POSTER
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Overall Survival of Recurrent Glioblastoma (rGBM) in Patients on Bizaxofusp (MDNA55), an IL-4R Targeting Toxin – Phase 2b Study

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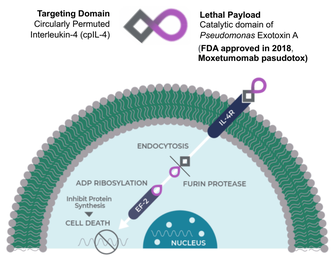
Bizaxofusp (MDNA55)

Potent IL4R Targeted Toxin



- **Target:** IL4R expressed in CNS tumors but not healthy brain
- **CED Delivery :** Bypasses Blood Brain Barrier
- **Highly Selective:** Avoids collateral damage to healthy brain
- **Disrupts the TME:** Targets IL4R positive MDSCs and disrupts Th2 bias
- **Immunogenic Cell Death:** Anti-tumor immunity is initiated and remains active after Bizaxofusp is cleared

Study Design of Bizaxofusp and External Control Arm (ECA)

Arm 1: Bizaxofusp

1. Eligibility

- Adults ≥ 18 yrs
- De novo GBM at initial diagnosis
- 1st or 2nd relapse
- No resection
- KPS ≥ 70
- IDH wild-type only
- Retrospective IL4R analysis from initial Dx

N = 44
Per Protocol Population

2. Characteristics

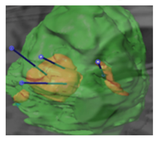
	N (%)
Total Patients	**44**
Age (median, range)	56 years (34 – 77)
Sex (Male)	27 / 44 (61%)
KPS at Enrolment: 70, 80 90, 100	22 / 44 (50%) 22 / 44 (50%)
De novo GBM	44 / 44 (100%)
Poor candidates for repeat surgery	44 / 44 (100%)
IDH Wild-type	37 / 37 (100%)
Unmethylated MGMT	23 / 40 (58%)
IL4R over-expression	21 / 40 (53%)
Steroid use during study > 4mg/day	23 / 44 (52%)
Max Tumor Diameter	29.6 mm (8 – 59)
# Prior Relapse: 1 , 2	35 (80%) , 9 (20%)

3. Bizaxofusp Administration

Single infusion of bizaxofusp by Convection Enhanced Delivery (CED)

Benefits of CED:

- Bypasses blood-brain barrier
- Maximizes drug exposure at tumor
- Avoids systemic toxicities.
- Uniform drug distribution



Blue: Catheters
Orange: Tumor
Green: Bizaxofusp

4. Bizaxofusp Study Objectives

- **Primary Endpoint:**
  - Overall Survival (OS)
- **Secondary Endpoints:**
  - Safety
  - ORR (mRANO)
  - PFS (mRANO)
  - OS vs. IL4R expression

Arm 2: External Control Arm (ECA)

1. Eligibility

- Adults ≥ 18 yrs
- De novo GBM at initial diagnosis
- 1st or 2nd relapse
- No resection
- KPS ≥ 70
- IDH wild-type only
- Retrospective IL4R analysis from initial Dx

N = 81
Eligibility matched

2. Baseline Parameters for Matching Patients in ECA with Experiment Arm (Bizaxofusp)

- Age
- Sex
- KPS
- MGMT methylation status
- IL4R expression level
- Time from initial diagnosis to relapse
- Number of prior relapses
- Extent of resection at initial diagnosis
- Tumor size at relapse
- Tumor location at relapse
- Steroid use prior to treatment

3. Construction of ECA

[**STEP 1**] Data preparation: feasibility and quality, mapping, standardization, covariates

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[**STEP 2**] Estimate propensity scores: statistical models

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[**STEP 3**] Propensity score balancing algorithm - weighting

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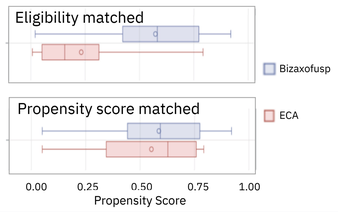
[**STEP 4**] Evaluation of balance in baseline characteristics

4. ECA Arm Objectives

Unblinding of treatment outcome of propensity matched ECA for comparative analysis with bizaxofusp data



