

# 高雄榮民總醫院

## 甲狀腺癌臨床診療指引

2023 年第一版

癌症中心甲狀腺癌醫療團隊擬定

2019 年第一版為參考美國癌症聯合委員會於 2018 年 3 月出版之甲狀腺癌臨床指引、2015 年美國甲狀腺協會治療指引及其他參考文獻，於 2023.02.16 由甲狀腺癌團隊相關人員梁宗榮、佘筠瑩、朱志勳、譚弘遠、邱宇莉、張益銘、許碩修等討論後共同修訂。

注意事項：這個診療準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，直接引用這個研究資訊及診療準則並不恰當。

只有你的醫師才能決定給你最恰當的治療。

## Summary of the Guidelines Updates (與上一版差異)

### 上一版

#### 1.標靶治療處方 (Kinase Inhibitor Therapy or metastasis)

Regimen	Agents/Dosages	Frequency
Dabrafenib (Tafinlar) and Trametinib (Mekinist)	150 mg and 2 mg Oral	Twice daily (BID) and once daily (QD)
Pralsetinib (Gavreto)	400 mg Oral	Once daily (QD)

### 新版

#### 1.標靶治療處方 (Kinase Inhibitor Therapy or metastasis)

Regimen	Agents/Dosages	Frequency
Sorafenib (Nexavar)	400mg Oral	Twice daily (BID)
Lenvatinib(Lenvima)	24mg Oral	Once daily (QD)
Dabrafenib (Tafinlar) and Trametinib (Mekinist)	150 mg and 2 mg Oral	Twice daily (BID) and once daily (QD)
Pralsetinib (Gavreto)	400 mg Oral	Once daily (QD)
Cabozantinib (Cabometyx)	60 mg Oral	Once daily (QD)
Everolimus (Afinitor, Votubia, Certican)	10 mg Oral	Once daily (QD)
Selpercatinib (Retevmo)	160 mg Oral	Twice daily (BID)
Larotrectinib (Vitrakvi)	100 mg Oral	Twice daily (BID)

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## 甲狀腺結節評估 - 超音波特徵

	<u>Threshold for FNA</u>		
Solid nodule			
• With suspicious sonographic features <sup>1</sup>	$\geq 1.0$ cm	Yes	FNA
• Without suspicious sonographic features	$\geq 1.5$ cm		
Mixed cystic-solid nodule			
• With suspicious sonographic features <sup>1</sup>	Solid component $>1$ cm		
• Without suspicious sonographic features	Solid component $>1.5$ cm	No	Observe
Spongiform nodule <sup>2</sup>	$\geq 2.0$ cm		
Suspicious cervical lymph node <sup>3, 4</sup>	FNA node $\pm$ FNA-associated thyroid nodule(s)		

<sup>1</sup>Suspicious sonographic features: Hypoechoic, microcalcifications, infiltrative margins, and taller than wide in transverse plane. Sonographic features associated with a low risk of malignancy including spongiform nodules, isoechoic or hyperechoic solid nodules, and mixed solid-cystic nodules without any of the suspicious features listed above.

<sup>2</sup>Aggregation of multiple microcystic components in more than 50% of the volume of the nodule.

<sup>3</sup>Tg washout may be helpful in diagnosis of lymph node metastases.

<sup>4</sup>Suspicious lymph node features may include hypoechoic, rounded, absence of fatty hilum, cystic or partially cystic, and/or microcalcifications.

## 甲狀腺細胞病理學報告

<b>Benign form 良性的格式</b>	
<b>1. Nondiagnostic</b>	
	<i>Specimen processed and examined, but nondiagnostic due to insufficient cellularity.</i>
<b>2. Benign</b>	
	<i>Presence of some benign-appearing follicular cells</i>
<b>3. BENIGN.</b>	
	<i>Consistent with lymphocytic (Hashimoto's) thyroiditis. Numerous polymorphic lymphoid cells and scattered follicular cells. Lymphocytic (Hashimoto's) thyroiditis is considered. Suggest clinical correlation.</i>
<b>Atypia 不確定的格式</b>	
<b>4. Atypia of Undetermined Significance, favor reactive</b>	
	<i>Presence of groups of proliferative benign-looking follicular cells. Suggest follow-up and repeat FNA cytology in the next visit.</i>
<b>5. Atypia of Undetermined Significance, neoplasm cannot be excluded</b>	
	<i>Presence of groups/sheets of proliferating follicular cells with obvious nucleoli/ with focal papillary arrangement, the possibility of malignancy cannot be excluded totally. Suggest further evaluation and either repeat FNA cytology 3 months later or do biopsy if clinically indicated.</i>
<b>Suspicious for a Follicular Neoplasm. 針對濾泡型腫瘤</b>	
<b>6. Suspicious for a Follicular Neoplasm.</b>	
	<i>Cellular aspirate of follicular cells with a predominantly microfollicular architecture, scattered isolated cells, and scant colloid.</i>

<b>Suspicious for malignancy 疑似惡性</b>	
<b>7.</b>	<b>Suspicious for malignancy</b>
	<i>Presence of some sheets of proliferating follicular cells, of which some having intranuclear pseudoinclusions. Suspicious for papillary carcinoma. Presence of some atypical follicular cells with obvious nucleoli and a few pseudo-inclusion nuclei, of which the possibility of papillary carcinoma should be considered. Suggest further evaluation and do biopsy.</i>
<b>8.</b>	<b>Suspicious for malignancy, particularly medullary carcinoma cannot be excluded.</b>
	<i>Presence of some small groups of small hyperchromatic cells, of which the possibility of malignancy, particularly medullary carcinoma cannot be excluded. Suggest do biopsy if clinically indicated.</i>
<b>Malignant 確定惡性</b>	
<b>9.</b>	<b>Positive for malignant cells.</b>
	<i>The sections show groups of atypical follicular cells with obvious pseudo-inclusions, which is consistent with papillary carcinoma.</i>

