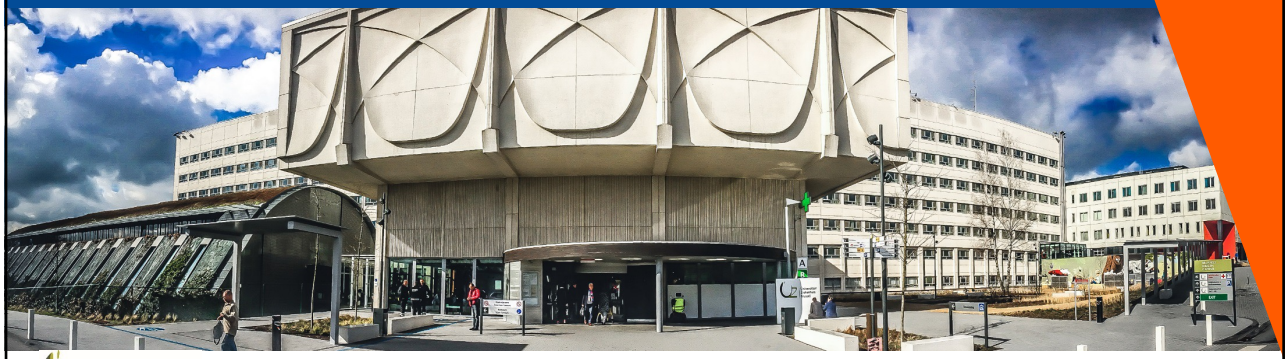
Is er een vaccin op komst tegen melanoom?

Professor Bart Neyns MD PhD
Head of the Department of Medical Oncology
Universitair Ziekenhuis Brussel, Brussels, Belgium



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Bart.Neyns@UZBrussel.be

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DISCLOSURES

- **Personal financial compensation** from Roche, Bristol-Myers Squibb, Merck Sharp & Dohme, and Novartis for public speaking, consultancy and participation in advisory board meetings
- My institution (UZ Brussel) received **research funding** related to research projects conducted by my team from Pfizer, Novartis, Roche, Merck-Serono

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vaccine

(vak-SEEN)

A substance or group of substances meant to cause the immune system to respond to a tumor or to microorganisms, such as bacteria or viruses. A vaccine can help the body recognize and destroy cancer cells or microorganisms.

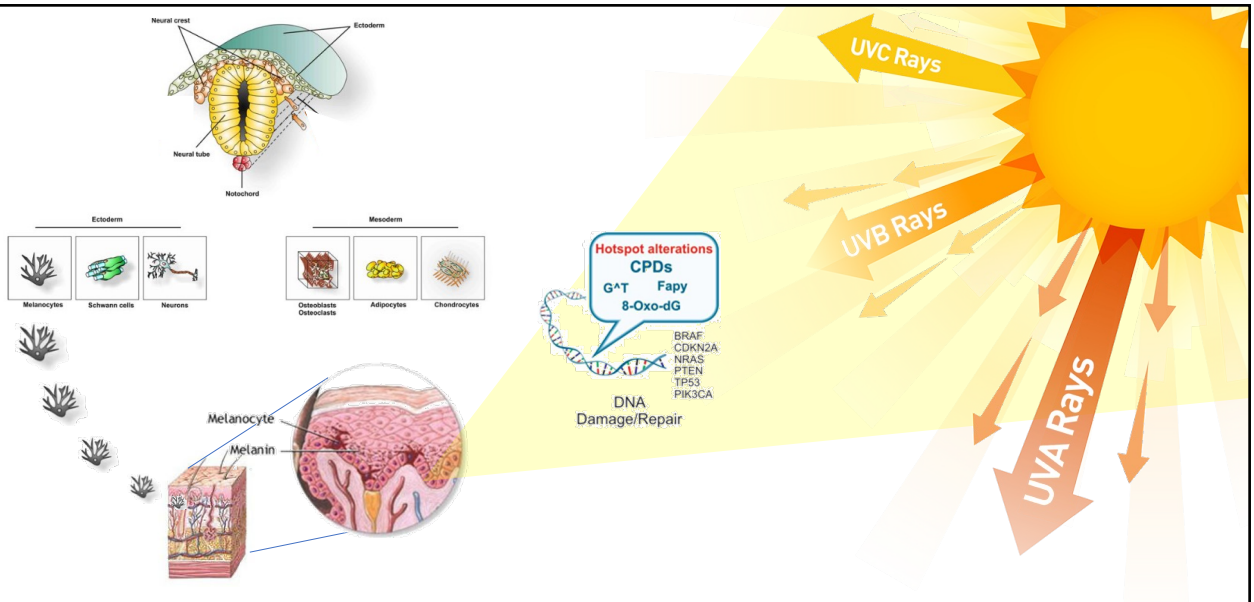
Prophylactic Vaccines are designed to build immunity in a healthy person. A prophylactic, or preventative, vaccine involves introducing antigens into a person's body. The goal is that the individual's immune system will create humoral (: antibodies) and cellular immunity for those antigens, and become "immune" to the associated illness.

Example of successful cancer preventing vaccines = HPV-, HBV-vaccines

Therapeutic vaccines differs from prophylactic vaccines in that prophylactic vaccines are administered to individuals as a precautionary measure to avoid the infection or disease while therapeutic vaccines are administered after the individual is already affected by the disease (: cancer) or infection.

