Oncology Clinical Pathways
Esophageal Cancer
September 2022 – V1.2022
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Esophageal Cancer – Stage 1A T1aN0M0
Adenocarcinoma or Squamous Cell Carcinoma

Stage 1A T1aN0M0
Adenocarcinoma or
Squamous Cell Carcinoma

Endoscopically
eradicated?

Yes ➔ Surveillance

No ➔ Multidisciplinary
discussion

Clinical trial(s) always considered on pathway.

*a Staging confirmed during Endoscopic Mucosal Resection (EMR) or Endoscopic Submucosal Dissection (ESD)*

*b Multidisciplinary discussion includes surgery, radiation oncology, and medical oncology*
Esophageal Cancer – Stage I T1bN0M0
Adenocarcinoma or Squamous Cell Carcinoma

Stage I T1bN0M0 Adenocarcinoma or Squamous Cell Carcinoma → Multidisciplinary discussion → Surgical candidate?

Yes → Resection → R0 lymph node positive?

Yes → Refer to Medical Oncology
No → Surveillance

No → High risk features present? b

Yes → Refer to Medical Oncology and Radiation Oncology
No → Refer to Radiation Oncology

Clinical trial(s) always considered on pathway.

a Multidisciplinary discussion confirm stage

b High risk features include lymphovascular invasion, poorly differentiated tumors, tumor size ≥ 2cm, SM1, SM2, or positive margin on EMR

EMR Endoscopic Mucosal Resection
Esophageal Cancer – Stage T1N1(IIA), T2N0(IIIB), T2N1 (III), T3 N0-1(III), T4aN0-1(III), T1-4AN2(IVA), T1-3 N3 (IVA) Adenocarcinoma

Clinical trial(s) always considered on pathway.

- **Multidisciplinary discussion** includes surgery, radiation oncology, and medical oncology
- Surgical candidate discussion with or evaluation by a surgeon
- Carboplatin and paclitaxel with radiation preferred treatment for predominantly esophageal tumors
- Perioperative chemotherapy preferred treatment for predominantly gastric tumors or patient is not a candidate for radiation
- FLOT4 candidates include fit patients with ECOG 0-1 due to expected Grade 3/4 toxicities of neutropenia, infection, diarrhea and peripheral neuropathy
- FLOT4 candidates include fit patients with ECOG 0-1 due to expected Grade 3/4 toxicities of neutropenia, infection, diarrhea and peripheral neuropathy
- Quality for immune checkpoint inhibitor patients without active autoimmune disease, primary immune deficiency, concurrent immunosuppression (including prednisone equivalent >10mg/day) or prior allogeneic HSCT/solid organ transplant

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Stage T1N1(IIA), T2N0(IIIB), T2N1 (III), T3 N0-1(III), T4aN0-1(III), T1-4AN2(IVA), T1-3 N3 (IVA) Adenocarcinoma

**Clinical trial(s) always considered on pathway:**

- Multidisciplinary discussion includes surgery, radiation oncology, and medical oncology
- Surgical candidate? **Yes**
- Carboplatin and paclitaxel weekly with radiation
- Assess response by PET/CT
- Unresectable or new metastases? **Yes**
- Follow First Line Adenocarcinoma Metastatic pathway
- **No**
- Proceed to surgery
- Complete response? **Yes**
- pet/ct
- Unresectable or new metastases? **Yes**
- Follow metastatic pathway
- **No**
- Surveillance

- Surgical candidate? **No**
- Carboplatin and paclitaxel weekly with radiation
- Surveillance

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Surveillance

Assess response by PET/CT

Preoperative FLO T4

Complete response? **Yes**

Postoperative chemotherapy

Surgery

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Surveillance

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Adjuvant nivolumab (1 year)
Esophageal Cancer – Stage T2-T3 N0 (IB-IIB), T1-T2 N1(IIB), T1-2 N2 (IIIA), T3N1 (IIIA), T4aN0-1 (IIIA), T3N2(IIIB), T4aN2 (IVA)

Non-Cervical Squamous Cell Carcinoma

**Multidisciplinary discussion** includes surgery, radiation oncology, and medical oncology

**Surgical candidate** discussion with or evaluation by a surgeon

**Qualify for immune checkpoint inhibitor** patient without active autoimmune disease, primary immune deficiency, concurrent immunosuppression (including prednisone equivalent >10mg/day) or prior autologous HSCT/solid organ transplant

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Clinical trial(s) always considered on pathway.
Esophageal Cancer – Stage IVB Adenocarcinoma Molecular Testing

Stage IVB Adenocarcinoma Molecular Testing

- Order MSI or MMR status testing
- Order HER2 IHC testing
- Order PD-L1 by CPS

Clinical trial(s) always considered on pathway.

