Roche setting the standards of cancer care  
Oncology Event for Investors, June 19

Kapil Dhingra, VP Medical Science

Developing a drug to the standard of care
Superior clinical benefit, resources and time (!)

Changing the standard of care requires
• superior clinical benefit
• cutting edge research
• excellence in clinical development leading to realization of the full potential of the drug for patient benefit
• meeting the needs of patients, providers, payors, and regulators
A multitude of Roche products becoming crucial components of the standard of care

Proven efficacy
In development

Colorectal Cancer

Non-small Cell Lung Cancer
Breast Cancer
Other solid tumor types
Non-Hodgkin’s Lymphoma
Conclusions
**Colorectal Cancer**

*Characteristics and treatment practice*

- Second most common cause of cancer-related death
- Early diagnosis feasible
- Relapse pattern often predictable
- Early diagnosis of relapse possible
- Rapidly changing treatment landscape
  - Number of novel active agents identified
    - (e.g. Xeloda, Avastin, Erbitux, Panitumomab)
  - Increasing use of adjuvant treatment

**Potential for cure in selected patients with metastatic disease in the future**

**Evolution of standards of care in colorectal cancer**

*Progressive improvement in survival over the past decade*

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Median overall survival</th>
<th>Disease-free survival at 3 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-FU/LV or Xeloda mono</td>
<td>12.6 months</td>
<td>Being tested</td>
</tr>
<tr>
<td>FOLFOX</td>
<td>16–17 months</td>
<td>Being tested</td>
</tr>
<tr>
<td>FOLFIRI or FOLOFOX</td>
<td>20.3 months</td>
<td>Being tested</td>
</tr>
<tr>
<td>Avastin + IFL</td>
<td>20–22 months</td>
<td>Being tested</td>
</tr>
<tr>
<td>FOLFOX → FOLFIRI or FOLFIRI → FOLFOX</td>
<td>Being tested</td>
<td>Being tested</td>
</tr>
<tr>
<td>XELOX/FOLFOX + Avastin</td>
<td>Being tested</td>
<td>Being tested</td>
</tr>
<tr>
<td>Surgery alone</td>
<td>XELOX/FOLFOX + Avastin</td>
<td>Being tested</td>
</tr>
<tr>
<td>Mayo regimen</td>
<td>Being tested</td>
<td>Being tested</td>
</tr>
<tr>
<td>LV5FU2</td>
<td>Being tested</td>
<td>Being tested</td>
</tr>
<tr>
<td>Xeloda mono</td>
<td>Being tested</td>
<td>Being tested</td>
</tr>
<tr>
<td>FOLFOX</td>
<td>Being tested</td>
<td>Being tested</td>
</tr>
<tr>
<td>XELOX</td>
<td>Being tested</td>
<td>Being tested</td>
</tr>
<tr>
<td>Avastin combo</td>
<td>Being tested</td>
<td>Being tested</td>
</tr>
</tbody>
</table>
Current treatment paradigm for CRC

Roche Oncology Event, June 19 2006

Key ongoing phase III clinical trials in adjuvant and metastatic CRC

Roche Oncology Event, June 19 2006
Future treatment paradigm for CRC

Incident cases CRC

Early stage

Loco-regional therapy

No adjuvant chemotherapy
Fluoropyrimidine monotherapy
Fluoropyrimidine based combination

XELOD

Locally advanced/metastatic

1st line Fluoropyrimidine-based chemotherapy

XELOX/FOLFOX + Avastin

Xeloda

2nd line

XELOX

Irinotecan
Cetuximab

Colorectal Cancer

Non-small Cell Lung Cancer

Breast Cancer

Other solid tumor types

Non-Hodgkin’s Lymphoma

Conclusions
Non-Small Cell Lung Cancer
*Characteristics and treatment practice*

- Most common cause of cancer related deaths
- Usually diagnosed at a late stage
- Low cure rate with loco-regional therapy
- Limited benefit of chemotherapy
- Patients generally sicker with comorbidities
  - Need for low toxicity targeted therapies
- Rapid change in treatment paradigms expected over next 5 years

**Current treatment paradigm for NSCLC**

- Incident cases NSCLC
  - Early stage
    - Loco-regional therapy +/− adjuvant chemotherapy
  - Locally advanced/ metastatic
    - Platinum-based chemotherapy
      - 1st line
      - 2nd/ 3rd line
      - Tarceva
### Key ongoing clinical trials in metastatic NSCLC