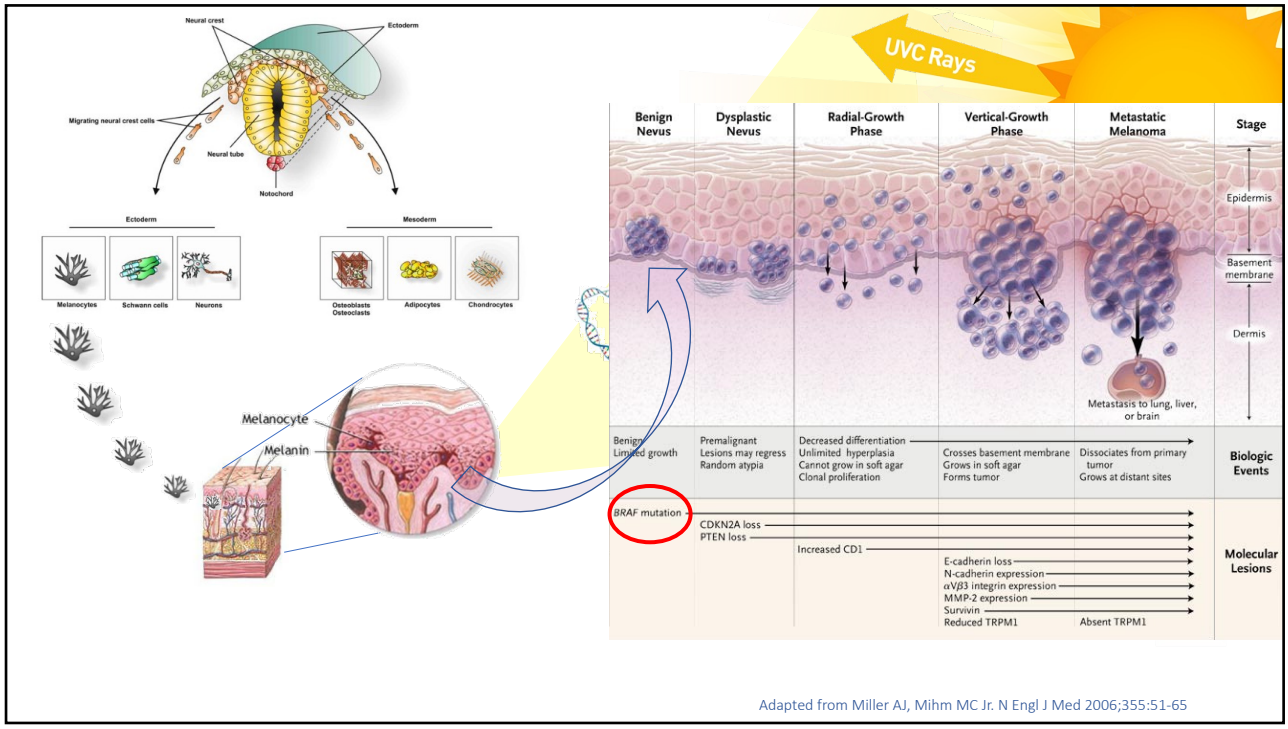
Immune response: Self-foreignness

3



Adapted from Miller AJ, Mihm MC Jr. N Engl J Med 2006;355:51-65

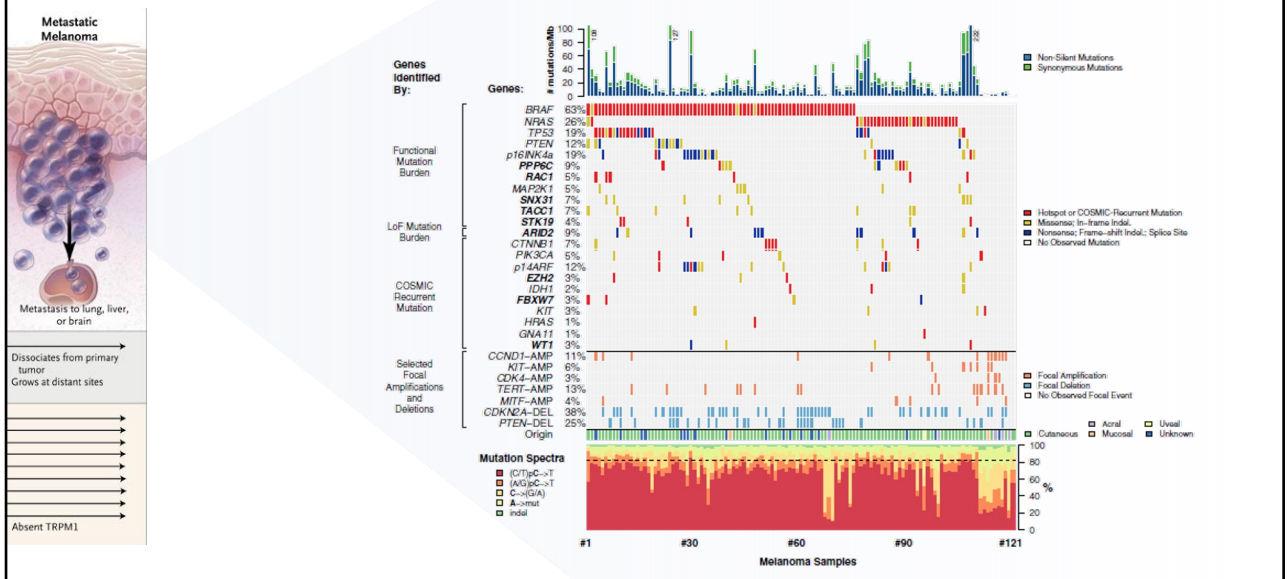
4



Adapted from Miller AJ, Mihm MC Jr. N Engl J Med 2006;355:51-65

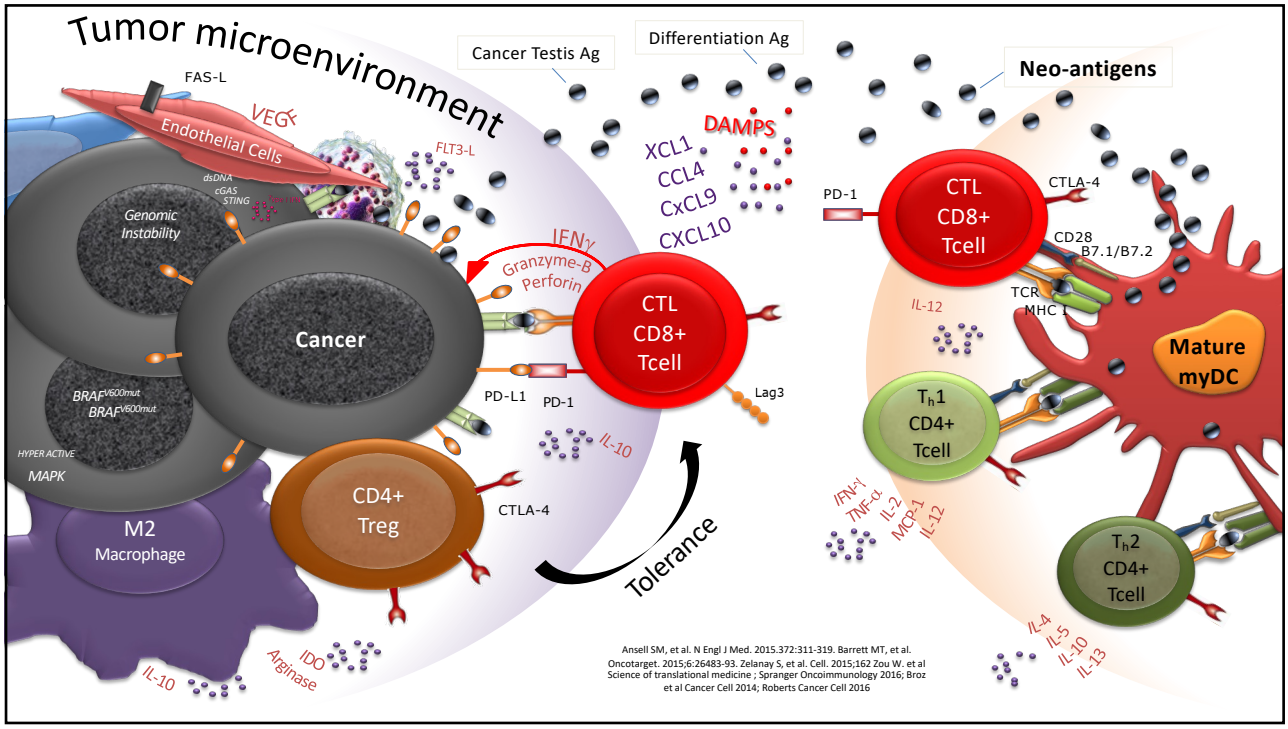
5

BRAF V600- vs. *RAS*- vs. *NF1-mut, vs. triple-WT vs cKIT- or GNA11-/GNAQ mut* subsets (significant heterogeneity within subsets)



Hodis E et al. Cell 150, 251-263, July 20, 2012; Akbani R, et al. Cell 2015;161:1681–1696

6


Tumor microenvironment
FAS-L
VEGF
Endothelial Cells
FLT3-L
Cancer Testis Ag
Differentiation Ag
DAMPS
XCL1
CCL4
CXCL9
CXCL10
Neo-antigens
PD-1
CTL CD8+ Tcell
CTLA-4
CD28
B7.1/B7.2
TCR
MHC 1
IL-12
Mature myDC
Genomic Instability
dsDNA
cGAS
STING
IFNγ
Granzyme-B
Perforin
Cancer
PD-L1
PD-1
Lag3
IL-10
HYPER ACTIVE MAPK
CD4+ Treg
CTLA-4
Tolerance
M2 Macrophage
IL-10
IDO
Arginase
Th1 CD4+ Tcell
IFN-γ
TNF-α
IL-2
MCP-1
IL-12
Th2 CD4+ Tcell
IL-4
IL-5
IL-10
IL-13
Ansell SM, et al. N Engl J Med. 2015;372:311-319. Barrett MT, et al. Oncotarget. 2015;6:26483-93. Zelanay S, et al. Cell. 2015;162 Zou W. et al Science of translational medicine ; Spranger Oncoimmunology 2016; Broz et al Cancer Cell 2014; Roberts Cancer Cell 2016

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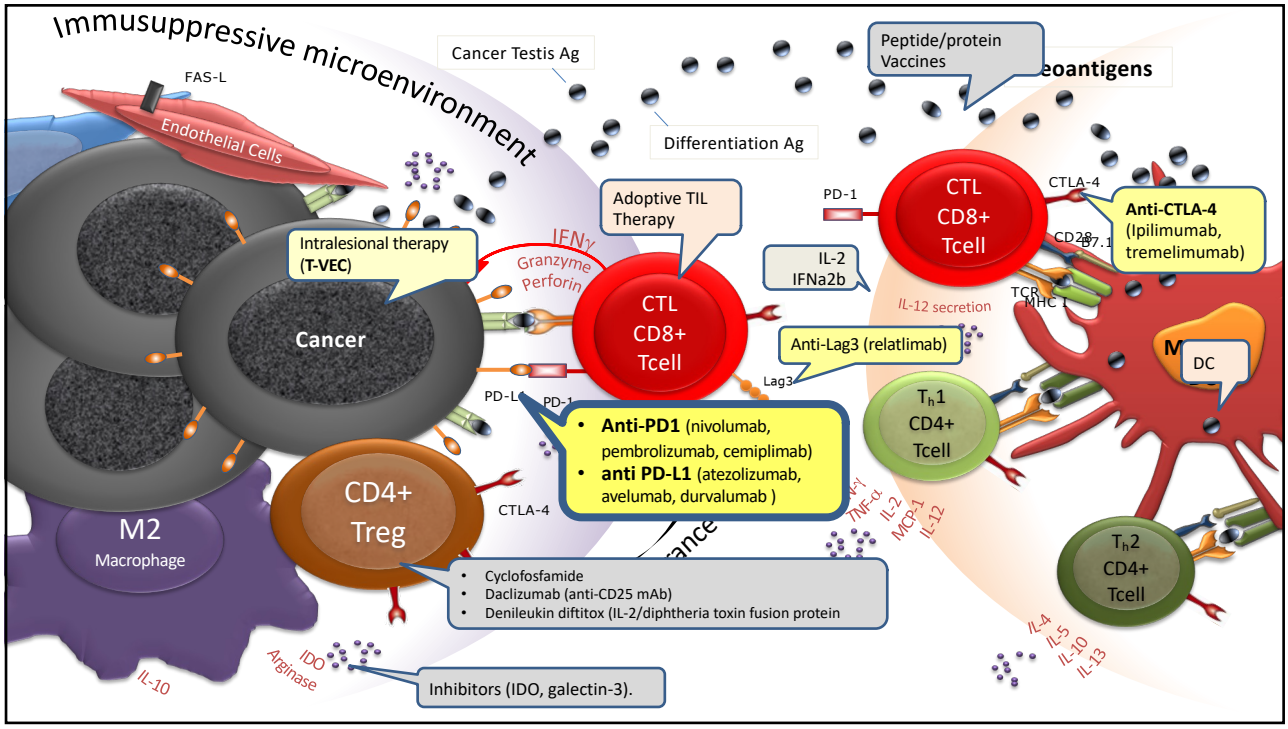
Immusuppressive microenvironment
FAS-L
Endothelial Cells
Cancer Testis Ag
Differentiation Ag
Peptide/protein Vaccines
Adoptive TIL Therapy
Intralesional therapy (T-VEC)
IFNγ
Granzyme
Perforin
CTL CD8+ Tcell
PD-1
CTLA-4
Anti-CTLA-4 (Ipilimumab, tremelimumab)
IL-2 IFNa2b
IL-12 secretion
TCR
MHC 1
Anti-Lag3 (relatlimab)
Lag3
Cancer
PD-L
PD-1
DC
Th1 CD4+ Tcell
Anti-PD1 (nivolumab, pembrolizumab, cemiplimab)
anti PD-L1 (atezolizumab, avelumab, durvalumab)
CD4+ Treg
CTLA-4
IFN-γ
TNF-α
IL-2
MCP-1
IL-12
Th2 CD4+ Tcell
IL-4
IL-5
IL-10
IL-13
M2 Macrophage
Cyclofosfamide
Daclizumab (anti-CD25 mAb)
Denileukin diftitox (IL-2/diphtheria toxin fusion protein
IL-10
IDO
Arginase
Inhibitors (IDO, galectin-3).

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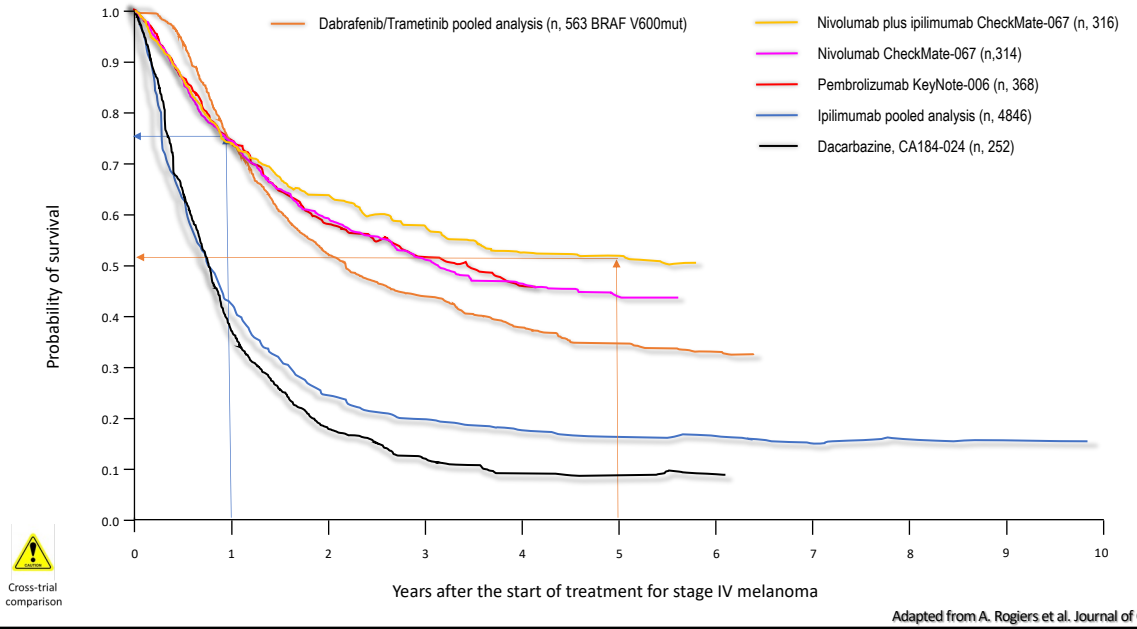
Overall Survival of Advanced Melanoma Patients According to First Line Therapy



Cross-trial comparison

Adapted from A. Rogiers et al. Journal of Oncology, 2019

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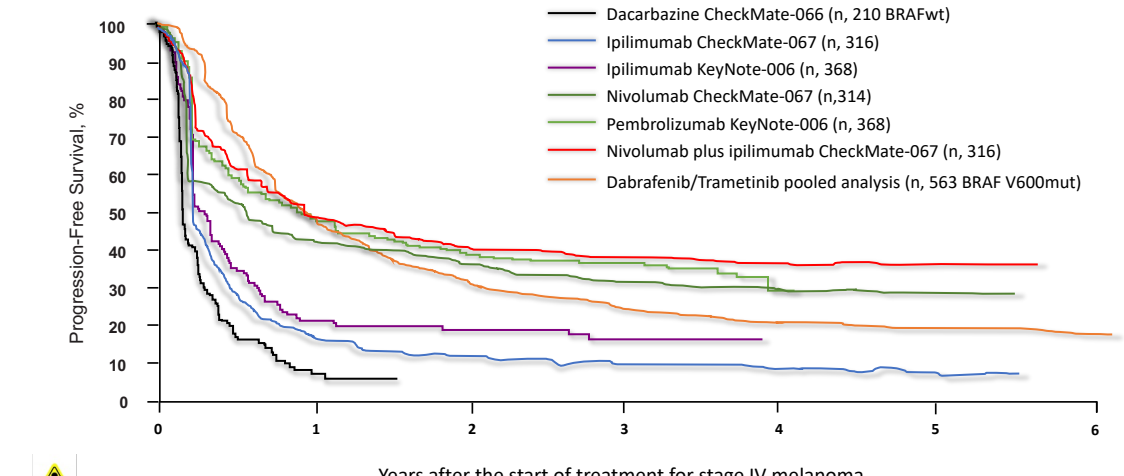
Progression-Free Survival of Advanced Melanoma Patients on First Line Therapy

