HAUTE AUTORITÉ DE SANTÉ

The legally binding text is the original French version

TRANSPARENCY COMMITTEE

Opinion

24 July 2013

ZALTRAP, 25 mg/ml, concentrate for solution for infusion

B/1 glass vial of 4 ml (CIP 3400958418563)
B/3 glass vials of 4 ml (CIP 3400958418624)
B/1 glass vial of 8 ml (CIP 3400958418792)

Applicant: SANOFI-AVENTIS FRANCE

INN	aflibercept
ATC code (2012)	L01XX44 (aflibercept)
Reason for the request:	**Inclusion**
List(s) concerned	**Hospital use** (French Public Health Code L.5123-2)
Indication(s) concerned	**"ZALTRAP in combination with irinotecan/5-fluorouracil/folinic acid (FOLFIRI) chemotherapy is indicated in adults with metastatic colorectal cancer (MCRC) that is resistant to or has progressed after an oxaliplatin-containing regimen."**

Actual Benefit	**The AB is substantial in the treatment of metastatic colorectal cancer that is resistant to or has progressed after an oxaliplatin-containing regimen.**
Improvement in Actual Benefit	**In light of the current data, the Committee believes that ZALTRAP in combination with irinotecan/5-fluorouracil/folinic acid (FOLFIRI) chemotherapy does not provide any improvement in actual benefit (level V, nonexistent) in the management of metastatic colorectal cancer that is resistant to or has progressed after an oxaliplatin-containing regimen.**
Therapeutic use	**ZALTRAP in combination with irinotecan/5-fluorouracil/folinic acid (FOLFIRI) chemotherapy is a second-line treatment for metastatic colorectal cancer that is resistant to or has progressed after an oxaliplatin-containing regimen. However, its therapeutic use taking account of the KRAS status of the tumour has still to be determined.**
Committee recommendation	**The Transparency Committee recommends inclusion on the list of medicines approved for hospital use in the indication in the Marketing Authorisation.**

01 ADMINISTRATIVE AND REGULATORY INFORMATION

Marketing Authorisation	Date of Marketing Authorisation (centralised procedure): 01 February 2013
Prescribing and dispensing conditions / special status	List I Reserved for hospital use Prescription restricted to cancer treatment or clinical oncology specialists and departments. Medicine requiring special monitoring during treatment.

ATC Classification	2012	
	L	Antineoplastic and immunomodulating agents
	L01	Antineoplastic agents
	L01X	Other antineoplastic agents
	L01XX	Other antineoplastic agents
	L01XX44	aflibercept

02 BACKGROUND

This is an application for inclusion of ZALTRAP, anti-VEGF (vascular endothelial growth factor) inhibiting the growth of new vessels that supply tumours in colorectal cancer. The first anti-VEGF medicinal product to have Marketing Authorisation in the treatment of colorectal cancer was bevacizumab (AVASTIN) in 2005.
The Committee notes that, in the European assessment, 7 CHMP member countries, including France, voted for an unfavourable risk-benefit ratio for the proprietary medicinal product ZALTRAP in this indication (EPAR p 90).

03 THERAPEUTIC INDICATIONS

“ZALTRAP in combination with irinotecan/5-fluorouracil/folinic acid (FOLFIRI) chemotherapy is indicated in adults with metastatic colorectal cancer (MCRC) that is resistant to or has progressed after an oxaliplatin-containing regimen.”

04 DOSAGE

“ZALTRAP should be administered under the supervision of a physician experienced in the use of antineoplastic medicinal products.

Posology
The recommended dose of ZALTRAP, administered as an intravenous infusion over 1 hour, is 4 mg/kg of body weight, followed by the FOLFIRI regimen. This is considered as one treatment cycle.
The FOLFIRI regimen to be used is irinotecan 180 mg/m^2 intravenous infusion over 90 minutes and folinic acid (dl racemic) 400 mg/m² intravenous infusion over 2 hours at the same time on day 1 using a Y-line, followed by 5-fluorouracil (5-FU) 400 mg/m² intravenous bolus, followed by 5-FU 2400 mg/m² continuous intravenous infusion over 46 hours.

