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Karolinska Comprehensive Cancer Center

Immunterapi vid esofagus

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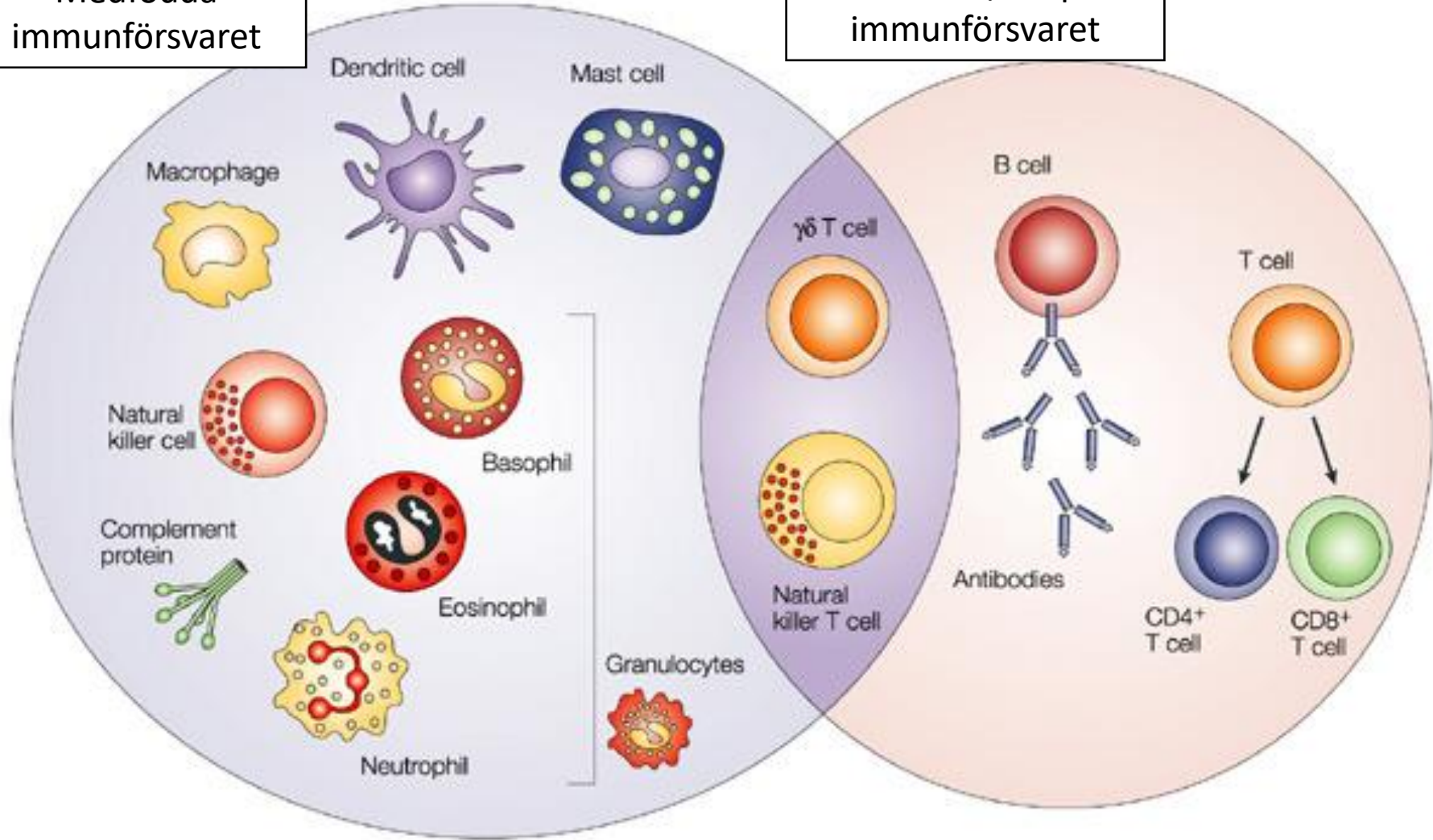


Dave Simonds

Snabbkurs i immunologi

Medfödda
immunförsvaret

Förvärvade/adaptiva
immunförsvaret

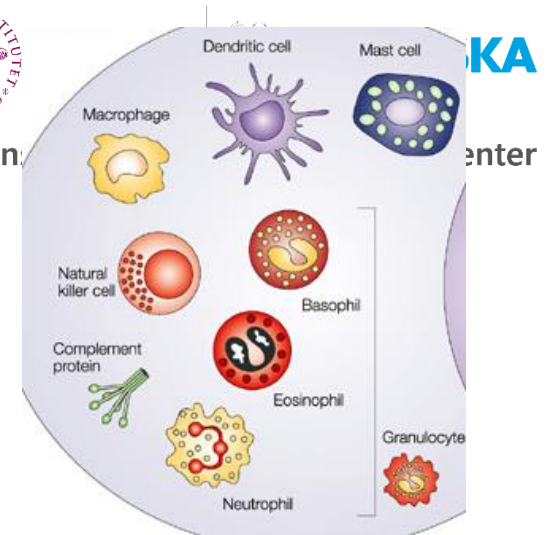


Medfödda immunförsvaret

- Snabbt svar
- Aktiveras av förutbestämda strukturer

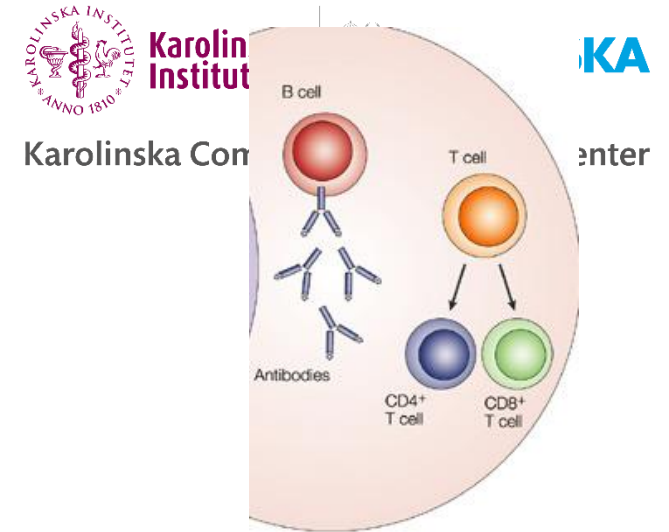


Karolin



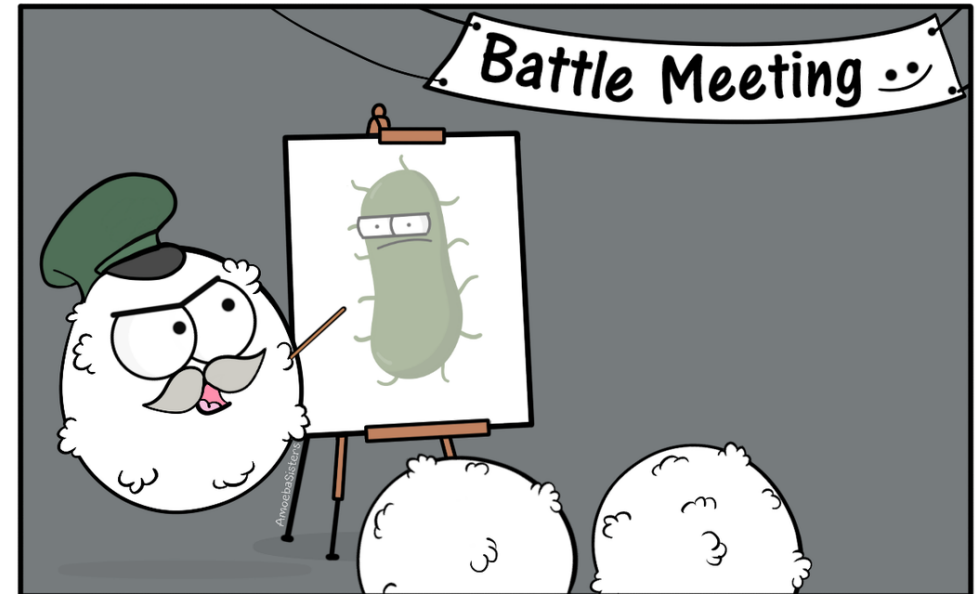
Förvärvade, adaptiva immunförsvaret

- Långsamt svar, men mer kraftfullt
- Anpassar sig efter vem som inkräktar
- Kräver aktivering av medfödda immunförsvaret

