

## Management of Intermediate HCC with Sorafenib and Drug-Eluting Bead, Doxorubicin (DEBDOX™)

Chairman: Professor Josep Llovet, Barcelona Clinic Liver Cancer (BCLC) Group, Spain & Mount Sinai School of Medicine, New York, USA

Saturday 3 September, 2011  
5:30 – 6.30pm

Plenary Room  
Hong Kong Convention and Exhibition Centre



Overview of HCC management and rationale for SPACE trial

**Professor Josep Llovet**

Barcelona Clinic Liver Cancer (BCLC) Group, Spain & Mount Sinai School of Medicine, New York, USA



Is DEBDOX™ the new standard for chemoembolisation?

**Professor Riccardo Lencioni**

Pisa University Hospital and School of Medicine, Italy



Asian experience with Drug-Eluting Beads for HCC and rationale for the TRACER study

**Professor Ronnie Poon**

Queen Mary Hospital, The University of Hong Kong



Five-year follow up with DEBDOX in intermediate HCC, BCLC experience

**Professor Jordi Bruix**

Barcelona Clinic Liver Cancer (BCLC) Group, Spain

# ***Is DEBDOX the New Standard for Chemoembolization?***

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***Professor Riccardo Lencioni, MD***

***Director, Division of Diagnostic Imaging and Intervention  
Department of Hepatology and Liver Transplantation  
Pisa University Hospital and School of Medicine  
Pisa, Italy***

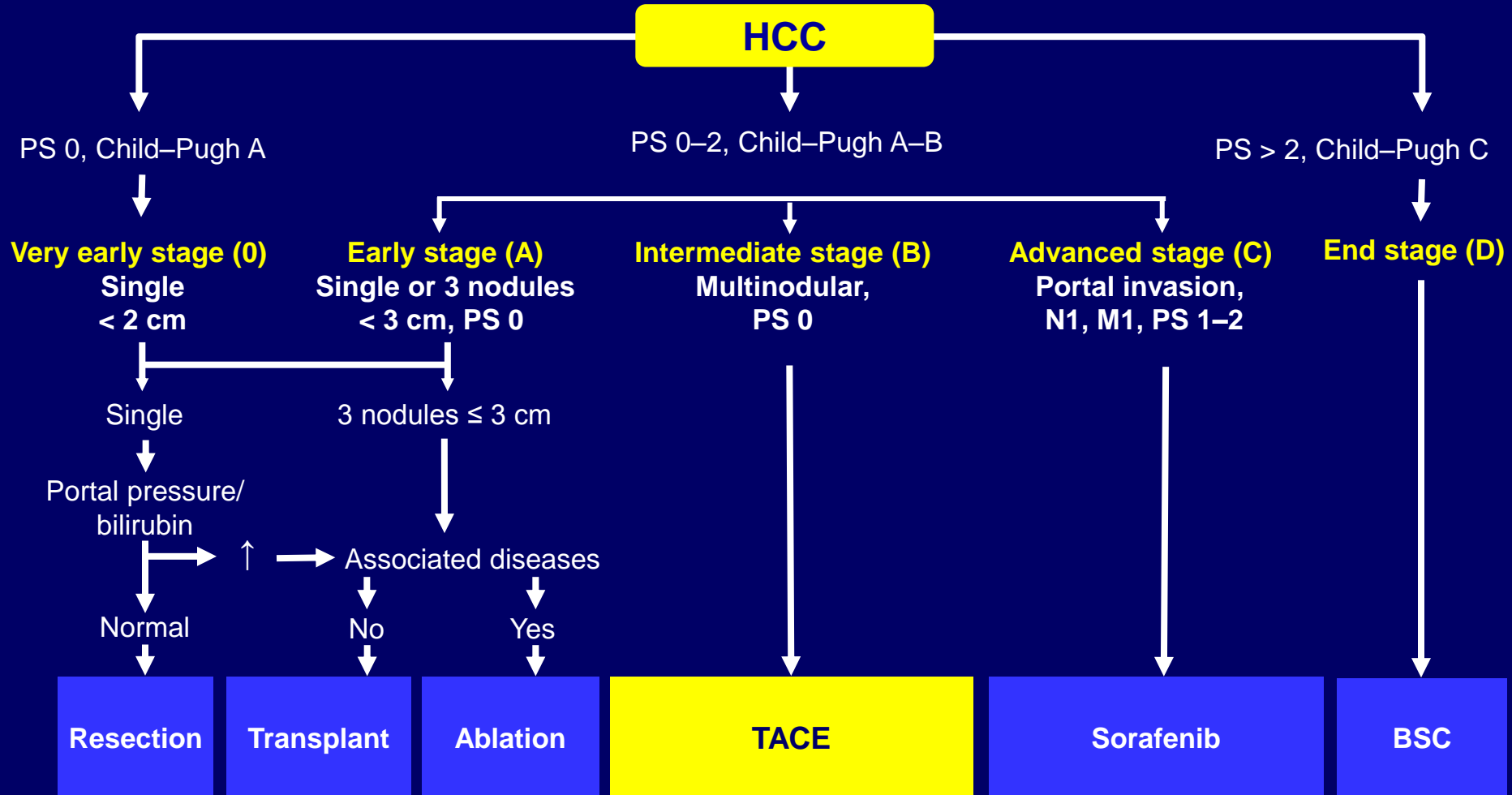


# *Disclosure*

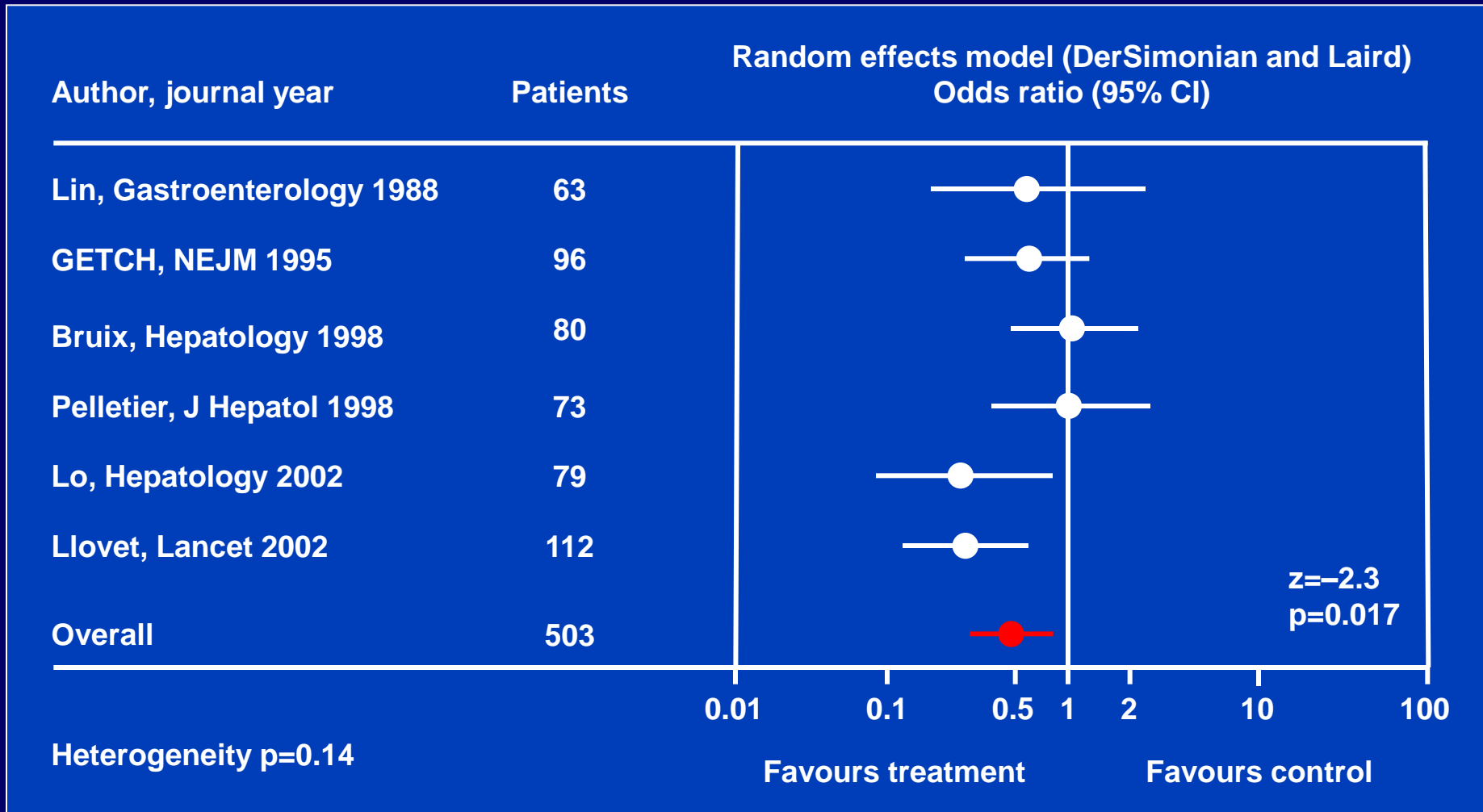
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- **Consultant, Biocompatibles UK Ltd**

