

Chimerix January 2022 Corporate Presentation



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; risks that the Company will not obtain a procurement contract for TEMBEXA in smallpox in a timely manner, on favorable terms or at all; 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.



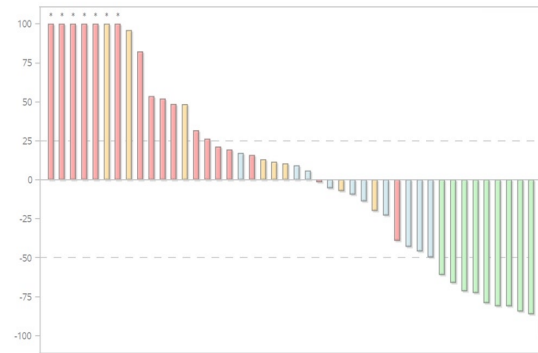
Potential TEMBEXA® stockpiling to fund oncology development

Source of non-dilutive capital directed toward innovative oncology development

TEMBEXA approved June 4, 2021 for the treatment of smallpox

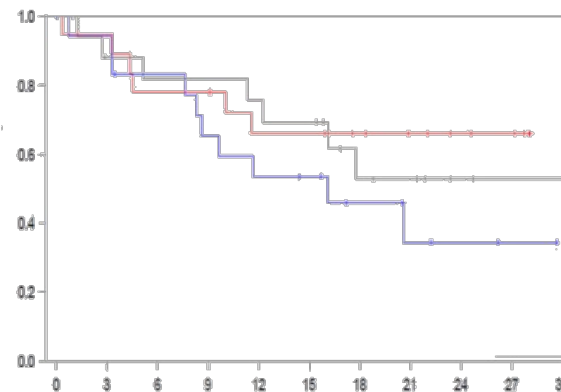
December 23, 2021, BARDA announced a sole source contract for up to 1.7m courses of therapy for TEMBEXA for national preparedness for treatment of smallpox

Focus on oncology areas of high unmet need supported by strong clinical data



ONC201/ONC206/ONC212

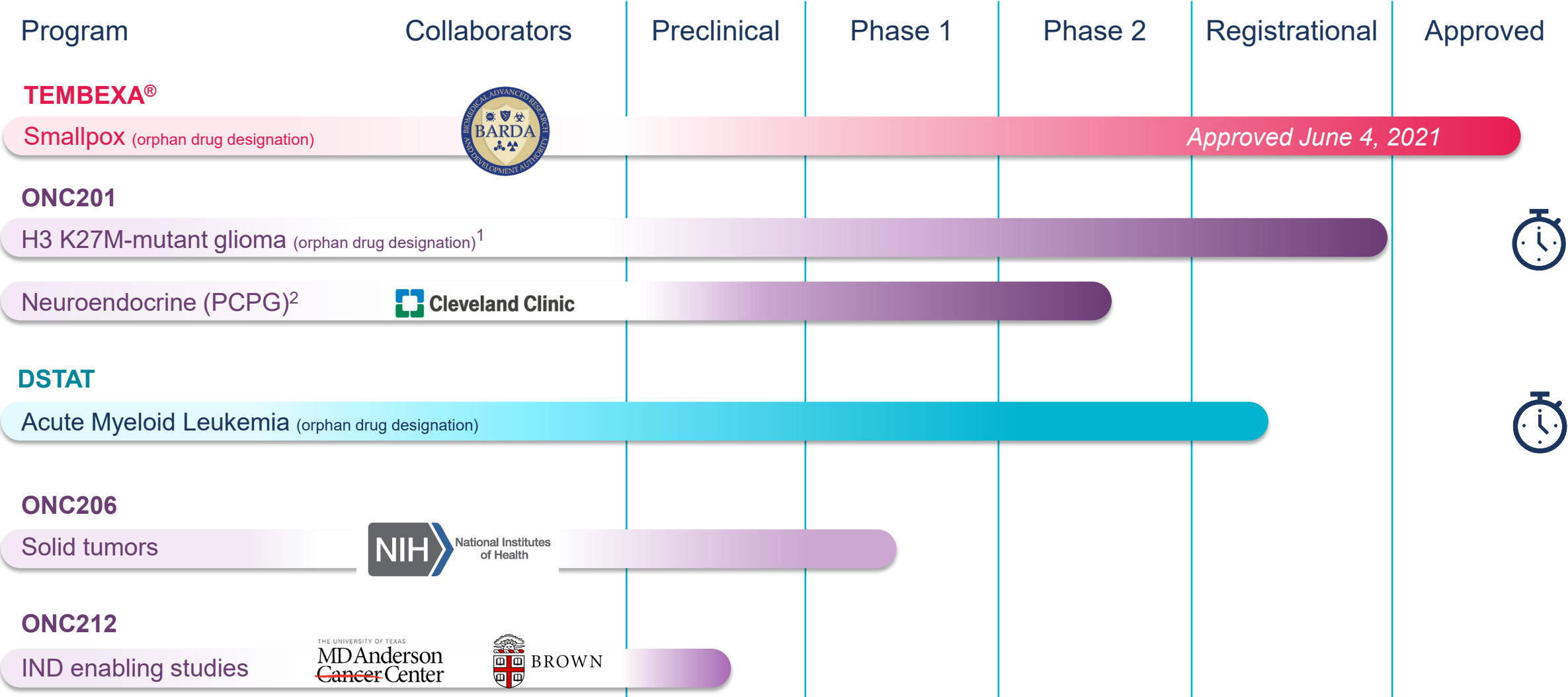
- Positive ORR data in recurrent H3 K27M-mutant glioma
- New indications & pipeline expansion



DSTAT

- Phase 3 front-line AML trial

Deep pipeline across all development stages



TEMBEXA®

Approved for Treatment of Smallpox as a Medical Countermeasure



The value of preparedness has never been more evident

- Highly infectious virus with ~30% mortality¹
- Population is unvaccinated since early '70s
- Considered a Class A security threat by PHEMCE², CDC and NIAID
- Weaponized virus could be engineered to increase transmission and resistance
- BARDA announced 1.7m sole source contract TEMBEXA into the national stockpile (\$500 to \$600m at historical pricing)
- SIGA Technologies awarded >\$1B in contracts for development and stockpile of TPOXX
- TEMBEXA[®] approved June 4, 2021 for the treatment of smallpox



Two labs in the world keep a live smallpox sample. The one in Russia just had an explosion

N'dea Yancey-Bragg USA TODAY

Published 12:46 p.m. ET Sep. 17, 2019



How Canadian researchers reconstituted an extinct poxvirus for \$100,000 using mail-order DNA

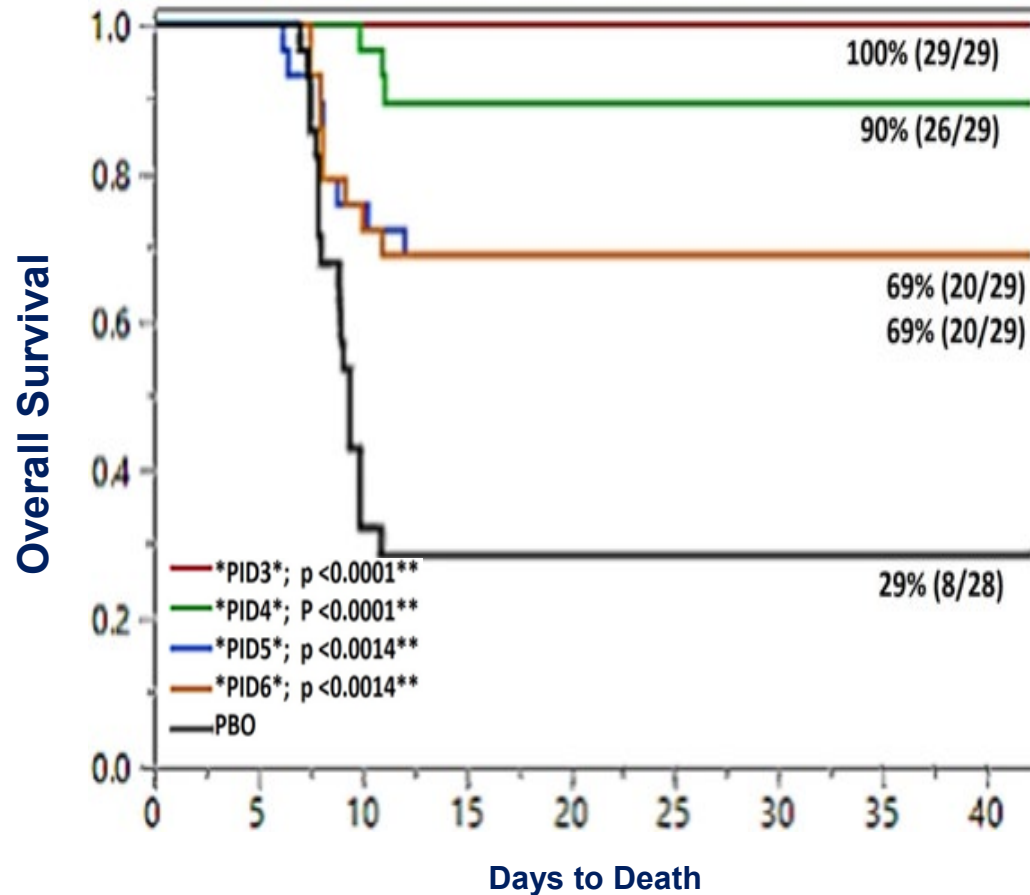
By Kai Kupferschmidt | Jul. 6, 2017, 5:00 PM

Posted in: [Health, Science and Policy, Scientific Community](#)
doi:10.1126/science.aan7069

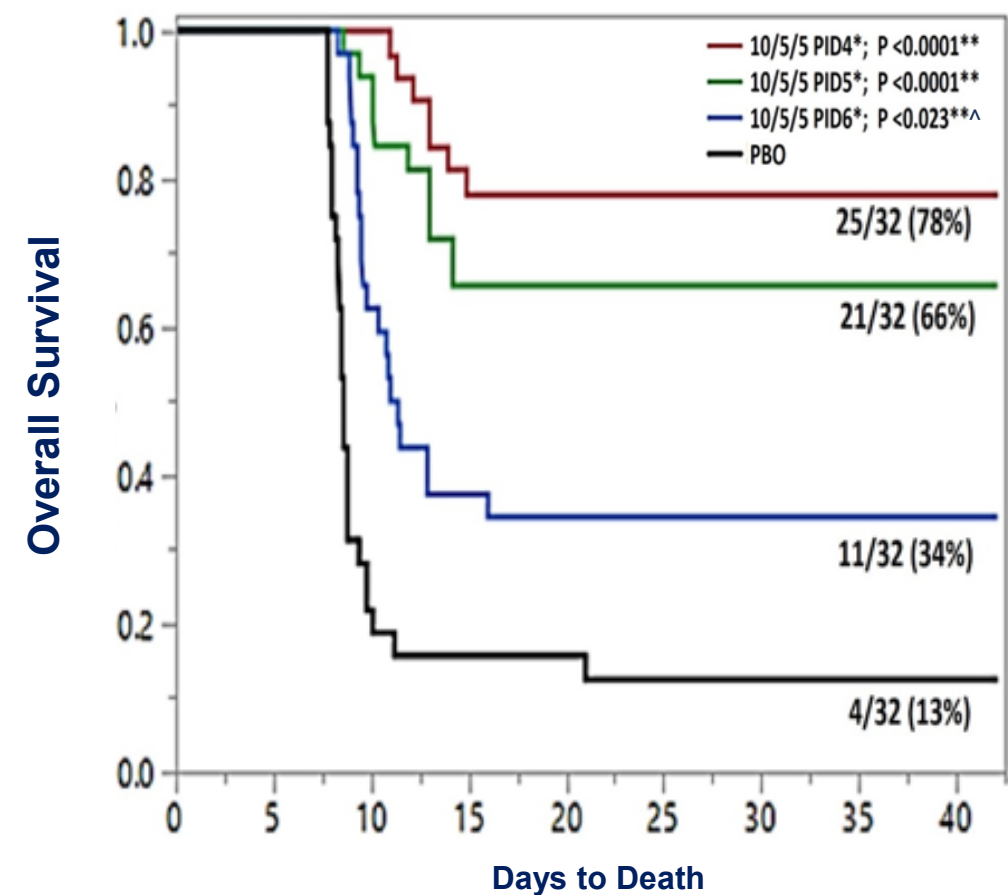
TEMBEXA[®] significantly reduced mortality in required models

Survival improved even with administration of TEMBEXA well beyond midpoint of disease progression

Rabbit Model



Mouse Model



* PID = Post Inoculation Day

** Versus Placebo (PBO); Boschloo one-sided

[^] Day 6 was not determined to be statistically significant in mouse



TEMBEXA® an attractive addition to SNS

- Approved by the FDA in tablet and oral suspension formulations for the treatment of smallpox disease in adult and pediatric patients, including neonates/infants
- TEMBEXA impairs viral replication with a different mechanism of action than TPOXX®, important hurdle to an engineered bioterror attack¹
- Short-course therapy, oral tablet and suspension (two tablets once weekly for 2 doses oral suspension once weekly for 2 doses)
- Complementary with existing countermeasures and vaccines
- TEMBEXA has a higher barrier to resistance compared to TPOXX¹
- TEMBEXA and TPOXX work well in combination in animal studies¹
- Initial quantities available for delivery to the SNS once contract is finalized

TEMBEXA®
brincidofovir
10 mg/mL oral suspension | 100 mg tablets



Imipridone Oncology Pipeline

Lead Candidate,
ONC201 Positive Top-
line Data



Topline results for ONC201 in recurrent H3 K27M DMG

- 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%)
 - ORR 30% including HGG and/or LGG
 - 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 considered possibly ONC201 related by investigator and unlikely related to ONC201 by sponsor



Efficacy analysis of ONC201 in recurrent H3 K27M DMG

Objective

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

Eligibility

- Age ≥ 2 yo 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 hist., leptomeningeal spread, CSF dissemination

