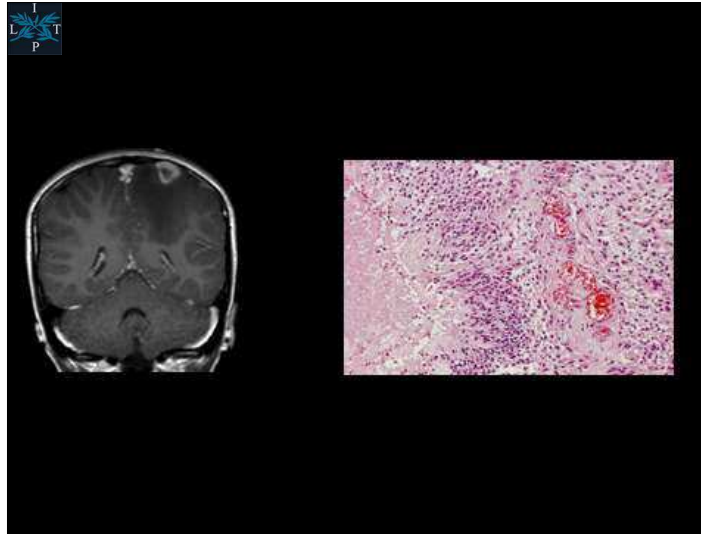
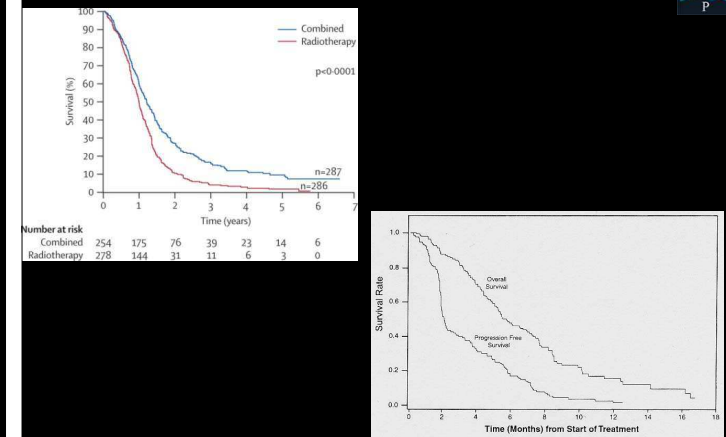


## Tumor vaccinatie

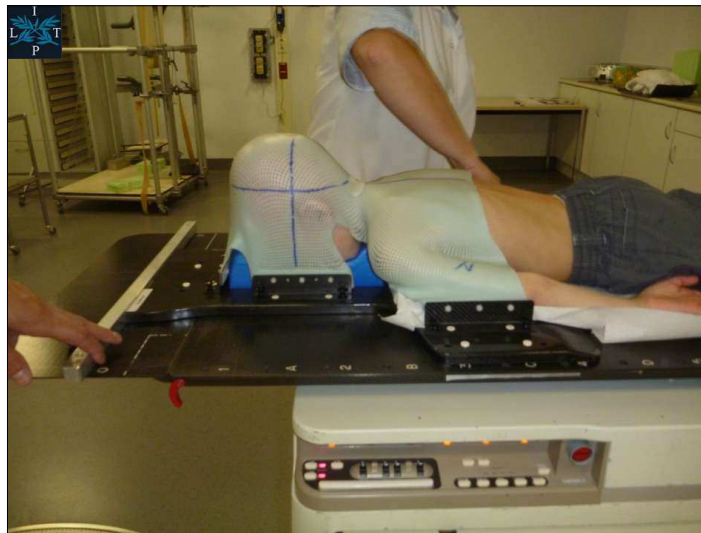
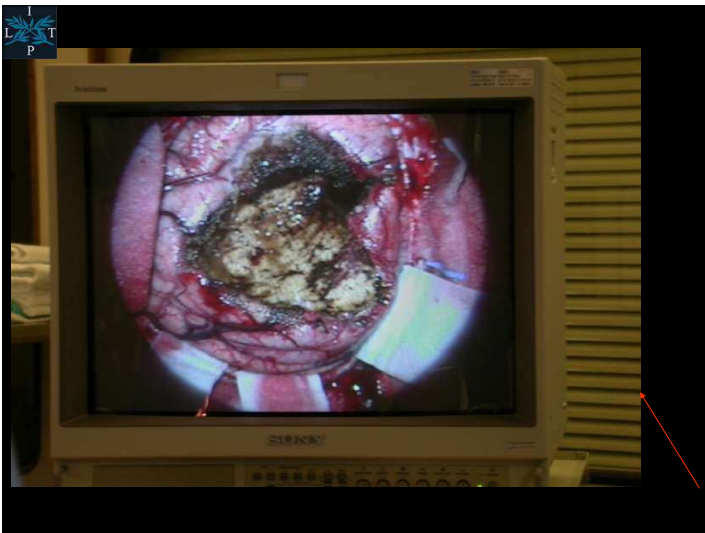
**Stefaan Van Gool, Steven De Vleeschouwer, Frank Van Calenbergh, (Chris Plets), Jan Goffin, (Martine Ade), Katja Vandenbrande, (Wim Maes), (Isabel Spencer), Dominique Bullens, Jan Ceuppens, Hilko Ardon, Goedele Stegen, Vallentina Chaiko, Tina Verschuere, Sofie Van Cauter, Pascal Cadot, (Elke Nackers), Anaïs Van Hoylandt, Carolien Koks, Lien Vandenberg, Femke Pauwels, Jeroen Plessers, Kelly Verstraete, Jochen Belmans, Melissa D'Hooghe**



