

## Roche setting the standards of cancer care

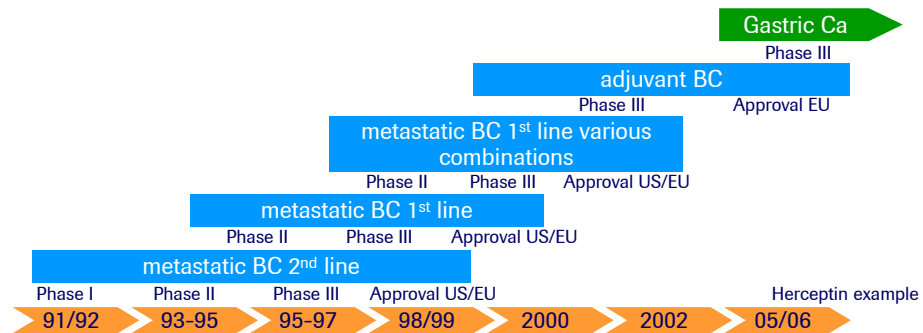
### Oncology Event for Investors, June 19

*Kapil Dhingra, VP Medical Science*



## Developing a drug to the standard of care

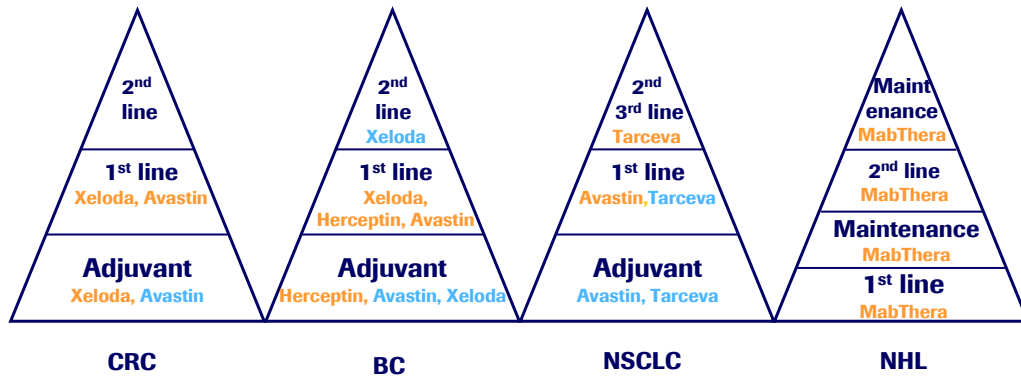
### *Superior clinical benefit, resources and time (!)*



#### 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

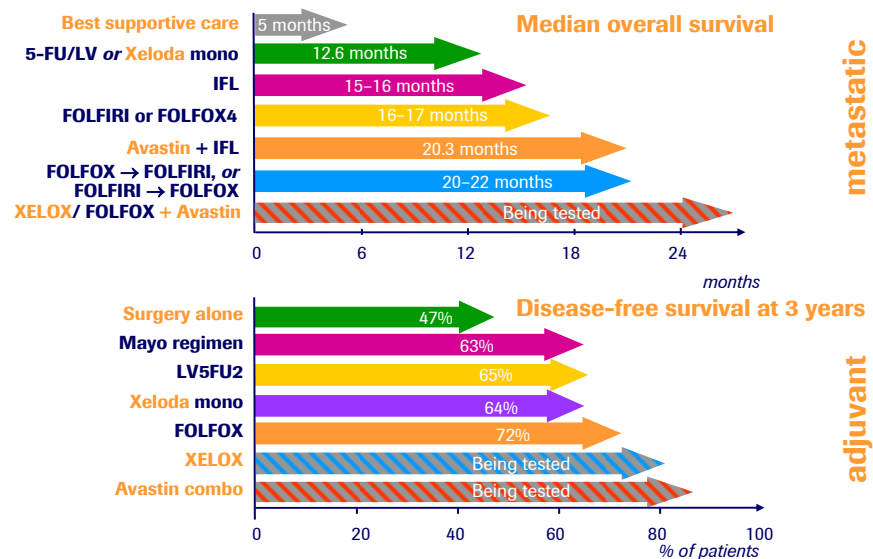
### *Characteristics and treatment practice*

