Post Society for Neuro-Oncology Management Conference Call

November 22, 2021

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Forward-Looking Statements

These slides contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that are subject to risks and uncertainties that could cause actual results to differ materially from those projected. Forward-looking statements include those relating to, among other things, the status of Chimerix's oncology programs, and the results of the 50-patient efficacy analysis of ONC201, including those related to the potential safety and benefit of ONC201 or the prevalence or severity of H3K27M mutant glioma. Among the factors and risks that could cause actual results to differ materially from those indicated in the forward-looking statements are risks that the current clinical study data for ONC201 will not support accelerated, or any, regulatory approval; the anticipated benefits of the acquisition of Oncoceutics may not be realized; the ability to generate positive results in a Phase 3 study in acute myeloid leukemia and subsequent approval for DSTAT; risks that ongoing or future trials may not be successful or replicate previous trial results, or may not be predictive of real-world results or of results in subsequent trials; risks and uncertainties relating to competitive products and technological changes that may limit demand for our drugs; risks that our drugs may be precluded from commercialization by the proprietary rights of third parties; and additional risks set forth in the Company's filings with the Securities and Exchange Commission. These forward-looking statements represent the Company's judgment as of the date of this release. The Company disclaims, however, any intent or obligation to update these forward-looking statements.

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Clinical Efficacy of ONC201 in Recurrent H3 K27M- Mutant Diffuse Midline Glioma Patients

Review: Society for Neuro-Oncology 2021 Presentation

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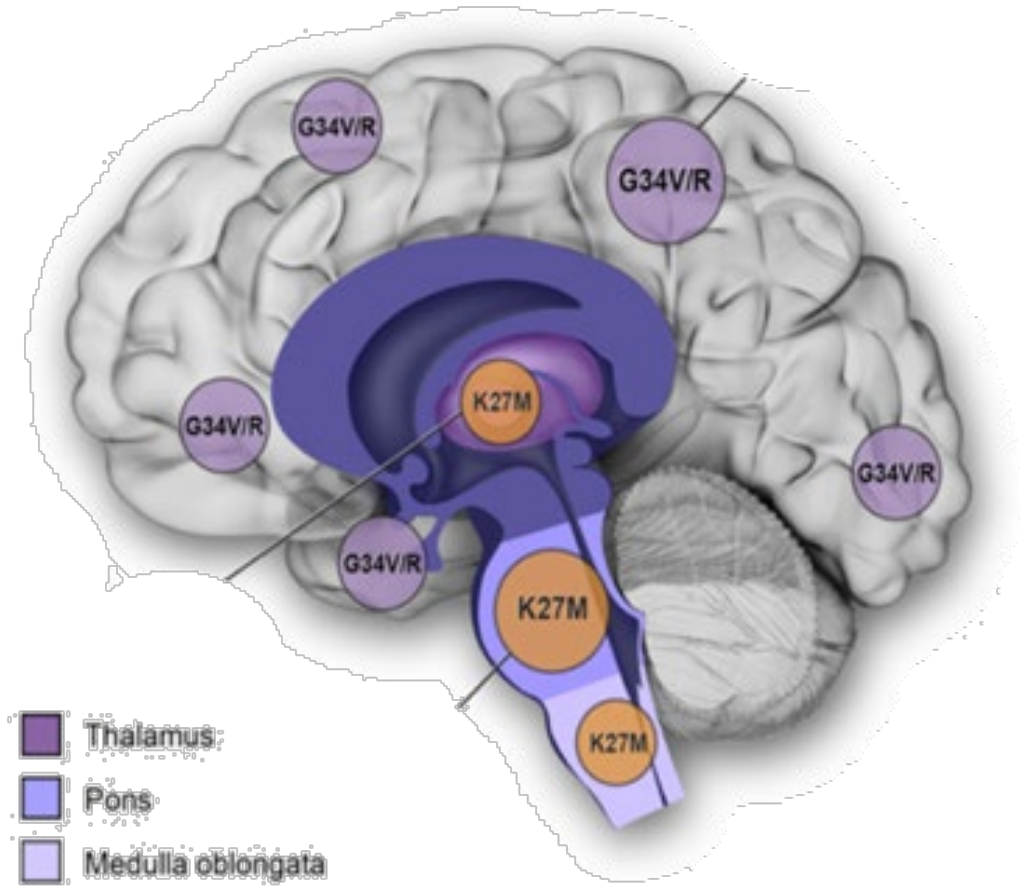
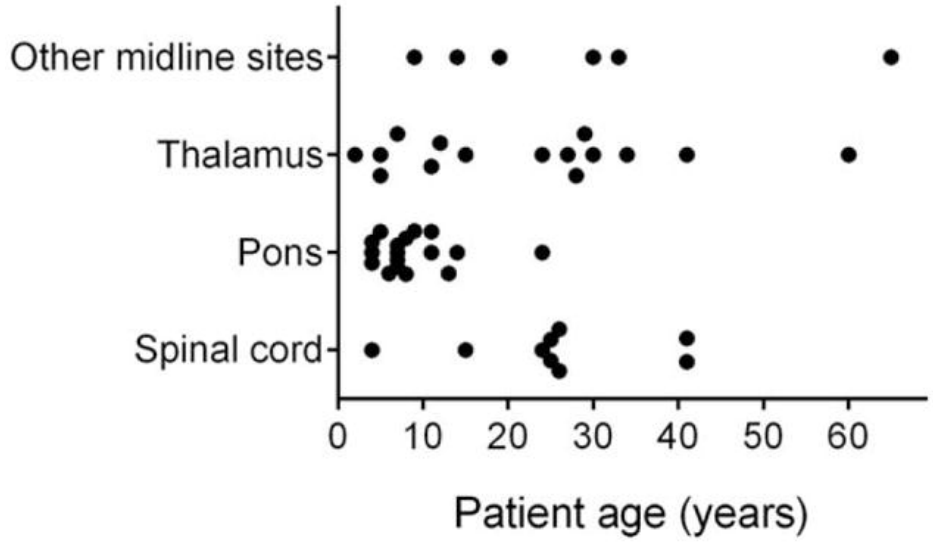
Diffuse Midline Glioma, H3 K27M-mutant



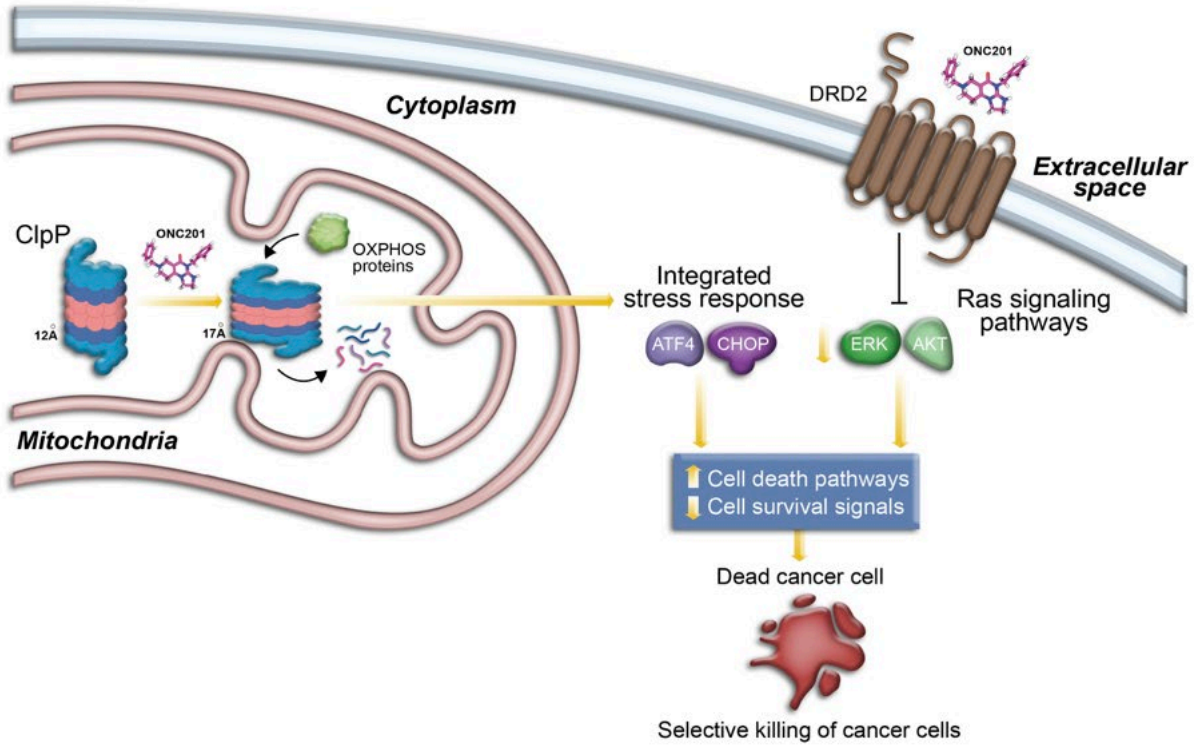
Lulla et al., *Science Advances,* 2016

- H3 K27M is detected in 50-90% of midline gliomas
- More prevalent in pediatric populations but also prevalent adults as well
- Highly aggressive malignancy; invariably lethal
- No effective drug therapies to date for recurrence
- No definite objective responses to systemic therapies by RANO HGG reported in literature in the recurrent setting



Solomon et al., *Brain Pathology* 26 (2016) 569–580

ONC201 Is a DRD2 Antagonist/ClpP Agonist



- Oral small molecule
- Once weekly dosing based on pharmacodynamics
- Well tolerated
- DRD2 antagonist and ClpP agonist that induces tumor cell apoptosis

Allen et al., *Science Translational Medicine,* 2013
Ishizawa et al, *Science Signaling*, 2016
Kline et al, *Science Signaling*, 2016
Siegelin et al, *Clinical Cancer Research*, 2018
Ishizawa et al, *Cancer Cell*, 2019

Integrated Efficacy Analysis: Objective and Eligibility Criteria

Objective

- To evaluate monotherapy efficacy of ONC201 in recurrent H3 K27M-mutant diffuse midline glioma