Stupp R et al. Lancet Oncol 2009;10:459-466

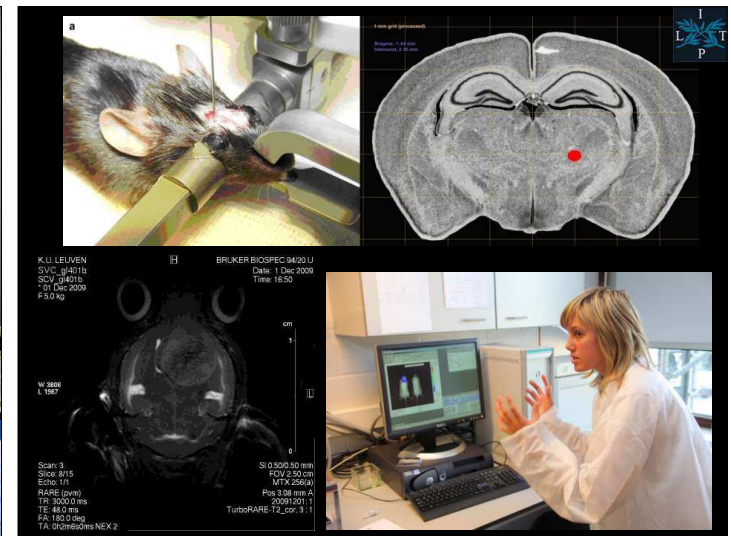
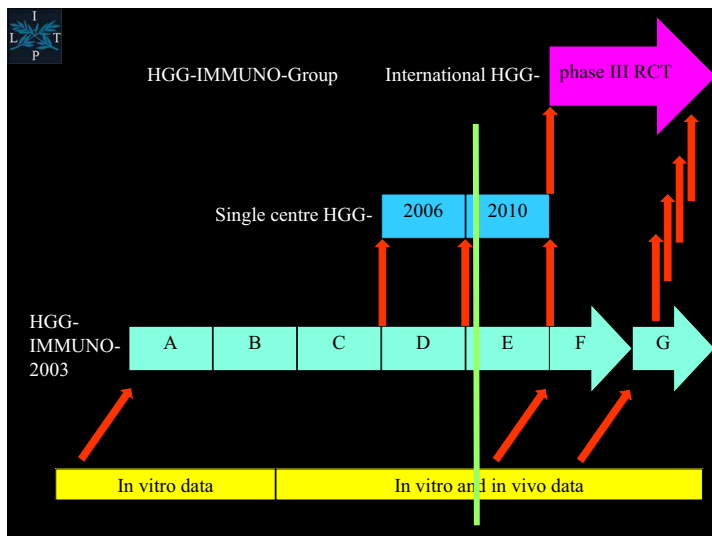
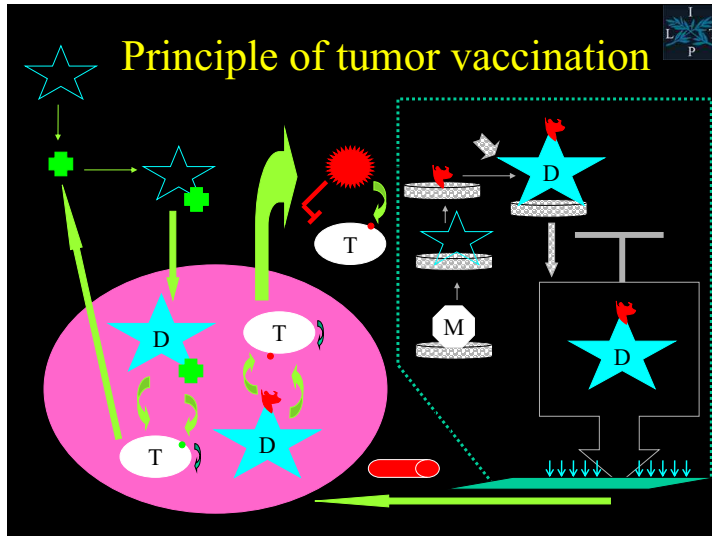


