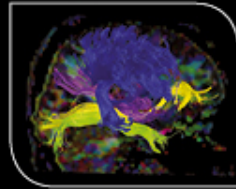




SOCIÉTÉ FRANÇAISE DE NEURORADIOLOGIE



du **30 mars** au **1^{er} avril 2016**

Novotel Paris Tour Eiffel

Président du congrès : Pr François Cotton

Président de la SFNR : Pr Alexandre Krainik

43^{ème} CONGRÈS ANNUEL de la Société
Française de NeuroRadiologie

Marqueurs tumoraux des gliomes

Marc SANSON

Neurologie 2 &

Institut du Cerveau et de la Moelle (ICM)

GH Pitié-Salpêtrière

www.sfnrcongres.net

43^{ème} CONGRÈS ANNUEL
de la Société Française
de NeuroRadiologie



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Novotel Paris Tour Eiffel

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Conflit d'intérêt

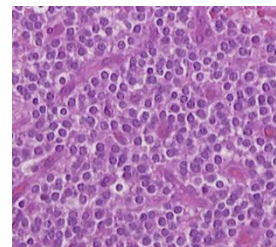
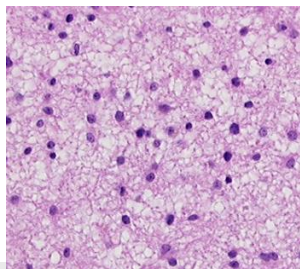
Nom de l'orateur: Marc SANSON

.....

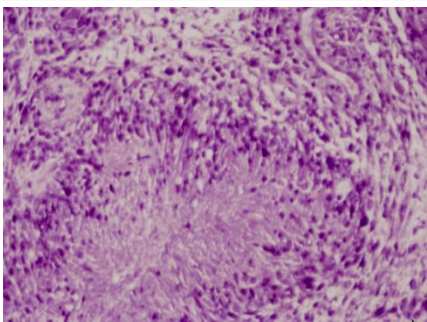
Je n'ai aucun conflit d'intérêt

Classification of gliomas

30% of discrepancy in diagnosis

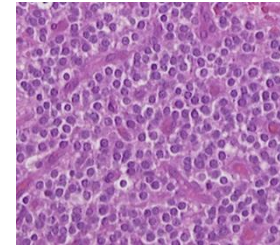
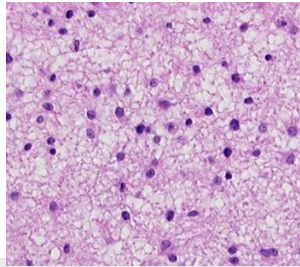


Grade	Astrocytic	Mixed	Oligodendroglial	Survival
Grade I	Pilocytic Astro			>20 y
Grade II	Low grade Astro	Low grade Oligoastro	Low grade Oligo	5-20 y
Grade III	Anaplastic Astro	Anaplastic Oligoastro	Anaplastic Oligo	2-15 y
Grade IV	Glioblastoma			1-2 y

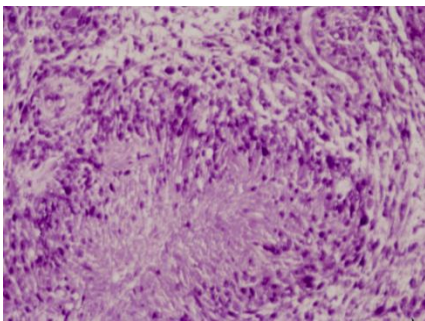


Classification of gliomas

30% of discrepancy in diagnosis

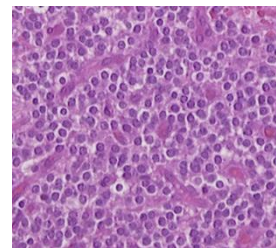
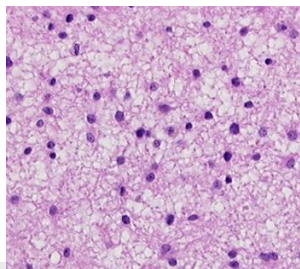


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Grade IV	Glioblastoma			1-2 y



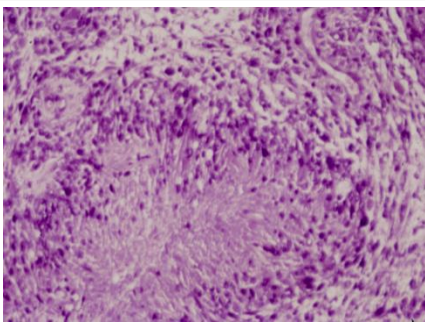
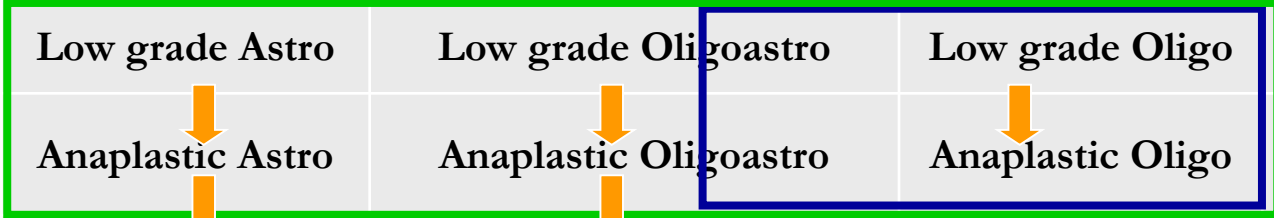
Classification of gliomas

30% of discrepancy in diagnosis



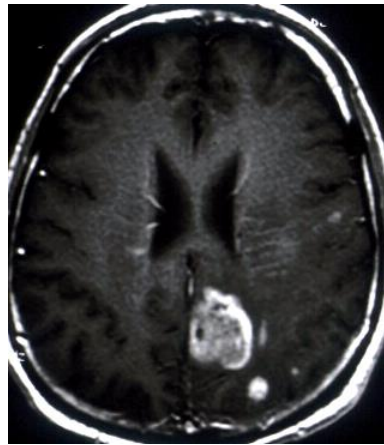
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IDH