Eligibility

- Age ≥2yo and received ONC201 under studies ONC006, ONC013, ONC014, ONC016, or ONC018
- Diffuse glioma with a known H3K27M mutation and involvement of a midline structure of the brain
- Progressive and measurable disease on contrast-enhanced brain MRI by RANO-High Grade Glioma (HGG) criteria
- Prior therapy with at least radiation
- Washouts prior to first ONC201 dose:
- Radiation: 90 days
- Temozolomide: 23 days / Antibodies (e.g., bevacizumab): 42 days / Other anticancer therapies: 28 days
- Baseline Performance Status ≥60
- Corticosteroids stable or decreasing for at least 3 days prior to baseline scan
- Excluded: DIPG, primary spinal tumors, atypical and non-astrocytic histologies, leptomeningeal spread, CSF dissemination

Endpoints

Primary Endpoint

- Overall response rate by RANO-HGG criteria

Secondary Endpoints

- Overall response rate by RANO-Low Grade Glioma (LGG) criteria
- Duration of response[1]
- Time to response[1]
- Best overall response[1]
- Disease Control Rate[1]
- Progression-free survival[1]
- Overall survival
- Corticosteroid response rate
- Performance status response rate

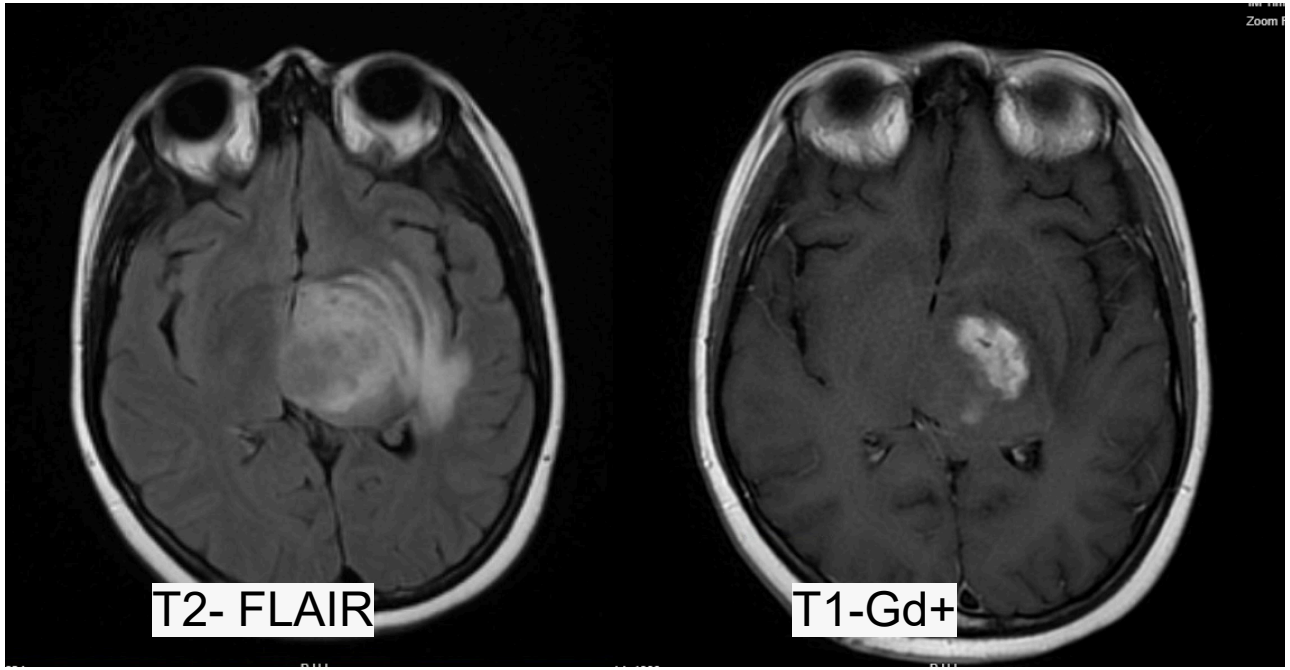
Analysis

- First 50 patient enrolled who meet eligibility for integrated efficacy analysis[2]
- Censored for all endpoints except overall survival upon eligibility criteria initiation of any additional anti-cancer therapy

[1]Assessed by RANO-HGG and RANO-LGG criteria with dual-reader blinded independent central review (BICR).
[2]As discussed and prespecified with regulatory authorities

Response Assessment Criteria for Glioma

- DMG with H3K27M typically have *both* enhancing and non-enhancing disease components
- RANO-HGG responses defined by decrease in enhancing disease
- RANO LGG response defined by decrease in T2 FLAIR

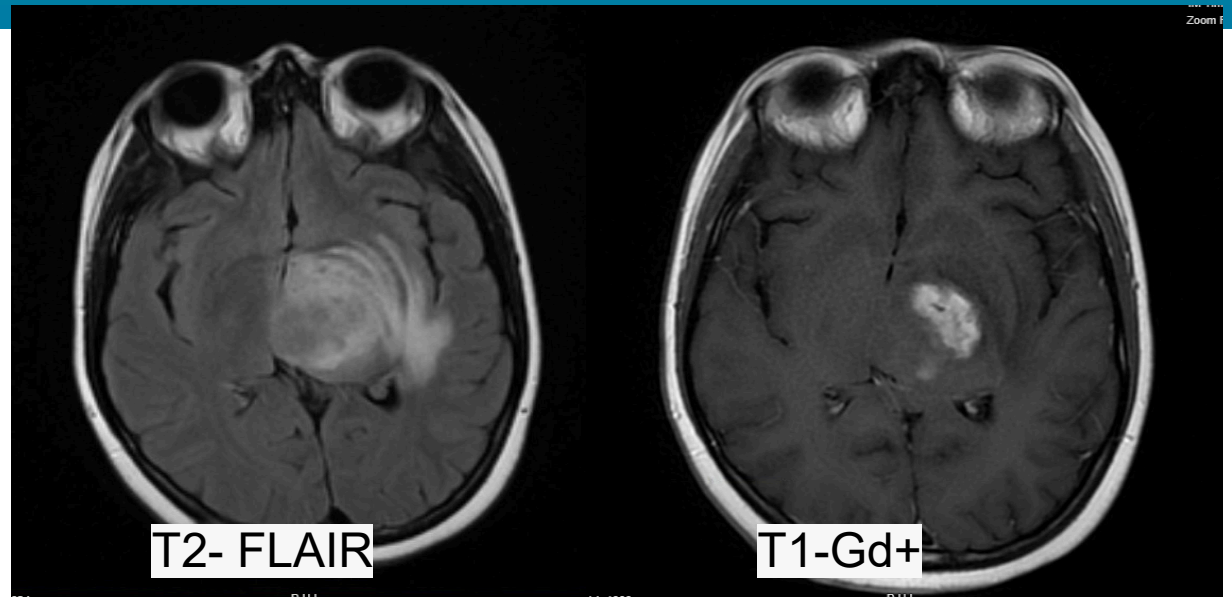


RANO- HGG

Criterion	CR	PR	SD	PD
T1-Gd +	None	≥50% ↓	<50% ↓ to <25% ↑	≥25% ↑†
T2/FLAIR	Stable or ↓	Stable or ↓	Stable or ↓	↑†
New lesion	None	None	None	Present†
Corticosteroids	None	Stable or ↓	Stable or ↓	NA‡
Clinical status	Stable or ↑	Stable or ↑	Stable or ↑	↓†
Requirement for response	All	All	All	Any‡

Response Assessment Criteria for Glioma

- RANO LGG response defined by decrease in T2 FLAIR



RANO- LGG

Criterion	CR	PR	MR	SD	PD
T2/FLAIR	Disappearance of all lesions	≥50% ↓ in perpendicular diameters of lesion, sustained for 4 weeks	25–50% ↓ in perpendicular diameters of lesion	<25% ↓ to <25% ↑	≥25% ↑[†]
New lesion	None (apart from those consistent with radiation effects, and no new or increased enhancement)	None (apart from those consistent with radiation effects, and no new or increased enhancement)	None (apart from those consistent with radiation effects, and no new or increased enhancement)	None (apart from those consistent with radiation effects, and no new or increased enhancement)	Present[†]
Corticosteroids	None	Stable or ↓	Stable or ↓	Stable or ↓	NA[‡]
Clinical status	Stable or ↑	Stable or ↑	Stable or ↑	Stable or ↑	↓[†] (not attributable to other causes apart from the tumor, or decrease in corticosteroid dose)
Requirement for response	All	All	All	All	Any[‡]

Patient Demographics and Disease Characteristics

	N=50
Age (years), median (range)	30 (8 – 70)
<18 years, N(%)	4 (8%)
18 - <40 years, N(%)	32 (64%)
≥40 years, N(%)	14 (28%)
Gender, N(%)	
Male	27 (54%)
Female	23 (46%)
Race, N(%)	
White	39 (78%)
Other	6 (12%)
Black	3 (6%)
Asian	1 (2%)
Not reported	1 (2%)
Body weight (kg), median (range)	88 (29 – 199)
Performance status (KPS/LPS), N(%)	
60-70	14 (28%)
80	20 (40%)
90-100	16 (32%)

	N=50
Primary tumor location, N(%)	
Thalamic	33 (66%)
Other midline	17 (34%)
Multifocal disease[1], N(%)	23 (46%)
>1 Target lesion, N(%)	9 (18%)
Tumor size[2] (cm^2), median (range)	10.4 (1.6 – 40.8)
H3 K27M detection method	
IHC, N(%)	47 (94%)
NGS, N(%)	3 (6%)
First recurrence, N(%)	37 (74%)
Prior temozolomide, N(%)	44 (88%)
Time from recurrence, days, median (range)	20 (1 – 126)
Time from prior radiation, months, median (range)	7.5 (3 – 104)
Time from initial diagnosis, months, median (range)	10.9 (5 – 105)
Daily steroid dose (mg, dex equiv): median (range)	1.1 (0.0 – 12.0)

[1]Multifocal disease includes non-target lesions
[2]Sum of product of diameters of enhancing target lesions per BICR

Dosing & Disposition

- Dosing
  - Oral 625 mg ONC201 (scaled by body weight for pediatric patients)
  - Once every week with exception of one patient dosed once every 3 weeks
- Last patient enrolled February 26, 2020
- Data cutoff for analysis May 31, 2021
- Median follow-up 18.8 months
- Disposition
  - Five patients remain on study drug; four patients continue post-progression

Serious Adverse Events

	Any attribution, N (%)	Related, N (%)
Any SAE[1]	**25 (50%)**	**1 (2%)**
Gastrointestinal disorders		
Nausea	2 (4%)	0
Vomiting	2 (4%)	0
General disorders and administration site conditions		
Disease progression	2 (4%)	0
Nervous system disorders		
Brain oedema	2 (4%)	0
Encephalopathy	4 (8%)	0
Headache	3 (6%)	0
Respiratory, thoracic and mediastinal disorders		
Dyspnoea	2 (4%)	0
Vascular disorders		
Embolism	2 (4%)	0
Pulmonary embolism	2 (4%)	1 (2%)[2]