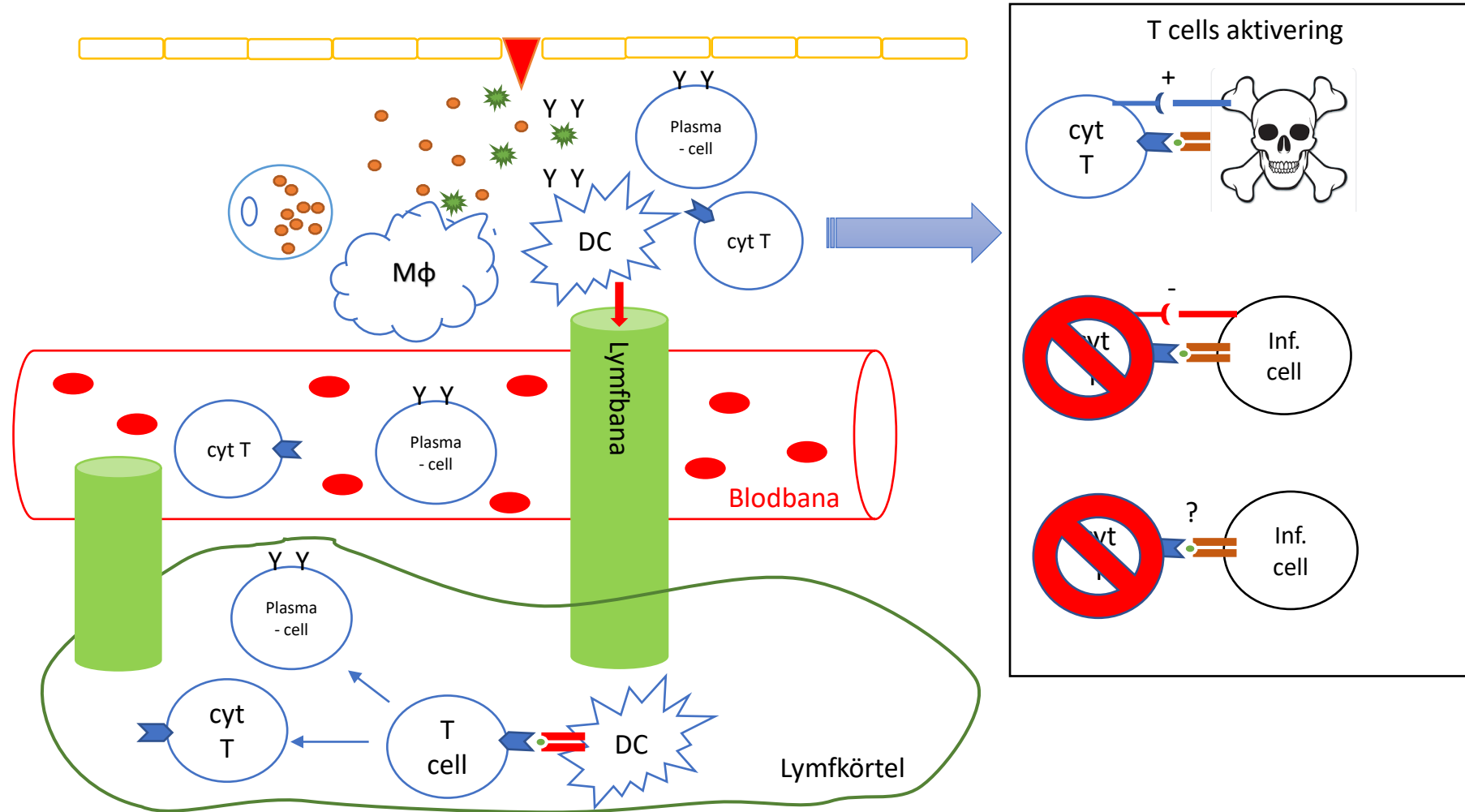


Paramecium Parlor

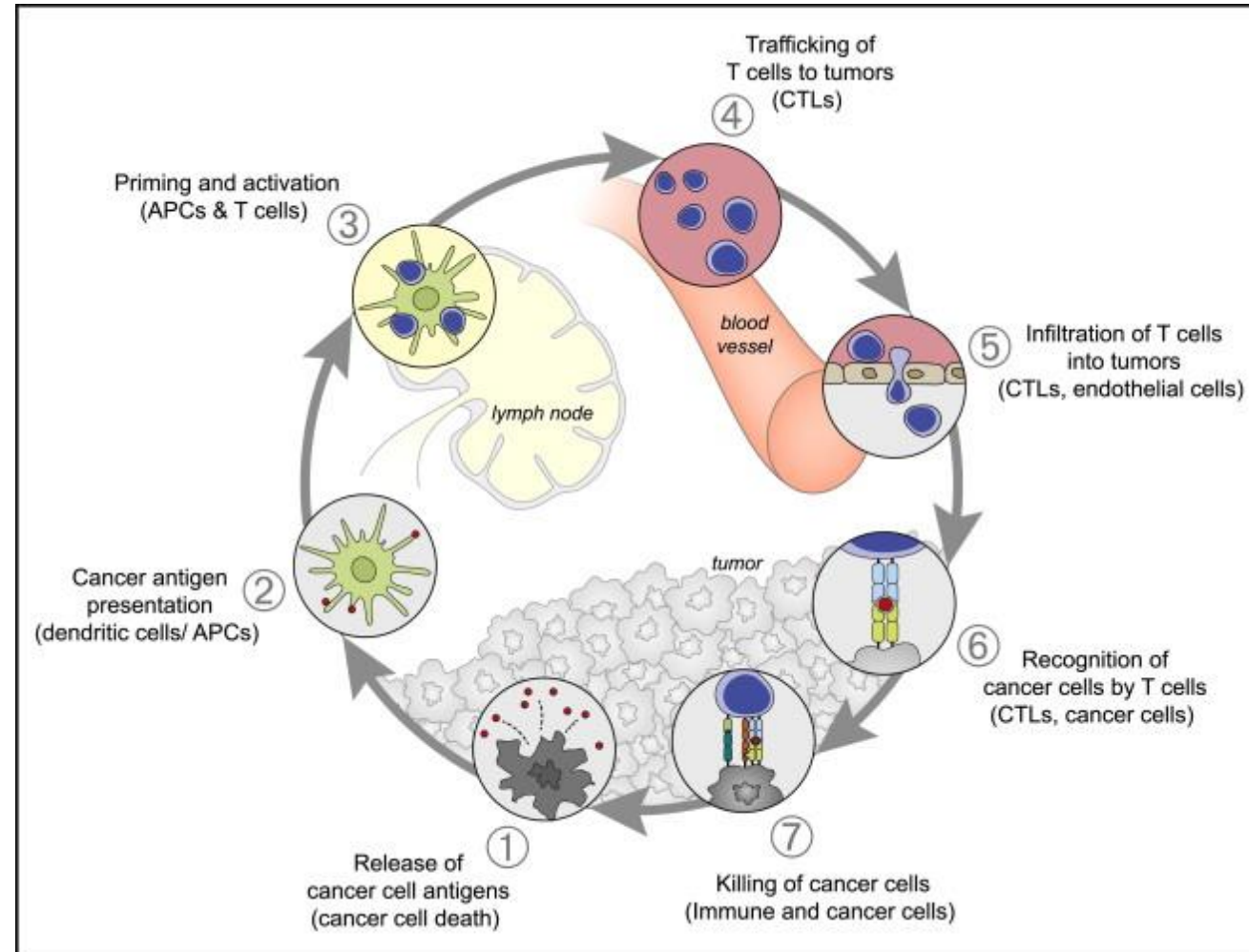
@AmoebaSisters



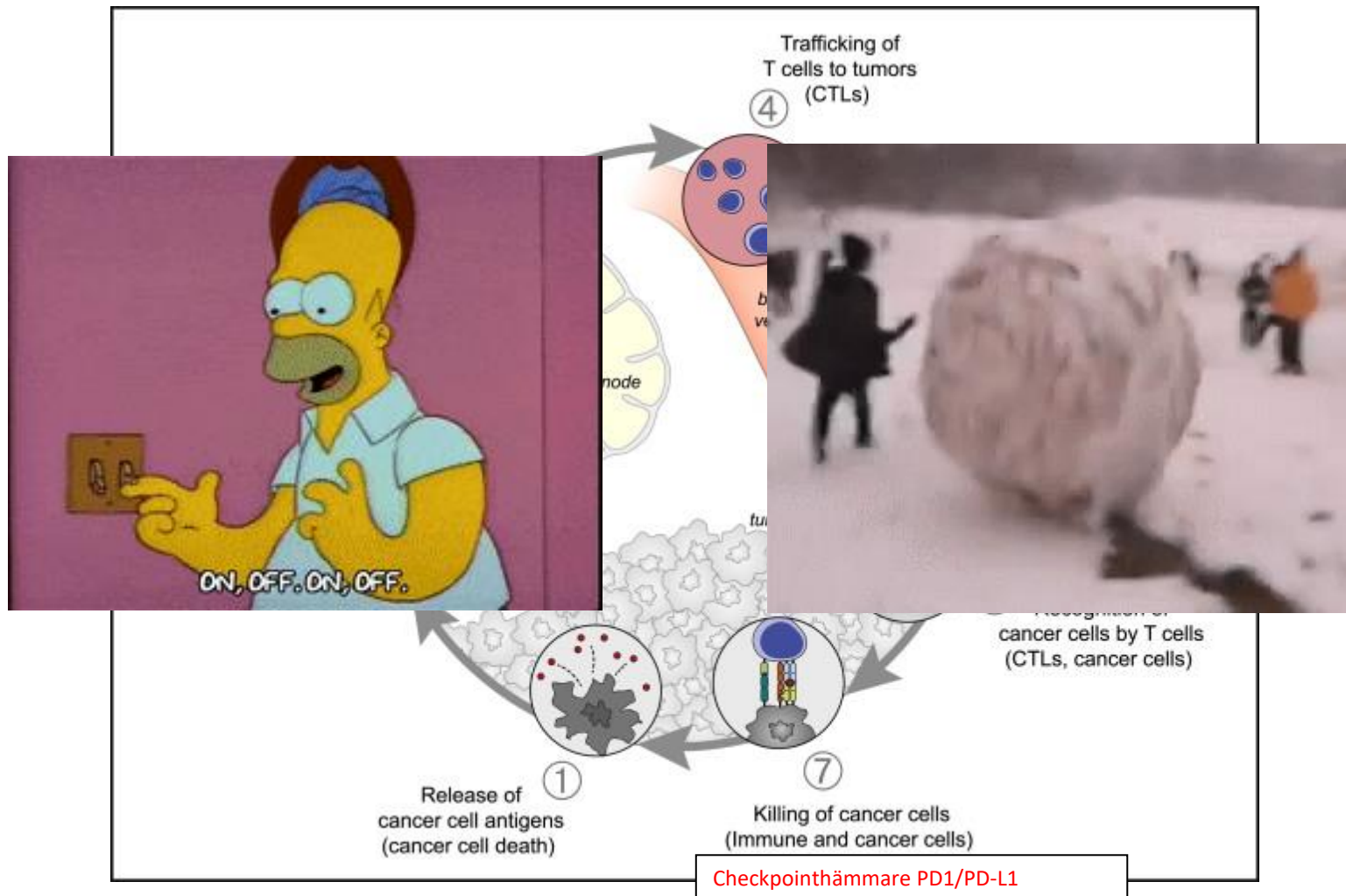
White blood cells: waging war with pathogens