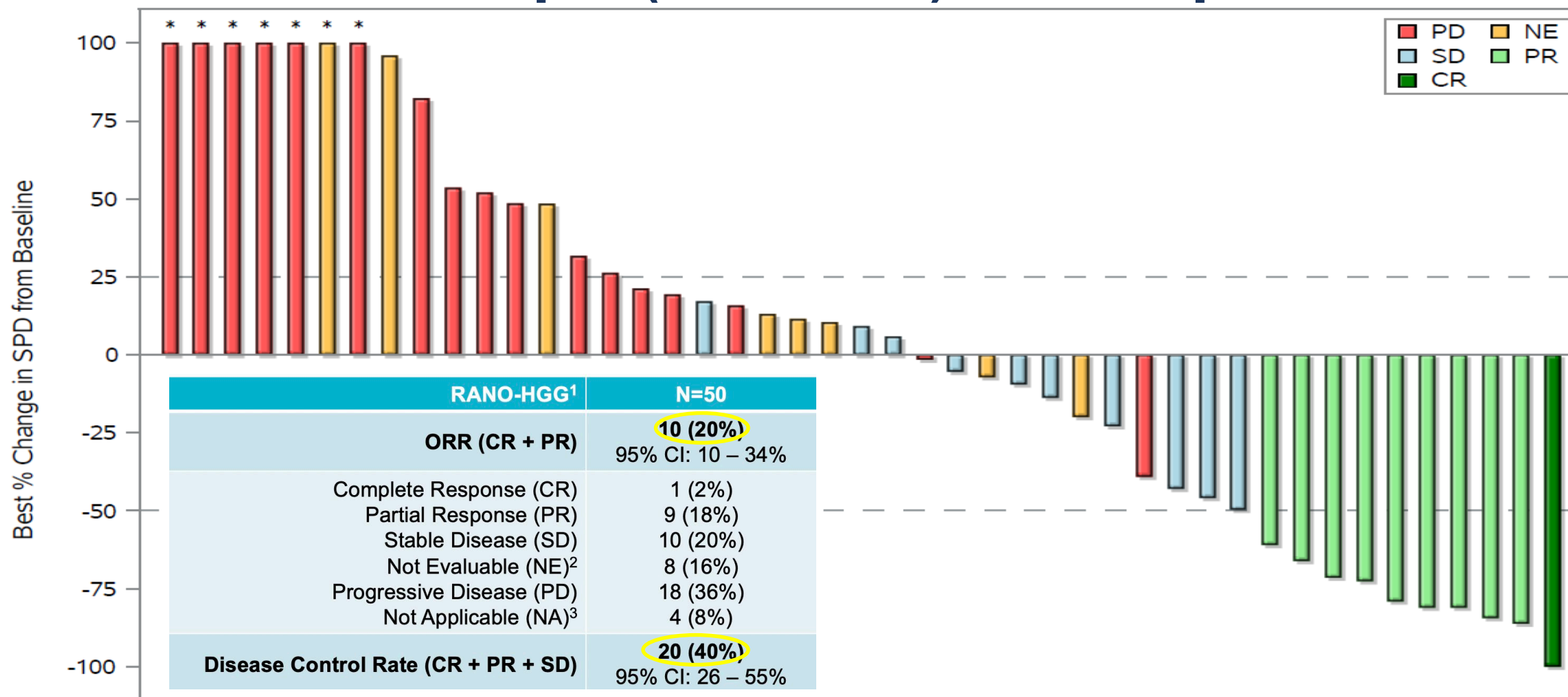
Patient demographics and disease characteristics

	N=50		N=50
Age (years), median (range)	30 (8 – 70)	Primary tumor location, N(%)	
<18 years, N(%)	4 (8%)	Thalamic	33 (66%)
18 - <40 years, N(%)	32 (64%)	<u>Other</u> midline	17 (34%)
≥40 years, N(%)	14 (28%)	Multifocal disease ¹ , N(%)	23 (46%)
Gender, N(%)		>1 Target lesion, N(%)	9 (18%)
Male	27 (54%)	Tumor size ² (cm ²), median (range)	10.4 (1.6 – 40.8)
Female	23 (46%)	H3 K27M detection method	
Race, N(%)		IHC, N(%)	47 (94%)
White	39 (78%)	NGS, N(%)	3 (6%)
Other	6 (12%)	First recurrence, N(%)	37 (74%)
Black	3 (6%)	Prior temozolomide, N(%)	44 (88%)
Asian	1 (2%)	Time from recurrence, days, median (range)	20 (1 – 126)
Not reported	1 (2%)	Time from prior radiation, months, median (range)	7.5 (3 – 104)
Body weight (kg), median (range)	88 (29 – 199)	Time from initial diagnosis, months, median (range)	10.9 (5 – 105)
Performance status (KPS/LPS), N(%)		Daily steroid dose (mg, <u>dex equiv</u>): median (range)	1.1 (0.0 – 12.0)
60-70	14 (28%)		
80	20 (40%)		
90-100	16 (32%)		

¹Multifocal disease includes non-target lesions

²Sum of product of diameters of enhancing target lesions per BICR

Waterfall plot (RANO-HGG) – 20% response



* 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.

¹Integrated RANO HGG criteria assessment by dual reader BICR

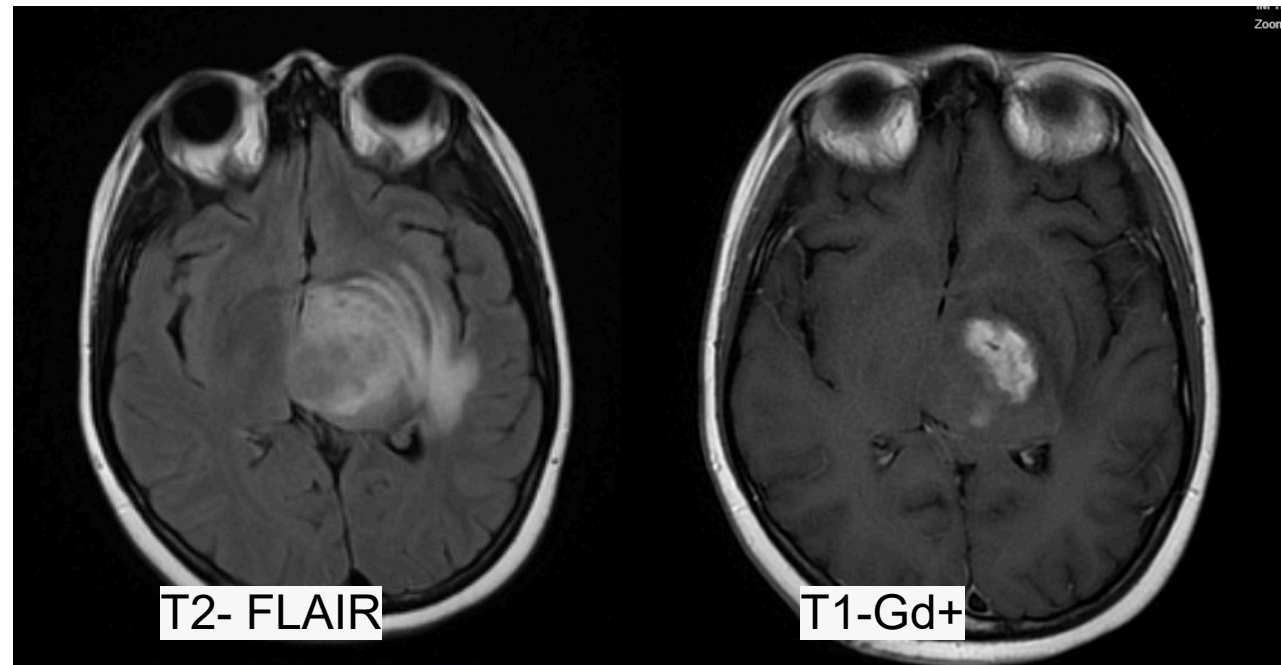
²Five overall radiographic SD accompanied by increase in corticosteroids; 3 overall radiographic PD accompanied by decrease in corticosteroids

³Three patients did not have on-treatment monotherapy MRIs available for BICR; one patient censored prior to first on-treatment MRI



Response assessment criteria for glioma

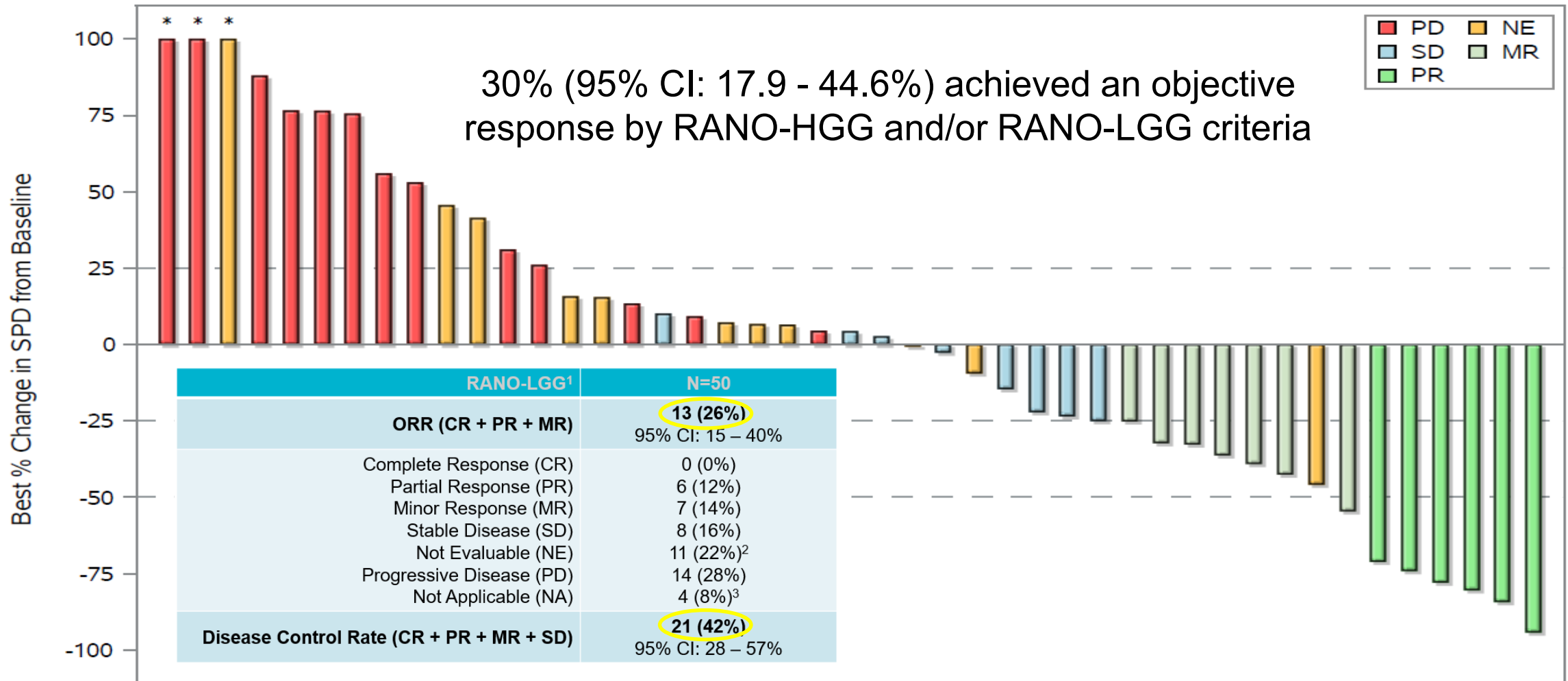
- DMG with H3K27M typically have *both* enhancing and non-enhancing disease components
- RANO-HGG responses defined by decrease in enhancing disease
- RANO LGG response defined by decrease in T2 FLAIR



RANO- HGG

Criterion	CR	PR	SD	PD
T1-Gd +	None	$\geq 50\%$ ↓	$< 50\%$ ↓ to $< 25\%$ ↑	$\geq 25\%$ ↑ [†]
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 [‡]

Waterfall plot (RANO-LGG) – 26% response



*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.

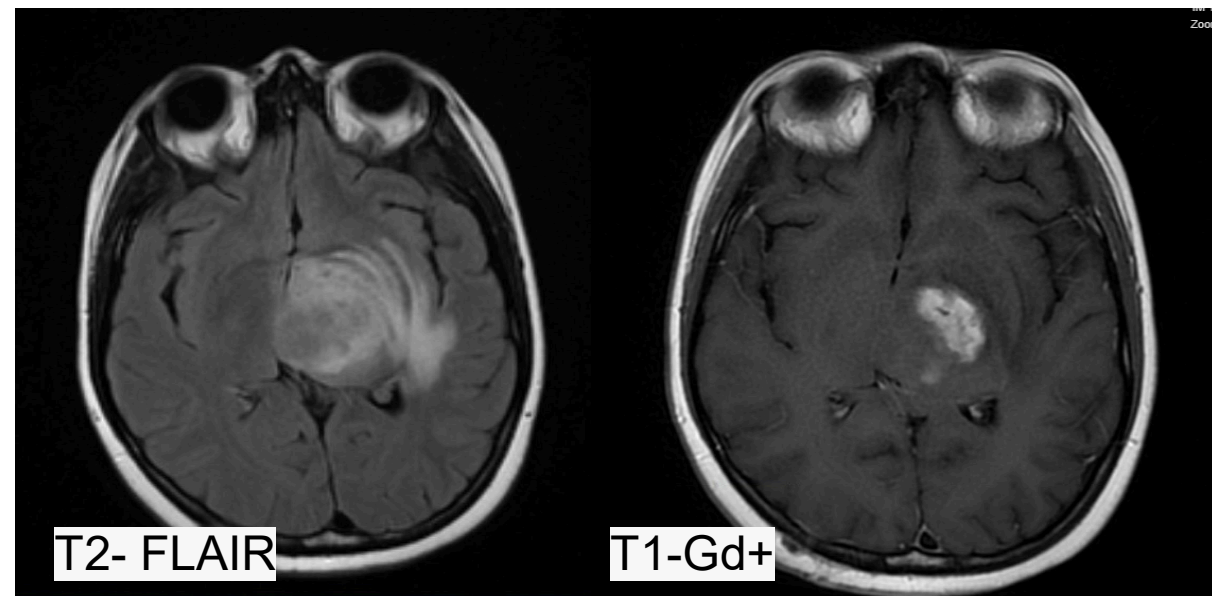
¹Integrated RANO LGG criteria assessment by dual reader BICR

²Eight overall radiographic SD accompanied by increase in corticosteroids; 3 overall radiographic PD accompanied by decrease in corticosteroids

³Three patients did not have on-treatment monotherapy MRIs available for BICR; one patient censored prior to first on-treatment MRI

