**UNITED STATES**
**SECURITIES AND EXCHANGE COMMISSION**
**WASHINGTON, D.C. 20549**

# FORM 8-K
# CURRENT REPORT

**Pursuant to Section 13 or 15(d) of the**
**Securities Exchange Act of 1934**

Date of Report (Date of earliest event reported): June 27, 2011 (June 25, 2011)

**REGENERON PHARMACEUTICALS, INC.**
(Exact Name of Registrant as Specified in Charter)

| **New York** | **000-19034** | **13-3444607** |
|---|---|---|
| (State or other jurisdiction of Incorporation) | (Commission File No.) | (IRS Employer Identification No.) |

**777 Old Saw Mill River Road, Tarrytown, New York 10591-6707**
(Address of principal executive offices, including zip code)

**(914) 347-7000**
(Registrant's telephone number, including area code)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

**Item 7.01 Regulation FD Disclosure.**

On April 26, 2011, Regeneron Pharmaceuticals, Inc. and Sanofi announced that the Phase 3 VELOUR trial evaluating the investigational agent ZALTRAP™ (aflibercept), also known as VEGF Trap, in combination with the FOLFIRI chemotherapy regimen [folinic acid (leucovorin), 5-fluorouracil, and irinotecan] versus a regimen of FOLFIRI plus placebo met its primary endpoint of improving overall survival (OS) in the second-line treatment of metastatic colorectal cancer (mCRC). On June 25, 2011, at the ESMO World Congress on Gastrointestinal Cancer in Barcelona, Spain, data were presented related to the results of the VELOUR trial. A copy of the slides that were presented is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

99.1 Presentation entitled Intravenous (IV) Aflibercept Versus Placebo in Combination With Irinotecan/5-FU (FOLFIRI) For Second-line Treatment of Metastatic Colorectal Cancer (mCRC): Results Of A Multinational Phase III Trial.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: June 27, 2011

REGENERON PHARMACEUTICALS, INC.

By: /s/ Murray A Goldberg
Name: Murray A. Goldberg
Title: Senior Vice President, Finance and Administration, Chief Financial Officer, Treasurer, and Assistant Secretary

Exhibit Index

| Number | Description |
| --- | --- |
| 99.1 | Presentation entitled Intravenous (IV) Aflibercept Versus Placebo in Combination With Irinotecan/5-FU (FOLFIRI) For Second-line Treatment of Metastatic Colorectal Cancer (mCRC): Results Of A Multinational Phase III Trial. |

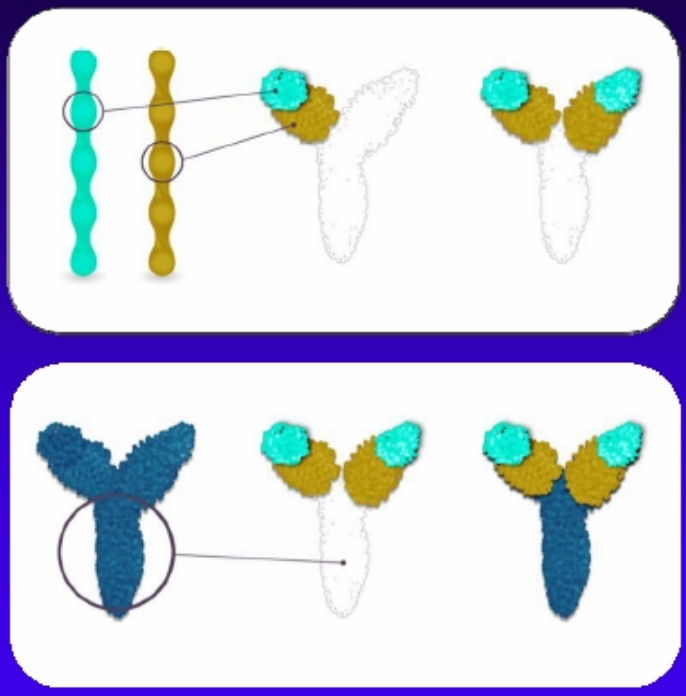
# VELOUR

## Intravenous (IV) Aflibercept Versus Placebo in Combination With Irinotecan/5-FU (FOLFIRI) For Second-line Treatment of Metastatic Colorectal Cancer (mCRC): Results Of A Multinational Phase III Trial (EFC10262-VELOUR).

