BIOS-03 - Real world clinical outcomes of patients with diffuse midline glioma in a longitudinal outcomes registry

Timothy J. Stuhlmiller[1], Asher Wasserman[1], Jameson Quinn[1], Zac Cole[1], Alaa Awawda[1], Sabrina Irizarry[1], Sebastian Williams[1], Mark Shapiro[1], Al Musella[2], Santosh Kesari[3]

[1]xCures, Inc., Oakland, CA; [2]The Musella Foundation, Hewlett, NY; [3]Pacific Neuroscience Institute, Santa Monica, CA

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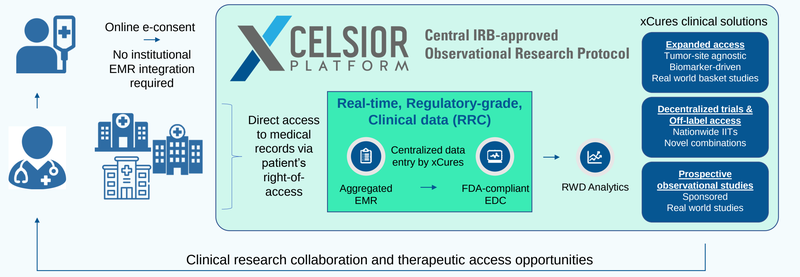
Abstract



We utilized the longitudinal clinical outcomes registry XCELSIOR (NCT03793088) to understand real world outcomes and treatment patterns among patients with diffuse midline glioma. A total of 85 patients were identified with a diagnosis of diffuse midline gliomas by pathology or imaging (42 pediatric and 43 adult patients). Median age at diagnosis was 19 years. As of 11/1/2022, 53 patients had expired. Median overall survival (mOS) of the entire cohort was 1.58 years (19 months). Cox proportional hazard ratio analysis identified age, tumor location, and exposure to ONC201 as significant covariates for OS. Pediatric patients had a mOS of 12.0 months and adult patients a mOS of 27.0 months from diagnosis (pediatric HR = 1.0, p = 0.01). Most frequent primary tumor locations in this dataset were pons (33%) and thalamus (21%). Pons location was associated with worst survival (mOS 12.0 months, N=30 patients). The most common anti-cancer interventions among all patients were temozolomide (44 patients), ONC201 (39 patients), bevacizumab (27 patients), panobinostat (7 patients), and immune checkpoint inhibitors (4 patients pembrolizumab, 3 patients nivolumab, and 1 patient ipilimumab/nivolumab combination). In this dataset, ONC201 was statistically significant in a Cox proportional hazard model (HR = -1.15, p=0.03, mOS for patients exposed vs. not exposed to ONC201 = 19.6 months vs. 11.4 months). Treatment with immune checkpoint inhibitors trended toward benefit in the entire population (HR = -0.21, p=0.74). The subpopulation of patients treated with ONC201 whose tumor also harbored a TP53 mutation displayed a tendency toward activity (n=12); TP53-mutant patients treated with ONC201 had a mOS of 25.0 months vs. TP53 wild-type patients treated with ONC201 had a mOS of 15.7 months. This abstract text is updated based on additional patient enrollment and data annotation since submission.

Summary of Real-World Dataset

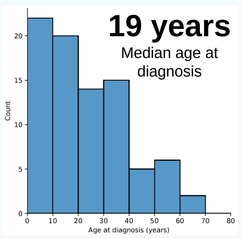
As of November 1st, 2022:

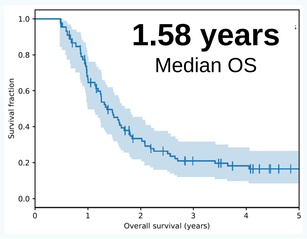
117 patients with diffuse midline glioma (DMG) in XCELSIOR registry

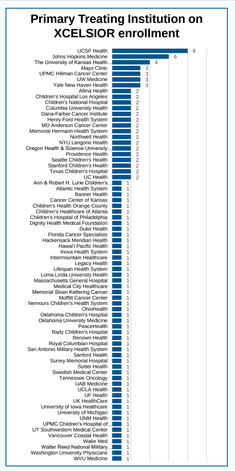
85 patients with annotated longitudinal history

Patients seen at **211** Institutions

10.7 mo Median follow-up from diagnosis

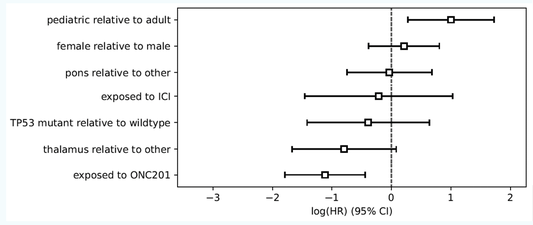






Results

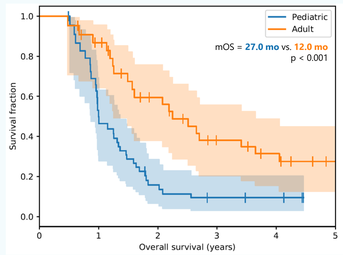
1A Cox Proportional Hazard analysis identifies adult age at diagnosis and exposure to ONC201 as associated with better overall survival



