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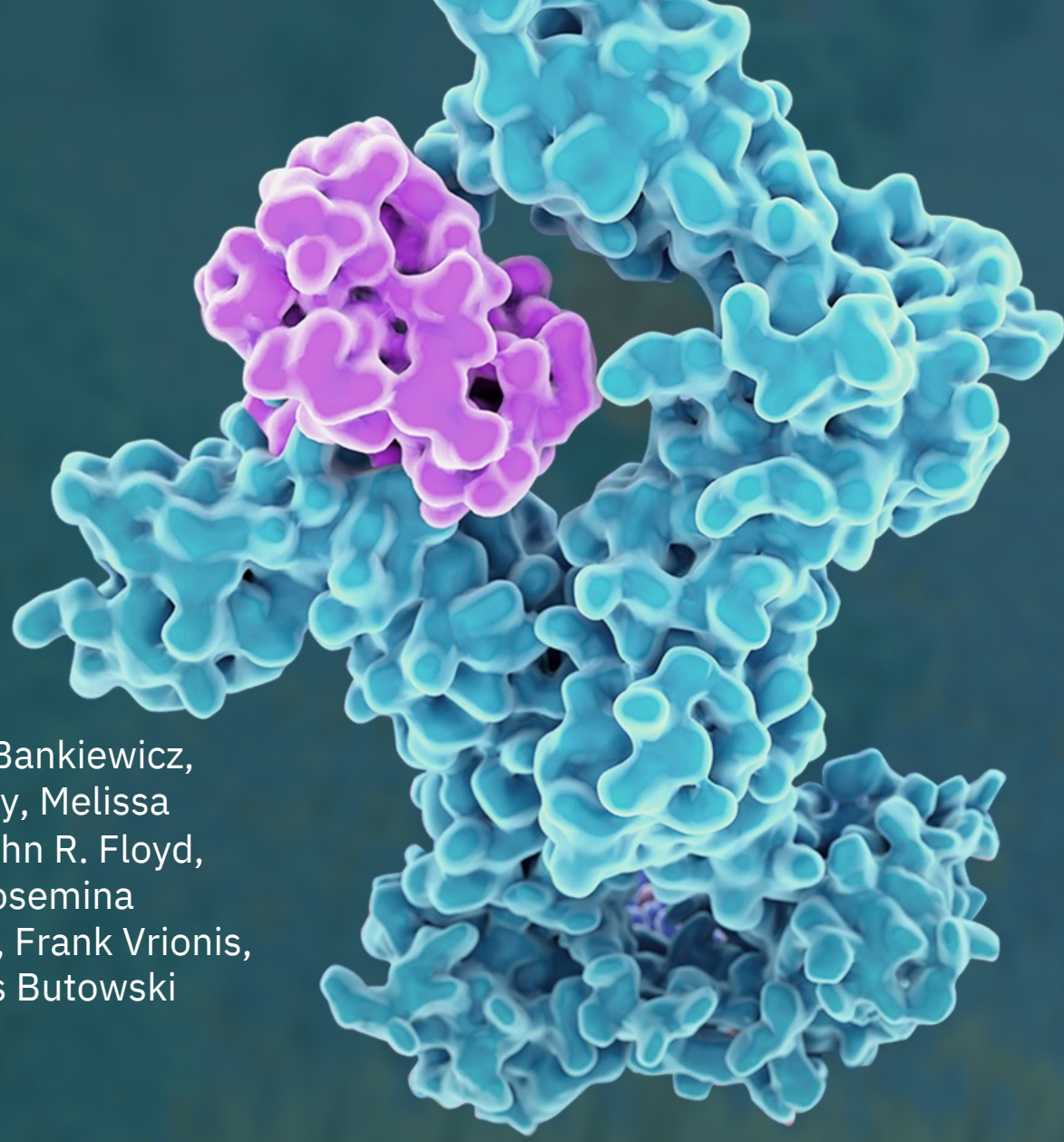
2023 SNO

