

BPGTMbio

Results from Phase 2 Study of BPM31510 in Combination With Standard of Care (SOC) RT and TMZ in Newly Diagnosed Glioblastoma (GB)

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Low Expression of CoQ10 Genes in GB Correlates with Poor Survival

Human Proteome Atlas TCGA analysis COQ10 synthesis enzymes mRNA expression level and survival.

BPM31510 Mechanism of Action: Reversing the Warburg Effect

BPM31510IV-11 Study

Abbreviations: MRI = magnetic resonance imaging; RT = radiation therapy; TMZ = temozolomide; PFS = progression free survival

Study Design:

- An open-label study to assess efficacy of BPM31510 plus standard of care RT and TMZ in newly diagnosed GB.
- The study enrolled 51 subjects for ~90% power in rejecting the null hypothesis of PFS6 of ≤ 30%.

Primary Endpoint:

- PFS at 6 and 12 months (defined as meeting RANO 1.0 criteria for complete response, partial response, or stable disease).

Secondary Endpoints:

- Overall survival (defined as time from start of BPM31510 to date of death or last follow-up).
- Safety and tolerability of BPM31510 + vitamin K1 administered with standard RT and TMZ in newly diagnosed GB.

Demographics : ITT Population (N=51)

	MGMT Status	Methylated	Unmethylated	Unknown	Total
Age at screening	N	17	33	1	51
	Mean (SD)	65 (13.8)	58.2 (9.36)	64.0 (-)	60.6 (11.29)
	Median	70.0	58.0	64.0	64.0
Sex at birth – n (%)					
	Female	8 (47.1)	14 (42.4)	1 (100)	23 (45.1)
	Male	9 (52.9)	19 (57.6)	0	28 (54.9)
Race – n (%)					
	American Indian or Alaska Native	1 (5.9)	0	0	1 (2.0)
	Asian	0	2 (6.1)	0	2 (3.9)
	Black or African American	0	0	0	0
	White	14 (82.4)	27 (81.8)	1 (100)	42 (82.4)
	Others	0	4 (12.1)	0	4 (7.8)
	Not Reported	2 (11.8)	0	0	2 (3.9)

Tumor Response at 6 Months Based on RANO 1.0 - PP Population

MGMT Status	Methylated	Unmethylated	Total
N	15	28	44
Best overall response - n (%)			
Complete response (CR)	0	1 (3.6)	1 (2.3)
Partial response (PR)	0	3 (10.7)	3 (6.8)
Stable disease (SD)	5 (33.3)	10 (35.7)	15 (34.1)
Progressive disease (PD)	9 (60.0)	13 (46.4)	22 (50.0)
Not evaluable (NE)	1 (6.7)	0	1 (2.3)
Overall response rate (CR or PR) - n (%)	0	4 (14.3)	4 (9.1)
95 % CI for ORR	(0.0, 21.8)	(4.0, 32.7)	(2.5, 21.7)
Disease control rate (CR or PR or SD) - n (%)	5 (33.3)	14 (50.0)	19 (43.2)
95 % CI for DCR	(11.8, 61.6)	(30.6, 69.4)	(28.3, 59.0)

PP = Per-Protocol (subjects completed first 2 weeks BPM31510 and started RT and TMZ); CI = Confidence Interval; 95% CI is estimated using the Clopper-Pearson method. Overall Response is assessed up to day 183 after first BPM31510 infusion; Patients with no post-baseline tumor assessment are included in the population denominator but are not shown in any response categories; therefore, the sum of response categories may not equal the total population.

Tumor Response at 12 Months Based on RANO 1.0 - PP Population

MGMT Status:	Methylated	Unmethylated	Total
N	15	28	44
Best overall response - n (%)			
Complete response (CR)	0	1 (3.6)	1 (2.3)
Partial response (PR)	0	4 (14.3)	4 (9.1)
Stable disease (SD)	5 (33.3)	12 (42.9)	17 (38.6)
Progressive disease (PD)	9 (60.0)	10 (35.7)	19 (43.2)
Not evaluable (NE)	1 (6.7)	0	1 (2.3)
Overall response rate (CR or PR) - n (%)	0	5 (17.9)	5 (11.4)
95 % CI for ORR	(0.0, 21.8)	(6.1, 36.9)	(3.8, 24.6)
Disease control rate (CR or PR or SD) - n (%)	5 (33.3)	17 (60.7)	22 (50.0)
95 % CI for DCR	(11.8, 61.6)	(40.6, 78.5)	(34.6, 65.4)

