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9. Litigation;
10. Loss of key executives or other employees; and...
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Agenda Analyst briefing - part 1

Introduction

William M. Burns, CEO Roche Pharmaceuticals

AVADO study results

Dr. David Miles, Consultant Medical Oncologist, Mount Vernon Cancer Centre, Middlesex, UK

Avastin development program in breast cancer and other key data presented at ASCO so far

Dr. Stefan Frings, Life Cycle Leader Avastin, Roche

Conclusions

Dr. Karl Mahler, Head of Investor Relations, Roche
Roche products: impressive presence at ASCO
Almost 300 posters and oral presentations

Presence by brand (n=286)
Roche: what it takes to establish standard of care
Aiming for first and best in class

• Meaningful medical benefit, preferably on overall survival
• Broad combinability, especially with established backbones
• Balanced safety-efficacy profile, improving quality of life
• Confirmation with a breadth of clinical evidence, building trust through theory and practice
Roche oncology products

Existing and future components of standards of care

Proven efficacy
In development
AVADO study results

Avastin development program in breast cancer

Other key data presented so far at ASCO 2008

Q&A
AVADO

A randomized, double-blind study of bevacizumab in combination with docetaxel as first-line treatment of patients with HER2-negative locally recurrent or metastatic breast cancer: efficacy and safety

Dr. David Miles
Mount Vernon Cancer Centre, Middlesex, United Kingdom

On behalf of the AVADO investigators
Introduction

• Bevacizumab is a monoclonal antibody to vascular endothelial growth factor (VEGF) that inhibits tumor angiogenesis

• In a phase III trial (E2100) the addition of bevacizumab to first-line paclitaxel significantly increased progression-free survival (PFS) in patients with metastatic breast cancer (mBC)¹

• Docetaxel is a widely used and active taxane in mBC

• AVADO was designed to investigate the addition of bevacizumab to docetaxel in first-line mBC

10

AVADO: double-blind, placebo-controlled trial

1st-line locally recurrent or mBC (n=705)

Stratification factors:
- region
- prior taxane/time to relapse since adjuvant chemo
- measurable disease
- hormone receptor status

Docetaxel* 100mg/m²
+ placebo q3w

Docetaxel* + bevacizumab
7.5mg/kg q3w

Docetaxel* + bevacizumab
15mg/kg q3w

Treat with placebo/bevacizumab to disease progression

All patients given option to receive bevacizumab with 2nd-line chemotherapy

*Docetaxel was administered for a maximum of 9 cycles, but earlier discontinuation was permitted

- Primary endpoint: progression-free survival
- Secondary endpoints: overall response rate, duration of response, time to treatment failure, overall survival, safety, quality of life
AVADO: statistical design

• Sample size assumptions were based upon
  – 80% power to detect PFS hazard ratio of 0.7
    • median 6.0 vs 8.6 months
  – 705 patients required

• Planned analyses were
  – to compare PFS between each bevacizumab-containing arm versus control using a closed-test procedure (unstratified test)
  – to investigate PFS with censoring for non-protocol antineoplastic therapy given prior to progression (stratified test) = primary analysis for US FDA
AVADO: results

• 736 patients recruited from 104 sites in 26 countries between March ‘06 & April ‘07
• Data cut-off 31 October ‘07
• Median follow-up = 10.15 months (range 0–17.5)
• Analysis
  – intent-to-treat population (all randomized patients), n=736
  – safety population (patients receiving at least one dose of study therapy), n=730
AVADO: patient and disease characteristics well balanced ITT

