



# Functional Ex Vivo Testing Prospectively Identifies Newly Diagnosed Glioblastoma Patients Sensitive to Temozolomide Treatment Irrespective of MGMT Methylation Status

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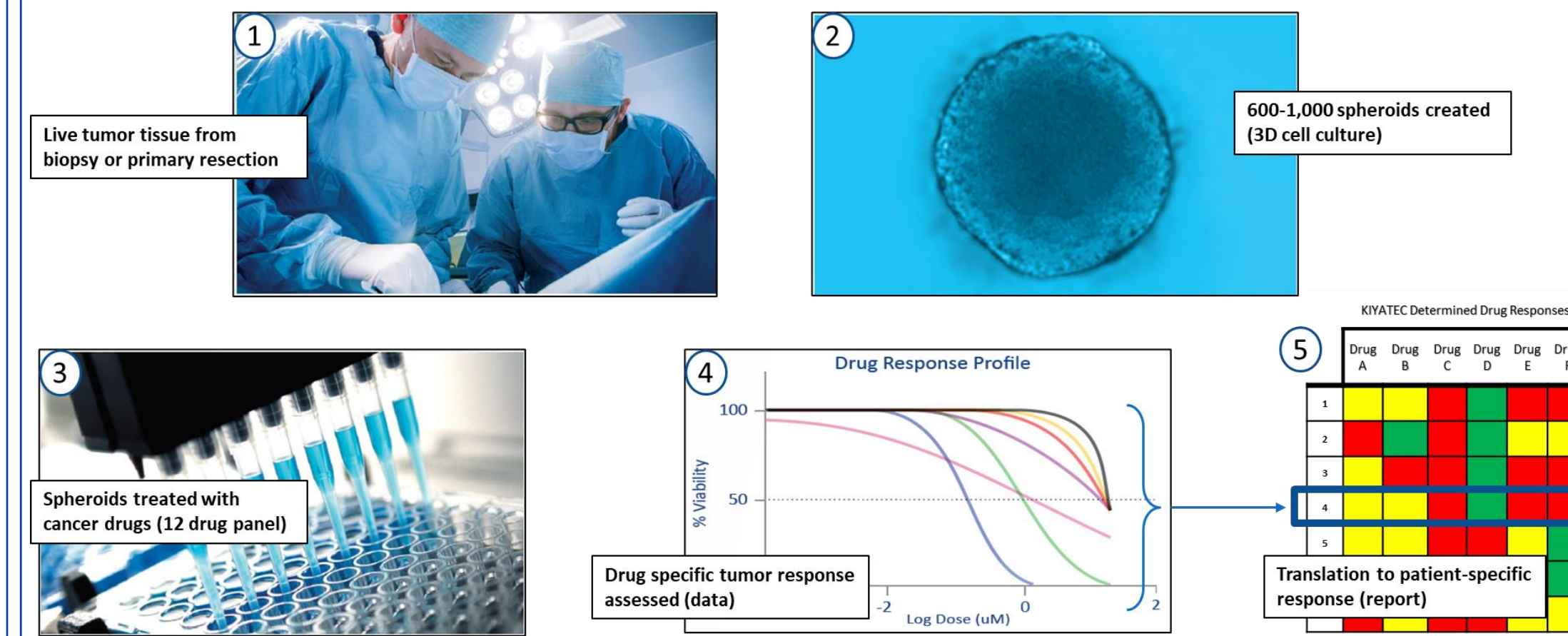
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## Abstract

Standard of care (SOC) therapy for newly diagnosed (ND) glioblastoma (GBM) patients consists of temozolomide (TMZ) concurrent with radiation therapy. It is well known that patients with an unmethylated *MGMT* promoter are less likely to respond to TMZ. However, this is not universal. We have previously shown that 3D Predict™ Glioma can identify patient response to TMZ, often differentially than the methylation status would predict. Here we present expanded clinical data relating to functional *ex vivo* testing capable of identifying patients responsive to TMZ, regardless of methylation status.

