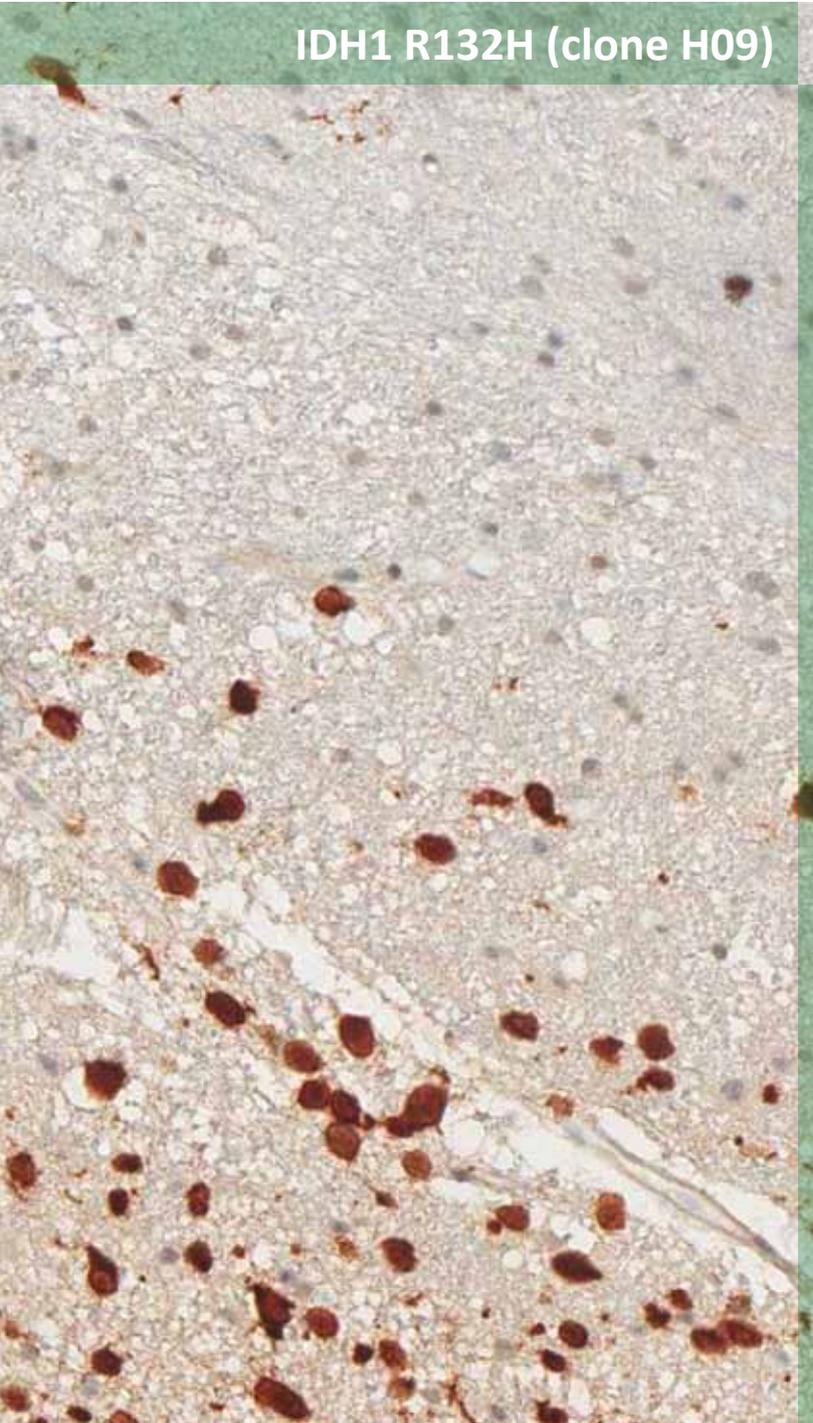


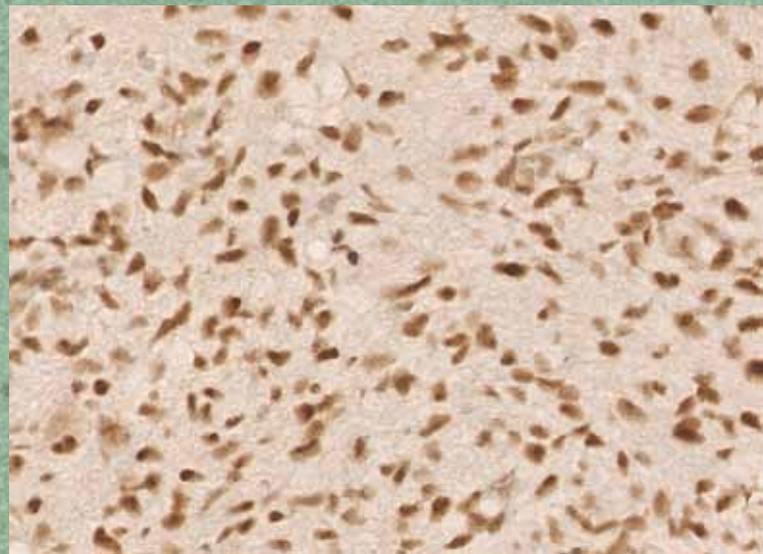
Classification of diffuse Gliomas

Combined Immunohistochemistry on IDH1 R132H and ATRX substitutes molecular testing.

IDH1 R132H (clone H09)



ATRX (clone AX1)



ATRX positive 1p/19q deleted



ATRX loss 1p/19q intact



Characteristics of the 3 most important molecular groups of adult glioma

	Diffuse glioma with IDH mutation and 1p/19q-codeletion (oligodendroglioma)	Diffuse glioma with IDH mutation	Diffuse glioma without IDH mutation
Biomarker			
IDH1/2	mutated	mutated	non mutated
1p/19q	co-deleted	intact	intact
ATRX	nuclear expression	loss of nuclear expression	nuclear expression
hTERT-Promotor mutations	common	rare	common
Typical histological finding and prognosis			
Histology	oligodendroglial	astrocytic	astrocytic
WHO grading	II or III	II or III (rare IV)	IV (rare II or III)
Median Survival	>15 years ?	8-12 years	<2-3 years

The routine practical approach for diagnosing astrocytomas and oligodendrogliomas begins with performing IHC for ATRX and IDH1 R132H expression. Stepwise analysis of molecular parameters with initial IHC for ATRX and IDH1 R132H followed by 1p/19q analysis and then by IDH sequencing significantly reduces the number of molecular tests required for unequivocal diagnosis (Reuss et al., 2015).

IDH1 R132H

The 2016 CNS WHO classification recommends IDH1 R132H IHC as a backbone for differential diagnosis of glioma. IDH1 R132H IHC is widely applied as a favorable prognostic marker.

ATRX

ATRX mutations in gliomas result in the loss of nuclear ATRX expression, which can be diagnosed by IHC. Loss of ATRX expression is close to being mutually exclusive to 1p/19q co-deletion.

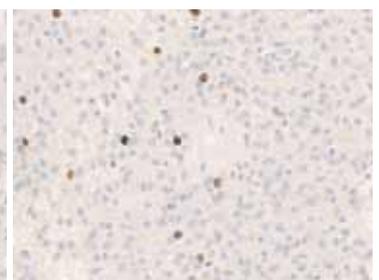
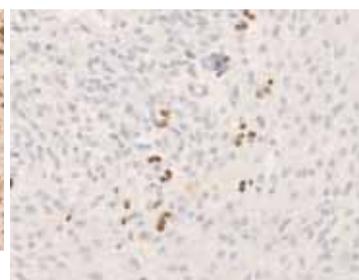
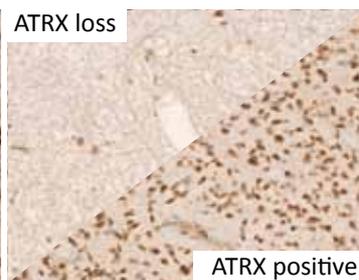
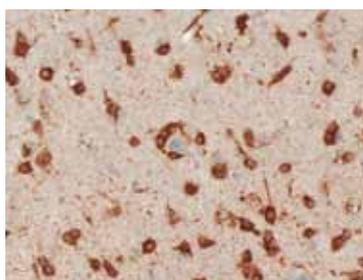
p53

p53 can be selected as a marker since prominent staining is mutually exclusive to 1p/19q deletion, suggesting the usefulness of ATRX and p53 IHC should 1p/19q analysis not be possible.

Ki-67

High Ki-67 labeling index is high in IDH wild type gliomas and lower in IDH1 mutant glioma. The mitotic index is associated with outcome in IDH wild type tumors.

NEW



Anti-IDH1 R132H

clone H09

#DIA-H09

0.5 ml

1:20-1:50

Anti-ATRX

clone AX1

#DIA-AX1

0.5 ml

1:100-1:200

Anti-p53

clone CC53

#DIA-530

0.5 ml

1:100-1:200

Anti-Ki67

clone Ki67P

#DIA-670

0.5 ml

1:100-1:200

References:

1. Reuss DE et al. ATRX and IDH1-R132H immunohistochemistry with subsequent copy number analysis and IDH sequencing as a basis for an „integrated“ diagnostic approach for adult astrocytoma, oligodendroglioma and glioblastoma. Acta Neuropathol. 129(1):133-146, 2015
2. Jinquan Cai et al. Detection of ATRX and IDH1-R132H immunohistochemistry in the progression of 211 paired gliomas. Oncotarget 2016 Mar 29; 7(13): 16384-16395.