台北榮民總醫院
Taipei Veterans General Hospital

Anal Cancer

大腸直腸癌醫療團隊
2014年6月13日 第一版
2015年7月24日 第二版
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2022年8月26日 第十版

Before Guidelines

- Elder (individual consideration)
- For squamous cell carcinoma
- This panel is for medical fitted patients, adjustment might be considered for medical unfitted patients or for individual considerations under clinical practices.
- Although the guidelines are believed to represent the optimal treatment strategy, the panel believes that, when appropriate, patients should preferentially be included in a clinical trial over standard or accepted therapy.

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- Flowchart and information
- Principles of Radiation Therapy
- Chemotherapy

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AJCC VII

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Flowchart

Initial Workup

- Present illness
- Physical examination, Personal and family history
- CBC, chemistry profile SCC, Cyfra21-1, aPTT/PT
- Abdominal/Chest CT ± MRI
- Rectal untrasound
- Anoscopy/Colonoscopy
- Inguinal LN evaluation
  - ± FNA and/or excisional biopsy of the inguinal LNs
- ±PET scan for T3-4,N0 or anyT, N+
- Education of vaccine treatment
- Education of HIV and STD studies/GYN consultation

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2022
Anal Carcinoma

NCCN Guidelines Index
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Discussion

American Joint Committee on Cancer (AJCC)
TNM Staging Classification for Anal Carcinoma (8th ed., 2017)
***Table 1.* Definitions for T, N, M**

T	**Primary Tumor**
TX	Primary tumor not assessed
T0	No evidence of primary tumor
Tis	High-grade squamous intraepithelial lesion (previously termed carcinoma in situ, Bowen disease, anal intraepithelial neoplasia II–III, high-grade anal intraepithelial neoplasia)
T1	Tumor 2 cm or less
T2	Tumor more than 2 cm but not more than 5 cm
T3	Tumor more than 5 cm
T4	Tumor of any size invades adjacent organ(s), such as the vagina, urethra, bladder

N	**Regional Lymph Nodes**
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in inguinal, mesorectal, internal iliac, or external iliac nodes
N1a	Metastasis in inguinal, mesorectal, or internal iliac lymph nodes
N1b	Metastasis in external iliac lymph nodes
N1c	Metastasis in external iliac with any N1a nodes

M	**Distant Metastasis**
M0	No distant metastasis
M1	Distant metastasis

***Table 2.* AJCC Anatomic Stage/Prognostic Groups**

	T	N	M
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T2	N0	M0
Stage IIB	T3	N0	M0
Stage IIIA	T1-T2	N1	M0
Stage IIIB	T4	N0	M0
Stage IIIC	T3-T4	N1	M0
Stage IV	Any T	Any N	M1

