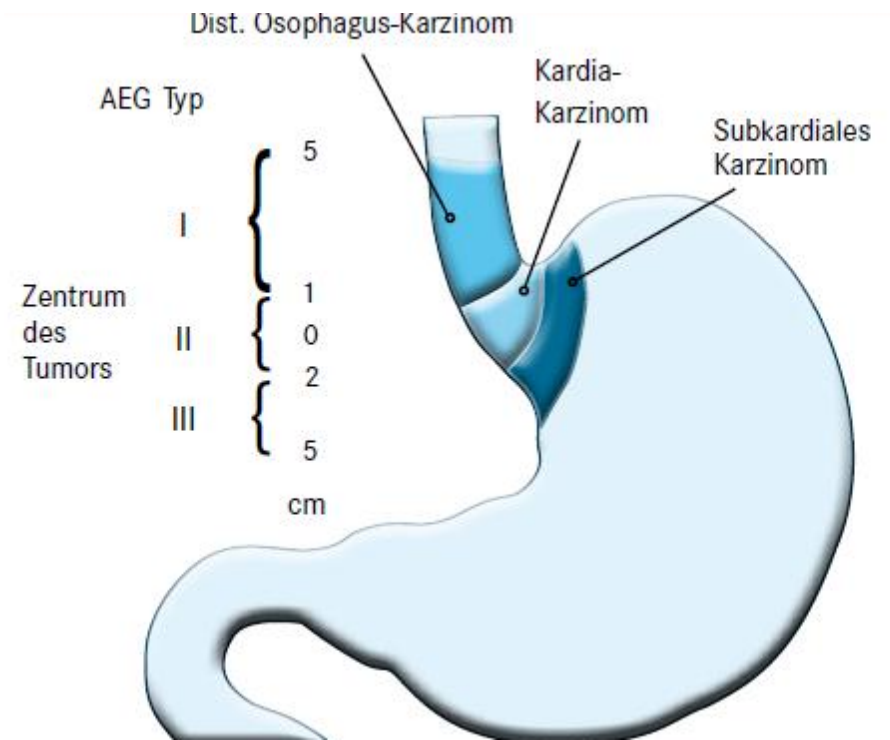


Perioperative Therapie des Magenkarzinoms – immer noch MAGIC?



PD Dr. Salah-Eddin Al-Batran
Klinik für Hämatologie und
Onkologie am
Krankenhaus Nordwest
Frankfurt am Main

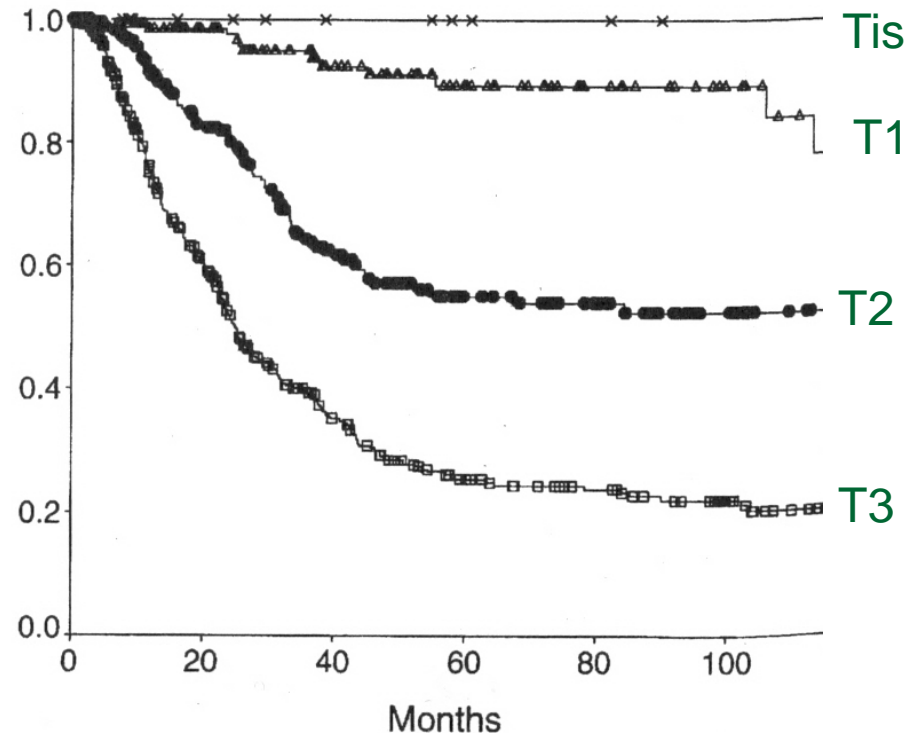
Einführung



AEG Siewert Klassifikation

Prognose Faktoren

- T-Kategorie
- N-Kategorie
- Resektionsstatus
 - (R0 vs. R1/2)