## 3D Predict™ Glioma

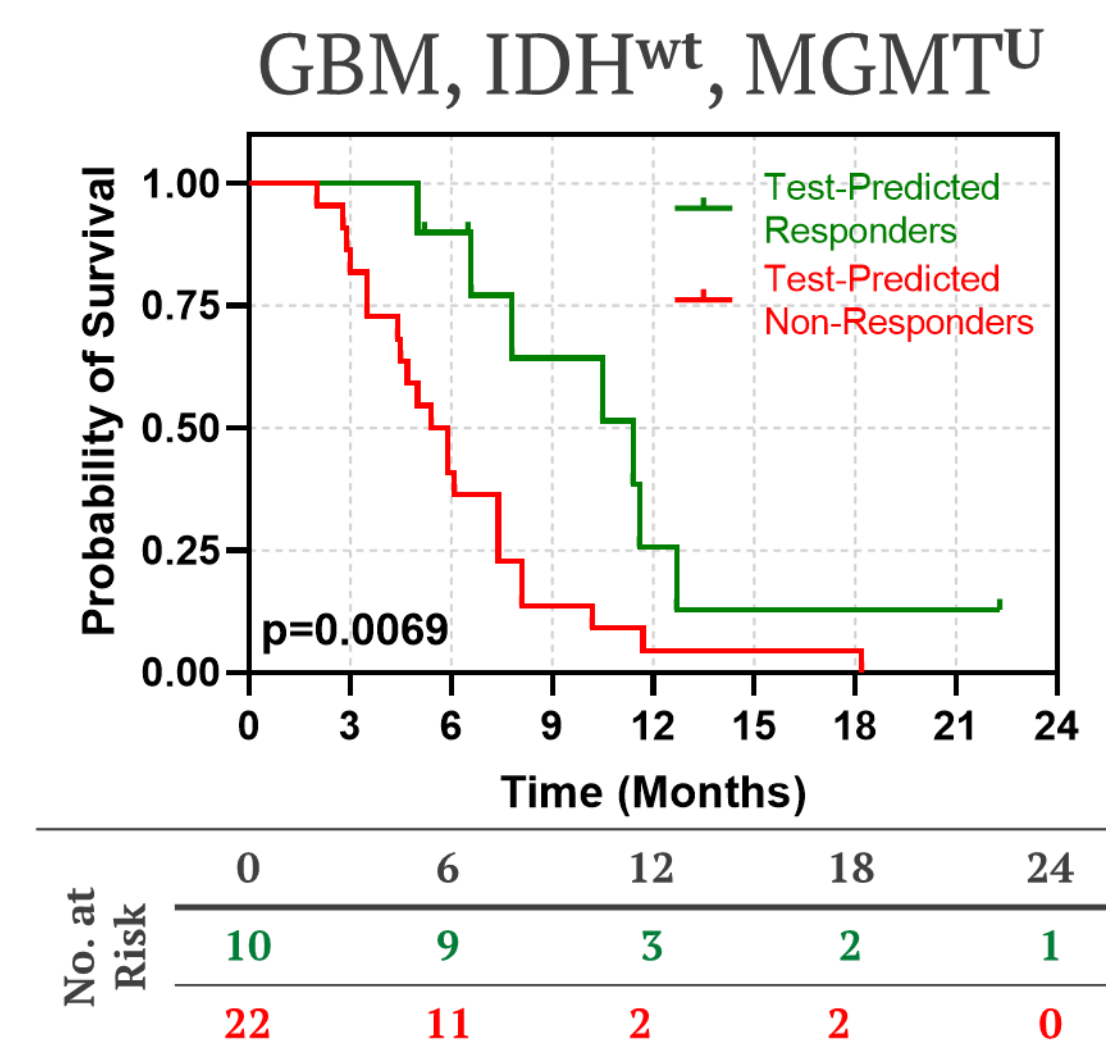
