Chimerix 1Q2022 Corporate Presentation

CHIMERIX

Forward-Looking Statements

These slides contain 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, results from the BICR of the 50- patient cohort of ONC201 for the treatment of recurrent H3 K27M-mutant glioma, the status of Chimerix's oncology programs, and the manufacturing, potential benefits and government procurement of TEMBEXA. 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 pre-clinical or clinical study data for ONC201 or CMX521 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 Chimerix will not obtain a procurement contract for TEMBEXA in smallpox in a timely manner or at all; Chimerix's current BCV manufacturing efforts may not satisfy the requirements of any procurement award; Chimerix's reliance on a sole source third-party manufacturer for drug supply; 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.

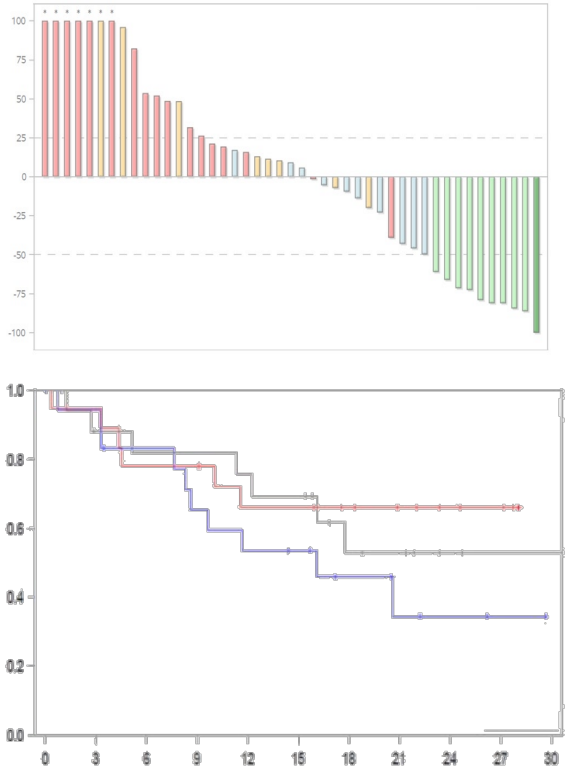
Potential TEMBEXA® stockpiling to fund oncology development

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



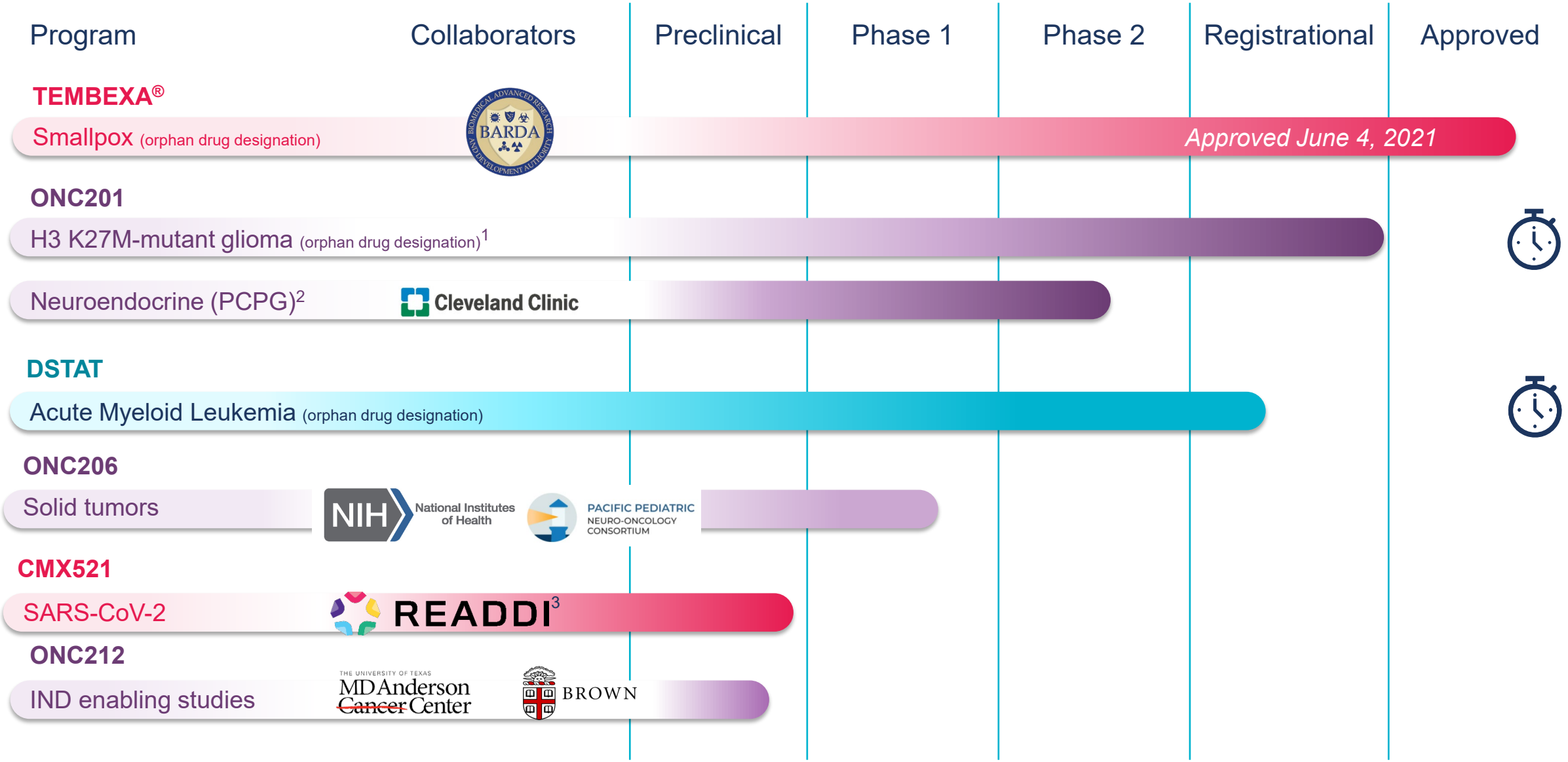
ONC201/ONC206/ONC212

- 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



1 Recurrent diffuse midline glioma H3 K27M mutant positive
2 Pheochromocytoma/paraganglioma
3 Rapidly Emerging Antiviral Drug Development Initiative

Denotes US FDA Fast Track Designation

TEMBEXA®
Approved for Treatment of Smallpox as a Medical Countermeasure

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The value of preparedness has never been more evident

- Highly infectious virus with ~30% mortality[1]
- Population is unvaccinated since early ‘70s
- Considered a Class A security threat by PHEMCE[2], 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


The Siberian Times

'Since 1902 there was a daily 'butter' train, leaving Novosibirsk to Riga, Latvia, with 25 carriages, each loaded with 7 000 kg of butter'

The chronicles of Novosibirsk

Home News Features Business City Focus Sport Culture Science Health & Lifestyle Ecology Weird & Wonderful

Case study Opinion Profile

Experts warn of threat of born-again smallpox from old Siberian graveyards

By The Siberian Times reporter

12 August 2016

This summer's melting of permafrost is more than THREE TIMES greater than usual, unlocking long-frozen deadly diseases.

Yamal and the anthrax outbreak now underway - the first for 75 years - should act as a warning. Picture: EMERCOM


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

CDC

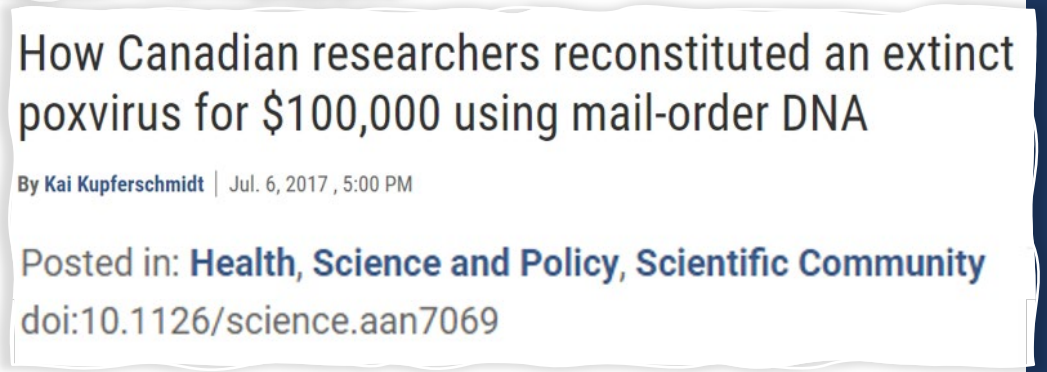
Vector


CNN Health » Diet + Fitness | Living Well | Parenting + Family Live TV U.S. Edition

CDC: Smallpox found in NIH storage room is alive

By Jen Christensen, CNN

Updated 3:07 PM ET, Fri July 11, 2014


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

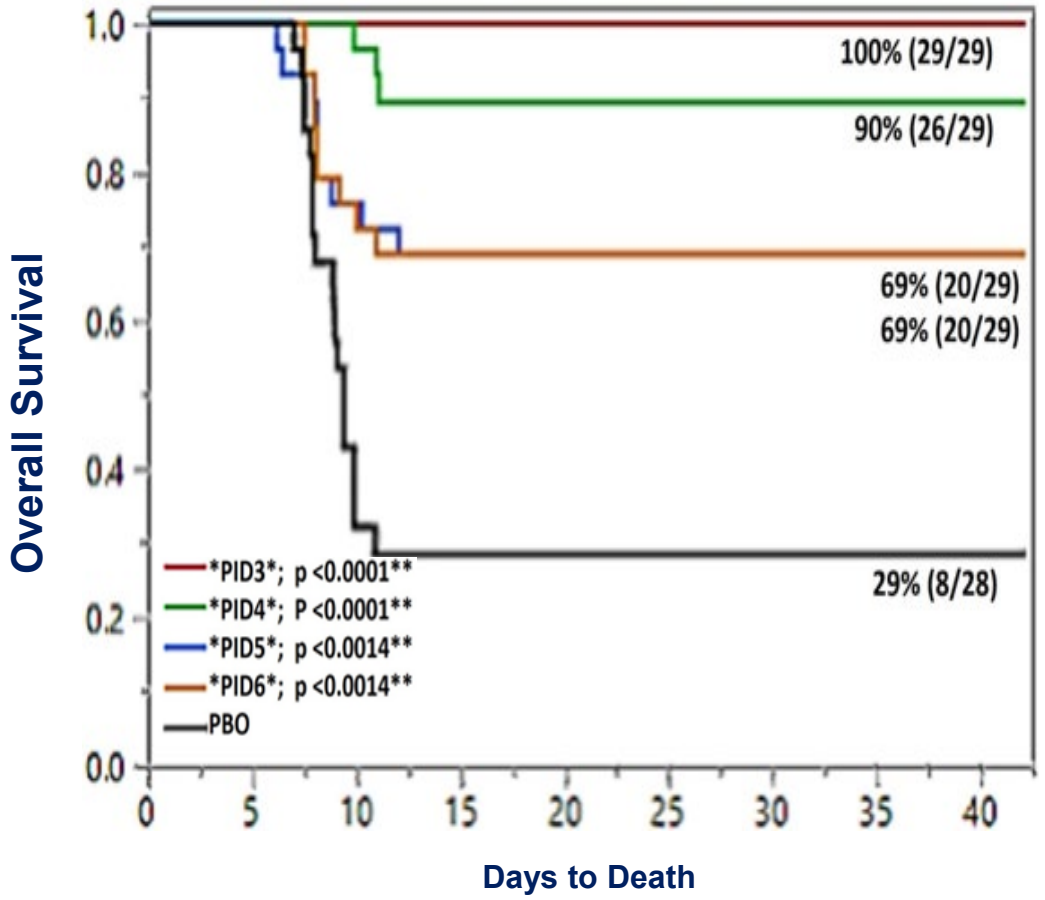
doi:10.1126/science.aan7069

1. World Health Organization, estimate for the more common variola major form of smallpox (vs variola minor of 1%), January 13, 2014
2. Public Health Emergency Medical Counter Measures Enterprise

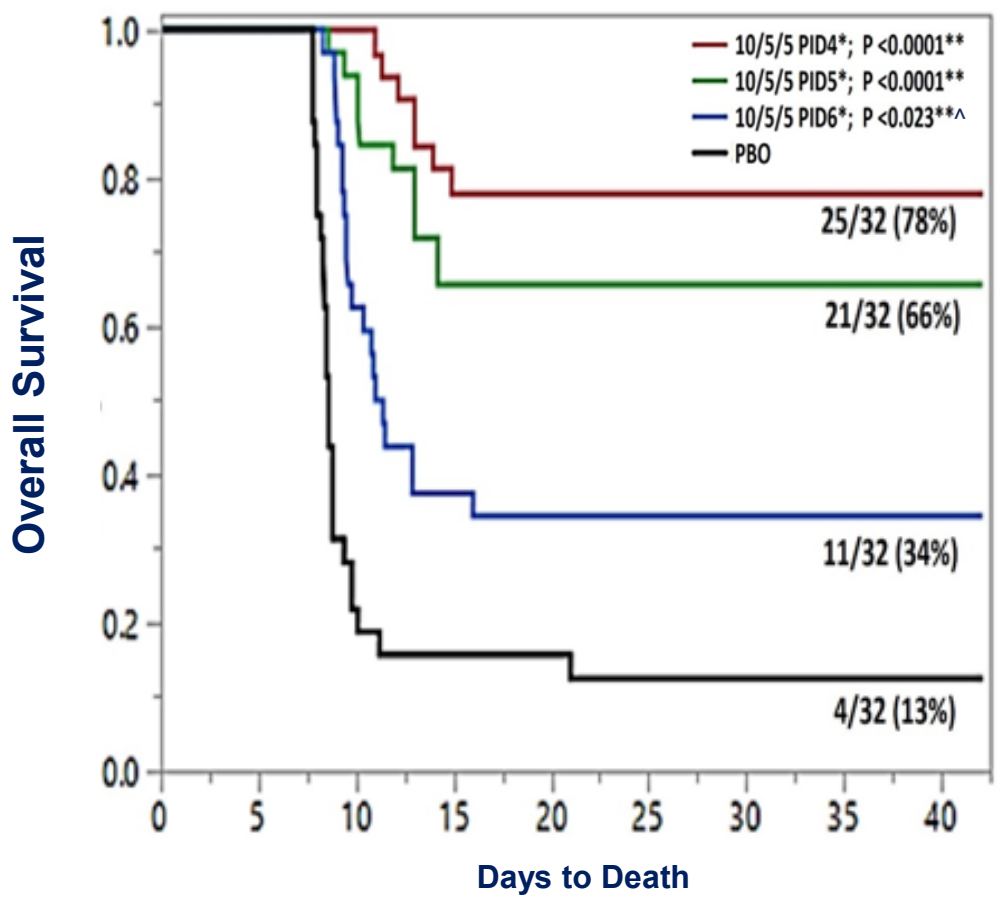
TEMBEXA® significantly reduced mortality in required models