# BCLC staging system and treatment strategy

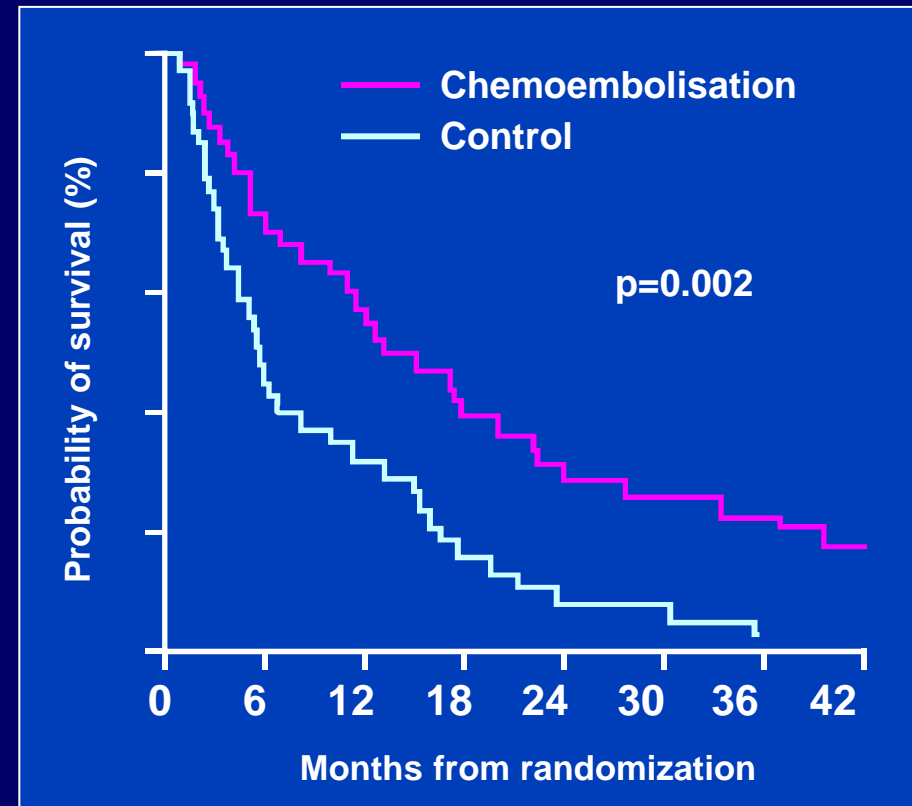
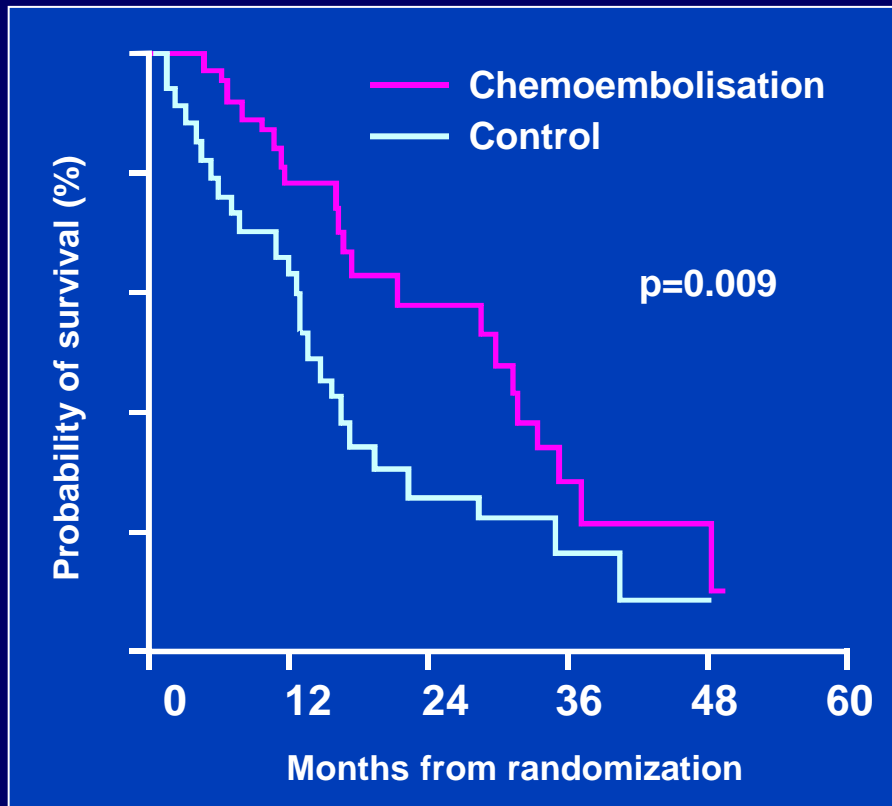


