Overzicht van de behandelingen (dr. Meert)

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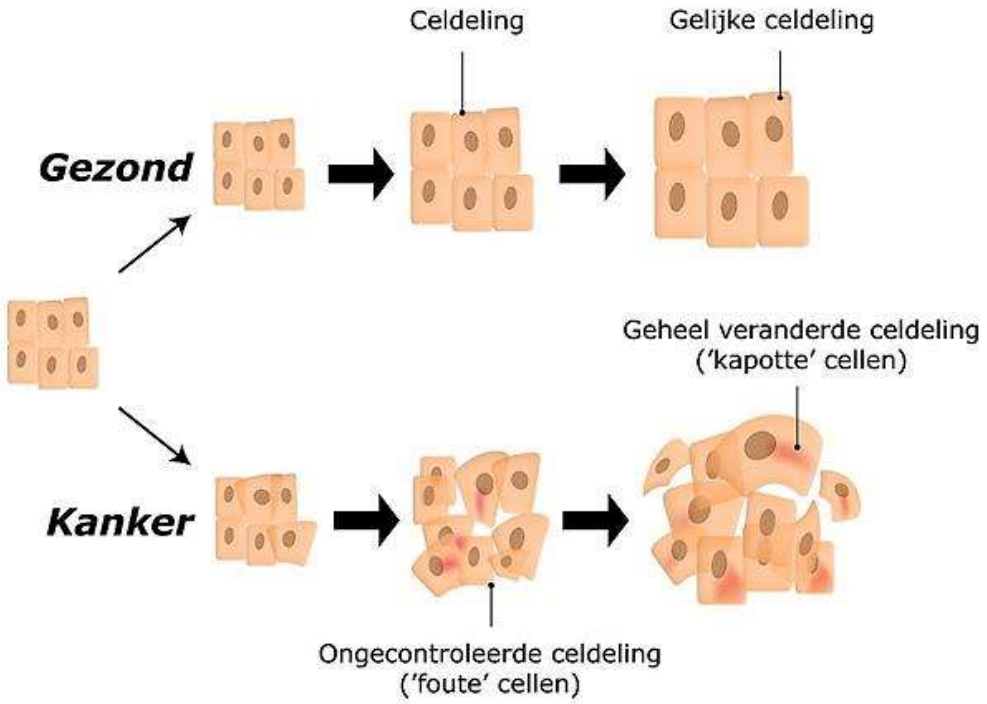
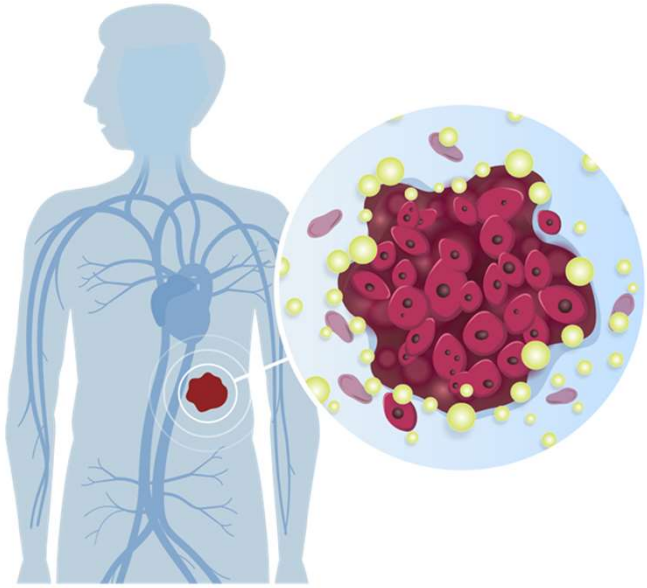
Lymfklierkanker-Vereniging Vlaanderen vzw

Overzicht van de behandelingen

1. Wat is kanker?
2. Wat is lymfeklierkanker (lymfoom)?
3. Chemotherapie
4. Radiotherapie
5. Doelgerichte therapie
6. Immunotherapie
7. Stamceltransplantatie
8. Conclusie

1. Wat is kanker?





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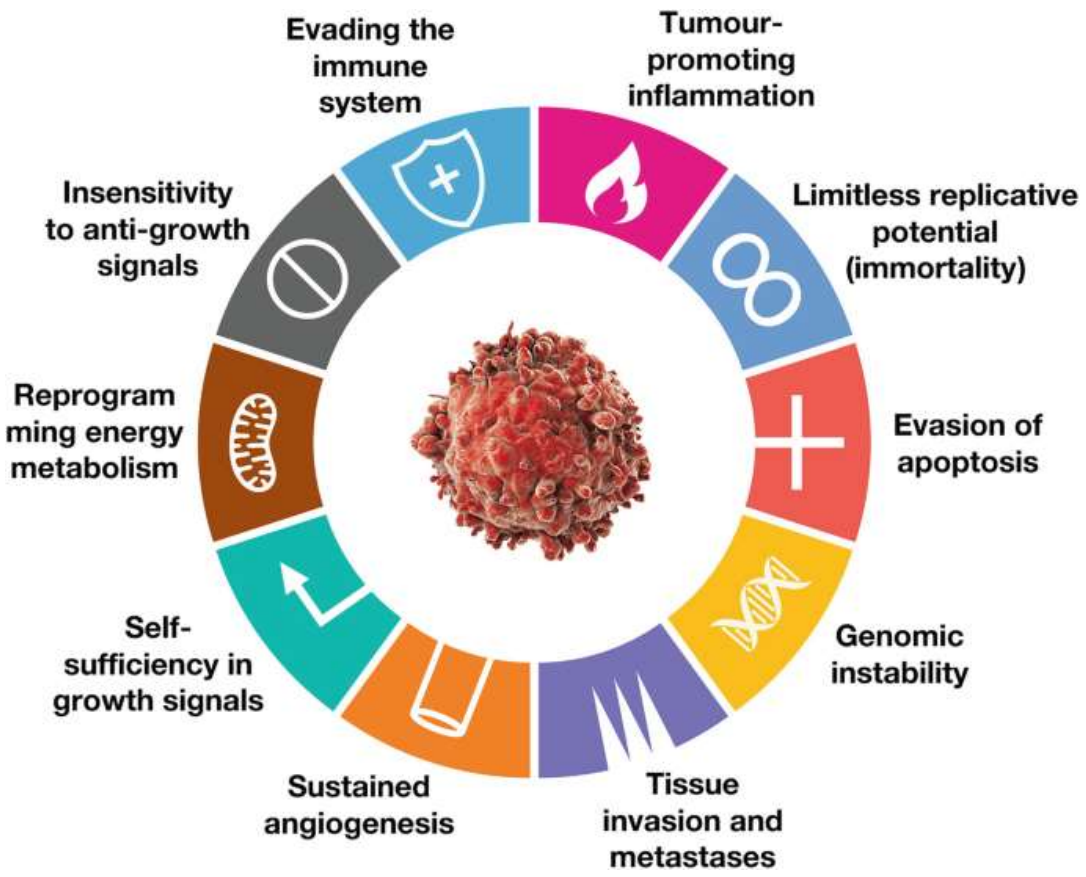
1. Wat is kanker?



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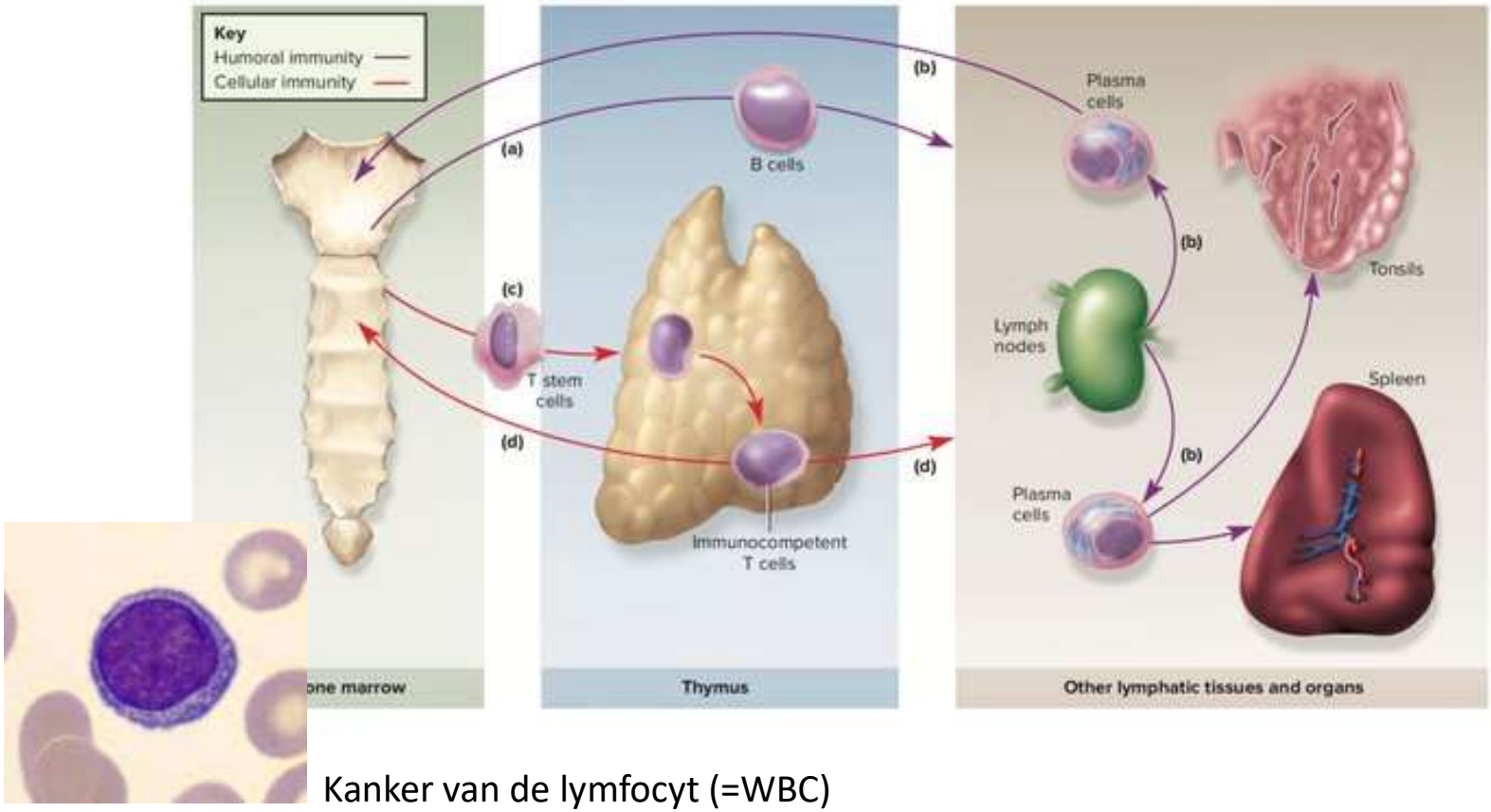
Hanahan et al. Cell 2000 Jan 7;100(1):57-70.