while you're watching cat videos.



Tumörimmunologi

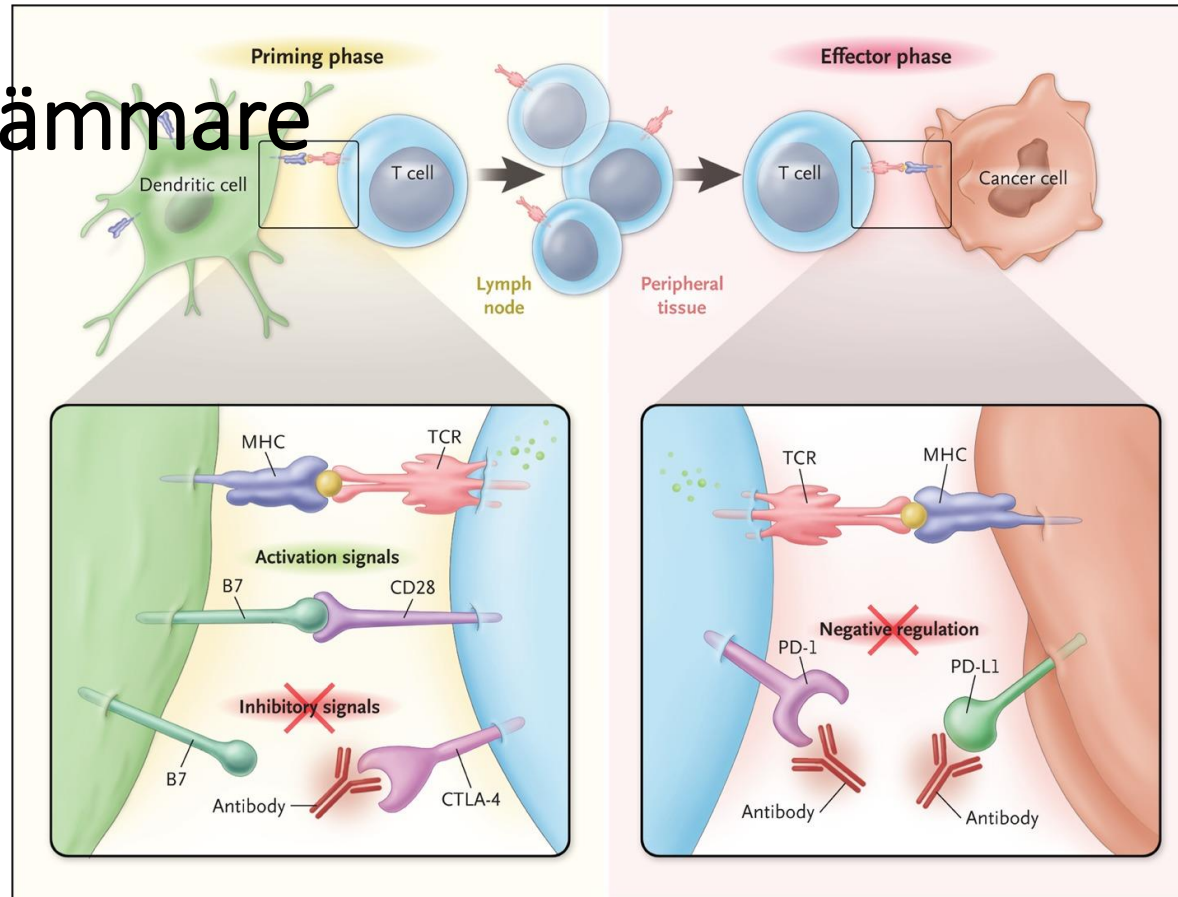


Tumörimmunologi



Chen et al *Immunity* 2013

Checkpointhämmare



Anti-CTLA4

Ipilimumab (Yervoy®)

