

The broader view of Immunotherapy in Gastric Cancer- Recent Progress in Cellular Therapy Trials

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Topics to be discussed

- How does our immune system handle cancer cells?
- What comprises immunotherapy?
- What are other forms of immunotherapy beyond pembrolizumab and nivolumab?
- What is the hope for these treatments to change the face of gastric cancer?
- What trials are ongoing?



**How does our immune system
handle cancer cells?**



Immune cells recognize foreign objects such as infections, cancer cells and tries to attack them

Immune cells protect normal cells from self-destruction



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Immune
ne...

IMMUNESURVEILLANCE

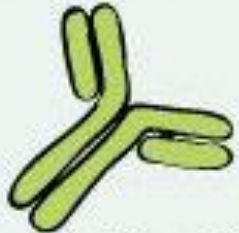


**What comprises
immunotherapy?**



TYPES OF IMMUNOTHERAPY

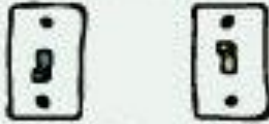
ANTIBODIES



A version of a protein that can attach themselves to cancer cells, tagging them for immune destruction.



CHECKPOINT INHIBITORS



Some proteins help to control the immune system. When these are turned off immune cells are able to kill cancer cells better.



VACCINES

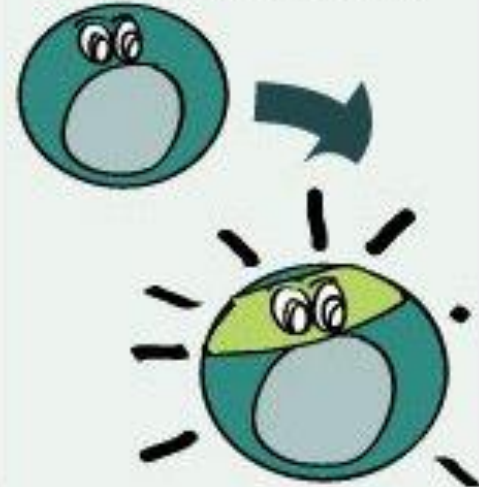


Vaccines work by putting substances into the body that train the immune cells to respond better to cancer.



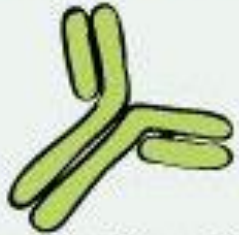
T-CELL TRANSFERS

Upgrade and improve a patient's T-cells (an immune cell that helps to eliminate cancer)



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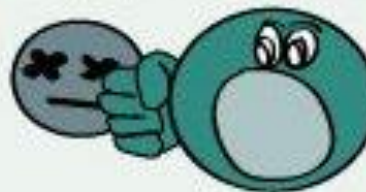
CHECKPOINT INHIBITORS

