Field Direction Memo

Date: March 4, 2025

To: Solid Tumor Account Managers, Division Managers

Cc: RSDs, Market Access, Learning & Development, Marketing, Field Medical Directors, PRC, CLT, Mark Riedl, Ashley Riley, Matt Shaulis

From: Andrew Sawyer

Subject: TEVIMBRA added to NCCN Guidelines for Esophageal and Esophagogastric Junction Cancers and Gastric Cancer

– APPROVED FOR DISSEMINATION –

Objective To inform Solid Tumor team of recent updates to the National Comprehensive Cancer Network® (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Esophageal and Esophagogastric Junction Cancers (Version 1.2025) and Gastric Cancer (Version 1.2025).

Background (internal only)
TEVIMBRA (tislelizumab-jsgr) was added to the esophageal and esophagogastric junction cancers guidelines as a preferred, first-line regimen for both esophageal squamous cell carcinoma with PD-L1 CPS ≥1 (category 1) and HER2-negative esophageal/gastroesophageal junction adenocarcinoma with a category 2A recommendation in PD-L1 CPS 1 - <5 and category 1 recommendation for PD-L1 CPS ≥5.

Additionally, TEVIMBRA was added to the gastric cancer guidelines as a preferred, first-line regimen for HER2-negative, unresectable, locally advanced, recurrent, or metastatic disease (where local therapy is not indicated) with a category 2A recommendation in PD-L1 CPS 1 - <5 and category 1 recommendation for PD-L1 CPS ≥5.

See below for NCCN guidance for PD-1 inhibitors in ESCC:

Esophageal Squamous Cell Carcinoma (ESCC)			
tislelizumab-jsgr	• Fluoropyrimidine (fluorouracil or capecitabine), oxaliplatin, and tislelizumab-jsgr • Fluoropyrimidine (fluorouracil or capecitabine), cisplatin, and tislelizumab-jsgr	PD-L1 CPS ≥1	Category 1
pembrolizumab	• Fluoropyrimidine (fluorouracil or capecitabine), oxaliplatin, and pembrolizumab • Fluoropyrimidine (fluorouracil or capecitabine), cisplatin, and pembrolizumab	PD-L1 CPS ≥1	Category 1
nivolumab	• Fluoropyrimidine (fluorouracil or capecitabine), oxaliplatin, and nivolumab	All-Comers	Category 1

See below for NCCN guidance for PD-1 inhibitors in HER2-negative EAC/EGJ adenocarcinoma and Gastric Cancer:

Esophageal Adenocarcinoma (EAC)/ Esophagogastric Junction (EGJ) adenocarcinoma/ Gastric Cancer			
tislelizumab-jsgr	• Fluoropyrimidine (fluorouracil or capecitabine), oxaliplatin, and tislelizumab-jsgr • Fluoropyrimidine (fluorouracil or capecitabine), cisplatin, and tislelizumab-jsgr	PD-L1 CPS ≥5	Category 1
		PD-L1 CPS 1 - <5	Category 2A
pembrolizumab	• Fluoropyrimidine (fluorouracil or capecitabine), oxaliplatin, and pembrolizumab • Fluoropyrimidine (fluorouracil or capecitabine), cisplatin, and pembrolizumab	PD-L1 CPS ≥5	Category 1
		PD-L1 CPS 1 - <5	Category 2A
nivolumab	• Fluoropyrimidine (fluorouracil or capecitabine), oxaliplatin, and nivolumab	PD-L1 CPS ≥5	Category 1
		PD-L1 CPS 1 - <5	Category 2A

Field Direction

- Materials that include the NCCN recommendation are currently under development.
- You may **proactively** verbalize the following regarding the NCCN recommendation:
    - TEVIMBRA is a preferred, first-line regimen for ESCC in patients with a PD-L1 CPS ≥1. Preferred regimens include:
        - Fluoropyrimidine (fluorouracil or capecitabine), oxaliplatin, and tislelizumab-jsgr
        - Fluoropyrimidine (fluorouracil or capecitabine), cisplatin, and tislelizumab-jsgr
    - TEVIMBRA is a preferred, first-line regimen for gastric cancer and gastroesophageal junction adenocarcinoma with a category 1 recommendation in patients with a PD-L1 CPS ≥5 and a category 2A recommendation in patients with a PD-L1 CPS 1 - <5. Preferred regimens include:
        - Fluoropyrimidine (fluorouracil or capecitabine), oxaliplatin, and tislelizumab-jsgr
        - Fluoropyrimidine (fluorouracil or capecitabine), cisplatin, and tislelizumab-jsgr
- If a customer brings up the inclusion of tislelizumab in the NCCN guideline for esophageal adenocarcinoma, acknowledge you are aware of the update and inform them that tislelizumab is not approved in this indication.
    - Remind the customer that TEVIMBRA tislelizumab is approved for
    - Esophageal Cancer
        - in combination with platinum-containing chemotherapy, for the first-line treatment of adults with unresectable or metastatic ESCC whose tumors express PD-L1 (≥1).
        - as monotherapy for the treatment of adult patients with unresectable or metastatic ESCC after prior systemic chemotherapy that did not include a PD-(L)1 inhibitor.
    - Gastric Cancer

- in combination with platinum and fluoropyrimidine-based chemotherapy, for the first-line treatment of unresectable or metastatic HER2-negative G/GEJ adenocarcinoma in adults whose tumors express PD-L1 (≥1).