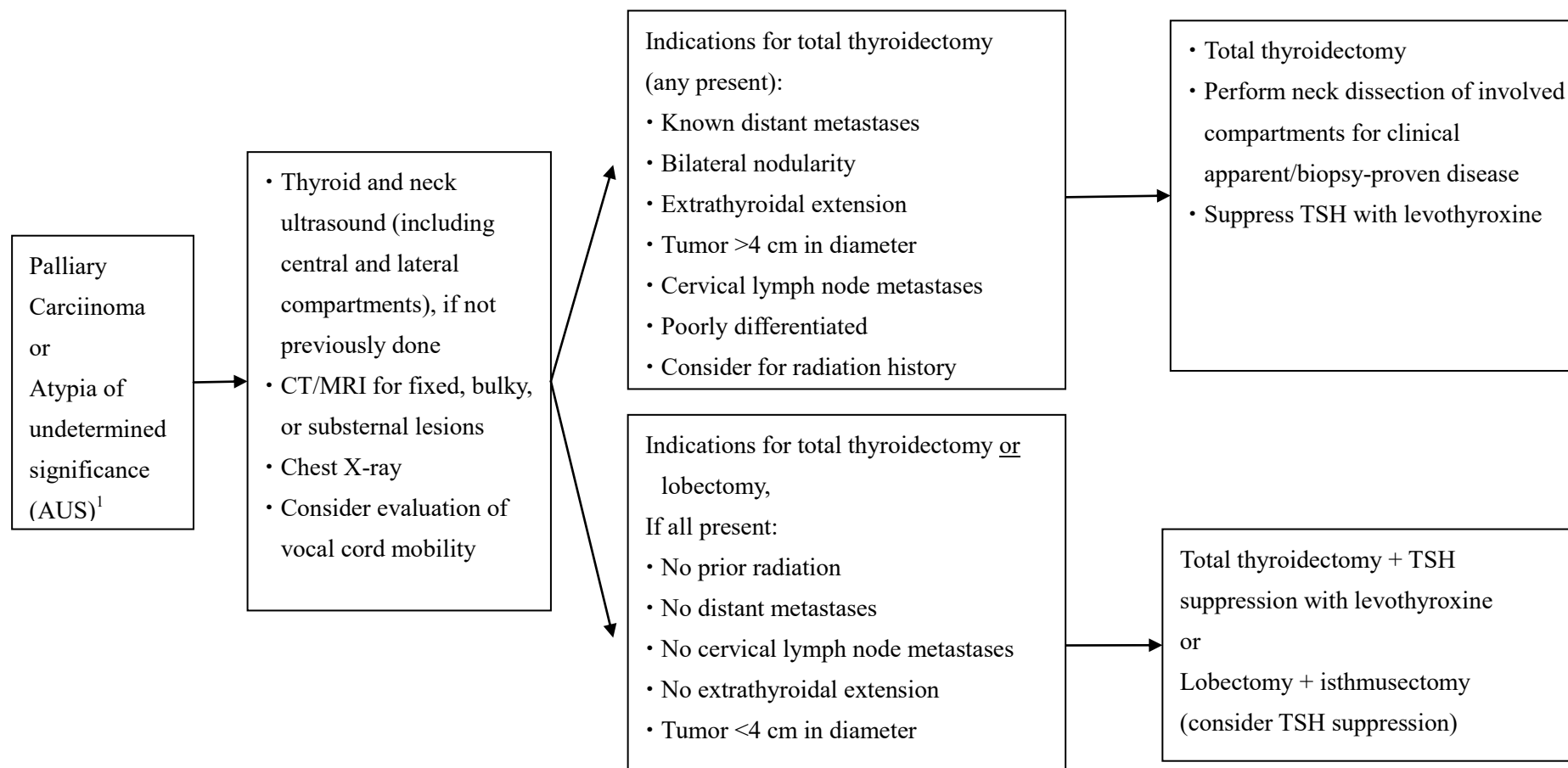
## 乳突癌 (Papillary Carcinoma)

### 細針抽吸結果

### 評估

### 手術方式考量

### 治療



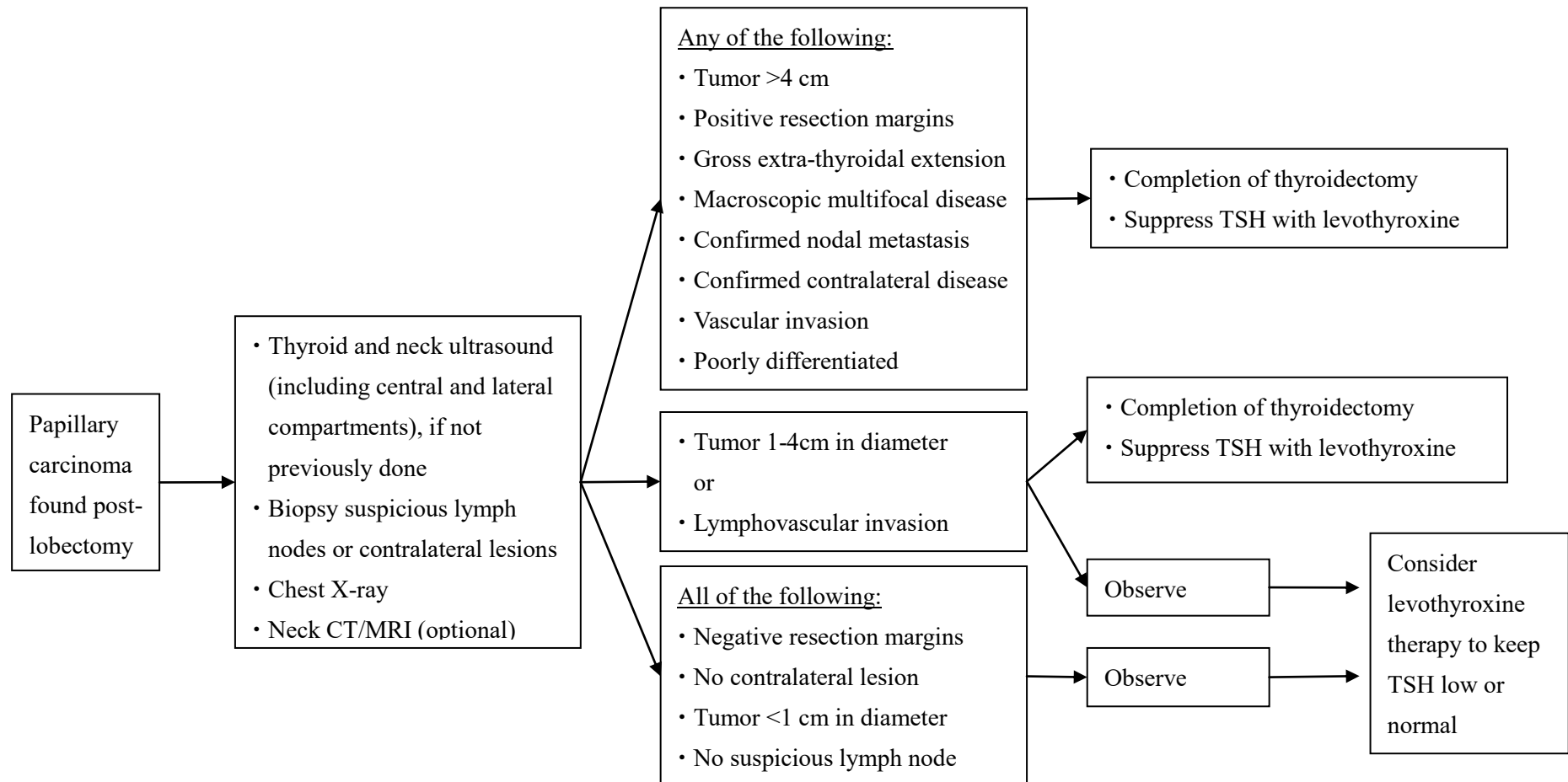
<sup>1</sup>AUS with high clinical suspicion of malignancy may consider lobectomy or total thyroidectomy for definitive diagnosis/treatment.