# TAE / TACE versus BSC / suboptimal therapy: meta-analysis of RCTs (2-year survival)

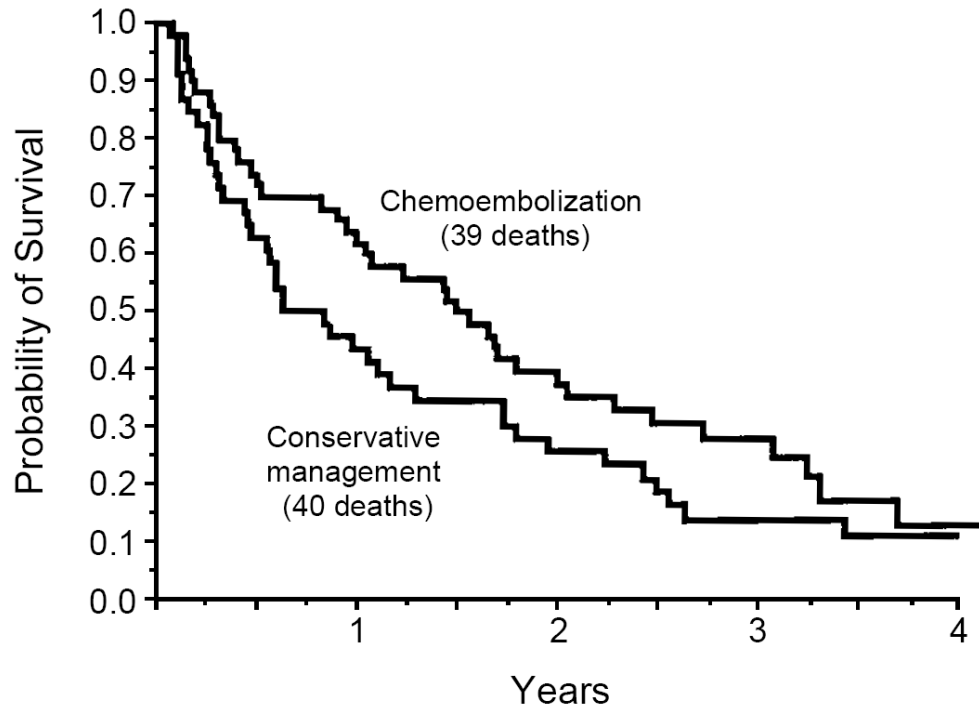


# Conventional TACE: long-term outcomes are unsatisfactory

- 3-year overall survival in the TACE treatment arm: 26% – 29%
- Sustained objective response (lasting > 3–6 months): 27% – 35%



# Conventional TACE: liver toxicity is a major limitation of Lipiodol-based regimens



COMPLICATION	OF PATIENTS WITH COMPLICATION (%)*
Abdominal pain	40 (80)
Vomiting	40 (80)
Temperature $\geq 38^{\circ}\text{C}$	38 (76)
Death	1 (2)
Ascites	5 (10)
Encephalopathy	1 (2)
Gastrointestinal hemorrhage	4 (8)
Cholecystitis	2 (4)
Serum AST or ALT activity $\geq 5 \times$ upper limit of normal 3 days after treatment <sup>†</sup>	27 (54)
Increase in serum bilirubin of $\geq 0.9$ mg/dl <sup>‡</sup>	29 (58)
Other complications <sup>§</sup>	9 (18)

**“In a group of patients with unresectable HCC but without severe liver disease, Lipiodol chemoembolization often caused acute liver failure and did not significantly improve survival”**

# Conventional TACE: treatment discontinuation due to AEs or technical issues is common

- Reasons for treatment discontinuation among HCC patients who received a conventional TACE regimen with doxorubin, Lipiodol, and gelatine sponge fragments

	Chemoembolisation (n=40)
<b>Reason</b>	
Tumour progression (portal thrombosis, extrahepatic spread, or performance status >2)	9
Liver failure without tumour progression	2
Technical problems (arterial hepatic obstruction, collateral or hepatofugal blood flow, low ejection fraction)	8
Adverse events (leucopenia, ischaemic biliary stricture, transient ischaemic attack, allergic dermatitis)	4
Patient's decision	4
Death on treatment	3
Other (lung cancer, percutaneous ethanol injection)	0
Treatment discontinuation	31 (77%)
Active treatment at end of follow-up	9 (23%)

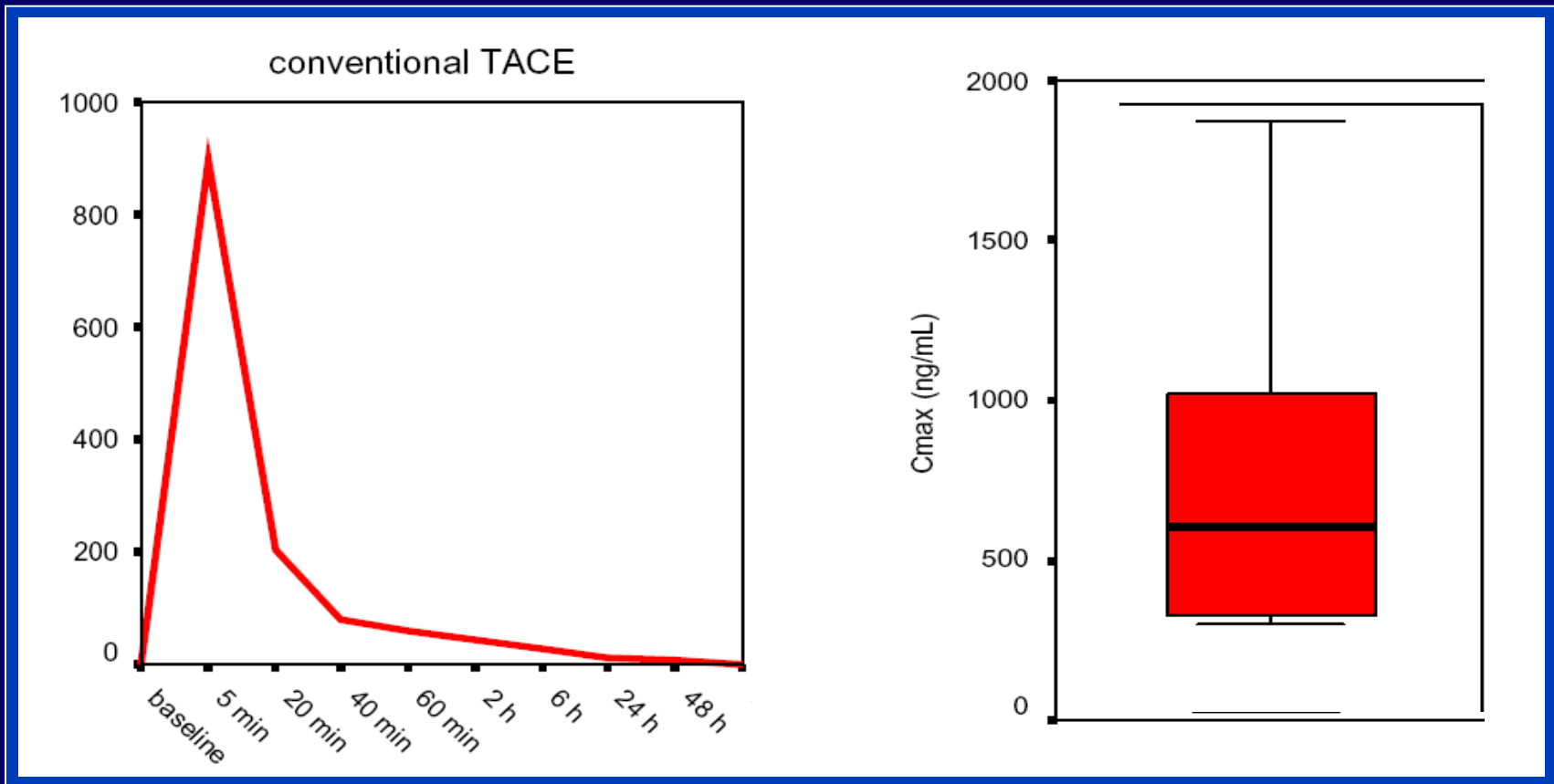
# Conventional TACE is a home-made technique with inherent inconsistencies

- **Gelatin sponge particles:** manually-prepared embolic agents – heterogeneous size distribution results in poor predictability and reproducibility
- **Anticancer-in-oil mixture:** unstable emulsion – the belief that it allows for a sustained drug release to the tumor is untrue