Eric Van Cutsem*, J. Tabernero,
R. Lakomy, J. Prausova, P. Ruff, G. Van Hazel, V. Moiseyenko, D. Ferry,
J. Mckendrick, A. Tellier, R. Castan, C. Allegra, on the behalf of the
VELOUR investigators

*University Hospital Gasthuisberg / Leuven / Belgium

# Aflibercept



- Soluble fusion protein
- Consists of portion of extracellular domains of human VEGF receptors 1 and 2 fused to human IgG1 Fc portion
- Binds all VEGF-A isoforms, VEGF-B and PlGF
- High affinity: binds VEGF-A and PlGF more tightly than native receptors
- Half-life in humans ~17 days

# Background and Study Rationale

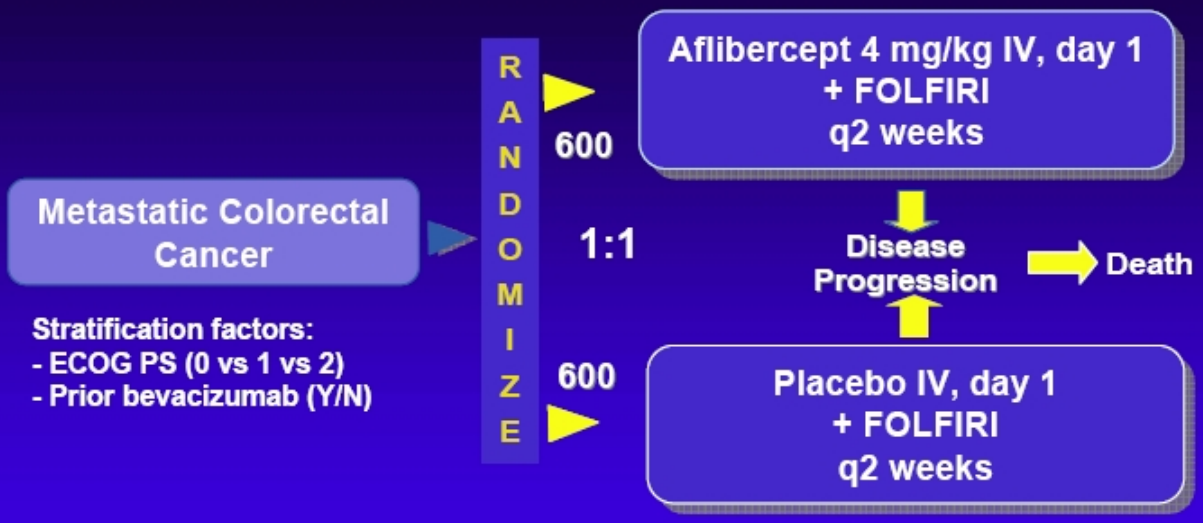
- In the preclinical setting, aflibercept exhibited improved activity when combined with irinotecan and with 5-FU
- Objective tumor responses were observed in patients with mCRC who received aflibercept in combination with irinotecan and 5-FU/FA in the phase I TCD 6118 study

# Background:
## Benefit of Angiogenesis Inhibitors in mCRC

| 1st Line | 2nd Line |
|---|---|
| IFL +/- bevacizumab<br>ORR, PFS, OS (1) | ? |
| FOLFOX/XELOX +/- bevacizumab<br>PFS (3) | FOLFOX +/- bevacizumab<br>ORR, PFS, OS (2) |


