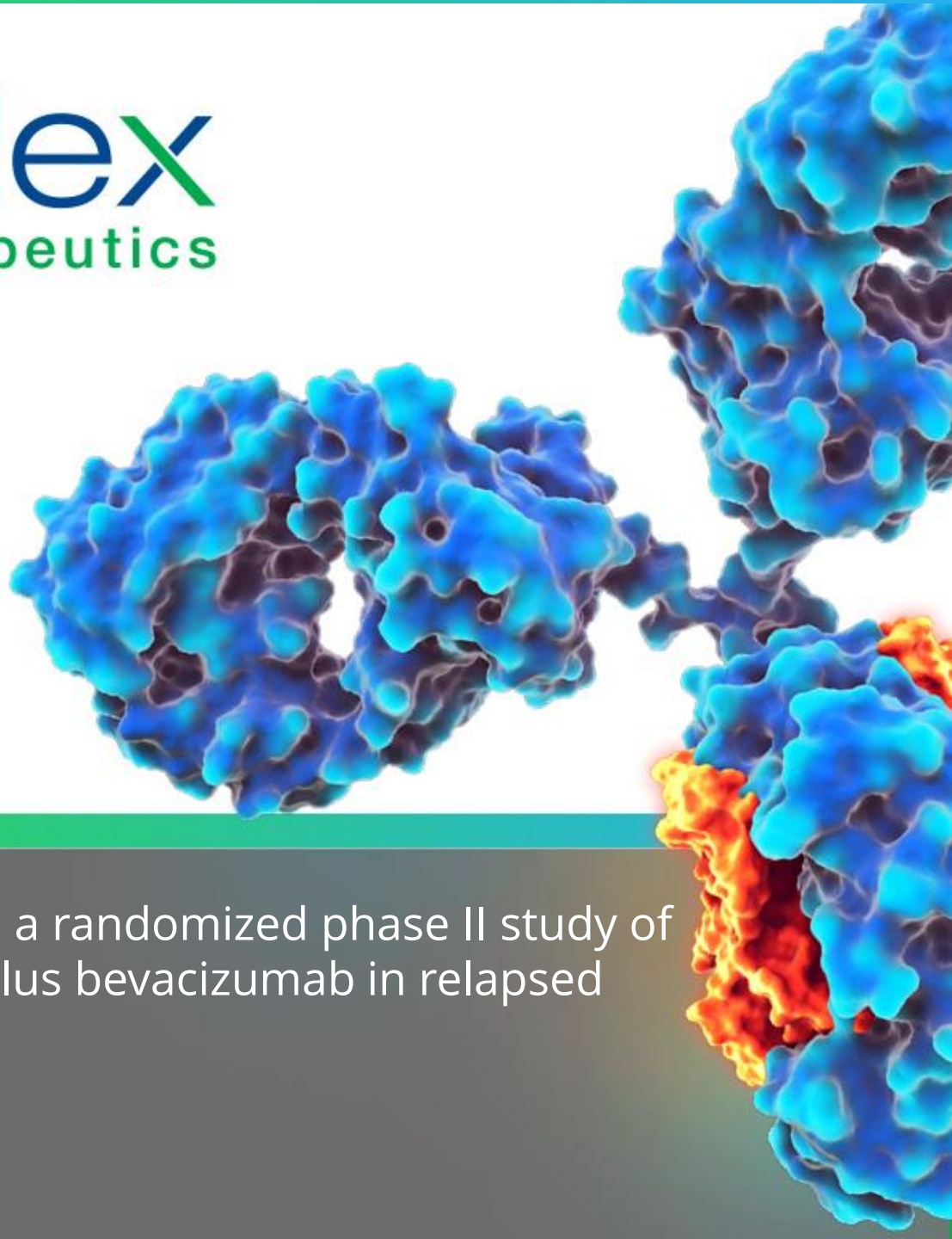
Celldex therapeutics



ReACT: Overall survival from a randomized phase II study of RINTEGA® (rindopepimut) plus bevacizumab in relapsed glioblastoma