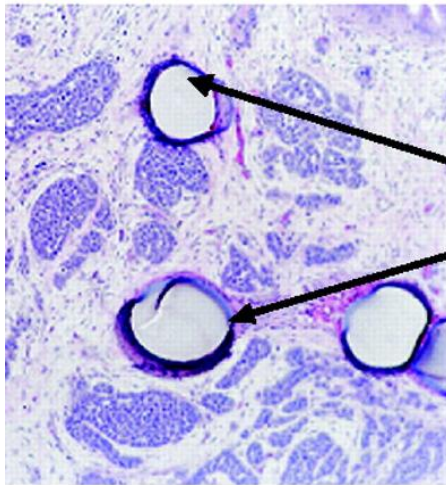


# Conventional Lipiodol TACE: Pharmacokinetic profile

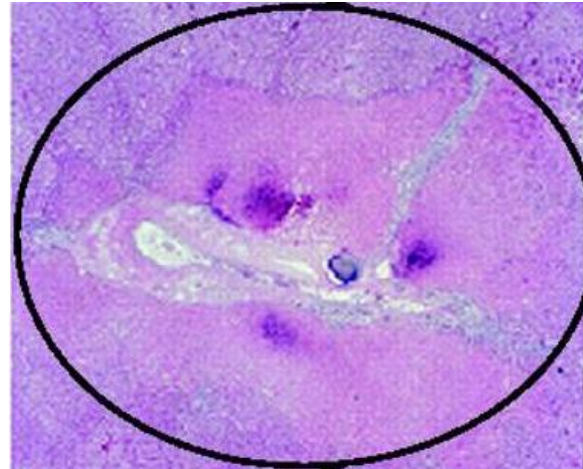
- Serum doxorubicin levels at different time points in patients receiving conventional TACE and maximum serum doxorubicin concentration



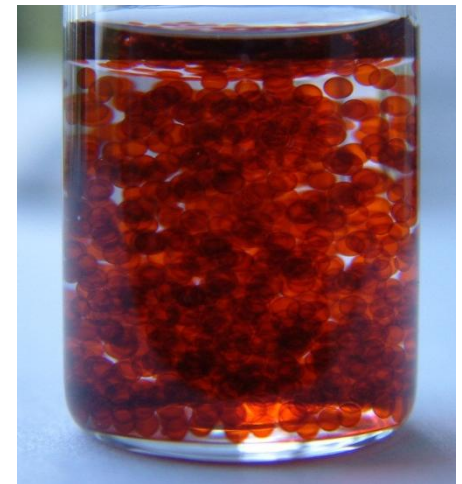
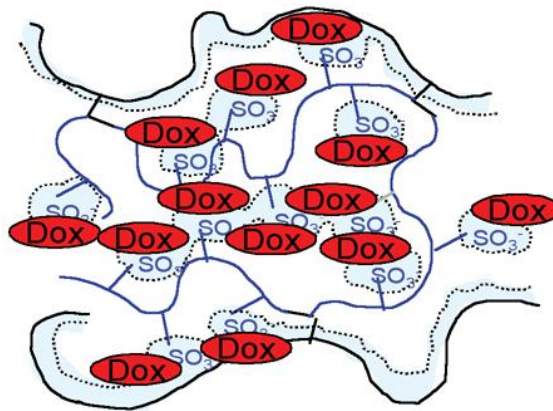
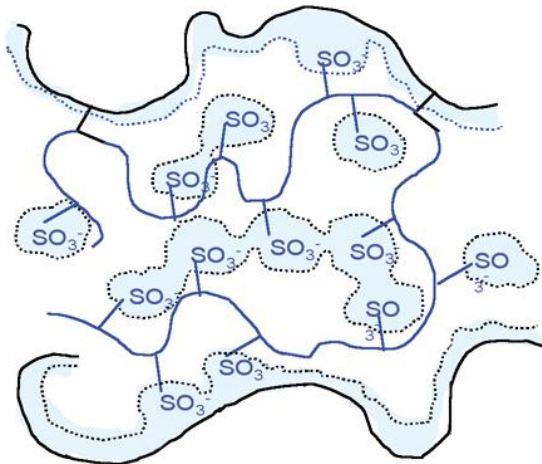
# Drug eluting bead doxorubicin (DEBDOX) changes the paradigm of TACE



DEB

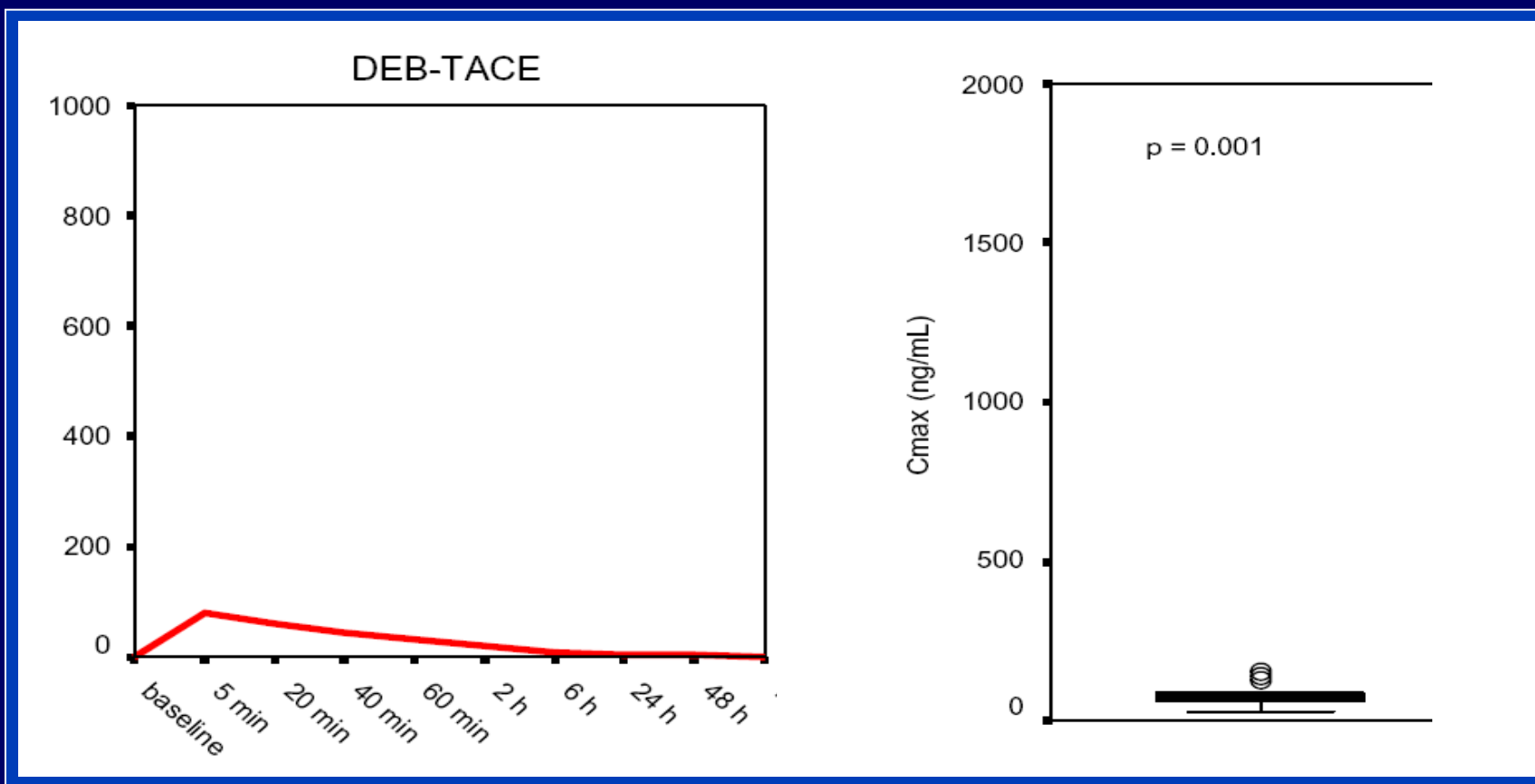


Necrotic Tumor



# Drug eluting bead doxorubicin (DEBDOX): Pharmacokinetic profile

- Serum doxorubicin levels at different time points in patients receiving DEB-TACE and maximum serum doxorubicin concentration