- 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

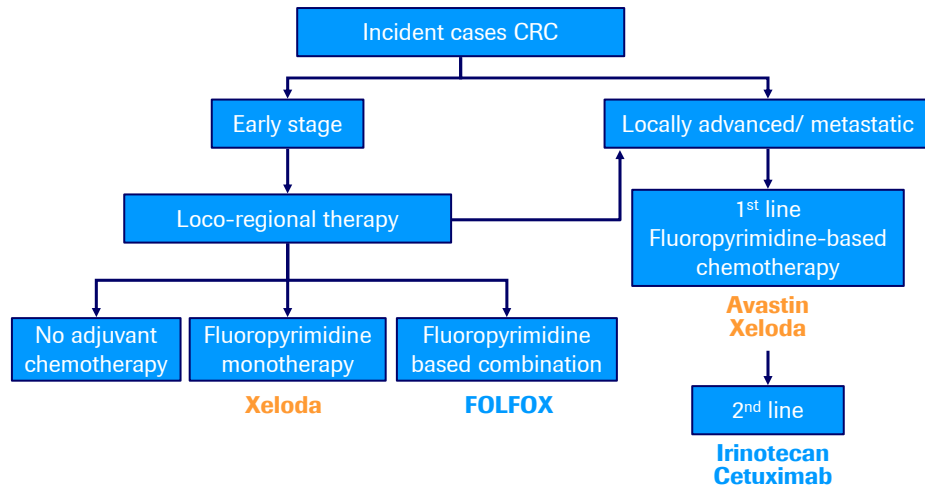
Potential for cure in selected patients with metastatic disease in the future

## Evolution of standards of care in colorectal cancer

### *Progressive improvement in survival over the past decade*



## Current treatment paradigm for CRC



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## Key ongoing phase III clinical trials in adjuvant and metastatic CRC

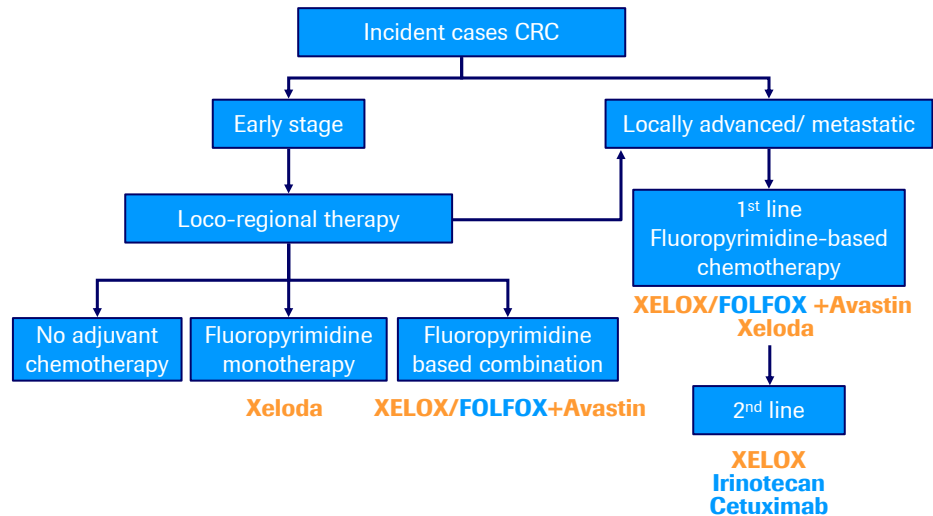


Trial	Avastin		Avastin + Xeloda		Xeloda	
	NSABP	E5204	AVANT	NO16966	NO16968	NO16967
Patient population	Adjuvant CC	Adjuvant Rectal Ca	Adjuvant CC	1 <sup>st</sup> line mCRC	Adjuvant CC	2 <sup>nd</sup> line mCRC
Treatment regimen	FOLFOX ± Avastin	FOLFOX ± Avastin	FOLFOX vs. FOLFOX + Avastin vs. XELOX + Avastin	XELOX ± Avastin vs. FOLFOX ± Avastin	XELOX vs. 5FU/LV	XELOX vs. FOLFOX
Status	Started Q3'04	Started Q1'06	Started Q4'04	Final analysis 2006	Recruitment completed	Recruitment completed

Filings expected in 2006 for Avastin (combo oxaliplatin) and Xeloda in 1<sup>st</sup> line mCRC

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## Future treatment paradigm for CRC



