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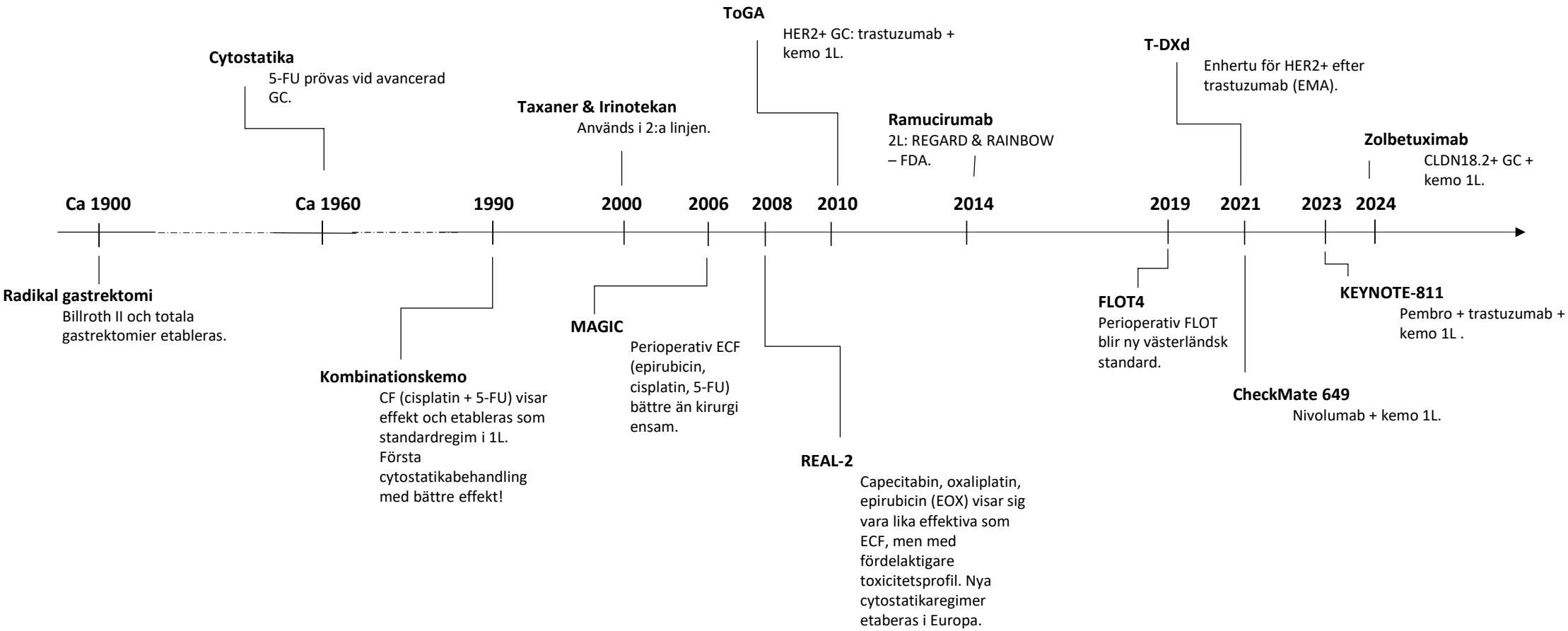
Nya onkologiska behandlingar för Ventrikelcancer

260925

Lisa Liu Burström, MD PhD
Specialistläkare onkologi
Tema Cancer, Karolinska Universitetssjukhuset

Ventrikelcancer – behandlingsutveckling över tid



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Relativ 5-årsöverlevnad över tid

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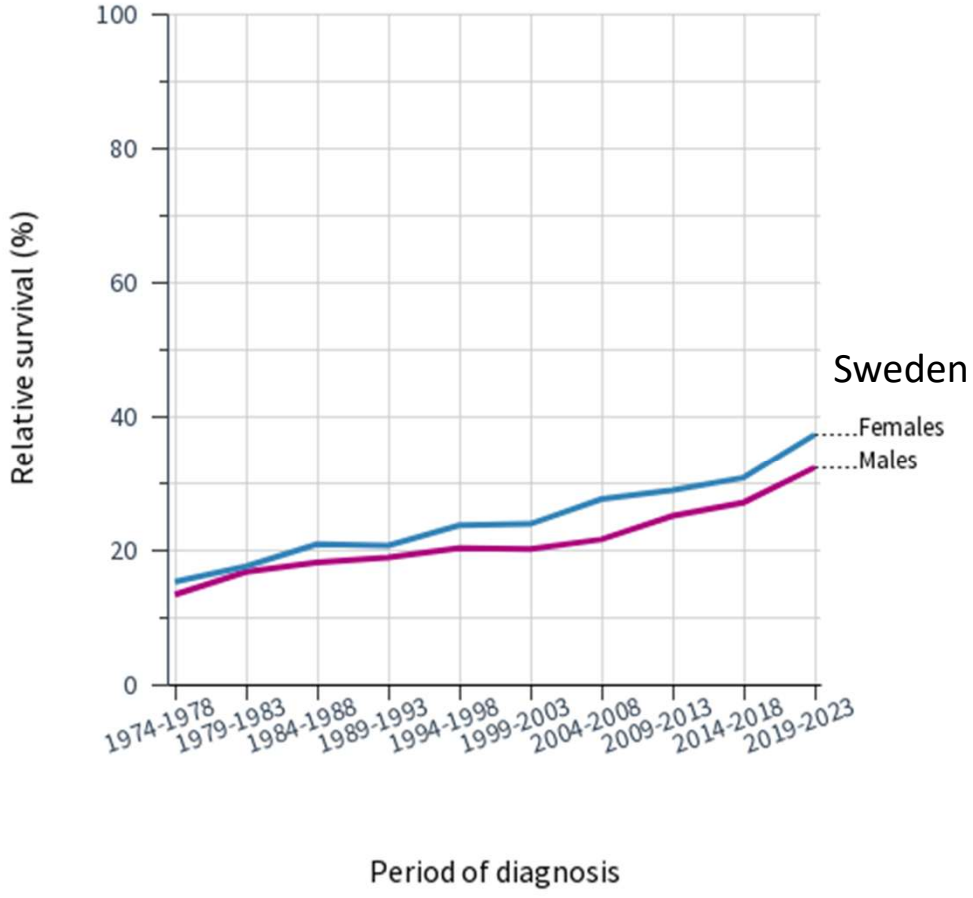
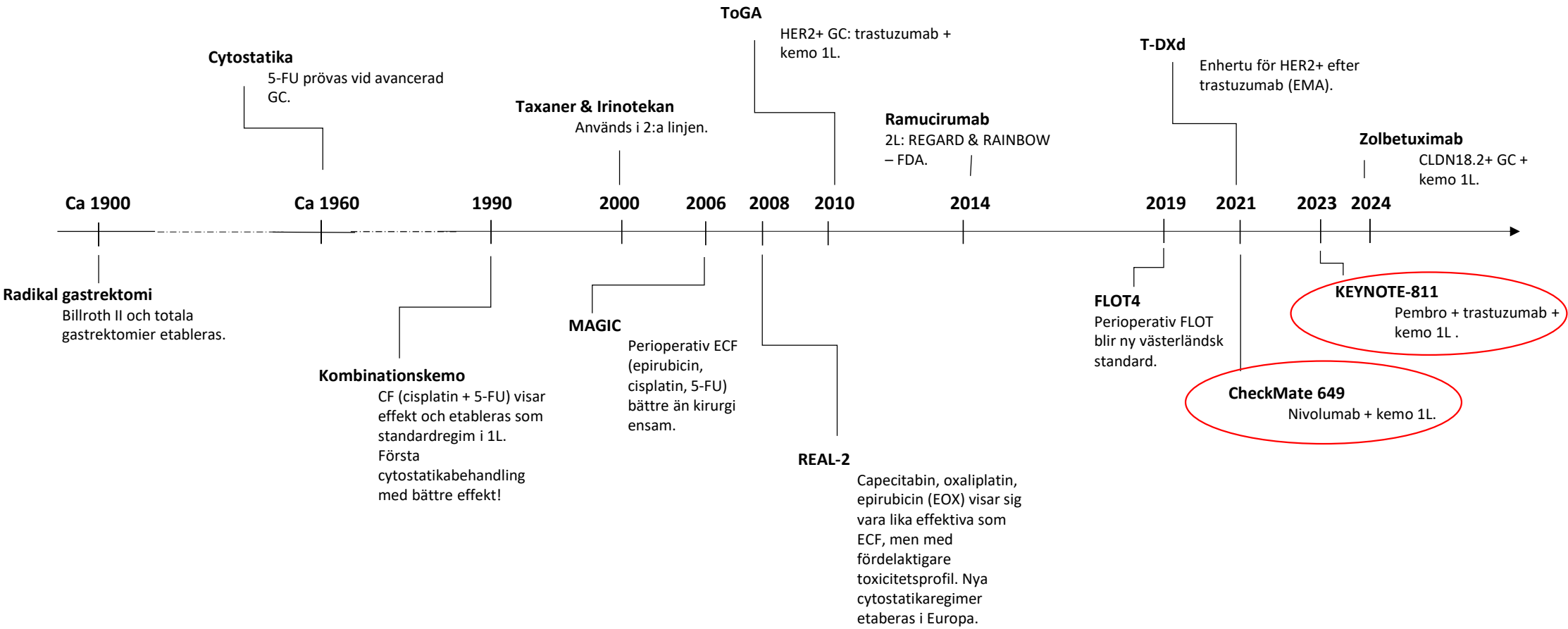


NORDCAN | IARC - https://gco.iarc.who.int
Data version: 9.5 - 06.2025

Ventrikelcancer – behandlingsutveckling över tid



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James P. Allison

Prize share: 1/2

Tasuku Honjo

Prize share: 1/2

Immunterapi – hur fungerar det?

