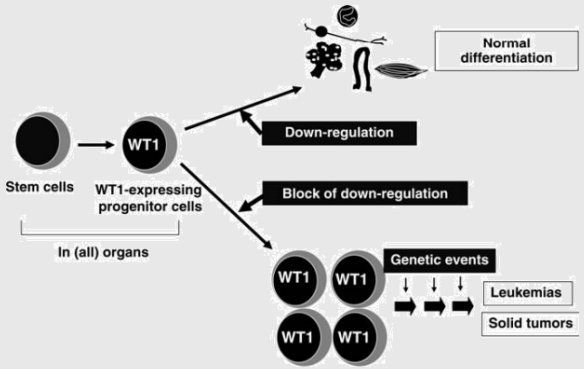
From Vein to Vaccine: A safety feasibility trial assessing dendritic cell vaccination in Children with High-Grade glioma and Diffuse Intrinsic Pontine Glioma

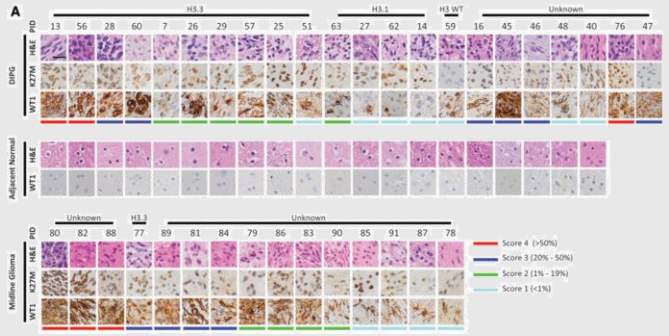
Dr. Toon Van Genechten
Senior Staff, pediatric Oncology, UZA
PhD student, CCRG, UAntwerp

Background

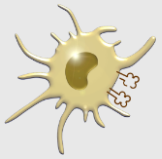
Wilms' tumor 1 antigen[1, 2]



Wilms' Tumor 1 antigen in pHGG[3]



Dendritic Cell Immunotherapy in children[4]



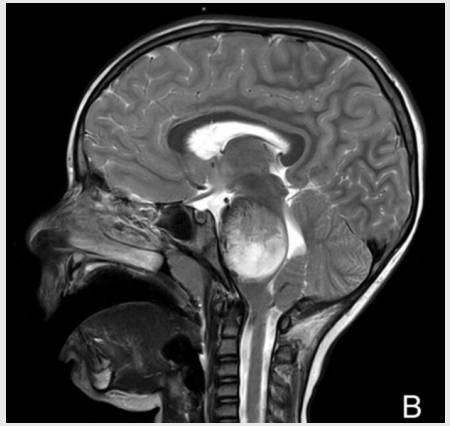
Safe
Feasible
Combinational therapy

Diffuse mideline glioma and pediatric type High grade glioma

Better molecular understanding (H3K27M)

Early phase clinical trials and preclinical research

Transient respons to radiotherapy



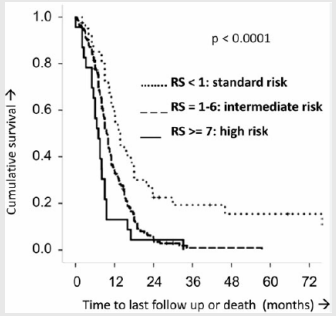
I: 1,5/100 000

Rapid onset of symptoms

Irresectable

Effect chemotherapy?

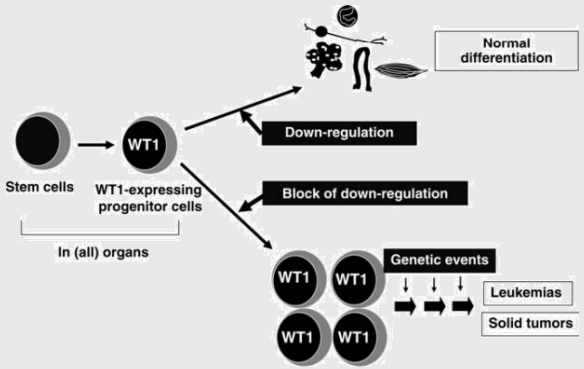
OS: <5% 2 year, mOS 10-12months
no long term survivors



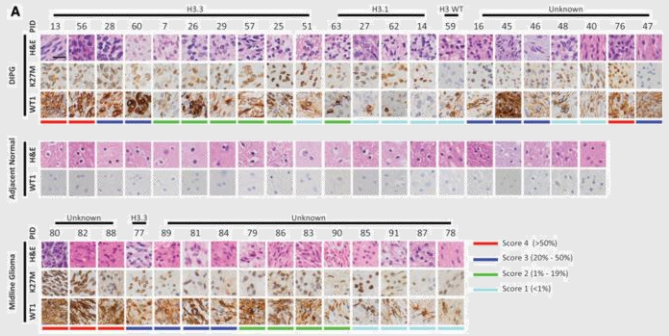
[1] Cheever et al. 2009
[2] Sugiyama et al. 2010
[3] Lee et al. 2019
[4] De Bruyn et al. 2019
[5] Van Genechten et al. 2024

Background

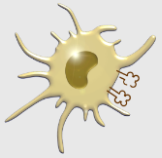
Wilms' tumor 1 antigen[1, 2]



Wilms' Tumor 1 antigen in pHGG[3]



Dendritic Cell Immunotherapy in children[4]