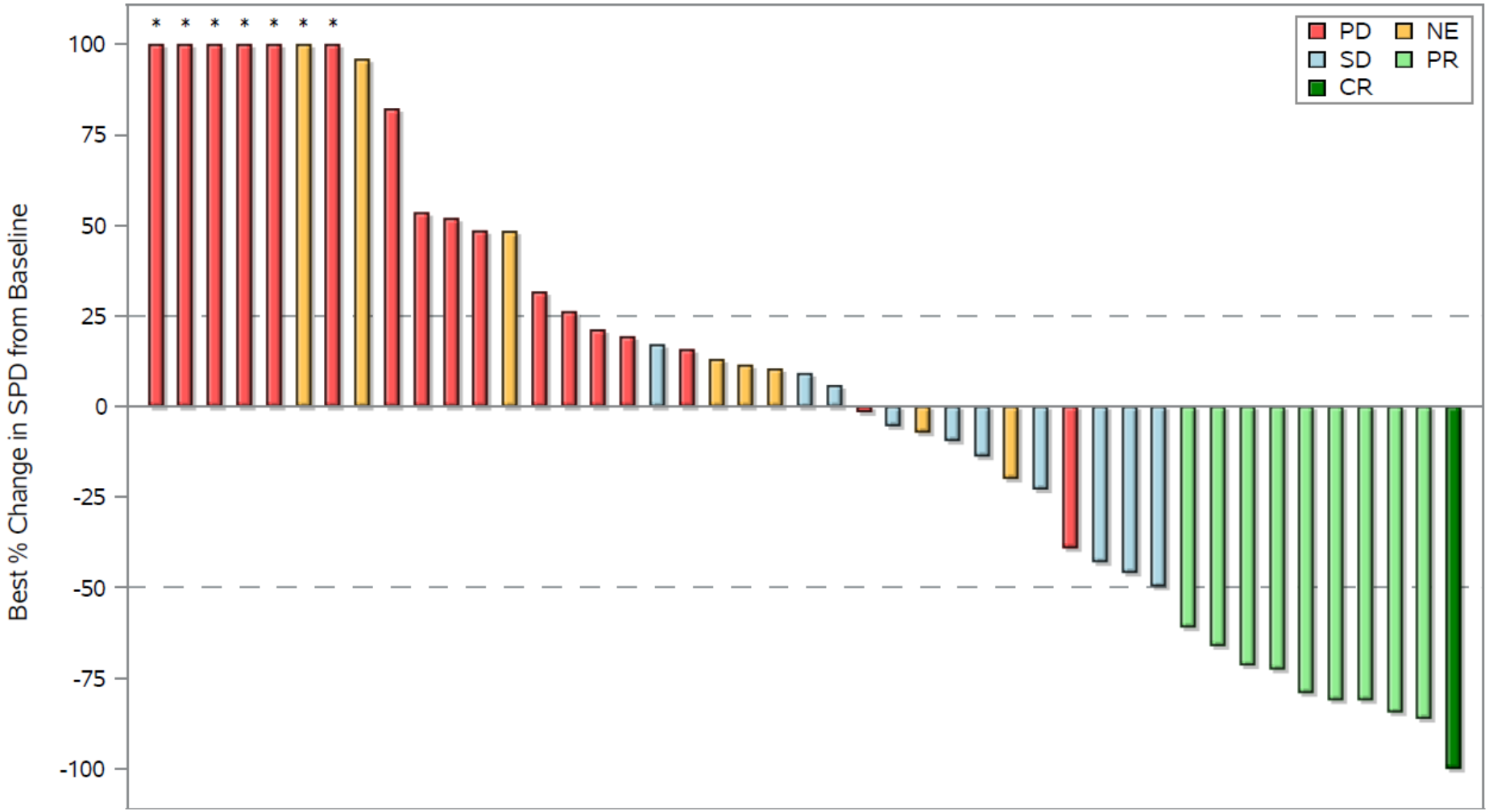
[1]Specific preferred terms occurring in more than one patient are listed; 25 patients had at least one SAE
[2]Possibly related per investigator assessment; unlikely related per sponsor assessment

Overall Response Rate (RANO-HGG)

RANO-HGG[1]	N=50
ORR (CR + PR)	**10 (20%)** 95% CI: 10 – 34%
Complete Response (CR) Partial Response (PR) Stable Disease (SD) Not Evaluable (NE)[2] Progressive Disease (PD) Not Applicable (NA)[3]	1 (2%) 9 (18%) 10 (20%) 8 (16%) 18 (36%) 4 (8%)
Disease Control Rate (CR + PR + SD)	**20 (40%)** 95% CI: 26 – 55%

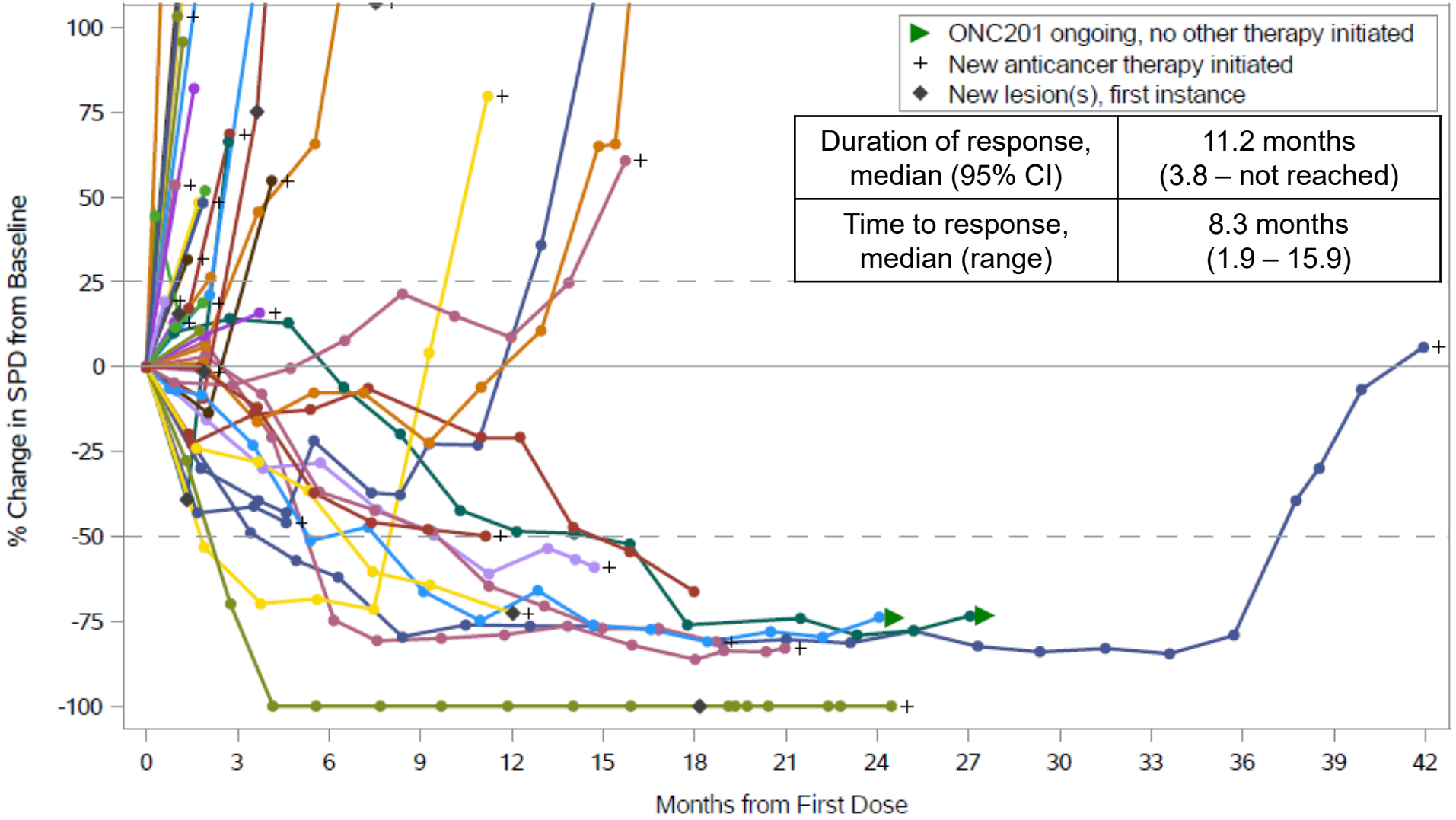
[1]Integrated RANO HGG criteria assessment by dual reader BICR
[2]Five overall radiographic SD accompanied by increase in corticosteroids; 3 overall radiographic PD accompanied by decrease in corticosteroids
[3]Three patients did not have on-treatment monotherapy MRIs available for BICR; one patient censored prior to first on-treatment MRI

Waterfall Plot (RANO-HGG)



* Change > 100%, CR=complete response, PR=partial response, SD=stable disease, NE=not evaluable, PD=progressive disease
SPD=sum of products of perpendicular diameters (target enhancing lesions per BICR)
Only patients with measurable target enhancing lesions by BICR at baseline and with post-baseline evaluations are included.
Three patients did not have on-treatment monotherapy MRIs available for BICR; one patient censored prior to first on-treatment MRI; one patient did not have measurable target lesion.

Spider Plot (RANO-HGG)



Duration of response, median (95% CI)	11.2 months (3.8 – not reached)
Time to response, median (range)	8.3 months (1.9 – 15.9)

SPD=sum of products of perpendicular diameters (target enhancing lesions per BICR)
Only patients with measurable target enhancing lesions by BICR at baseline and with post-baseline evaluations are included.
Three patients did not have on-treatment monotherapy MRIs available for BICR; one patient censored prior to first on-treatment MRI ; one patient did not have measurable target lesion.