Response assessment criteria for glioma

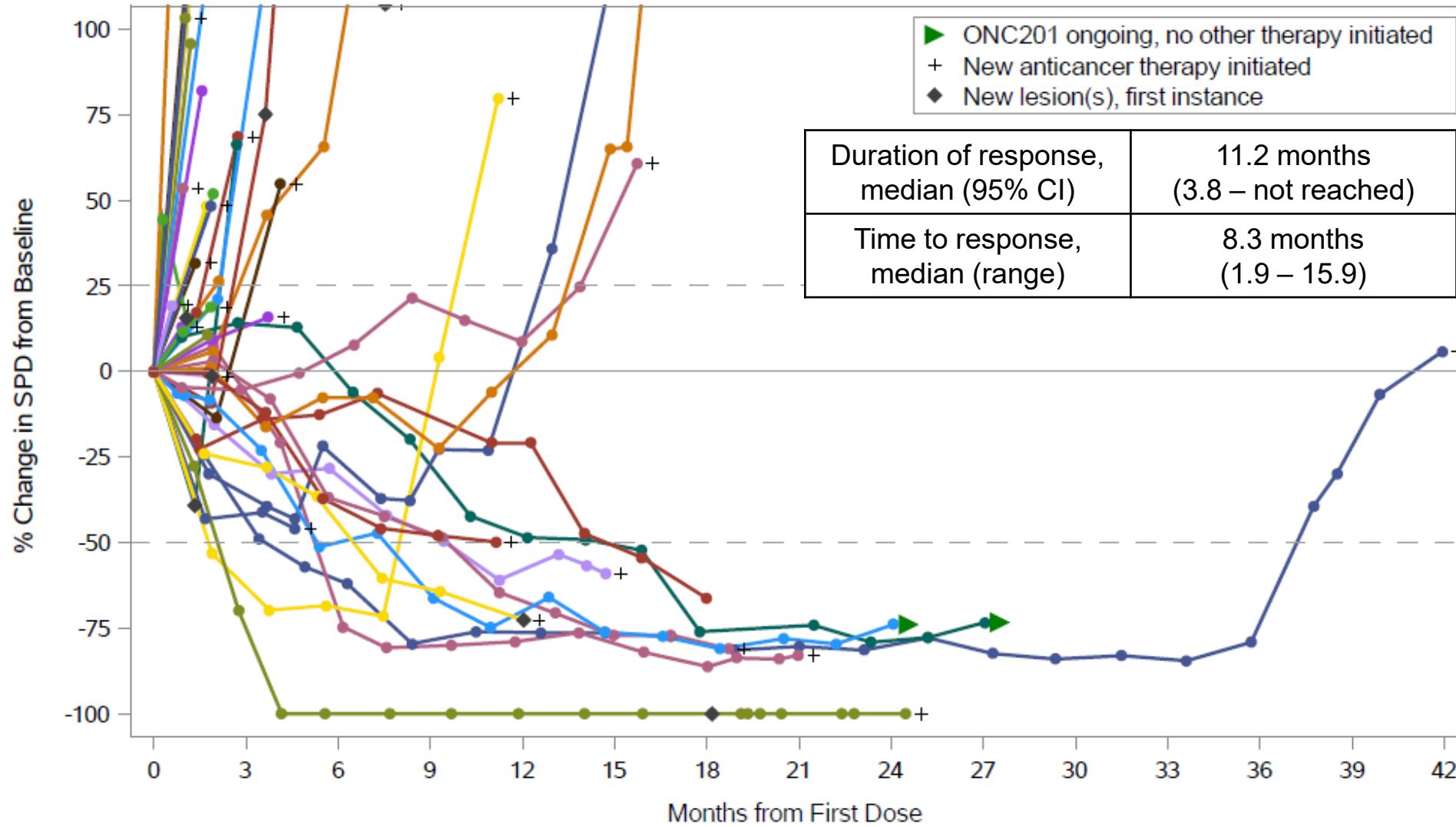
- RANO LGG response defined by decrease in T2 FLAIR



RANO- LGG

Criterion	CR	PR	MR	SD	PD
T2/FLAIR	Disappearance of all lesions	$\geq 50\%$ \downarrow in perpendicular diameters of lesion, sustained for 4 weeks	25–50% \downarrow in perpendicular diameters of lesion	$<25\%$ \downarrow to $<25\%$ \uparrow	$\geq 25\%$ \uparrow^{\dagger}
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 \downarrow	Stable or \downarrow	Stable or \downarrow	NA [‡]
Clinical status	Stable or \uparrow	Stable or \uparrow	Stable or \uparrow	Stable or \uparrow	\downarrow^{\dagger} (not attributable to other causes apart from the tumor, or decrease in corticosteroid dose)
Requirement for response	All	All	All	All	Any [‡]

Spider plot (RANO-HGG)



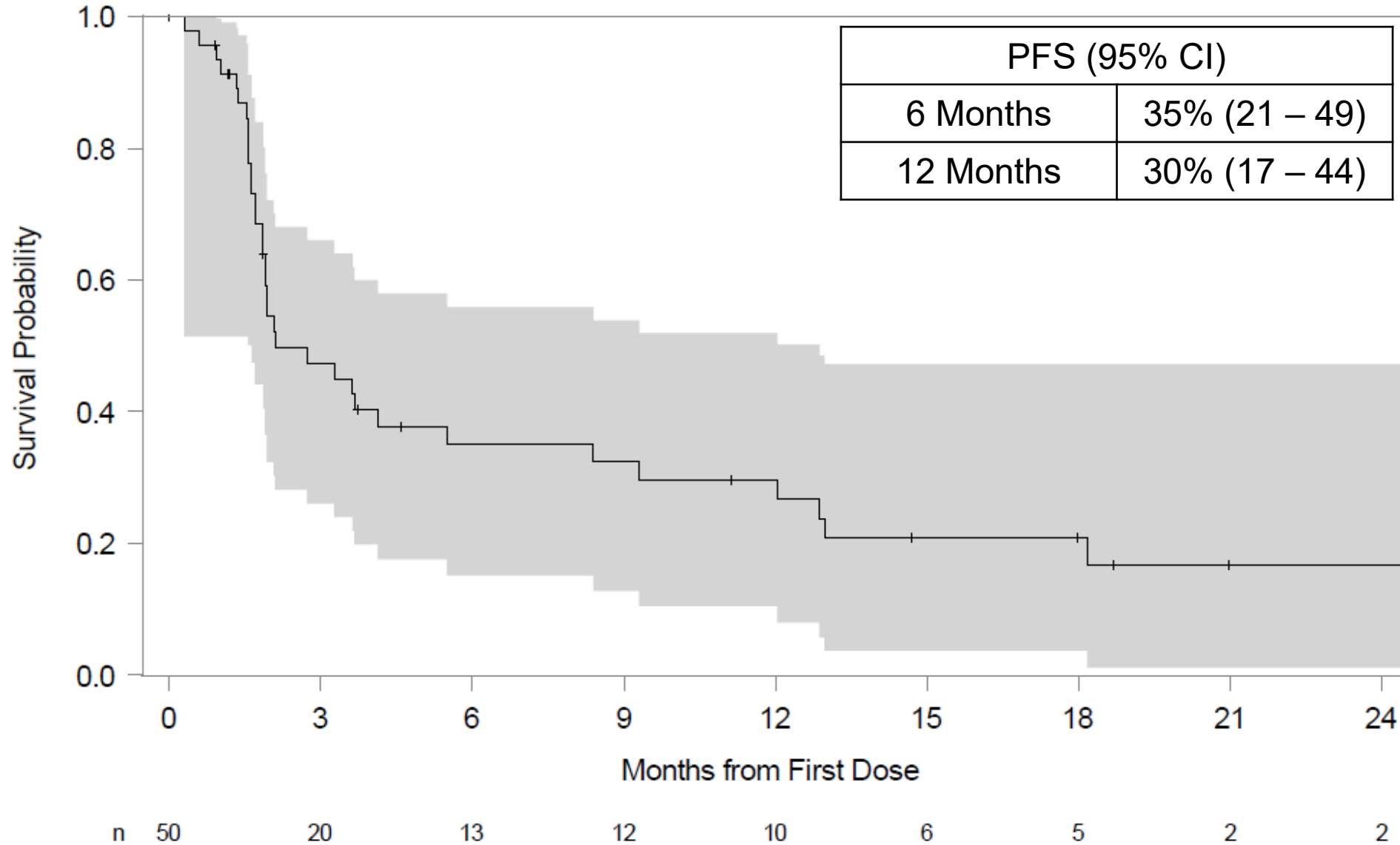
SPD=sum of products of perpendicular diameters (target enhancing lesions per BICR)

Only patients with measurable target enhancing lesions by BICR at baseline and with post-baseline evaluations are included.

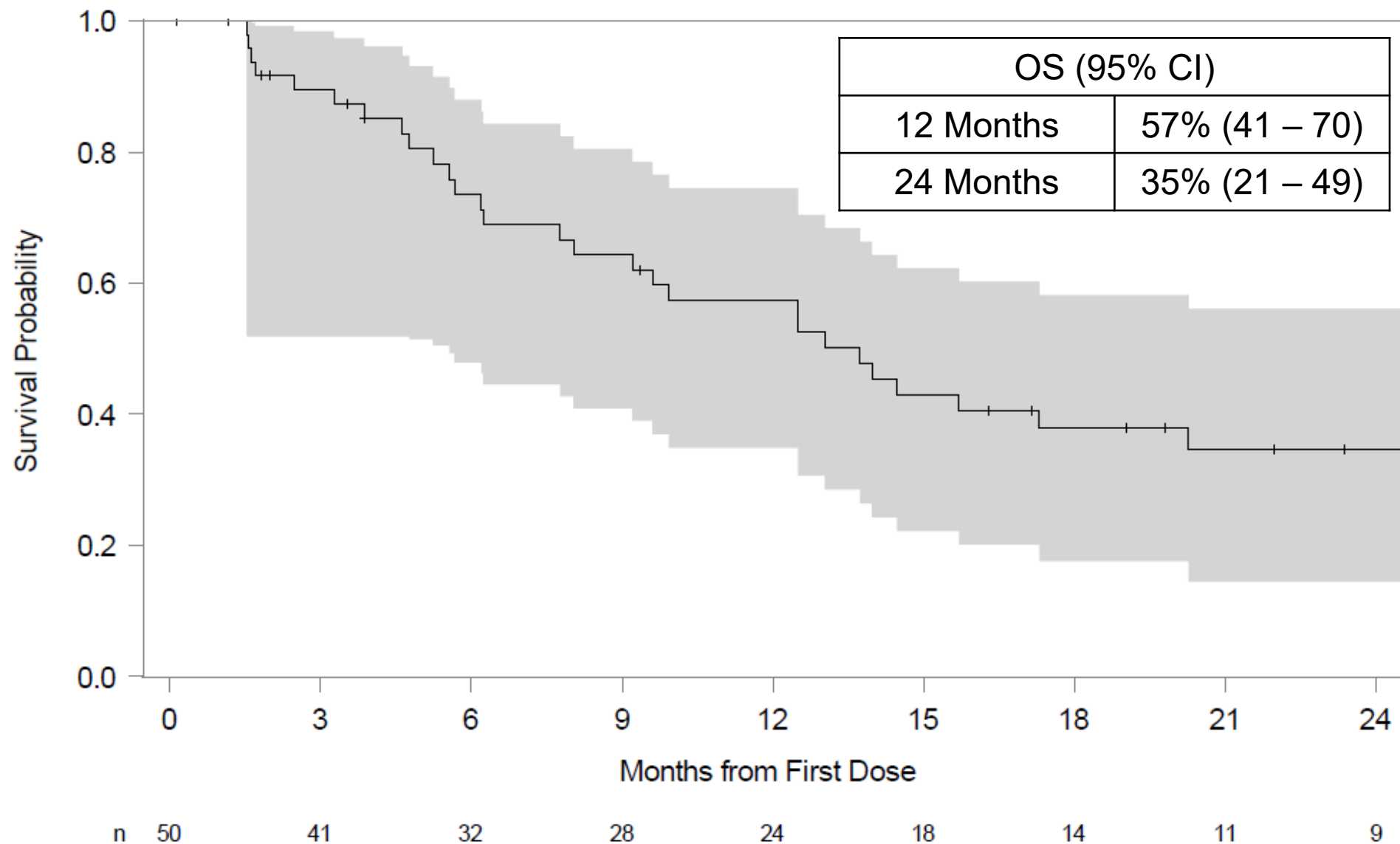
Three patients did not have on-treatment monotherapy MRIs available for BICR; one patient censored prior to first on-treatment MRI ; one patient did not have measurable target lesion.



Progression-free survival



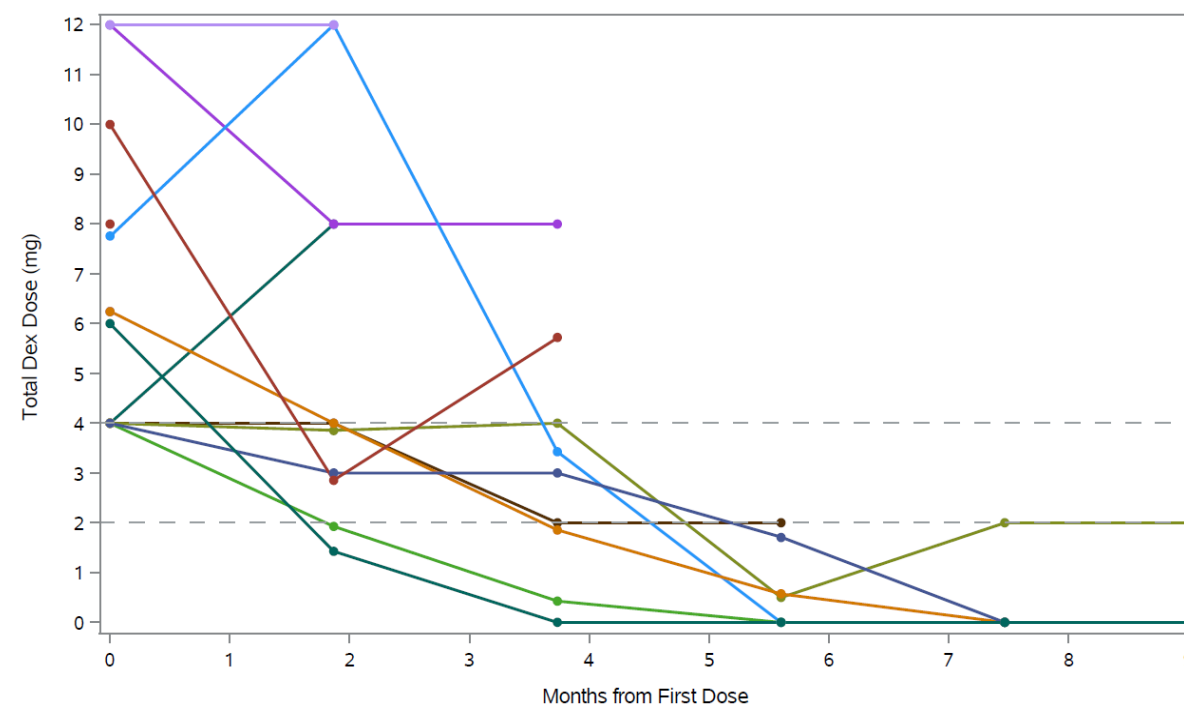
Overall survival



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)

Corticosteroids³



¹Corticosteroid response: $\geq 50\%$ 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 $\geq 4\text{mg}$ dexamethasone at baseline were evaluable.