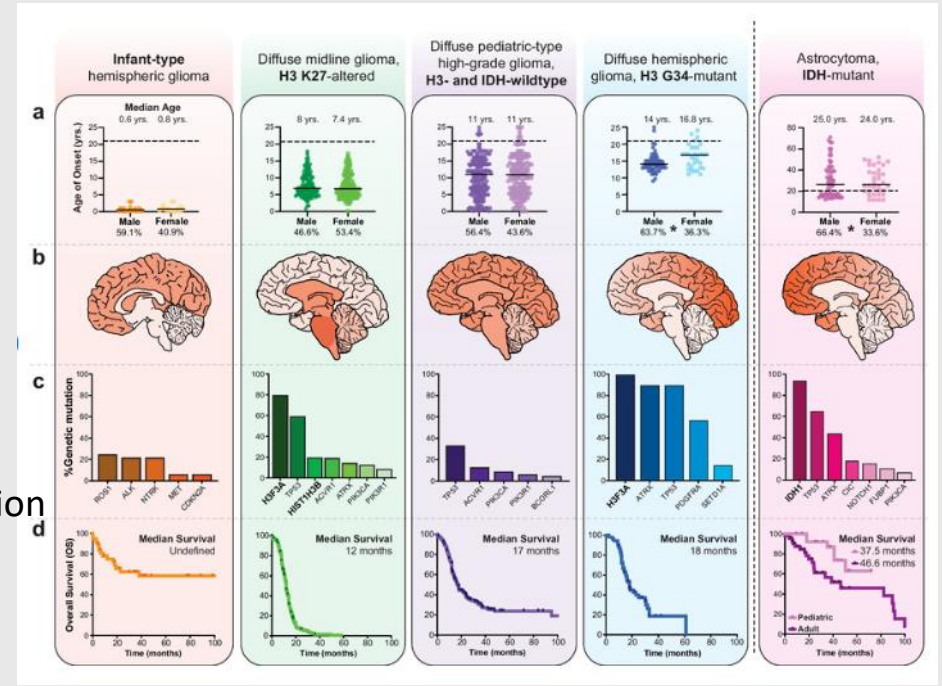
Safe
Feasible
Combinational therapy

Diffuse mideline glioma and pediatric type High grade glioma

I: 0,85/100 000

3-5% pediatric CNS tumors

Symptoms depend on localisation



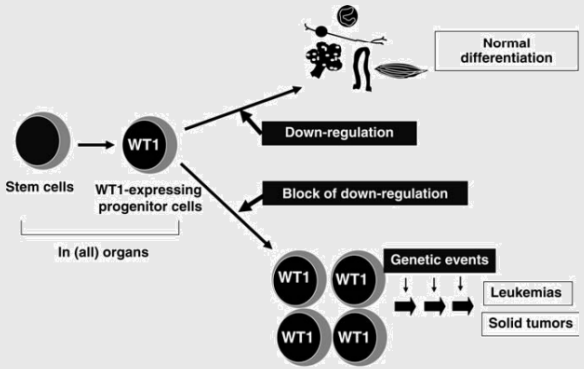
Molecular different from adult counterpart
MGMT over-expression / IDH WT

OS HGG: 5%

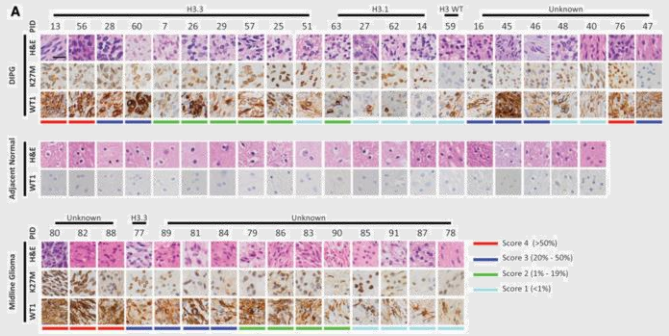
[1] Cheever et al. 2009
[2] Sugiyama et al. 2010
[3] Lee et al. 2019
[4] De Bruyn et al. 2019

Background

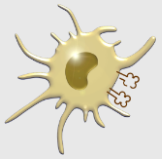
Wilms' tumor 1 antigen[1, 2]



Wilms' Tumor 1 antigen in pHGG[3]

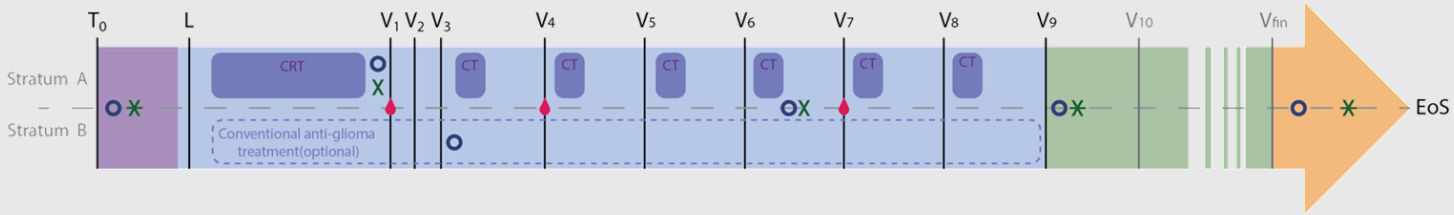


Dendritic Cell Immunotherapy in children[4]