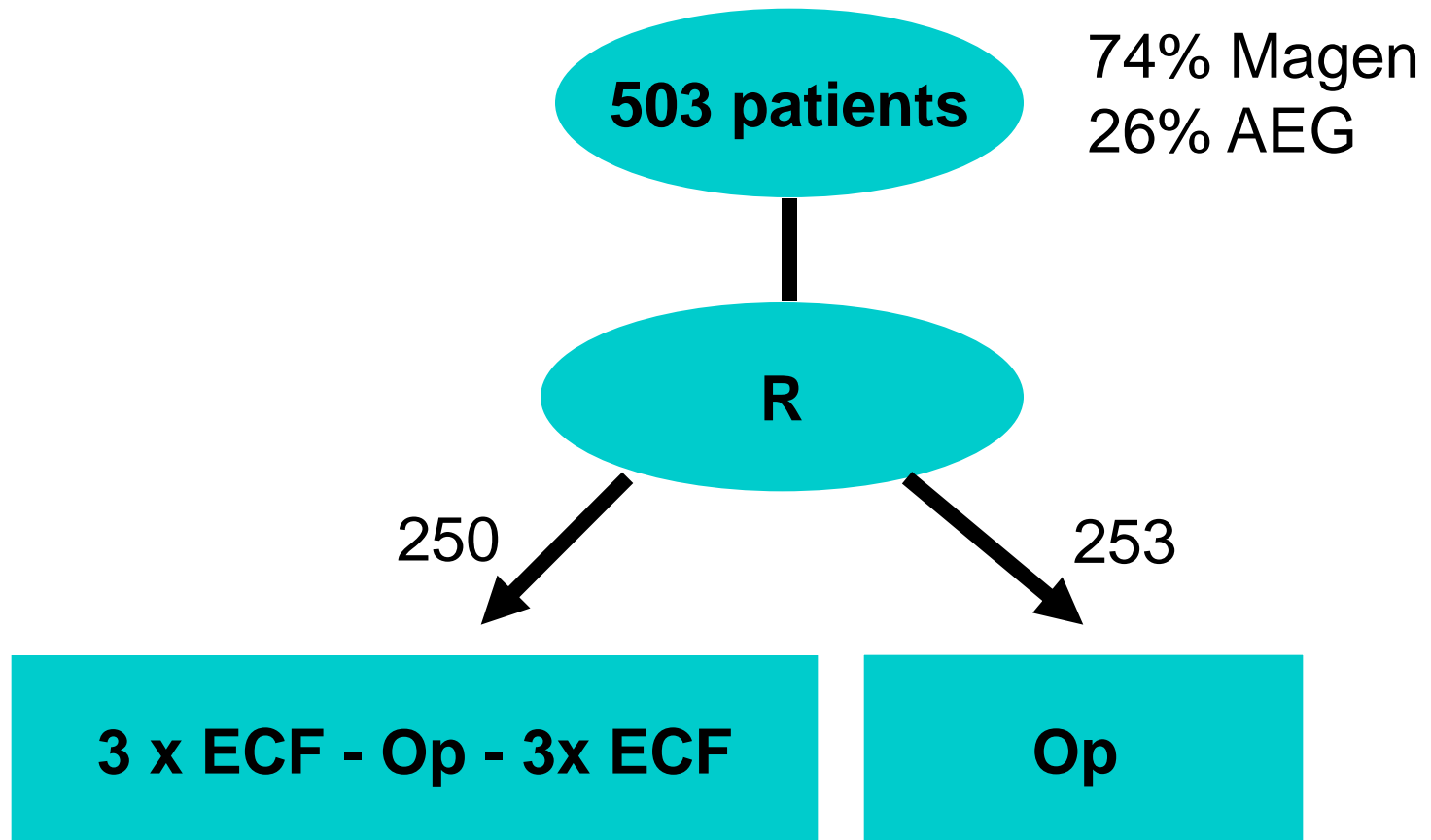


Überleben nach T-Kategorie

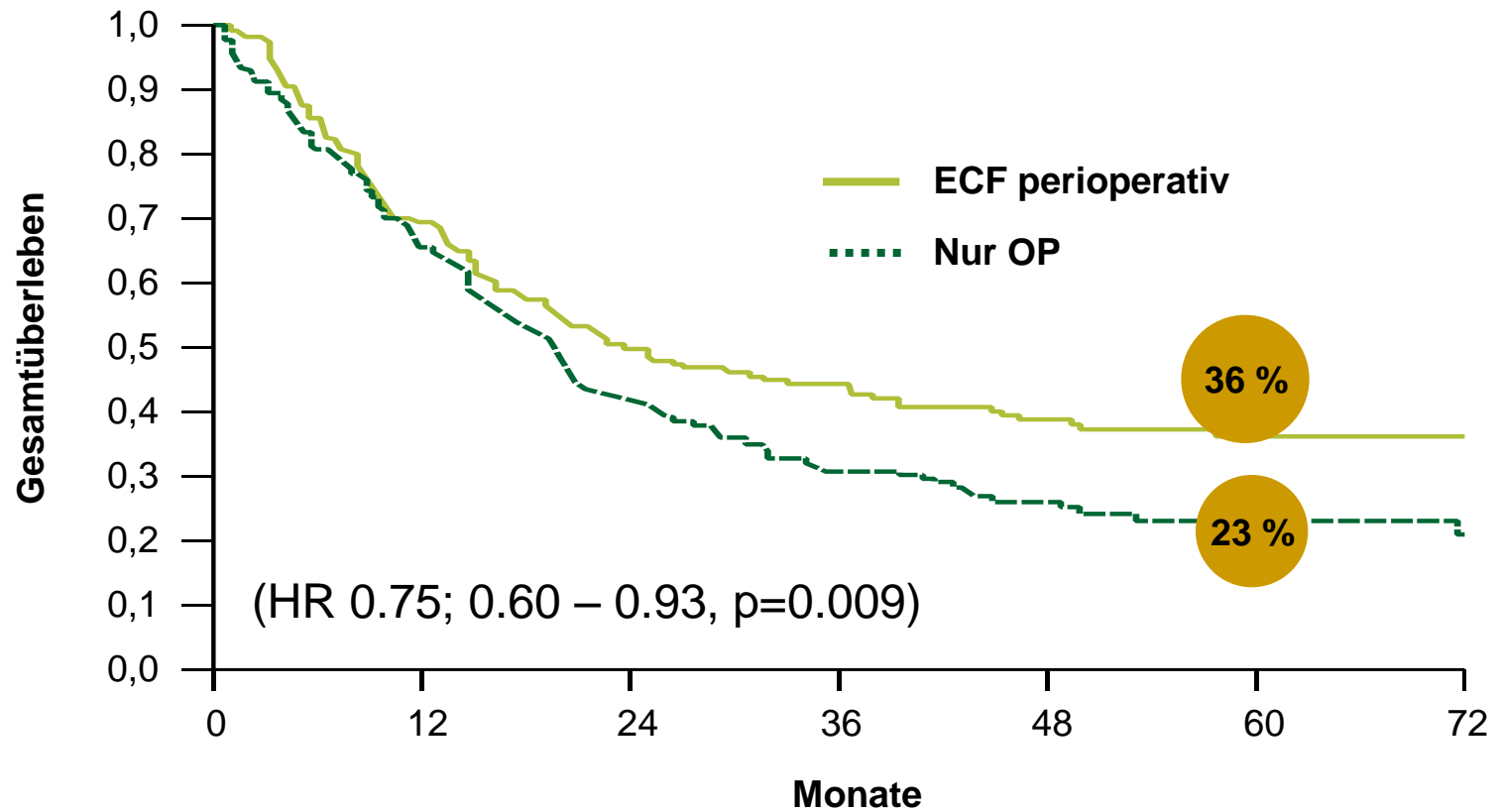


Multimodale Ansätze
bei T3 oder N+ =
UICC II oder III

MAGIC Studie



MAGIC Studie: OS



MAGIC: keine Erhöhung der postoperativen Komplikationsrate

| | CSC | S |
|------------------------------|---------|---------|
| Postoperative Todesfälle | 6% | 6% |
| Postoperative Komplikationen | 46% | 46% |
| KH-Aufenthalt [Median] | 13 Tage | 13 Tage |

Perioperative Therapie Magen-/AEG: 3 randomisierte Phase-III-Studien

- UK: MAGIC (n=503)
- Frankreich: ACCORD / FFCD (n=224)
- Deutschland (EU): EORTC 40954 (n=144)

Cunningham D et al. *N Engl J Med* 2006;355:11-20

Boige V. et al. ASCO 2007 #4510

Schuhmacher C. et al. ASCO 2009 #4510

MAGIC – FFCD – EORTC

| Studie | N | Lokalisation | Schema | Setting | HR OS | Δ OS* |
|---------------------------------|-----|---|--------|--------------------------------|-----------------------|--------------|
| MAGIC 2006 | 503 | Magen 74 % Kardia 12 % Ösoph. 14% | ECF | 9w vor + 9w nach OP | 0,75 (0,60 - 0,93) | 13 % |
| ACCORD 9703 2007 | 224 | Magen 25% Kardia 65% Ösoph.10% | CF | 8w vor + ggf. 8w nach OP | 0,69 (0,50 - 0,96) | 14 % |
| EORTC 2009 | 114 | Magen 47% Kardia 53% Ösoph. - | PLF | 12w vor OP | 0,84 (0,52 - 1,35) | - |