²Performance 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.

³Average daily over 1 week around analysis window presented (every 8 weeks)

Serious adverse events

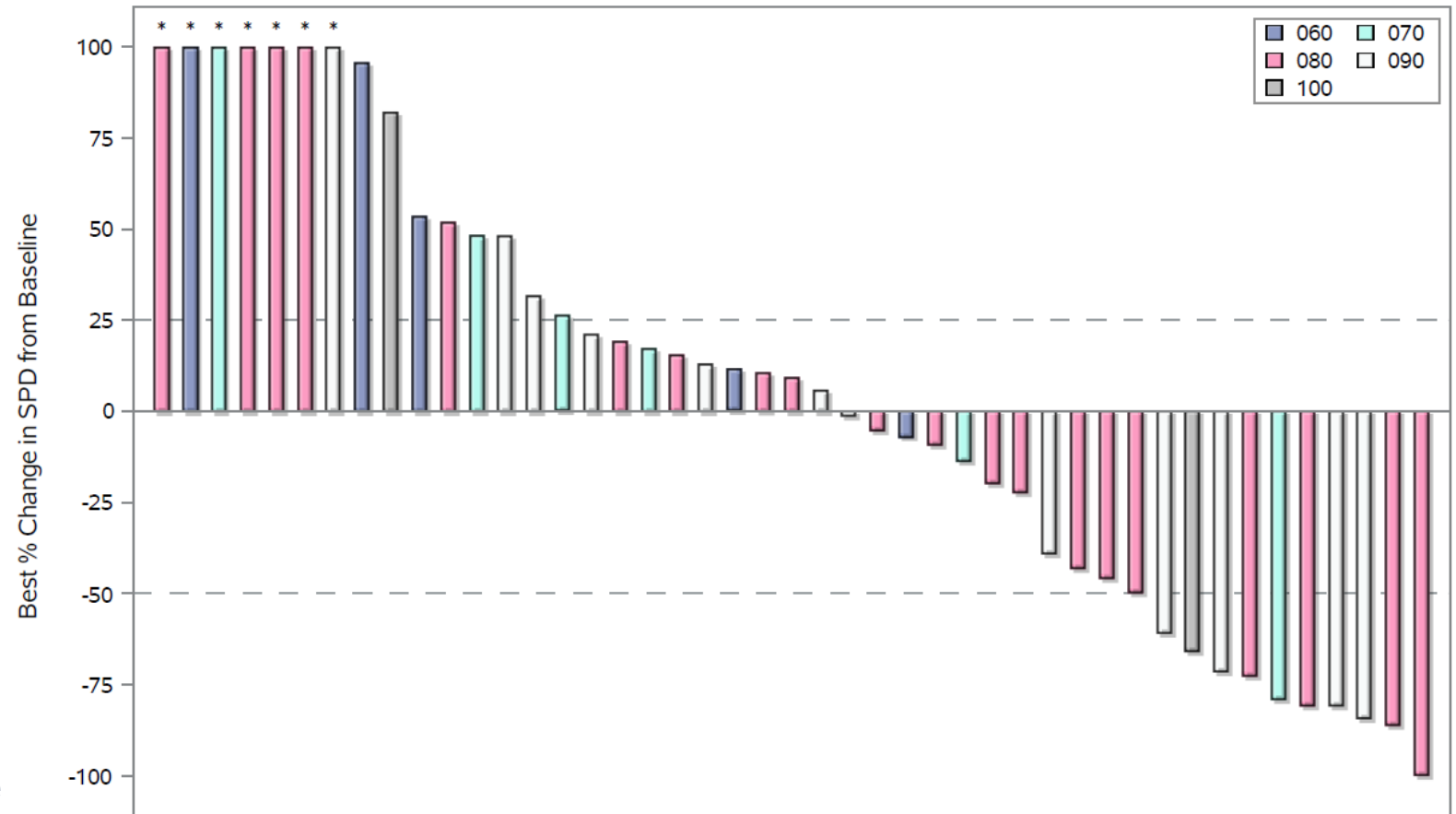
	Any attribution, N (%)	Related, N (%)
Any SAE¹	25 (50%)	1 (2%)
Gastrointestinal disorders		
Nausea	2 (4%)	0
Vomiting	2 (4%)	0
General disorders and administration site conditions		
Disease progression	2 (4%)	0
Nervous system disorders		
Brain oedema	2 (4%)	0
Encephalopathy	4 (8%)	0
Headache	3 (6%)	0
Respiratory, thoracic and mediastinal disorders		
<u>Dyspnoea</u>	2 (4%)	0
Vascular disorders		
Embolism	2 (4%)	0
Pulmonary embolism	2 (4%)	1 (2%) ²

¹Specific preferred terms occurring in more than one patient are listed; 25 patients had at least one SAE

²Possibly related per investigator assessment; unlikely related per sponsor assessment

Waterfall plot (RANO-HGG) stratified by performance status

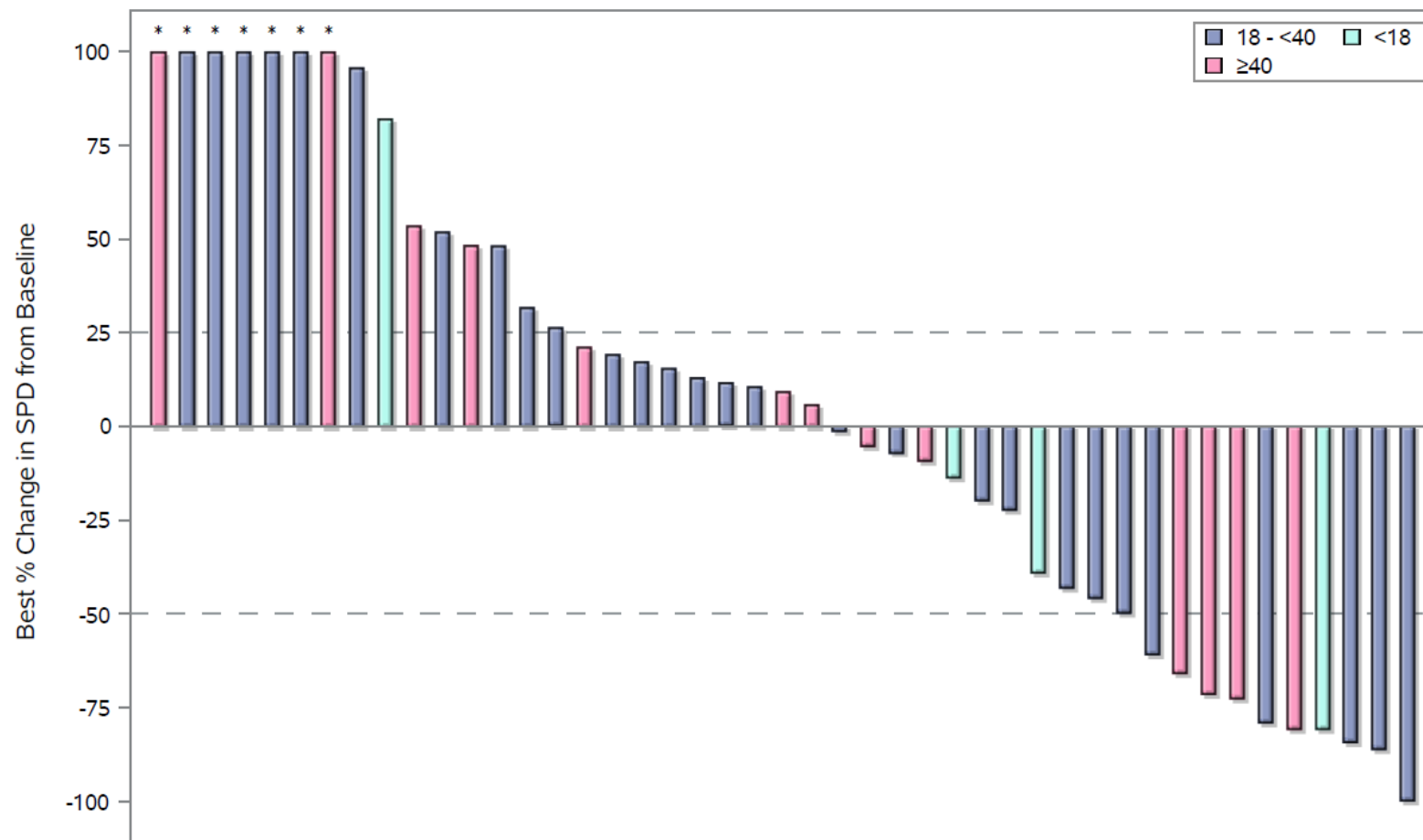
- Expectedly, patients with higher PS were more likely to respond to treatment
 - 100: 1/2 (50%)
 - 90: 4/14 (29%)
 - 80: 4/20 (20%)
 - 70: 1/7 (14%)
 - 60: 0/7 (0%)
- Consistent with hypothesis that treating earlier in disease course may enhance efficacy



* 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.

Waterfall plot (RANO-HGG) stratified by age

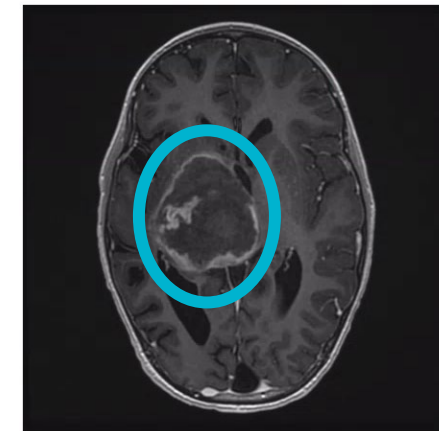
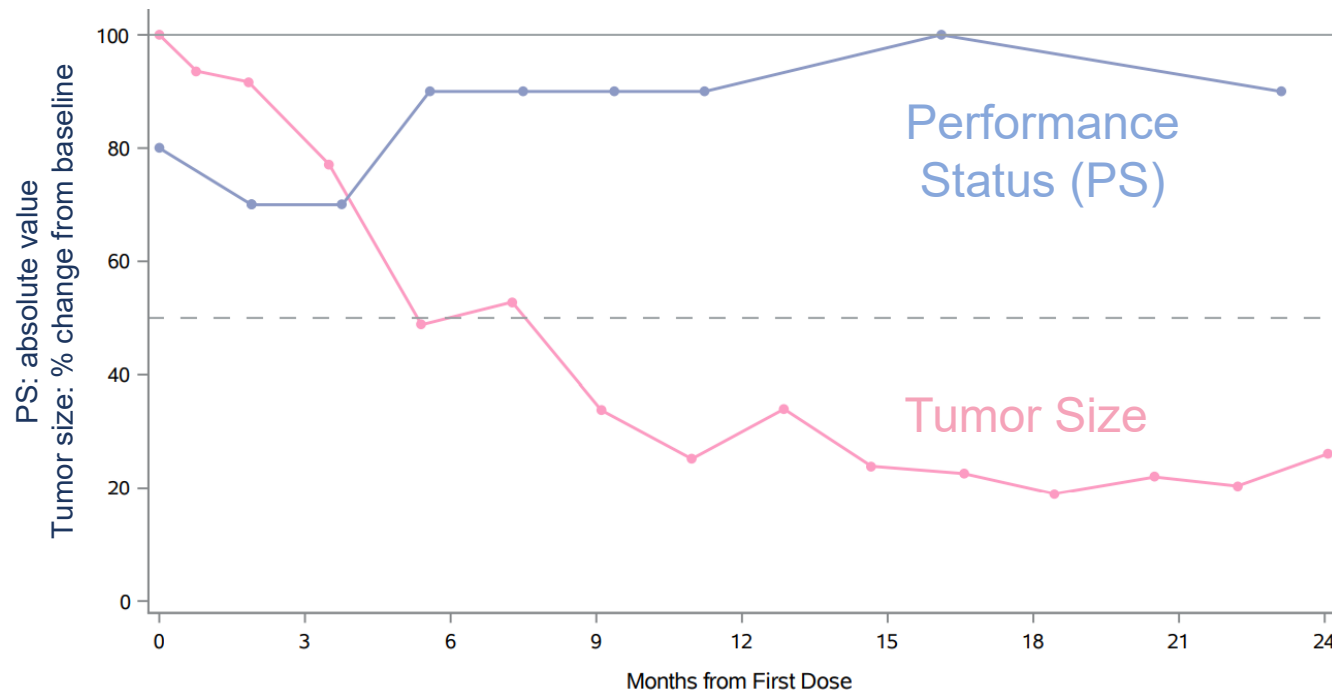
- Responses observed across age groups:
 - <18 years: 1/4 (25%)
 - 18-40 years: 5/32 (16%)
 - ≥40 years: 4/14 (29%)
- RANO-HGG response of 8-year-old subject confirms activity in this population



* 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.

