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1 Drug description

Generic/Brand name:

Panitumumab/Vectibix ®

Panitumumab/ Vectibix ®

Developer/Company:

Amgen Europe B.V.

Description:

Panitumumab is a fully human monoclonal antibody targeting the epidermal growth factor receptor (EGFR) which can be found on the surface of certain cancer cells such as colorectal cancer (CRC) cells. Consequently, the EGFR expressing tumour cells no longer receive messages needed for growth transmitted via EGFR and therefore progression and spreading of the tumour cells is stopped [1]. Further, panitumumab shows no clinical efficacy in tumour cells expressing mutated KRAS [2], because the growth of tumour cells containing mutated KRAS is no longer controlled by EGF receptors [1].

monoclonal antibody targeting EGFR

KRAS status

KRAS gene analysis in metastatic disease is recommended as it is very important regarding responsiveness to treatment with EGFR targeted therapies such as panitumumab and cetuximab [3]. Cetuximab, the second EGFR targeting antibody is – in contrast to panitumumab, a chimeric monoclonal antibody approved for the treatment of colorectal carcinoma and for the treatment of squamous cell cancers of the head and neck [2, 4].

KRAS genotyping recommended at diagnosis

The recommended dose of panitumumab is 6mg/kg body weight given once every other week as an intravenous infusion (iv) over 60 minutes when the administered infusion is ≤1000ml. Infusion time is extended to 90 minutes when the infusion is >1000 ml [1].

i.v. infusion of 6mg/kg body weight every 2 weeks

2 Indication

Within this assessment, the indication of interest for panitumumab is the 1st- and 2nd-line treatment of patients with metastatic colorectal cancer (mCRC) in combination with chemotherapy, either FOLFOX or FOLFIRI. The FOLFOX regimen consists of fluorouracil, leucovorin and oxaliplatin and the FOLFIRI regimen combines fluorouracil, leucovorin and irinotecan [5].

1st- and 2nd-line treatment of mCRC

combination with chemotherapy

3 Current regulatory status

Since December 2007 Vectibix ® is approved in Europe for the treatment of patients with EGFR expressing metastatic colorectal cancer with non-mutated, so called wild-type, KRAS after failure of previous chemotherapy regimens based on one of the following chemotherapeutic agents: fluoro-

approved as monotherapy in 3rd- line treatment of mCRC

pyrimidine, oxaliplatin or irinotecan. Panitumumab is approved as 3rd-line mono-therapy [1].

conditional marketing authorisation

Conditional marketing authorization was granted to Vectibix ® by European Medicines Agency (EMA). They requested further information particularly regarding safety and effectiveness in patients whose tumour contain non-mutated KRAS and their quality of life. This request includes studies that investigate the use of panitumumab in different combinations with other drugs at different treatment lines and the effectiveness of panitumumab as mono-therapy [1].

request for mature data on clinical and patient relevant benefit

FDA approved Vectibix ® for the same indication as EMA in 2006. As EMA, FDA granted accelerated marketing authorization, requesting mature data on clinical benefit and patient relevant outcomes of panitumumab, not only surrogate endpoints [6].

4 Burden of disease

worldwide 3rd most common type of cancer

Colorectal cancer is worldwide the third most common type of cancer [7]. In 2007, there were 4462 (2478 men, 1984 women) new cases of colorectal cancer diagnosed in Austria. These are about 13% of all new cancer cases in Austria in 2007 [8]. In the same year 2210 (1178 men, 1032 women) CRC patients died in Austria [9].

approx. 50% of CRC pts develop metastatic disease

At time of diagnosis between 15-25% of colorectal cancer patients suffer from advanced disease and approximately 50% of all CRC patients will develop metastatic disease [10]. Applying these estimates to the Austrian context, approximately 2231 patients are eligible for 1st-line metastatic CRC treatment (mCRC).

5-year survival depends on spread of metastases at time of diagnosis

The 5-year survival rate for colorectal cancer patients suffering from metastatic disease at time of diagnosis is between 44-83% [3]. The most widely applied staging system in colorectal cancer patients is the TNM staging system [3, 11-12]. Besides the prognostic value of the staging system it is used as the basis for discussion on the choice of therapy[3].