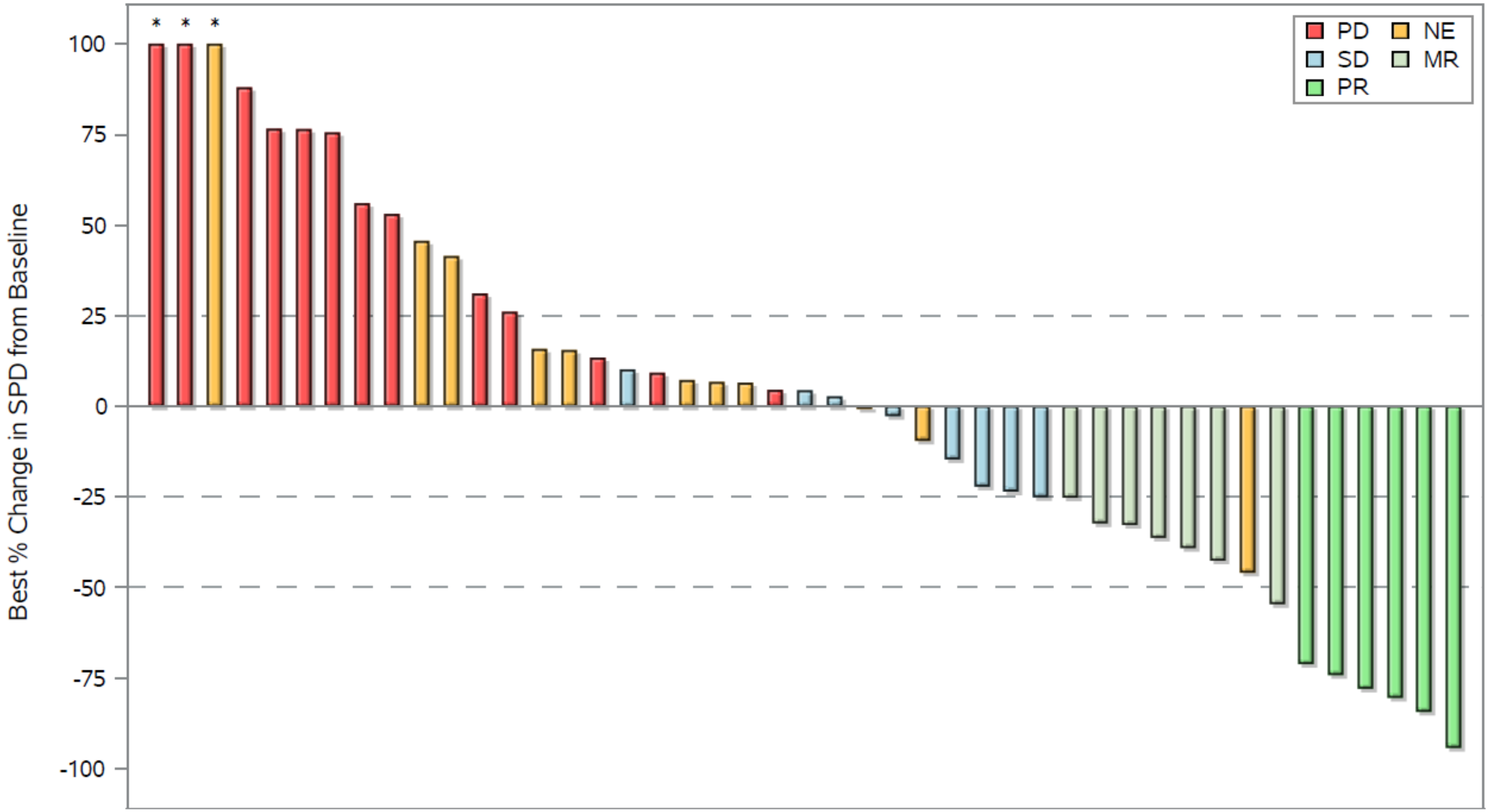
Overall Response Rate (RANO-LGG)

RANO-LGG[1]	N=50
ORR (CR + PR + MR)	**13 (26%)** 95% CI: 15 – 40%
Complete Response (CR)	0 (0%)
Partial Response (PR)	6 (12%)
Minor Response (MR)	7 (14%)
Stable Disease (SD)	8 (16%)
Not Evaluable (NE)	11 (22%)[2]
Progressive Disease (PD)	14 (28%)
Not Applicable (NA)	4 (8%)[3]
Disease Control Rate (CR + PR + MR + SD)	**21 (42%)** 95% CI: 28 – 57%

30.0% (95% CI: 17.9 - 44.6%) achieved an objective response by RANO-HGG and/or RANO-LGG criteria

[1]Integrated RANO LGG criteria assessment by dual reader BICR
[2]Eight overall radiographic SD accompanied by increase in corticosteroids; 3 overall radiographic PD accompanied by decrease in corticosteroids
[3]Three patients did not have on-treatment monotherapy MRIs available for BICR; one patient censored prior to first on-treatment MRI

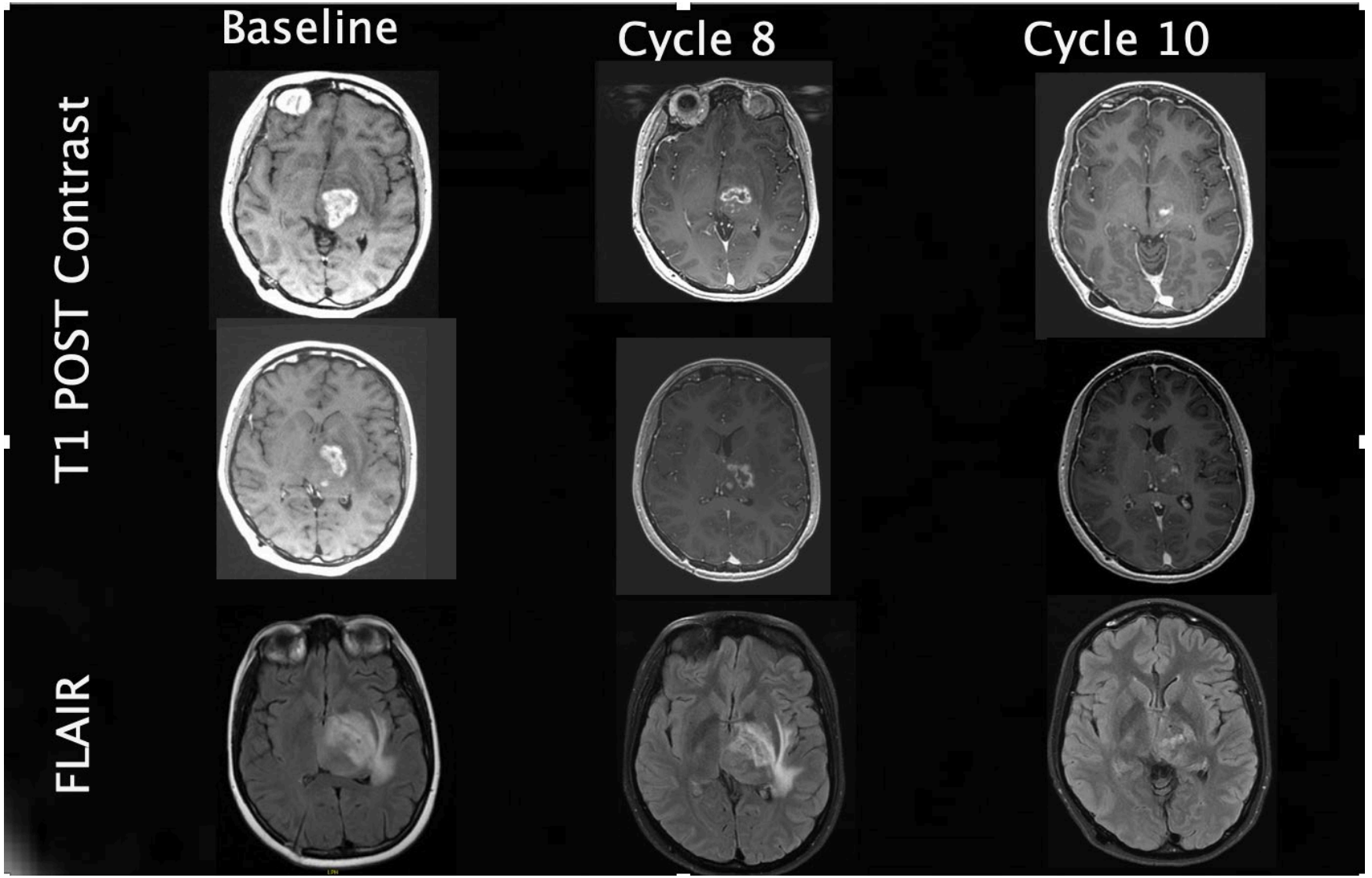
Waterfall Plot (RANO-LGG)



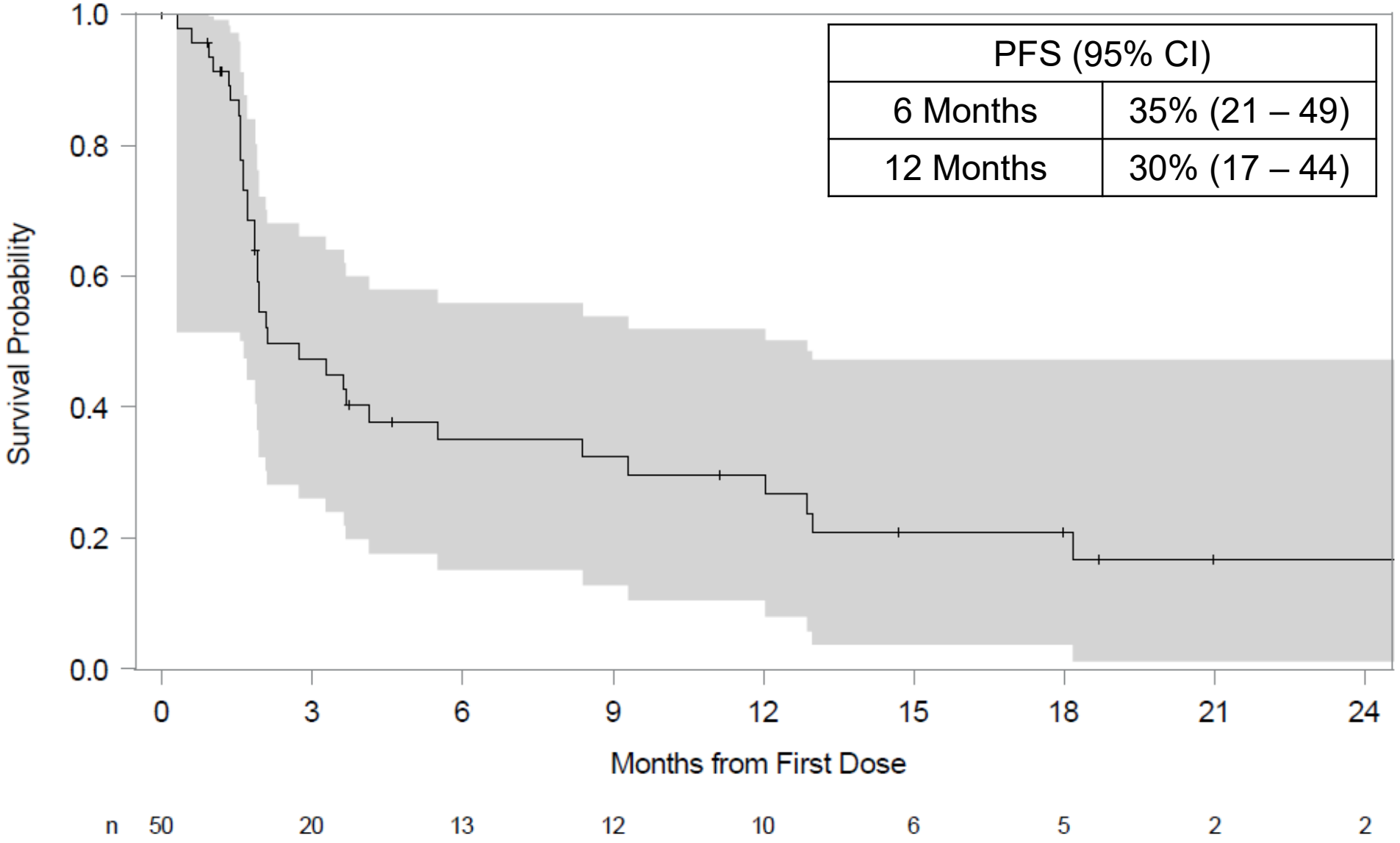
* Change > 100%, PR=partial response, MR=minor response, SD=stable disease, NE=not evaluable, PD=progressive disease
SPD=sum of products of perpendicular diameters (target non-enhancing lesions per BICR)
Only patients with measurable target lesions by BICR at baseline and with post-baseline evaluations are included.
Three patients did not have on-treatment monotherapy MRIs available for BICR; one patient censored prior to first on-treatment MRI.