Safe
Feasible
Combinational therapy

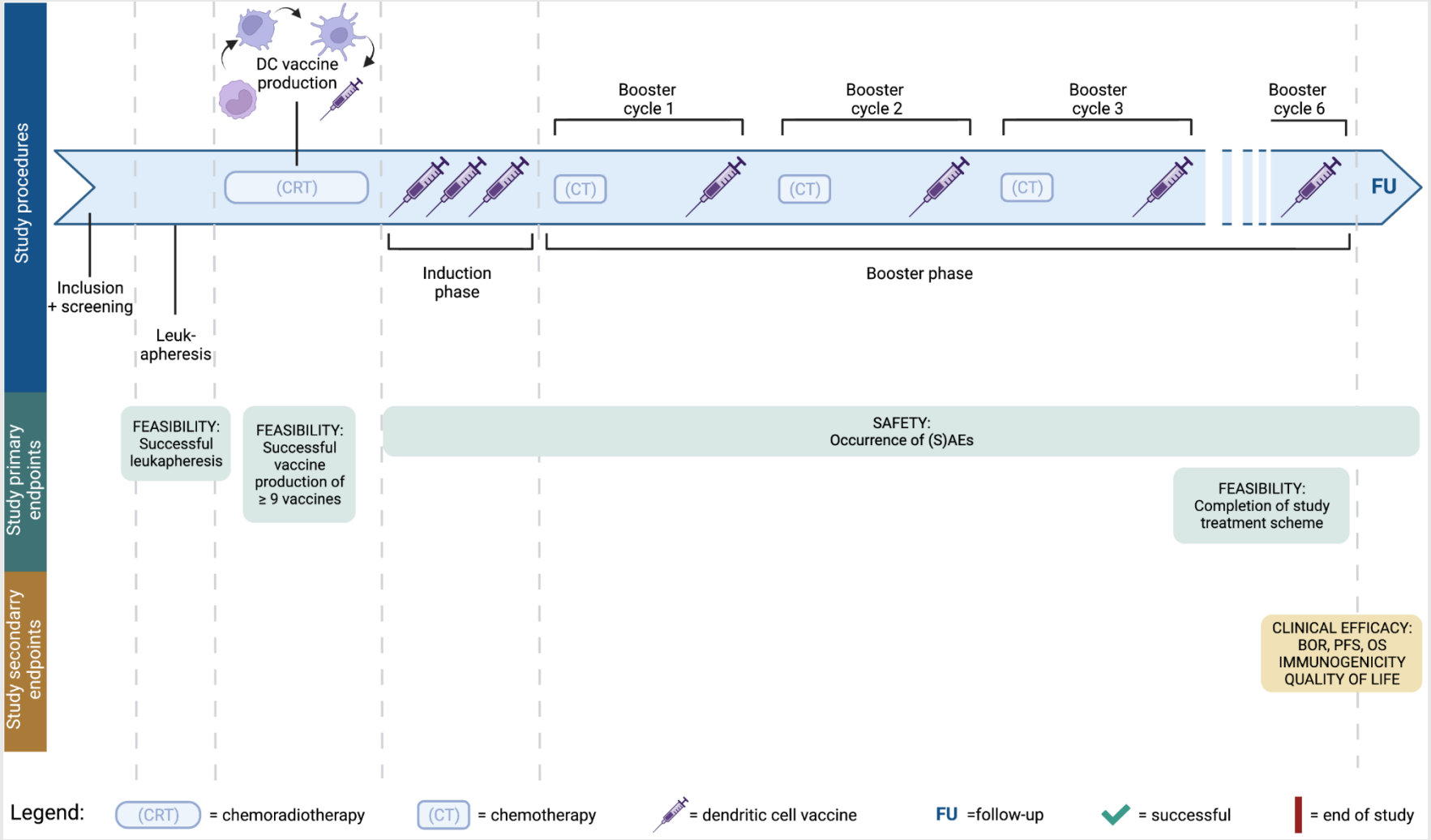
ADDICT-pedGLIO: Adjuvant Wilms' tumour 1-specific dendritic cell immunotherapy complementing conventional therapy for paediatric patients with high-grade glioma and diffuse intrinsic pontine glioma: protocol of a monocentric phase I/II clinical trial in Belgium[5]



T_0	Inclusion
L	Leukapheresis
$V_{1\text{-}9}$	Autologous WT1/DC vaccination 3 induction vaccines (weekly ± 3 days) + 6 booster vaccines (on day 21 (± 3 days) of every 28-day cycle)
$V_{10/fin}$	Additional WT1/DC vaccination (optional, fin = final)
CRT	Chemoradiation therapy 54 Gy in 1.8 Gy fractions 5 days/week for 6 weeks + 90 mg/m²/day temozolomide (p.o.) daily
CT	Maintenance chemotherapy 150-200 mg/m²/day temozolomide (p.o.) daily, day 1-5 of 28-day (± 3 days) cycle, for a total of 6 cycles
EoS	End of study (90 days post V_{fin} or 24 months post diagnosis (whichever occurs later))
	Blood sampling for immunomonitoring purposes On the day of V_1, V_4 and V_7
	MRI at screening, after chemoradiation (statum A) or as medically appropriate before start of the booster phase (stratum B), every 3 booster cycles and at least every 15 weeks during booster phase, every 12 ± 1 weeks during additional V administrations and follow-up
X	PedsQL + BRIEF questionnaires
X	PedsQL questionnaires at screening, once during chemoradiation (stratum A), before start of induction phase and after completion of chemoradiation (stratum A), after the induction phase and before start of the booster phase, around the time of disease assessment during booster phase and optional continuation of V, 90 days (± 1 week) post V_{fin}

[1] Cheever et al. 2009
[2] Sugiyama et al. 2010
[3] Lee et al. 2019
[4] De Bruyn et al. 2019
[5] Van Genechten et al. 2024

ADDICT-pedGLIO: Adjuvant Wilms' tumour 1-specific dendritic cell immunotherapy complementing conventional therapy for paediatric patients with high-grade glioma and diffuse intrinsic pontine glioma: protocol of a monocentric phase I/II clinical trial in Belgium[5]