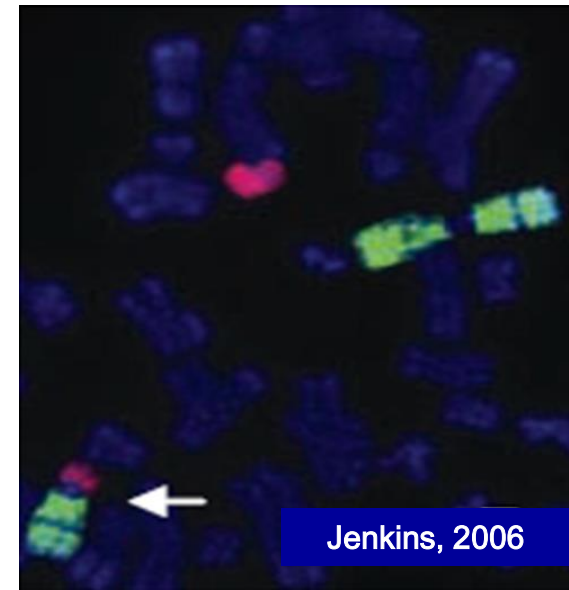
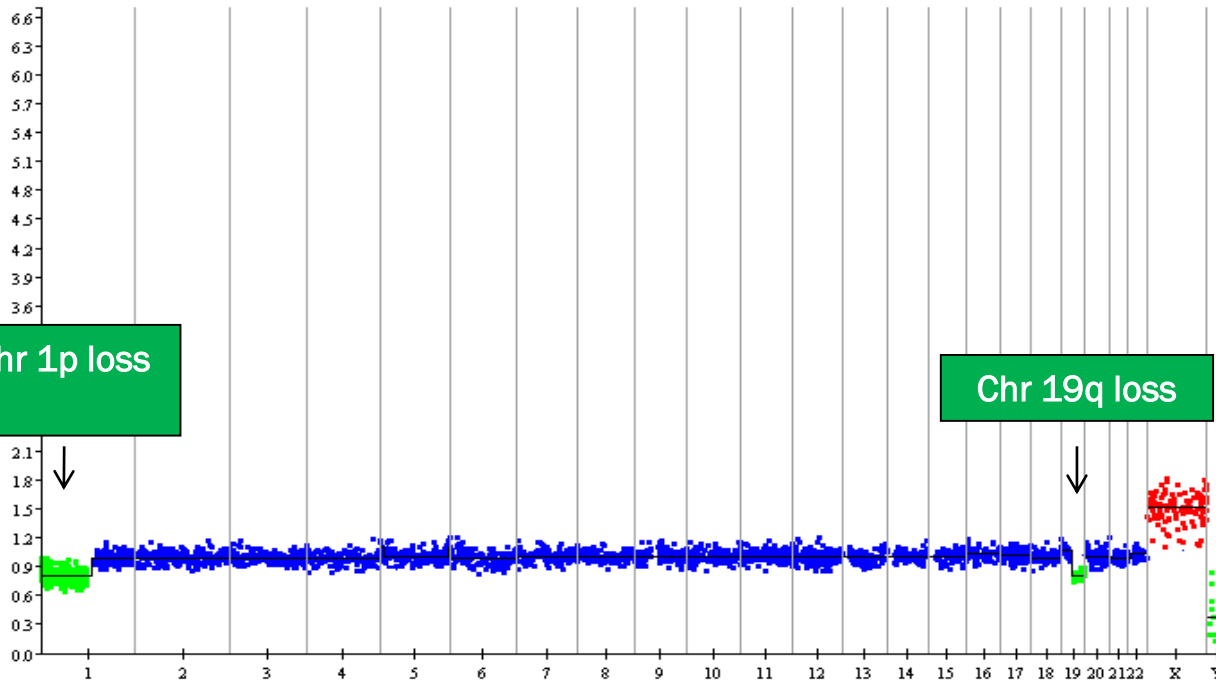
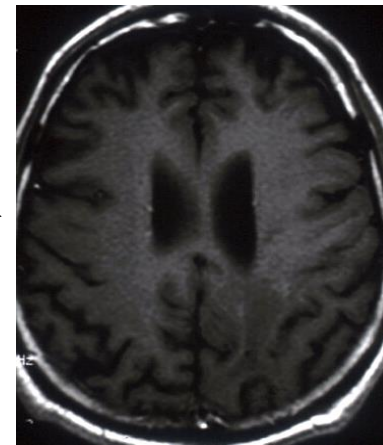


1p19q
codeletion

anaplastic oligodendroglioma



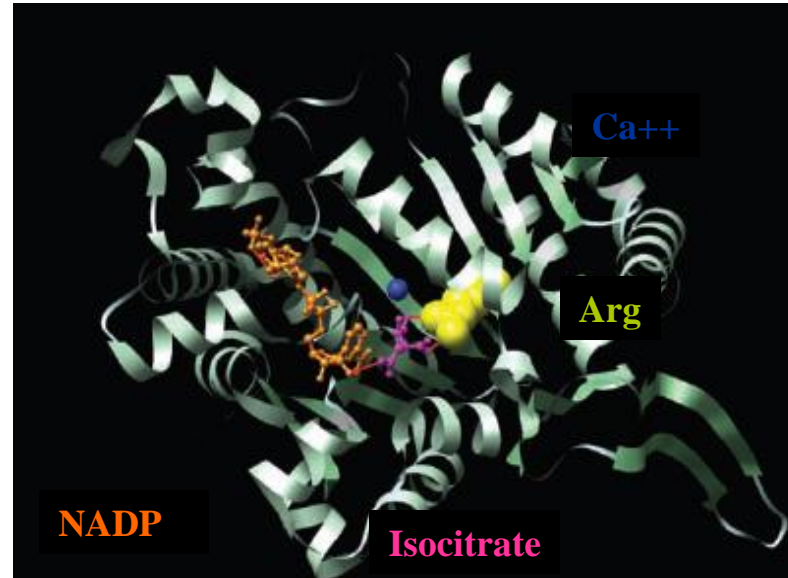
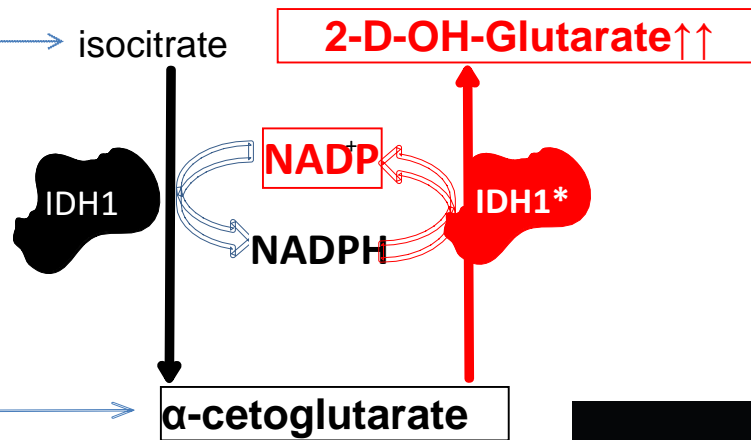
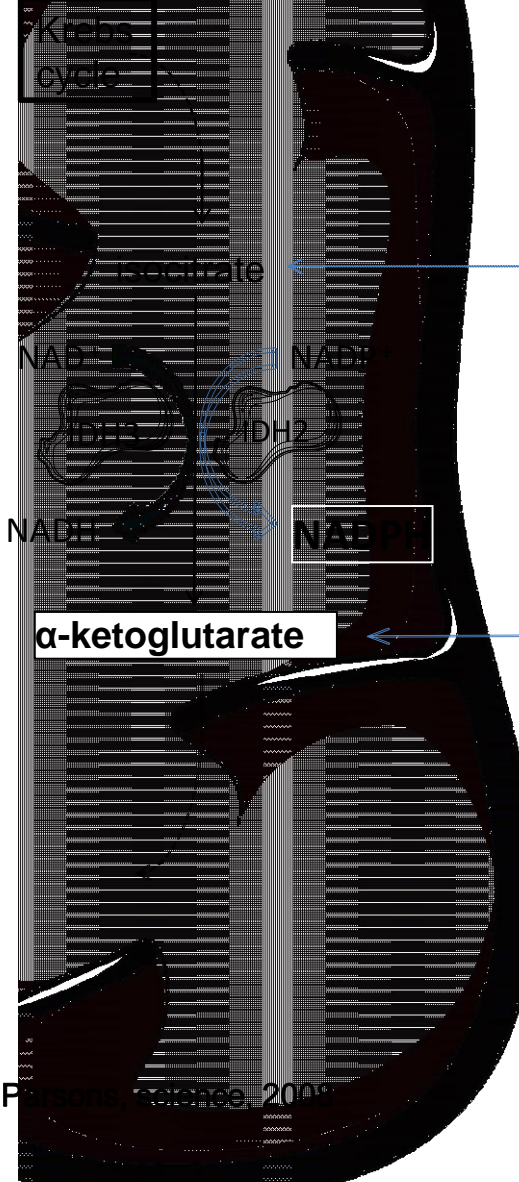
2 cycles
chemotherapy



