



## Helmut – Kraatz- Preis

# Innovative Modelle in der Behandlung des Ovarialkarzinoms



PD Dr. Christina Fotopoulou

Klinik für Gynäkologie

Europäisches Kompetenzzentrum für Eierstockkrebs

Charité –Universitätsmedizin Berlin

Campus Virchow-Klinikum

*Charité*

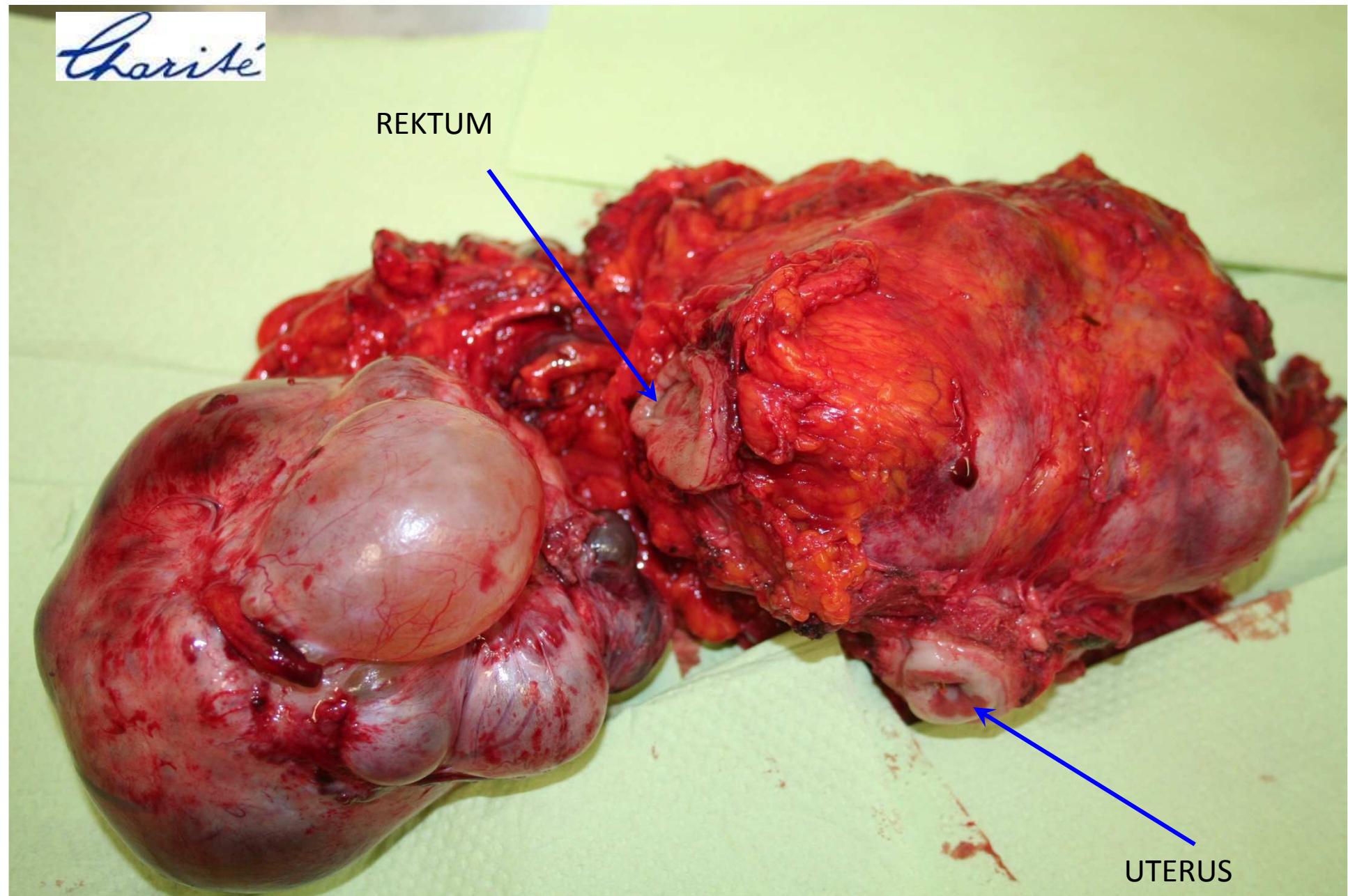
## Fall I

- 53j. Patientin mit der Primärdiagnose eines serösen-Zystadenokarzinoms des Ovars FIGO IIIc

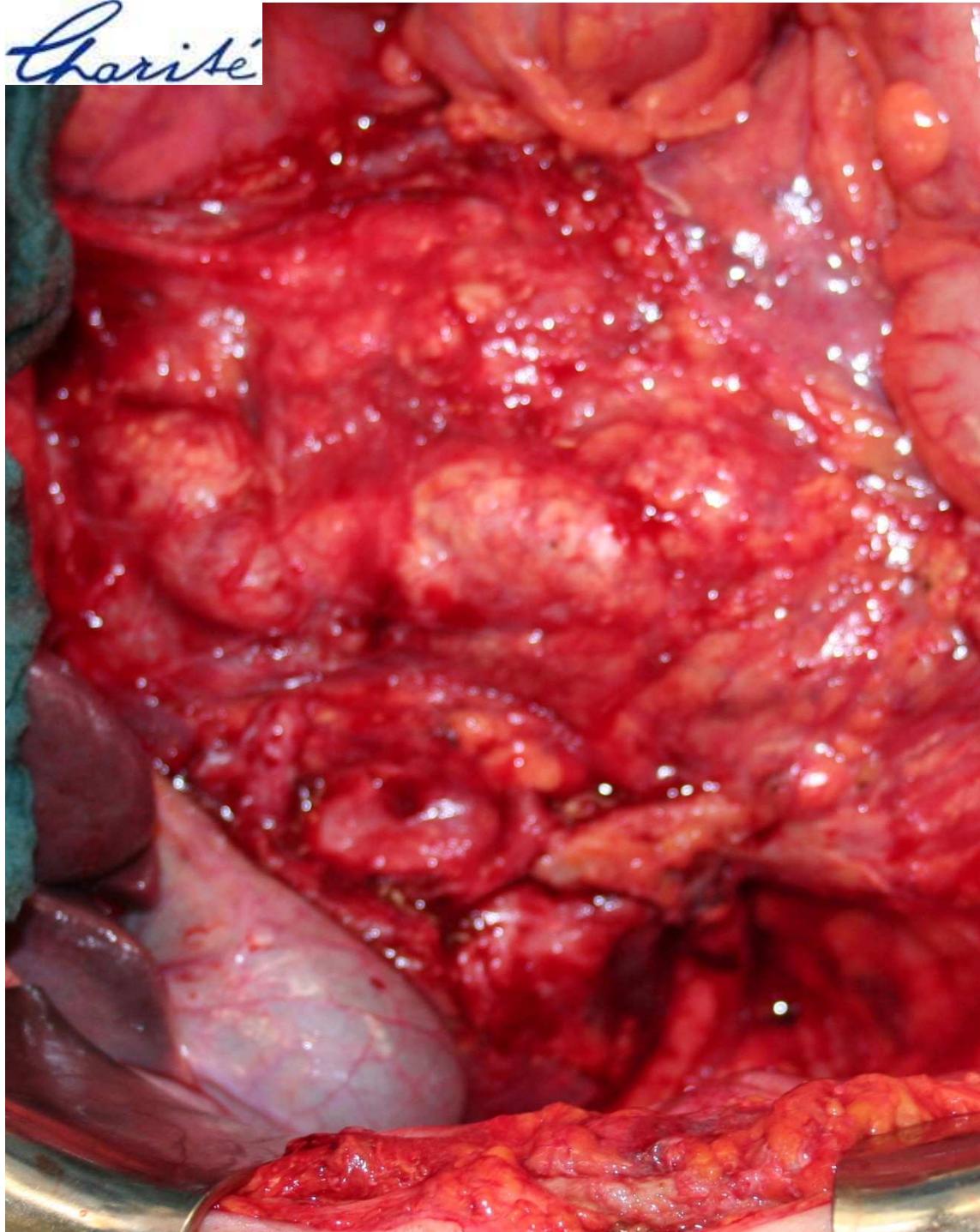
Tumorstadium: pT3c, N1 (**101/117**), G3, L1, V1

