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Abstract #2053

Phase 1 Study of Pritumumab in Brain Cancer

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BACKGROUND

- Gliomas are the most common primary malignant central nervous system (CNS) tumors with glioblastoma, representing approximately 57% of all gliomas.[1]
- GBM remains an incurable disease, with the median survival of approximately 15 months.[2]
- **Pritumumab** is a natural human IgG1 kappa monoclonal antibody (mAb) originally isolated from a regional lymph node of a patient with cervical carcinoma. This antibody was then produced using a human lymphoblast-like B cell line (UC729-6) and a human lymphocyte (B cell).[3]
- This mAb recognizes an altered form of the cytoskeletal protein vimentin, referred to as **ectodomain vimentin (EDV).**
- Pritumumab binds to a malignant tumor associated antigen TA226 (a form of ectovimentin).[4-5]
- EDV is an ideal target as it is expressed on the surface of tumor cells and is significantly overexpressed in GBM.
- Antitumor effect is mainly mediated by antibody dependent cellular cytotoxicity (ADCC).[6]

PHASE 1 TRIAL DESIGN

Dose Escalation Schema:

Dose Cohort	Dose Level	Patients
1	1.6 mg/kg	n = 3
2	4.8 mg/kg	n = 3
3	8.0 mg/kg	n = 3
4	12.0 mg/kg	n = 3
5	16.2 mg/kg	n = 3
	Total	15

Key Inclusion
- Age ≥18 years
- Histologically confirmed diagnosis of a CNS cancer

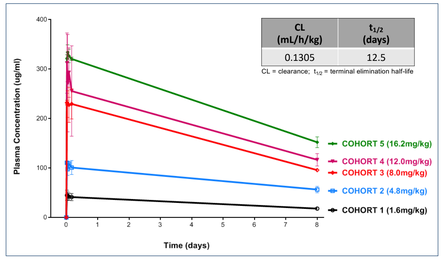
Key Exclusion
- Less than 28 days from cytotoxic therapy or less than 14 days from non-cytotoxic investigational agent

Demographics:

Characteristics	N=15
Age, years	
Median	58
Range	40-84
Gender	
Female	4 (27%)
Male	11 (73%)
Racial Origin	
White	15 (100%)
Ethnicity	
Hispanic or Latino	3 (20%)
Not Hispanic or Latino	12 (80%)
Pathology	
Glioblastoma, Grade IV	12 (80%)
Anaplastic Astrocytoma, Grade III	1 (7%)
Oligodendroglioma, Grade III	1 (7%)
NSCLC with Brain Metastases	1 (7%)
Karnofsky Performance Status	
90	3 (20%)
80	5 (33%)
70	6 (40%)
60	1 (7%)

RESULTS

Pritumumab Clinical Pharmacokinetics Profile



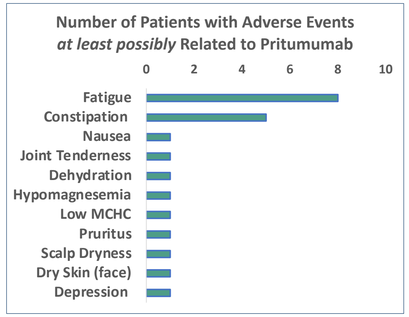
Pritumumab PK profile appears to be linear with no observed sink effect.

The PK profile for Pritumumab dosing at 16.2 mg/kg allows for an increase in therapeutic efficacy without toxicity.

Safety Data

Safety Population	15
Number of subjects with TEAE	15 (100%)
Drug-related	10 (66.7%)
Number of subjects with Grade 3-4 TEAEs	12 (80.0%)
Drug-related	0 (0%)
Number of subjects with SAEs	8 (53.3%)
Drug-related	0 (0%)

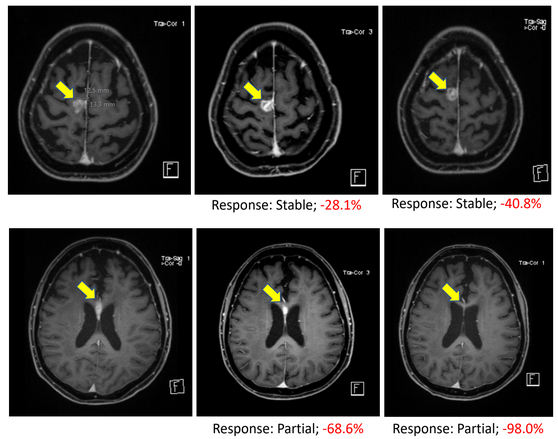
Adverse Events



Biomarker Profile

MGMT: Methylated
BRCA1: Mutated
CDKN2A: Copy Number Loss
EGFR: Amplified
LZTR1: Somatic Variant
PD-1: Positive, 2-5/HPF
PD-L1: Positive, 2+, 100%
TOPO1: 2+, 100%
TS: Positive, 2+, 25%
TMB: Intermediate, 11 mut/Mb

Subject Response



CONCLUSIONS

- This study evaluated the safety of pritumumab in brain tumor patients
- No Grade 3 or 4 toxicities related to Pritumumab
- No Serious Adverse Events related to Pritumumab
- Results from Phase 1 NAS-101 trial (NCT04396717) show that single agent Pritumumab is **safe**
- Phase 1 study established a **Maximum Feasible Dose (MFD)*** of Pritumumab as 16.2 mg/kg every 7 days
- Drug levels were in similar range to other antibodies commercially available

*Note: Maximum Tolerated Dose (MTD) was not reached

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FUTURE DIRECTION

Phase 2 studies are being planned as single agent and in combination with standard chemotherapy and checkpoint inhibitors in recurrent gliomas and upfront with chemoradiation in newly diagnosed gliomas.

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