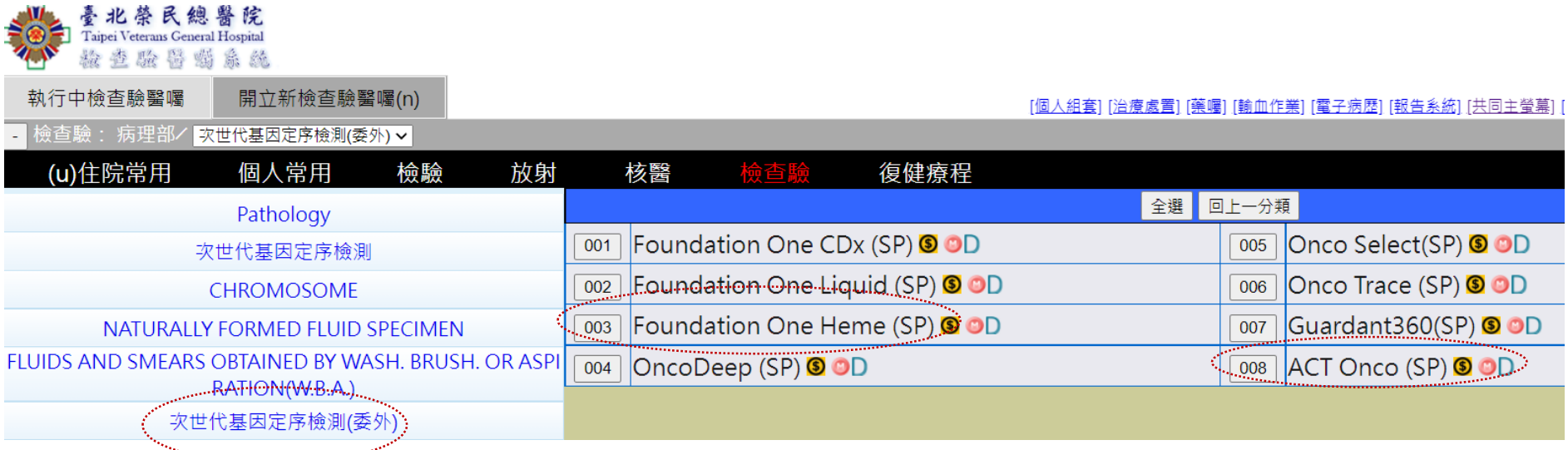
Long-Term Follow-up and Surveillance/Survivorship

- Patients should have a survivorship prescription to schedule follow-up with a multidisciplinary team.
- Life-long follow-up is recommended for surveillance and treatment of late effects of surgery, radiation, and chemotherapy in long-term survivors.

NCCN Guidelines v1.2022 Updates結論

1. **IDH1 mutation & CGP (Comprehensive genomic profiling): 診斷時，復發時都要考慮做。Chondrosarcoma 有IDH1 mutation者可使用ivosidenib。**
2. **Ewing sarcoma無轉移者，可做PET/CT就好，省略BMBA。CIC-DUX4者可以考慮使用其他治療方式。**
3. **Giant Cell Tumor of Bone: chest imaging 每6-12月追蹤4年(原為2年)，使用denosumab前，先會診牙科。**
4. **切片前，骨科，放射科，病理科醫師要先有良好的溝通**
5. **安寧緩和治療對某些病患很重要**
6. **化療前要考慮保存生育功能**
7. **Osteosarcoma 一線建議MAP，MAP+IFO歸類在Other recommended regimen: 繼續使用**
8. **Ewing sarcoma一線使用VDC/IE, 可以考慮interval compressed化療(q3w→q2w)**

病理部: 次世代基因定序(委外)



正式報告

臺北榮民總醫院病理部報告

病患資訊：	中正０９３ - 21 陳妍萱 4617956-0 女性 13歲 GPED	
申請序號 / 工作號：	0BKRENL/S110-99552	開立時間：
開醫囑者：	DOC8059J 許雅筑	簽收時間：
報告人 ：	DOC5452C 周德盈	報告時間：
檢體 ：	Tissue	
醫囑名稱：	Foundation One Heme (SP)	

PATHOLOGICAL DIAGNOSIS:

Test Name: FoundationOne Heme

Relevant Biomarkers

Biomarker Findings
Microsatellite Status -MS-Stable
Tumor Mutation Burden - 7 Muts/Mb

Genomic Findings alternation [VAF%]
MYC amplification
C17orf39 amplification
CDKN2A/B CDKN2B loss, CDKN2A loss

討論: NCCN第一線建議MAP，而MAP+IFO歸類在Other recommended regimen。
結論: 目前本院的protocol是根據本院過去研究結果，顯示治療成績與歐美一致，建議繼續使用。