June 1, 2015

Forward Looking Statement

This communication contains "forward-looking" statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical fact are statements that could be forward-looking statements. You can identify these forward-looking statements through our use of words such as “may,” “will,” “can,” “anticipate,” “assume,” “should,” “indicate,” “would,” “believe,” “contemplate,” “expect,” “seek,” “estimate,” “continue,” “plan,” “point to,” “project,” “predict,” “could,” “intend,” “target,” “potential” and other similar words and expressions of the future. These forward-looking statements are subject to risks and uncertainties that may cause actual future experience and results to differ materially from those discussed in these forward-looking statements. Important factors that might cause such a difference include, but are not limited to, the timing, cost and uncertainty of obtaining regulatory approvals for product candidates; our ability to develop and commercialize products before competitors that are superior to the alternatives developed by such competitors; the validity of our patents and our ability to avoid intellectual property litigation, which can be costly and divert management time and attention; and the other factors listed under “Risk Factors” in our filings with the SEC, including Forms 10-K, 10-Q and 8-K.

Celldex does not undertake any obligation to release publicly any revisions to such forward-looking statement to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events.

Celldex therapeutics

EGFR Mutation Variant III (EGFRvIII)

- Tumor-specific oncogene expressed in one-third of primary GBM, seldom expressed with IDH mutations but not in normal tissue
- EGFRvIII(+) cells may induce growth in EGFRvIII(-) cells via paracrine signaling, membrane-derived microvesicles, and tumor stem cells[1-4]
- RINTEGA consists of EGFRvIII peptide conjugated to Keyhole Limpet Hemocyanin (KLH)
  - Generates a specific immune response against EGFRvIII-expressing GBM
  - "Ready to use" formulation
  - Delivered as intradermal injection of 500 µg RINTEGA with 150 µg GM-CSF as an adjuvant

EGFRvIII Linked to Poor Long Term Survival

	EGFRvIII+		EGFRvIII-	
Dataset	Median OS	3-year OS	Median OS	3-year OS
Heimberger 2005	12	<5%		
Pelloski 2007	12.7	6%		
RTOG 0525, TMZ 5/28	14.2	7%	18.2	25%
RTOG 0525, matched*	16.0	13%	22.2	36%
Lai 2010, matched*	15.2	6%		
German glioma network, all patients	11.3	8%	11.9	17%
German glioma network, matched*	17.0	17%	15.4	26%

* Matched for eligibility for Phase II RINTEGA trials (EGFRvIII+, GTR, radiation/TMZ, no progression through ~3 months post-diagnosis)

1. Inda, Genes Dev. 2010
2. Al-Nedawi, Nat Cell Biol. 2008
3. Wong, JCO. 2008
4. Fan, Cancer Cell 2013

Celldex therapeutics

Rationale for RINTEGA Plus Bevacizumab in Relapsed GBM

- Promising PFS/OS from Phase 2 studies in newly diagnosed, resected, EGFRvIII-expressing GBM[1-3]
- Anecdotal evidence suggests that RINTEGA may induce specific immune responses and regression in multifocal and bulky tumors
  - Marked tumor regression with RINTEGA in combination with standard treatments (compassionate use experience)
- Bevacizumab (BV) may optimize EGFRvIII-specific immune response[4-6]
  - VEGF may mediate immunosuppression (impairs DC maturation, alters tumor endothelium, potentially decreasing immune cell infiltration)
  - BV enhances immune-mediated anti-tumor effect in tumor models

Expected Outcome for Relapsed GBM Treated with BV[7]

ORR (%)	PFS6 (%)	Median PFS (months)	Median OS (months)
28	43	4.2	9.2

1. Sampson, JCO 2010
2. Sampson, Neuro-Onc 2010
3. Schuster, Neuro-Onc 2015
4. Johnson, Expert Opin. Biol. Ther. 2007
5. Shrimali, Cancer Research 2010
6. Osada, Cancer Immunol Immunother 2008
7. Friedman, JCO 2009

Celldex therapeutics

Study Design

BV-naïve GBM
1st or 2nd relapse
(n=70)
No prior bevacizumab or VEGF/ VEGFR therapy

Randomization (1:1)