2. Wat is lymfeklierkanker (lymfoom)?



Kanker van de lymfocyt (=WBC)

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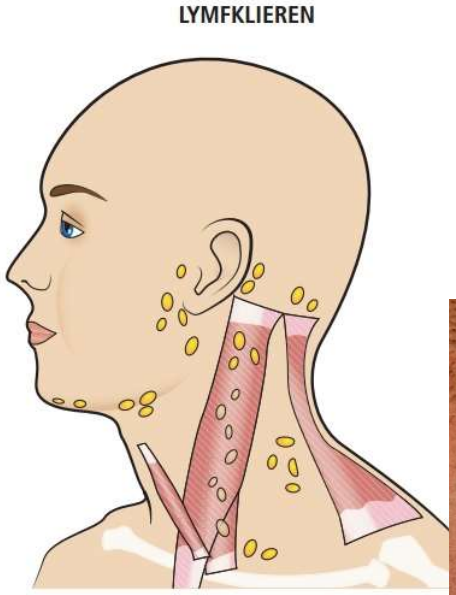
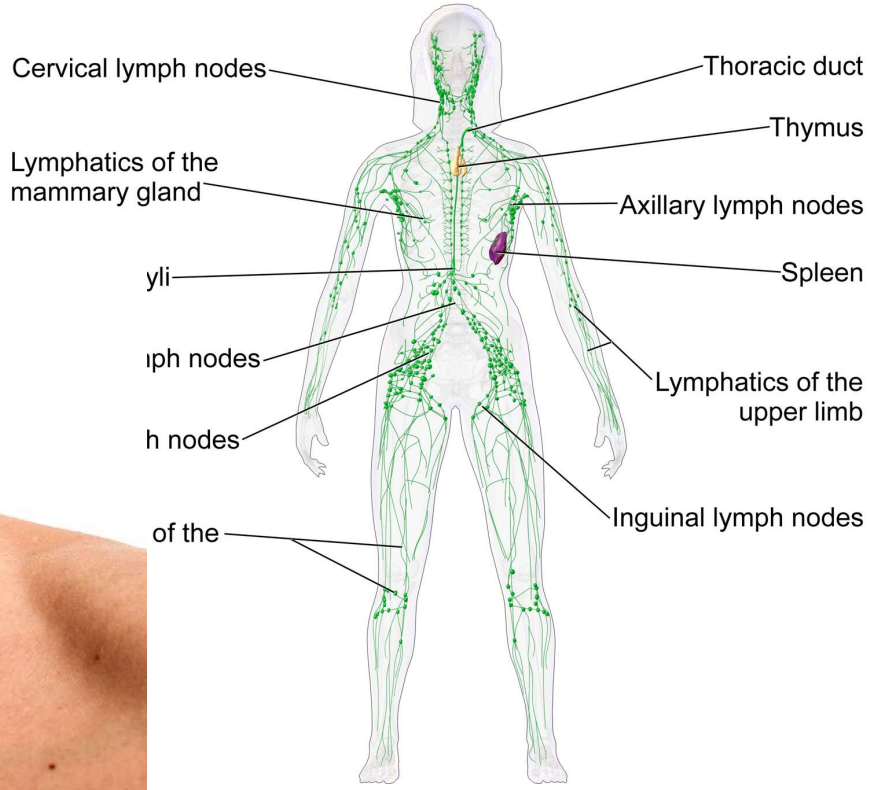
2. Wat is lymfeklierkanker (lymfoom)?





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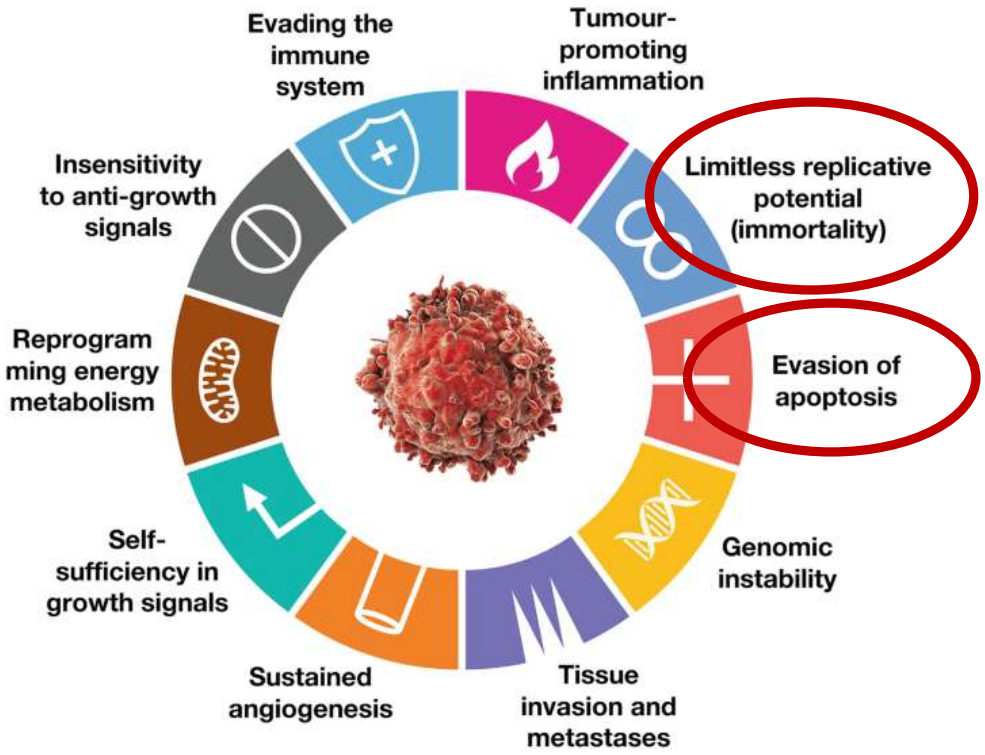
3. Chemotherapie

- Cytostatica
- verzamelnaam van allerlei chemische stoffen die als doel hebben de celdeling te verstoren

- Niet specifiek: werkt in op elk soort van snel delend weefsel, dus ook haarfollikels, slijmvliezen en het beenmerg.

- Curatief of palliatief
- Adjuvant of neo-adjuvant: niet bij lymfoom
- Voor en/of na stamceltransplantatie
- Synergie



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Chemotherapie: soorten

ANTIMETABOLITES
Azacitidine
5-fluorouracil
6-mercaptopurine
Capecitabine
Cladribine
Clofarabine
Cytarabine
Decitabine
Floxuridine
Fludarabine
Gemcitabine
Hydroxyurea
Methotrexate
Nelarabine
Pemetrexed
Pentostatin
Pralatrexate
Thioguanine
Trifluridine/tipiracil

ALKYLATING AGENTS
Altretamine
Bendamustine
Busulfan
Carboplatin
Carmustine
Chlorambucil
Cisplatin
Cyclophosphamide
Dacarbazine
Ifosfamide
Lomustine
Mechlorethamine
Melphalan
Oxaliplatin
Temozolomide
Thiotepa
Trabectedin

OTHER CHEMOTHERAPY DRUGS
All-trans-retinoic acid
Arsenic trioxide
Asparaginase
Eribulin
Hydroxyurea
Ixabepilone
Mitotane
Omacetaxine
Pegaspargase
Procarbazine
Romidepsin
Vorinostat

CORTICOSTEROIDS
Prednisone
Methylprednisolone
Dexamethasone

NITROSOUREAS
Carmustine
Lomustine
Streptozocin

TOPOISOMERASE INHIBITORS
Irinotecan
Topotecan
Etoposide
Mitoxantrone
Teniposide

ANTI-TUMOR ANTIBIOTICS
Daunorubicin
Doxorubicin
Epirubicin
Idarubicin
Valrubicin
Bleomycin
Dactinomycin
Mitomycin-C
Mitoxantrone

MITOTIC INHIBITORS
Cabazitaxel
Docetaxel
Nab-paclitaxel
Paclitaxel
Vinblastine
Vincristine
Vinorelbine

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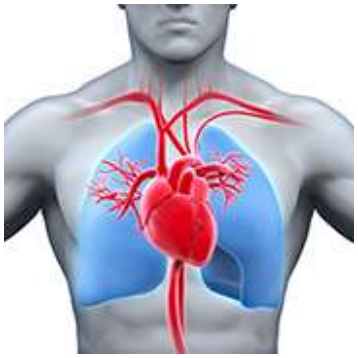
Chemotherapie: voorbeeld ABVD voor klassiek Hodgkin lymfoom

- 6 cycli met 2 toedieningen per cyclus van 28 dagen

Drug	Dosage and Route	Days of Treatment
Doxorubicin	25 mg/m^2 I.V	1 and 15
Bleomycin	10 mg/m^2 I.V	1 and 15
Vinblastine	6 mg/m^2 I.V	1 and 15
Dacarbazine	375 mg/m^2 I.V	1 and 15



- Dosering obv lichaamsoppervlakte, gewicht, ideaal lichaamsgewicht, UAC …
- Dosisaanpassingen ifv leeftijd en orgaanfunctie, bv longen, nieren, hart etc
- Kiezen van juiste katheter
- IV vocht toedieningen, ondersteunende medicatie, tumorlyse preventie, diurese; alkalyseren van urine, etc
- Cytoprotectie
- Opvolgen van orgaanfunctie: echo van het hart en longfunctie

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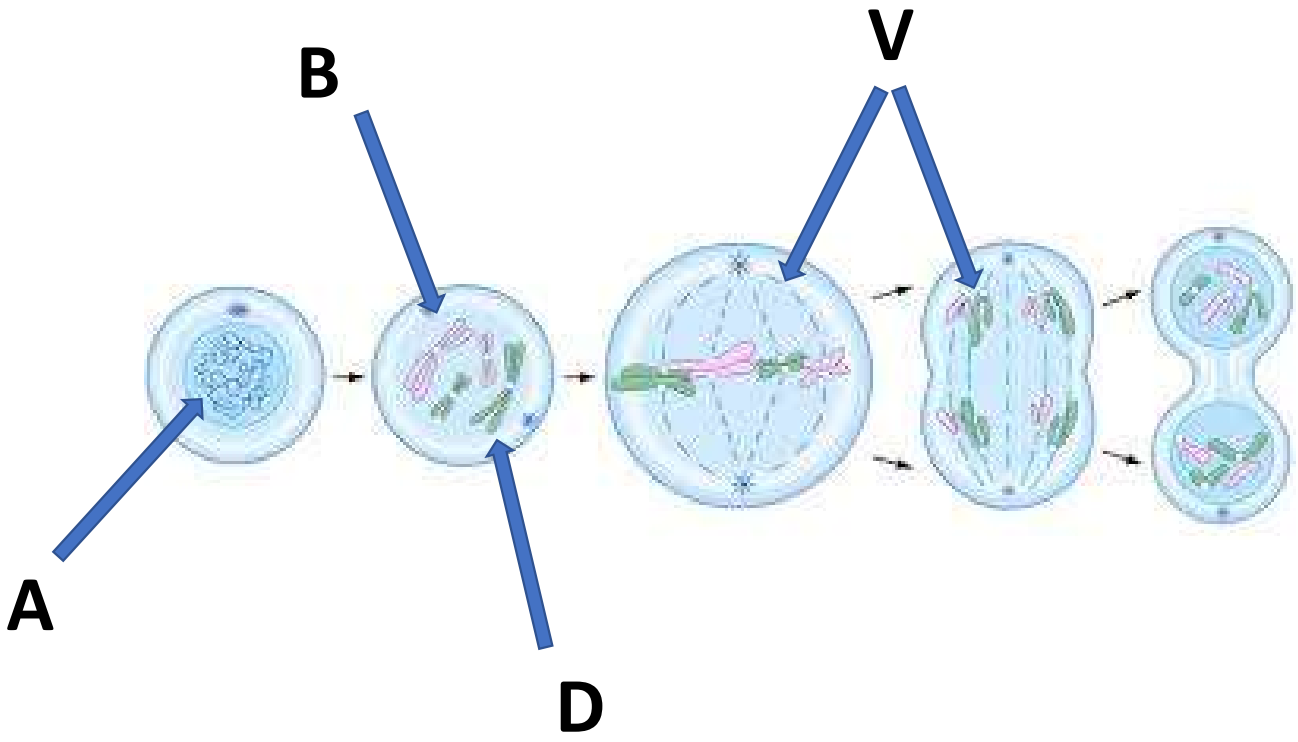
ABVD chemotherapie: mode of action



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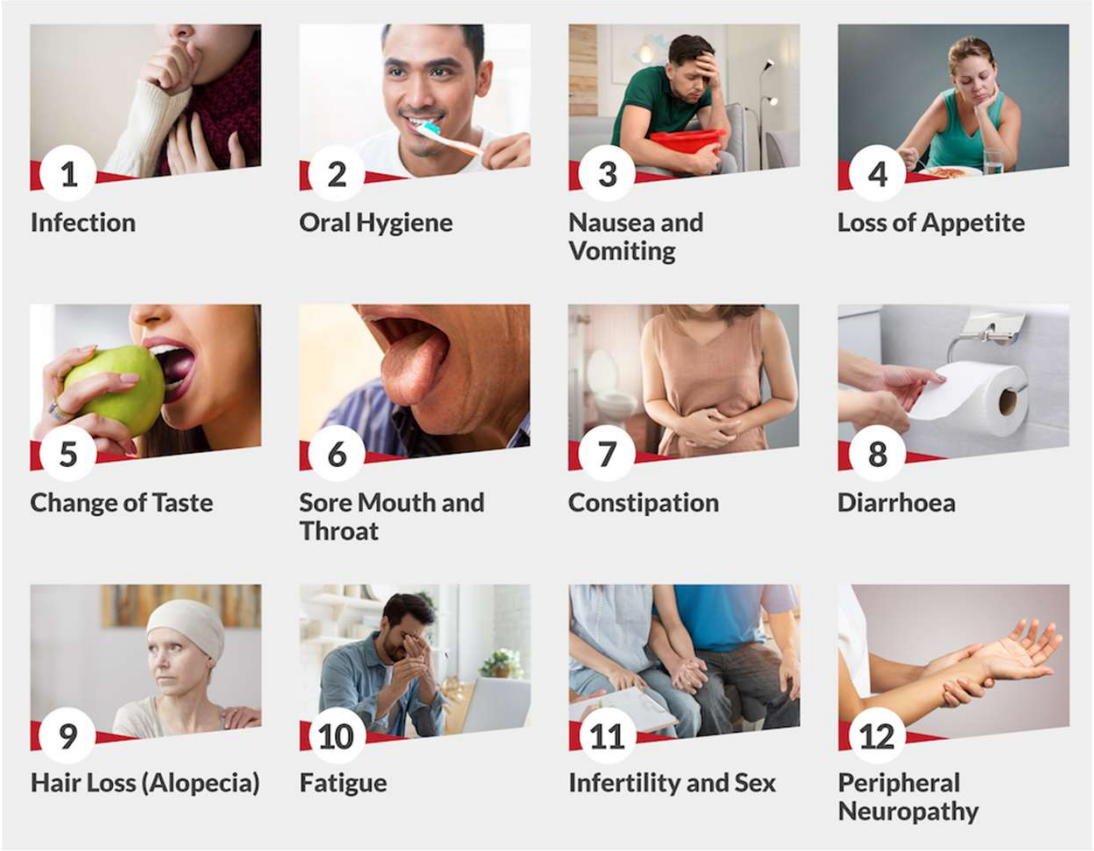
Chemotherapie:

Nevenwerkingen:

- Korte en lange termijn



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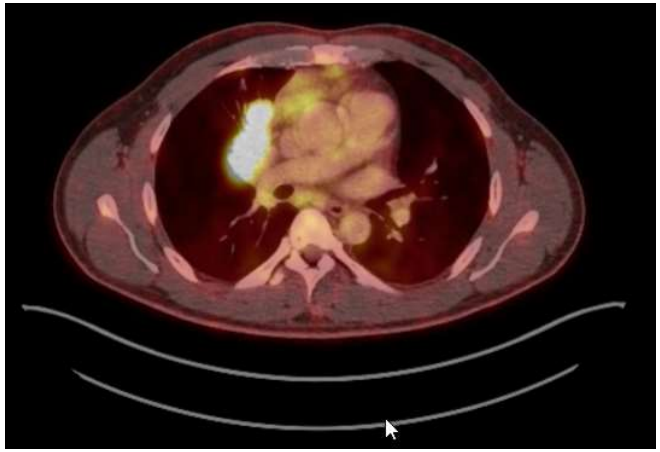
Chemotherapie: voorbeeld ABVD voor klassiek Hodgkin lymfoom

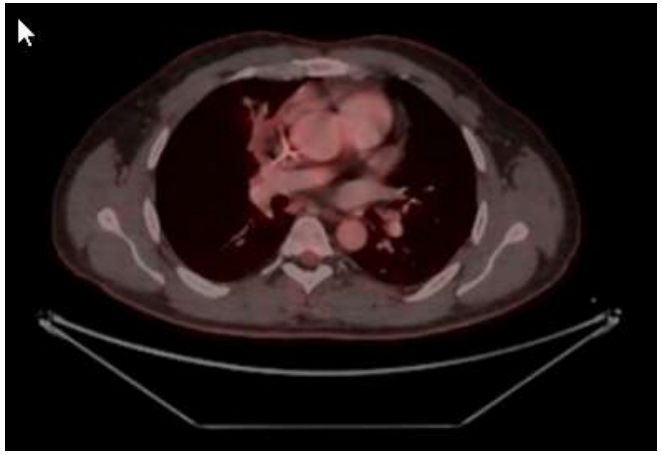
- Waarom geven we chemo?

Chemotherapie: voorbeeld ABVD voor klassiek Hodgkin lymfoom

- Waarom geven we chemo?

Effect na 2 cycli ABVD





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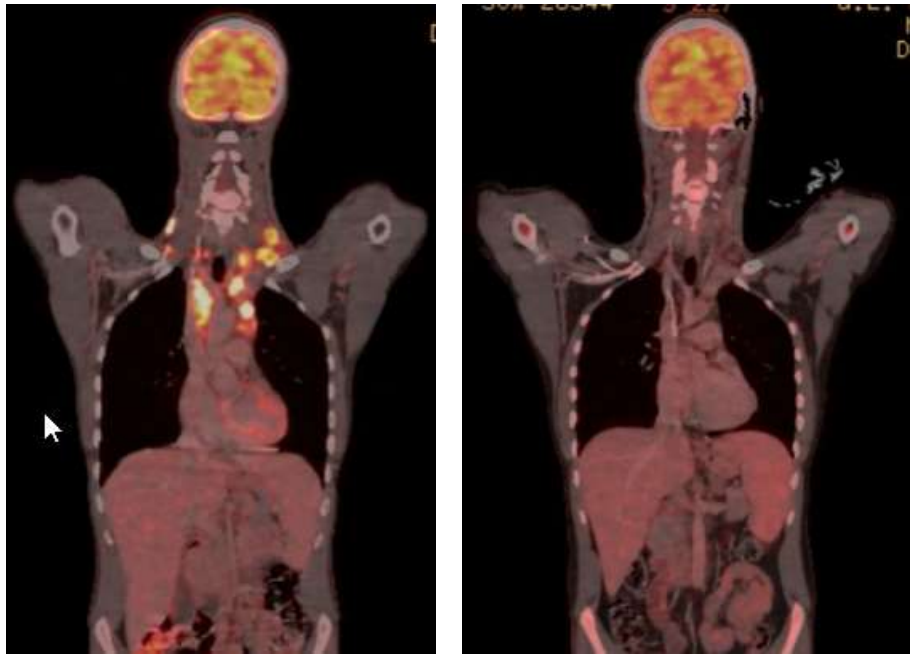
Chemotherapie: voorbeeld ABVD voor klassiek Hodgkin lymfoom

- Waarom geven we chemo?

Effect na 2 cycli A+AVD



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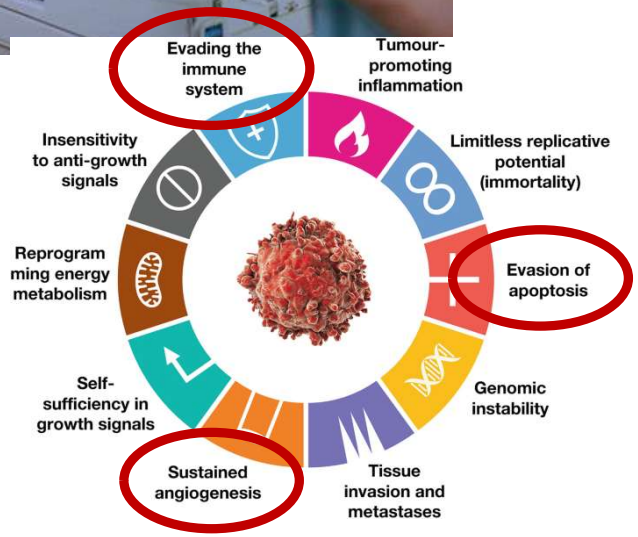
2. Radiotherapie

- Ioniserende straling
- Lineaire deeltjesversneller
- DNA schade en celdood

- Curatief of palliatief
- Symptomatisch/supportief
- Voor stamceltransplantatie of andere celtherapie

- Stralingsveld zo beperkt mogelijk houden



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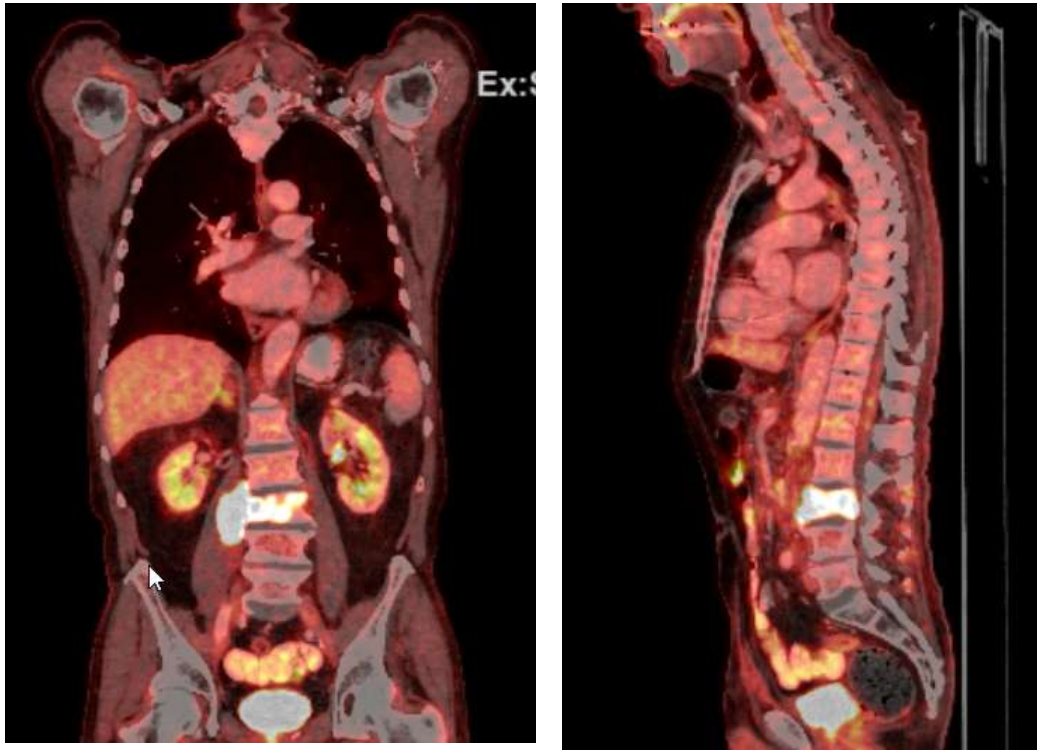
2. Radiotherapie: voorbeeld



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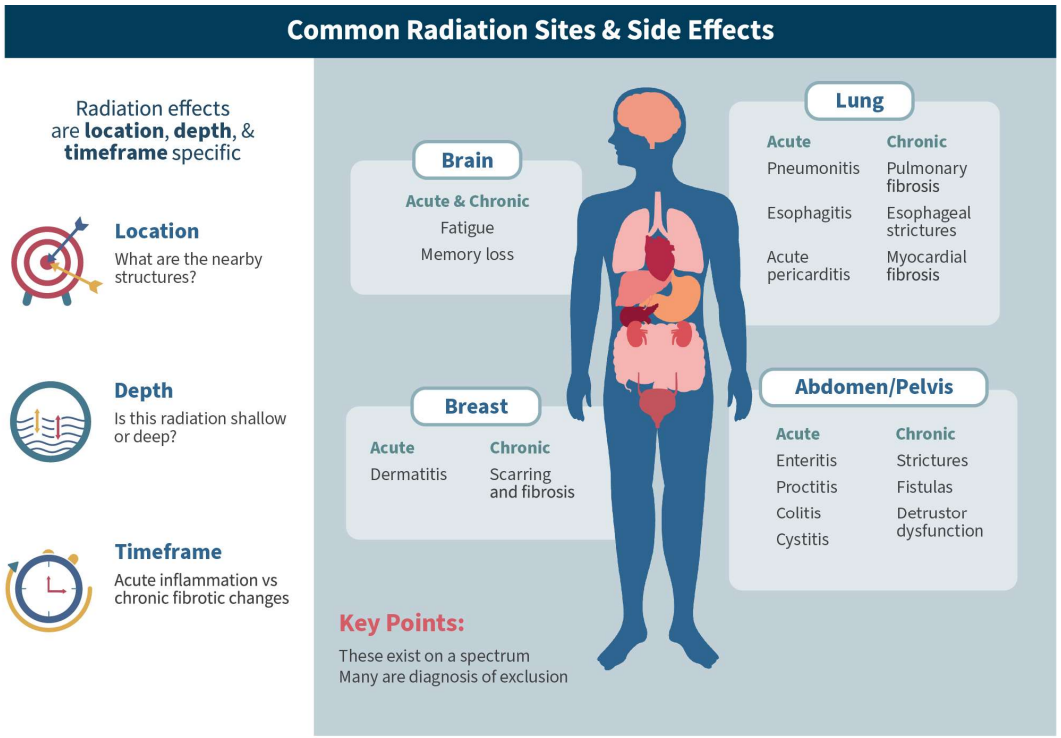
2. Radiotherapie: nevenwerkingen