[5] Van Genechten et al. 2024

Production of a personalized dendritic cell vaccine

Insertion tumor marker

Mature DC

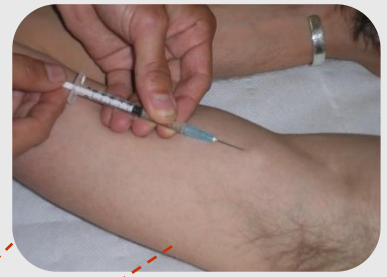
MATURATION

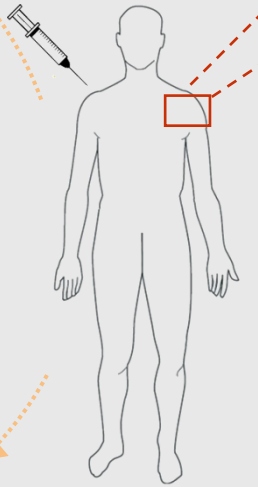
Immature DC

DIFFERENTIATION

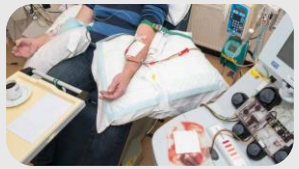
monocyte

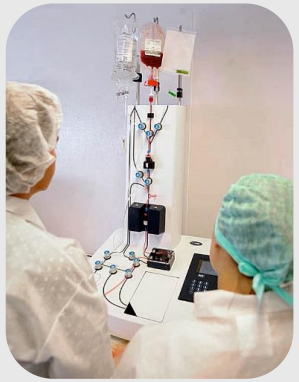
= DC vaccine ADMINISTRATION via skin





LEUKAPHERESIS
white blood cell collection
↓
Monocyte isolation





Parameter	n (%)
Successful leukapheresis	10/10 (100%)
Successful vaccine production	8/10 (80%)
Completion of study treatment schedule	4/10 (40%)
Proportion of efficacy evaluable patients in the intention-to-treat population	10/10 (100%)

TABLE 1. FEASIBILITY PARAMETERS.

ADDICT-pedGLIO: feasibility & safety

Patient characteristics	(n=10)	
	mean	range
Age (years)	11	4 – 15
Blood volume (ml)	2410	870 – 3155
Monocytic cell count (/µl)	660	190 – 1110
Apheresis procedures	**(n=13)**	
Venous acces	proportion	percentage
Femoral catheter	8/13	61%
Successful procedure	8/8	100%
Peripheral catheter	5/13	39%
Successful procedure	3/5	60%
Priming required	3/13	23%
Corticosteroid use at apheresis	2/13	15%
Suppletion		
Calcium	7/13	54%
Potassium	3/13	23%
	mean	range
Yield ($CD14^+$ cells, $x10^9$)	1,73	0,69 – 3,3

TABLE 2. APHERESIS RELATED DATA

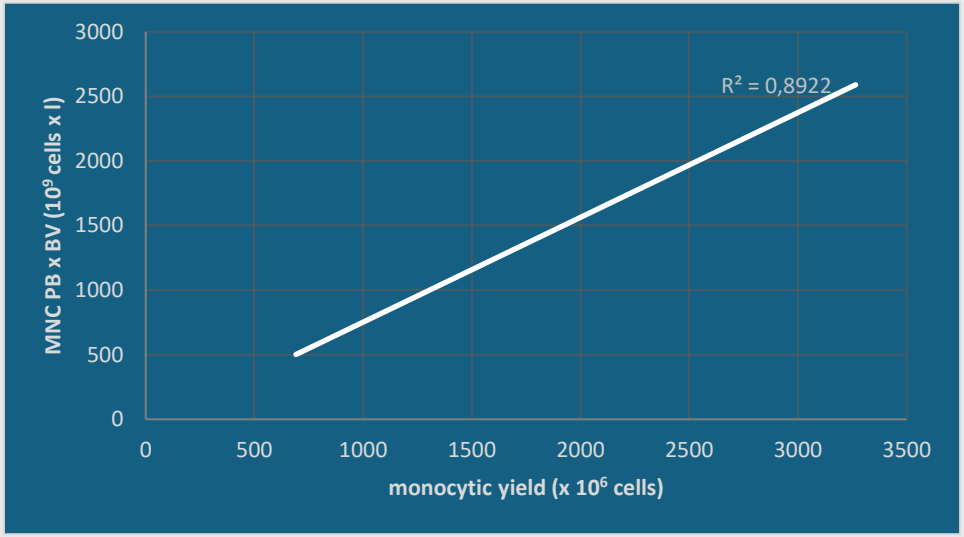


FIGURE 1. Correlation between total blood volume x pre-apheresis monocytic count and monocytic yield. *Bloodvolume adjusted for age, weight, sex and pubertal stage in females

AE relationship	Number of patients	Number of AEs	Number of G1 AEs	Number of G2 AEs	Number of G3 AEs	Number of G4 AEs	Number of AEs with unknown grade
Disease under study	8	53	12	26	13	1	1
Chemotherapy and/or radiotherapy	9	75	43	26	6	0	0
Leukapheresis	9	20	15	5	0	0	0
DC vaccination	7	20	20	0	0	0	0
Other	9	37	27	9	1	0	0

TABLE 3. ADVERSE EVENTS IN RELATION TO STUDY COMPONENT

ADDICT-pedGLIO: preliminary results

Patients	n=10	%
Gender		
male	4	40
female	6	60
Histology		
DIPG	6	60
pHGG	3	30
Anaplastic astrocytoma	1	10
WT1 staining		
Strong	3	30
weak	2	20
negative	1	10
Not available	4	40
First-line therapy	5	50
second or >2-line therapy	5	50
	range	mean
Disease duration at inclusion (months)	0,8 - 21,4	7,1
Age (years)	4 - 15	11