Tremelimumab

Anti-PD-1

Nivolumab (Opdivo®)

Pembrolizumab (Keytruda®)

Cemiplimab (Libtayo®)

Dostarlimab (Jemperli®)

Tislelizumab

Camrelizumab

Pidilizumab

Sintilimab

Sugemalimab

Gemtanolimab

Cetrelimab

KL-A167



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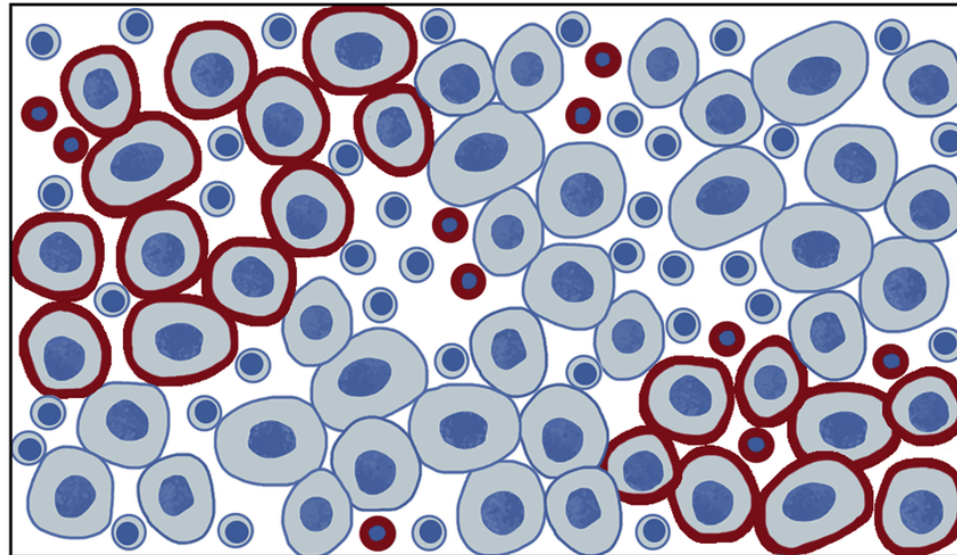
Anti-PD-L1

Atezolizumab (Tecentriq®)

Durvalumab (Imfinzi®)

Avelumab (Bavencio®)

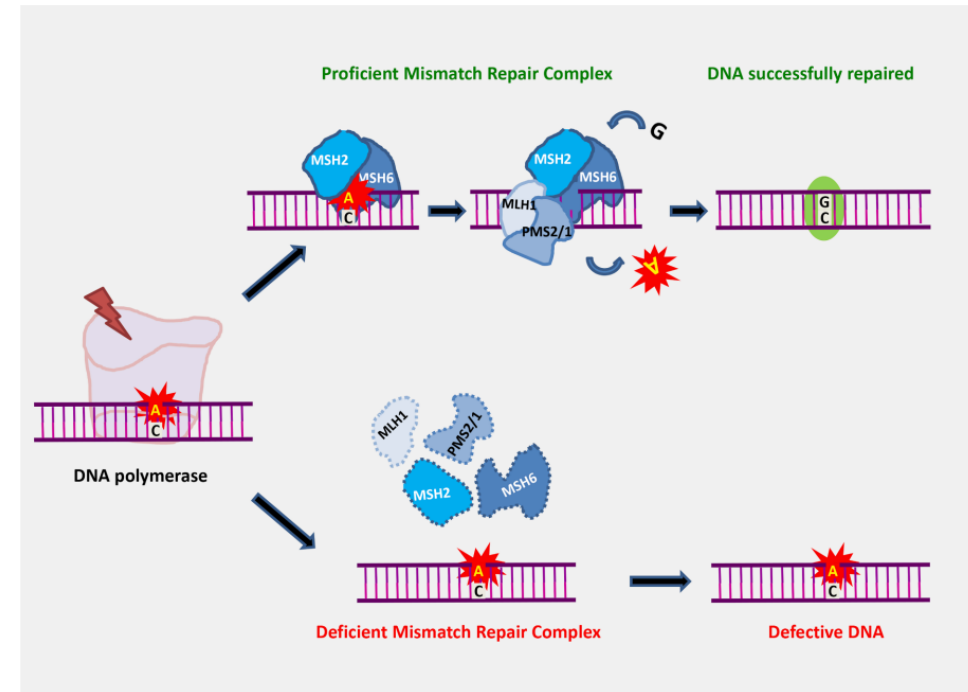
PD-L1 och MSI



- PD-L1 negative tumor cell
- PD-L1 negative immune cell
- PD-L1 positive tumor cell
- PD-L1 positive immune cell

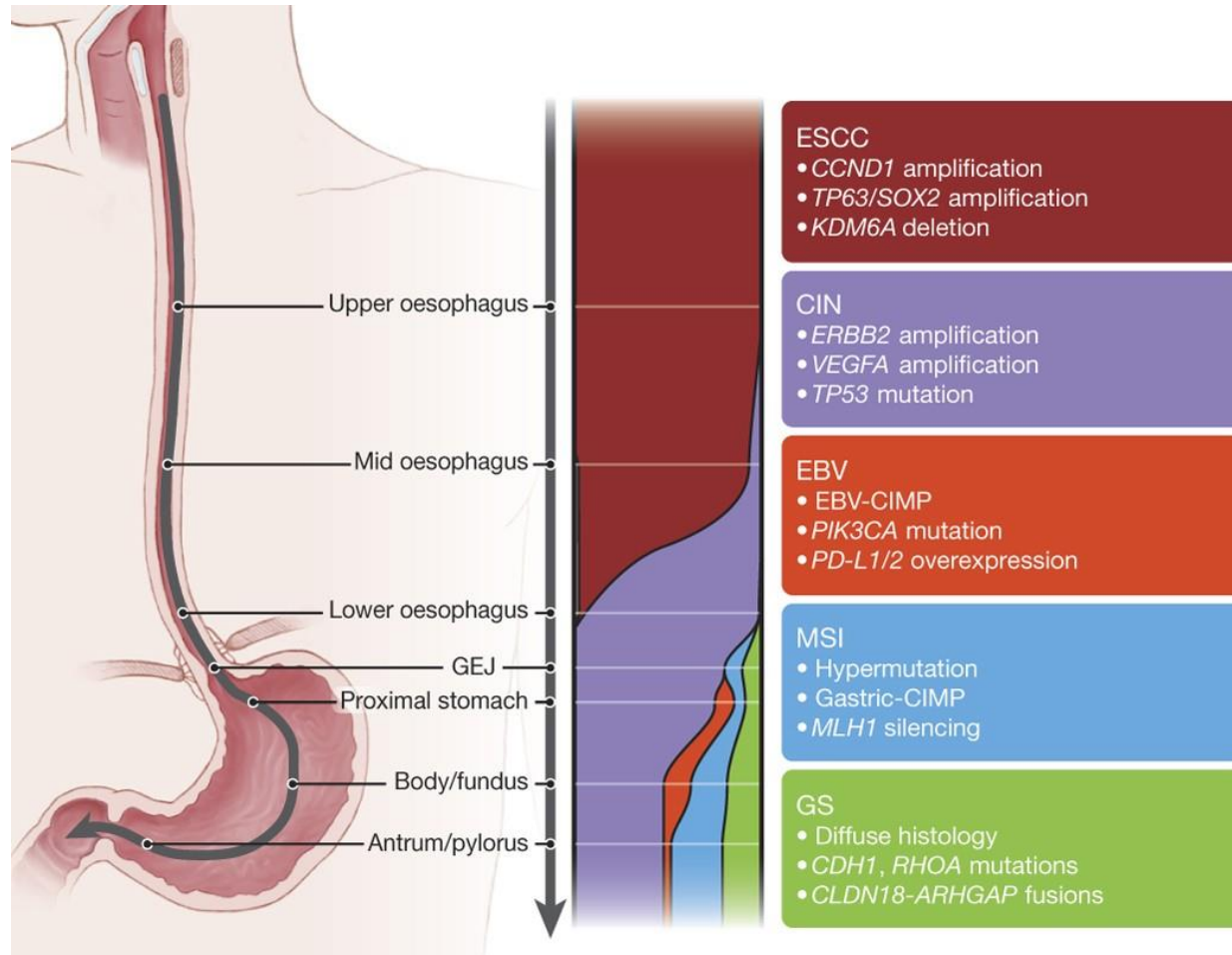
$$\text{TPS} = \frac{\text{No. PD-L1 positive tumor cells}}{\text{Total No. of viable tumor cells}} \times 100$$

$$\text{CPS} = \frac{\text{No. PD-L1 positive cells (tumor cells, lymphocytes, macrophages)}}{\text{Total No. of viable tumor cells}} \times 100$$