EXAMPLES INCLUDE PEMBROLIZUMAB AND NIVOLUMAB

VACCINES

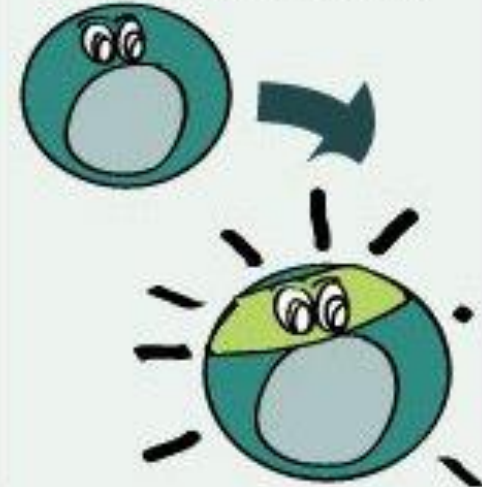


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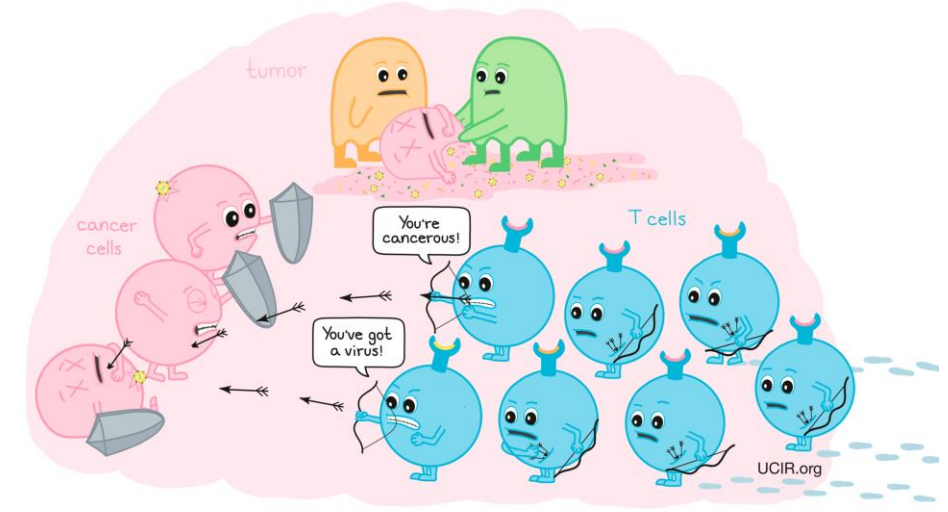
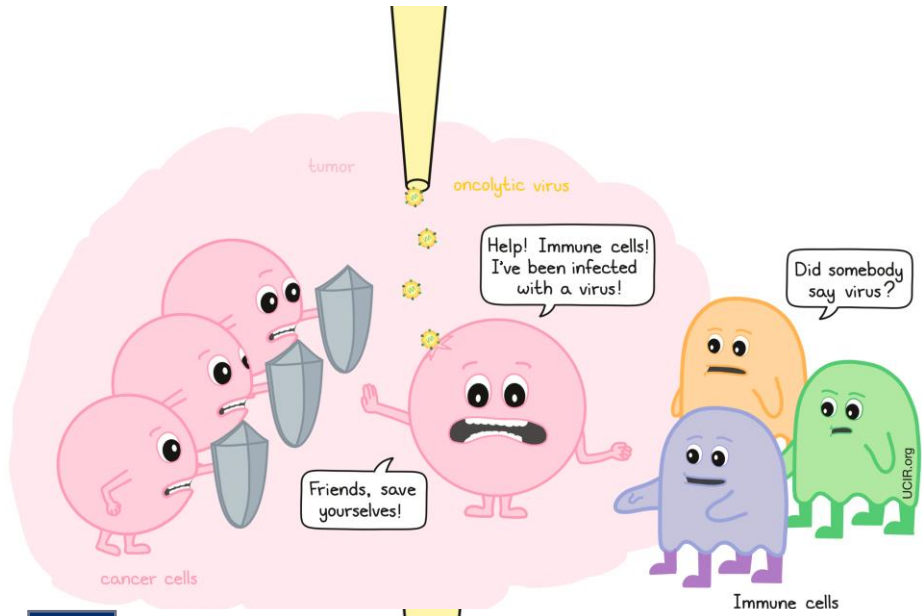