KRAS as prognostic factor

Study results show, that KRAS status is an essential prognostic factor in respect to responsiveness of tumours to EGFR targeting anticancer medicine. Approximately 40% of all patients suffering from metastatic colorectal cancer have KRAS-mutated tumour cells. Consequently, the treatment with EGFR-targeting antibodies is not considered to be effective [11-12].

development of targeted therapies – bevacizumab, cetuximab, panitumumab

Within the last 10 years, different targeted therapies such as monoclonal antibodies (moAbs) were developed and approved for the treatment of CRC. These moAbs target different receptors at the surface of the tumour cell and inhibit the growth and spreading of the tumour. The currently most widely used receptors for the choice of therapy are vascular endothelial growth factor (VEGF) and epidermal growth factor receptor (EGFR) [13]. Bevacizumab, a moAb targeting the VEGF demonstrated a clinical relevant improvement of overall survival from 15.6 to 20.3 months when added to irinotecan and 5-fluorouracil (5-FU) compared to these regimens alone in the 1st-line setting [10]. The two other relatively new agents, cetuximab and panitumumab are targeting the EGFR of tumour cells. Cetuximab is ap-

proved for 1st-, 2nd- and 3rd-line therapy in KRAS wild-type (WT) metastatic colorectal cancer [4, 14].

combination of 2 targeted anticancer agents

The rationale behind the PACCE study, the basis of this assessment, is to investigate, if the addition of panitumumab to bevacizumab and chemotherapy is more effective than bevacizumab and chemotherapy alone, as these two monoclonal antibodies bind to different growth factors.

5 Current treatment

resection primary choice of therapy in eligible patients

Patients diagnosed with metastatic colorectal cancer should first be evaluated if they are eligible for surgery. Patients who cannot undergo resection are considered to be candidates for radiofrequency ablation (RFA) which is, according to study results considered to be inferior to surgery in terms of local recurrence and 5-year overall survival [12].

5 different drug classes for chemotherapy

Those patients who suffer from unresectable disease should receive chemotherapy for advanced or metastatic disease [12]. Currently there are five different classes of drugs available which show significant anti-tumour activity when used as single agents or in different combinations in mCRC. These classes of drugs are:

- Fluoropyrimidines (5-fluorouracil, also widely known as 5-FU)
- Irinotecan
- Platinum agent Oxaliplatin
- Monoclonal antibody targeting EGFR (cetuximab and panitumumab)
- Monoclonal antibody targeting VEGF (bevacizumab)[15]

The choice of therapy is based on consideration of the goal of the therapy, the type and timing of the prior therapy that has been administered and the differing toxicity profiles of the constituent drugs [12].

development of chemo- and immunotherapy combinations

Until the beginning of the 20th century the combination of 5-fluorouracil and leucovorin (5-FU/LV) was the basis of therapy for mCRC. In the following years, studies were conducted either adding irinotecan or oxaliplatin to 5-FU/LV (FOLFIRI or FOLFOX, respectively[1]) [16]. Due to increases in disease free survival and overall survival these two regimens are currently considered to be standard of care in combination with bevacizumab and cetuximab in the 1st-line treatment of metastatic colorectal cancer. Both, FOLFIRI and FOLFOX are considered to be adequate choices for 1st-line therapy [15] and study results also suggest that they are effective when used interchangeable for 1st- and 2nd-line therapy [16-17].

The development of therapy for mCRC is described elsewhere in more detail [11-13].

[1] FOLFIRI – combination therapy consisting of 5-fluorouracil, leucovorin and irinotecan; FOLFOX – combination therapy consisting of 5-fluourouracil, leucovorin and oxaliplatin

6 Evidence

2 phase III trials

Two phase III studies (PRIME trial and PACCE trial) assessing the efficacy of panitumumab in combination with standard of care versus standard of care (PRIME trial [18-20]) and bevacizumab in combination with chemotherapy with or without panitumumab (PACCE trial [5, 17]) for the 1st-line treatment of metastatic colorectal cancer could be identified.

PRIME ongoing – panitumumab + chemotherapy

The PRIME trial is an ongoing trial investigating the treatment effect of panitumumab in combination with FOLFOX in 1183 mCRC patients. Interim results on safety and efficacy presented at the Gastrointestinal Cancers Symposium 2010 and at the meeting of the European Society for Medical Oncology (ESMO) in 2009 are listed in table 6.1-1.