Therapie: Multiviszeraler Eingriff am 25.11.2008 mit optimaler Zytoreduktion (makroskopische Tumorfreiheit) und adjuvanter Chemotherapie

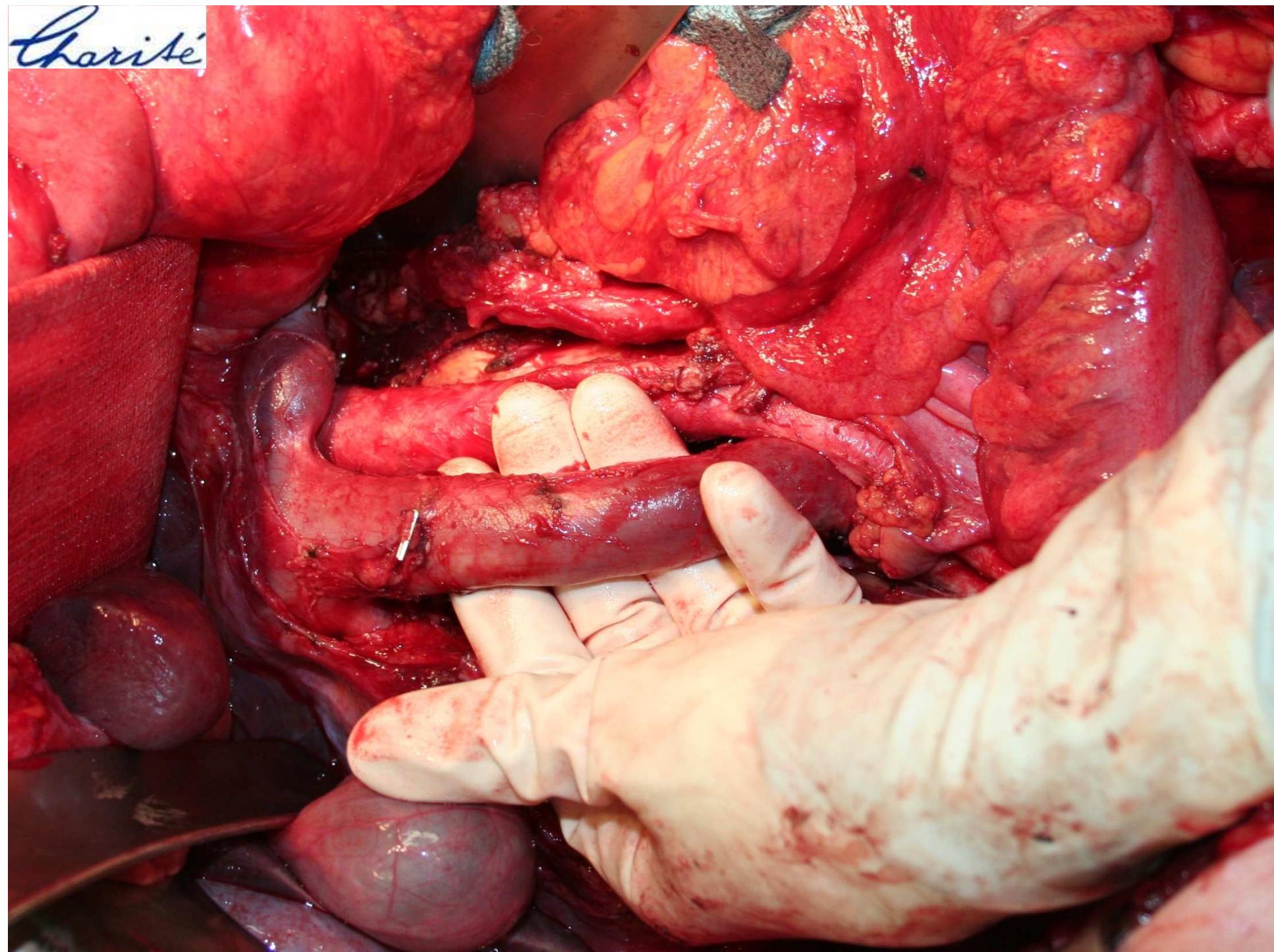
Follow-up: Patientin bis heute im Wohlbefinden, rezidivfrei.



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## Fall II

- 48j. Patientin mit der Primärdiagnose eines serösen Zystadenokarzinoms des Ovars FIGO IIc