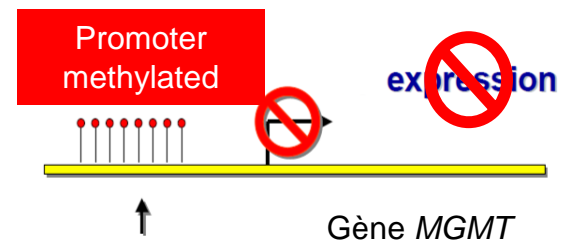
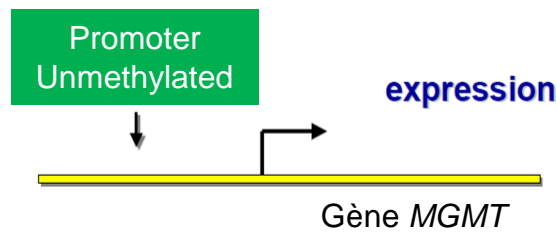
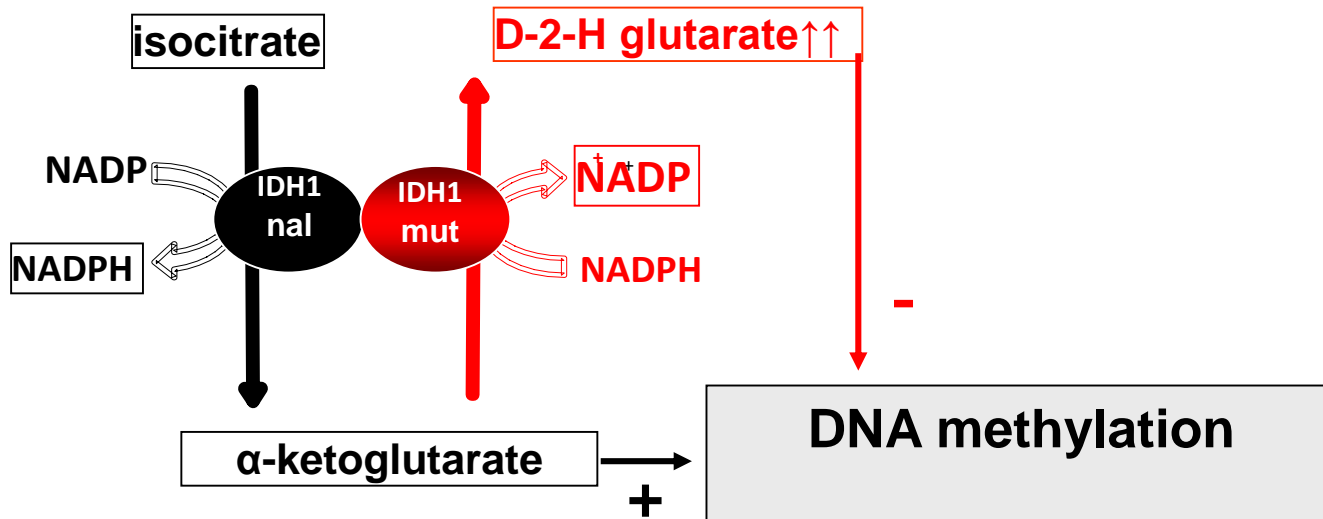
Cytoplasm

Cancer-associated IDH1 mutations produce 2-hydroxyglutarate

Lenny Dang¹, David W. White¹, Stefan Gross¹, Bryson D. Bennett², Mark A. Bittinger¹, Edward M. Driggers¹, Valeria R. Fantin¹, Hyun Gyung Jang¹, Shengfang Jin¹, Marie C. Keenan¹, Kevin M. Marks¹, Robert M. Prins³, Patrick S. Ward⁴, Katharine E. Yen¹, Linda M. Liao³, Joshua D. Rabinowitz², Lewis C. Cantley⁵, Craig B. Thompson⁴, Matthew G. Vander Heiden¹† & Shinsan M. Su¹



IDH mutated gliomas: D2HG, an « oncometabolite »



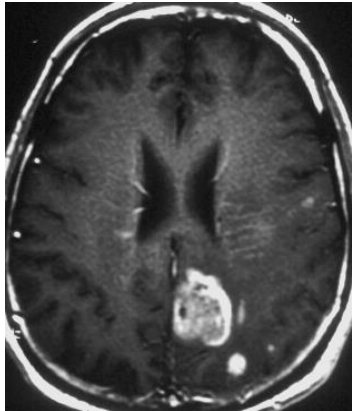
La mutation IDH est un facteur pronostique majeur, quel que soit le grade



Oligo II

Mixed II

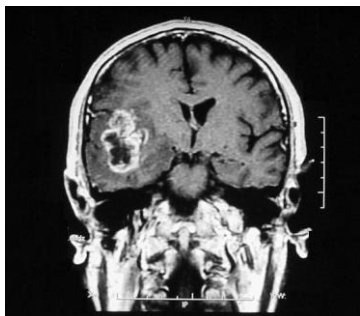
Astro II



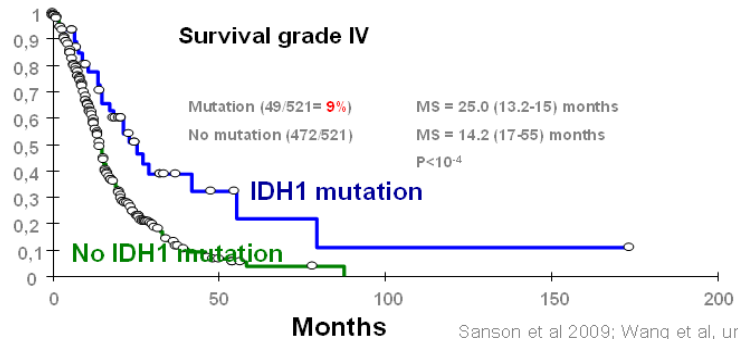
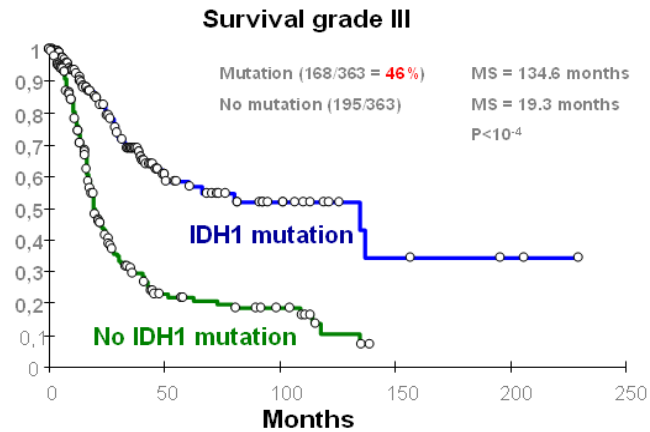
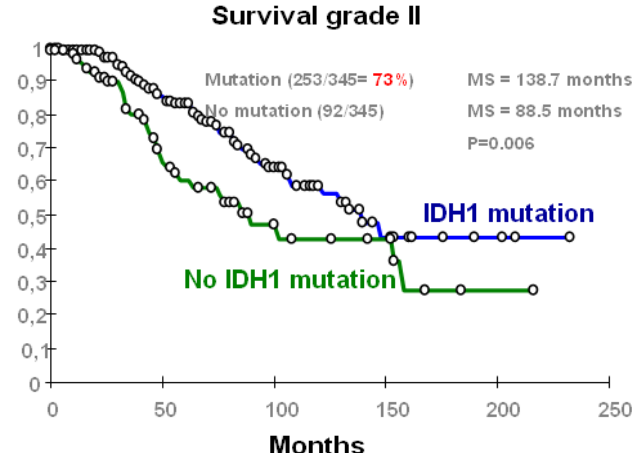
Oligo III