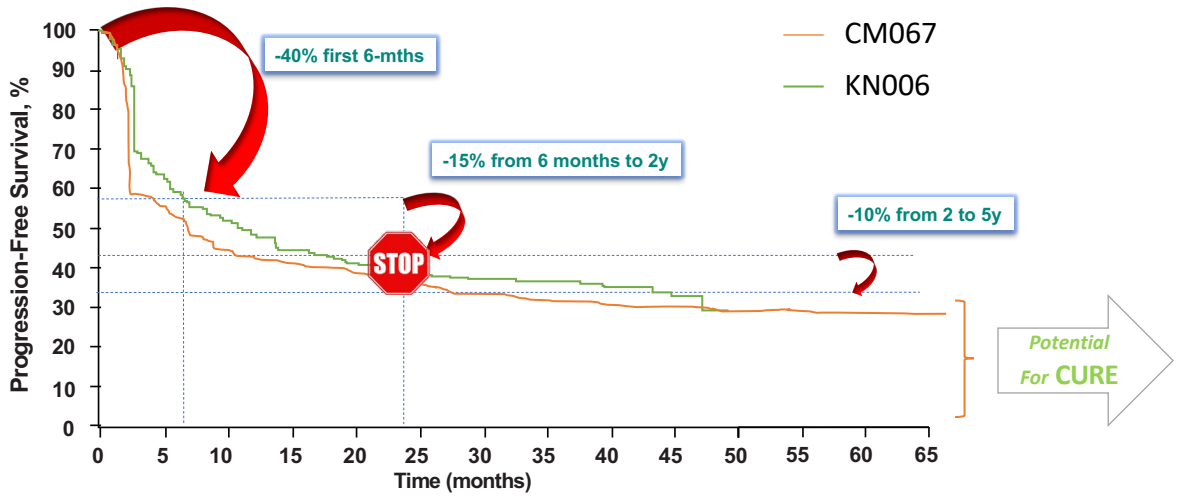


Cross-trial comparison

Adapted from A. Rogiers et al. Journal of Oncology, 2019

11

Overlay of Progression-Free Survival Estimates of First-Line Treatment with Pembrolizumab (KeyNote-006) or Nivolumab (CeckMate-067)

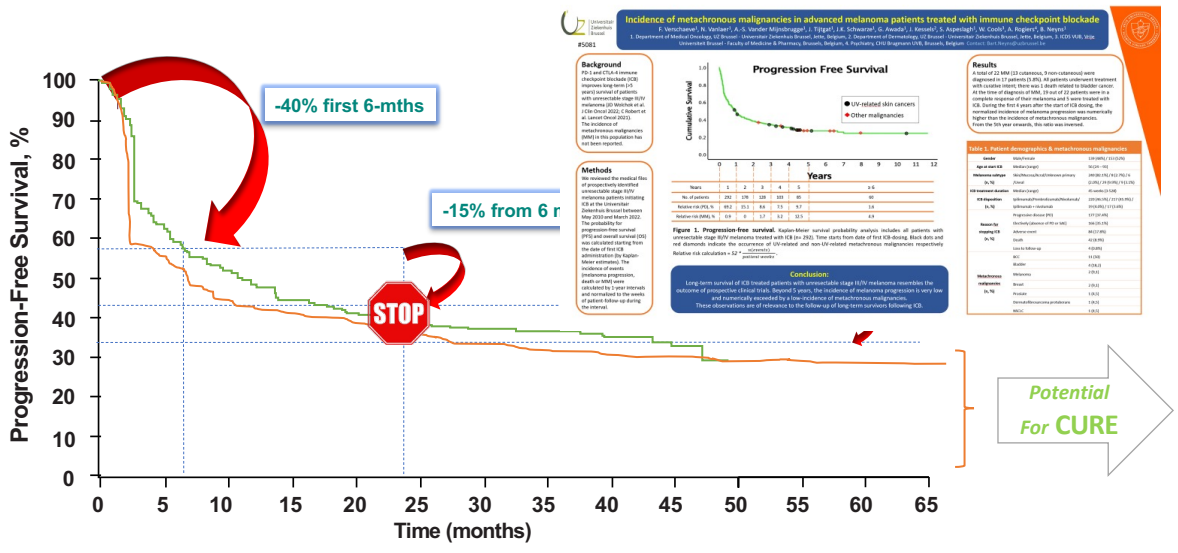


Adapted from Larkin J. et al. NEJM 2019

Adapted from Robert et al. Lancet Oncology 2019

12

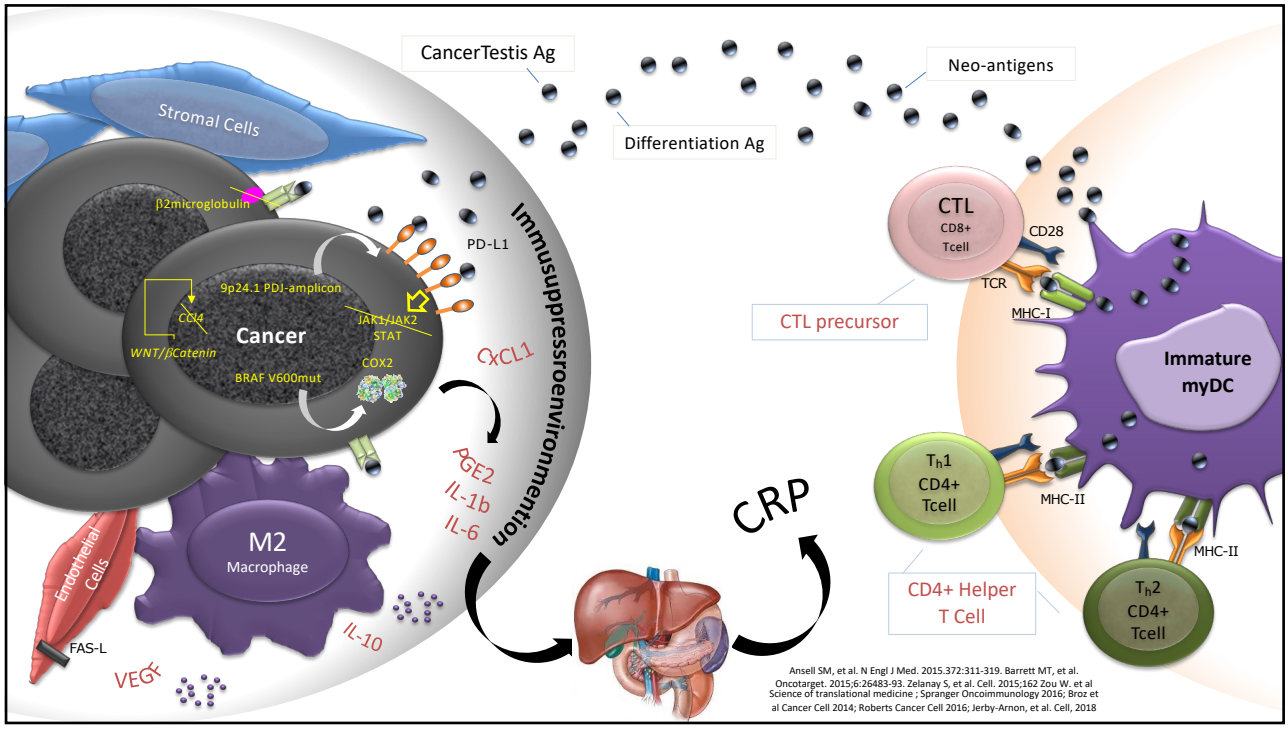
Overlay of Progression-Free Survival Estimates of First-Line Treatment with Pembrolizumab (KeyNote-006) or Nivolumab (CeckMate-067)



Adapted from Larkin J. et al. NEJM 2019

Adapted from Robert et al. Lancet Oncology 2019

13


CancerTestis Ag
Neo-antigens
Differentiation Ag
Stromal Cells
β2microglobulin
PD-L1
9p24.1 PDJ-amplicon
CCL4
WNT/βCatenin
Cancer
JAK1/JAK2
STAT
COX2
BRAF V600mut
CXCL1
PGE2
IL-1b
IL-6
Immunosuppressroenvironmention
M2
Macrophage
Endothelial Cells
FAS-L
VEGF
IL-10
CRP
CTL
CD8+
Tcell
CD28
TCR
MHC-I
CTL precursor
Immature
myDC
Th1
CD4+
Tcell
MHC-II
MHC-II
Th2
CD4+
Tcell
CD4+ Helper
T Cell
Ansell SM, et al. N Engl J Med. 2015.372:311-319. Barrett MT, et al.
Oncotarget. 2015;6:26483-93. Zelanay S, et al. Cell. 2015;162 Zou W. et al
Science of translational medicine ; Spranger Oncoimmunology 2016; Broz et
al Cancer Cell 2014; Roberts Cancer Cell 2016; Jerby-Arnon, et al. Cell, 2018

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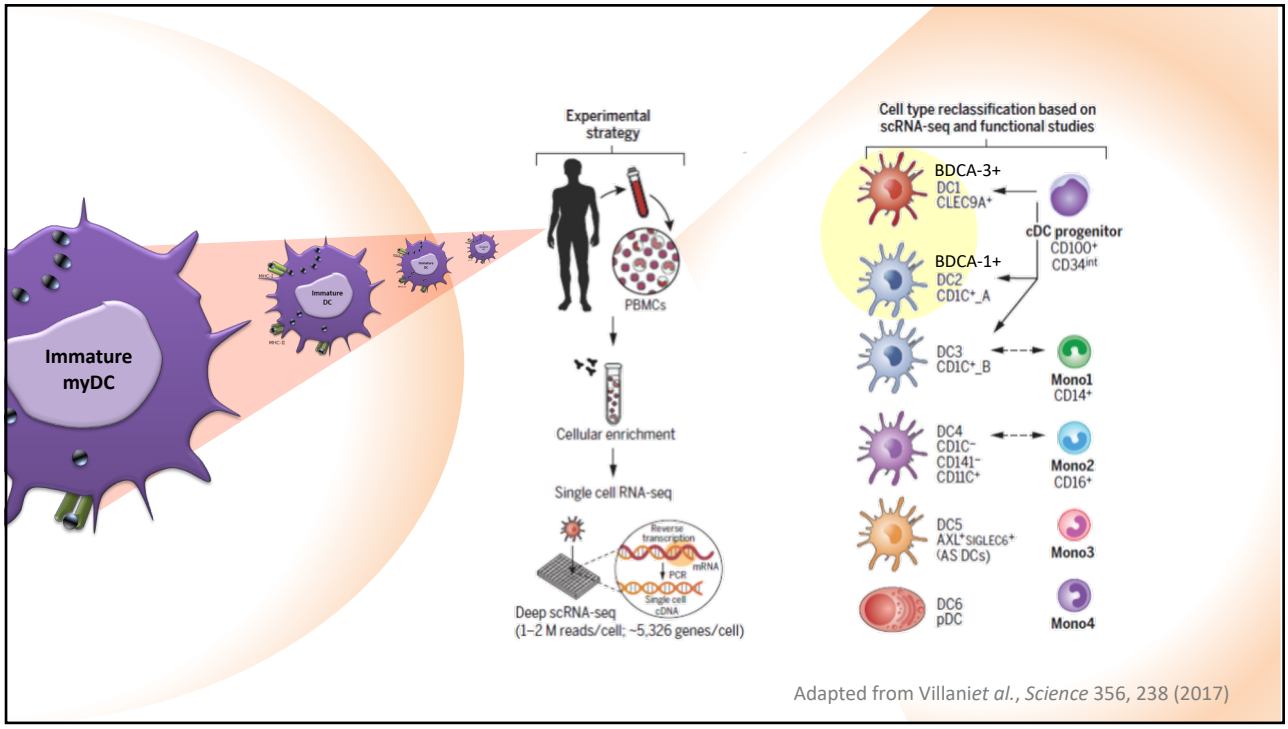
Immature
myDC
Experimental
strategy
PBMCs
Cellular enrichment
Single cell RNA-seq
Deep scRNA-seq
(1–2 M reads/cell; ~5,326 genes/cell)
Cell type reclassification based on
scRNA-seq and functional studies
BDCA-3+
DC1
CLEC9A+
BDCA-1+
DC2
CD1C+_A
cDC progenitor
CD100+
CD34int
DC3
CD1C+_B
Mono1
CD14+
DC4
CD1C−
CD141−
CD11C+
Mono2
CD16+
DC5
AXL+SIGLEC6+
(AS DCs)
Mono3
DC6
pDC
Mono4
Adapted from Villani et al., Science 356, 238 (2017)