PP = Per-Protocol (subjects completed first 2 weeks BPM31510 and started RT and TMZ); CI = Confidence Interval; 95% CI is estimated using the Clopper-Pearson method. Overall Response is assessed up to day 365 after first BPM31510 infusion; Patients with no post-baseline tumor assessment are included in the population denominator but are not shown in any response categories; therefore, the sum of response categories may not equal the total population.

Safety: ITT Population (N=51)

Number of patients with:	Overall N=51; n (%)	Related to BPM31510; n (%)
Any TEAE	50 (98.0)	37 (72.5)
Any serious TEAE	18 (35.3)	7 (13.7)
Any TEAE leading to treatment discontinuation	5 (9.8)	3 (5.9)
Any TEAE leading to death	4 (7.8)	1 (2.0)*
Any AESIs	5 (9.8)	
TEAE by NCI-CTCAE	grade 1 48 (94.1) 33 (64.7)	grade 2 24 (47.1) 6 (11.8)
	grade 3 6 (11.8)	grade 4 4 (7.8)
	grade 5 4 (7.8)	
TEAE by System Preferred Term	Any CTC grade; n (%) [Events]	TEAESI by Preferred Term
Fatigue	21 (41.2) [26]	Platelet count decreased
Nausea	20 (39.2) [23]	Alanine aminotransferase increased
Headache	18 (35.3) [22]	Lymphocyte count decreased
Constipation	18 (35.3) [20]	Aspartate aminotransferase increased
Alopecia	11 (21.6) [12]	Activated partial thromboplastin time prolonged
Seizure	8 (15.7) [9]	
Pruritus	7 (13.7) [10]	International normalized ratio increased
Brain oedema	7 (13.7) [7]	Haemorrhage intracranial

Note: MedDRA v29.0. CTCAE v5.0, TEAE = Treatment-Emergent Adverse Event, If there is more than one TEAE with maximum NCI CTCAE grade within a system organ class (SOC), the patient is counted only once under that SOC. If there is more than one TEAE with maximum NCI CTCAE grade within a SOC and preferred term (PT), the patient is counted only once in that SOC and PT. Only PTs > 9% are included in table. [Events] presents the number of TEAEs by primary SOC and PT regardless of severity. *Patient expired due to progressive disease with pancytopenia "possibly related" to BPM31510.

Overall Survival PP Population (N=44)

PP= Per Protocol (subjects completed at least 2 weeks BPM31510 and started RT and TMZ), CI = Confidence Interval, OS = Overall Survival, NR = Not Reached; OS is the time from first date of BPM31510 exposure to death

Overall Survival PP Population
MGMT: Methylated (N=15) vs Unmethylated (N=28)

PP= Per Protocol (subjects completed at least 2 weeks BPM31510 and started RT and TMZ), CI = Confidence Interval, OS = Overall Survival, NR = Not Reached; OS is the time from first date of BPM31510 exposure to death

Conclusions

- BPM31510 was well-tolerated and does not exacerbate toxicity profile of RT +TMZ in a front-line setting.
- Median OS of ~20 months observed in **unmethylated** patients is a clinically meaningful improvement in OS compared to historical cohorts shown below.

	MGMT - Unmethylated	
Study	N	Median OS (95% CI)
This Study	24	19.9 (14.2, NR)
Gilbert'13*	254	14.60 (13.20, 16.50)
Gilbert'14*	214	14.60 (13.60, 15.60)
Stupp'05*	60	12.70 (11.60, 14.40)
Stupp'17*	95	14.70 (12.80, 19.10)
Westphal'15*	32	15.50 (13.80, 24.00)

*Alnahhas, Iyad et al. *Neuro-oncology advances* vol. 2,1 vdaa082. 30 Oct. 2020. doi:10.1093/noonjnl/vdaa082

- BPM31510IV-11 (NCT04752813) has completed recruiting.
- Planning for a future registrational trial is underway.

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The safety and efficacy of BPM31510 has not been determined yet by the FDA.