Pediatric case study

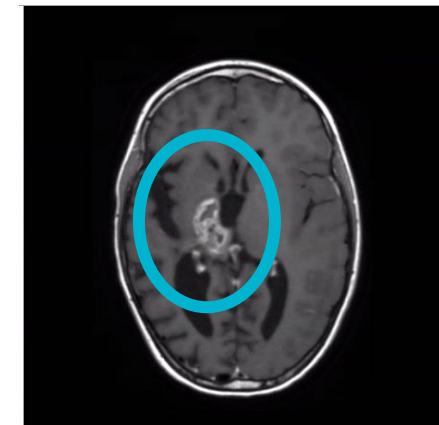
- 8-year-old thalamic H3.3 K27M DMG initially diagnosed in May 2018
- First-line therapy: radiation, dasatinib, everolimus and bevacizumab
- Second-line therapy: 375mg weekly ONC201 monotherapy initiated Apr 2019 following progression on first-line therapy
 - Clinical and radiographic improvement over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



**Pre-ONC201
baseline**



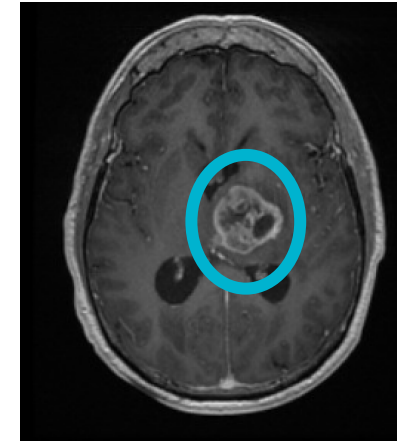
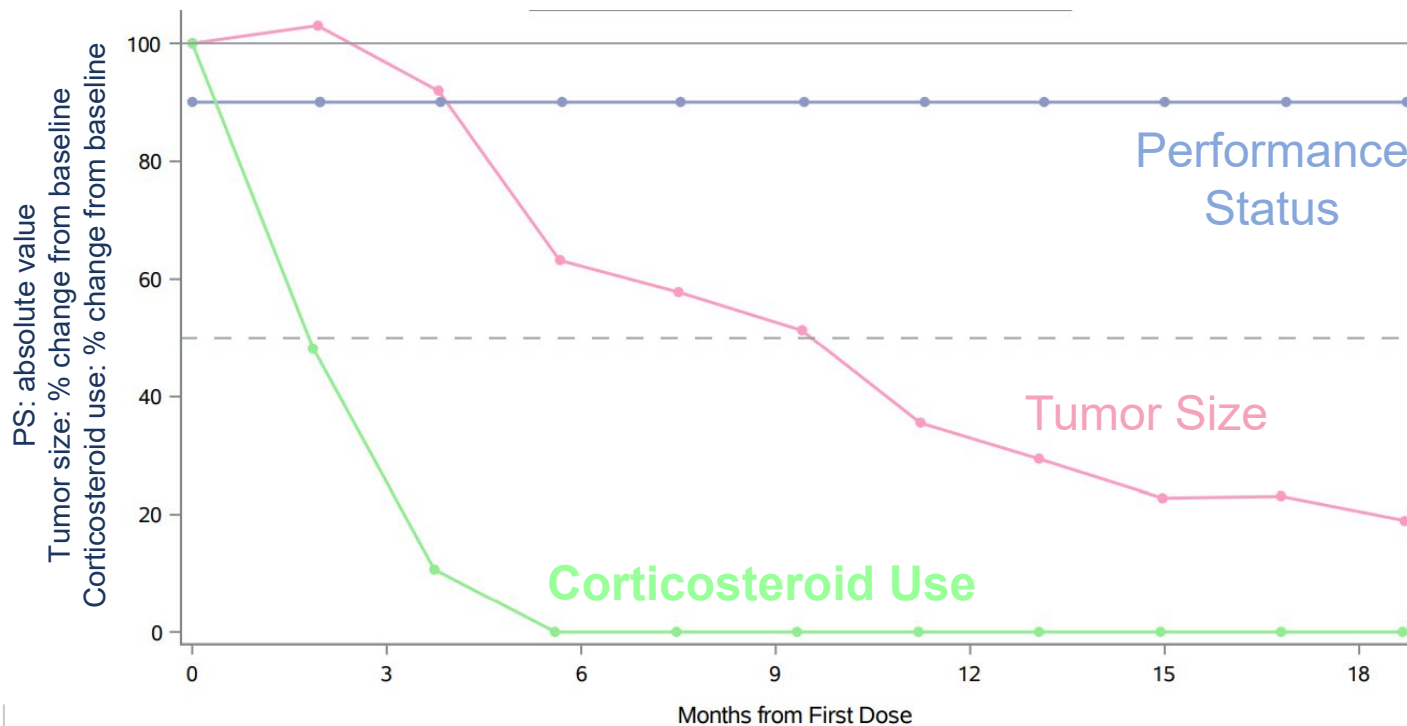
**9 months
on ONC201**



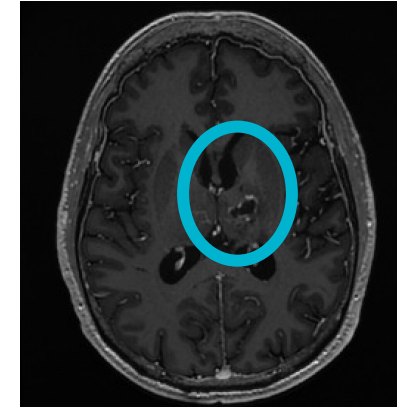
**18 months
on ONC201**

Adult case study

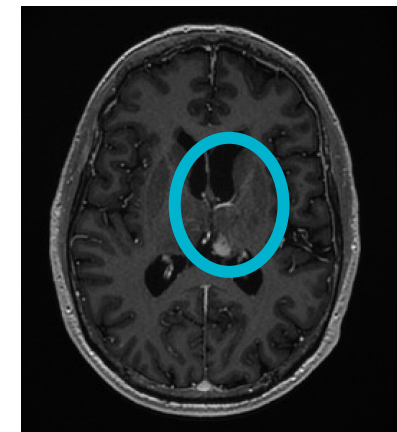
- 54-year-old thalamic H3 K27M DMG diagnosed in Nov 2018
- First-line therapy: radiation and temozolomide
- Second-line therapy: 625mg weekly ONC201 monotherapy initiated May 2019
 - Corticosteroid elimination and radiographic regression over >1.5 years of therapy



***Pre-ONC201
baseline***



***12.9 months
on ONC201***



***18.5 months
on ONC201***

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)

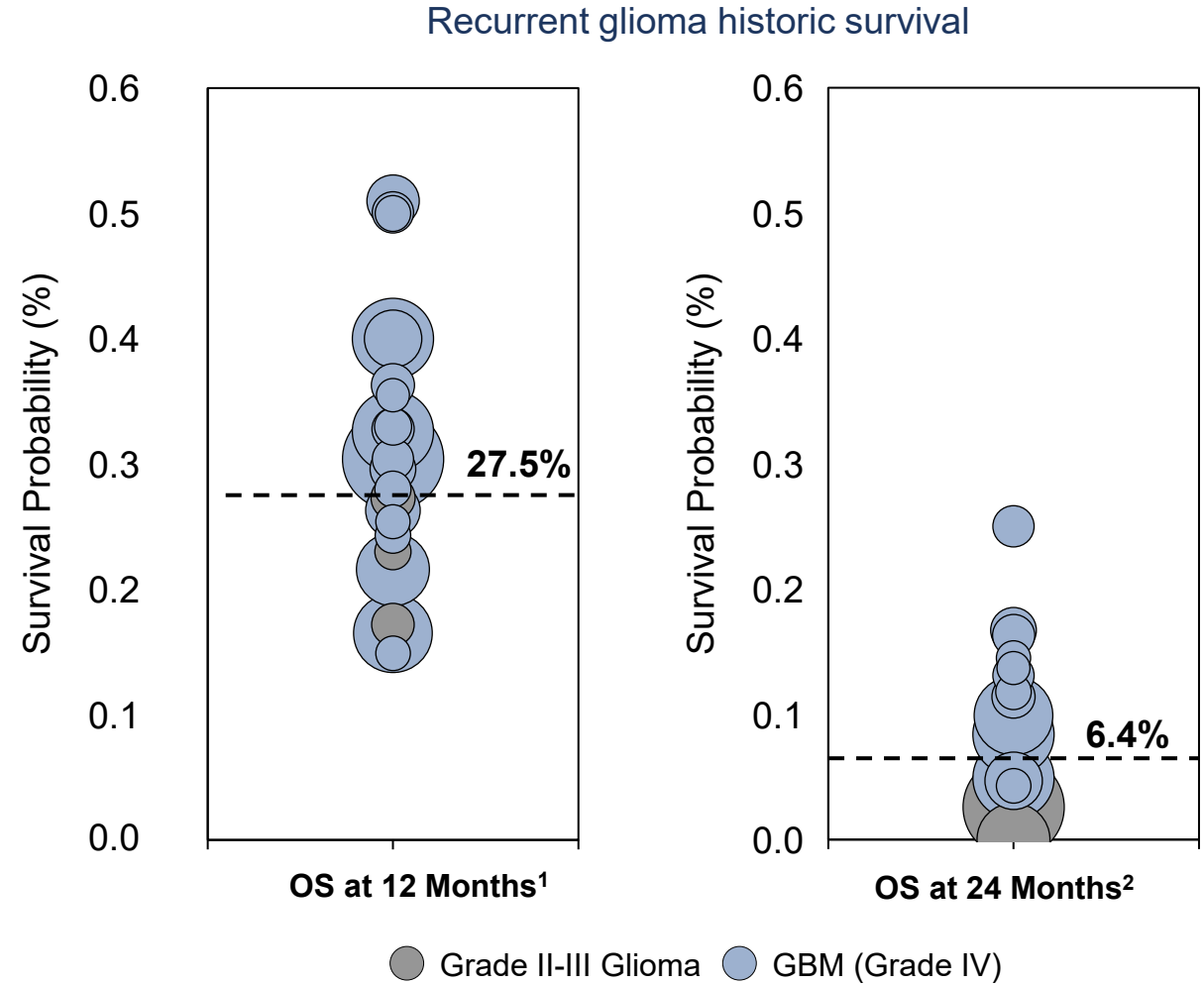
3. Corticosteroid response: ≥50% reduction in average daily corticosteroid dose compared to baseline with stable or improved KPS/LPS. Must be confirmed at next analysis timepoint. Corticosteroids were converted into a dexamethasone equivalent dose. Baseline ≥4mg dexamethasone at baseline were evaluable.

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.



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 months¹ and 6.4% at 24 months²
- Survival in pediatric recurrent H3 K27M DMG reported to be 0% at 24 months³
- 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

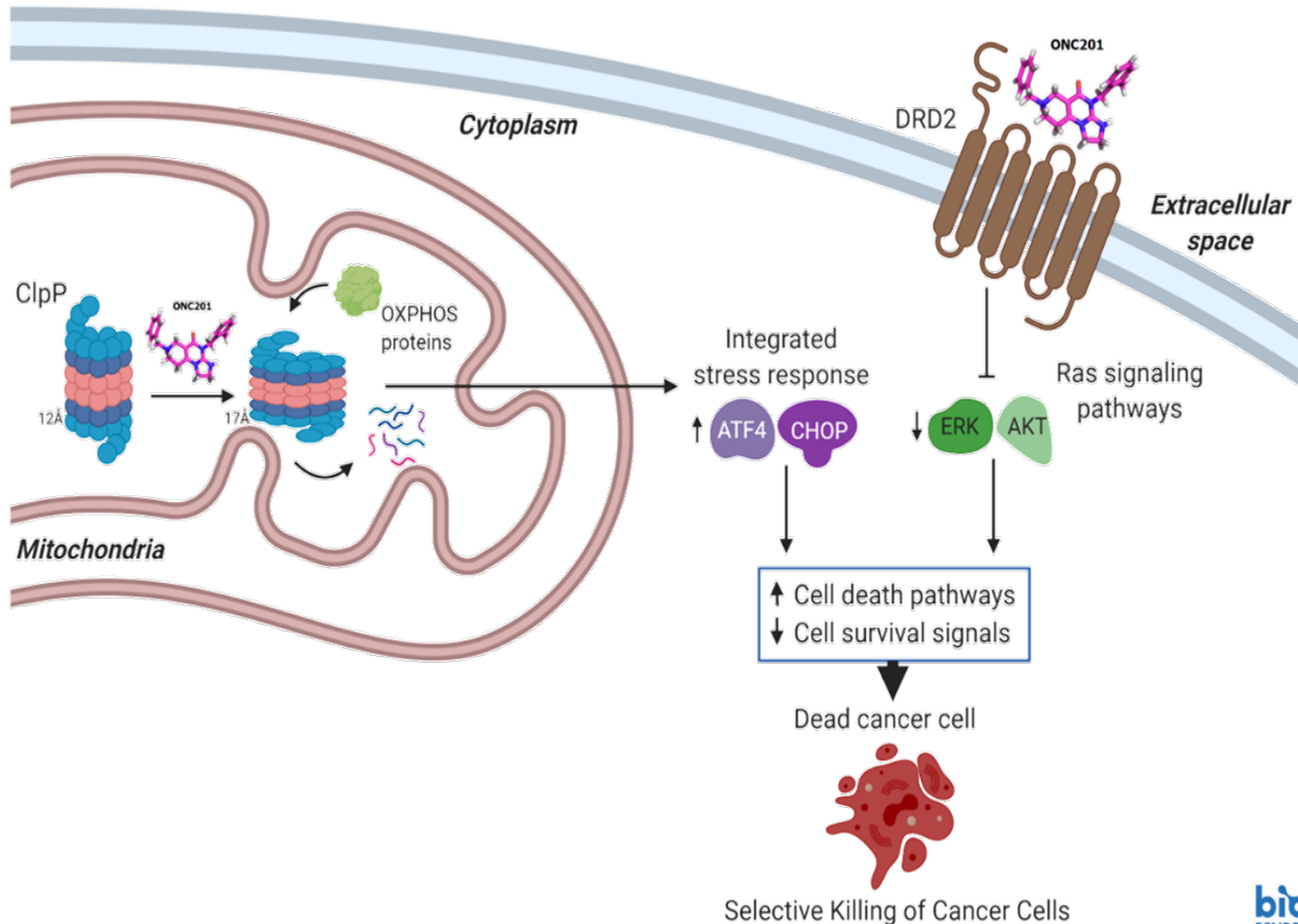
H3 K27M-mutant glioma: market dynamics and opportunity

- U.S. annual incidence of ~2,000
- Market research
 - Nearly all mid-line glioma patients tested for H3 K27M-mutation; rate to increase with targeted therapy
 - ~20% ORR and/or clinically relevant durability deemed clinically meaningful
 - ONC201 use expected in >80% of H3 K27M-mutant glioma patients based on current profile
 - Interest in combination with radiation, if possible, in the front-line setting
- Competitive landscape: chemotherapy and bevacizumab ineffective; targeted agents, vaccines and CAR-T therapies are in early development with limited efficacy analysis available
- Low barriers to adoption
 - No effective treatment options available
 - K27M already on commercial and site-specific NGS panels, oral dosing (QW), good safety profile
 - High unaided awareness of ONC201 among neuro-oncologists
 - Longer-term, potential combinable with other glioma therapies