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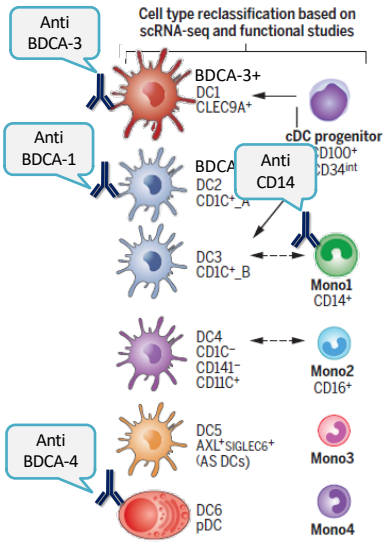
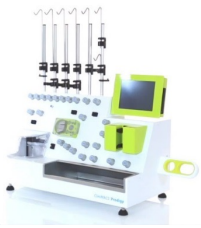
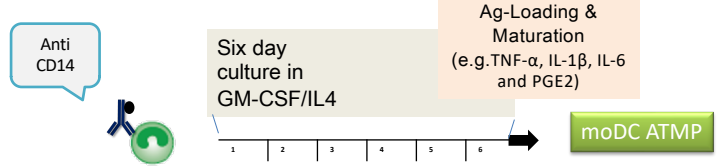
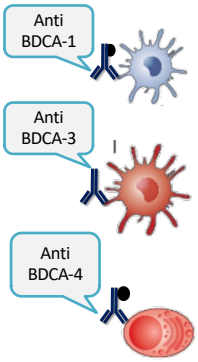


16







Sabado et al Cell Research (2017) 27:74-95; Schreibelt et al. Clin Cancer Res; 22(9) May 1, 2016; Jurjen *Cancer Res* 2013;73:1063-1075

17

Clinical Research Program of moDC-Therapy for Melanoma
Universitair Ziekenhuis Brussel & Vrije Universiteit Brussel

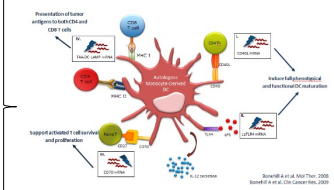

2002 → Cytokine matured moDC loaded with 1 up to 6 CT-Ag derived HLA-restricted peptide(s)

2005 → PolyI:C matured moDC electroporated with up to 6 CT-Ag mRNA (HLA-unrestricted) +/- Interferon alfa2b

moDC *Vaccine*

<5% ORR
Good prognosis patients

2007 / 2009 / 2011 / 2012



- ID pilot trial
- ID/IV phase I
- + Ipilimumab Phase II
- Randomized phase II adjuvant setting

moDC *Cellular Immunotherapy*

>10% ORR
Incl stage IV-M1c pretreated patients

Bonehill A et al. Mol Ther. 2008
Bonehill A et al. Clin Cancer Res. 2009

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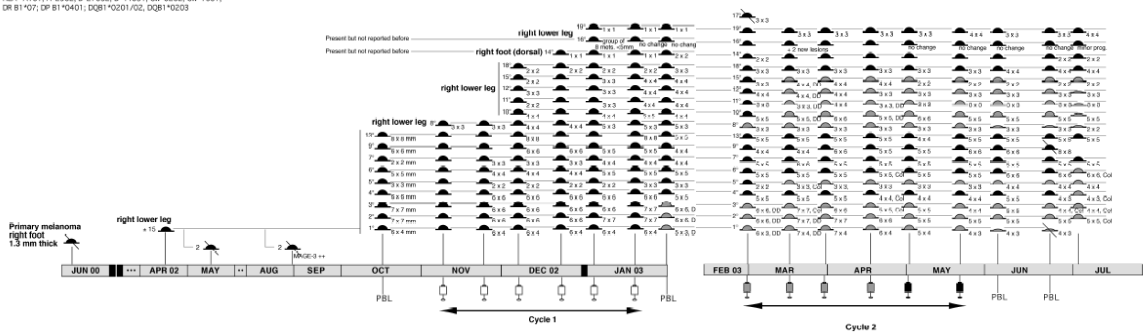
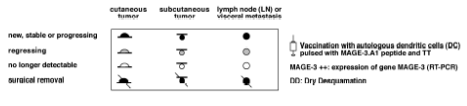
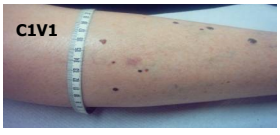
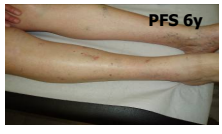
Response to MAGE3.A1 peptide loaded moDC-Vaccination

Study VUB 02-001
MELANOMA PATIENT BAGM (1)
HLA *A101, A*2902; B*27052, B*44031; Cw*0202, Cw*1601; DR B1*07; DP B1*0401; DQB1*0201/02, DQB1*0203









Godelaine et al. Immunol Immunoth 2007;
Carrasco et al. J Immunol 2008

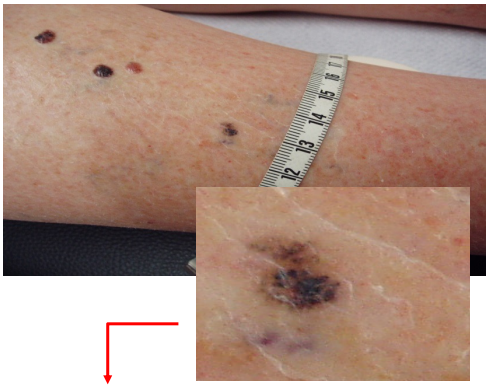
19

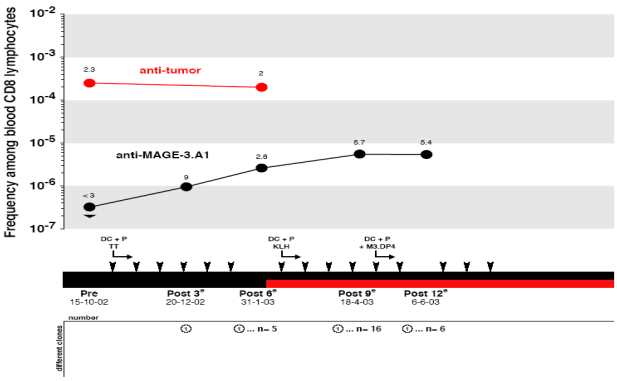
Immunological Analysis of Responding Patient Vaccinated with MAGE-3.A1 Pulsed DC

BAGM

A*0101 - 2902
B*2705 - 4403
C*0202 - 1601
DPB1*0401
DRB1*07
DQB1*0201/2 - 0203

DC + MAGE-3.A1
VUB 02-001 K. Thielemans





Discovery of NEW HLA-B44 restricted MAGE-C2 peptide recognized by TIL[1] ➡ **"Epitope spreading"**

Godelaine et al. Immunol Immunoth 2007 ; Carrasco et al. J Immunol 2008

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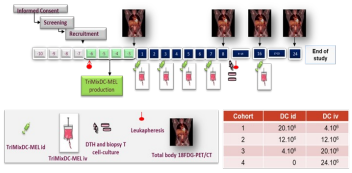
TriMixDC-MEL Pilot ID & Phase IB id/iv Clinical Trials

Safety of TriMixDC-MEL by ID and escalating doses by iv/id-admin.
Sequential cohorts (3+3 patients)

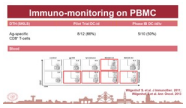


Tumor response to TriMixDC-MEL

	BORR by RECIST			
No. pts	CR	PR	SD	PD
Pilot Trial DC-id				
20	0	0	11	9
%BORR*	0			
%DCR		55		
Phase IB TriMixDC-MEL id/iv				
15	2	2	4	7
%BORR	27			
%DCR		53		

*Fisher's Exact Test: p = 0.026

=



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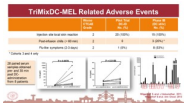
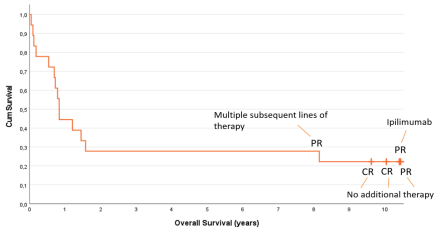
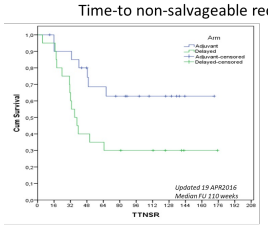
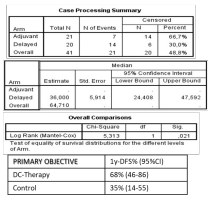


Overall Survival Phase Ib TriMixDC-MEL ID/IV



Primary objective/Endpoint ITT-analysis
Time-to non-salvageable recurrence or death*





PRIMARY OBJECTIVE	1y-DFS% (95%CI)
DC-Therapy	68% (46-86)
Control	35% (14-55)

* One patient on the DC-treatment arm died without melanoma recurrence

Wilgenhof S. et al. J Immunother. 2011; Wilgenhof S et al. Ann Oncol. 2013; Jansen Y et al. Cancer Immunol Immunotherapy 2019

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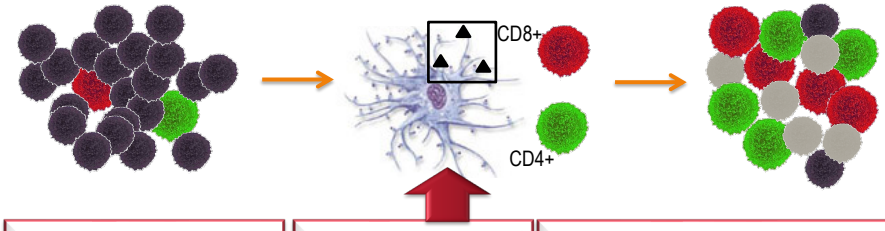
Antigen-specified Therapeutic Cancer Vaccines



Peptide(s) +/- adjuvant
- ✓ HLA-restricted
- ✓ Excellent safety profile
- ✓ Many MAA are poorly immunogenic
- ✓ BORR <5% in stIV-M1a/b (but durable)

Protein + adjuvant
E.g. MAGE-A3, PRAME protein combined with AS15 [a combination of QS21, monophosphoryl lipid A, and CpG7909, a TLR-9 agonist, in a liposomal formulation]

Rec. viral vaccines
E.g. ALVAC-MAGE-1.A1/MAGE-3.A1 mini-genes virus

DNA or mRNA

Nanoparticle vaccines
MAA + appropriate immune-stimulatory signals directed to T-cells or APC's

Marchand M. et al. Int J Cancer 1999; Rosenberg Nat Med 2004; Coulie PG et al. Immunol Rev 2002; Marchand M. et al. 2005; Van Baren et al. JCO 2006

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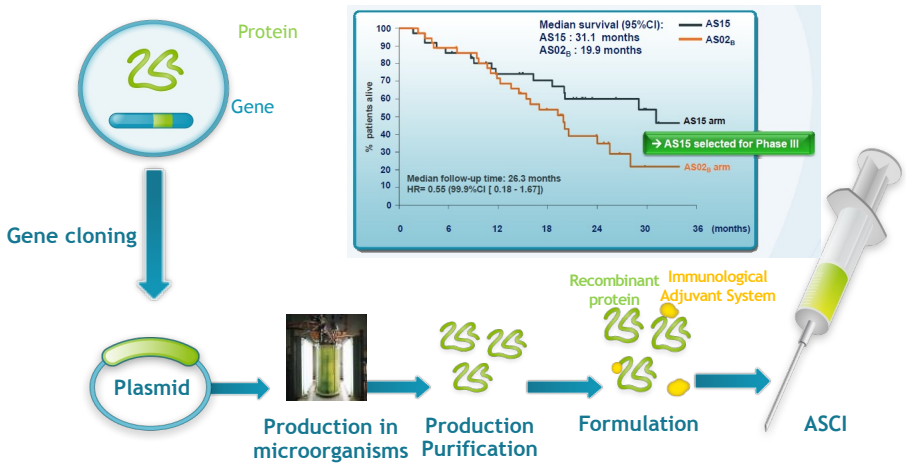
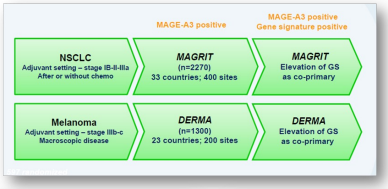
MAGE-A3/AS15 Ag-Specific Therapeutic Vaccine



W. H. [illegible], et al. 2013

23



The investigational MAGE-A3 antigen-specific cancer immunotherapeutic does not meet first co-primary endpoint in Phase III melanoma clinical trial

- In line with the Independent Data Monitoring Committee's (IDMC) unanimous recommendation, GSK will continue the DERMA trial until the second co-primary endpoint is assessed

Issued: Thursday 5 September 2013, London UK – LSE announcement

GlaxoSmithKline plc (LSE:GSK) today announced that an independent analysis of the DERMA[1] study, a Phase III randomised, blinded, placebo-controlled trial of the MAGE-A3 cancer immunotherapeutic,[2] showed that the study did not meet its first co-primary endpoint as it did not significantly extend disease-free survival (DFS[3]) when compared to placebo in the MAGE-A3 positive population.