The treatment cycle is repeated every 2 weeks.
ZALTRAP treatment should be continued until disease progression or unacceptable toxicity occurs."

05 THERAPEUTIC NEED

In France in 2011, colorectal cancer was the number three cancer in terms of incidence and number two in terms of mortality.
Colorectal cancer is a cancer with a good prognosis when it is diagnosed early: relative 5-year survival is 91% for localised stages, 70% for stages with locoregional invasion. On the other hand, 5-year survival is about 11% in metastatic cases which account for about 25% of patients at the time of diagnosis.[1]
First- and second-line chemotherapy was based on irinotecan or oxaliplatin, each combined with 5-FU and folinic acid. These treatments have also evolved to include targeted therapies such as bevacizumab, an anti-VEGF, cetuximab and panitumumab, both targeting the unmutated KRAS gene. Despite these advances, the prognosis for second-line metastatic colorectal cancer remains poor and median overall survival is about one year.

[1] Survival of patients with cancer in France: status report – INCa - April 2010

06 CLINICALLY RELEVANT COMPARATORS

06.1 Medicinal products

INN	*Company*	*Indication*	*Date of TC opinion*	*AB*	*IAB (Wording)*
bevacizumab	Roche	MCRC in combination with a fluoropyrimidine-based chemotherapy	1st line: 08/06/2005	*Substantial*	II
			2nd line: 04/04/2009		"AVASTIN in combination with the FOLFOX-4 protocol provides a minor improvement in actual benefit (level IV) in terms of efficacy by comparison with the FOLFOX-4 protocol administered alone."

MCRC: metastatic colorectal cancer

When the pivotal study was set up to evaluate aflibercept + FOLFIRI in 2nd-line treatment in patients who had already received oxaliplatin (first patient included on 19 November 2007), bevacizumab (another anti-VEGF) did not yet have Marketing Authorisation in 2nd-line treatment. It received that Marketing Authorisation in 2008 on the basis of a study comparing the combination of FOLFOX4+bevacizumab versus FOLFOX4, after first-line, irinotecan-based treatment. Thus, the comparator used in the pivotal study for ZALTRAP, the combination of FOLFIRI (irinotecan, 5-fluorouracil, folinic acid) + placebo was a relevant comparator at that time.
Today, bevacizumab (AVASTIN) can be regarded as a comparator, particularly in one subgroup of the pivotal study for ZALTRAP: patients who failed first-line oxaliplatin-based chemotherapy without bevacizumab.

◗ Conclusion

AVASTIN (bevacizumab) can be regarded as the relevant comparator for ZALTRAP, particularly in the subgroup of patients not previously treated with first-line bevacizumab.

07 INTERNATIONAL INFORMATION ON THE MEDICINAL PRODUCT

Country	REIMBURSEMENT	
	YES/NO If no, why not	Population(s) That of the Marketing Authorisation or restricted
EU	No (procedures in progress)	
USA	Yes	Indication identical to that in Europe

08 ANALYSIS OF AVAILABLE DATA

The dossier of the application for inclusion comprises:
- 7 phase I dose-finding studies
- 4 phase II studies evaluating the efficacy, safety and pharmacokinetics of aflibercept (ZALTRAP) in monotherapy. Since these studies do not provide any information on the quantity of the medicine's effect, they are not examined in this document.
- a pivotal phase III placebo-controlled study (the VELOUR study) which will be analysed below.

08.1 Efficacy

VELOUR study[2]

Randomised double-blind phase III study evaluating the efficacy and safety of ZALTRAP (aflibercept) versus placebo, both combined with irinotecan-based chemotherapy (FOLFIRI protocol), in patients with metastatic colorectal cancer who failed oxaliplatin-based chemotherapy, with or without bevacizumab.
Assignment to treatment was stratified according to the ECOG performance status (0 versus 1 versus 2) and according to prior treatment with bevacizumab (yes or no).