Brada et al. Annals of Oncology 2001;12:259-266

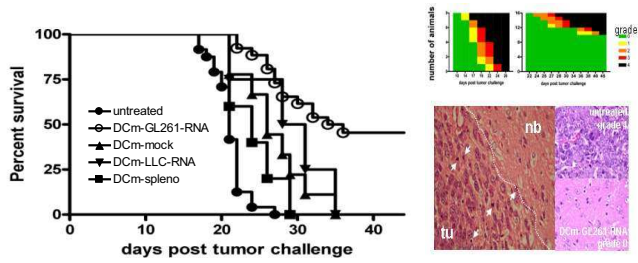


**Temodar**  
temozolomide  
Capsules

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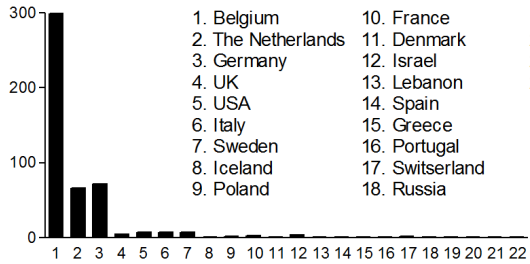
### Vaccination with RNA-loaded DC induces a protective antitumor immune response in vivo



Maes, et al. *J Neurooncol* 2009;91:127-39  
 Maes, et al. *Neuro-Oncol* 2009;11:529-542  
 Van Gool, et al. *Brain Pathol* 2009;19:694-712  
 Maes, et al. *Cancer Immunol Immunother* 2011;60:153-160

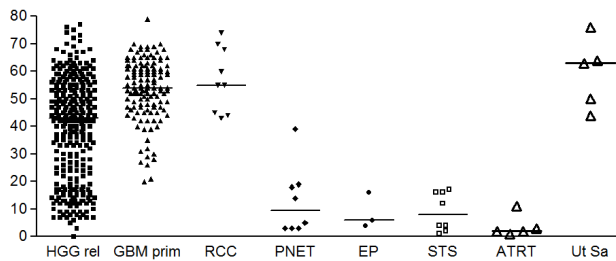
### Current research projects

- Knocking down galectin-1
- Knocking down IDO
- Immunotherapy + oncolytic virus therapy
- Nanoparticle loading
- Photo Dynamic Therapy

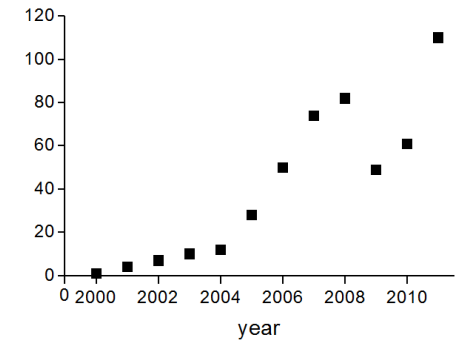


1. Belgium
2. The Netherlands
3. Germany
4. UK
5. USA
6. Italy
7. Sweden
8. Iceland
9. Poland
10. France
11. Denmark
12. Israel
13. Lebanon
14. Spain
15. Greece
16. Portugal
17. Switzerland
18. Russia
19. Croatia
20. Kazakhstan
21. Luxemburg
22. Mexico

### Diagnosis - Age: n = 485



### Number of HGG patients per year

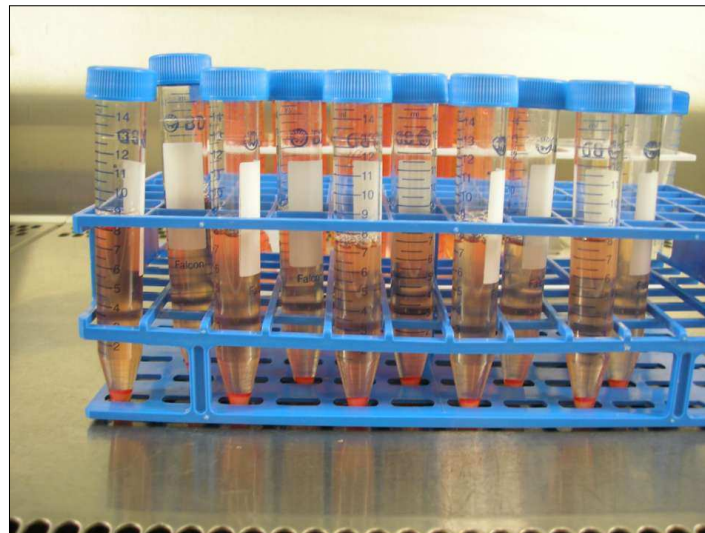


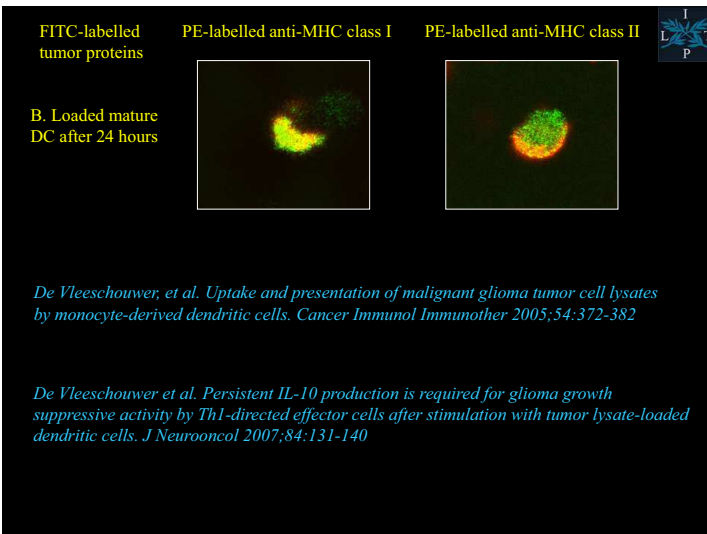
# HGG-IMMUNO-2003 Cohort comparison study Cohort A - E