Update on phase III clinical trial of investigational MAGE-A3 antigen-specific cancer immunotherapeutic in non-small cell lung cancer

Issued: 2 April 2014, London UK

GlaxoSmithKline plc (LSE:GSK) today announced its decision to stop the MAGRIT[1] trial, a Phase III trial of its MAGE-A3[2] cancer immunotherapeutic[3] in non-small cell lung cancer (NSCLC) patients, after establishing that it will not be possible to identify a sub-population of gene-signature positive NSCLC patients that may benefit from the treatment.

Data from the trial announced on 20 March 2014 showed that it did not meet its first or second co-primary endpoints as it did not significantly extend disease-free survival (DFS[4]) when compared to placebo in either the overall MAGE-A3 positive population (first co-primary endpoint) or in those MAGE-A3-positive patients who did not receive chemotherapy (second co-primary endpoint).

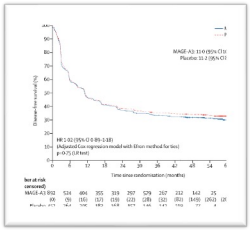
THE LANCET
Oncology

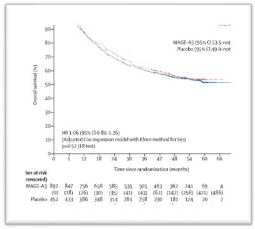
ARTICLES | VOLUME 19, ISSUE 7, P916-929, JULY 2018

MAGE-A3 immunotherapeutic as adjuvant therapy for patients with resected, MAGE-A3-positive, stage III melanoma (DERMA): a double-blind, randomised, placebo-controlled, phase 3 trial

Prof Brigitte Dreno, MD • Prof John F Thompson, MD • Prof Bernard Mark Smithers, FRACS • Mario Santinami, MD • Thomas Jouary, MD • Prof Ralf Gutzmer, MD • Evgeny Levchenko, MD • Prof Piotr Rutkowski, MD • Prof Jean-Jacques Grob, MD • Sergii Korovin, MD • Kamil Drucis, MD • Prof Florent Grange, MD • Prof Laurent Machet, MD • Prof Peter Hersey, MD • Ivana Krajsova, MD • Alessandro Testori, MD • Robert Conry, MD • Prof Bernard Guillot, MD • Wim H J Kruit, MD • Prof Lev Demidov, MD • Prof John A Thompson, MD • Prof Igor Bondarenko, MD • Jaroslaw Jaroszek, MD • Susana Puig, MD • Gabriela Cinat, MD • Prof Axel Hauschild, MD • Prof Jelle J Goeman, PhD • Prof Hans C van Houwelingen, PhD • Fernando Lilloa-Montoya, PhD • Andrea Callegaro, PhD • Benjamin Dôzer, MPH • Bart Spiessens, PhD • Muriel Debois, MSc • Vincent G Brichard, MD • Jamila Louahed, PhD • Patrick Therasse, MD • Channa Debruyne, MD • Prof John M Kirkwood, MD • Show less

Published: June 13, 2018 • DOI: https://doi.org/10.1016/S1470-2045(18)30254-7 • Check for updates

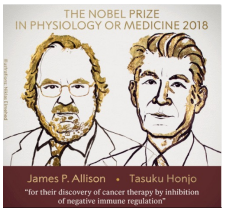


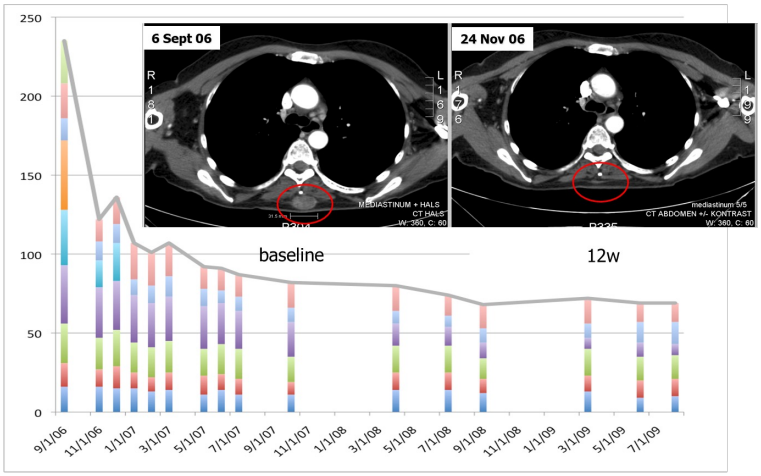


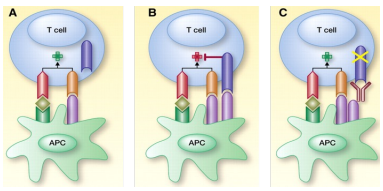
24

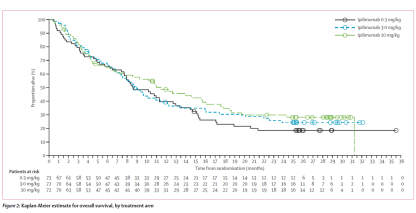
Ipilimumab monotherapy in patients with pretreated advanced melanoma: a randomised, double-blind, multicentre, phase 2, dose-ranging study

Jedd D Wolchok, Bart Neyns, Gerald Linette, Sylvie Negrier, Jose Lutzky, Luc Thomas, William Waterfield, Dirk Schadendorf, Michael Smylie, Troy Guthrie Jr, Jean-Jacques Grob, Jason Chesney, Kevin Chin, Kun Chen, Axel Hoos, Steven J O'Day, Celeste Lebbé









Lancet Oncol 2010; 11: 155–64

25

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

Phase II Study of Autologous Monocyte-Derived mRNA Electroporated Dendritic Cells (TriMixDC-MEL) Plus Ipilimumab in Patients With Pretreated Advanced Melanoma

Sofie Wilgenhof, Jurgen Corthals, Carlo Heirman, Nicolas van Baren, Sophie Lucas, Pia Kvistborg, Kris Thielemans, and Bart Neyns

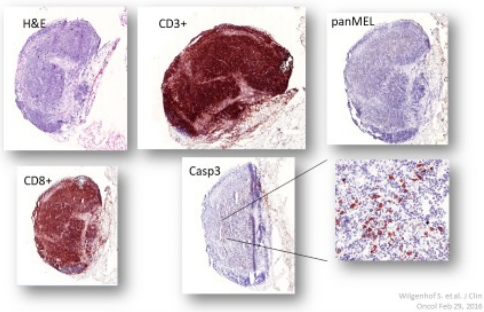
Tumor response by irRC and duration of response

Best objective tumor response by irRC				Duration of response * (months)
CR	8	BORR 38%	DCR 53%	20, 95+, 101+, 110+, 110+, 114+, 112+, 120+
PR	7			3, 8, 10, 11, 24, 33, 44
SD	6			
PD	18			
Tot. patient No.	39			

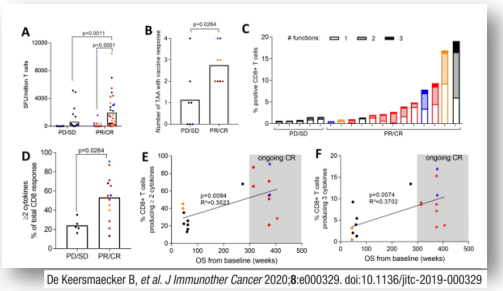
BORR: best overall response rate; DCR: disease control rate; +: response ongoing at latest evaluation; * updated on 19 SEP PR 2019

Wilgenhof S. et al. J Clin Oncol Feb 29, 2016;

Immune response "*caught in the act*"



Wilgenhof S. et al. J Clin Oncol Feb 29, 2016

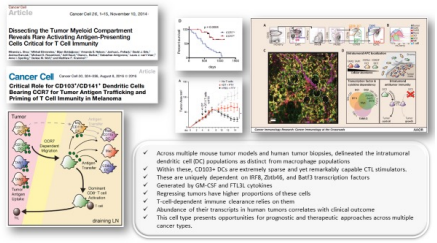


De Keersmaecker B, *et al. J Immunother Cancer* 2020;**8**:e000329. doi:10.1136/jitc-2019-000329

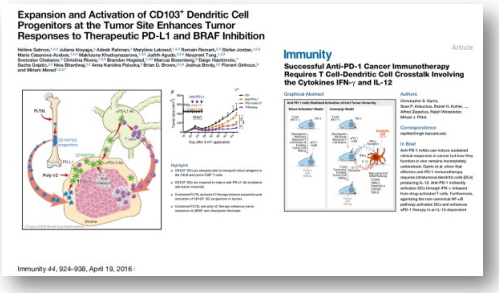
26

The pivotal role of myeloid DC in cancer immunity

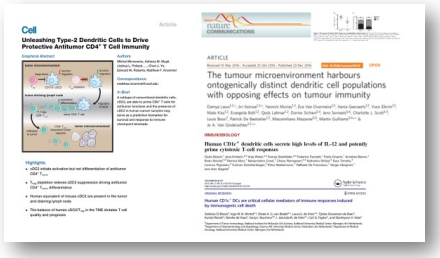
cDC1 (BDCA-3$^+$/CD141$^+$, Batf3$^+$)

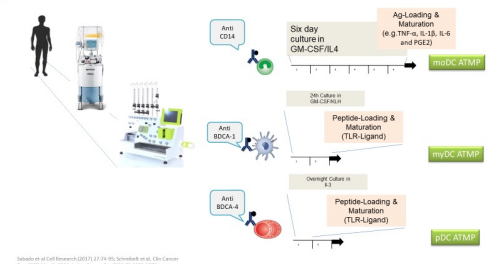


- Across multiple mouse tumor models and human tumor biopsies, delineated the intratumoral dendritic cell (DC) populations as distinct from macrophage populations
- Within these, CD103+ DCs are extremely sparse and yet remarkably capable CTL stimulators.
- These are uniquely dependent on IRF8, Zbtb46, and Batf3 transcription factors
- Generated by GM-CSF and FTLR cytokines
- Regressing tumors have higher proportions of these cells
- T-cell-dependent immune clearance relies on them
- Abundance of their transcripts in human tumors correlates with clinical outcome
- This cell type presents opportunities for prognostic and therapeutic approaches across multiple cancer types.



cDC2 (BDCA-1$^+$/CD1c$^+$)