- All other questions on the guidelines should be directed to your respective Field Medical Director or Medical Information.

See here for the gastric cancer guidelines and here for the esophageal and esophagogastric junction guidelines (login required).

See below for thumbnails of the updates and definitions of NCCN Categories of Evidence and Consensus.

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2025
Esophageal and Esophagogastric Junction Cancers

NCCN Guidelines Index
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Discussion

PRINCIPLES OF SYSTEMIC THERAPY

Systemic Therapy for Unresectable Locally Advanced, Recurrent, or Metastatic Disease (where local therapy is not indicated)

SQUAMOUS CELL CARCINOMA

First-Line Therapy
- Oxaliplatin is preferred over cisplatin due to lower toxicity.

Preferred Regimens
- Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and nivolumab (category 1)[d,e,60]
- Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and pembrolizumab for PD-L1 CPS ≥1 (category 1)[d,e,28]
- Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and tislelizumab-jsgr for PD-L1 CPS ≥1 (category 1)[d,e,61]
- Fluoropyrimidine (fluorouracil[a] or capecitabine) and oxaliplatin[33-35]
- Fluoropyrimidine (fluorouracil[a] or capecitabine), cisplatin, and nivolumab (category 1)[d,e,60]
- Fluoropyrimidine (fluorouracil[a] or capecitabine), cisplatin, and pembrolizumab for PD-L1 CPS ≥1 (category 1)[d,e,28]
- Fluoropyrimidine (fluorouracil[a] or capecitabine), cisplatin, and tislelizumab-jsgr for PD-L1 CPS ≥1 (category 1)[d,e,61]
- Fluoropyrimidine (fluorouracil[a] or capecitabine) and cisplatin[33,36-38]
- Nivolumab and ipilimumab[d,e,60]
- MSI-H/dMMR tumors (independent of PD-L1 status)[c]
  - Pembrolizumab[d,e,39-41]
  - Dostarlimab-gxly[d,e,42]
  - Nivolumab and ipilimumab[d,e,27]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and nivolumab[d,e,27]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and pembrolizumab[d,e,28]

Other Recommended Regimens
- Fluorouracil[a,f] and irinotecan[43]
- Paclitaxel with or without carboplatin or cisplatin[44-48]
- Docetaxel with or without cisplatin[49-52]
- Fluoropyrimidine[37,53,54] (fluorouracil[a] or capecitabine)
- Docetaxel, cisplatin or oxaliplatin, and fluorouracil[a,55,56]

Useful in Certain Circumstances
- Entrectinib, larotrectinib, or repotrectinib for *NTRK* gene fusion-positive tumors (category 2B)[57-59]

[a] Leucovorin is indicated with certain fluorouracil-based regimens. Depending on availability, these regimens may be used with or without leucovorin. For important information regarding the leucovorin shortage, please see the Discussion.
[c] Principles of Pathologic Review and Biomarker Testing (ESOPH-B).
[d] NCCN Guidelines for Management of Immunotherapy-Related Toxicities.
[e] If no prior checkpoint inhibitor therapy or no tumor progression while on therapy with a checkpoint inhibitor.
[f] Capecitabine cannot be used interchangeably with fluorouracil in regimens containing irinotecan.

Note: All recommendations are category 2A unless otherwise indicated.

Continued
References

PRINCIPLES OF SYSTEMIC THERAPY

Systemic Therapy for Unresectable Locally Advanced, Recurrent, or Metastatic Disease (where local therapy is not indicated)

ADENOCARCINOMA

First-Line Therapy
- Oxaliplatin is preferred over cisplatin due to lower toxicity.