* Δ OS nach 5 Jahren

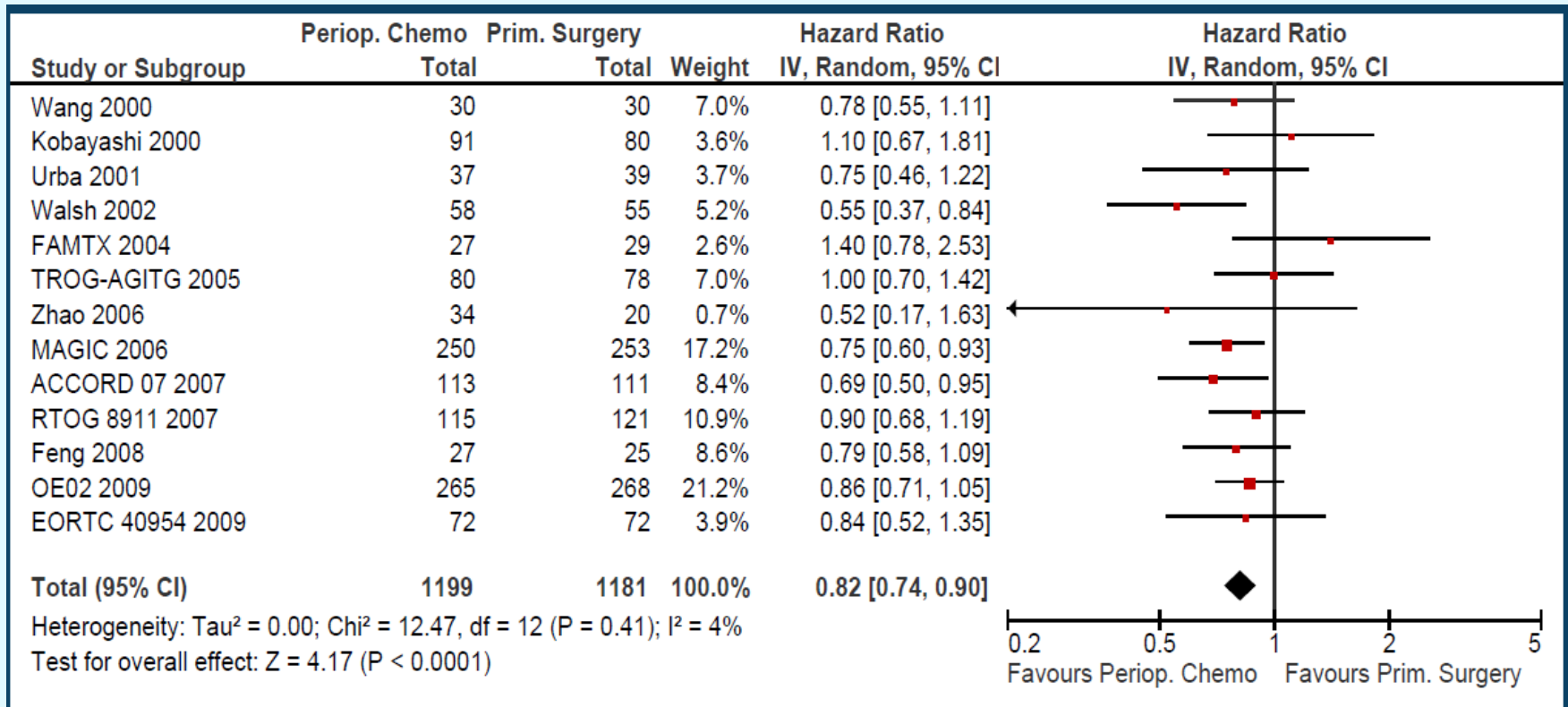
Cunningham D et al. *N Engl J Med* 2006;355:11-20

Boige V. et al. ASCO 2007 #4510

Schuhmacher C. et al. ASCO 2009 #4510

Ronellenfitsch et al. ASCO 2010

Meta-analysis of preoperative chemotherapy (CTX) versus primary surgery for locoregionally advanced adenocarcinoma of the stomach, gastroesophageal junction and lower esophagus (GE adenocarcinoma)



Ronellenfitsch et al. ASCO 2010

ösophogastraler Übergang

| | | | | |
|-------------------|-----|-----|--------|-------------------|
| Wang 2000 | 30 | 30 | 29.5% | 0.78 [0.55, 1.11] |
| Urba 2001 | 0 | 0 | | Not estimable |
| Walsh 2002 | 23 | 16 | 9.4% | 0.35 [0.15, 0.80] |
| MAGIC 2006 | 28 | 30 | 23.3% | 0.61 [0.39, 0.94] |
| ACCORD 07 2007 | 0 | 0 | | Not estimable |
| RTOG 8911 2007 | 47 | 46 | 22.2% | 1.06 [0.67, 1.69] |
| OE02 2009 | 0 | 0 | | Not estimable |
| EORTC 40954 2009 | 37 | 39 | 15.6% | 0.71 [0.39, 1.30] |
| Subtotal (95% CI) | 165 | 161 | 100.0% | 0.72 [0.54, 0.96] |

Heterogeneity: $\text{Tau}^2 = 0.04$; $\text{Chi}^2 = 6.41$, $\text{df} = 4$ ($P = 0.17$); $I^2 = 38\%$

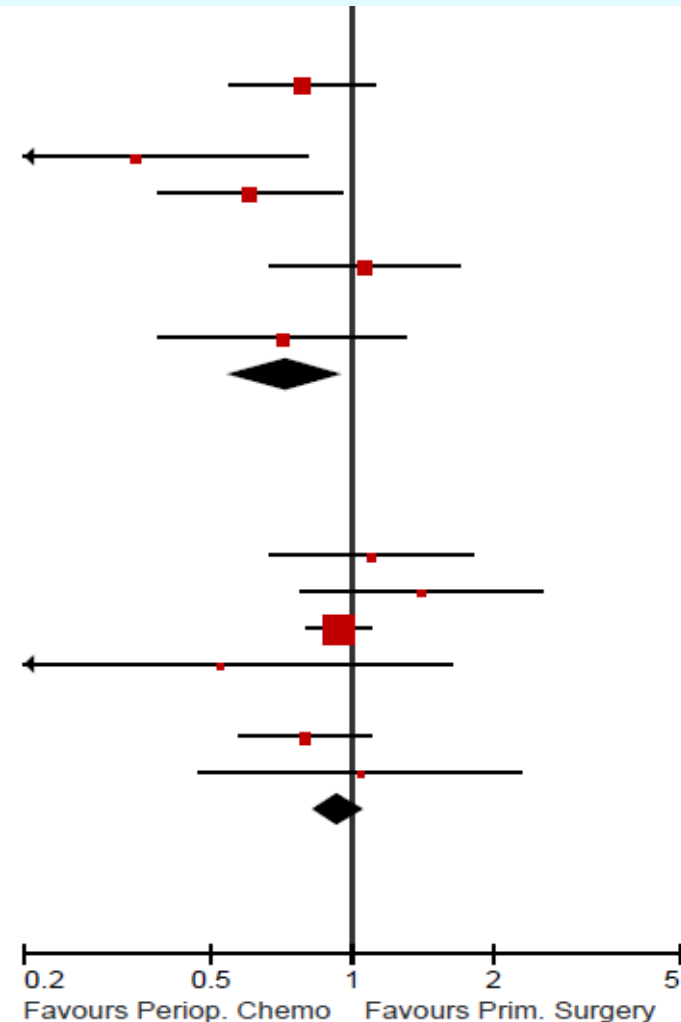
Test for overall effect: $Z = 2.27$ ($P = 0.02$)