<table>
<thead>
<tr>
<th></th>
<th>Placebo + docetaxel (n=241)</th>
<th><strong>Bev 7.5</strong>† + docetaxel (n=248)</th>
<th><strong>Bev 15</strong>† + docetaxel (n=247)</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median age, years (range)</td>
<td>55.0 (29–83)</td>
<td>54.0 (26–83)</td>
<td>55.0 (27–76)</td>
</tr>
<tr>
<td>ECOG PS 0/1</td>
<td>62/38</td>
<td>61/39</td>
<td>61/39</td>
</tr>
<tr>
<td>ER/PgR positive</td>
<td>78</td>
<td>78</td>
<td>76</td>
</tr>
<tr>
<td>DFI* ≥12 months</td>
<td>82</td>
<td>75</td>
<td>81</td>
</tr>
<tr>
<td>Adjuvant chemotherapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>taxane</td>
<td>65</td>
<td>65</td>
<td>68</td>
</tr>
<tr>
<td>anthracycline</td>
<td>15</td>
<td>15</td>
<td>17</td>
</tr>
<tr>
<td>≥3 metastatic sites</td>
<td>41</td>
<td>49</td>
<td>49</td>
</tr>
<tr>
<td>Sites</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bone</td>
<td>59</td>
<td>60</td>
<td>55</td>
</tr>
<tr>
<td>liver</td>
<td>50</td>
<td>40</td>
<td>46</td>
</tr>
<tr>
<td>lung</td>
<td>38</td>
<td>42</td>
<td>48</td>
</tr>
<tr>
<td>Measurable disease</td>
<td>86</td>
<td>81</td>
<td>83</td>
</tr>
</tbody>
</table>

†mg/kg q3w; *disease-free interval
AVADO: superior progression-free survival for both bevacizumab doses

Placebo + docetaxel (n=241)  
Bev 7.5† + docetaxel (n=248)  
Placebo + docetaxel (n=241)  
Bev 15† + docetaxel (n=247)  

HR + 95% CI (unstratified)  
0.79 (0.63–0.98)  
p=0.0318  
0.72 (0.57–0.90)  
p=0.0099  

HR + 95% CI (stratified*)  
0.69 (0.54–0.89)  
p=0.0035  
0.61 (0.48–0.78)  
p<0.0001  

Median 8.0  
8.7  
8.8  

†mg/kg q3w  
*Data censored for non-protocol therapy before PD
### AVADO: PFS subgroup analysis

*Consistent treatment effect in subgroups*

<table>
<thead>
<tr>
<th>Baseline risk factor</th>
<th>Bev 7.5mg/kg q3w</th>
<th>Bev 15mg/kg q3w</th>
<th>Favors bevacizumab</th>
<th>Favors placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All patients</strong></td>
<td>489 0.79</td>
<td>488 0.72</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ER/PgR combined</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>negative</td>
<td>105 0.76</td>
<td>111 0.60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>positive</td>
<td>382 0.78</td>
<td>376 0.73</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Prior adjuvant chemotherapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>318 0.67</td>
<td>323 0.65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>171 1.04</td>
<td>165 0.85</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Prior taxane therapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>73 0.59</td>
<td>77 0.42</td>
<td></td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>416 0.84</td>
<td>411 0.77</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Measurable disease at baseline</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>408 0.76</td>
<td>413 0.70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>81 1.14</td>
<td>75 0.89</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

†mg/kg q3w
AVADO: high overall response rate with 63%

<table>
<thead>
<tr>
<th></th>
<th>Placebo + docetaxel (n=207)</th>
<th>Bev 7.5(^\dagger) + docetaxel (n=201)</th>
<th>Bev 15(^\dagger) + docetaxel (n=206)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall response rate</td>
<td>44</td>
<td>55</td>
<td>63</td>
</tr>
<tr>
<td>p value (vs control)</td>
<td>–</td>
<td>0.0295</td>
<td>0.0001</td>
</tr>
<tr>
<td>Best response</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>1</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>PR</td>
<td>44</td>
<td>52</td>
<td>62</td>
</tr>
<tr>
<td>SD</td>
<td>39</td>
<td>35</td>
<td>25</td>
</tr>
<tr>
<td>PD</td>
<td>12</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

(patients with measurable disease)