- **MSI or MMR** NGS or IHC
- **HER2 IHC** if results 2+, HER2 IHC with reflex to FISH required (in-situ hybridization)
Esophageal Cancer – Stage IVB Adenocarcinoma Any T, Any N, M1 MSS HER2 Positive First Line

Stage IVB Adenocarcinoma Any T, Any N, M1 MSS HER2 Positive First Line

Assess nutritional status

Candidate for cytotoxic chemotherapy?

Assess nutritional status

Assess nutritional status

Assess nutritional status

Candidate for trastuzumab?

Candidate for immune checkpoint inhibitor?

No

Patient preference after shared decision making

Trastuzumab and CAPOX combination

Candidate for immune checkpoint inhibitor?

No

Patient preference after shared decision making

Trastuzumab pembrolizumab and CAPOX combination

Candidate for immune checkpoint inhibitor?

Yes

Yes

Patient preference after shared decision making

Trastuzumab pembrolizumab and CAPOX combination

Assess nutritional status and consider palliative stent or other nutritional support modalities when clinically appropriate

Candidate for cytotoxic chemotherapy consider if patient can tolerate a platinum- and fluoropyrimidine-based doublet

Qualify for trastuzumab or biosimilar patient with HER2-positive disease and no clinically significant CV disease (defined as LVEF < 50%, MI within prior 6 months, symptomatic CHF (NYHA class II to IV), unstable angina or cardiac arrhythmia requiring therapy)

Radiation Oncology consider palliative radiation when clinically appropriate

Qualify for immune checkpoint inhibitor patient without active autoimmune disease, primary immune deficiency, concurrent immunosuppression (including prednisone equivalent >10mg/day) or prior allogeneic HSCT/solid organ transplant

Pembrolizumab for two years

Clinical trial(s) always considered on pathway.
Esophageal Cancer – Stage IVB Adenocarcinoma Any T, Any N, M1 MSS HER2 Positive Second Line

- Patient preference after shared decision making
  - Proceed to treatment
    - Candidate for fam-trastuzumab deruxtecan?
      - Yes
        - Fam-trastuzumab deruxtecan
      - No
        - Candidate for ramucirumab?
          - Yes
            - Paclitaxel and ramucirumab
          - No
            - Irinotecan or taxane

Clinical trial(s) always considered on pathway.

- **Candidate for fam-trastuzumab deruxtecan** received trastuzumab in the first-line setting; baseline LVEF > 50% and/or no clinically significant cardiac disease (defined as LVEF < 50%, MI within prior 6 months, symptomatic CHF (NYHA class II to IV), unstable angina or cardiac arrhythmia requiring therapy); no ILD or pneumonitis; ANC > 1500/mm$^3$

- **Candidate for ramucirumab** received fluoropyrimidine and platinum agent in the first-line setting; ECOG PS 0-2; ANC > 1500/mm$^3$. Note: Due to anti-VEGF effects patients with the following should not receive ramucirumab: non-healing wound/fracture, major surgery in prior 4 weeks, bleeding disorder or coagulopathy, recent history of GI perforation, unstable cardiac condition (uncontrolled HTN, arterial thromboembolism, symptomatic CHF (NYHA II-IV) or arrhythmia), or active cocaine use.
Esophageal Cancer – Stage IVB Adenocarcinoma Any T, Any N, M1 MSS HER2 Negative First Line

Stage IVB Adenocarcinoma Any T, Any N, M1 MSS HER2 Negative First Line

- Assess nutritional status
- Refer to Palliative Care
- Order PD-L1 by CPS
- Cytotoxic chemotherapy candidate?

PD-L1 by CPS ≥1%?
- Yes: Nivolumab and mFOLFOX6 or CAPOX
- No: mFOLFOX6 or CAPOX

Candidate for immune checkpoint inhibitor?
- Yes: Nivolumab and mFOLFOX6 or CAPOX
- No: mFOLFOX6 or CAPOX

Patient preference after shared decision making?
- Yes: Nivolumab and mFOLFOX6 or CAPOX
- No: mFOLFOX6 or CAPOX

Clinical trial(s) always considered on pathway.

