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Early Safety Data From a Randomized, Multicenter, Double-Blind, Phase 2b Study of IGV-001, an Autologous Cell Immunotherapy, Versus Placebo, in Newly Diagnosed Glioblastoma

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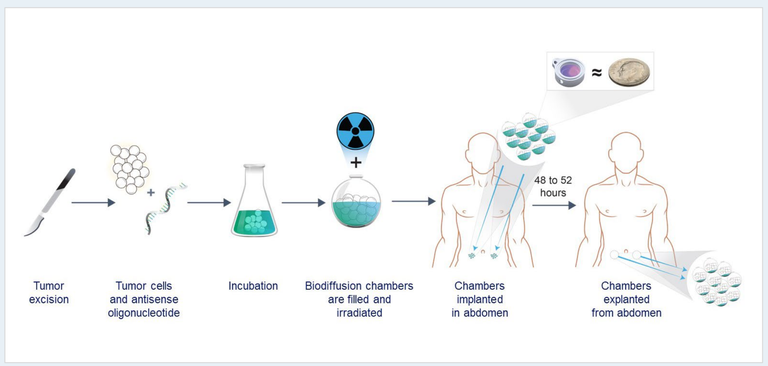
INTRODUCTION

- Standard of care (SOC) for first-line therapy in patients with newly diagnosed glioblastoma (GBM) is surgery followed by concurrent radiotherapy (RT) and temozolomide (TMZ) followed by adjuvant TMZ alone as maintenance[1]
- With SOC, overall survival (OS) was 14.6 months and progression-free survival (PFS) was 6.9 months in the Stupp trial[1]
- Insulin-like growth factor type 1 receptor (IGF-1R) is overexpressed in malignant cells, including GBM,[2] where it promotes cell growth, cell survival, and tumor progression, and is implicated in the pathophysiology of several human cancers[3-6]
- IGV-001 is the first product developed using Goldspire™, the proprietary platform of Imvax (**Figure 1**)

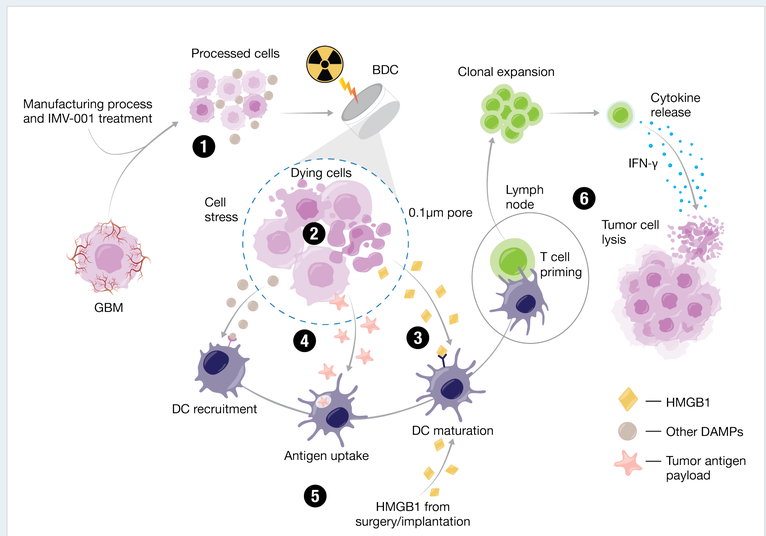
Figure 1. The Goldspire Platform



Resected glioblastoma cancer cells treated with IMV-001 are encapsulated in biodiffusion chambers (BDC) of 0.1 µm pore size, which allow tumor antigens and immune-stimulating molecules but not tumor cells to diffuse. BDCs are irradiated, producing IGV-001, which is implanted into 2 abdominal sites (between the rectus abdominis muscle and fascia) of patients for 48-52 hours, then explanted.