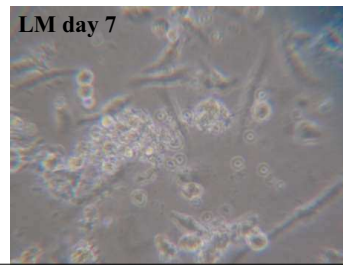
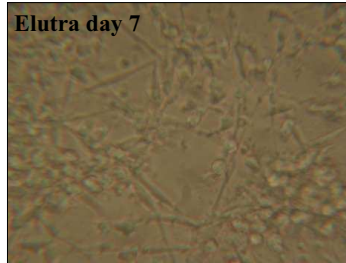
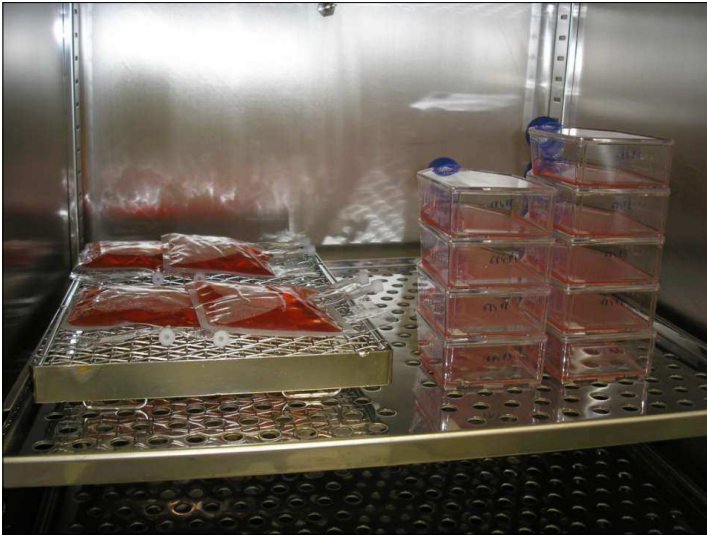
Surgery  
Immunotherapy

Vaccination in relapsed HGG patients: cohort comparison Trial

	induction vaccines	boost vaccines	DC maturation	adjuvants
<b>Cohort A</b>	DC week 1 and 3	DC monthly	TNFa, IL-1b, PGE2	none
<b>Cohort B</b>	DC week 1,3,5 and 7	DC monthly	TNFa, IL-1b, PGE2	none
<b>Cohort C</b>	DC week 1,2,3,4	Lysate monthly	TNFa, IL-1b, PGE2	none
<b>Cohort D</b>	DC week 1,2,3,4	Lysate monthly	TNFa, IL-1b	imiquimod
<b>Cohort E</b>	ElutraDC week 1,2,3,4	Lysate monthly	TNFa, IL-1b	Imiquimod



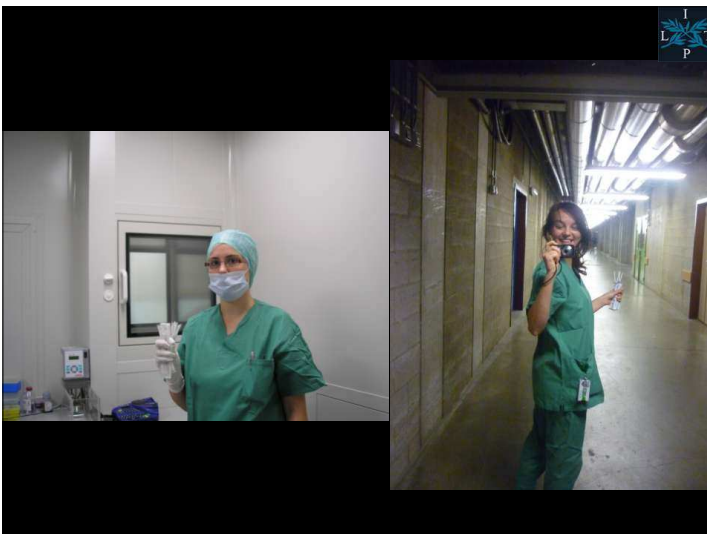




**V**iability  
**I**dentify  
**P**urity  
**P**otency  
**S**terility

Medicinal product: Dir 2001/83/EC, Dir 2004/27/EC  
 ATMP: defined in Part VI Annex I to Dir 2001/83/EC  
 Investigational ATMP: Clinical trials Dir 2001/20/EC  
 GCP Dir 2005/28/EC; all IMP in GMP  
 Non-commercial trials; member state authorisation

Regulation 2007/1394/EC; Hospital exemption; implicit no clinical trial  
 Dir 2004/23/EC includes Clinical trial material; member state; GTP



Relapsed GBM; Injection at 17-12-2003; still alive

**Inclusion criteria HGG-IMMUNO-2003 for Relapsed High Grade Glioma**

Age: > 3 years

recurrent diagnosis of high grade glioma (grade III or IV, or malignant progression of former low grade glioma), histologically proven

Total or subtotal resection of tumor mass, confirmed by assessment by the neurosurgeon and by postoperative MRI scan within 72 hours (-/+ Gd).

