

Immune modulating effects of TACE

Trans-arterial chemoembolization as a loco-regional inducer of immunogenic cell death in hepatocellular carcinoma: implications for immunotherapy.

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The relationship between intra-tumoral (IT) and non-tumoral (NT) T-cell density expressed in cells/mm² of tissue in T+ patients stratified on the basis of achievement of necrosis (N) in <50% (N-, n=37) or >50% (n=21) of the assayed tumoural tissue post-TACE.

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The expression of a panel of biomarkers of immune-tolerance in patients samples with (T+) or without (T-) prior TACE treatment.

*Immunotherapy Toxicity in HCC***Supplementary Table 1.** Patient disposition across participating institutions.

Participating Institution	Patient samples (n, %)
Imperial College London, London, United Kingdom	3 (2.5)
Istituto Nazionale Tumori, Milan, Italy	21 (17.6)
Hospital Clinic, Barcelona, Spain	18 (15.1)
Vall D'Hebron Hospital, Barcelona, Spain	5 (4.2)
San Martino University Hospital, Genova, Italy	10 (8.4)
University of Udine, Hepatology and Liver Transplantation Unit, Udine, Italy	62 (52.1)
Total	119 (100)

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Supplementary Table 2. The relationship between T-cell density across intra-tumoural (IT), peri-tumoural (PT) and non-tumoural background liver (NT) and prior treatment with TACE in patients with HCC.

	Multiplex IHC	TACE Group	Median cell density (cells/mm ²)	IQR	p value
IT	CD4 ⁺	TACE-	151.1	166.3	0.62
		TACE+	40.8	191.8	
	CD4 ⁺ FoxP3 ⁺	TACE-	40.8	61.7	0.006*
		TACE+	8.2	32.7	
	CD8 ⁺	TACE-	118.4	129.9	0.002*
		TACE+	32.7	141.8	
CD8 ⁺ PD-1 ⁺	TACE-	36.7	34.7	<0.001*	
	TACE+	16.3	40.8		
PT	CD4 ⁺	TACE-	608.6	656.8	0.41
		TACE+	600.0	580.1	
	CD4 ⁺ FoxP3 ⁺	TACE-	24.7	89.9	0.95
		TACE+	40.8	81.8	
	CD8 ⁺	TACE-	526.9	430.9	0.67
		TACE+	580.0	531.0	
CD8 ⁺ PD-1 ⁺	TACE-	98.0	83.7	0.85	
	TACE+	100.0	77.0		
NT	CD4 ⁺	TACE-	167.5	190.4	0.27
		TACE+	200.0	147.0	
	CD4 ⁺ FoxP3 ⁺	TACE-	8.2	24.5	0.74
		TACE+	1.0	32.7	
	CD8 ⁺	TACE-	251.7	200.0	0.12
		TACE+	253.2	188.0	
CD8 ⁺ PD-1 ⁺	TACE-	146.4	89.9	<0.001*	
	TACE+	9.4	57.2		

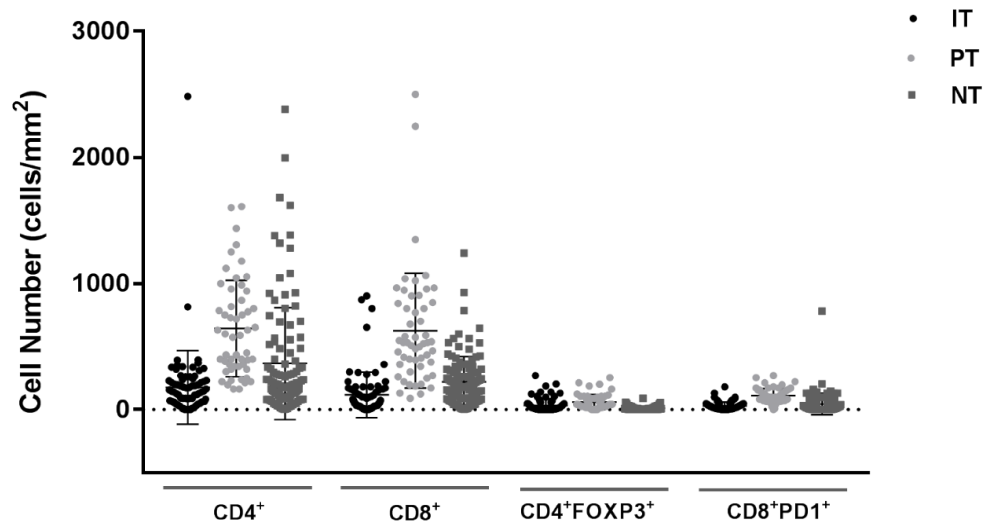
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Supplementary Table 3. Multivariable analysis of recurrence-free survival (RFS).