Mixed III

Astro III



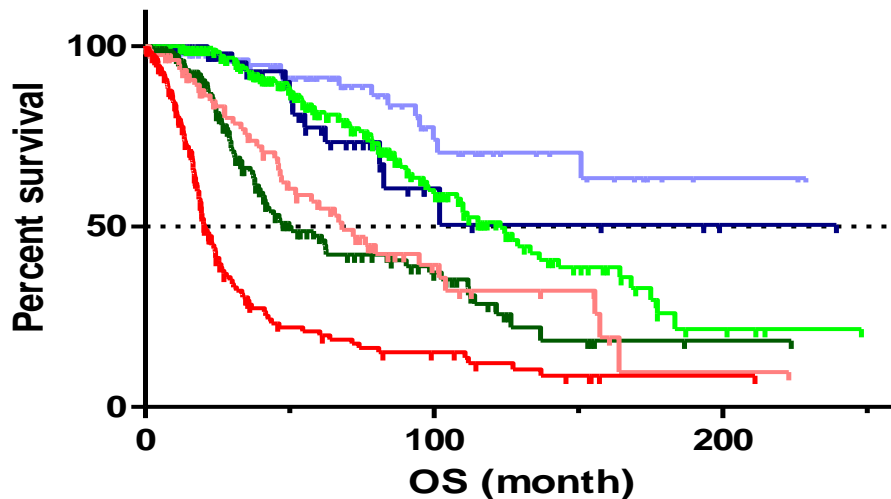
GBM



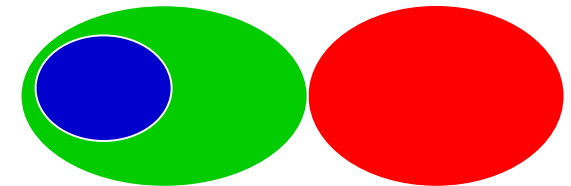
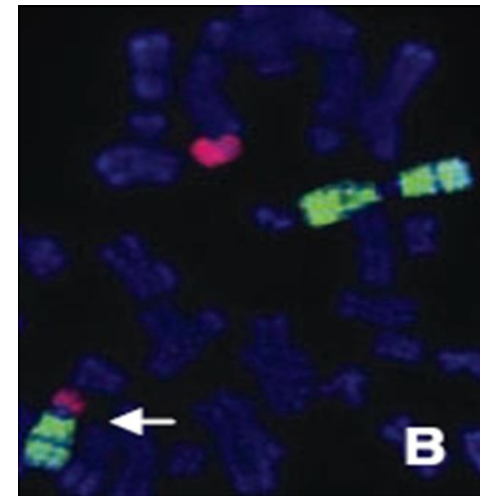
Tous les gliomes avec codéletion 1p19q
sont mutés sur IDH1 ou IDH2

3 catégories pronostiques

Overall survival grade II and III gliomas

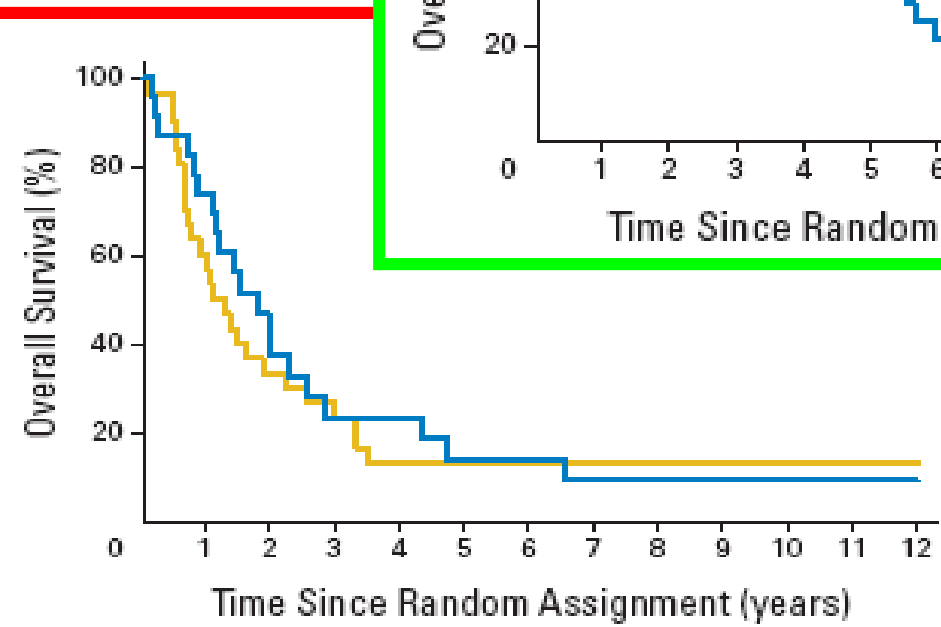
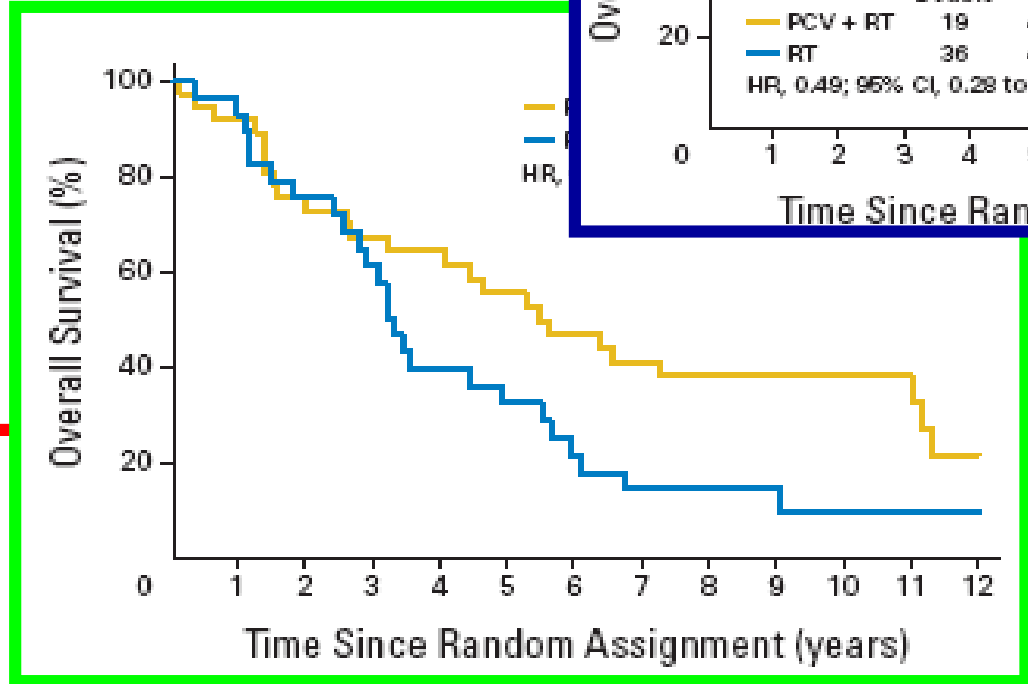
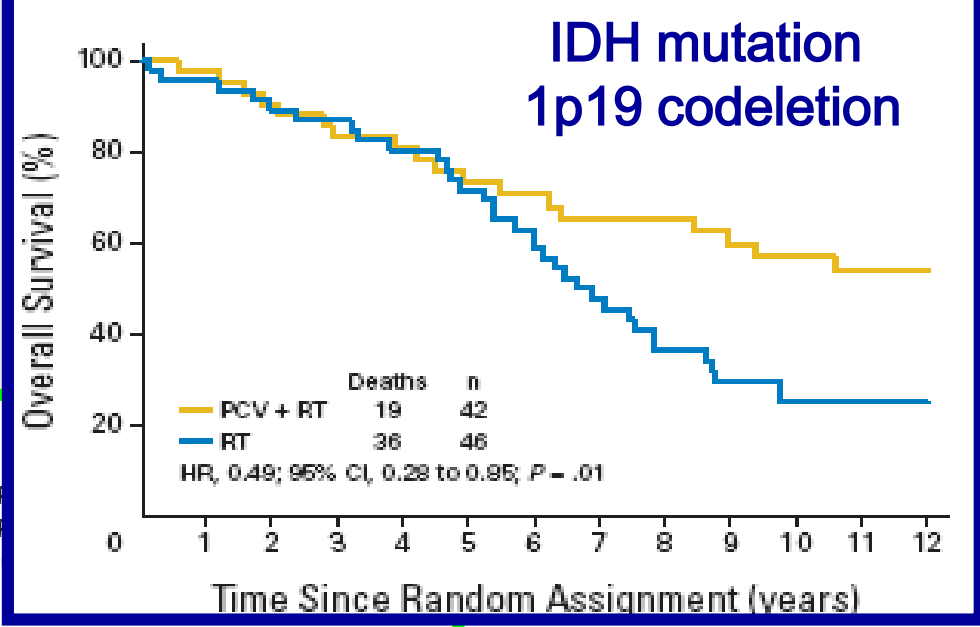


- Codel II n=89
 - Codel III n=96
 - IDHmut non-codel II n=208
 - IDHmut non-codel III n=166
 - IDHwt II n=81
 - IDHwt III n=169
- $p=0.13$
- *** $p<0.001$
- *** $p<0.001$