Patients had to receive the study treatment within 3 days after randomisation then every 2 weeks (= 1 cycle of treatment):
- Group A: aflibercept: 4 mg/kg over 1 hour i.v. on day 1.
- Group B: placebo: over 1 hour i.v. on day 1.

The administration of the investigational medicinal product (aflibercept or placebo) was immediately followed by the administration of FOLFIRI as follows:
- folinic acid 400 mg/m² by i.v. infusion over 2 hours and irinotecan 180 mg/m² as an infusion over 90 minutes,
- followed by a bolus of 400 mg/m² 5-FU and continuous infusion of 5-FU in a dose of 2400 mg/m² over 46 hours.

The treatment cycles in both groups had to be repeated every 2 weeks. Patients had to be treated until the disease progressed or unacceptable toxicity occurred.

The primary efficacy endpoint was overall survival defined as the time between the date of randomisation and the date of death from any cause.

The secondary endpoints were:
- progression-free survival, defined as the time between the date of randomisation and the date of the first observation of disease progression or the date of death from any cause (whichever happened first).
- the objective response (complete response (CR) and partial response (PR) according to the RECIST criteria[3]).

[2] Van Cutsem E, Tabernero J, Lakomy R, et al. Addition of aflibercept to fluorouracil, leucovorin, and irinotecan improves survival in a phase III randomized trial in patients with metastatic colorectal cancer previously treated with an oxaliplatin-based regimen. J Clin Oncol 2012; 30: 3499-3506.

[3] Corresponds to criteria used to evaluate the response in solid tumours and summarised as follows:
- Complete response: disappearance of all tumoral lesions
- Partial response: reduction of 30% in the largest lesion diameter

Inclusion criteria:

- patients with adenocarcinoma of the colon or rectum, confirmed histologically or cytologically.
- incurable (i.e. inoperable) metastatic disease.
- disease measurable or unmeasurable (according to the RECIST criteria).
- a previous single line of chemotherapy administered for metastatic disease. This previous chemotherapy had to be an oxaliplatin-based treatment. The disease had to have progressed during or after the last administration of the oxaliplatin-based chemotherapy. Patients who had had a recurrence within 6 months after the end of the adjuvant oxaliplatin-based chemotherapy were eligible.

Non-inclusion criteria:

- prior treatment with irinotecan.
- less than 28 days between a previous radiotherapy, previous surgery or previous chemotherapy and randomisation. Less than 42 days between previous major surgery and randomisation.
- age < 18 years.
- ECOG performance status > 2.
- history of cerebral metastases, uncontrolled compression of the spinal cord or carcinomatous meningitis, or new signs of cerebral or leptomeningeal disease.
- existence of an event linked to use of an anti-VEGF: proteinuria, uncontrolled arterial hypertension, uncontrolled thromboembolic event within 3 months before randomisation, deep vein thrombosis within 4 weeks before randomisation, coagulopathy, unhealed wound.
- contraindications to FOLFIRI: known deficiency of dihydropyrimidine dehydrogenase, uncontrolled disorders of the colon or the small intestine, history of intestinal disease, chronic diarrhoea, unresolved occlusion/partial occlusion of the intestine, known Gilbert syndrome.
- inadequate bone marrow function: absolute neutrophil count < 1.5 x 10^9/l, platelet count < 100 x 10^9/l, haemoglobin < 9.0 g/dl.
- serum creatinine > 14.5 x ULN (upper limit of normal), creatinine clearance < 60 ml/min, calculated using the Cockroft-Gault formula.
- inadequate liver function test results: total bilirubin > 1.5 x ULN, transaminases > 3 x ULN (if liver metastasis > 5 x ULN), alkaline phosphatases > 3 x ULN (if liver metastasis > 5 x ULN).