- IGV-001 is a first-in-class autologous immunotherapy product that combines personalized whole tumor–derived cells with an antisense oligonucleotide against IGF-1R (IMV-001), in implantable biodiffusion chambers (BDC). The BDC device combination product is irradiated and implanted at abdominal acceptor sites of patients and removed ~48 hours later[7]
- IGV-001 can induce cellular stresses on GBM cells in the product, resulting in immunogenic cell death and consequent antitumor immunity[8]
- Antigens from dying/dead tumor cells, IMV-001, and damage-associated molecular patterns (DAMP) immune stimulators diffuse from the BDCs into the surrounding tissue and combine with locally generated DAMPs at the implantation site to train the immune system to generate tumor-specific T-cell responses that reduce/eliminate tumor burden (**Figure 2**)[8,9]

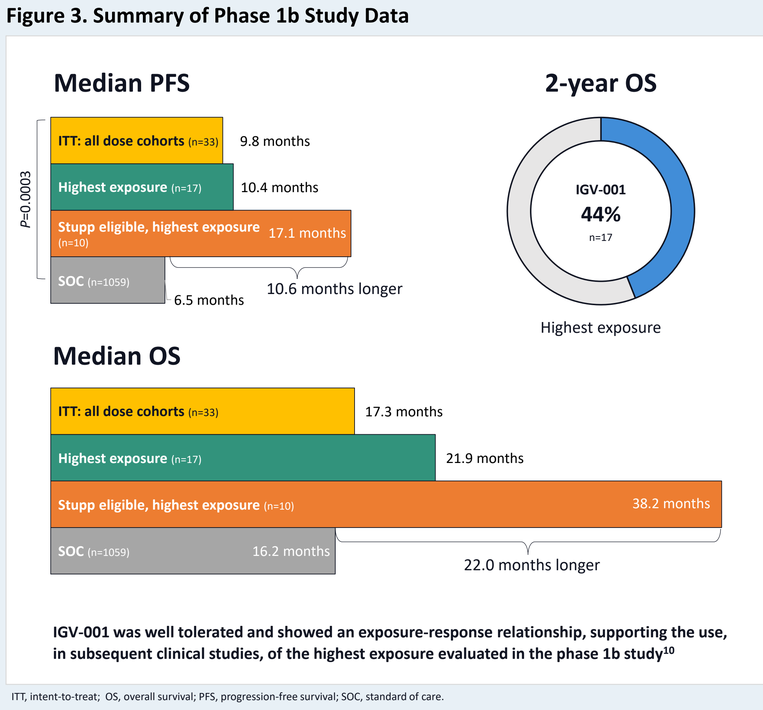
Figure 2. The IGV-001 Manufacturing Assembly and 6-Stage Mechanism of Action



Processed cells removed at the time of glioblastoma (GBM) resection are treated with IMV-001. Specifically, the following stages occur: (1) after manufacturing process (which takes approximately half day), combination drug product (IMV-001–treated autologous tumor cells plus additional IMV-001) is placed in biodiffusion chambers (BDC), which are then irradiated and sent to the clinical site for implantation into the abdomen of the patient; (2) due to the irradiation, isolated IMV-001 treatment, low-nutrient environment, and inability to adhere inside the BDC, tumor cells are exposed to cellular stresses that ultimately result in cell death; (3) high mobility group box 1 (HMGB1), and damage-associated molecular patterns (DAMP) produced during immunogenic cell death (ICD), are released from stressed/dying cells inside the BDCs and from the surrounding damaged tissue at the implantation site; (4) also released from the BDCs is a tumor antigen payload (<0.1 µm in size); (5) dendritic cells (DC) are recruited by DAMPs adjuvanticity and mature upon tumor antigen uptake; (6) DC-primed T cells undergo clonal expansion and tumor antigen-specific T cells kill tumor cells.
IFN-γ, interferon gamma.