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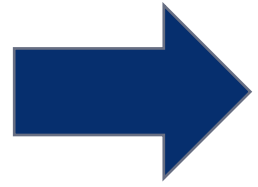
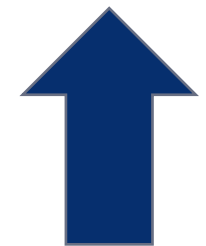
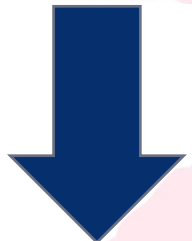
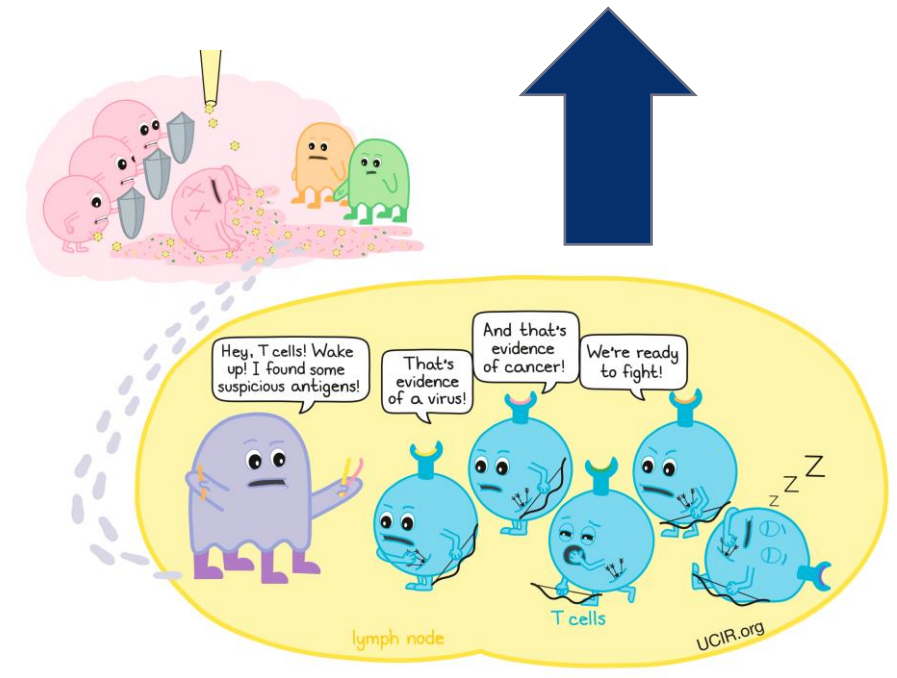
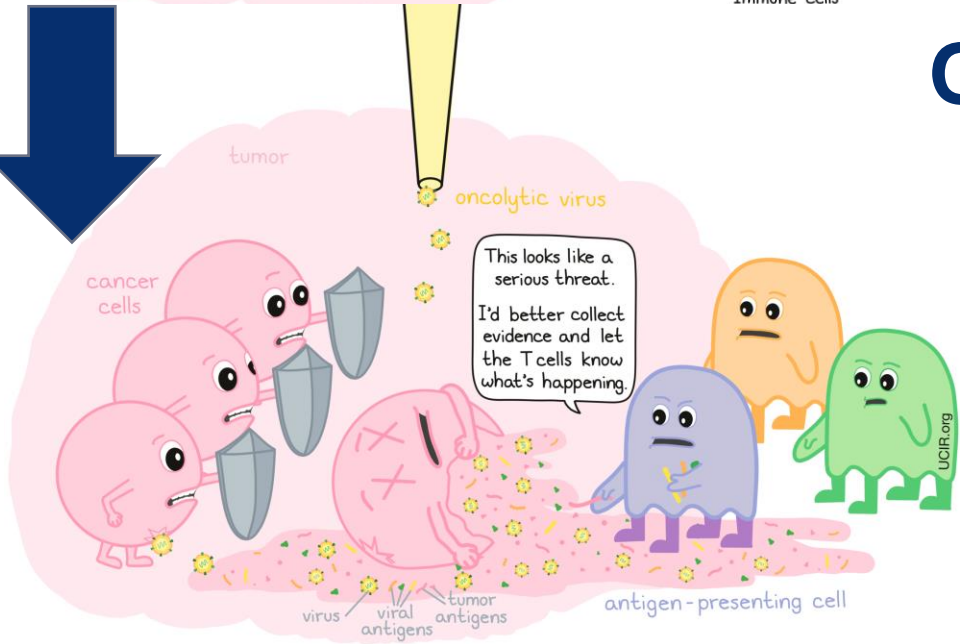