(1) Hurwitz H et al. N Engl J Med 2004 (350) 2335-2342
(2) Giantonio BJ et al. ECOG E3200. J Clin Oncol 2007(25) 1539-1544
(3) Saltz LB et al. J Clin Oncol 2008 (26) 2013-2019

# Study Design




**Stratification factors:**
- ECOG PS (0 vs 1 vs 2)
- Prior bevacizumab (Y/N)

DMC review every 6 months

# Primary Endpoint: Overall Survival

- Demonstrate a HR of 0.8 with 90% power and a 2-sided type I error of 0.05
- Analysis with log-rank comparison and Kaplan Meier method, stratified by
  - ECOG PS 0 *vs* 1 *vs* 2
  - Prior treatment with bevacizumab Yes *vs* No
- Final analysis of OS~863 death events using a 2-sided nominal significance level of 0.0466 (α spending function)
- Interim analysis: OS interim analysis at 65% of death events (n= 561)

# Secondary Endpoints

- Progression free survival and response rate:
  - RECIST 1.0 criteria, independent third party review
  - Imaging every 6 weeks
  - Analysis using a 2-sided nominal significance level of 0.0001
- Safety (NCI CTC v.3.0)
- PK and immunogenicity

# Patient Population

- Histologically proven metastatic colorectal cancer
- One prior treatment with an oxaliplatin based regimen
- No prior irinotecan
- Prior bevacizumab permitted
- Age ≥ 18 years old
- ECOG PS: 0, 1, 2
- Adequate organ functions
- Measurable or non-measurable disease
- Written informed consent

# Patient Disposition - Analysis Populations

| N (%) | Placebo/ FOLFIRI | Aflibercept/ FOLFIRI |
|---|---|---|
| ITT population | 614 (100) | 612 (100) |
| Randomized not treated | 5 (0.8) | 5 (0.8) |
| Evaluable population* | 530 (86.3) | 531 (86.8) |
| Safety population | 605 | 611 |

* Response rate analysis excluded patients with only non target lesion as well as those patients who did not consent to third-party review

# Main Demographic Characteristics

| ITT Population | | Placebo N = 614 | Aflibercept N = 612 |
|---|---|---|---|
| Age, yrs | | | |
| Median (Range) | | 61.0 (19:86) | 61.0 (21:82) |
| Age >65 | | 38.8 | 33.5 |
| Gender, % | | | |
| Male | | 57.5 | 59.6 |
| ECOG PS*, % | 0 | 57.0 | 57.0 |
| | 1 | 40.7 | 40.8 |
| | 2 | 2.3 | 2.1 |

*as reported per IVRS

# Prior Chemotherapy

| ITT Population<br>% | Placebo<br>N = 614 | Aflibercept<br>N = 612 |
|---|---|---|
| Chemotherapy | 100 | 100 |
| Adjuvant only (relapse <6 mos end adjuvant) | 10.4 | 9.8 |
| Adjuvant + metastatic | 17.6 | 16.7 |
| Metastatic only | 72.0 | 73.5 |
| **Last Chemotherapy Prior to Randomization** | | |
| Oxaliplatin based | 99.8 | 99.8 |
| Oxaliplatin single agent | 0.7 | 0.3 |
| Oxaliplatin + fluoropyrimidine only | 64.5 | 66.8 |
| Oxaliplatin + fluoropyrimidine + biologic | 34.9 | 32.7 |
| Prior Bevacizumab | 28.8 | 27.6 |

* Patients who became metastatic within 6 months of completion of adjuvant were eligible

# Main Disease Characteristics

| ITT Population<br>% | Placebo<br>N = 614 | Aflibercept<br>N = 612 |
|---|---|---|
| Primary site | | |
| Colon | 49.2 | 47.2 |
| Rectosigmoid | 22.1 | 20.1 |
| Rectum | 28.3 | 32.2 |
| Other | 0.3 | 0.5 |
| > 1 metastatic sites | 54.9 | 57.8 |
| Main metastatic organs involved | | |
| Liver (overall) | 70.2 | 75.0 |
| Liver only | 23.8 | 25.0 |
| Lung | 45.1 | 44.3 |
| Peritoneum | 14.3 | 11.1 |