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



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MEDICENNA

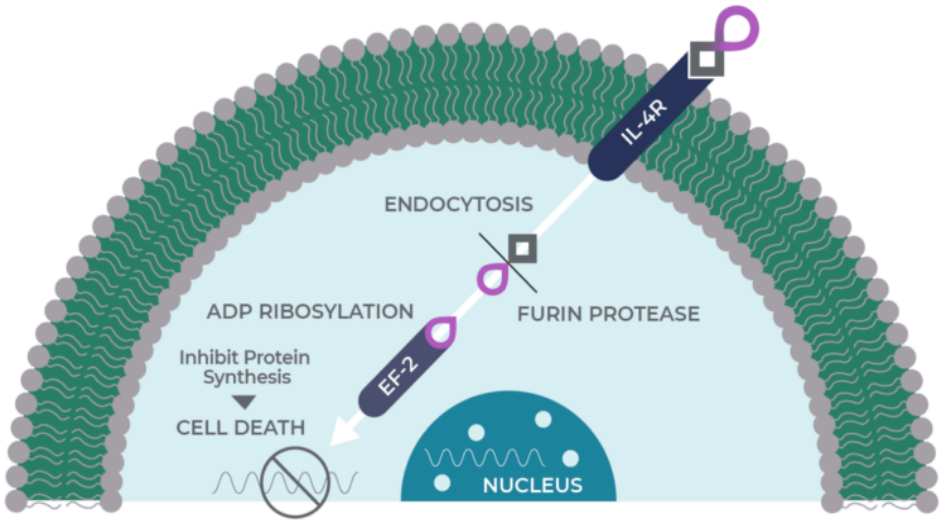
Bizaxofusp (MDNA55): Potent IL4R Targeting Toxin

- **Target:** IL4R expressed in CNS tumors but not healthy brain
- **CED:** 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

Targeting Domain
Circularly Permuted Interleukin-4 (cpIL-4)

Lethal Payload
Catalytic domain of *Pseudomonas* Exotoxin A

(FDA approved in 2018, Moxetumomab pasudotox)



Study Design: Bizaxofusp Treatment Arm

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

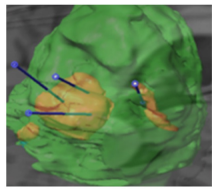
2. Characteristics	N (%)
Total Patients	**44**
Age (median, range)	56 years (34 – 77)
Sex (Male)	27 / 44 (61%)
KPS at Enrolment: 70, 80 90, 100	22 / 44 (50%) 22 / 44 (50%)
De novo GBM	44 / 44 (100%)
Poor candidates for repeat surgery	44 / 44 (100%)
IDH Wild-type	37 / 37 (100%)
Unmethylated MGMT	23 / 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)
  - mOS vs. IL4R expression

Study Design: 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
- IL4R analysis from initial Dx

N = 81
Eligibility matched

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

- 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

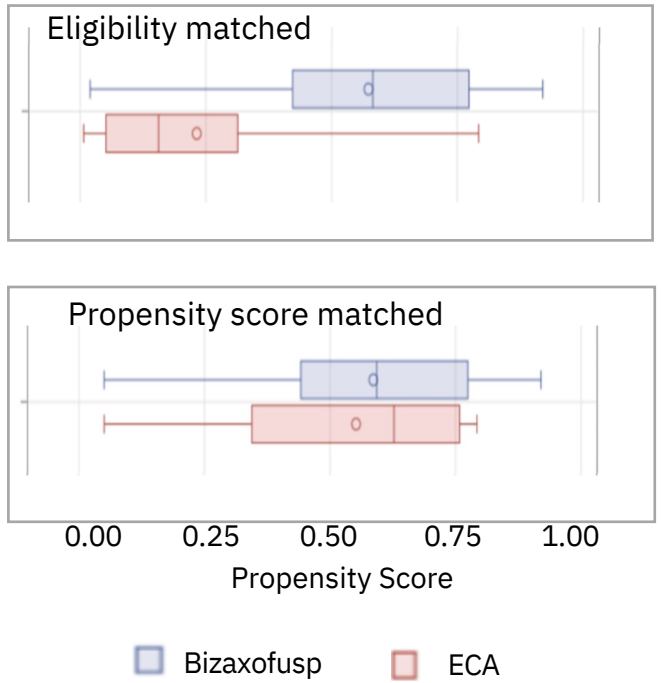
[STEP 2] Estimate propensity scores: statistical models