TPOG-OS 2017 protocol

化學治療藥物與時程

	←手術前化療→						←手術後化療→							
Cycle	1			2			3				4			
	M	P A	I	M	P A	*OP*	I	M	P*	A*	I	M	P*	A*
週	0	1	4	7	8	11	13	16	17	20	23	26	27	30
劑量 (mg)														
日期														

OP = 原發部位手術

腫瘤壞死率 = _____ % (GR=化療反應佳者, 腫瘤壞死率≥ 90%; PR=化療反應不佳者, 腫瘤壞死率< 90%)

M	=	Methotrexate	(MTX)	**12000** mg/m^2 靜脈注射 4 小時 with leucovorin rescue
P*	=	Cisplatin	(CDDP)	**75** mg/m^2/day 靜脈連續滴注 24 hrs x 2 days
P	=	Cisplatin	(CDDP)	**60** mg/m^2/day 靜脈連續滴注 24 hrs x 2 days
A*	=	Adriamycin	(ADR)	**45** mg/m^2/day 靜脈連續滴注 24 hrs x 2 days
A	=	Adriamycin	(ADR)	**37.5** mg/m^2/day 靜脈連續滴注 24 hrs x 2 days
I	=	Ifosfamide	(IFO)	**3000** mg/m^2/day 靜脈連續滴注 24 hrs x 5 days with 等量 mesna

VDC/IE: 可以考慮Interval compressed

TPOG-ES 2017

化學治療藥物與時程

	←手術前化療			→		←			手術後化療						→	
Cycle	*C1*	*C2*	*C3*	*C4*	*OP*	*C5*	*C6*	*C7*	*C8*	*C9*	*C10*	*C11*	*C12*	*C13*	*C14*
						R/T	*R/T*	*R/T*							
	V	**I**	**V**	**I**		**V**	**I**	**V**	**I**	**V**	**I**	**V**	**I**	**V**	**I**
	D	**E**	**D**	**E**		**D**	**E**		**E**	**D**	**E**	**D**	**E**		**E**
	C		**C**			**C**		**C**		**C**		**C**		**C**	
	(e)				*(e)*				*(e)*				*(e)*		
週	**0**	**3**	**6**	**9**	**12**	**14**	**17**	**20**	**23**	**26**	**29**	**32**	**35**	**38**	**41**
劑量(mg)															
日期															

*轉移者或復發之高危險群建議加上 Anti-angiogenic 藥物如下(全部療程；從 C1 第一天至 C14 第 21 天，開刀後**暫停 1 週，放療期間亦暫停**):

Vin**bla**stine	**1** mg/m^2/dose, IV push 3 times/week	該週若化療使用 vin**cri**stine，則下降為 2 times/week
Celecoxib 自費	**250** mg/m^2/dose, BID 口服[四捨五入為半顆(100 mg)、一顆(200 mg)…以此類推)	Total daily dose **500** mg/m^2

OP =手術

R/T =放療 Week 13，有肺轉移者開始 whole lung irradiation 1500 cGy (請病患戒菸)，暫停 anti-angiogenic drugs (總劑量=_____cGy，共_____次)(日期:_____至_____)

(e) =檢查與評估

V	=	Vincristine	*Day 1*	**1.5** mg/m^2 (最大劑量 **2** mg) IV drip **15** min
D	=	Doxorubicin	*Day 1-2*	**37.5** mg/m^2/day 靜脈連續滴注 **24** 小時
C	=	Cyclophosphamide with Mesna	*Day 1*	**1200** mg/m^2 靜脈滴注 **1** 小時 Mesna= 20% of the endoxan dose in the bag with the drug and 2 boluses of the same dose at hours 4 and 8 after the infusion.
I	=	Ifosfamide with Mesna	*Day 1-5*	**1800** mg/m^2/day 靜脈滴注 **1** 小時 (最大總劑量 **9000** mg/m^2) Mesna =20% of the ifosfamide dose in the bag with the drug and 2 boluses of the same dose at hours 4 and 8 after the infusion.
E	=	Etoposide	*Day 1-5*	**100** mg/m^2/day 靜脈滴注 **1-2** 小時 (etoposide 濃度需 ≤ 0.4 mg/mL in D5W or NS)

TPOG-BC 2017-rel (2)

(For osteosarcoma, group A~H; for Ewing sarcoma, group A, C, D, F, VIT)

