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Supplementary information

Biological and clinical significance of tumour-infiltrating lymphocytes in the era of immunotherapy: a multidimensional approach

In the format provided by the authors and unedited

Supplementary Table 1 | Associations between TIL abundance and clinical outcomes with ICI therapy for solid tumours

Study	Treatment	Analytical method	TIL type	Outcome	
				Association	Parameter
Melanoma					
Helmink et al. (2020)[1]	Nivolumab ± ipilimumab	RNA-seq and IHC	$CD8^+$ T cells	None	NA
			$CD4^+$ T cells	None	NA
			B cells	Improved	Clinical response
			TLS	Improved	Clinical response
Chen et al. (2016)[2]	Anti-CTLA4 and/or anti-PD-1 mAbs	IHC	$CD8^+$ T cells	Improved	Clinical response
			$CD4^+$ T cells	None	NA
			B cells	None	NA
Cabrita et al. (2020)[3]	Anti-CTLA4 and/or anti-PD-1 mAbs	IHC, mIF and RNA-seq	$CD8^+$ T cells	Improved	OS
			B cells	Improved	OS
			TLS	Improved	Clinical response, OS
Balatoni et al. (2018)[4]	Ipilimumab	IHC	$CD8^+$ T cells	Improved	Clinical response
			$CD4^+$ T cells	Improved	Clinical response
			B cells	Improved	Clinical response
Wong et al. (2019)[5]	Pembrolizumab, or nivolumab ± ipilimumab	mIF	$CD8^+$ T cells	Improved	Clinical response, PFS
			$CD4^+$ T cells	Improved	Clinical response, PFS
			B cells	Improved	PFS
Amaria et al. (2018)[6]	Nivolumab ± ipilimumab (neoadjuvant)	IHC	$CD8^+$ T cells	Improved	Clinical response
			$CD4^+$ T cells	None	NA
			B cells	None	NA
Daud et al. (2016)[7]	Pembrolizumab or nivolumab	Flow cytometry	$CD8^+$ T cells	None	NA
			$CD4^+$ T cells	None	NA
			T_{reg} cells	None	NA
Mastracci et al. (2020)[8]	Ipilimumab	IHC	$CD8^+$ T cells	Improved	Clinical response
			$CD4^+$ T cells	None	NA
			B cells	None	NA
Tumeh et al. (2014)[9]	Pembrolizumab	IHC	$CD8^+$ T cells	Improved	Clinical response
			$CD4^+$ T cells	None	NA
Uryvaev et al. (2018)[10]	Pembrolizumab or nivolumab	IHC	$CD8^+$ T cells	Improved	Clinical response
			$CD4^+$ T cells	Improved	Clinical response
Hamid et al. (2019)[11]	Atezolizumab	IHC	$CD8^+$ T-cells	Improved	Clinical response, PFS, OS
Harder et al. (2019)[12]	Ipilimumab	IHC	$CD8^+$ T cells	Improved	OS
Gide et al. (2020)[13]	Pembrolizumab or ipilimumab + nivolumab	mIF	$CD8^+$ T cells	Improved	Clinical response
Madonna et al. (2018)[14]	Ipilimumab	mIF	$CD8^+$ T cells	Reduced	OS
van Duin et al. (2024)[15]	Anti-PD-1 mAb or ipilimumab + nivolumab	H&E	T cells	Improved	Clinical response, PFS, OS
Non-small-cell lung cancer					
Lopez de Rodas et al. (2022)[16]	Nivolumab or atezolizumab	mIF and WES	$CD8^+$ T cells	Improved	PFS, OS
			$CD4^+$ T cells	None	NA
			B cells	Improved	OS
Patil et al. (2022)[17]	Atezolizumab	RNA-seq and H&E	Plasma cells	Improved	OS
			TLS	Improved	OS
Niemeijer et al. (2020)[18]	Nivolumab	IHC	$CD8^+$ T cells	Improved	Clinical response
			$CD4^+$ T cells	Improved	Clinical response
Uryvaev et al. (2018)[10]	Nivolumab or pembrolizumab	IHC	$CD8^+$ T cells	Improved	Clinical response
			$CD4^+$ T cells	None	Clinical response
Kaira et al. (2023)[19]	Pembrolizumab	mIF	$CD4^+$ T cells	Improved	PFS, OS
			$CD8^+$ T cells	Improved	OS
Hu-Lieskovan et al. (2019)[20]	Pembrolizumab	IHC	$CD8^+$ T cells	Improved	Clinical response, PFS
			$CD4^+$ T cells	None	NA
Cottrell et al. (2018)[21]	Nivolumab (neoadjuvant)	H&E	TLS	Improved	Clinical response