PACCE – panitumumab + bevacizumab + chemotherapy

trial halted by the sponsor

The intention of the PACCE trial was to determine whether the addition of panitumumab to standard of care FOLFOX and FOLFIRI regimens, both in combination with bevacizumab, will help patients being treated for previously untreated mCRC [5, 17]. Due to decrease in PFS and unacceptable toxicity in the investigational arm, treatment with panitumumab was halted in March 2007. The descriptive analysis regarding safety and efficacy presented in the table below is based on data available as of May 2007.

All in all, these 2 trials include 2236 patients suffering from previously untreated metastatic colorectal cancer.

one phase II trial consisting of 2 parts

Further, one phase II multicenter trial [21] of panitumumab for first-line treatment of metastatic colorectal cancer consisting of two parts was identified. The aim of part1 (n=19) was to assess PFS and of part2 to determine the incidence of grade 3/4 diarrhoea.

6.1 Efficacy and safety - Phase III studies

Table 6.1-1: Phase III trials - efficacy and safety of panitumumab in mCRC

Reference	Hecht et al. (2009) [5] (PACCE)	Siena et al. (2010) [18, 20] (PRIME); Abstract only
Sponsor	Supported by Amgen Inc.	Amgen
Country	USA	116 study locations worldwide [22]
Design	Randomized, open-label multicenter (200) phase III study	Randomized, multicenter phase III study
Participants characteristics	N=1053 (randomized pts), overall median age 60.5 years; I: 528 (Ox-CT: 413; Iri-CT: 115) C: 525 (Ox-CT: 410; Iri-CT: 115)	N=1183; demographics were balanced I: 593 patients C: 590 patients 1096/1183 pts had *KRAS* results: 656 WT; 440 mutant (MT)
Treatments	I(ntervention): 2 cohorts both with bevacizumab every 2 weeks (Q2W); doses were chosen by the investigator - Ox-CT: fluorouracil, leucovorin, oxaliplatin - Iri-CT: fluorouracil, leucovorin, irinotecan Pts received concomitant panitumumab of 6 mg/kg Q2W C(ontrol): The same treatment regimen as intervention group but without panitumumab	Intervention: 6.0 mg/kg panitumumab Q2W + FOLFOX4 Q2W Control: FOLFOX4 Q2W alone

In-/exclusion criteria	Inclusion: pathologic diagnosis of mCRC with measurable disease per RECIST[2] ECOG PS[3] 0 or 1, adequate hematologic, hepatic and renal functions Exclusion: prior chemotherapy or biologic therapy for metastatic disease; adjuvant chemotherapy within 6 months of undergoing random assignment, major surgery within 28 days of random assignment, pre-existing bleeding diathesis or coagulopathy	Inclusion: histologically/cytologically-confirmed adenocarcinoma of the colon or rectum with metastatic disease, no prior chemotherapy or systemic therapy for mCRC, no prior oxaliplatin, ECOG PS 0-2 No EGFR staining required for inclusion.
Follow-up	Study drug discontinuation in March 2007, cut-off date May 2007.	Trial ongoing – estimated completion time March 2011[22]
Outcomes	Primary: Ox-CT arm: progression free survival (PFS); Iri-CT arm: safety Secondary (both cohorts): objective response rate (RR), overall survival (OS) and safety	Primary: PFS Secondary: OS, objective response rate, time to progression, duration of response and safety
Key results	Median PFS time I vs. C in May 2007: - Ox-CT: 10 months (mths) (95% CI, 8.9 to 11) vs. 11.4 mths (95% CI, 10.5 to 11.9) - Iri-CT: 10.1 vs. 11.7 mths (HR 1.19; 95% CI, 079 to 1.79) Secondary endpoints I vs. C in May 2007: RR: - Ox-CT: 46% vs. 48% (OR 0.92; 95% CI, 0.7 to 1.22) - Iri-CT: 43% vs. 40% (OR 1.11; 95% CI, 0.65 to 1.90 OS: - Ox-CT: 19.4 mths (95% CI, 18.4 to 20.8) vs. 24.5 mths (95% CI, 20.4 to 24.5), (HR 1.43; 95% CI, 1.11 to 1.83) - Iri-CT: 20.7 vs. 20.5 mths (HR 1.42; 95% CI, 0.77 to 2.62)	Pts with wild type KRAS tumours : median PFS – I: 9.6 mths vs. C: 8.0 mths (HR 0.8, 95% CI, 0.66-0.97; p=0.02); RR – I: 55% vs. C: 48% Pts with mutant KRAS tumours: median PFS – I: 7.3 mths vs. C: 8.8 mths (HR 1.29, 95% CI, 1.04-1.62; p=0.02) No OS data presented in the available ASCO abstract
Adverse effects	Safety analysis included 804pts Ox-CT-cohort and 224 pts Iri-CT cohort: Worst grade 3 or higher AEs I vs. C: - Ox-CT: 367 (90%) vs. 305 (77%) - Iri-CT: 100 (90%) vs. 71 (63%) Adverse events included garde 3/4 skin toxicity, diarrhoea, infections, pulmonary embolism 7 of 293 deaths were attributed by the investigator to be panitumumab related (pulmonary embolism, cardiac arrest, cancer progression, arrhythmia, intestinal perforation, sepsis)	AE s were comparable across arms with exception of known toxicities associated with anti-EGFR therapy. Grade 3/4 infusion reactions related to panitumumab treatment were observed in less than 1% of patients.
Commentary	Study was halted in 2007 due to decrease of PFS and increase of toxicity when panitumumab was added to chemotherapy KRAS analysis showed adverse outcomes for the panitumumab arm in both wild-type and mutant groups Administration of chemotherapy and dual EGFR/VEGF inhibition (panitumumab plus bevacizumab) not recommended for treatment of mCRC in clinical practice	PFS superior in wild type KRAS tumours than in mutant KRAS tumours No data available on OS No details available on adverse events (no full publication)