Tumorstadium: pT2c, N0 (0/65), G3, L0, V0

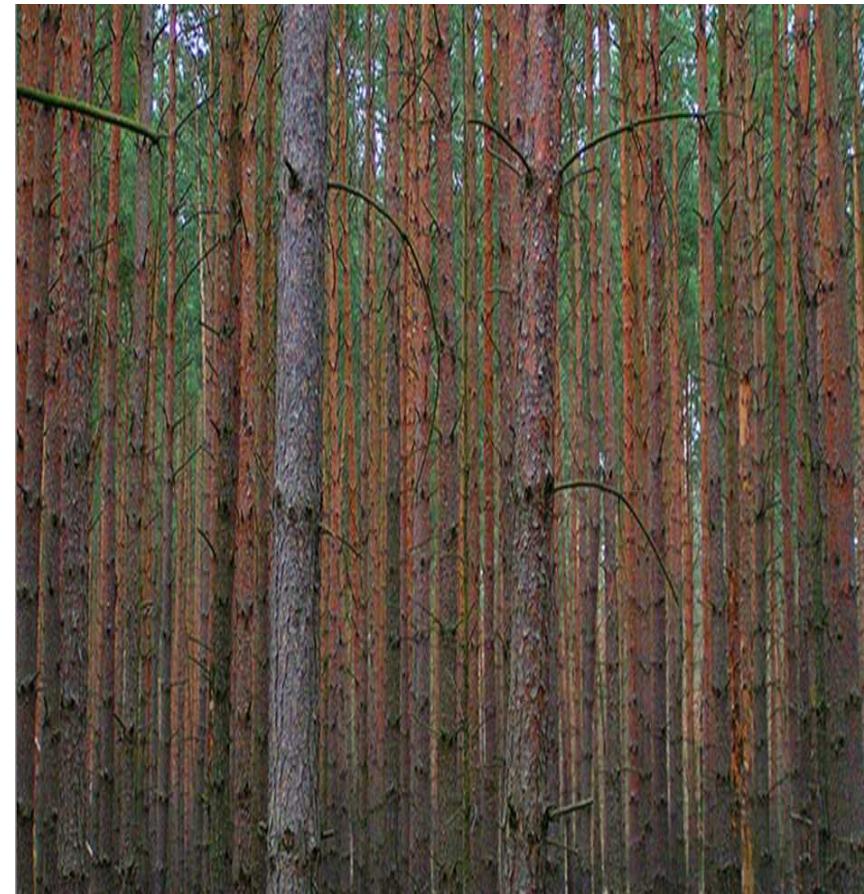
Therapie: Primäre Operation am 29.04.2010 mit Deperitonealisierung des kleinen Beckens, und makroskopischer Tumorfreiheit.  
Anschliessende adjuvante Chemotherapie

Follow-up: 14 Monate nach Chemo-Ende multifokales Rezidiv: LK Tr. coeliacus, Leberparenchym, Mesenterium, Nebennieren, Aszites

# ....Unterschiedliches Outcome

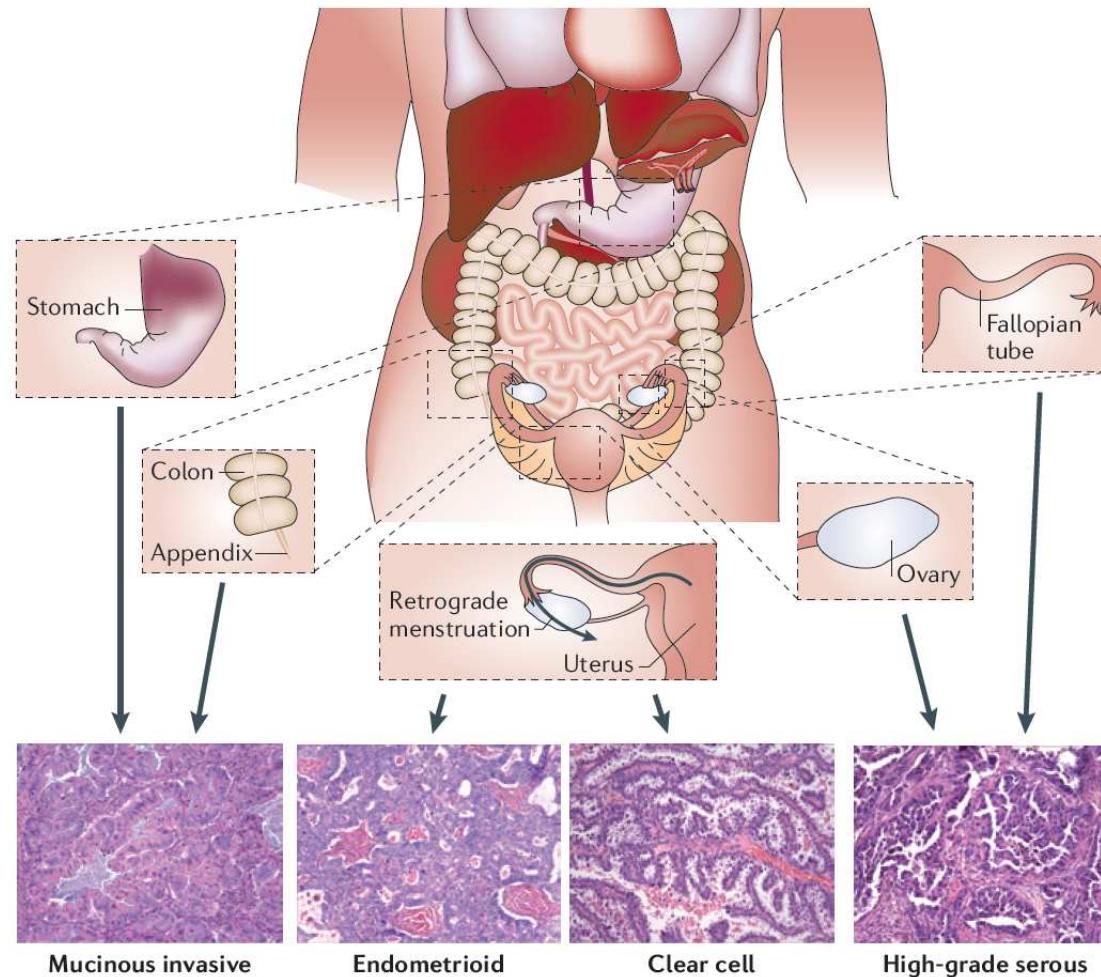
- Faktor: Operateur/  
Team?
- Faktor: Zentrum?
- Faktor:  
Anschlußtherapie?
- Faktor: Histologie?
- Faktor: Tumorstadium?

✓ Faktor:  
Tumorbiologie?