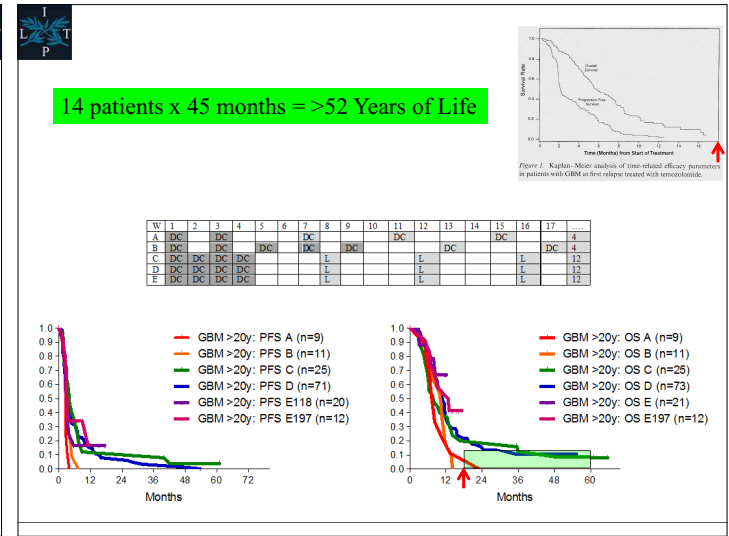
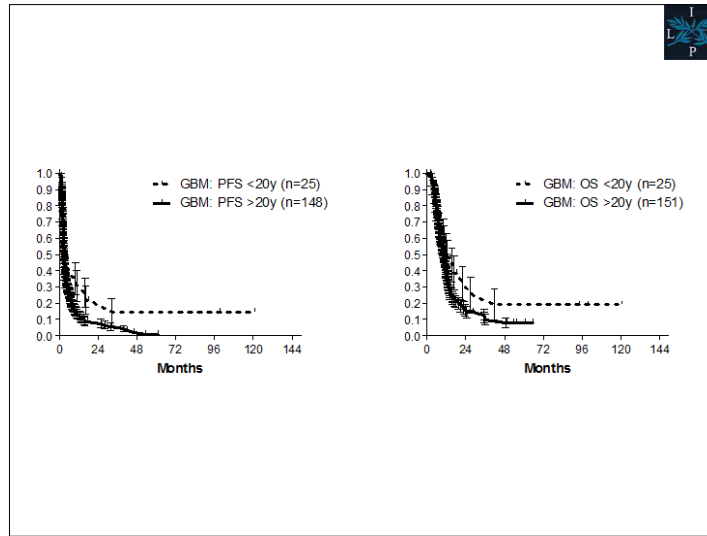
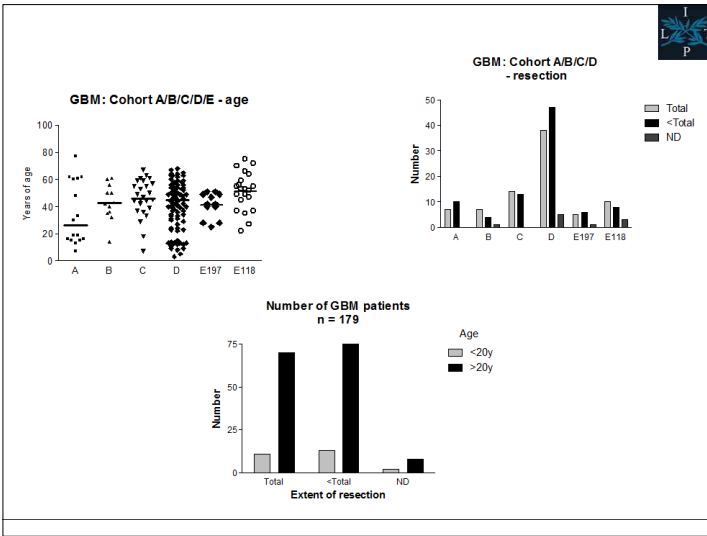
Availability of enough tumor tissue (<3cc), kept dry in a sterile vial at -80°C

Possibility to send the sterile tumor specimen on enough dry ice to the vaccination center (Leuven).

Perioperative administration of corticosteroids tapered within 7 days postoperatively: no ongoing need for steroids.