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## Colorectal Cancer

### Non-small Cell Lung Cancer

### Breast Cancer

### Other solid tumor types

### Non-Hodgkin's Lymphoma

### Conclusions



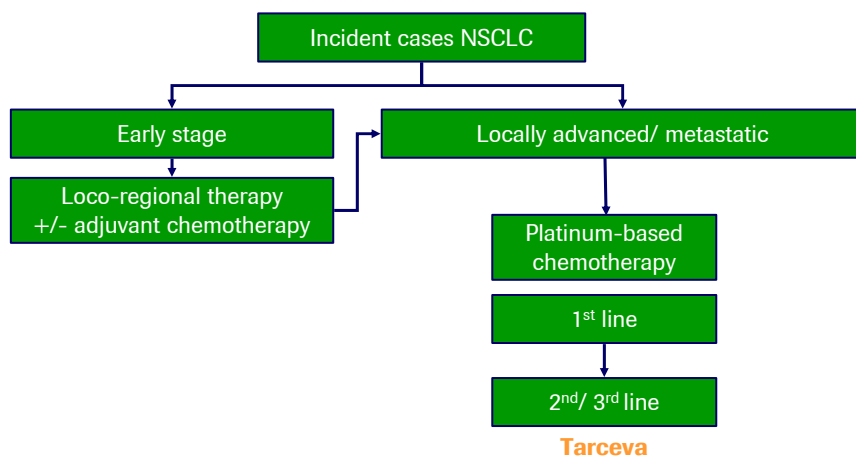
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## Non-Small Cell Lung Cancer

### *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



## Key ongoing clinical trials in metastatic NSCLC

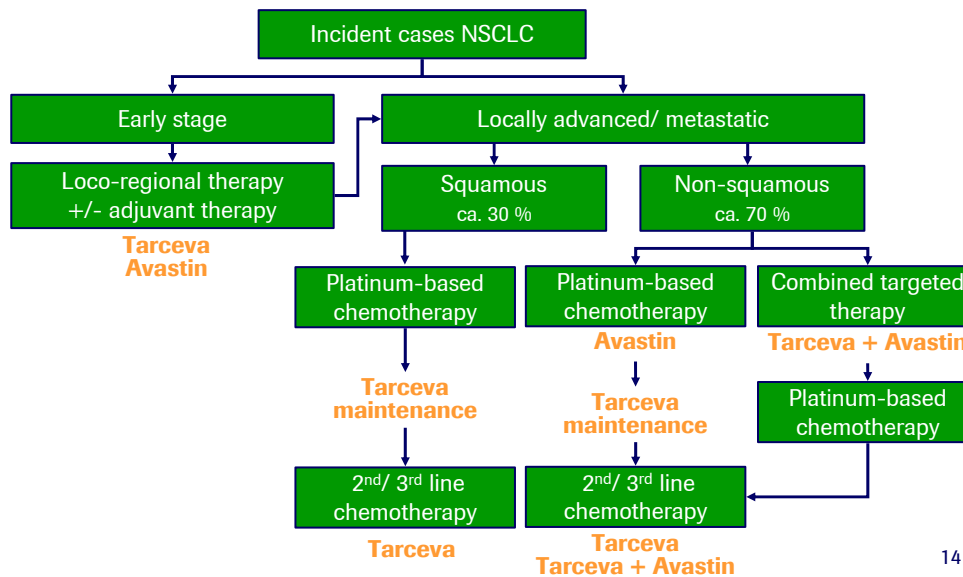


	Avastin	Avastin		Avastin + Tarceva			Tarceva	
<b>Trial</b>	<b>E4599</b> phase III	<b>AVAIL</b> phase III	<b>GENE 3744</b> phase II	<b>GENE</b> phase II	<b>ATLAS</b> phase III	<b>BETA Lung</b> phase III	phase II	<b>SATURN</b> phase III
<b>Patient population</b>	1 <sup>st</sup> line, non-squamous	1 <sup>st</sup> line, non-squamous	1 <sup>st</sup> line, squamous	1 <sup>st</sup> or 2 <sup>nd</sup> line, treated CNS metastases	1 <sup>st</sup> line maintenance non-squamous	2 <sup>nd</sup> line	2 <sup>nd</sup> line	1 <sup>st</sup> line
<b>Treatment regimen</b>	Carboplatin/Taxol ± Avastin	Cisplatin/Gemcitabine ± Avastin	RT -> CT -> CT + Avastin	CT + Avastin or Tarceva + Avastin	CT + Avastin -> Avastin ± Tarceva	Tarceva ± Avastin	Avastin + Tarceva vs. Avastin + CT vs. CT	CT -> Tarceva vs. placebo
<b>Status</b>	Completed ASCO'05	Recruitment to complete Q3'06	Started Q2'06	Started Q1'06	Started Q4'06	Started Q2'06	Completed ASCO'06	Started Q4'05

