Original Study

Evaluation of Guideline Adherence in Colorectal Cancer Treatment in The Netherlands: A Survey Among Medical Oncologists by the Dutch Colorectal Cancer Group

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Abstract

Guideline adherence for the systemic treatment of (metastatic) colorectal cancer was surveyed among oncologists in The Netherlands. Reported overtreatment patterns (adjuvant setting) and undertreatment patterns for targeted therapies (metastatic setting) were identified, possibly explained by unawareness or disagreement with the guidelines, or local financial restrictions. Additional support for guideline implementation and monitoring besides investigating underlying causes for nonadherence is recommended.

Background: Clinical guidelines are generated to preserve high-quality evidence-based care. Data on the implementation of guidelines into clinical practice are scarce, despite that guideline adherence prevents over- and undertreatment and correlates with survival. Therefore, we investigated guideline adherence for the systemic treatment in high-risk stage II and stage III colon cancer and metastatic colorectal cancer. **Patients and Methods:** In all Dutch hospitals (n = 88) 1 medical oncologist involved in colorectal cancer care was approached to participate. An online survey was conducted regarding the local standard of care for adjuvant chemotherapy in high-risk stage II and stage III colon cancer and first-line treatment regimens in metastatic colorectal cancer. Frequency tables were provided for categorical variables and compared for differences in guideline adherence according to hospital type (academic/teaching/regional). **Results:** The overall response rate was 70% (62 of 88). Reported guideline adherence was at least 60% of all presented settings. For high-risk stage II and stage III colon cancer, treatment strategies agreed with national guidelines in 66% and 84% of hospitals, and overtreatment patterns were identified in 28% and 13%, respectively. Targeted therapy was not routinely administered as first-line treatment in metastatic colorectal cancer (range from 63% to 71% in different settings). No differences in guideline adherence were observed among different hospital types. **Conclusion:** Guideline adherence as reported by medical oncologists in The Netherlands is suboptimal. Possible explanations include unawareness or disagreement with the guidelines, or local financial restrictions. Our results recommend additional support of guideline implementation and monitoring in clinical practice, and investigating underlying causes in case of nonadherence.

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Introduction

Clinical practice guidelines are generated to improve high-quality evidence-based care of patients and to prevent undesirable practice variation. In The Netherlands, a team of medical experts of all relevant specialties is responsible for updating the guideline recommendations every few years on the basis of recent literature or consensus if no evidence-based data exist. The national guideline serves as a basis for clinical practice, but it is known that hospitals in The Netherlands might differ in their interpretation of the guidelines.

In 2014, a new Dutch guideline for colorectal cancer was published, which included updated recommendations for adjuvant chemotherapy for high-risk stage II and stage III colon cancer and systemic treatment for metastatic colorectal disease.[1] In patients with early stage (I and II) colon cancer, the use of adjuvant chemotherapy has been restricted, which implies that fewer patients should be exposed to the morbidity (and sometimes mortality) that is associated with this treatment.[2] In the metastatic setting, treatment options have been expanded by the incorporation of novel targeted drugs in treatment regimens, leading to improved survival.[2] There are no significant differences between Dutch guideline recommendations and international European Society for Medical Oncology (ESMO)[3,4] and National Comprehensive Cancer Network (NCCN) guidelines.[5] American Society of Clinical Oncology colorectal cancer guidelines for systemic therapy are lacking, except for an outdated (2004) guideline regarding adjuvant chemotherapy for stage II colon cancer.[6]

Guideline adherence for adjuvant treatment strategies in colorectal cancer has been investigated earlier.[7-10] In The Netherlands a suboptimal adherence during 2001 to 2007 was observed,[7] despite that the survival benefit of adjuvant chemotherapy had been demonstrated.[11] For metastatic colorectal cancer, the current guideline provides clear recommendations for the use of anti-vascular endothelial growth factor (VEGF) and anti-epidermal growth factor receptor (EGFR) agents, but the use of these drugs in several Dutch hospitals is restricted, at least partly because of the high costs of these drugs. However, data on this topic are scarce. Recent studies showed that bevacizumab was not administered in 41% to 49% of Dutch patients as part of first-line treatment for metastatic colorectal cancer.[12,13] Therefore, the aim of our provider-based study was to compare the reported use of adjuvant and metastatic colorectal treatment regimens with the recommendations in the most recent Dutch colorectal cancer guideline.

