# Tumoren der Leber: Update der Therapieoptionen

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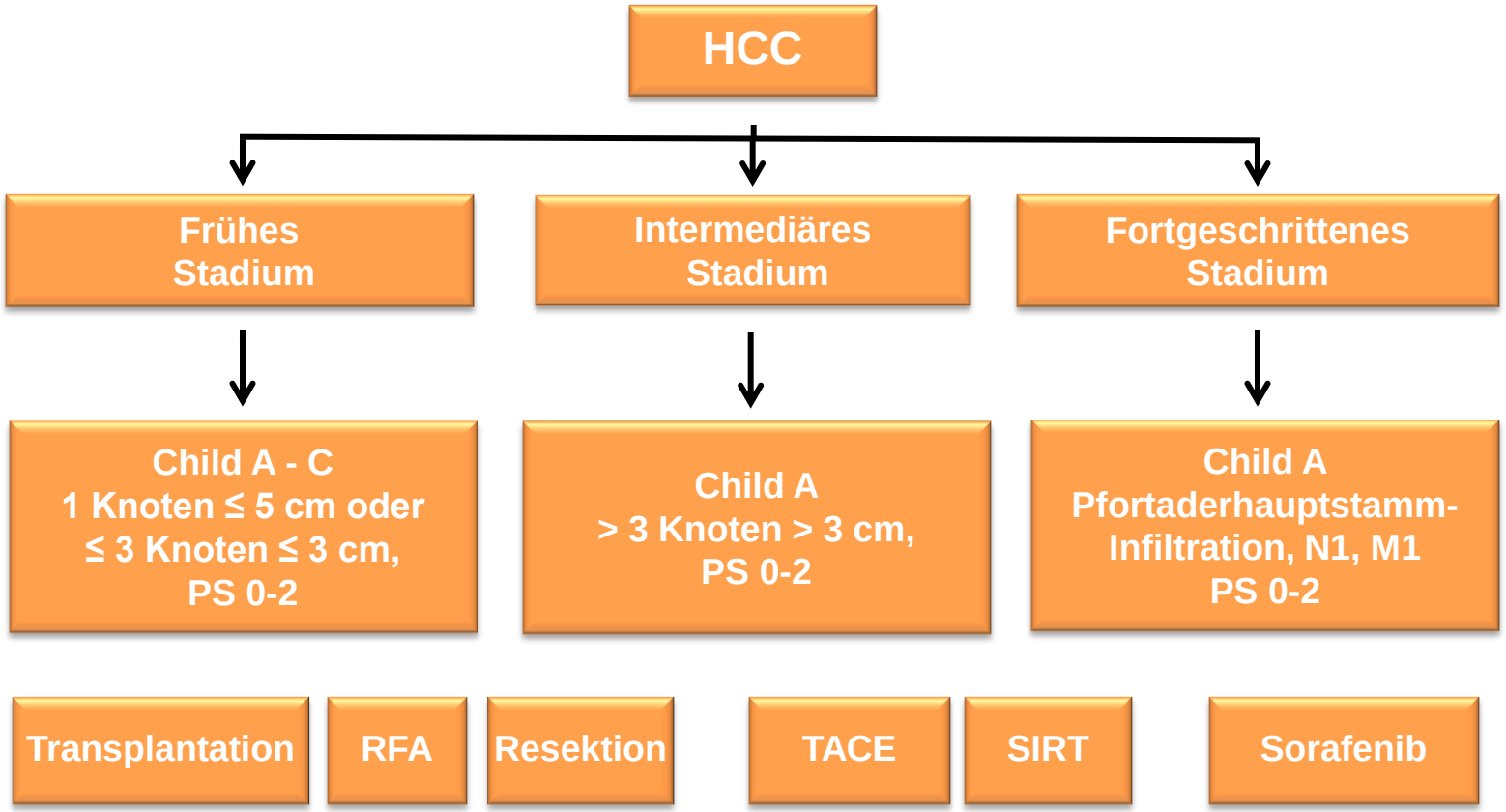
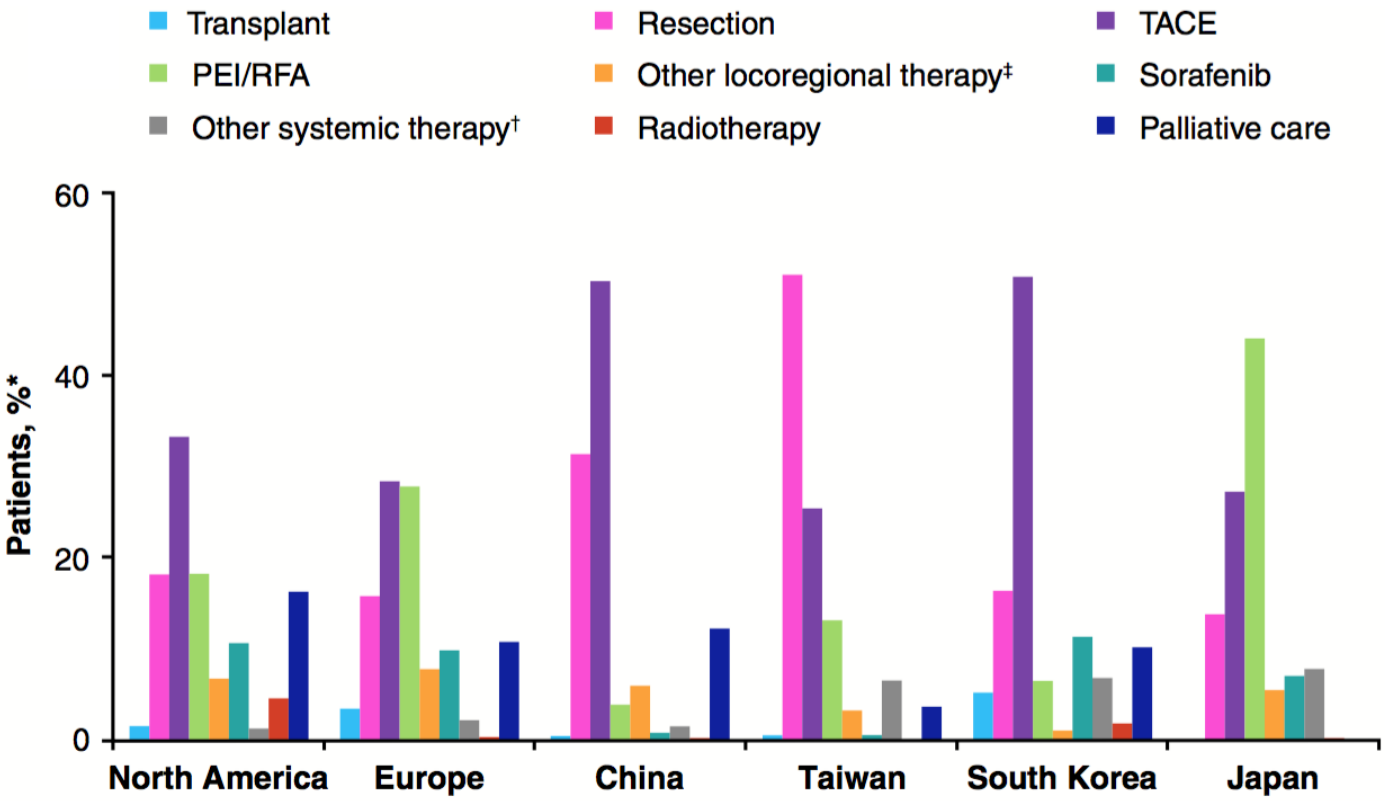
# Therapie des HCC




Vogel und Manns, Dtsch Arztebl 2014

# Wie wird welt-weit behandelt?

BRIDGE Study: 18301 Patienten in 14 Ländern




**Viel TACE, wenig Systemische Therapie!**

Park et al., Liver International2015

# Systemische Therapie des HCC

**10 Jahre**

**1 Substanz**

2007 - 2017

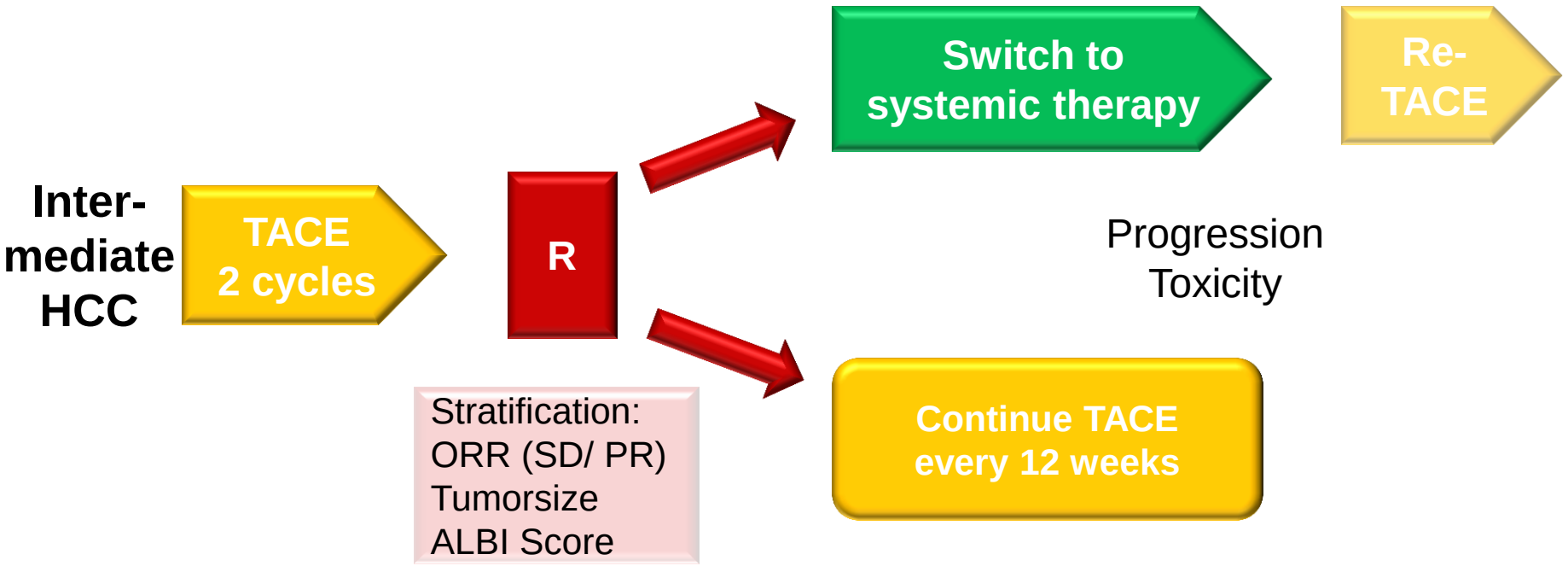
**2 Jahre**

**5 Substanzen!**

2016 - 2018

# TACEnd Phase-II Study

TACE followed by systemic therapy compared to continious TACE in intermediate stage hepatocellular carcinoma (HCC)