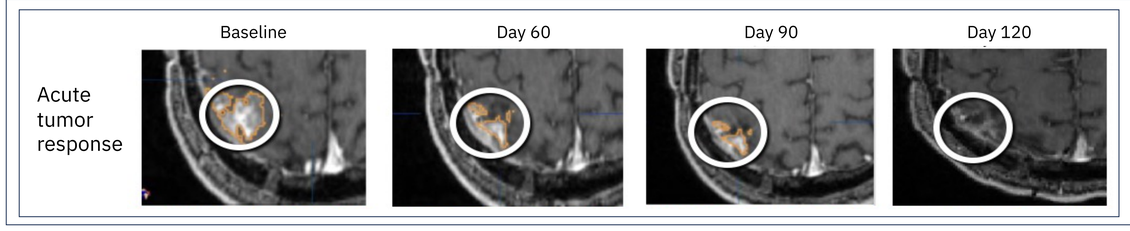
Bizaxofusp Safety

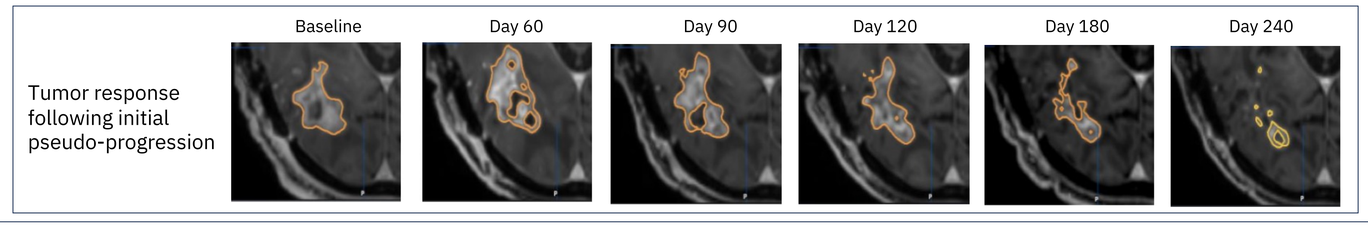
RELATED AEs ≥ GRADE 3 OCCURRING IN ≥ 5% SUBJECTS (SOC / PREFERRED TERM)	TOTAL N=47 [n (%)]
# of Subjects	10 (21.3)
Nervous system disorders	**10 (21.3)**
Brain Edema / Hydrocephalus	4 (8.5)
Hemiparesis	3 (6.3)
Seizure	3 (6.3)

RELATED SAEs OCCURRING IN ≥ 5% SUBJECTS (SOC / PREFERRED TERM)	TOTAL N=47 [n (%)]
# of Subjects	9 (19.1)
Nervous system disorders	**4 (8.5)**
Seizure	4 (8.5)

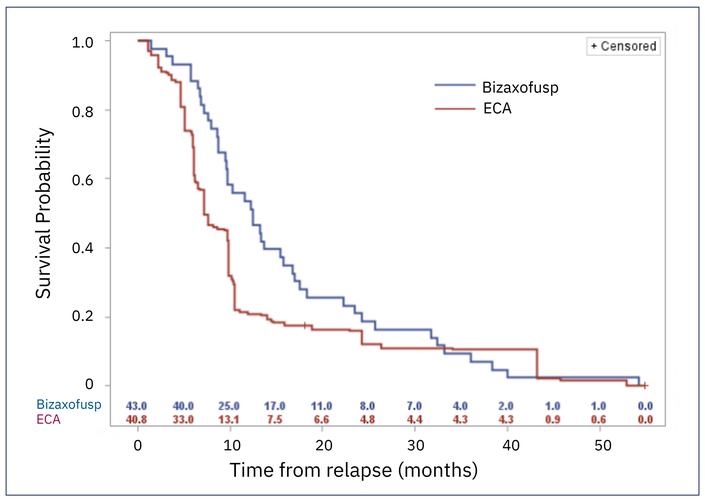
Safety data on Intended to Treat (ITT) Population (N = 47)

Tumor Response Following a Single Dose of Bizaxofusp in Patients with Unresectable Recurrent GBM