[2] *RECIST – Response Evaluation Criteria in Solid Tumours*

[3] *ECOG PS – Eastern Cooperative Oncology Group performance status*

HR – hazard ratio, OR – odds ratio, RR – response rate, pts – patients, Q2W – every two weeks, WT – wild type, MT – mutated; AEs – adverse events, FOLFOX4 – combination therapy of 5-fluorouracil, leucovorin and oxaliplatin

decrease in PFS

increase toxicities

PFS favoured control arm regardless of KRAS status

Due to decrease in PFS and increase of toxicity observed in the panitumumab arm, panitumumab was discontinued on both, bevacizumab + FOLFIRI and bevacizumab + FOLFOX cohorts in March 2007 in the PACCE trial. At time of data analysis in May 2007, 94% of the Ox-CT cohort and 87% in the Iri-CT cohort had ended study treatment. Most of these patients discontinued the study treatment due to AEs, treatment refusal and requirement of alternative therapy. KRAS mutation status was analysed in 82% of patient tumour samples. Results show that PFS favoured the control arm in both chemotherapy cohorts, regardless of KRAS status. Differentiating between FOLFIRI and FOLFOX cohorts, response rates (RR) were similar between intervention and control arm in both KRAS groups in the FOLFOX cohort. For the irinotecan-based cohort RR was numerically higher in the wild-type group for the intervention group and for the mutant group in the control arm [5].

KRAS as predictive biomarker for choice of therapy

importance of KRAS status confirmed

The PRIME trial was designed to demonstrate the importance of KRAS status as a predictive biomarker for the selection of 1st-line therapy for metastatic colorectal cancer with panitumumab (anti-EGFR monoclonal antibody) in combination with oxaliplatin-based chemotherapy (FOLFOX). Results of the PRIME trial confirm the importance of determining the KRAS status as a predictive biomarker for the choice of therapy [18]. Besides the interim safety analysis presented 2010 at the annual meeting of the American Society of Clinical Oncology (ASCO) [18], another ASCO abstract from 2008 is available presenting the pooled safety data on the first 601 patients [19]. The most common grade 3/4 AEs observed were skin and subcutaneous tissue of system organ class (11%), diarrhoea (10%), nausea (3%), neutropenia (25%), fatigue (4%), hypomagnesaemia (2%) and dehydration [19].

panitumumab improves PFS in combination with chemotherapy

Whereas, the PACCE trial was started in June 2005 and halted in March 2007 due to decrease in PFS and unacceptable toxicities, the PRIME trial started in July 2006 and is still ongoing. OS results and safety results are available from the abstracts of presentations at ESMO meeting 2009 [20] and the 2010 ASCO Gastrointestinal Cancer Symposium [18]. These results show that the addition of panitumumab to chemotherapy in 1st-line treatment is superior with respect to PFS in wild-type KRAS tumours compared to chemotherapy alone [18, 20].