組合	藥物劑量	天數	註
A	Ifosfamide* **2400** mg/m²/day CIVD 22 hrs Etoposide **60** mg/m²/day IVD for 2 hrs	D1~5 D1~5	*IFO 要給等量 **mesna** CIVD 22 hrs (共五天); hydration 3000cc/m²/day.
C	Endoxan **625** mg/m²/day IVD for 4 hrs Topotecan **1.25** mg/m²/day IVD 30 minutes 自費	D1,2 D1,2,3	*Hydration 3000 cc/m²/day.
D	Gemcitabine **900** mg/m²/day IVD 90 分鐘，自費 Taxotere **75** mg/m²/day IVD 60 分鐘，自費 *Premedication:* *D1, D8 化療前先給 Allermin+kytril IV.* *D7~9 每天口服兩次:* dexamethasone 4~8 mg, periactin 1#, 與 ranitidine (自費) 1#.	D1, ***D8*** ***D8***	*不需特別 hydration, *可以門診打藥*. **Day 8 先給 Gemzar,再給 taxotere.*
E	Cyclophosphamide* **4000** mg/m² IVD 4 hrs Etoposide **100** mg/m² IVD 2 hrs, **twice daily** *Day1 給 cyclophosphamide 時要給 **mesna** 1400 mg/m² 共三次: bolus at 0, 4, 8 hrs from cyclophosphamide start	D1 D2,3,4	Day 1 hydration 3000cc/m²/day. (注意: Etoposide 100 mg/m²每天給兩次，三天總劑量為 600 mg/m²)
F	Carboplatin **100** mg/m²/day IVD 1 hr (hr 0-1) Etoposide **150** mg/m²/day IVD 2 hrs (hr 1-3) Ifosfamide* **1500** mg/m²/day CIVD 21 hrs (hr 3-24)	D1~4 D1~4 D1~4	*IFO 要給等量 **mesna** CIVD 21 hrs (共 4 天). *Hydration 3000cc/m²/day.
G	Gemcitabine **1000~1200** mg/m² IVD 100~120 minutes 自費	D1,8,15	10 mg/m²/min fixed infusion. *不需特別 hydration, *可以門診打藥*.
H	Sorafenib **400** mg PO twice daily 自費	**Daily**	Dose reduction according to toxicity .
VIT	Vincristine **1.5** mg/m² (max: 2 mg/dose) Irinotecan **50** mg/m²/d IVD 1 hour for **5** d 自費 Temozolomide **125~150** mg/m²/d orally for **5** d (> 1 hour prior to irinotecan) 自費	D1, D8 D1~5 D1~5	Vincristine max 2 mg. Irinotecan max 100 mg/dose, 2 天前要先開始吃 cefixime，至少連續吃 10 天。如果腹瀉，使用 loperamide and hydration support.

GCSF support: all needed except for sorafenib (組合代號 H).

上述化藥組合除 sorafenib 為每天連續性使用外，其他組合每 21 天為一個 cycle。

MRI Protocol for Bone Cancer

T Stage

Tx: Primary tumor cannot be assessed
T0: No evidence of primary tumor
T1: Tumor 8 cm or less in greatest dimension
T2: Tumor more than 8 cm in greatest dimension
T3: Discontinuous tumors in the primary bone site

N Stage

Nx: Regional lymph nodes cannot be assessed
N0: No regional lymph node metastasis
N1: Regional lymph node metastasis

M Stage

M0: No distant metastasis
M1: Distant metastasis
- **M1a: Lung Metastases**
- **M1b: Other distant sites / lymphadenopathy**

TNM Staging System: UICC/AJCC 2010 7th Edition

T Stage

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TNM Staging System: UICC/AJCC 2010 7th Edition
Stage Grouping

GROUP	T	N	M	Grade
IA	T1	N0	M0	G1,2 Low grade GX
IB	T2	N0	M0	G1,2 Low grade GX
	T3	N0	M0	G1,2 Low grade GX
IIA	T1	N0	M0	G3,4 High grade
IIB	T2	N0	M0	G3,4 High grade
III	T3	N0	M0	G3,4*
IVA	Any T	N0	M1a	Any G
IVB	Any T	N1	Any M	Any G
	Any T	Any N	M1b	Any G

*Ewing's sarcoma is classified as G4

Follow-Up

- **If the patient develops of symptoms and signs for recurrent disease during the follow-up, the following studies may be arranged ahead of the fixed follow-up schedule.**
- **Physical examination**
- **MRI of primary tumor**
  - Every 6 months or as clinically indicated
- **Sonography of primary site**
  - Every 6 months
- **CT Chest**
  - Every 6 months for the first 5 years
  - Once a year thereafter
- **Bone scan**
- **Serum metabolite analysis for liver and renal function**
  - Every 3 months in the first 2 years
  - Every 4 months in the 3rd year
  - Every 6 months thereafter up to 5 years

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感謝您的聆聽~
敬請多多指教!

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