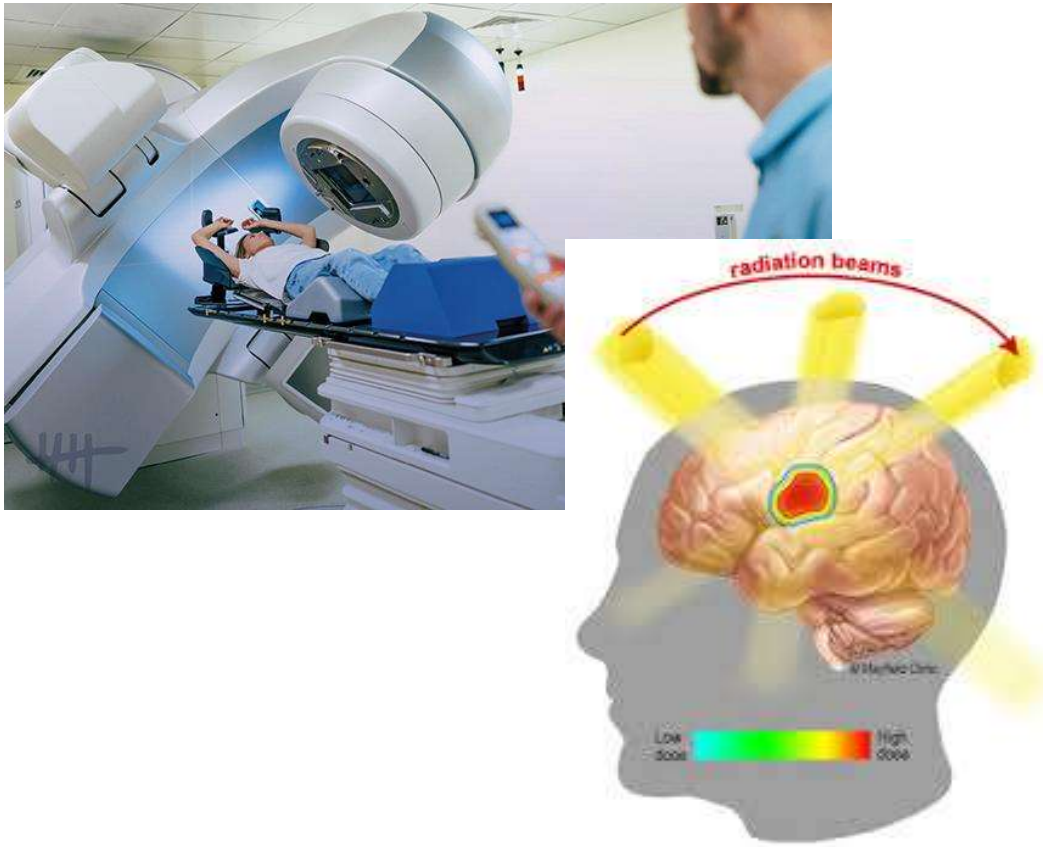
- Nevenwerkingen zijn sterk afhankelijk van de locatie die bestraald wordt en de grootte van het bestralingsveld.
- Acute inflammatie vs fibrotische veranderingen
- Secundaire kanker



azdelta

2. Radiotherapie: nevenwerkingen

- Nevenwerkingen zijn sterk afhankelijk van de locatie die bestraald wordt en de grootte van het bestralingsveld.
- Acute inflammatie vs fibrotische veranderingen
- Secundaire kanker
- Stereotactisch bestralen



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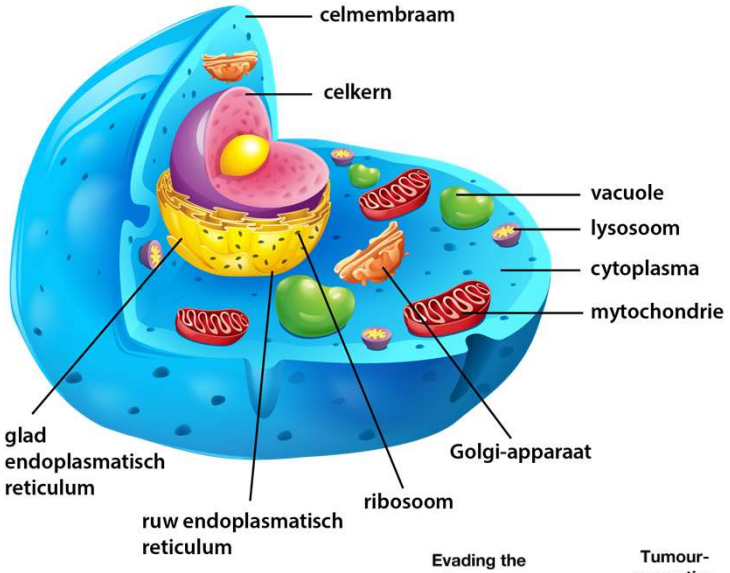
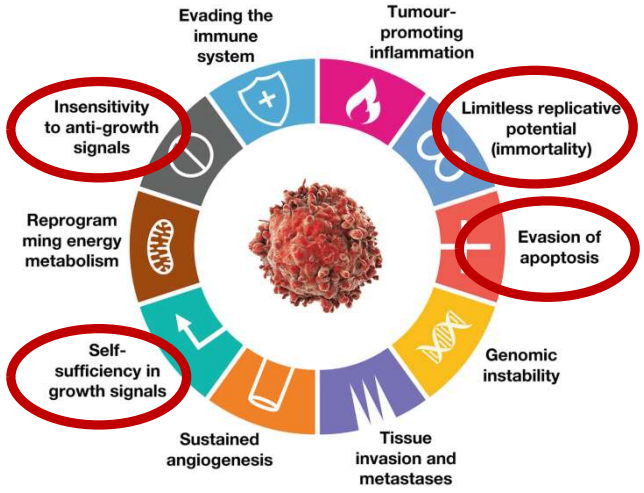
3. Doelgerichte therapie

- Type behandeling die direct inwerkt op proteïnen in de cel die celgroei en celdood aansturen
- Meestal behandeling in pilvorm

- Precision medecine
- Voordeel: erg specifiek en gunstig nevenwerkingen profiel
- Nadeel: langdurige therapie en vaak niet minder actief tegen agressief lymfoom





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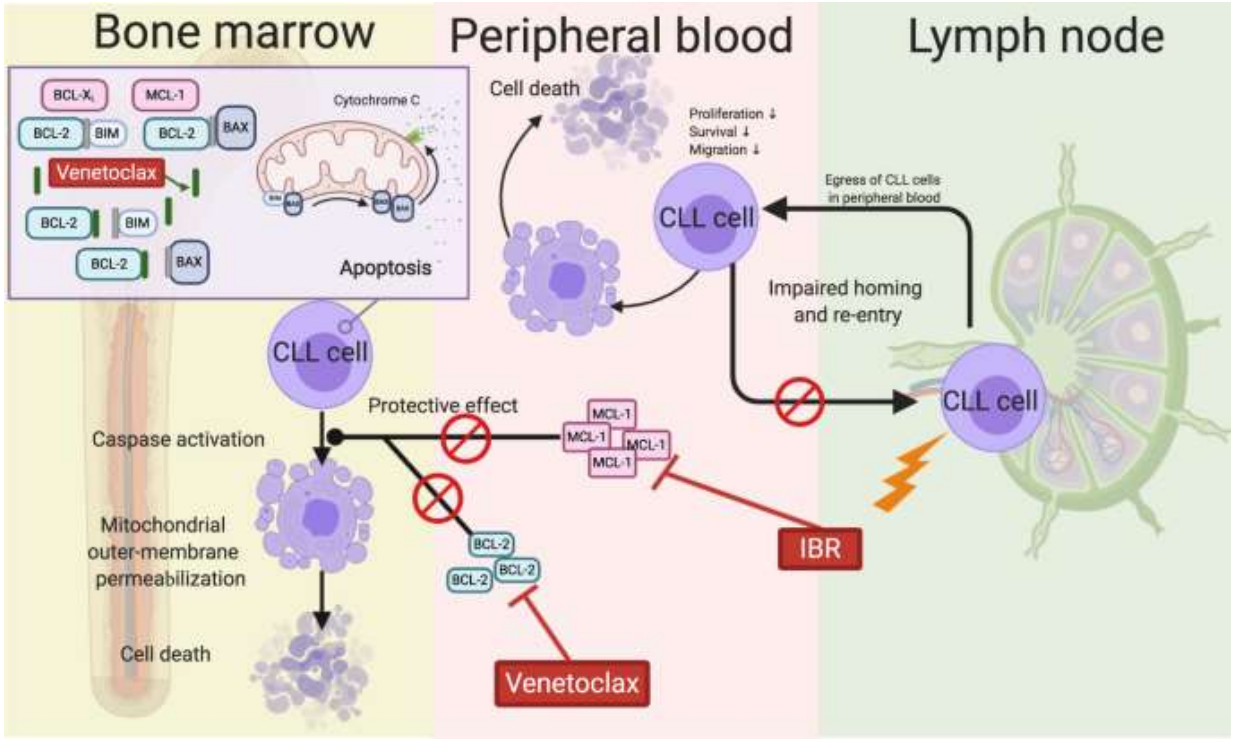
3. Doelgerichte therapie: mechanisme



3. Doelgerichte therapie: Casus CLL

	21-12-2021 13:01 KCL Meert	28-09-2021 13:44 Deeren	24-06-2021 12:58 Deeren	16-03-2021 13:47 Meert	29-12-2020 13:17 Meert	03-11-2020 13:20 Meert	13-10-2020 13:22 Meert
leucocytose	4.89	9.38	17.92	39.37	60.11	100.74	91.59
erythrocyten	4.55	4.76	4.67	5.10	4.59	4.18	4.02
hemoglobine	13.6	14.2	14.2	14.7	13.6	12.8	12.2
Hematocriet	40.0	41.9	41.1	44.9	41.9	40.1	37.9
MCV	87.9	88.0	88.0	88.0	91.3	95.9	94.3
MCH	29.9	29.8	30.4	28.8	29.6	30.6	30.3
MCHC	34.0	33.9	34.5	32.7	32.5	31.9	32.2
Red blood cell distribution width	-	-	-	-	-	-	-
thrombocyten	110	113	89	111	91	100	78
Staalcommentaar PLT	<Memo>	<Memo>	<Memo>	<Memo>	<Memo>	-	<Memo>
Microscopisch nazicht PLT	-	-	<Memo>	-	-	-	<Memo>
reticulocyten	0.7	1.0	0.8	0.7	0.5	1.0	1.2
reticulocytose	33.7	46.2	37.4	35.7	23.4	43.5	46.2
reticulocyten Hgb	-	-	-	-	-	-	-
Delta He	-	-	-	-	-	-	-

