Prognostic value of circulating progastrin (hPG80) in IDH-wild type glioblastoma treated with radio-chemotherapy

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Abstract 2049

Background

Glioblastoma patients treated with radio-chemotherapy have dismal prognosis and no circulating predictive or prognostic biomarker have been identified. hPG80 is a circulating precursor of the hormone gastrin and has oncogenic properties[1]. A new method of detection yields a very low threshold (1.2 pM)[2]. With this method, hPG80 is a prognostic biomarker in metastatic renal cell carcinoma[3] and hepatocellular carcinoma[4]. We evaluated the prognostic value of hPG80 in glioblastoma patients.

Methods

We conducted a retrospective study of *IDH* wt glioblastoma patients treated with radiochemotherapy[5,6]. We evaluated the prognostic value of postoperative hPG80 detection using the kit DxPG80.Lab on progression-free (PFS) and overall survival (OS) in combination with known prognostic factors.

Results

70 patients were evaluable. Characteristics are resumed in Table 1. Median PFS is 7.8 months (IC95 6.7 - NA) and median OS is 17.8 months (IC95 13.9 - NA). Median time from surgery to post-operative plasma collection was 27 days (IQR 5.5 - 42). hPG80 was detected in 48 (69%) patients (hPG80+) with a median concentration of 5.37 pM (IQR 0 - 13.9). hPG80 detection rate and concentration were lower in patients with complete resection (Fig.1). hPG80+ was associated with poorer outcome (Fig. 2 and 3, Table 2 and 3).

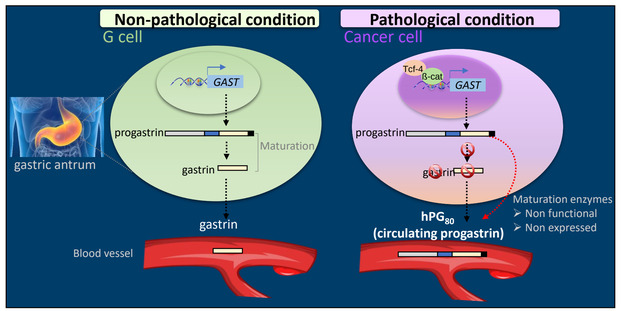


Table 1 - Demographic and Clinical Characteristics of the Patients

Characteristic	N=70
Median age (range) — yr	64 (19–84)
Sex — no. of patients	
Female	32 (46%)
Male	38 (54%)
Surgery type — no. of patients	
Biopsy	22 (31%)
Partial resection	25 (36%)
Complete resection	23 (33%)
MGMT promoter methylation — no. of patients	N= 55
Present (≥ 12%)	22 (40%)
Absent (< 12%)	33 (60%)
Median percentage (IQR)	7.2 (2.7–30.2)
ATRX status — no. of patients	N=54
Present	49 (91%)
Loss	5 (9%)
Postoperative radiochemotherapy — no. of patients	N=70
Stupp	61 (87%)
Short-course (Perry)	9 (13%)
Median interval from surgery to radiotherapy (IQR) — days	39 (33—49)
Karnofski index — no. of patients	N=57
≥ 80%	52 (91%)
< 80%	5 (9%)
Median lymphocytes count (IQR) — Giga per Litre	1. 6 (1.1—2.3)
Corticosteroids use	N=44
Median (IQR) — mg prednisone equivalent	20 (0—40)
No corticosteroid	14 (32%)
Proton pump inhibitor usage — no. of patients	N=45
No	27 (60%)
Yes	18 (40%)