<table>
<thead>
<tr>
<th>Trial</th>
<th>Phase</th>
<th>Treatment regimen</th>
<th>Patient population</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>E4599</td>
<td>phase III</td>
<td>Carboplatin/Avastin</td>
<td>1st line, non-squamous</td>
<td>Completed ASCO'05</td>
</tr>
<tr>
<td>AVAIL</td>
<td>phase III</td>
<td>Cisplatin/Gemcitabine ± Avastin</td>
<td>1st line, squamous</td>
<td>Recruitment to complete Q3'06</td>
</tr>
<tr>
<td>GNE 3744</td>
<td>phase II</td>
<td>RT -&gt; CT -&gt; CT + Avastin or Tarceva + Avastin</td>
<td>1st or 2nd line, treated CNS metastases</td>
<td>Started Q2'06</td>
</tr>
<tr>
<td>GNE</td>
<td>phase II</td>
<td>CT + Avastin</td>
<td>1st line maintenance non-squamous</td>
<td>Started Q1'06</td>
</tr>
<tr>
<td>ATLAS</td>
<td>phase III</td>
<td>Tarceva + Avastin</td>
<td>2nd line</td>
<td>Started Q4'06</td>
</tr>
<tr>
<td>BETA</td>
<td>phase III</td>
<td>Avastin + Tarceva vs. Avastin + CT vs. CT</td>
<td>2nd line</td>
<td>Completed ASCO'06</td>
</tr>
<tr>
<td>SATURN Lung</td>
<td>phase III</td>
<td>CT -&gt; Tarceva vs. placebo</td>
<td>1st line</td>
<td>Started Q4'05</td>
</tr>
</tbody>
</table>

### Future treatment paradigm for NSCLC

- **Incident cases NSCLC**
  - **Early stage**
    - Loco-regional therapy +/- adjuvant therapy
      - Tarceva
  - **Locally advanced/metastatic**
    - Squamous ca. 30%
      - Tarceva maintenance
      - Platinum-based chemotherapy
    - Non-squamous ca. 70%
      - Tarceva maintenance
      - Platinum-based chemotherapy

- **2nd/3rd line chemotherapy**
  - **Platinum-based chemotherapy**
    - Tarceva
  - **Avastin**
    - Tarceva + Avastin
  - **Tarceva + Avastin**
Breast Cancer

Characteristics and treatment practice

- Usually diagnosed at an early stage
- Long natural history
- High cure rate with loco-regional therapy
- Still 2nd most common cause of cancer related deaths in women
- Large number of active drugs
  - Widespread use of chemotherapy and hormonal therapy for adjuvant as well as metastatic disease
- Strong patient advocacy involvement in driving the direction of research and treatment guidelines
Current paradigm for adjuvant treatment of BC

Stage I-III BC
85-90% of incident cases

Routine HER2 testing
+ usual prognostic/predictive factors

Appropriate loco-regional therapy

Very low risk (<10%) of recurrence

No adjuvant therapy

Medium-high risk of recurrence

HER2+

Chemo +/- hormonal therapy

HER2-

Chemo +/- hormonal therapy

HERceptin (1 year)

Key ongoing/planned clinical trials in adjuvant BC

<table>
<thead>
<tr>
<th>Trial</th>
<th>Xeloda</th>
<th>Avastin</th>
<th>Avastin + Herceptin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient population</td>
<td>HER2-</td>
<td>HER2-</td>
<td>HER2-</td>
</tr>
<tr>
<td>Treatment regimen</td>
<td>AC--&gt; Docetaxel ± Xeloda</td>
<td>AC --&gt; P vs. AC/Avastin --&gt; P/Avastin (6 months) vs. AC/Avastin --&gt; P/Avastin (12 months)</td>
<td>Under development</td>
</tr>
<tr>
<td>Status</td>
<td>Recruitment completed</td>
<td>Protocol in preparation</td>
<td></td>
</tr>
</tbody>
</table>

Filings expected in 2009 for Xeloda and post 2009 for Avastin
Future paradigm for adjuvant treatment of BC

Stage I-III BC
85-90 % of incident cases

Routine HER2 testing
+ usual prognostic/predictive factors

Appropriate loco-regional therapy

Very low risk (<10 %)
of recurrence

No adjuvant therapy

Medium-high risk of recurrence

HER2+

Chemo +/-
hormonal therapy

Herceptin (2 years)
+ Avastin

HER2-

Chemo +/-
hormonal therapy

Avastin
Xeloda

Current treatment paradigm for metastatic BC

Stage IV BC

Hormone receptor status

Candidate for hormonal therapy

Hormonal therapy
1st line/ 2nd line

Progression

Not a candidate for hormonal therapy

HER2+

Chemotherapy
(multiple lines)

Herceptin
Xeloda

HER2-

Chemotherapy
(multiple lines)