Case Study

- Integrated Diagnosis: DMG, H3K27m mutation
- Molecular Features: MGMT promoter unmethylated, IDH wildtype.
- Significant response to treatment both by RANO-HGG and RANO-LGG by cycles 8 and 10; response was sustained for over one year

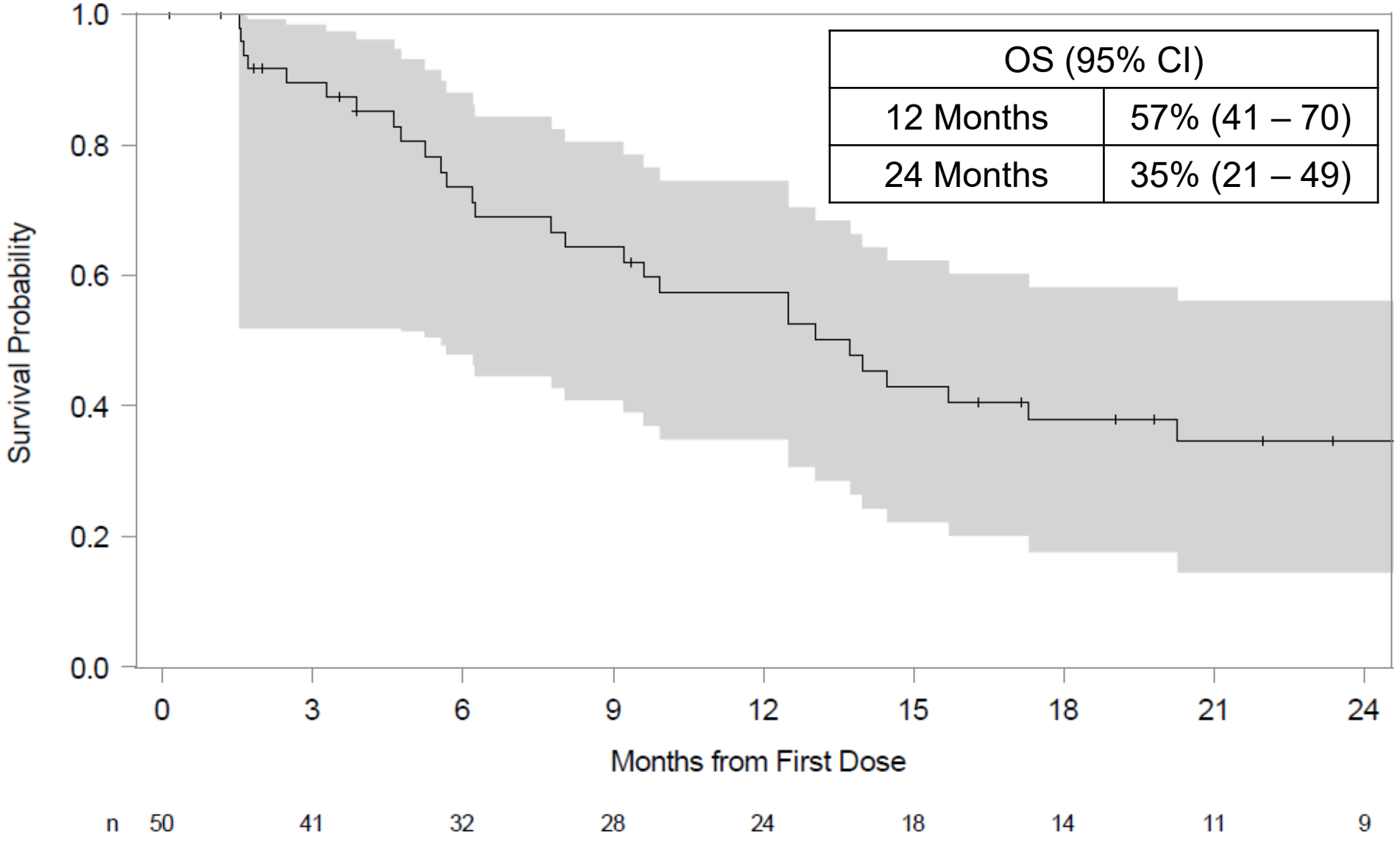


Progression-Free Survival



PFS (95% CI)	
6 Months	35% (21 – 49)
12 Months	30% (17 – 44)

Overall Survival

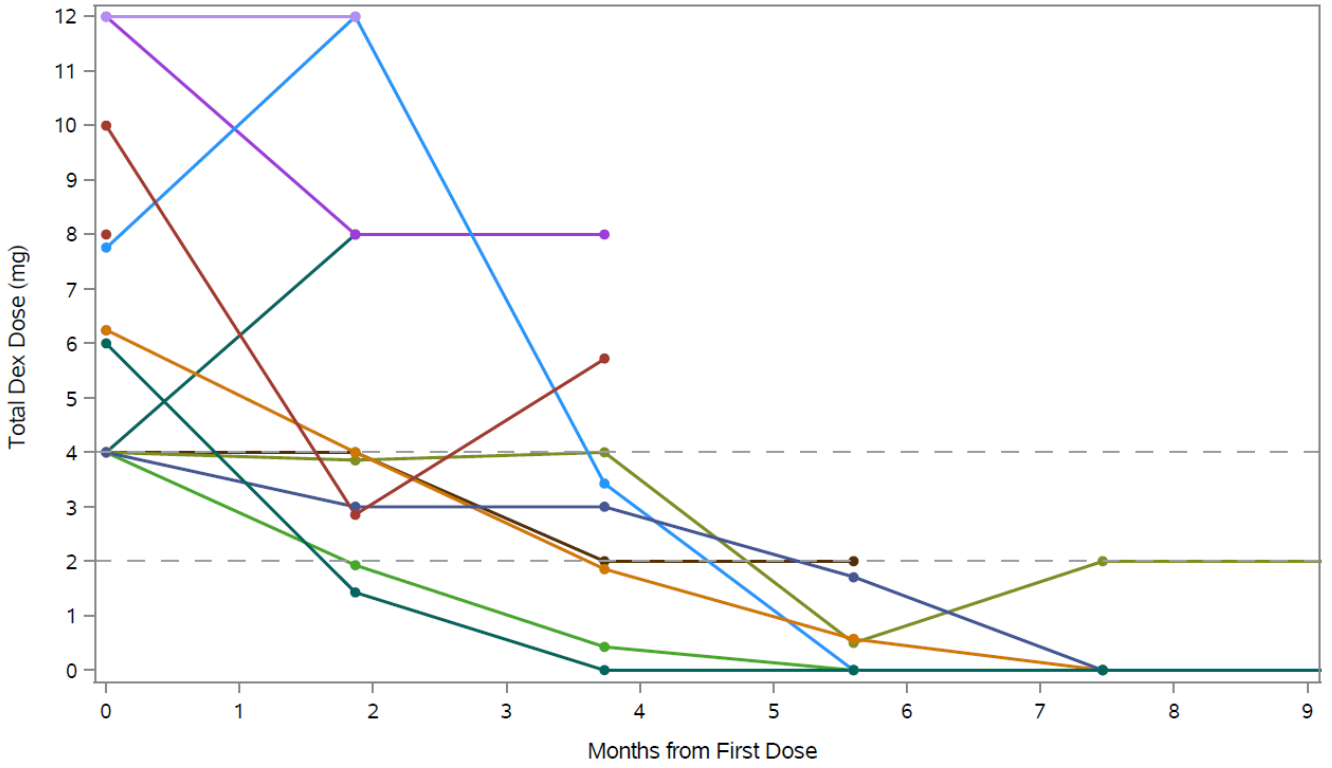


OS = overall survival

Performance Status and Corticosteroid Use

Corticosteroid Response[1]	
Evaluable, N	15
Response rate, N(%) (95%CI)	7 (47%) (21 – 73%)
Time to response, months median (range)	3.7 (1.9 – 5.6)
Performance Status Response[2]	
Evaluable, N	34
Response rate, N(%) (95% CI)	7 (21%) (9 – 38%)
Time to response, months median (range)	3.5 (1.9 – 22.4)

Corticosteroids[3]



[1]Corticosteroid response: ≥50% reduction in average daily corticosteroid dose compared to baseline with stable or improved KPS/LPS. Must be confirmed at next analysis timepoint. Corticosteroids were converted into a dexamethasone equivalent dose. Baseline ≥4mg dexamethasone at baseline were evaluable.
[2]Performance status response: increase in KPS/LPS compared to baseline with stable or reduced corticosteroid use. Must be confirmed at next analysis timepoint. Baseline KPS/LPS ≤80 were evaluable.
[3]Average daily over 1 week around analysis window presented (every 8 weeks)

Summary

- Integrated response analysis results
  - RANO-HGG criteria assessed by dual reader BICR
    - ORR 20% (95% CI: 10 – 34%)
    - Median DOR 11.2 months (95% CI: 3.8 – not reached)
    - Median time to response 8.3 months (range 1.9 – 15.9)
    - Disease control rate 40% (95% CI: 26 – 55%)
    - PFS at 6 months 35% (95% CI: 21 – 49%); PFS at 12 months 30% (17 – 44)
  - RANO-LGG criteria assessed by dual reader BICR
    - ORR 26% (95% CI: 15 – 40%)
  - Overall survival
    - 12 months: 57% (41 – 70%)
    - 24 months: 35% (95% CI: 21 – 49%)
- ONC201 monotherapy exhibited apparent durable and clinically meaningful efficacy in recurrent H3 K27M-mutant DMG patients

Acknowledgments

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  - Cancer Commons
  - Michael Mosier Defeat DIPG Foundation
  - The Musella Foundation
  - The Cure Starts Now Foundation
  - xCures

Supplemental Material and Management Discussion

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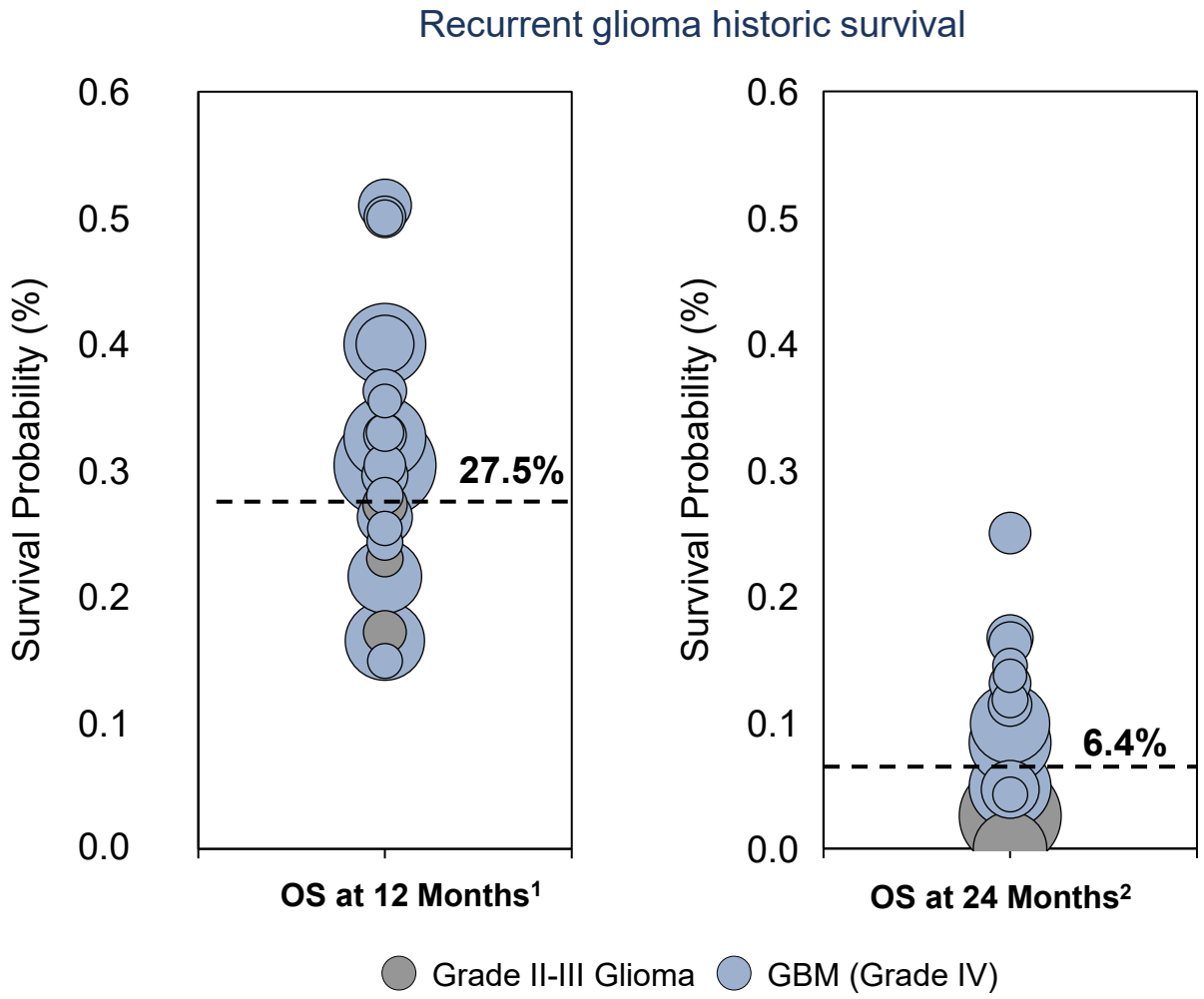
Recurrent Glioma Remains a High Unmet Need

- H3 K27M-mutant DMG is a grade IV by WHO
- FDA has acknowledged available therapy is palliative
  - Often not possible to resect
  - Recurrence inevitable after first-line radiation
  - Chemotherapy ineffective; objective responses by RANO-HGG have not been reported
- Survival in grade II-IV recurrent glioma reported to be 27.5% at 12 months[1] and 6.4% at 24 months[2]
- Survival in pediatric recurrent H3 K27M DMG reported to be 0% at 24 months[3]
- Survival in ONC201-treated recurrent H3 K27M DMG was 57% OS at 12 months and 35% at 24 months



1. Data collected from 15 literature sources since 2010 with trial arms size >30 pts each reporting data on 1816 pts with recurrent, unstratified disease.
2. 10 literature sources that describes OS with 1279 patients
3. Koschmann et al, 2020; DOI:10.21203/rs.3.rs-69706/v1

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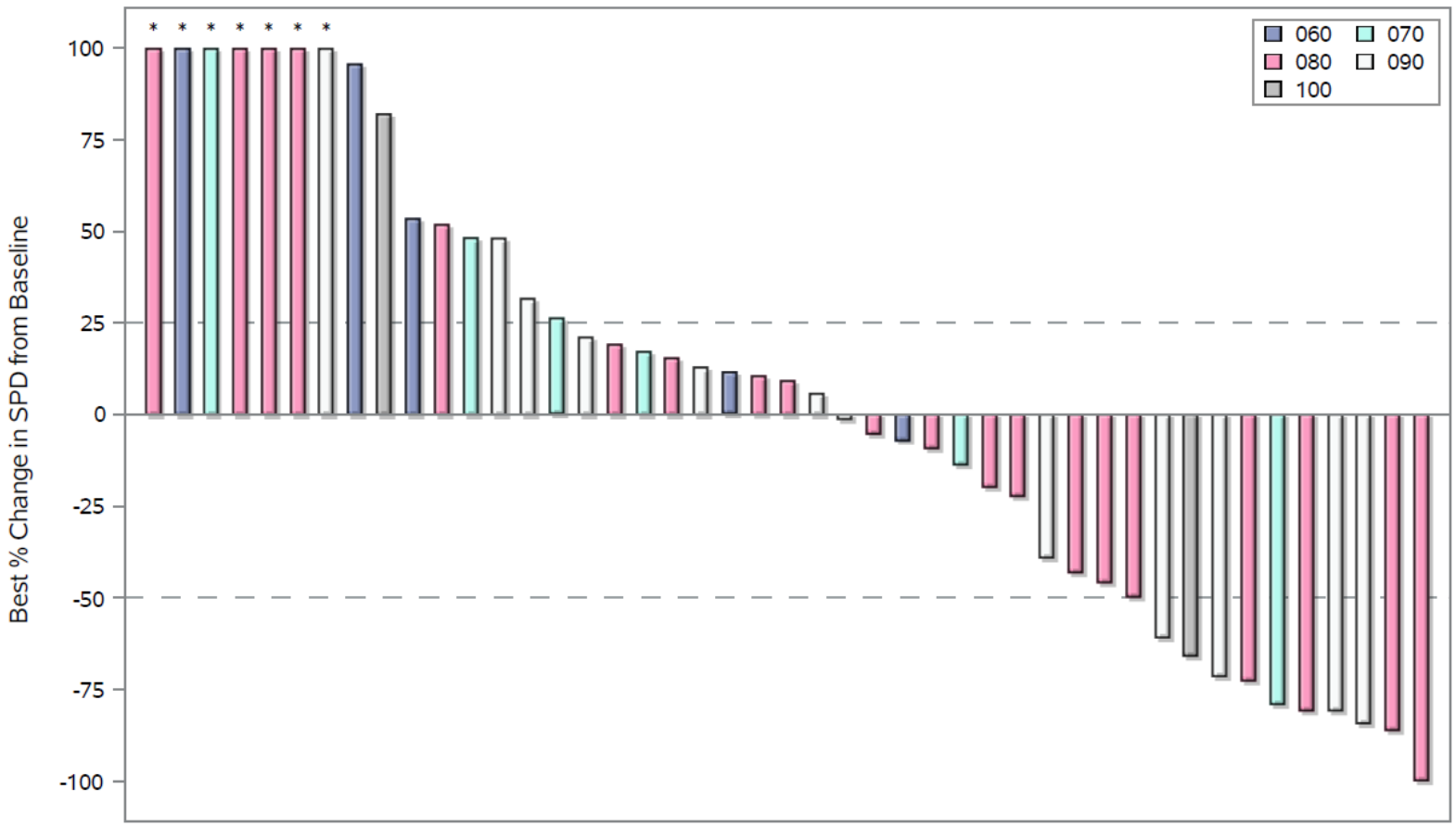
Waterfall Plot (RANO-HGG) Stratified by Performance Status

- Expectedly, patients with higher PS were more likely to respond to treatment
  - 100: 1/2 (50%)
  - 90: 4/14 (29%)
  - 80: 4/20 (20%)
  - 70: 1/7 (14%)
  - 60: 0/7 (0%)
- Consistent with hypothesis that treating earlier in disease course may enhance efficacy



* Change > 100%, SPD=sum of products of perpendicular diameters (target enhancing lesions per BICR)
Only patients with measurable target enhancing lesions at both baseline and post-baseline are included.