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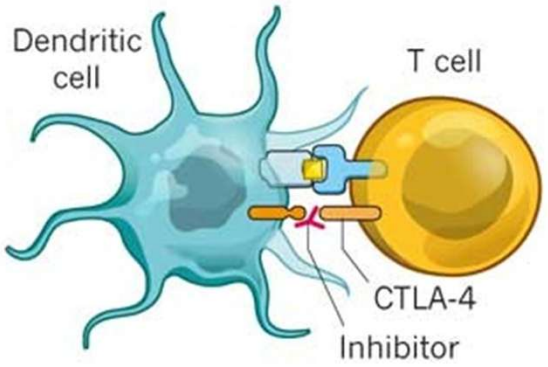
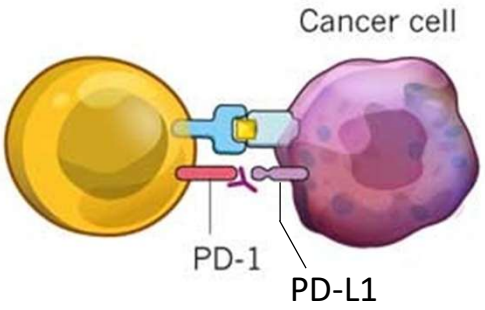
- Anti-CTLA-4 (ipilimumab)
- Anti-PD-1/PD-L1 (nivolumab, pembrolizumab)

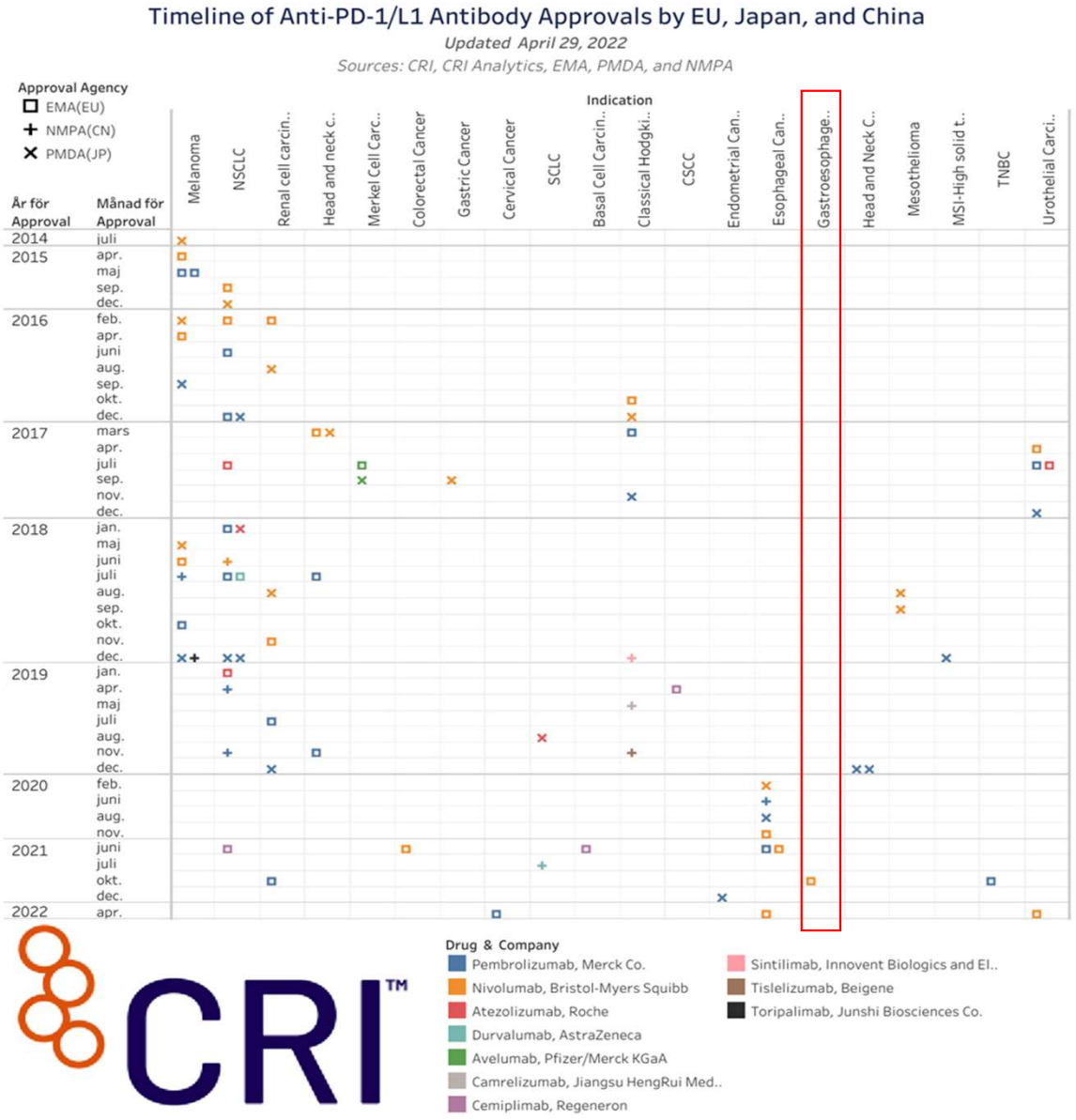


The CTLA-4 checkpoint protein prevents dendritic cells from priming T cells to recognize tumours. Inhibitor drugs block the checkpoint.



The PD-1 checkpoint protein prevents T cells from attacking cancer cells. The inhibitor drug allows T cells to act.

Ledford H. Nature 2014.



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Vilka patienter kan få immunterapi för sin magsäckscancer?

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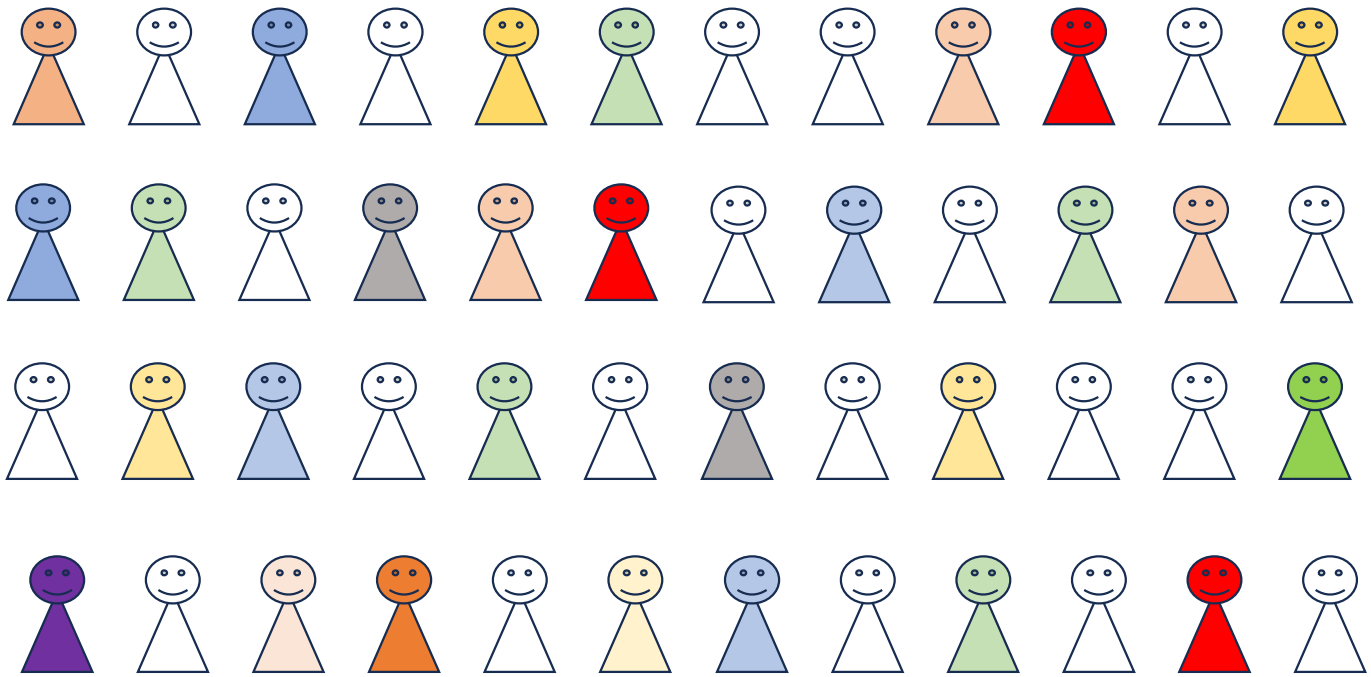