- In a phase 1b study (NCT02507583),[10] median PFS and OS compared favorably with SOC arms of published studies (**Figure 3**)[11-13]

Figure 3. Summary of Phase 1b Study Data



IGV-001 was well tolerated and showed an exposure-response relationship, supporting the use, in subsequent clinical studies, of the highest exposure evaluated in the phase 1b study[10]

ITT, intent-to-treat; OS, overall survival; PFS, progression-free survival; SOC, standard of care.

OBJECTIVE

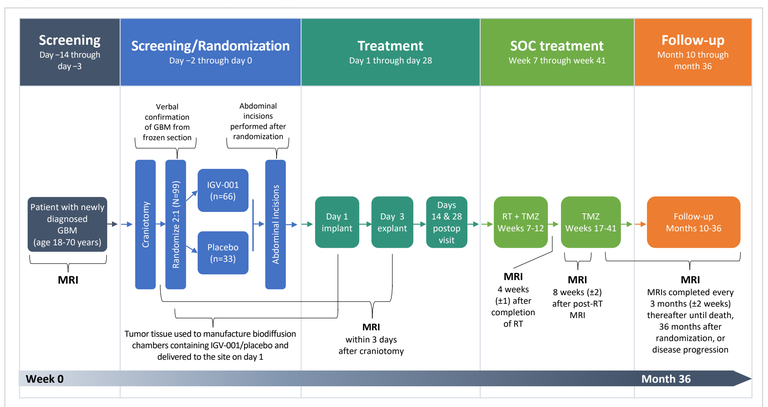
- Here, we present early blinded safety data of a phase 2b randomized, multicenter, double-blind, placebo-controlled study (NCT04485949) evaluating IGV-001 versus placebo, both followed by SOC treatment in patients with newly diagnosed GBM[7]

METHODS

Study Design

- The IGV-001 study (NCT04485949) is a multicenter, randomized, double-blind, placebo-controlled phase 2b study investigating the safety and efficacy of IGV-001 plus SOC (RT and TMZ treatments) versus placebo plus SOC in patients with newly diagnosed GBM (**Figure 4**)
- Study design and treatment plan, objectives, eligibility criteria, and statistical analyses were detailed in a prior publication[7]
- Briefly, patients were randomized 2:1 to either receive IGV-001 at 16-20 BDCs or placebo for 48-52 hours and stratified by age groups (≤50 years vs >50 years at randomization)
  - The BDCs implanted in patients in the placebo group contained inactive solution without GBM tumor cells and without IMV-001
- Six weeks after randomization, patients received RT (54-60 Gy total dose delivered as 2 Gy per fraction) per institutional standards (hence per investigators' choice) for 5 days per week along with TMZ (75 mg/m^2 orally) once daily for 6 weeks
- Four weeks after completion of RT, patients received TMZ maintenance (150-200 mg/m^2 orally) on days 1-5 of each 28-day cycle for 6 cycles (week 41)

Figure 4. Phase 2b Study Design



GBM, glioblastoma; MRI, magnetic resonance imaging; RT, radiotherapy; SOC, standard of care; TMZ, temozolomide.

Primary and Secondary Endpoints

- The primary outcome is PFS, defined as the time from randomization to first progression, as determined by blinded central radiology review, or death
- Secondary outcomes include OS, defined as the time from randomization to death due to any cause, and safety

Safety Assessments

- Safety is reported as the incidence of procedure-related adverse events (AE), treatment-emergent AEs, and serious AEs from the time the informed consent was signed during screening until the 30-day safety visit (occurring 30 days after SOC treatment or 30 days after early termination)
- AEs were coded by the investigator using the Medical Dictionary for Regulatory Activities (MedDRA) and summarized using System Organ Class and Preferred Term
- The severity (intensity) of each AE was graded by the investigator according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0
- The causal relationship between AEs and the experimental treatment was assessed by the investigator

