

This is a repository copy of *Immunotherapy in gastrointestinal cancer: Recent results,* current studies and future perspectives.

White Rose Research Online URL for this paper: http://eprints.whiterose.ac.uk/109941/

Version: Accepted Version

Article:

Moehler, M, Delic, M, Goepfert, K et al. (14 more authors) (2016) Immunotherapy in gastrointestinal cancer: Recent results, current studies and future perspectives. European Journal of Cancer, 59. pp. 160-170. ISSN 0959-8049

https://doi.org/10.1016/j.ejca.2016.02.020

© 2016 Elsevier Ltd. Licensed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International http://creativecommons.org/licenses/by-nc-nd/4.0/

Reuse

Unless indicated otherwise, fulltext items are protected by copyright with all rights reserved. The copyright exception in section 29 of the Copyright, Designs and Patents Act 1988 allows the making of a single copy solely for the purpose of non-commercial research or private study within the limits of fair dealing. The publisher or other rights-holder may allow further reproduction and re-use of this version - refer to the White Rose Research Online record for this item. Where records identify the publisher as the copyright holder, users can verify any specific terms of use on the publisher's website.

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.



Table 1 Technologies/methods to target potential biomarker

Targets	Potential Biomarker	Technologies / Methods	References
Checkpoint inhibitors	PD-L1	PD-L1, PD-L2 staining ELISA	(20, 21, 31) (62)
Cytokine/chemokine levels	IFN-γ, CXCR4	ELISPOT ELISA IHC	(9, 63) (9) (24, 26)
Incidence of specific immune cells	CD8+, CD4+, iDC, mDC, Tregs, MDSC	IHC FACS	(19, 20) (9, 16, 64, 65)
TILs	CD3, CD8, granzyme B, FOXP3	IHC	(15, 16, 65)
MMR deficiency	MMR status	IHC of MMR proteins	(37, 39)
Immune gene panels	PD-L1/2, PIK3CA, CDH1	PCR/NGS	(30, 66, 67)
RNA stability and gene expression	miRNAs	PCR	(68, 69)

Abbreviations: CXCR4, chemokine CXC motif receptor 4; iDC, immature dendritic cell (DC); mDC, mature DC; ELISA, enzyme linked immunosorbent assay; ELISPOT, enzyme linked immuno spot assay; FACS, fluorescence-activated cell sorting; IFN-γ, interferon-γ; IHC, immunohistochemical staining; MDSC, myeloid-derived suppressor cells; miRNA, MicroRNA; MMR, mismatch repair; NGS, next-generation sequencing; PCR, polymerase chain reaction; TIL, tumor-infiltrating lymphocytes; Treg, regulatory T cell

Table 2 Studies with immune checkpoint inhibitors in gastric and colon cancer

	Drug	Stage of development*	Trials for gastric cancer	Trials for colon cancer
CTLA-4	Tremelimumab	FDA approved for malignant mesothelioma		
	Ipilimumab	FDA approved for unresectable or metastatic melanoma	NCT01585987	
	Tremelimumab + Durvalumab	Phase lb/II	NCT02340975	
PD-1	Nivolumab (ONO-4538)	FDA approved for melanoma + NSCLC	NCT02267343	NCT02423954 NCT02335918 NCT02327078
	Pembrolizumab (MK3475)	FDA approved for unresectable or metastatic melanoma + NSCLC	NCT02335411 NCT01848834 NCT02370498 NCT02494583	NCT02318901 NCT02460198 NCT01876511 NCT02563002 NCT02437071 NCT02375672 NCT02260440 NCT02268825 NCT02298959
	Nivolumab + Ipilimumab	FDA approved for melanoma	NCT01928394	NCT02060188
PD-L1	Durvalumab (MEDI4736)	Phase III		NCT02227667
	Atezolizumab (MPDL3280A)	Phase III	NCT02471846	NCT02291289
	Avelumab (MSB0010718C)	Phase III	NCT02625623	

^{*}Highest stage of clinical development, regardless of tumor type.

Abbreviations: FDA, US Food and Drug Administration; NSCLC, Squamous Non-Small Cell Lung Cancer