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 attack[1]
- 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 TPOXX[1]
- TEMBEXA and TPOXX work well in combination in animal studies[1]
- Initial quantities available for delivery to the SNS once contract is finalized

TEMBEXA®

brincidofovir

10 mg/mL oral suspension | 100 mg tablets

1. Chan-Tack, et al. Antiviral Research 195 September 25, 2021

Imipridone Oncology Pipeline

Lead Candidate, ONC201 Positive Top-line Data

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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 ≥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 hist., leptomeningeal spread, CSF dissemination

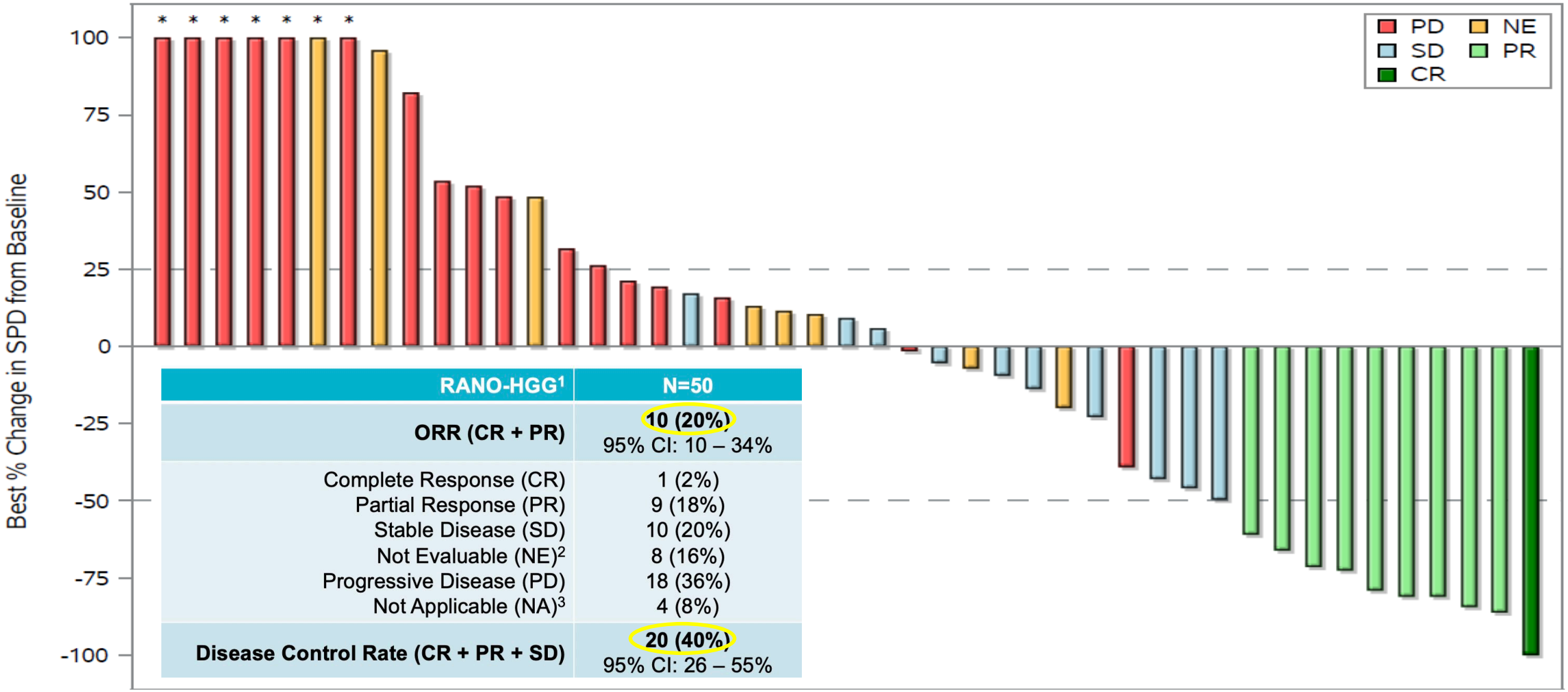
Patient demographics and disease characteristics

	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

Waterfall plot (RANO-HGG) – 20% response



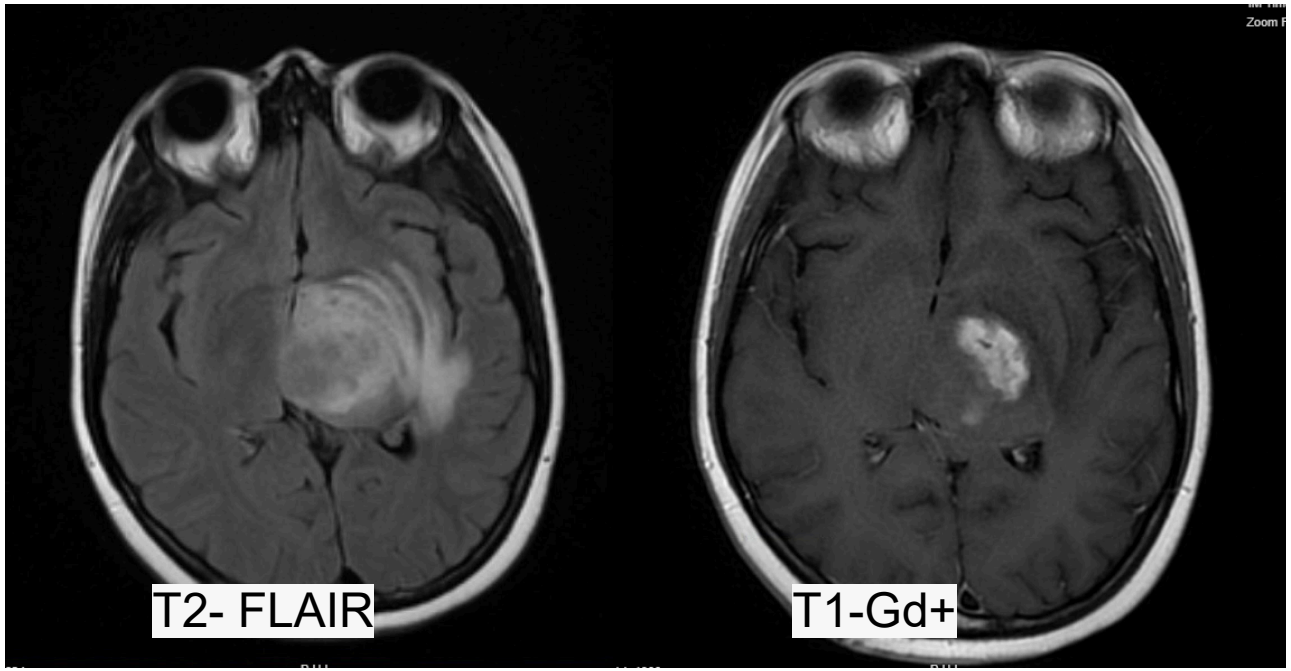
RANO-HGG[1]	N=50
ORR (CR + PR)	**10 (20%)** 95% CI: 10 – 34%
Complete Response (CR)	1 (2%)
Partial Response (PR)	9 (18%)
Stable Disease (SD)	10 (20%)
Not Evaluable (NE)[2]	8 (16%)
Progressive Disease (PD)	18 (36%)
Not Applicable (NA)[3]	4 (8%)
Disease Control Rate (CR + PR + SD)	**20 (40%)** 95% CI: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

* 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.

[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

Response assessment criteria for glioma

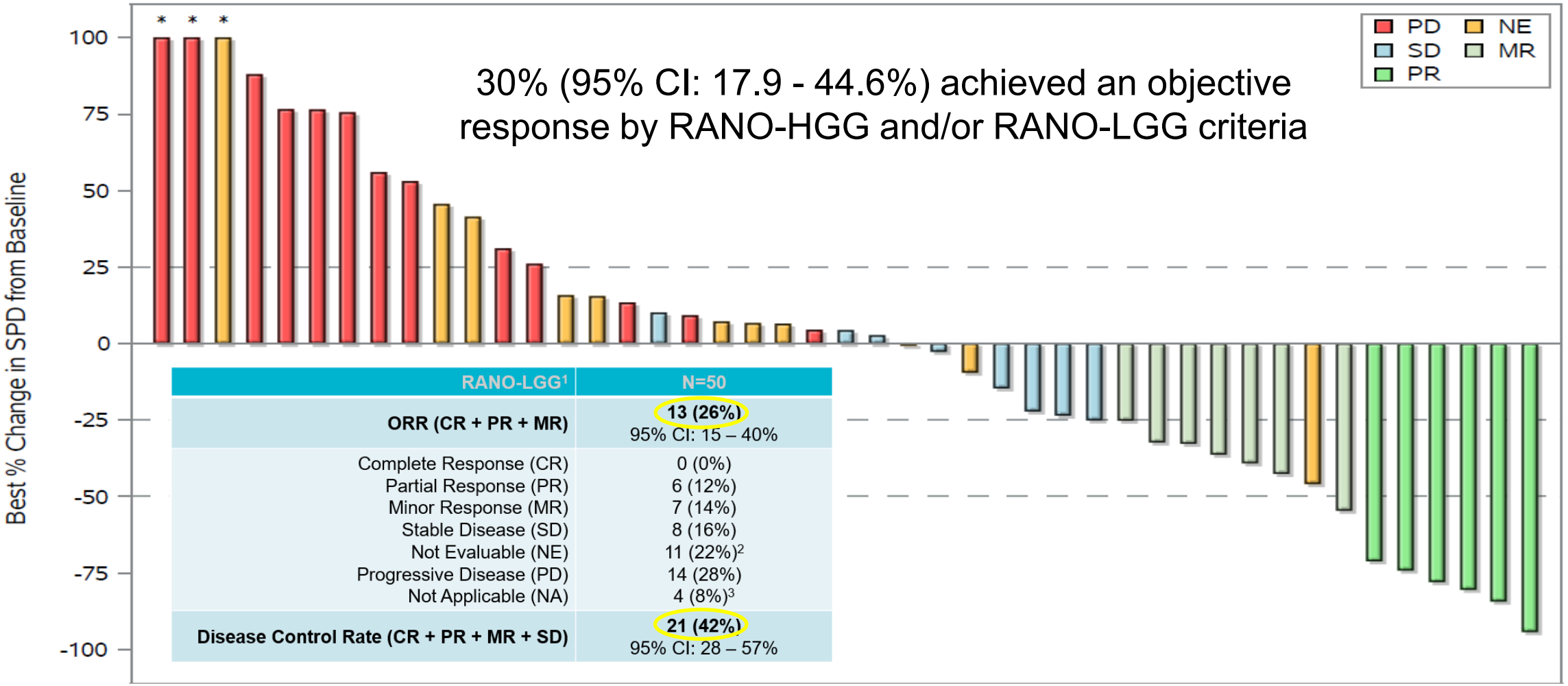
- DMG with H3K27M typically have *both* enhancing and non-enhancing disease components
- RANO-HGG responses defined by decrease in enhancing disease
- RANO LGG response defined by decrease in T2 FLAIR



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‡

Waterfall plot (RANO-LGG) – 26% response



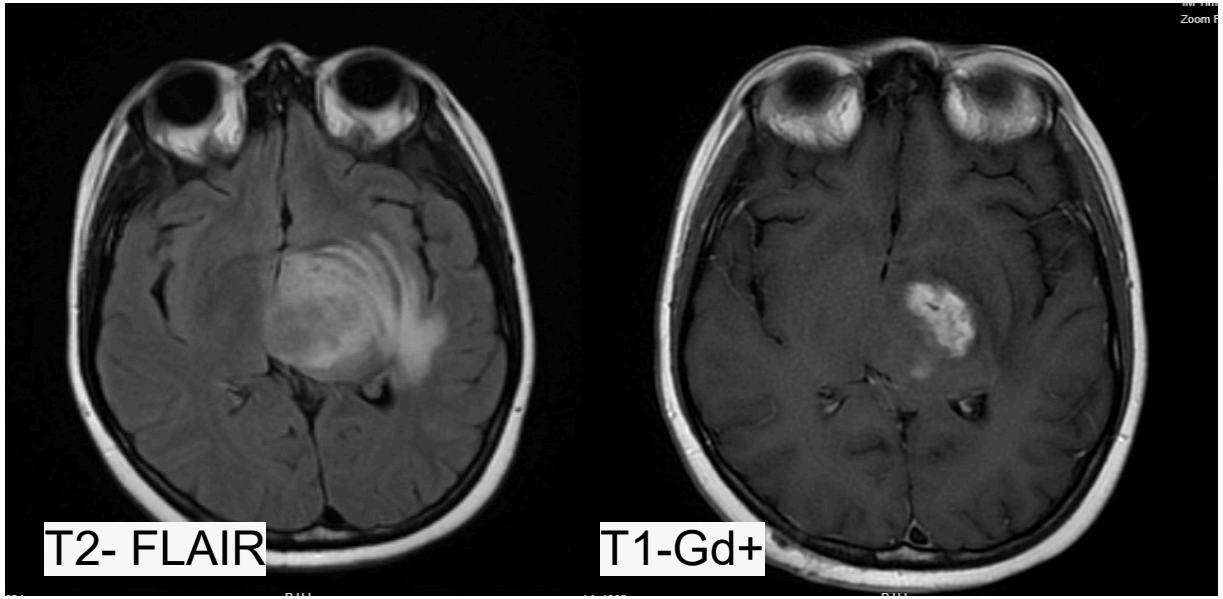
RANO-LGG[1]	N=50
ORR (CR + PR + MR)	**13 (26%)** 95% CI: 15 – 40%
Complete Response (CR)	0 (0%)
Partial Response (PR)	6 (12%)
Minor Response (MR)	7 (14%)
Stable Disease (SD)	8 (16%)
Not Evaluable (NE)	11 (22%)[2]
Progressive Disease (PD)	14 (28%)
Not Applicable (NA)	4 (8%)[3]
Disease Control Rate (CR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

*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.