Primary Endpoint: OS

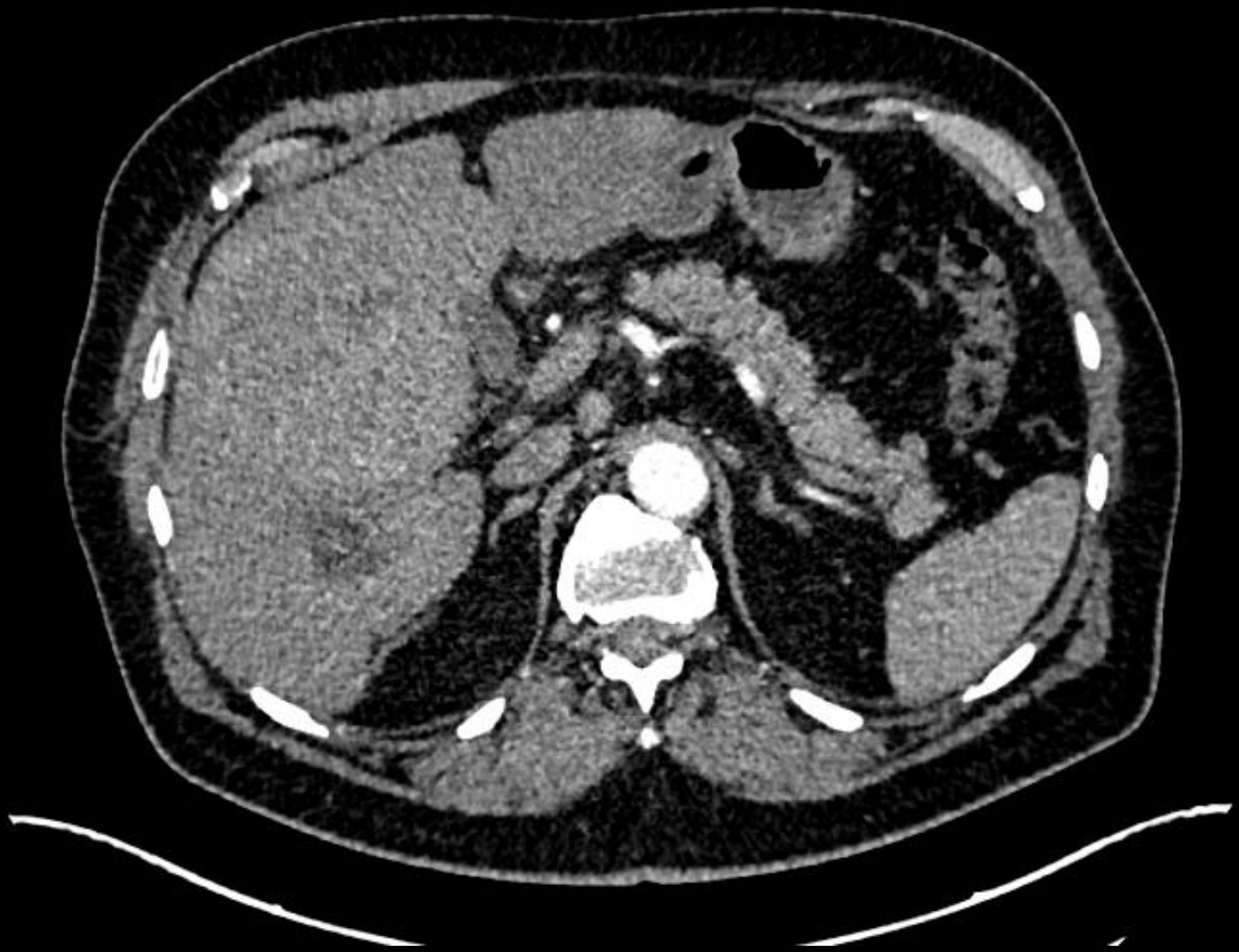
2nd EP: PFS, TTP, ORR, QoL

# Fall – Herr S., 73 Jahre

09/2015 ED pulm.+ lymph. metastasiertes HCC

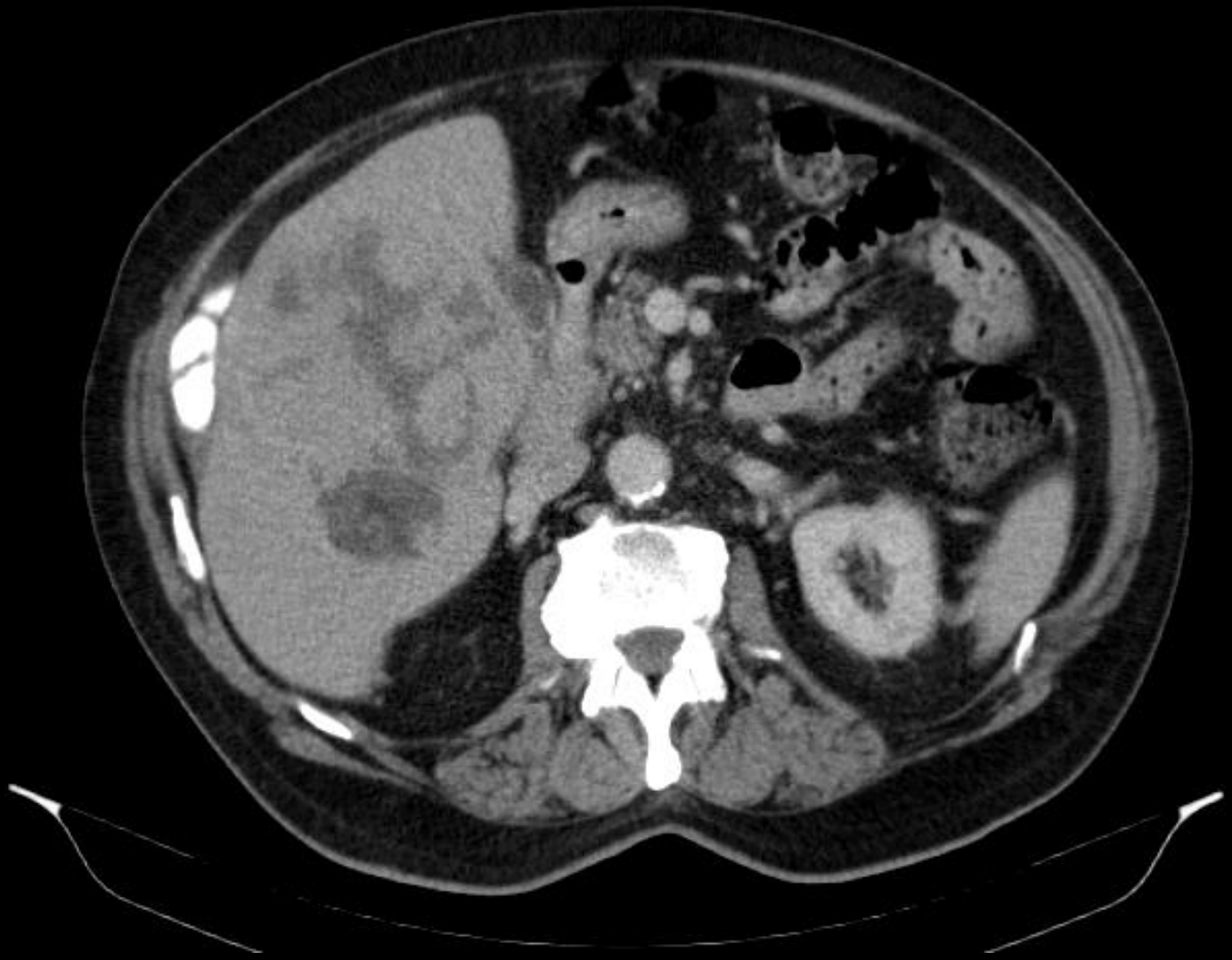
Keine Zirrhose, exzellenter AZ

**09/ 15**



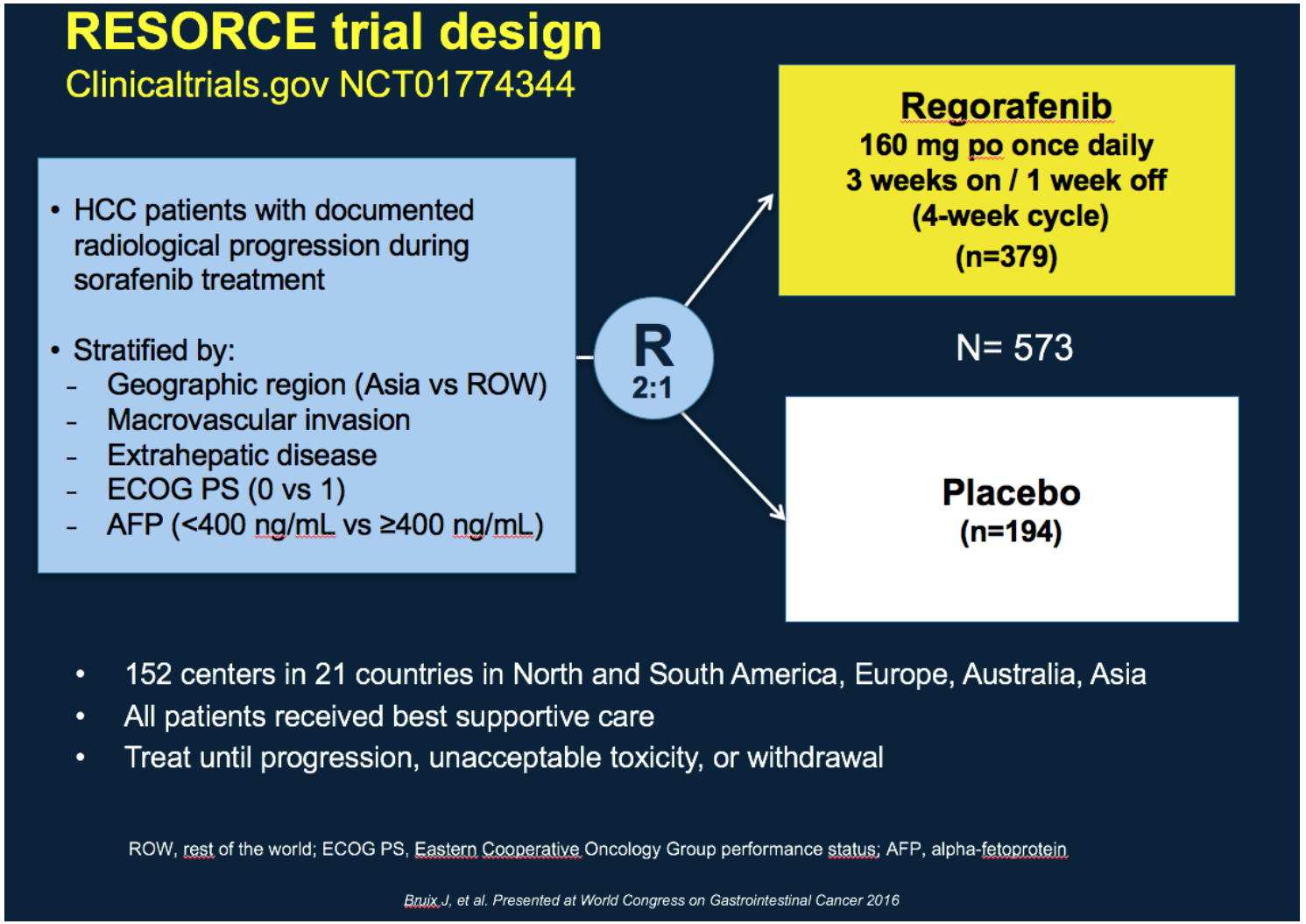
Start Sorafenib

**09/ 15 - 08/ 16**

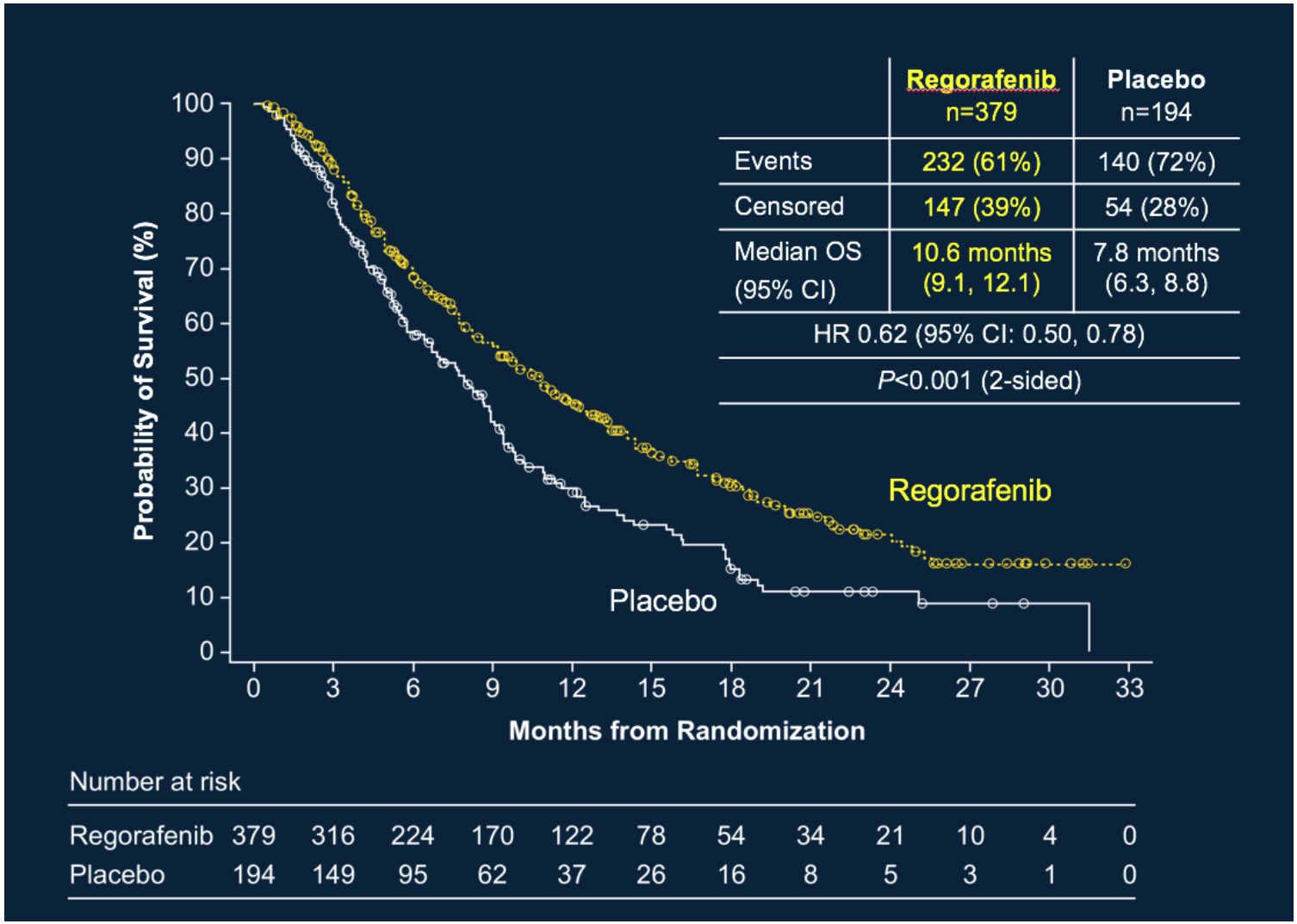