[STEP 3] Propensity score balancing algorithm - weighting

[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



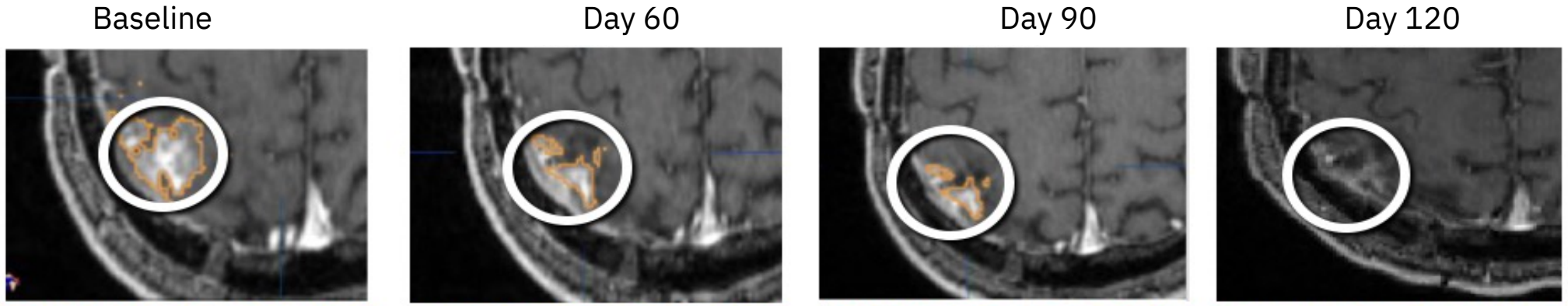
Bizaxofusp Safety Profile

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)

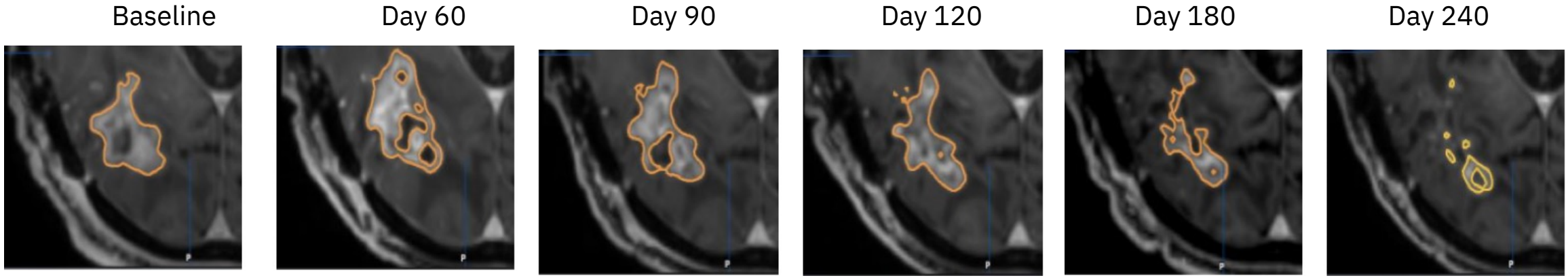
RELATED SAEs OCCURRING IN ≥ 5% SUBJECTS (SOC / PREFERRED TERM)	TOTAL N=47 [n (%)]
# of Subjects	9 (19.1)
Nervous system disorders	**4 (8.5)**
Seizure	4 (8.5)