[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

Response assessment criteria for glioma

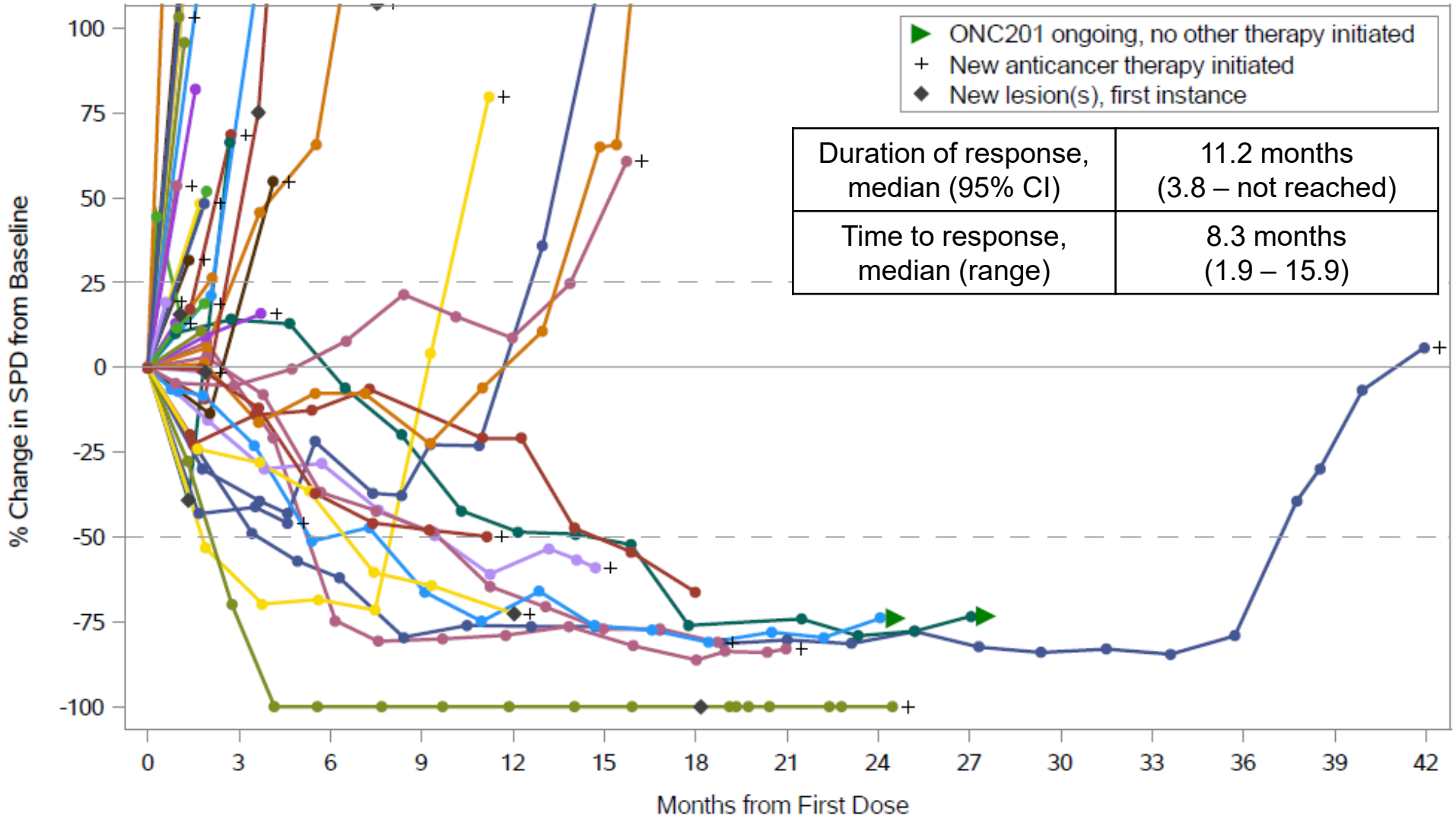
- RANO LGG response defined by decrease in T2 FLAIR



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[‡]

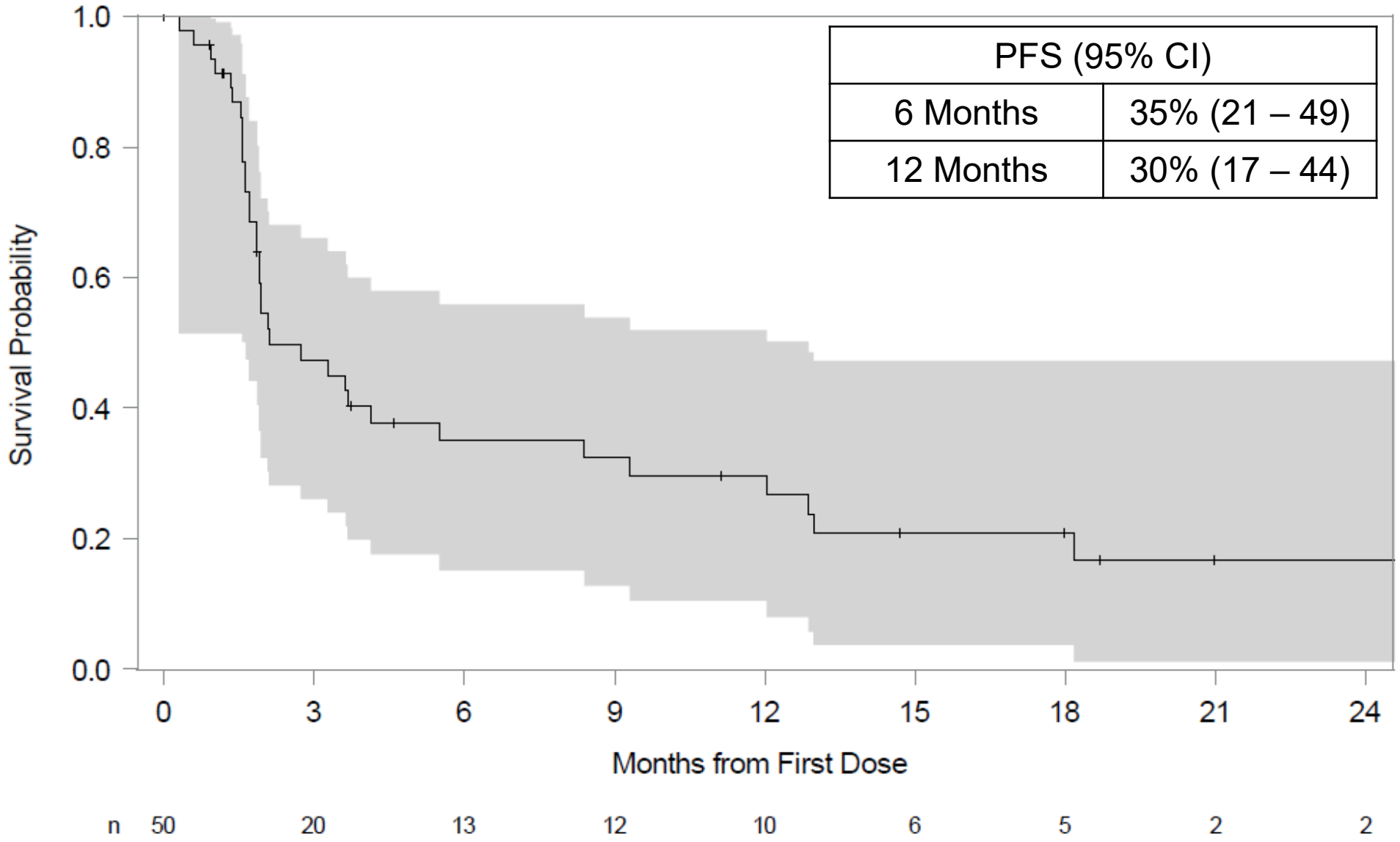
Spider plot (RANO-HGG)



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)

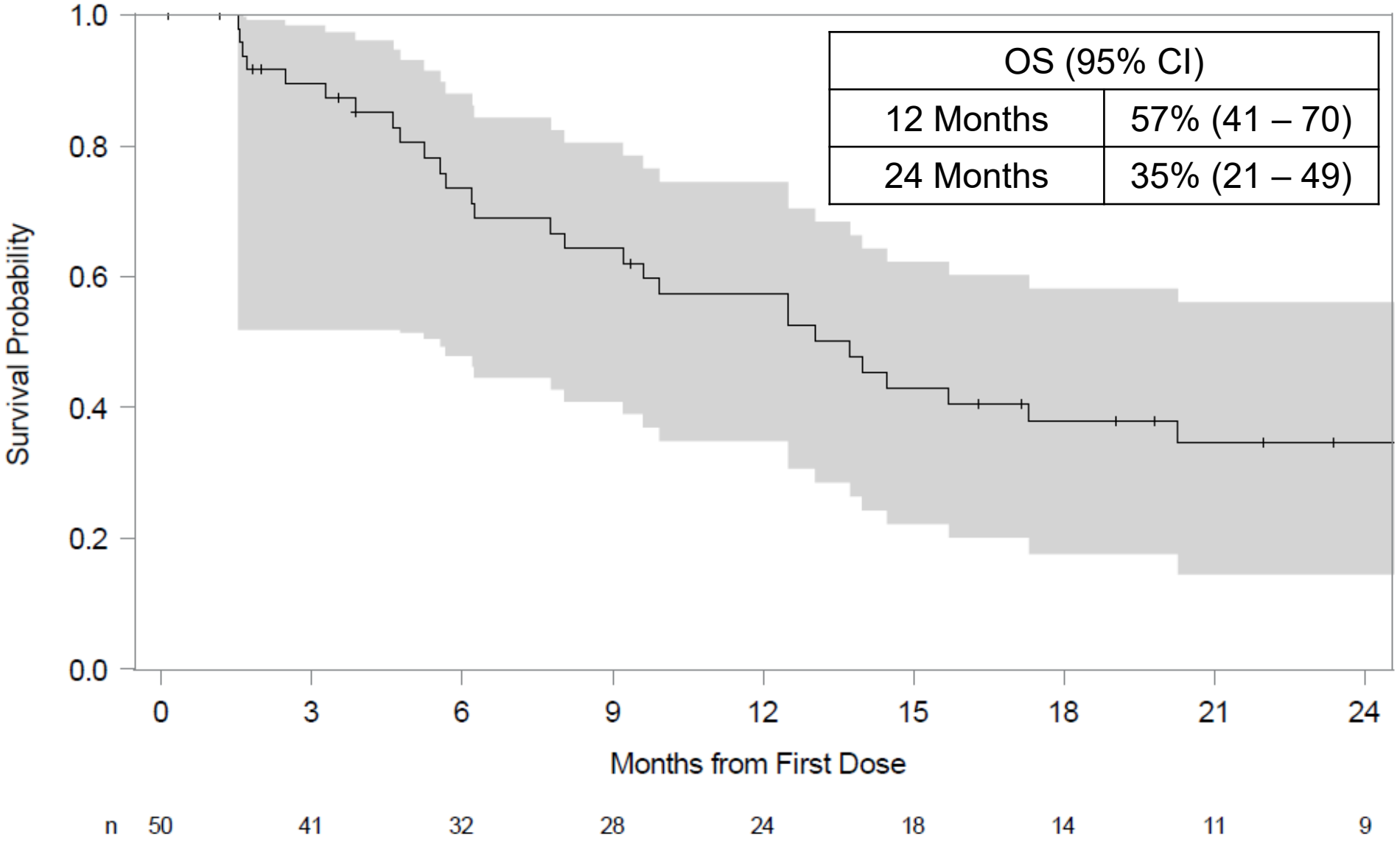
SPD=sum of products of perpendicular diameters (target enhancing lesions per BICR)
Only patients with measurable target enhancing lesions by BICR at baseline and with post-baseline evaluations are included.
Three patients did not have on-treatment monotherapy MRIs available for BICR; one patient censored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

Progression-free survival



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

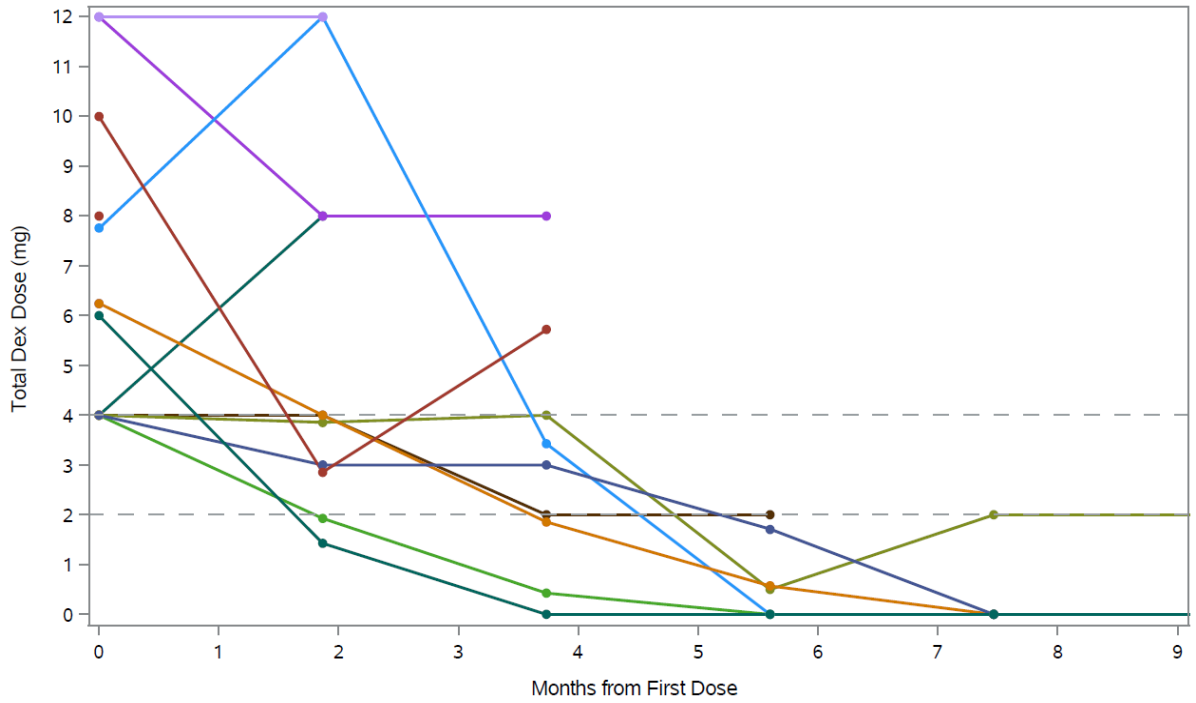
Overall survival



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)