Prediktiva biomarkörer som stöd för behandlingsval

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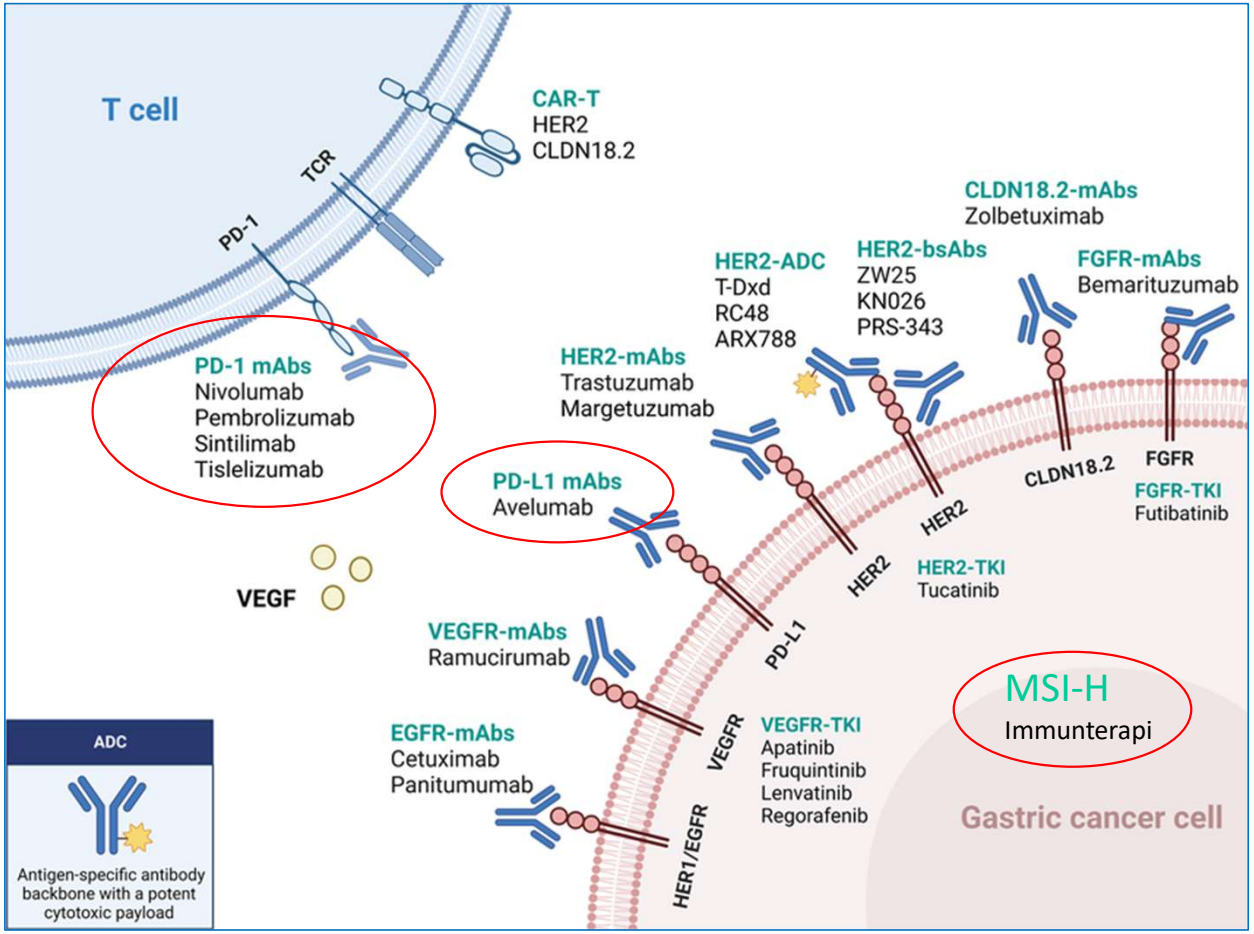
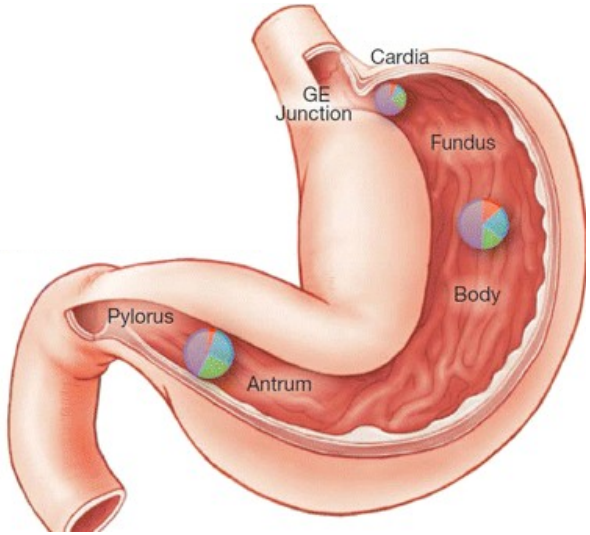
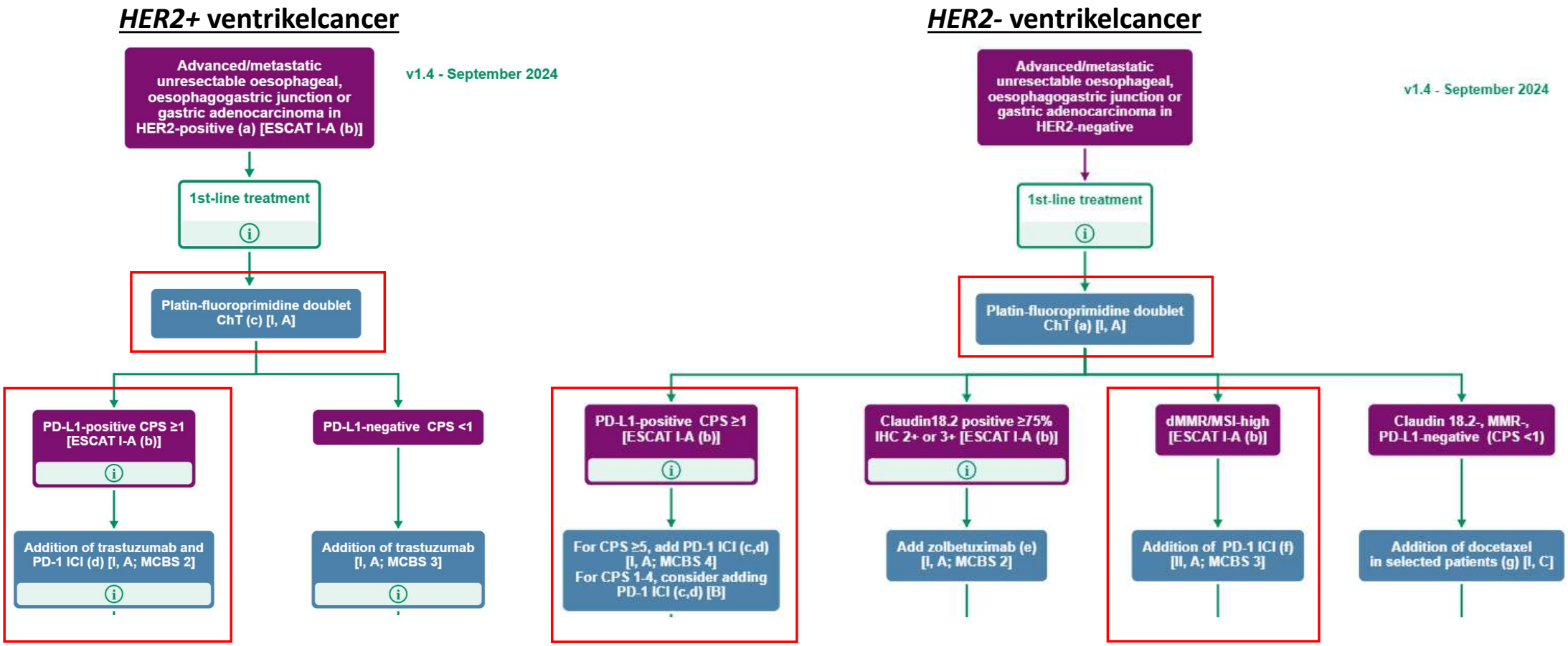




Wen-Long et al. Journal of Hematology & Oncology 2023

Behandlingslandskap - metastaserad ventrikelcancer



Avgörande immunterapistudier

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Pembrolizumab plus trastuzumab and chemotherapy for HER2-positive gastric or gastro-oesophageal junction adenocarcinoma: interim analyses from the phase 3 KEYNOTE-811 randomised placebo-controlled trial

*Yelena Y Janjigian, Akihito Kawazoe, Yuxian Bai, Jianming Xu, Sara Lonardi, Jean Phillipe Metges, Patricio Yanez, Lucjan S Wyrwicz, Lin Shen, Yuriy Ostapenko, Mehmet Bilici, Hyun Cheol Chung, Kohei Shitara, Shu-Kui Qin, Eric Van Cutsem, Josep Tabernero, Kan Li, Chie-Schin Shih, Pooja Bhagia, Sun Young Rha, on behalf of the KEYNOTE-811 Investigators**

Clinical Trial > Lancet. 2021 Jul 3;398(10294):27-40. doi: 10.1016/S0140-6736(21)00797-2. Epub 2021 Jun 5.

First-line nivolumab plus chemotherapy versus chemotherapy alone for advanced gastric, gastro-oesophageal junction, and oesophageal adenocarcinoma (CheckMate 649): a randomised, open-label, phase 3 trial

Yelena Y Janjigian [1], Kohei Shitara [2], Markus Moehler [3], Marcelo Garrido [4], Pamela Salman [5], Lin Shen [6], Lucjan Wyrwicz [7], Kensei Yamaguchi [8], Tomasz Skoczylas [9], Arinilda Campos Bragagnoli [10], Tianshu Liu [11], Michael Schenker [12], Patricio Yanez [13], Mustapha Tehfe [14], Ruben Kowalyszyn [15], Michalis V Karamouzis [16], Ricardo Bruges [17], Thomas Zander [18], Roberto Pazo-Cid [19], Erika Hitre [20], Kynan Feeney [21], James M Cleary [22], Valerie Poulart [23], Dana Cullen [23], Ming Lei [23], Hong Xiao [23], Kaoru Kondo [23], Mingshun Li [23], Jaffer A Ajani [24]

Clinical Trial > Lancet Oncol. 2023 Nov;24(11):1181-1195. doi: 10.1016/S1470-2045(23)00515-6. Epub 2023 Oct 21.

Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for HER2-negative advanced gastric cancer (KEYNOTE-859): a multicentre, randomised, double-blind, phase 3 trial

Sun Young Rha [1], Do-Youn Oh [2], Patricio Yañez [3], Yuxian Bai [4], Min-Hee Ryu [5], Jeeyun Lee [6], Fernando Rivera [7], Gustavo Vasconcelos Alves [8], Marcelo Garrido [9], Kai-Keen Shiu [10], Manuel González Fernández [11], Jin Li [12], Maeve A Lowery [13], Timuçin Çil [14], Felipe Melo Cruz [15], Shukui Qin [16], Suxia Luo [17], Hongming Pan [18], Zev A Wainberg [19], Lina Yin [20], Sonal Bordia [21], Pooja Bhagia [21], Lucjan S Wyrwicz [22]; KEYNOTE-859 investigators

CheckMate 649

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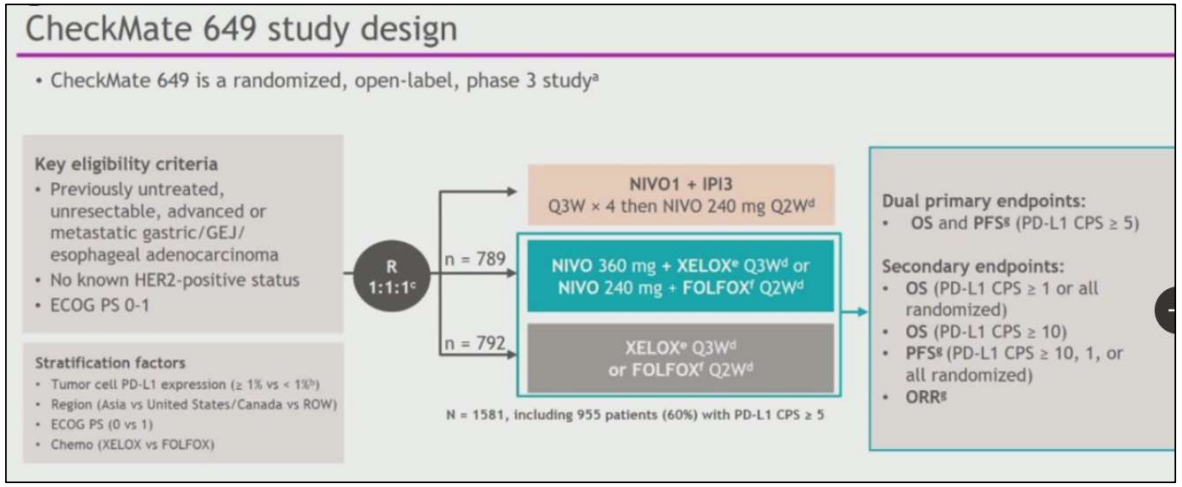

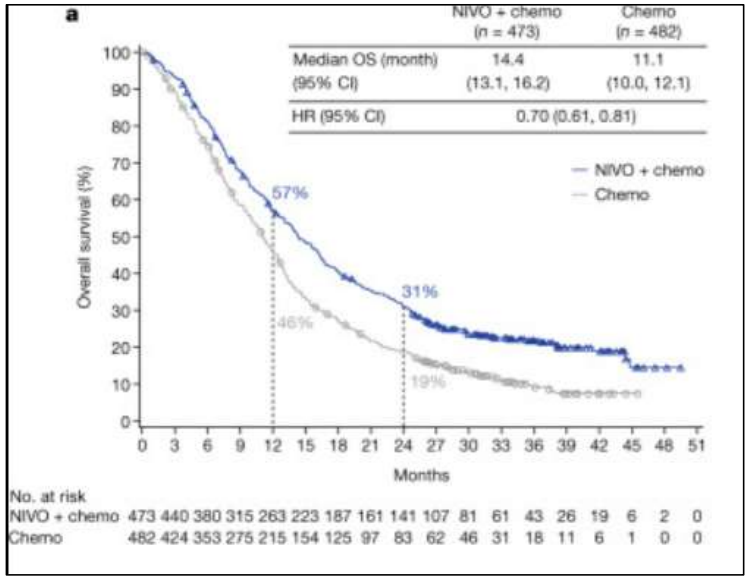

Nivo + kemo vs kemo.
All randomized patients, CPS >=5

Janjigian et al. Lancet 2021

KEYNOTE-811

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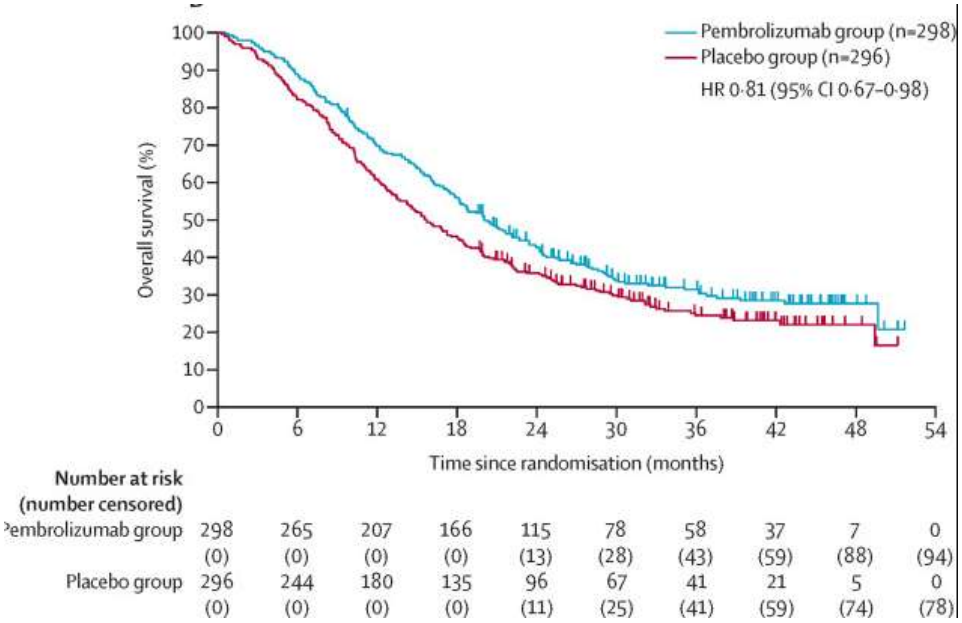
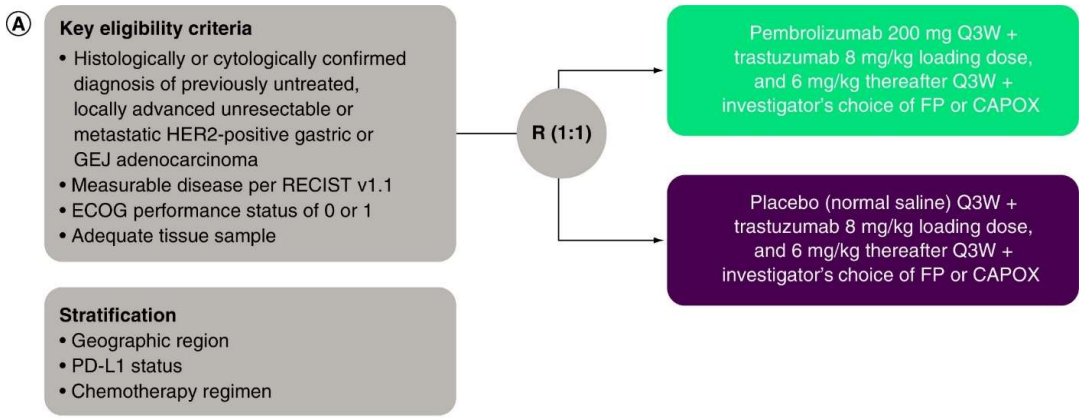