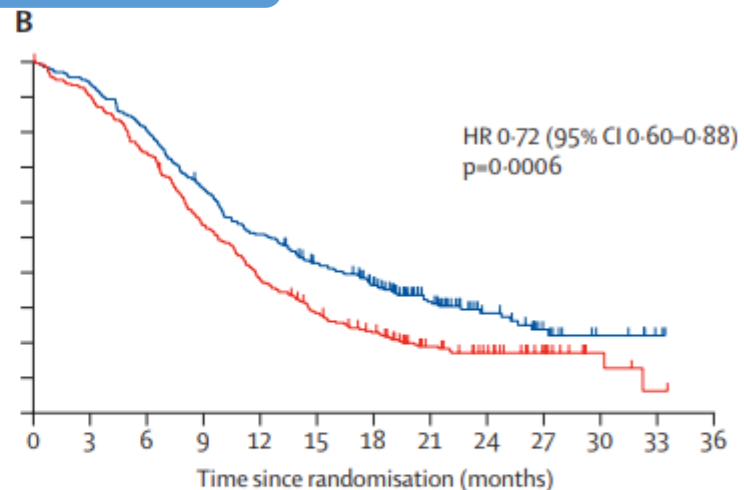
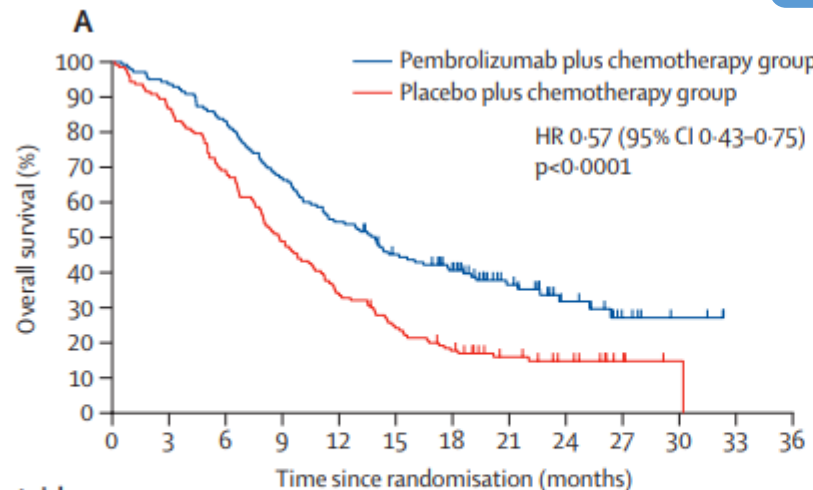
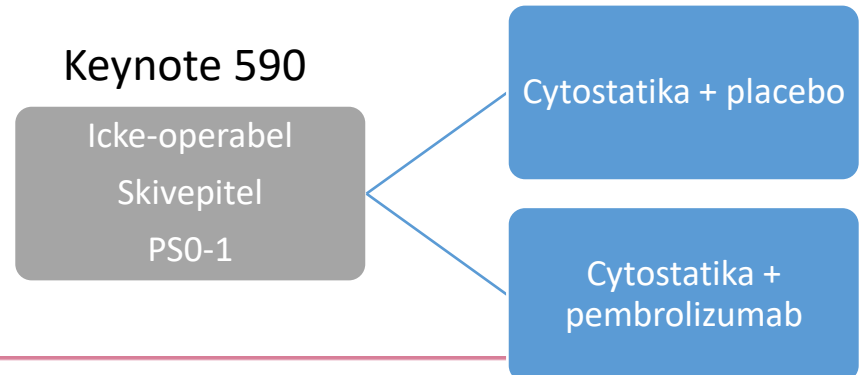
MSI = microsatellit instabilitet -> hög mutationsbörda i tumören -> högre sannolikhet att svara på immunterapi

Vilken typ av esofaguscancer?



- Skivepitelcancer
- Adenocarcinom

Immunterapi i skivepitelcancer



Skivepitelcancer
+ CPS >10%

	0	3	6	9	12	15	18	21	24	27	30	33	36
Number at risk	143	134	119	96	78	61	51	29	16	7	3	0	0
(number censored)	(0)	(0)	(0)	(0)	(0)	(4)	(8)	(25)	(35)	(42)	(46)	(49)	(49)
Pembrolizumab plus chemotherapy group	143	124	99	70	48	34	24	15	10	4	1	0	0
Placebo plus chemotherapy group	(0)	(0)	(0)	(0)	(0)	(1)	(2)	(9)	(13)	(19)	(22)	(22)	(22)

	274	258	221	175	139	111	89	50	27	14	6	2	0
	(0)	(0)	(0)	(1)	(1)	(7)	(13)	(43)	(62)	(71)	(78)	(82)	(82)
Pembrolizumab plus chemotherapy group	274	247	203	146	103	75	57	34	23	13	4	1	0
Placebo plus chemotherapy group	(0)	(1)	(1)	(2)	(2)	(5)	(9)	(23)	(31)	(42)	(50)	(51)	(51)