# ***Drug eluting bead doxorubicin (DEBDOX) vs conventional TACE: A RCT (PRECISION V)***

CLINICAL INVESTIGATION

## **Prospective Randomized Study of Doxorubicin-Eluting-Bead Embolization in the Treatment of Hepatocellular Carcinoma: Results of the PRECISION V Study**

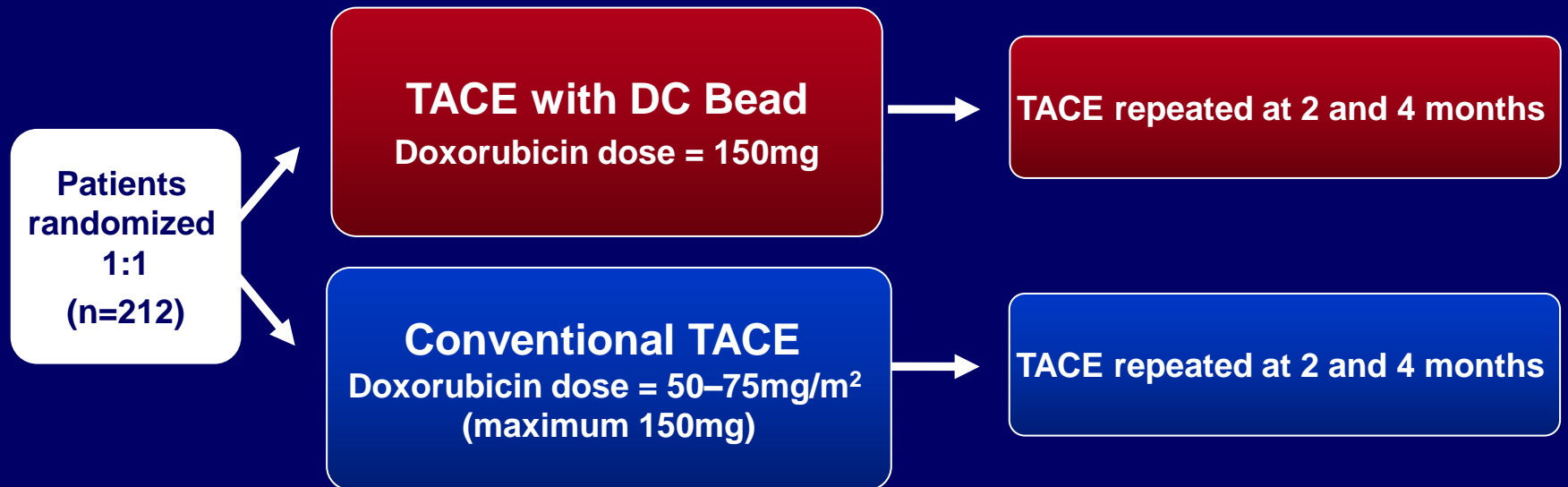
**Johannes Lammer · Katarina Malagari · Thomas Vogl · Frank Pilleul · Alban Denys · Anthony Watkinson · Michael Pitton · Geraldine Sergent · Thomas Pfammatter · Sylvain Terraz · Yves Benhamou · Yves Avajon · Thomas Gruenberger · Maria Pomoni · Herbert Langenberger · Marcus Schuchmann · Jerome Dumortier · Christian Mueller · Patrick Chevallier · Riccardo Lencioni · On Behalf of the PRECISION V Investigators**

**CVIR**

**The Editors' Medal 2011**

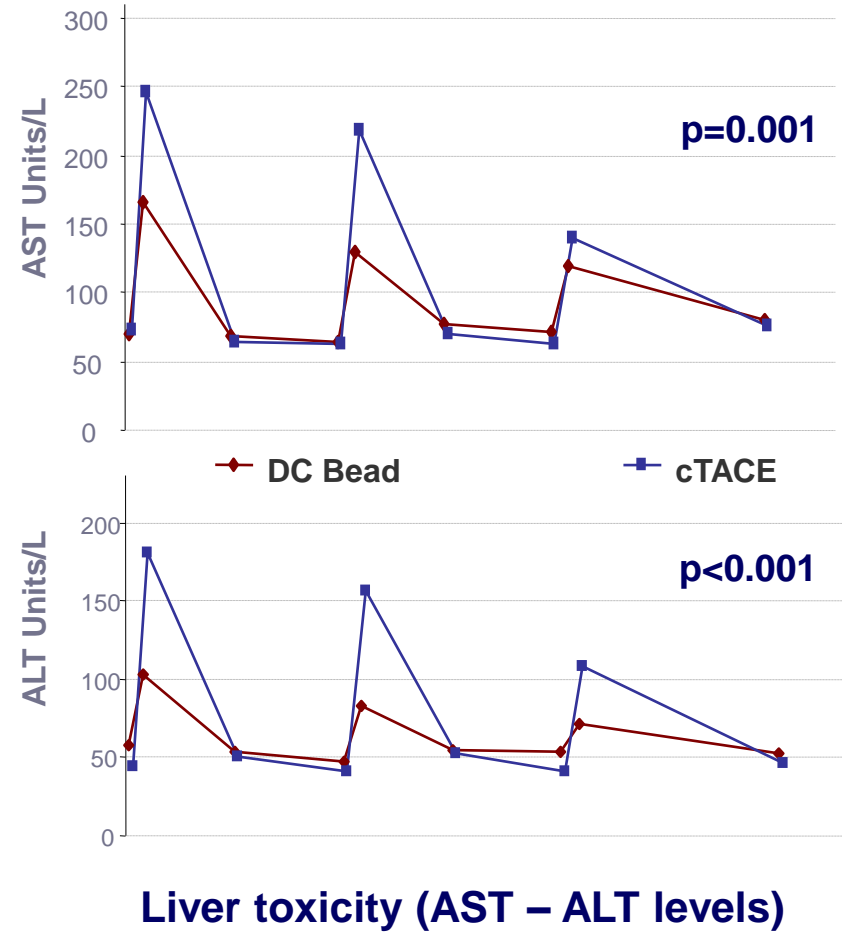
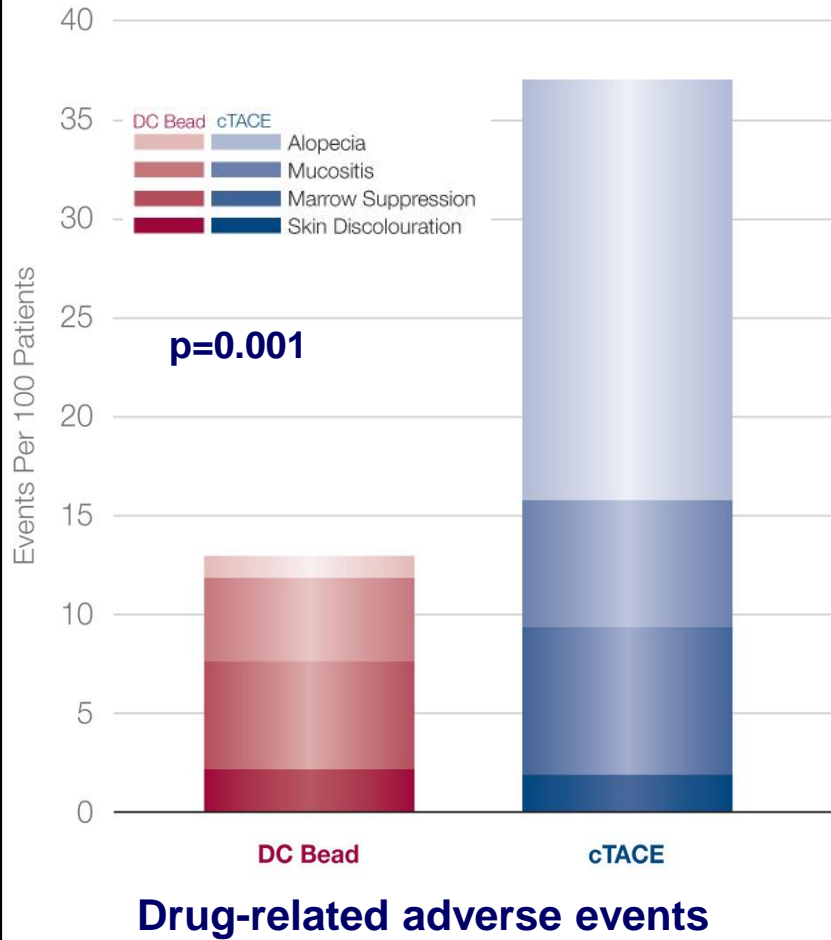
# ***Drug eluting bead doxorubicin (DEBDOX) vs conventional TACE: A RCT (PRECISION V)***