Progress unter Sorafenib

# Regorafenib beim HCC, 2. Linie

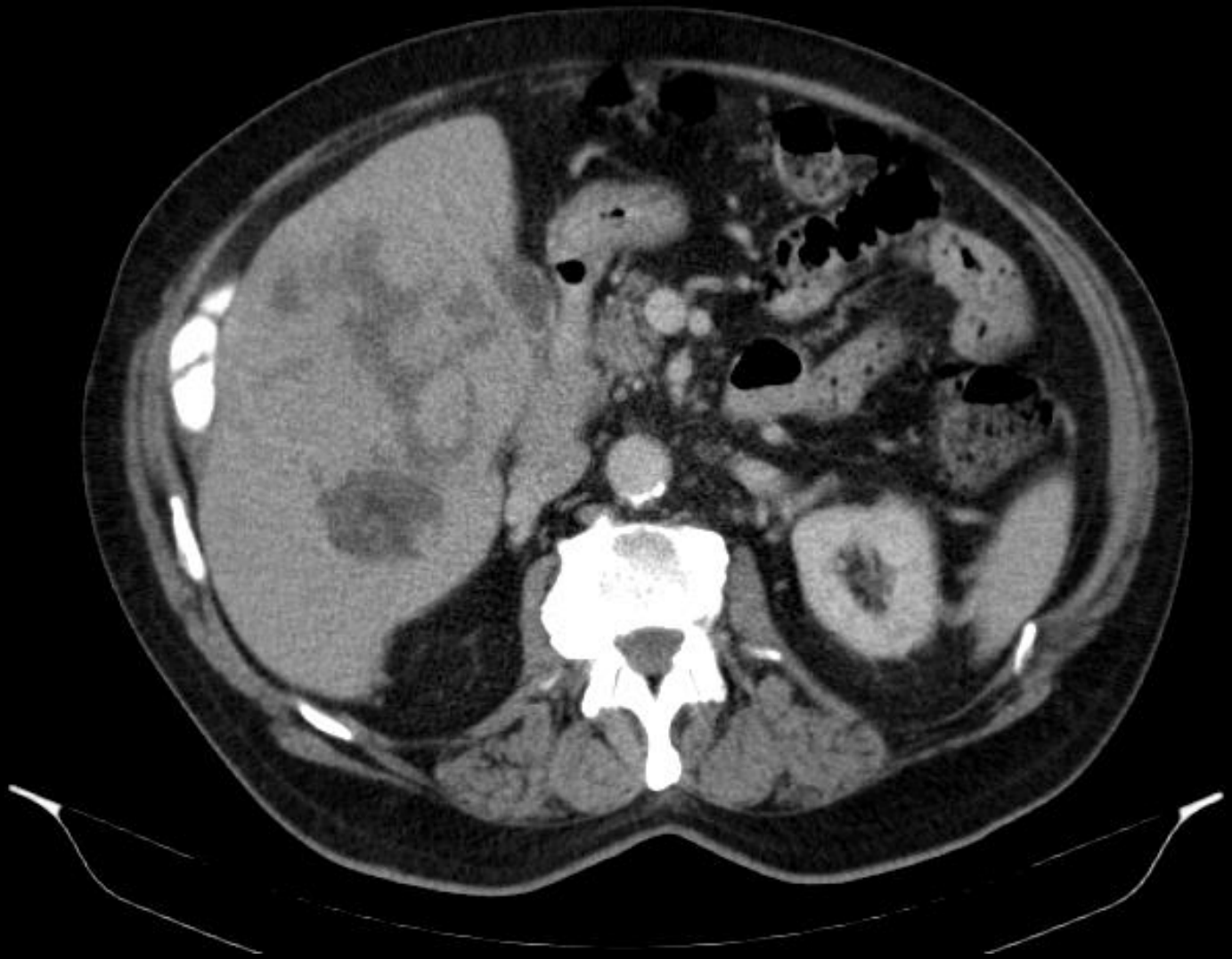


# Regorafenib beim HCC, mOS



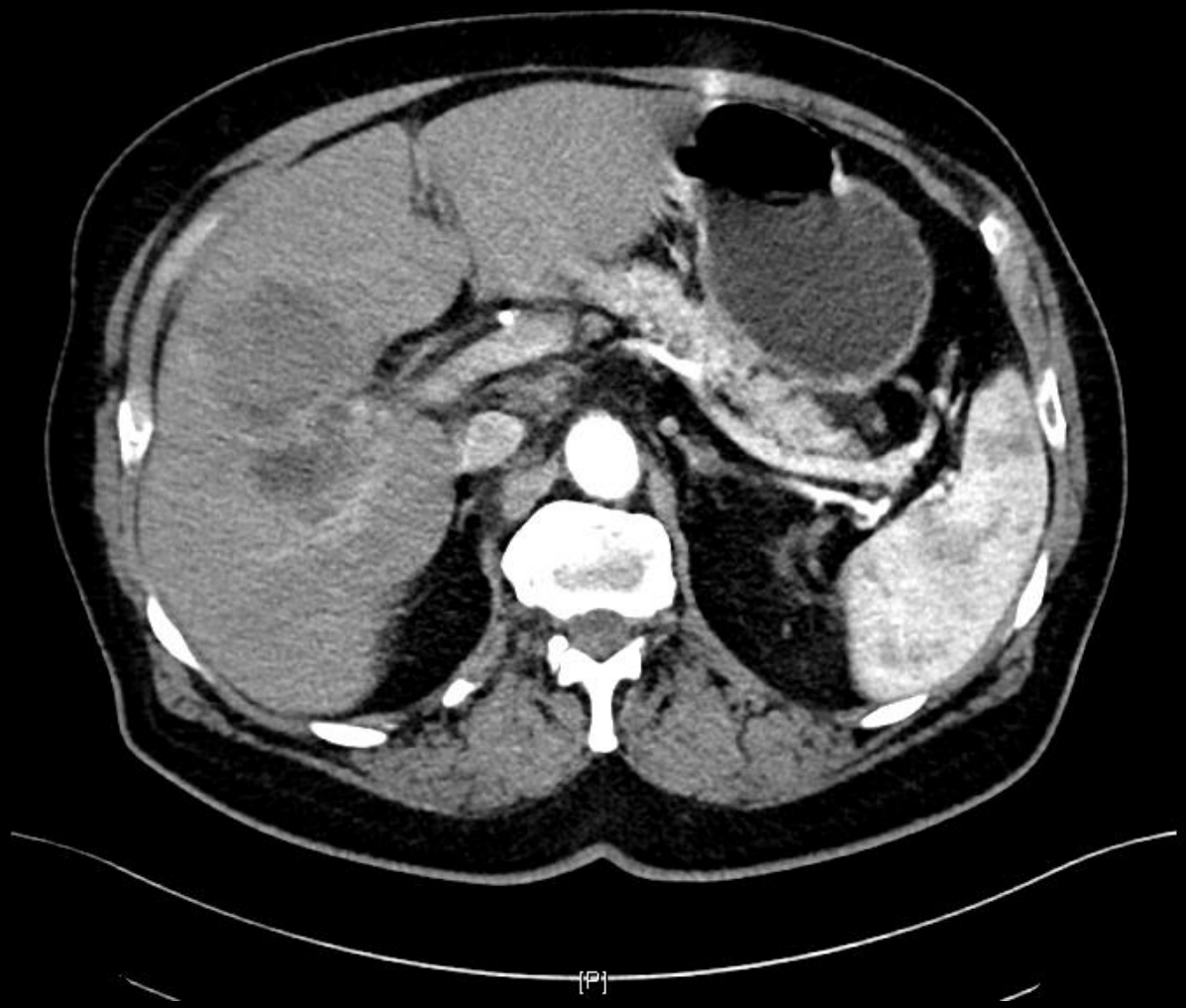

Bruix J, et al. WCGI 2016

**08/ 16**



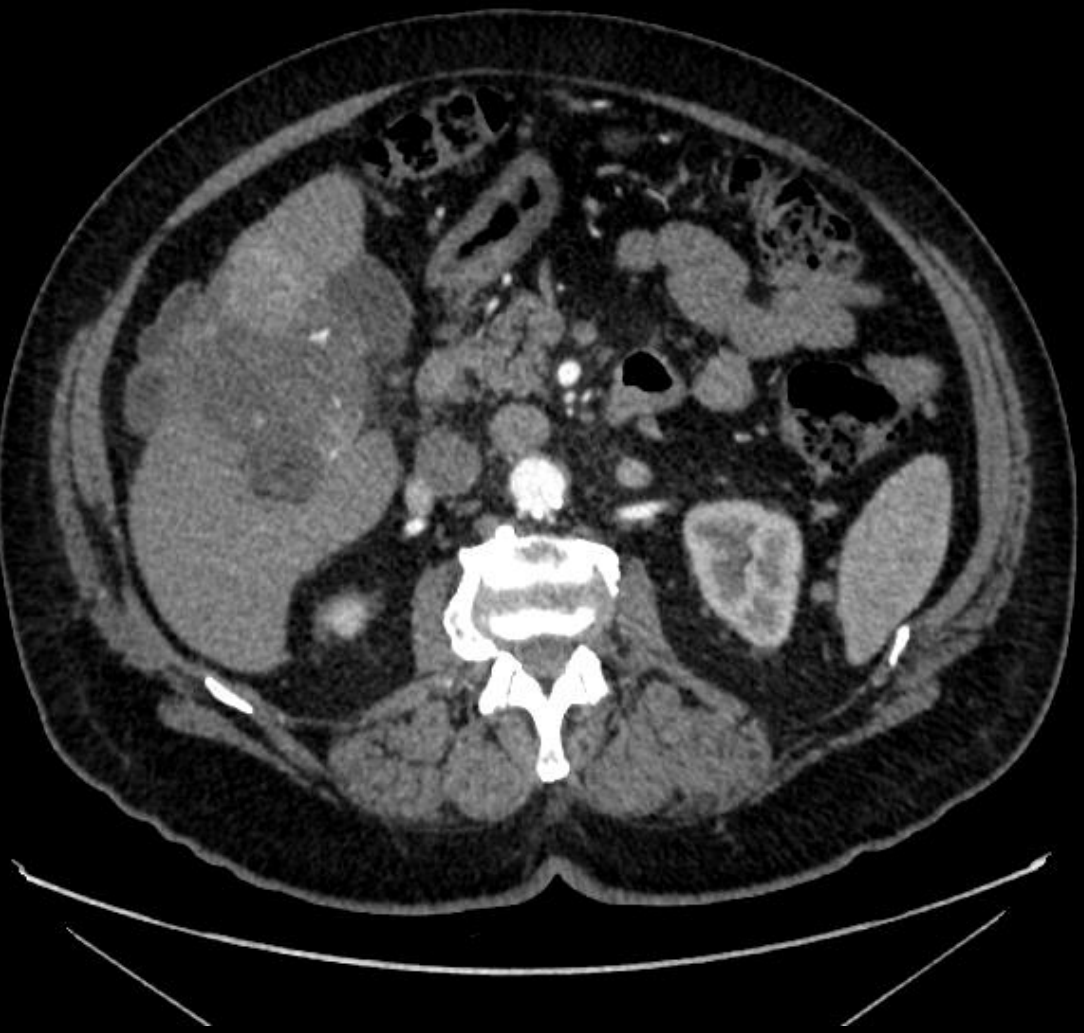
Start Regorafenib

**11/ 16**



Response unter Regorafenib

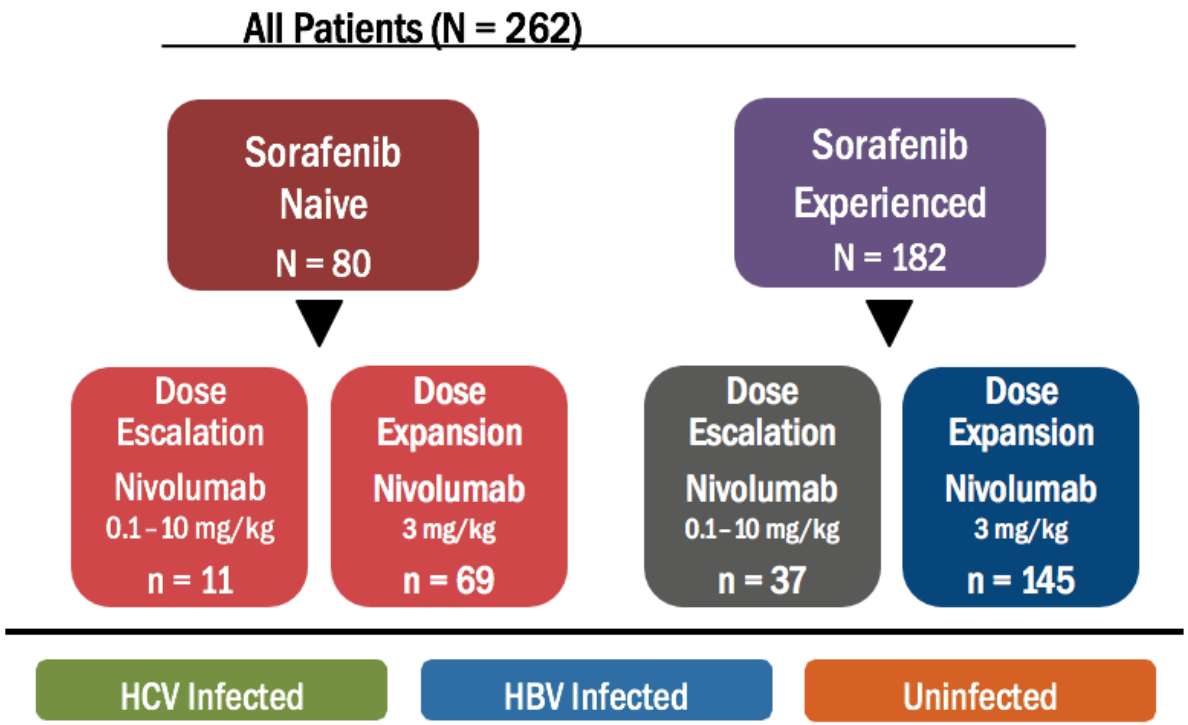
