Tumori Cerebrali

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Padova

2023 ASCO ANNUAL MEETING

INDIGO: a Phase 3 global, randomized, double-blinded study of vorasidenib versus placebo in patients with residual or recurrent grade 2 glioma with an IDH1/2 mutation

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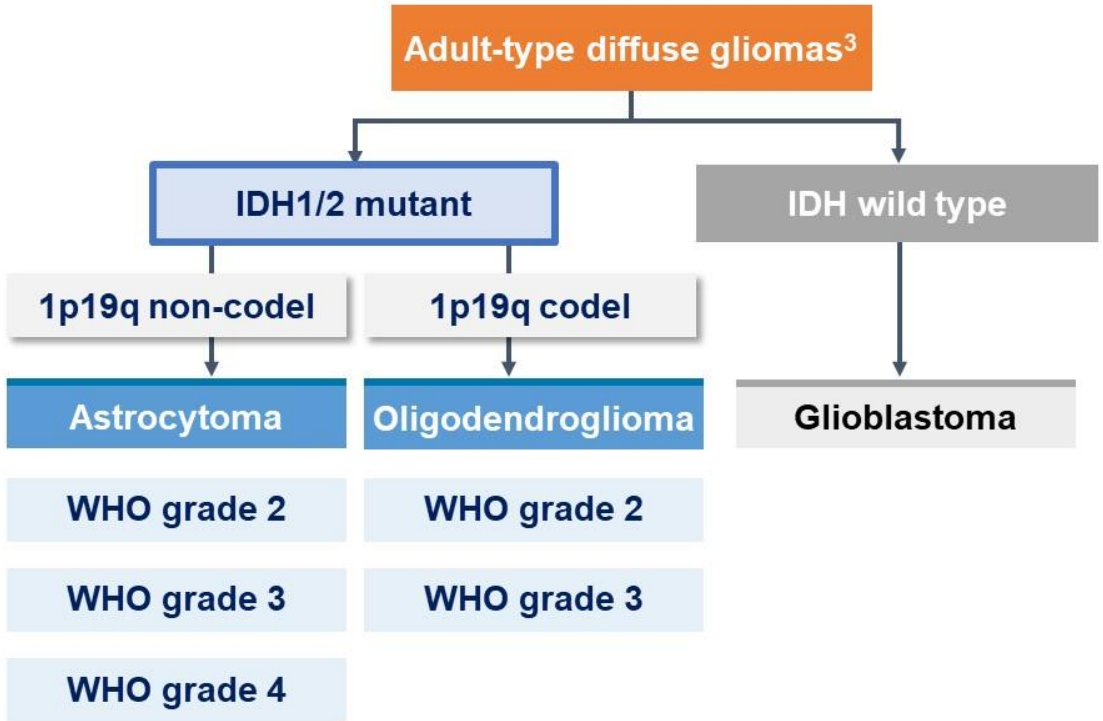
ClinicalTrials.gov identifier: NCT04164901. This study was sponsored by Servier

IDH1/2-mutant diffuse gliomas

- IDH1/2 mutations occur in most low-grade diffuse gliomas[1,2]
- Characteristic molecular and clinical features[3]
- Distinct disease entity in revised WHO classification (2021)[3]
- Median age ~40 years[4]



1. Yan H *et al. N Engl J Med* 2009;360:765–73; 2. Hartmann C *et al. Acta Neuropathol* 2009;118:469–74; 3. Louis DN *et al. Neuro Oncol* 2021;23:1231–51; 4. Ostrom QT *et al. Neuro Oncol* 2022;24:v1–v95.
codel, codeletion.

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Current treatment approach to newly diagnosed IDH1/2-mutant glioma

No curative therapy

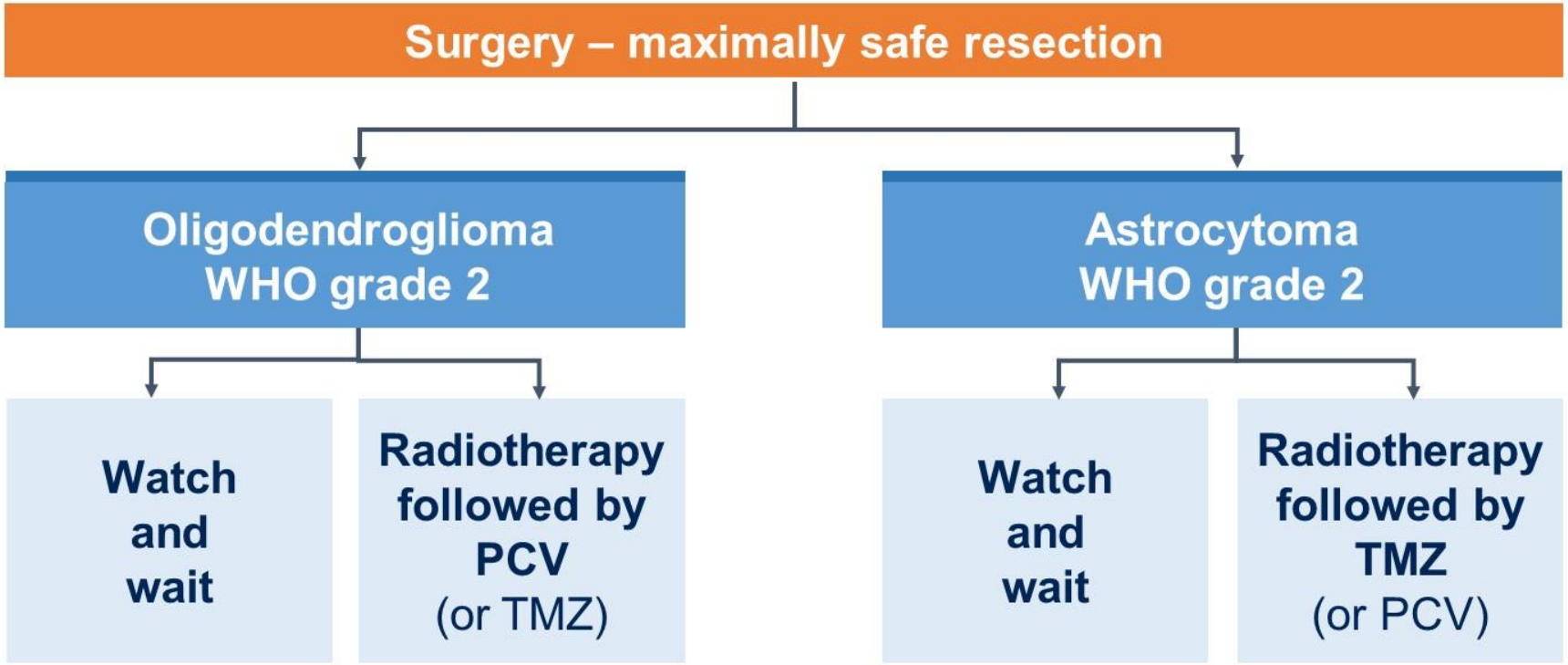
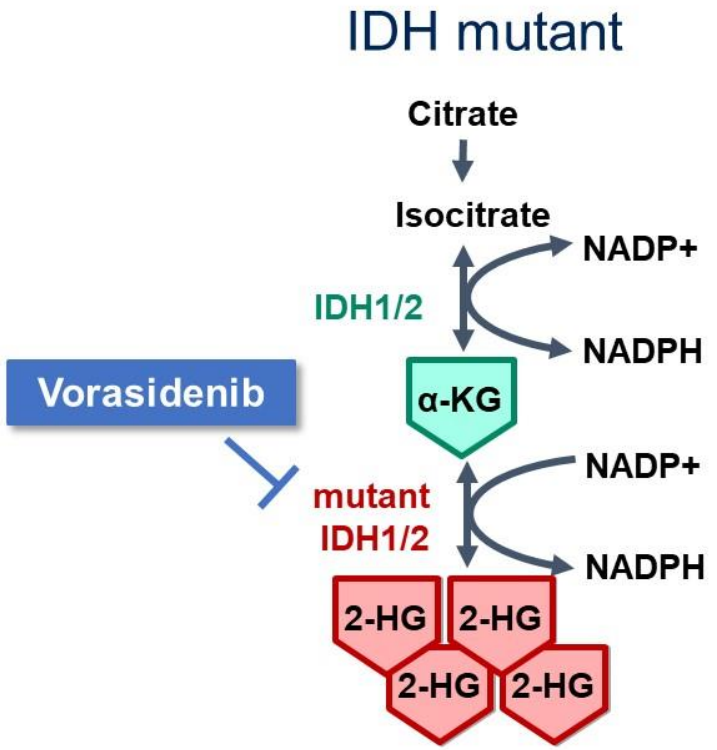


Figure modified from: Weller M *et al*. *Nat Rev Clin Oncol* 2021;18:170–86, with permission.
PCV, procarbazine, lomustine and vincristine; TMZ, temozolomide.

Vorasidenib

- Oral inhibitor of mutant IDH1 and IDH2[1]
- Specifically designed for brain penetrance[1]
- Reduced tumor 2-HG by >90% in resected grade 2/3 non-enhancing diffuse glioma[1]
- 2-HG reduction associated with:[2]
  - Lower tumor cell proliferation
  - Reversal of IDH1/2 mutation-associated gene expression programs
  - Increased DNA 5-hydroxy-methylcytosine
  - Increased tumor infiltrating lymphocytes



Competitive inhibition of α-KG-dependent enzymes

1. Mellinghoff I *et al. Nat Med* 2023;29:615–22; 2. Lu M et al. Presented at the American Association for Cancer Research Virtual Annual Meeting II June 22–24, 2020: abstract 2046.