Statistical Analysis

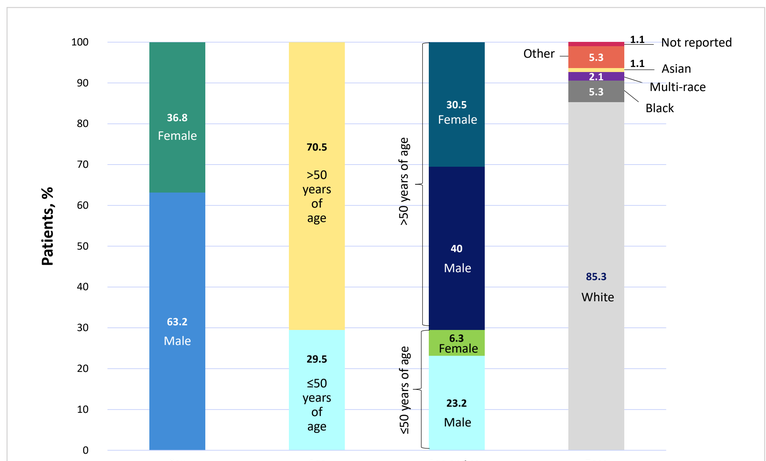
- The safety population corresponds to the intent-to-treat population and includes all randomized patients with a median follow-up of 8 months
- Each AE Preferred Term was counted once only for a given patient. If the same AE occurred on multiple occasions, the highest severity was assumed. Thus, patients were not counted multiple times in a given numerator in the calculation of frequencies for a specific AE
- SAS version 9.4 (SAS Institute, Cary, NC, USA) was used for all analyses

RESULTS

Patients' Disposition and Baseline Characteristics

- As of July 14, 2024, a total of 99 patients have been randomized and of those, 95 have been implanted with IGV-001 or placebo plus SOC
- A total of 84/94 (89.4%) patients with enough follow-up time initiated treatment with concurrent RT and TMZ
- A total of 36/95 (37.9%) randomized patients discontinued treatment during the SOC treatment period
- A total of 14/95 (14.7%) randomized patients discontinued the study after randomization
- There were 2 patients who experienced fatal AEs that led to study discontinuation (sepsis [n=1] and hypotension [n=1])
- The median age was 60.0 years (range, 24-70)
- Most randomized patients were 51-70 years of age (70.5%), male (63.2%), and White (85.3%; **Figure 5**)

Figure 5. Baseline Demographic Characteristics (Safety Population, N=95)



Early Blinded Safety

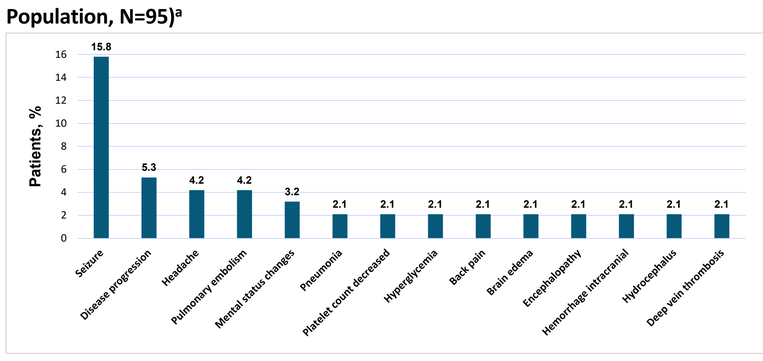
- A total of 86 SAEs have been reported from this study:
  - 85 treatment-emergent SAEs and 1 nontreatment-emergent SAE that occurred in a patient who failed screening
- SAEs occurred most frequently in the SOC Nervous system disorders (n=36 [37.9%]), the SOC General disorders and administration site conditions (n=7 [7.4%]) and the SOC Infections and infestations (n=7 [7.4%]; **Table 1**)
  - The most frequently reported Preferred Terms in these 3 SOCs include seizure (n=15 [15.8%]), disease progression (n=5 [5.3%]), and pneumonia (n=2 [2.1%]), respectively (**Figure 6**)