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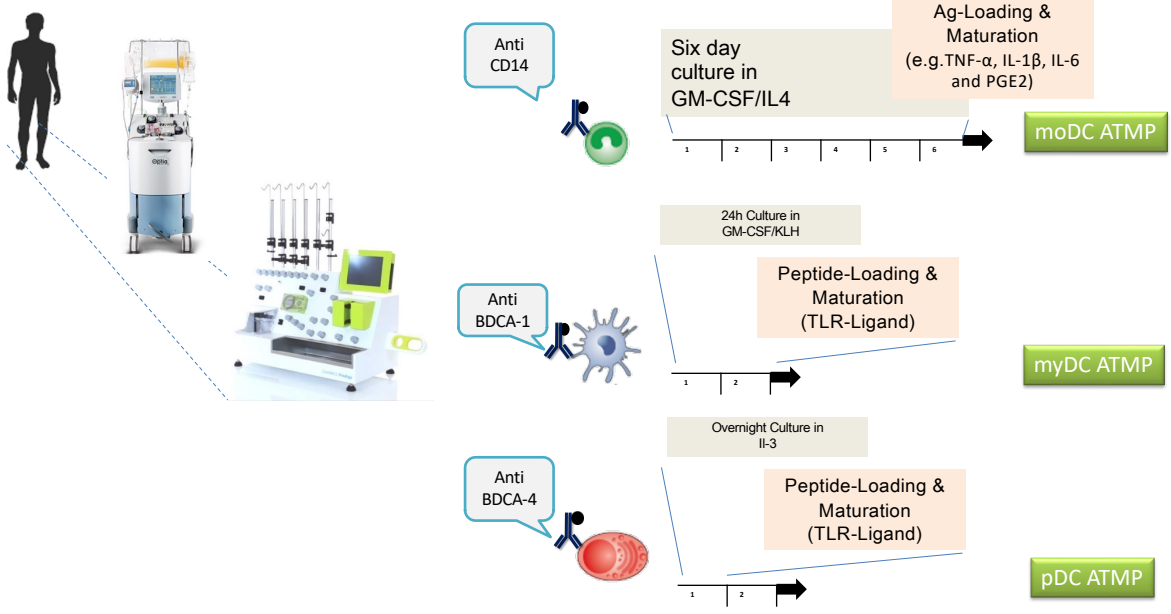
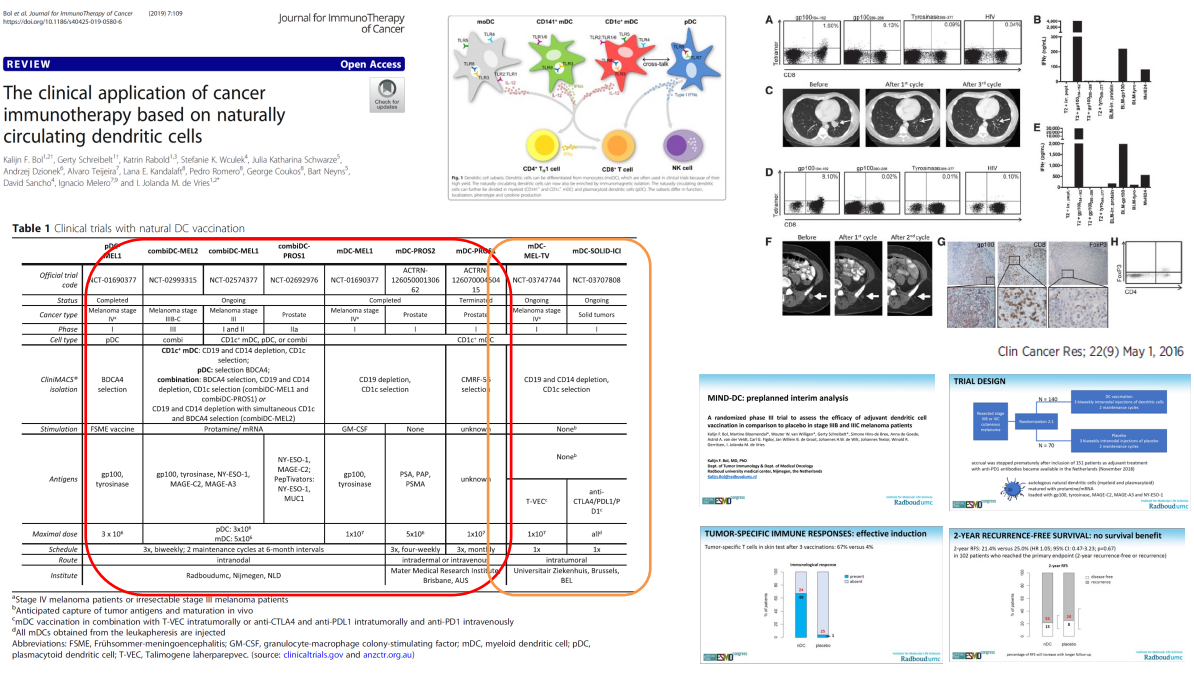


Sabado et al Cell Research (2017) 27:74-95; Schreibelt et al. Clin Cancer Res; 22(9) May 1, 2016; Jurjen *Cancer Res* 2013;73:1063-1075

28



Journal for ImmunoTherapy of Cancer

REVIEW — Open Access

The clinical application of cancer immunotherapy based on naturally circulating dendritic cells

Kalijn F. Bol[1,2†], Gerty Schreibelt[1†], Katrin Rabold[1,3], Stefanie K. Wculek[4], Julia Katharina Schwarze[5], Andrzej Dzionek[6], Alvaro Teijeira[7], Lana E. Kandalaft[8], Pedro Romero[9], George Coukos[8], Bart Neyns[5], David Sancho[4], Ignacio Melero[7,9] and I. Jolanda M. de Vries[1,2*]

Table 1 Clinical trials with natural DC vaccination

	pDC-MEL1	combiDC-MEL2	combiDC-MEL1	combiDC-PROS1	mDC-MEL1	mDC-PROS2	mDC-PROS1	mDC-MEL-TV	mDC-SOLID-ICI
Official trial code	NCT-01690377	NCT-02993315	NCT-02574377	NCT-02692976	NCT-01690377	ACTRN-12605001306 62	ACTRN-12607000 4504 15	NCT-03747744	NCT-03707808
Status	Completed	Ongoing			Completed		Terminated	Ongoing	Ongoing
Cancer type	Melanoma stage IV[a]	Melanoma stage IIIB-C	Melanoma stage III	Prostate	Melanoma stage IV[a]	Prostate	Prostate	Melanoma stage IV[a]	Solid tumors
Phase	I	III	I and II	IIa	I	I	I	I	I
Cell type	pDC	combi	CD1c[+] mDC, pDC, or combi				CD1c[+] mDC		
ClinMACS® isolation	BDCA4 selection		**CD1c[+] mDC**: CD19 and CD14 depletion, CD1c selection; **pDC**: selection BDCA4; **combination**: BDCA4 selection, CD19 and CD14 depletion, CD1c selection (combiDC-MEL1 and combiDC-PROS1) or CD19 and CD14 depletion with simultaneous CD1c and BDCA4 selection (combiDC-MEL2)		CD19 depletion, CD1c selection		CMRF-5[b] selection	CD19 and CD14 depletion, CD1c selection	
Stimulation	FSME vaccine	Protamine/ mRNA			GM-CSF	None	unknown[b]	None[b]	
Antigens	gp100, tyrosinase	gp100, tyrosinase, MAGE-C2, MAGE-A3		NY-ESO-1, MAGE-C2; PepTivators: NY-ESO-1, MUC1	gp100, tyrosinase	PSA, PAP, PSMA	unknown	None[b] T-VEC[c]	anti-CTLA4/PDL1/PD1[c]
Maximal dose	3 x 10[6]	pDC: 3x10[6] mDC: 5x10[6]			1x10[7]	5x10[6]	1x10[7]	1x10[7]	all[d]
Schedule	3x, biweekly; 2 maintenance cycles at 6-month intervals				3x, four-weekly	3x, monthly		1x	1x
Route	intranodal				intradermal or intravenous			intratumoral	
Institute	Radboudumc, Nijmegen, NLD				Mater Medical Research Institute, Brisbane, AUS			Universitair Ziekenhuis, Brussels, BEL	

[a]Stage IV melanoma patients or irresectable stage III melanoma patients
[b]Anticipated capture of tumor antigens and maturation in vivo
[c]mDC vaccination in combination with T-VEC intratumorally or anti-CTLA4 and anti-PDL1 intratumorally and anti-PD1 intravenously
[d]All mDCs obtained from the leukapheresis are injected
Abbreviations: FSME, Frühsommer-meningoencephalitis; GM-CSF, granulocyte-macrophage colony-stimulating factor; mDC, myeloid dendritic cell; pDC, plasmacytoid dendritic cell; T-VEC, Talimogene laherparepvec. (source: clinicaltrials.gov and anzctr.org.au)

Clin Cancer Res; 22(9) May 1, 2016

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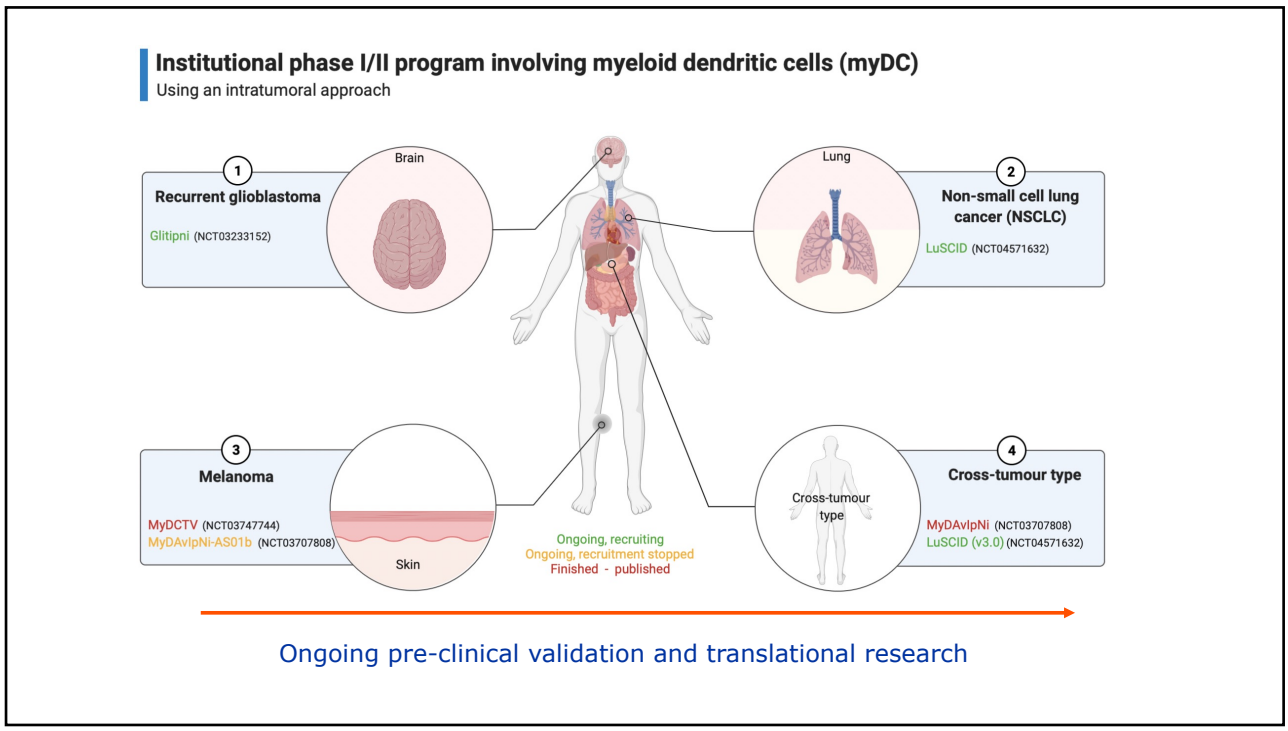
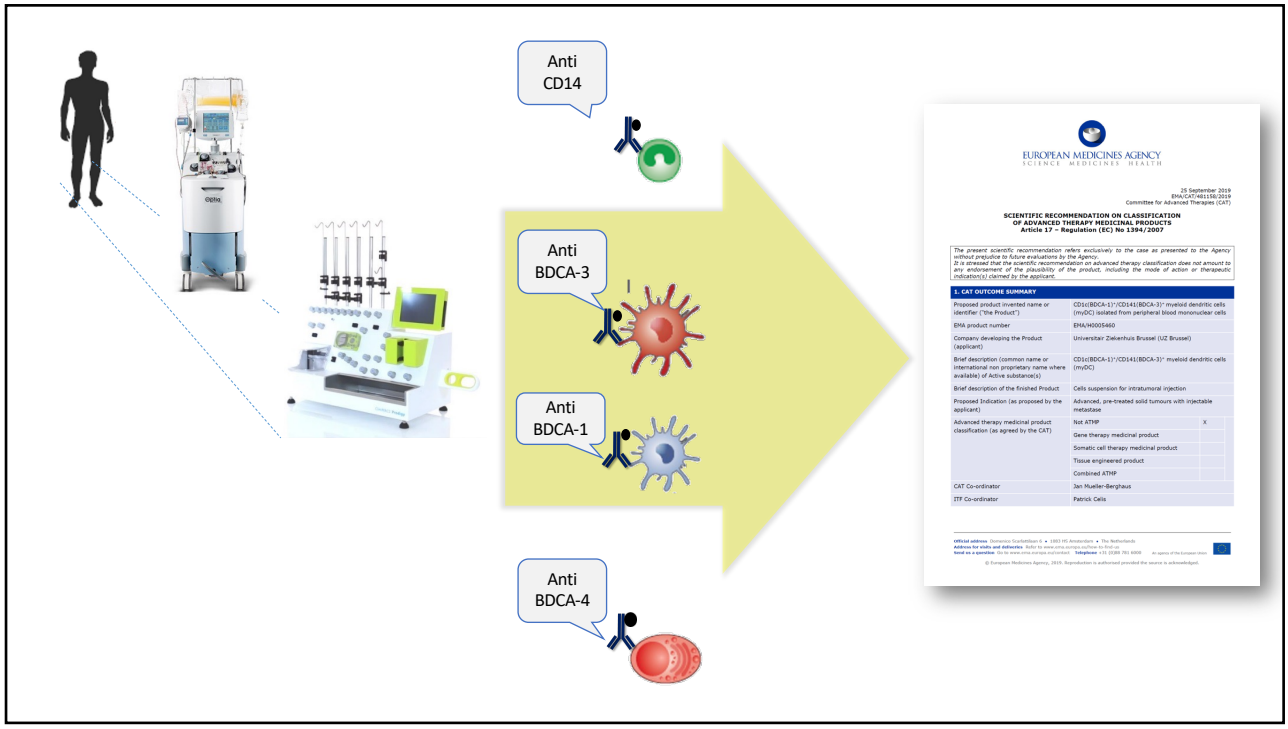