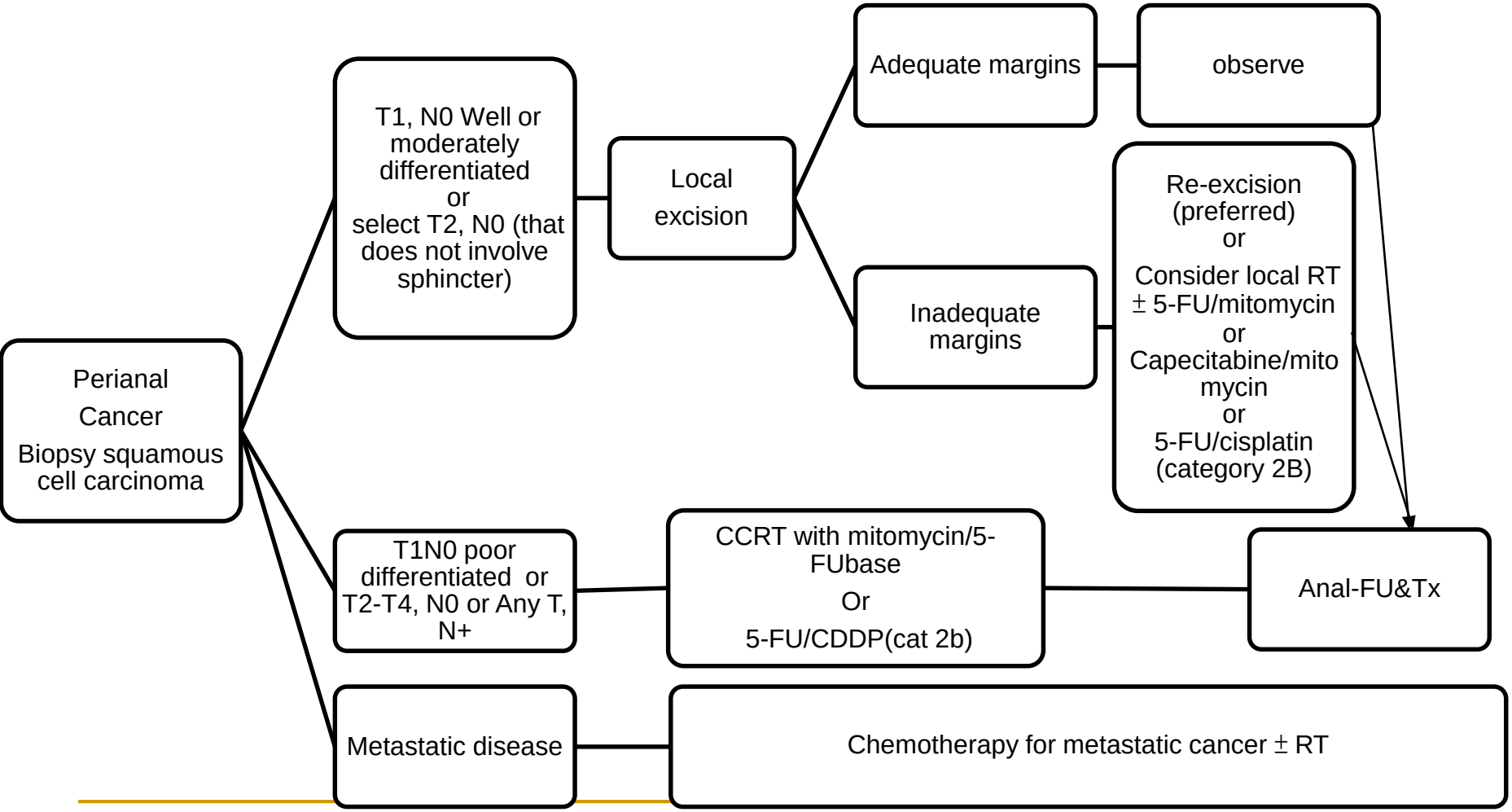
Anal cancer

Anal canal cancer: (squamous cell carcinoma)

- Locoregional disease
  - Mitomycin/5-FU + RT
    or
    Mitomycin/capecitabine + RT
    or
    5-FU/cisplatin + RT (category 2B)
    - **Anal-FU&Tx**
- Metastatic disease
  - **Carboplatin/paclitaxel ± RT**
    or
    FOLFOX ± RT
    or
    FOLFCIS ± RT
    Or
    5-FU/cisplatin ± RT
    (category 2B)
    or
    Modified docetaxel/cisplatin/
    fluorouracil (DCF)
    (category 2B)
    - Nivolumab
      or
      Pembrolizumab

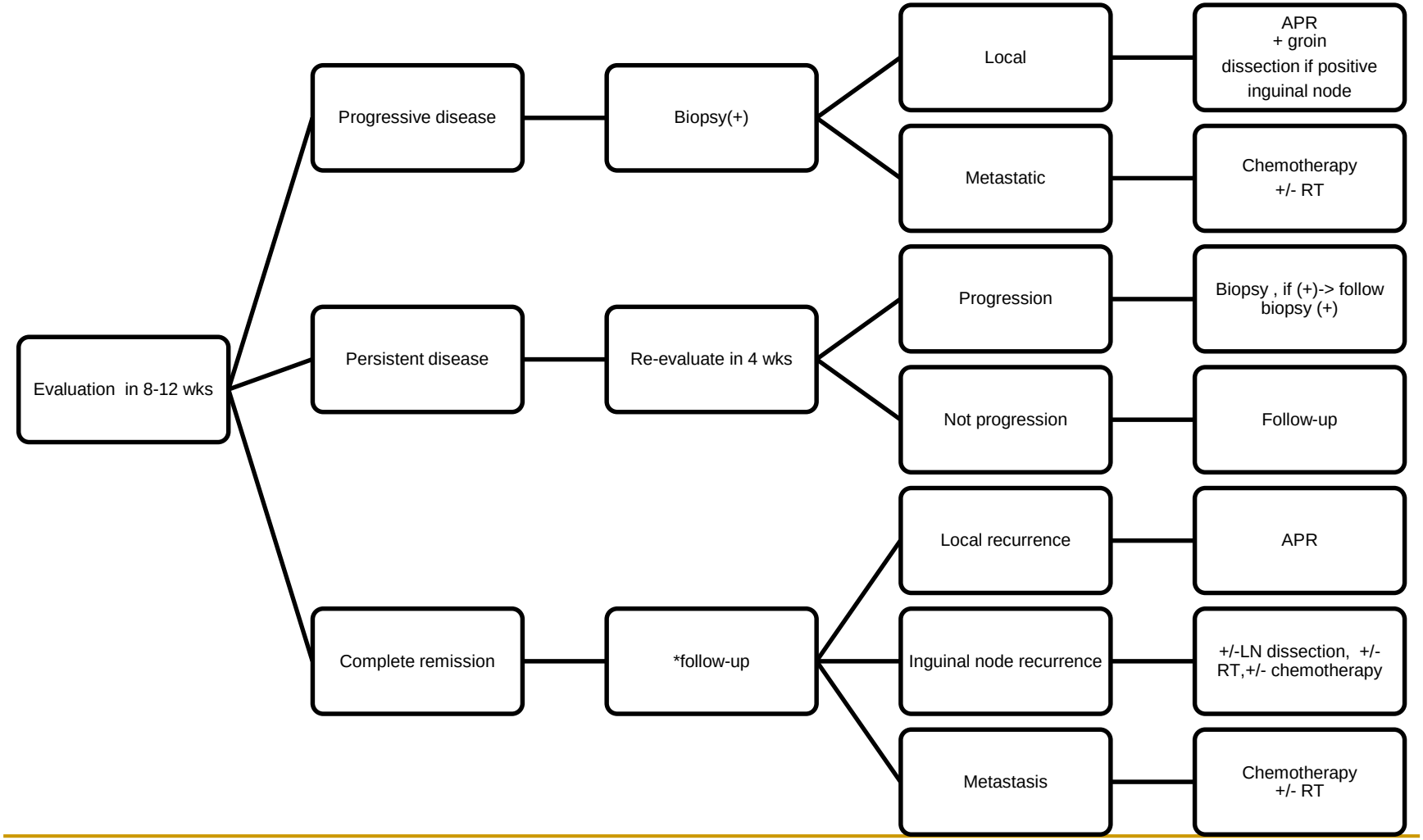
A malignant polyp is defined as one with cancer invading the submucosa (pT1).
Favorable histologic features include lesions of grade 1 or 2, no angiolymphatic invasion, and a negative resection margin

