SurVaxM with standard therapy in newly diagnosed glioblastoma: Phase II trial update.

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Abstract #2016

Background: SVN53-67/M57-KLH (SurVaxM) is a novel cancer vaccine designed to stimulate an immune response targeting the tumor-specific antigen survivin. A multi-center, single-arm phase 2 clinical trial of SurVaxM in survivin-positive newly diagnosed glioblastoma (nGBM, NCT02455557) is now fully enrolled and data updated.

Methods: Patients (n = 63) with nGBM were enrolled at 5 US cancer centers and followed for safety, 6-month progression-free survival (PFS6), 12-month overall survival (OS12) and immunologic response. All patients underwent craniotomy with near-total resection (< 1 cm3 residual contrast enhancement), TMZ chemoradiation, adjuvant TMZ and SurVaxM. Patients received 4 doses of SurVaxM (500 mcg) in Montanide with sargramostim (100 mcg) biweekly, followed by maintenance SurVaxM with adjuvants every 12 weeks until tumor progression. Immunogenicity of SurVaxM was assessed by detection of survivin-specific antibody (IgG) and CD8+ T-cell levels.

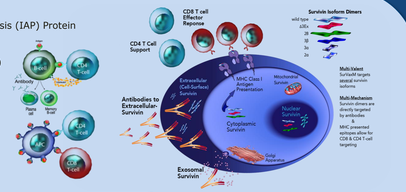
Results: Median age was 60 yrs (range, 20-82), 53% methylated MGMT, 46% unmethylated MGMT (1 N/A) and 60% were male. Survivin expression ranged from 1-40% (median 12%) by immunohistochemistry. Median time to first immunization was 3.0 mo (1.9-4.0 mo) from diagnosis. There have been no RLT or grade ≥ 3 SAE attributable to SurVaxM. The most common AE was grade 1-2 injection site reactions. OS12 was 86.3% from first immunization and 93.5% from diagnosis. OS12 for meMGMT was 93.4% and unMGMT was 78.2% from first immunization. Median time to tumor progression (mPFS) was 15.5 months from diagnosis. Median OS is 30.5 months from diagnosis at present follow-up. SurVaxM produced an increase in survivin-specific IgG titre from pre-vaccine baseline to ≥ 1:10,000 in 67% of pts and ≥ 1:100,000 in 27%. CD8+ T cell responses were observed. Anti-survivin IgG and OS were correlated.

Conclusions: SurVaxM immunotherapy generated encouraging efficacy and immunogenicity in nGBM and has minimal toxicity. A randomized, prospective trial of SurVaxM in nGBM is planned.

SurVaxM

Drug – SurVaxM (DRU-2017-5947)

- Mimic of "Survivin" an Inhibitor of Apoptosis (IAP) Protein
- 15 amino acid novel, synthetic long peptide (SLP)
- High-Density Peptide Delivery conjugated to Keyhole Limpet Hemocyanin (KLH)



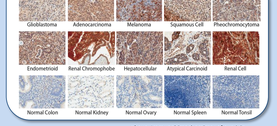
MOA

- Circumvents immune tolerance through activation of mid-affinity multi-clonal CD8 & CD4 T cells
- Multi-valent targeting of survivin in several isoforms & localizations
- Stimulates unique IgG recognition of cell surface survivin

Administration

- Cell-free subcutaneous administration
- 500µg SurVaxM in Montanide ISA 51 VG + 100µg GM-CSF,
- 1st dose after resection & chemoradiation, before adjuvant temozolomide
- 4 Biweekly doses; followed by every 12 week maintenance dosing

below, multi-clonal CD8 & CD4 T-cell epitopes contained within the 15AA SurVaxM peptide



above, Immunohistochemistry of survivin expressing tumors and normal control tissues

Trial Design

Primary Objective:

- To evaluate 6-month progression-free survival (PFS6) in patients with survivin positive newly diagnosed glioblastoma (nGBM) treated with SurVaxM and standard of care temozolomide.

Rationale for newly diagnosed glioblastoma:

- Low immunosuppression post-tumor resection
- Window of opportunity (1 mo.) prior to adjuvant chemotherapy
- Over 90% of glioblastomas are survivin-positive

Trial Design:

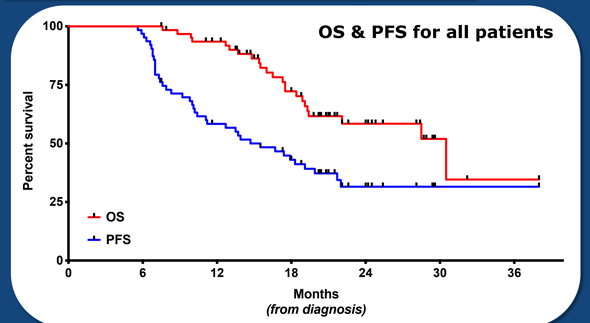
- Single arm SurVaxM® (prime-boost) + adjuvant temozolomide
- Multi-center trial performed at Roswell Park, Cleveland Clinic, Dana-Farber, Mass General & Beth Israel Deaconess Hospital