Magen

| | | | | |
|-------------------|-----|-----|--------|-------------------|
| Kobayashi 2000 | 91 | 80 | 6.7% | 1.10 [0.67, 1.81] |
| FAMTX 2004 | 27 | 29 | 4.8% | 1.40 [0.78, 2.53] |
| MAGIC 2006 | 185 | 187 | 68.2% | 0.94 [0.80, 1.09] |
| Zhao 2006 | 34 | 20 | 1.3% | 0.52 [0.17, 1.63] |
| ACCORD 07 2007 | 0 | 0 | | Not estimable |
| Feng 2008 | 27 | 25 | 16.4% | 0.79 [0.58, 1.09] |
| EORTC 40954 2009 | 35 | 33 | 2.7% | 1.04 [0.47, 2.29] |
| Subtotal (95% CI) | 399 | 374 | 100.0% | 0.93 [0.82, 1.06] |

Heterogeneity: $\text{Tau}^2 = 0.00$; $\text{Chi}^2 = 4.37$, $\text{df} = 5$ ($P = 0.50$); $I^2 = 0\%$

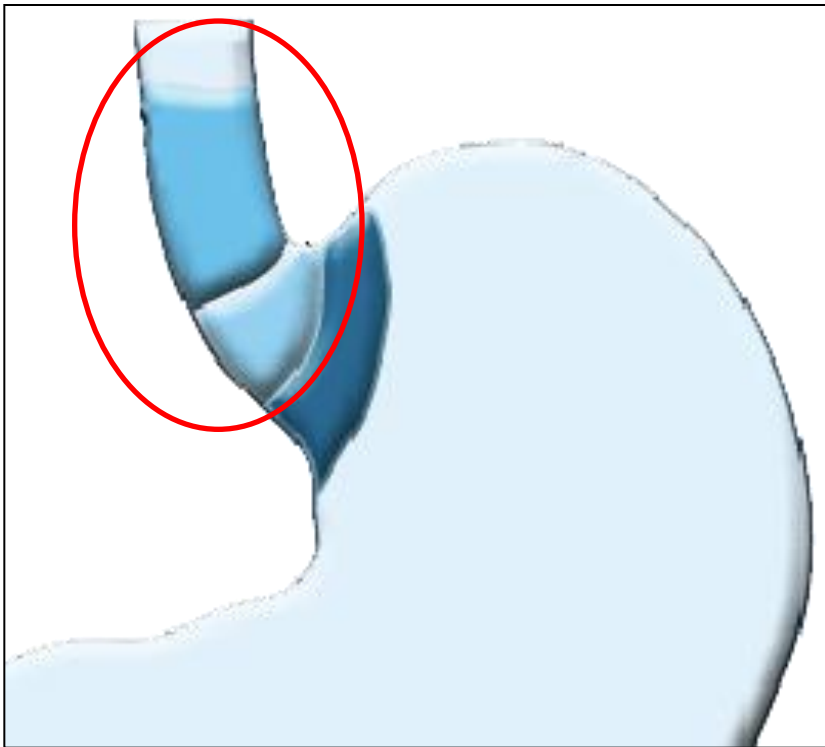
Test for overall effect: $Z = 1.03$ ($P = 0.30$)



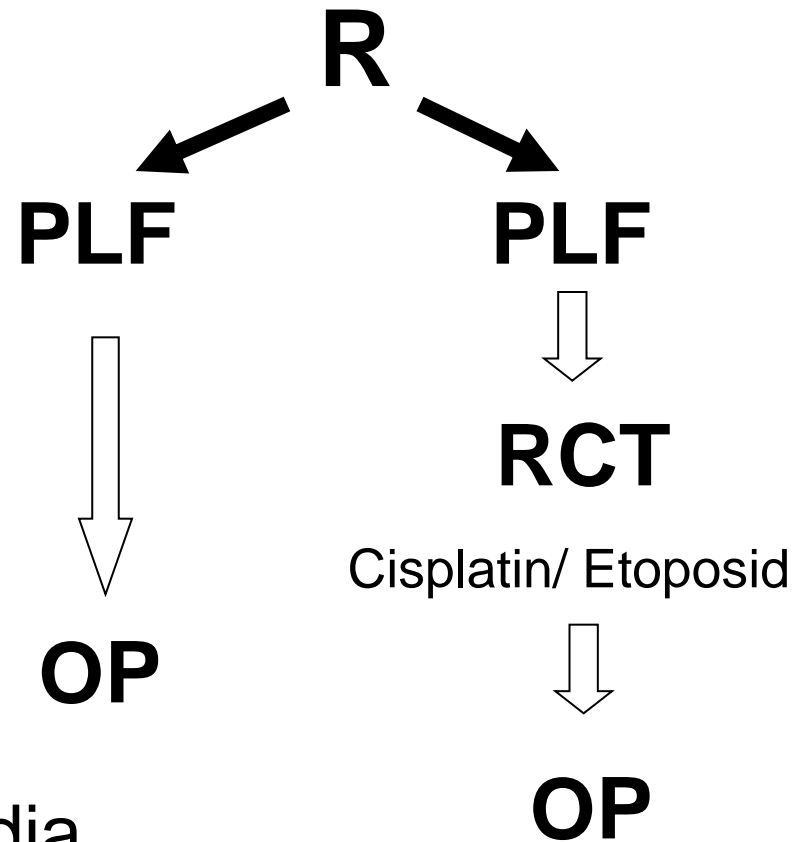
Rolle der additiven Radiotherapie?