\(^\dagger\)mg/kg q3w
### AVADO: overall survival currently immature

<table>
<thead>
<tr>
<th></th>
<th>Placebo + docetaxel (n=241)</th>
<th><strong>Bev 7.5</strong>&lt;sup&gt;†&lt;/sup&gt; + docetaxel (n=248)</th>
<th><strong>Bev 15</strong>&lt;sup&gt;†&lt;/sup&gt; + docetaxel (n=247)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths, n (%)</td>
<td>50 (21)</td>
<td>49 (20)</td>
<td>37 (15)</td>
</tr>
<tr>
<td>Median overall survival, months</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>hazard ratio</td>
<td>–</td>
<td>0.92</td>
<td>0.68</td>
</tr>
<tr>
<td>[95% CI]</td>
<td></td>
<td>[0.62–1.37]</td>
<td>[0.45–1.04]</td>
</tr>
<tr>
<td>1-year survival, %</td>
<td>73</td>
<td>78</td>
<td>83</td>
</tr>
<tr>
<td>patients still at risk, n</td>
<td>63</td>
<td>73</td>
<td>79</td>
</tr>
</tbody>
</table>

Cut-off for final survival analysis 24 months after last patient recruited (April 2009)

*Unstratified analysis; †mg/kg q3w; NR = not reached
## AVADO: safety summary

<table>
<thead>
<tr>
<th></th>
<th>Placebo + docetaxel</th>
<th>Bev 7.5† + docetaxel</th>
<th>Bev 15† + docetaxel</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=233)</td>
<td>(n=250)</td>
<td>(n=247)</td>
</tr>
<tr>
<td>Any AE</td>
<td>99.6</td>
<td>100.0</td>
<td>99.6</td>
</tr>
<tr>
<td>Any grade ≥3 AE</td>
<td>67.0</td>
<td>74.8</td>
<td>74.1</td>
</tr>
<tr>
<td>AEs leading to death*</td>
<td>2.6</td>
<td>1.6</td>
<td>1.6</td>
</tr>
<tr>
<td>AEs leading to discontinuation† of:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>docetaxel</td>
<td>24.0</td>
<td>20.8</td>
<td>24.3</td>
</tr>
<tr>
<td>bevacizumab or placebo</td>
<td>11.2</td>
<td>8.0</td>
<td>11.7</td>
</tr>
</tbody>
</table>

†mg/kg q3w; *during study phase; ‡not mutually exclusive
**AVADO: selected key grade ≥3 adverse events**

<table>
<thead>
<tr>
<th>Adverse event, %</th>
<th>Placebo + docetaxel (n=233)</th>
<th>Bev 7.5† + docetaxel (n=250)</th>
<th>Bev 15† + docetaxel (n=247)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>3.4</td>
<td>6.8</td>
<td>6.9</td>
</tr>
<tr>
<td>Fatigue</td>
<td>5.2</td>
<td>8.4</td>
<td>6.5</td>
</tr>
<tr>
<td>Palmar-plantar erythema</td>
<td>0.9</td>
<td>5.2</td>
<td>6.1</td>
</tr>
<tr>
<td>Mucosal inflammation</td>
<td>0.4</td>
<td>4.0</td>
<td>4.9</td>
</tr>
<tr>
<td>Peripheral sensory neuropathy</td>
<td>1.7</td>
<td>3.2</td>
<td>4.5</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>0.4</td>
<td>2.8</td>
<td>3.2</td>
</tr>
<tr>
<td>Myalgia</td>
<td>0.9</td>
<td>1.2</td>
<td>3.6</td>
</tr>
<tr>
<td>Skin exfoliation</td>
<td>0</td>
<td>2.4</td>
<td>1.2</td>
</tr>
<tr>
<td>Anemia</td>
<td>2.6</td>
<td>0.4</td>
<td>1.2</td>
</tr>
<tr>
<td>Infection</td>
<td>3.0</td>
<td>0.8</td>
<td>0.4</td>
</tr>
</tbody>
</table>

*With a ≥2% difference in incidence between study arms; †mg/kg q3w
AVADO: grade ≥3 adverse events of special interest*