Perianal cancer
(squamous cell carcinoma)



A malignant polyp is defined as one with cancer invading the submucosa (pT1).
Favorable histologic features include lesions of grade 1 or 2, no angiolymphatic invasion, and a negative resection margin

Anal-FU&Tx



*Every 3-6 mo for 5 y {DRE, Anoscopy, Inguinal node palpation}; T3-T4 or inguinal node positive{ chest/abd/pelvic imaging annually for 3 y}

Principles of Surgery

- Local excision
  - Superficially Invasive Squamous Cell Carcinoma(SISCCA)
    - SISCCA are anal cancers that are generally found incidentally in the setting of a biopsy or excision of what is thought to be a benign lesion such as a condyloma, hemorrhoid, or anal skin tag.
    - For such lesions that are noted to have histologically negative margins in carefully selected patients followed by an experienced provider and/or team, local excision alone with a structured surveillance plan may represent adequate treatment
  - Perianal Cancer
    - T1N0, moderately to well-differentiated or select T2N0 squamous cell carcinoma of the perianal region may be adequately treated by local excision with 1-cm margins
- Radical Surgery
  - Local Recurrence/Persistence
    - APR
  - Inguinal Recurrence
    - inguinal node dissection

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Principles of Radiation Therapy

Principles of Radiation Therapy

- Multifield techniques with supervoltage radiation (photon energy of > 6 mV) should be used to deliver a minimum dose of 45 Gy in 1.8 Gyfractions (25 fractions over 5 weeks) to the primary cancer
- The inguinal nodes and the pelvis, anus, and perineum should be included in the initial radiation fields. The superior field border should be at L5-S1, and the inferior border should include the anus with a minimum 2.5 cm-margin around the anus and tumor. The lateral border should include the lateral inguinal nodes (as determined from imaging or bony landmarks). There should be attempts to reduce the dose to the femoral heads.
- After 17 fractions (30.6 Gy), an additional 14.4 Gy should be given in 8 fractions with the superior field reduced to the bottom of the sacroiliac joints. Additional field reduction off inguinal nodes should occur after 36 Gy for node-negative lesions. This protocol brings the total dose to 45 Gy in 25 fractions over 5 weeks.

- For T2 lesions with residual disease after 45 Gy, T3/4 lesions, or N1 lesions, an additional boost of 9-14 Gy in 1.8-2 Gy fractions to the original primary tumor volume and involved nodes plus a 2-2.5 cm margin is usually delivered. This boost brings the total dose to 54-59 Gy in 30-32 fractions over 6-7.5 weeks. Simultaneous integral boost may be used to give the same total dose in 25 fractions.
- The consensus of the panel is that IMRT is preferred over 3-D conformal RT in the treatment of anal carcinoma. IMRT requires expertise and careful target design to avoid reduction in local control by so-called “marginal-miss.” The clinical target volumes for anal cancer used in the RTOG-0529 trial have been described in detail. Also see for more details of the contouring atlas defined by RTOG.
- Image-guided RT (IGRT) with cone beam CT imaging should be used during IMRT.