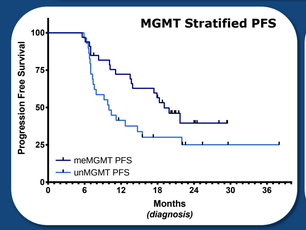
Eligibility Criteria:

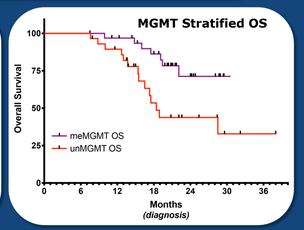
- Age ≥ 18years of age.
- Karnofsky performance status ≥ 70
- Survivin-positive tumor status.
- Pathologically confirmed diagnosis of glioblastoma.
- HLA-A*02, HLA-A*03, HLA-A*11 or HLA-A*24 (+) patients.
- No evidence of progressive disease.
- MRI documenting 1 cm3 or less tumor volume post resection
- Dexamethasone dose less than or equal to 4 mg daily.
- Completed radiation therapy (RT) with initial temozolomide (SOC)
- Participant or legal representative must understand the investigational nature of this study, signed Independent Ethics Committee/IRB approved informed consent.

Status:
Fully enrolled (63 patients), no longer recruiting

Survival – OS & PFS







measured from Diagnosis	OS12	95% CI	OS18	95% CI	OS24	95% CI
SurVaxM	93.5%	(-10, 4)	72.2%	(-14, 10)	58.4%	(-15, 13)
meMGMT	96.9%	(-17, 3)	86.2%	(-19, 8)	71.3%	(-24, 15)
unMGMT	89.4%	(-19, 7)	53.5%	(-22, 18)	43.8%	(-21, 19)
median follow-up	*at risk = 56*		*at risk = 36*		*at risk = 16*	

measured from first immunization	OS12	95% CI	OS18	95% CI	OS24	95% CI
SurVaxM	86.3%	(-12, 7)	61.6%	(-15, 12)	58.2%	(-16, 13)
meMGMT	93.4%	(-17, 5)	78.4%	(-20, 11)	71.3%	(-24, 15)
unMGMT	78.2%	(-21, 11)	44.0%	(-21, 19)	44.0%	(-21, 19)
median follow-up	*at risk = 44*		*at risk = 22*		*at risk = 12*	

measured from Diagnosis	mOS	mPFS	PFS6	95% CI	PFS12	95% CI
SurVaxM	30.5 mos.	15.5 mos.	96.8%	(-9, 2)	58.4%	(-13, 11)
meMGMT	30.5 mos.	19.1 mos.	97.0%	(-17, 3)	72.3%	(-19, 12)
unMGMT	18.4 mos.	10.0 mos.	96.6%	(-19, 3)	41.4%	(-18, 17)
median follow-up	*21.7 mos.*	*22.6 mos.*	*at risk = 62*		*at risk = 36*	

measured from first immunization	mOS	mPFS	PFS6	95% CI	PFS12	95% CI
SurVaxM	26.0 mos.	12.1 mos.	71.3%	(-13, 10)	50.0%	(-13, 12)
meMGMT	28.2 mos.	16.3 mos.	81.7%	(-18, 10)	78.2%	(-21, 11)
unMGMT	15.6 mos.	7.9 mos.	58.6%	(-20, 15)	62.9%	(-19, 14)
median follow-up	*18.7 mos.*	*19.8 mos.*	at risk = 45		*at risk = 32*	

Patient Characteristics & Safety

Patient Characteristics

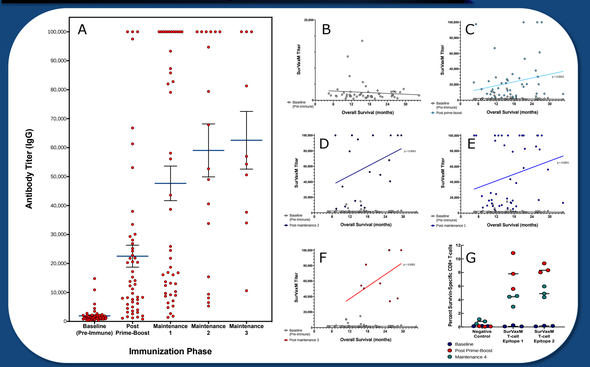
Age	Sex	IDH1	MGMT	Temozolomide use meGMT	Temozolomide use unMGMT	KPS	Survivin	Time to 1st immunization	mAb Titer
Range 20 - 82	Male 38 (60%)	IDH1 53 (84%)	Methylated 33 (52%)	Range 5–21 mos.	Range 4–18 mos.	Range 70-100	Range 1-40%	Range 2.1–4.0 mos.	Range 1,800 to >100,000
Mean 56.5	Female 25 (40%)	IDH1-R32h 8 (13%)	Unmethylated 29 (46%)	Mean 11 mos.	Mean 8 mos.	Mean 86.3	Mean 13%	Mean 3.0 mos.	Mean 53,437
Median 60		unknown 2	unknown 1	Median 9 mos.	Median 7 mos.	Median 90	Media n 12%	Median 3.0 mos.	Median 51,650