INvestigating vorasiDenIb in GliOma (NCT04164901)

Key eligibility criteria

- ≥12 years of age
- IDH1/2-mutated* grade 2 oligodendroglioma or astrocytoma per WHO 2016 guidelines
- Prior surgery only
- Measurable non-enhancing disease (≥1 target lesion measuring ≥1 cm × ≥1 cm), confirmed by blinded review
- Not in need of immediate chemotherapy or radiotherapy per investigator assessment

1:1 double-blind randomization (N=331)

Stratified by 1p19q status and baseline tumor size

Vorasidenib 40 mg (N=168)

Orally, once daily, 28-day cycles

Centrally confirmed progressive disease permitted unblinding and crossover†

Placebo (N=163)

IDMC regularly reviewed safety and other clinical data, as well as the efficacy data following prespecified interim analyses

*Centrally confirmed using an investigational clinical trial assay, based on the Oncomine Dx Target Test and developed in partnership with Thermo Fisher Scientific Inc.;
†Real-time single BIRC reader.
IDMC, independent data monitoring committee.

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Endpoints and planned analyses

1 Primary endpoint

PFS: time from randomization to the first imaging-based disease progression as assessed by BIRC or death because of any cause

- MRI every 3 months for 3 years, then every 6 months

2 Key secondary endpoint

TTNI: time from randomization to the initiation of first subsequent anticancer therapy or death because of any cause

Three prespecified analyses*

IA1: futility
(~55 PFS events) – Jan 2022

↓

IA2: futility/superiority
(~123 PFS events) – Sep 2022

Final analysis (~164 events) → no longer needed after IA2 superiority outcome

Other secondary/exploratory endpoints include: safety, tumor growth rate by volume, objective response rate, overall survival, HRQoL, seizure activity and neuro-cognitive function.
*With multiplicity adjustment and alpha spending.
HRQoL, health-related quality of life; IA, interim analysis; MRI, magnetic resonance imaging.

Patient disposition

As of Sep 2022 data cutoff (IA2):

- Enrollment:
  - Jan 2020 to Feb 2022
- 77 centers across 10 countries
- Median follow-up:
  - 14.0 months with vorasidenib
  - 14.3 months with placebo
- No deaths
- No patients lost to follow-up for the primary outcome

	Vorasidenib	Placebo
Randomized to treatment – n (%)	168 (100)	163 (100)
Received treatment (safety set)	167 (99.4)*	163 (100)
Discontinued treatment – n (%)	36 (21.4)	68 (41.7)
Centrally confirmed disease progression†	24 (14.3)	59 (36.2)
Patient decision	5 (3.0)	5 (3.1)
Adverse event	6 (3.6)	2 (1.2)
Investigator decision	1 (0.6)	1 (0.6)
Clinical disease progression‡	0	1 (0.6)
Crossed over to vorasidenib – n (%)	–	52 (31.9)

Study unblinded in Mar 2023 following IDMC recommendation based on early demonstration of efficacy, after which the majority of patients randomized to placebo crossed over to vorasidenib

*One patient withdrew consent from study treatment and later withdrew consent from the study overall;
†Real-time single BIRC reader; ‡In absence of imaging-based progression.

Baseline patient characteristics

	Vorasidenib (N=168)	Placebo (N=163)
Median age (range) – year	40.5 (21–71)	39.0 (16–65)
Sex – n (%)		
Male/female	101/67 (60.1/39.9)	86/77 (52.8/47.2)
Karnofsky performance score – n (%)		
100	90 (53.6)	87 (53.4)
90–80*	77 (45.8)	76 (46.6)
Time from last surgery for glioma to randomization – year		
Median (range)	2.5 (0.2–5.2)†	2.2 (0.9–5.0)
Chromosome 1p19q codeletion status – n (%)‡		
Codeleted/non-codeleted	88/80 (52.4/47.6)	84/79 (51.5/48.5)
Tumor size at baseline – n (%)‡		
Longest diameter of ≥2 cm/<2 cm	139/29 (82.7/17.3)	137/26 (84.0/16.0)

*One additional patient (0.6%) met eligibility criteria during screening, but then had score of 70 on Day 1 of the first cycle; †One patient had a biopsy during prescreening to obtain tumor tissue for IDH mutation status testing, which was allowed per protocol; ‡Data are reported as collected by electronic case report forms.

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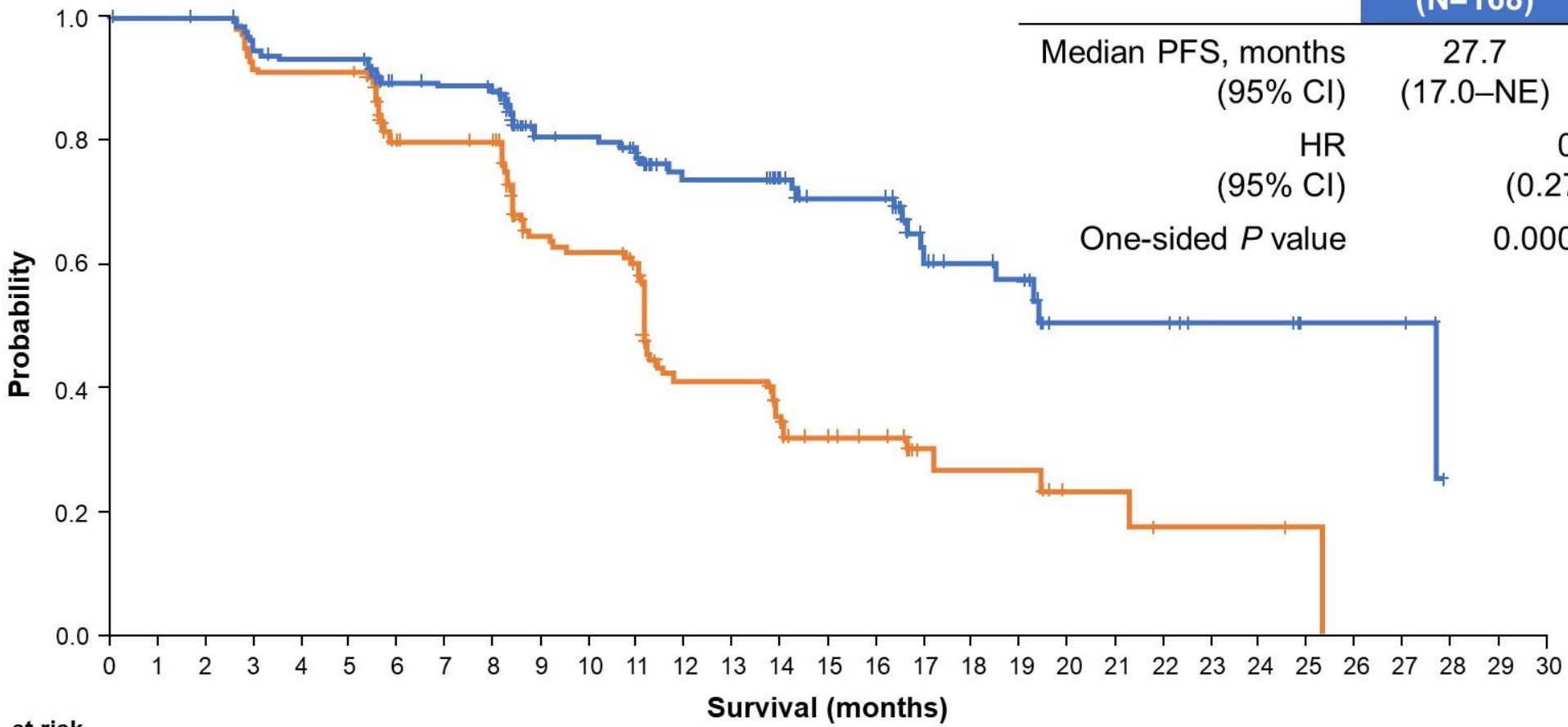
Primary endpoint: PFS per BIRC

	Vorasidenib (N=168)	Placebo (N=163)
Median PFS, months (95% CI)	27.7 (17.0–NE)	11.1 (11.0–13.7)
HR (95% CI)	0.39 (0.27–0.56)	
One-sided *P* value	0.000000067	



No. at risk

VOR	168	166	166	157	154	154	133	131	129	93	91	81	63	63	52	45	45	25	22	20	11	11	11	7	7	4	4	4	0
PBO	163	162	161	146	145	145	117	116	114	73	70	65	38	38	29	21	19	9	8	8	4	4	2	2	2	1	0		

+ Censored.
P value is from one-sided stratified log-rank test.
NE, not estimable; PBO, placebo; VOR, vorasidenib.