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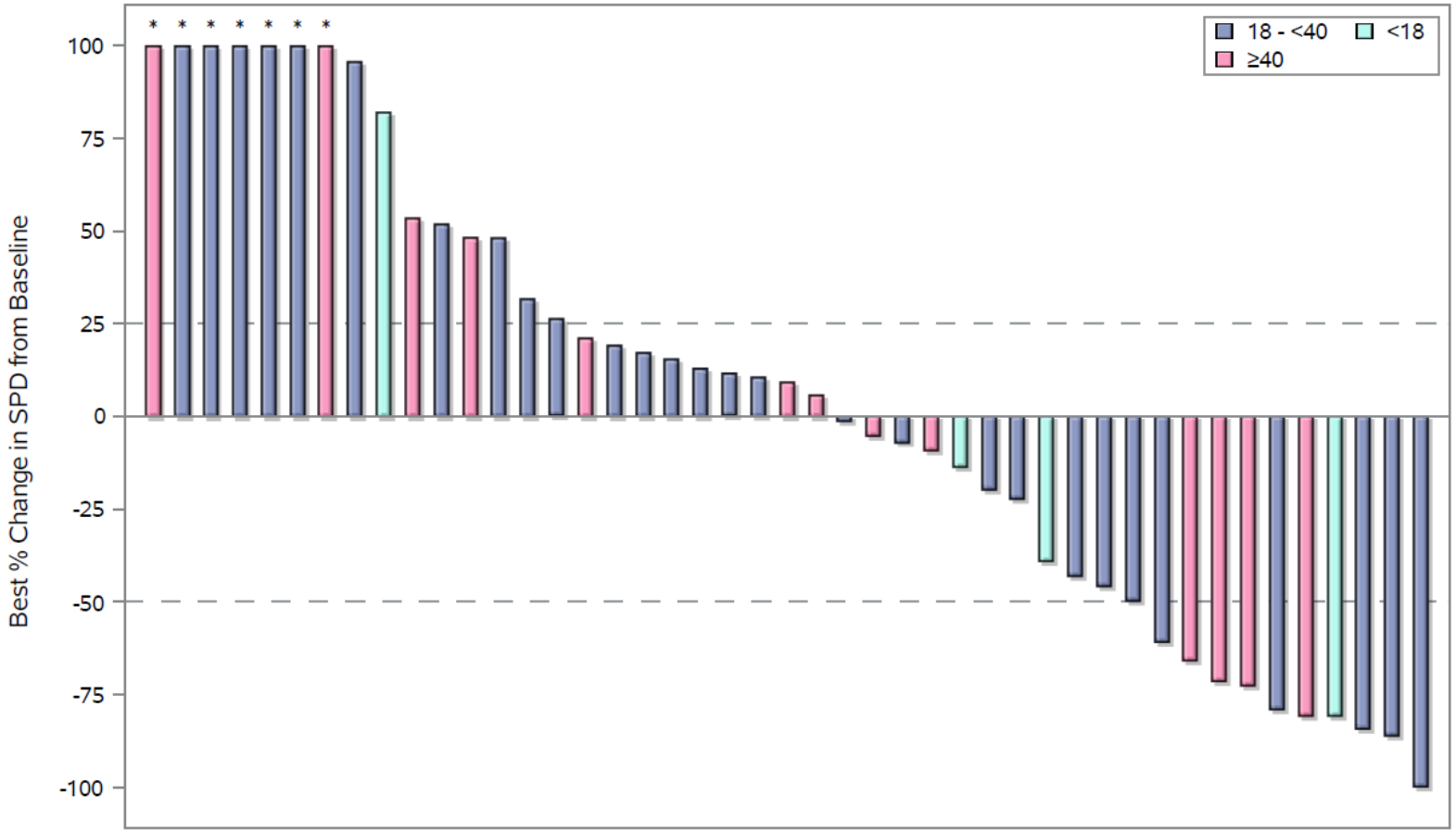
Waterfall Plot (RANO-HGG) Stratified by Age

- Responses observed across age groups:
  - <18 years: 1/4 (25%)
  - 18-40 years: 5/32 (16%)
  - ≥40 years: 4/14 (29%)
- RANO-HGG response of 8-year-old subject confirms activity in this population



* Change > 100%, SPD=sum of products of perpendicular diameters (target enhancing lesions per BICR)
Only patients with measurable target enhancing lesions at both baseline and post-baseline are included.

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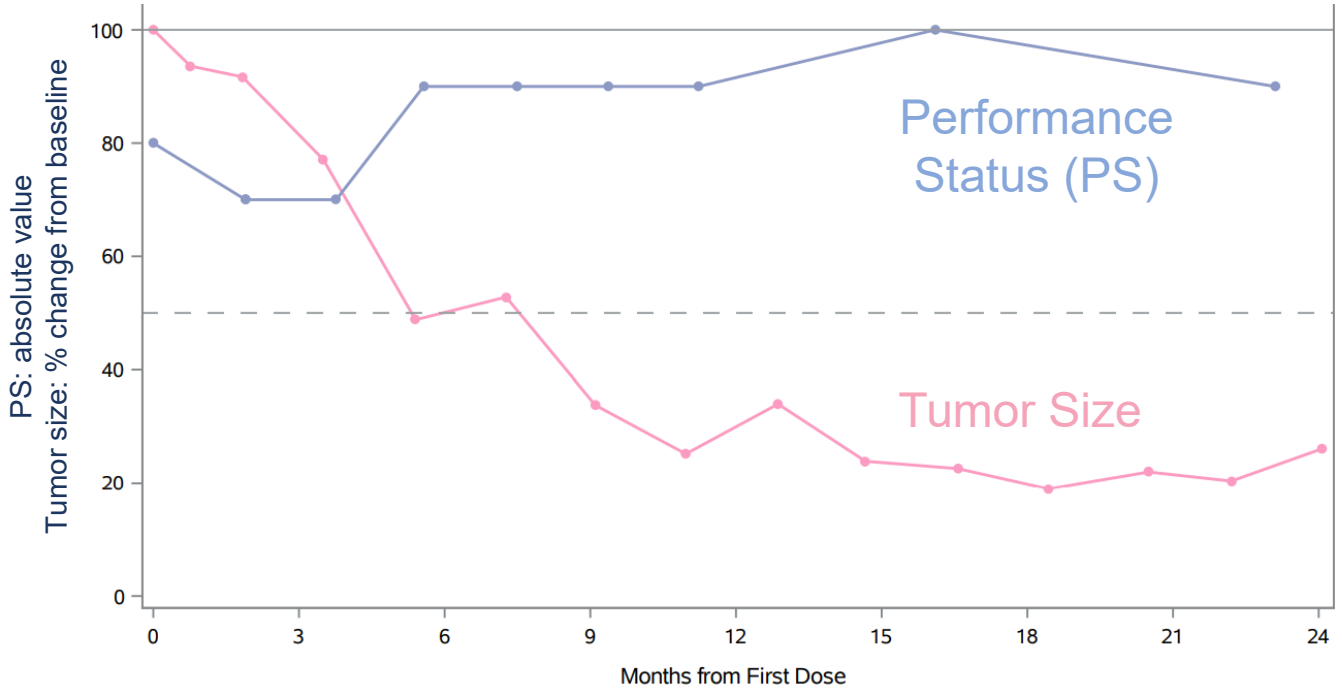
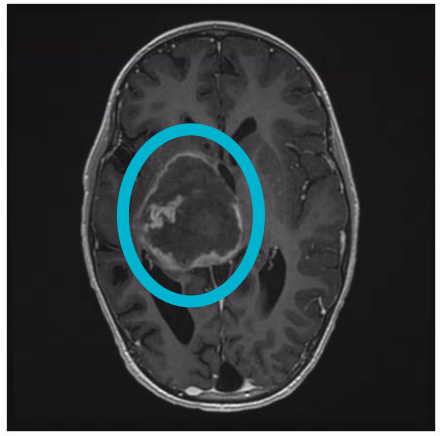
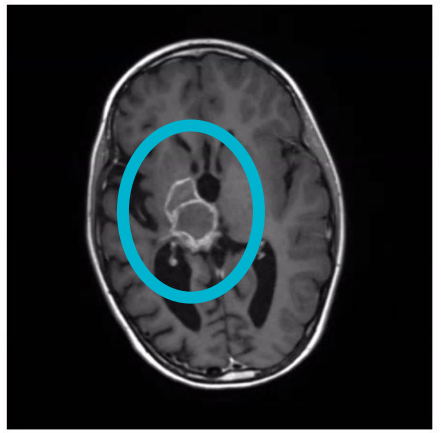
Pediatric Case Study

- 8-year-old thalamic H3.3 K27M DMG initially diagnosed in May 2018
- First-line therapy: radiation, dasatinib, everolimus and bevacizumab
- Second-line therapy: 375mg weekly ONC201 monotherapy initiated Apr 2019 following progression on first-line therapy
  - Clinical and radiographic improvement over >2 years of therapy