Variable	RFS HR (95% CI)	P value
IT CD4+FOXP3+ <median/≥median	3.51 (1.14-10.81)	0.028*
TNM Stage I/≥II	1.05 (0.19-5.69)	0.952
Child-Turcotte Pugh class A/B-C	1.76 (0.33-9.56)	0.504
AFP <median/≥median	1.10 (0.35-3.40)	0.869

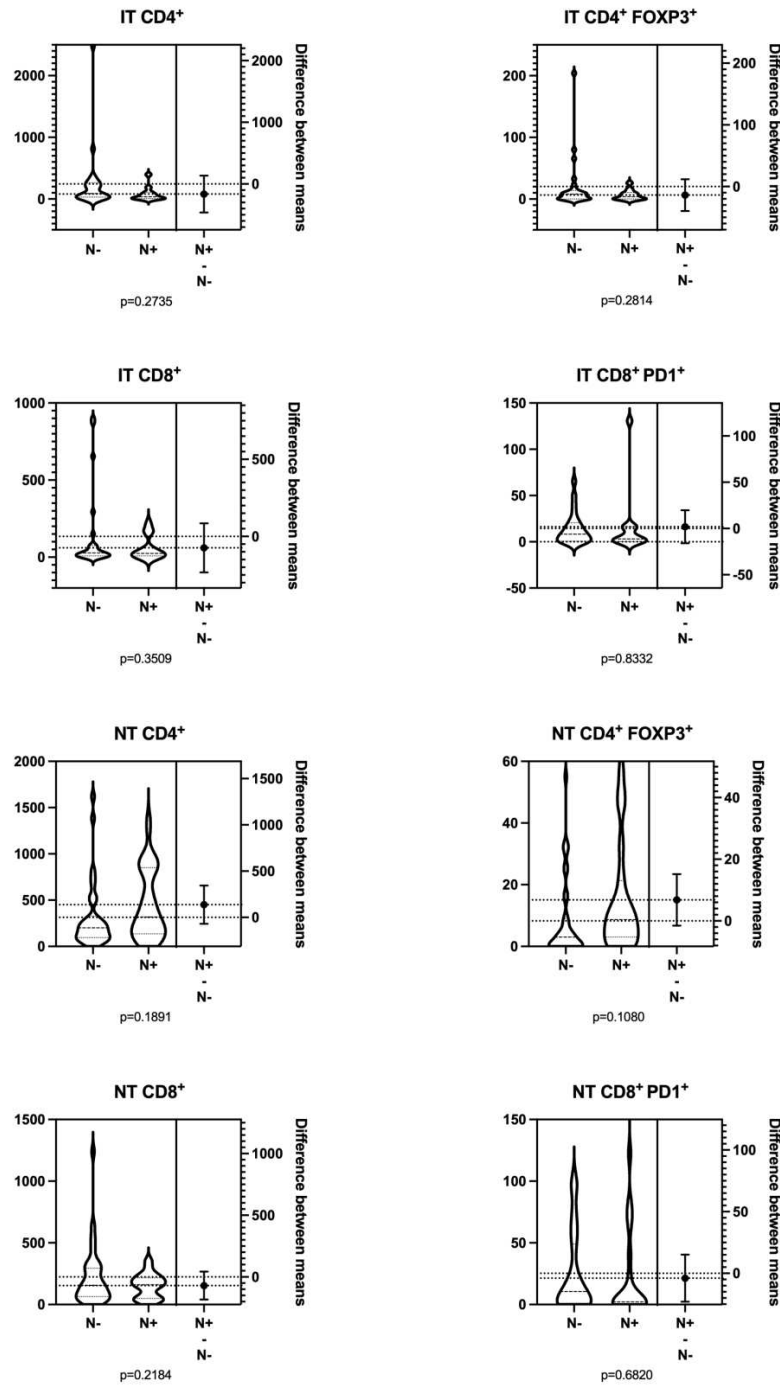
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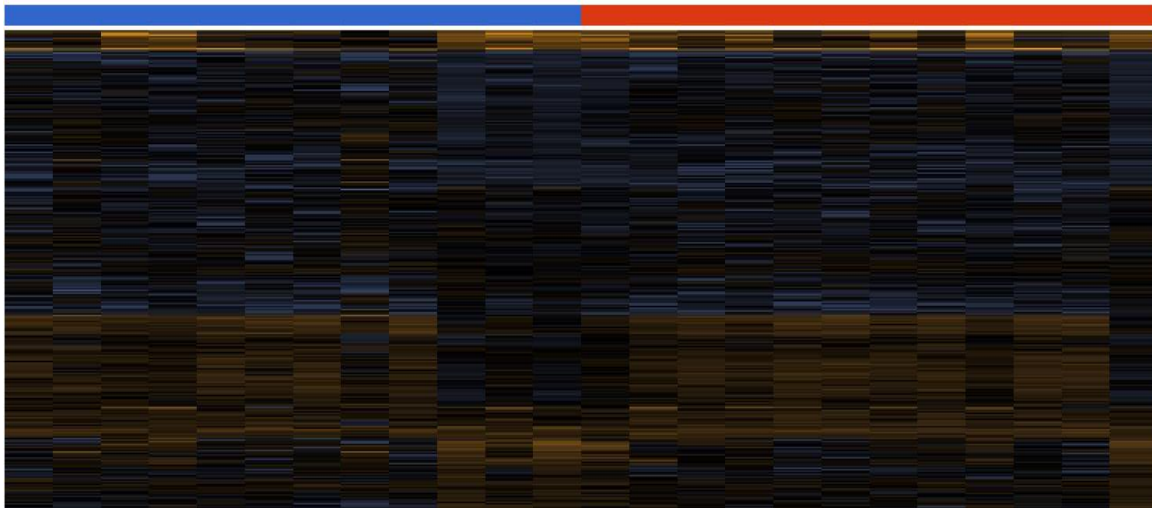
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Supplementary Figure 4. The expression of a panel of biomarkers of immune-tolerance in patients samples with (T+) or without (T-) prior TACE treatment.