<table>
<thead>
<tr>
<th>Adverse event, %</th>
<th>Placebo + docetaxel (n=233)</th>
<th>Bev 7.5† + docetaxel (n=250)</th>
<th>Bev 15† + docetaxel (n=247)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>31.3</td>
<td>35.2</td>
<td>36.4</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>17.2</td>
<td>19.2</td>
<td>19.8</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>12.0</td>
<td>15.2</td>
<td>16.6</td>
</tr>
<tr>
<td>VTE</td>
<td>3.4</td>
<td>1.2</td>
<td>1.2</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.3</td>
<td>0.4</td>
<td>3.2</td>
</tr>
<tr>
<td>Bleeding</td>
<td>0.9</td>
<td>1.2</td>
<td>1.2</td>
</tr>
<tr>
<td>Wound-healing complication</td>
<td>0.9</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>GI perforation</td>
<td>0.9</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>CHF</td>
<td>0</td>
<td>0.8</td>
<td>0</td>
</tr>
<tr>
<td>ATE</td>
<td>0.4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>0</td>
<td>0</td>
<td>0.4</td>
</tr>
<tr>
<td>RPLS</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Protocol-defined; †mg/kg q3w
AVADO: conclusions

• Double-blind, placebo-controlled trial AVADO confirms the clinical benefit of combining first-line bevacizumab with taxane chemotherapy for patients with HER2-negative mBC

• Both the 7.5 and 15mg/kg doses significantly increased PFS and response rate compared with placebo
  - Numerically higher activity was noted with the bevacizumab 15mg/kg dose compared with the 7.5mg/kg dose

• Overall survival data are not yet mature

• No new safety signals were detected and bevacizumab had limited impact on the toxicity profile of docetaxel 100mg/m2
AVADO study results

Avastin development program in breast cancer

Other key data presented so far at ASCO 2008

Q&A
Avastin in Breast Cancer

Avastin: approved based on E2100 for the first-line treatment of mBC

- March 2007 in the EU
  - Avastin in combination with paclitaxel is indicated for first-line treatment of patients with metastatic breast cancer

- February 2008 in the USA (accelerated approval)
  - Avastin in combination with paclitaxel is indicated for the treatment of patients who have not received chemotherapy for metastatic HER2-negative breast cancer
E2100: unprecedented progression-free survival confirmed by Independent Review Facility (IRF)

Paclitaxel (n=354)
Avastin + paclitaxel (n=368)

PFS by investigator
HR=0.42

PFS by IRF*
HR=0.48

Avastin Summary of Product Characteristics (SmPC); Klencke, ASCO 2008 poster (3-06-08)
E2100: doubling objective response rate

Investigator assessment (n=525)

- CR + PR: 23% (p<0.0001)

IRF assessment (n=472)

- CR + PR: 22% (p<0.0001)

- CR = complete response
- PR = partial response

Avastin Summary of Product Characteristics (SmPC);
Klencke, ASCO 2008 poster (3-06-08)
Avastin: effective anti-angiogenic therapy for metastatic breast cancer

**E2100**
- Avastin: unprecedented efficacy by doubling PFS in 1st-line mBC in combo with paclitaxel
- Avastin in combination with paclitaxel doubles response rates versus paclitaxel alone

**AVADO**
- Avastin significantly increases PFS in mBC patients in combination to docetaxel
  - Up to 64% increase depending on dose and analysis
  - Unprecedented overall response rate of 63%
  - Numerical difference for efficacy in favor of the 15mg/kg dose arm

**Conclusions**
- Avastin can be safely combined with taxanes and provides a meaningful clinical benefit
- AVADO along with E2100 supports 5mg/kg/week (twice the mCRC dose) as standard dose
### Avastin in metastatic breast cancer