# Other Baseline Characteristics

| ITT Population | Placebo | | Aflibercept | |
|---|---|---|---|---|
| % | N = 614 | | N = 612 | |
| | All grades | Grade 3-4 | All grades | Grade 3-4 |
| Anemia | 47.6 | 0 | 44.2 | 0 |
| Elevated alkaline phosphatase | 54.0 | 0.8 | 52.5 | 1.0 |
| Hypoalbuminemia | 15.6 | 0.2 | 15.0 | 0 |
| | > ULN | | > ULN | |
| Elevated LDH | 55.2 | | 53.6 | |

# Discontinuation of Study Treatment

| ITT Population<br>% | Placebo<br>N = 614 | Aflibercept<br>N = 612 |
|---|---|---|
| Discontinued study treatment | 97.4 | 96.9 |
| Disease progression | 71.2 | 49.8 |
| Adverse event | 12.1 | 26.6 |
| Patient request | 7.0 | 12.6 |
| Investigator decision | 3.4 | 3.3 |
| Metastatic surgery | 1.6 | 2.0 |
| Other causes* | 2.1 | 2.6 |
| Study treatment ongoing | 1.8 | 2.3 |

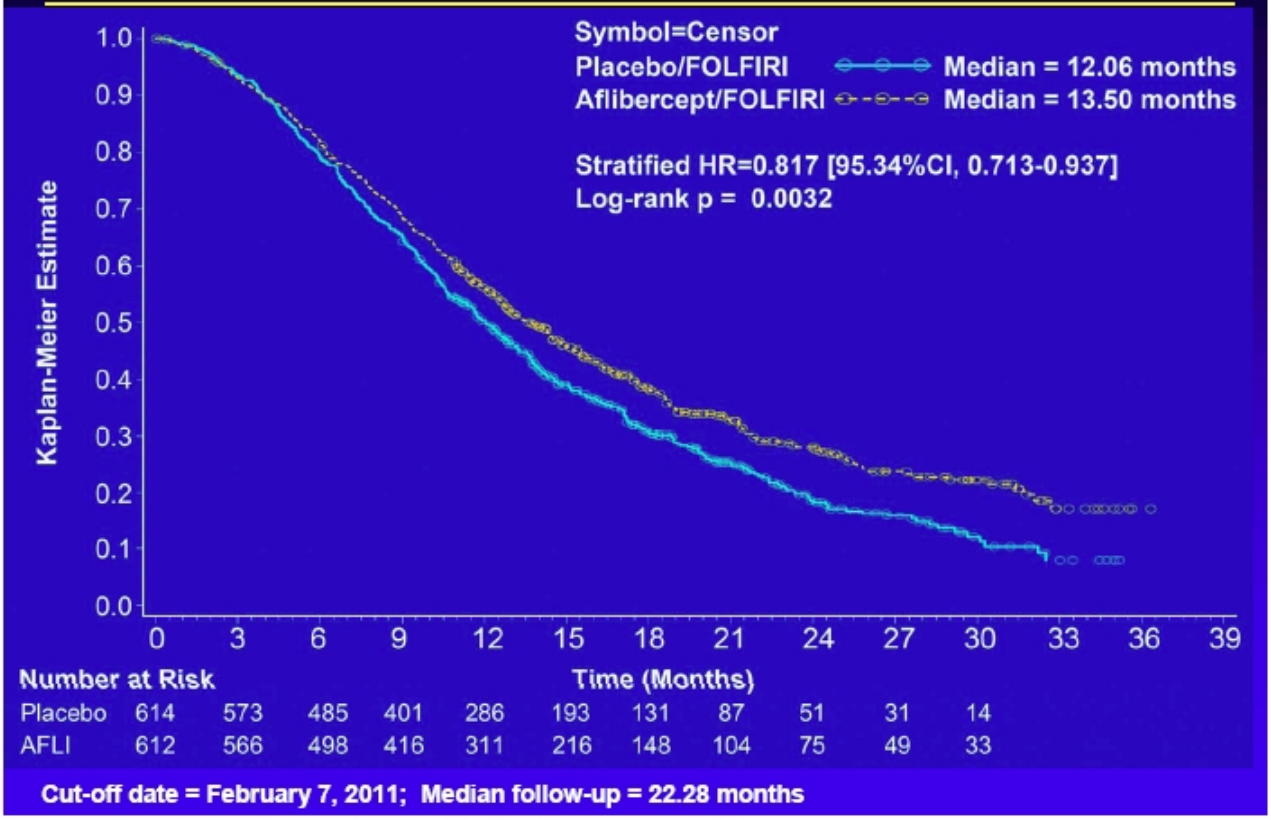
*Other causes include consent withdrawal, lost to FUp, poor compliance and other not classified reasons