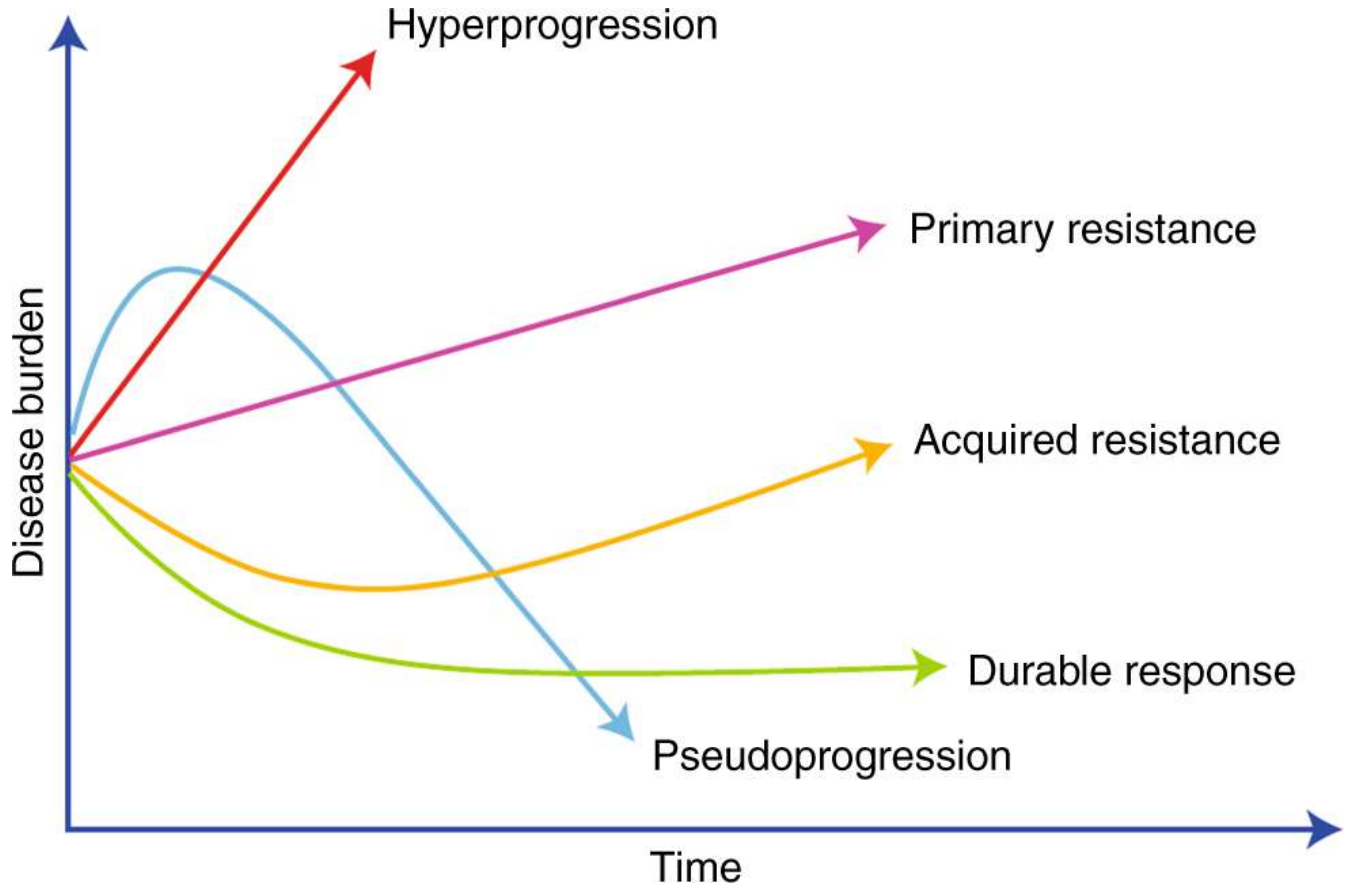


CPS >=1

HR 0.79, mOS 20.1 vs 15.7 mån

Janjigian et al. Annals of Oncology 2024.

Behandlingsutfall vid behandling med immunterapi



Baxter, M.A., Middleton, F., Cagney, H.P. *et al.* Resistance to immune checkpoint inhibitors in advanced gastro-oesophageal cancers. *Br J Cancer* **125**, 1068–1079 (2021).

Pseudoprogress vid immunterapi

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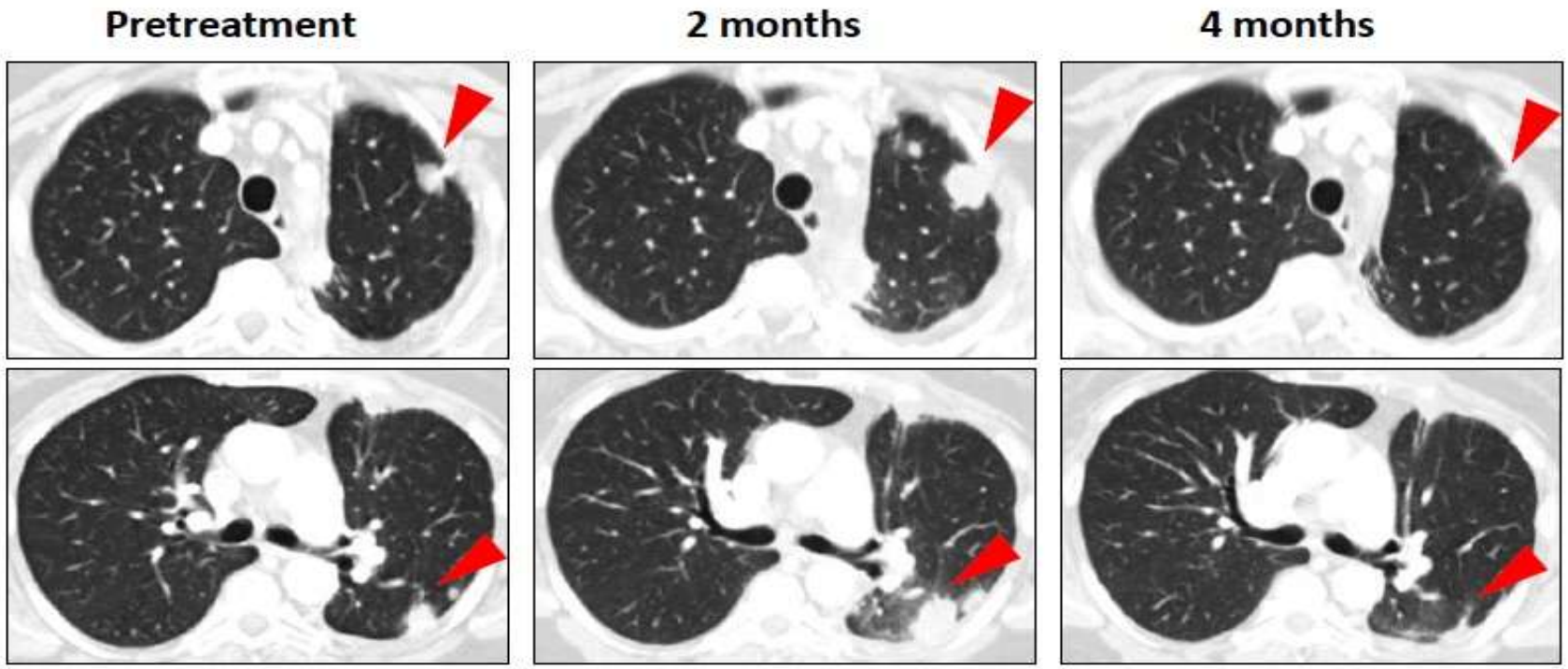
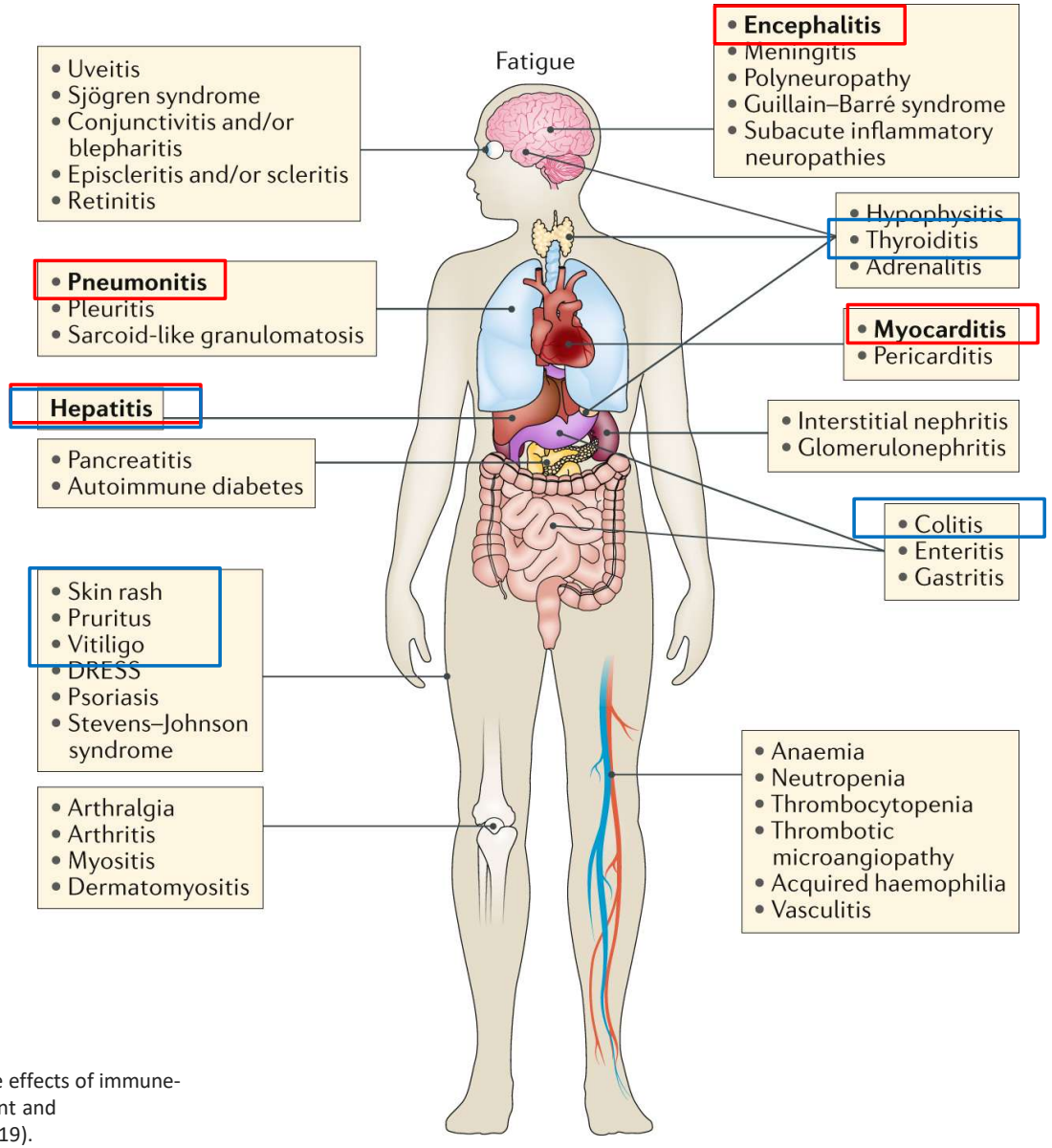


Pseudoprogression is seen in 7-10% of the patients



Martins, F., Sofiya, L., Sykiotis, G.P. *et al.* Adverse effects of immune-checkpoint inhibitors: epidemiology, management and surveillance. *Nat Rev Clin Oncol* **16**, 563–580 (2019).