Start BTKI

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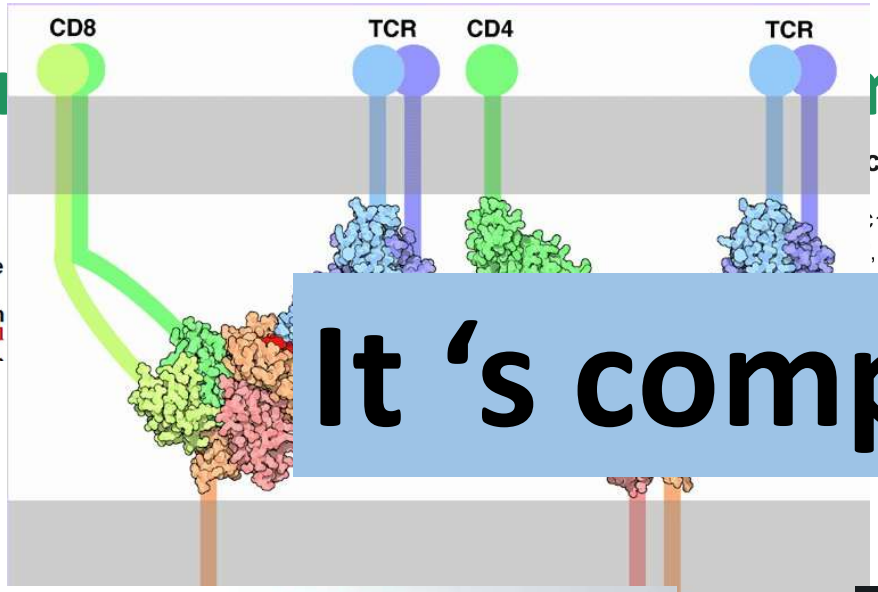
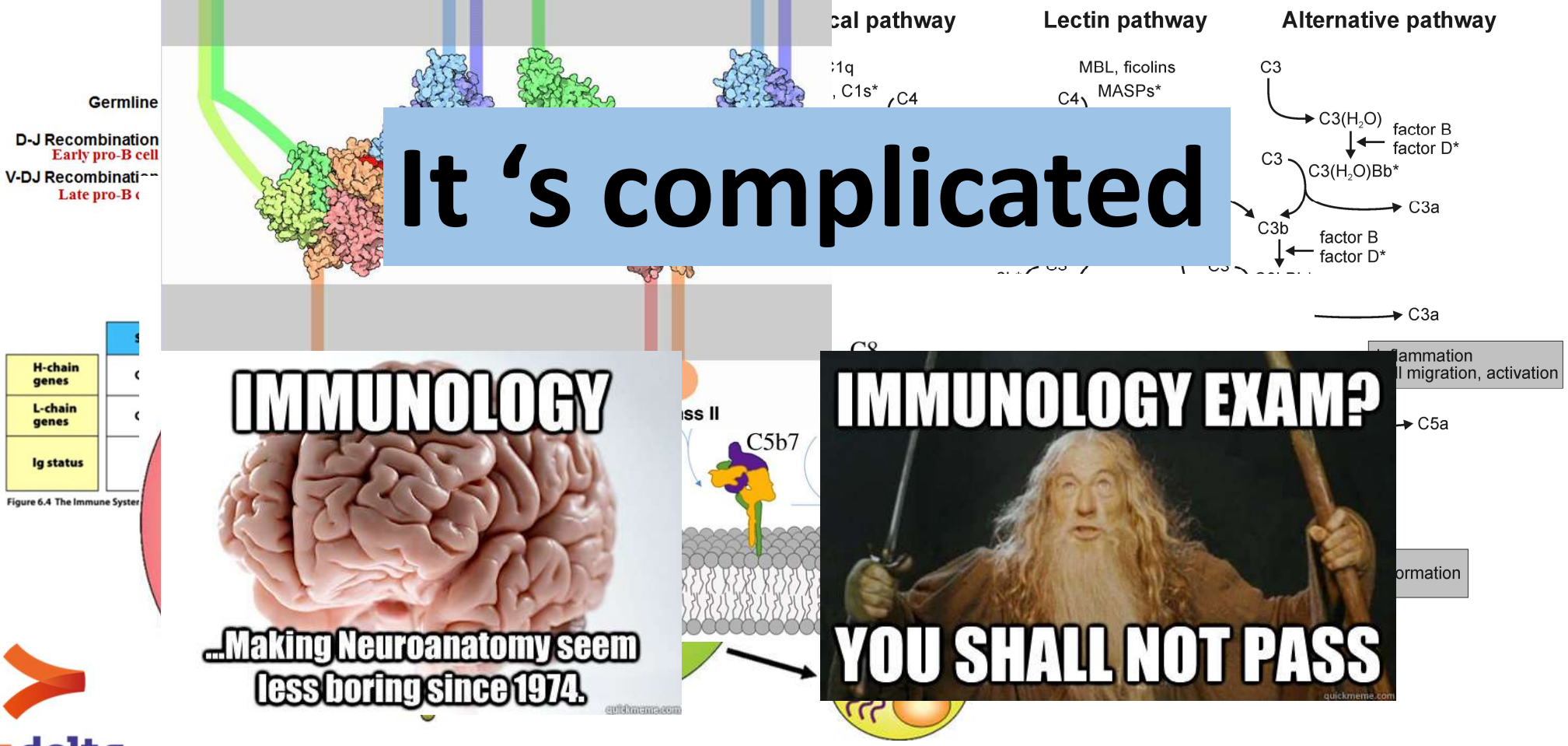
4. I nies





It ‘s complicated

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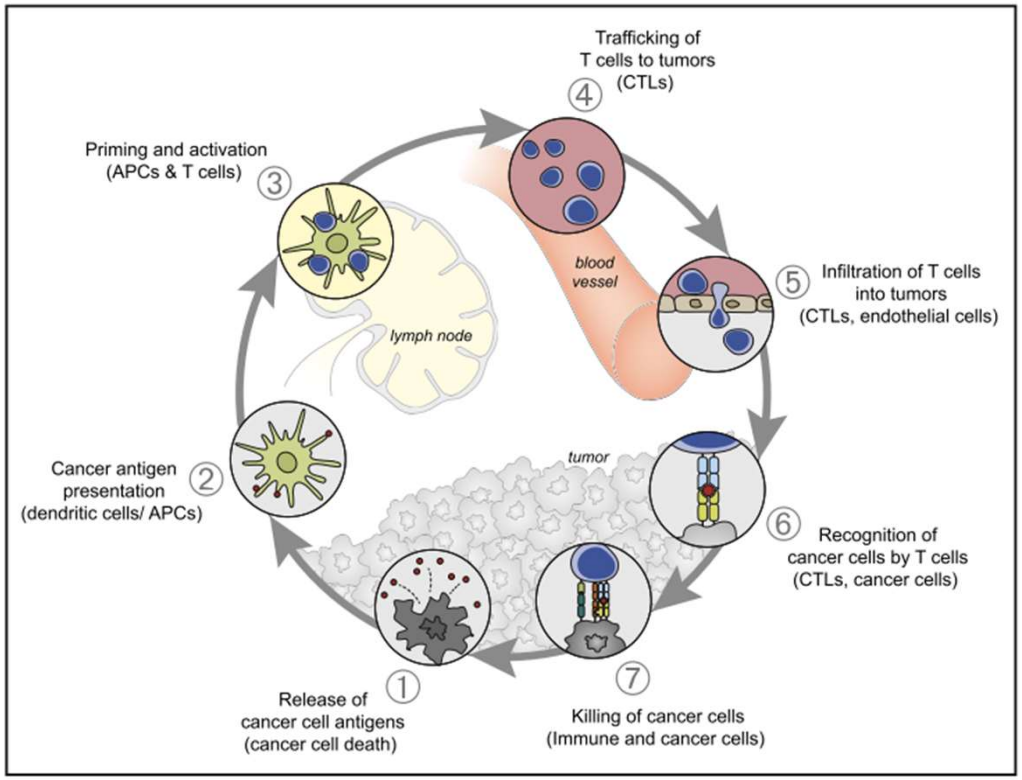
4. Onco-immunologie: the Cancer-Immunity Cycle



1. Tumorcel necrose

2. Presentatie van tumorantigenen door APC

3. Activatie van de T-cellen (=MVP) 

4. Toenadering en infiltratie van de T-cellen in de tumor

5. Herkenning van tumorcel

6. Killing van de tumorcel

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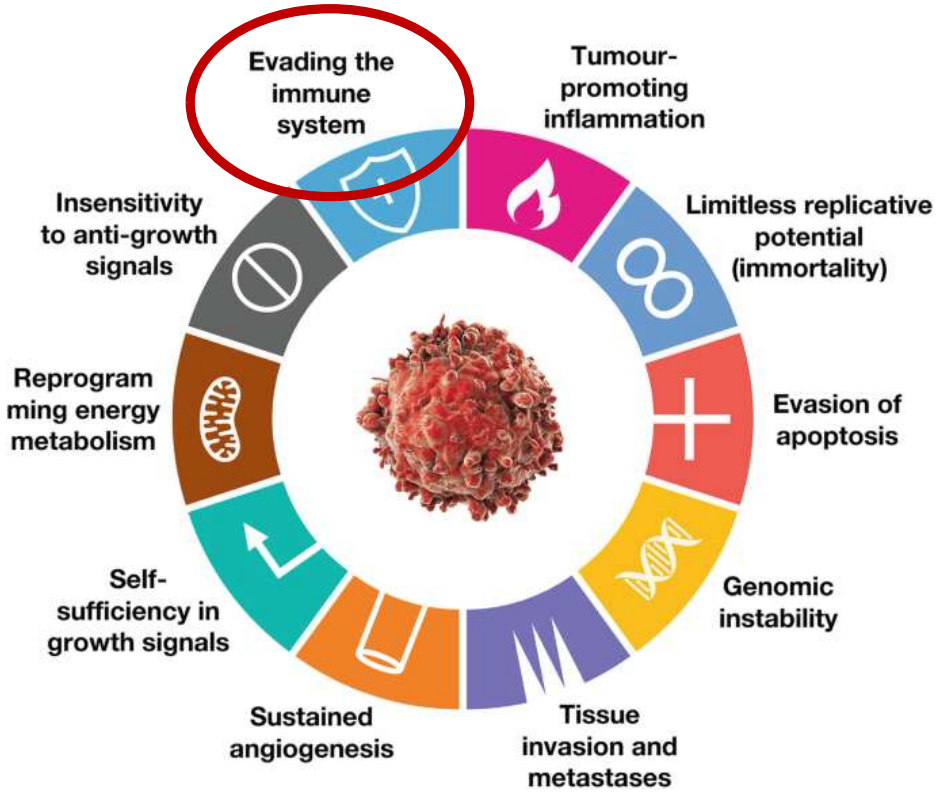
Chen S, Mellman I. Immunity 2013.

4. Immuuntherapie



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4. Immuuntherapie

4.1 Antibodies

4.2 Immuunmodulatoren

4.3 Bispecifieke antistoffen

4.4 CAR T celtherapie

4.5 Stamceltransplantatie

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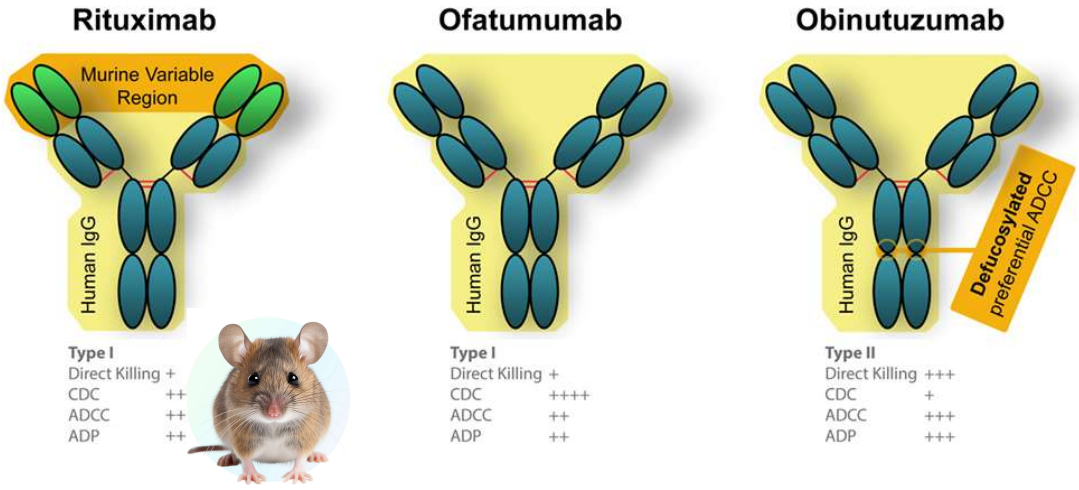
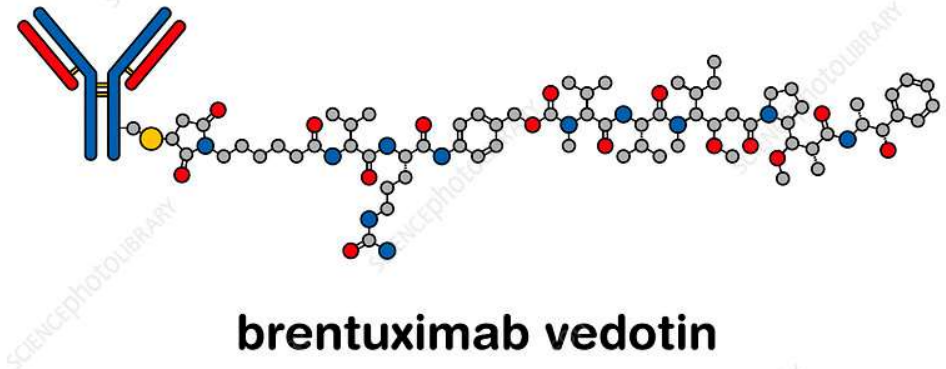
4.1 Antibodies