## 單葉切除術後發現之乳突癌(Papillary carcinoma found post-lobectomy)

臨床表現

評估

治療



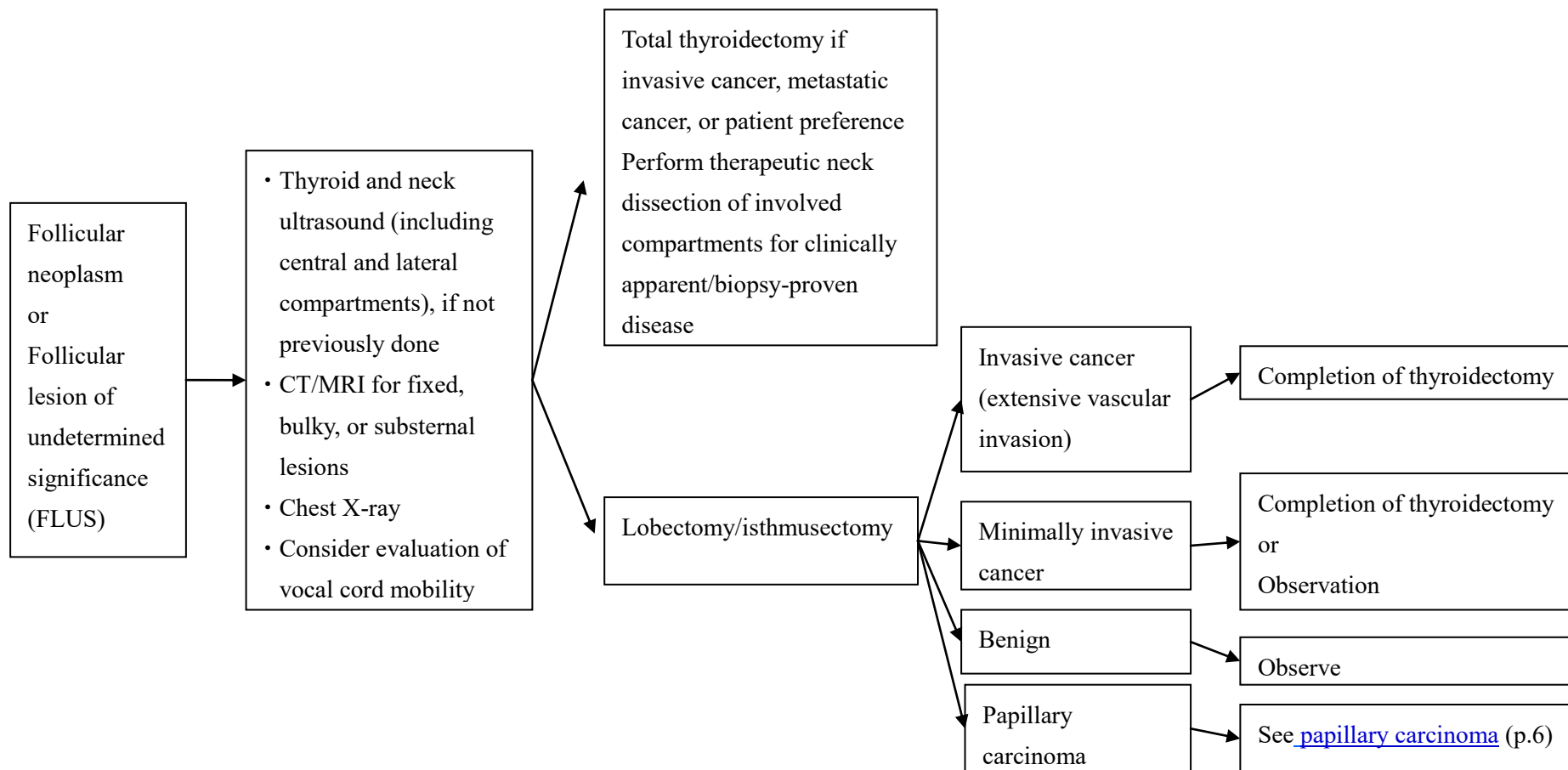


## 濾泡癌(Follicular Carcinoma)

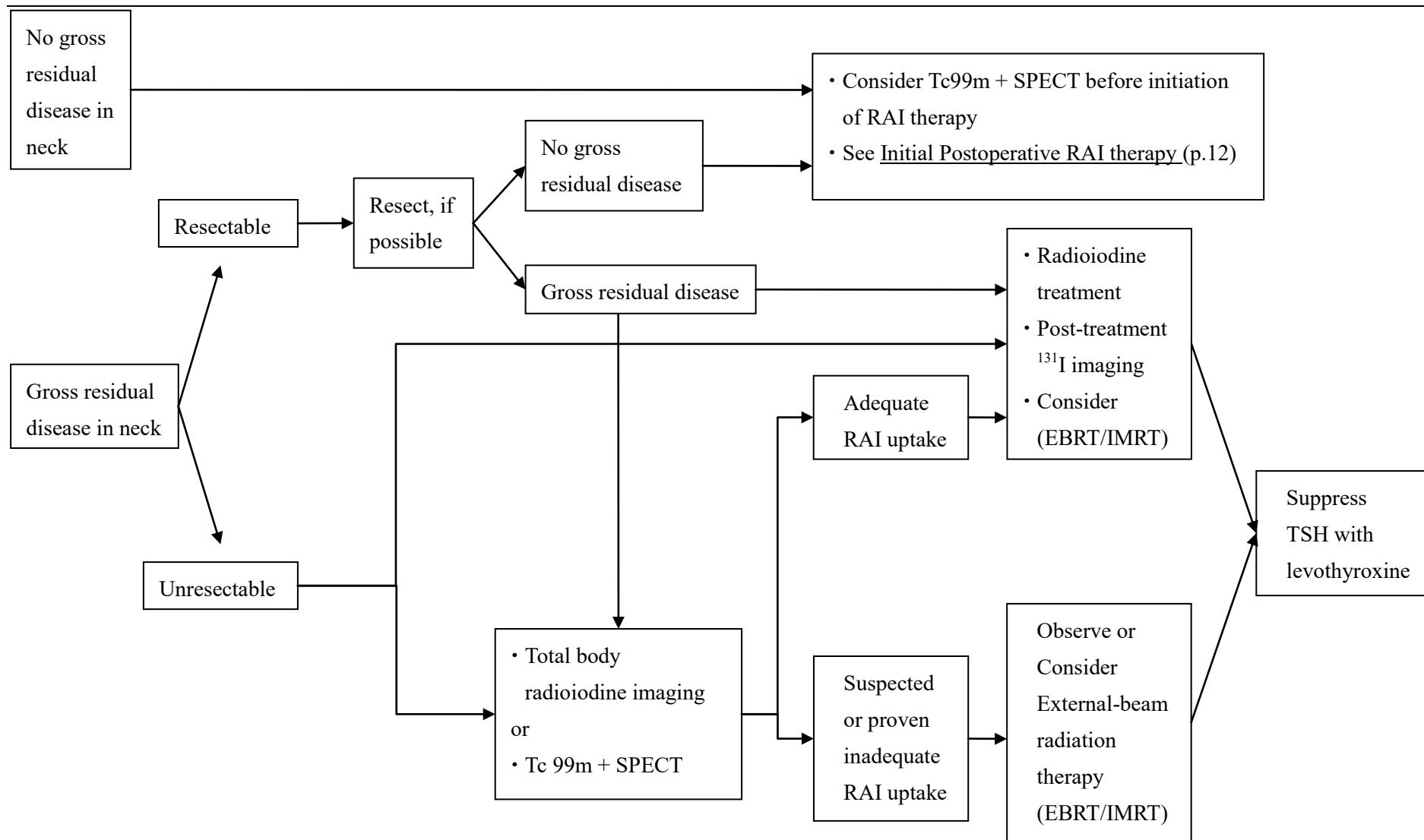
### 細針抽吸結果

### 評估

### 治療



## 術後評估與治療(Postsurgical Evaluation & Treatment)



## 美國甲狀腺協會危險分層系統(ATA risk stratification system with Proposed Modifications)

<p style="text-align: center;">低風險 Low risk</p>	<p>Papillary thyroid cancer (with all of the following):</p> <ul style="list-style-type: none"> <li>• No local or distant metastases;</li> <li>• All macroscopic tumor has been resected</li> <li>• No tumor invasion of loco-regional tissues or structures</li> <li>• The tumor does not have aggressive histology (e.g., tall cell, hobnail variant, columnar cell carcinoma)</li> <li>• If 131-I is given, there are no RAI-avid metastatic foci outside the thyroid bed on the first posttreatment whole-body RAI scan</li> <li>• No vascular invasion</li> <li>• Clinical N0 or <math>\leq 5</math> pathologic N1 micrometastases (<math>&lt;0.2</math> cm in largest dimension)<sup>a</sup></li> </ul> <p>Intrathyroidal, encapsulated follicular variant of papillary thyroid cancer<sup>a</sup></p> <p>Intrathyroidal, well differentiated follicular thyroid cancer with capsular invasion and no or minimal (<math>&lt;4</math> foci) vascular invasion<sup>a</sup></p> <p>Intrathyroidal, papillary microcarcinoma, unifocal or multifocal, including BRAF<sup>V600E</sup> mutated (if known)<sup>a</sup></p>
<p style="text-align: center;">中度風險 Intermediate risk</p>	<p>Microscopic invasion of tumor into the perithyroidal soft tissues</p> <p>RAI-avid metastatic foci in the neck on the first posttreatment whole-body RAI scan</p> <p>Aggressive histology (e.g., tall cell, hobnail variant, columnar cell carcinoma)</p> <p>Papillary thyroid cancer with vascular invasion</p> <p>Clinical N1 or <math>&gt;5</math> pathologic N1 with all involved lymph nodes <math>&lt;3</math> cm in largest dimension<sup>a</sup></p> <p>Multifocal papillary microcarcinoma with ETE and BRAF<sup>V600E</sup> mutated (if known)<sup>a</sup></p>