# Treatment Exposure

| Safety Population | Placebo N = 605 | Aflibercept N = 611 |
|---|---|---|
| Total number of cycles | 6127 | 6362 |
| Median (range) | 8.0 (1 : 67) | 9.0 (1: 50) |
| Aflibercept or placebo infusions | | |
| Total number | 6035 | 5632 |
| Median (range) | 8 (1 : 67) | 7 (1 : 35) |
| Relative dose intensity (%) | 92 | 83 |
| Patients with at least 1 dose modification (%) * | 4.8 | 16.7 |
| Patients with at least 1 dose modification (%) * | | |
| Irinotecan | 22.6 | 37.2 |
| 5-FU | 21.7 | 39.1 |

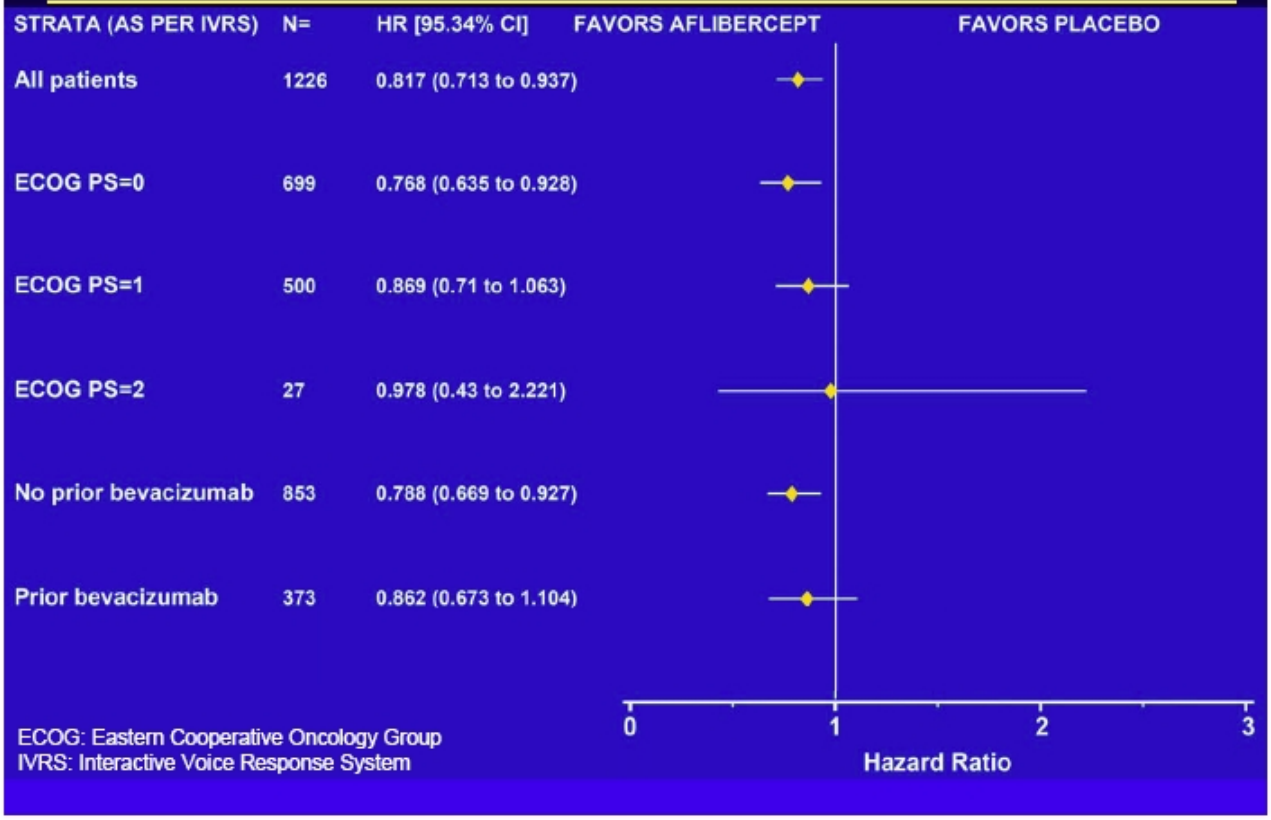
* dose reduction or dosing omission

# Overall Survival - ITT Population




Cut-off date = February 7, 2011; Median follow-up = 22.28 months

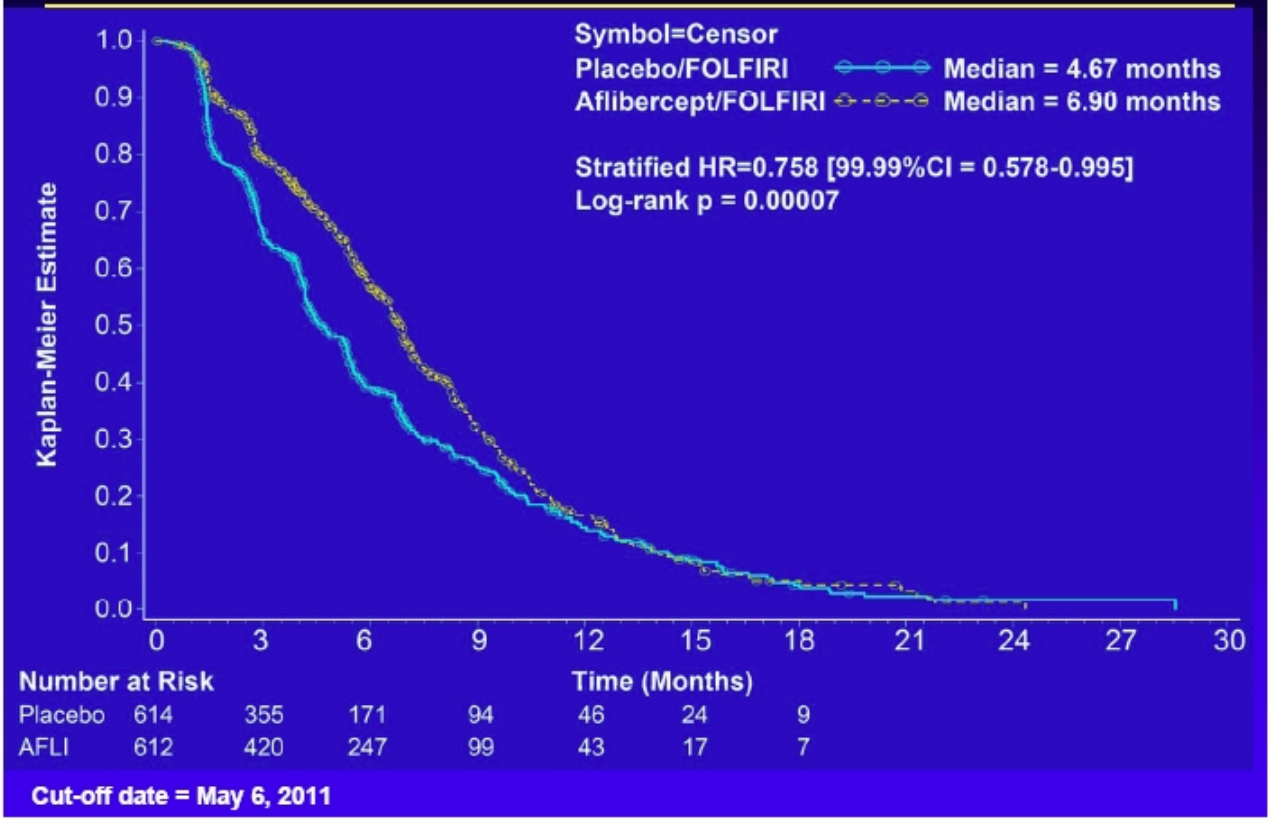
# Overall Survival
## by Stratification Factors – ITT Population