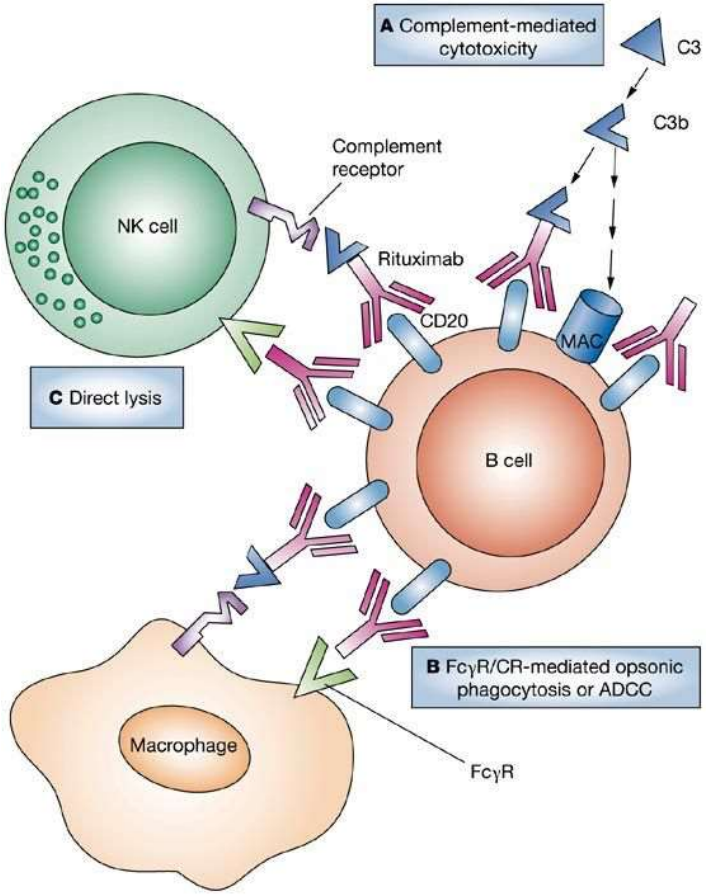
- Nabouwen van menselijke antistoffen
- Naked vs armed
- Infusiereacties
- Verminderde vaccinrespons





Naked antibodies: Rituximab

- anti-CD20: B-NHL
- Mechanisme: apoptose + fagocytose + complementactivatie
- Nevenwerkingen: infusiegerelateerd, infectierisico, neutropenie



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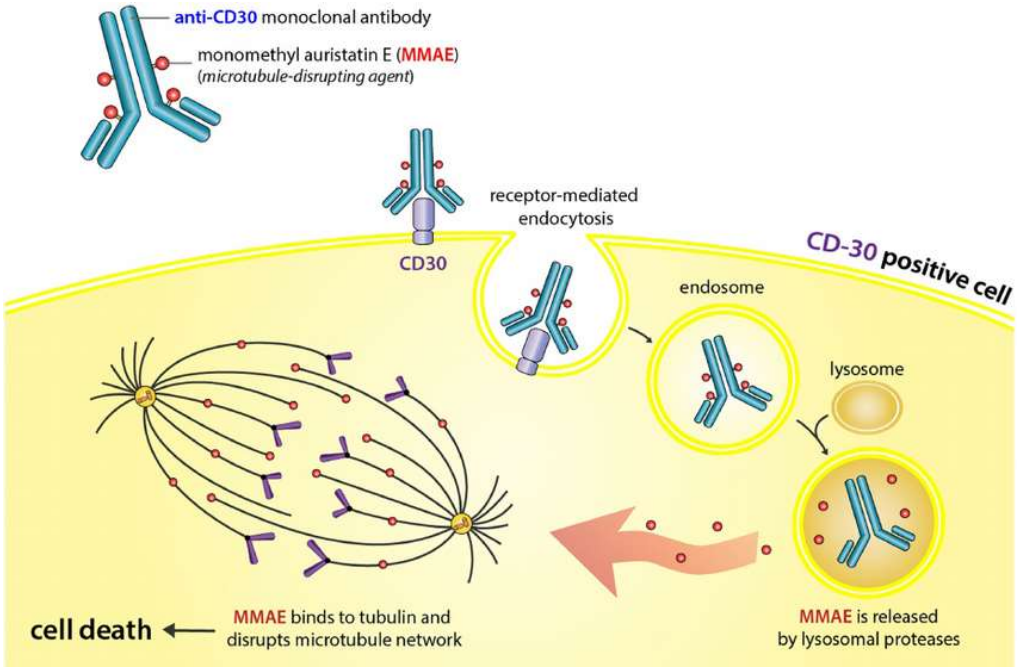
Armed antibodies: Brentuximab-vedotin

- Anti-CD30: HL en perifeer T-cel lymfoom
- Antibody gekoppeld aan chemotherapie
- Mechanisme: endocytose
- 1.2mg/kg q2w voor max 12 toedieningen (HL)
- 1.8mg/kg q3w voor max 6-8 toedieningen (T-NHL)
- Nevenwerkingen: neuropathie, neutropenie



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CHOP CHEMOTHERAPY PLUS RITUXIMAB COMPARED WITH CHOP ALONE IN ELDERLY PATIENTS WITH DIFFUSE LARGE-B-CELL LYMPHOMA

BERTRAND COIFFIER, M.D., ERIC LEPAGE, M.D., PH.D., JOSETTE BRIÈRE, M.D., RAOUL HERBRECHT, M.D., HERVÉ TILLY, M.D., REDA BOUABDALLAH, M.D., PIERRE MOREL, M.D., ERIC VAN DEN NESTE, M.D., GILLES SALLES, M.D., PH.D., PHILIPPE GAULARD, M.D., FELIX REYES, M.D., AND CHRISTIAN GISSELBRECHT, M.D.

ABSTRACT

Background The standard treatment for patients with diffuse large-B-cell lymphoma is cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP). Rituximab, a chimeric monoclonal antibody against the CD20 B-cell antigen, has therapeutic activity in diffuse large-B-cell lymphoma. We conducted a randomized trial to compare CHOP chemotherapy plus rituximab with CHOP alone in elderly patients with diffuse large-B-cell lymphoma.

Methods Previously untreated patients with diffuse large-B-cell lymphoma, 60 to 80 years old, were randomly assigned to receive either eight cycles of CHOP every three weeks (197 patients) or eight cycles of CHOP plus rituximab given on day 1 of each cycle (202 patients).

Results The rate of complete response was significantly higher in the group that received CHOP plus rituximab than in the group that received CHOP alone (76 percent vs. 63 percent, P=0.005). With a median

event-free and overall survival ra
and 35 to 40 percent, respectively
crease the efficacy of CHOP by a
toxic drugs have not succeeded,
these additional drugs cannot be
less the doses of cyclophosphamid
are reduced below those given in
men.[5,7] Intensified chemotherapy
prove the outcome in young pat
prognosis,[8] but they are not well t
patients. Indeed, CHOP itself ma
elderly patients.[9,10] More easily
have been designed for elderly pati
they cause fewer side effects, they
and no more beneficial than CHO

Rituximab, a chimeric anti-CI
clonal antibody, is effective when
agent in the treatment of relapse
delent lymphomas and has activit

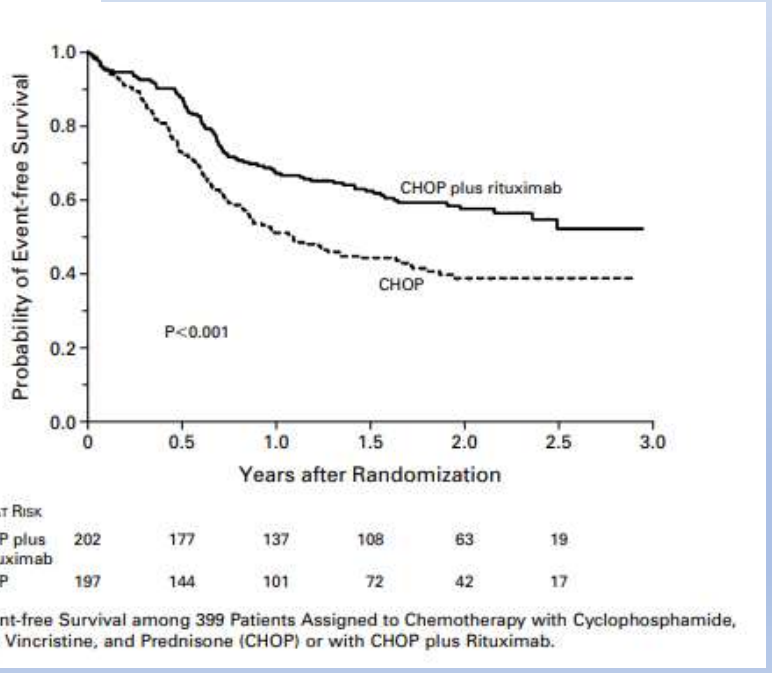

Figure 1. Event-free Survival among 399 Patients Assigned to Chemotherapy with Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (CHOP) or with CHOP plus Rituximab.

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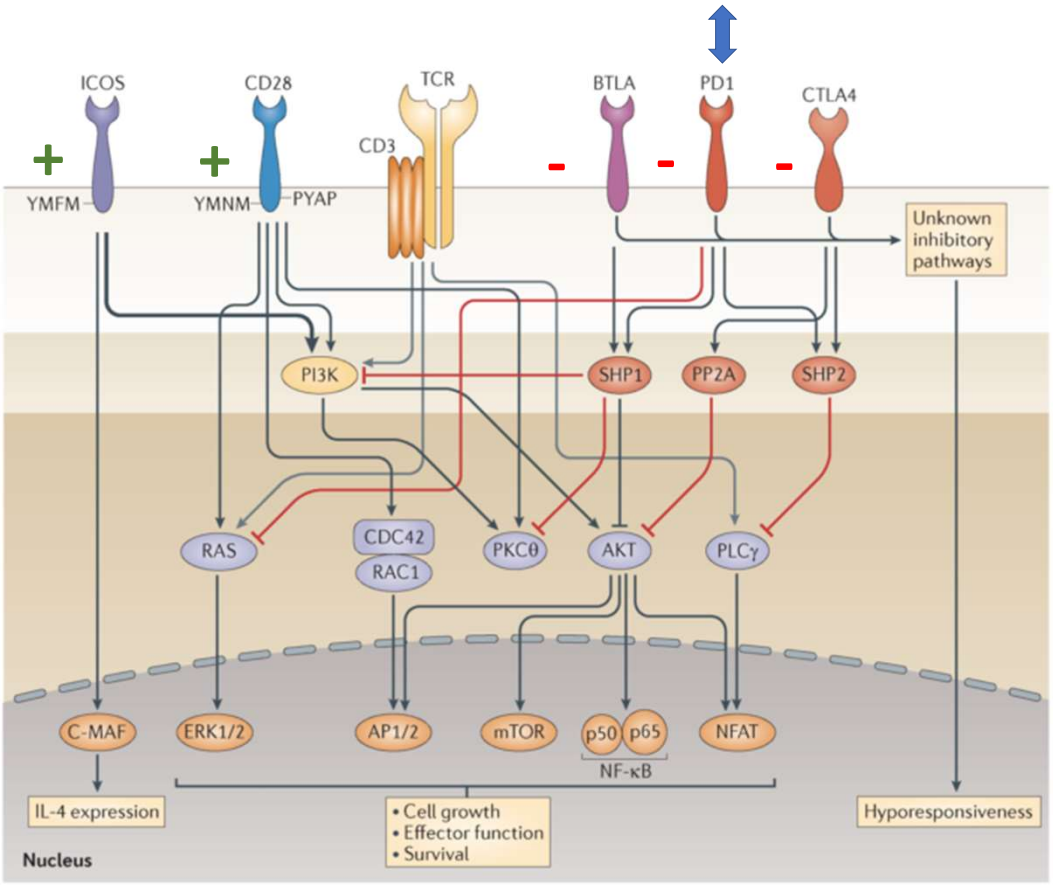
Coiffier et al. N Engl J Med, Vol. 346, No. 4 · January 24, 2002

4.2 Immuunmodulatoren (checkpointinhibitoren)

PD L-1 en PD L-2



= moleculen die de schakelaar van immuunrespons van de T-cel terug aanzetten

Cheng L & Flies DB. Nat Rev Immunol 2013

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Casus: 22 jarige man

- 7/2014: diagnose klassiek hodgkin lymfoma stadium IV, NS, IPS 2

-> ABVD 8# – eindbilan: CMR?