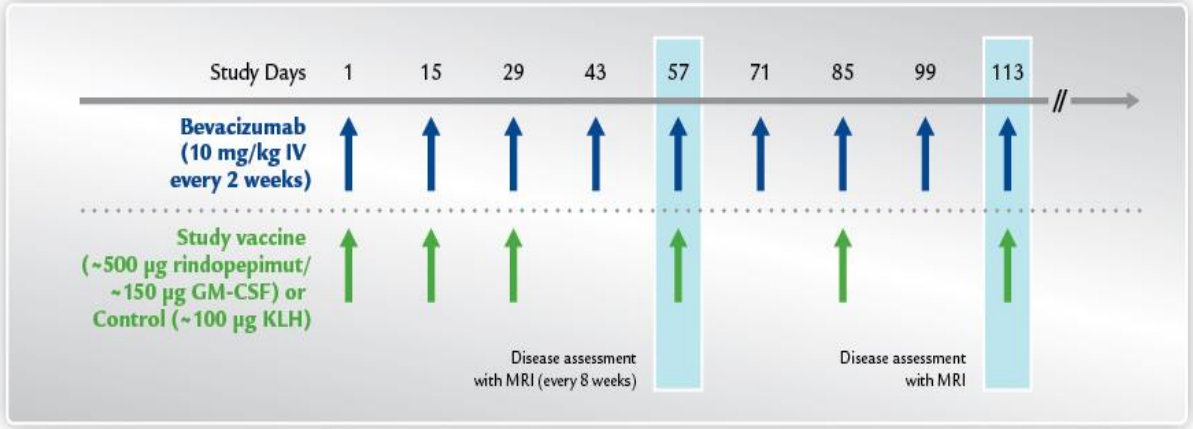
Double-blind treatment

RINTEGA + BV

Control (KLH) + BV

Additional eligibility requirements

- EGFRvIII+ (as per centralized IDE-approved RT-PCR assay)
- Prior conventional radiation and temozolomide
- ≤ 4 mg of dexamethasone daily
- No gliomatosis cerebri, infratentorial, leptomeningeal or metastatic disease
- No prior intracerebral agents, antibody-based therapy within 28 days, non-protein based agents within 14 days, or radiation within 3 months of entry



Design and results of a single-arm study portion evaluating RINTEGA for BV-refractory GBM have been presented previously (Reardon, Neuro Onc 2013; Reardon ,Neuro Onc 2014).

Celldex therapeutics

Study Analyses

Randomized Phase 2 study designed to estimate outcome for patients with relapsed EGFRvIII+ GBM treated with standard of care +/- RINTEGA

- Primary Analysis: PFS at 6 mos (PFS6) for intent-to-treat (ITT) population
  - Study Design: PFS6 of 40%[1] vs 60%, 1-sided α = 0.2, power = 80%
  - Assessed by a blinded independent review committee (IRC)
- Secondary Analyses: ORR, PFS, OS, safety and tolerability, EGFRvIII-specific immune response
- Supportive/sensitivity analyses: Per-Protocol (PP) population
  - Excludes patients with significant protocol deviations:
    - Randomized but did not receive study treatment (n=1)
    - Screening scan after initiation of BV (n=2)
    - Screening scan > 28 days prior to Day 1 (n=3)
- Tumor response evaluation by RANO criteria:[2] assessment incorporates radiographic data, steroid use and clinical status

1. Friedman, JCO 2009 2. Wen, JCO. 2010

Patient Characteristics

		RINTEGA + BV (n=36)	Control + BV (n=37)
Age, years (median [range])		59 (44-79)	55 (30-75)
≥50 years (n [%])		35 (97%)	27 (73%)
Male (n [%])		19 (53%)	22 (59%)
KPS (n [%])	100	2 (6%)	5 (14%)
	90	13 (36%)	13 (35%)
	80	14 (39%)	12 (32%)
	70	7 (19%)	7 (19%)
Primary GBM (n [%])		35 (97%)	35 (95%)
Time from diagnosis to study entry, months (median [range])		10.8 (3.7-55.2)	11.6 (4.7-38.3)
Prior relapses (n [%])	1	33 (92%)	28 (76%)
	2	3 (8%)	9 (24%)
Surgery after last relapse (n [%])		15 (42%)	10 (27%)
Gross-total resection		14 (39%)	6 (16%)
Partial resection/unspecified		1 (3%)	4 (11%)
On steroids at study entry (n [%])		18 (50%)	19 (51%)

Celldex therapeutics

Safety

- Mean (range) number of vaccinations
  - RINTEGA + BV: 9.1 (3, 35)
  - Control + BV: 6.3 (2, 23)
- RINTEGA + BV was well-tolerated
  - No unexpected toxicity associated with BV administration
  - No SAEs attributed to RINTEGA
  - No discontinuations due to RINTEGA treatment-related AEs
  - Frequent grade 1-2 injection site reactions
  - One G2 hypersensitivity reaction
  - No evidence of increased cerebral edema