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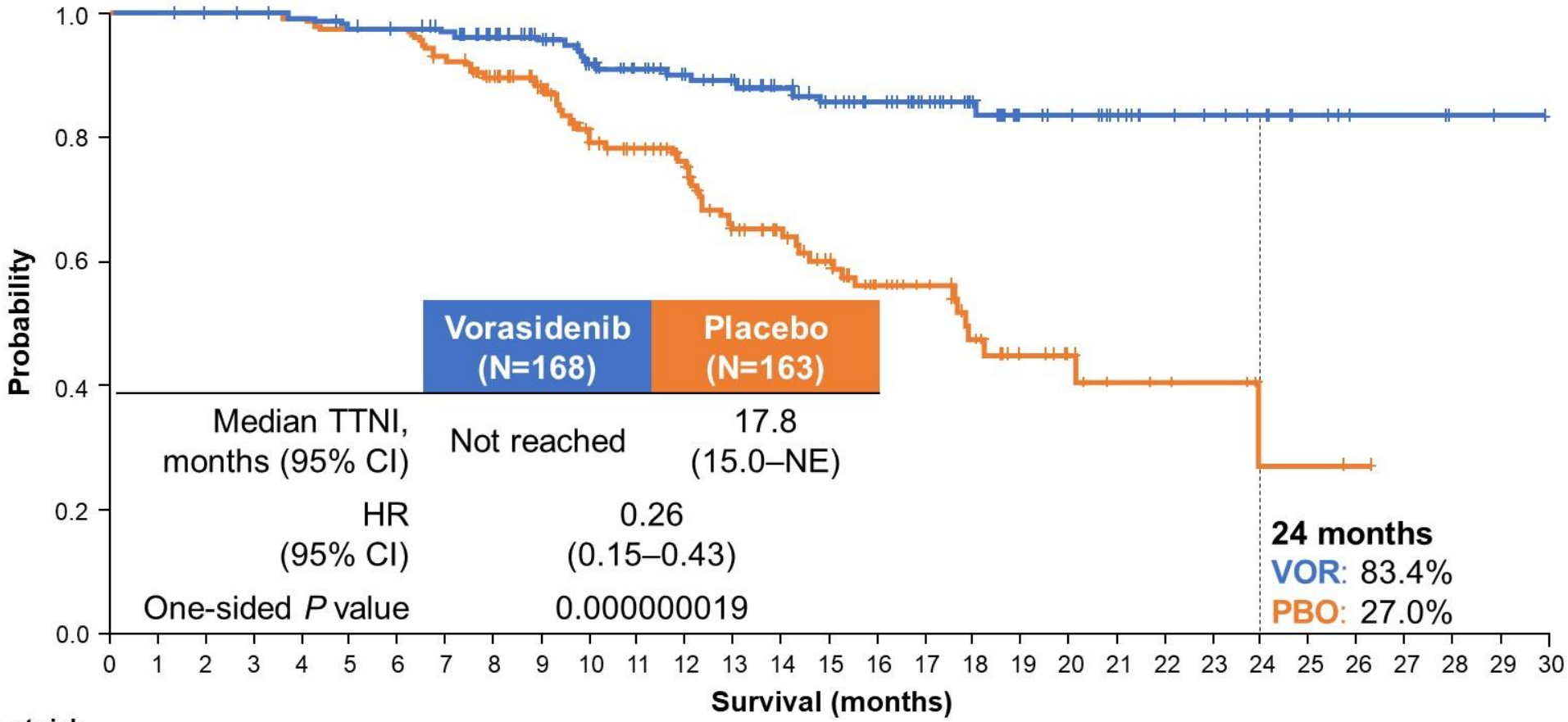
Key secondary endpoint: TTNI



No. at risk

VOR	168	168	167	167	165	161	160	156	146	130	117	105	95	86	75	65	57	48	38	27	25	18	15	13	11	7	4	4	2	1	0
PBO	163	163	162	161	159	156	155	146	134	119	97	88	77	60	54	45	35	30	21	14	11	7	6	5	2	2	1	0			

+ Censored.
P value is from one-sided stratified log-rank test.

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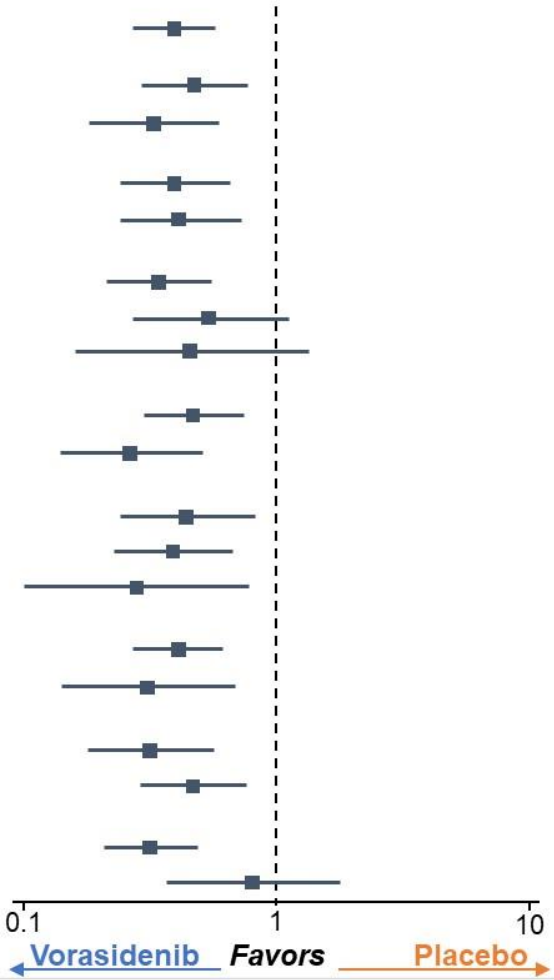
Subgroup analysis for PFS by BIRC

Subgroup	Events/N (%)	HR (95% CI)
Overall	135/331 (40.8)	0.39 (0.27–0.56)
18–<40 years	80/163 (49.1)	0.47 (0.29–0.75)
40–<65 years	53/164 (32.3)	0.32 (0.18–0.58)
Male	72/187 (38.5)	0.39 (0.24–0.64)
Female	63/144 (43.8)	0.41 (0.24–0.70)
North America	89/193 (46.1)	0.34 (0.21–0.54)
Western Europe	31/97 (32.0)	0.54 (0.27–1.10)
Rest of the World	15/41 (36.6)	0.45 (0.16–1.31)
Frontal tumor at initial diagnosis	92/222 (41.4)	0.47 (0.30–0.73)
Non-frontal tumor at initial diagnosis	43/109 (39.4)	0.26 (0.14–0.50)
<2 years from last surgery to randomization	51/130 (39.2)	0.44 (0.24–0.82)
2–<4 years from last surgery to randomization	59/145 (40.7)	0.39 (0.23–0.66)
≥4 years from last surgery to randomization	25/56 (44.6)	0.28 (0.10–0.76)
1 prior surgery	106/260 (40.8)	0.41 (0.27–0.61)
≥2 prior surgeries	29/71 (40.8)	0.31 (0.14–0.68)
Codeleted chromosome 1p19q*	59/172 (34.3)	0.32 (0.18–0.57)
Non-codeleted chromosome 1p19q	76/159 (47.8)	0.47 (0.29–0.75)
Longest tumor diameter of ≥2 cm at baseline*	109/269 (40.5)	0.32 (0.21–0.48)
Longest diameter of <2 cm at baseline	26/62 (41.9)	0.81 (0.37–1.77)



*Data are reported as collected by the interactive web response system.

Safety: TEAEs

	Vorasidenib (N=167)	Placebo (N=163)
Any grade ≥3 AE – n (%)	38 (22.8)	22 (13.5)
Increased alanine aminotransferase	16 (9.6)	0
Increased aspartate aminotransferase	7 (4.2)	0
Seizure	7 (4.2)	4 (2.5)
Increased gamma-glutamyltransferase	5 (3.0)	2 (1.2)
Syncope	3 (1.8)	1 (0.6)
Hypertension	2 (1.2)	3 (1.8)
Decreased neutrophil count	2 (1.2)	0

- Treatment interruption due to TEAE
  - **Vorasidenib** 29.9% (n=50)
  - **Placebo** 22.7% (n=37)
- Dose reduction due to TEAE
  - **Vorasidenib** 10.8% (n=18)
  - **Placebo** 3.1% (n=5)
- Discontinuation due to TEAE
  - **Vorasidenib** 3.6% (n=6)
  - **Placebo** 1.2% (n=2)
- No fatal TEAE

The safety set included all the patients who received at least one dose of study treatment.
Preferred terms listed are those that occurred at Grade ≥3 in two or more patients in the vorasidenib group.
AE, adverse event; TEAE, treatment-emergent adverse event.