Results:

A total of 1226 patients were randomised in the study; their median age was 61 years. Almost all patients (97.8%) had an ECOG performance status of 0 or 1, and 2.2% had an ECOG performance status of 2.

Among the 1226 randomised patients, 89.4% of the patients treated with placebo/FOLFIRI and 90.2% treated with ZALTRAP/FOLFIRI had previously received a combined oxaliplatin-based chemotherapy in the context of their metastatic/advanced disease. A total of 10.4% of the patients on placebo/FOLFIRI and 9.8% of the patients on ZALTRAP/FOLFIRI previously received adjuvant, oxaliplatin-based chemotherapy; their disease had progressed during the adjuvant chemotherapy or within 6 months after the end of it.

Oxaliplatin-based treatment regimens were administered in combination with bevacizumab in 373 patients (30.4%).

Table 1: Baseline characteristics of patients – ITT population

	ZALTRAP + FOLFIRI *n*=612	placebo + FOLFIRI *n*=614
Age, years		
Median (range)	61. 0 (21:82)	61. 0 (19:86)
Age > 65 years (%)	33. 5	38. 8
Men (%)	59. 6	57. 5
ECOG performance status (%)		
0	57. 2	57. 7
1	40. 7	40. 4
2	2. 1	2. 0
Primary site (%)		
Colon	47.2	49. 2
Rectosigmoid	20.1	22. 1
Rectum	32.2	28. 3
Other	0. 5	0. 3
>1 metastatic site (%)	57. 8	54. 9
Main organs with metastatic invasion (%)		
Liver	75. 0	70. 2
Lung	44. 3	45. 1
Peritoneum	11. 1	14. 3

Median overall survival (primary efficacy endpoint) was 13.5 months in the ZALTRAP + FOLFIRI arm versus 12.06 months in the placebo+FOLFIRI arm (HR = 0.81 95.34% CI [0.71 – 0.93]; p = 0.0032), a gain in absolute terms of 1.44 months.

Median progression-free survival was 6.90 months in the ZALTRAP+FOLFIRI arm versus 4.67 months in the placebo+FOLFIRI arm (HR = 0.75 99.99% CI [0.57-0.99]; p = 0.00007), a gain in absolute terms of 2.23 months in favour of the ZALTRAP arm.
The percentage objective response based on a review of the radiological images in the evaluable population was 19.8% in the ZALTRAP+FOLFIRI arm versus 11.1% in the placebo+FOLFIRI arm (p = 0.0001).

Analyses of overall survival and progression-free survival were performed as a function of stratification factors. The effect of treatment with ZALTRAP/FOLFIRI on overall survival was found to be numerically smaller in patients who had already received bevacizumab than in patients who had not previously received bevacizumab, with no evidence of any variation in the treatment effect (nonsignificant interaction test, p = 0.567). The results as a function of prior exposure to bevacizumab are summarised in Table 2.