<p style="text-align: center;">高風險 High risk</p>	<p>Macroscopic invasion of tumor into the perithyroidal soft tissues (gross ETE) 腫瘤沒有完整切除</p> <p>Incomplete tumor resection</p> <p>Distant metastases</p> <p>Postoperative serum thyroglobulin suggestive of distant metastases</p> <p>Pathologic N1 with any metastatic lymph node <math>\geq 3</math> cm in largest dimension<sup>a</sup></p> <p>Follicular thyroid cancer with extensive vascular invasion (<math>&gt; 4</math> foci of vascular invasion)<sup>a</sup></p> <div style="border: 1px solid black; padding: 5px; margin-top: 10px;"> <p><sup>a</sup>Proposed modifications, not present in the original 2009 initial risk stratification system</p> </div>

## 促甲狀腺激素抑制原則[Principles of Thyroid-Stimulating Hormone (TSH) Suppression]

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- Because TSH is a trophic hormone that can stimulate the growth of cells derived from thyroid follicular epithelium, the use of levothyroxine to maintain low TSH levels is considered optimal in treatment of patients with papillary, follicular, or Hurthle cell carcinoma. However, data are lacking to permit precise specification of the appropriate serum levels of TSH.
- Given the potential toxicities associated with TSH-suppressive doses of levothyroxine—including cardiac tachyarrhythmias (especially in the elderly) and bone demineralization (particularly in post-menopausal women) as well as frank symptoms of thyrotoxicosis—the risk and benefit of TSH-suppressive therapy must be balanced for each individual patient.
- Patients whose TSH levels are chronically suppressed should be counseled to ensure adequate daily intake of calcium and vitamin D.