Methods

Study Population

We conducted an online questionnaire on the local implementation of the most recent Dutch colorectal cancer guideline recommendations for the use of systemic treatment in high-risk stage II and stage III colon cancer and in first-line for metastatic colorectal cancer outside the context of clinical trials (see Supplemental Appendix 1 in the online version. In the beginning of 2016 we invited 1 medical oncologist involved in colorectal cancer care in each of all 88 Dutch hospitals to participate. We sent 2 online reminders after initial invitation and 1 by regular mail.

Adjuvant Chemotherapy According to the 2014 Dutch Guidelines

Adjuvant chemotherapy after curative resection has been the standard recommended treatment for stage III colon cancer, with fluoropyrimidine (5-fluorouracil or capecitabine) with oxaliplatin being the most effective regimen.[11,14] In the most recent 2014 Dutch guideline,[1] several recommendations have been updated. Fluoropyrimidine monotherapy might be considered in stage III patients not eligible for oxaliplatin treatment, provided that the tumor is microsatellite stable (MSS). Fluoropyrimidine monotherapy is not indicated in patients with microsatellite instable (MSI) tumors. For patients with high-risk stage II tumors, only oxaliplatin-based adjuvant chemotherapy is recommended, provided that the tumor is MSS. A tumor is defined as high-risk stage II if at least 1 of the following characteristics is present: stage T4, <10 regional lymph nodes examined, presentation with obstruction or perforation, extramural vascular invasion, or poorly/undifferentiated tumors. Fluoropyrimidine monotherapy is not recommended because of the lack of data on this regimen in these patients. There is no indication for adjuvant chemotherapy in patients with high-risk stage II MSI tumors because of the good prognosis in this group. Any adjuvant chemotherapy should preferably be initiated within 8 weeks but not later than 12 weeks after surgery. There is no specific age limit for the administration of adjuvant chemotherapy, but the added value of oxaliplatin in elderly people (age older than 70 years) is questionable. The 2014 guideline does not recommend the use of adjuvant chemotherapy in rectal cancer patients or in patients having undergone a resection of (liver) metastases.

First-Line Systemic Treatment of Metastatic Colorectal Cancer According to the 2014 Dutch Guidelines

Currently available cytotoxic drugs with efficacy in metastatic colorectal cancer concern the fluoropyrimidines (5-fluorouracil, capecitabine), irinotecan, and oxaliplatin. More recently the targeted drugs bevacizumab (targeting the VEGF receptor pathway)[15,16] and cetuximab and panitumumab (targeting the EGFR pathway) have been implemented in the standard of care according to the 2014 Dutch guideline for colorectal cancer.[1] For patients with permanently unresectable metastases (palliative intent), a fluoropyrimidine-containing schedule (monotherapy or combination with irinotecan or oxaliplatin) in combination with bevacizumab is recommended as the standard of care. Anti-EGFR treatment is reserved for salvage treatment in patients with *RAS* (*KRAS* and *NRAS)* wild type tumors. Patients with initially unresectable but potentially resectable metastases (curative intent) of *RAS* mutant tumors are to be treated with doublet or even triplet chemotherapy in combination with bevacizumab, and there is no preference between bevacizumab and anti-EGFR therapy in these patients with *RAS* wild type tumors. Anti-EGFR therapy is contraindicated in patients with a *RAS* mutated tumor.

Outcomes

The survey consisted of 16 questions with 2 general questions on hospital type and time since registration as medical oncologist. Hospital type was classified as academic hospital/cancer institute,

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