- 5/2015: recidief HL

-> DHAP 2#

- 7/2015: PET-CT toont mixed respons

-> Brentuximab 6#

- 11/2015: PET-CT toont PD

-> radiotherapie

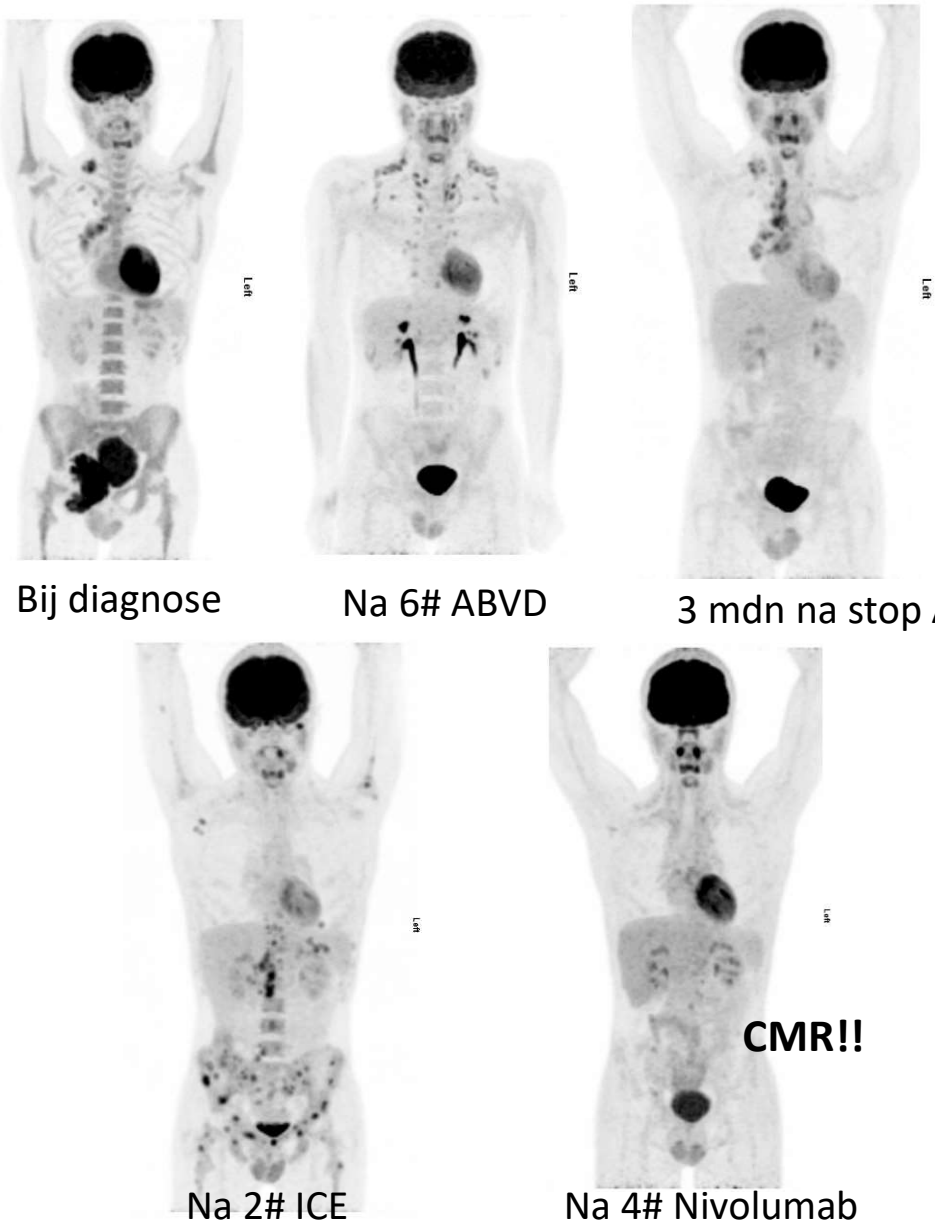
- 2/2016: PD

-> start ICE

- 4/2016: PET-CT na 2# toont SD

-> start Nivolumab 4#

- Allogene stamceltransplantatie



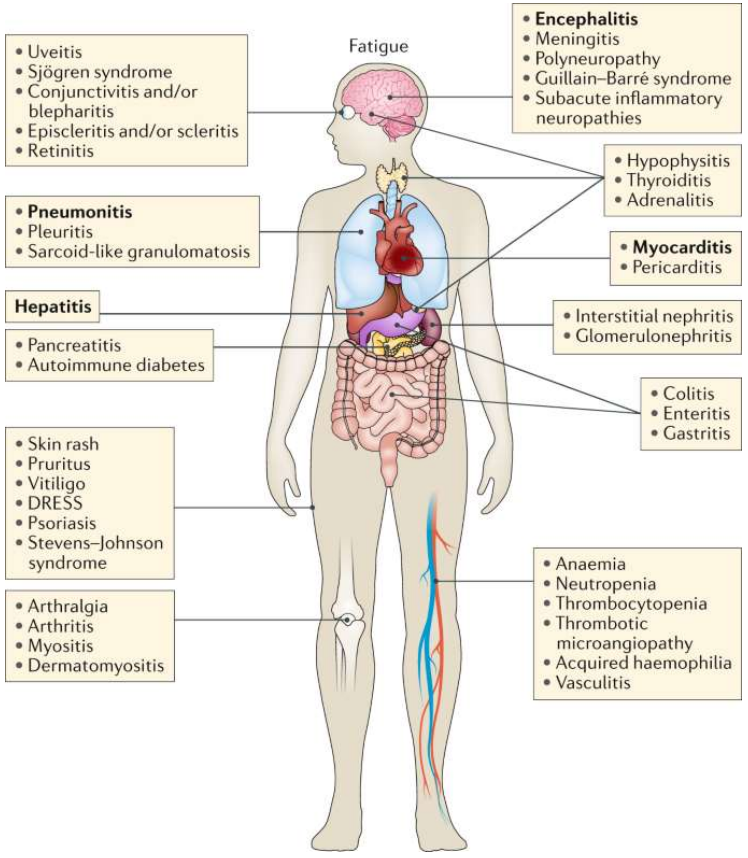
Bij diagnose | Na 6# ABVD | 3 mdn na stop ABVD

Na 2# ICE | Na 4# Nivolumab

4.2 Immuunmodulatoren: nevenwerkingen

Ontsteking door auto-immuun reactie:

- Longen
- Lever
- Darmen
- Gewrichten
- Schildklier
- Huid
- Hartspier



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4.3 Bispecifieke antistoffen (BiTE-antibodies)

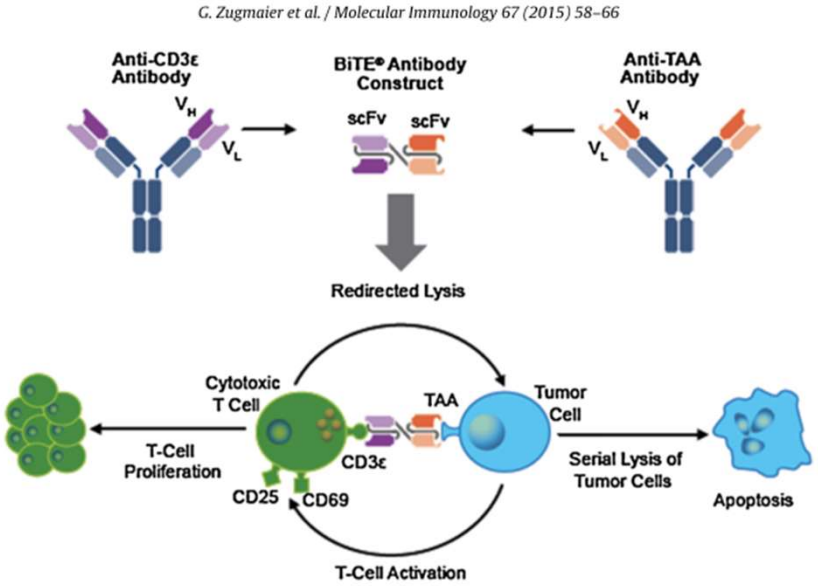

Fig. 1. Design and mode of action of BiTE® antibody constructs. TAA, tumor-associated antigens.

- Koppeleiwit tussen de tumorcel en de T-cel

- Nevenwerking: cytokine release syndroom CRS (= overactivatie van het immuunsysteem)

Casus: 44-jarige man

- Recidief **DLBCL** na voorgaande therapieën met R-CHOP, R-ICE, Auto HCT na BEAM, Copanlisib, Gem-Ox
- Start **Blinatumomab:** opname voor eerste dosisverhoging (9 -> 112 µg/dag)

- 4:30am: pt belt verpleegkundige en geeft aan: 'ik voel mij niet goe'
- Vpl: koorts? Nee – andere parameters oké? Ja – pijn? Nee – nausea? Nee – kort van adem? Nee – angor? Nee – Wat dan wel?
- Pt:

- ASO bellen?

- Klinische evaluatie door ASO: suf voorkomen, maar wekbaar. Geen motorische of sensorische uitval, wel duidelijke afasie. (ICANS)

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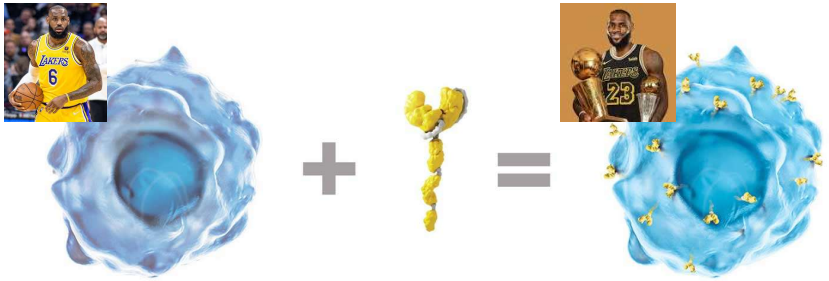
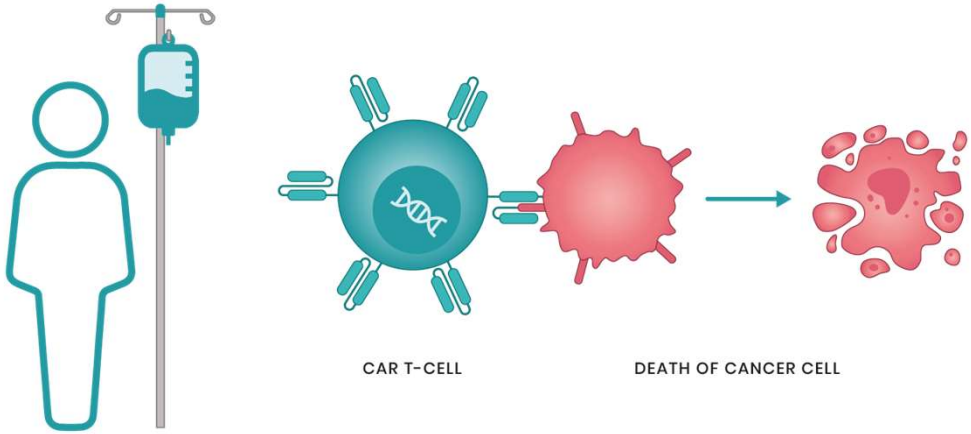
4.4 CAR T celtherapie

- Chimeric antigen receptor
- Genetische gemanipuleerde cel
- Brengt eiwitten tot expressie die rechtstreeks koppelen aan de tumorcel