“estimated” life expectancy > 3 months

Informed consent by patient



**HGG-2006**

Surgery  
Leukapheresis  
Radiochemotherapy  
4 weekly DC-HGG-L  
Maintenance chemotherapy + HGG-L

**Inclusion criteria HGG-2006**

Age: > 18 years and < 70 years

First diagnosis of high grade glioma (glioblastoma multiforme WHO grade IV), histologically proven

Diagnosis confirmed by the reference pathology

Total or subtotal resection of tumor mass (<2 cc), confirmed by assessment by the neurosurgeon and by postoperative MRI scan within 72 hours.

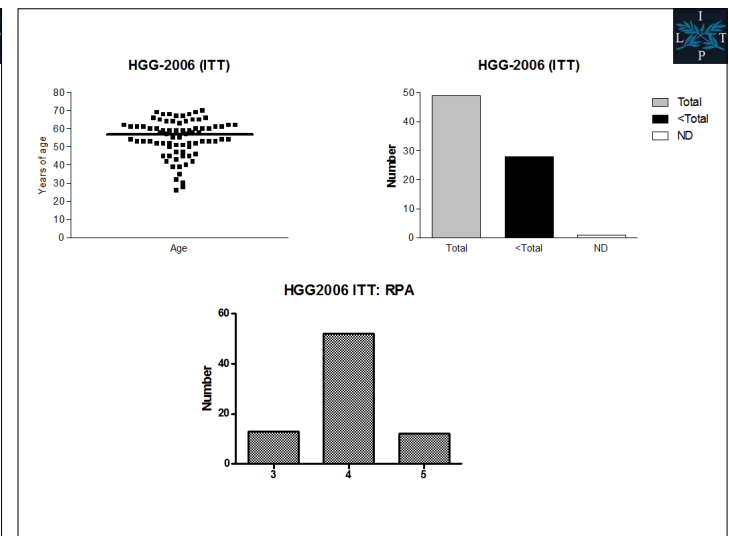
Availability of enough tumor tissue, kept dry in a sterile vial at -80°C

Postoperative radiological assessment by the reference radiology

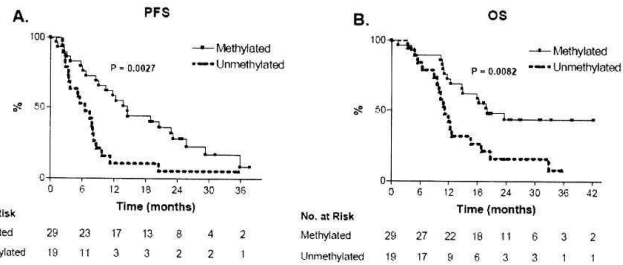
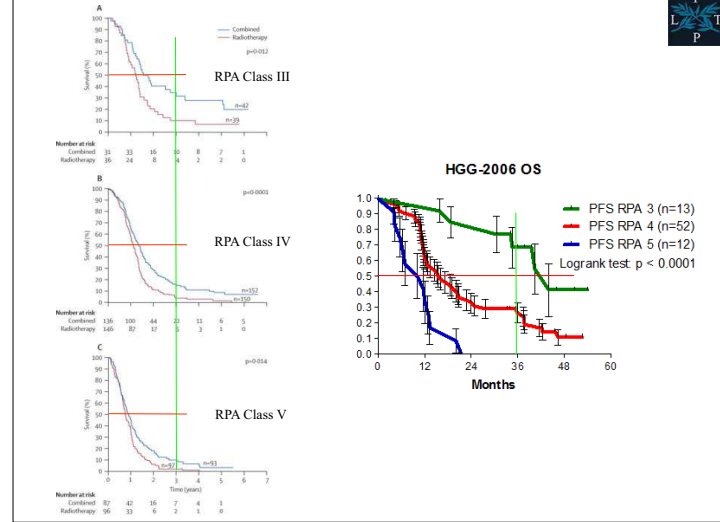
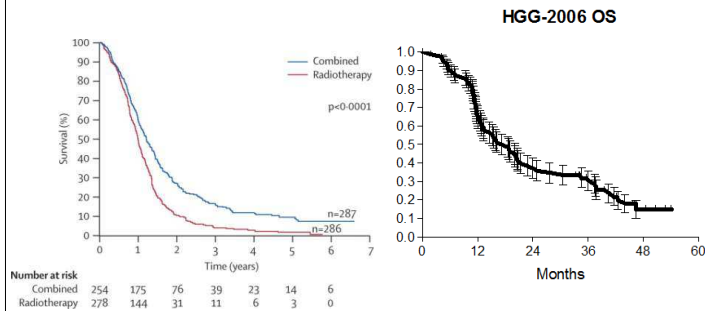
Perioperative administration of corticosteroids tapered within 5 days postoperatively