6.2 Efficacy and safety - further studies

2 parts – different mode of administration of 5-FU

Berlin et al. [21] conducted a phase II multicenter, open-label study consisting of two parts to assess the efficacy of panitumumab in combination with irinotecan-based chemotherapy (irinotecan, leucovorin and 5-fluorouracil) for untreated mCRC. The two parts of the study differed regarding the mode of administration of 5-fluorouracil which was given either as bolus intravenous (part1; n=19) or as an intravenous (i.v.) infusion (FOLFIRI, part2; n=24). The dose of panitumumab was 2.5 mg/kg given intravenously once weekly. The primary objective of part1 was to assess progression free survival (PFS) and as patients experienced unacceptable toxicity in part1 of the study, the protocol was amended to replace part1 by part2 and also the primary endpoint was changed to assess the incidence of grade 3/4 diarrhoea. 11 (58%) and 6 (25%) patients suffered from grade 3 or 4 diarrhoea in part1 and 2, respectively. All in all, 4 patients discontinued treatment due to grade 3/4 diarrhoea, 3 in part1 and one in part2. Other treatment related grade 3/4 adverse events observed in both parts were pain, dehydration, hypokalaemia and fatigue and grade 4 hypomagnesaemia which was considered to be treatment related. Skin-related toxicities – common AEs of EGFR-targeting agents – related to treatment occurred in all patients included in the trial. 16% of patients in part1 and 13% in part2 had grade 3 skin-related reactions. Rash was the most common event of skin-related toxicities. Overall, 6 (32%) patients and 11 (46%) patients in part1 and 2 discontinued treatment due to adverse events – 5 and 8 patients suffered from AEs considered to be panitumumab related, respectively. Whereas in part1 2 patients died during the panitumumab treatment, none of the deaths was study drug related. No patient died in part2. The median PFS time was 5.6 months (95% CI, 4.4-8.3 months) in part1 and 10.9 months (95% CI, 7.7-22.5) in part2 and the median overall survival (CI 95%) was 17 months (13.7 to not estimable) and 22.5 months (14.4 to not estimable), respectively.

dose of panitumumab: 2.5mg/kg every week

primary endpoints: PFS and diarrhoea

4 pts discontinued treatment

common AEs related to EGFR-targeting agents

2 pts died – non was study drug related

7 Estimated costs

monthly therapy costs €4,250.-

It is recommended that panitumumab is administered as an intravenous infusion at 6mg/kg over 60 (≤1000 ml) or 90 (>1000 ml) minutes every 14 days [23]. In Austria, the price for one vial of 5ml containing 20mg/ml panitumumab is €425.- (manufacturer's price [24]; pharmacy retail price: €707.20 [25]). Assuming an average weight of 70kg of patients, 5 vials are needed for one treatment cycle of two weeks. Therefore the monthly treatment costs for panitumumab mono-therapy would be €4,250.- (€7,072.-).

additional to standard of care

KRAS genotyping

If the immunotherapy with panitumumab would be used as 1st-line therapy in combination with standard of care (see chapter 5) these costs would be additional to the treatment costs of standard of care. Further, as study results show that EGFR-targeting agents are not effective in KRAS-mutated tumours, genotyping is strongly recommended prior the therapy, ideally at time of diagnosis of mCRC [11-12].

8 Ongoing research

several phase III trials registered at www.clinicaltrial.gov

At the trial registry website ClinicalTrials.gov of the U.S. National Institutes of Health are several phase III trials registered, investigating the efficacy and safety in different treatment options (June 2010). Most of the studies investigate the anti-cancer ability of panitumumab in the second-line setting. Two studies, briefly described below, are conducted in the first-line setting:

pre-operative therapy combination

- FOxTROT trial (NCT00647530) – fluoropyrimidine, oxaliplatin and targeted receptor pre-operative therapy: a controlled trial in high-risk operable colon cancer. The aim of this trial is to investigate whether the addition of panitumumab to fluorouracil and oxaliplatin is superior in terms of efficiency and safety to fluorouracil and oxaliplatin alone in the treatment of patients with high-risk colon cancer that can be removed by surgery. The estimated completion date of this trial is January 2012.

panitumumab with standard of care in 1st-line therapy of mCRC

- PRIME trial (NCT00364013I) – the purpose of this study is again to investigate the efficacy and safety of adding panitumumab to standard of care in the 1st-line treatment of mCRC. In chapter 6 of this assessment interim safety and efficacy results presented at ASCO meetings in 2008 and 2010 are described [18-19]. As mentioned above, the PRIME trial is estimated to be completed in March 2011.