TABLE 4. PATIENT CHARACTERISTICS

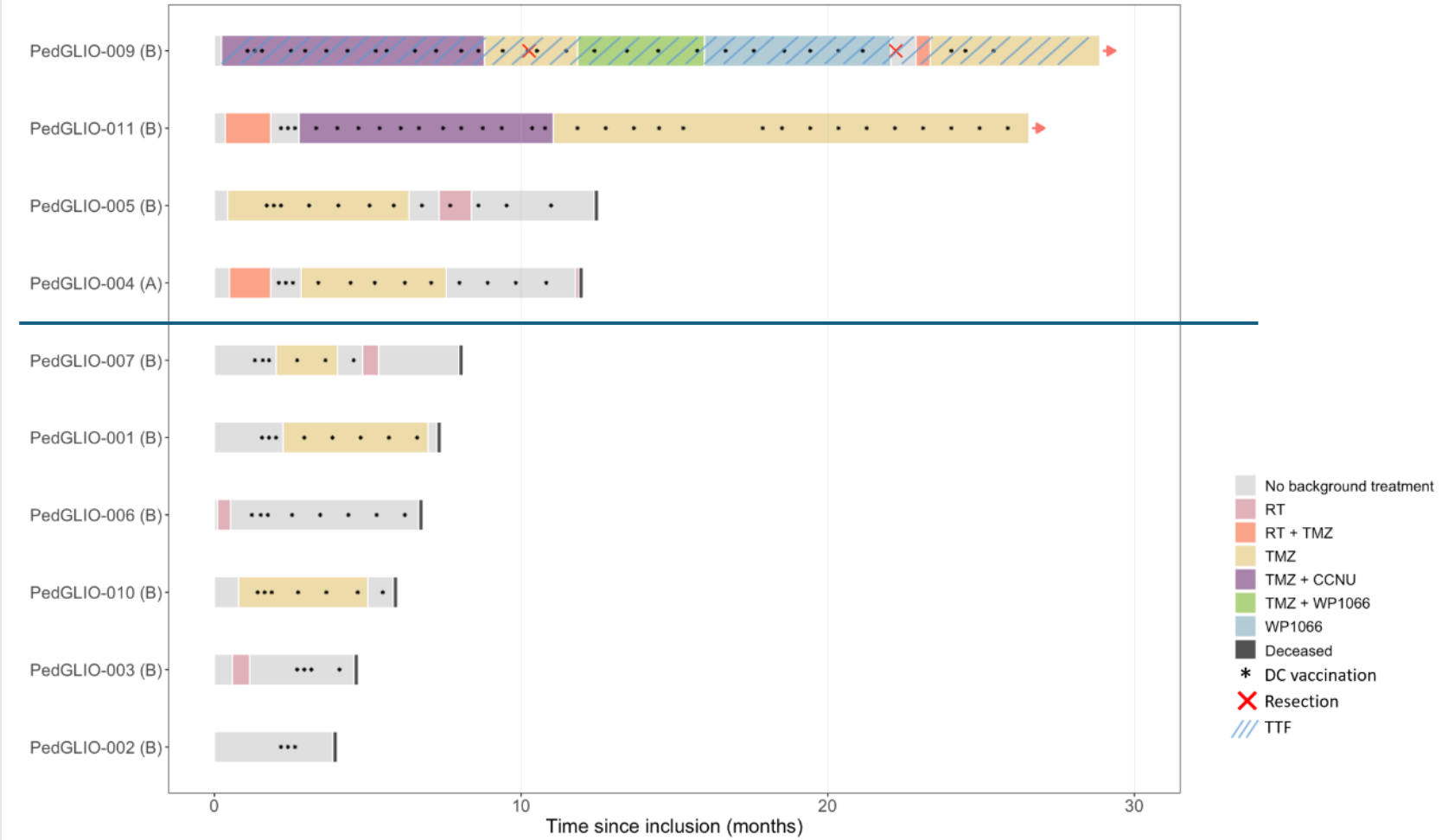


Figure 2. SWIMMER PLOT AND CONCOMITTANT TREATEMENTS

ADDICT-pedGLIO Patient-009

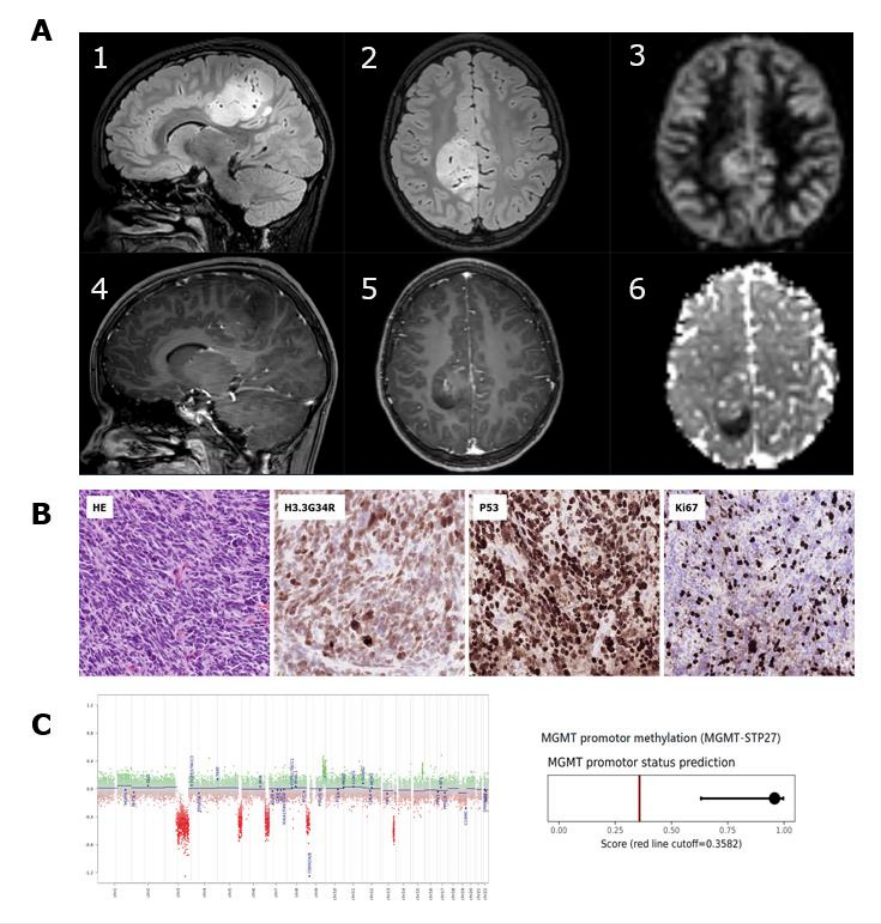