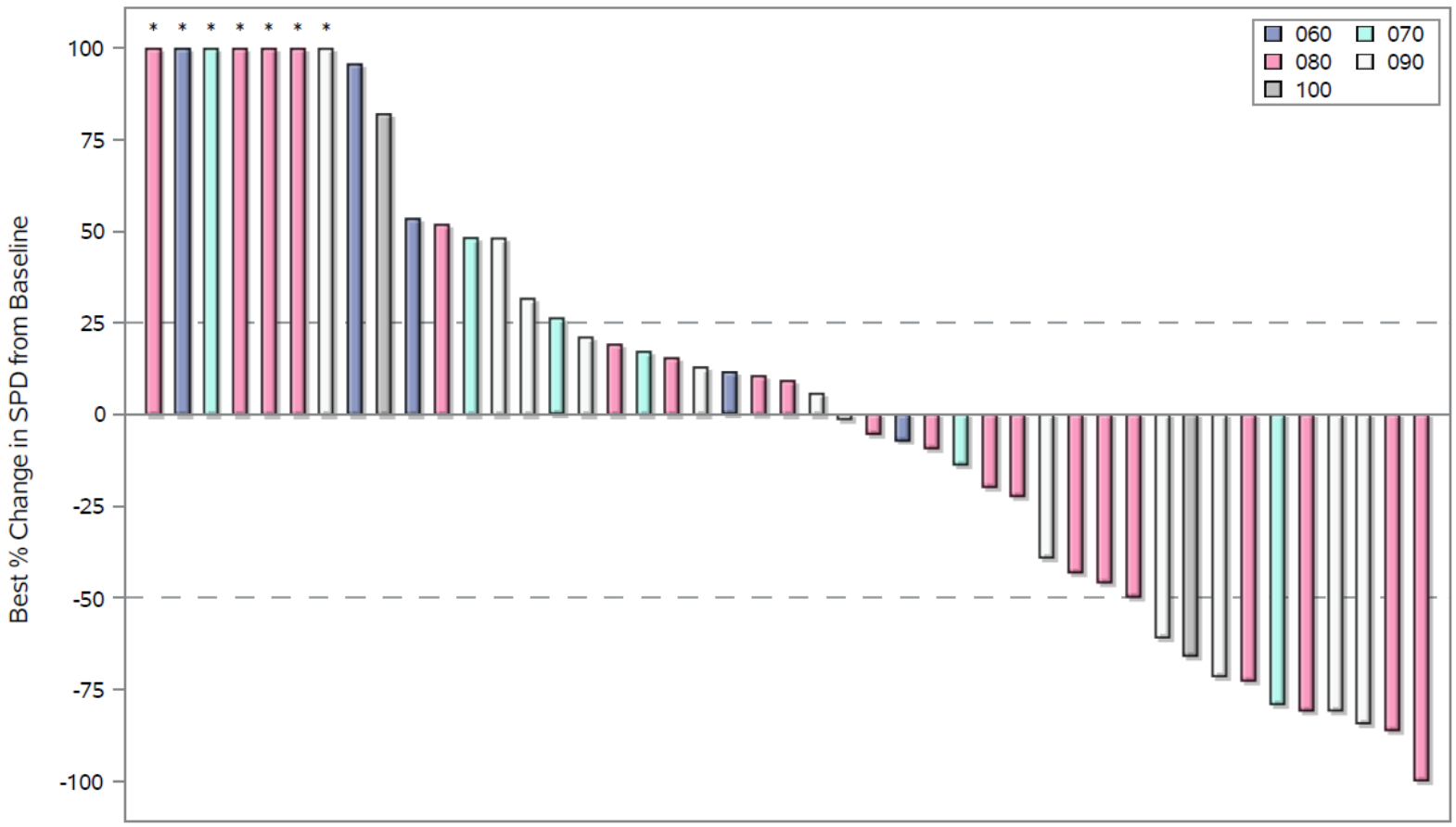
Serious adverse events

	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

Waterfall plot (RANO-HGG) stratified by performance status

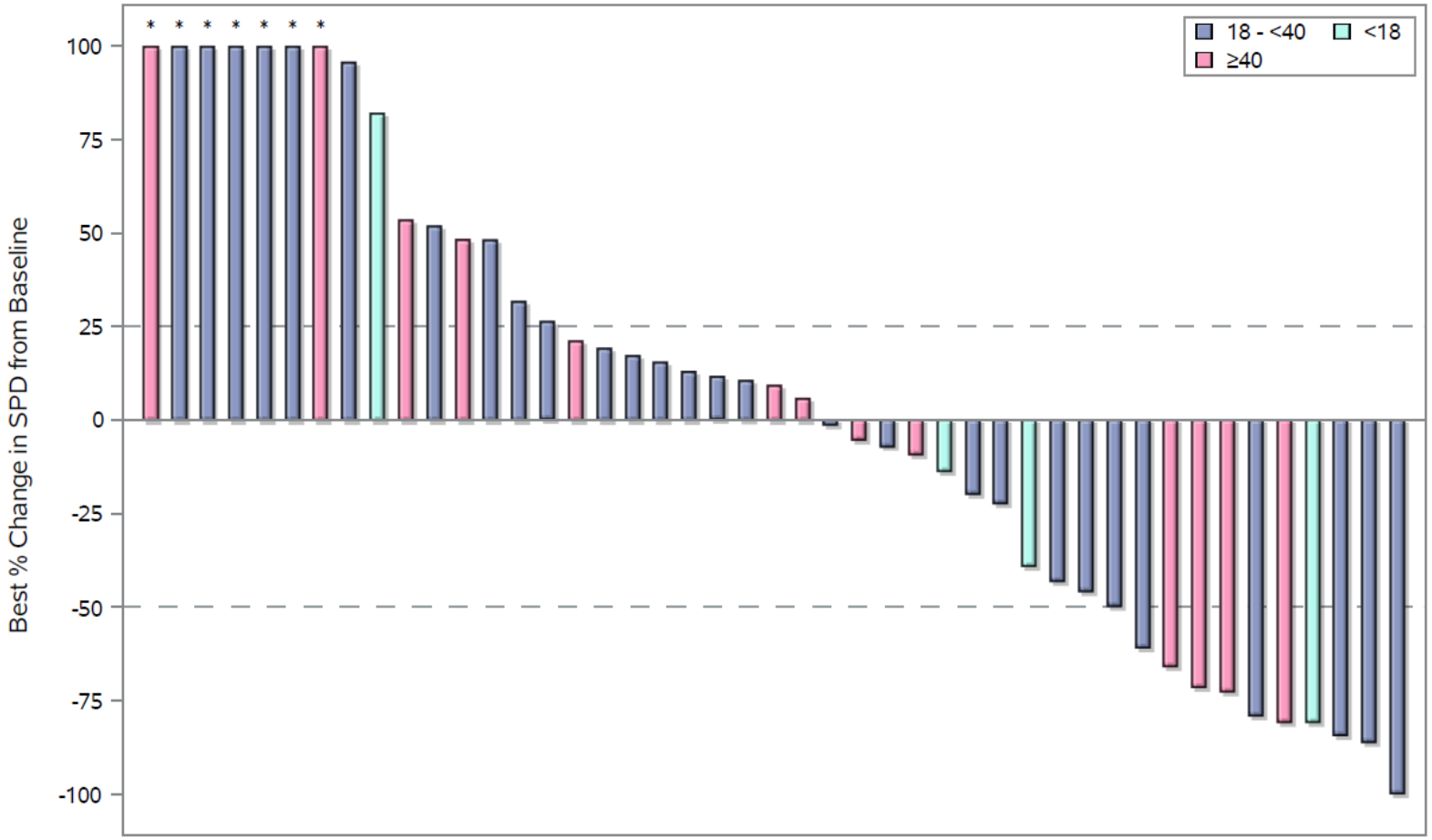
- Expectedly, patients with higher PS were more likely to respond to treatment
  - 100: 1/2 (50%)
  - 90: 4/14 (29%)
  - 80: 4/20 (20%)
  - 70: 1/7 (14%)
  - 60: 0/7 (0%)
- Consistent with hypothesis that treating earlier in disease course may enhance efficacy



* 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

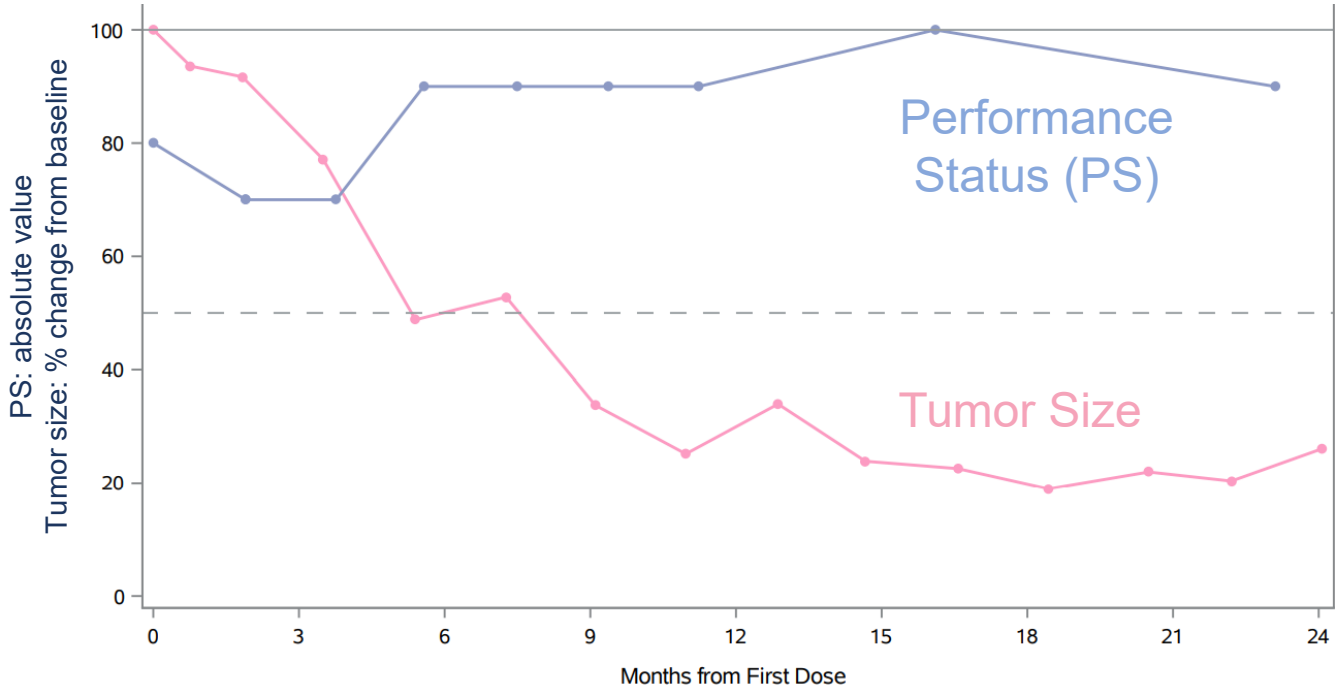
- Responses observed across age groups:
  - <18 years: 1/4 (25%)
  - 18-40 years: 5/32 (16%)
  - ≥40 years: 4/14 (29%)
- RANO-HGG response of 8-year-old subject confirms activity in this population

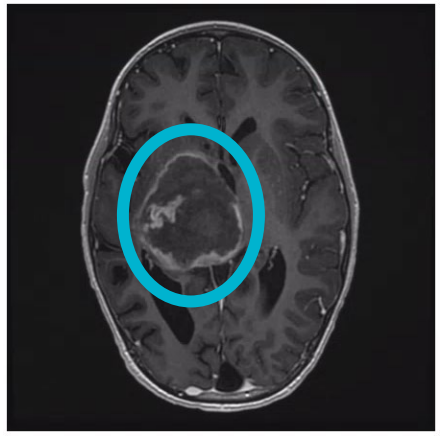


* Change > 100%, SPD=sum of products of perpendicular diameters (target enhancing lesions per BICR)
Only patients with measurable target enhancing lesions at both baseline and post-baseline are included.