# „Ovarian cancer is many diseases...”

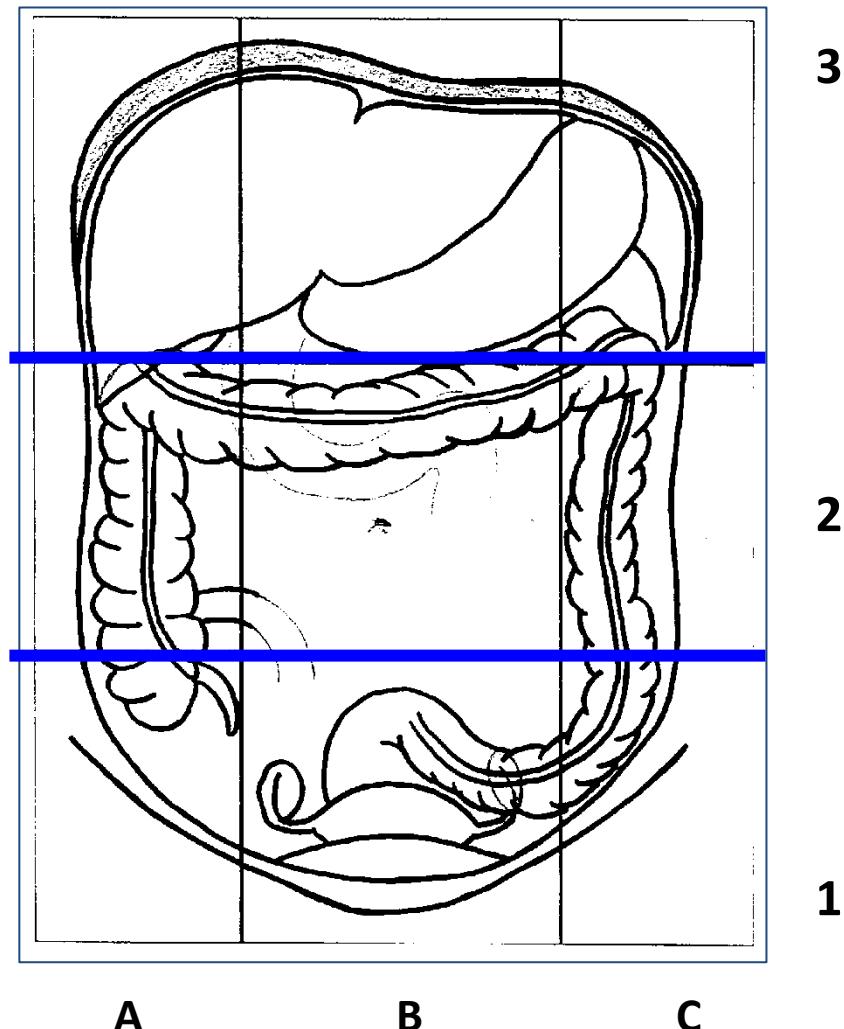
NATURE REVIEWS | CANCER



Vaughan et.al. 2011

## IMO: Intraoperative Mapping Ovarian Cancer

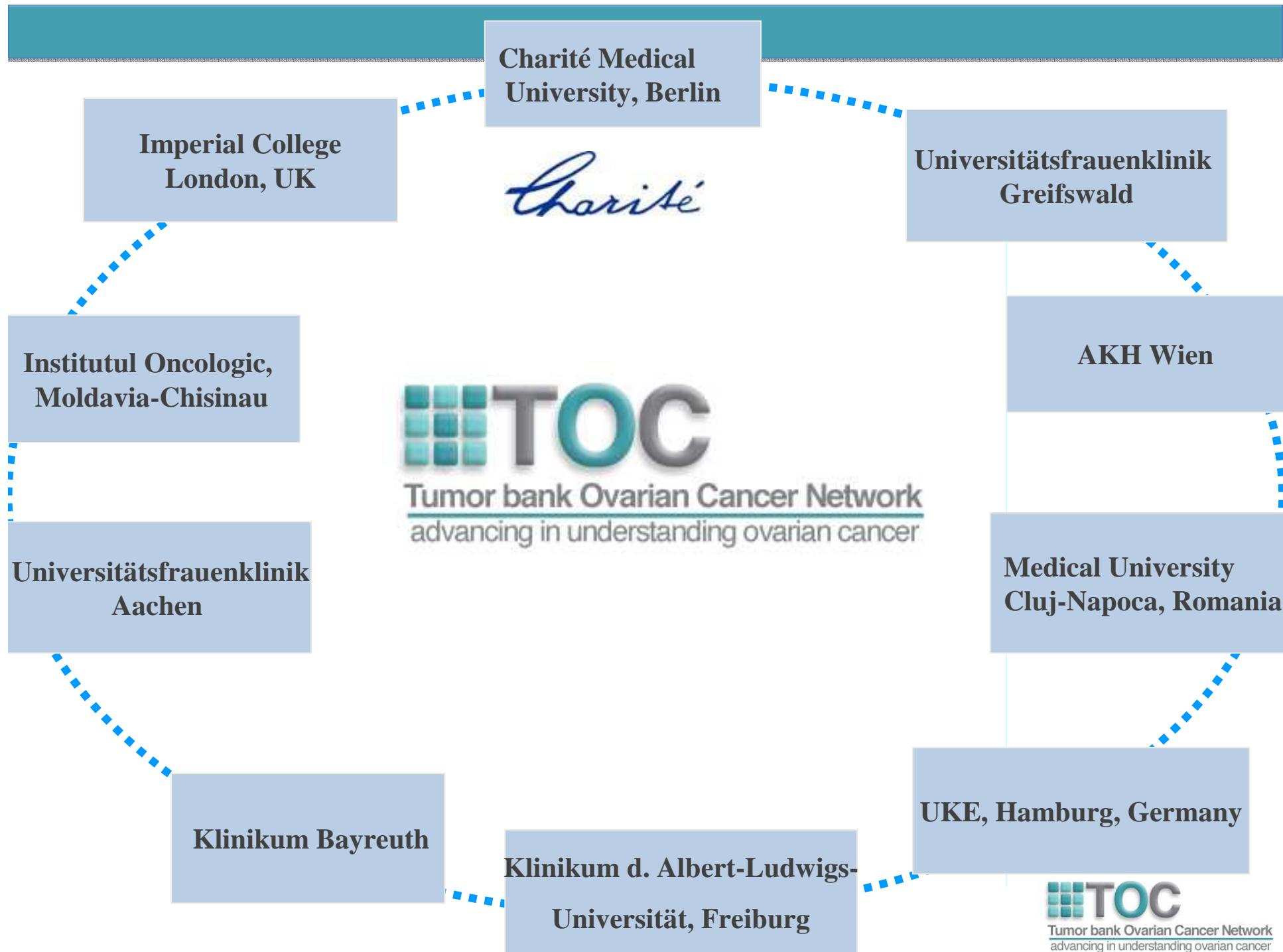
*Prospektive  
Erfassung  
operativer,  
klinischer und  
histopatho-  
logischer Daten*



# Entwicklung des TOC-Networks

- **2000-2004**
  - Systematische prospektive Asservierung von Tumorgewebe: Charité (monozentrisch), Definierung von SOP's, software Entwicklung
- **2004**
  - Tumorbank Ovarian Cancer (TOC-Network) (multizentrisches Projekt)
  - 1. Berliner Symposium „Molecular biology“
- **2005-2010**
  - Translationale Forschungsprojekte
  - I-IV. Berlin International Symposium Molecular biology
  - 5. International Symposium Molecular biology (2009)
  - Etablierung von Audits und Zertifizierung (2009)
  - EUROC – European network for translational research in ovarian cancer





# Recruitment

Start: 19.04.2004 / Status: 15.11.2011



European Network for Translational Research in Ovarian Cancer

## Top Center

1. Berlin Charité, GER
2. Wien, AUS
3. Chisinau/MOD
4. Freiburg, GER
5. Greifswald, GER
6. Bayreuth, GER
7. Cluj-Napoca
8. London, UK
9. Hamburg, GER

**Total**

## Patients

- 1274  
163  
102  
72  
145  
37  
14  
18  
15  
**1867**



Tumor bank Ovarian Cancer Network  
advancing in understanding ovarian cancer

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  - 5. International Symposium Molecular biology, Istanbul (2009)
  - Etablierung von Audits und Zertifizierung (2009)
  - **EUTROC – European network for translational research in ovarian cancer**



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**EUTROC DRUG DISCOVERY**

Optimize the development of targeted therapies in ovarian cancer

**PRECLINICAL CLINICAL DRUG DISCOVERY**

EUTROC is a leading European interdisciplinary network including scientists with high expertise in: patient care, pathology, translational research, epigenomics, molecular biology, bioinformatics, drug development, aiming to reduce fragmentation in clinical management and translational research in ovarian cancer.