FIGURE 5. BACKGROUND pedGLIO-009

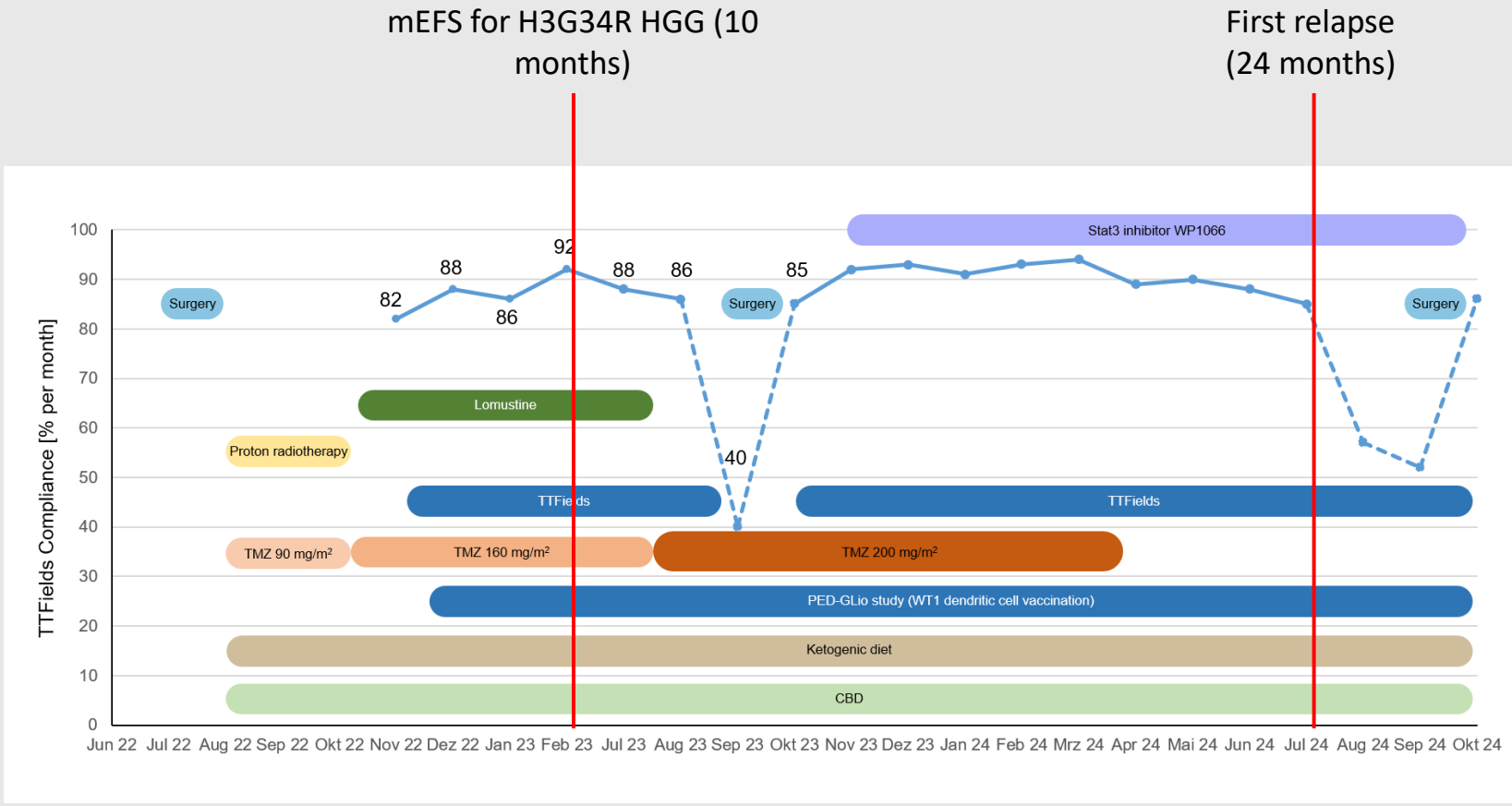


FIGURE 6. TREATMENT PLAN pedGLIO-009

ADDICT-pedGLIO Patient-009

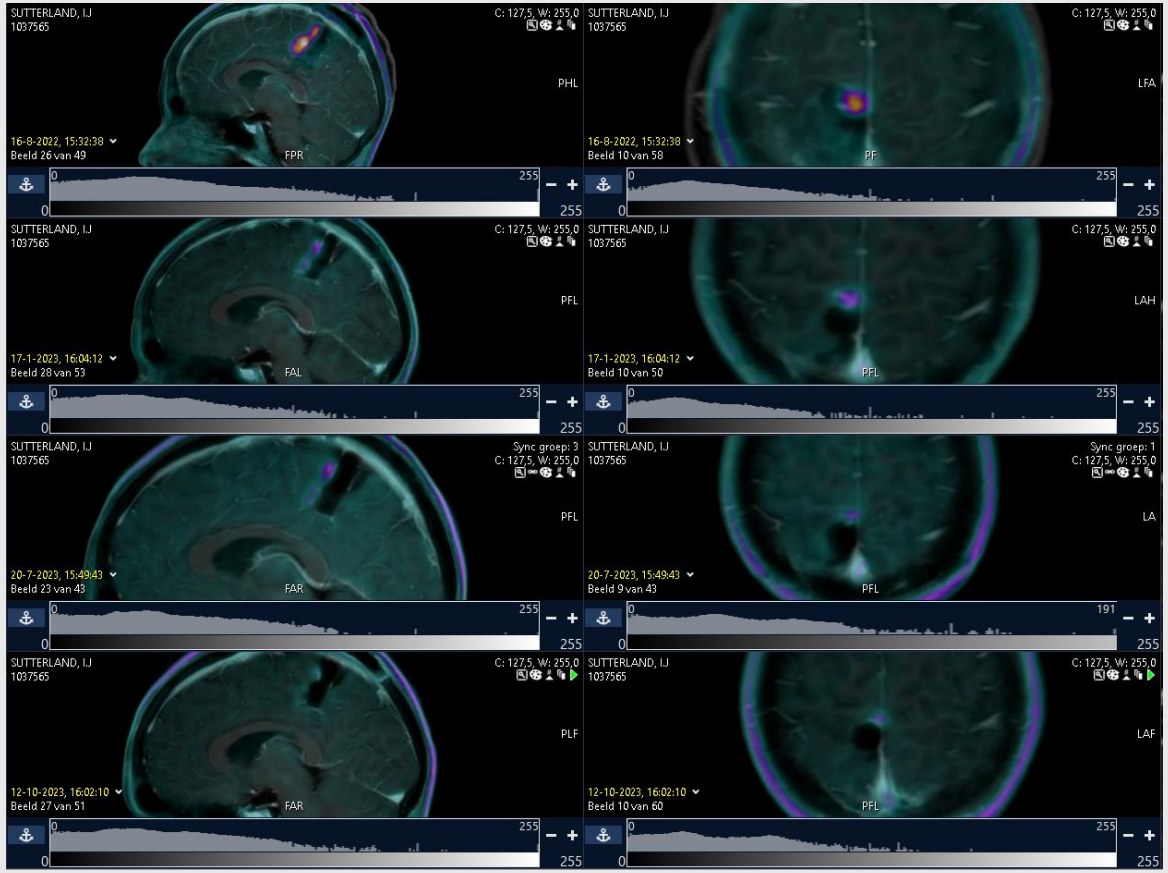