**08/ 16 – 01/ 17**



Progress unter Regorafenib

# Immuntherapie beim HCC

## CHECKMATE-040




### Study Endpoints

**Primary**

- Safety and tolerability (ESC)
- ORR (EXP)[a]

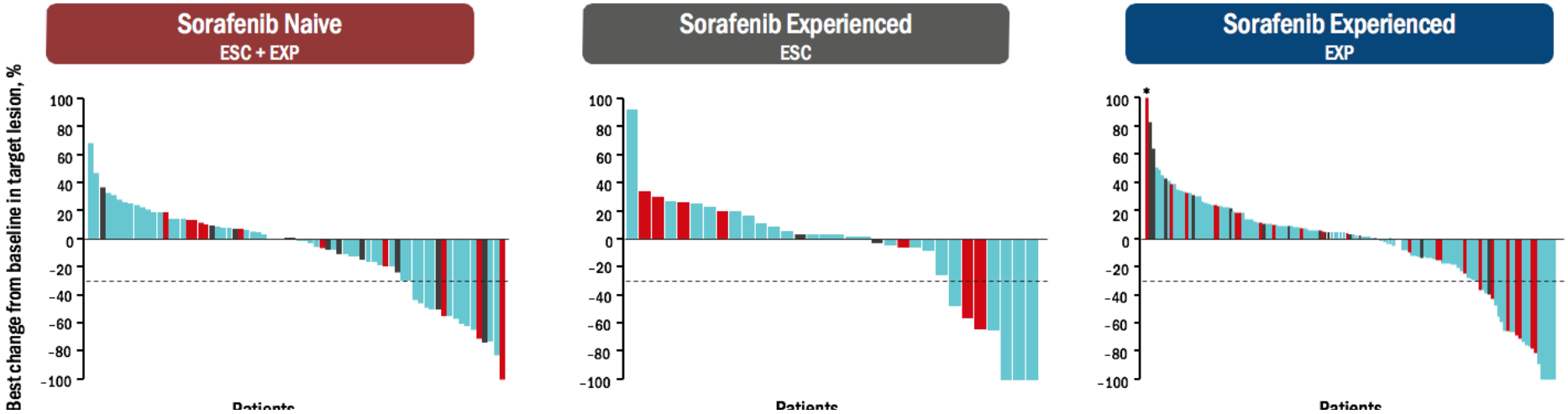
**Secondary**

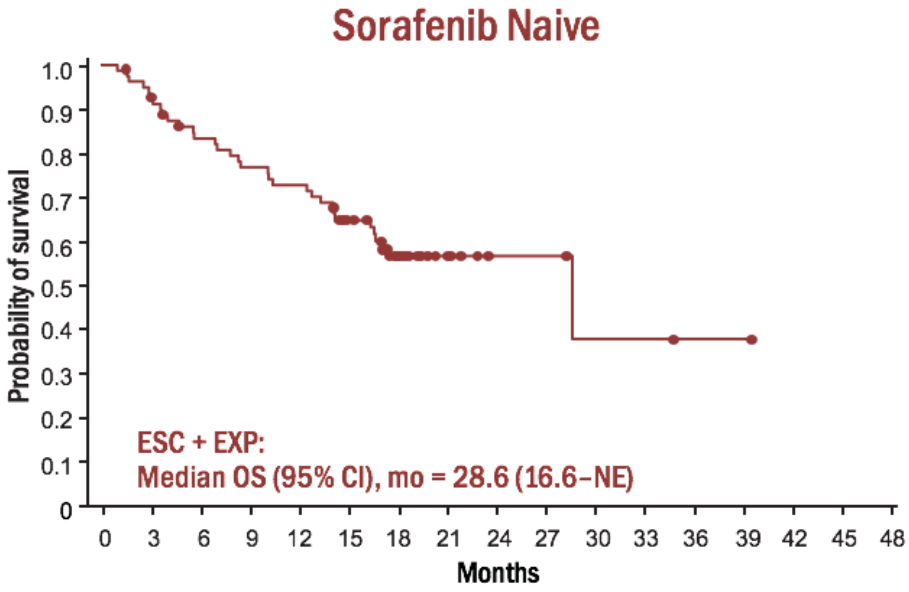
- ORR (ESC)[a]
- Disease control rate
- Time to response
- Duration of response
- Overall survival