- International multicenter phase II study of DC Bead (BTG-Biocompatibles) with doxorubicin versus conventional Lipiodol TACE with doxorubicin

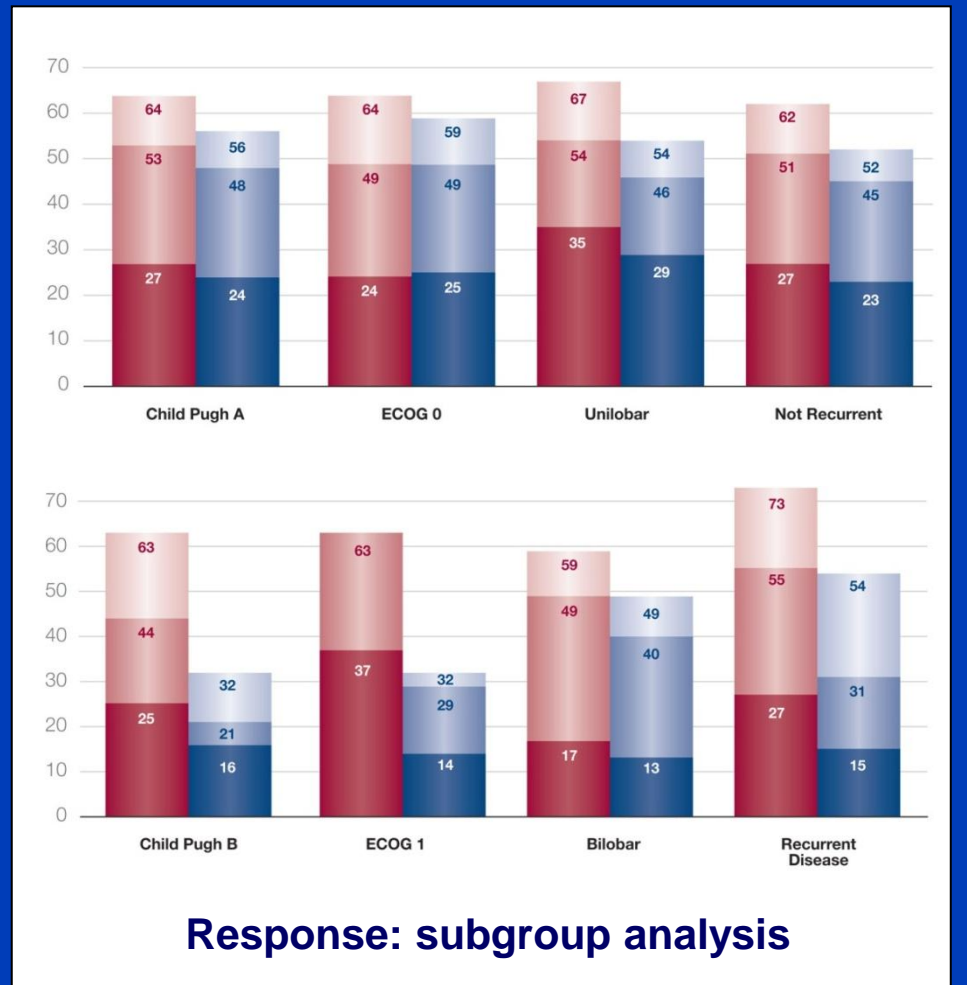
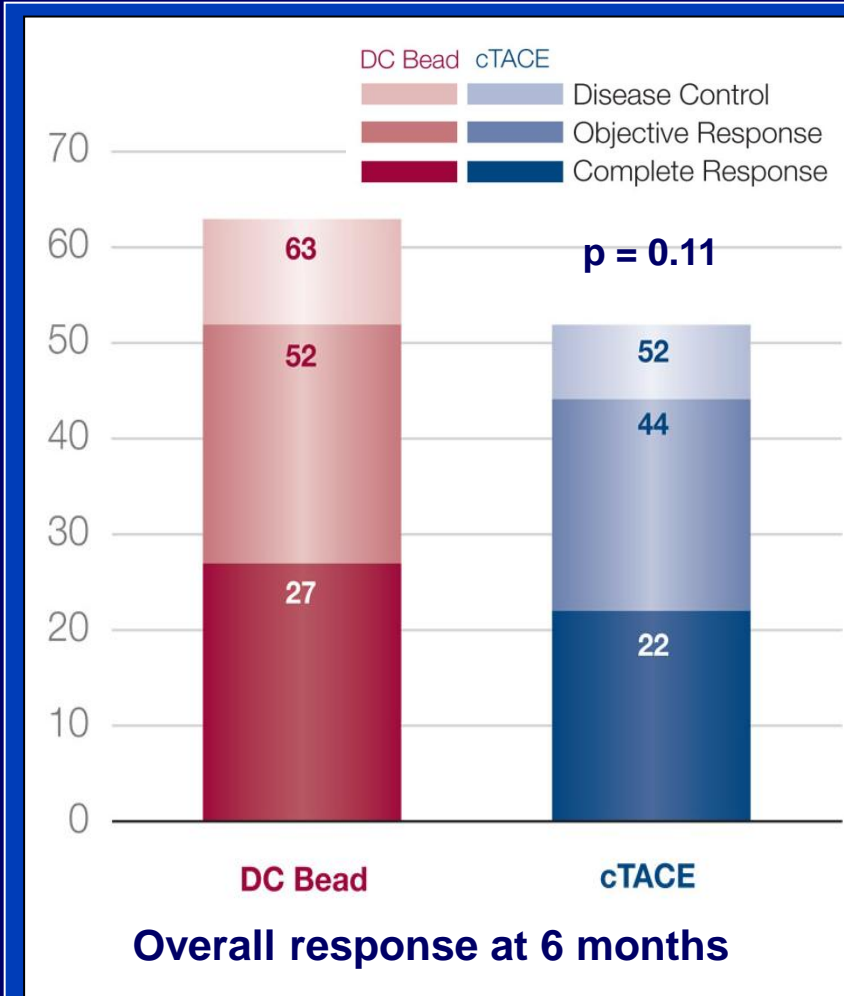


- Primary endpoint: 6-month tumor response by central independent review
- Secondary endpoints included safety (toxicity according to SWOG)