FIGURE 7. EVOLUTION IMAGING (FET-PET) pedGLIO-009

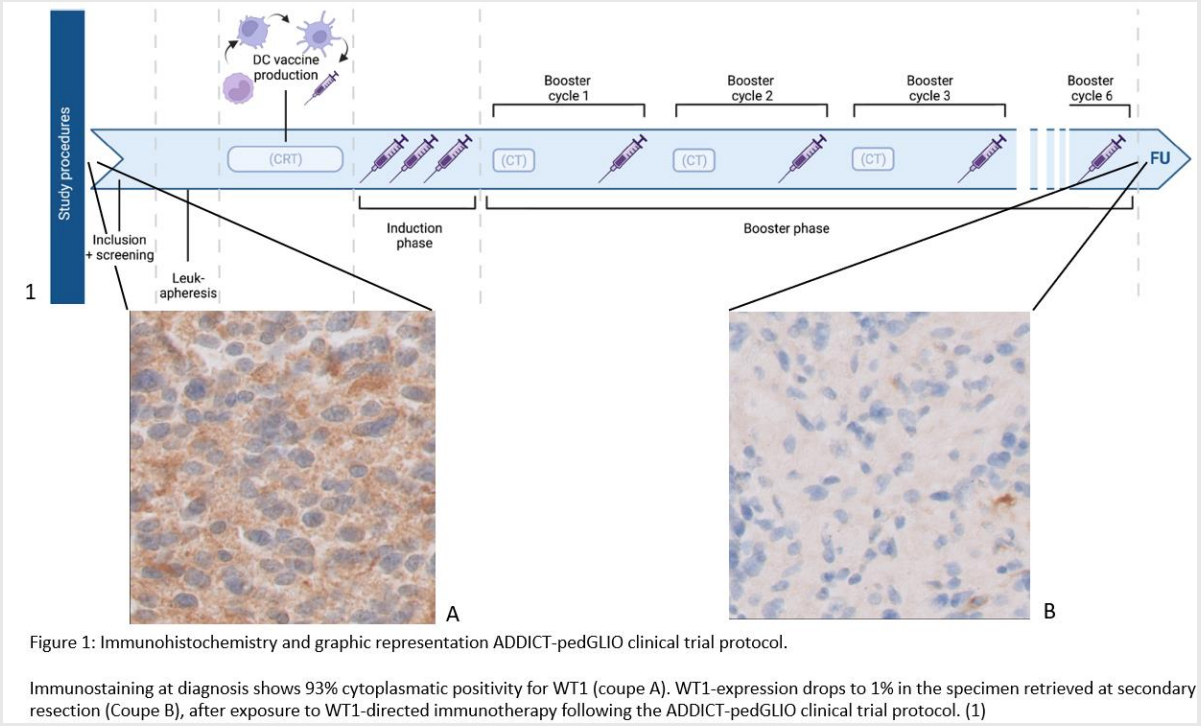


Figure 1: Immunohistochemistry and graphic representation ADDICT-pedGLIO clinical trial protocol.

