

*Il mio primo abstract AIOM*  
*AIOM Giovani 5-6 Luglio 2019*

***Tumor infiltrating lymphocytes after transarterial chemoembolization of colorectal cancer liver metastases***

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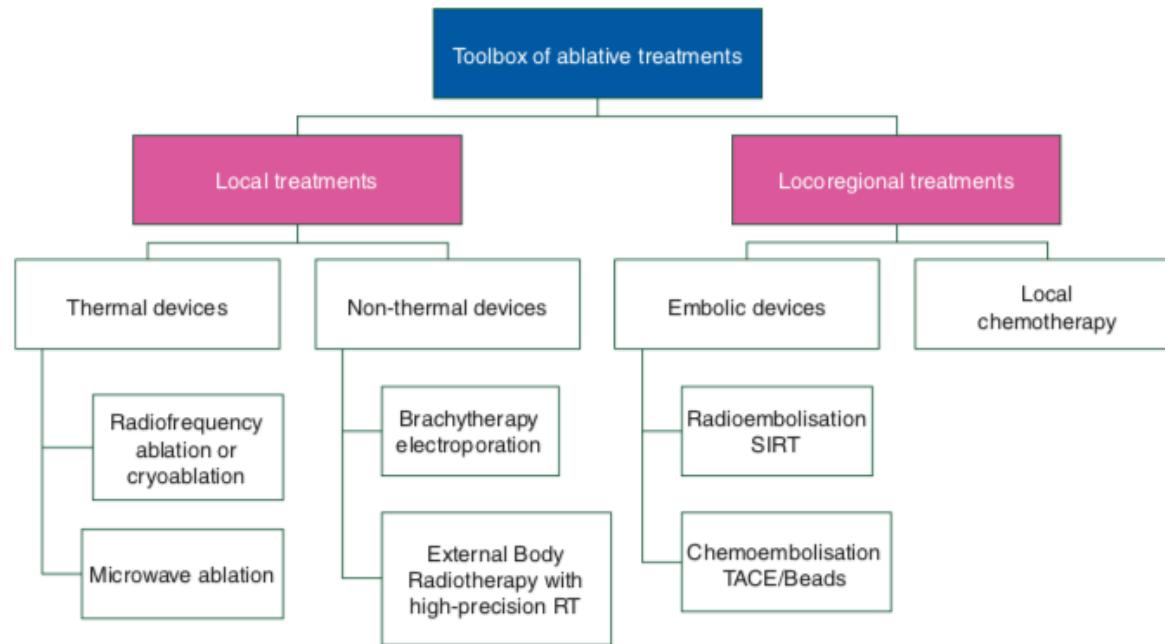
*Istituto Oncologico Veneto – IRCCS, Padova*



Regione del Veneto

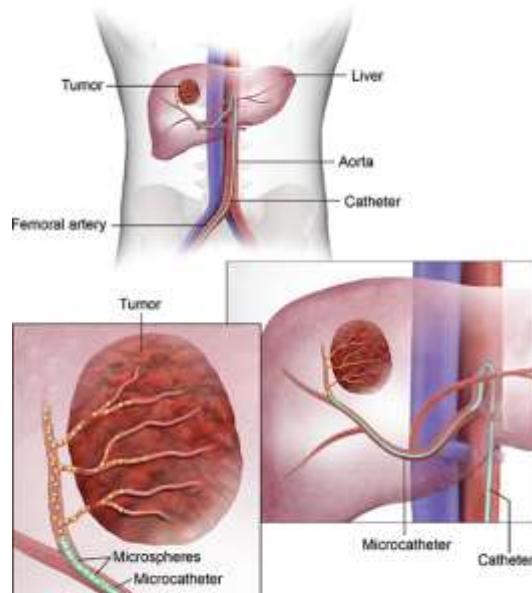
# Background: indications of loco-regional therapies in mCRC

In patients with unresectable liver metastases only or oligometastatic disease, local ablation techniques can be considered



# Background: what is TACE ?

- ❖ Trans-arterial chemoembolization (TACE) is the most commonly performed procedure for liver tumors
- ❖ Technique: infusion of chemotherapeutic agents followed by embolic particles into the hepatic arteries supplying the liver tumors



Source: Khaled M. Elsayes, Sandra A. A. Oldham: Introduction to Diagnostic Radiology:  
www.acsmedmedicine.com  
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# Background: the effects of loco – regional therapies on liver

Preclinical models have shown that liver loco-regional treatments induce local inflammation and enhance systemic adaptive T-cells response

[CANCER RESEARCH 63, 6496–6500, October 1, 2003]

## Activation of Tumor-specific T Lymphocytes by Radio-Frequency Ablation of the VX2 Hepatoma in Rabbits<sup>1</sup>

Thädaus Till Wissniowski,<sup>2</sup> Johannes Hünsler,<sup>2</sup> Daniel Neureiter, Markus Frieser, Stefan Schaber, Birgit Esslinger, Reinhard Voll, Deike Strobel, Eckhart G. Hahn, and Detlef Schuppan<sup>3</sup>

Department of Medicine I (J. H., T. T. W., M. F., S. S., B. E., D. St., E. G. H., D. Sc.), Institute of Pathology (D. N.), and Department of Medicine III (R. V.), Friedrich-Alexander University, Erlangen-Nürnberg, 91054 Erlangen, Germany



## Activation of dendritic cells by local ablation of hepatocellular carcinoma

Mona Y. Ali<sup>1,\*</sup>, Christian F. Grimm<sup>1,\*</sup>, Marcus Ritter<sup>1</sup>, Leonhard Mohr<sup>1</sup>, Hans-Peter Allgaier<sup>1</sup>, Robert Weth<sup>1</sup>, Wulf O. Bocher<sup>2</sup>, Katja Endrulat<sup>1</sup>, Hubert E. Blum<sup>1</sup>, Michael Geissler<sup>1,\*</sup>

<sup>1</sup>Department of Medicine II, University Hospital Freiburg, Hugstetter Strasse 55, D-79106 Freiburg, Germany  
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# Background: role of TILs in mCRC

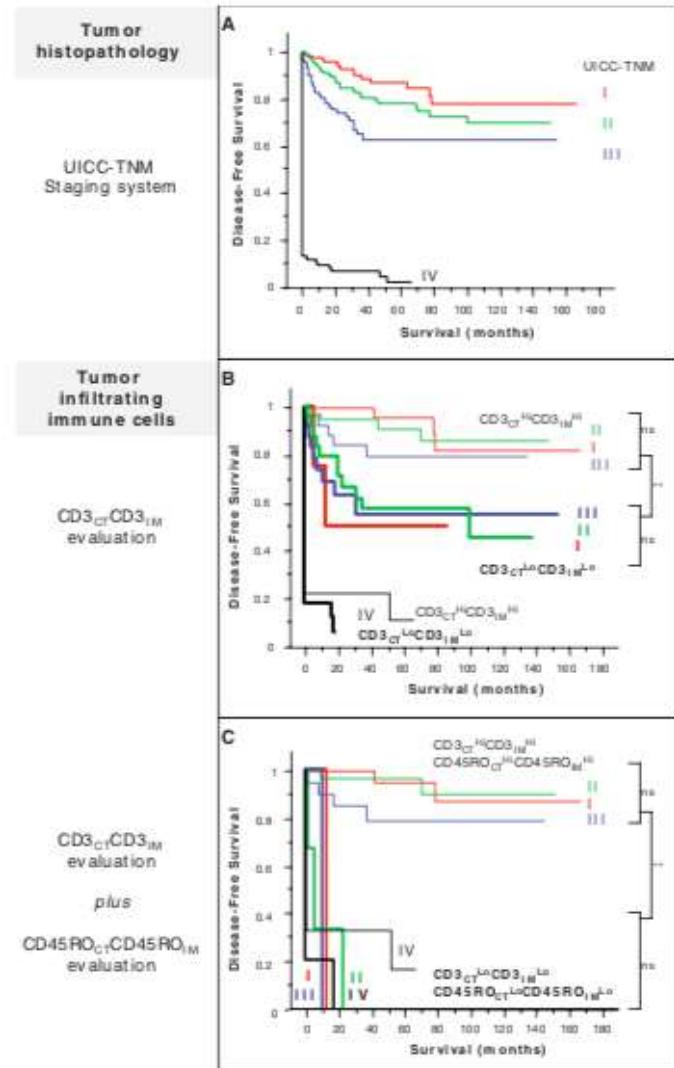
## Type, Density, and Location of Immune Cells Within Human Colorectal Tumors Predict Clinical Outcome

Jérôme Galon,<sup>1,\*†</sup> Anne Costes,<sup>1</sup> Fatima Sanchez-Cabo,<sup>2</sup> Amos Kirilovsky,<sup>1</sup> Bernhard Mlecnik,<sup>2</sup> Christine Lagorce-Pagès,<sup>3</sup> Marie Tosoloni,<sup>1</sup> Matthieu Camus,<sup>1</sup> Anne Berger,<sup>4</sup> Philippe Wind,<sup>4</sup> Franck Zinzindohoué,<sup>5</sup> Patrick Bruneval,<sup>6</sup> Paul-Henri Cugnenc,<sup>5</sup> Zlatko Trajanoski,<sup>2</sup> Wolf-Herman Fridman,<sup>1,7</sup> Franck Pagès<sup>1,7,†</sup>