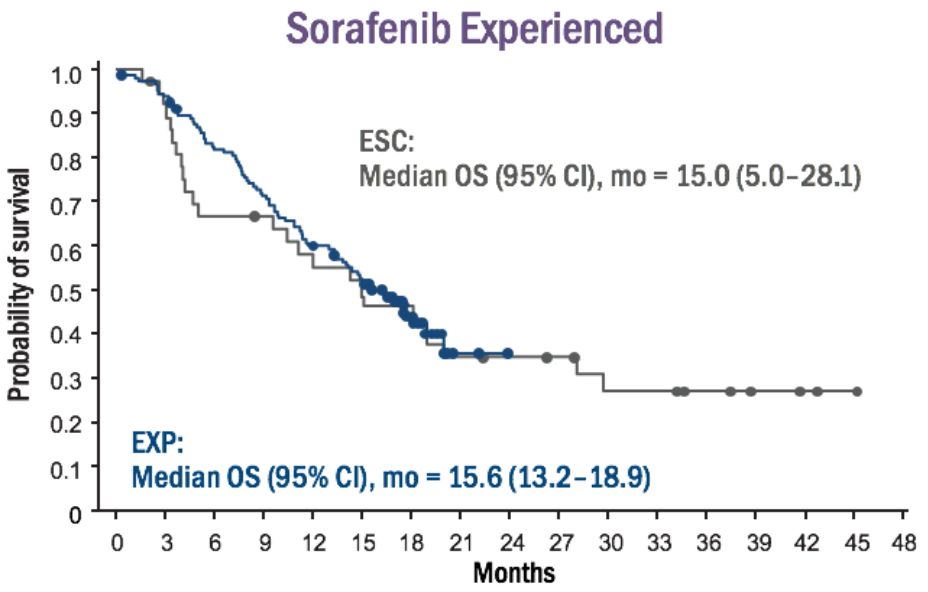
**Other**

- Biomarker assessments

# Immuntherapie & down-staging/ neoadjuvante Therapie?



# Immuntherapie des HCC

**IMMULAB**

Frühes HCC

RFA, d1 of cycle 3

Pembrolizumab q3w 200 mg

**IMMUTACE**

Intermediäres HCC

TACE, d1 of cycle 1 and 3

Nivolumab q2w 3 mg/kg

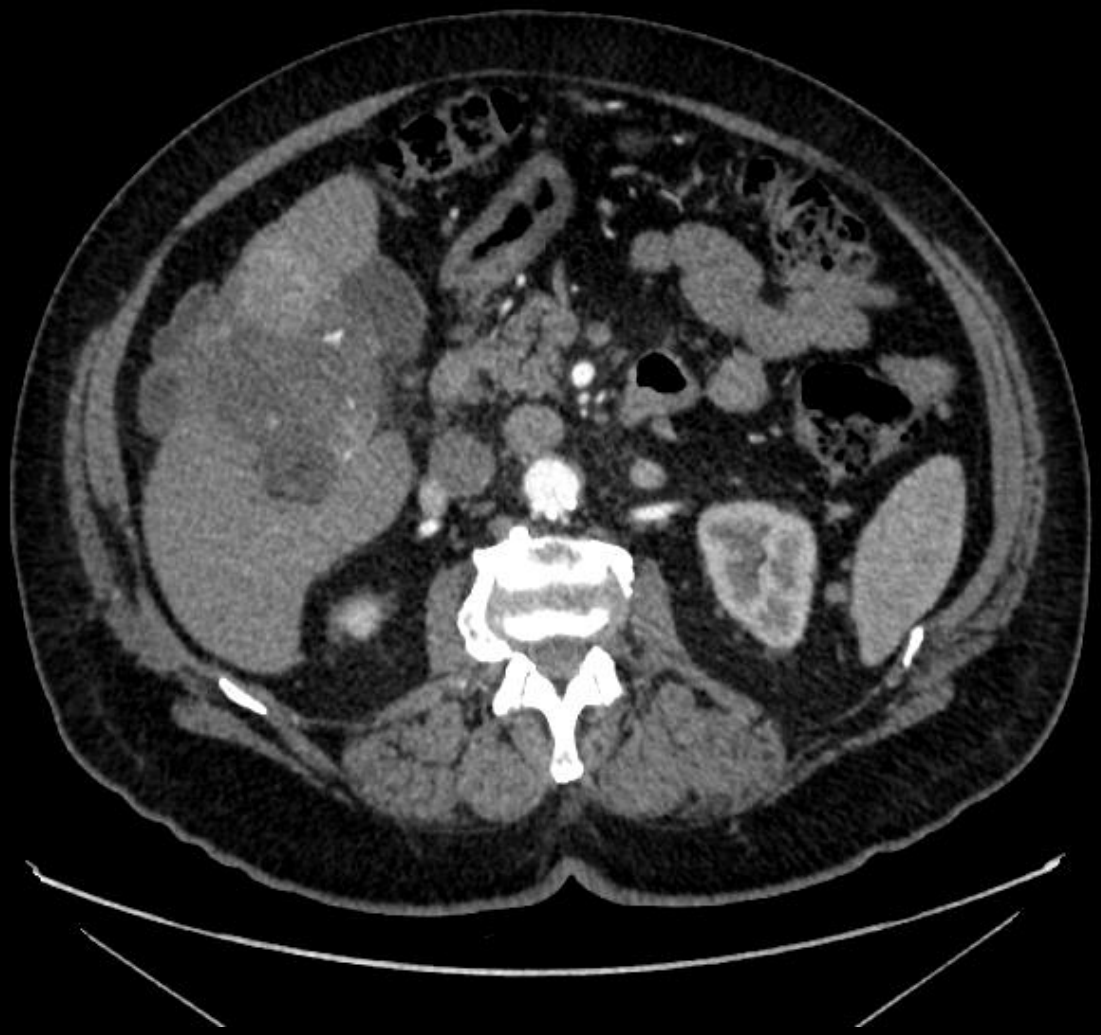
**IMMUNIB**

Fortgeschrittenes HCC

Lenvatinib 12/ 16 mg

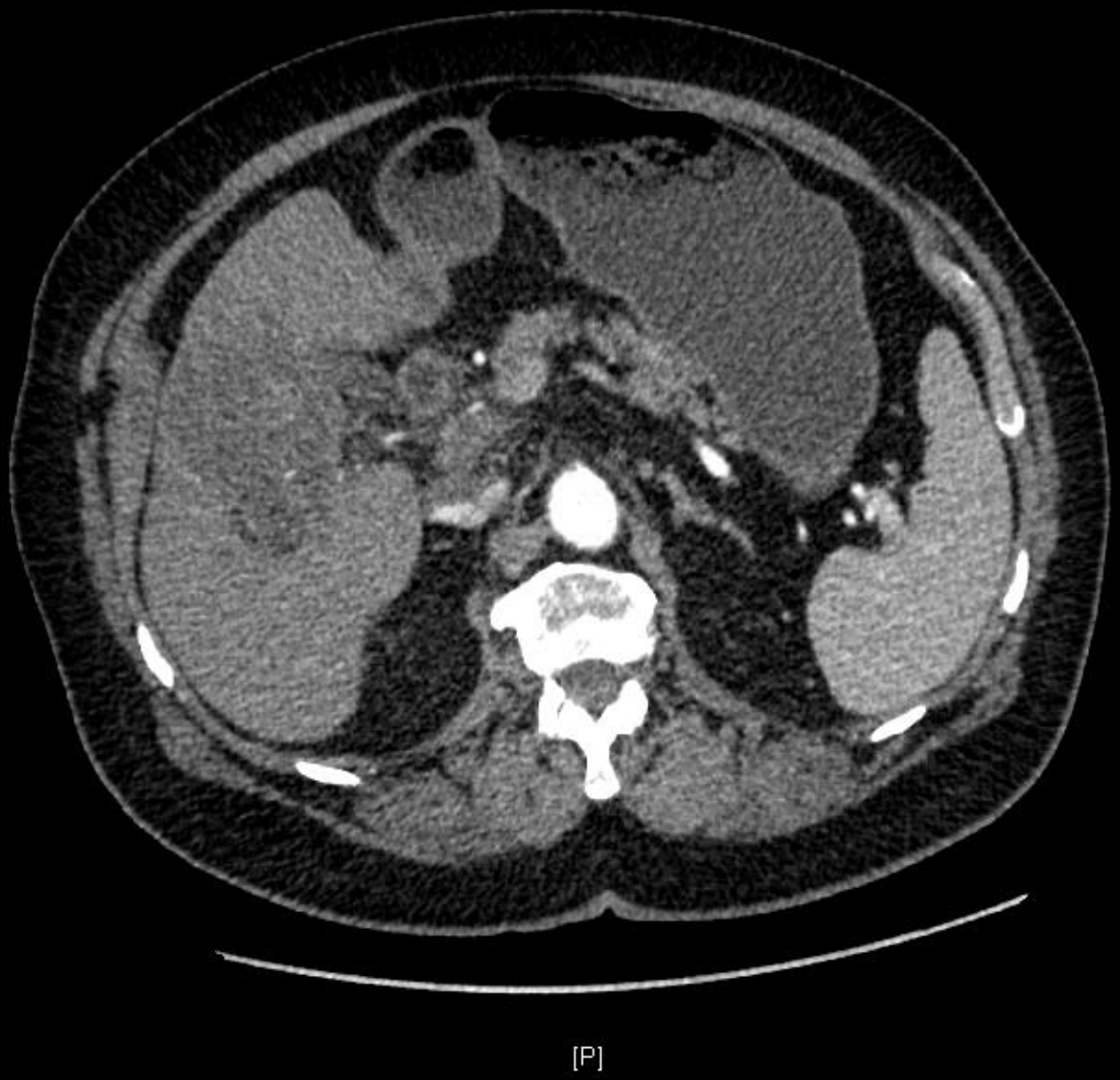
Nivolumab q2w 3 mg/kg

01/ 17



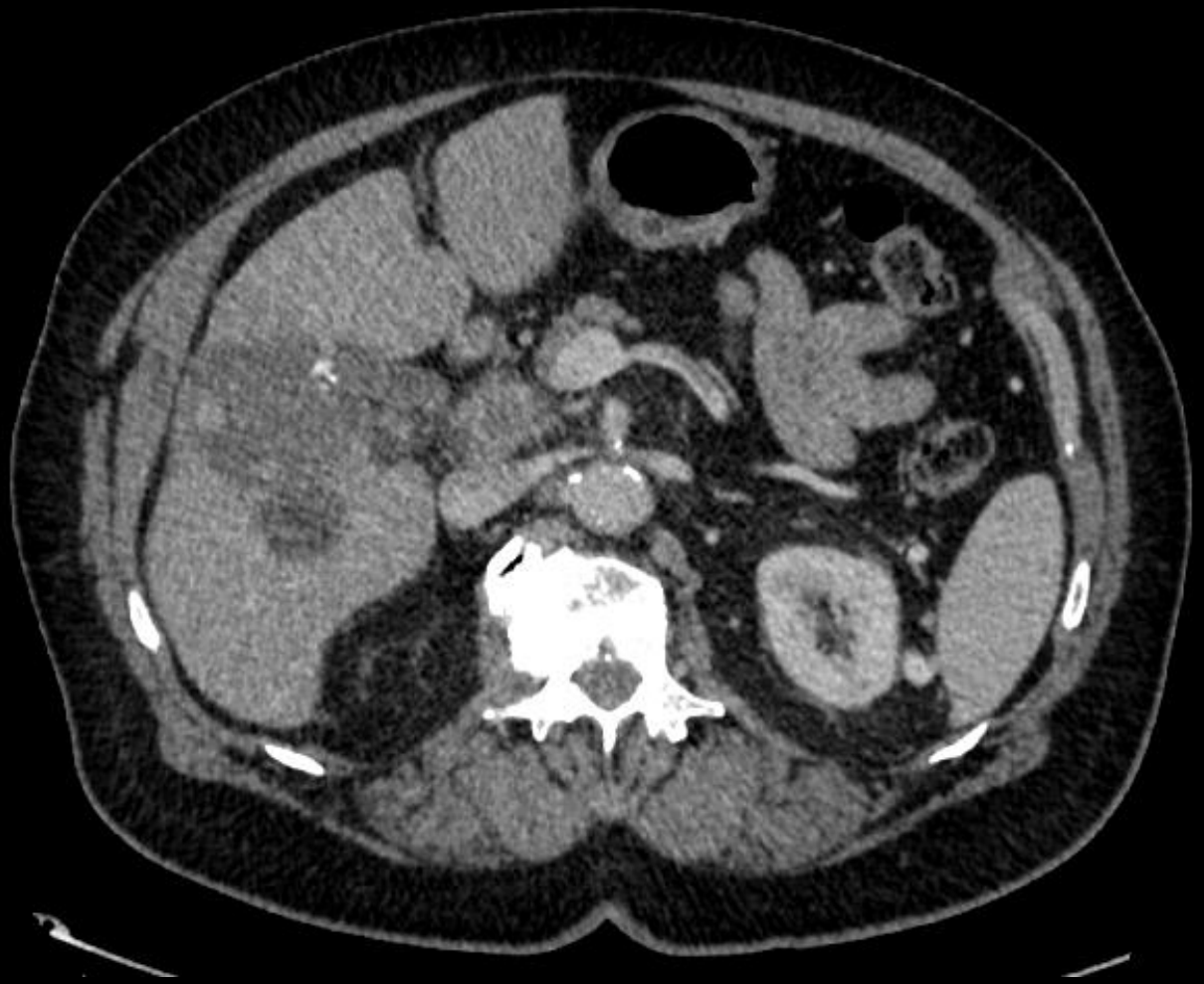
Start Nivolumab