## 術後放射線碘治療 (Initial Postoperative RAI therapy)

### Papillary Carcinoma

#### **RAI not typically recommended (if all present) :**

- Classic papillary thyroid carcinoma (PTC)
- Primary tumor < 2 cm
- Intrathyroidal
- Unifocal or multifocal

#### **RAI selectively recommended (if any present):**

- Primary tumor 2-4cm
- High-risk histology
- Lymphovascular invasion
- Cervical lymph node metastases
- Macroscopic multifocality (one focus >1 cm)

#### **RAI typically recommended (if any present):**

- Gross extrathyroidal extension
- Primary tumor >4 cm
- Known or suspected distant metastases at presentation (if amenable to RAI)

### Follicular carcinoma

#### **RAI not typically recommended (if all present) :**

- Primary tumor <2 cm
- Intrathyroidal
- No vascular invasion
- Clinical N0

#### **RAI selectively recommended (if any present):**

- Primary tumor 2-4cm
- Minor vascular invasion
- Cervical lymph node metastases

#### **RAI typically recommended (if any present):**

- Gross extrathyroidal extension
- Primary tumor >4 cm
- Extensive vascular invasion
- Known or suspected distant metastases at presentation (if amenable to RAI)

#### **Recommended Dosage :**

- RAI not typically recommended: 0-30 mCi
- RAI selectively recommended: 30-150 mCi
- RAI typically recommended: 100-200 mCi

## 放射線治療 (External Beam Radiation Therapy/Intensity Modulated Radiation Therapy)

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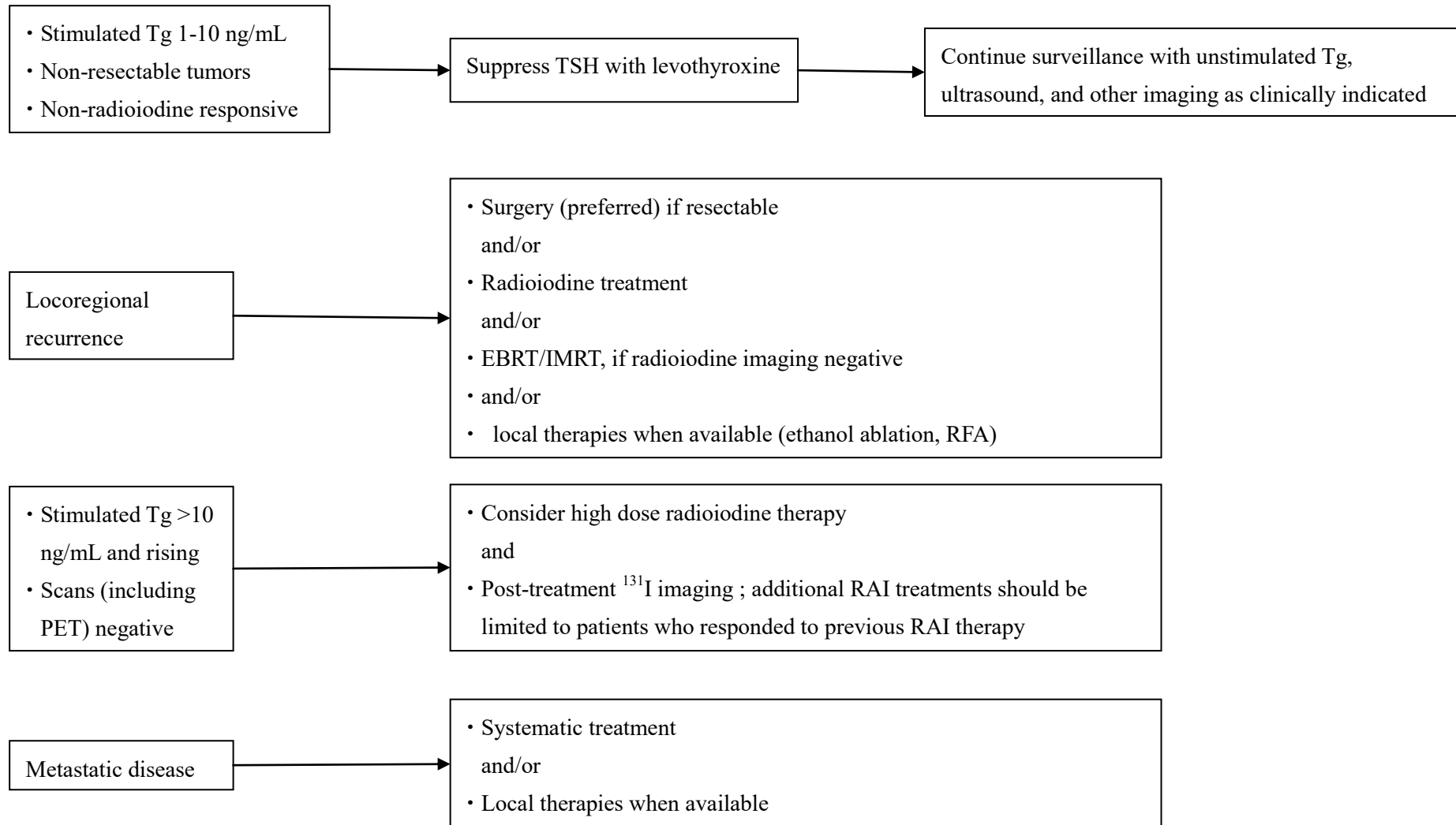
- There is no major prospective, randomized trials in external beam radiotherapy but some retrospective studies showed beneficial in local control or cancer-specific survival.
- Indication of considering R/T
  - gross residual tumor/unresectable tumor, esp in no/poor RAI uptake tumor
  - extrathyroidal extension or extranodal extension.
- Dosage:
  - low-risk : 54 Gy,
  - microscopic disease: 59.4–63 Gy,
  - positive margins: 63–66 Gy,
  - macroscopic disease: 66–70 Gy.