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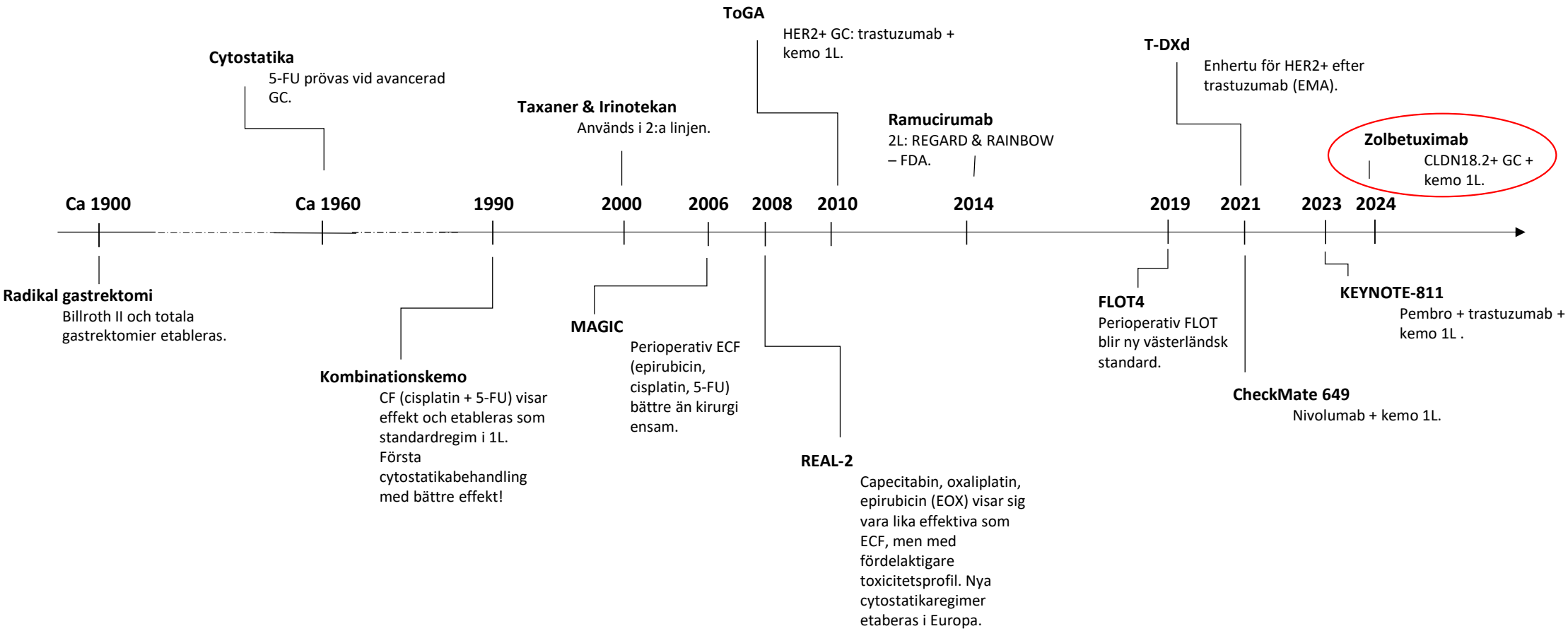

Billroth T. 1881, Heidelberger C et al. Science 1957, Lokich J etl al. J Clin Oncol 1980, Boku et al. J Clin Oncol. 1999, Cunningham D et al. N Engl J Med, 2006, Bang YJ et al. Lancet 2010. Cunningham D et al. N Engl J Med 2008, Fuchs CS et al, Lancet 2014. Al-Batran SE et al. Lancet. 2019. Shitara K et al. N Engl J Med. 2020, Janjigian YY et al. N Engl J Med. 2021.Sun JM et al. J Clin Oncol 2023, Shitara K et al. Lancet Oncol 2023.

Anti-claudin18.2 i ESMO behandlingsriktlinjer

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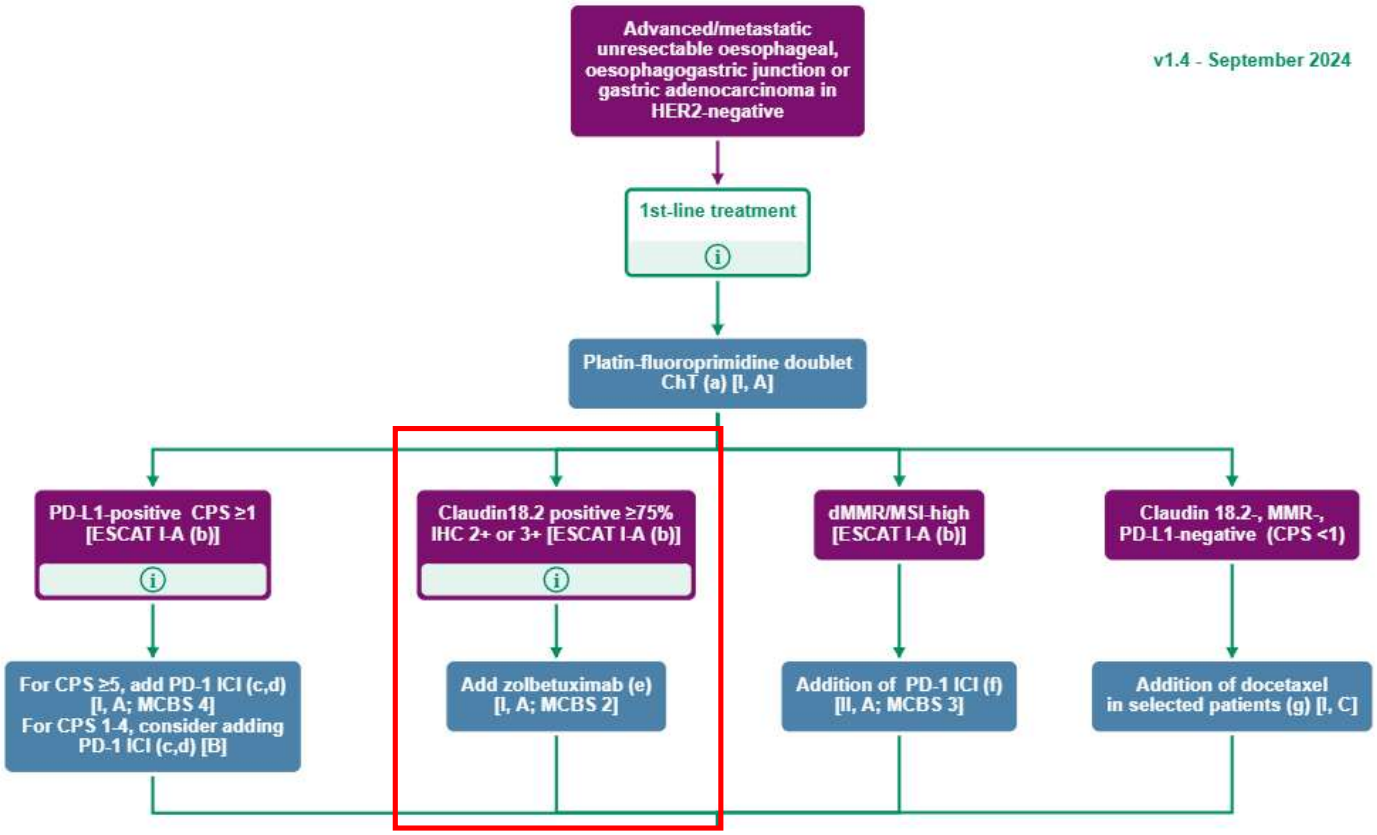

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Article | Open access | Published: 31 July 2023

Zolbetuximab plus CAPOX in CLDN18.2-positive gastric or gastroesophageal junction adenocarcinoma: the randomized, phase 3 GLOW trial

Manish A. Shah, Kohei Shitara, Jaffer A. Ajani, Yung-Jue Bang, Peter Enzinger, David Ilson, Florian Lordick, Eric Van Cutsem, Javier Gallego Plazas, Jing Huang, Lin Shen, Sang Cheul Oh, Patrapim Sunpaweravong, Hwoei Fen Soo Hoo, Haci Mehmet Turk, Mok Oh, Jung Wook Park, Diarmuid Moran, Pranob Bhattacharya, Ahsan Arozullah & Rui-Hua Xu ✉

Nature Medicine **29**, 2133–2141 (2023) | Cite this article

Zolbetuximab plus mFOLFOX6 in patients with CLDN18.2-positive, HER2-negative, untreated, locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma (SPOTLIGHT): a multicentre, randomised, double-blind, phase 3 trial

Kohei Shitara, Florian Lordick, Yung-Jue Bang, Peter Enzinger, David Ilson, Manish A Shah, Eric Van Cutsem, Rui-Hua Xu, Giuseppe Aprile, Jianming Xu, Joseph Chao, Roberto Pazo-Cid, Yoon-Koo Kang, Jianning Yang, Diarmuid Moran, Pranob Bhattacharya, Ahsan Arozullah, Jung Wook Park, Mok Oh, Jaffer A Ajani

Summary

Background Zolbetuximab, a monoclonal antibody targeting claudin-18 isoform 2 (CLDN18.2), has shown efficacy in patients with CLDN18.2-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma. We report the results of the SPOTLIGHT trial, which investigated the efficacy and safety of first-line zolbetuximab plus mFOLFOX6 (modified folinic acid [or levofolinate], fluorouracil, and oxaliplatin regimen) versus placebo plus mFOLFOX6 in patients with CLDN18.2-positive, HER2-negative, locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma.