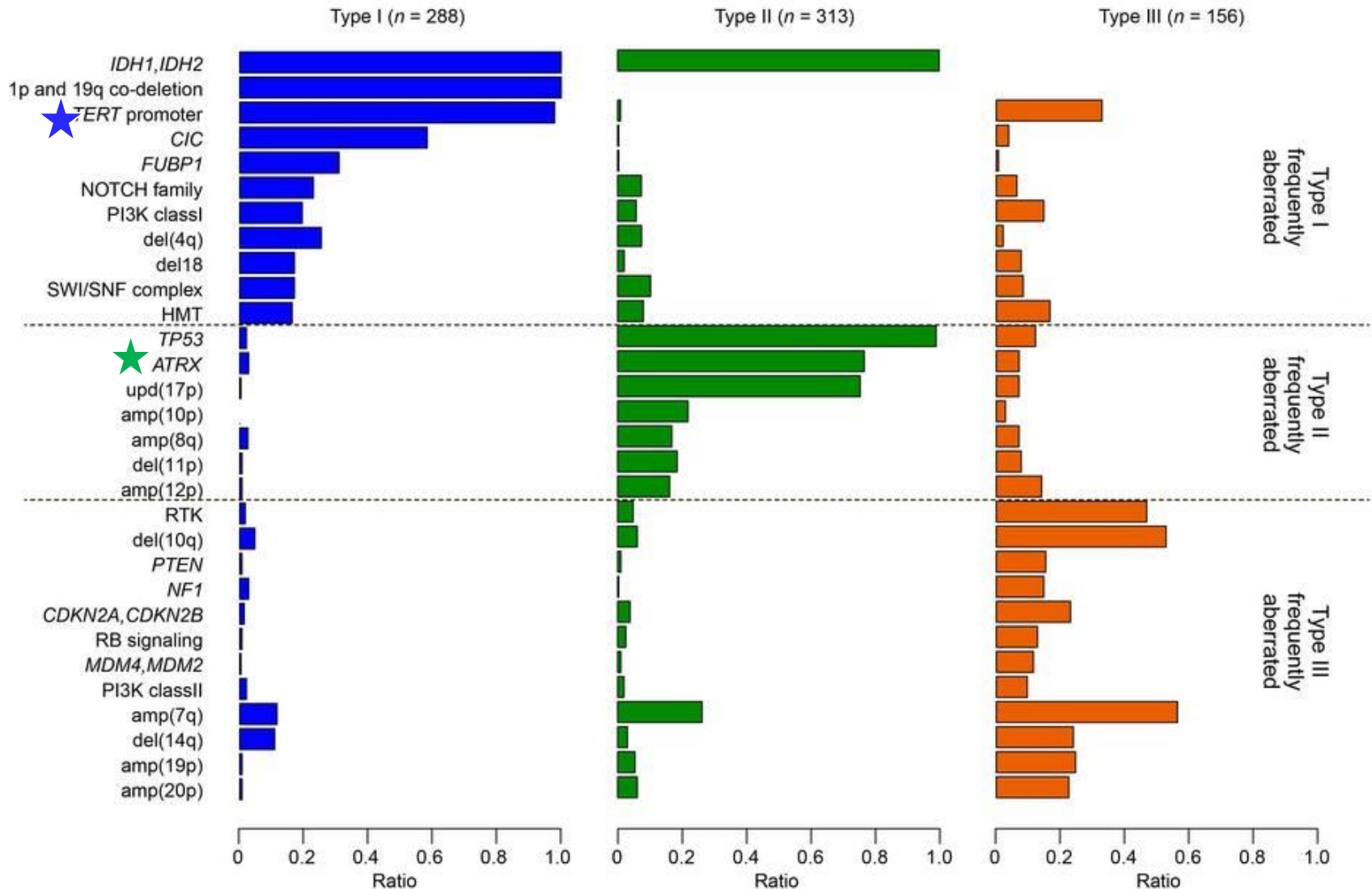
- 1p19q codeletion and IDH mutation
- Only IDH mutation
- None of these alterations

IDH and 1p19q status
predict
the benefit of adjuvant
chemotherapy



Cairncross 2013-2014, RTOG 9402
Van den Bent 2013, EORTC 26951

Whole exome sequencing

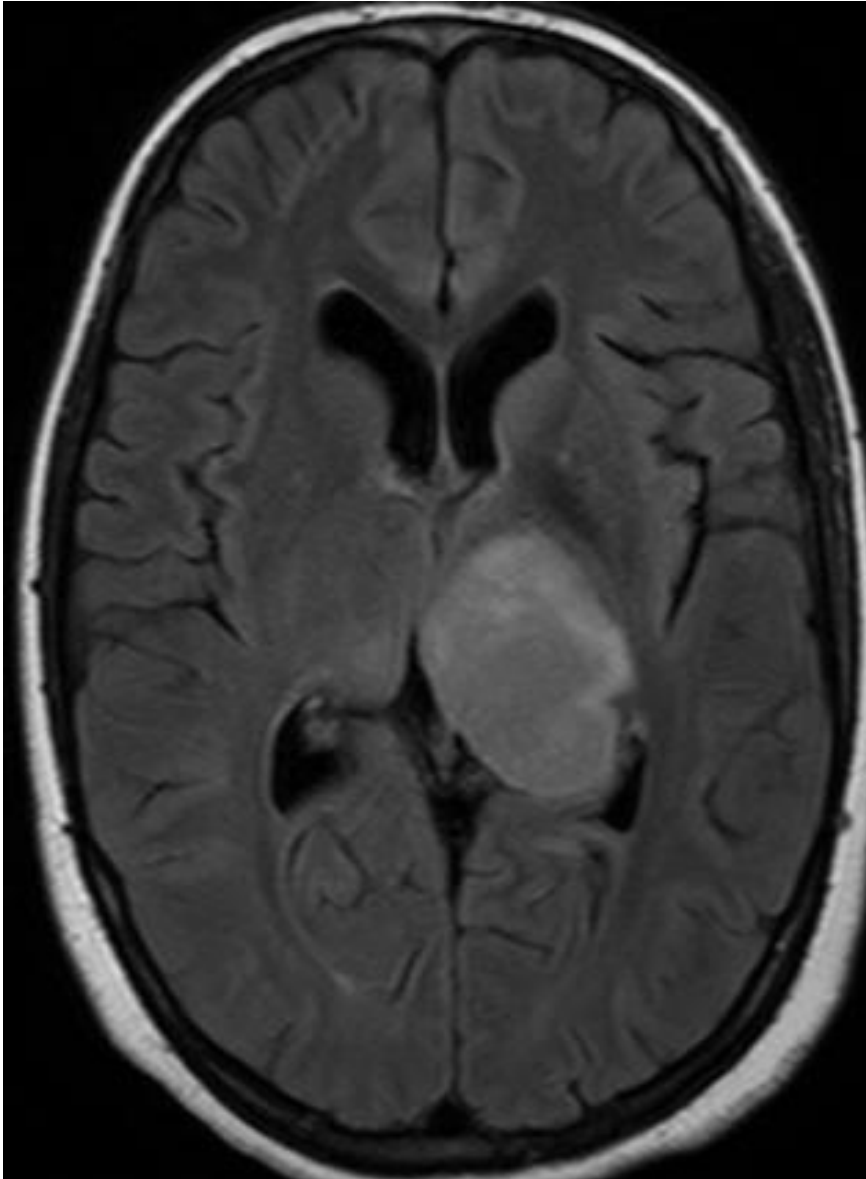


A simple, prognostic classification of the main molecular gliomas entities

IDH	Mutated		Non mutated	
Telomere maintenance	hTERT promoter mutation	ATRX mutation ALT (alternative lengthening telomeres)	ATRX mutation	hTERT promoter mutation
Other frequent alterations	1p19q codeletion	TP53 mut	Histone genes mutations	<i>Gene amplif (EGFR)</i>
Predominant histology	Oligo	Astro	"Molecular Glioblastoma »	
Median Survival	>15 y	6-7 y	1.5-2 y	