Xeloda
Key ongoing clinical trials in metastatic BC

<table>
<thead>
<tr>
<th>Study</th>
<th>Herceptin + Avastin</th>
<th>Avastin</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAnDEM</td>
<td>TaenDEM phase III</td>
<td>Roche phase III</td>
</tr>
<tr>
<td>1st line</td>
<td>1st line</td>
<td>1st line</td>
</tr>
<tr>
<td>Taxotere ± Avastin</td>
<td>Taxol ± Avastin</td>
<td>Taxotere ± Avastin</td>
</tr>
<tr>
<td>Completed ESMO'06</td>
<td>Completed ASCO'06</td>
<td>Started Q1'06</td>
</tr>
</tbody>
</table>

Filing expected in 2006 for Herceptin, 2006 and 2008 for Avastin

Future treatment paradigm for metastatic BC

Stage IV BC

HER2 Status

HER2+

Herceptin based therapy

Herceptin + Avastin

2nd line

Xeloda

Herceptin

HER2-

Candidate for hormonal therapy

Not a candidate for hormonal therapy

Chemotherapy 1st line

Chemotherapy 2nd line

Xeloda

Avastin

Hormonal therapy

Chemotherapy 1st line

Chemotherapy 2nd line

Xeloda

Avastin
Colorectal Cancer

Non-small Cell Lung Cancer

Breast Cancer

Other solid tumor types

Non-Hodgkin’s Lymphoma

Conclusions

Pancreatic Cancer

*Incremental gains with new drugs in a difficult to treat disease*

- Very high unmet medical need
  - Diagnosis usually late
  - >90% mortality rate
- Gemcitabine only approved drug until now
  - Many drugs failed in phase III
- New drugs with survival benefit
  - Tarceva
  - Xeloda
- Progress slow and incremental

<table>
<thead>
<tr>
<th></th>
<th>Avastin</th>
<th>Xeloda</th>
<th>Tarceva</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trial</strong></td>
<td>AVITA</td>
<td>CALGB</td>
<td>GEM-CAP</td>
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<tr>
<td></td>
<td>phase III</td>
<td>80303</td>
<td>phase III</td>
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<tr>
<td><strong>Patient</strong></td>
<td>1st line</td>
<td>1st line</td>
<td>1st line</td>
</tr>
<tr>
<td><strong>population</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Gemcitabine /Tarceva ± Avastin</td>
<td>Gemcitabine ± Avastin</td>
<td>Gemcitabine ± Xeloda</td>
</tr>
<tr>
<td><strong>regimen</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Status</strong></td>
<td>Started H1’06</td>
<td>Recruitment completed Q2’06</td>
<td>Interim analysis ECCO’05</td>
</tr>
</tbody>
</table>

**Tarceva:** approved US / filed EU

**Xeloda:** filing to be discussed with health authorities

**Avastin:** filing in 2008
Gastric cancer
Emerging new drugs

- Greater prevalence in the Far East
  - Significant commercial potential in emerging markets
- High unmet medical need
  - Diagnosis often late
- 5-FU based chemotherapy mainstay of systemic therapy
- Emerging new standards
  - Xeloda / Cisplatin
  - Docetaxel based combinations
  - Herceptin for HER2-positive patients

<table>
<thead>
<tr>
<th>Herceptin</th>
<th>Xeloda</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial</td>
<td>ToGA</td>
</tr>
<tr>
<td></td>
<td>phase III</td>
</tr>
<tr>
<td>Patient population</td>
<td>1st line</td>
</tr>
<tr>
<td>Treatment regimen</td>
<td>Cisplatin/(5FU or Xeloda) ± Herceptin</td>
</tr>
<tr>
<td>Status</td>
<td>Started Q3'05</td>
</tr>
</tbody>
</table>

Filings expected for Xeloda in 2006 and Herceptin in 2008

Renal Cell Carcinoma
A time of rapid progress

- Resistant to conventional chemotherapy
- Responsive to immunomodulators
  - Roferon, Interleukin-2
- Multiple new active drugs
  - e.g. Avastin, Sunitinib, Sorafenib, Temsirolimus
- Optimum first line standard yet to be determined
  - Possibility of using doublets of targeted therapy

<table>
<thead>
<tr>
<th>Avastin</th>
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<tbody>
<tr>
<td>Trial</td>
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</tr>
<tr>
<td>Patient population</td>
</tr>
<tr>
<td>Treatment regimen</td>
</tr>
<tr>
<td>Status</td>
</tr>
</tbody>
</table>