Phase III in adjuvant NSCLC with Avastin and Tarceva in preparation

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## Future treatment paradigm for NSCLC



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**Colorectal Cancer**

**Non-small Cell Lung Cancer**

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**Breast Cancer**

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**Other solid tumor types**

**Non-Hodgkin's Lymphoma**

**Conclusions**

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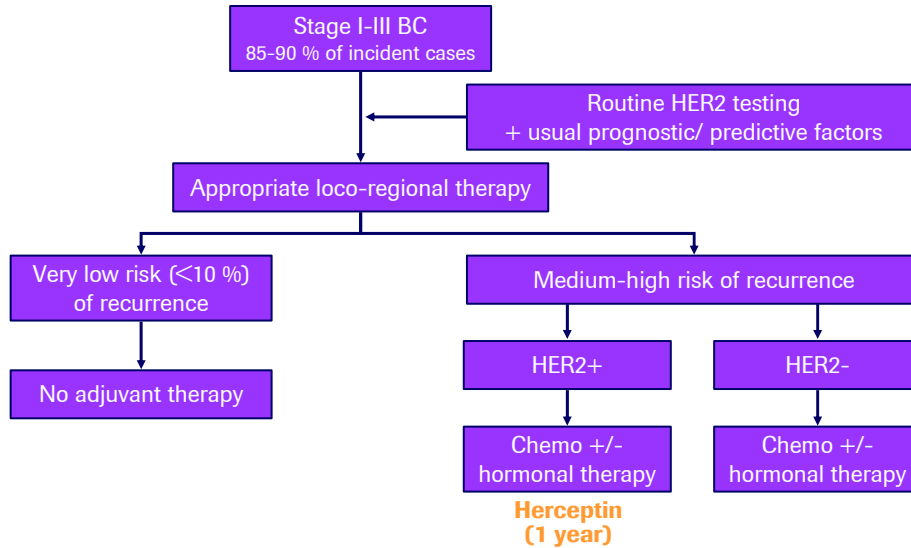
**Breast Cancer**

*Characteristics and treatment practice*

- Usually diagnosed at an early stage
- Long natural history
- High cure rate with loco-regional therapy
- Still 2<sup>nd</sup> 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

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## Current paradigm for adjuvant treatment of BC



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## Key ongoing/planned clinical trials in adjuvant BC

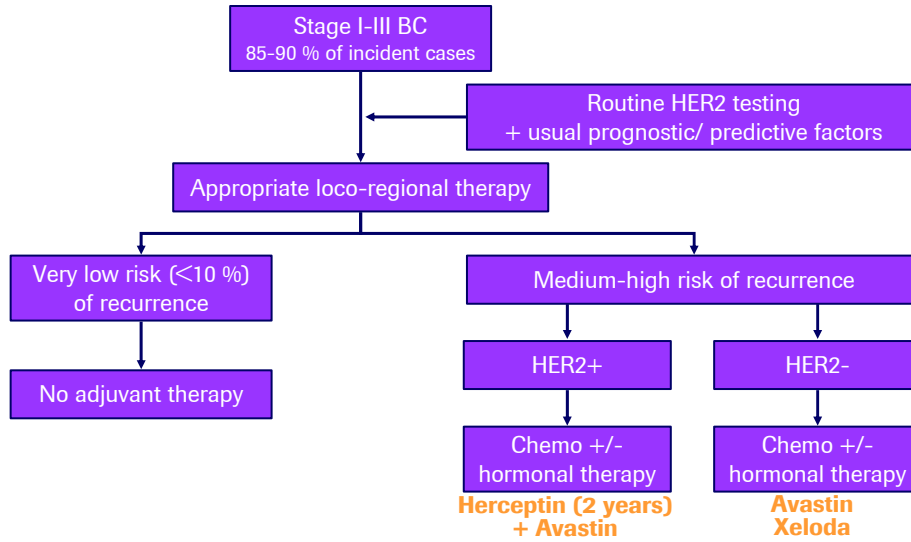


	Xeloda	Avastin		Avastin + Herceptin
<b>Trial</b>	<b>NO17629</b> phase III	<b>E5103</b> phase III	Roche phase III	Roche phase III
<b>Patient population</b>	HER2-	HER2-	HER2-	HER2+
<b>Treatment regimen</b>	AC-> Docetaxel ± Xeloda	AC --> P vs. AC/Avastin --> P/Avastin (6 months) vs. AC/Avastin --> P/Avastin (12 months)	Under development	Under development
<b>Status</b>	Recruitment completed	Protocol in preparation		