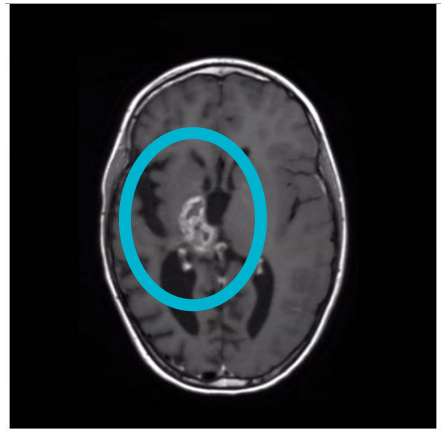




Pre-ONC201 baseline



9 months on ONC201



18 months on ONC201

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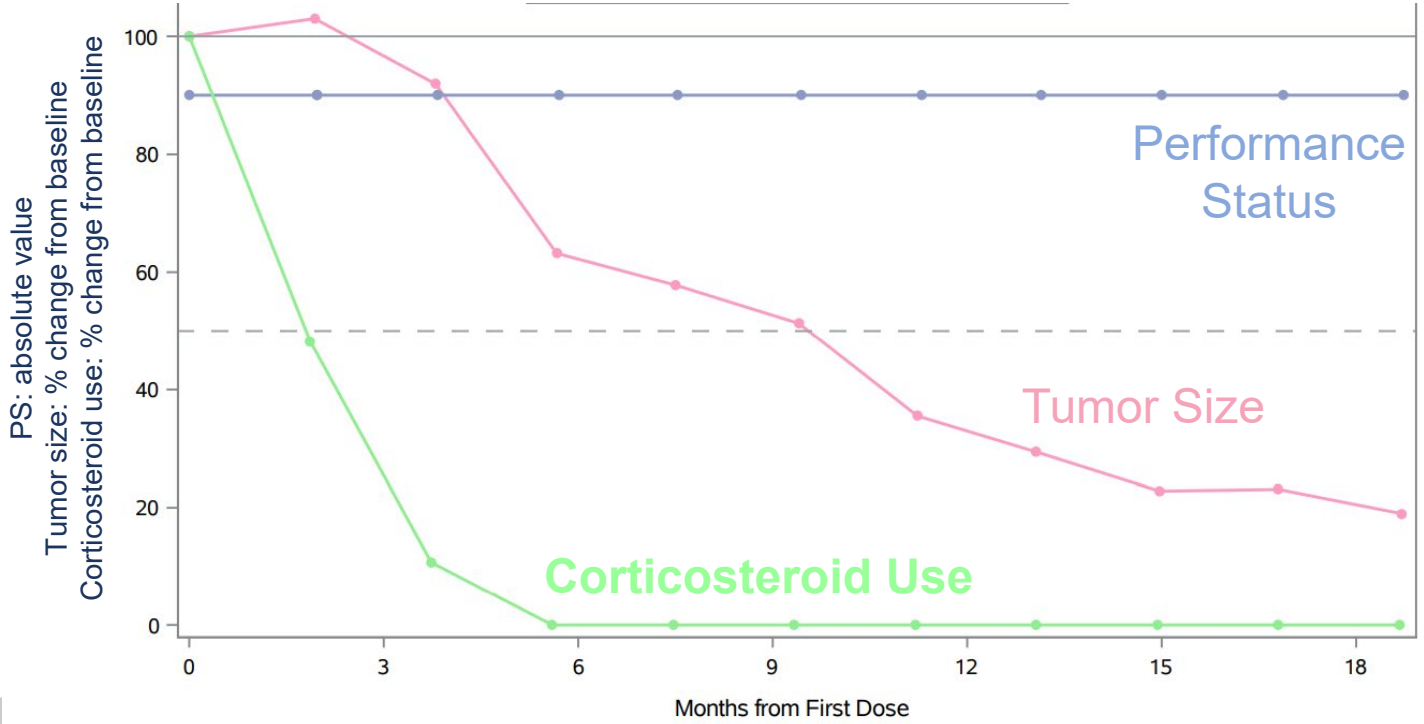
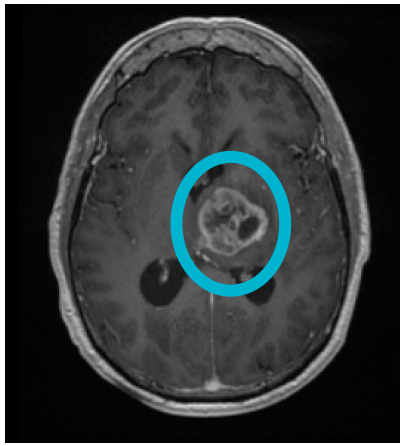
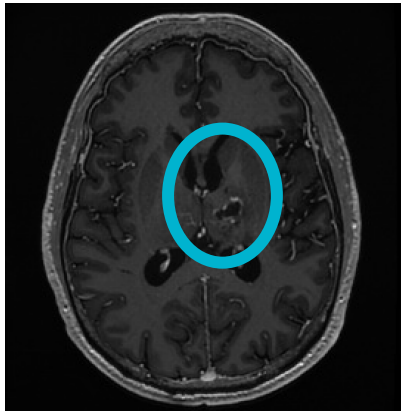
Adult Case Study

- 54-year-old thalamic H3 K27M DMG diagnosed in Nov 2018
- First-line therapy: radiation and temozolomide
- Second-line therapy: 625mg weekly ONC201 monotherapy initiated May 2019
  - Corticosteroid elimination and radiographic regression over >1.5 years of therapy

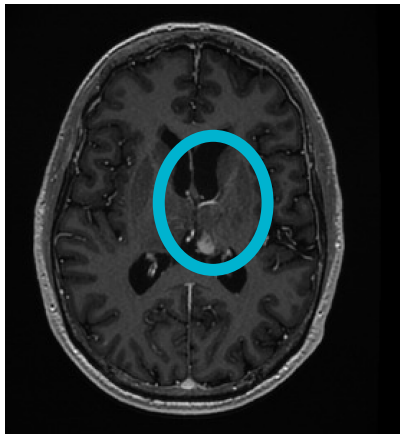




Pre-ONC201 baseline



12.9 months on ONC201



18.5 months on ONC201

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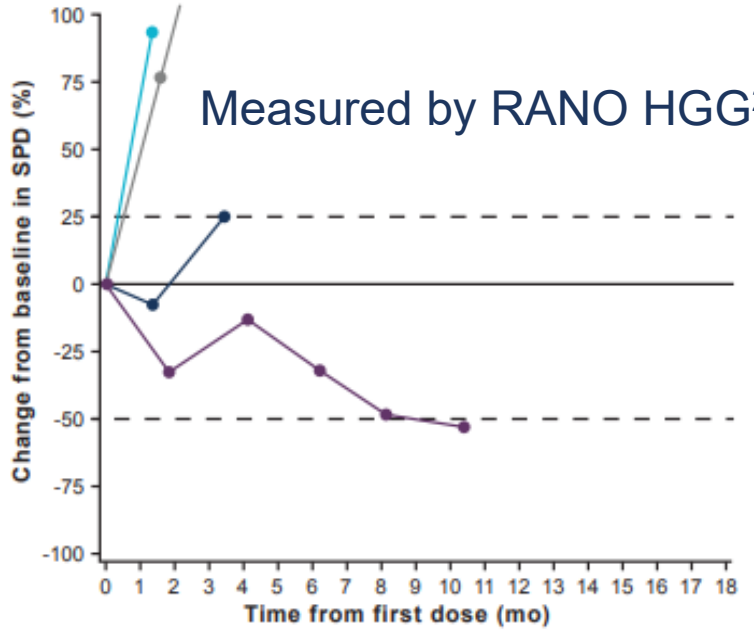
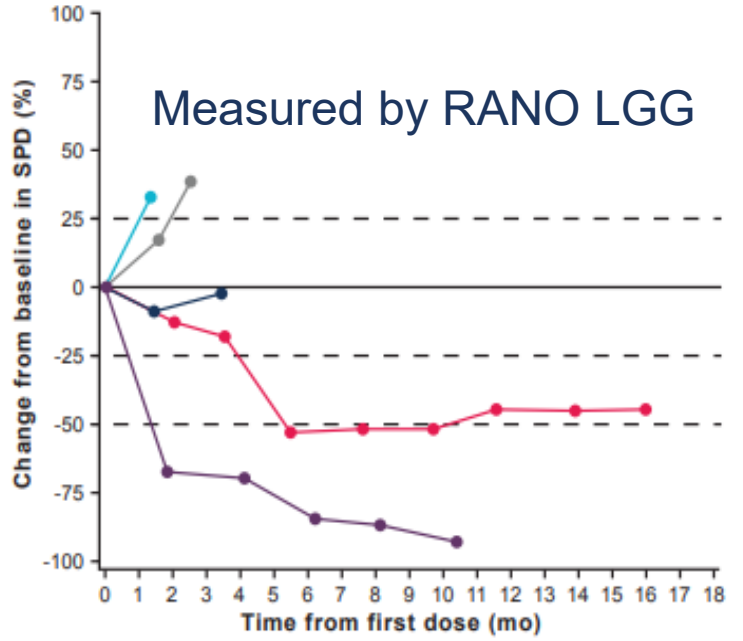
ONC201 Activity in Non-Midline H3 K27M Diffuse Glioma

- Two of five patients had objective responses by RANO-HGG per investigator but not BICR[1]
  - Both patients had a response by RANO-LGG per BICR
    - Patients were on-treatment for 14 and 23 months
  - Responses were associated with increased mobility and alertness
- Suggest activity may not be restricted by location





1. Odia et al, SNO 2021
2. One of these five patients did not have a measurable lesion per BICR

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RANO Responses Correspond with Survival & Clinical Benefit

	All patients	RANO HGG Responders	RANO HGG and/or LGG Responders	All Other Patients
N	50	10	15	35
PFS at 12 months (number of patients censored)	30%[1]	90% (0)	67% (2)	0% (8)
OS at 24 months (number of patients censored)[2]	35%[1]	80% (2)	53% (5)	0% (8)
Corticosteroids response[3] (number of patients evaluable)	47% (15)	100% (4)	100% (5)	20% (10)
Performance status response[4] (number of patients evaluable)	21% (34)	60% (5)	67% (9)	4% (25)

1. Kaplan-Meier median Progression-Free Survival or Overall Survival
2. Censored patients include those who are lost to follow-up or have withdrawn prior to the time point, as well as those who have not yet reached the time point. These patients are counted in the denominator but not counted as survivors (i.e., imputed as failure)
3. Corticosteroid response: ≥50% reduction in average daily corticosteroid dose compared to baseline with stable or improved KPS/LPS. Must be confirmed at next analysis timepoint. Corticosteroids were converted into a dexamethasone equivalent dose. Baseline ≥4mg dexamethasone at baseline were evaluable.
4. Performance status response: increase in KPS/LPS compared to baseline with stable or reduced corticosteroid use. Must be confirmed at next analysis timepoint. Baseline KPS/LPS ≤80 were evaluable.

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Summary

- ONC201 monotherapy exhibited durable and clinically meaningful efficacy in recurrent H3 K27M-mutant DMG patients
  - RANO-HGG criteria assessed by dual reader BICR
    - ORR 20% (95% CI: 10 – 34%)
    - Median DOR 11.2 months (95% CI: 3.8 – not reached)
    - Median time to response 8.3 months (range 1.9 – 15.9)
    - Disease control rate 40% (95% CI: 26 – 55%)
    - PFS at 6 months 35% (95% CI: 21 – 49%); PFS at 12 months 30% (95% CI: 17 – 44%)
  - RANO-LGG criteria assessed by dual reader BICR
    - ORR 26% (95% CI: 15 – 40%)
  - Overall survival
    - 12 months: 57% (95% CI:41 – 70%)
    - 24 months: 35% (95% CI: 21 – 49%)
- Improvements observed in performance status and reduction in corticosteroid use
- One SAE was considered possibly related to ONC201 by investigator and unlikely related to ONC201 by sponsor

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