**Additional studies to set standard of care**

<table>
<thead>
<tr>
<th></th>
<th>Phase III RIBBON-1</th>
<th>Phase III RIBBON-2</th>
<th>Phase III AVEREL</th>
<th>Phase III E1105</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient population</strong></td>
<td>HER2-negative</td>
<td>HER2-negative</td>
<td>HER2-positive</td>
<td>HER2-positive</td>
</tr>
<tr>
<td><strong>Number of patients</strong></td>
<td>1200</td>
<td>700</td>
<td>410</td>
<td>490</td>
</tr>
<tr>
<td><strong>Design</strong></td>
<td>Chemo (anthracycline-based, or taxanes +/- Avastin or Xeloda +/- Avastin)</td>
<td>Chemo (taxane, vinorelbine, capecitabine or gemcitabine) +/- Avastin</td>
<td>Herceptin+ docetaxel +/-Avastin</td>
<td>Herceptin+ paclitaxel (+/-carboplatin) +/-Avastin</td>
</tr>
<tr>
<td><strong>Primary endpoint</strong></td>
<td>PFS</td>
<td>PFS</td>
<td>PFS</td>
<td>PFS</td>
</tr>
<tr>
<td><strong>Status</strong></td>
<td>Completed enrollment Q3 2007, Expect data late 08</td>
<td>Expect data 2009</td>
<td>Initiated Q3 2006</td>
<td>Initiated Q1 2008</td>
</tr>
</tbody>
</table>
## Avastin as adjuvant therapy for breast cancer

*Large opportunity – major phase III trials ongoing*

### Phase II

**E2104**

- **Patient population**: HER2-negative
- **Number of patients**: 226
- **Design**: Anthracylines + Avastin followed by paclitaxel + Avastin
  - Anthracylines followed by paclitaxel + Avastin (2 cohorts)
- **Primary endpoint**: Safety
- **Status**: Updated safety results ASCO 2008 Monday, abstr. 520

### Phase III

**E 5103**

- **Patient population**: HER2-negative
- **Number of patients**: 4950
- **Design**: Arm A: AC followed by paclitaxel
  - Arm B: AC + Av, followed by paclit.+ Avastin
  - Arm C: AC + Av, followed by paclit. + Avastin, followed by Avastin up to 1 y
- **Primary endpoint**: DFS
- **Status**: FPI Q4 2007

**BEATRICE**

- **Patient population**: HER2-, ER-, PR-negative
- **Number of patients**: 2530
- **Design**: Anthracycline- and taxane-based therapies +/- Avastin up to 1 year
- **Primary endpoint**: DFS
- **Status**: FPI Q4 2007

**BETH**

- **Patient population**: HER2-positive
- **Number of patients**: ~3600
- **Design**: Herceptin + chemo +/-Avastin up to 1 year
- **Primary endpoint**: DFS
- **Status**: FPI Q2 08
AVADO study results

Avastin development program in breast cancer

Other key data presented so far at ASCO 2008

Q&A
Roche oncology products
Existing and future components of standards of care

Proven efficacy
In development
Avastin as adjuvant therapy for colon cancer

**NSABP C-08**

- **Stage II or III Colon Cancer**
- **Stratification: # of +LN**
- **Randomization (1:1)**
  - **mFOLFOX6 (6 mo)**
  - **mFOLFOX6 (6 mo) + Avastin (5 mg/kg q2 wk X 12 mo)**

N= 2710
(enrolled 9/04- 10/06)

C. J. Allegra, ASCO 2008, abstract 4006 (Saturday)
C-08 Safety Summary

Overall rate of Grade 4/5 toxicities*

- FOLFOX 15.2% (n=1356)
- Avastin + FOLFOX 15.3% (n=1354)

Treatment associated mortality excluding death after relapse or second primary progression

- Within 6 months of randomization
  - FOLFOX 0.96%
  - Avastin + FOLFOX 0.90%  p=1.0

- Within 18 months of randomization
  - FOLFOX 1.33%
  - Avastin + FOLFOX 1.35%  p=1.0

*C. J. Allegra, ASCO 2008, abstract 4006 (Saturday)
**C-08 Safety Conclusions**

Avastin treatment up to one year in combination with FOLFOX is well-tolerated in the adjuvant setting in patients with stage II or III colon cancer