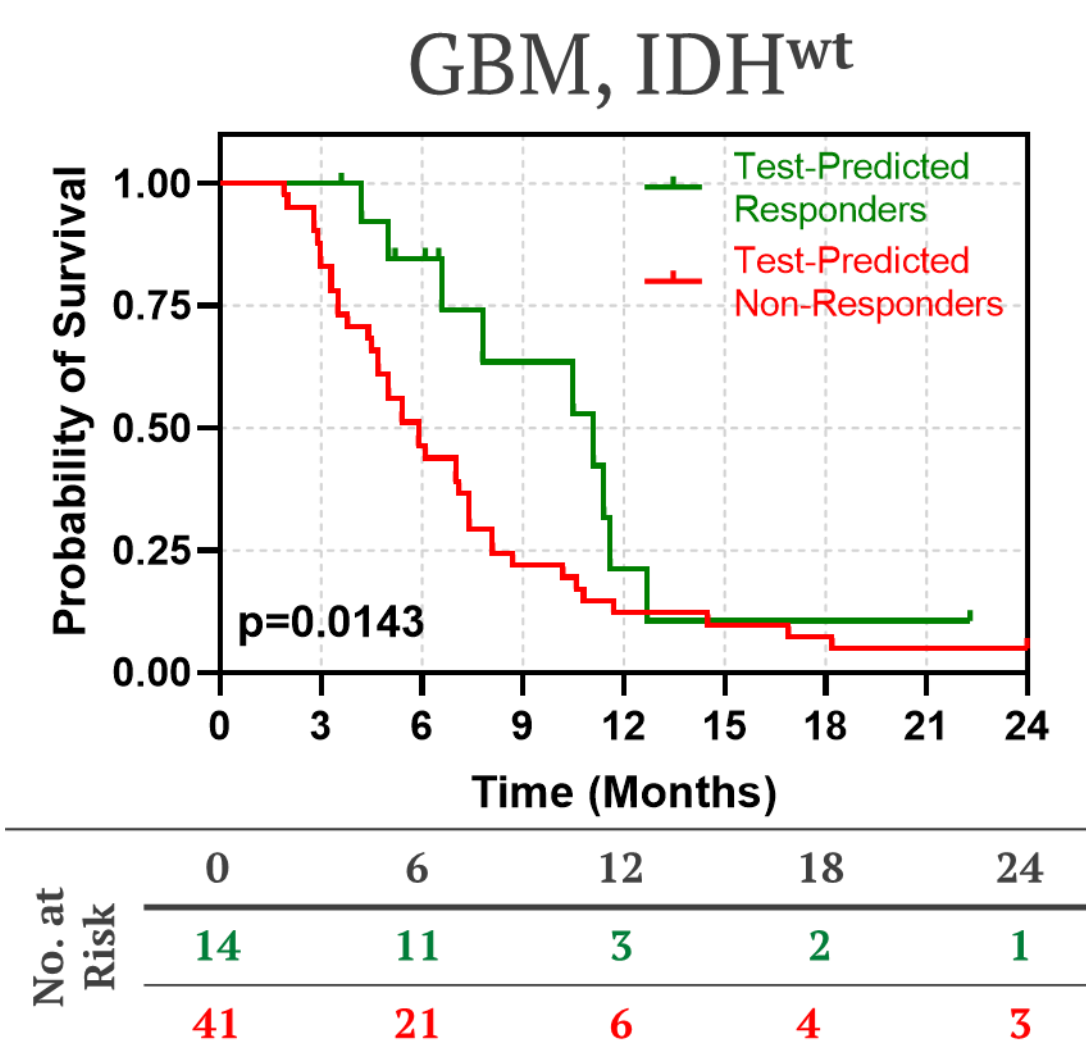
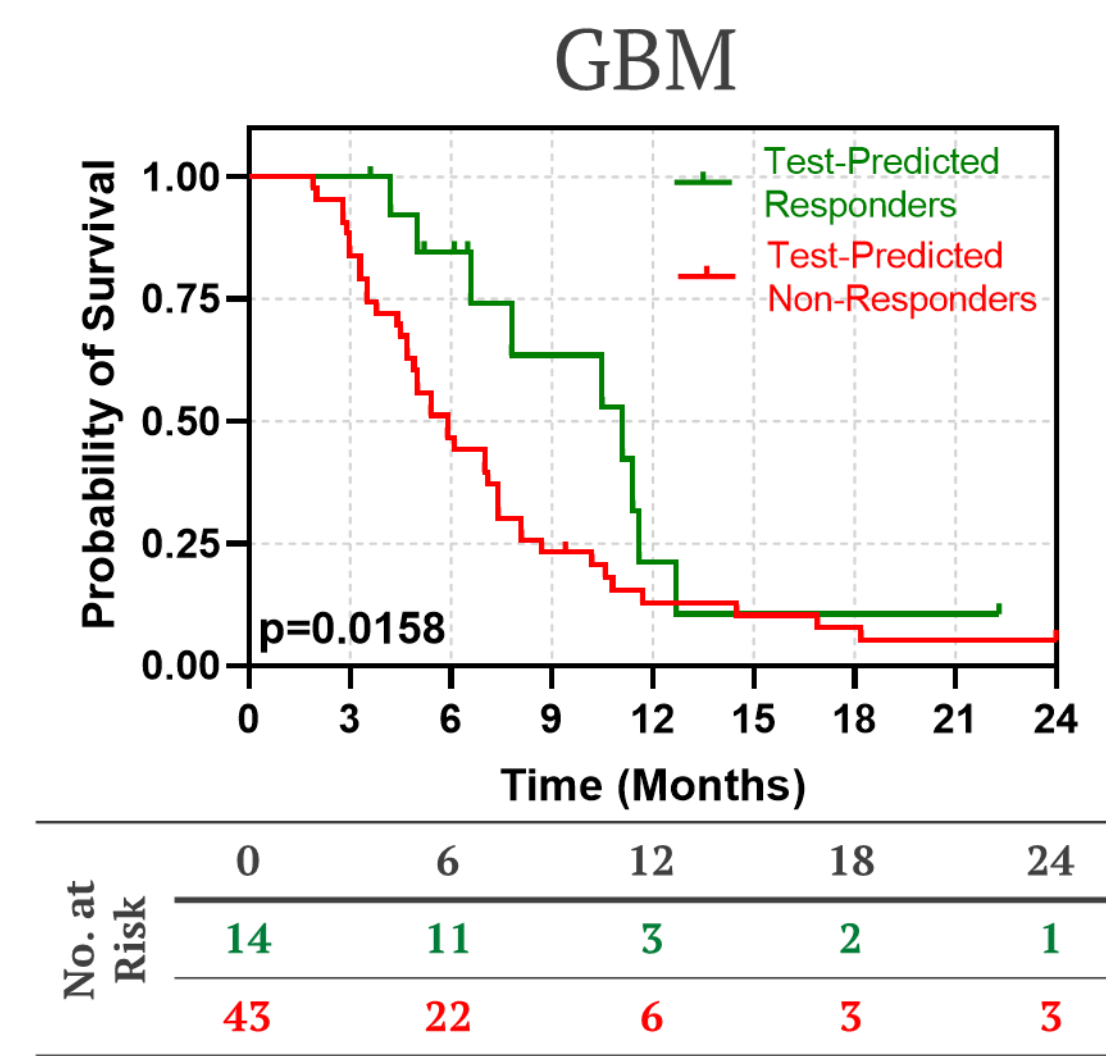