**Filings expected in 2009 for Xeloda and post 2009 for Avastin**

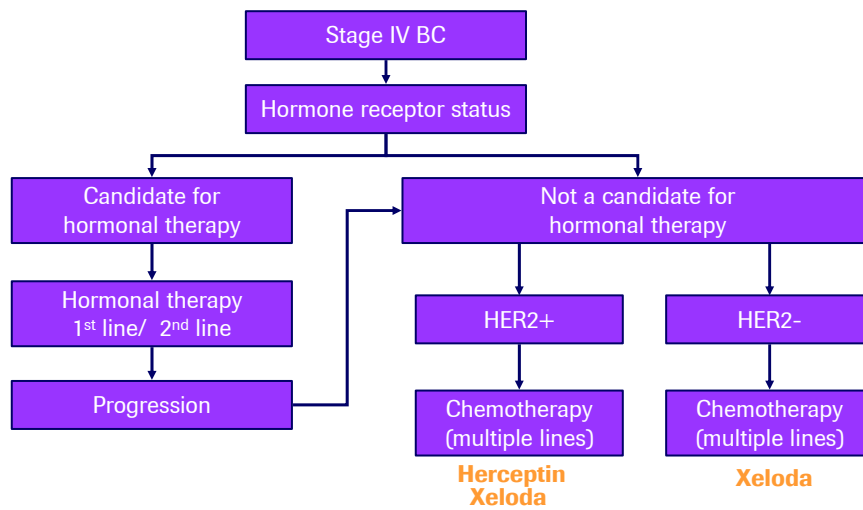
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## Future paradigm for adjuvant treatment of BC



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## Current treatment paradigm for metastatic BC



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## Key ongoing clinical trials in metastatic BC

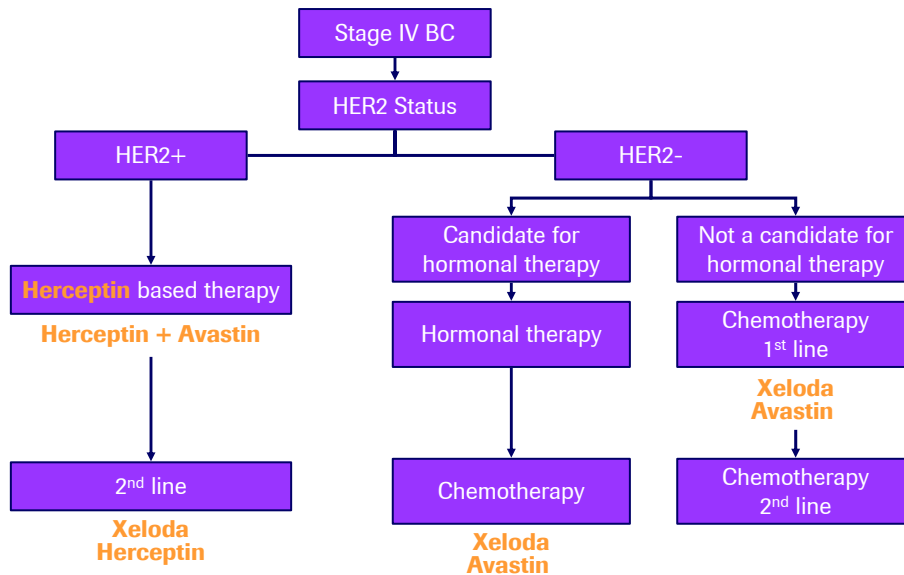


	Herceptin	Herceptin + Avastin	Avastin			
Study	<b>TAnDEM</b> phase III	Roche phase III	<b>E2100</b> phase III	<b>AVADO</b> phase III	<b>RIBBON-1</b> phase III	<b>RIBBON-2</b> phase III
Patient population	1 <sup>st</sup> line	1 <sup>st</sup> line	1 <sup>st</sup> line	1 <sup>st</sup> line	1 <sup>st</sup> line	2 <sup>nd</sup> line
Treatment regimen	Arimidex ± Herceptin	Herceptin + Docetaxel ± Avastin	Taxol ± Avastin	Taxotere ± Avastin	Any CT ± Avastin	Any CT ± Avastin
Status	Completed ESMO'06	To start H2'06	Completed ASCO'05	Started Q1'06	Started Q4'05	Started Q1'06