Mutation H3.3 K27M

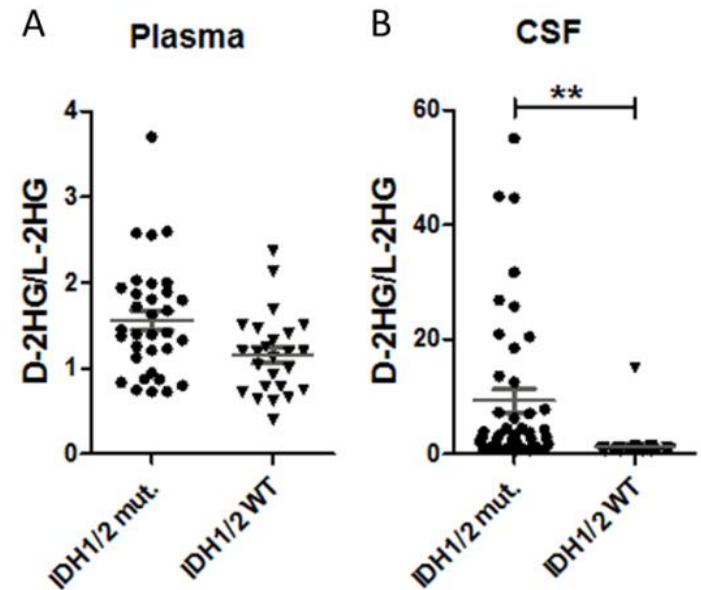
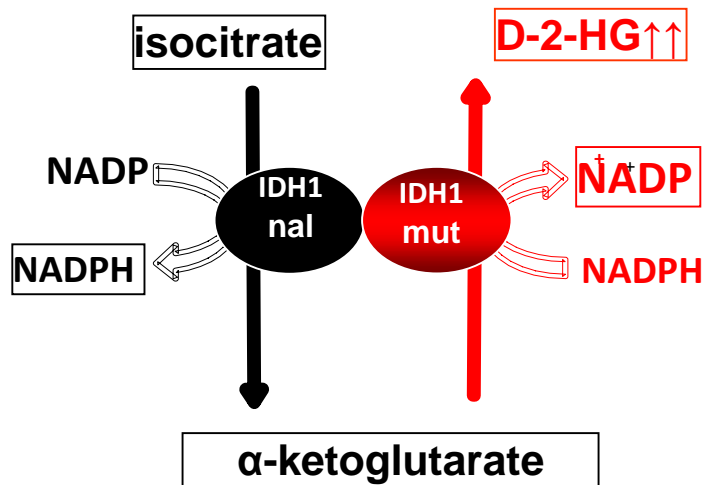
=Caractéristique des gliomes de la ligne médiane



Non mutated	
ATRX mutation	hTERT promoter mutation
Histone genes mutations	Gene amplif (EGFR)
«Molecular Glioblastoma »	
1.5-2 y	

Non invasive determination of IDH1 status

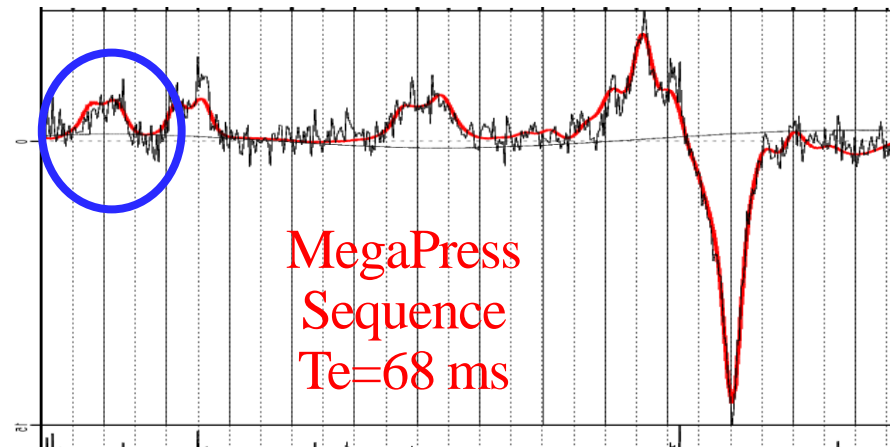
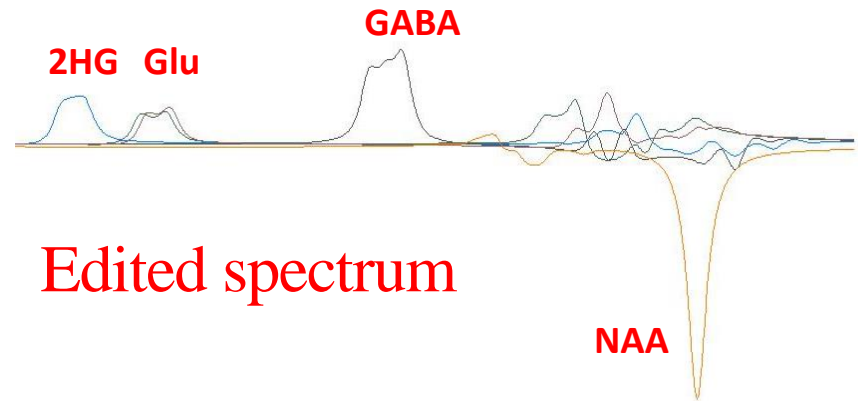
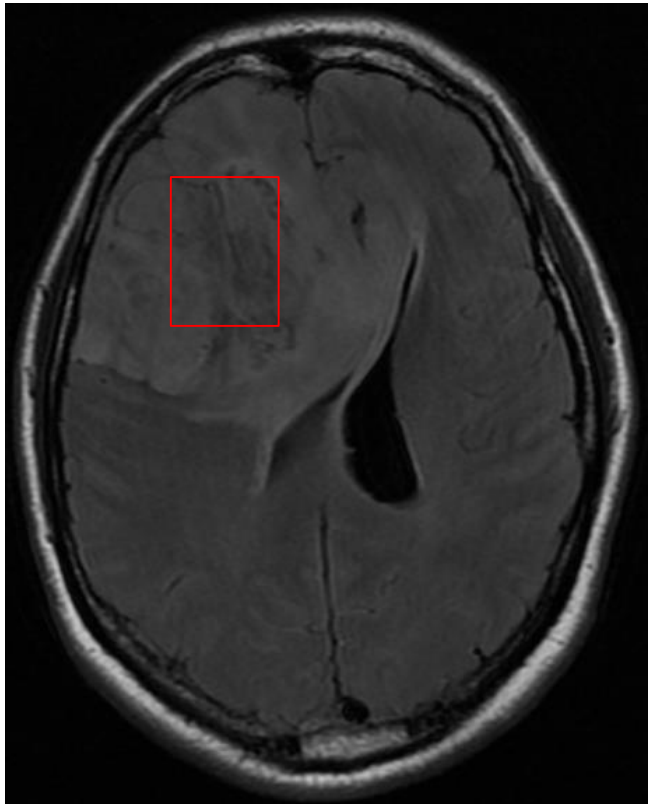
Detection of D-HG in biological fluids