ECOG: Eastern Cooperative Oncology Group
IVRS: Interactive Voice Response System

# Progression Free Survival – ITT Population

## Independent Review Committee




**Number at Risk**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Placebo | 614 | 355 | 171 | 94 | 46 | 24 | 9 |
| AFLI | 612 | 420 | 247 | 99 | 43 | 17 | 7 |

**Cut-off date = May 6, 2011**

# Response Rate,
## Independent Review Committee

| Evaluable population*, % | Placebo N = 530 | Aflibercept N = 531 |
|---|---|---|
| **Best Overall Response** | | |
| Complete response | 0.4 | 0 |
| Partial response | 10.8 | 19.8 |
| Stable disease | 64.9 | 65.9 |
| Progressive disease | 21.5 | 10.4 |
| Not evaluable | 2.5 | 4.0 |
| **Overall Response Rate** | | |
| (CR or PR) | 11.1 | 19.8 |
| 95% CI | 8.5 to 13.8 | 16.4 to 23.2 |
| | p= 0.0001** | |

*Evaluable population: patients with measurable target lesions that have agreed for third party review

** Stratified, Cochran Mantel test

## Safety – Most frequent AEs, with ≥ 5% difference in incidence between treatment arms, excluding anti-VEGF class events

| Safety Population, % of patients | Placebo, N = 605 | | Aflibercept N = 611 | |
|---|---|---|---|---|
| PT, SOC, HLT* | All Grades | Grade 3-4 | All Grades | Grade 3-4 |
| Diarrhea | 56.5 | 7.8 | 69.2 | 19.3 |
| Neutropenia** | 56.3 | 29.5 | 67.8 | 36.7 |
| Complicated neutropenia | | 2.8 | | 5.7 |
| Asthenic conditions (HLT) | 50.2 | 10.6 | 60.4 | 16.9 |
| Stomatitis & ulceration (HLT) | 34.9 | 5.0 | 54.8 | 13.7 |
| Thrombocytopenia** | 33.8 | 1.7 | 47.4 | 3.3 |
| Infections (SOC) | 32.7 | 6.9 | 46.2 | 12.3 |
| Decrease appetite | 23.8 | 1.8 | 31.9 | 3.4 |
| Weight decreased | 14.4 | 0.8 | 31.9 | 2.6 |
| Palmar plantar erythrodysaesthesia | 4.3 | 0.5 | 11.0 | 2.8 |
| Skin hyperpigmentation | 2.8 | 0 | 8.2 | 0 |
| Dehydration | 3.0 | 1.3 | 9.0 | 4.3 |

* PT:Preferred Term, SOC: system organ class, HLT: High Level Term, grouping: grouping of selected PTs