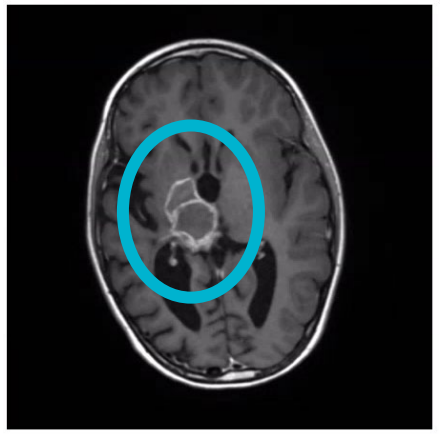
Pediatric case study

- 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

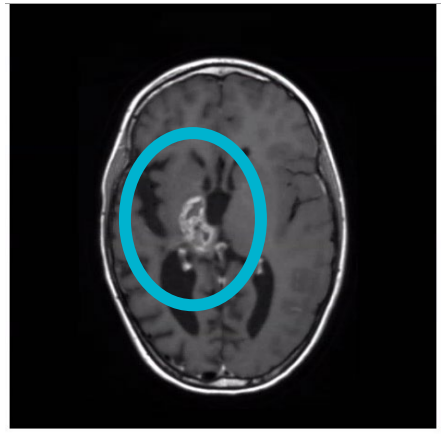




Pre-ONC201 baseline



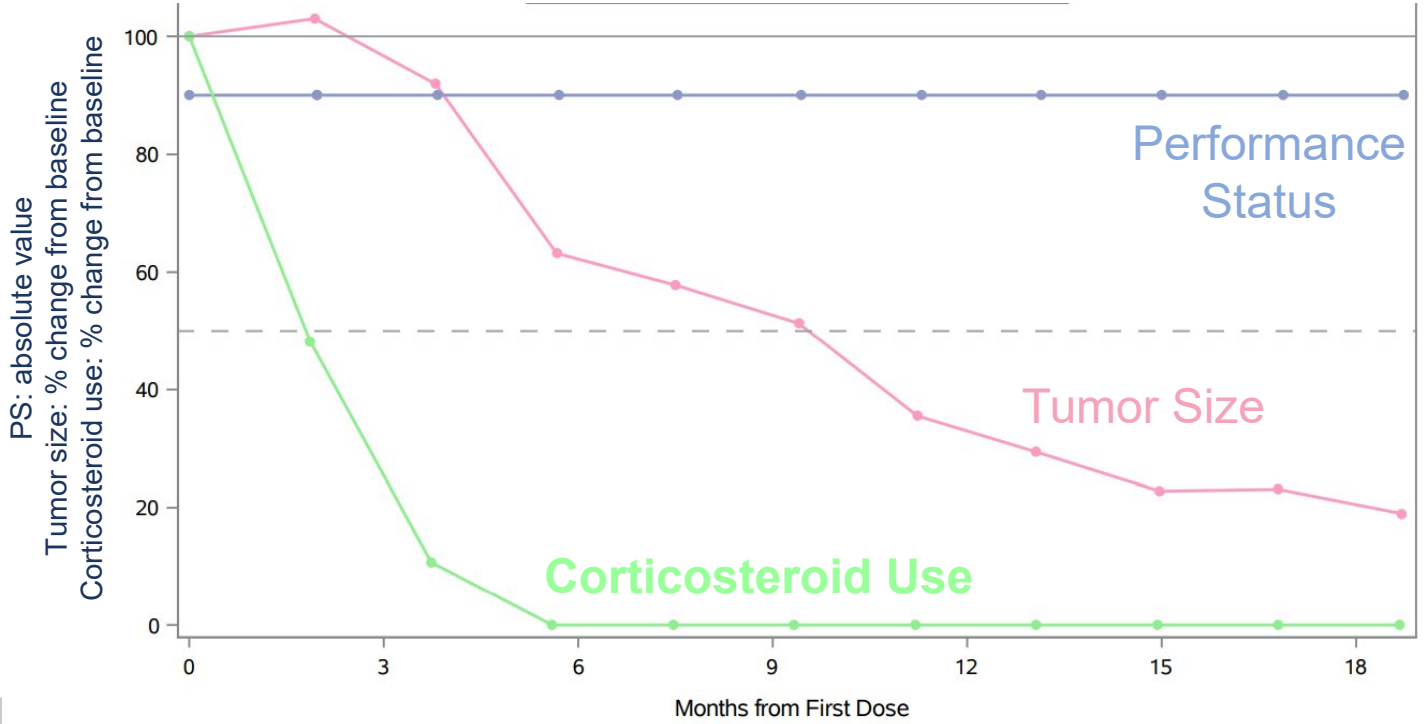
9 months on ONC201

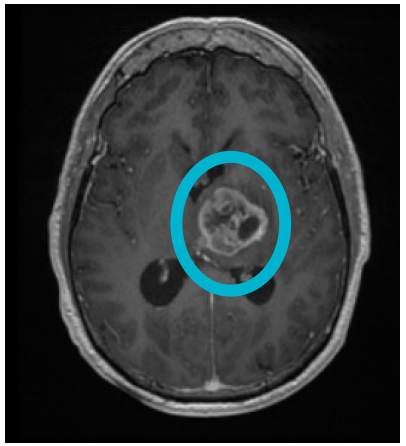


18 months on ONC201

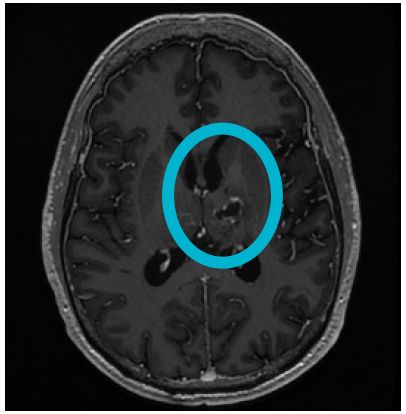
Adult case study

- 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

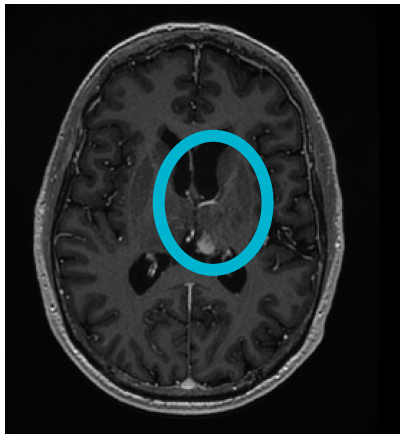




Pre-ONC201 baseline



12.9 months on ONC201



18.5 months on ONC201

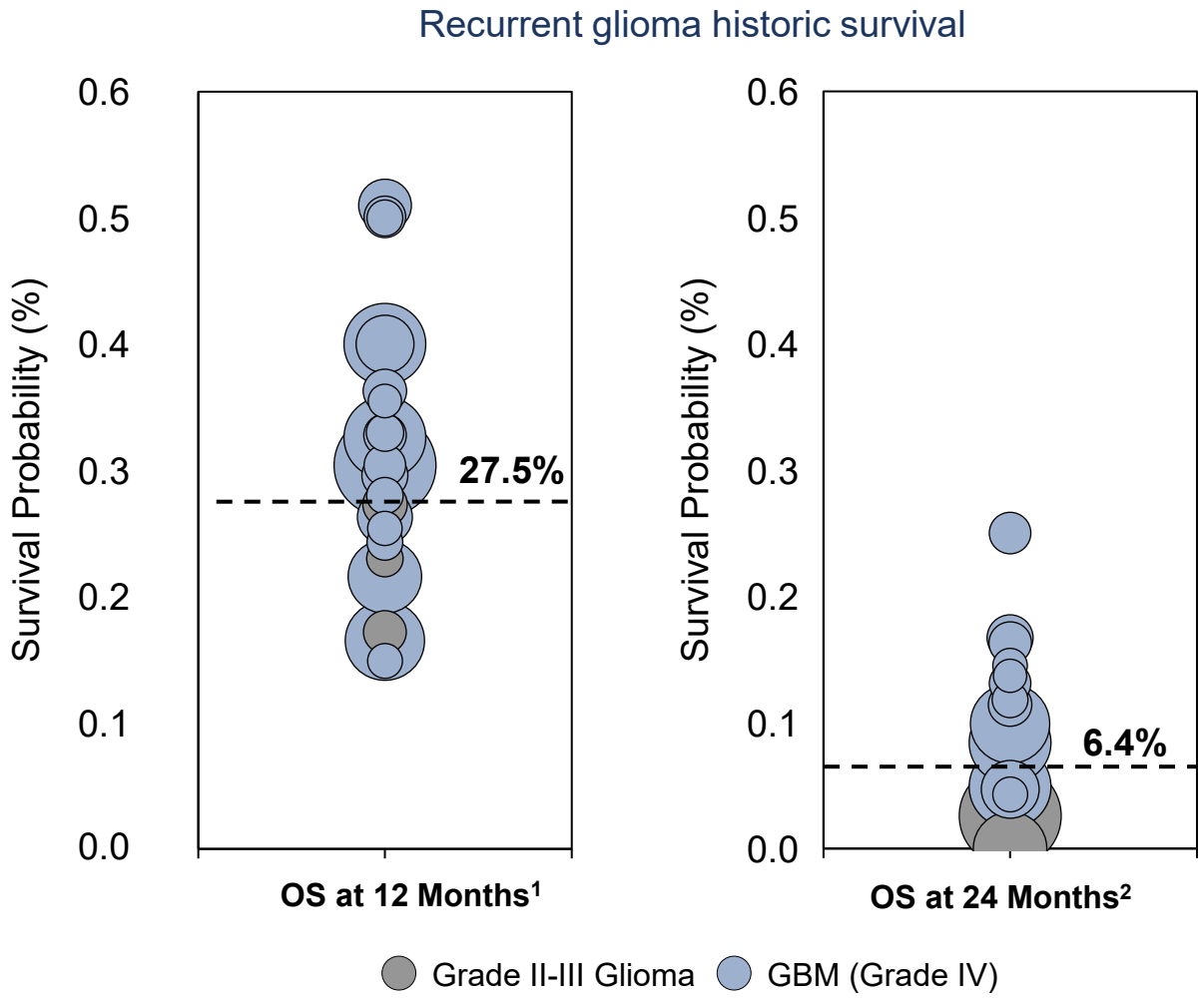
RANO responses correspond with survival & clinical benefit

	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 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



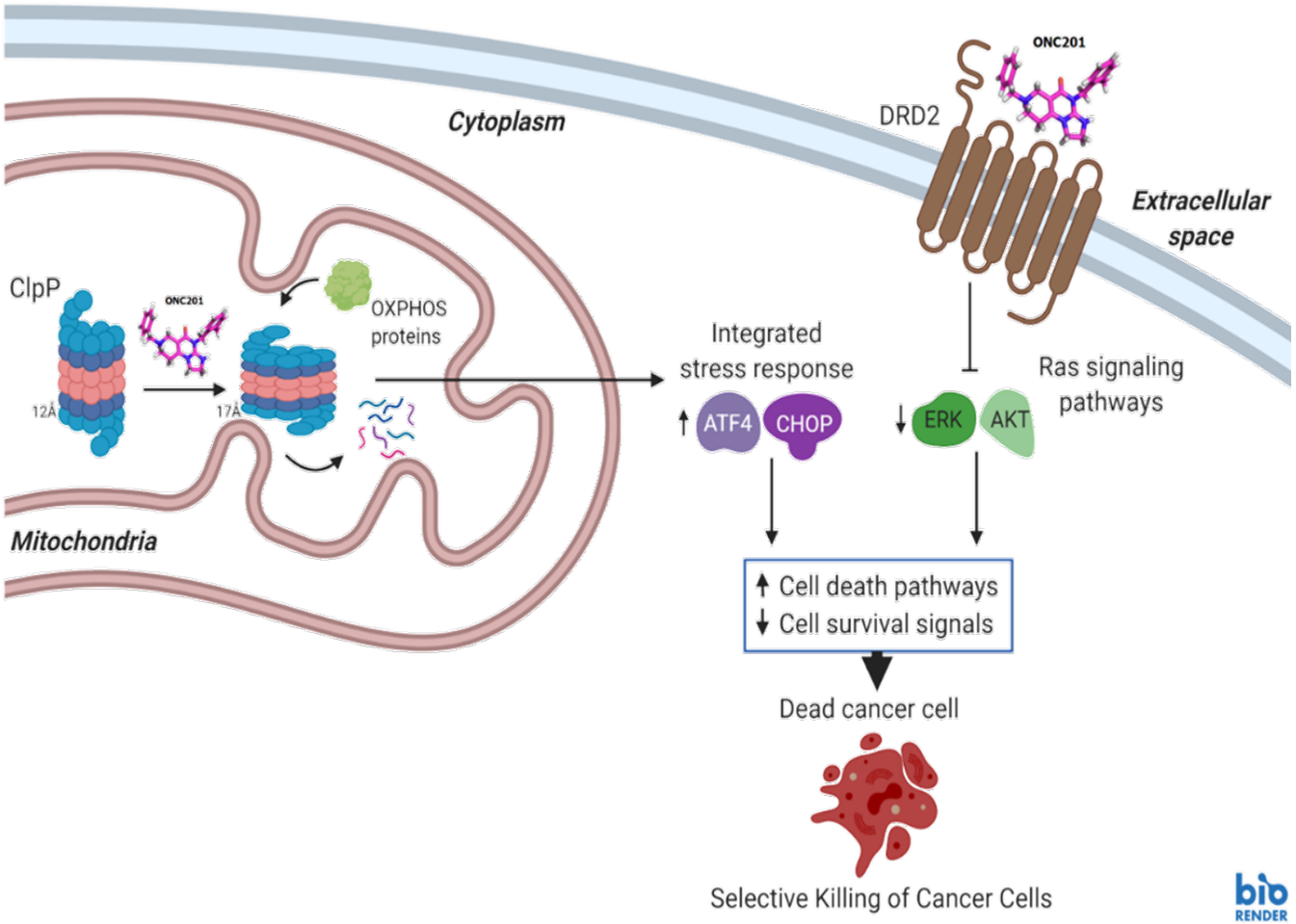
1. Data collected from 15 literature sources since 2010 with trial arms size >30 pts each reporting data on 1816 pts with recurrent, unstratified disease.
2. 10 literature sources that describes OS with 1279 patients
3. Koschmann et al, 2020; DOI:10.21203/rs.3.rs-69706/v1

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

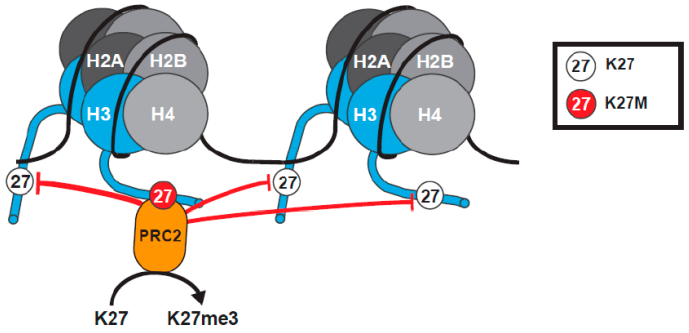


- ONC201 can selectively induce apoptosis in cancer cells by altering activity of two proteins
- DRD2 antagonism
  - DRD2 is a G protein-coupled neuroreceptor that regulates Ras signaling
  - ONC201 antagonizes DRD2, inhibiting Ras signaling pathways
- ClpP agonism
  - ClpP normally degrades misfolded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