Skivepitelcancer
Oavsett CPS

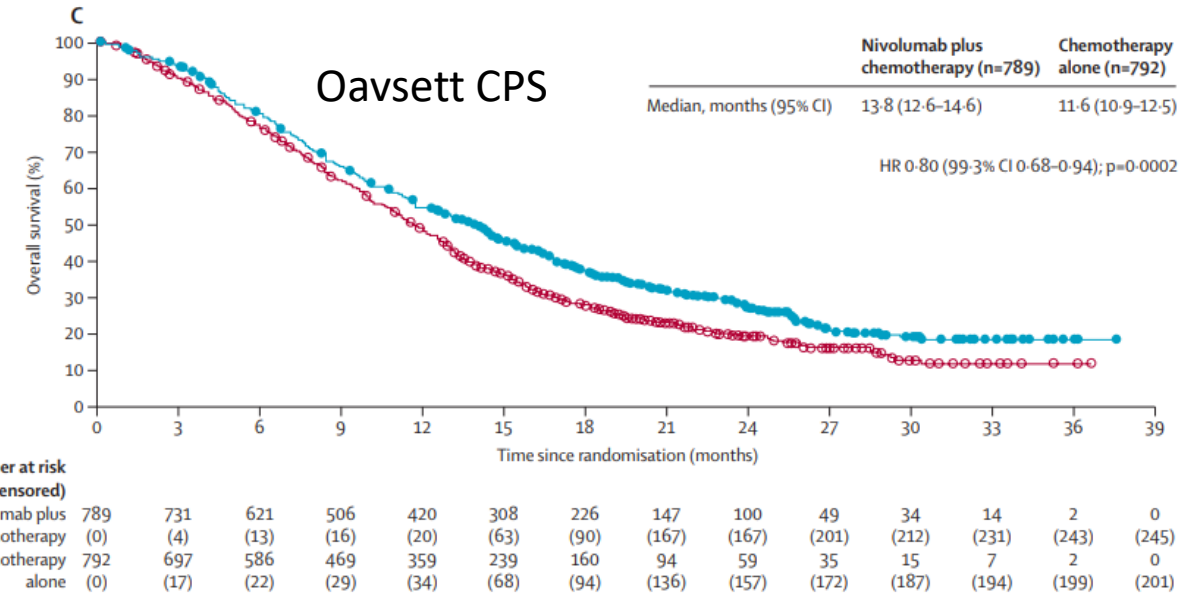
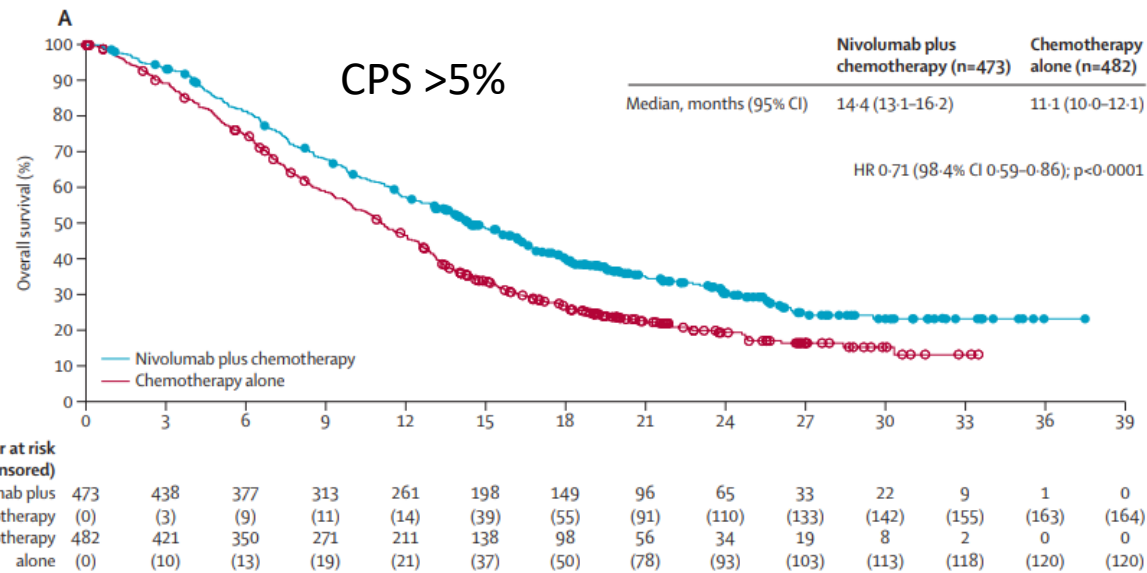
Immunterapi i adenocarcinom