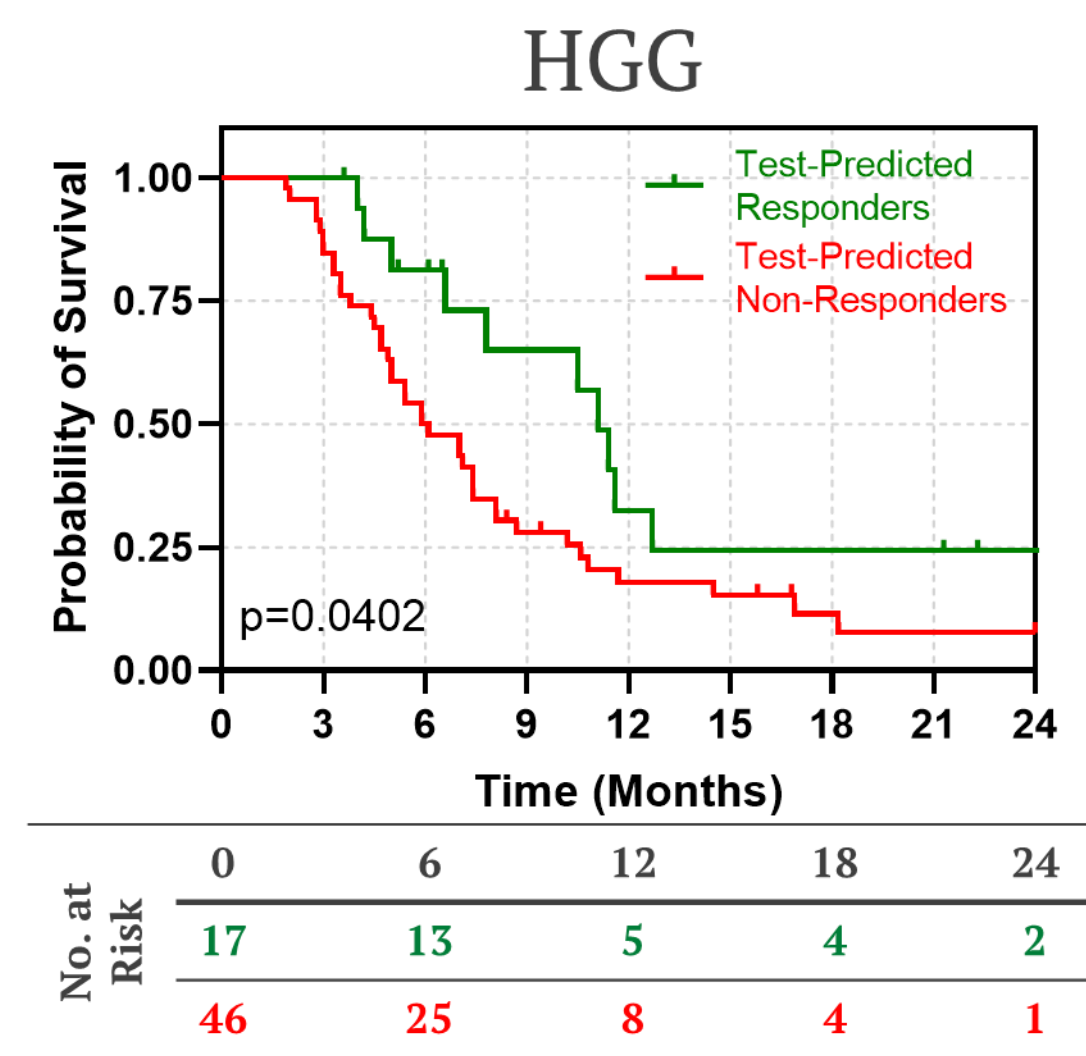