Institutional phase I/II program involving myeloid dendritic cells (myDC)
Using an intratumoral approach
1
Recurrent glioblastoma
Glitipni (NCT03233152)
Brain
2
Non-small cell lung cancer (NSCLC)
LuSCID (NCT04571632)
Lung
3
Melanoma
MyDCTV (NCT03747744)
MyDAvIpNi-AS01b (NCT03707808)
Skin
4
Cross-tumour type
MyDAvIpNi (NCT03707808)
LuSCID (v3.0) (NCT04571632)
Cross-tumour type
Ongoing, recruiting
Ongoing, recruitment stopped
Finished - published
Ongoing pre-clinical validation and translational research

30


Anti CD14
Anti BDCA-3
Anti BDCA-1
Anti BDCA-4
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH
SCIENTIFIC RECOMMENDATION ON CLASSIFICATION OF ADVANCED THERAPY MEDICINAL PRODUCTS
Article 17 – Regulation (EC) No 1394/2007
1. CAT OUTCOME SUMMARY

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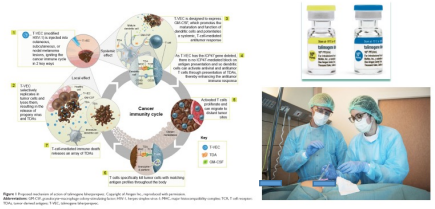
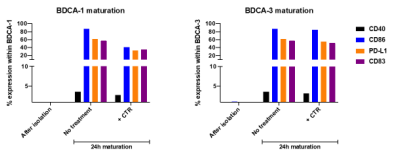
Combining myDC with HSV derived Oncolytic Viruses

Talimogene laherparepvec (T-VEC, Imlygic™)



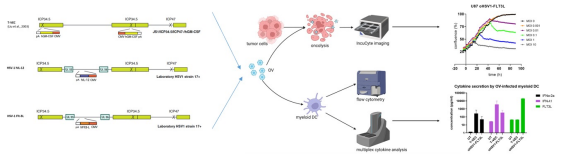
BDCA-1/-3 myDC maturation



- Peripheral blood isolated BDCA-1/-3 myDC without treatment upregulate maturation markers to the same extent as BDCA-1/-3 myDC exposed to protamin/dubbelstranded RNA complexes (+CTR)
- Additional interventions (co-culture with irradiated tumor cells, addition of T-VEC, PD-1/-L1 blockade (addition of nivolumab or avelumab) did not alter expression of maturation markers.

Collaborative study on the effect of FLT-3L and IL-12 producing HSV-derived OV on human myDC

Prof. Arianna Calistri
Dr. Alberto Reale
University of Padova



ORIGINAL RESEARCH article
Front. Immunol., 28 October 2021 | https://doi.org/10.3389/fimmu.2021.733506

Unraveling the Effects of a Talimogene Laherparepvec (T-VEC)-Induced Tumor Oncolysate on Myeloid Dendritic Cells

Jens Tijtgat[†], Jolien De Munck[†], Inès Dufait, Julia Katharina Schwarze, Ivan Van Riet, Lorenzo Franceschini, Karine Breckpot, Joeri L. Aerts, Bart Neyns and Sandra Tuyaerts*

JK Schwarze et al. ESMO AM 2021; JK Schwarze et al accepted JITC 2022

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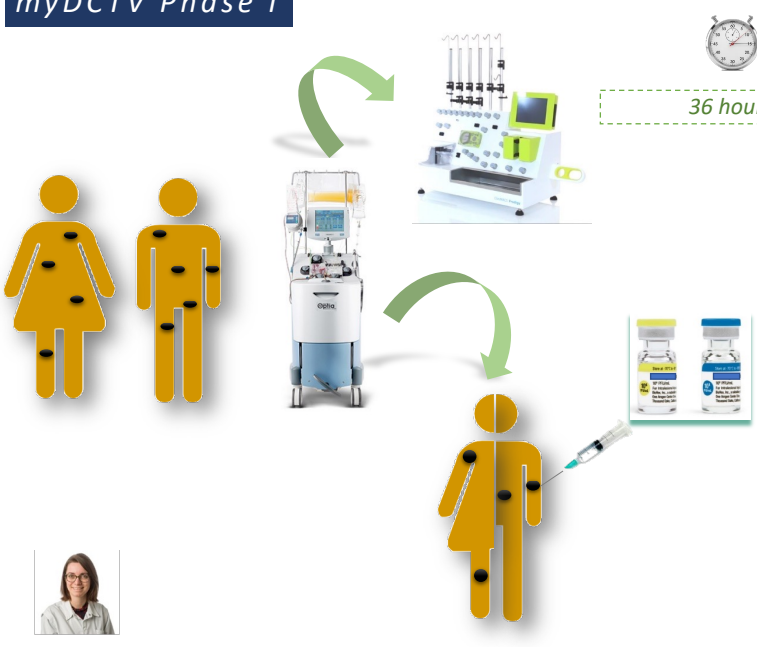
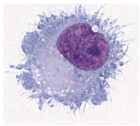
myDCTV Phase I



36 hours



CD1c(BDCA-1)⁺ DC *or* CD1c(BDCA-1)⁺/CD141(BDCA-3)⁺ DC

3 Cohorts – 3 dose levels
Cohort 1 – 0.5x10^6 myDC
Cohort 2 – 1 x 10^6 myDC
Cohort 3 – 10 x 10^6 myDC

IT injection of talimogene laherparepvec

Injection volume based on lesion size

> 5 cm up to 2 mL
> 2.5 cm to 5 cm up to 1 mL
> 1.5 cm to 2.5 cm up to 0.50 mL
> 0.5 cm to 1.5 cm up to 0.25 mL
≤ 0.5 cm up to 0.05 mL

Julia Katharina Schwarze MD

JK Schwarze et al. ESMO AM 2021; JK Schwarze et al accepted JITC 2022

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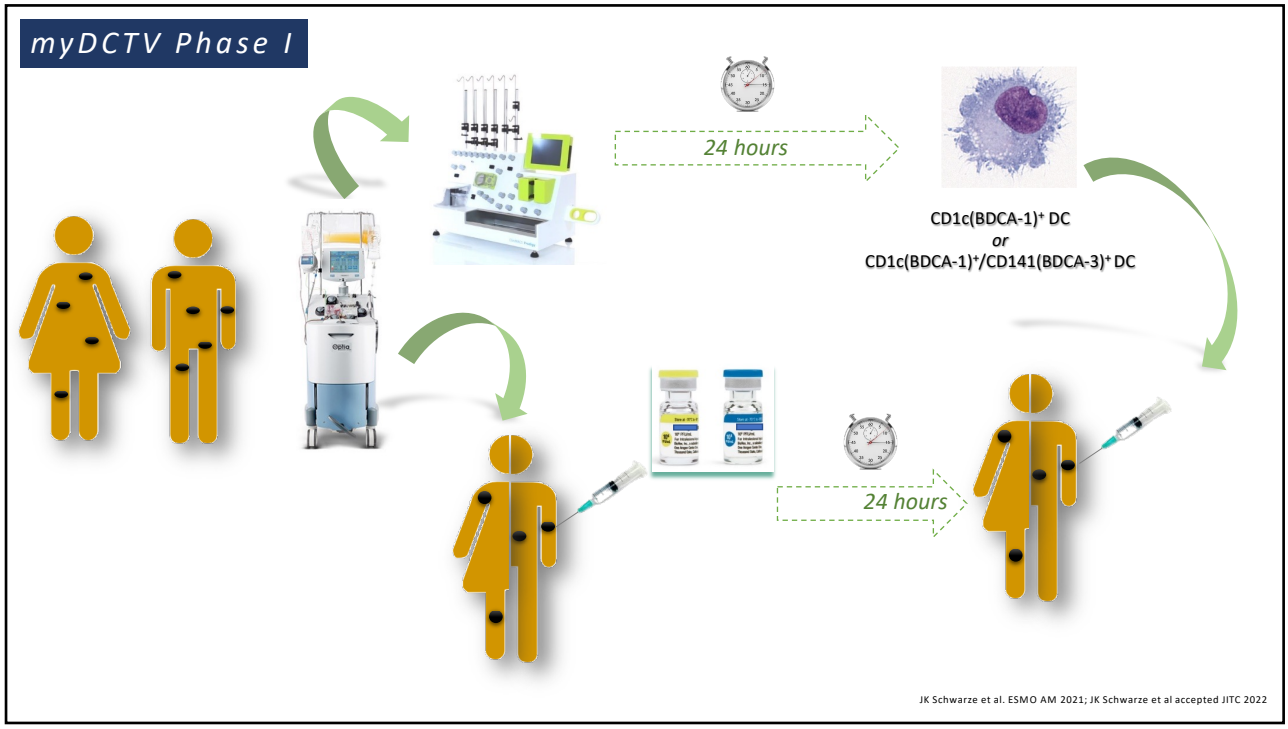

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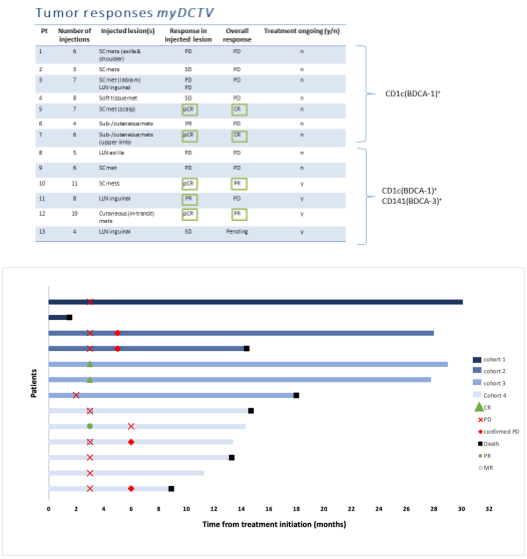
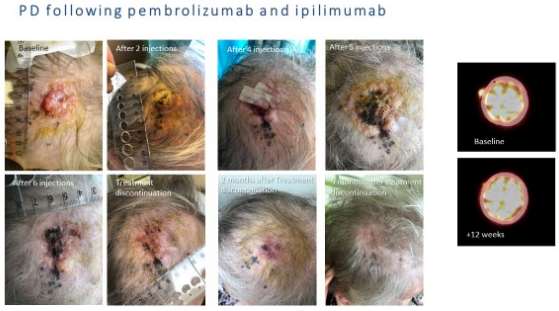
myDCTV: tumor response