ONC201 targets DRD2 and ClpP

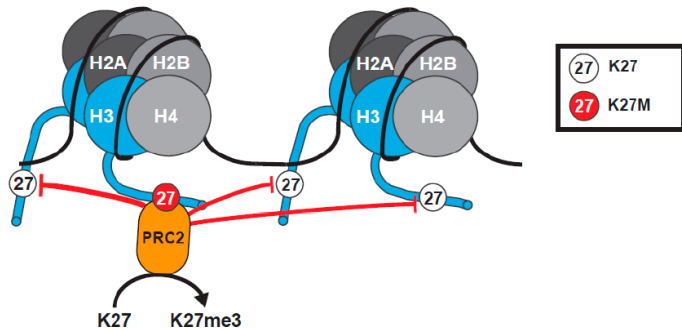
ONC201 upregulates integrated stress response, inactivates Akt/ERK, selectively inducing tumor cell death



- ONC201 can selectively induce apoptosis in cancer cells by altering activity of two proteins
- DRD2 antagonism
 - DRD2 is a G protein-coupled neuroreceptor that regulates Ras signaling
 - ONC201 antagonizes DRD2, inhibiting Ras signaling pathways
- ClpP agonism
 - ClpP normally degrades misfolded proteins in mitochondria
 - ONC201 modifies ClpP conformation, promoting excess degradation of specific mitochondrial proteins important for cancer cell viability

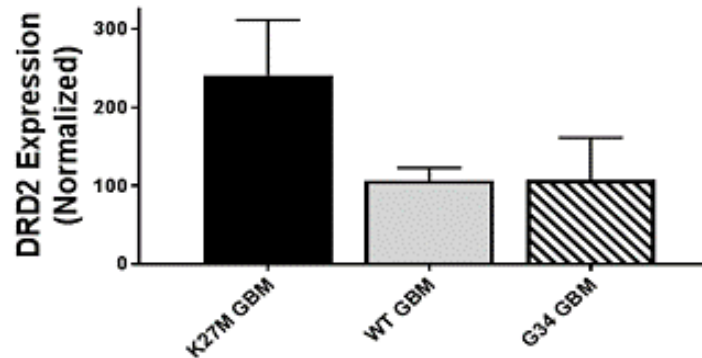
H3 K27M-mutant gliomas exhibit enhanced sensitivity to ONC201

Lysine to methionine (“K-to-M”) histone H3 mutation reduces H3 K27 methylation



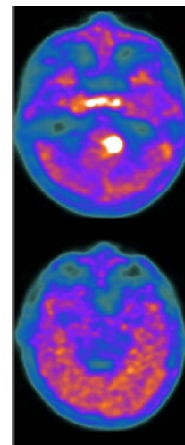
K27M-mutants bind PRC2 which normally methylates H3 K27 via EZH1/2; binding/tethering PRC2 prevents methylation of even nonmutant H3 K27

H3 K27M elevates DRD2 expression



H3 K27M
Grade IV
DMG

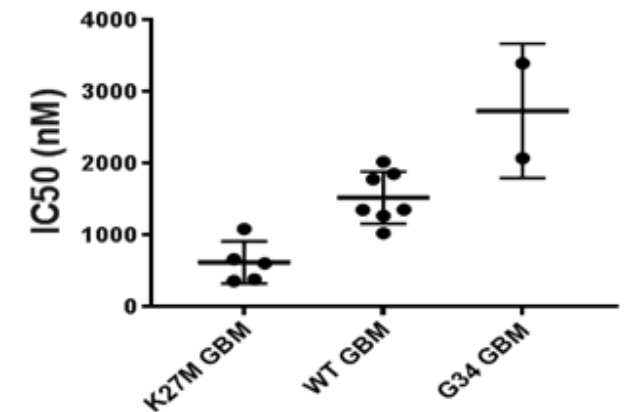
H3 WT
Grade IV
DMG



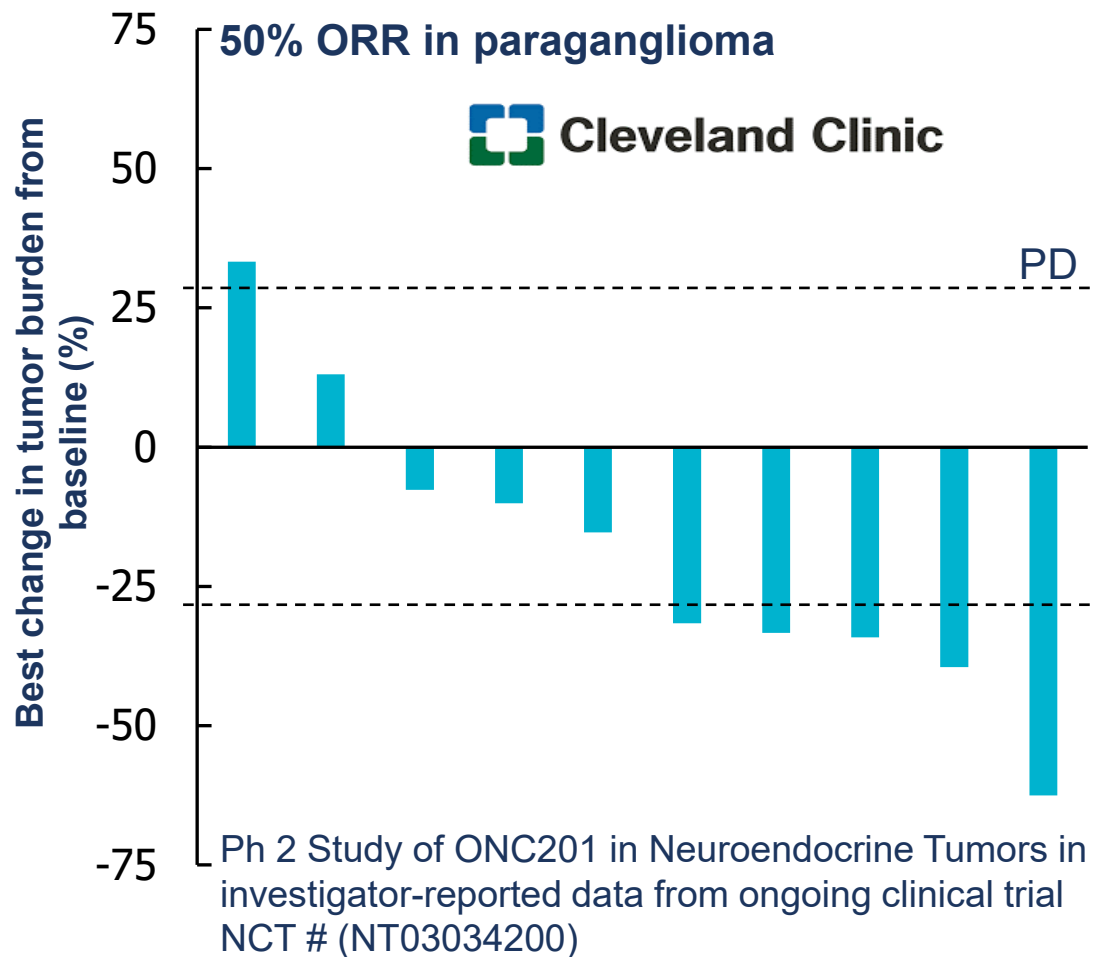
18F-DOPA PET

Midline tumors occur in dopamine-rich regions of the brain

High sensitivity to ONC201



ONC201 interim efficacy results in dopamine-secreting tumors outside the brain



- Single agent responses in Ph 2 neuroendocrine trial of ONC201 observed in subset (paraganglioma)
- Paraganglioma are adrenal-related tumors with elevated DRD2 expression
- Five patients have been treated > 1 year
- Less short-term and potential long-term toxicities than other paraganglioma therapies
- Objective responses in patients with tumor genetic driver alterations in metabolic enzymes (SDHA, SDHB, SDHD) and diverse prior therapy

ONC201 FDA designations



Orphan Drug Designation (ODD) (treatment of glioblastoma and treatment of malignant glioma)



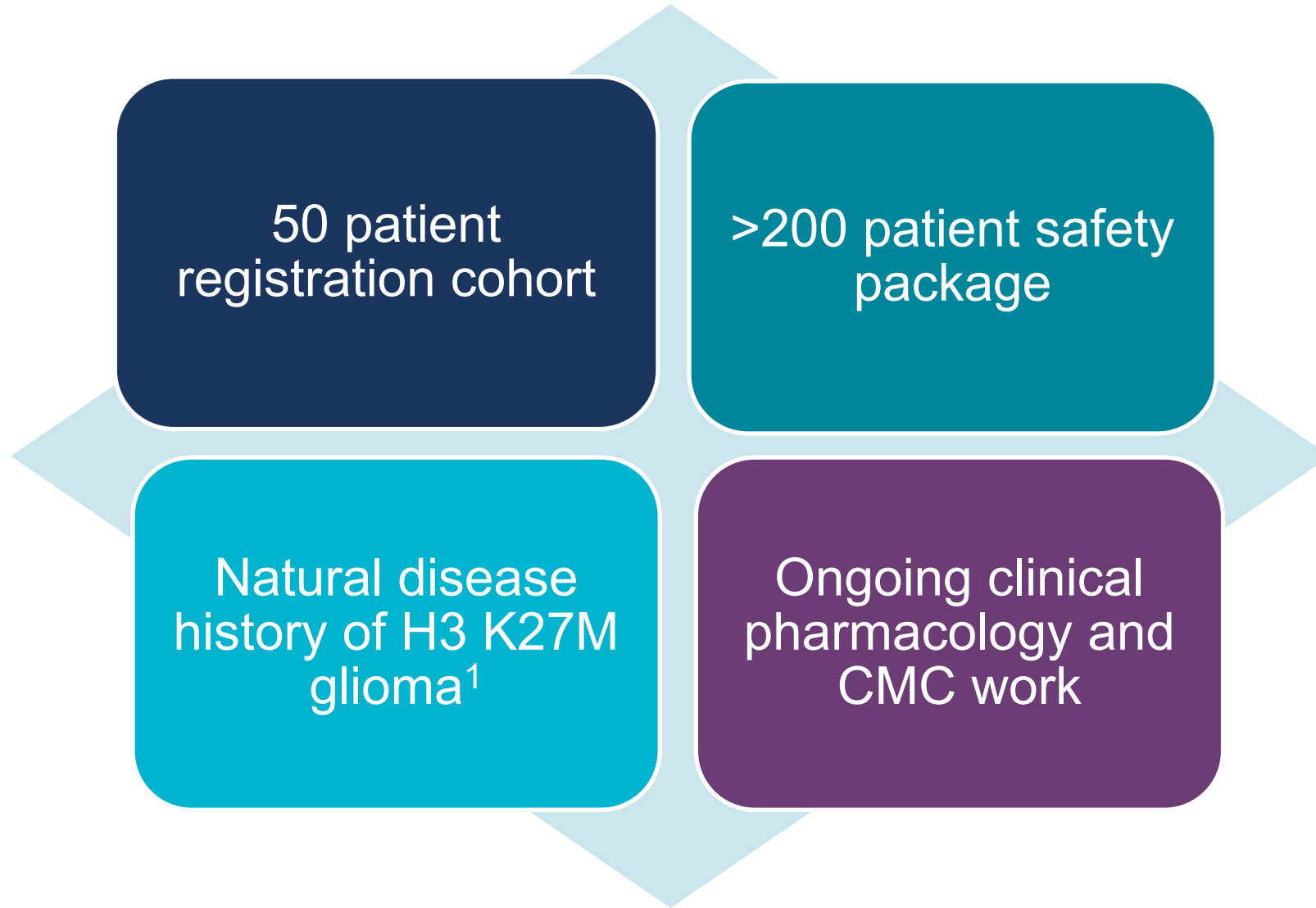
Fast Track Designation (FTD) for adult recurrent H3 K27M-mutant high-grade glioma



Rare Pediatric Disease Designation for treatment of H3 K27M mutant glioma

- Potential to receive rare pediatric voucher¹

Key elements of regulatory package



1. One population mirroring 50 patient cohort and second providing broader population to identify prognostic drivers

Promising pipeline in development

ONC206:

- Differentiated DRD2 antagonist + ClpP agonist
- Phase 1 for recurrent CNS tumors



ONC212:

- GPR132 agonist + ClpP agonist
- IND-enabling studies



Dociparstat Sodium (DSTAT) for First-line Treatment in AML



More than 21,000 new cases of AML annually in the U.S.