Most Frequent Adverse Events
(Regardless of relationship to study treatment)

	RINTEGA + BV (n=35)		Control + BV (n=37)	
	≥ Grade 3	Overall	≥ Grade 3	Overall
Arthralgia	-	8(23%)	1(3%)	2(5%)
Back pain	2(6%)	6(17%)	-	3(8%)
Convulsion	4(11%)	7(20%)	-	9(24%)
Diarrhea	-	6(17%)	-	2(5%)
Fatigue	-	9(26%)	2(5%)	9(24%)
Headache	-	8(23%)	2(5%)	9(24%)
Hemiparesis	-	2(6%)	2(5%)	6(16%)
Hyperglycaemia	-	3(9%)	3(8%)	4(11%)
Hypertension	1(3%)	8(23%)	3(8%)	9(24%)
Musculoskeletal pain	-	-	2(5%)	4(11%)
Nausea	-	8(23%)	1(3%)	4(11%)
Vomiting	-	6(17%)	-	2(5%)

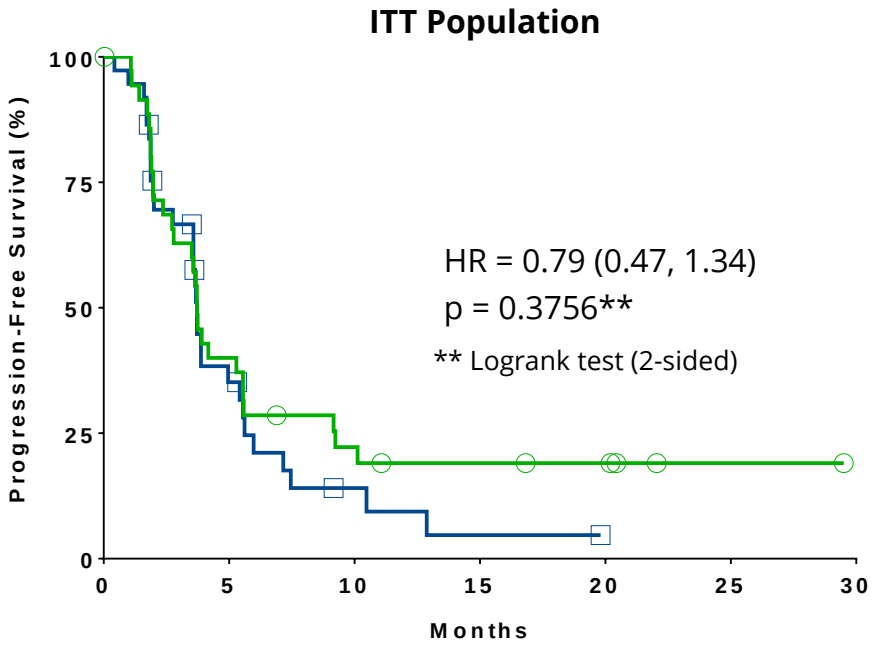
Includes any adverse event occurring at ≥15% frequency, or in >2 patients at severity Grade ≥3, in either treatment group (excluding injection site reactions).