9 Commentary

approved as mono-therapy in 2nd-line treatment of mCRC

Vectibix ® was approved by FDA and EMA in 2006 and 2007, respectively as mono-therapy for the treatment of mCRC after irinotecan- or oxaliplatin-based chemotherapy has failed [1, 23]. Both, EMA and FDA granted accelerated/conditional approval based on one open-label, randomized multinational study (n=463 patients) not showing a survival difference between the intervention and the control arms, but superior PFS in the panitumumab arm [14, 26-27]. If drugs are granted accelerated or conditional approval based on surrogate endpoint(s) that are likely to predict effects on OS, the marketing authorization holder is obliged to conduct further studies to verify the clinical benefit of the medicine [26]. These new results of the trials are then reviewed every year by the regulatory authority [14].

conditional approval based on surrogate endpoints

investigation of antitumor activity of two moAbs targeting EGFR and VEGF

The PACCE trial was conducted to find out whether panitumumab is effective in the 1st-line therapy of mCRC. One very important point to note is that this trial investigated the antitumor activity of two monoclonal antibodies, each targeting a different receptor on the surface of tumour cells in combination with chemotherapy. Recent studies demonstrated the superiority of adding bevacizumab to either FOLFOX or FOLFIRI compared to one of these regimens alone. The rationale behind the PACCE trial was, to improve efficacy by blocking two growth factors on the surface of cancer cells – VEGF with bevacizumab and EGFR with panitumumab.

Within the FDA review, Giusti et al. (2009) expressed 3 major concerns on the PACCE trial. First of all, they criticized that the assessment, whether the risks of panitumumab treatment could outweigh its benefit was conducted at the time of interim analysis. The time when to conduct the interim analysis was event driven and all patients had already been accrued. Originally, the purpose of the data safety monitoring board (DSMB) was to stop accrual when the risks of panitumumab are superior to its benefit. Further, the FDA advised the sponsor in advance about its concerns regarding the study design and the lack of phase II trial data with the combination of panitumumab and bevacizumab plus chemotherapy. And finally Giusti et al. expressed concern about the consistency of the results of retrospective KRAS analysis and the hypothesis that response in patients with wild-type KRAS is superior to that in patients with mutated KRAS tumours [26].

3 major concerns:

first benefit-risk analysis was event driven

lack of phase II trials

relevance of KRAS status for mCRC therapy

Several retrospective analyses and studies show that the monoclonal antibodies panitumumab and cetuximab are not suitable for therapy in patients with KRAS mutated cancer cells [28]. It is estimated that about 40% of colorectal cancer have mutated KRAS. Therefore, guidelines suggest KRAS status testing at time of diagnosis of mCRC. The early establishment of the KRAS status does not necessarily influence the therapy selection for 1st-line setting, but enables oncologists and patients to develop a targeted, continuous treatment strategy – especially in deciding whether to use EGFR-targeting argents or not [11-12].

moAbs targeting EGFR not effective in pts with KRAS mutated tumour

KRAS testing at time of diagnosis

At the beginning of June 2010 EMA released a summary of the European Public Assessment Report on Vectibix ® [14] stating among other things that they are still awaiting results of studies investigating the clinical benefit of panitumumab in combination with other medicines or as a single agent in different treatment lines of patients with colorectal cancer with and without KRAS mutation. Further, the quality of life of patients treated with panitumumab needs to be determined [14].

clinical benefit still needs to be proven

Based on the results of the PACCE trial and also of the CAIRO-2 trial, when cetuximab was added to capecitabine, oxaliplatin and bevacizumab for the 1st-line treatment of mCRC [29-30] guidelines strongly advise against the concurrent use of bevacizumab with either cetuximab or panitumumab [11-12]. In both studies the progression free survival in the investigational study arm was inferior to the control arm [5, 29].

guidelines advise not to use bevacizumab in combination with EGFR-targeting moAbs

To date, there are no data available on the quality of life (QoL) of patients treated with panitumumab [14] and currently trial results have only demonstrated benefit of panitumumab in treatment of chemotherapy refractory mCRC [13].

to date no quality of life data available

Though, panitumumab is approved in the US and in Europe, there still remain questions to be answered in terms of patient relevant benefit for mCRC patients. Based on trial results the concomitant use of panitumumab and bevacizumab is not recommended. Further, data demonstrating the effectiveness regarding OS and QoL of mCRC patients treated with panitumumab in the 1st-line setting should be provided before the widespread clinical use.

patient relevant benefit still remains to be answered more precisely

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