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

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## Future treatment paradigm for metastatic BC



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**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

	Avastin		Xeloda	Tarceva
<b>Trial</b>	<b>AVITA</b> phase III	<b>CALGB 80303</b> phase III	<b>GEM-CAP</b> phase III	<b>PA3</b> phase III
<b>Patient population</b>	1 <sup>st</sup> line	1 <sup>st</sup> line	1 <sup>st</sup> line	1 <sup>st</sup> line
<b>Treatment regimen</b>	Gemcitabine / Tarceva ± Avastin	Gemcitabine ± Avastin	Gemcitabine ± Xeloda	Gemcitabine ± Tarceva
<b>Status</b>	Started H1'06	Recruitment completed Q2'06	Interim analysis ECCO'05	Completed ASCO GI'05

**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

	Herceptin	Xeloda
<b>Trial</b>	<b>ToGA</b> phase III	<b>ML17032</b> phase III
<b>Patient population</b>	1 <sup>st</sup> line	1 <sup>st</sup> line
<b>Treatment regimen</b>	Cisplatin/(5FU or Xeloda) ± Herceptin	Cisplatin + Xeloda vs. Cisplatin + 5FU
<b>Status</b>	Started Q3'05	Completed ASCO'06

**Filings expected for Xeloda in 2006 and Herceptin in 2008**

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## 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

	Avastin	
<b>Trial</b>	<b>AVOREN</b> phase III	<b>CALGB90206</b> phase III
<b>Patient population</b>	1 <sup>st</sup> line	1 <sup>st</sup> line
<b>Treatment regimen</b>	Interferon ± Avastin	Interferon ± Avastin
<b>Status</b>	Recruitment completed	Recruitment completed

**Data expected in 2006 / Filing expected in 2007**

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**Colorectal Cancer**

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**Other solid tumor types**

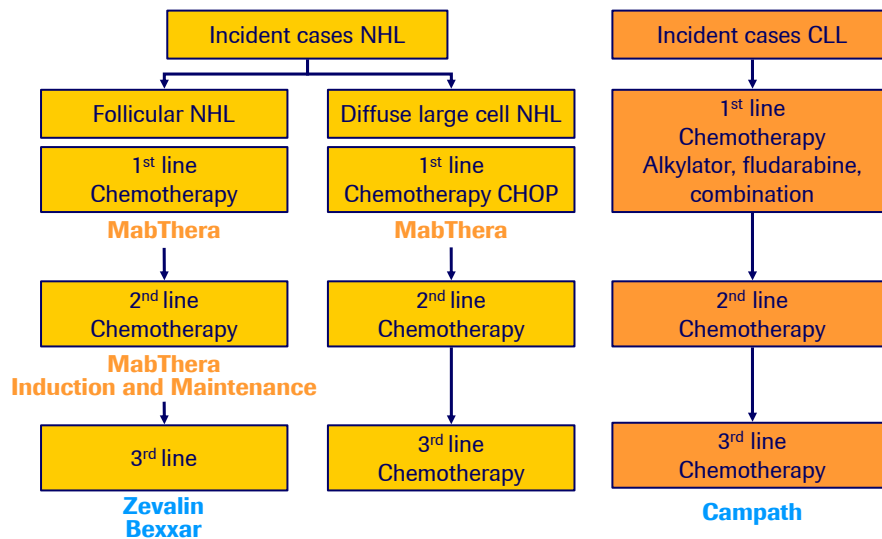
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**Non-Hodgkin's Lymphoma**