**03/ 17**



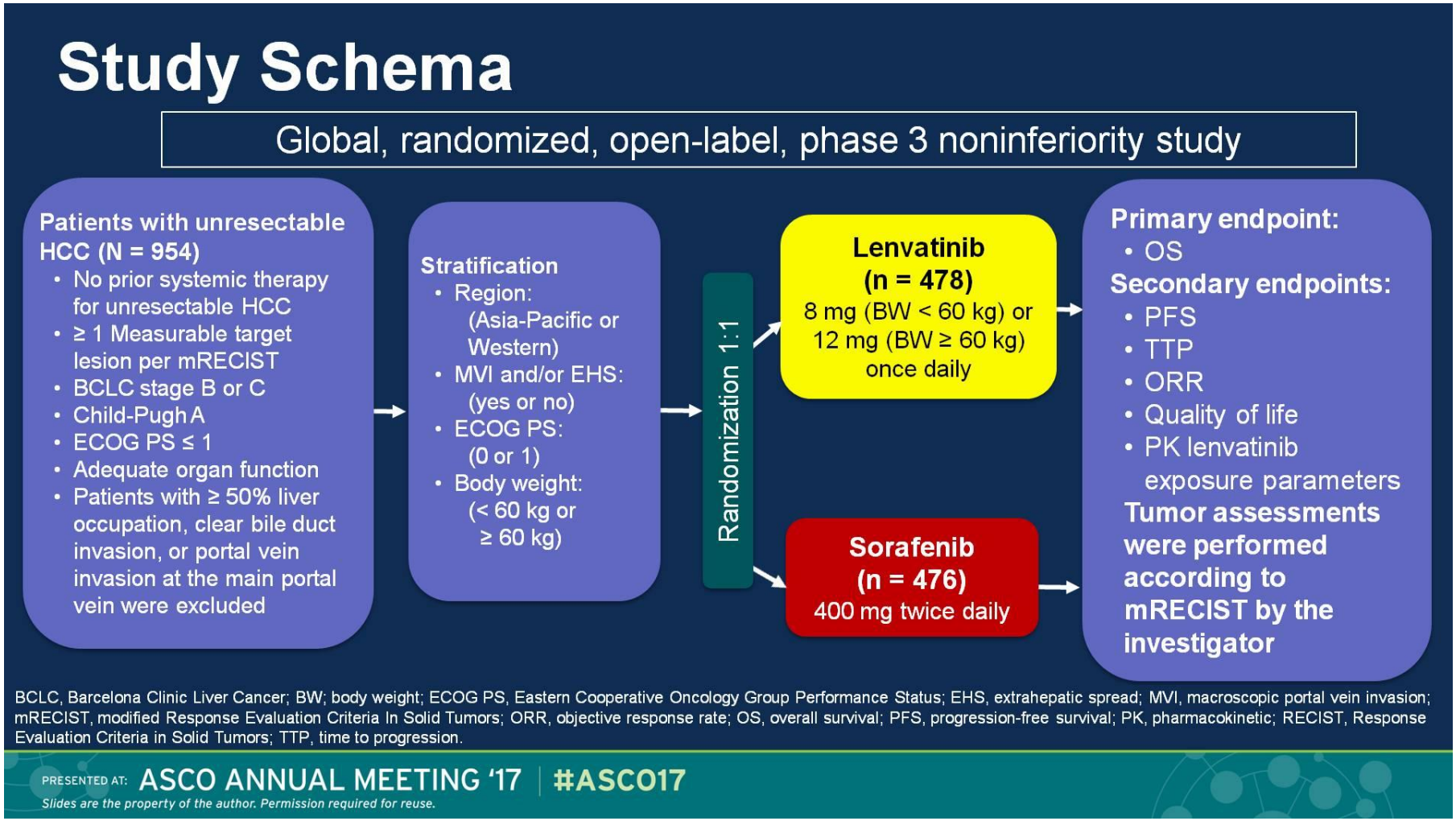

Response unter Nivolumab

**01/ 17 – 09/ 17**

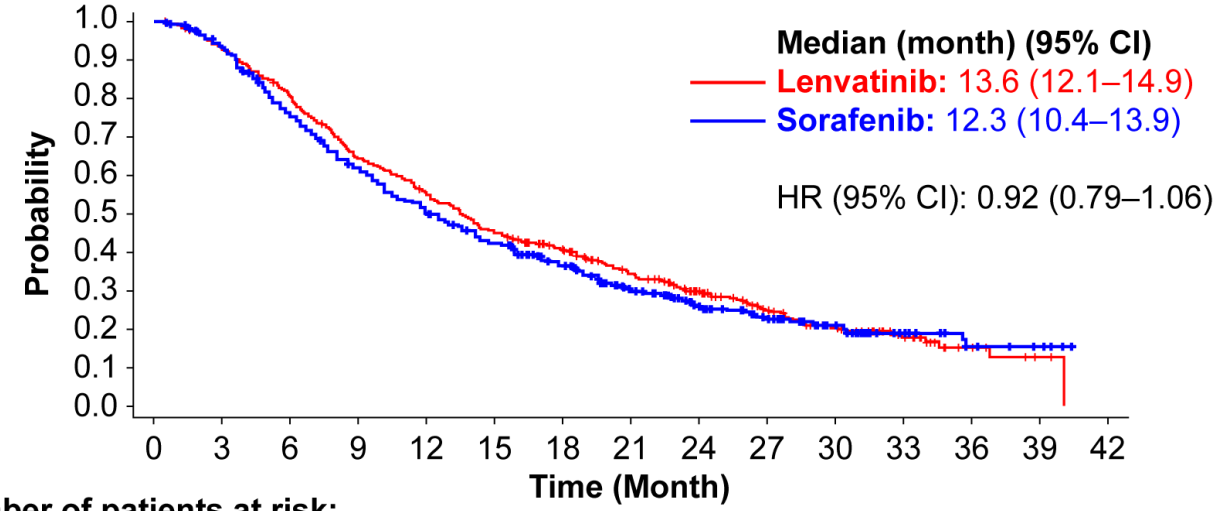


Progress unter Nivolumab

# Lenvatinib beim HCC, 1. Linie



# REFLECT Studie: Gesamtüberleben und Ansprechen

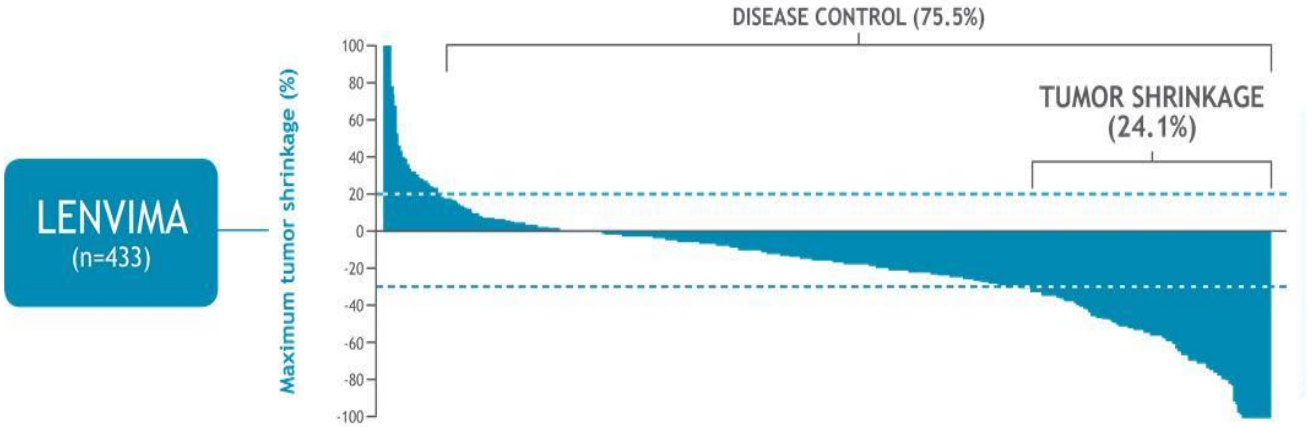



**Number of patients at risk:**

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Lenvatinib** | 478 | 436 | 374 | 297 | 253 | 207 | 178 | 140 | 102 | 67 | 40 | 21 | 8 | 2 | 0 |
| **Sorafenib** | 476 | 440 | 348 | 282 | 230 | 192 | 156 | 116 | 83 | 57 | 33 | 16 | 8 | 4 | 0 |