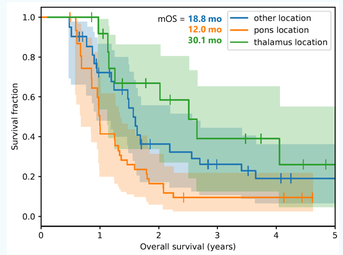
1B

log(HR) [95% confidence]	p-value
1.0 [0.28-1.72][a]	0.01
0.21 [-0.38-0.81]	0.48
-0.03 [-0.75-0.68]	0.93
-0.21 [-1.46-1.03]	0.74
-0.39 [-1.42-0.64]	0.46
-0.79 [-1.67-0.08]	0.08
-1.12 [-1.79–-0.44][b]	<0.001

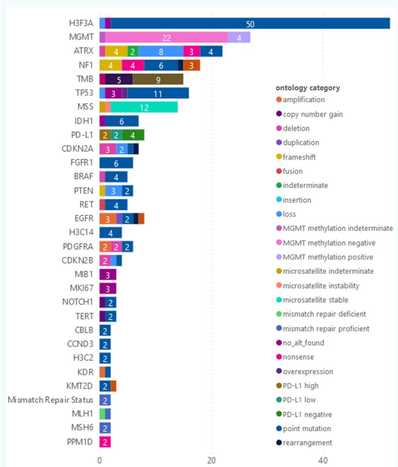
1C Pediatric age at diagnosis is associated with worse overall survival



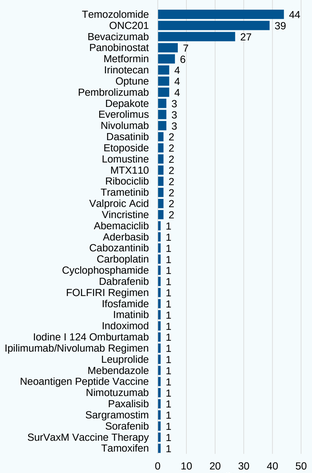
1D Pons location is associated with worst overall survival; thalamus location is associated with best overall survival



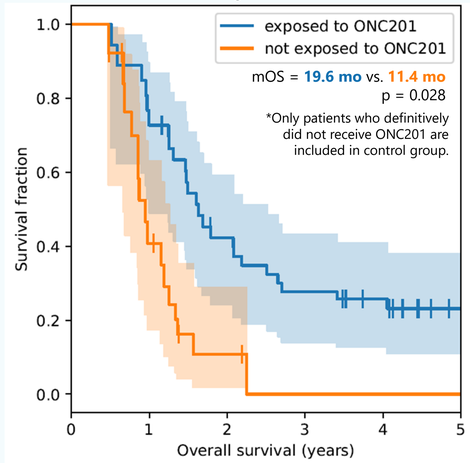
2A Genomic alterations across cohort (2+ patients with altered biomarker)



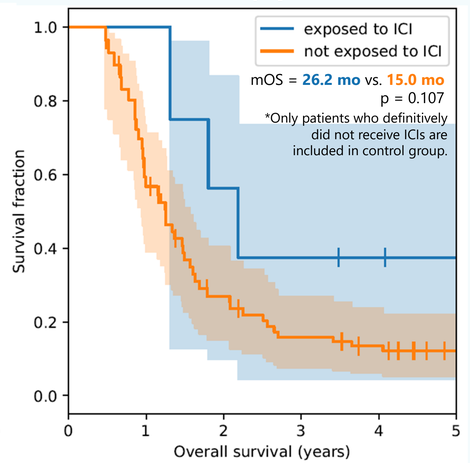
2B Anti-cancer agents utilized in DMG patients



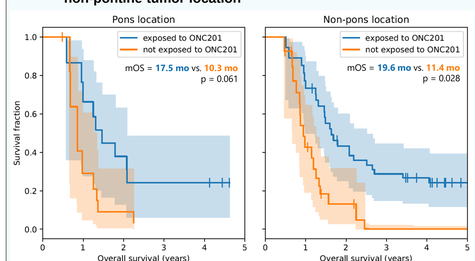
3A ONC201 significantly extends OS vs. a cohort of patients who did not receive ONC201 during their treatment*



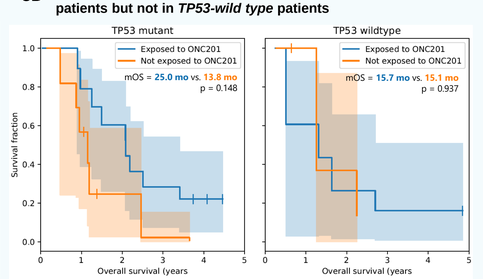
3B Immune checkpoint inhibitor (ICI) exposure numerically extends OS but is not statistically significant*



3C ONC201 exposure significantly extends OS in patients with non-pontine tumor location



3D ONC201 numerically extends OS in *TP53-mutant* patients but not in *TP53-wild type* patients



Conclusions

- **xCures clinical research platform:** XCELSIOR is a master observational research protocol designed to generate ***Real-time, Regulatory-grade, Clinical data (RRC)*** on patients with advanced cancer. Clinical data elements are abstracted into an FDA-compliant EDC from EMR – each data element is source-verified by electronic documents.
- **DMG findings:** ONC201 significantly extends OS in patients with DMG. In patients with pontine tumor location (DIPG), ONC201 numerically increases mOS. *TP53* mutation status may impact ONC201 activity, but greater numbers of patients are required. Patients undergoing active treatment will be included in subsequent analyses.
- **Collaboration opportunities:** xCures manages a patient-centric platform for observational research under a central IRB approved research protocol and is open to academic research collaborations. Patient-granted access to entire longitudinal EMR including clinic notes, lab reports, imaging reports, raw DICOMS, raw NGS data, and other diagnostic testing offers potential to answer multiple real-world research questions.

Scan here to learn more about collaboration opportunities and to refer patients for observational research!