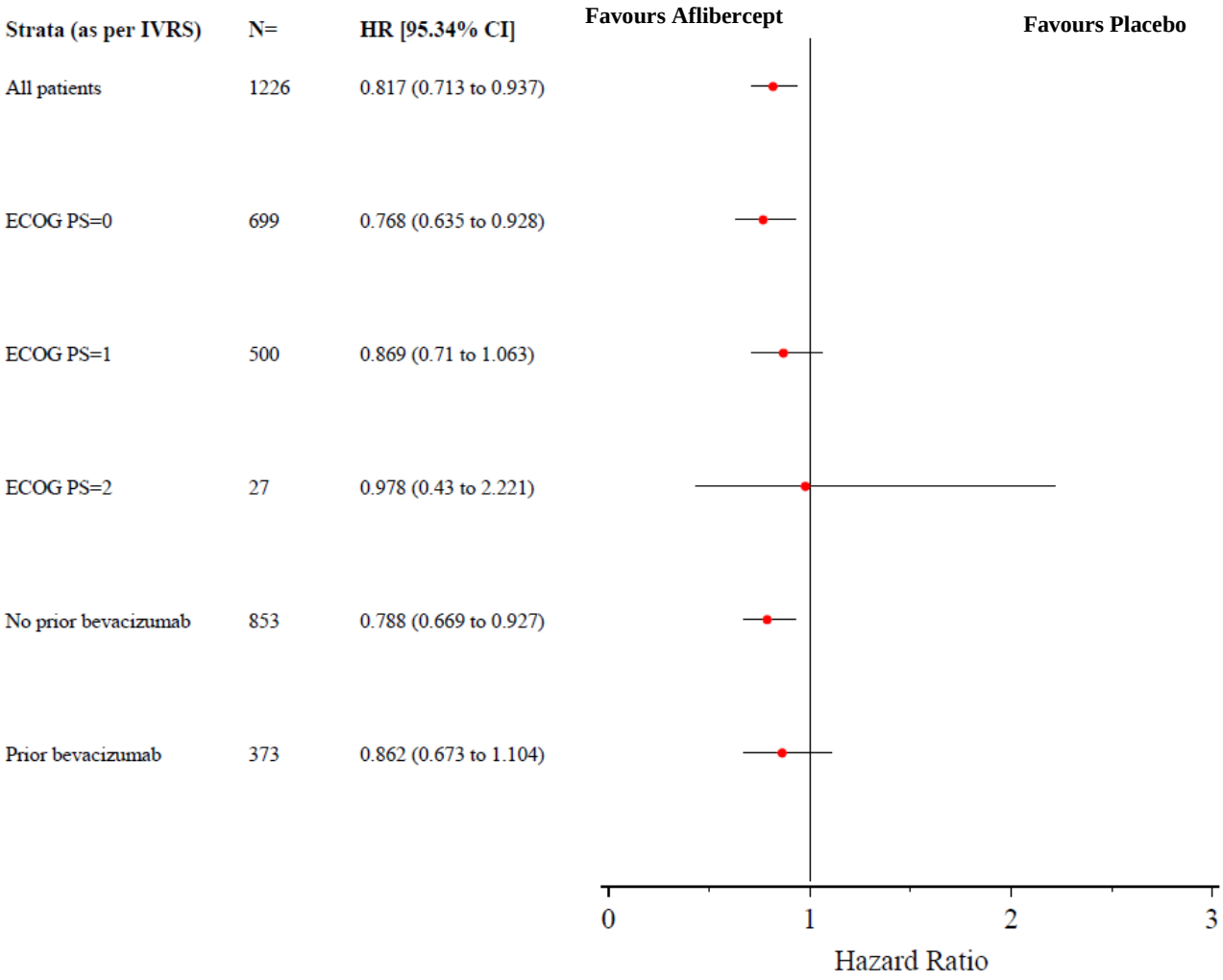
Table 2: Overall survival and progression-free survival according to prior exposure to bevacizumab – ITT population

	Placebo/FOLFIRI	ZALTRAP/FOLFIRI
Overall survival		
Patients who had received prior treatment with bevacizumab, n (%)	187 (30.5%)	186 (30.4%)
Median overall survival, months, [95% CI]	11.7 [9.96 to 13.77]	12.5 [10.78 to 15.47]
Hazard ratio [95% CI]	0.862 [0.676 to 1.100]	
Patients who had not received prior treatment with bevacizumab, n (%)	427 (69.5%)	426 (69.6%)
Median overall survival, (months) [95% CI]	12.4 (11.17 to 13.54)	13.9 (12.72 to 15.64)
Hazard ratio [95% CI]	0.788 (0.671 to 0.925)	
Progression-free survival		
Patients who had received prior treatment with bevacizumab, (n (%)),	187 (30.5%)	186 (30.4%)
Median PFS (95% CI) (months)	3.9 (3.02 to 4.30)	6.7 (5.75 to 8.21)
Hazard ratio (95% CI)	0.661 (0.512 to 0.852)	
Patients who had not received prior treatment with bevacizumab (n (%))	427 (69.5%)	426 (69.6%)
Median PFS (95% CI) (months)	5.4 (4.53 to 5.68)	6.9 (6.37 to 7.20)
Hazard ratio (95% CI)	0.797 (0.679 to 0.936)	