Lancet 2023; 401: 1655-68

Published Online
April 14, 2023
https://doi.org/10.1016/S0140-6736(23)00620-7

This online publication has been corrected. The corrected version first appeared at thelancet.com on December 12, 2023

Verkningsmekanism för Zolbetuximab

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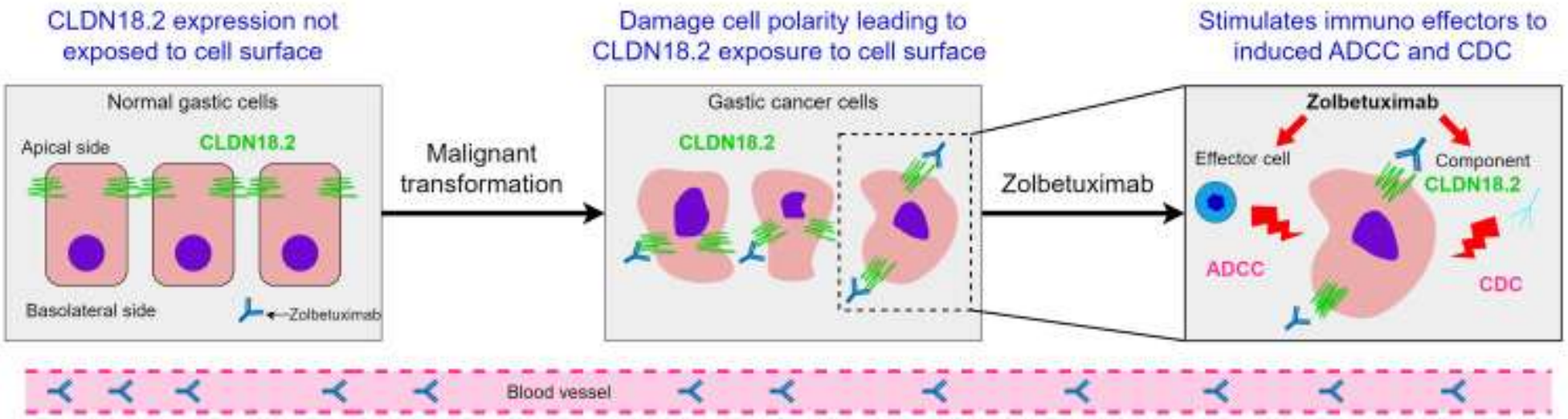

Samanta A et al. Zolbetuximab for Unresectable and Metastatic Gastric and Gastroesophageal Junction Adenocarcinoma: A Review of Literature. Cureus. 2024 Dec

Antibody-dependent cellular toxicity (ADCC)

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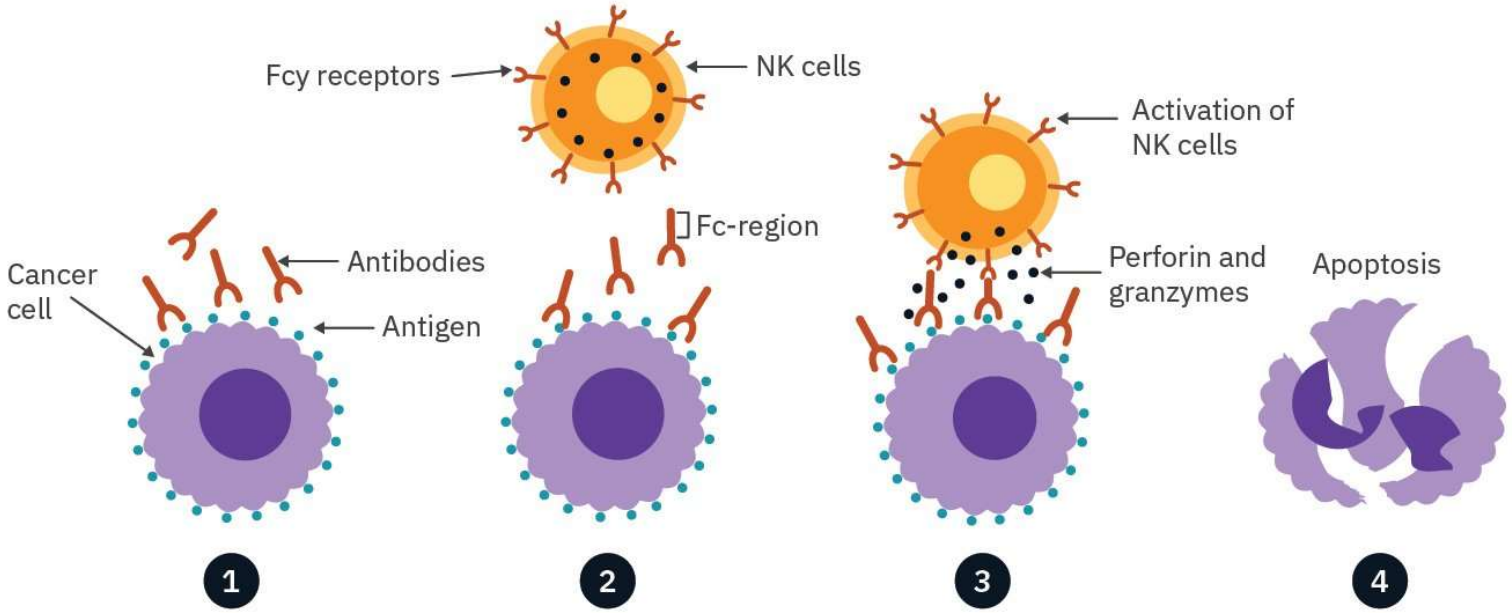

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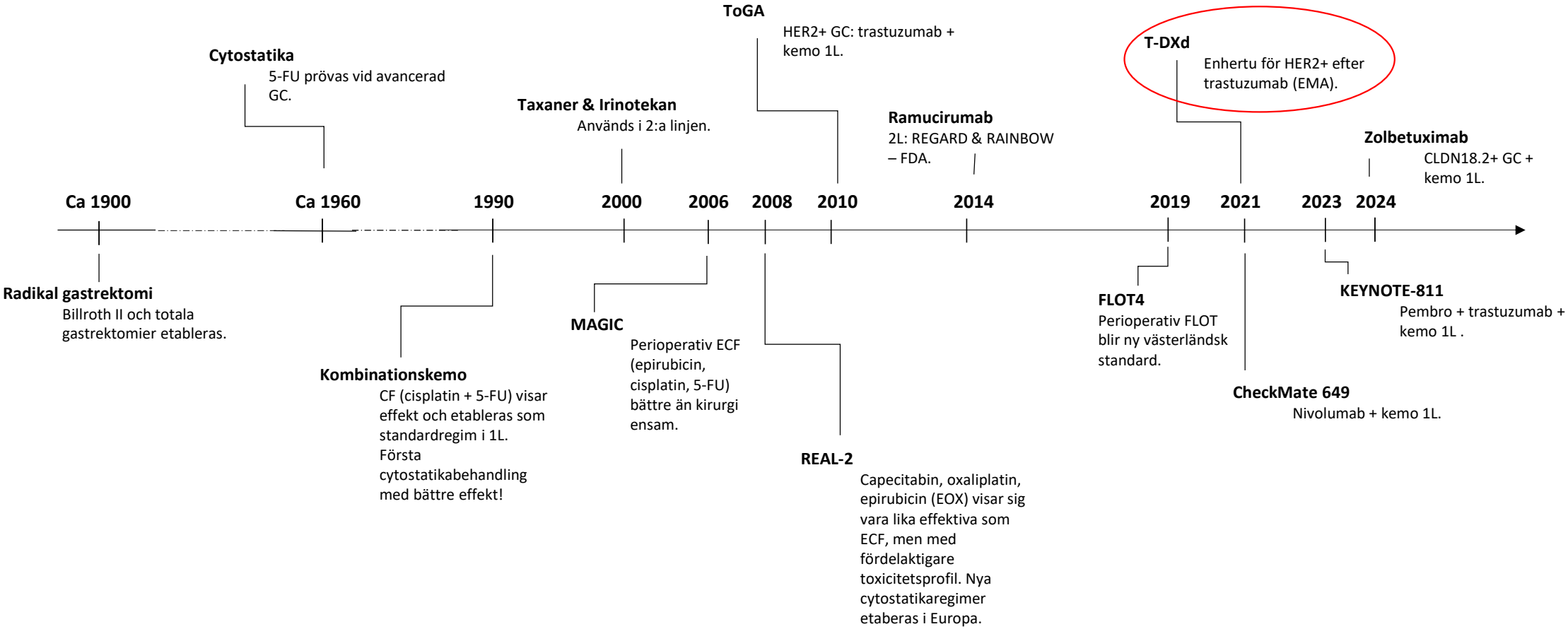