- “No increase in ATE, hemorrhage, GI perforations, or death from any cause as a result of the addition of bevacizumab to mFOLFOX6”*
- Grade 5 event rate is in-line with previous adjuvant colon cancer phase III results
- Long-term follow-up for late effects ongoing

*C. J. Allegra, ASCO 2008, abstract 4006 (Saturday)
Roche oncology products

Existing and future components of standards of care

- Adjuvant: Xeloda, Avastin
- 1st line: Avastin, Xeloda
- 2nd line: Xeloda, Avastin

- Adjuvant: Herceptin, Avastin, Xeloda
- 1st line: Herceptin, Avastin, Xeloda
- 2nd line: Xeloda, Avastin, Herceptin, pertuzumab, TDM-1

- Adjuvant: Tarceva, Avastin
- 1st line: Tarceva, Avastin
- 2nd line: 3rd line: Tarceva

Proven efficacy
In development
**CAIRO-2 (1st line mCRC): Confirms efficacy of Avastin**  
*Cetuximab: increased toxicity and less efficacy*

<table>
<thead>
<tr>
<th></th>
<th>XELOX+Avastin median</th>
<th>XELOX+Avastin +cetuximab median</th>
<th>Hazard ratio/ p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PFS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(primary endpoint)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ITT</td>
<td>10.7</td>
<td>9.8</td>
<td>HR: 1.22 p=0.019</td>
</tr>
<tr>
<td>K-Ras Wild-type</td>
<td>10.7</td>
<td>10.5</td>
<td></td>
</tr>
<tr>
<td>K-Ras Mutant</td>
<td>12.5</td>
<td>8.6</td>
<td></td>
</tr>
<tr>
<td><strong>OS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>K-Ras Wild-type</td>
<td>23.0</td>
<td>22.2</td>
<td></td>
</tr>
<tr>
<td>K-Ras Mutant</td>
<td>24.9</td>
<td>19.1</td>
<td></td>
</tr>
</tbody>
</table>

Grade 3/4 toxicity significantly increased in cetuximab arm (p=0.0012)

C.J. Punt et al., ASCO 2008, abstract LBA4011 (Saturday)
Our current understanding of K-Ras in mCRC

- Roche is committed to personalized healthcare

- Our current understanding of K-Ras in mCRC:
  - If K-Ras status is unknown, cetuximab’s use is potentially harmful
    - OPUS, CAIRO-2
  - In K-Ras wild-type Avastin has substantially better efficacy and is better tolerated than cetuximab
    - CRYSTAL vs. PACCE and AVF2107g
  - Avastin works independently of K-Ras
  - Avastin’s position as standard of care in mCRC is unchallenged
AZD2171 vs. Avastin head-to-head

VEGFR-TKIs - difficult to match Avastin’s safety & efficacy

• Phase II, FOLFOX + Avastin vs. FOLFOX + cediranib in mCRC
  – Response rates
    • Cediranib 20mg +FOLFOX 18% (n=71)
    • Cediranib 30mg +FOLFOX 19% (n=73)
    • Avastin +FOLFOX 27% (n=66)
  – PFS hazard ratios
    • Cediranib 20mg vs. Avastin 1.26 (p=0.29)
    • Cediranib 30mg vs. Avastin 1.17 (p=0.79)

Grade 3/4 events were in general more frequent with AZD2171 vs. Avastin

“Overall there were more adverse events leading to discontinuation of study medication/placebo in the two cediranib groups than the bevacizumab group”

D. Cunningham et al., ASCO 2008, abstract 4028 (Sunday)
Roche oncology products
Existing and future components of standards of care

Proven activity
Development planned

Glioblastoma Multiforme

1st line
Avastin

refractory
Avastin
Case Study: Avastin randomised Ph II BRAIN Trial
Refractory Glioblastoma Multiforme (GBM)

- Incident Primary Brain Tumors population in line with mRCC
  - 20,000 incident patients in top 5 EU countries (mRCC: 17,000)
- High unmet medical need