## 追蹤

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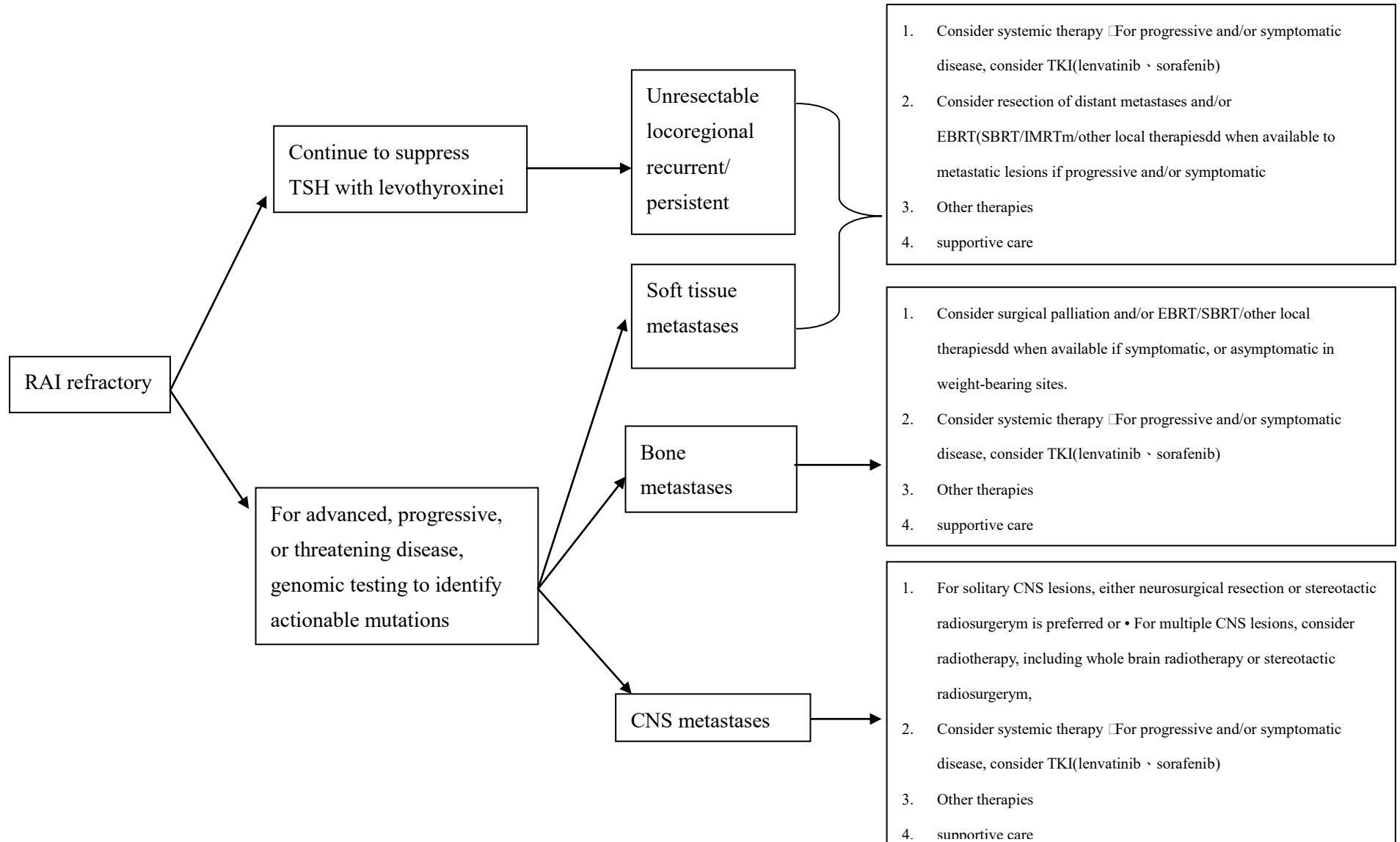
- Physical examination, TSH and Tg measurement + antithyroglobulin antibodies
- Neck ultrasound every 6-12 months
- Chest X-ray every 6-12 months
- For patients underwent total thyroidectomy and postoperative RAI therapy, consider radioiodine imaging in the first year postoperatively
- Consider TSH-stimulated radioiodine imaging in high-risk patients, patients with previous RAI-avid metastases, or patients with abnormal Tg levels (either TSH-suppressed or TSH-stimulated), rising antithyroglobulin antibodies, or abnormal ultrasound during surveillance.
- Consider FDG-PET/CT for patients with abnormal Tg level but negative  $^{131}\text{I}$  imaging.