[Read more »](#)

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**Vice President:** J. Sehouli, MD, PhD, Prof.  
**Executive officer:** J. Green, MD, PhD  
**Treasurer:** E.I. Braicu, MD

<b>Office</b> Berlin, Germany <b>Coordinator:</b> E.I. Braicu, MD	<b>Office</b> London, UK
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**WG1: Education**  
Leader: J. Green, MD, PhD

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Leader: I. Vergote, MD, PhD, Prof.

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Leader: Ch. Fotopoulou, MD, PhD

**WG 7: Biostatistics and Bioinformatics**  
Leader: R. Agarwal, MD, PhD

**WG8: Dissemination and exploitation**  
Leader: F. Esposito, MD, PhD, Prof.

**WG 9: Quality management**  
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European Network for Translational Research in Ovarian Cancer

News:

**TOC**  
Tumor bank Ovarian Cancer Network advancing in understanding ovarian cancer

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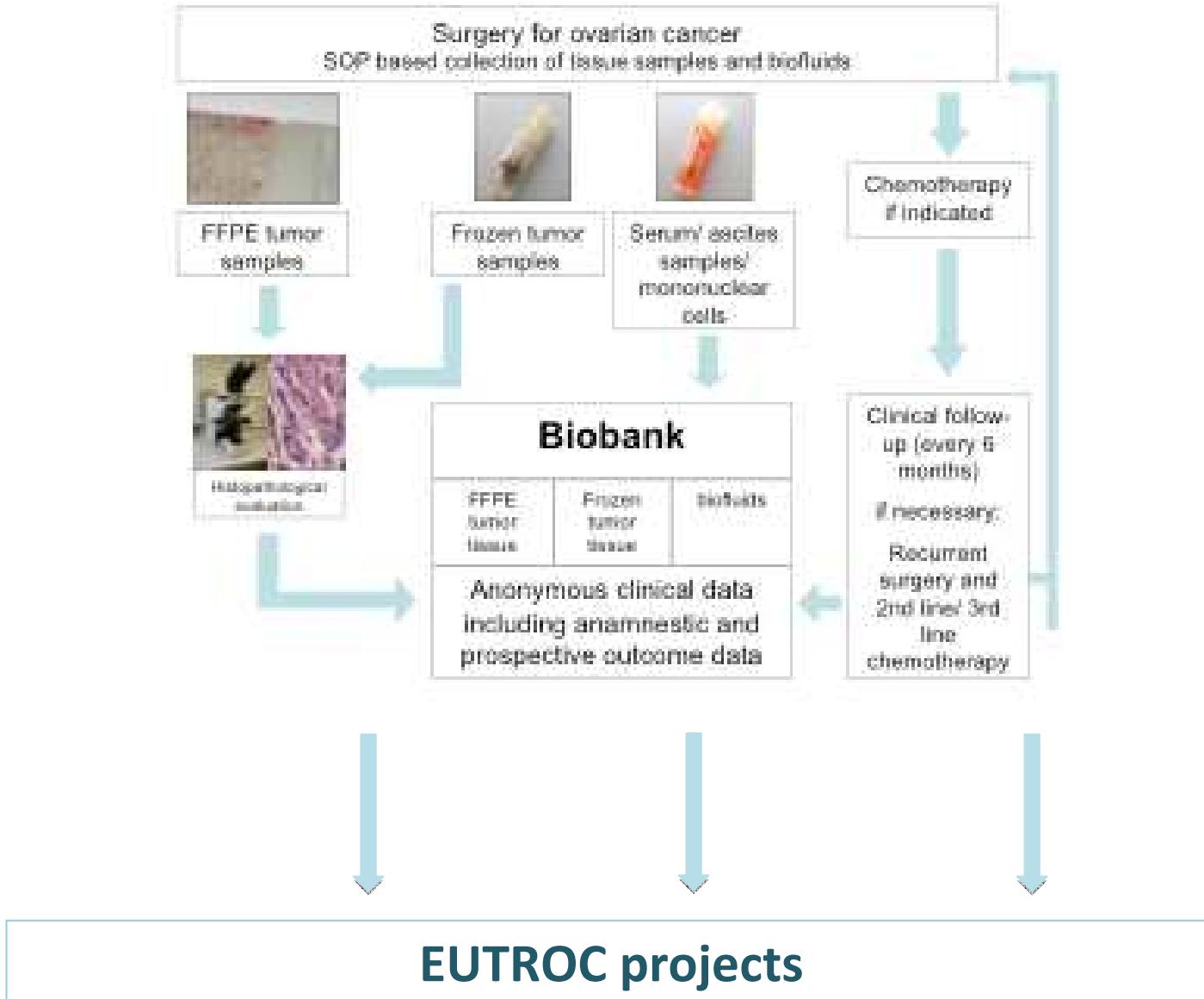
**Centers**

- Universitätsklinikum Charité Berlin
- Medizinische Universität Wien
- Imperial College London

**Tumor bank Ovarian Cancer Network (TOC)**  
advancing in understanding ovarian cancer

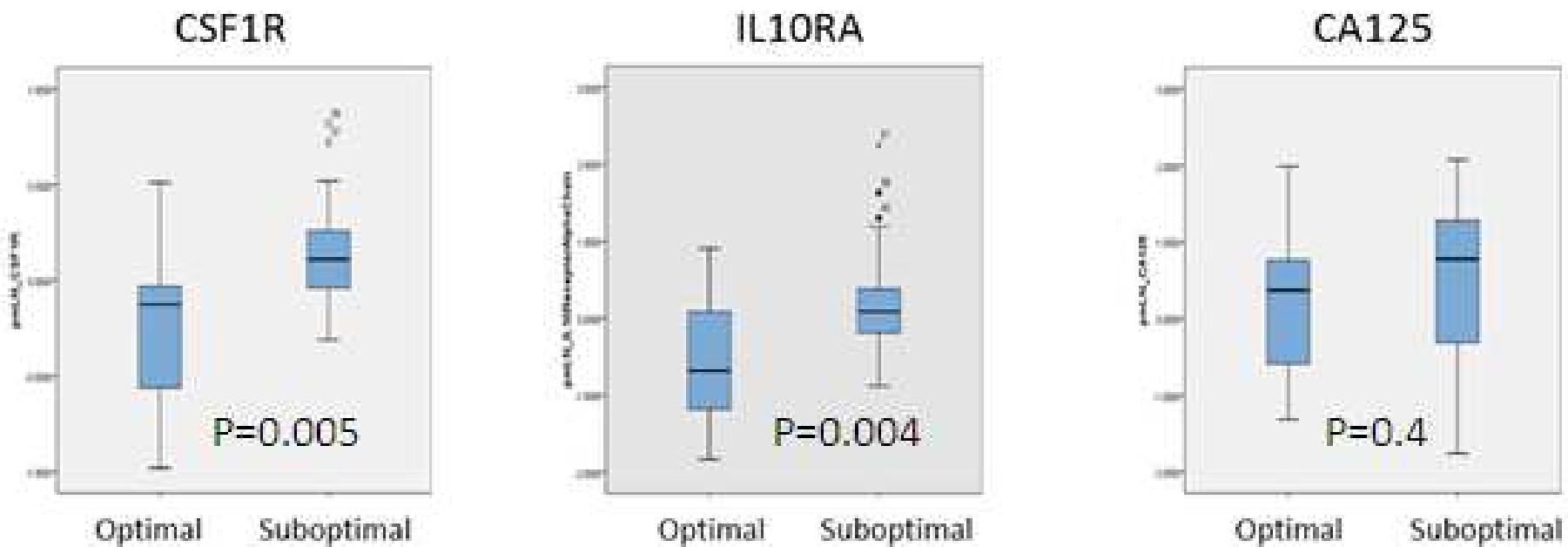
Koordination: Dr. Ioana Braicu, Dr. Radislav Chekerov, Dr. Gülen Oksay-Ozcelik

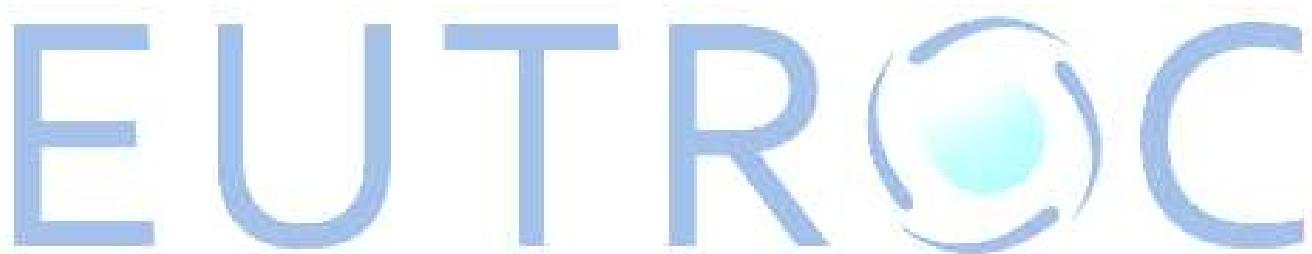
[www.eutroc.org](http://www.eutroc.org)



# Aktuelle Projekte

**Figure 1** Box plots of serum protein expression in Stage 3/ 4 serous ovarian cancer patients optimally (n=14) and sub-optimally (n=21) debulked





European Network for Translational Research in Ovarian Cancer

## Aktuelle Projekte:

Diagnostik

Operative Therapie

Systemische Therapie

Rezidiv

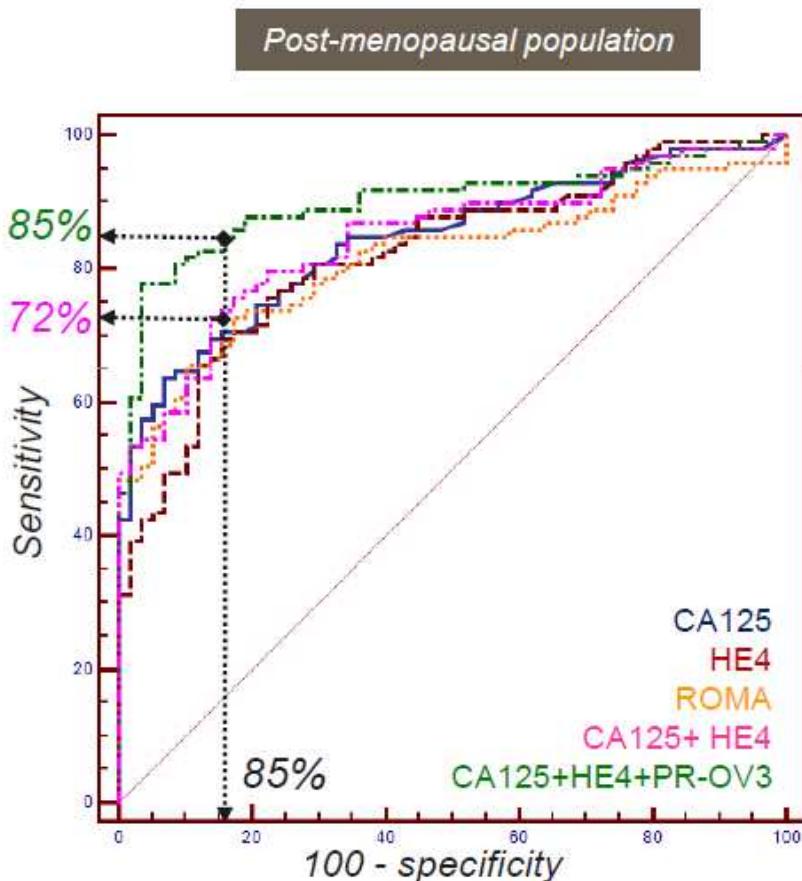


Tumor bank Ovarian Cancer Network

advancing in understanding ovarian cancer

# Biomarker in der Diagnostik des Ov Ca

PR-OV3 systematically adds value to CA125 - HE4



KATHOLIEKE UNIVERSITEIT  
**LEUVEN**

Post menopausal women	AUC	Significance of improvement*
CA125 (central lab)	0.84 (0.78-0.90)	na
CA125 + PR-OV3	0.88 (0.82-0.92)	0.069
HE4 (Fujirebio/BD/Roche)	0.82 (0.75-0.88)	na
HE4 + PR-OV3	0.89 (0.83-0.94)	0.006
ROMA test	0.82 (0.75-0.87)	na
CA125 + HE4	0.85 (0.78-0.90)	na
CA125 + HE4 + PR-OV3	0.90 (0.84-0.94)	0.011

250 Ov Ca  
60 BOT  
100 benigne Tumore  
40 Metastasen

\*by adding PR-OV3

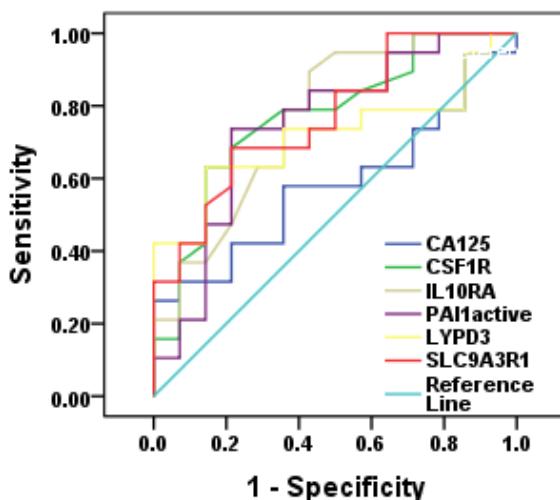
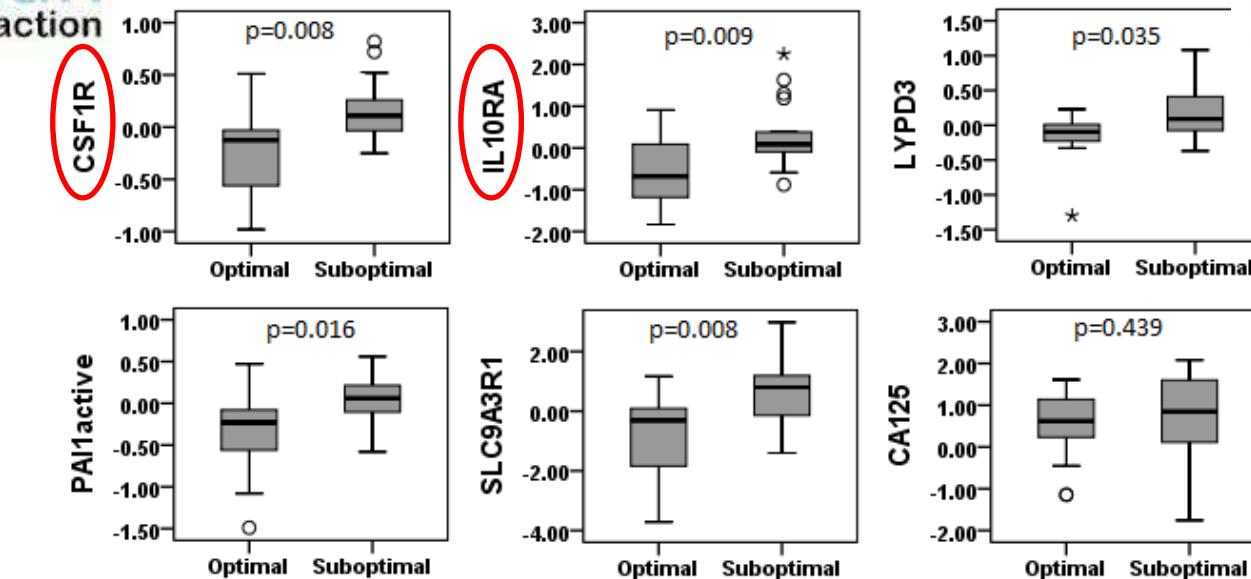
Charité

# Predicting optimal debulking in ovarian cancer: tumour bulk or biology?



Imperial College London

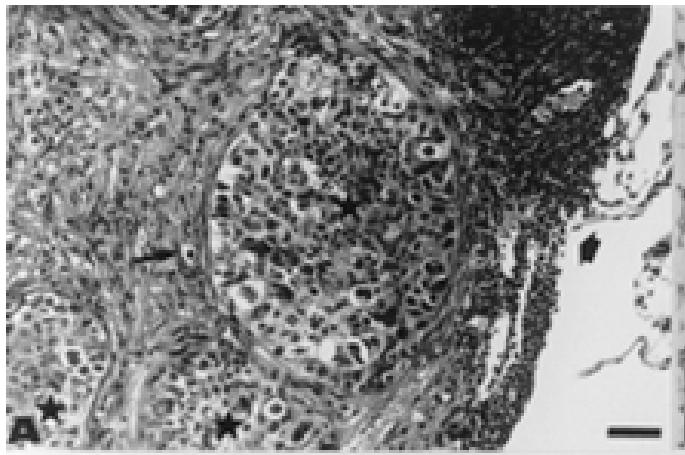
*charité*



Markers	Area	Std. Error <sup>a</sup>	p-value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
CA125	.583	.100	.423	.387	.779
CSF1R	.771	.084	.009	.605	.936
IL10RA	.767	.086	.010	.599	.935
PAI1active	.748	.091	.016	.571	.926
LYPD3	.718	.090	.035	.541	.895
SLC9A3R1	.769	.082	.009	.608	.929