ClpP=caseinolytic protease P; DRD2=Dopamine receptor D2; ATF4=activating transcription factor 4; CHOP=C/EBP-homologous protein; ERK=extracellular-regulated kinase; AKT=protein kinase B

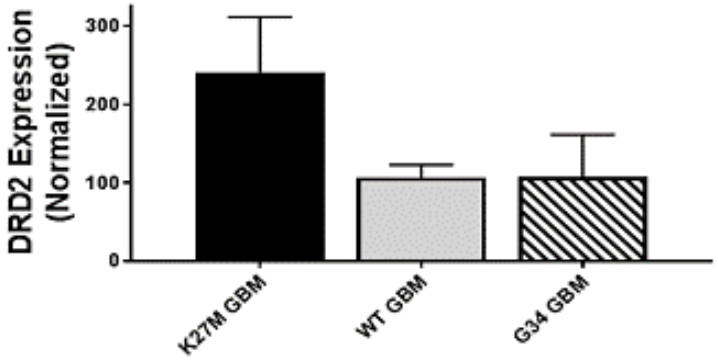
H3 K27M-mutant gliomas exhibit enhanced sensitivity to ONC201

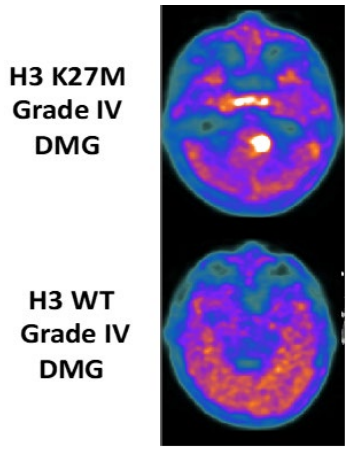
Lysine to methionine ("K-to-M") histone H3 mutation reduces H3 K27 methylation



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

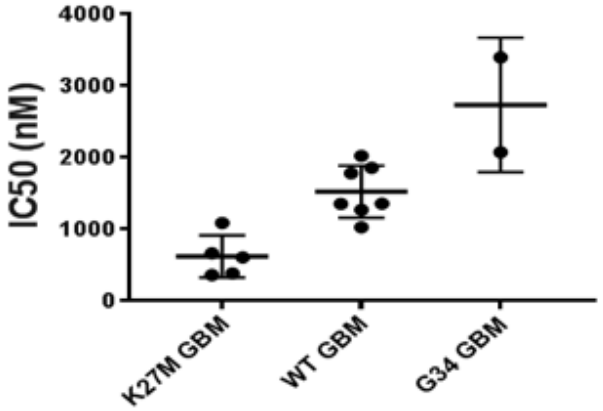




18F-DOPA PET

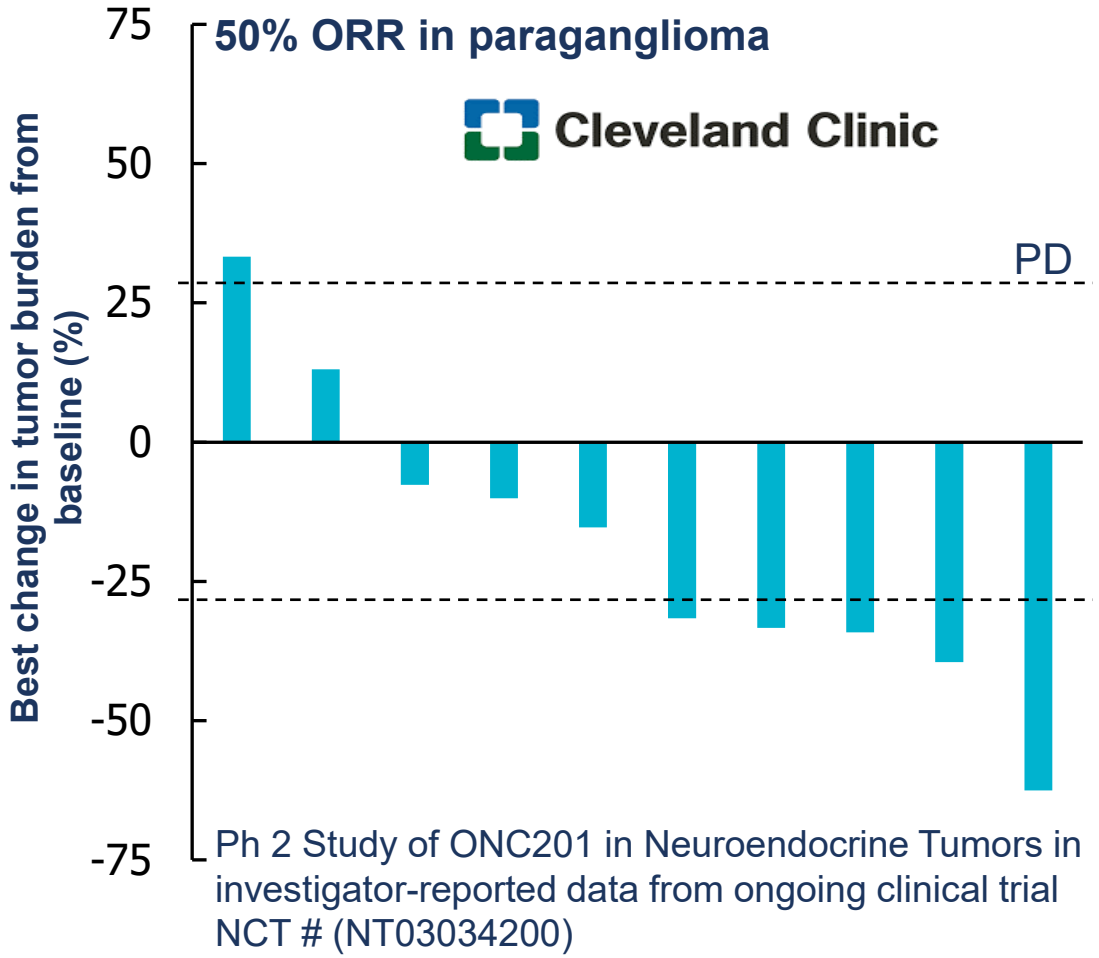
Midline tumors occur in dopamine-rich regions of the brain

High sensitivity to ONC201



Lowe et al., Cancers, 2019; Chi et al., Society of Neuro-Oncology, 2017; Kawakibi et al, Society of Neuro-Oncology, 2019; Koschmann et al., Pediatric Society of Neuro-Oncology 2019; Prabhu et al, Clinical Cancer Research, 2018; Ishizawa et al, Cancer Cell, 2019; Prabhu et al., Society of Neuro-Oncology, 2019, Piccardo et al., Eur J. Nucl Med Mol Imaging, 2019

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

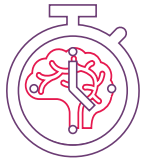


- Single agent responses in Ph 2 neuroendocrine trial of ONC201 observed in subset (paraganglioma)
- Paraganglioma are adrenal-related tumors with elevated DRD2 expression
- Five patients have been treated > 1 year
- Less short-term and potential long-term toxicities than other paraganglioma therapies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

1. ASCO oral presentation June 2021

ONC201 FDA designations

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



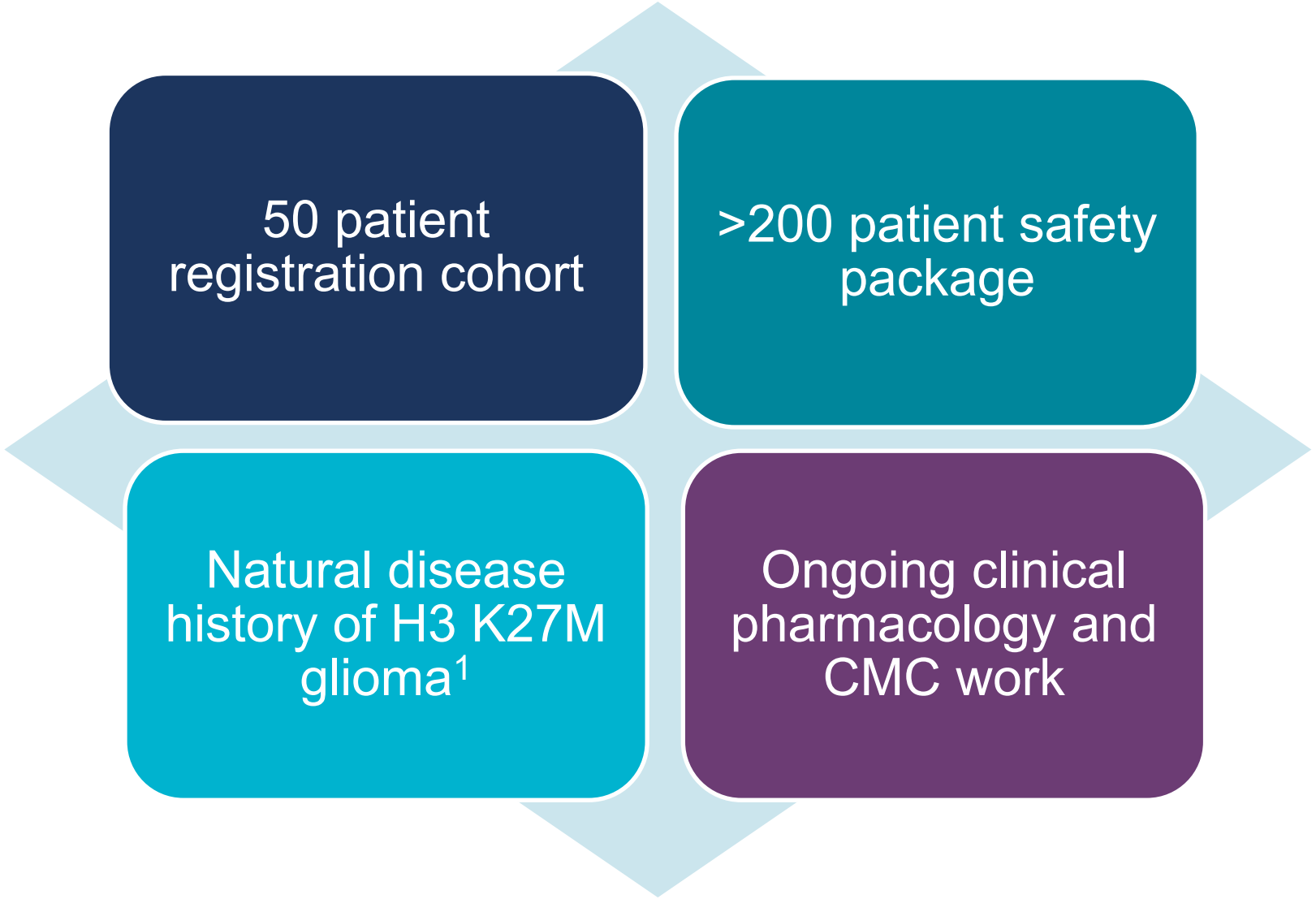
Fast Track Designation (FTD) for adult recurrent H3 K27M-mutant high-grade glioma

Rare Pediatric Disease Designation for treatment of H3 K27M mutant glioma

- Potential to receive rare pediatric voucher[1]

1. Subject to continuation of Rare Pediatric Disease Voucher Program and proceeds from voucher will be split 50/50 with legacy Oncoceutics shareholders

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

CHIMERIX

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 out of 10

  - 5-year survival for older patients

1 out of 10

  - Relapse can occur if not all AML blasts and stem cells are eradicated
- AML is heterogenous and has multiple mechanisms of resistance to treatment

Walter RB, Othus M, Burnett AK, et al. Resistance prediction in AML: analysis of 4601 patients from MRC/NCRI, HOVON/SAKK, SWOG and MD Anderson Cancer Center. Leukemia. 2015;29(2):312-320. doi: 10.1038/leu.2014.242

Compelling pilot study results in treatment-naïve AML patients

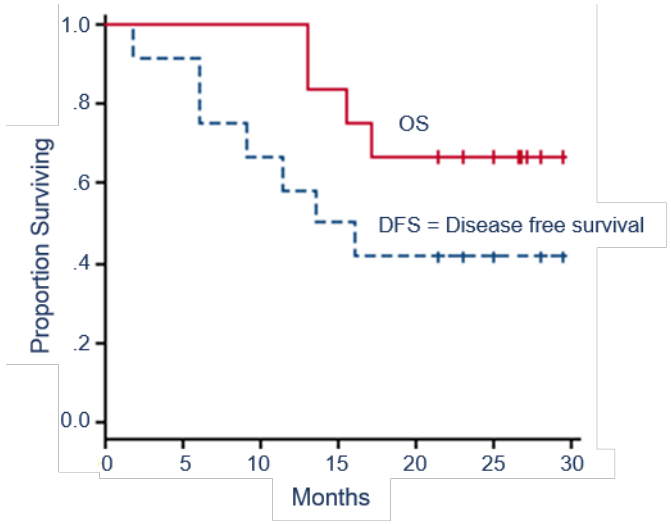
Strong Complete Response, Overall Survival and improved hematologic recovery

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



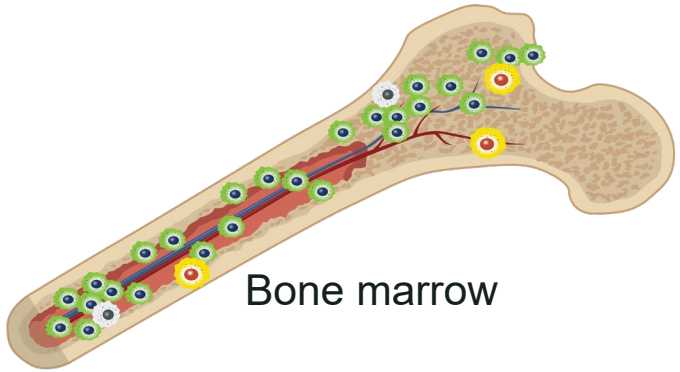
Count Recovery

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

Tibor J. Kovacsovics, Alice Mims, Mohamed E. Salama, et al. Combination of the low anticoagulant heparin CX-01 with chemotherapy for the treatment of acute myeloid leukemia. Blood Advances. 16 October 2017; accepted 21 January 2018. DOI 10.1182