# DEBDOX vs cTACE: Drug-related AEs and liver toxicity are markedly reduced

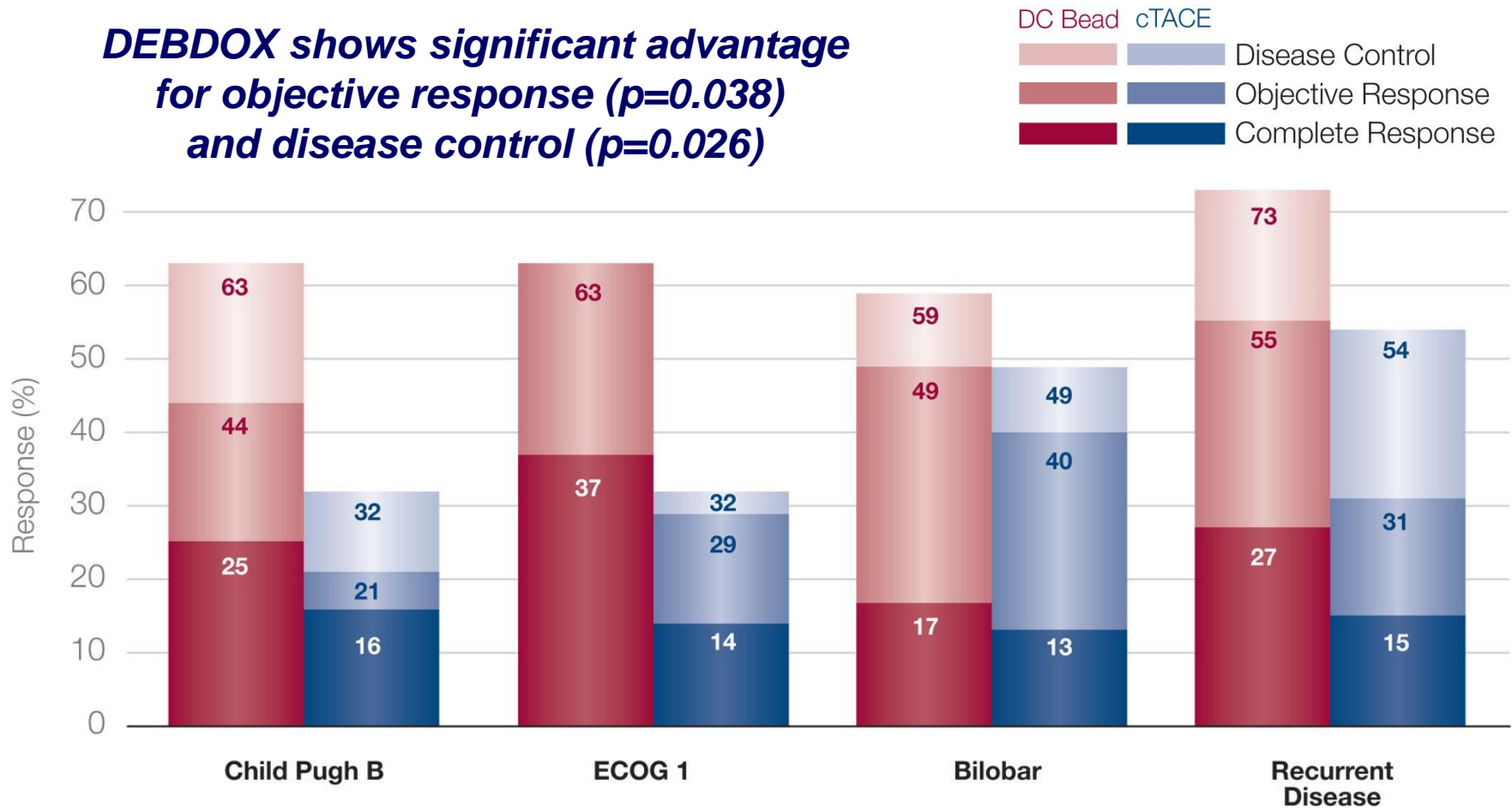


# DEBDOX vs cTACE: Response rates are higher in patients with more advanced disease

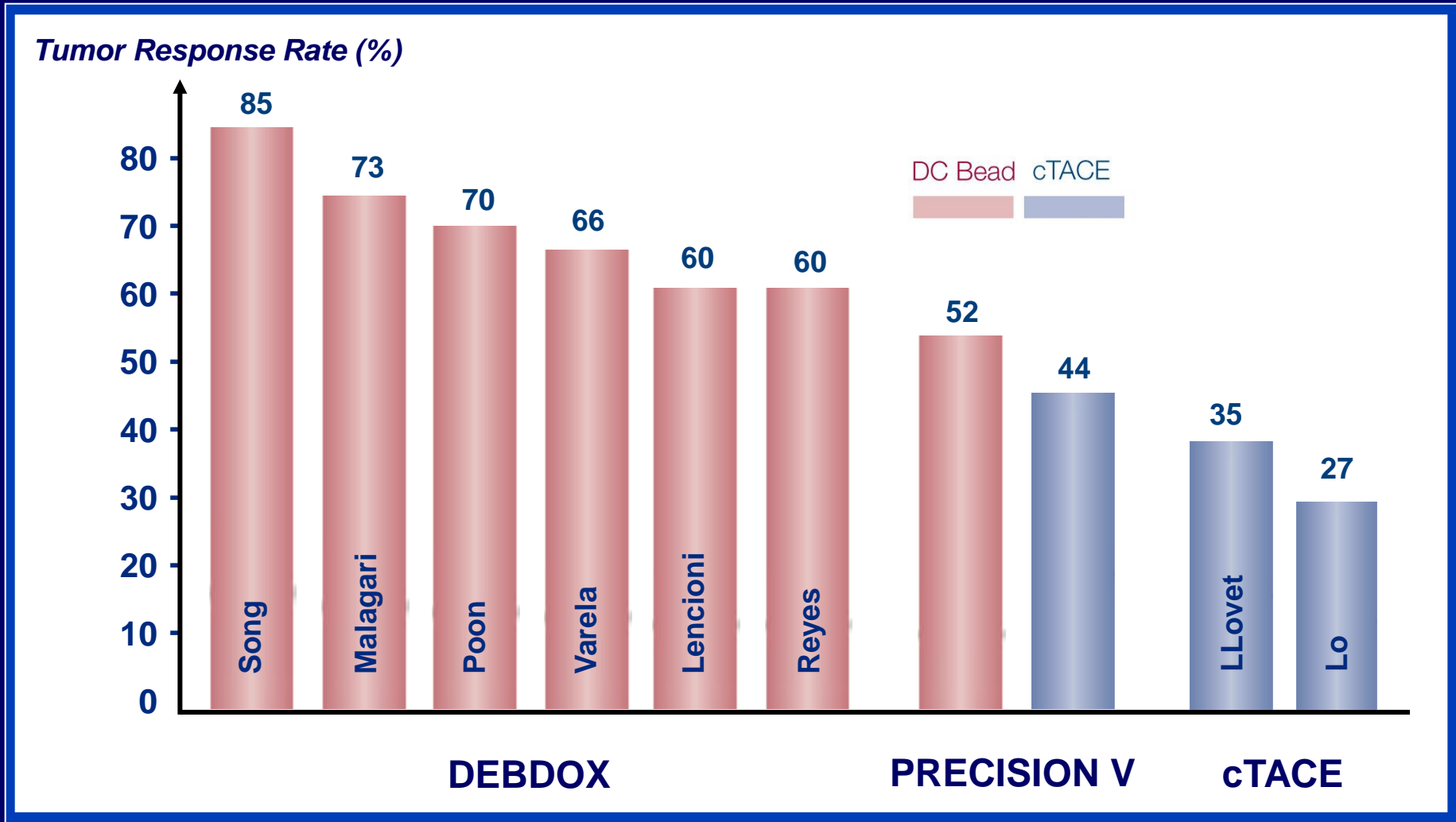


# DEBDOX vs cTACE: Response rates are higher in patients with more advanced disease

**DEBDOX shows significant advantage for objective response ( $p=0.038$ ) and disease control ( $p=0.026$ )**



# ***DEBDOX vs conventional Lipiodol TACE: Tumor response rates***



# ***DEBDOX: Development of procedural standards and technical recommendations***

## **Transcatheter Treatment of Hepatocellular Carcinoma with Doxorubicin-Loaded DC Bead: Technical Recommendations**

Riccardo Lencioni <sup>1</sup>, Thierry de Baere <sup>2</sup>, Martha Burrel <sup>3</sup>, James G. Caridi <sup>4</sup>, Johannes Lammer <sup>5</sup>, Katerina Malagari <sup>6</sup>, Robert C. Martin <sup>7</sup>, Elisabeth O'Grady <sup>8</sup>, Maribel Real <sup>3</sup>, Thomas J. Vogl <sup>9</sup>, Anthony Watkinson <sup>10</sup>, Jean-Francois H. Geschwind <sup>11</sup>

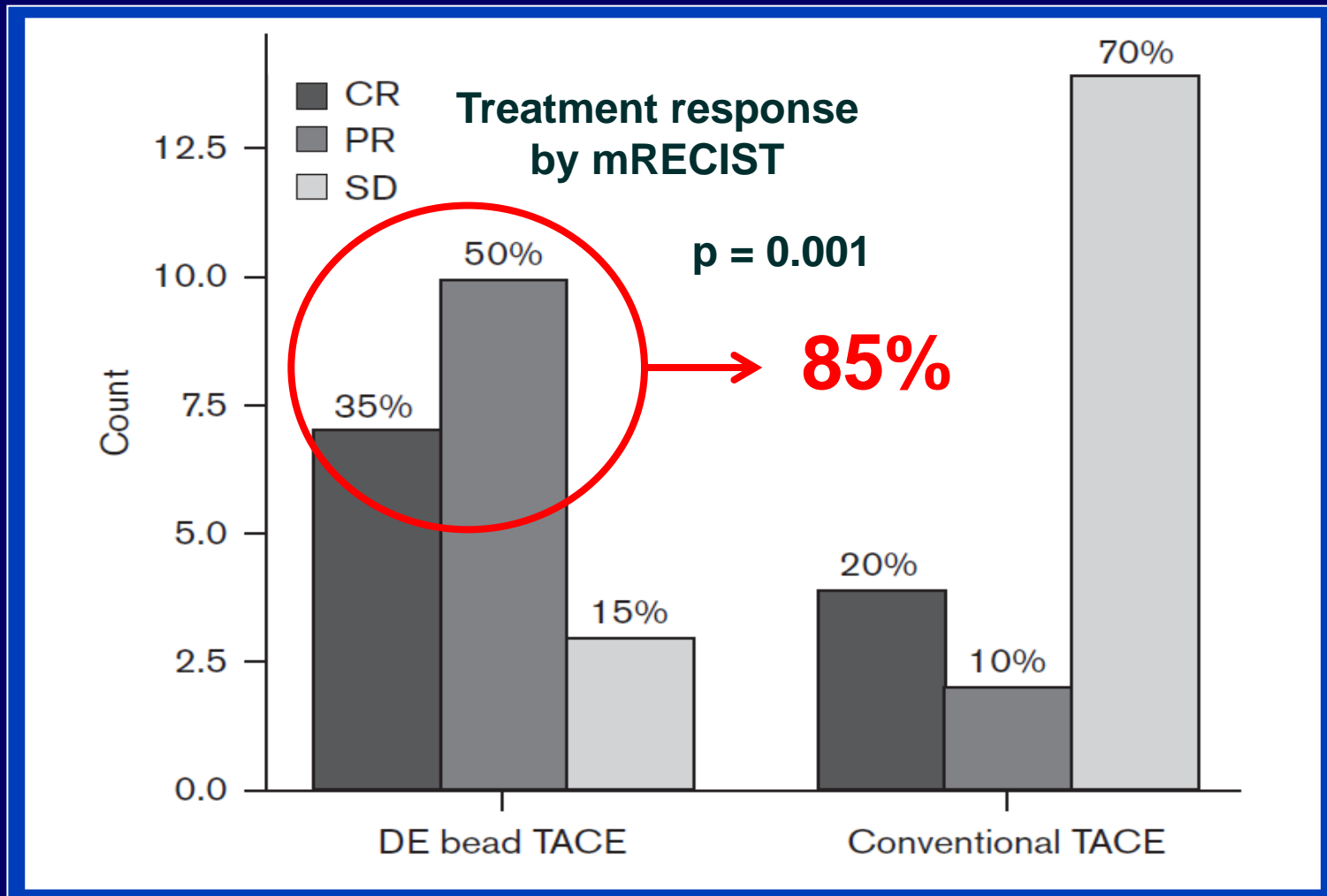
- **Bead size: 100-300µm**
- **Loading dose: 25-37.5 mg doxorubicin / ml of beads**
- **Dilution: 5-10 ml contrast / ml of beads**
- **Injection rate: 1 ml / minute**
- **Tumor response by mRECIST for HCC**

# DEBDOX vs conventional Lipiodol TACE: A case-control study in Asian patients

**Table 1 Baseline patients characteristics**

Variable	DEB (N= 20)	cTACE (N= 20)	P value