Safety Data

ADVERSE EVENT & Grade	1	2	3	ADVERSE EVENT & Grade	1	2	3
Alopecia	1			Injection site swelling	2		
Amnesia	12			Lymphocyte count decreased	2	3	1
Arthralgia	3			Malaise	2	1	
Asthenia		1		Myalgia	4		
Back pain	1			Nausea	1		
Chills	1			Neutrophil count decreased	2		
Confusional state			1	Paraesthesia	3		
Decreased appetite	1			Platelet count decreased	2		
Fatigue	12	1		Pruritus	2	1	
Hyperhidrosis	1			Pyrexia	5		
Hypertension aggravated		1		Rash	2	1	1
Influenza like illness	7			Rash maculo-papular			1
Injection site haematoma	5			Skin hypertrophy	1		
Injection site induration	5			Subcutaneous nodule	3		
Injection site pain	12			Transaminases increased		1	
Injection site pruritus	2			Urticaria	1		
Injection site reaction	37	2		White blood cell ct. decreased	4		

- There have been no RLT or grade ≥ 3 SAE attributable to SurVaxM.
- The most common AE was grade 1-2 injection site reactions

Immunomonitoring

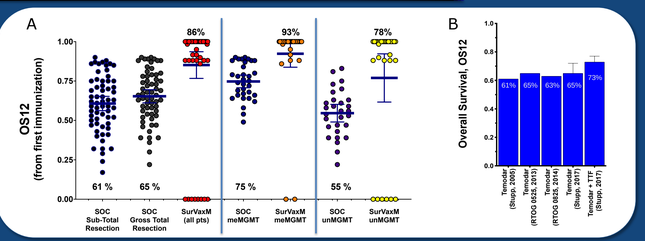


A) Antibody titers of patients receiving SurVaxM. SurVaxM produced an increase in survivin-specific IgG titre from pre-vaccine baseline to ≥ 1:10,000 in 67% of pts and ≥ 1:100,000 in 27%.

B-F) Patient titers vs overall survival. Increasing anti-SurVaxM antibody levels was observed to be correlated with better survival.

G) CD8+ T cell responses were observed and continue to be assessed.

Historical Comparators



A) Nomogram* prediction of overall survival and stratification for MGMT status.

The glioblastoma nomogram incorporates individual patient characteristics to predict expected "standard of care" (SOC) response.

- Here, OS is measured from first immunization to better align with historical randomized studies as a comparator.
- SOC O12 prediction is based upon age, sex, KPS, gross total resection (GTR) & MGMT status.
- The predicted SOC OS12 is compared to the actual SurVaxM OS12 of each patient.

***B)** Historical OS12 for SOC from several large Phase 3 clinical trials, shown for reference*

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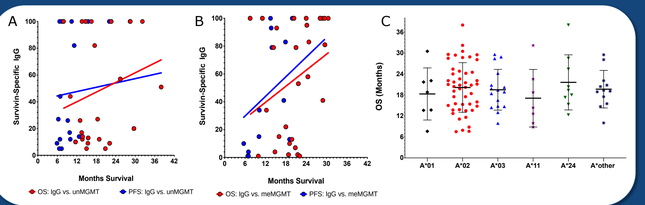
Immune Response Correlations



A) Correlation of anti-SurVaxM IgG and OS in unMGMT pts; **B)** Correlation of anti-SurVaxM IgG and OS in meMGMT pts;

- Survivin is known to be a poor prognostic marker for patients with glioblastoma.
- SurVaxM immunization appears to alter this association. Anti-survivin IgG and OS were correlated.

C) Comparison of different patient HLA allele status vs. Overall Survival (OS)

- SurVaxM is expected to not be HLA restricted

Conclusions

SurVaxM immunotherapy generated encouraging efficacy and immunogenicity in nGBM with minimal toxicity. A randomized, prospective trial of SurVaxM in nGBM is planned.

- Median PFS of 15.5 mos. from diagnosis (12.1 mos. from first immunization)
- PFS6 of 97% from diagnosis (71% from first immunization)
- OS12 of 94% from diagnosis (86% from first immunization)

Acknowledgements

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MimiVax, LLC holds the worldwide license for development of SurVaxM.
MSA, MJC & RAF are equity shareholders of MimiVax, LLC.

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