T. F. Cloughesy et al., ASCO 2008, abstract 2010b (Monday)
**Avastin in relapsed Glioblastoma multiforme**

*Very encouraging efficacy in a difficult-to-treat cancer*

<table>
<thead>
<tr>
<th></th>
<th>Avastin</th>
<th>Avastin + irinotecan</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months PFS</td>
<td>43%</td>
<td>50%</td>
</tr>
<tr>
<td>Response rate</td>
<td>28.2%</td>
<td>37.8%</td>
</tr>
<tr>
<td>Median OS</td>
<td>9.2</td>
<td>8.7</td>
</tr>
</tbody>
</table>

- Phase II data demonstrated encouraging six-month PFS and ORR in patients with relapsed GBM, exceeding historical estimates of 15%
- GBM data for Avastin on course to be filed by end 2008

T. F. Cloughesly et al., ASCO 2008, abstract 2010b (Monday)
Roche oncology products
Existing and future components of standards of care

Proven efficacy
In development
Herceptin is the foundation of care across all stages of HER2-positive breast cancer

<table>
<thead>
<tr>
<th>EGF104900</th>
<th>GBG-26</th>
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</thead>
<tbody>
<tr>
<td>n=296</td>
<td>n=156</td>
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</tbody>
</table>

Herceptin pre-treatment

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Herceptin + lapatinib</th>
<th>lapatinib</th>
<th>Herceptin + Xeloda</th>
<th>Xeloda</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR (%)</td>
<td>10</td>
<td>7</td>
<td>48</td>
<td>27</td>
</tr>
<tr>
<td>TTP/PFS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR</td>
<td>0.73 ( (p=0.008) )</td>
<td></td>
<td>0.69 ( (p=0.034) )</td>
<td></td>
</tr>
<tr>
<td>Median (m)</td>
<td>2.8</td>
<td>1.9</td>
<td>8.2</td>
<td>5.6</td>
</tr>
<tr>
<td>OS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR</td>
<td>0.75 ( (p=0.106) )</td>
<td></td>
<td>0.76 ( (p=0.26) )</td>
<td></td>
</tr>
<tr>
<td>Median (m)</td>
<td>11.9</td>
<td>9.0</td>
<td>25.5</td>
<td>20.4</td>
</tr>
</tbody>
</table>

“Continuation of trastuzumab is the best option for patients who develop progressive disease on or after trastuzumab-based therapy” F. J. Esteva

J. O’Shaughnessy et al., ASCO 2008, abstract 1015 (Sunday); Von Minckwitz et al., ASCO 2008, abstract 1025 (Tuesday)
Roche oncology products

Existing and future components of standards of care

Proven efficacy
In development
Avastin’s position as standard of care in first-line mNSCLC remains unchallenged

• Lack of PFS benefit questions efficacy of cetuximab with all platinum backbones
  – FLEX: median PFS 4.8 months in both arms (HR 0.94)
  – BMS – 099: median PFS 4.2 vs. 4.4 months (failed primary endpoint)

• Marginal OS data with borderline p-value in FLEX

• Incidence of febrile neutropenia (22%) unacceptable
Avastin’s position as standard of care in first-line mNSCLC remains unchallenged

- Avastin remains the best option for the vast majority of patients with NSCLC based on:
  - Robustness and consistency of data across all endpoints
  - ARIES and SAiL data presented further establish safety/tolerability and broad applicability for non-squamous mNSCLC
    - Including patients with PS2, treated CNS metastases and receiving full anticoagulation
  - The longest median overall survival in first-line non-squamous mNSCLC
Conclusions for Roche in oncology

Leading position reinforced

Avastin

- Position in major tumor types (mCRC, mBC, and NSCLC) solidified based on data displayed at ASCO 2008
- Glioblastoma multiforme - major medical advance, filing 2008
- Strong Avastin data raising the bar for competitors

Herceptin

- Foundation of care across all stages of HER2-positive breast cancer
- Clear rationale to continue Herceptin in combination with a different cytotoxic or biologic agent after initial progression
AVADO study results

Avastin development program in breast cancer

Other key data presented so far at ASCO 2008

Q&A
We Innovate Healthcare