Rolle der additive Radiotherapie?

POET Studie



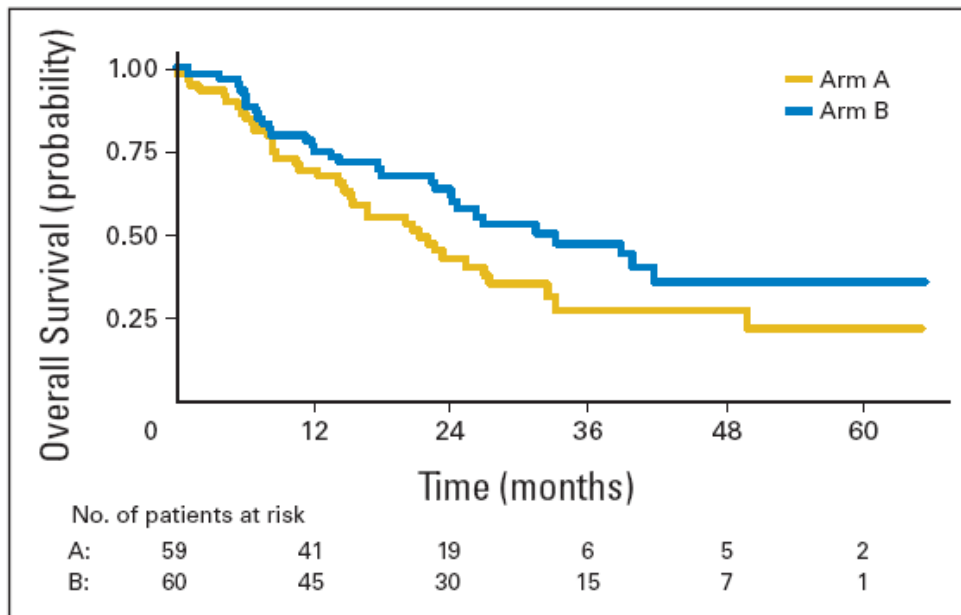
N=126 dist. Ösophagus/Kardia
AEG I oder II



Chemotherapie oder Chemoradiotherapie?

POET Studie

Gesamtüberleben



Arm Chemotherapie:
medianes Überleben 21,1 Mo,
3-Jahres Überleben 27,7%

Arm Chemoradiotherapie:
medianes Überleben 33,1 Mo
3-Jahres Überleben 47,7%

P = 0.07

Postoperative Letalität
3.8% vs. 10.2%

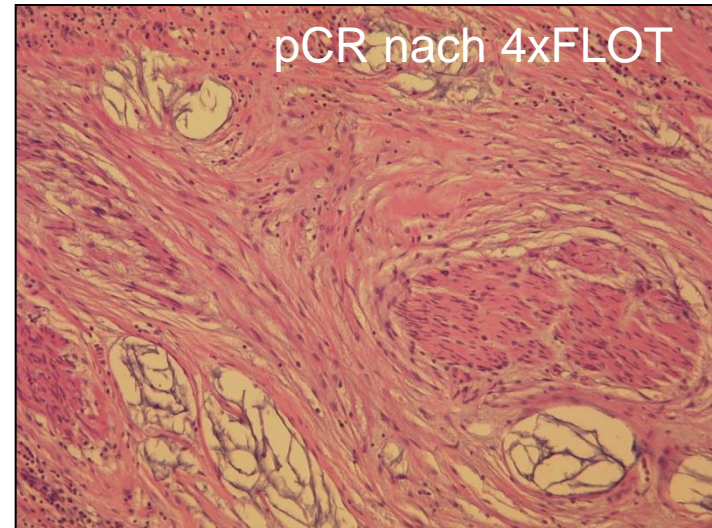
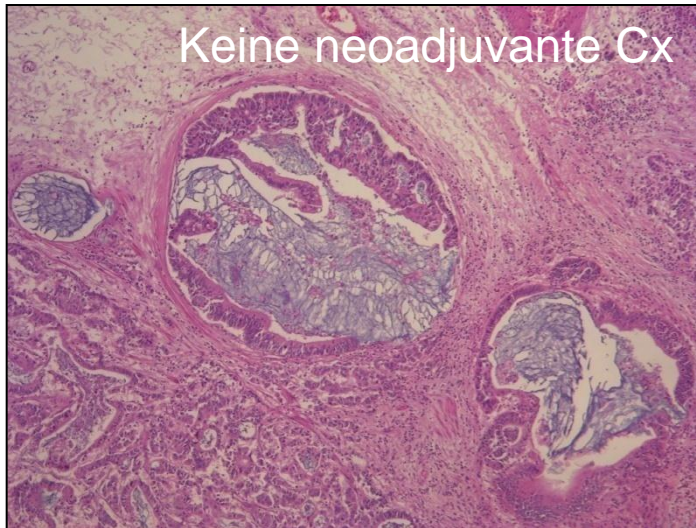
Rolle der molekular-gezielten Therapie?