- Rapidly progressive disease with low survival rates

- Existing therapies are seldom cures

- 1-year survival for older patients



- 5-year survival for older patients



- Relapse can occur if not all AML blasts and stem cells are eradicated

- AML is heterogenous and has multiple mechanisms of resistance to treatment

Compelling pilot study results in treatment-naïve AML patients

Strong Complete Response, Overall Survival and improved hematologic recovery

Complete Response

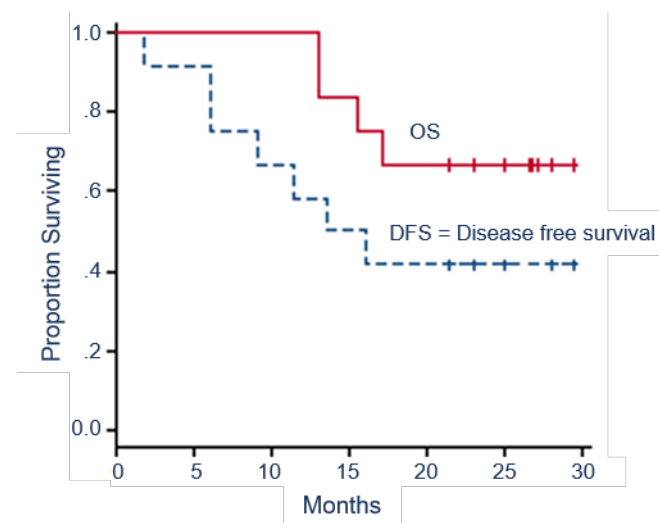
- **11 of 11 (100%)** patients with treatment-naïve primary AML achieved a CR with single induction cycle of 7+3 chemotherapy plus DSTAT; none reported serious adverse events related to DSTAT
- 12th patient enrolled with granulocytic sarcoma secondary to chronic myelomonocytic leukemia achieved a CR with second induction cycle without DSTAT
- All 5 baseline FLT3+ patients achieved CR with single induction cycle

Survival Rates

- Median survival not yet reached after 29.4 months
- Median disease-free survival of 14.8 months
- 4 patients remained in remission

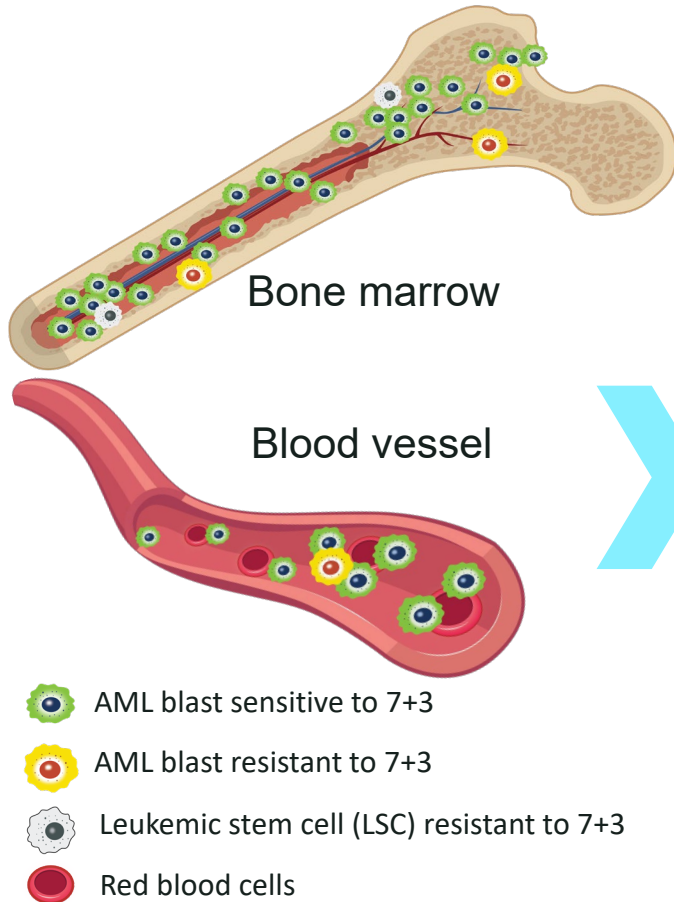
Count Recovery

- Median time to recovery of an untransfused platelet count of at least $50 \times 10^9/L$ of 23.5 days
- Median time to ANC recovery of at least $0.5 \times 10^9/L$ of 22 days



DSTAT may improve duration of response & overall survival

DSTAT targets proteins involved in resistance pathways and LSC/blast quiescence, including HMGB1, PF4, CXCR4 / CXCL12, neutrophil elastase and selectins



'7+3' Chemotherapy + DSTAT

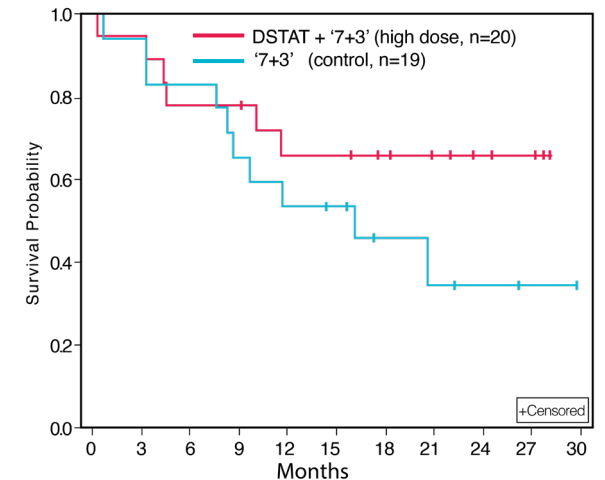
- 1) Inhibit AML survival and chemoresistance pathways
- 2) Reverse quiescence of AML blasts and LSCs

'7+3' Chemotherapy

- 1) Residual AML blasts cause relapse
- 2) Low abundance LSCs cause relapse

DSTAT appears to reduce AML relapse

Overall Survival (OS)



Relapse driven by resistant blasts & LSCs

Randomized Phase 2B AML study in U.S. cancer centers

Design^{1,2}

Subjects

- Treatment-naïve AML patients
- Age 60+
- N = 75

Treatment Arms

- Cytarabine + idarubicin (control)
- Cytarabine + idarubicin + low dose DSTAT (4 mg/kg IV bolus followed by 0.125 mg/kg/hr for 7 days)
- Cytarabine + idarubicin + higher dose DSTAT (4 mg/kg IV bolus followed by 0.25 mg/kg/hr for 7 days)

1. 4th arm in this study (4 mg/kg bolus followed by 0.325 mg/kg/hr infusion plus 7+3) discontinued after two patients were enrolled (one patient had hemorrhage deemed possibly related to DSTAT)
2. Low dose was deemed sub-therapeutic and the following data presented is limited to the high dose arm and the control arm

DSTAT potentially amplifies efficacy without significant toxicity

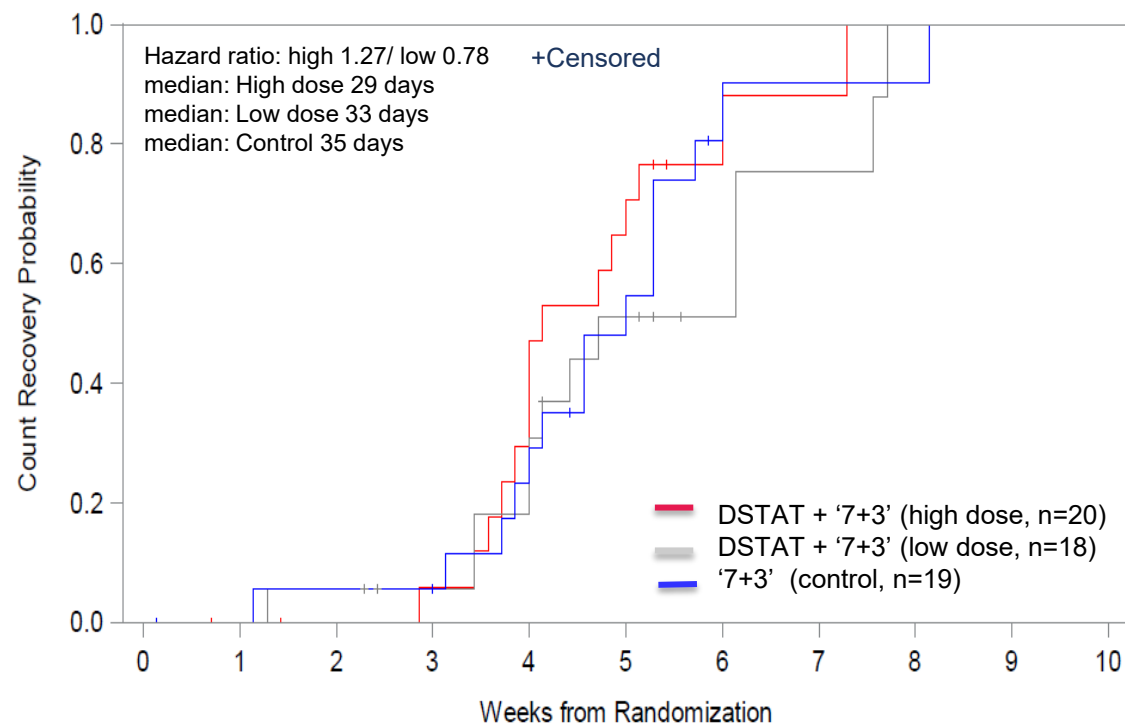
Generally well tolerated in newly diagnosed AML patients

- Most common serious adverse event in DSTAT arms was febrile neutropenia
 - 3 on high DSTAT arm, 1 on control arm
 - No difference in infection SOC SAEs (3 each)
- Four gastrointestinal SAEs on DSTAT arm none deemed related to DSTAT (colitis, ileus/gastric ulcer, small bowel obstruction, vomiting – single events and did not increase rate of mucositis)
- One SAE of lower gastrointestinal hemorrhage was reported in the control group
- Asymptomatic, transient elevation of hepatic transaminases observed in both arms
 - Well-described and non-adverse effect of cytarabine therapy
- aPTT remained in the normal range for most patients in DSTAT and control arms
- Comparable incidence of Gr>3 hemorrhagic events (1 on high DSTAT arm, 2 control)

DSTAT may not delay hematologic recovery, may accelerate

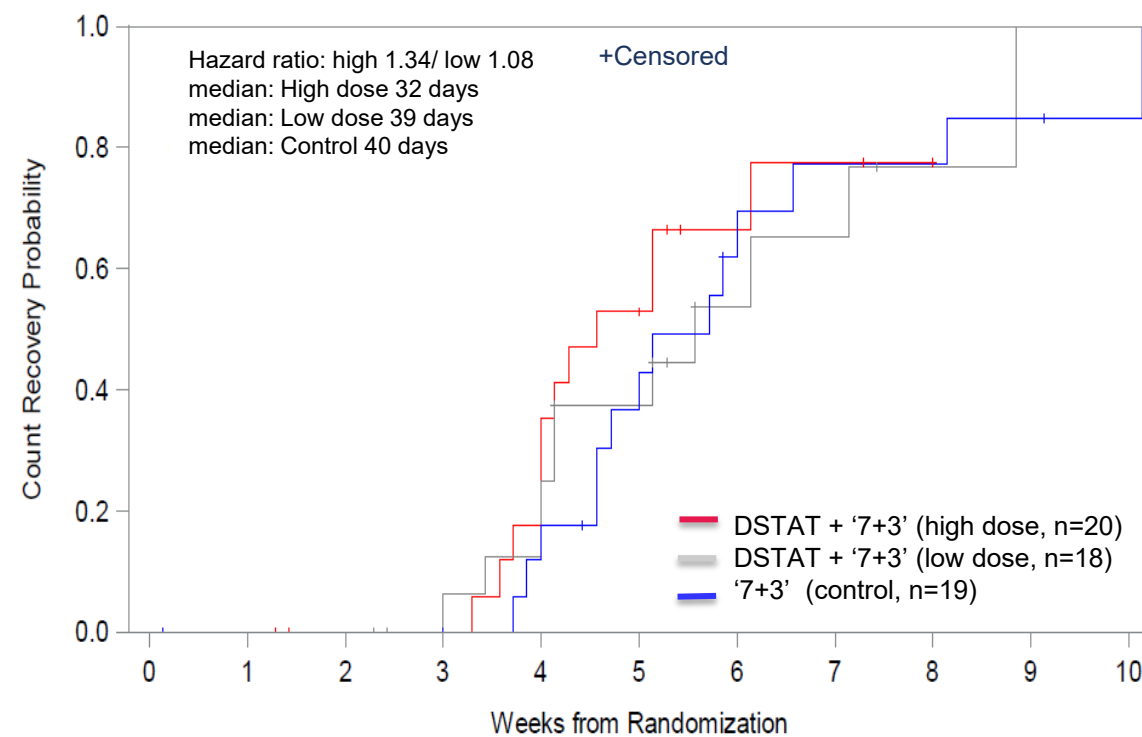
Median days to neutrophil and platelet recovery reduced by 17% and 20%, respectively on high dose

Likely Ph 3 ITT Neutrophil recovery > 500 cells/uL



DSTAT High	20	18	17	16	12	6	2	1	0	
DSTAT Low	18	18	17	15	13	7	4	2	0	
Control	19	18	17	17	13	8	2	1	1	0

Likely Ph 3 ITT Platelet recovery > 100,000 cells/uL



DSTAT High	20	19	17	17	14	8	3	2	1	
DSTAT Low	18	18	18	16	14	9	4	3	1	0
Control	19	18	18	18	15	10	5	3	3	2

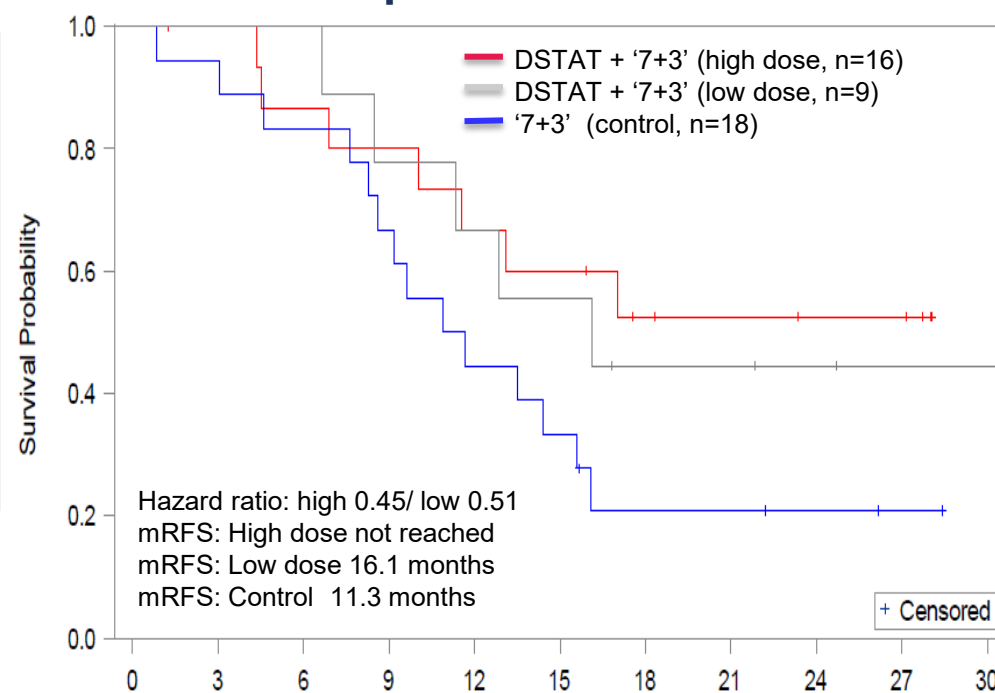
Full ITT population outperforms standard 7+3 chemo