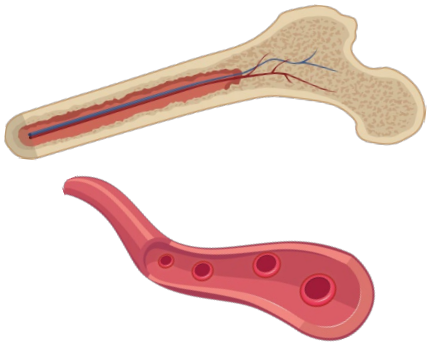
DSTAT may improve duration of response & overall survival

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



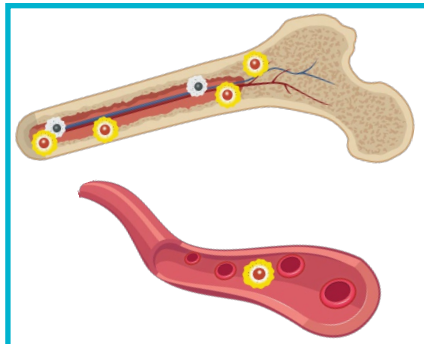
- AML blast sensitive to 7+3
- AML blast resistant to 7+3
- Leukemic stem cell (LSC) resistant to 7+3
- Red blood cells

'7+3' Chemotherapy + DSTAT



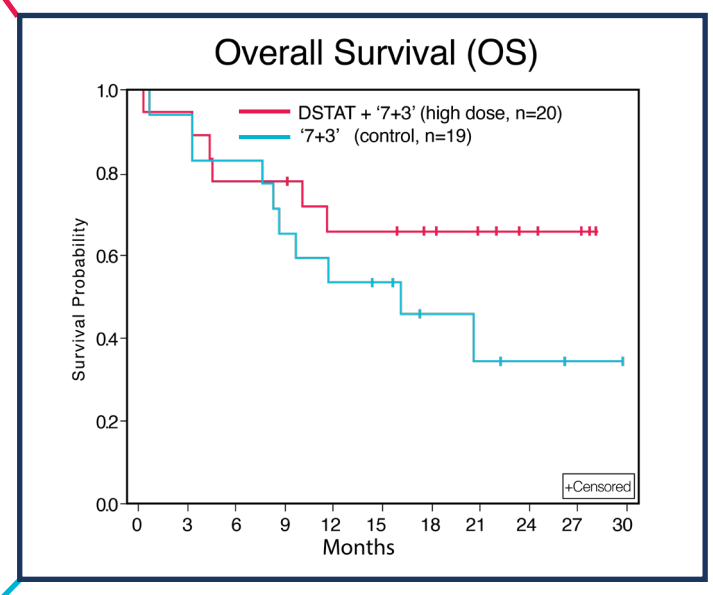
1) Inhibit AML survival and chemoresistance pathways
2) Reverse quiescence of AML blasts and LSCs

'7+3' Chemotherapy



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

DSTAT appears to reduce AML relapse



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

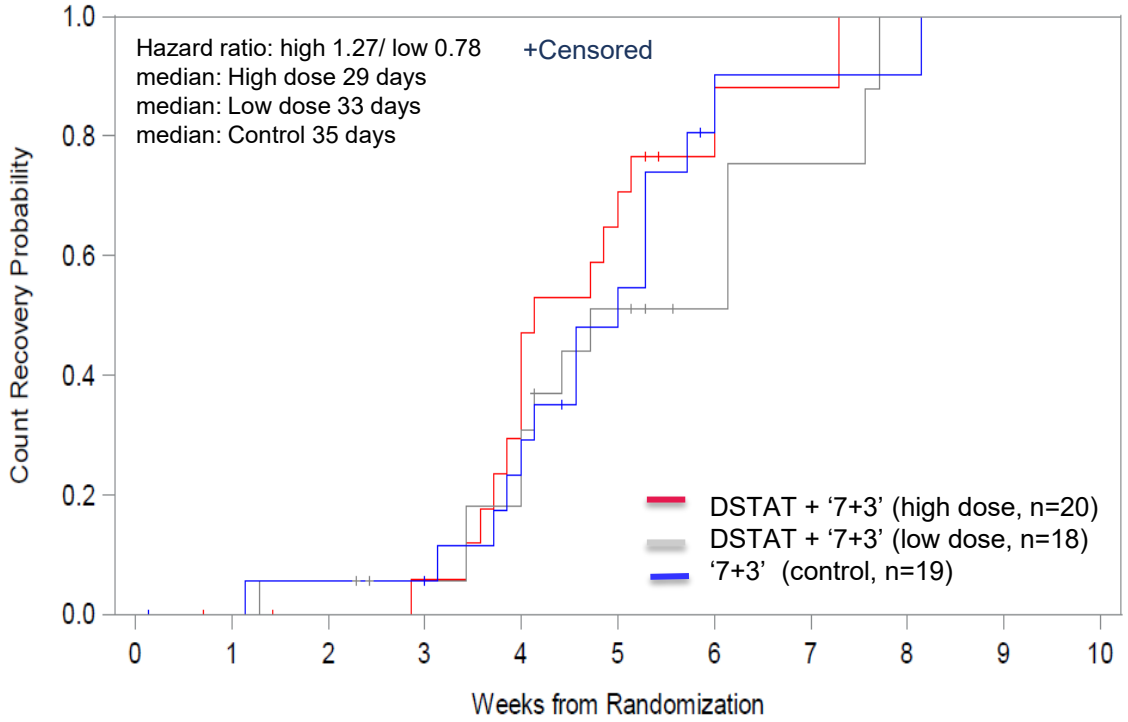
Generally well tolerated in newly diagnosed AML patients

- 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

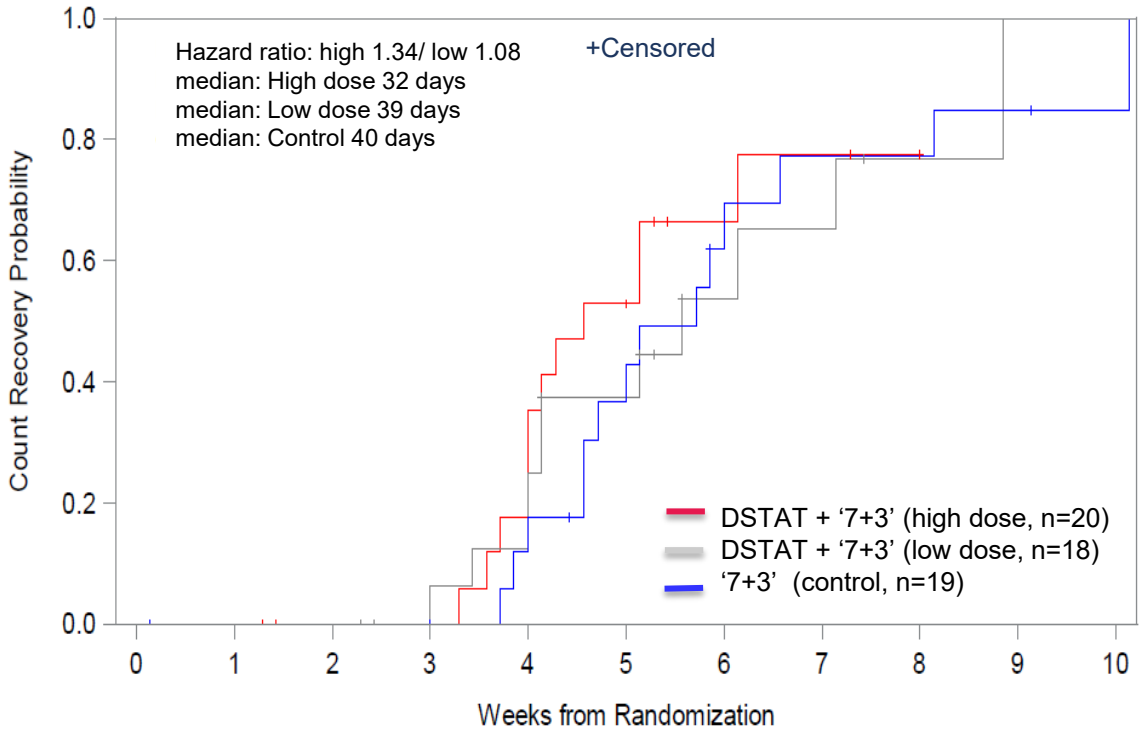
Median days to neutrophil and platelet recovery reduced by 17% and 20%, respectively on high dose

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	1

Median Time to Recovery
Kaplan-Meier curves do not include sub therapeutic low dose arm

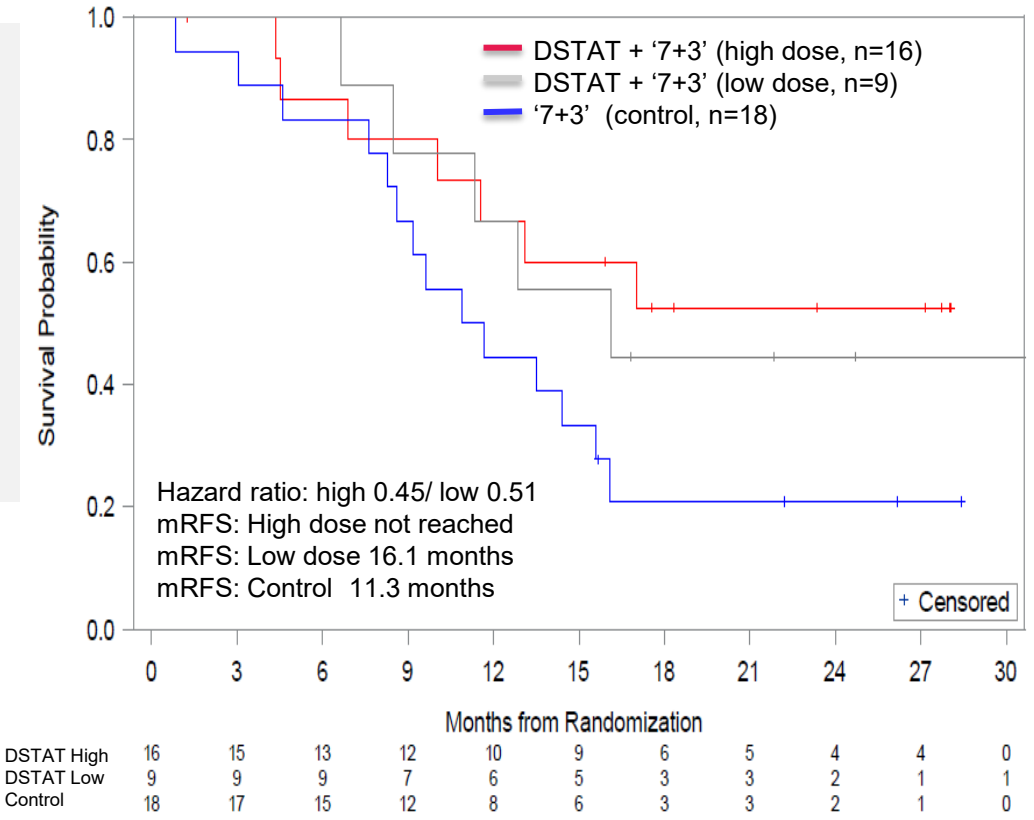
Full ITT population outperforms standard 7+3 chemo

RFS and OS benefit in full ITT Ph 2 population

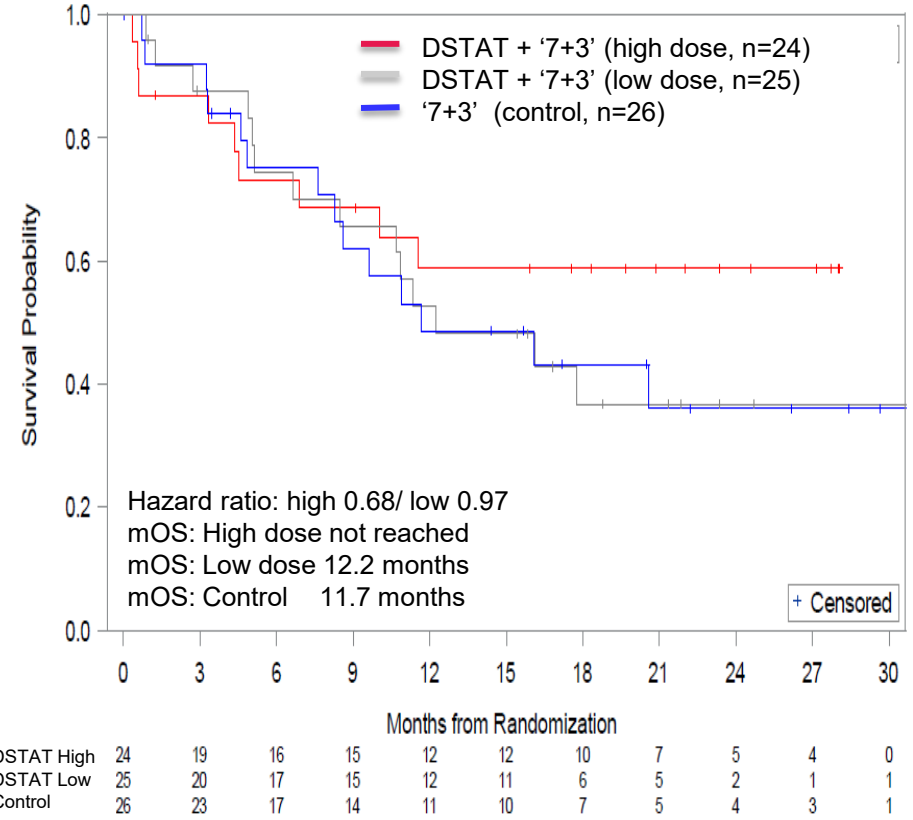
Response Summary

	% 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 Survival[3]