Figure 1 - Postoperative hPG80 concentration according to the extent of surgery

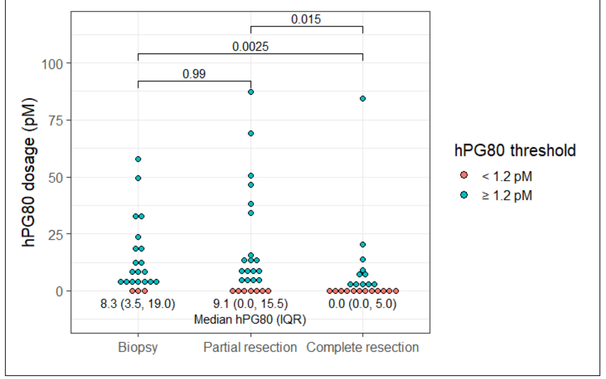


Figure 2 – (A) PFS and (B) OS according to postoperative hPG80 detection

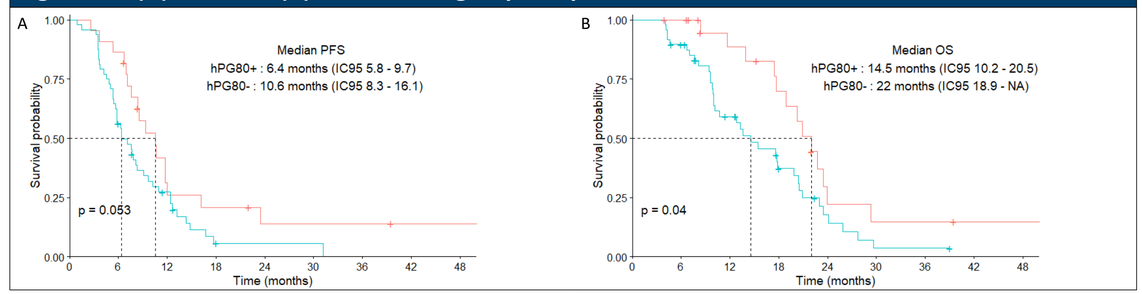


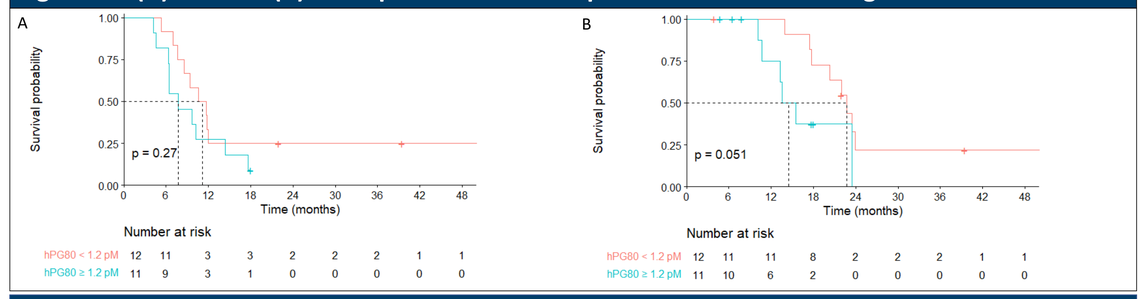
Table 2 - Uni- and multivariate analysis of prognostic factors of PFS

			PFS	
Variable	Category	N (%)	HR (univariable)	HR (multivariable)
Complete resection	No	47 (67.1)	-	-
	Yes	23 (32.9)	0.60 (0.35-1.04, p=0.070)	0.65 (0.29-1.46, p=0.295)
Age at diagnosis	< 45	6 (8.6)	-	-
	≥ 45	64 (91.4)	2.28 (0.80-6.52, p=0.124)	-
hPG80+	No	22 (31.4)	-	-
	Yes	48 (68.6)	1.75 (0.99-3.08, p=0.055)	1.50 (0.61-3.72, p=0.378)
ATRX	Loss	5 (9.3)	-	-
	Present	49 (90.7)	5.00 (1.18-21.22, p=0.029)	4.39 (0.99-19.50, p=0.052)
MGMT promoter methylation	< 12%	33 (60.0)	-	-
	≥ 12%	22 (40.0)	0.53 (0.29-1.00, p=0.049)	0.84 (0.39-1.80, p=0.649)
Interval surgery-radiotherapy	< 56 days	61 (87.1)	-	-
	≥ 56 days	9 (12.9)	0.37 (0.16-0.87, p=0.022)	0.29 (0.09-1.00, p=0.050)
Lymphocytes count (G/L)	< 2.44	34 (79.1)	-	-
	≥ 2.44	9 (20.9)	0.54 (0.23-1.23, p=0.142)	-

Table 3 - Uni- and multivariate analysis of prognostic factors of OS

			OS	
Variable	Category	N (%)	HR (univariable)	HR (multivariable)
Complete resection	No	47 (67.1)	-	-
	Yes	23 (32.9)	0.60 (0.32-1.11, p=0.105)	-
Age at diagnosis	< 50	9 (12.9)	-	-
	≥ 50	61 (87.1)	2.76 (1.08-7.02, p=0.033)	1.84 (0.55-6.12, p=0.320)
hPG80+	No	22 (31.4)	-	-
	Yes	48 (68.6)	1.93 (1.02-3.66, p=0.044)	2.33 (1.01-5.38, p=0.048)
ATRX	Loss	5 (9.3)		-
	Present	49 (90.7)	6.51 (1.48-28.57, p=0.013)	4.72 (1.09-20.39, p=0.038)
MGMT promoter methylation	< 12%	33 (60.0)	-	-
	≥ 12%	22 (40.0)	1.24 (0.62-2.49, p=0.541)	-
Interval surgery-radiotherapy	< 56 days	61 (87.1)	-	-
	≥ 56 days	9 (12.9)	0.33 (0.10-1.06, p=0.063)	0.00 (0.00-Inf, p=0.998)
Lymphocytes count (G/L)	< 0.84	6 (14.0)	-	-
	≥ 0.84	37 (86.0)	0.51 (0.21-1.23, p=0.134)	-

Figure 3 – (A) PFS and (B) OS in patients with complete resection according to hPG80 detection



hPG80 is detected in the plasma of *IDH* wt glioblastoma patients and could serve as a new circulating prognostic biomarker. Further explorations are ongoing in larger cohorts including longitudinal evaluation during the course of the disease.

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1- You B et al., EBioMedicine 2020; 2- Cappellini M et al., Anal Methods 2021; 3- Kohli M et al., Cancers 2021; 4- Dupuy M et al., Cancers 2022; 5- Stupp R et al., NEJM 2005; 6- Perry JR et al., NEJM 2017