OS: Bizaxofusp vs Propensity Matched ECA

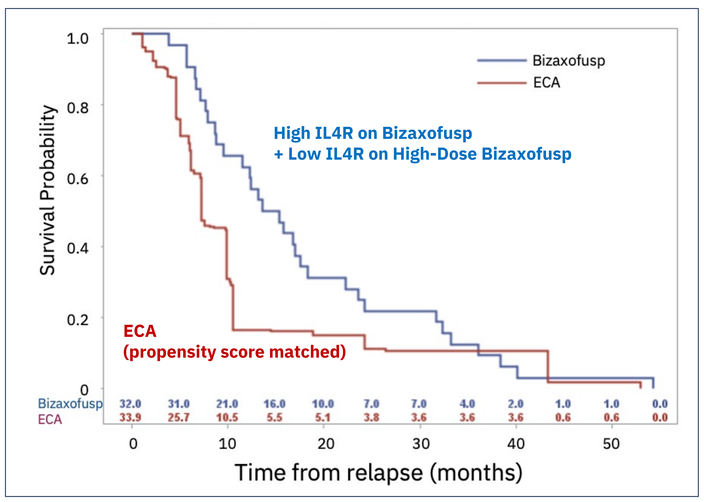


- Bizaxofusp increased mOS by 72% vs ECA
- OS-12 increased by > 2.5-fold in bizaxofusp arm

	Bizaxofusp	ECA
OS-12 (%) (95% CI)	53.5 (37.6, 67.0)	20.8 (6.5, 40.6)
OS-24 (%) (95% CI)	20.9 (10.4, 34.0)	16.1 (4.2, 35.0)
mOS* (months)	12.4	7.2

* P = 0.2717 (Log-rank test)

Bizaxofusp Doubled mOS Irrespective of IL4R Expression vs ECA



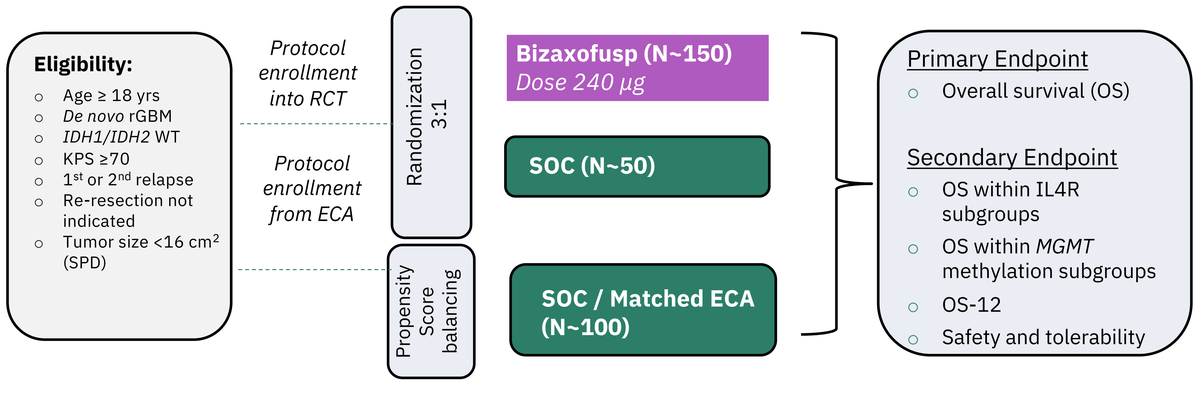
- OS increased by 370% at 1 year
- OS at 2 years improved by > 50%

	Bizaxofusp	ECA
OS-12 (%) (95% CI)	62.5 (43.5, 76.7)	16.7 (2.4, 42.1)
OS-24 (%) (95% CI)	25.0 (11.8, 40.7)	16.1 (2.1, 39.8)
mOS* (months)	14.5	7.2

* P = 0.2142 (Log-rank test)

Compelling survival benefit justifies registration trial endorsed by FDA

FDA Endorsed Design of a Phase 3 Study: Bizaxofusp vs Hybrid Control



Summary

- Among all comers, mOS was 12.4 months in the bizaxofusp arm vs 7.2 months for propensity matched ECA
- High dose bizaxofusp in planned Phase 3 population doubled mOS vs propensity matched ECA irrespective of IL-4R expression
  - mOS of 14.5 months on bizaxofusp vs 7.2 months of propensity matched ECA
- **FDA endorsed Phase 3 study design with high dose bizaxofusp and a Hybrid Control Arm that leverages propensity score balancing for the following reasons:**
  - **Large effect size demonstrated in Phase 2b study**
  - **Significant unmet medical need**
  - **Buy-in and, in fact, encouragement from FDA statistical review group**
- No systemic or clinically significant laboratory abnormalities were reported; TRAEs were primarily neurological or aggravation of pre-existing neurological deficits due to rGBM

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