Fumet et al. (2018)[22]	Nivolumab or pembrolizumab	IHC and RNA-seq	$CD8^+$ T cells	Improved	PFS
Althammer et al. (2019)[23]	Durvalumab	IHC	$CD8^+$ T cells	Improved	OS
Hurkmans, et al. (2020)[24]	Nivolumab	IHC	$CD8^+$ T-cells	Improved	PFS
Hashemi et al. (2021)[25]	Nivolumab or pembrolizumab	IHC	$CD8^+$ T cells	Improved	PFS, OS
Rakaee et al. (2023)[26]	Pembrolizumab, nivolumab or atezolizumab	H&E	T cells	Improved	PFS
Liu et al. (2023)[27]	Anti-PD-(L)1 mAbs	RNA-seq	TLS	Improved	Clinical response, OS
Sun et al. (2022)[28]	Anti-PD-1 + chemotherapy (neoadjuvant)	H&E and IHC	TLS	Improved	PFS
Provencio et al. (2020)[29]	Nivolumab + chemotherapy (neoadjuvant)	mIF	$CD8^+$ T cells	Improved	Clinical response
Breast cancer					
Hammerl et al. (2021)[30]	Anti-PD-1 mAbs	RNA-seq	TLS	None	NA
Dieci et al. (2022)[31]	Nivolumab (neoadjuvant)	mIF	$CD8^+$ T cells	Improved	Clinical response
			$CD4^+$ T cells	Improved	Clinical response
			T_{reg} cells	Improved	Clinical response
Emens et al. (2019)[32]	Atezolizumab	IHC	$CD8^+$ T cells	Improved	PFS, OS
Voorwerk et al. (2019)[33]	Nivolumab + chemotherapy	IHC	$CD8^+$ T cells	Improved	Clinical response
Emens et al. (2021)[34]	Atezolizumab + nab-paclitaxel	IHC	$CD8^+$ T cells	Improved	PFS, OS
Adams et al. (2019)[35]	Atezolizumab + nab-paclitaxel	IHC	$CD8^+$ T cells	None	NA
Bachelot et al. (2021)[36]	Durvalumab	mIF	$CD8^+$ T cells	None	NA
Colorectal cancer					
Le et al. (2015)[37]	Pembrolizumab	IHC	$CD8^+$ T cells	Improved	Clinical response
Loupakis et al. (2020)[38]	Pembrolizumab, or nivolumab ± ipilimumab	H&E	T cells	Improved	Clinical response, PFS, OS
Urothelial carcinoma					
Gao et al. (2020)[39]	Durvalumab + tremelimumab (neoadjuvant)	IHC	$CD8^+$ T cells	Improved	Clinical response
			$CD4^+$ T cells	Improved	Clinical response
			B cells	Improved	Clinical response
			TLS	Improved	Clinical response, PFS, OS
Van Dijk et al. (2020)[40]	Ipilimumab + nivolumab	mIF	$CD8^+$ T cells	None	NA
			B cells	Reduced	Clinical response
			TLS	None	NA
Rosenberg et al. (2016)[41]	Atezolizumab	IHC	$CD8^+$ T cells	Improved	Clinical response
Deng et al. (2018)[42]	Pembrolizumab, atezolizumab or durvalumab	IHC	$CD8^+$ T cells	Improved	PFS
Mariathasan et al. (2018)[43]	Atezolizumab	WES	$CD8^+$ T cells	Improved	Clinical response
Wang et al. (2018)[44]	Nivolumab	IHC	$CD8^+$ T cells	Improved	Clinical response, PFS, OS
Powles et al. (2019)[45]	Atezolizumab (neoadjuvant)	IHC	$CD8^+$ T cells	Improved	Clinical response
Renal cell carcinoma					
Pignon et al. (2019)[46]	Nivolumab	mIF	$CD8^+$ T cells	Improved	Clinical response, PFS
Ficial et al. (2021)[47]	Nivolumab	mIF	$CD8^+$ T cells	Improved	Clinical response, PFS
Braun et al. (2020)[48]	Nivolumab	mIF	$CD8^+$ T cells	None	NA
Motzer et al. (2020)[49]	Avelumab + axitinib	IHC	$CD8^+$ T cells	None	NA
Helmink et al. (2020)[1]	Nivolumab ± ipilimumab	RNA-seq	B cells	Improved	Clinical response

Head and neck squamous cell carcinoma					
Hanna et al. (2018)[50]	Anti-PD-(L)1 mAb	Flow cytometry	$CD8^+$ T cells	Improved	Clinical response
Hecht et al. (2020)[51]	Chemotherapy and durvalumab + tremelimumab	IHC	$CD8^+$ T cells	Improved	Clinical response
Liu et al. (2022)[52]	Anti-PD-(L)1 mAbs	RNA-seq	TLS	Improved	Clinical response, OS
Sarcoma					
Petitprez et al. (2020)[53]	Pembrolizumab	RNA-seq	$CD8^+$ T cells	None	NA
			B cells	Improved	OS
Italiano et al. (2022)[54]	Pembrolizumab	IHC and RNA-seq	T_{reg} cells	Reduced	Clinical response, PFS, OS
			Plasma Cells	Improved	Clinical response
Keung et al. (2020)[55]	Pembrolizumab	mIF	$CD8^+$ T cells	Improved	Clinical response, PFS
Gastric cancer					
Tong et al. (2022)[56]	Sintilimimab or pembrolizumab + chemotherapy	mIF	$CD8^+$ T cells	Improved	Clinical response, PFS
Oesophageal cancer					
Kato et al. (2020)[57]	Nivolumab	IHC	$CD8^+$ T cells	None	NA
Multiple tumour types					
Vanhersecke et al. (2021)[58]	Anti-PD-(L)1 mAbs ± other ICIs	H&E and IHC	$CD8^+$ T cells	Improved	PFS
			TLS	Improved	PFS, OS
Prat et al. (2017)[59]	Nivolumab or pembrolizumab	RNA-seq	$CD8^+$ T cells	Improved	PFS
			$CD4^+$ T cells	Improved	PFS
			T_{reg} cells	Improved	PFS
			B cells	None	NA

H&E, haematoxylin and eosin staining; ICI, immune-checkpoint inhibitor; IHC, immunohistochemistry; mAb, monoclonal antibody; mIF, multiplex immunofluorescence imaging; NA, not applicable; OS, overall survival; PFS, progression-free survival; RNA-seq; RNA sequencing; TIL, tumour-infiltrating lymphocyte; TLS, tertiary lymphoid structures; T_{reg}, regulatory T; WES, whole-exome sequencing.

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