CheckMate 649

Icke-operabel
Adenocarcinom
PS 0-1

Cytostatika + placebo

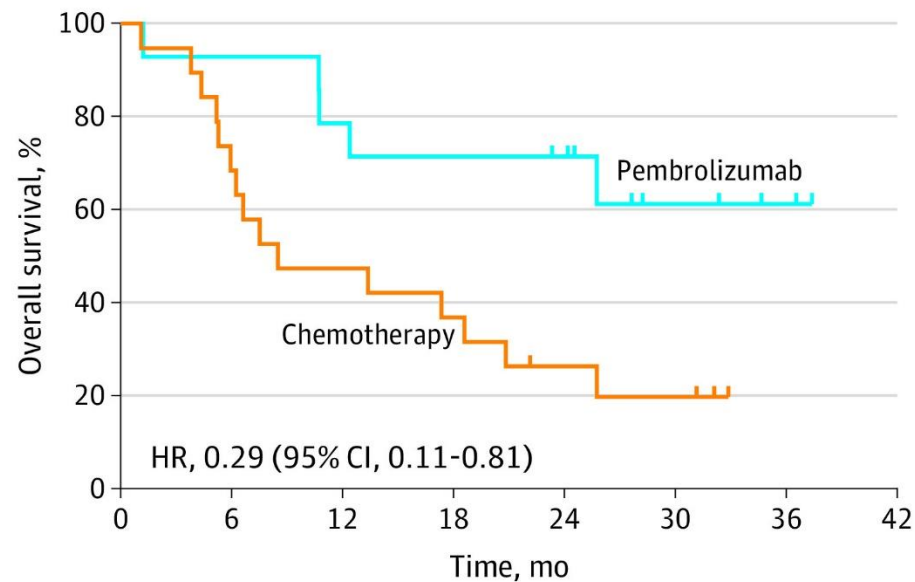
Cytostatika +
nivolumab



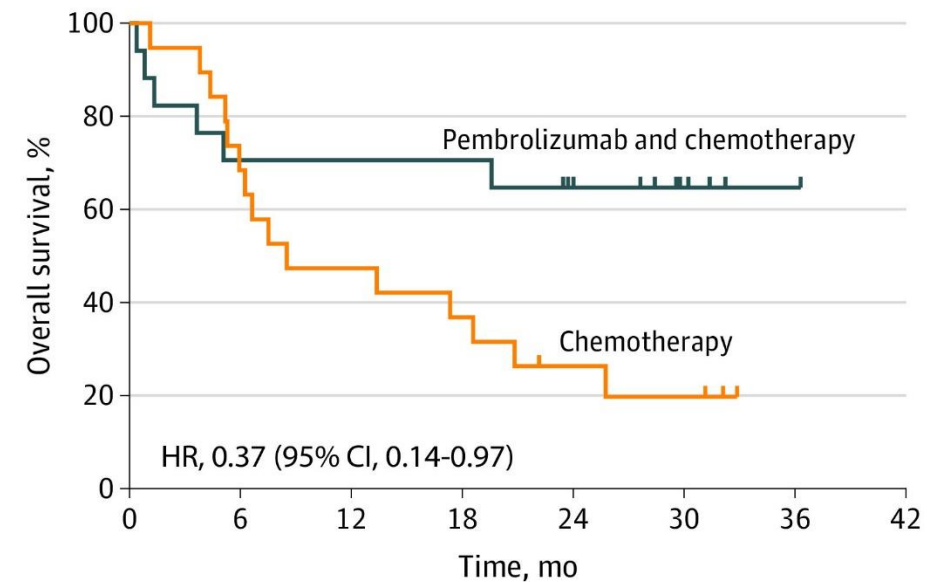
Immunterapi i MSI-H tumör

Pembrolizumab

A Pembrolizumab



B Pembrolizumab and chemotherapy



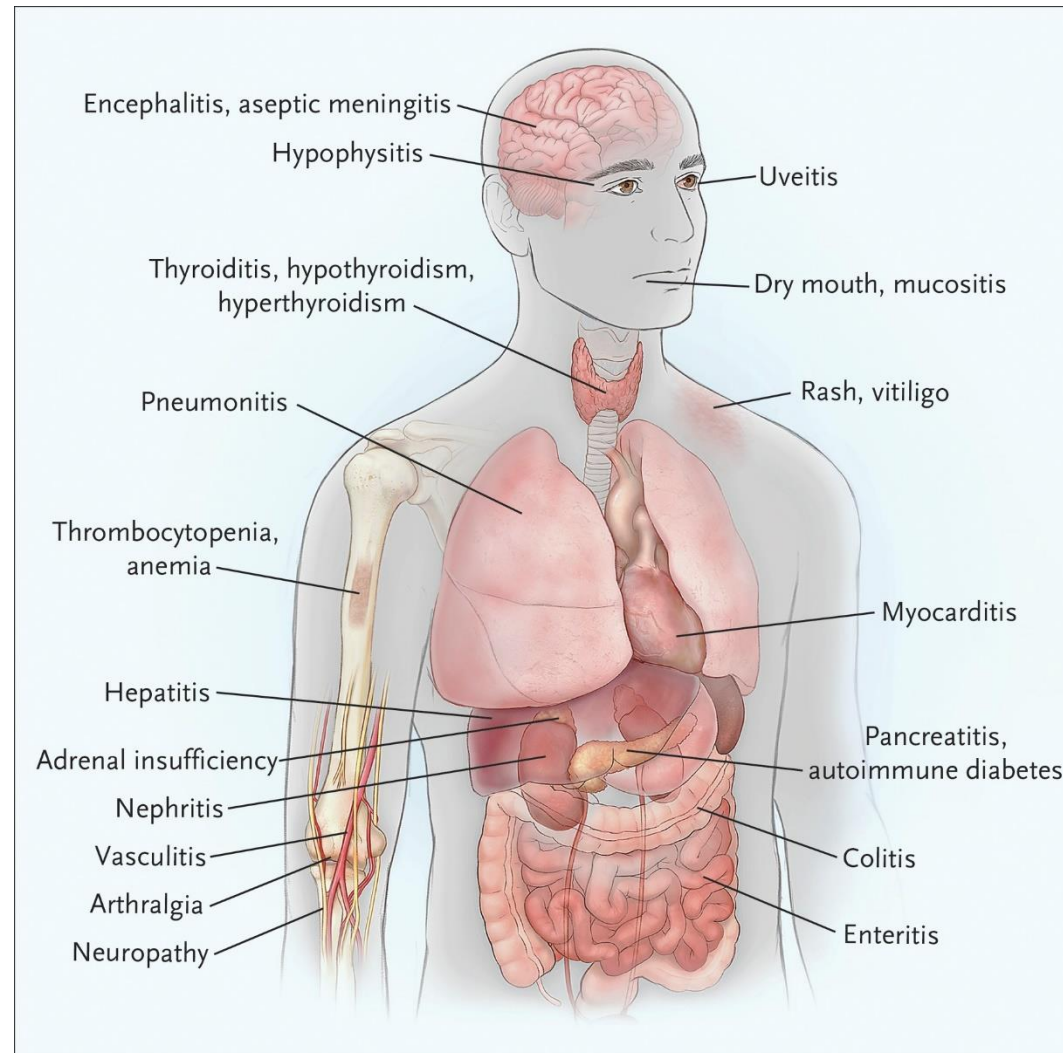
No. at risk (No. censored)

Pembrolizumab	14 (0)	13 (0)	11 (0)	10 (0)	9 (0)	4 (3)	2 (6)	0 (9)
Chemotherapy	19 (0)	13 (0)	9 (0)	7 (0)	4 (0)	3 (1)	0 (4)	0 (4)

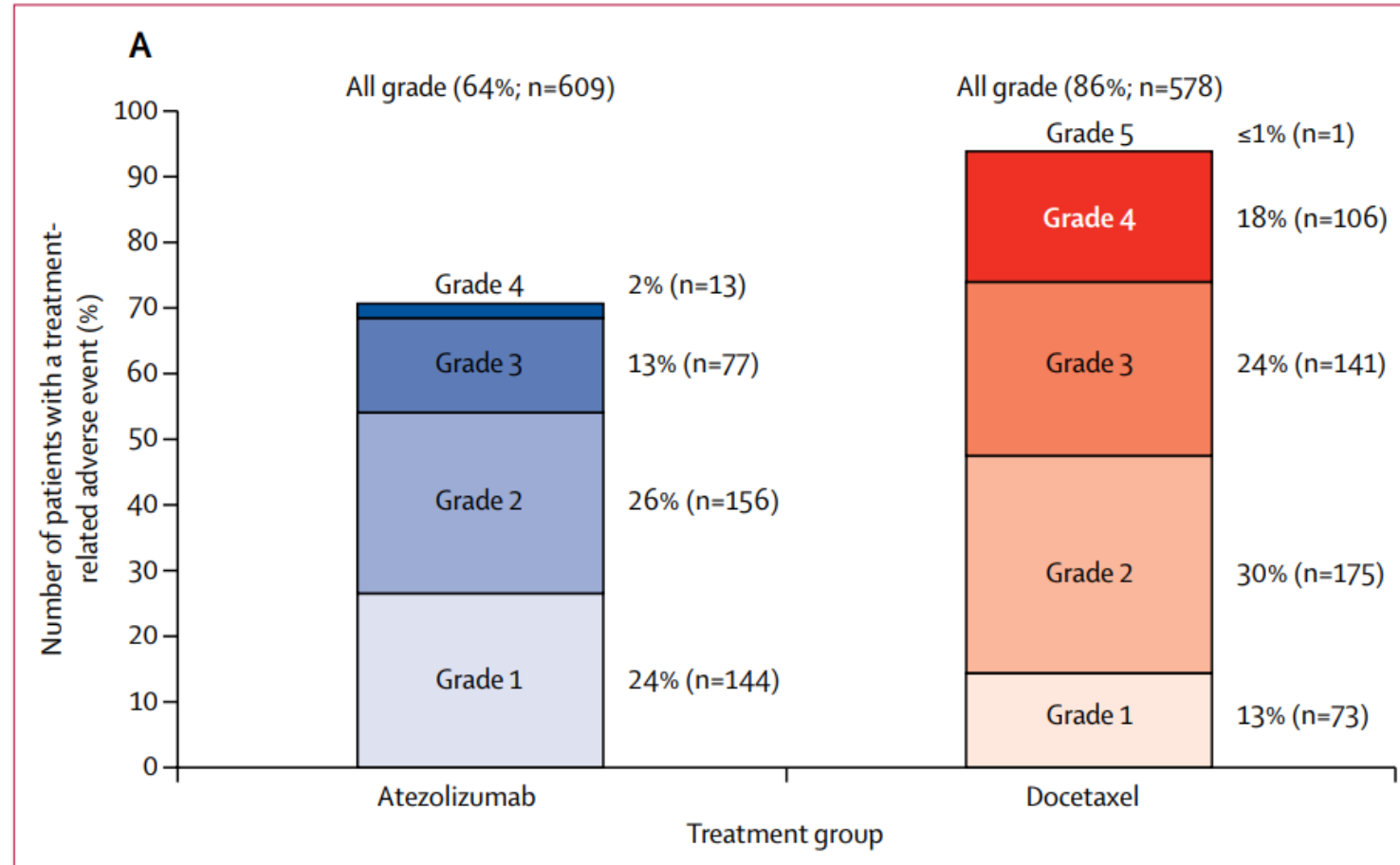
No. at risk (No. censored)

Pembrolizumab and chemotherapy	17 (0)	12 (0)	12 (0)	12 (0)	9 (0)	4 (3)	1 (10)	0 (11)
Chemotherapy	19 (0)	13 (0)	9 (0)	7 (0)	4 (0)	3 (1)	0 (4)	0 (4)