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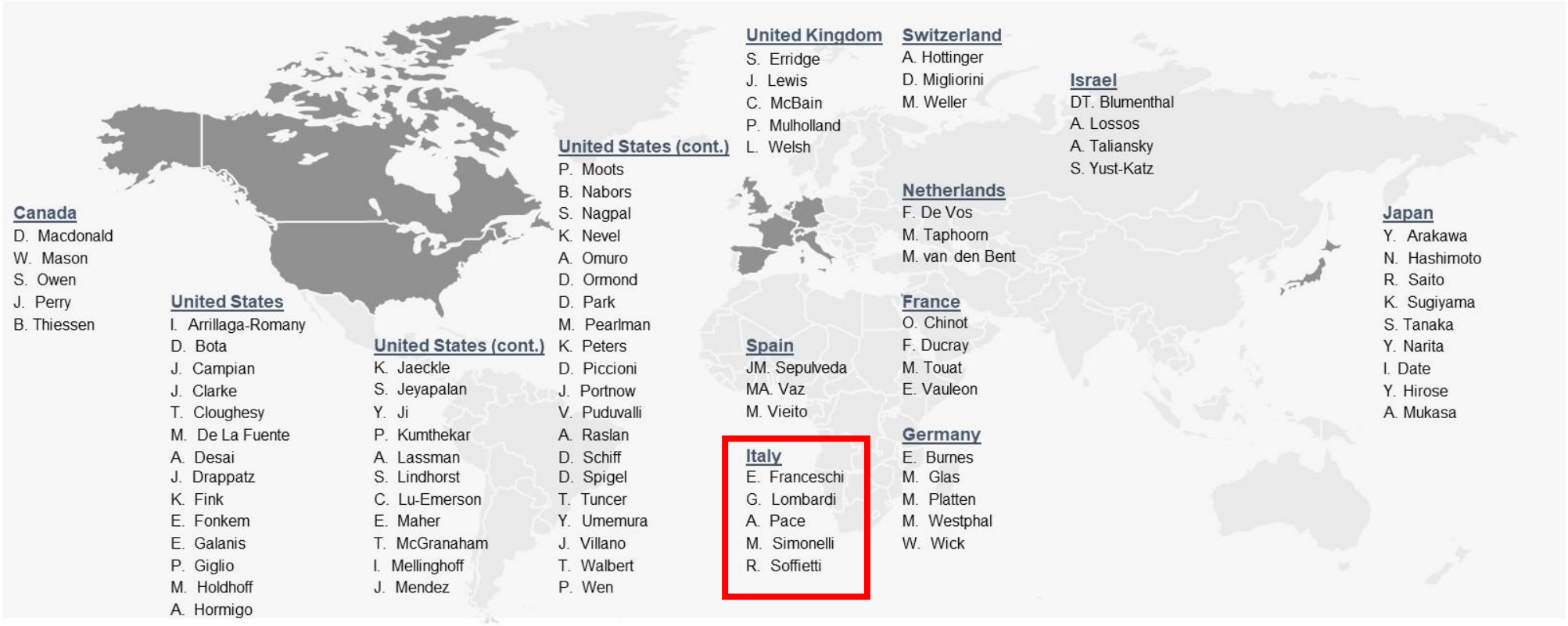
Summary

- Diffuse gliomas with IDH1/2 mutations are not curable with current therapies and infiltrate the brain in the absence of treatment
- Vorasidenib is an oral inhibitor of the mutant IDH1/2 enzymes with proven brain penetrance
- Treatment with vorasidenib significantly improved imaging-based PFS and TTNI with a manageable safety profile in patients who were not in need of immediate chemotherapy or radiotherapy

Acknowledgments

We would like to thank the principal investigators, their institutions, and most importantly the patients who took part in this study



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2023 ASCO ANNUAL MEETING

Anti-Telomerase vaccine in patients with newly diagnosed, unmethylated MGMT glioblastoma: a phase II study

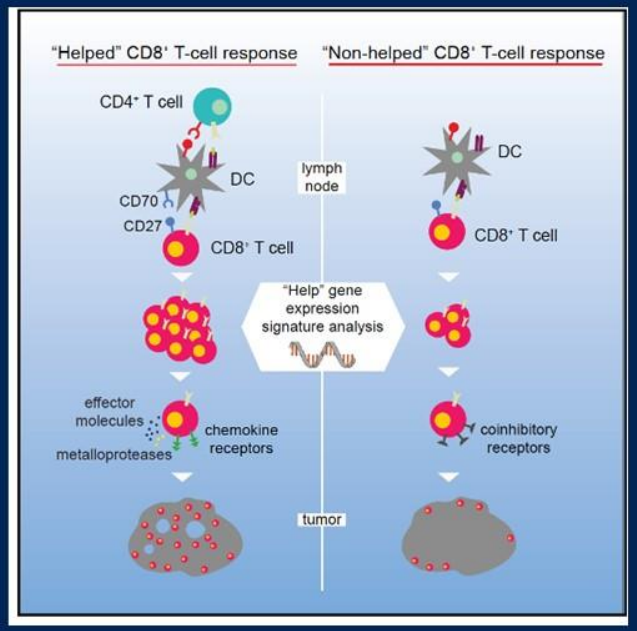
Antoine F Carpentier, Clotilde Verlut, François Ghiringhelli, Charlotte Bronnimann, Renata Ursu, Jean David Fumet, Elisabeta Gherga, Felix Lefort, Catherine Belin, Dewi Vernerey, Alice Hervieu, Caroline Laheurte, Aurelia Meurisse, Marion Jacquin, Marine Malfroy, Christine Fagnoni-Legat, Jacqueline Lehmann-Che, Laura Boullerot, Stefania Cuzzubbo, Olivier Adotevi

Investigating Centers : University hospitals of Paris, Besançon, Dijon and Bordeaux; France

UCPvax clinical trial

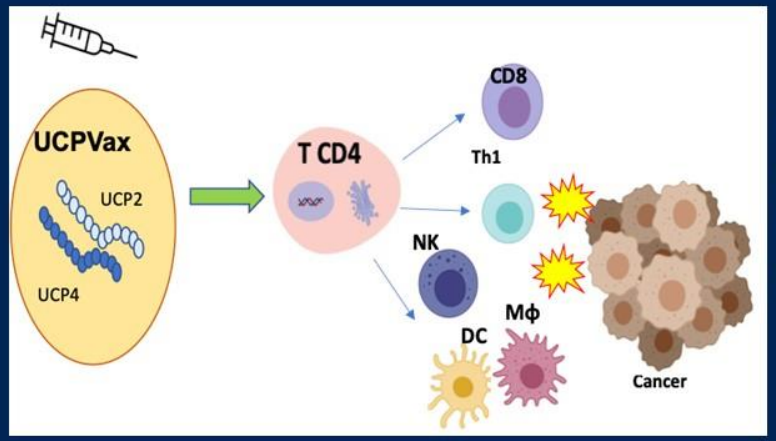
Introduction

Crucial role of CD4 Th1 T-cell in cancer vaccine efficacy



Ahrends et al. Immunity 2018, Borst et al. Nat Rev Immnunol 2018; Saxena et al Nat Rev Can 2021, Speiser et *al*, Nat Cancer, 2023

UCPVax is a cancer vaccine against UCP2 and UCP4, two CD4 helper peptides derived from TERT protein (telomerase)



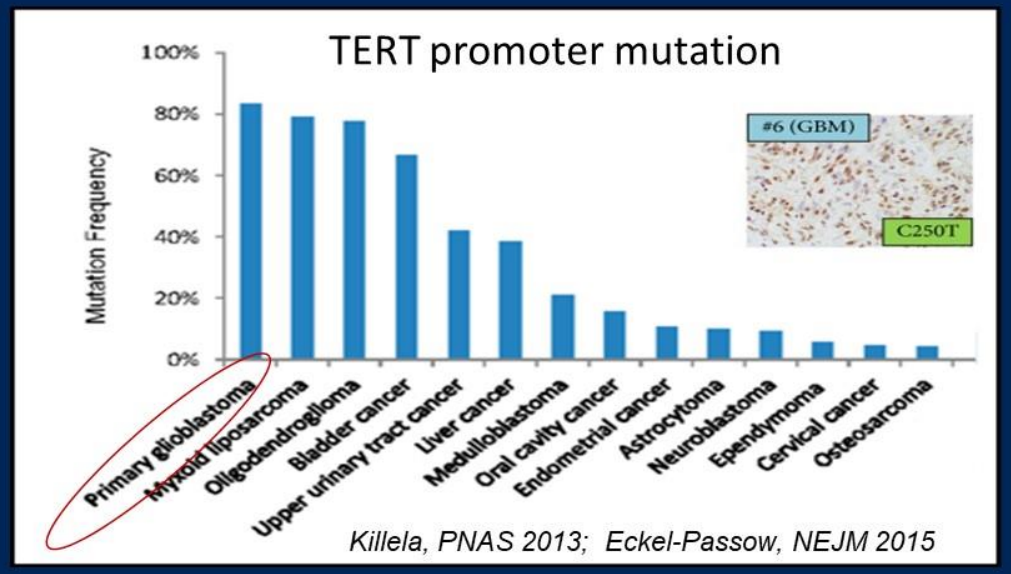
Godet et al. Clin Can Res 2012
Dosset et al. Clin Can Res 2012
Galaine et al. J Immunol 2016
Dosset et al Cancers 2020

UCPvax showed encouraging signs of efficacy in advanced NSCLC (phase I/II trial). *Adotévi et al. J Clin Oncol 2023*

UCPvax clinical trial

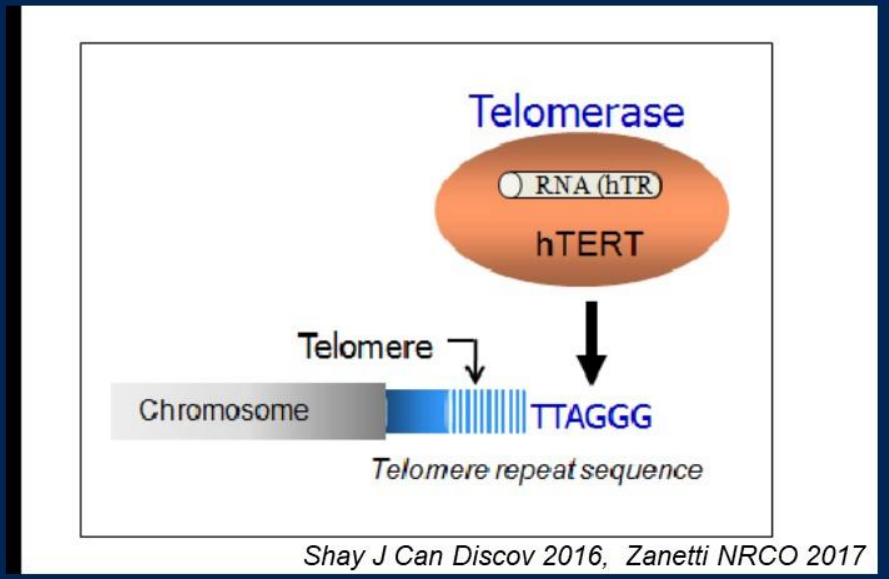
Introduction

High incidence of activating TERT promoter mutation in glioblastomas (GBM)



Killela, PNAS 2013; Eckel-Passow, NEJM 2015

TERT is strongly expressed in GBM, but not in normal brain



Shay J Can Discov 2016, Zanetti NRCO 2017

→ phase IIa trial to test the efficacy of UCPvax in GBM.