Tumor Response Following Single Dose of Bizaxofusp

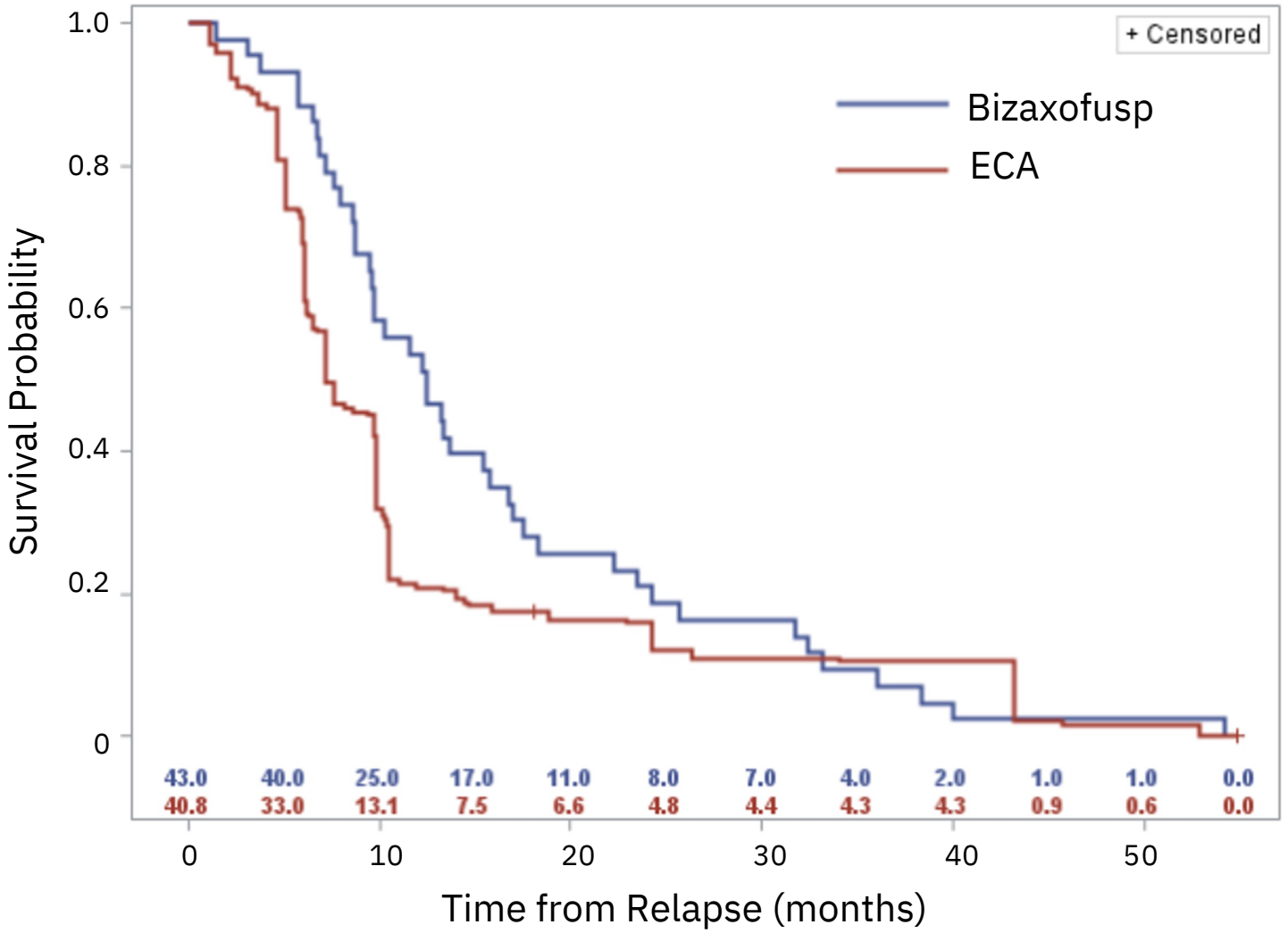
Acute tumor response



Tumor response following initial pseudo-progression



Overall Survival : Bizaxofusp vs. Propensity Matched ECA

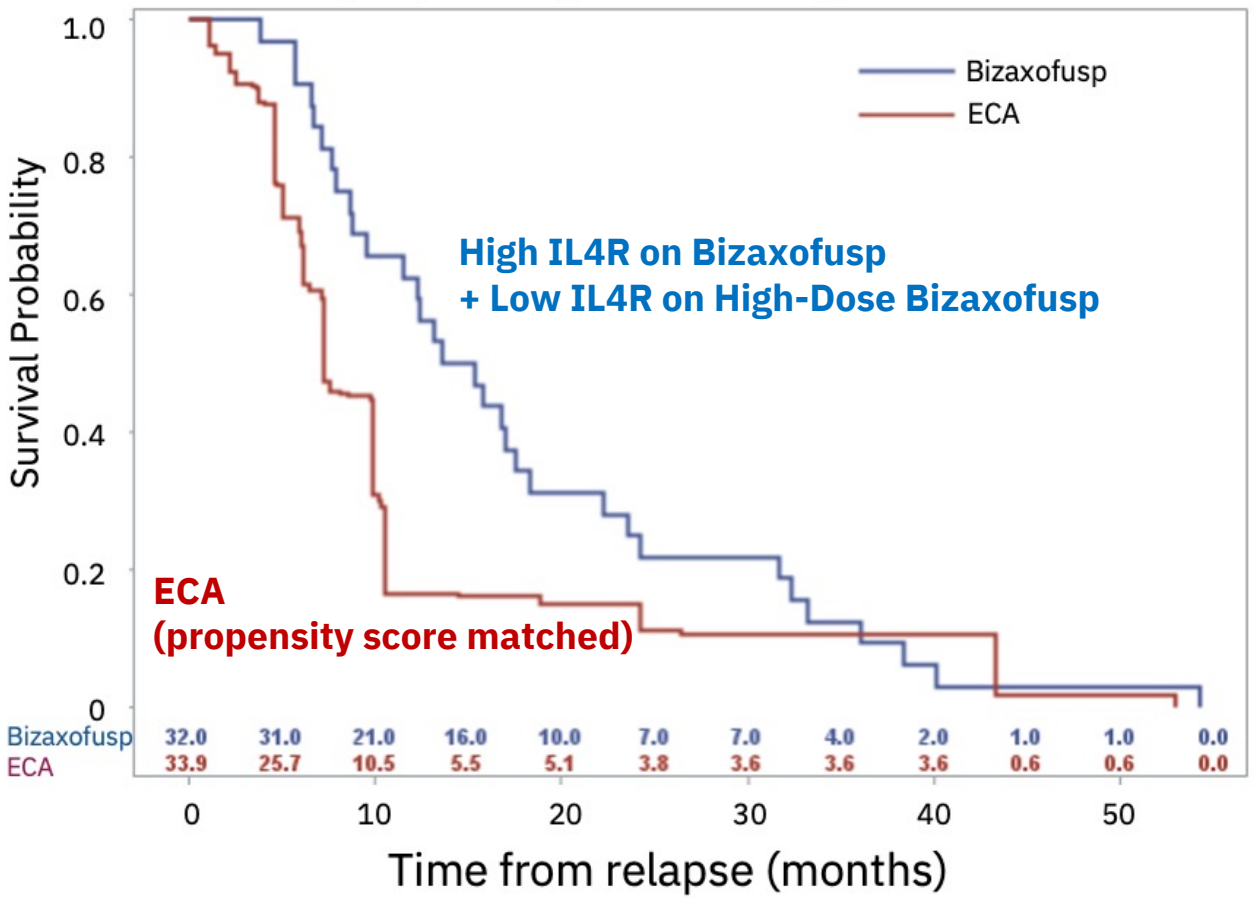


- Bizaxofusp increased mOS by 72% vs ECA
- OS-12 Increased by > 2.5-fold in bizaxofusp arm

	Bizaxofusp (all comers)	**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)

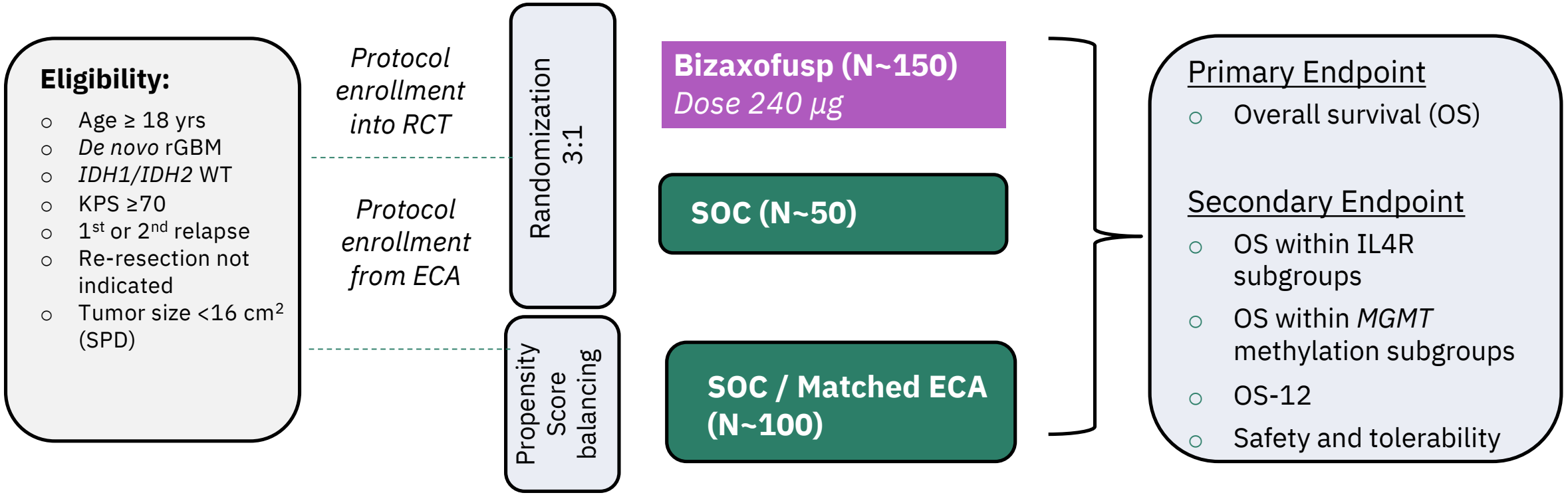
Compelling survival benefit justifies registration trial endorsed by FDA

Interim and Complete Survival Data for Bizaxofusp

	Interim Survival Data	Complete Survival Data
	30 months follow up	52 months follow up
All Comers [N = 43]		
mOS	12.4 months	12.4 months
OS-12	53.5%	53.5%
OS-24	18.6%	21%
OS-36	N/A	9.3%
Patients Censored*	6	None
Phase 3 Population [N = 32; High IL-4R (all bizaxofusp doses) + Low IL-4R (high dose bizaxofusp)]		
mOS	14.5 months	14.5 months
OS-12	62.5%	62.5%
OS-24	21.8%	25%
OS-36	N/A	12.5%
Patients Censored	6	None

*Patients censored for analysis

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 of 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 score 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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.....And most of all, to the patients & their families

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