** From lab

# Safety – Anti-VEGF Associated Events

| Safety population, % of patients | Placebo N = 605 | | Aflibercept N = 611 | |
|---|---|---|---|---|
| Grouped Term, PT | All Grade | Grade 3/4 | All Grade | Grade 3/4 |
| Proteinuria* | 40.7 | 1.2 | 62.2 | 7.9 |
| Hypertension | 10.7 | 1.5 | 41.4 | 19.3 |
| Haemorrhage | 19.0 | 1.7 | 37.8 | 2.9 |
| Epistaxis | 7.4 | 0 | 27.7 | 0.2 |
| GI origin | 5.1 | 1.0 | 10.0 | 2.0 |
| Dysphonia (PT) | 3.3 | 0 | 25.4 | 0.5 |
| Headache (PT) | 8.8 | 0.3 | 22.3 | 1.6 |
| Venous thromboembolic event | 7.3 | 6.3 | 9.3 | 7.9 |
| Pulmonary embolism | 3.5 | 3.5 | 4.7 | 4.7 |
| Arterial thromboembolic event | 1.5 | 0.5 | 2.6 | 1.8 |
| Fistula (GI origin) | 0.3 | 0.2 | 1.1 | 0.3 |
| Wound healing | 0.8 | 0 | 0.5 | 0.3 |
| GI perforation | 0.5 | 0.3 | 0.5 | 0.5 |

*Systematic pre-dosing urine spot urinalysis

# Deaths During Study Treatment

| % – Safety Population | Placebo N = 605 | Aflibercept N = 611 |
|---|---|---|
| Number of deaths within 30d from last dose | 3.1 | 4.9 |
| Disease progression | 2.1 | 2.3 |
| Adverse events: | 1.0 | 2.6 |
| Infections (sepsis and neutropenic sepsis) | 0.5 | 0.7 |
| Death/sudden death | 0.3 | 0.3 |
| Pulmonary embolism | 0 | 0.2 |
| GI hemorrhage (duodenal ulcer) | 0 | 0.2 |
| GI disorders (inflammation/obstruction) | 0 | 0.3 |
| Respiratory disorders | 0.2 | 0.3 |
| Other** | 0 | 0.7 |

**Other: dehydration (2pts), metabolic encephalopathy (1pt), hypovolemic shock (1pt)

# Conclusions

- **Adding aflibercept to FOLFIRI in mCRC previously treated with an oxaliplatin based regimen provided benefits that are both statistically and clinically significant:**
  - Improvement in overall survival (HR=0.817 [95.34%CI, 0.713-0.937], p = 0.0032)
  - Improvement in PFS (HR=0.758 [99.99%CI, 0.578-0.995], p=0.00007)
  - Improvement in overall RR (11.1% vs 19.8%, p=0.0001)
- **The safety profile of aflibercept was acceptable and consistent with known anti-VEGF adverse effects. Adding aflibercept increases the specific CT related toxicity in the combination arm: neutropenic complications and diarrhea/stomatitis.**

# Conclusions:
## benefit of angiogenesis inhibitors in mCRC

| 1st Line | 2nd Line |
|---|---|
| IFL +/- bevacizumab<br>ORR, PFS, OS (1) | FOLFIRI +/- aflibercept<br>OS, PFS, RR (4)<br>VELOUR |
| FOLFOX/XELOX +/- bevacizumab<br>PFS only (3) | FOLFOX +/- bevacizumab<br>ORR, PFS, OS (2) |


(1) Hurwitz H et al. N Engl J Med 2004 (350) 2335-2342
(2) Giantonio BJ et al. ECOG E3200. J Clin Oncol 2007(25) 1539-1544
(3) Saltz LB et al. J Clin Oncol 2008 (26) 2013-2019
(4) Van Cutsem E et al, ESMO/WCGIC, Ann Oncol, june 2011

# Acknowledgements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