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| Table 2. Characteristics of the Included Studies | | | | | | | | | | | | | |
| **Reference** | **Country** | **N** | **Age range (yrs)** | **Mean age (yrs)** | **Factor** | **Method** | **MSpos**  **(mos.)** | **MSneg (mos.)** | **MSdif (mos.)** | **MSDIF CI** | **MS\_P** | **HR** | **HR, 95% CI** |
| Cheng et al (2015) | China | 19 | ND | ND | miR-222, -145, -20a, -132, -129 | Chinese Glioma Genome Atlas; high vs low risk mirVana miRNA Isolation 27 Kit | 4.3 | 22.1 | 17.8 | ND | 0.0113 | 3.39 | 1.44-12.91 |
| Yin et al (2018) | France (RAUH) Neurosurgery Departments of Rennes and Angers University Hospitals | 79 | 36-75 | 58.9 | Epigenetic silencing (TRIM58, ADRA2C); restatement (TRIM38, MS4A7); | Infinium Human Methylation 450k platform (Illumina Inc) | 10.3 | 13.9 | 3.6 | ND | 0.008 | ND | ND |
| Yin et al (2018) | Canada/Germany (GSE36278-Gen expression omnibus series) | 57 | 18-57 | 42.2 | Epigenetic silencing (TRIM58, ADRA2C); restatement (TRIM38, MS4A7); | Infinium Human Methylation 450k platform (Illumina Inc) | 8.3 | 48 | 39.7 | ND | 0.0001 | ND | ND |
| Marziali et al (2017) | Italy | 35 | 30-80 | 59.5 | miR-23a, miR-27a, miR-9 expression | qPCR | 5 | 4 | 1 | ND | 0.4921 | ND | ND |
| MGMT methylation | MSP | 14 | 8 | 6 | ND | 0.0167 | ND | ND |
| EGFRvIII overexpression | IHQ | 8 | 10.5 | 2.5 | ND | 0.5389 | ND | ND |
| PTEN little expression | IHQ | 9 | 8 | 1 | ND | 0.0284 | ND | ND |
| VEGF overexpression | IHQ | 9 | 3 | 6 | ND | 0.1459 | ND | ND |
| Adam et al (2012) | Germany | 60 | 33-86 | 61 | ALDH1A1 expression | IHQ | 8 | 6 | 2 | ND | 0.267 | 0.826 | 0.48-1.41 |
| MGMT methylation | MSP | 11 | 6 | 5 | ND | 0.016 | 0.516 | 0.29-0.92 |
| Weller et al (2014) | Germany | 179 | 24-84 | 60.6 | EGFRvIII overexpression | MLPA, IHQ, RTPCR | 7.4 | 6.6 | 0.8 | ND | 0.803 | ND | ND |
| Dréan et al (2018) | France | 51 | ND | ND | ABCA13 overexpression | Accutase StemPro RT qPCR, IHQ | ND | ND | ND | ND | 0.0064 | 1.12 | ND |
| MGMT methylation | MSP | ND | ND | ND | ND | ND | 3.13 | ND |
| Ohba et al (2019) | Japan | 59 | 17-86 | 54.5 | cMET overexpression | IHQ | 5.3 | 8.3 | 3 | ND | 0.045 | ND | ND |
| Swellam et al (2019) | Egypt | 20 | >18 | 60 | miR-221 overexpression | miRNeasy Mini kit qPCR | 7.3 | 10.4 | 3.1 | ND | 0.001 | ND | ND |
| miR-222 overexpression | miRNeasy Mini kit qPCR | 7.6 | 10.4 | 2.8 | ND | 0.0001 | ND | ND |
| Lalezari et al (2013) | USA | 355 | 22.3- 90.0 | 57.6 | MGMT >=30 vs <30% | IHQ | 7.8 | 10.9 | 3.1 | ND | 0.0001 | 1.49 | 1.18-1.89 |
| IDH1 not mutated | ND | ND | ND | ND | ND | 0.0436 | 0.54 |  |
| MGMT methylation | MSP | 13.3 | 7.8 | 5.5 | ND | 0.0001 | 0.53 | 0.42-0.67 |
| IDH1 not mutated | ND | ND | ND | ND | ND | 0.081 | 0.62 | 0.36-1.06 |
| MGMT BISEQ >=3 vs <3 | BiSEQ | 11.5 | 7.9 | 3.6 | ND | 0.0001 | 0.64 | 0.49-0.82 |
| IDH1 not mutated | ND | ND | ND | ND | ND | 0.1162 | 0.54 | 0.29-0.99 |
| De Carlo et al (2018) | Italy | 53 | 26-82 | 61 | MGMT (>= 6) | Pyrosequencing | 9.5 | 6.4 | 3.1 | ND | 0.038 | 0.54 | 1.18-1.89 |
| MGMT (>= 6) | Pyrosequencing | ND | ND | ND | ND | 0 | 0.4188 | 0.28-0.64 |
| IDH1 mutated | Pyrosequencing | ND | ND | ND | ND | ND | 0.42 | 0.19-0.93 |
| Etcheverry et al (2014) | France | 399 | 21-88 | 59 | IDH1 not mutated | Sequencing (ABI PRISM 310 Genetic Analyzer) | 18.3 | 56.7 | 38.4 | ND | <0.001 | 4.1 | 1.3-13.3 |
| MGMT not methylated | PCR Pyrosequencing | 14.9 | 30.2 | 15.3 | ND | <0.001 | 3 | 2.2-4.2 |
| DGKI not methylated | PCR Pyrosequencing | 19.6 | 16.9 | ND | ND | 0.004 | 0.7 | 0.5-1.0 |
| Tini et al (2018) | Italy | 129 | 34-84 | 66 | EGFR overexpression | IHQ | 6 | 13 | 7 | ND | 0.003 | 1.79 | 1.15-2.8 |
| MGMT not methylated | MSP | 5 | 18 | 13 | ND | 0.001 | 2.3 | 1.29-4.11 |
| Meng et al (2014) | China | 110 | ND | 53 | TCTN1 overexpression | IHQ | ND | ND | ND | ND | 0.029 | 1.6 | 1.01-2.52 |
| Purkait et al (2016) | India | 54 | ND | ND | DNMT1 overexpression | IHQ | ND | ND | ND | ND | ND | 2.63 | 1.1-6.2 |
| DNMT3B overexpression | IHQ | ND | ND | ND | ND | ND | 2.6 | 1.0-8.4 |
| EZH2 overexpression | IHQ | ND | ND | ND | ND | ND | 4.17 | 1.3-13.5 |
| Toraih et al (2019) | Egypt | 57 | 25-67 | 52 | LINC-ROR overexpression | qPCR, IHQ | ND | ND | ND | ND | 0.02 | ND | ND |
| MGMT methylation | MSP | 15 | 15 | 0 | ND | 0.8 | 1.06 | 0.63-1.8 |
| Zhang et al (2016) | China | 70 | 17-79 | 59 | IFIT1 little expression | IHQ | ND | ND | ND | ND | 0.03 | 0.42 | 0.21-0.86, |
| MGMT not methylated | IHQ | ND | ND | ND | ND | 0.018 | 2.04 | 1.05-3.95 |
| Shouwei et al (2015) | China | 30 | 14-65 | 41.1 | p53 little expression | IHQ | 17.4 | 8.9 | ND | ND | 0.0299 | ND | ND |
| Kim et al (2017) | South Korea | 76 | 29.4-81.6 | 52.4 | Histone H3 lysine 4 methyltransferase, MLL4, Histone H3 lysine 27 demethylase UTX, Little expression | IHC Pyrosequencing | 8.8 | 9.7 | 0.9 | ND | 0.174 | 1.29 | 0.95–1.63 |
| MGMT not methylated | MSP | 7 | 10.4 | 3.4 | ND | 0.026 | 2.24 | 1.28-3.19 |
| Dong et al (2017) | Japan | 39 | 17-85 | 65 | LAPTM4B-35 overexpression | IHQ | 5.13 | 12 | 6.87 | ND | 0.001 | 2.922 | 1.332-6.409 |
| MGMT methylation | Pyrosequencing | 6.37 | 7.4 | 1.03 | ND | 0.55 | ND | ND |
| Wang et al (2017) | China | 36 | 16-76 | 48 | miR-485-3p overexpression | qPCR | ND | ND | ND | ND | 0.004 | 0.135 | 0.048–0.382 |
| miR-451a overexpression | qPCR | ND | ND | ND | ND | 0.464 | 1.372 | 0.586-3.214 |
| miR-4289 overexpression | qPCR | ND | ND | ND | ND | 0.542 | 0.756 | 0.319-1.793 |
| MGMT not methylated | IHQ | ND | ND | ND | ND | 0.097 | 2.162 | 0.87-5.37 |
| Pinel et al (2017) | France | 80 | 30-83 | 60.3 | MGMT methylation | ND | 8.3 | 8.2 | 0.1 | ND | 0.26 | ND | ND |
| DNA-PKcs overexpression | IHQ | ND | ND | ND | ND | 0.102 | ND | ND |
| Ku70 overexpression | IHQ | ND | ND | ND | ND | 0.359 | ND | ND |
| Ku80 overexpression | IHQ | ND | ND | ND | ND | 0.247 | ND | ND |
| CD44 overexpression | IHQ | 8.7 | 5.5 | ND | ND | 0.012 | ND | ND |
| Olig2 overexpression | IHQ | 8.5 | 8.2 | ND | ND | 0.26 | ND | ND |
| Eoli et al (2017) | Italy | 86 | 28-67 | 52.8 | MGMT methylation | MSP | 10 | 7 | 3 | ND | 0.006 | 0.57 | 0.35-0.93 |
| TP53 mutations | Sequencing (ABI Prism 377) | 8 | 8 | 0 | ND | NS | ND | ND |
| EGFR overexpression | PCR Sequencing (Alf Express II) | 8 | 8 | 0 | ND | NS | ND | ND |
| Kim et al (2012) | South Korea | 78 | 24-78 | 58 | MGMT not methylated | MSP | 9 | 18 | 9 | ND | 0.017 | 1.6 | 1.1-2.2 |
| Sadones et al (2018) | Belgium | 22 | 23-80 | 55 | MGMT methylation | MSP | ND | ND | ND | ND | 0.311 | ND | ND |
| Olmez et al (2014) | Turkey | 69 | 23-81 | 52.2 | cMET overexpression | IHQ | 12.3 | 19.1 | 6.8 | ND | <0.05 | 1.7 | 1.1-2.2 |
| Sana et al (2014) | Czech Republic | 58 | 24-71 | 56 | miR-3,miR-224, miR-432, miR-454, miR-672, miR-885-5p expression | TaqMan Human MicroRNA v3.0 | ND | ND | ND | ND | 0.001 | 1.98 | 1.33–2.94 |
| MGMT methylation | EpiTect Bisulfite Kit high-resolution melting analysis | 9 | 6.75 | 2.25 | ND | 0.0309 | NS | NS |
| Tabouret et al (2015) | France | 29 | 37-74 | 57 | CXCR4 | RTqPCR | ND | ND | ND | ND | 0.003 | 0.303 | 0.119-0.770 |
| HIF1α | RTqPCR | ND | ND | ND | ND | 0.009 | 0.275 | 0.111-0.679 |
| VEGFR2 overexpression | RTqPCR | ND | ND | ND | ND | 0.003 | 4.119 | 1.432-11-846 |
| CXCL12 | RTqPCR | ND | ND | ND | ND | 0.122 | ND | ND |
| VEGFA | RTqPCR | ND | ND | ND | ND | 0.190 | ND | ND |
| VEGFR1 | RTqPCR | ND | ND | ND | ND | 0.337 | ND | ND |
| Adrenomedullin | RTqPCR | ND | ND | ND | ND | 0.413 | ND | ND |
| uPA | RTqPCR | ND | ND | ND | ND | 0.026 | 0.349 | 0.133-0.914 |
| Wang et al (2014) | China | 78 | 21-62 | 45 | IDH1 mutated | Pyrosequencing | ND | ND | ND | ND | 0.006 | 0.124 | 0.128-0.553 |
| TP53 mutated | IHQ | ND | ND | ND | ND | 0.012 | 0.149 | 0.144-0.664 |
| MGMT methylated | MSP | ND | ND | ND | ND | 0.031 | 0.595 | 0.320-0.831 |
| Lee et al (2013) | South Korea | 36 | 38-70 | 54.6 | Tetraspanin CD151 overexpression | IHQ | 9.5 | 14.5 | 5 | ND | 0.043 | 1.841 | 0.765, 4.432 |
| MGMT not methylated | RT-qPCR | 9.9 | 19.1 | 9.2 | ND | 0.011 | 2.505 | 0.930-6.747 |
| Limam et al (2019) | Tunisia | 74 | 38-89 | 54 | p53 overexpression | IHQ | ND | ND | ND | ND | 0.621 | 0.983 | 0.2-4.837 |
| MDM2 overexpression | IHQ | ND | ND | ND | ND | 0.228 | 0.427 | 0.118-1.541 |
| PTEN little expression | IHQ | ND | ND | ND | ND | 0.025 | 1.336 | 0.277-6.446 |
| EGFR overexpression | IHQ | ND | ND | ND | ND | 0.816 | 0.792 | 0.09-6.955 |
| MGMT expression | IHQ | ND | ND | ND | ND | 0.308 | 2.04 | 0.706-5.897 |
| MGMT methylation | MSP | ND | ND | ND | ND | 0.0001 | 0.096 | 0.020-0.460 |
| Griguer et al (2013) | USA | 53 | ND | ND | CcO elevated | Spectrophotometry | 5.5 | 9.75 | 4.25 | ND | 0.0087 | 3.57 | 1.38-9.22 |
| Switzerland | 26 | ND | ND | CcO elevated | Spectrophotometry | 4.7 | 9.43 | 4.73 | ND | 0.0274 | 5.31 | 1.2-23.58 |
| Fan et al (2013) | China | 199 | ND | 53 | SLC7A7 overexpression | IHQ | 7 | 14 | 7 | ND | 0.001 | 2.31 | 1.34–3.97 |
| Shastry et al (2016) | India | 136 | ND | ND | PP1A overexpression | IHQ | ND | ND | ND | ND | 0.076 | 1.01 | 0.991-1.029 |
| Kim et al (2017) | South Korea | 129 | 15-82 | 53 | GLI1 little expression | IHQ | ND | ND | ND | ND | 0.034 | 1.7 | 1.04-2.79 |
| PTCH1 little expression | IHQ | ND | ND | ND | ND | 0.12 | ND | ND |
| USA (TCGA) | 295 | 15-82 | 53 | GLI1 little expression | IHQ | ND | ND | ND | ND | 0.043 | 1.69 | 1.02-2.82 |
| PTCH1 little expression | IHQ | ND | ND | ND | ND | 0.003 | 2.17 | 1.3-3.61 |
| South Korea | 170 | 15-82 | 53 | MGMT methylation | MSP | ND | ND | ND | ND | 0.003 | 0.45 | 0.27-0.76 |
| IDH1 mutated | IHQ | ND | ND | ND | ND | 0.26 | ND | ND |
| Abbreviations: ADN, methyltransferases; CcO, cytochrome oxidase; cMET, hepatocyte growth factor receptor; CXCL12, CXC motif chemokine ligand 12; CXCR, chemokine receptor family; DGKI, diacylglycerol kinase iota; DNA-PKcs, DNA-dependent protein kinase; DNMT, DNA methyltransferases; GLI1, glioma-associated oncogene homologue 1; HIF1a, inducible factor for hypoxia; HMT, histone methyl transferase; IDH, isocitrate dehydrogenase; IFIT1, interferon-induced protein with tetratricopeptide repeats 1; LAPTM4B-35, lysosomal protein transmembrane 4 beta; lncRNA, long noncoding RNA; MDM2, murine double minute 2; MGMT, O-6-methylguanine DNA methyltransferase; miR, microRNA; MS\_P, statistical significance log rank test; MS4A7, membrane spanning 4-domains A7; MSdif, median survival difference; MSneg, mean survival in negative (unexposed); MSpos, mean survival in positive (exposed); N, number of patients; ND, no data; P53, protein 53; PTCH, patched; PP1A, nuclear protein phosphatase 1; PTEN, phosphatase and tensin homologue; SLC7A7, solute carrier family 7 member 7; TCTN1, tectonic family member 1; TRIM38, tripartite motif containing 38. | | | | | | | | | | | | | |