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**Conclusions**

**Current standard for treatment of NHL and CLL**



## Key phase III clinical trials in NHL and CLL

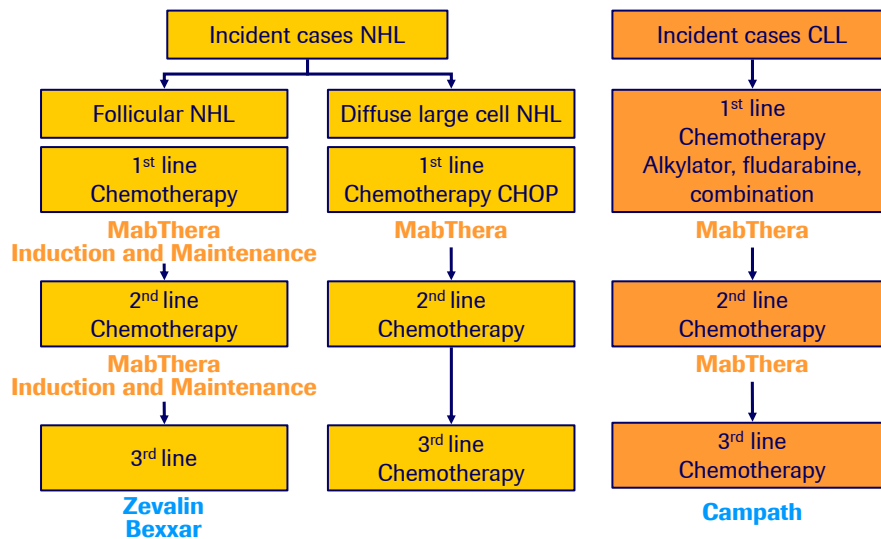


	MabThera in NHL		MabThera in CLL	
Trial	<b>EORTC 20891</b>	<b>ECOG 1496</b>	<b>REACH</b>	<b>ML17102</b>
Patient population	Maintenance relapsed iNHL	Maintenance 1 <sup>st</sup> line iNHL	CLL relapsed	CLL 1 <sup>st</sup> line
Treatment regimen	8 infusions in 2 years	16 infusions in 2 years	FC ± R	FC ± R
Status	Completed ASH'05	Completed ASH'05	Started Q3'03	Recruitment completed

**Filing for MabThera in CLL expected in 2009**

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## Future standard for treatment of NHL and CLL



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**Conclusions**

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**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

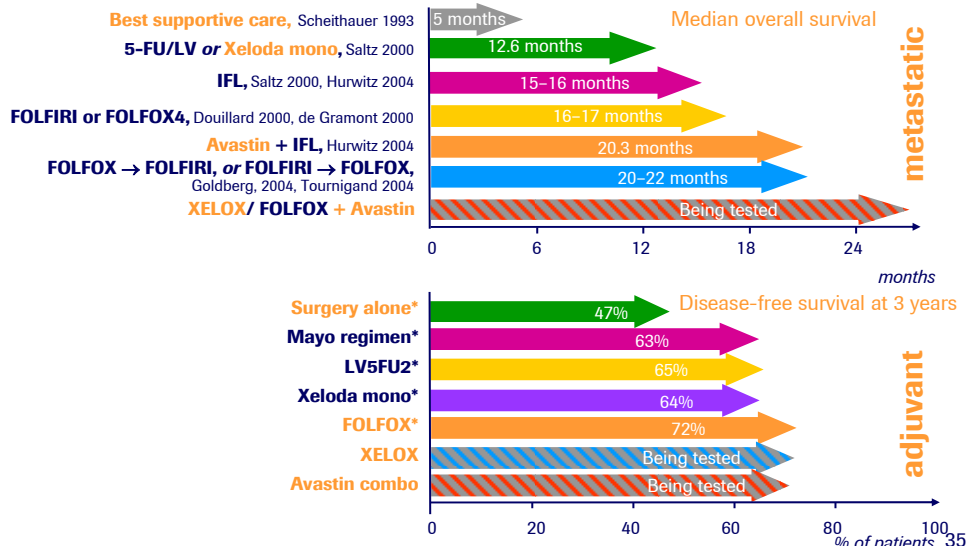
## Appendix

## Other cancer types

	Ovarian Ca		Prostate Ca
	Avastin		Avastin
<b>Trial</b>	<b>GOG 218</b> phase III	<b>ICON7</b> phase III	<b>CALGB 90401</b> phase III
<b>Patient population</b>	1 <sup>st</sup> line	1 <sup>st</sup> line	Hormone-refractory
<b>Treatment regimen</b>	Carboplatin/ Paclitaxel ± Avastin	Carboplatin/ Paclitaxel ± Avastin	Docetaxel ± Avastin
<b>Status</b>	Started Q3'05	To start H2'06	Started Q2'05

# Evolution of standards of care in colorectal cancer

## Progressive improvement in survival over the past decade



\*LaBianca R et al. Lancet 1995;345:939-44, Topham C et al. Eur J Cancer 2003;1(Suppl. 5):S324 (Abst 1085)