3D Predict™ Glioma starts with fresh tissue acquired during standard of care surgery or biopsy. *Fresh, live tissue* (1) is digested and reformed into 600 – 1,000 individual 3D spheroids (2) and exposed to TMZ and up to 11 other compounds commonly used in HGG treatment (3). Therapeutic response assessment is evaluated using Kiyatec's proprietary algorithms (4), with patient specific results delivered to physicians within 10 business days (5).

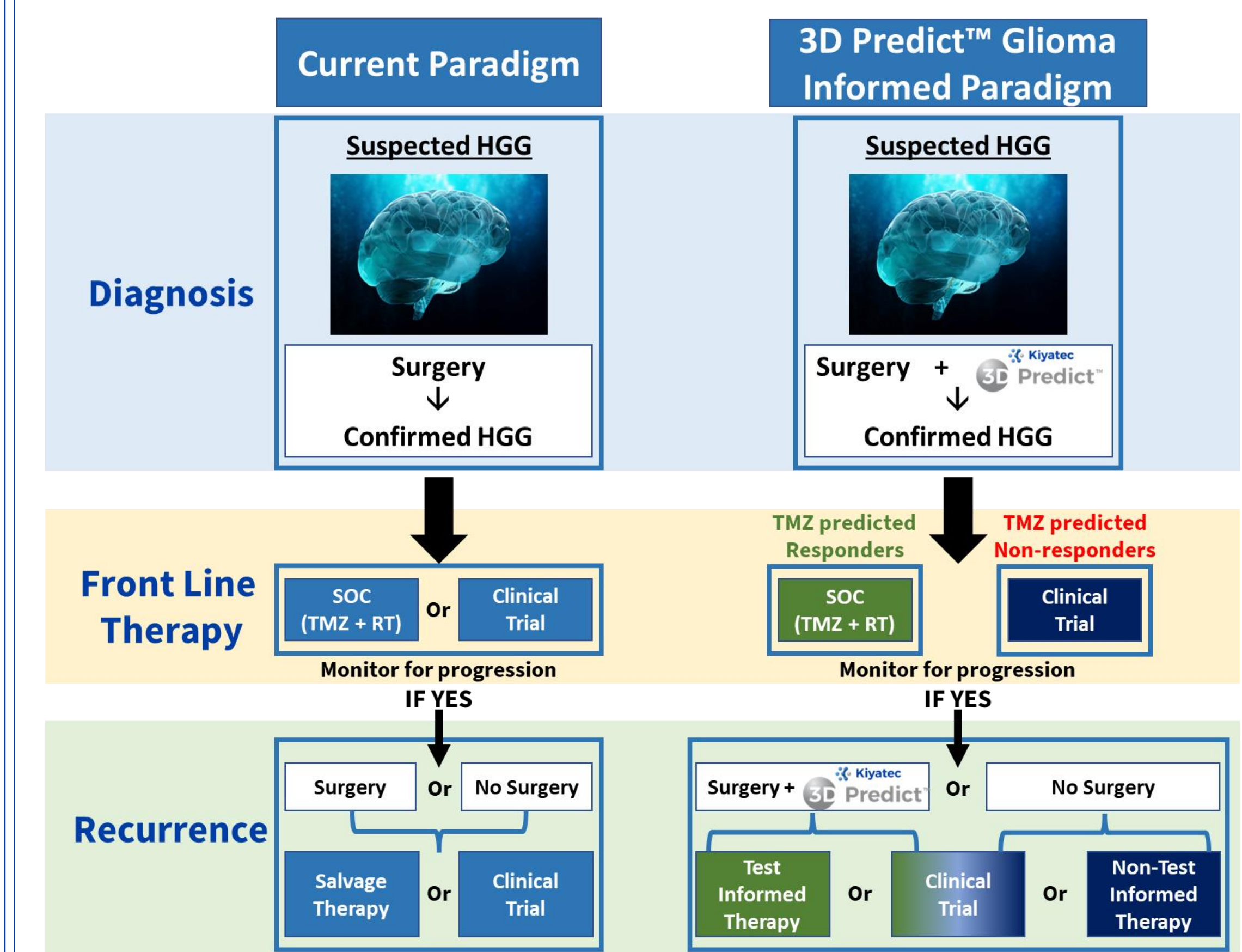
❖ Shuford S, et al. Prospective prediction of clinical drug response in high-grade gliomas using an *ex vivo* 3D cell culture assay. *Neurooncol Adv.* 2021. 3 (1): 1-13