Non-inferiority margin assumption: 1.08
Upper HR limit, 95% CI

Actual result:
1.06
Upper HR limit, 95% CI




Cheng AL et al. J Clin Oncol 35, 2017 (suppl; abstr 4001); oral presentation

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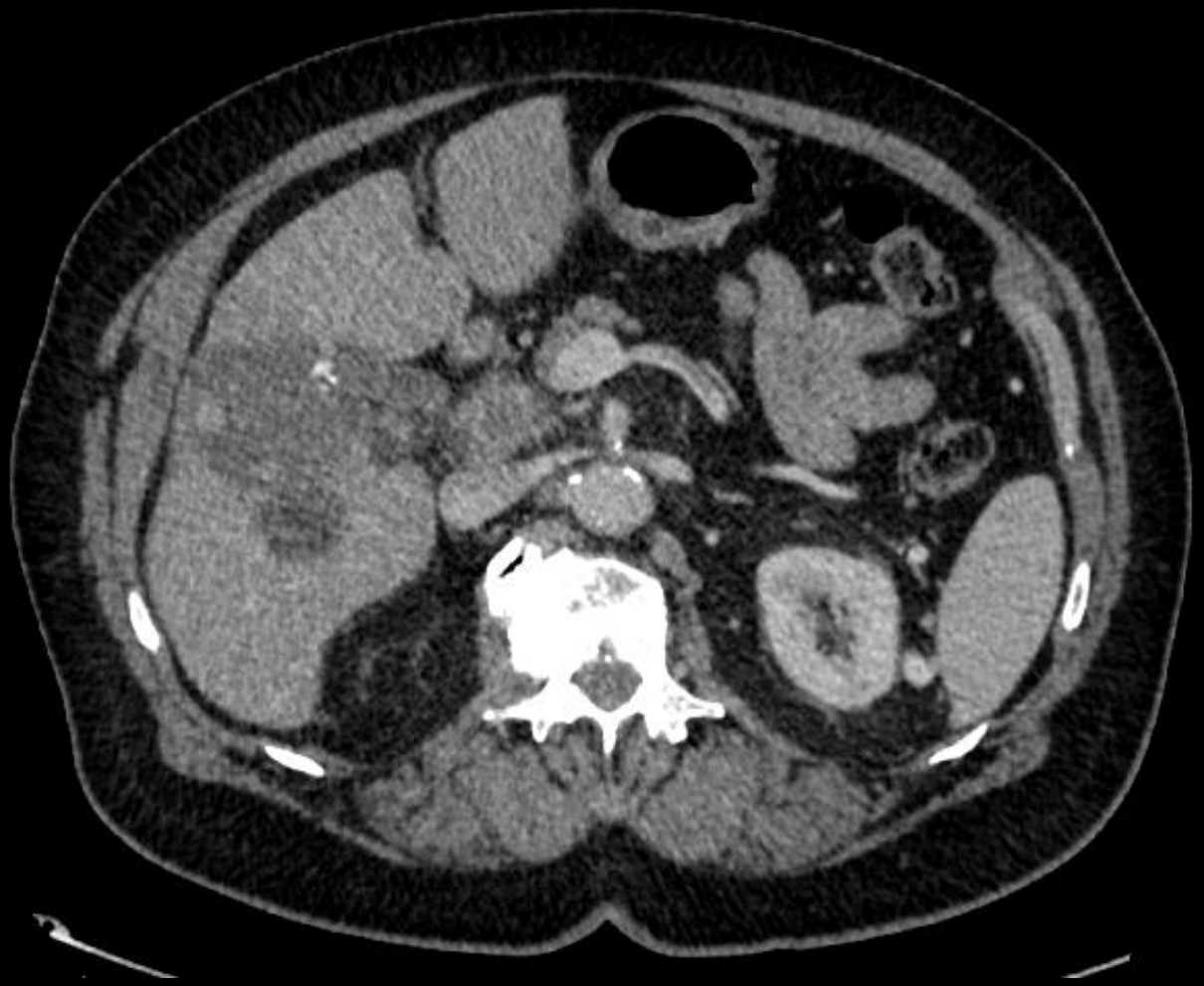
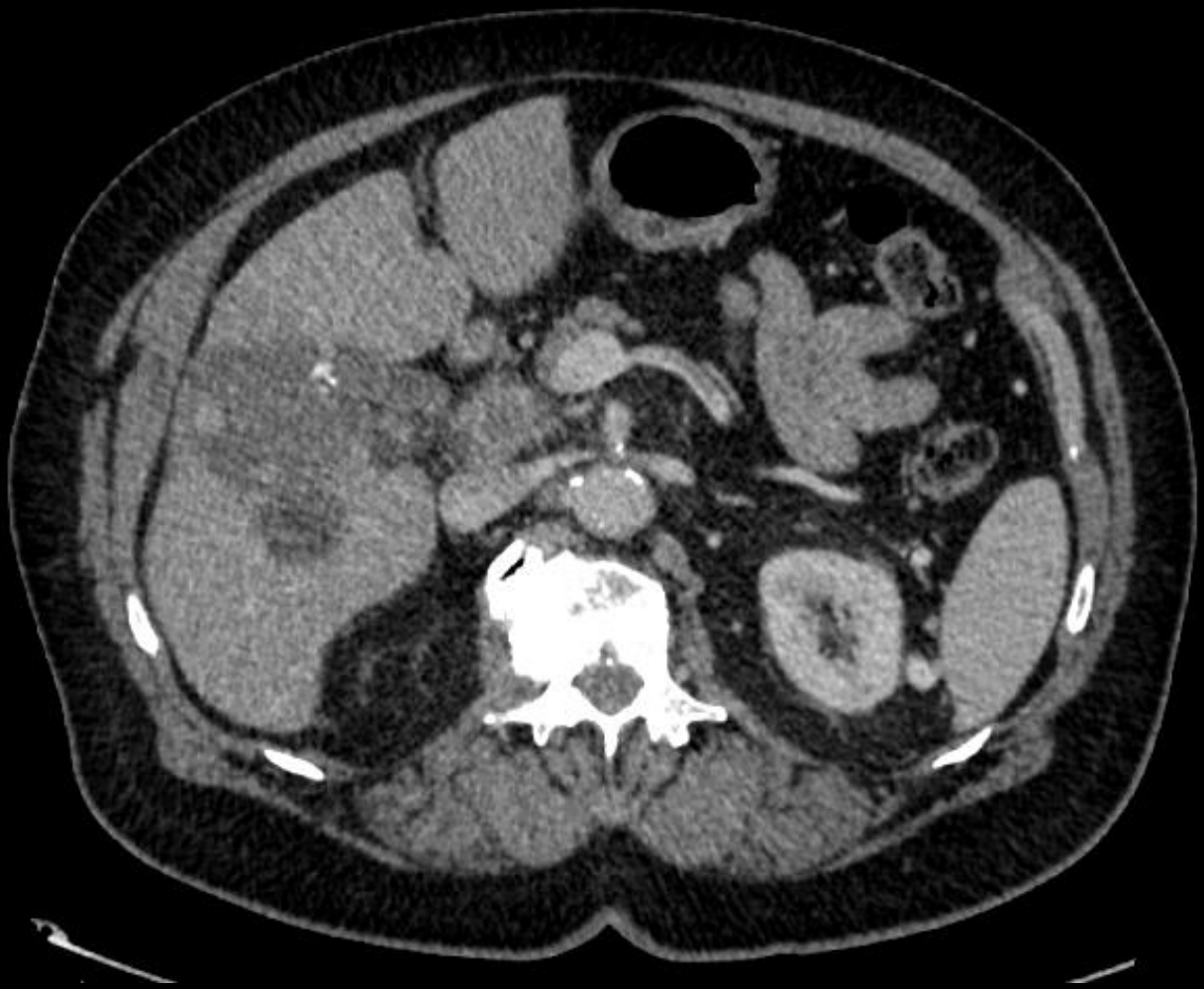
**09/ 17**



Start Lenvatinib

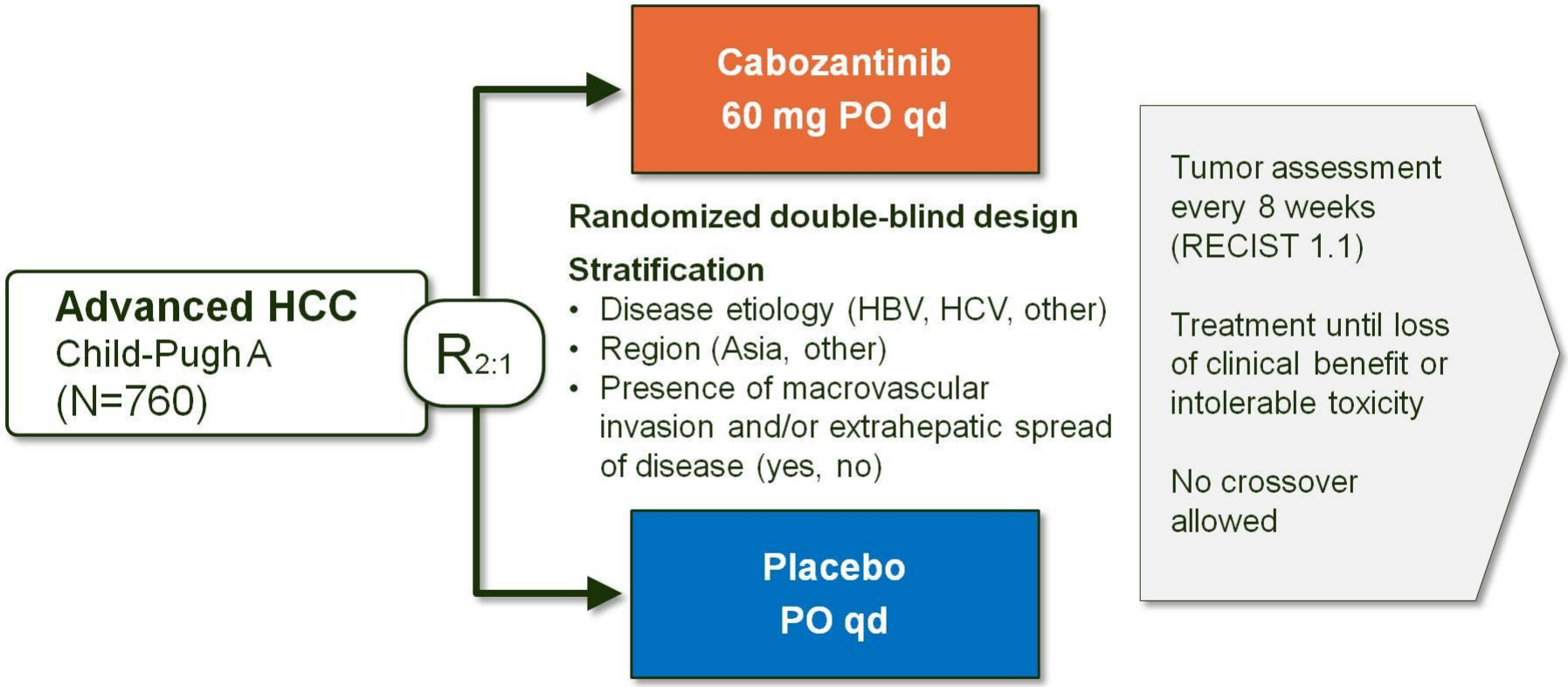
**01/ 18**



SD unter Lenvatinib

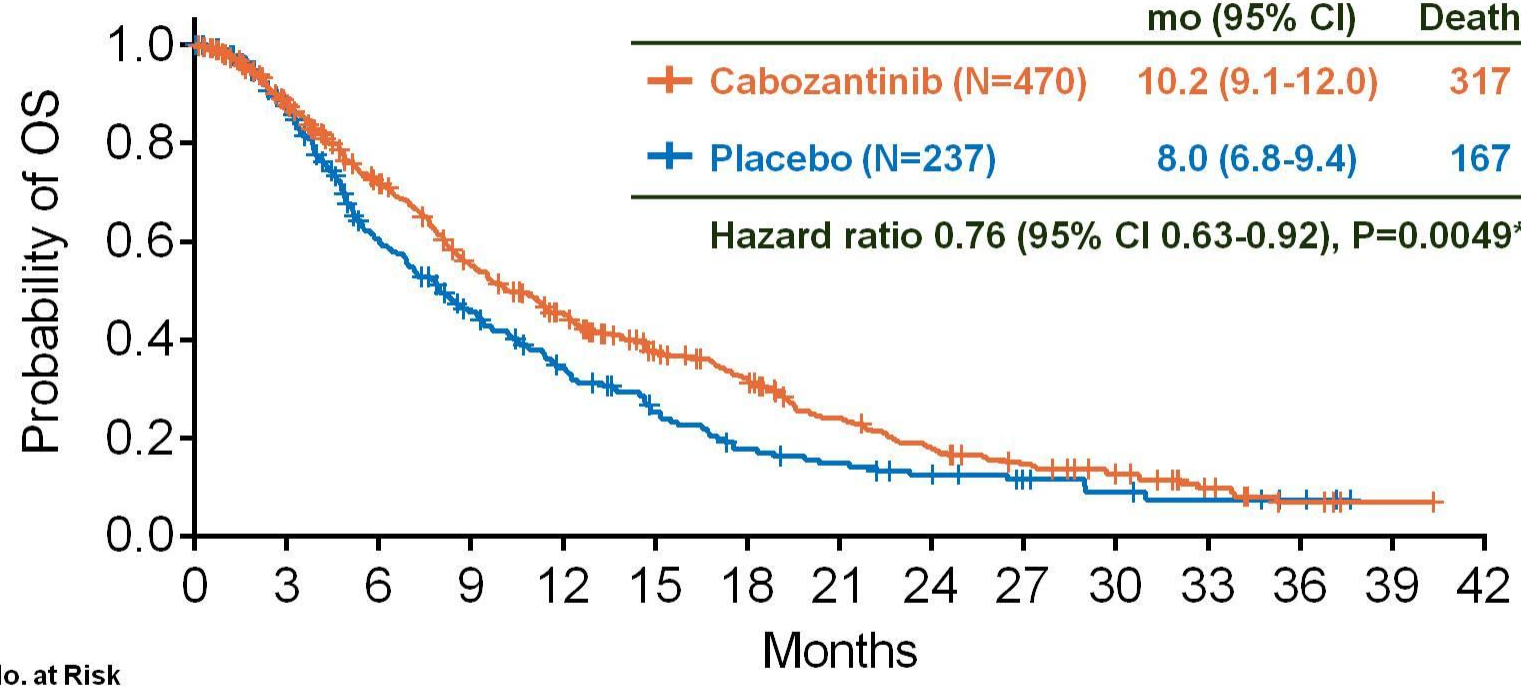
# Carbozantinib beim HCC, 2. und 3. Linie

## CELESTIAL Study Design



# Carbozantinib beim HCC, 2. Linie

## Overall Survival




| | Median OS mo (95% CI) | No. of Deaths |
|---|---|---|
| Cabozantinib (N=470) | 10.2 (9.1-12.0) | 317 |
| Placebo (N=237) | 8.0 (6.8-9.4) | 167 |

Hazard ratio 0.76 (95% CI 0.63-0.92), P=0.0049*

**No. at Risk**

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cabozantinib | 470 | 382 | 281 | 206 | 159 | 116 | 93 | 63 | 44 | 31 | 22 | 12 | 4 | 1 | 0 |
| Placebo | 237 | 190 | 117 | 82 | 57 | 37 | 25 | 20 | 15 | 10 | 7 | 5 | 3 | 0 | 0 |

*Critical p-value ≤ 0.021 for second interim analysis

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09/2015 ED pulm.+ lymph. metastasiertes HCC