Analyses of overall survival and progression-free survival were also performed according to the ECOG PS performance score. The hazard ratio for overall survival was 0.77 (95% CI: [0.64 – 0.93]) for ECOG performance status 0, and 0.87 (95% CI: [0.71 – 1.06]) for ECOG performance status 1.

The hazard ratio for progression-free survival was 0.76 (95% CI: [0.63 - 0.91]) for ECOG performance status 0, and 0.75 (95% CI: [0.61 – 0.92]) for ECOG performance status 1.

Efficacy results (overall survival) in the stratified subgroups



Retrospective analyses excluding patients whose disease progressed during or within 6 months after the end of the adjuvant treatment, according to whether or not they were previously treated with bevacizumab, are given in the dossier. They are exploratory in nature and will not be described in this document.

There are no data on quality of life.

08.2 Safety/Adverse effects

The frequency of treatment discontinuations due to adverse events was 26.8% in the ZALTRAP+FOLFIRI arm versus 12.1% in the placebo + FOLFIRI arm.
Grade 3 or 4 adverse events were observed in 83.5% of patients in the ZALTRAP/FOLFIRI arm versus 62.5% in the placebo/FOLFIRI arm. The main grade 3 or 4 adverse events that occurred with greater frequency in the ZALTRAP/FOLFIRI arm than in the comparator group were: diarrhoea (19.3% versus 7.8%), hypertension (19.3% versus 1.5%), asthenia (16.9% versus 10.6%), stomatitis and ulceration (13.7% versus 5%), and dehydration (4.3% versus 1.3%).

08.3 Summary & discussion

A randomised double-blind phase III study compared aflibercept (ZALTRAP) with placebo, both combined with irinotecan-based chemotherapy (FOLFIRI protocol), in patients with metastatic colorectal cancer and failure of oxaliplatin-based chemotherapy, with or without bevacizumab.
Assignment to treatment was stratified according to the ECOG performance status (0 versus 1 versus 2) and according to prior treatment with bevacizumab (yes or no).
The primary efficacy endpoint was overall survival, defined as the time between the date of randomisation and the date of death from any cause.

The 1226 patients included had a median age of 61 years, 97.8% had an ECOG performance status of 0 or 1 and 30.4% had received bevacizumab in prior oxaliplatin-based treatment regimens.

In the aflibercept/FOLFIRI vs placebo/FOLFIRI arm

- For all included patients:
  - Median overall survival (primary efficacy endpoint) was longer: 13.5 months versus 12.06 months, a gain in absolute terms of 1.44 months (HR = 0.81 95.34% CI: [0.71 – 0.93] p = 0.0032).
  - Median progression-free survival was longer: 6.90 months versus 4.67 months (HR = 0.75 99.99% CI [0.57 – 0.99]; p = 0.00007), a gain in absolute terms of 2.23 months.
  - Efficacy according to the KRAS mutation in the tumour is unknown (not required by the protocol). The same is true for quality of life.
- As a function of stratification factors, the effect on overall survival
  - was smaller in patients who had already previously received bevacizumab than in those who had not received it, with no evidence of variation in the treatment effect (non-significant interaction test, p = 0.567).
  - was greater in patients with a low ECOG score
    for ECOG 0 hazard ratio 0.77 [0.64 – 0.93]
    for ECOG 1 hazard ratio 0.87 [0.71 – 1.06].