Table 1. Serious Adverse Events (SAE) by SOC (Safety Population, N=95)

System Organ Class	n (%)
Nervous system disorders	36 (37.9)
General disorders and administration site conditions	7 (7.4)
Infections and infestations	7 (7.4)
Injury, poisoning and procedural complications	5 (5.3)
Psychiatric disorders	5 (5.3)
Gastrointestinal disorders	4 (4.2)
Musculoskeletal and connective tissue disorders	4 (4.2)
Respiratory, thoracic and mediastinal disorders	4 (4.2)
Metabolism and nutrition disorders	3 (3.2)
Renal and urinary disorders	3 (3.2)
Vascular disorders	3 (3.2)
Blood and lymphatic system disorders	2 (2.1)
Investigations (platelet count decreased)	2 (2.1)
Surgical and medical procedures	1 (1.1)

SOC, System Organ Class.

Figure 6. Serious Adverse Events (SAE) Occurring in ≥2 Patients (Safety Population, N=95)[a]



[a]The following AEs occurred in 1 patient each (1.1%): acute kidney injury, agitation, anemia, aphasia, asthenia, Bell's palsy, *Clostridium difficile* infection, delirium, depressed level of consciousness, diarrhea, dysphagia, epilepsy, extradural hematoma, fall, gait disturbance, hematoma evacuation, hemiparesis, hyponatremia, intestinal mass, ischemic stroke, *Klebsiella* sepsis, muscular weakness, musculoskeletal stiffness, nausea, nephrolithiasis, pancytopenia, paraparesis, partial seizures, postprocedural infection, procedural pain, renal hematoma, sepsis, third cranial nerve disorder, wound complication, wound dehiscence, and wound infection.

- Overall, there were 16 (16.8%) deaths reported, regardless of causality
  - There were 2 (2.1%) deaths due to SAEs (1 death was reported due to sepsis, and the other was reported due to hypotension). These 2 SAEs were deemed not related to the blinded study product
  - Two (2.1%) deaths occurred in patients ≤50 years of age and 14 (14.7%) deaths occurred in patients >50 years of age

CONCLUSIONS

- To date, in the ongoing phase 2b randomized study designed to assess the efficacy and safety of IGV-001 in patients with newly diagnosed GBM (NCT04485949), the review of the blinded safety data did not show any emerging risk and supports that there is no change to the benefit-risk profile of treatment with IGV-001 versus placebo
- Overall, the benefit-risk profile remains positive and supports the continued development of IGV-001

LISTING OF ALL PARTICIPATING SITES AND THEIR PRINCIPAL INVESTIGATORS

State	Site (Institution)	Authors
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New Hampshire	Dartmouth Hitchcock Medical Center	Linton Evans
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New York	Columbia University Medical Center	Brian Gill
	Lenox Hill Hospital	John Boockvar,[a] Morana Vojnic
	Memorial Sloan Kettering Cancer Center	Cameron Brennan
	Montefiore Medical Center	Vijay Agarwal
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	North Shore University Hospital	Michael Schulder,[a] Samuel Singer
	Weill Cornell Medicine	Rohan Ramakrishna,[a] Rajiv Magge
	Westchester Medical Center	Simon Hanft,[a] Synphen H. Wu
North Carolina	University of North Carolina	Soma Sengupta
Ohio	Ohio State University	Brad Elder,[a] Pierre Giglio
Pennsylvania	Penn State Medical Center	Brad Zacharia,[a] Dawit Aregawi
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Rhode Island	Rhode Island Hospital	Eric T. Wong
Wisconsin	University of Wisconsin – Madison	Ankush Bhatia

[a]Site principal investigators.

DISCLOSURES

Simon Hanft reports consulting fees from Omniscient and honoraria from GT Medical Technologies.

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