Overall Survival

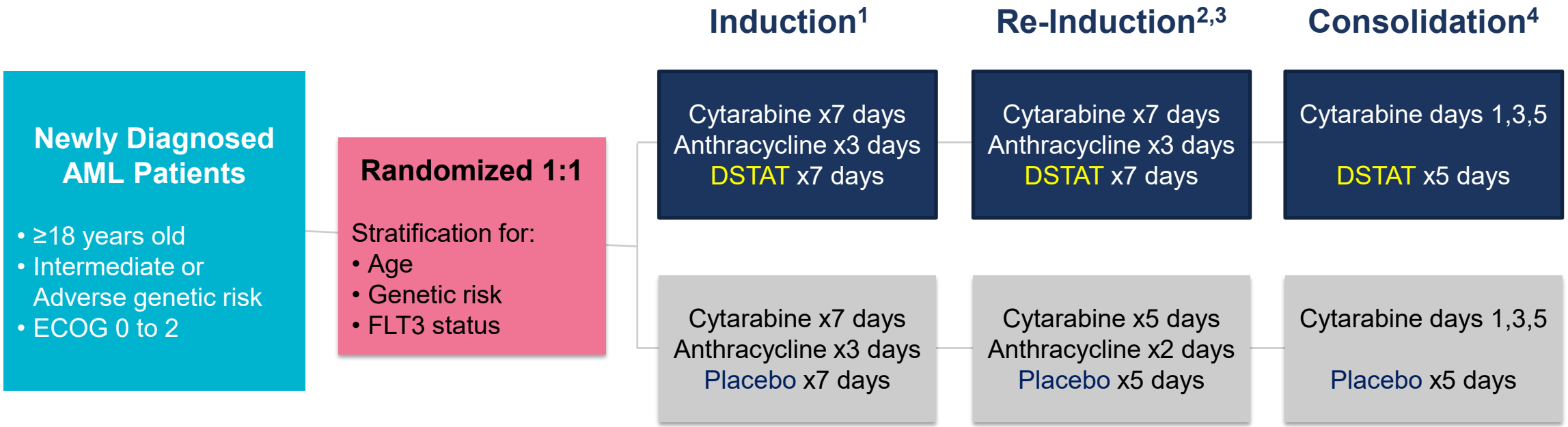


1. Complete Response (CR) or Complete Response without complete hematologic recovery (CRi)
2. Confirmed with post day 14 (D14) bone marrow (BM) biopsy and less than 5% blasts. If no post D14 was performed, the D14 BM biopsy was used to determine response.
3. Relapse-Free Survival (RFS) is survival without 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 evaluable[1] patients for MRD status[2]
- 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 data[3]
- 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

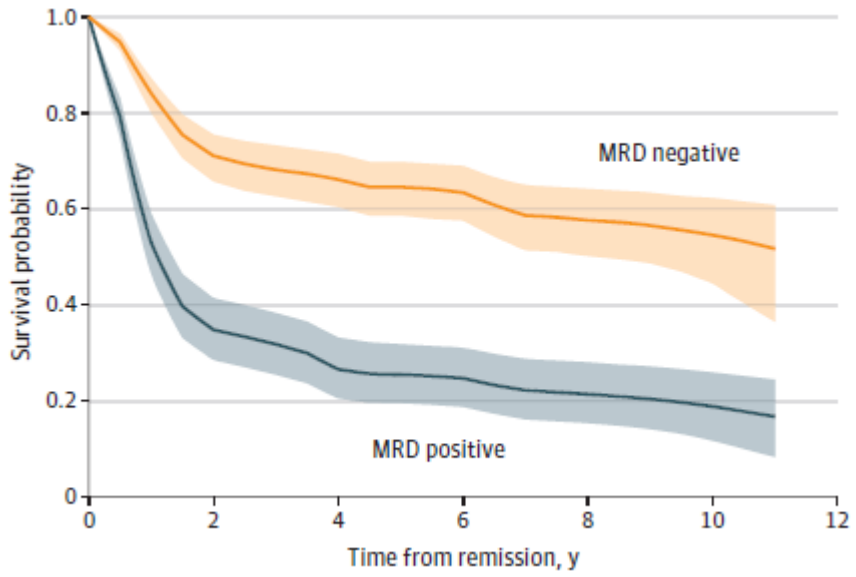
1. Evaluable patients include those who have valid MRD results following induction or re-induction, discontinue due to AE or die during induction or re-induction
2. Following induction or re-induction if applied
3. Data from early assessment would be excluded from final analysis if unblinded

MRD negativity is associated with superior DFS and OS

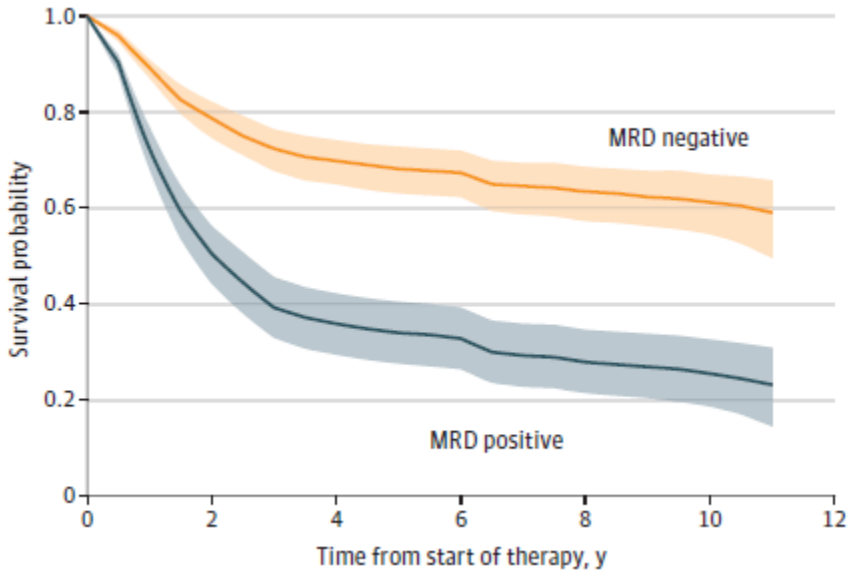
80 Patient Assessment likely strong predictor of success

- 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



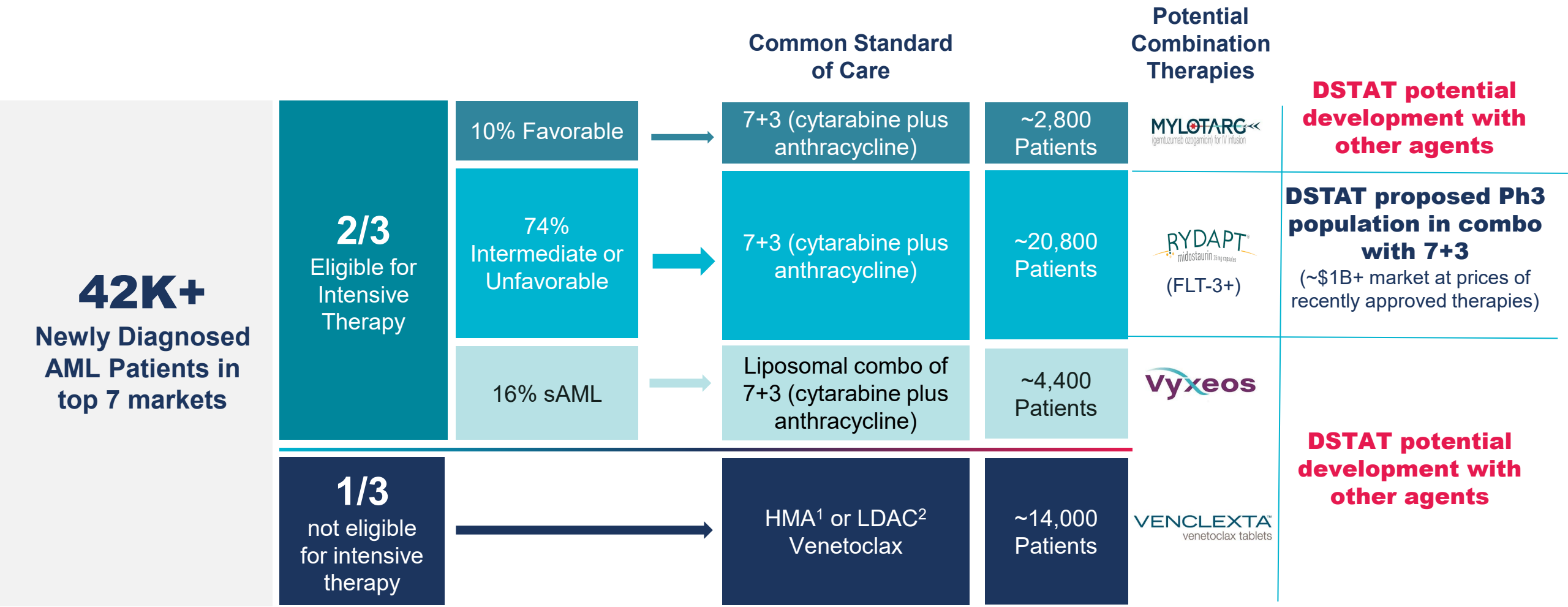
Overall Survival



Short, et al. JAMA Oncology, October 8,2020

Significant commercial opportunity and potential to expand

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



1. Hypomethylating agents
2. Low dose cytarabine

CMX521

CHIMERIX

CMX521: SARS-CoV-2 antiviral with established safety profile

Late-breaker oral presentation at ICAR (Seattle, March 23; 12:15-1pm PT)

CMX521

- Ribonucleoside analog known to inhibit viral RdRp*
- Uptake and conversion to triphosphate demonstrated in human epithelial cells
- Oral formulation developed through Phase I
- 27 kg of GMP API available for development/ clinical
- COM patent through 2038, with Method of Use through 2040

Data in SARS-CoV-2

- In vitro activity in human airway epithelial cells (EC50 = 0.3-0.9uM)
- In vivo efficacy with aerosol delivery in SARS-CoV-2-MA10 mouse model established by UNC School of Medicine
- Low µM activity across diverse coronaviruses suggests broad variant activity

Safety Profile

- Not mutagenic, clastogenic, cytotoxic or mitotoxic
- Excellent safety profile in IND enabling tox studies (oral) in rats and dogs
- Inhaled aerosol formulation well-tolerated in mice
- Well-tolerated in healthy volunteer Phase I study at ≤ 2400 mg oral, safety in human of an aerosolized formulation needs to be established

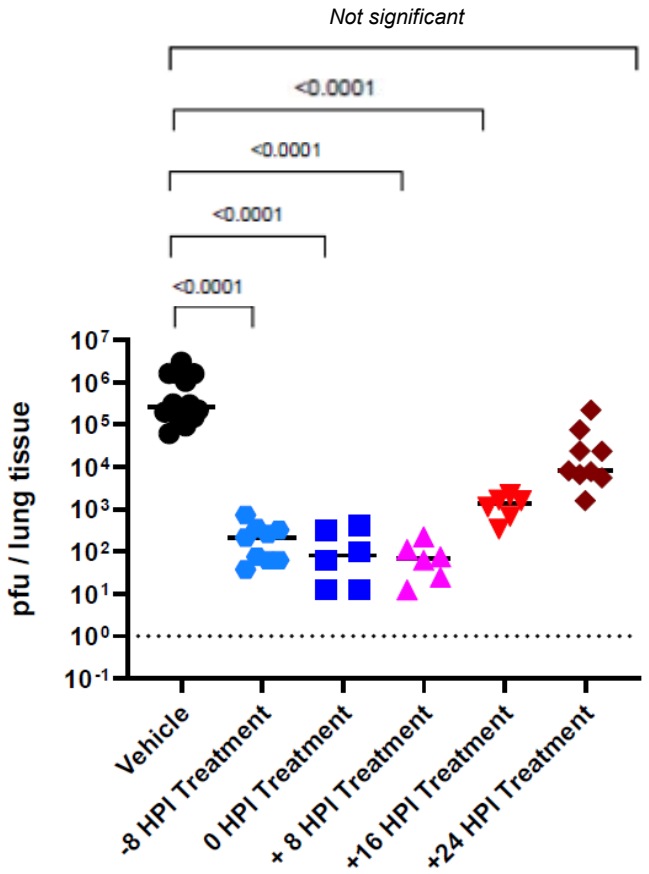
Inhalation administration maximizes respiratory exposure while minimizing systemic exposure

*Confirmation in SARS-CoV-2 RdRp ongoing

Significant antiviral effect demonstrated in nonclinical SARS-CoV-2 model conducted in collaboration with UNC-CH

- Mouse-adapted SARS-CoV-2-MA10 model
  - Replicates lung pathology of human infection 4-days post infection
    - **1 day in mouse = 5-7 days in humans (adjusted disease course)**
- CMX521 delivered as inhaled nebulized liquid aerosol
  - 3x daily from initiation through Day 4
- Minimal systemic exposure
- CMX521 treatment significantly decreased lung viral titer
  - 365-fold decrease with treatment initiation 16 hours post-infection
  - 3,000-fold decrease with treatment initiation at time of infection
- Clinical scoring (animal health), lung pathology, animal weight loss and viral RNA parallel viral lung titer (plaque forming unit) data
- Dose-range, PK, comparative and combination studies ongoing

Viral Lung Titer
Replicating SARS-COV-2-MA10



Corporate Update

CHIMERIX

Financial summary

Dollars (millions)	Dec 31, 2021
R&D	$ 73.8*
G&A	18.7
Acquired in process R&D	82.9
Total operating expenses	175.4
Net loss	(173.2)
Ending Cash balance	$ 90.4
Shares outstanding	86.9

- 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 includes the $20m success milestone payment due to Oncoceutics shareholders for BICR readout of ≥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

- Preclinical data from CMX521 program as a potential prophylaxis and treatment for COVID-19
  - Developed in collaboration with READDI
  - Monotherapy aerosol administration in preclinical model reduced viral titers in lungs by 99.9% on day four post infection

Chimerix Corporate Presentation

CHIMERIX