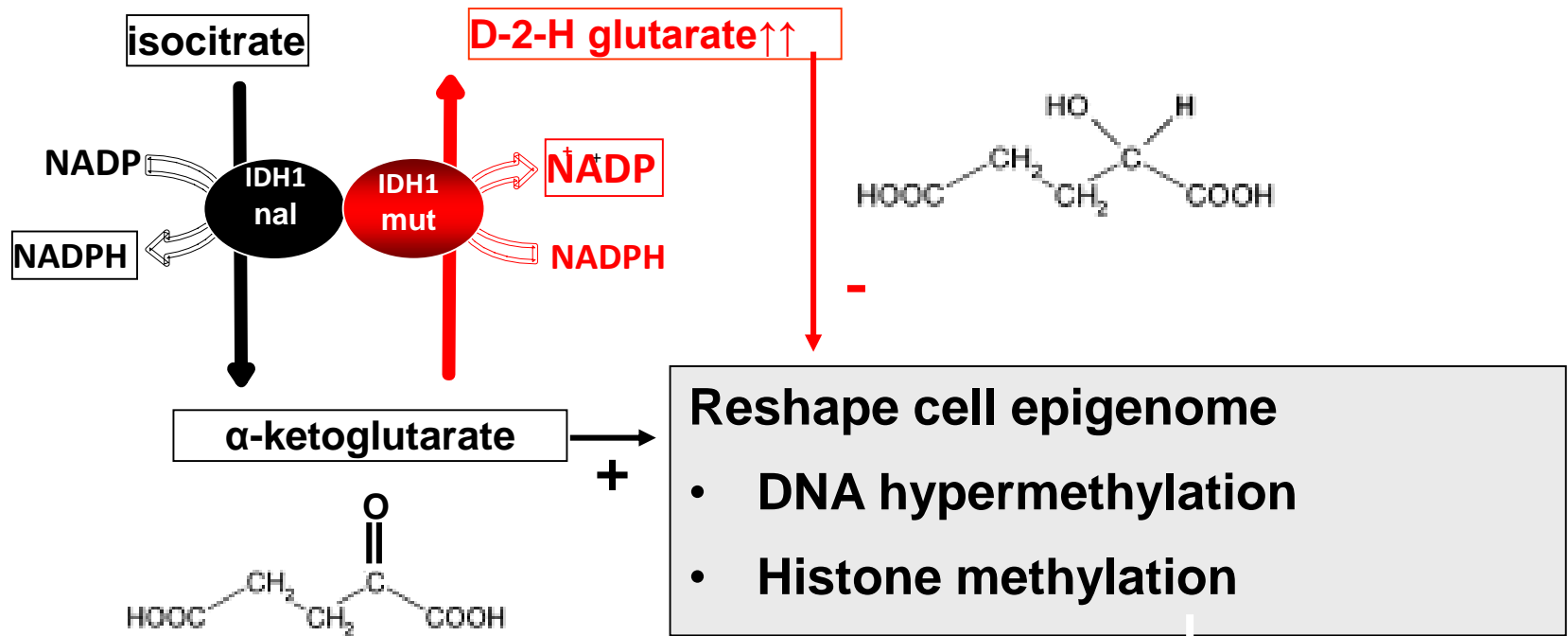


Non invasive determination of IDH1 status

Detection of D-HG by spectro-MRI



Thérapies personnalisées

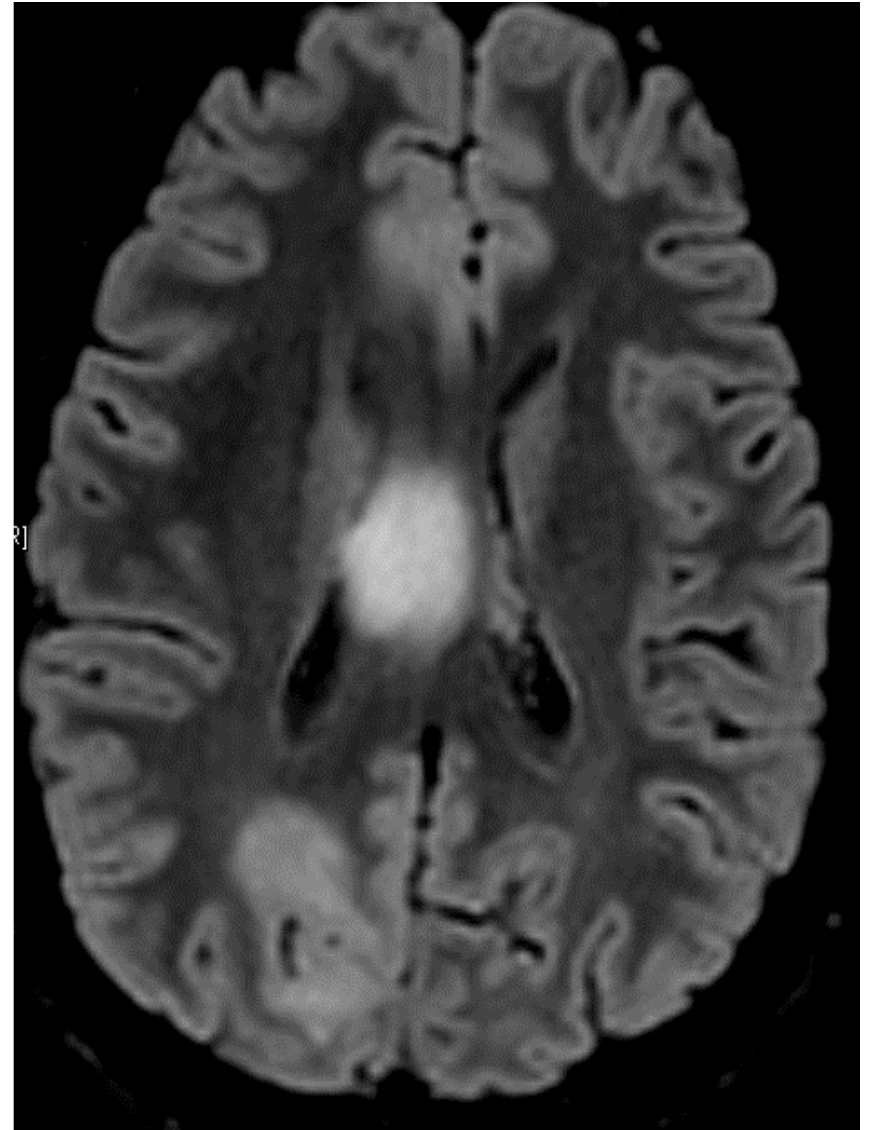
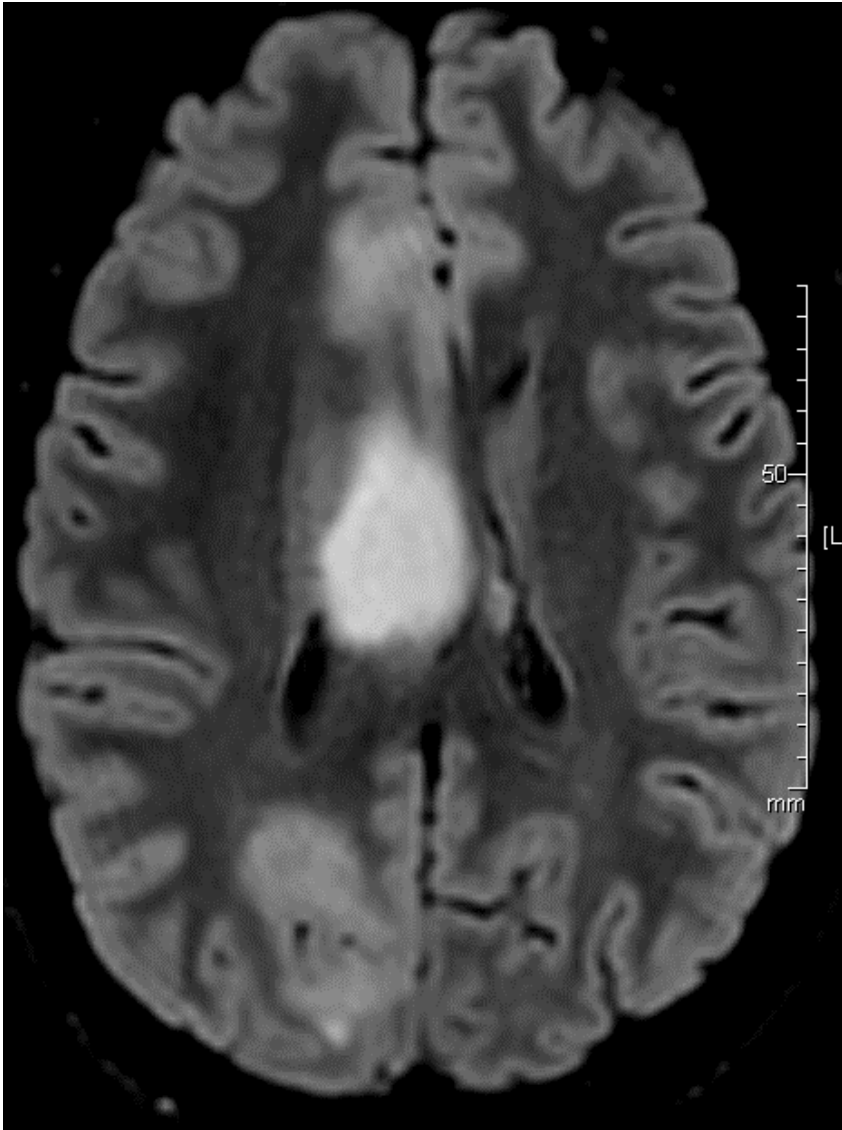