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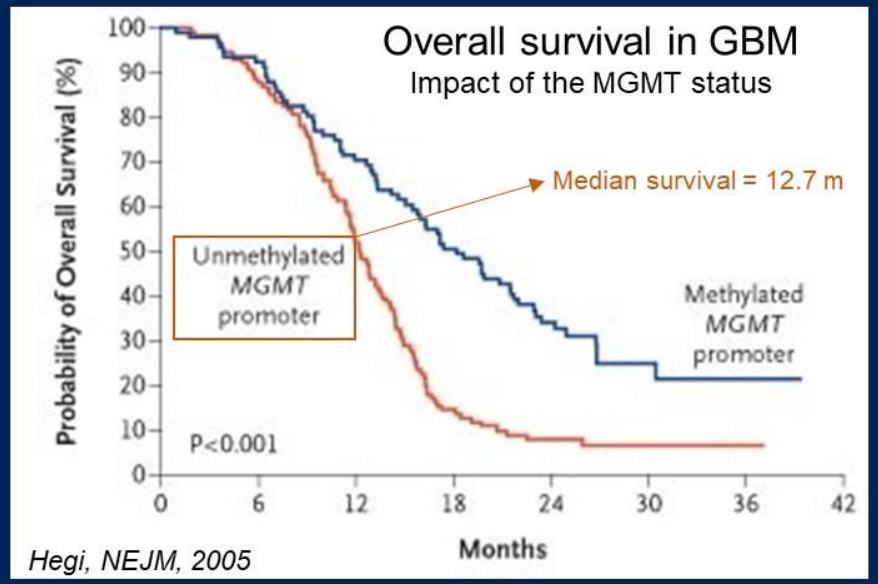
UCPvax clinical trial

Target population and inclusion criteria

In GBM treated with RT /TMZ,
MGMT methylation status has a prognostic value.



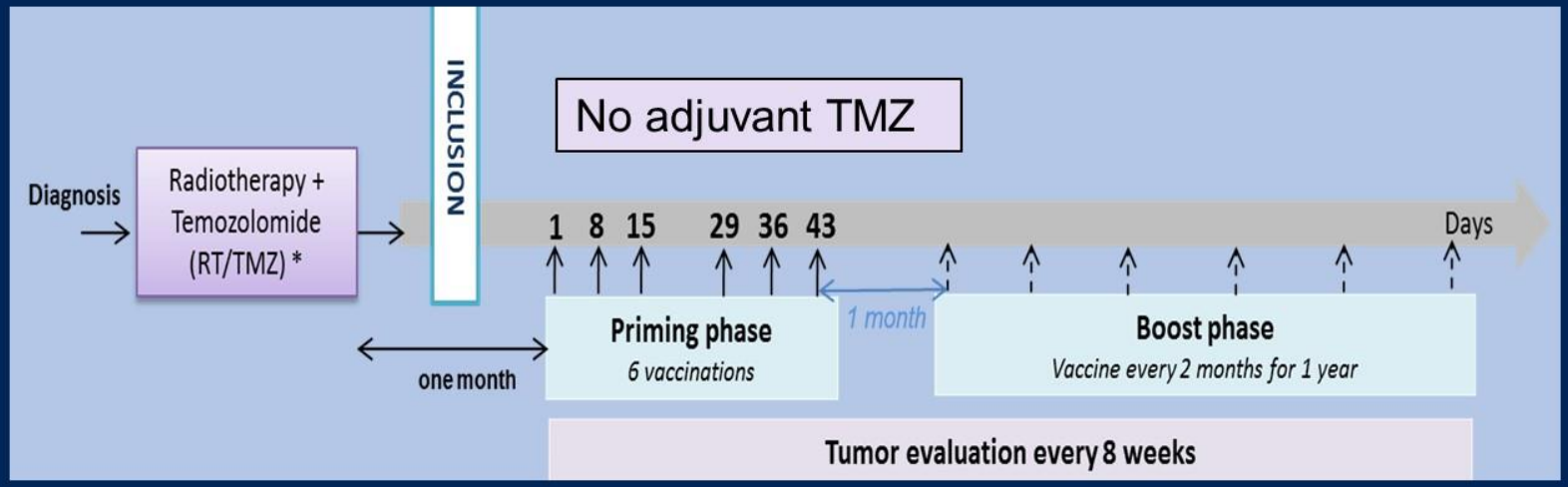
Main inclusion/exclusion criteria in UCPvax:

- non-mutated IDH1 glioblastoma
- ***unmethylated MGMT promoter status***
- Completed RT/TMZ (concomitant phase)
- Karnofsky Performance Status (KPS) ≥ 70%
- steroids <1.5mg/day dexamethasone

UCPvax clinical trial

Design and objectives

Multi-center, prospective, non-controlled, phase II trial. (NCT04280848)



s.c. injections : UCP2 and UCP4 (0,5mg each) + Montanide ISA-51

Primary endpoint:
TERT-specific CD4 T-cell response in peripheral blood (IFN-gamma ELISPOT)

Secondary endpoints:
- safety (CTCAE v 4.03)
- OS & PFS

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UCPvax clinical trial

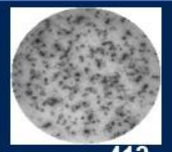
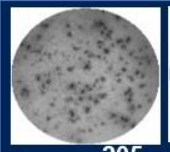
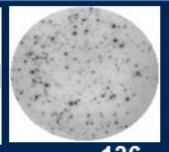
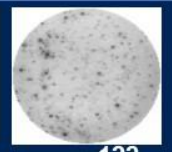
Baseline characteristics

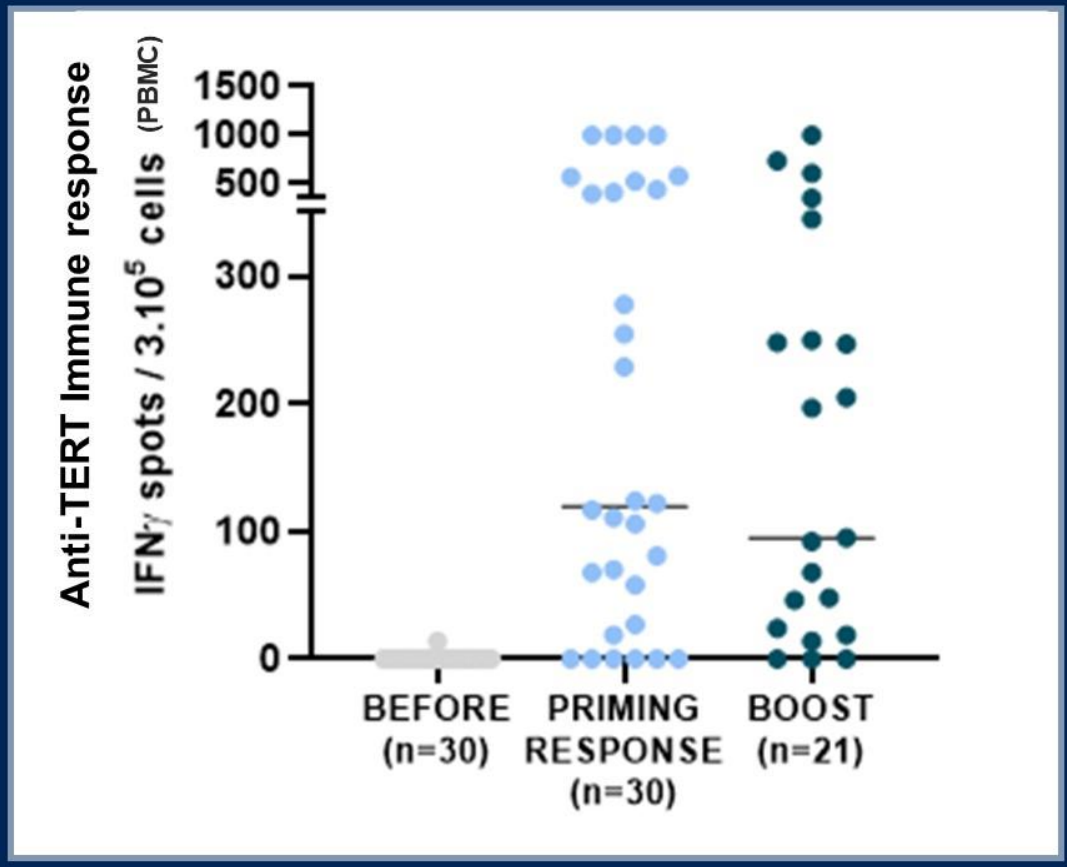
	Number of patients	% of patients
Glioblastoma, IDH1 wild-type	31	100%
Age, median (range), years	60.2 (37.5-85.5)	
Gender, female/male	12 / 19	39% / 61%
KPS 70-80 % **KPS 90-100 %**	6 25	19% 81%
***MGMT* promoter methylation (Yes/No)**	0 / 31	0% / 100%
Initial surgical procedure **biopsy** **partial resection** **complete resection**	 3 13 15	 10% 46% 54%
Baseline steroid use (at inclusion) **No** **Yes (dexamethasone ≤ 1.5 mg/d)**	 26 5	 84% 16%