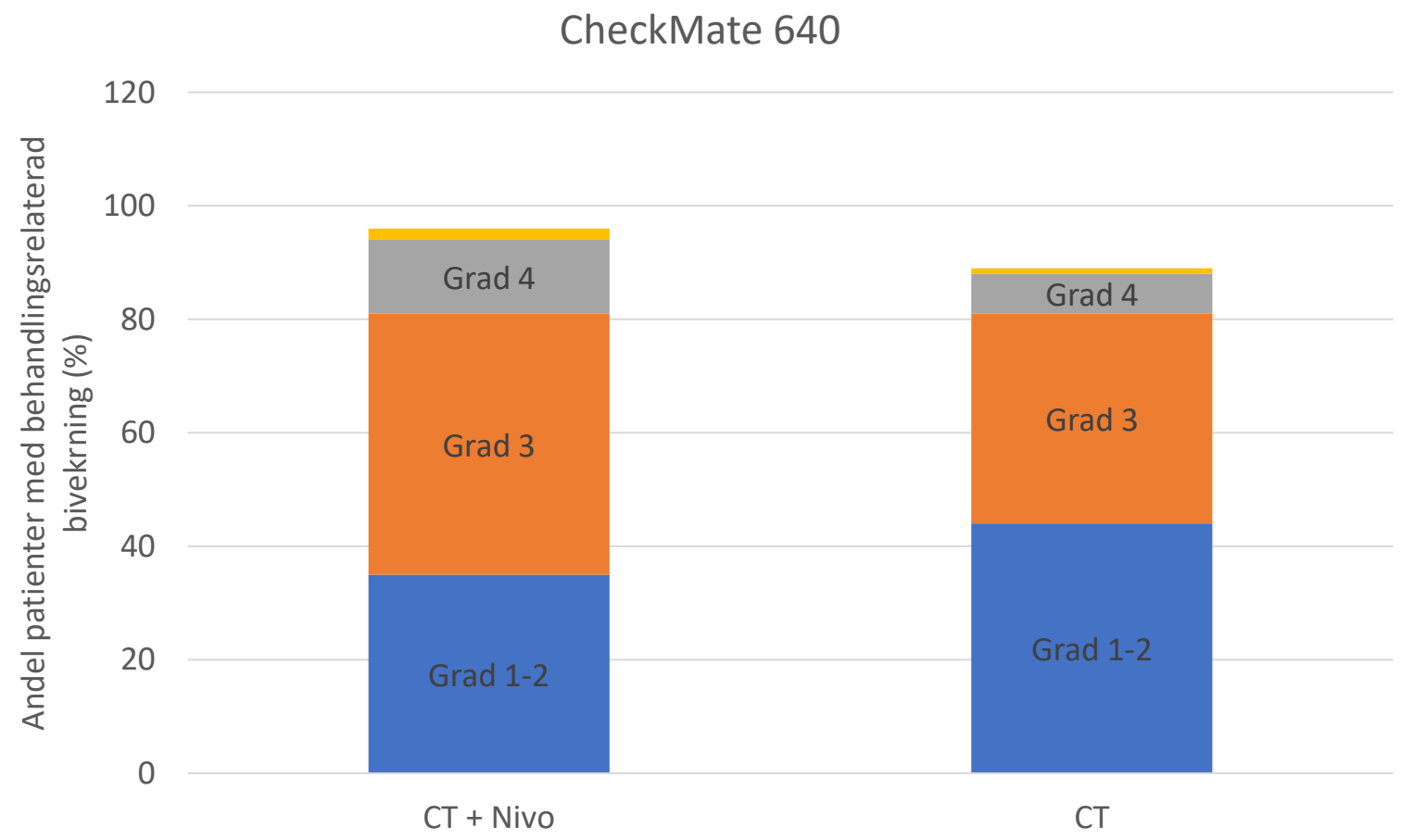
Vilka biverkningar?



Hur mycket biverkningar?

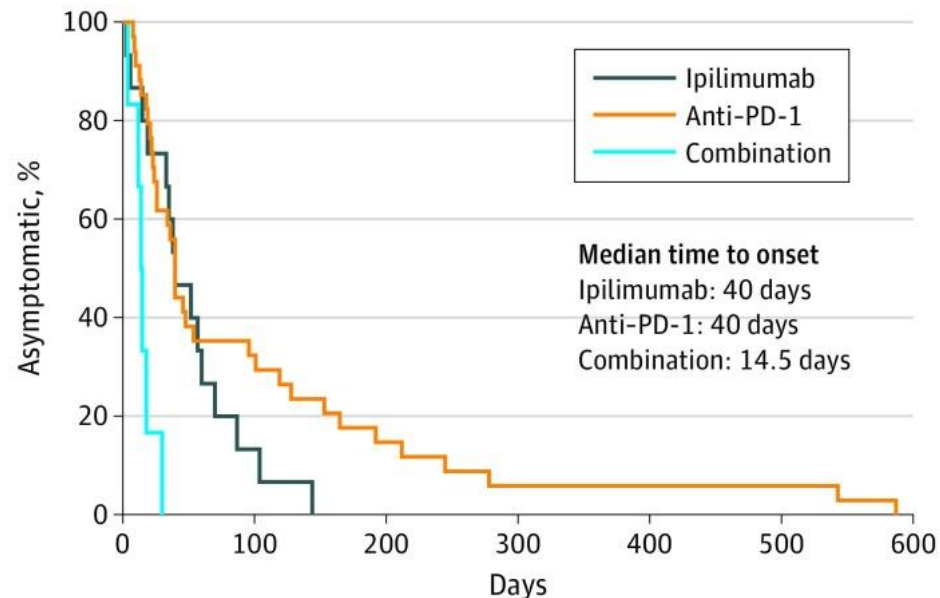


Hur mycket biverkningar egentligen?



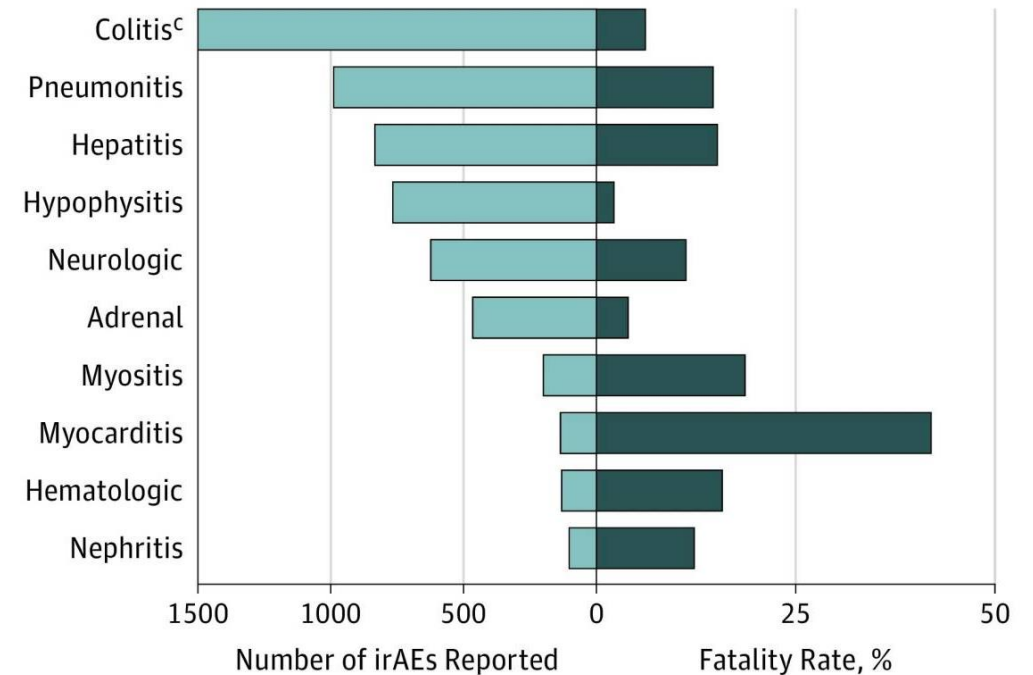
Adenocarcinom
ventrikel,
esofagus, GEJ

Hur dödliga är dem?



No. at risk	0	100	200	300	400	500	600
Ipilimumab	15	2	0	0	0	0	0
Anti-PD-1	34	11	5	2	2	2	0
Combination	6	0	0	0	0	0	0

C Cases and fatality rates



- Mortaliteten beräknas till ca 0,3-1,3%



Avslutande ord

- Immunterapi är äntligen ett vanligt behandlingsalternativ för onkologer.
 - Fortfarande något begränsad effekt hos patienter med esofagus och ventrikelcancer.
 - Förutsägande faktorer som CPS och MSI-H behövs för att bättre välja rätt patient.
 - Biverkningarna är utmanande pga den förändrade karaktären och behandling i kombinationer.
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Tack för uppmärksamheten!

Frågor? Kommentarer!