Life expectancy > 3 months

Informed consent by patient



Adverse Events	No. of patients	Grade according to NCI CTCAE (version 3.0)
Fatigue	34	I
General rash/itching	4	I
Shoulder pain	2	I
Anorexia	2	I
Myalgia	1	I
Nausea / vomitus	11	I-II
Memory impairment	5	I-III
Epileptic seizure	13	II
Confusion	3	II
Humeral fracture	3	II
Lethargy	2	II
Bleeding (ectopic cerebral lesion)	1	II
Depression	1	II
Dysphasia	1	II
Oesophagitis	1	II
Otitis media serosa	1	II
Epileptic seizures	5	III
Allergic reaction on TMZ	1	III
Cerebral abscess (surgery required)	1	III
DVT	1	III
Hydrocephalus (surgery required)	1	III
Ischemic bowel perforation	1	III
Lung- and peripheral edema	1	III
Osteoporotic D10 fracture	1	III
Dementia (Alzheimer)	1	III-IV
Focal status epilepticus	2	IV
Ischemic stroke (full recovery)	1	IV
Status epilepticus	2	IV
Overwhelming infection	1	V
<b>Hematotoxicity</b>		
lymphopenia	17	I
leukopenia	16	I
lymphopenia	7	II
leukopenia	5	II
lymphopenia	12	III
thrombopenia	2	III
leukopenia	1	III
thrombopenia	3	IV
lymphopenia	1	IV

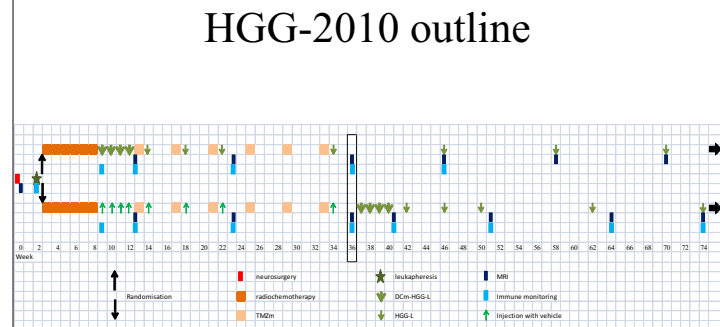


**HGG-2010**

Surgery  
 Leukapheresis  
 Radiochemotherapy

Ⓜ 4 weekly DC-HGG-L

Maintenance chemotherapy + Ⓜ HGG-L



**Inclusion criteria HGG-2010**

Age: > 18 years and < 70 years

First diagnosis of high grade glioma (glioblastoma multiforme WHO grade IV), histologically proven

Diagnosis confirmed by the reference pathology

Total or subtotal resection of tumor mass (<2 cc), confirmed by assessment by the neurosurgeon and by postoperative MRI scan within 72 hours.