Auswahl randomisierter Studien zur molekular-gezielten Therapie

| Ziel | Akronym | Design | n |
|------|--------------|---------------------------|------|
| VEGF | MAGIC 2 | 3x/3x ECX +/- Bevacizumab | 1100 |
| EGFR | AIO CAO 0108 | 3x/3x ECX +/- Panitumumab | 150 |

Rolle der Chemotherapie- Intensivierung?

Histopathologische Remission



Grading of Histopathologic Regression in the Primary Tumor Bed

| Grade | Description |
|-------|---------------------------------|
| 1a | No residual tumor/tumor bed |
| 1b | < 10% residual tumor/tumor bed |
| 2 | 10-50% residual tumor/tumor bed |
| 3 | > 50% residual tumor/tumor bed |

36 Patienten erhielten 4x
Etoposid/Doxorubicin/Cisplatin
1a → 0 Patienten

➔ **ECF ?**

A phase II trial of preoperative chemotherapy with epirubicin, cisplatin and capecitabine for patients with localised gastro-oesophageal junctional adenocarcinoma

N Starling¹, A Okines¹, D Cunningham^{*.1}, W Allum², A Wotherspoon³, M Benson¹, J Thompson², J Thomas¹, G Brown⁴, A Riddell⁴, F Stavridi¹, S Ashley⁵, J Oates¹ and I Chau¹

¹Department of Medicine, Royal Marsden Hospital NHS Foundation Trust, Surrey and London, UK; ²Department of Surgery, Royal Marsden Hospital NHS Foundation Trust, Surrey and London, UK; ³Department of Histopathology, Royal Marsden Hospital NHS Foundation Trust, Surrey and London, UK; ⁴Department of Radiology, Royal Marsden Hospital NHS Foundation Trust, Surrey and London, UK; ⁵Department of Computing and Statistics, Royal Marsden Hospital NHS Foundation Trust, Surrey and London, UK

34 Patienten erhielten 4x ECX → Operation
pCR bei 5.9%

Pathologische Komplettremission mit Docetaxel-basierten 3-Fachkombinationen

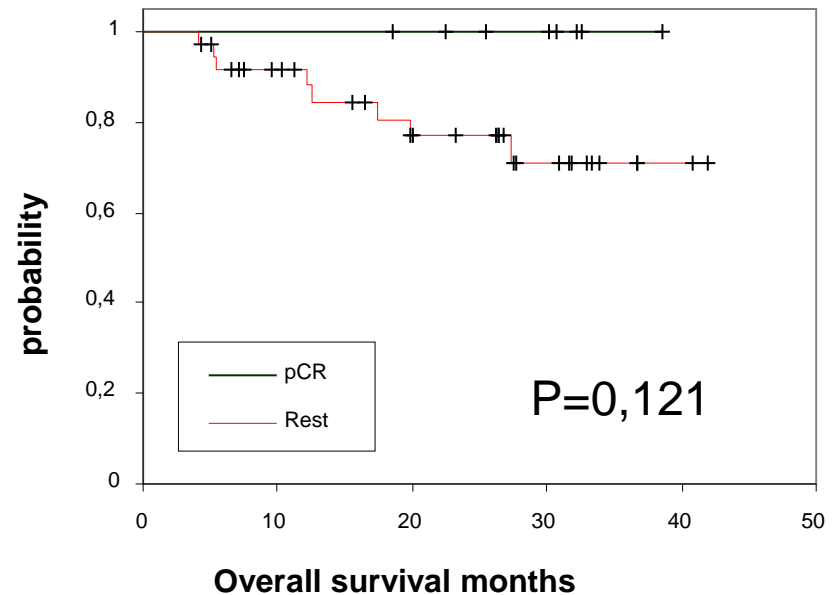
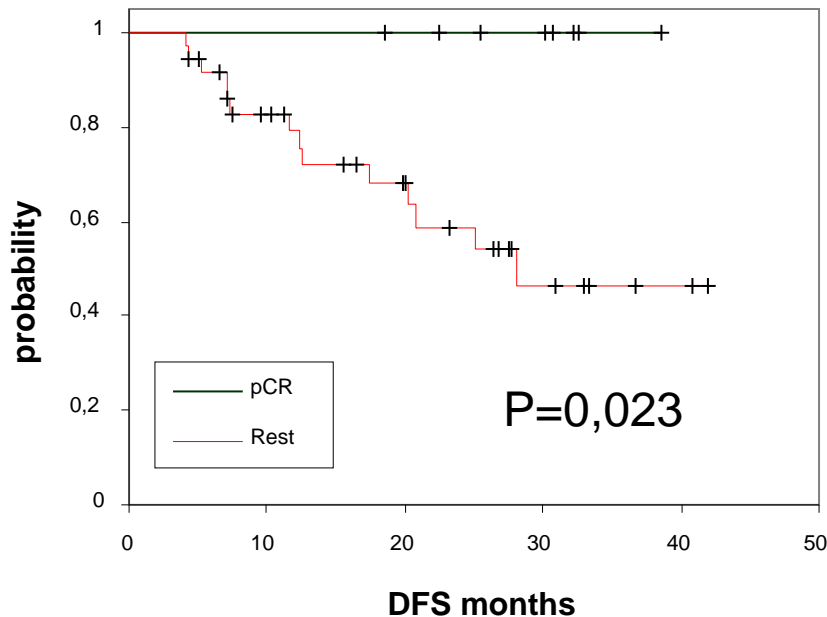
| Autor | N | Schema | pCR* n(%) |
|---------------------|----|--------------------------------------|-----------------|
| Lorenzen 2008 | 24 | Cisplatin/5-FU/Docetaxel (GastroTax) | 4 (17,4) |
| Al-Batran 2008 | 46 | Oxaliplatin/5-FU/Docetaxel (FLOT) | 8 (17,4) |
| Thuss-Patience 2010 | 44 | Cisplatin/Cape/Docetaxel (DCX) | 7 (15,9) |