Immunostaining at diagnosis shows 93% cytoplasmatic positivity for WT1 (coupe A). WT1-expression drops to 1% in the specimen retrieved at secondary resection (Coupe B), after exposure to WT1-directed immunotherapy following the ADDICT-pedGLIO clinical trial protocol. (1)

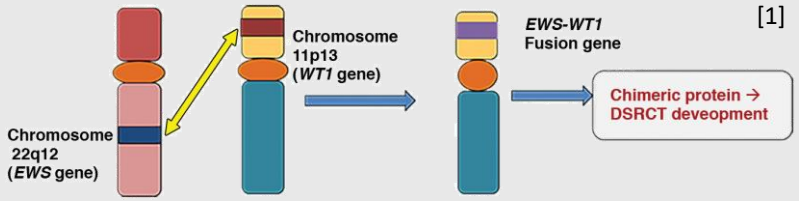
FIGURE 8. WT1 IMMUNOHISTOCHEMESTRY pedGLIO-009

Future research

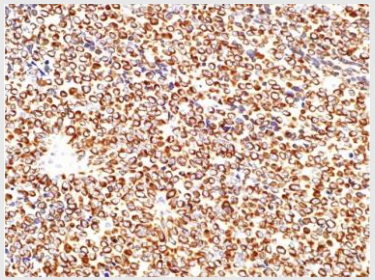
Immune-monitoring ADDICT-pedGLIO cohort

- Flow cytometry
- Functional assays
- RNA-sequencing
- Loss of antigen
- Radiological and clinical response evaluation

WT1/DC in Demoplastic Small Round Cell Tumor



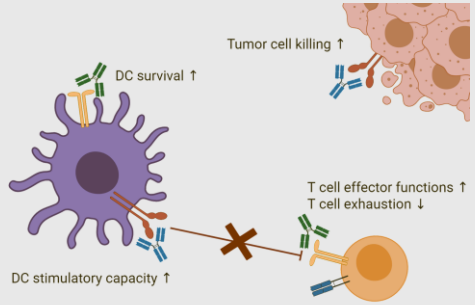
[1]



WT1 staining DSRCT

- I: < 0,1/1.000.000
- EWSR1-WT1 t(11;22) (p13:q12)
- OS: 15-25%, lower in metastazised disease
- Addition to SOC chemotherapy

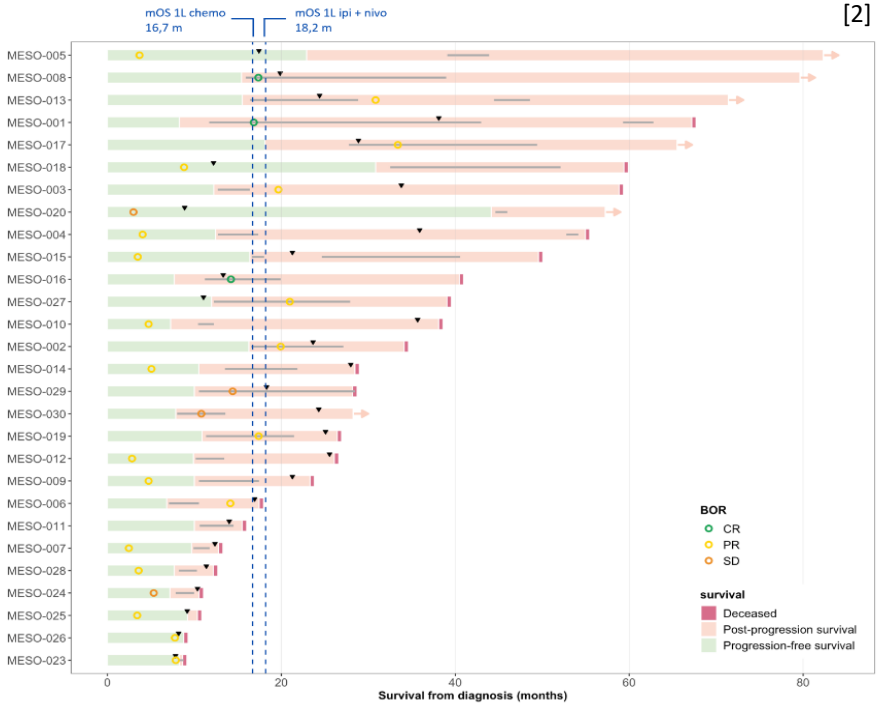
Combinational therapy: checkpoint inhibition



Addition of PD1-blockade in a WT1/DC vaccine treated Mesothelioma cohort

anti-PD-1/anti-PD-L1

[2]



[1] Morani et al. 2019
[2] Mesodec clinical trial UZA, unpublished

Thank you

patients and families

Pediatric Oncology UZA

Dr. Joris Verlooy
Prof. Dr. Koen Norga
Dr. Jaques Van Heerden
Renke Peeters
Lien Leyten

Anicells

Prof. Dr. Nathalie Cools
Bram Keymolen
Sam Vanleene
Linsey Claes
Jolien Van den Heuvel
Karen Segers
Julie Peeters

Nephrology, UZA

Prof. Dr. Marie-Madeleine Couttenye
Katrien Vandewalle
& colleagues

CCRG, UZA

Prof. Dr. Zwi Berneman
Prof. Dr. Sébastien Anguille
Eva Lion
Maxime De Laere
Barbara Stein
Griet Nijs
Kim Caluwaerts
Chantal Talboom
Sandy Van den Eynde
Michaël Vercauteren
Natacha Ottschytsch

Oncology, UZA

Katja Hazes
Caroline De Schepper

Anaesthesia, UZA

Dr. Sabine Maes
& colleagues

- Sponsors: