Supplementary Table 11: Details of included studies: predictors of therapy efficacy

Study (year) - **Design**	**Population (*n*)**	**Treatment regimen**	**Mean duration of follow-up in months (range)**	**Radiological response (*n*)**	**Predictors of therapy efficacy**
TEMOZOLOMIDE					
Bengtsson (2015) - Cohort	APT (16) - somatotroph (2) - lactotroph (7) - lactotroph becoming somatotroph (1) - corticotroph (1) - NFPA (5) PC (8) - somatotroph (2) - lactotroph (2) - lactotroph becoming somatotroph (1) - corticotroph (3), of which 1 Nelson	150 - 200 mg/m^2 in a 5/28 regimen for a median of 6 months (range 1-23) NB two persons received concurrent capecitabine because of non-responsiveness, two persons received concurrent radiotherapy	Median 32.5 (4-91)	APT: PR 46% (6) SD 15% (2) PD 38% (5) PC: CR 25% (2) PD 75% (6), of which 3 patients initially had PR NB treatment response data are based on 21/24 patients One patient with concurrent RT could be evaluated and had SD	MGMT status assessed in 20 patients: Responders median 9% (range 5-20) Non-responders median 93% (range 50-100) p <0.001 MLH1 stained positive in all patients MSH2 and MSH6 stained positive in all patients except one who had an initial response but became resistant to TMZ within 6 months No relation between TMZ response and Ki-67 indices or p53 immunostaining patterns
Hirohata (2013) - Cohort	APT (3) - corticotroph (Crooke cell) (1) - lactotroph (2) PC (10) - corticotroph (3, of which 2 Crooke cell) - lactotroph (3) - nonfunctioning (4)	n.r. NB 1 person with APT and 1 person with PC received concurrent RT	Length of treatment 10.5 (1.5-24)	APT: CR* 33% (1) PR* 33% (1) PD* 33% (1) PC: CR* 20% (2) PR* 50% (5) SD* 20% (2) PD* 10% (1)	100% MSH6 positive staining cells in responders vs. 33% in non-responders (p = 0.015) No relation between TMZ response and Ki-67 indices, MGMT immunoexpression or p53 labeling indices
Lamas (2023) - Cohort	APT (24) - somatotroph (3) - lactotroph (8) - corticotroph (11) - gonadotroph (1) - NFPA (1) PC (4) - lactotroph (2) - NF (2)	Mean initial dose of 265 ± 73 mg in a 5/28 regimen median of 13 cycles (range 3-66) NB 5 persons received concurrent RT (Stupp)	n.r. (≥ 6 months follow-up was inclusion criterium)	APT: CR* 0 PR* 29% (7) SD* 46% (11) PD* 21% (5) PC: CR* 0 PR* 25% (1) SD* 75% (3) PD* 0	No relation between TMZ response and sex, age, clinical or pathological subtype, Ki67 index, p53 expression, tumour volume at diagnosis or preTMZ treatment, radiological invasion, presence of metastases, previous or concomitant radiotherapy, time from diagnosis to TMZ treatment, TMZ dose or duration of treatment or follow-up

McCormack (2018) - Cohort	Whole cohort (166): APT (125) - somatotroph (14) - lactotroph (25) - corticotroph (56) - thyrotroph (4) - gonadotroph (5) - immunonegative (21) PC (40), - somatotroph (2) - lactotroph (15) - corticotroph (19) - thyrotroph (0) - gonadotroph (1) - immunonegative (3) unclassified (1) TMZ was given to 157/166 patients (95%)	Mostly 150 - 200 mg/m^2 in a 5/28 regimen NB 6 persons received concurrent RT (Stupp), 6 persons an additional chemotherapeutic agent	Median treatment duration 9 months (range 1–36) in 136 patients	CR$^{\Diamond}$ 5.7% (9) PR$^{\Diamond}$ 31.2% (49) SD$^{\Diamond}$ 33.1% (52) PD$^{\Diamond}$ 29.9% (47)	Clinically functioning tumours were more likely to demonstrate regression on TMZ compared with non-functioning tumours (45% vs 17%, p = 0.01) Tumours with high MGMT expression had a higher rate of no response while complete response was only seen among tumours with low MGMT expression No relation between TMZ response and sex, APT or PC, pathological subtype, Ki-67 indices or p53 labeling indices
Minniti (2020) - Cohort	APT (17) + PC (4): - corticotroph (8, of which 3 silent) - lactotroph (6) - nonfunctioning (7)	TMZ + 2nd course fractionated stereotactic radiotherapy (re-SRT) TMZ: 75 mg/m^2 concurrent with re-SRT, subsequent cycles 150-200 mg/m^2 in a 5/28 regimen or 50 mg/m^2/day for 12 months Re-SRT: 36 Gy/18 fractions (*n* = 13) 37.5 Gy/15 fractions (*n* = 8)	Median 27 (12-58)	APT+PC: CR* 9.5% (2) PR* 52.4% (11) SD/PD* 38% (8) Estimated 2 year local control 73% Estimated 4 year local control 65%	Median local control 15 months for patients with MGMT unmethylated tumours and not reached for patients with methylated tumours (by PCR *p* = 0.01) No relation between clinical outcome and Ki-67 ≥3%, p53 expression or presence of mitosis No relation between local control and APTs and PCs
IMMUNE CHECKPOINT INHIBITION					
Ilie (2022) - Retrospective cohort	APT (9) - corticotroph (5) - lactotroph (4) PC (6) - corticotroph (4) - lactotroph (2)	Ipilimumab (5) Ipilimumab + nivolumab (10) NB 6 patients received concurrent cabergoline, 3 patients concurrent prednisone, 1 patient concurrent mitotane and RFA of liver metastases	12.9 (5-32)	Radiological response: APT: SD* 22% (2) PD* 78% (7) PC: PR* 67% (4) PD* 33% (2)	Three of nine corticotroph tumors (33.3%) showing tumor partial response in comparison with one of six lactotroph tumors (16.7%) Four of six carcinomas showed tumor partial response, while no APT showed tumor partial response.

				Biochemical response: APT: PR° 11% (1) PD° 56% (5) n.a. 33% (3) PC: CR° 33% (2) PR° 17% (1) PD° 17% (1) n.a. 33% (2)	

TMZ = temozolomide
RT = radiotherapy
MGMT = O6-Methylguanine-DNA Methyltransferase
APT = aggressive pituitary tumour
PC = pituitary carcinoma
PFS = progression-free survival

◊ According to the following criteria:
CR = complete response: disappearance of all lesions
PR = partial response: ≥ 30% reduction in tumour volume
SD = stable disease: change in tumour volume between ≤ 30% decrease and ≤ 10% increase from baseline
PD = progressive disease: ≥ 10% increase in tumour volume

* According to RECIST criteria:
CR = complete response: disappearance of all lesions
PR = partial response: ≥ 30% reduction in tumour volume
SD = stable disease: neither sufficient shrinkage to qualify for PR, nor sufficient increase to qualify for PD
PD = progressive disease: ≥ 20% increase in tumour volume

° According to the following criteria:
CR = complete response: normalization of hormone levels
PR = partial response: ≥ 20% reduction in hormone levels
SD = stable disease: < 20% change in hormone levels
PD = progressive disease: ≥ 20% increase in hormone levels