UCPvax clinical trial

Immune response

Strong and durable T-cell response against TERT in 27/30 patients (90%)

patient #16	BEFORE	PRIMING RESPONSE	BOOST		
Months	0	2	4	6	12
IFN-γ spots	 0	 412	 205	 136	 122



(ex vivo IFN-γ Response ELISpot assay)

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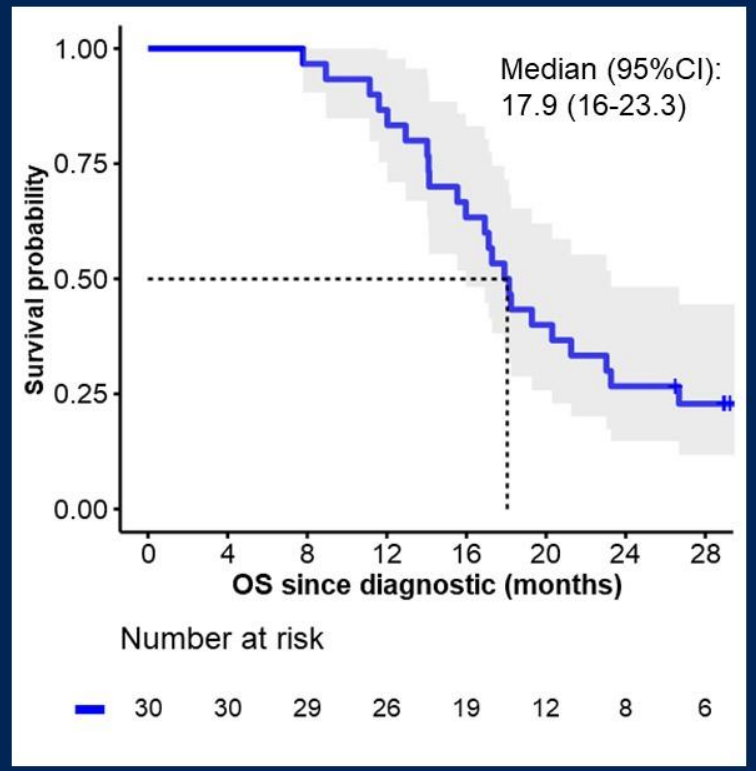
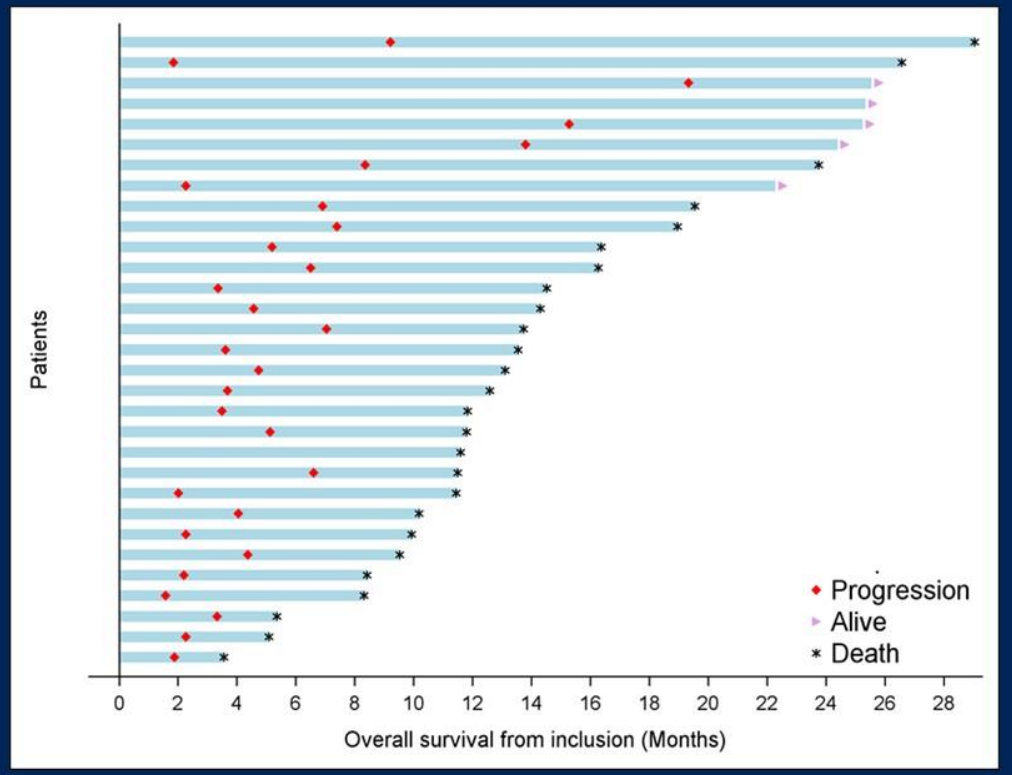
UCPvax clinical trial

Outcome

In the intent-to-treat population (n = 31):

Median PFS= 8.9 months , median OS: 17.9 months (No patients lost for follow-up)





UCPvax clinical trial

Outcome

	UCPvax (n=31 pts)		Historical data *	
OS since diagnosis:	**17.9 months**	⟷	**14.6 months** **14.9 months**	*Gilbert, NEJM, 2014* *Omuro, Neuro Oncol, 2023*
OS since end of radiotherapy				
• All patients	**15.0 months**	⟷	*No relevant historical data*	
• Pts without progression / pseudo-progression after RT	**18.1 months** (n=16 pts)	⟷	**14.7 months** **14.6 months**	*Stupp, JAMA, 2017* *Liau JAMA Oncol, 2023*

* unmethylated MGMT population, control groups

UCPvax clinical trial

Conclusions

UCPVax is:

- highly immunogenic
- provides an interesting survival in unmethylated MGMT GBM patients

This supports further clinical studies in newly-diagnosed GBM patients:

- UCPVax + TMZ (on-going)
- UCPVax + TMZ + anti-PD1 (MATVAC: Q1 2024)

PRESENTED BY: Antoine Carpentier, MD, PhD

2023 ASCO ANNUAL MEETING

PD1 inhibition and GITR agonism in combination with fractionated stereotactic radiotherapy for the treatment of recurrent glioblastoma: A phase 2, multi-arm study

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University of Pennsylvania

PRESENTED BY: Stephen J. Bagley, MD, MSCE

Background

- Recurrence of glioblastoma after standard of care chemoradiotherapy remains a major unmet medical need
  - Median OS ~ 9-12 months
- Glioblastoma is an immunologically “cold” tumor with low infiltration of T cells and poor response to immunotherapies[1]
  - Immune checkpoint inhibition has not demonstrated a signal of efficacy, with possible exception of neoadjuvant use in recurrent glioblastoma[2]
- Novel approaches are needed to sensitize glioblastoma to immune checkpoint inhibition

1. Jackson et al, *Nat Immunol* 2019.
2. Cloughesy et al, *Nat Med* 2019

Study Rationale

- Preclinical data have demonstrated the immunostimulatory effects of ***fractionated stereotactic radiotherapy (FSRT)***, with potential to convert immunologically "cold" tumors to "hot"/inflamed and sensitize to immune checkpoint inhibition[1]
  - FSRT is clinically available and increasingly used in routine practice for recurrent GBM[2]
  - Although optimal dose/fractionation for immune stimulation is not firmly established, a regimen of ***8 Gy x 3 fx*** (24 Gy) is strongly supported by murine studies[3]

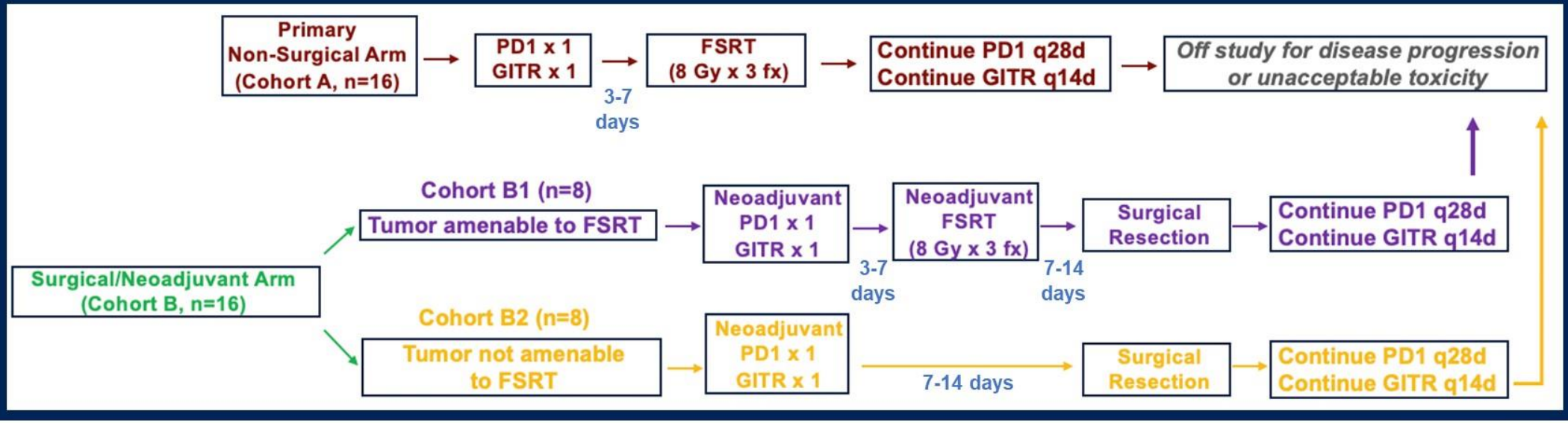
- The glucocorticoid-induced TNFR-related receptor (GITR) is an immune checkpoint constitutively expressed in immunosuppressive regulatory T cells (Tregs)
  - GITR activation using agonist mAbs leads to depletion and reduced immunosuppressive function of Tregs, and enhanced effector function of CD4/CD8 T cells[4]
  - Preclinical data suggest benefit of targeting GITR in GBM,[5] including in combination with PD1 inhibition[6] and with FSRT[7]

1. Demaria et al, *J Immunother Cancer* 2021
2. Bunevicius et al, *Neurosurg Clin N Am* 2021
3. Vanpouille-Box et al, *Nat Commun* 2017
4. Coe et al, *Cancer Immunol Immunother* 2010
5. Bagley et al, *J Neuroncol* 2019
6. Amoozgar et al, *Nat Commun* 2021
7. Patel M et al, *J Immunother Cancer* 2016

Study Design

- **Phase 2, open-label, single-center, investigator-initiated trial (N=32)**
  - Cohort A (n=16): Single-arm, primary nonsurgical cohort for determination of efficacy signal
  - Cohort B (n=16): Two-arm, non-randomized, neoadjuvant/surgical cohort for immune correlatives

- **Immunotherapy: 28 day-treatment cycles**
  - Anti-PD-1 inhibitor mAb: Retifanlimab 500mg IV, Day 1
  - Anti-GITR agonist mAb: INCAGN01876 300mg IV, Days 1 and 15
- **FSRT**:
  - 24 Gy (3 fractions of 8Gy/fraction)



Study Objectives

- Primary Objective:
  1. To determine the efficacy of the combination of retifanlimab, INCAGN01876, and FSRT in patients with recurrent GBM
     - Primary endpoint: objective radiographic response (ORR) in Cohort A (nonsurgical cohort), per mRANO
       - Null hypothesis: ORR in Cohort A, 5%
       - Alternative hypothesis: ORR in Cohort A, 25%
       - Exact single-stage design; n=16 evaluable patients for 80% power (one-sided alpha = 0.05)

- Secondary Objectives:
  1. To determine PFS and OS, separately in each cohort
  2. To evaluate the safety and tolerability of this regimen in patients with recurrent GBM

- Exploratory Objectives:
  1. To evaluate the systemic and tumor microenvironment immune effects of this regimen, with specific interest in the immune effects of FSRT
  2. To compare PFS and OS in Surgical/Neoadjuvant Arm patients (Cohort B) treated with vs. without neoadjuvant FSRT

Patient Eligibility

- Key Inclusion Criteria
  - 18 years or older with histopathologically confirmed GBM (WHO CNS5)
  - Recurrence following frontline radiotherapy (unlimited number of relapses allowed)
    - At least 12 weeks elapsed since completion of prior radiotherapy
  - ***Nonsurgical arm (Cohort A)***: Contrast-enhancing tumor at least 1cm and <= 4cm in largest dimension
  - ***Surgical arm (Cohort B):*** Candidate for surgical resection of tumor
  - Corticosteroid use <= 2mg of dexamethasone per day
  - Karnofsky Performance Status >= 60

- Key Exclusion Criteria
  - Prior bevacizumab or other VEGF inhibitors
  - Contrast-enhancing tumor in brainstem or spinal cord
  - Autoimmune or connective tissue disease either (a) actively flaring OR (b) has required systemic treatment in the past 2 years

Patient Characteristics

	Nonsurgical, Cohort A (n=16)	Neoadjuvant with FSRT, Cohort B1 (n=8)	Neoadjuvant without FSRT, Cohort B2 (n=8)	Total (n=32)	P value
Age (median, IQR)	61 (52, 66)	64 (63, 65)	63 (55, 72)	64 (55, 65)	0.61
Gender, n (%)					0.88
Female	7 (44)	3 (38)	4 (50)	14 (44)	
Male	9 (56)	5 (62)	4 (50)	18 (56)	
Karnofsky Performance Status					0.24
60-80	7 (44)	3 (38)	2 (25)	12 (38)	
90-100	9 (56)	5 (62)	6 (75)	20 (62)	
MGMT methylation status, n (%)					0.78
Methylated	6 (38)	4 (50)	4 (50)	14 (44)	
Unmethylated	10 (62)	4 (50)	4 (50)	18 (56)	
Preoperative CE tumor volume (cm^3) (median, IQR)		11.0 (8.9, 20.8)	17.5 (6.4, 22.4)		0.96
Percent CE tumor volume resected (median, IQR)		72 (42, 84)	61 (44, 63)		0.34

IQR, interquartile range MGMT, 06-methylguanine-DNA-methyltransferase CE, contrast-enhancing

Safety and tolerability

Adverse Events (CTCAE v 5.0)	No. (%)
Grade 3-4 AEs at least probably related to study interventions	
Cerebral edema	11 (34)
Fatigue	5 (16)
Decreased lymphocyte count	4 (12.5)
Cognitive disturbance	4 (12.5)
Immune-related AEs	
Grade 1-2 rash	10 (31)
Grade 1-2 diarrhea	9 (28)
Grade 4 immune thrombocytopenia	1 (3)
Grade 1 AST/ALT elevation	1 (3)

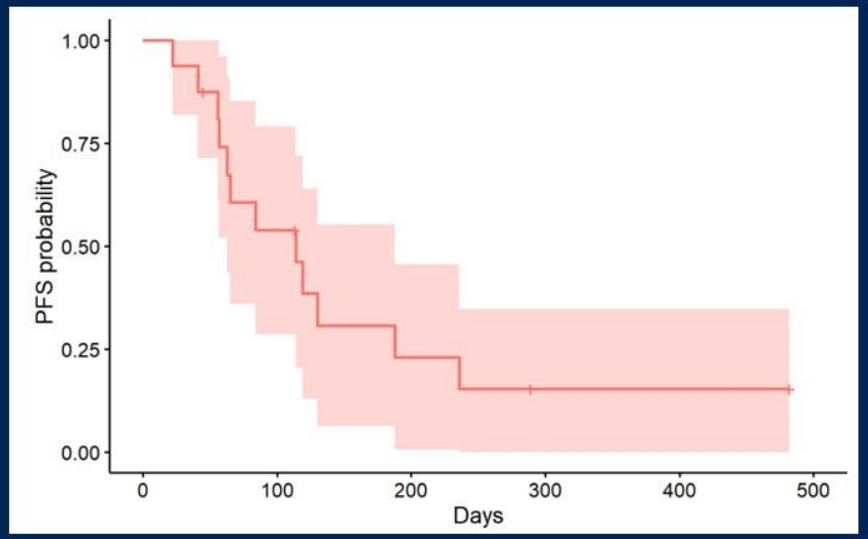
Efficacy Data

- Data cutoff for analyses: January 18, 2023
- Median follow-up 20.0 months (IQR, 11.1 – 22.3 months)

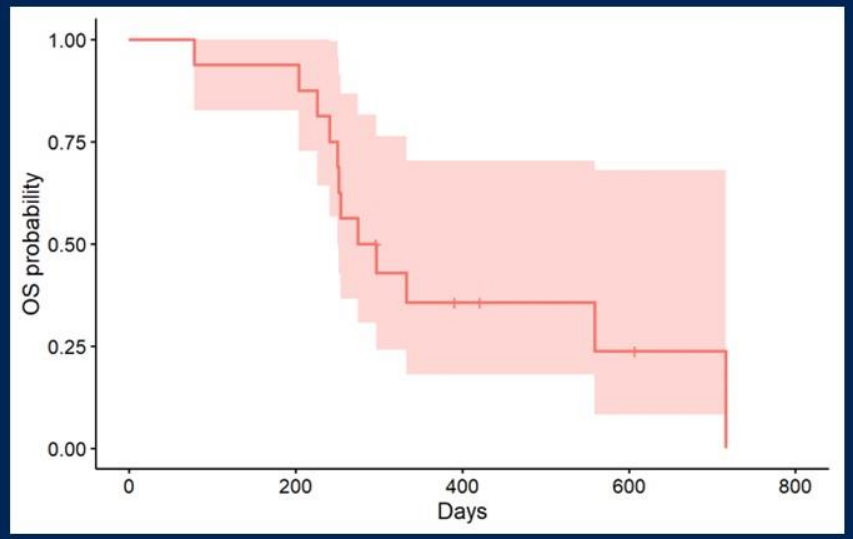
Efficacy Analysis – Cohort A (Primary/Non-Surgical, n=16)

- 0 / 16 patients achieved radiographic response per mRANO criteria (ORR, 0%)
- 9 / 16 patients (56%) achieved best response of Stable Disease

Median PFS 3.9 months (95% CI, 2.1 – 6 .2 months)