Preferred Regimens
- HER2 overexpression positive[c]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and trastuzumab
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, trastuzumab, and pembrolizumab for PD-L1 CPS ≥1 (category 1)[d,e,24,25]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), cisplatin, and trastuzumab (category 1)[26]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), cisplatin, trastuzumab and pembrolizumab for PD-L1 CPS ≥1 (category 1)[d,e,24,25]
- HER2 overexpression negative[c]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and nivolumab for PD-L1 CPS ≥1 (category 1 for PD-L1 CPS ≥5)[d,e,27]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and pembrolizumab for PD-L1 CPS ≥1 (category 1 for PD-L1 CPS ≥5)[d,e,28,29]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and tislelizumab-jsgr for PD-L1 CPS ≥1 (category 1 for PD-L1 CPS ≥5)[d,e,30]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and zolbetuximab-clzb for CLDN18.2 positive[c] (category 1 for EGJ adenocarcinoma; category 2A for esophageal adenocarcinoma)[31,32]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine) and oxaliplatin[33-35]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), cisplatin, and pembrolizumab for PD-L1 CPS ≥1 (category 1 for PD-L1 CPS ≥5)[d,e,28,29]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), cisplatin, and tislelizumab-jsgr for PD-L1 CPS ≥1 (category 1 for PD-L1 CPS ≥5)[d,e,30]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine) and cisplatin[33,36-38]
- MSI-H/dMMR tumors (independent of PD-L1 status)
  - Pembrolizumab[d,e,39-41]
  - Dostarlimab-gxly[d,e,42]
  - Nivolumab and ipilimumab[d,e,27]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and nivolumab[d,e,27]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and pembrolizumab[d,e,28]

Other Recommended Regimens
- Fluorouracil[a,f] and irinotecan[g,43]
- Paclitaxel with or without carboplatin or cisplatin[g,44-48]
- Docetaxel with or without cisplatin[i,49-52]
- Fluoropyrimidine[g,37,53,54] (fluorouracil[a] or capecitabine)
- Docetaxel, cisplatin or oxaliplatin, and fluorouracil[a,g,55,56]

Useful in Certain Circumstances
- Entrectinib, larotrectinib, or repotrectinib for *NTRK* gene fusion-positive tumors (category 2B)[57-59]

Continued
References

Note: All recommendations are category 2A unless otherwise indicated.

PRINCIPLES OF SYSTEMIC THERAPY

Systemic Therapy for Unresectable Locally Advanced, Recurrent, or Metastatic Disease (where local therapy is not indicated)

First-Line Therapy
- Oxaliplatin is preferred over cisplatin due to lower toxicity.

Preferred Regimens
- HER2 overexpression positive[c]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and trastuzumab
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, trastuzumab, and pembrolizumab for PD-L1 CPS ≥1 (category 1)[e,f,15-16]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), cisplatin, and trastuzumab (category 1)[17]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), cisplatin, trastuzumab, and pembrolizumab for PD-L1 CPS ≥1 (category 1)[e,f,15-16]
- HER2 overexpression negative[c]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and nivolumab for PD-L1 CPS ≥1 (category 1 for PD-L1 CPS ≥5)[e,f,18]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and pembrolizumab for PD-L1 CPS ≥1 (category 1 for PD-L1 CPS ≥5)[e,f,19]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and tislelizumab-jsgr for PD-L1 CPS ≥1 (category 1 for PD-L1 CPS ≥5)[e,f,20]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and zolbetuximab-clzb for CLDN18.2 positive[c] (category 1)[21,22]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine) and oxaliplatin[23-25]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), cisplatin, and pembrolizumab for PD-L1 CPS ≥1 (category 1 for PD-L1 CPS ≥5)[e,f,19]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), cisplatin, and tislelizumab-jsgr for PD-L1 CPS ≥1 (category 1 for PD-L1 CPS ≥5)[e,f,20]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine) and cisplatin[23,26-28]
- MSI-H/dMMR tumors (independent of PD-L1 status)[c]
  - Pembrolizumab[e,f,29-31]
  - Dostarlimab-gxly[e,f,32]
  - Nivolumab and ipilimumab[e,f,18]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and nivolumab[e,f,18]
  - Fluoropyrimidine (fluorouracil[a] or capecitabine), oxaliplatin, and pembrolizumab[e,f,30,31]

Other Recommended Regimens
- Fluorouracil[a,g] and irinotecan[h,33]
- Paclitaxel with or without carboplatin or cisplatin[h,34-38]
- Docetaxel with or without cisplatin[h,39-42]
- Fluoropyrimidine[h,27,43,44] (fluorouracil[a] or capecitabine)
- Docetaxel, cisplatin or oxaliplatin, and fluorouracil[a,h,45,46]

Useful in Certain Circumstances
- Entrectinib, larotrectinib, or repotrectinib for *NTRK* gene fusion-positive tumors (category 2B)[47-49]

Footnotes on GAST-F (4A of 20)

Note: All recommendations are category 2A unless otherwise indicated.

Continued
References

NCCN Categories of Evidence and Consensus

Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate

Category 2A: Based on lower-level evidence; there is uniform NCCN consensus that the intervention is appropriate

Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate

Category 3: Based on any level evidence, there is major NCCN disagreement that the intervention is appropriate
All recommendations are category 2A unless otherwise indicated.