- Assess nutritional status: consider palliative stent or other nutritional support modalities when clinically appropriate
- Assess Palliative Care: consider palliative radiation when clinically appropriate
- Candidate for cytotoxic chemotherapy: consider if patient can tolerate a platinum- and fluoropyrimidine-based doublet
- Qualify for immune checkpoint inhibitor: no active autoimmune disease, primary immune deficiency, concurrent immunosuppression (including prednisone equivalent >10mg/day) or prior allogeneic HSCT/solid organ transplant
Esophageal Cancer – Stage IVB Adenocarcinoma Any T, Any N, M1 MSS HER2 Negative Second Line

Stage IVB Adenocarcinoma Any T, Any N, M1 MSS HER2 Negative Second Line

Candidate for treatment?

- Yes
  - Candidate for ramucirumab? *a
    - Yes: Paclitaxel and ramucirumab
    - No: Irinotecan or taxane
  - No: Hospice

* Candidate for ramucirumab received fluoropyrimidine and platinum agent in the first-line setting; ECOG PS 0-2; ANC ≥ 1500/mm³; due to anti-VEGF effects patients with the following should not receive ramucirumab: non-healing wound/fracture, major surgery in prior 4 weeks, bleeding disorder or coagulopathy, recent history of GI perforation, unstable cardiac condition (uncontrolled HTN, arterial thromboembolism, symptomatic CHF (NYHA II-IV) or arrhythmia), or active cocaine use.

Clinical trial(s) always considered on pathway.
Esophageal Cancer – Stage IVB Adenocarcinoma Any T, Any N, M1
MSI High

Clinical trial(s) always considered on pathway.

* **Assess nutritional status** consider palliative stent or other nutritional support modalities when clinically appropriate

b **Qualify for immune checkpoint inhibitor** patient without active autoimmune disease, primary immune deficiency, concurrent immunosuppression (including prednisone equivalent >10mg/day) or prior allogeneic HSCT/solid organ transplant
Esophageal Cancer – Stage IVB Squamous Cell Carcinoma
Any T, Any N, M1 First Line

Stage IVB Squamous Cell Carcinoma Any T, Any N, M1 First Line

Assess nutritional status

Yes

Candidate for cytotoxic chemotherapy?

Yes

Nivolumab and mFOLFOX6 or CAPOX

No

Nivolumab and ipilimumab

Candidate for immune checkpoint inhibitor?

Patient preference after shared decision making?

Yes

CAPOX

No

mFOLFOX6

Refer to Palliative Care

Candidate for immune checkpoint inhibitor?

Candidate for cytotoxic chemotherapy?

Yes

No

Refer to Radiation Oncology

Clinical trial(s) always considered on pathway.

Assess nutritional status consider palliative stent or other nutritional support modalities when clinically appropriate

Qualify for immune checkpoint inhibitor patient without active autoimmune disease, primary immune deficiency, concurrent immunosuppression (including prednisone equivalent >10mg/day) or prior allogeneic HSCT/solid organ transplant

Candidate for cytotoxic chemotherapy consider if patient can tolerate a platinum- and fluoropyrimidine-based doublet

Radiation Oncology consider palliative or metastasis-directed radiation when clinically appropriate
Esophageal Cancer – Stage IVB Squamous Cell Carcinoma
Any T, Any N, M1 Second Line

Clinical trial(s) always considered on pathway.

*Qualify for immune checkpoint inhibitor patient without active autoimmune disease, primary immune deficiency, concurrent immunosuppression (including prednisone equivalent >10mg/day) or prior allogeneic HSC/Ts solid organ transplant

Pembrolizumab chosen due to FDA approval and patient convenience
Esophageal Cancer – Cervical Squamous or Unresectable Localized

Cervical Squamous or Unresectable Localized → Multidisciplinary discussion *

Assess nutritional status

Carboplatin and paclitaxel (weekly) with radiation → Progression or new metastases?

Yes → Follow Squamous Cell First Line pathway

No → Candidate for chemotherapy?

Yes → Adjuvant carboplatin and paclitaxel (2 cycles, every 3 weeks)

No → Surveillance

Clinical trial(s) always considered on pathway.

* Multidisciplinary discussion includes surgery, radiation oncology, and medical oncology; for mid-esophageal tumors, consider referral to Pulmonary to assess tracheal invasion.
Questions?

Contact VHAOncologyPathways@va.gov