Age, years (mean $\pm$ SD)	68 $\pm$ 9	59 $\pm$ 8	NS
Sex (male/female)	15/5	16/4	NS
Etiology (HBV/HCV/alcohol/others)	12/2/2/4	15/2/0/3	NS
Child-Pugh class (A/B)	18/2	16/4	NS
AFP(ng/ml)	2080 $\pm$ 7571	1945 $\pm$ 4974	NS
PIVKA-II	732 $\pm$ 869	812 $\pm$ 863	NS
Tumor size, cm (mean $\pm$ SD)	6.3 $\pm$ 3.8	6.2 $\pm$ 3.7	NS
Largest lesion diameter $\leq$ 5 cm/ >5 cm	8/12	8/12	NS
Uninodular/multinodular	8/12	12/8	NS
Tumor type <sup>a</sup>			NS
Nodular	14	14	
Massive	2	2	
Infiltrative	4	4	
Portal vein thrombosis (absent/ present)	17/3	13/7	NS
Extrahepatic disease (absent/present)	18/2	20/0	NS
BCLC stage (A/B/C)	6/10/4	7/6/7	NS

# DEBDOX vs conventional Lipiodol TACE: A case-control study in Asian patients



# DEBDOX vs conventional Lipiodol TACE: Where do we stand?

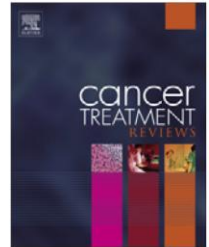


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Antitumour treatment

Evolving strategies for the management of intermediate-stage hepatocellular carcinoma: Available evidence and expert opinion on the use of transarterial chemoembolization

J.-L. Raoul <sup>a,\*</sup>, B. Sangro <sup>b,c</sup>, A. Forner <sup>d</sup>, V. Mazzaferro <sup>e</sup>, F. Piscaglia <sup>f</sup>, L. Bolondi <sup>f</sup>, R. Lencioni <sup>g</sup>

- ***Compared with conventional TACE, drug eluting bead has a standardized methodology, is more reproducible, and offers improved response and a significantly better safety profile.***

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