Patient Case: Derek

- Male, 68 years old
- Seeking first-line therapy for his advanced gastroesophageal (GEJ) cancer
- Relevant biomarker status:
 - CPS = <1%
 - Immunohistochemistry (IHC) = 3+ for HER2

Based on treatment recommendations by the NCCN Clinical Practice Guidelines for gastric cancer, what would you recommend for Derek?

Continue to Options





Select Option to Review in First-Line Setting Based on CPS = <1%; IHC = 3+ for HER2 expression

Option 1:

Pembrolizumab in combination with trastuzumab and a fluoropyrimidine - and platinum-containing regimen

Option 2:

Fluoropyrimidine and oxaliplatin and trastuzumab

or

Fluoropyrimidine and cisplatin and trastuzumab

Option 3:

Fluoropyrimidine and oxaliplatin and nivolumab

Option 4:

Fluoropyrimidine and oxaliplatin



NCCN Other Recommended Regimen

Option 1:

Pembrolizumab in combination with trastuzumab and a fluoropyrimidine - and platinum-containing regimen

 Other Recommended Regimen based on the May 2021 FDA approval of this combination for first-line treatment of locally advanced unresectable or metastatic HER2-positive gastric or GEJ adenocarcinoma



Preferred regimen with HER2 overexpression Category 1

Option 2:

Fluoropyrimidine and oxaliplatin and trastuzumab

or

Fluoropyrimidine and cisplatin and trastuzumab

- These regimens are an appropriate recommendation for Derek based on the NCCN panel consensus. Moreover, the regimen containing cisplatin is classified as **Category 1** (based upon high-level evidence, there is a uniform NCCN consensus that the intervention is appropriate)
- It is important to note that oxaliplatin is generally preferred over cisplatin due to lower toxicity

Select a different option

Continue on to second-line setting



Not preferred regimen with HER2 overexpression

Option 3:

Fluoropyrimidine and oxaliplatin and nivolumab

- Chemotherapy plus nivolumab would not be preferred due to Derek's CPS being <1% and HER2 overexpression
- Listed as Category 2B (based upon lower-level evidence, there
 is NCCN consensus the intervention is appropriate), Nivolumab
 would be useful in certain circumstances, such as HER2
 overexpression negative and PD-L1 CPS 1-4



Not preferred regimen with HER2 overexpression

Option 4:

Fluoropyrimidine and oxaliplatin

 Chemotherapy alone would not be preferred because Derek has no obvious indication for withholding the trastuzumab/chemotherapy regimen







- Disease progression following first-line fluoropyrimidine and oxaliplatin and trastuzumab or fluoropyrimidine and cisplatin and trastuzumab regimen:
 - HER2+ (IHC = 3+)
 - PD-L1 CPS = <1%

Based on treatment recommendations by the NCCN Clinical Practice Guidelines for gastric cancer, what would you now recommend to Derek?

Continue to Options



Select Option to Review in Second-Line Setting

Based on disease progression on fluoropyrimidine /oxaliplatin/trastuzumab and HER2+ (IHC = 3+); PD-L1 CPS = <1%

Option 1:

Ramucirumab and paclitaxel

Option 2:

Pembrolizumab

Option 3:

Trastuzumab deruxtecan



Not preferred regimen with HER2 overexpression

Option 1:

Ramucirumab and paclitaxel

 Ramucirumab/paclitaxel would be appropriate for Derek if he did not have HER2 overexpression

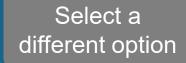


Not preferred regimen when CPS remains <1%

Option 2:

Pembrolizumab

 Pembrolizumab is not the preferred second-line selection since Derek's PD-L1 CPS remains <1%





NCCN Preferred
Regimen
Category 2A

Option 3:

Trastuzumab deruxtecan

- Based on NCCN guidance, the preferred second-line therapy for Derek's biomarker status would be trastuzumab deruxtecan
 - Derek remains HER2+ thus use of a trastuzumab-based antibody-drug conjugate (ADC) containing a high ratio cytotoxic payload is the preferred approach

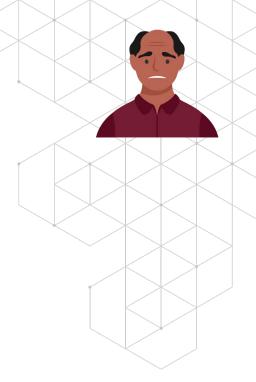
Select a different option

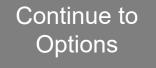
Continue to dosing



Patient Case: Derek – Second-Line Dosing

Based on treatment recommendations by the NCCN Clinical Practice Guidelines for gastric cancer, what would be the recommended dosing for Derek?







Select Dosing Option for Administration of Trastuzumab Deruxtecan

Option 1:

4.4 mg/kg IV on day 1, cycled every 21 days

Option 2:

5.4 mg/kg IV on day 1, cycled every 21 days

Option 3:

6.4 mg/kg IV on day 1, cycled every 21 days



Not Recommended Dosing

Option 1:

4.4 mg/kg IV on day 1, cycled every 21 days Dosing for trastuzumab deruxtecan is higher than is currently recommended for advanced/metastatic breast cancer, which is 5.4 mg/kg IV on day 1, cycled every 21 days



Not Recommended Dosing

Option 2:

5.4 mg/kg IV on day 1, cycled every 21 days Dosing for trastuzumab deruxtecan is higher than is currently recommended for advanced/metastatic breast cancer, which is 5.4 mg/kg IV on day 1, cycled every 21 days



Recommended Dosing

Option 3:

6.4 mg/kg IV on day 1, cycled every 21 days Dosing for trastuzumab deruxtecan in advanced HER2-positive gastric cancer is 6.4 mg/kg IV on day 1, cycled every 21 days, as currently recommended by both the FDA label and NCCN