In the aflibercept/FOLFIRI vs placebo/FOLFIRI arm

- the frequency of treatment discontinuations due to an adverse event was greater: 26.8% versus 12.1%
- the main, most common grade ≥ 3 events were: diarrhoea (19.3% versus 7.8%), hypertension (19.3% versus 1.5%), asthenia (16.9% versus 10.6%), stomatitis and ulceration (13.7% versus 5%), dehydration (4.3% versus 1.3%).

09 THERAPEUTIC USE

The treatment of metastatic colorectal cancer has changed substantially in recent years. First of all, overall survival has increased significantly thanks to the use in current practice of irinotecan or oxaliplatin, in combination with 5-fluorouracil (5FU) and folinic acid (FA), combinations called FOLFIRI and FOLFOX, respectively. A study had shown, in first- and second-line treatment, that the sequences FOLFIRI-FOLFOX and FOLFOX-FOLFIRI had equivalent efficacy.[4]
Since the appearance of targeted therapies, the value of combining chemotherapy with a targeted therapy seems to be accepted in first- and second-line treatment.[5] Determination of KRAS status is involved in the choice of treatment.[6]

In first-line treatment, the anti-VEGF antibody bevacizumab then the anti-EGFR antibody cetuximab have been assessed. Testing EGFR status by immunohistochemistry is no longer recommended since the method is not reliable and is not predictive of response, but the choice does involve checking for a mutation of the KRAS gene within the tumour. The indication for cetuximab is limited to tumours with an unmutated KRAS gene, whereas determination of KRAS status is not necessary for treatment with bevacizumab. In the absence of any comparative studies, the place of cetuximab in relation to bevacizumab has still to be determined.

In second-line treatment, in the event of progression with chemotherapy plus targeted therapy, the choice is either to change the chemotherapy (irinotecan if first-line FOLFOX or oxaliplatin if first line FOLFIRI), or to change the targeted therapy. Since January 2013, use in combination with FOLFOX is no longer in the indication of the Marketing Authorisation for second-line cetuximab.

ZALTRAP in combination with irinotecan/5-fluorouracil/folinic acid (FOLFIRI) chemotherapy is a second-line treatment for metastatic colorectal cancer that is resistant to or has progressed after an oxaliplatin-containing regimen. However, its therapeutic use taking account of the KRAS status of the tumour has still to be determined.

[4] Tournigand C, André T, Achille E, Lledo G, Flesh M, Mery-Mignard D, Quinaux E, Couteau C, Buyse M, Ganem G, Landi B, Colin P, Louvet C, de Gramont A (2004). FOLFIRI followed by FOLFOX6 or the reverse sequence in advanced colorectal cancer: a randomized GERCOR study. J Clin Oncol; 22(2): 229-37.
[5] French National Society of Gastroenterology (SNFGE) thesaurus of gastrointestinal oncology, metastatic colon cancer. Updated 14/10/2011
[6] Advanced colorectal cancer: European Society for Medical Oncology (ESMO) clinical practice guidelines for treatment, Annals of Oncology 2010; 21: 93-97.

010 TRANSPARENCY COMMITTEE CONCLUSIONS

In view of all the above information, and following the debate and vote, the Committee's opinion is as follows:

010.1 Actual benefit

- Colorectal cancer is a life-threatening disease.
- This medicinal product is intended as specific curative cancer therapy.
- The efficacy/adverse effects ratio is high.
- Alternative medicinal products exist.
- It is a second-line therapy.