Chemotherapy

PRINCIPLES OF SYSTEMIC THERAPY

Localized Cancer		Metastatic Cancer		Subsequent Therapy
Preferred Regimens	Other Recommended Regimens	Preferred Regimens	Other Recommended Regimens	Preferred Regimens
• 5-FU + mitomycin + RT • Capecitabine + mitomycin + RT	• 5-FU + cisplatin + RT	• Carboplatin + paclitaxel	• 5-FU + cisplatin • FOLFCIS • mFOLFOX6 • Modified DCF	• Nivolumab • Pembrolizumab if not previously received

Systemic Therapy Regimens and Dosing

- 5-FU + mitomycin + RT[1,2]
  - Continuous infusion 5-FU 1000 mg/m²/day IV days 1–4 and 29–32
    Mitomycin 10 mg/m² IV bolus days 1 and 29
    Concurrent radiotherapy (See ANAL-C)
    or
  - Continuous infusion 5-FU 1000 mg/m²/day IV days 1–4 and 29–32
    Mitomycin 12 mg/m² on day 1 (capped at 20 mg)
    Concurrent radiotherapy (See ANAL-C)
- Capecitabine + mitomycin + RT[3,4]
  - Capecitabine 825 mg/m² PO BID, Monday–Friday, on each day that RT is given, throughout the duration of RT (typically 28 treatment days)
    Mitomycin 10 mg/m² days 1 and 29
    Concurrent radiotherapy (See ANAL-C)
    or
  - Capecitabine 825 mg/m² PO BID days 1–5 weekly x 6 weeks
    Mitomycin 12 mg/m² IV bolus day 1
    Concurrent radiotherapy (See ANAL-C)
- 5-FU + cisplatin + RT[5]
  Cisplatin 75 mg/m² day 1
  Continuous infusion 5-FU 1000 mg/m²/day IV days 1–4
  Repeat every 4 weeks
  Concurrent radiotherapy (See ANAL-C)
- Carboplatin + paclitaxel
  - Carboplatin AUC 5 IV day 1
    Paclitaxel 175 mg/m² IV day 1
    Repeat every 21 days[6]
    or
  - Carboplatin AUC 5 IV day 1
    Paclitaxel 80 mg/m² IV days 1, 8, 15
    Repeat every 28 days[7]
- 5-FU + cisplatin
  - Cisplatin 60 mg/m² day 1
    Continuous infusion 5-FU 1000 mg/m²/day IV days 1–4
    Repeat every 3 weeks[8]
    or
  - Cisplatin 75 mg/m² day 1
    Continuous infusion 5-FU 750 mg/m²/day IV days 1–5
    Repeat every 4 weeks[9]
- FOLFCIS[10]
  Cisplatin 40 mg/m² IV over 30 minutes on day 1*
  Leucovorin 400 mg/m² IV day 1*
  5-FU 400 mg/m² IV bolus on day 1, then 1000 mg/m²/day x 2 days (total 2000 mg/m² over 46–48 hours)
  IV continuous infusion
  Repeat every 2 weeks

  *Cisplatin and leucovorin are given concurrently
- mFOLFOX6[11]
  Oxaliplatin 85 mg/m² IV day 1
  Leucovorin 400 mg/m² IV day 1
  5-FU 400 mg/m² IV bolus on day 1, then 1200 mg/m²/day x 2 days (total 2400 mg/m² over 46–48 hours)
  IV continuous infusion
  Repeat every 2 weeks
- Modified DCF[12]
  Docetaxel 40 mg/m² IV day 1
  Cisplatin 40 mg/m² IV day 1
  Fluorouracil 1200 mg/m²/day x 2 days (total 2400 mg/m² over 46–48 hours)
  Repeat every 2 weeks
- Nivolumab[13]
  Nivolumab 240 mg IV every 2 weeks
  or Nivolumab 3 mg/kg IV every 2 weeks
  or Nivolumab 480 mg IV every 4 weeks
- Pembrolizumab[14]
  Pembrolizumab 200 mg IV every 3 weeks
  or Pembrolizumab 2 mg/kg IV every 3 weeks
  or Pembrolizumab 400 mg IV every 6 weeks

Strategy in good clinical practice

- Induction/Neo-adjuvant systemic chemotherapy is a optional choice
- A short course of 5FU based regimen is optional before the CCRT.

Reference

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