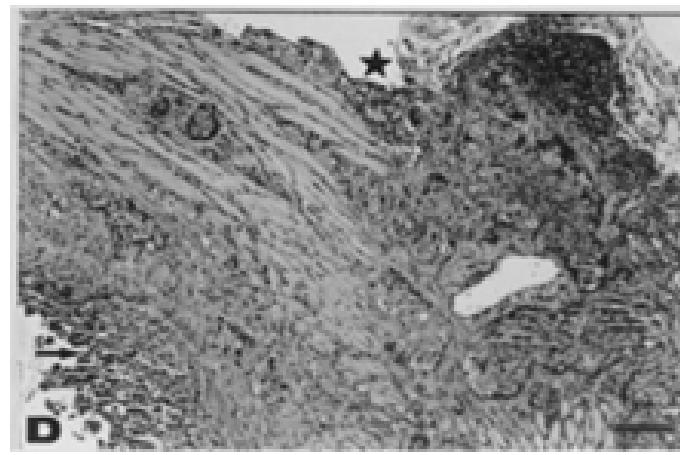
# CSF1R and *in vivo* metastasis

CSF1R LOW



Encapsulated

CSF1R HIGH

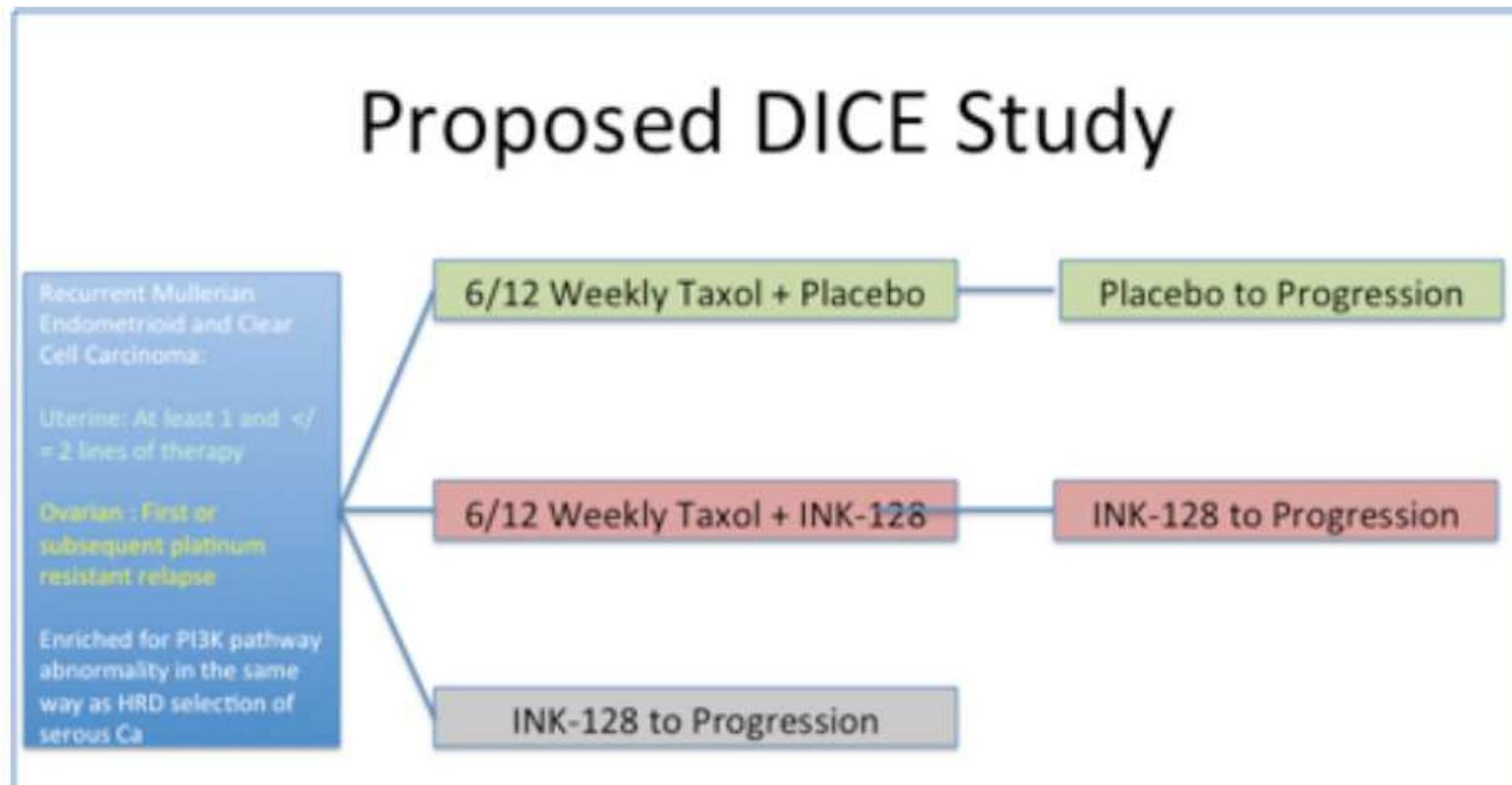


Infiltrative

Colony stimulating factor 1 receptor  
(CSF1R)

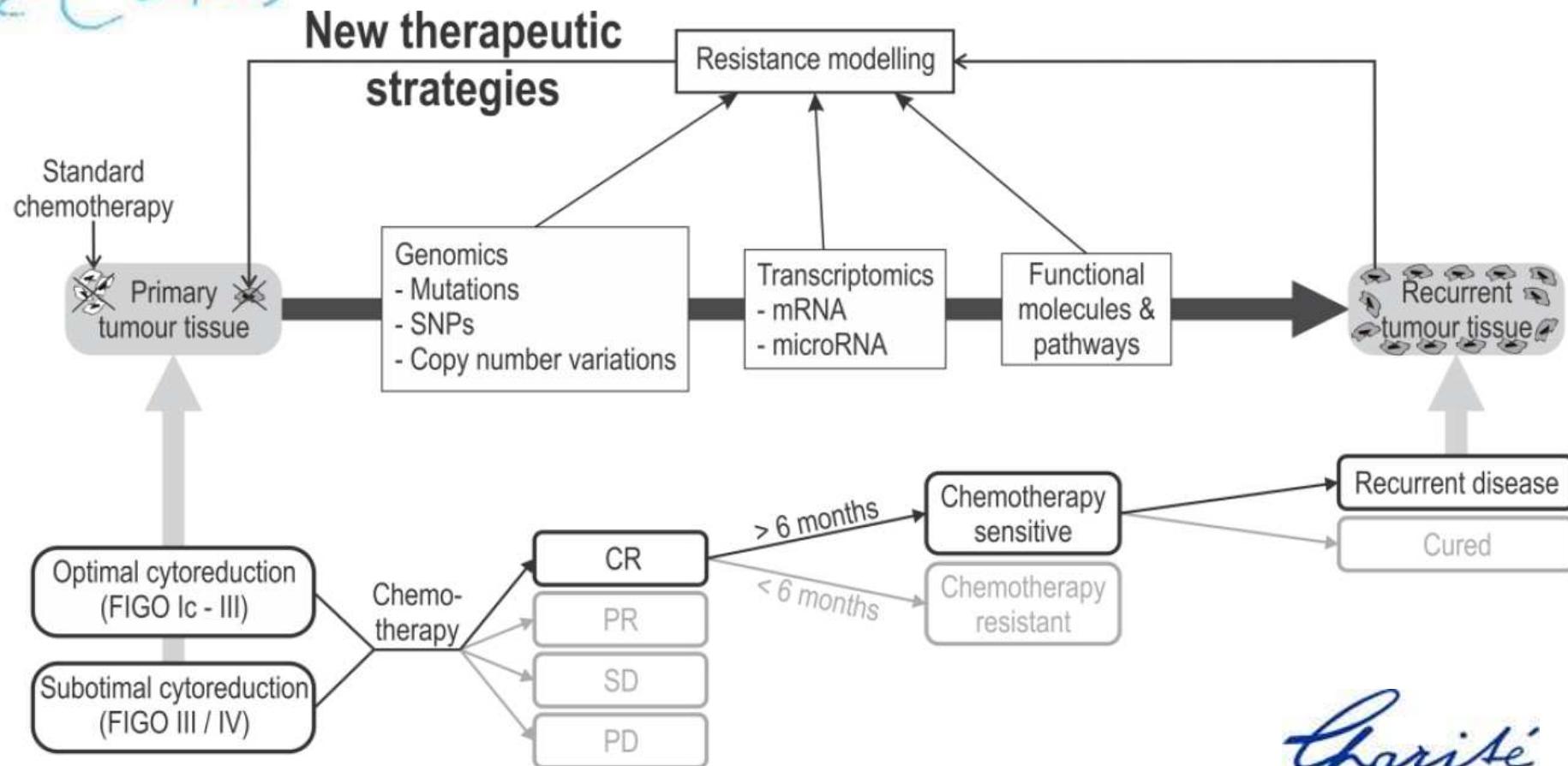
Toy et al. 2009, Neoplasia

# Zielgerichtete Therapien: mTOR Kaskade



INK128: oraler selektiver TORC1/2 Inhibitor

# OCTIPS



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# Individualisierte Medizin?