What are other forms of immunotherapy beyond pembrolizumab and nivolumab?



ONCOLYTIC VIRUSES





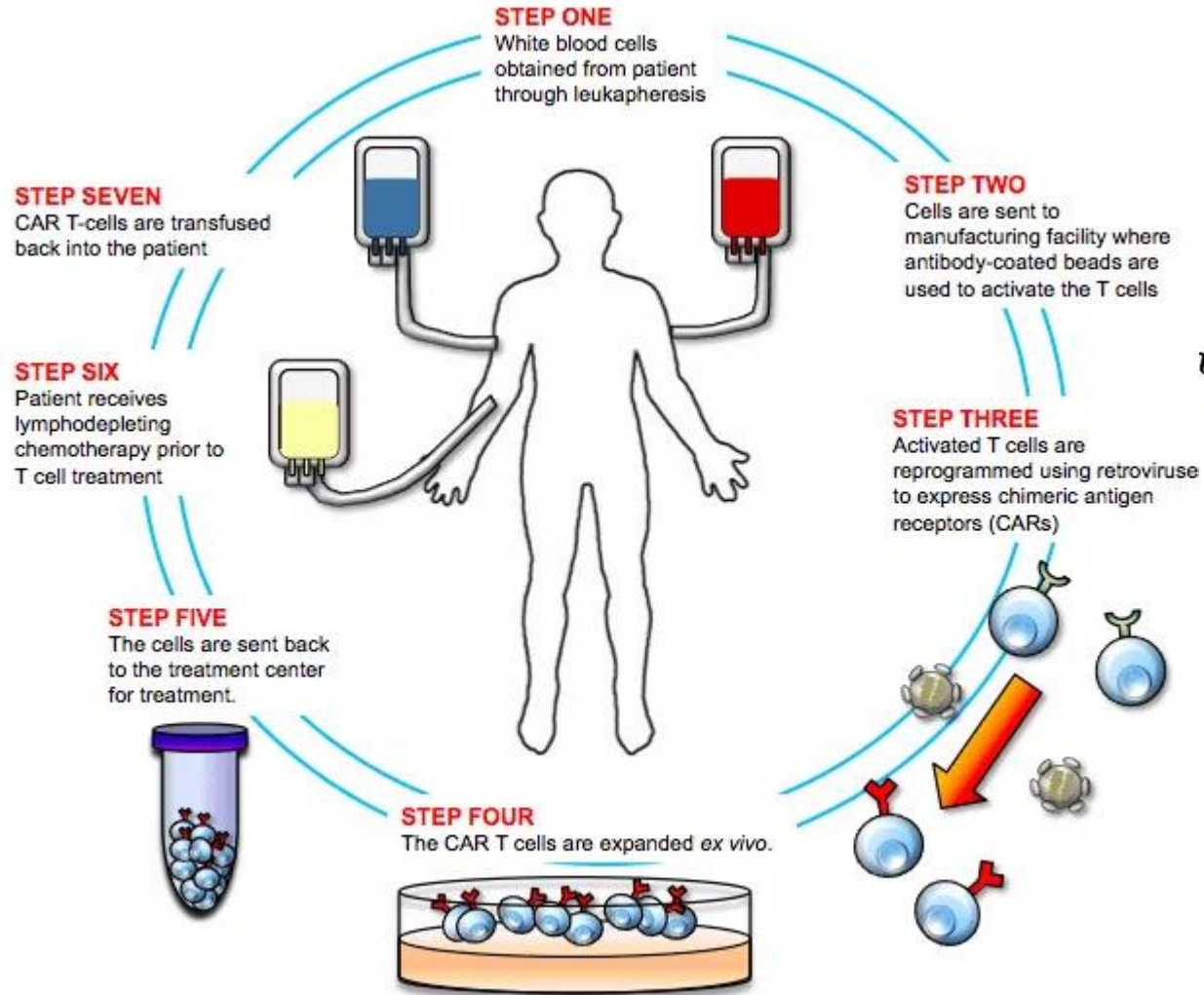
CANCER VACCINES



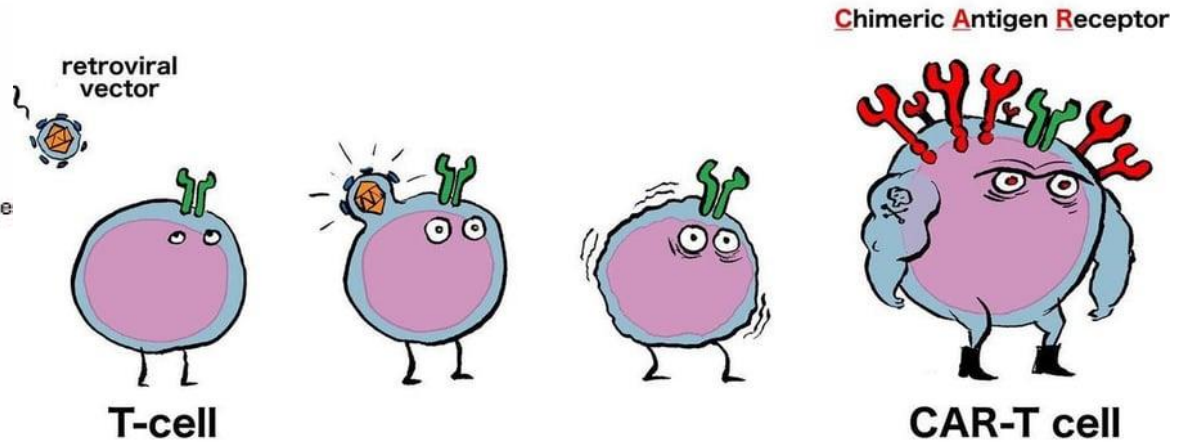
Medicines that train the immune system to recognize and destroy cancer cells. Unlike cancer prevention vaccines, these are designed for people who already have cancer.



CAR-T CELLS



Generating super-soldiers the production of CAR-T cells





What is the hope for these treatments to change the face of gastric cancer?



OPEN

Claudin18.2-specific CAR T cells in gastrointestinal cancers: phase 1 trial interim results

Changsong Qi^{1,5}, Jifang Gong^{1,5}, Jian Li^{1,5}, Dan Liu², Yanru Qin³, Sai Ge¹, Miao Zhang², Zhi Peng¹, Jun Zhou¹, Yanshuo Cao¹, Xiaotian Zhang¹, Zhihao Lu¹, Ming Lu¹, Jiajia Yuan¹, Zhenghang Wang¹, Yakun Wang², Xiaohui Peng⁴, Huiping Gao⁴, Zhen Liu⁴, Huamao Wang⁴, Daijing Yuan⁴, Jun Xiao⁴, Hong Ma⁴, Wei Wang⁴, Zonghai Li⁴ and Lin Shen¹  