* Rate pathologischer Komplettremissionen

Vs. 5.9% mit 4x ECX!

Lorenzen et al. *Ann Oncol* 2008
Al-Batran et al. *DGHO* 2008 *updated
Thuss-Patience et al. *ASCO* 2010
Starling et al. *B J cancer* 2009

DSF und OS bei Patienten mit pCR (Remissionsgrad 1a) versus Rest

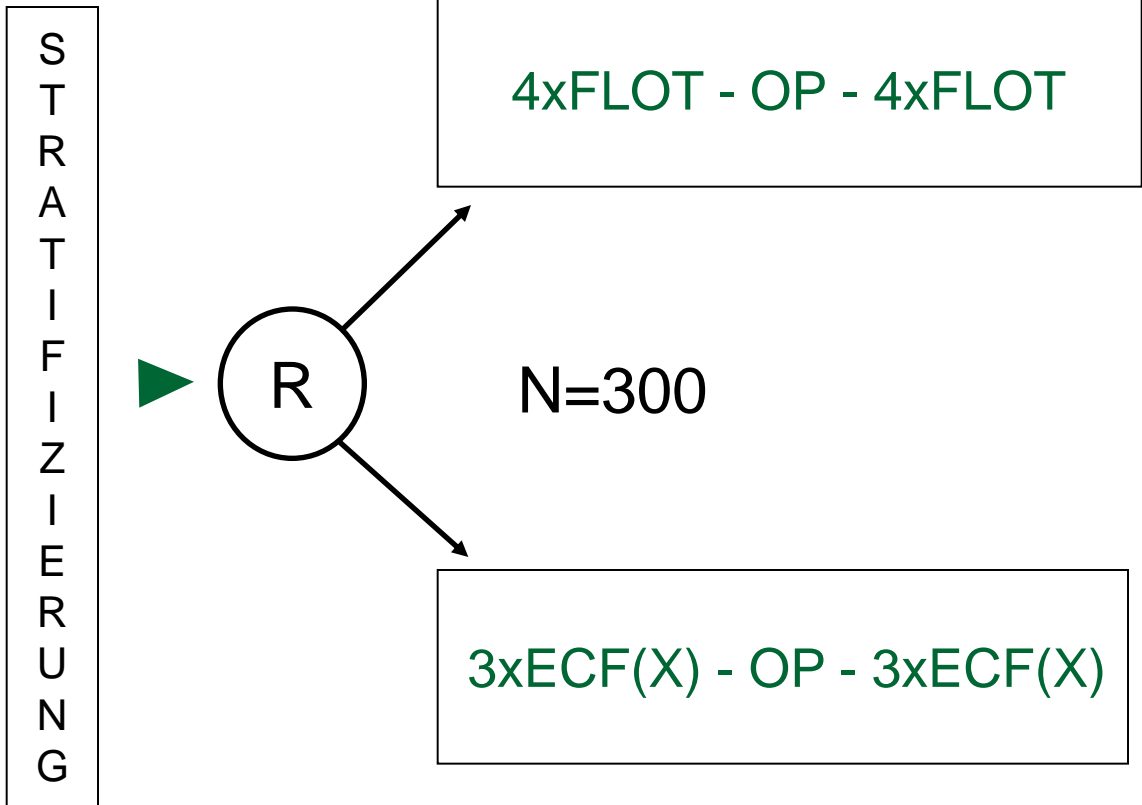


Studiendesign FLOT4

AIO

Phase II/III Studie der AIO

- Operables Magenkarzinom oder AEG
- ECOG ≤ 2
- Adäquate hämatologische/biochemische Parameter
- Keine vorherige Chemotherapie



Primärer Endpunkt: (f. Phase II Part) Rate pathologische Komplettremission (pCR)

Statistik: 80% Power für Unterschied von 5 \rightarrow 15% mit ECF vs. FLOT; $p < .05$ einseitig

Zentrale Pathologie: Prof. Tannapfel, Bochum, Prof. Wittekind, Leipzig

Schlussfolgerung

- Perioperative Therapie Standard
 - 1a Evidenz
 - Kardiakarzinom profitiert besonders
 - Additive Strahlentherapie bei AEG I und evtl. II eine Option
 - Hohe Rate an pCR durch Intensivierung der Chemotherapie mit docetaxel
-

Danke für die Aufmerksamkeit