In mCRC type, density and location of TILs have a prognostic significance superior to that of TNM classification system



Galon et al al. Science 2006;



# Endpoints

- ❖ **Primary:** assess the effects of TACE on intra- and peri-tumoral inflammatory infiltration in CRC liver metastases
- ❖ **Secondary:** to test if TACE could increase the number of TILs



# Study population

1406 CRC pts  
(Jan 2010 – Dec 2016)



586 pts with liver limited disease



41 pts underwent at least one TACE



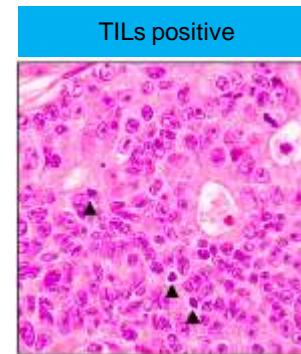
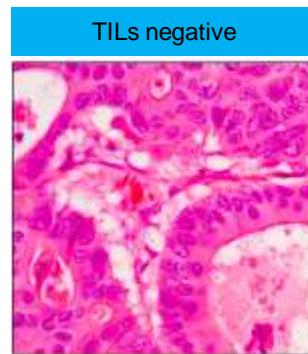
16 pts underwent liver resection after TACE

ELIGIBLE  
PATIENTS

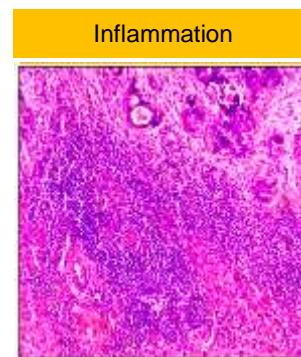
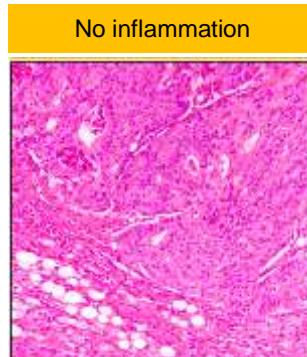
9 pts underwent liver resection also before TACE

# Materials and methods

- ❖ Evaluation of TILs: low < 2 per hpf, high  $\geq$  2 per hpf



- ❖ Evaluation of Peritumoral Inflammation (PI)



## Results: population features

- ❖ Median age 58 years
- ❖ Gender: 12 males and 4 females
- ❖ 1 pts with microsatellite instability
- ❖ Median n° of chemotherapy lines administered before TACE: 1 (range 0-2)

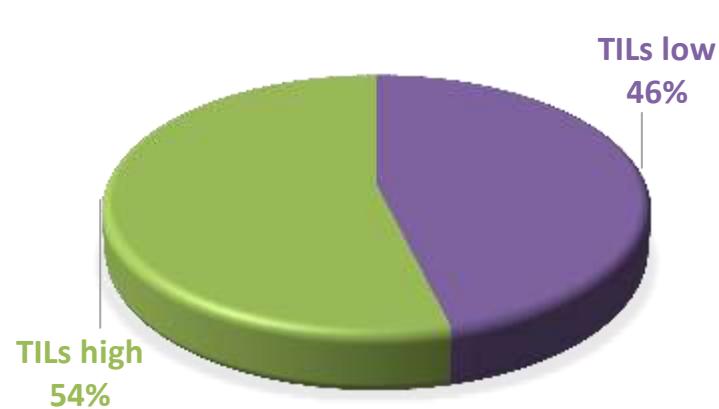


# Results: effect of TACE on TILs and PF

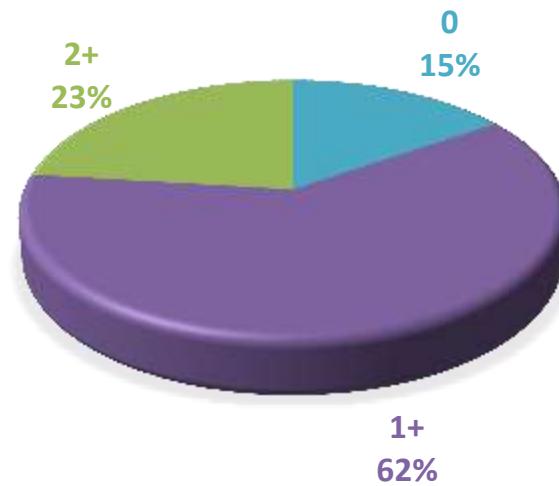
Pathological characteristics of colorectal liver metastases after TACE...