GC/GEJ patient characteristics	Dose escalation/de-escalation n = 12	Dose-expansion n = 16	Total n = 28
Histological (Lauren) classification, n (%)			
Intestinal type	6 (50)	4 (25.0)	10 (35.7)
Diffuse type	3 (25)	6 (37.5)	9 (32.1)
Mixed type	2 (16.7)	5 (31.3)	7 (25.0)
Unknown	1 (8.3)	1 (6.3)	2 (7.1)
Histological (WHO) classification, n (%)			
Mucinous adenocarcinoma	0	1 (6.3)	1 (3.6)
Signet-ring cell carcinoma	3 (25)	9 (56.3)	12 (42.9)
Other	9 (75)	5 (31.3)	14 (50.0)
HER2 status, n (%)			
Negative	11 (91.7)	16 (100)	27 (96.4)
Positive	0	0	0
Unknown	0	1 (20)	1 (3.6)
Numbers of metastatic organs, n (%)			
≤2	5 (41.7)	9 (56.3)	14 (50.0)
≥3	7 (58.3)	7 (43.8)	14 (50.0)
Peritoneal metastases, n (%)	9 (95.0)	10 (62.5)	19 (67.9)
Median no. of previous lines, n (%)			
1	2 (16.7)	3 (18.8)	5 (17.9)
2	7 (58.3)	8 (50.0)	15 (53.6)
≥3	3 (25.0)	5 (31.3)	8 (28.6)
Previous systemic therapies, n (%)			
Fluorouracil/analogs and derivatives	12 (100)	16 (100)	28 (100)
Taxanes	10 (83.3)	11 (68.8)	21 (75.0)
Platinum	12 (100)	15 (93.8)	27 (96.4)
Anti-PD-1/PD-L1 antibody	6 (50.0)	6 (37.5)	12 (42.9)
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- The most frequently reported adverse events (AEs) of grade 3 or higher were preconditioning-related hematologic toxicities in 37 patients (100%), leukopenia in 31 of 37 (83.8%), neutropenia in 25 of 37 (67.6%), anemia in 15 of 37 (40.5%) and thrombocytopenia in six of 37 (16.2%), which occurred within 28 days after the first infusion and generally recovered within a median of 4–9 days
- No grade 3 or higher CRS was observed
- 35 of 37 (94.6%) patients had grade 1 or 2 CRS. In the first cycle of treatment, the median onset of CRS was 2 days (1–3 days) after infusion and generally lasted for a median of 6 days (3–42 days).
- No immune effector cell-associated neurotoxicity syndrome (ICANS) was observed.
- No treatment-related death was reported.

**Table 3 | Efficacy evaluation according to tumor type***

Variable	Gastric <i>n</i> = 28	Other <i>n</i> = 9	All <i>n</i> = 37
Best overall response			
CR, <i>n</i> (%)	0	0	0
PR, <i>n</i> (%)	16 (57.1)	2 (22.2)	18 (48.6)
SD, <i>n</i> (%)	5 (17.9)	4 (44.4)	9 (24.3)
PD, <i>n</i> (%)	7 (25.0)	3 (33.3)	10 (27.0)
ORR, <i>n</i> (%) [95% CI]	16 (57.1) [37.2, 75.5]	2 (22.2) [2.8, 60.0]	18 (48.6) [31.9, 65.6]
DCR, <i>n</i> (%) [95% CI]	21 (75.0) [55.1, 89.3]	6 (66.7) [29.9, 92.5]	27 (73.0) [55.9, 86.2]
mPFS (months) [95% CI]	4.2 [3.7, 9.2]	2.6 [1.8, 3.5]	3.7 [2.6, 5.4]
6-month OS rate (%) [95% CI]	81.2 [60.3, 91.8]	77.8 [36.5, 93.9]	80.1 [62.5, 90.0]
6-month DOR rate (%) [95% CI]	53.3 [20.7, 77.8]	NA	44.8 [17.3, 69.3]

CR, complete response; NA, not applicable. *Tumor response was confirmed based on investigator assessment according to RECIST version 1.1.



What trials are ongoing?



NCT Number	Title	Tumor type	Type of trial
NCT05269381	Personalized Neoantigen Peptide-Based Vaccine in Combination With Pembrolizumab for the Treatment of Advanced Solid Tumors, The PNeoVCA Study	All solid tumors. Includes gastric cancer	Vaccine
NCT04111172	A Vaccine (Ad5.F35-hGCC-PADRE) for the Treatment of Gastrointestinal Adenocarcinoma	All gastrointestinal cancers. Includes gastric cancer.	Vaccine
NCT04246671	TAEK-VAC-HerBy Vaccine for Brachyury and HER2 Expressing Cancer	Different cancers. Includes gastric cancer	Vaccine
NCT04404595	Claudin18.2 CAR-T (CT041) in Patients With Gastric, Pancreatic Cancer, or Other Specified Digestive Cancers	Gastric cancer and pancreatic cancer	CAR-T
NCT04650451	Safety and Activity Study of HER2-Targeted Dual Switch CAR-T Cells (BPX-603) in Subjects With HER2-Positive Solid Tumors	All solid tumors. Includes gastric cancers	CAR-T