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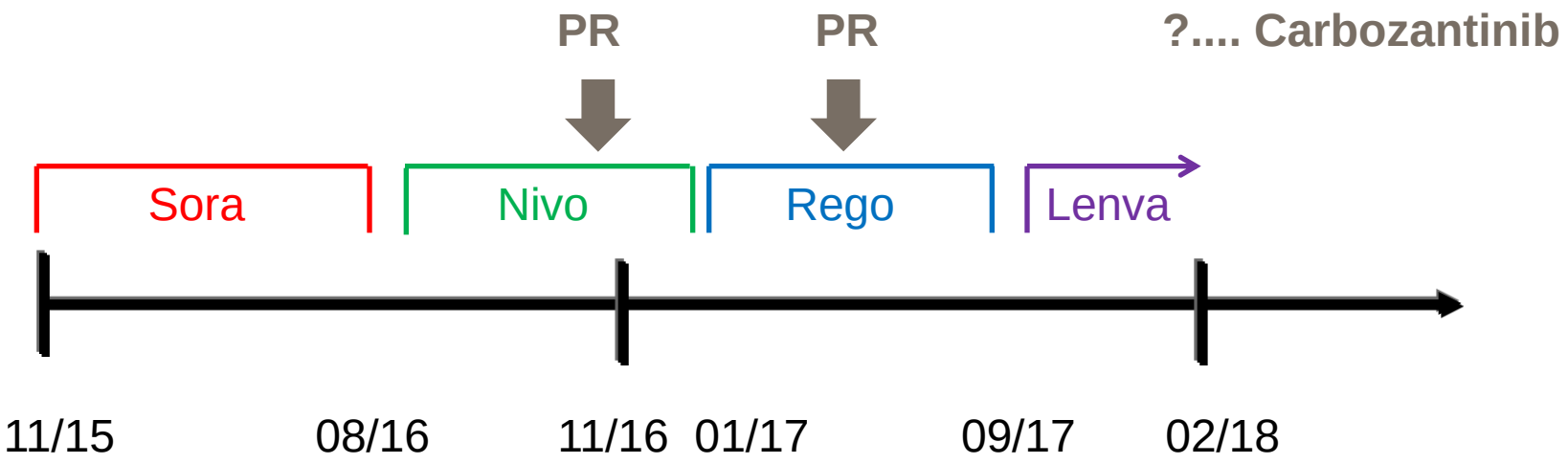
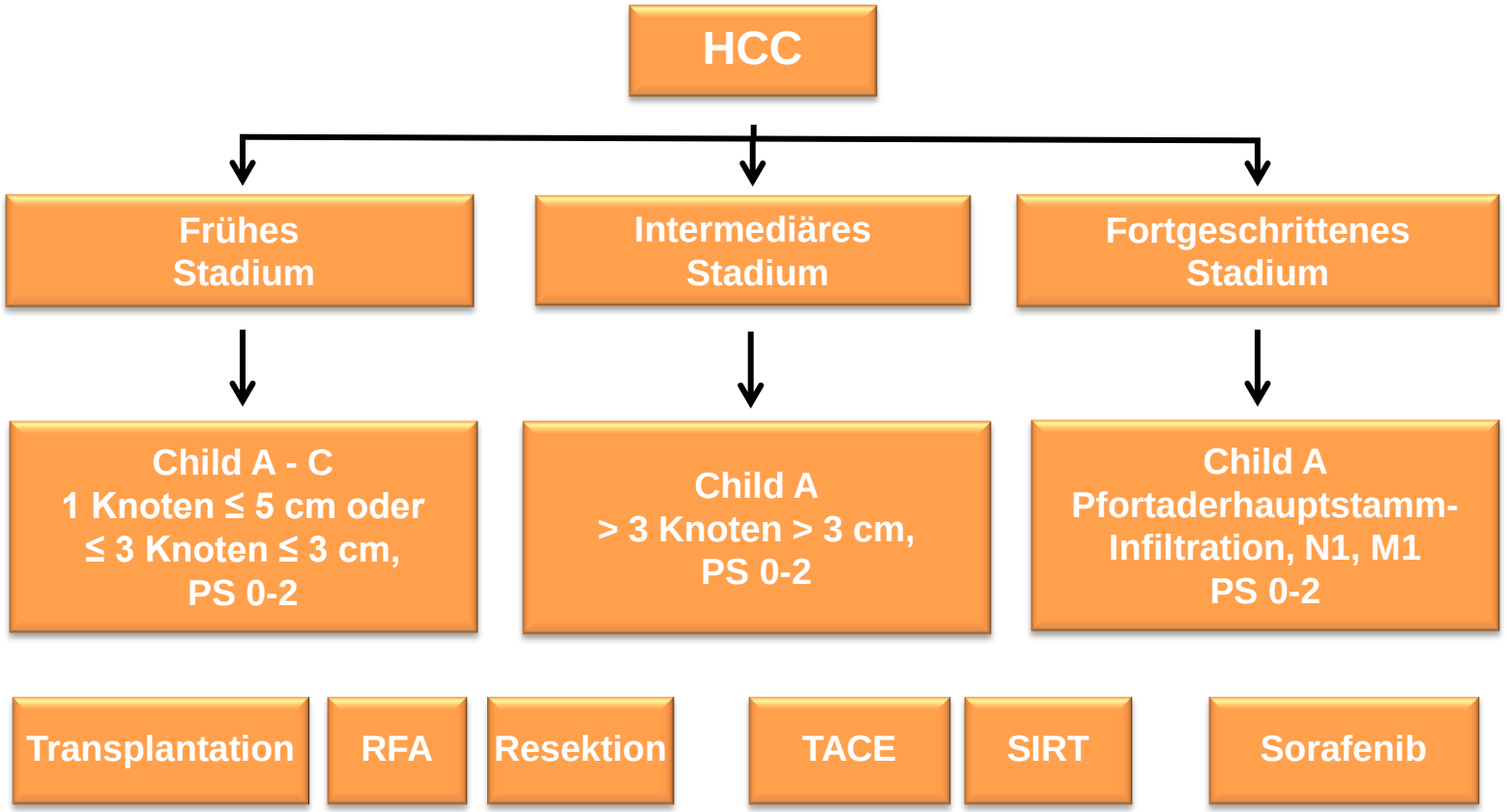
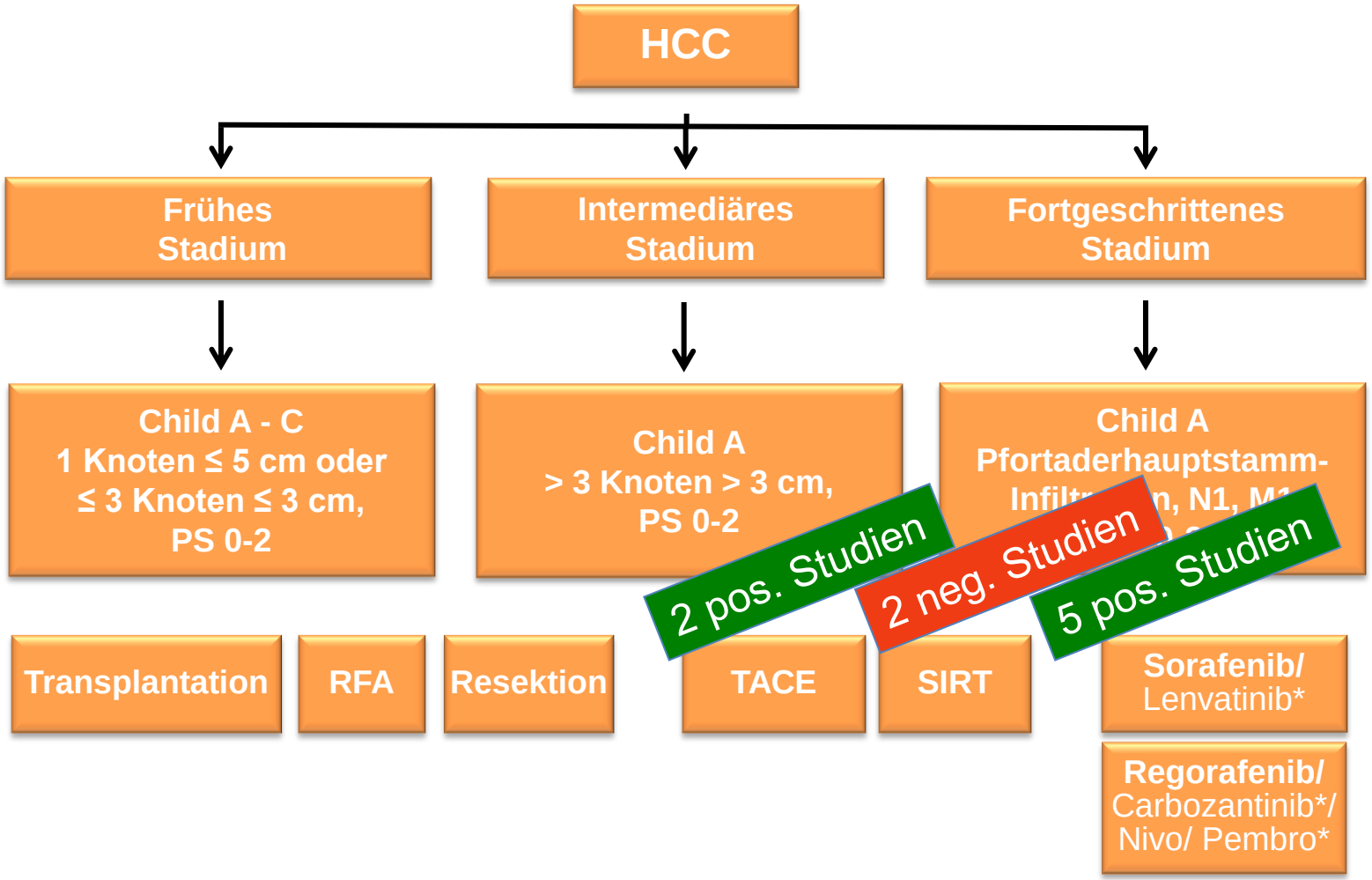


# Take Home HCC.....




Vogel und Manns, Dtsch Arztebl 2014

# Take Home HCC.....




Vogel und Manns, Dtsch Arztebl 2014

*noch nicht zugelassen

# HCC Phase-III Studien: 2011 - 2017

| | | | |
|---|---|---|---|
| **SPACE** | 20,4 | | |
| **BRISK** | 26,4 | vs. | 26,4 |
| **ORIENTAL** | 31,1 | vs. | 32.2 |
| **SHARP** | **7,9** | **vs** | **10,7** |
| **SUN** | 7,9 | vs. | 10,3 |
| **BRISK-FL** | 9,5 | vs. | 9,9 |
| **SEARCH** | 8,5 | vs. | 9,5 |
| **LIGHT** | 9,1 | vs. | 9,8 |
| **Nintendanib** | 11,9 | vs. | 11,5 |
| **Dovitinib** | 8,6 | vs. | 9,2 |
| **Axitinib** | 12,7 | vs. | 9,7 |
| **Sarah** | 9,9 | vs. | 9,9 |
| **Sirvenib** | 11,3 | vs. | 10,4 |
| **REFLECT** | **13,6** | **vs** | **12,3** |
| **EVOLVE-1** | 7,6 | vs. | 7,3 |
| **BRISK-SL** | 8,2 | vs. | 9,4 |
| **REACH** | 7,5 | vs. | 9,2 |
| **METIV** | 8,4 | vs. | 9,1 |
| **RESORCE** | **10,6** | **vs** | **7,8** |
| **CELESTIAL** | **10,2** | **vs** | **8,2** |

**TACE**
**≈ 26 Monate**

**1st line**
**Sorafenib/**
Lenvatinib
**≈ 12 Monate**

**2nd line**
**Regorafenib/**
Carbozantinib
**≈ 8 Monate**