RFS and OS benefit in full ITT Ph 2 population

Response Summary

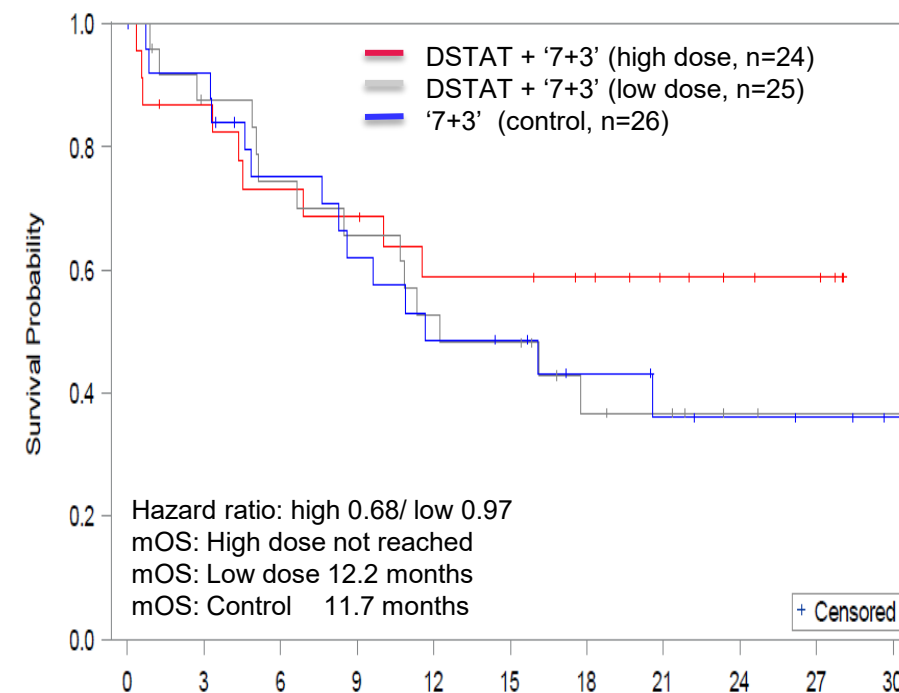
	% CR/CRi ^(1,2)
High Dose Arm	67% (16/24)
Low Dose Arm	36% (9/25)
Control Arm	69% (18/26)
(Historical Control ~50%)	

Relapse Free Survival³



	0	3	6	9	12	15	18	21	24	27	30
DSTAT High	16	15	13	12	10	9	6	5	4	4	0
DSTAT Low	9	9	9	7	6	5	3	3	2	1	1
Control	18	17	15	12	8	6	3	3	2	1	0

Overall Survival



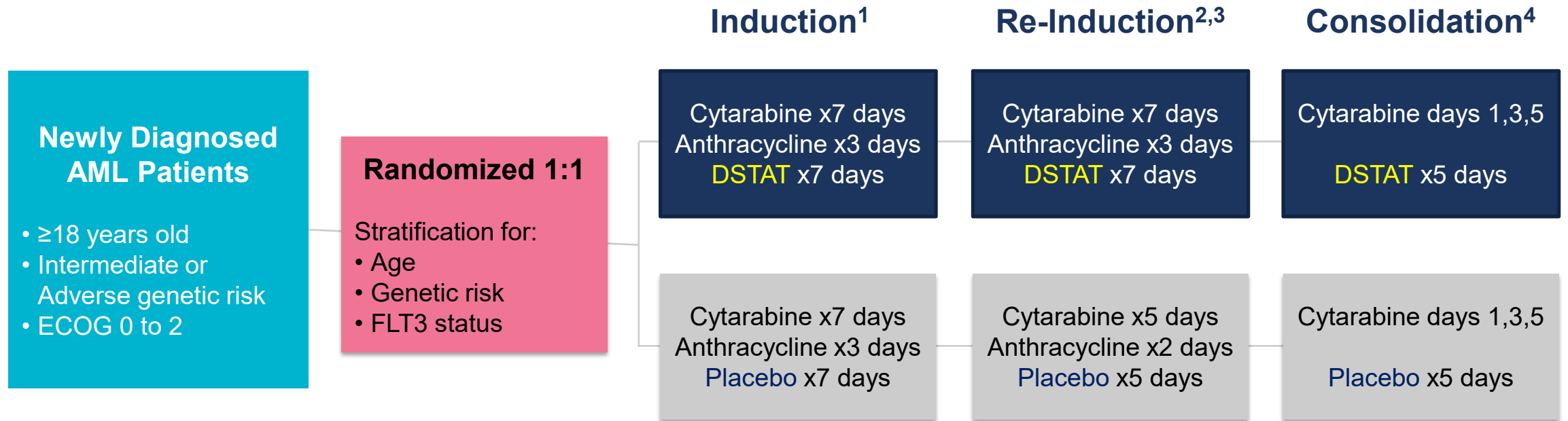
	0	3	6	9	12	15	18	21	24	27	30
DSTAT High	24	19	16	15	12	12	10	7	5	4	0
DSTAT Low	25	20	17	15	12	11	6	5	2	1	1
Control	26	23	17	14	11	10	7	5	4	3	1

1. Complete Response (CR) or Complete Response without complete hematologic recovery (CRi)
2. Confirmed with post day 14 (D14) bone marrow (BM) biopsy and less than 5% blasts. If no post D14 was performed, the D14 BM biopsy was used to determine response.
3. Relapse-Free Survival (RFS) is survival without relapse following induction success (CR/CRi)

Currently Enrolling DASH AML Ph 3 trial design

- 570 newly diagnosed adults with AML, fit for intensive chemotherapy
- Double-blind, placebo-controlled, randomized 1:1
 - DSTAT plus standard induction/consolidation chemotherapy (“7+3”)
 - Placebo plus standard induction/consolidation chemotherapy (“7+3”)
- FLT-3 positive subjects able to receive midostaurin
- Primary endpoints: overall survival and event free survival
- Secondary endpoints:
 - Minimal Residual Disease (MRD), Time to hematologic recovery, Response (CR, CR+CRi) and EFS with composite CR (CR+CRi)
- Early efficacy analysis: 80 evaluable patients
 - CR and MRD evaluated
 - Recent publications support predictive power MRD for OS, DFS
 - Data unblinded and published unless extraordinary benefit observed

DASH Phase 3 treatment plan



1. Cytarabine and DSTAT are given as continuous IV infusions
 2. For Reinduction: Patients age ≥ 60 receive cytarabine x5 days, anthracycline x2 days, and DSTAT or Placebo for 5 days.
 3. Re-induction if day 14 bone marrow shows persistent disease (≥5% blasts)
 4. Patients may proceed to HCT instead of consolidation chemotherapy

Early assessment to confirm mechanism

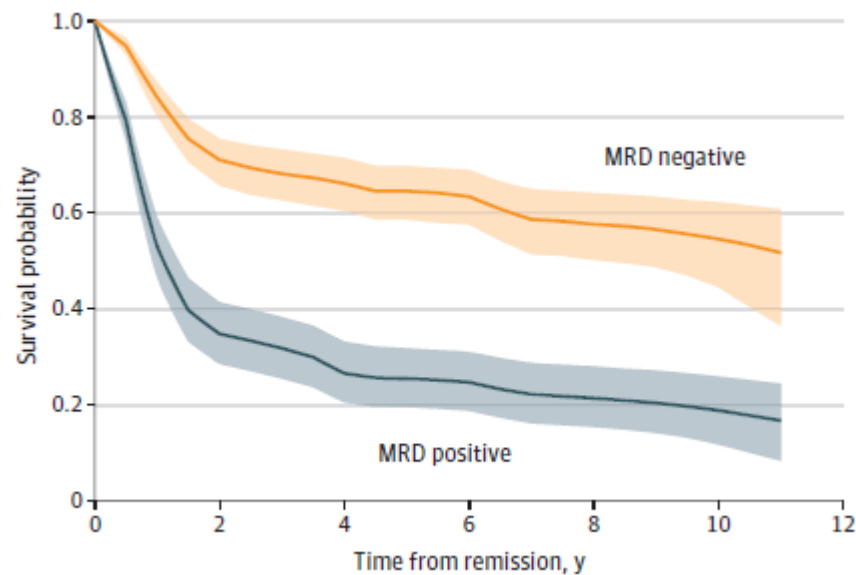
- Propose early assessment cohort of n=80 evaluable¹ patients for MRD status²
- MRD and CR are early indicators of potential OS and EFS advantage
- Patients continue to enroll during assessment
- Most likely unblind to assess and report data³
- Key benefits:
 - Confirmation of mechanism driving Phase 2 durable responses and OS
 - Prudent investment trigger
 - Ongoing reporting of cohort as data matures (including EFS and OS)
- IDMC discretion to maintain blinding if advantage is exceptional
 - Example: both CR and MRD advantage >20pp
- Allows for limited investment prior to proof of MRD advantage

MRD negativity is associated with superior DFS and OS

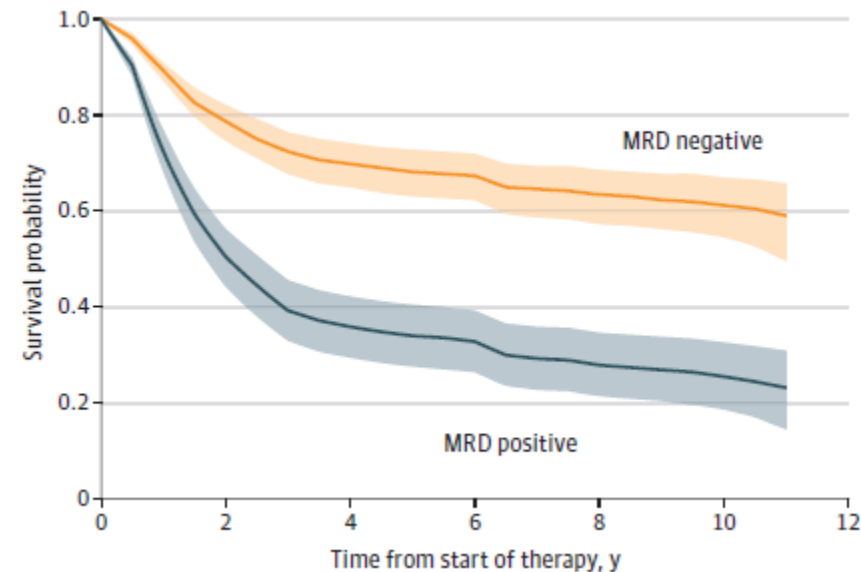
80 Patient Assessment likely strong predictor of success

- Meta-analysis of 81 studies (>11,000 patients) links MRD negativity with superior OS and disease-free survival (DFS)
- Results independent of age, subtype, time of assessment or detection method
- Average HR for achieving MRD activity was 0.37 for DFS and 0.36 for OS

Disease-free Survival

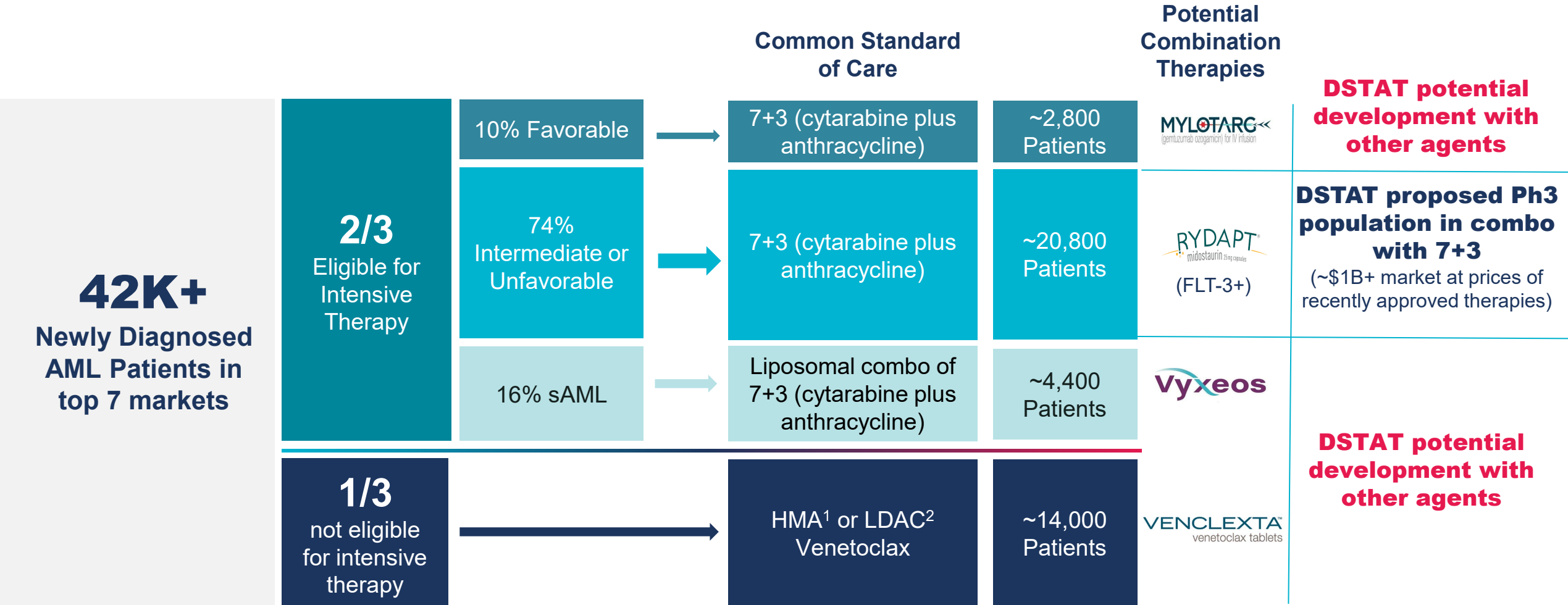


Overall Survival



Significant commercial opportunity and potential to expand

Phase 3 design may position DSTAT as standard of care for up to ~20,800 patients



Corporate Update



Financial summary

Dollars (millions)	Sept YTD 2021
R&D	\$ 39.5
G&A	13.4
Acquired in process R&D	82.9
Total operating expenses	135.8
Net income(loss)	(133.7)
Ending Cash balance	\$ 124.6*
Shares outstanding	86.8

- Several levers available for additional capital:
 - Expected significant non-dilutive proceeds from potential TEMBEXA[®] stockpiling
 - Global rights to most programs
 - Several catalysts provides additional optionality

*Amount is reported before \$20m milestone payment due to Oncoceutics shareholders for BICR readout of $\geq 20\%$



Major, near-term paths to value

- TEMBEXA® approved for the treatment of smallpox June 4, 2021
 - BARDA announced sole source contract of TEMBEXA for strategic national stockpile up to 1.7m courses of therapy
 - Potential \$80-\$100m annual cash flow next 5-12 years
- Synergistic acquisition of precision oncology platform
 - Positive data for ONC201, 20.0% ORR by blinded independent central review in recurrent H3 K27M mutant glioma
 - Opportunities for new indications and pipeline expansion with the imipridone program
- DSTAT development in front-line AML
 - Phase 3 DASH-AML, enrolling with an early assessment on the first 80 evaluable patients for MRD status



Chimerix Corporate Presentation