Data expected in 2006 / Filing expected in 2007
Colorectal Cancer

Non-small Cell Lung Cancer

Breast Cancer

Other solid tumor types

Non-Hodgkin’s Lymphoma

Conclusions

Current standard for treatment of NHL and CLL

Incident cases NHL

Follicular NHL

1st line
Chemotherapy

MabThera

2nd line
Chemotherapy

MabThera

Induction and Maintenance

Zevalin

Bexxar

3rd line
Chemotherapy

Diffuse large cell NHL

1st line
Chemotherapy CHOP

MabThera

2nd line
Chemotherapy

MabThera

Incident cases CLL

1st line
Chemotherapy

Alkylator, fludarabine, combination

2nd line
Chemotherapy

Bexxar

3rd line
Chemotherapy

Campath
Key phase III clinical trials in NHL and CLL

<table>
<thead>
<tr>
<th>Trial</th>
<th>MabThera in NHL</th>
<th>MabThera in CLL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient population</strong></td>
<td>EORTC 20891</td>
<td>REACH</td>
</tr>
<tr>
<td>Maintenance relapsed INHL</td>
<td>ECOG 1496</td>
<td>CLL relapsed</td>
</tr>
<tr>
<td>Maintenance 1st line INHL</td>
<td>REACH</td>
<td>CLL 1st line</td>
</tr>
<tr>
<td><strong>Treatment regimen</strong></td>
<td>FC ± R</td>
<td>FC ± R</td>
</tr>
<tr>
<td>8 infusions in 2 years</td>
<td>Completed ASH'05</td>
<td>Recruitment completed</td>
</tr>
<tr>
<td>16 infusions in 2 years</td>
<td>Completed ASH'05</td>
<td>Maintenance relapsed</td>
</tr>
</tbody>
</table>

Filing for MabThera in CLL expected in 2009

Future standard for treatment of NHL and CLL

Incident cases NHL

1st line Chemotherapy

Follicular NHL

1st line Chemotherapy

MabThera Induction and Maintenance

2nd line Chemotherapy

MabThera Induction and Maintenance

3rd line Chemotherapy

Zevalin Bexxar

Incident cases CLL

1st line Chemotherapy

Alkylator, fludarabine, combination

1st line Chemotherapy

Diffuse large cell NHL

MabThera

1st line Chemotherapy CHOP

MabThera

2nd line Chemotherapy

MabThera

3rd line Chemotherapy

Campath
Colorectal Cancer

Non-small Cell Lung Cancer

Breast Cancer

Other solid tumor types

Non-Hodgkin’s Lymphoma

Conclusions

The future

Complex but rational treatment algorithms in a crowded environment

• Segmentation of cancer based on histology and molecular genotypes / phenotypes
• Higher cure rates for most primary cancers
  - Early diagnosis
  - Increasing use of multiple and prolonged adjuvant treatments
• Substantial increase in number of available treatments
• Multiple lines of targeted therapies in metastatic disease
  - Metastatic cancer as chronic disease
• Increasing emphasis on long-term risk-benefit

New cancer medicines will have to provide clear and compelling differentiation to become the new standard of care for defined patient populations

Roche is in an excellent position to continue to set the standards and retain long-term leadership
Appendix

Other cancer types

<table>
<thead>
<tr>
<th>Trial</th>
<th>Ovarian Ca</th>
<th>Prostate Ca</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Avastin</td>
<td>Avastin</td>
</tr>
<tr>
<td>GOG 218</td>
<td>phase III</td>
<td>CALGB 90401</td>
</tr>
<tr>
<td>ICON7</td>
<td>phase III</td>
<td>phase III</td>
</tr>
<tr>
<td>Patient population</td>
<td>1st line</td>
<td>1st line</td>
</tr>
<tr>
<td>Treatment regimen</td>
<td>Carboplatin/ Paclitaxel ± Avastin</td>
<td>Carboplatin/ Paclitaxel ± Avastin</td>
</tr>
<tr>
<td>Status</td>
<td>Started Q3'05</td>
<td>To start H2'06</td>
</tr>
</tbody>
</table>
Evolution of standards of care in colorectal cancer

Progressive improvement in survival over the past decade

- Best supportive care, Scheithauer 1993
- 5-FU/LV or Xeloda mono, Saltz 2000
- IFL, Saltz 2000, Hurwitzy 2004
- FOLFIRI or FOLFOX, Douillard 2000, de Gramont 2000
- Avastin + IFL, Hurwitz 2004
- FOLFOX → FOLFIRI, or FOLFIRI → FOLFOX, Goldberg, 2004, Tournigand 2004
- XELOX/FOLFOX + Avastin

Median overall survival:
- Surgery alone*: 6 months
- Mayo regimen*: 12.0 months
- LV5FU2*: 15–16 months
- Xeloda mono*: 16–17 months
- FOLFOX*: 20–22 months
- XELOX + Avastin: Being tested

Disease-free survival at 3 years:
- Surgery alone*: 47%
- Mayo regimen*: 63%
- LV5FU2*: 60%
- Xeloda mono*: 64%
- FOLFOX*: 72%
- XELOX: Being tested
- Avastin combo: Being tested