## 復發 (Recurrent Disease)





## RAI refractory 的後續治療方式

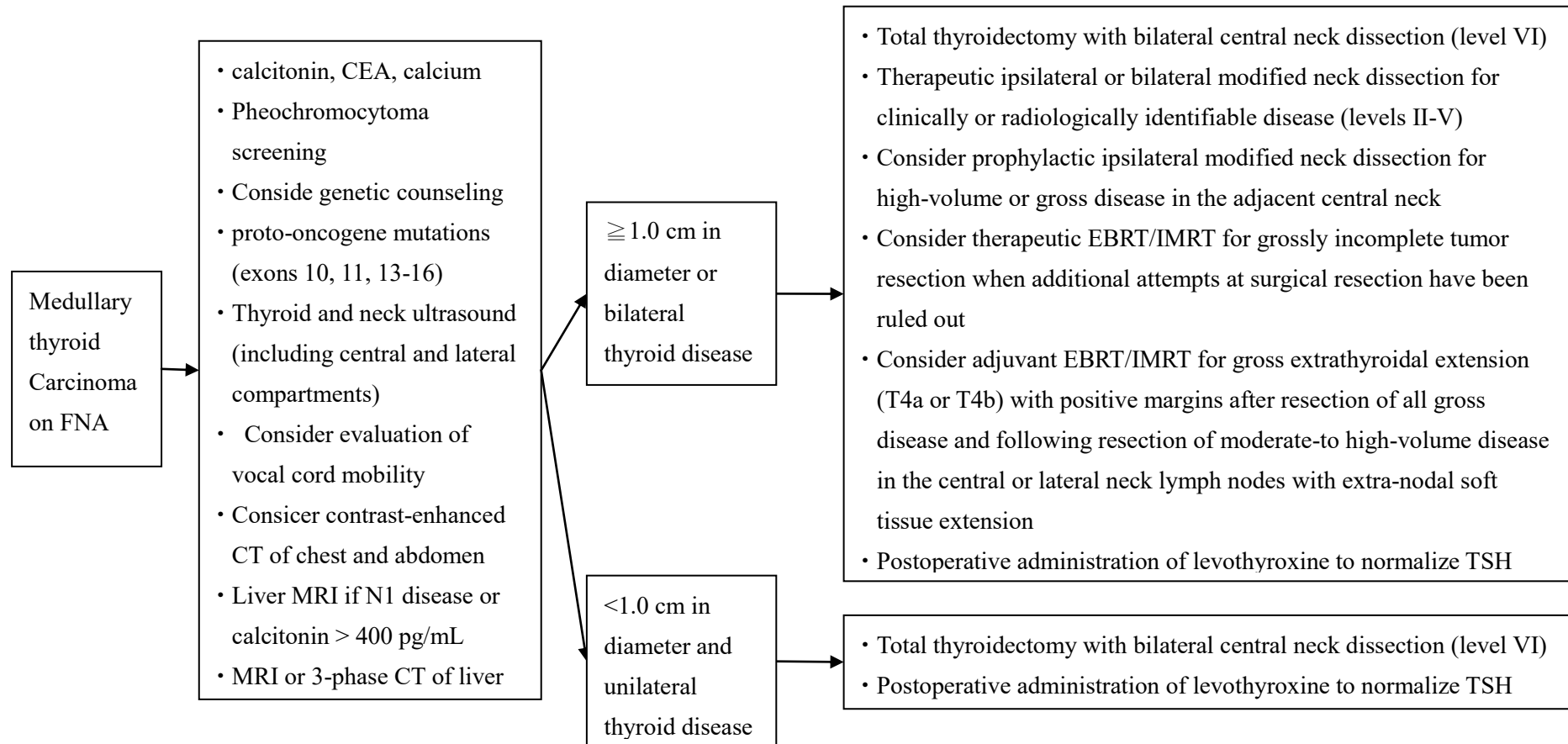


## 髓質癌 (Medullary Carcinoma)

### 細針抽吸結果

### 評估

### 治療



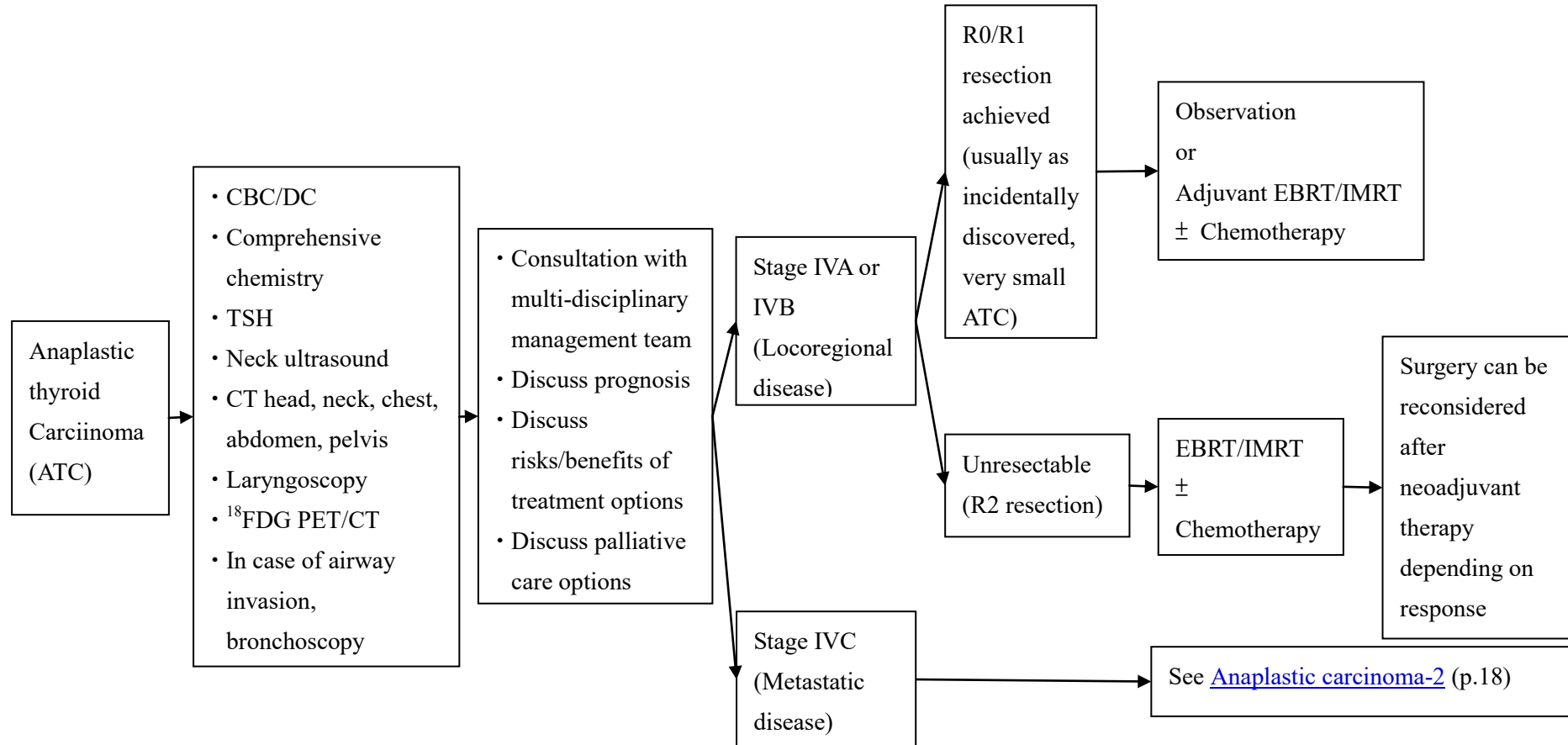
## 分化不良癌 (Anaplastic Carcinoma) -1

細針抽吸結果

評估

建立治療目標

依期別治療

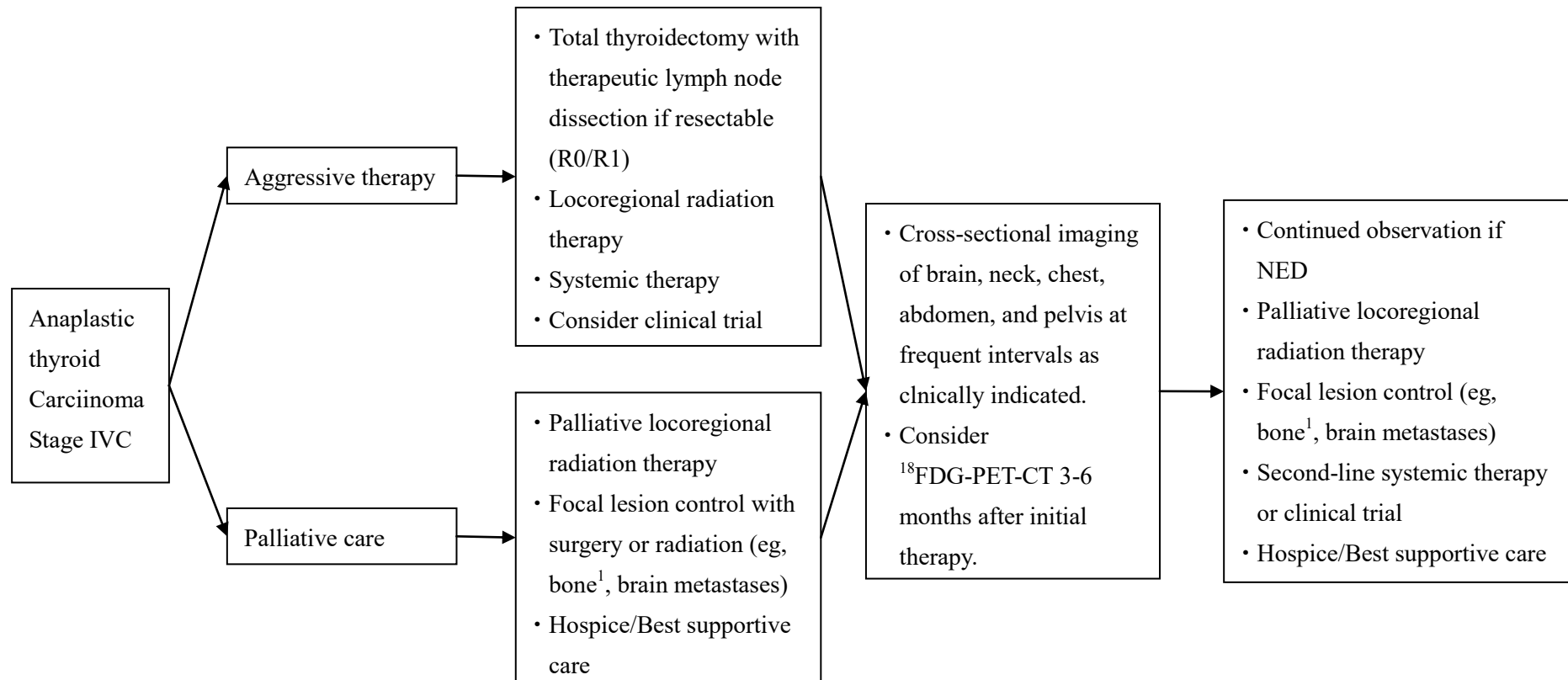


## 分化不良癌 (Anaplastic Carcinoma) -2

轉移性疾病

治療

追蹤 & 處置



<sup>1</sup>Consider use of intravenous bisphosphonates or denosumab. Denosumab and intravenous bisphosphonates can be associated with severe hypocalcemia; patients with hypoparathyroidism and vitamin D deficiency are at increase risk.

## Metastasis 第一線治療

### 1. RAI therapy

### 2. 標靶治療處方 (Kinase Inhibitor Therapy or metastasis)

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Regimen	Agents/Dosages	Frequency
Sorafenib (Nexavar)	400mg Oral	Twice daily (BID)
Lenvatinib(Lenvima)	24mg Oral	Once daily (QD)
