ESMO Clinical Practice Guidelines

Metastatic colorectal cancer: Clinical Case Presentation

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Disclosures

Dirk Arnold has declared no potential conflicts of interest
Patient profile and presentation

Patient details
- 68-year-old woman
- Teacher
- Single
- Enjoys hiking

Patient presented with
- Constipation and weight loss
- ECOG PS 0

Colonoscopy/biopsy
- Adenocarcinoma in descending colon

Laboratory tests
- CEA: 68 ng/mL

CT scans
- No distant metastases
Initial management: Surgical procedure

• Left-sided hemicolecctomy
• Pathology:
  • pT3 N1 M0 R0 G3
  • 3 of 15 lymph nodes positive
  • KRAS (exon 2) wild type
• Post-operative CEA: 15 ng/ml
• Adjuvant therapy refused by her (toxicity concerns)
At 6 month follow-up visit: CT scan
Patient case: 68 y/o female patient

- CT proven peritoneal and lymphatic relapse
- No symptoms, ECOG PS 0
- CEA: now 266 ng/ml
- Pathology:
  - Primary tumour: Adenocarcinoma G3; WT KRAS (exon 2)
Q1: What else is undoubtedly needed before decision making?

1. Nothing - information are complete
2. (expanded) RAS status only
3. RAS and BRAF status
4. RAS, BRAF and MSS status
5. all of those information are less relevant than PET
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- CT proven peritoneal and lymphatic relapse
- No symptoms, ECOG PS 0
- CEA: now 266 ng/ml
- Pathology:
  - Primary tumour: Adenocarcinoma G3; wild-type KRAS (exon 2)
  - wild-type RAS; wild-type BRAF
Q2: What would be your preferred suggestion for a 1st line (induction) treatment?

1. Fluoropyrimidine alone +/- bevacizumab
2. Combination chemo* alone
3. Combination chemo with Bevacizumab
4. Combination chemo with anti-EGFR (Cetuximab or Panitumumab)
5. Triplet chemotherapy (FOLFOXIRI) +/- Bevacizumab

* any fluoropyrimidine (5FU or Capecitabine) with oxaliplatin or FOLFIRI
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Patient case: 68 y/o female patient

• Discussion with the patient on decision making
  • „too aggressive“ disease for monotherapy
  • wanted to avoid symptomatic toxicity
  • upfront consideration of de-escalation

• after 2 mos.: CEA decreased

• after 4.5 mos.: Asthenia, neuropathy CTC 2°
At 4 mos.: Follow-up visit CT scan

- “minor response” ( = “stable disease” according to RECIST)
- no tumour-related symptoms, mild neuropathy
- CEA now normalized
Q3: What would be your preferred management here?

1. Stop all treatment – until progression
2. Continue with Bevacizumab alone
3. Continue with FP* alone
4. Continue with FP* plus Bevacizumab
5. Continue with FOLFIRI

* any fluoropyrimidine (5FU or Capecitabine)
Q3: What would be your preferred management here?

1. Stop all treatment – until progression
2. Continue with Bevacizumab alone
3. Continue with FP* alone
4. Continue with FP* plus Bevacizumab
5. Continue with FOLFIRI

* any fluoropyrimidine (5FU or Capecitabine)
Patient case: 68 y/o female patient

• So far: 4 mos. FOLFOX/Bev → 9 mos. Cape/Bev
  • well tolerated
  • discontinued for 4 weeks for holiday (cruise)

• Now:
  • CEA increases, lymph nodes with progressive disease
  • clinically excellent, neuropathy recovered
Q4: What would be your preferred management here?

1. Wait until she gets symptomatic
2. Re-start Oxaliplatin (Re-Induction)
3. FOLFIRI
4. FOLFIRI plus anti-EGFR
5. FOLFIRI plus Bevacizumab
6. FOLFIRI plus Afibercept
Q4: What would be your preferred management here?

1. Wait until she gets symptomatic
2. Re-start Oxaliplatin (Re-Induction)
3. FOLFIRI
4. FOLFIRI plus anti-EGFR
5. FOLFIRI plus Bevacizumab
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Q4: What would be your preferred management here?

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2. Re-start Oxaliplatin (Re-Induction)
3. FOLFIRI
4. FOLFIRI plus anti-EGFR
5. FOLFIRI plus Bevacizumab
6. FOLFIRI plus Aflibercept
Patient case: 68 y/o female patient

• So far:
  • 4 mos. FOLFOX/Bev ➔ 9 mos. Cape/Bev (= 13 in total)
  • 7 mos. FOLFIRI/Aflibercept (with some interruptions), stable disease

• Now:
  • (Few) ascites, CEA increases again
  • Some fatigue
  • ECOG PS 1
Q5: What would be your preferred management now?

1. Best supportive care
2. EGFR alone
3. Irinotecan & EGFR
4. Re-Induction of FOLFOX
5. Regorafenib
6. TAS 102 (if available)
Q5: What would be your preferred management now?

1. Best supportive care
2. EGFR alone
3. Irinotecan & EGFR
4. Re-Induction of FOLFOX
5. Regorafenib
6. TAS 102 (if available)
Patient case: 68 y/o female patient

• So far:
  • 4 mos. FOLFOX/Bev \rightarrow 9 mos. Cape/Bev (= 13 in total)
  • 7 mos. FOLFIRI/Aflibercept (with some interruptions), stable disease
  • 4 mos. Panitumumab single agent \rightarrow some response, then progression

• What now?
  • FOLFOX (Re-Induction) \rightarrow Regorafenib ?
  • Regorafenib \rightarrow FOLFOX (Re-Induction) ?
  • How to integrate TAS 102 ?
Patient case: 68 y/o female patient

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  • 4 mos. FOLFOX/Bev $\rightarrow$ 9 mos. Cape/Bev (= 13 in total)
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  • 4 mos. Panitumumab single agent $\rightarrow$ some response, then progression

• What now?
  • FOLFOX (Re-Induction) $\rightarrow$ Regorafenib ?
  • Regorafenib $\rightarrow$ FOLFOX (Re-Induction)
  • How to integrate TAS 102 ?
Treatment “lines“: Scenarios

Figure 1. Strategic scenarios in the continuum of care of metastatic CRC

A: Scenario 1
- 1\textsuperscript{st} line: Cytotoxic doublet\textsuperscript{1} + bevacizumab
- 2\textsuperscript{nd} line: Cytotoxic doublet\textsuperscript{1} + bevacizumab or aflibercept
- 3\textsuperscript{rd} line: Irinotecan or FOLIRI + anti-EGFR antibody\textsuperscript{2}
  - 4\textsuperscript{th} line: Regorafenib

B: Scenario 2
- Cytotoxic doublet\textsuperscript{1} + bevacizumab
- Cytotoxic doublet\textsuperscript{1} + anti-EGFR antibody\textsuperscript{2}
  - Regorafenib

C: Scenario 3
- Cytotoxic doublet\textsuperscript{1} + anti-EGFR antibody\textsuperscript{2}
- Cytotoxic doublet\textsuperscript{1} + bevacizumab
  - Regorafenib

\textsuperscript{1} cytotoxic doublets: fluoropyrimidine + oxaliplatin or irinotecan; \textsuperscript{2} RAS wild type

Van Cutsem, Cervantes, Nordlinger & Arnold; Ann Oncol 2014