Inhibiteur spécifique de l'enzyme IDH1 mutante (AG-120)

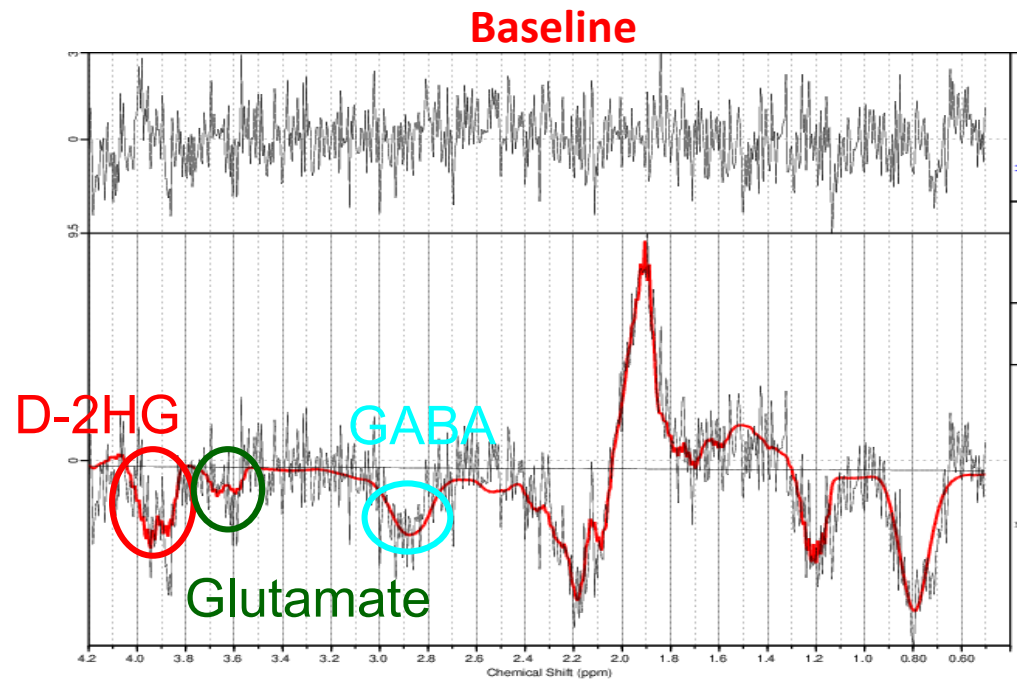
M 23y Oligoastrocytome grade II, IDH1^{R132H}, sans codeletion, traité par TMZ, puis AG120, inhibiteur IDHmut

11/05/15 (baseline)

04/11/15 (C7D1)



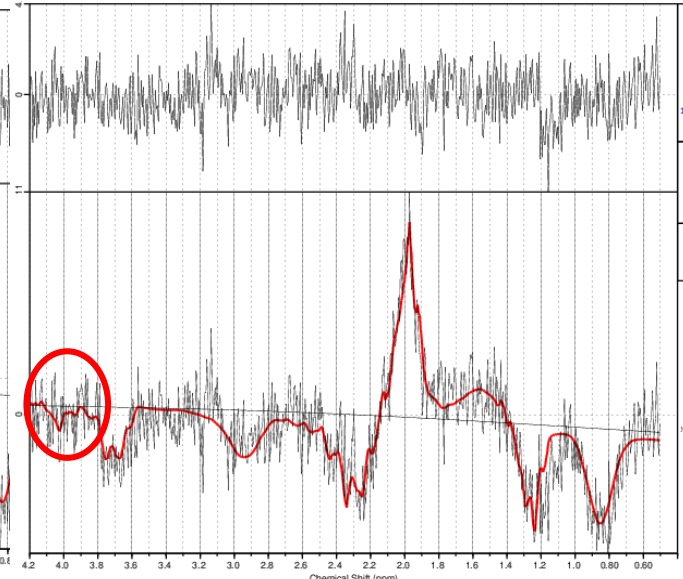
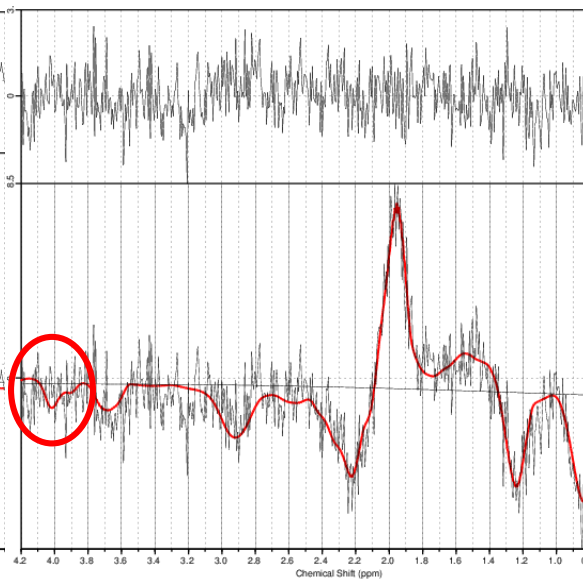
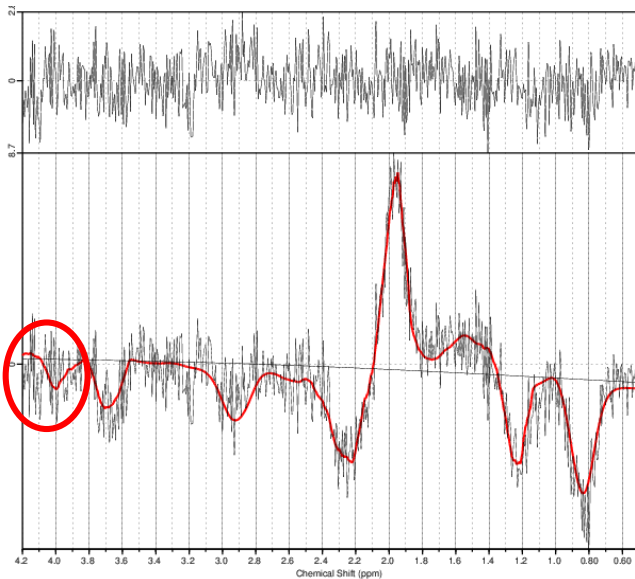
Effet de la thérapie sur le pic de D2HG



Follow up (15 days)

Follow up (23 days)

Follow up (56 days)



Messages

- Marqueurs moléculaires intégrés dans la future classification OMS 2016 des gliomes
- Intérêt diagnostique (IDH, Histones, 1p19q), pronostique (IDH, 1p19q), prédictif (IDH, 1p19q, MGMT)
- Identification non invasive du statut IDH

- **Jean-Yves Delattre**
 - **Khe Hoang-Xuan**
 - **Ahmed Idbaih**
 - **Agusti Alentorn**
 - **Caroline Dehais**
 - **Marianne Labussière**
 - **Vincent Gleize**
 - **Amithys Rahimian**
 - **Anna Luisa Di Stefano**
 - **Karim Labreche**

 - **François Ducray (Hosp civ Lyon)**

 - **Mehdi Touat (DITEP, IGR)**
- **Franck Bielkle**
 - **Karima Mokhtari (neuropathologie)**

 - **Laurent Capelle (neurochirurgie)**

 - **Francesca Branzoli (CENIR, Paris)**

 - **Chris Ottolenghi (Biochemistry-Paris Descartes)**



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