## Newly Diagnosed Patients

Patient Demographics at the Time of Tumor Resection				
Newly Diagnosed Patients				
	HGG	GBM	GBM, IDH <sup>wt</sup>	GBM, IDH <sup>wt</sup> , MGMT <sup>U</sup>
No. of Patients	63	57	55	32
Age				
Over 70	12 (19%)	12 (21%)	11 (20%)	6 (19%)
Under 70	46 (73%)	41 (72%)	40 (73%)	24 (75%)
Unknown	5 (8%)	4 (7%)	4 (7%)	2 (6%)
Sex				
Male	39 (62%)	36 (63%)	34 (62%)	24 (75%)
Female	19 (30%)	17 (30%)	17 (31%)	6 (19%)
Unknown	5 (8%)	4 (7%)	4 (7%)	2 (6%)
IDH				
Wild Type	56 (89%)	55 (96%)	55 (100%)	32 (100%)
Mutated	6 (10%)	1 (2%)		
Unknown	1 (1%)	1 (2%)		
MGMT				
Methylated	24 (38%)	21 (37%)	20 (36%)	
Unmethylated	36 (57%)	33 (58%)	32 (58%)	32 (100%)
Unknown	3 (5%)	3 (5%)	3 (5%)	
PFS (months)				
Test Predicted Responders	11.1	11.1	11.1	11.4
Test Predicted Non-Responders	6	5.9	5.9	5.7
P-value	0.0402	0.0158	0.0143	0.0069



## 3D Predict™ in the Patient Journey



3D Predict™ Glioma for newly diagnosed GBM patients can:

- Prospectively identify patients who may be better suited for clinical trials prior to initiation of SOC.
- Provide rationale for switching from TMZ to another compound (or therapeutic combination)
- Provide further support on how to treat *MGMT* unmethylated patients while identifying those that will respond to SOC

For recurrent patients it can inform the selection of salvage agents

Newly Diagnosed Patients were treated with radiation and concomitant TMZ followed by adjuvant TMZ. Progressionfree survival (PFS) was measured against the response prediction in the 3D Predict™ Glioma test. Importantly, the test is capable of identifying those patients with an unmethylated *MGMT* promoter who will still benefit from TMZ treatment. **Across all populations, test predicted responders had a greater than 5-month PFS benefit vs. test predicted non-responders.**