- Public health benefit:

Colorectal cancer is a serious and common clinical situation which is a major public health burden. The burden of metastatic colorectal cancer is substantial. That represented by the population of patients likely to benefit from this medicinal product (in combination with FOLFIRI, resistant to oxaliplatin-based treatment) may also be considered substantial.
Improving the management of this condition is a public health need which is an established priority (French 2004 Law on Public Health, Cancer plan).
In view of the data available from only one study in combination with the FOLFIRI protocol versus FOLFIRI, showing a modest improvement in median overall survival and progression-free survival (1.4 months and 2.2 months, respectively) and an improvement in objective response, at the expense of not inconsiderable toxicity [frequency of treatment discontinuations twice as high (26.8% vs 12.1%)], the expected additional impact of this medicinal product in terms of morbidity and mortality and quality of life can only be very small.
In addition, the transferability of the study results to clinical practice is not assured because of, in particular, the absence of clinical data on:
- the comparison of ZALTRAP in combination versus AVASTIN in combination. Whereas, for about 70% of the study patients, AVASTIN in combination would be the currently recommended comparator.
- the efficacy of treatment with ZALTRAP according to the presence or otherwise of the KRAS mutation in the tumour.

No impact on the organisation of healthcare is expected.
It is thus difficult to assume that the medicinal product ZALTRAP could provide any additional response to the identified public health need.
Consequently, in the current state of knowledge, it is not expected that the medicinal product ZALTRAP will benefit public health.

Taking account of these points, the Committee considers that the actual benefit of ZALTRAP in combination with the FOLFIRI protocol is substantial in the treatment of metastatic colorectal cancer that is resistant to or has progressed after an oxaliplatin-containing regimen.

010.2 Improvement in actual benefit (IAB)

In the light of the current data, the Committee considers that ZALTRAP in combination with irinotecan/5-fluorouracil/folinic acid (FOLFIRI) chemotherapy does not provide any improvement in actual benefit (level V, nonexistent) in the management of metastatic colorectal cancer that is resistant to or has progressed after an oxaliplatin-containing regimen.

010.3 Target population

The target population in the therapeutic indication of the Marketing Authorisation consists of patients with metastatic colorectal cancer, in combination with FOLFIRI, after failure of an oxaliplatin-containing regimen.
In 2011, according to the projections of the Health Monitoring Institute (InVS), the incidence of colorectal cancer is estimated to be 40,500 new cases.[7]
Metastatic stages are observed in about 25% cases on first diagnosis of the disease and in total almost 50% of patients will have metastases[8] (i.e. 20,250 cases).
Among patients with metastatic colorectal cancer, it is thought that 64.5% of patients will have chemotherapy (i.e. 13,060 patients), according to a National Health Insurance study[9] using data from 4273 incident cases of metastatic colorectal cancer diagnosed between April and September 2009 in France. This first-line chemotherapy can be oxaliplatin-based.
In the event of a relapse on oxaliplatin-based chemotherapy, it is thought that about 55% of patients will receive a new, second-line treatment, i.e. about 7500 patients a year.

The target population for ZALTRAP in this indication can be estimated at 7500 patients a year.

011 TRANSPARENCY COMMITTEE RECOMMENDATIONS

The Committee recommends inclusion of ZALTRAP on the list of medicines approved for hospital use in combination with irinotecan/5-fluorouracil/folinic acid (FOLFIRI) chemotherapy in adults with metastatic colorectal cancer (MCRC) that is resistant to or has progressed after an oxaliplatin-containing regimen, at the dosage in the Marketing Authorisation.

Packaging

Appropriate for the prescription conditions according to the indication, dosage and treatment duration.

[7] Civil Hospitals of Lyon, Health Monitoring Institute (InVs), National Cancer Institute (INCa), French Cancer Incidence and Mortality network (Francim), National Institute of Health and Medical Research (Inserm). Projection de l'incidence et de la mortalité par cancer en France en 2011, Technical report, June 2011
[8] Advanced colorectal cancer: ESMO clinical practice guidelines for treatment Annals of Oncology 2010; 21(5): 93-97.
[9] Study directed by Prof Guillemot and Prof Mitry using data from the National Salaried Workers' Health Insurance Fund (CNAMTS) with its support in the context of the RISE (Research Innovation Health Environment) research federation, INSERM unit U657, at the University of Versailles-St-Quentin