JK Schwarze et al. ESMO AM 2021; JK Schwarze et al accepted JITC 2022

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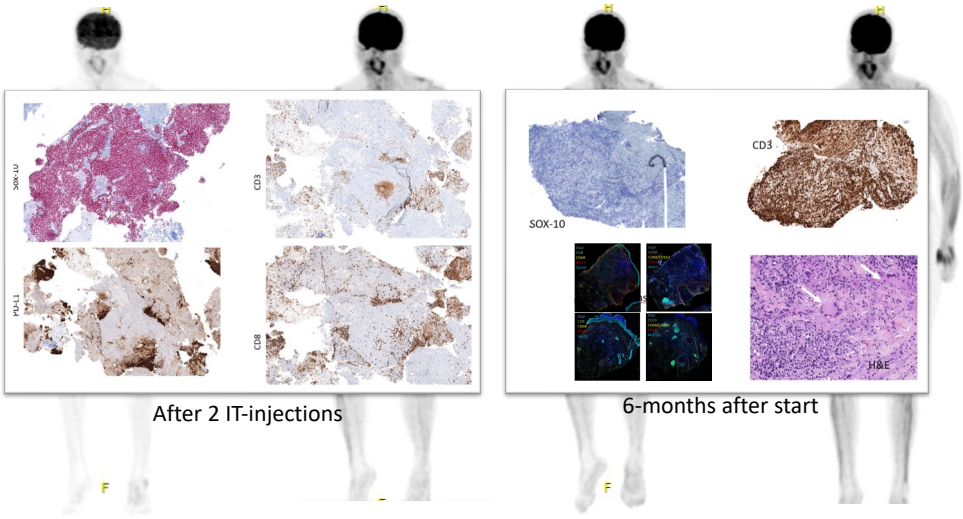
myDCTV Case illustration – 68y female, stage IIIC BRAFwt melanoma PD following pembrolizumab



After 2 IT-injections

6-months after start

28 MAR 2019

27 JUN (+12w)

1 AUG (+18w)

12 SEP (+24w)

JK Schwarze et al. ESMO AM 2021; JK Schwarze et al accepted JITC 2022

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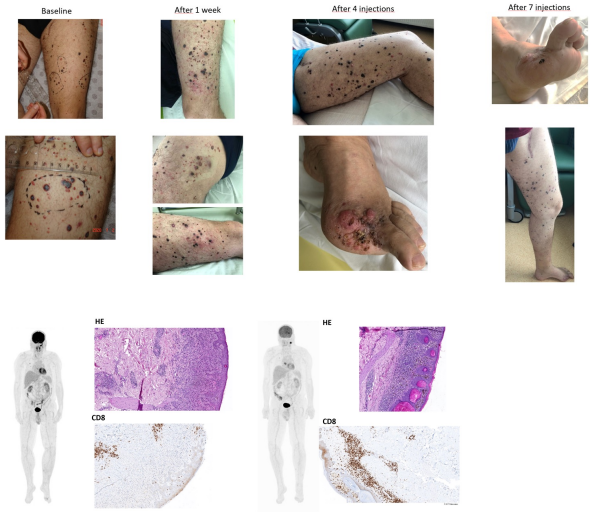
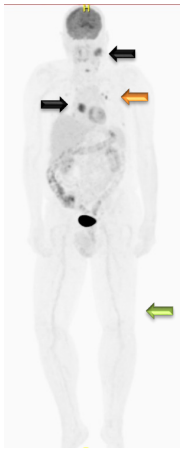
Case Illustration – 55y/o male PD following pembrolizumab and ipilimumab





W12 on Study Treatment

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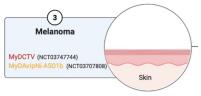
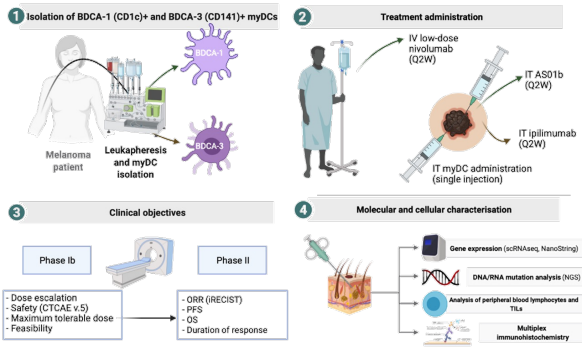
MyDAvIpNi-AS01$_b$ Phase I





QS-21: Quillaja saponaria
Soap bark tree – native to Chile
Hemolytic activity → liposomal formulation

MPL-A
3-O-desacyl–monophosphoryl lipid A
Derivative of LPS from Salmonella minnesota
TLR-4 agonist

J Tijtgat et al. Abstract accepted JITC AM 2022

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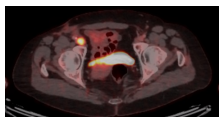
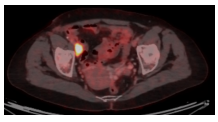
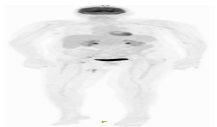
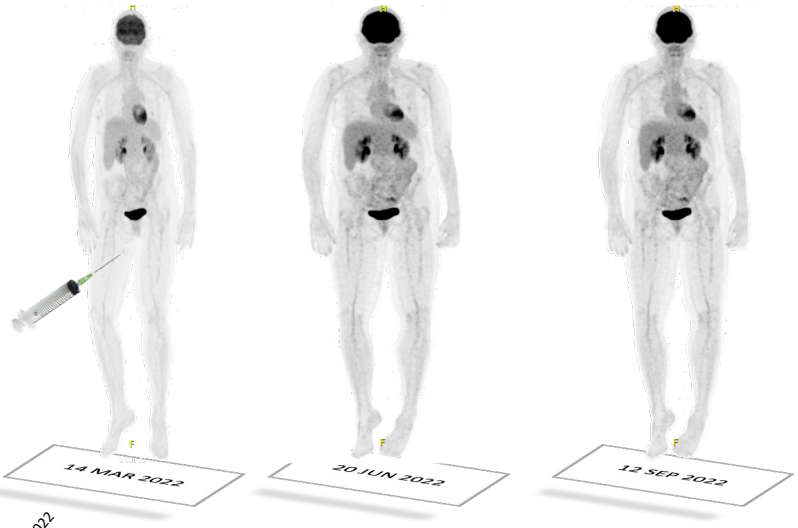
myDAvIpNi-AS01b Case Illustration:

Nodular melanoma right leg (BRAF V600wt), CLND, ILP (in transit metastases), resection gallbladder metastasis (stage IV-M1c), pembrolizumab, ipilimumab.









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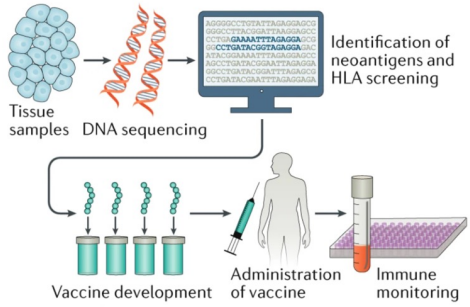
nature portfolio

MILESTONES | 28 September 2020

Individualized neoantigen vaccines

João H. Duarte



Credit: Springer Nature Limited (Waldman et al. https://doi.org/10.1038/s41577-020-0306-5)

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Moderna and Merck Announce mRNA-4157/V940, an Investigational Personalized mRNA Cancer Vaccine, in Combination With KEYTRUDA® (pembrolizumab), Met Primary Efficacy Endpoint in Phase 2b KEYNOTE-942 Trial

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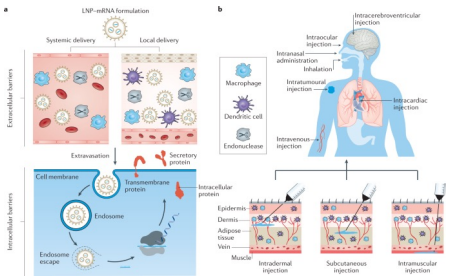

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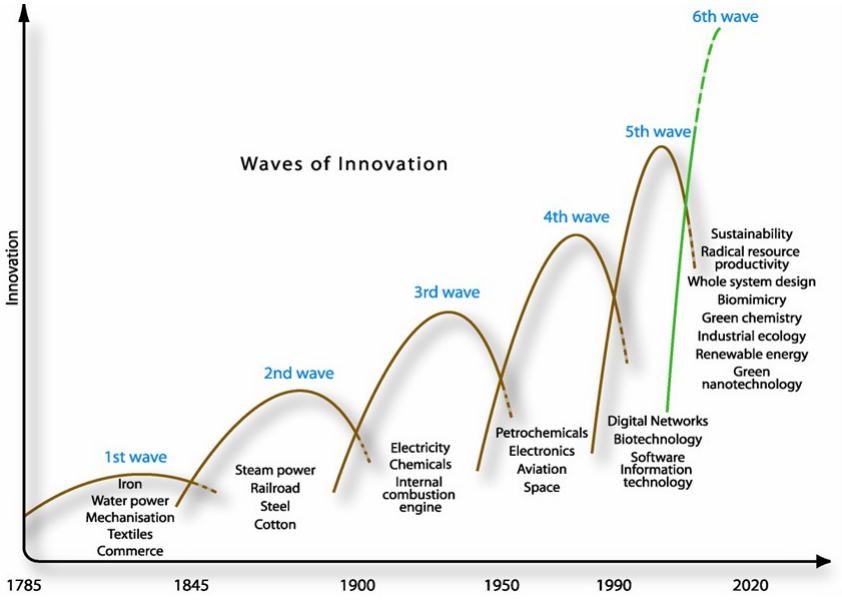

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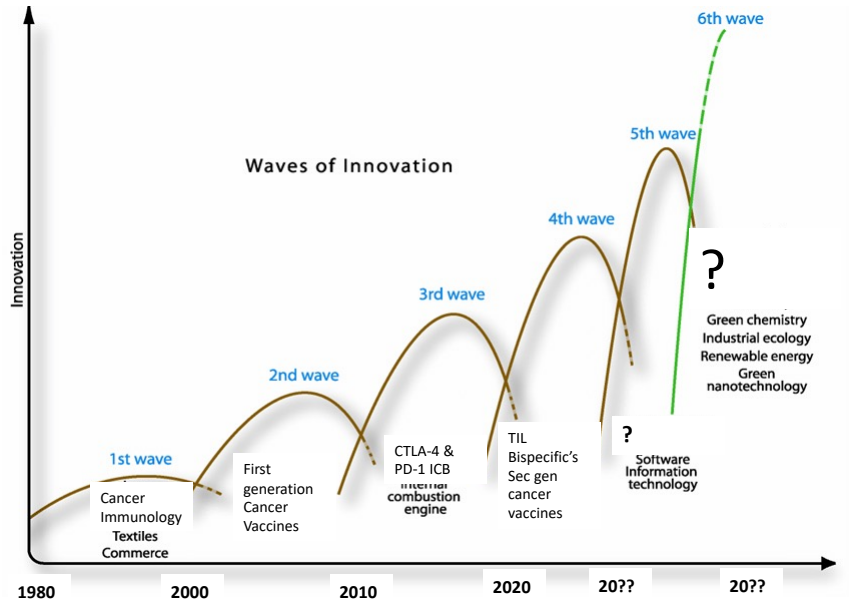

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Kom op tegen Kanker

Stichting tegen Kanker

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Thank you for your attention!

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