N° of evaluable patients = 13

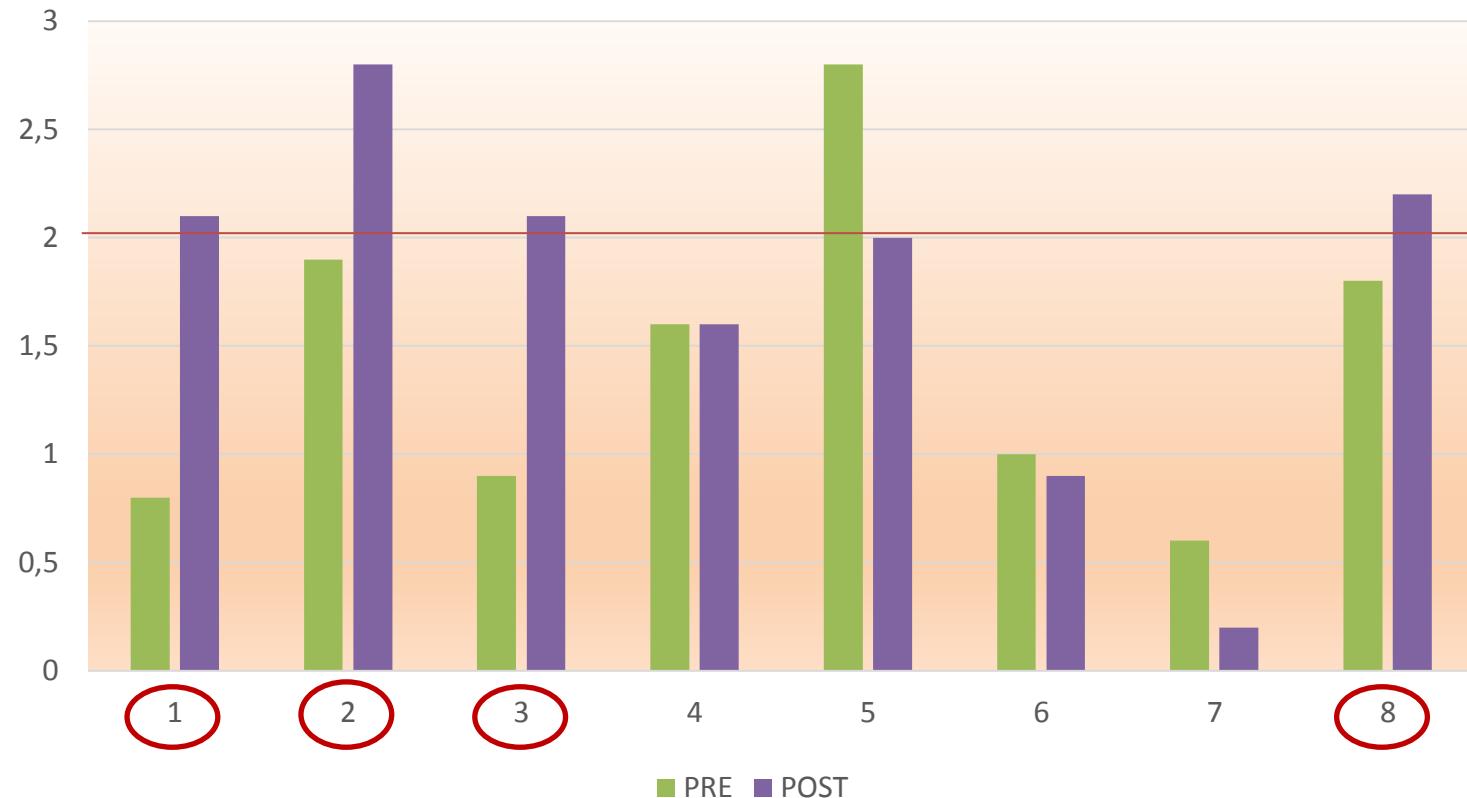
TILS



PF



# Results: could TACE enhance TILs?



**50 % of patients switched to “TILs high” following TACE**

# Conclusions

**TACE appears to stimulate immune response through an increased of number of TILs**

- ❖ After TACE TILs-high status was identified in **54%** of colorectal liver metastases

In literature TILs high status was identified in **30%** of colorectal adenocarcinoma

- ❖ **50%** of patients switched to TILs high following TACE

# Future perspectives

- ❖ In future the study through digital pathology of this selected population can help to better understand the effect of TACE on colorectal cancer liver metastases
- ❖ Could the enhancement of the immune response by TACE open the doors to a possible combination between TACE and immunotherapy?





TO...  
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