Availability of enough tumor tissue, kept dry in a sterile vial at -80°C

Postoperative radiological assessment by the reference radiology

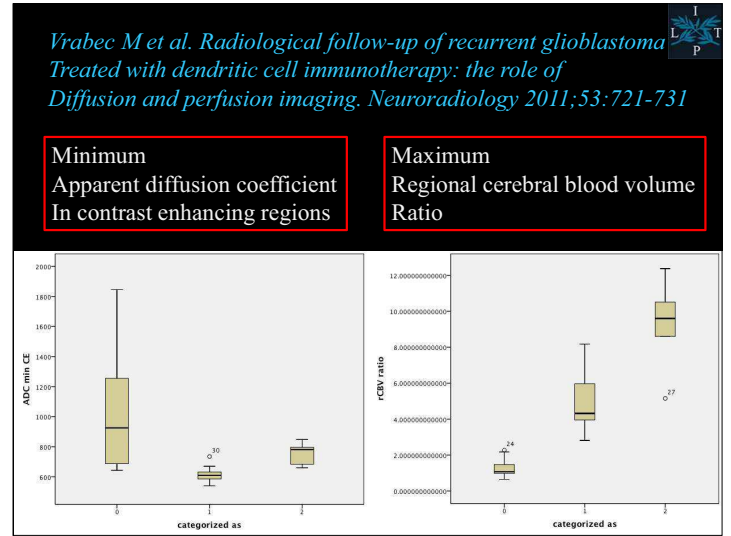
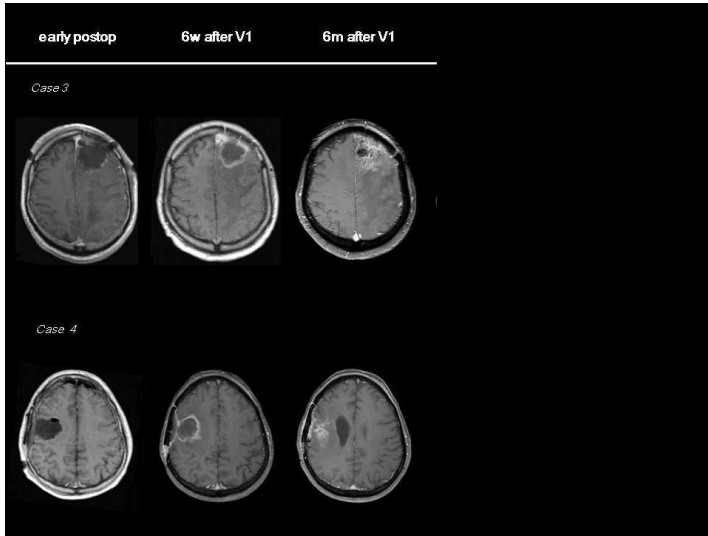
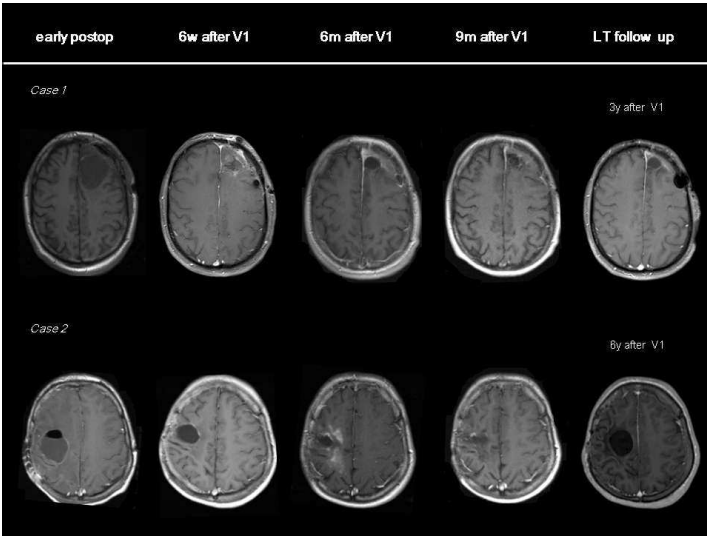
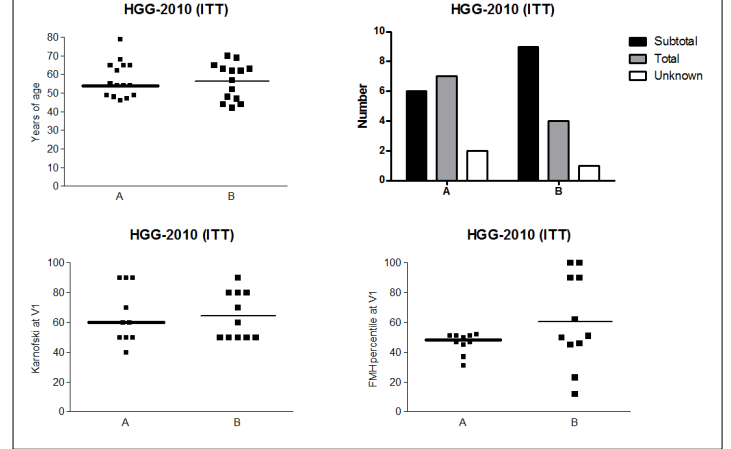
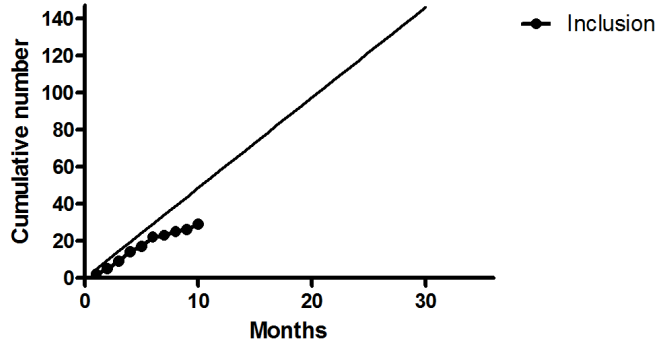
Perioperative administration of corticosteroids tapered within 5 days postoperatively

Life expectancy > 3 months

Informed consent by patient



**HGG2010 inclusion rate**



## Ongoing trials in Leuven:

- **HGG-IMMUNO-2003:** cohort E: towards GMP-DCm-HGG-L
- **HGG-IMMUNO-2003:** cohort D: Leuven method if needed (e.g. children)
- **HGG-2010:** single centre double blind placebo-controlled phase IIb randomised clinical trial

## immunotherapyplatformleuven

www.itpl.be

Other types of cancer:  
 \* WT1+ uterine tumors  
 \* ? RCC ?  
 \* ? pancreatic cancer ?

HGG-IMMUNO-Group  
 \* Global clinical strategies  
 \* Methodologies and SOPs  
 \* Science/economics

## 'Mijn ziekte heeft rust gebracht'



Remco heeft een hersentumor  
**De huisarts vroeg wat ik nog heel graag wilde doen. Ik zei: 'Nijs, ik wil mijn oude leven terug'**

Kan ik in een van andere mensen krijgen...  
 Het was een jongen van 34 jaar en twee keer geopereerd aan een kwaadaardige hersentumor. Volgens de arts in Nefertiti...  
 Het is een wonder van kennis van...  
 Het was een jongen van 34 jaar en twee keer geopereerd aan een kwaadaardige hersentumor. Volgens de arts in Nefertiti...  
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 Het is een wonder van kennis van...

Flair, the Netherlands, Nr. 48 23 nov. t/m 2 dec. 2007

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  - CAF, Baxter, Schering-Plough
  - Private families
  - Service Clubs
  - Belgian Federation Against Cancer
  - Actie zware apparatuur Van Mechelen
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  - Fund for Scientific Research – Flanders
  - IWT: TBM program



24 October 2011