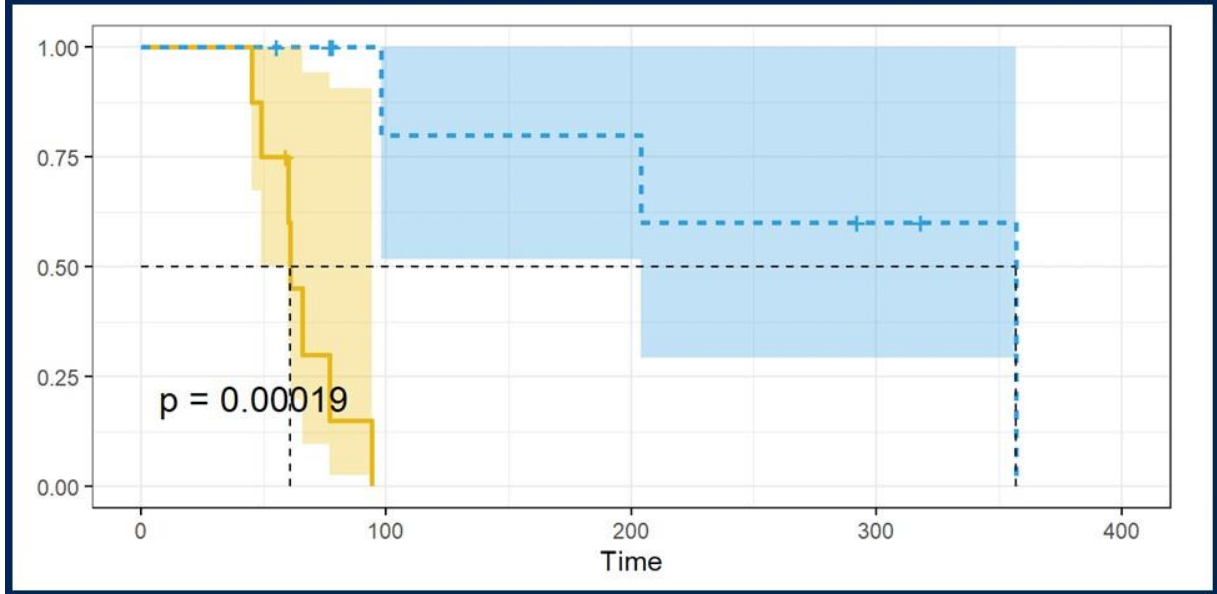
Median OS 9.4 months (95% CI, 8.2 – 10.6 months)



Efficacy Analysis – Cohort B (Surgical/Neoadjuvant Cohort)

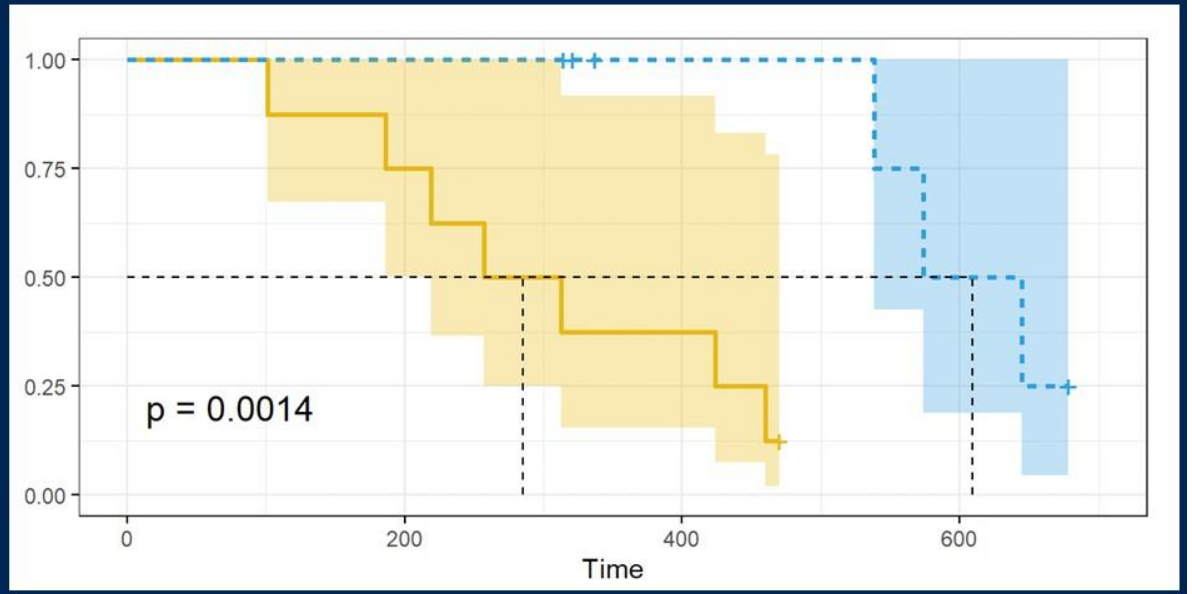
	Median PFS (*mo*)
Neoadjuvant ICB + FSRT (B1)	11.7
Neoadjuvant ICB (B2)	2.0

p=0.0002

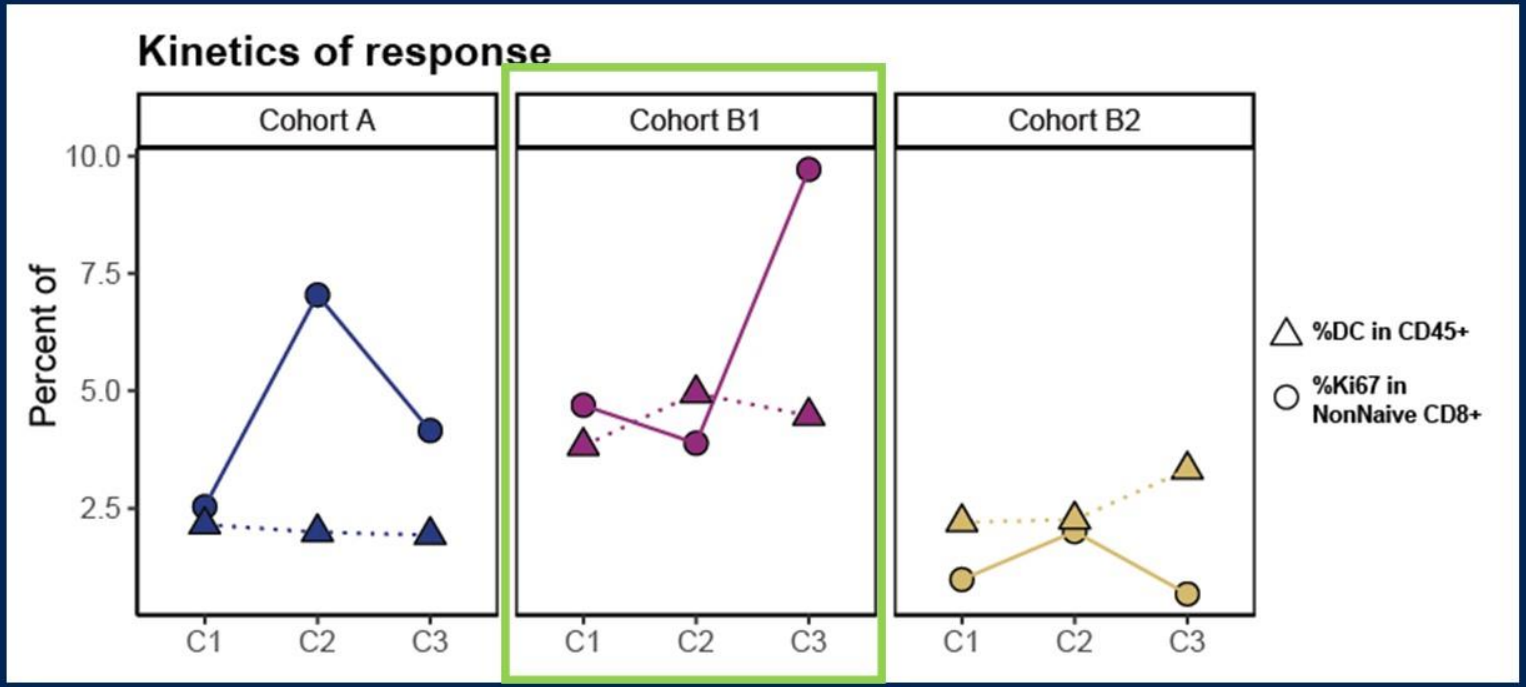


	Median OS (*mo*)
Neoadjuvant ICB + FSRT (B1)	20.1
Neoadjuvant ICB (B2)	9.4

p=0.0014



Flow cytometry of peripheral blood mononuclear cells (PBMCs)



- ***<u>In cohort B1 only (neoadjuvant ICB + FSRT):</u>***
  - Initial increase in dendritic cells (C1→C2), followed by an increase in proliferating CD8+ T cells (C2→C3)

Conclusions

- The combination of the PD1 inhibitor retifanlimab, GITR agonist INCAGN10876, and FSRT (8 Gy x 3 fx) was safe and well tolerated in patients with recurrent GBM
- There was no signal of efficacy in patients receiving this regimen in the absence of surgical tumor resection
- In patients receiving neoadjuvant doses of PD1/GITR prior to surgical tumor resection, the addition of neoadjuvant FSRT was associated with superior PFS and OS
  - The addition of neoadjuvant FSRT was also associated with stronger and more sustained systemic inflammation and greater proliferative T cell responses in the peripheral blood
  - Immune correlative studies analyzing effects of FSRT on the tumor microenvironment are ongoing
- These results warrant further evaluation of neoadjuvant ICB + FSRT in patients with recurrent GBM in a randomized phase 2 setting

Take Home Messages from ASCO 2023

- **Nuovi approcci di immunoterapia promettenti nel glioblastoma**
- Conferma efficacia delle Targeted therapies (anti-IDH) **in pazienti con glioma di basso grado**
- **Importanza** arruolamento in **studi sperimentali** paz neuro-oncologici

REGOMA-2 (no profit phase 1 study): enrolling!!