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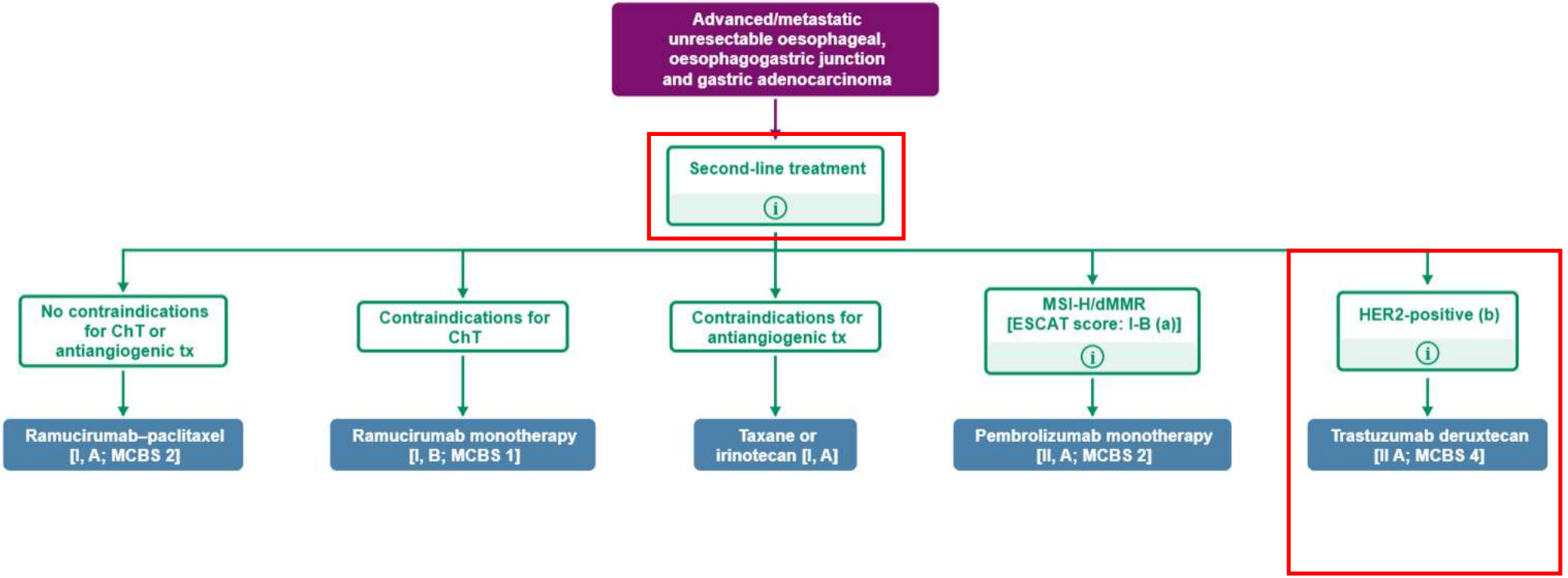
Trastuzumab deruxtecan i ESMOs behandlingsriktlinjer



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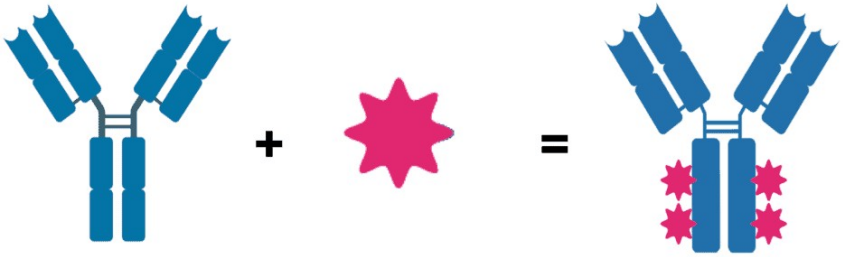
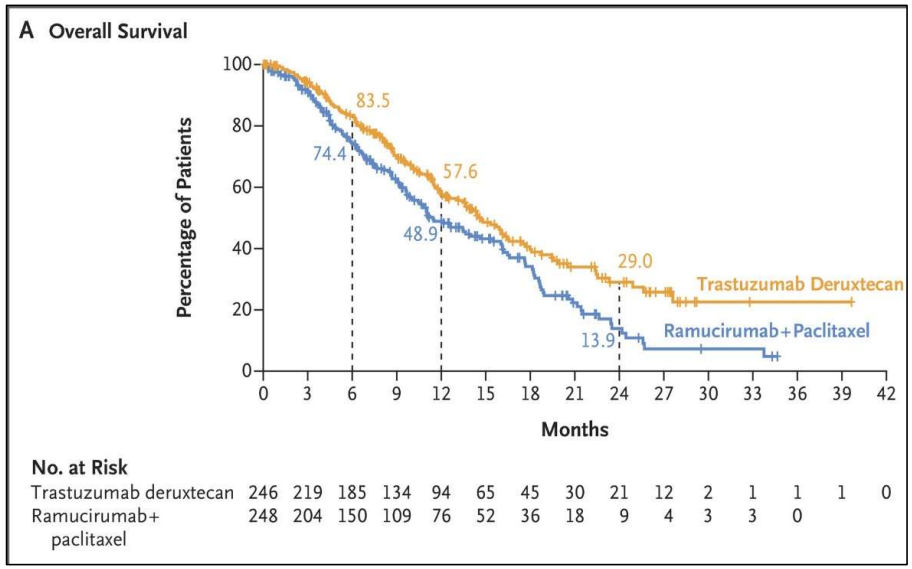
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trastuzumab Deruxtecan or Ramucirumab plus Paclitaxel in Gastric Cancer

K. Shitara,[1] E. Van Cutsem,[2,3] M. Gümüş,[4,5] S. Lonardi,[6] C. de la Fouchardière,[7] C. Coutzac,[7] J. Dekervel,[2,3] D. Hochhauser,[8] L. Shen,[9,10] W. Mansoor,[11] B. Liu,[12] L. Fornaro,[13] M.-H. Ryu,[14,15] J. Lee,[16] C. Faustino,[17] J.-P. Metges,[18] J. Tabernero,[19,20] F. Franke,[21] Y.Y. Janjigian,[22] F. Souza,[23] L. Jukofsky,[23] Y. Zhao,[23] T. Kamio,[23] A. Zaanan,[24,25] and F. Pietrantonio,[26] for the DESTINY-Gastric04 Trial Investigators*





Median OS, 14.7 vs. 11.4 months; HR 0.70

Potentiella framtida målsökande behandlingar

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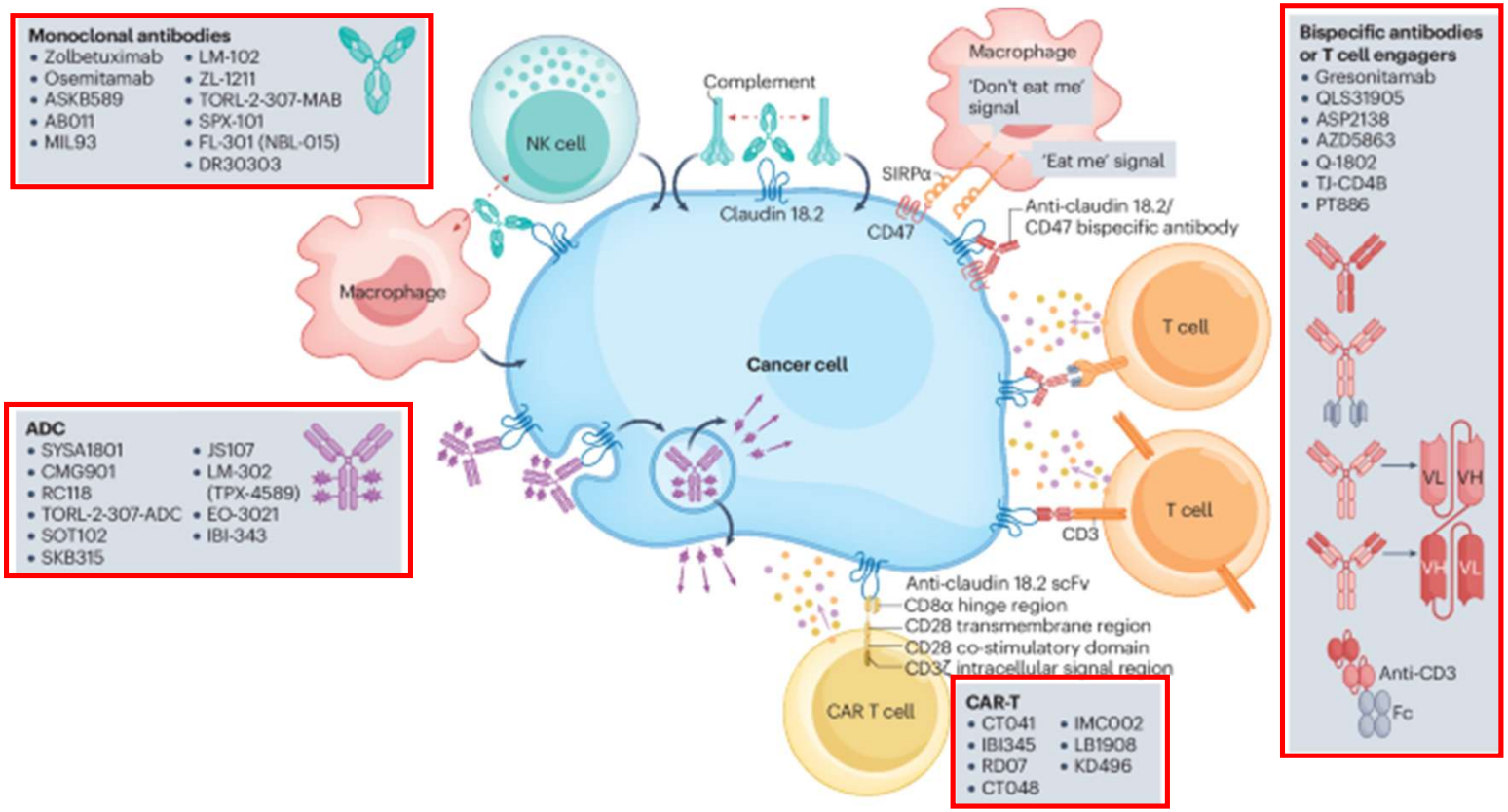

Nakayama, I., Qi, C., Chen, Y. *et al.* Claudin 18.2 as a novel therapeutic target. *Nat Rev Clin Oncol* **21**, 354–369 (2024). https://doi.org/10.1038/s41571-024-00874-2

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Tack för uppmärksamheten!