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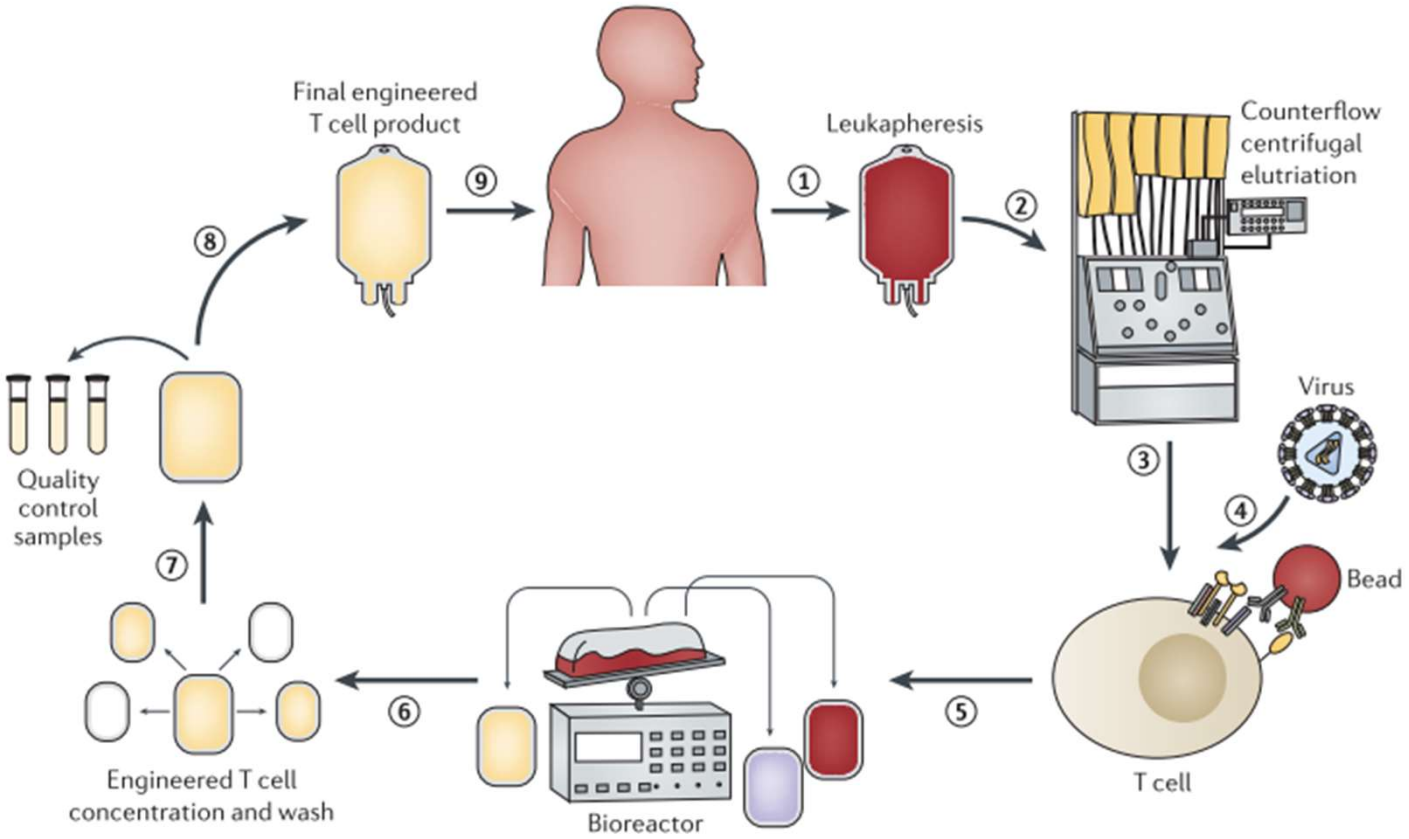
5. CAR T-cells



Fesnak AD, June CH et al. *Nature Reviews Cancer 2016*

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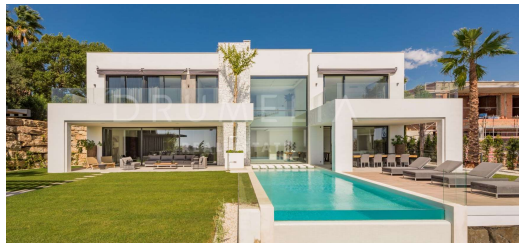
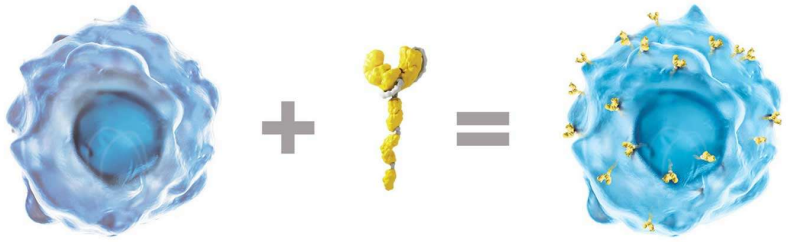
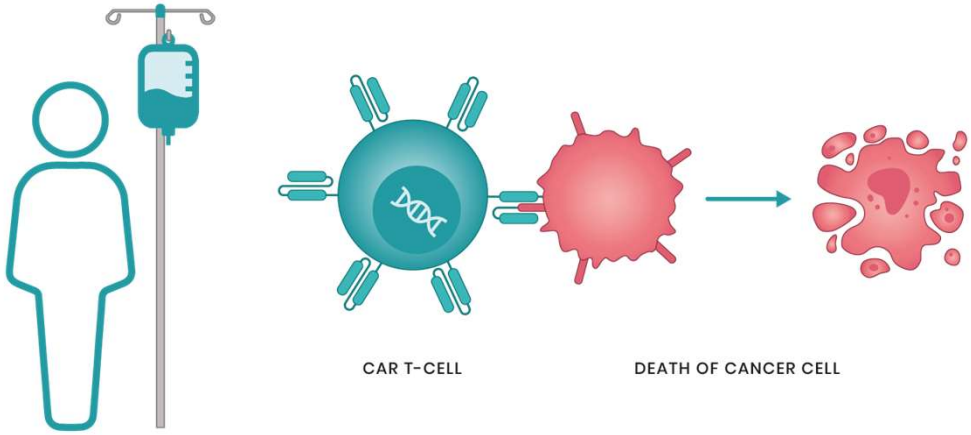
4.4 CAR T celtherapie

- Chimeric antigen receptor
- Genetische gemanipuleerde cel
- Brengt eiwitten tot expressie die rechtstreeks koppelen aan de tumorcel
- Activatie immuunsysteem
- (!) te veel activatie van het immuunsysteem: CRS en ICANS
- Lange termijn effecten
- Kostprijs



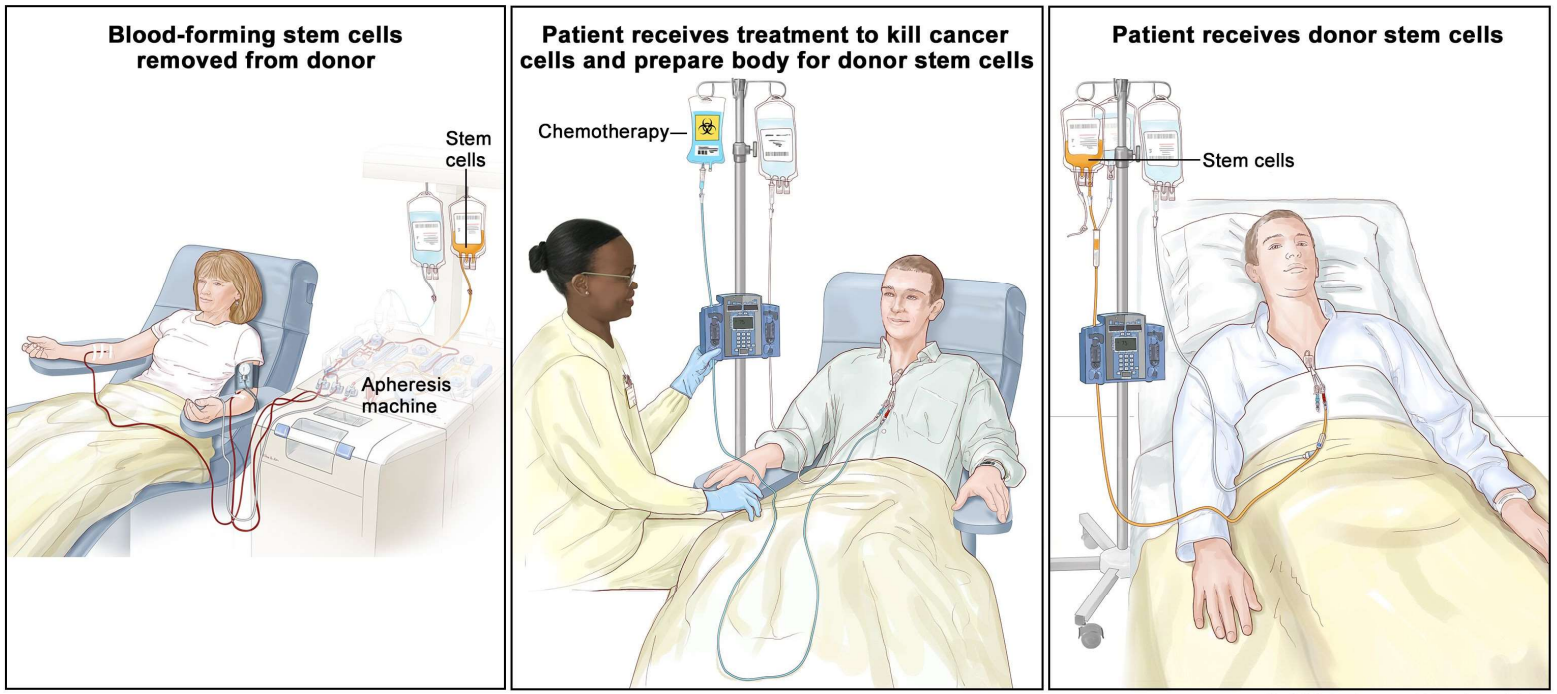




4.5 Stamceltransplantatie

Autoloog vs allogene stamceltransplantatie

Specifieke indicaties



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6. Conclusie

Therapie	+	-
Chemotherapie	Veel ervaring Snelwerkend Gouden standaard	Acute toxiciteit Secundaire kanker
Radiotherapie	Curatief in sommige settings Belangrijke supportieve rol Vaak goed verdragen Veel ervaring	Toxiciteit Secundaire kanker
Doelgerichte therapie	Goed verdragen Makkelijke toediening Weinig ziekenhuisopname Werkt erg goed, vooral bij indolente lymfomen	Langdurige therapie Werkt vaak minder goed in agressieve lymfomen
Immuuntherapie	Goede acute tolerantie Bewezen effectiviteit bij chemoresistentie	Verstoring van het immuunsysteem Lange termijn effecten

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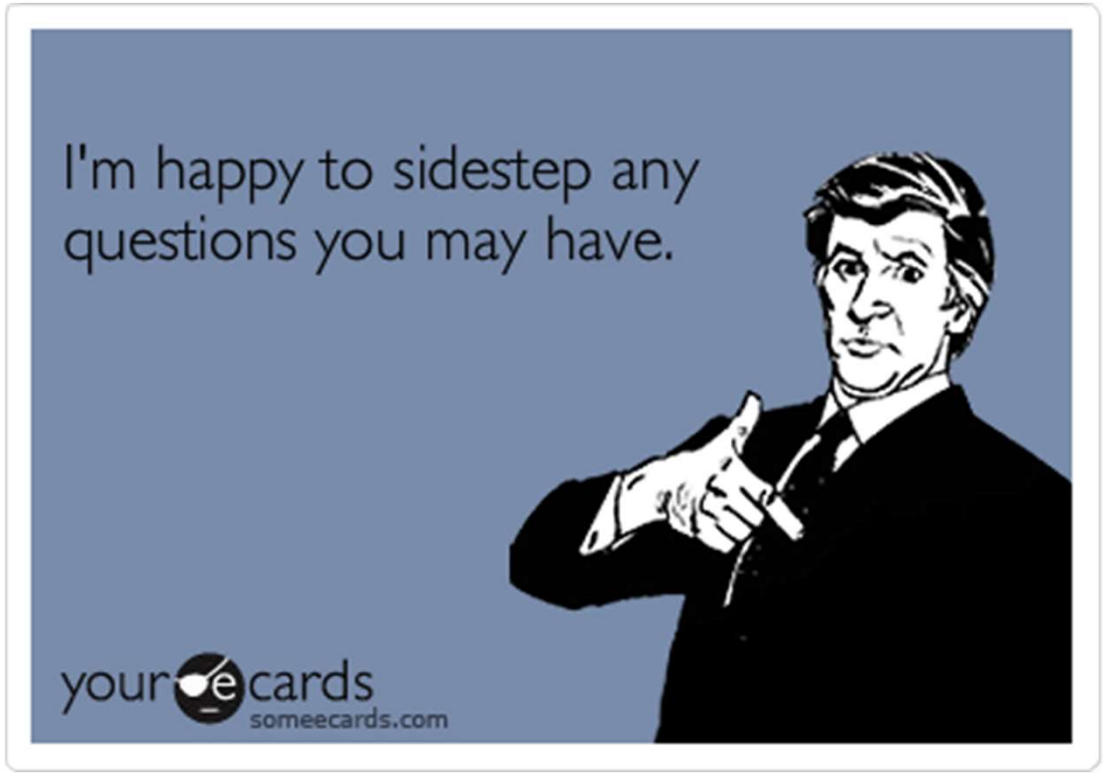
Take home messages

Nog vragen?


I'm happy to sidestep any questions you may have.
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