Dabrafenib (Tafinlar) and Trametinib (Mekinist)	150 mg and 2 mg Oral	Twice daily (BID) and once daily (QD)
Pralsetinib (Gavreto)	400 mg Oral	Once daily (QD)
Cabozantinib (Cabometyx)	60 mg Oral	Once daily (QD)
Everolimus (Afinitor, Votubia, Certican)	10 mg Oral	Once daily (QD)
Selpercatinib (Retevmo)	160 mg Oral	Twice daily (BID)
Larotrectinib (Vitrakvi)	100 mg Oral	Twice daily (BID)

### 3. 化學治療處方 (Chemotherapy Regimen or metastasis)

Regimen	Agents/Dosages	Frequency
Paclitaxel (weekly)	60-90 mg/m <sup>2</sup> IV	Weekly
Doxorubicin (weekly)	20 mg/ m <sup>2</sup> IV	Weekly
<u>Docetaxel (3-week)</u>	60 mg/ m <sup>2</sup> IV	<u>(3-week)</u>
<u>Docetaxel + Carboplatin</u> <u>( CCr &lt; 60)</u>	75 mg/ m <sup>2</sup> IV+Auc x 5 mg/CCR	<u>(3-week)</u>
<u>Docetaxel + Cisplatin</u> <u>( 3-week cycle)</u>	75 mg/ m <sup>2</sup> IV+60 mg/ m <sup>2</sup> IV	<u>(3-week)</u>

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