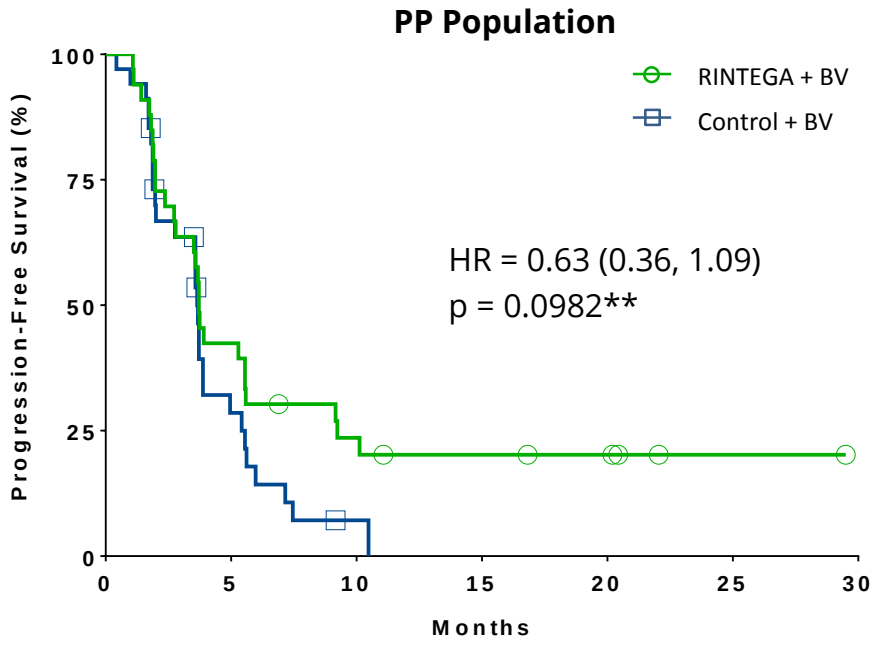
Celldex therapeutics

Progression-Free Survival

	Primary Endpoint: PFS6 (Crude rate)			
	ITT Population		PP Population	
RINTEGA + BV	10/36 (28%)	p = 0.1163*	10/33 (30%)	p = 0.0310*
Control + BV	6/37 (16%)		4/34 (12%)	

** Chi-square test (1-sided). Study is designed to detect a PFS6 difference with 1-sided $\alpha = 0.2$. Data based on independent expert radiographic review.*

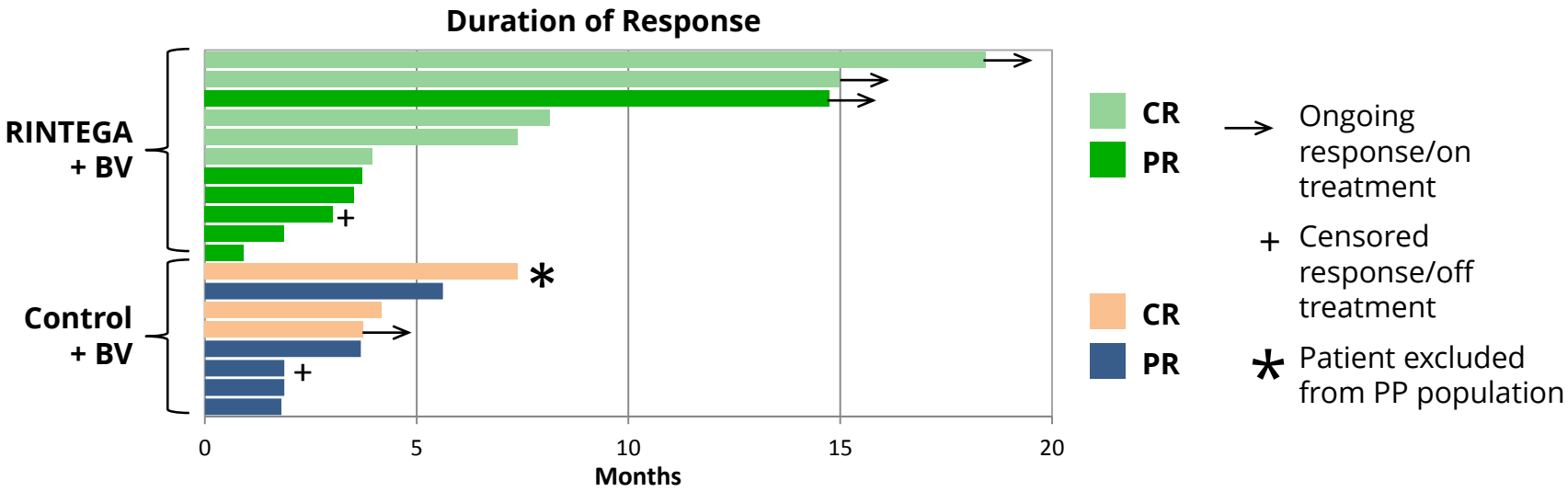




Radiographic Response

	ITT Population		PP Population	
	RINTEGA + BV	Control + BV	RINTEGA + BV	Control + BV
ORR (confirmed CR/PR)	9/30 (30%)	6/34 (18%)	9/29 (31%)	5/32 (16%)
Any response (≥50% shrinkage) including those not sustained at subsequent assessment	11/30 (37%)	8/34 (24%)	11/29 (38%)	7/32 (22%)

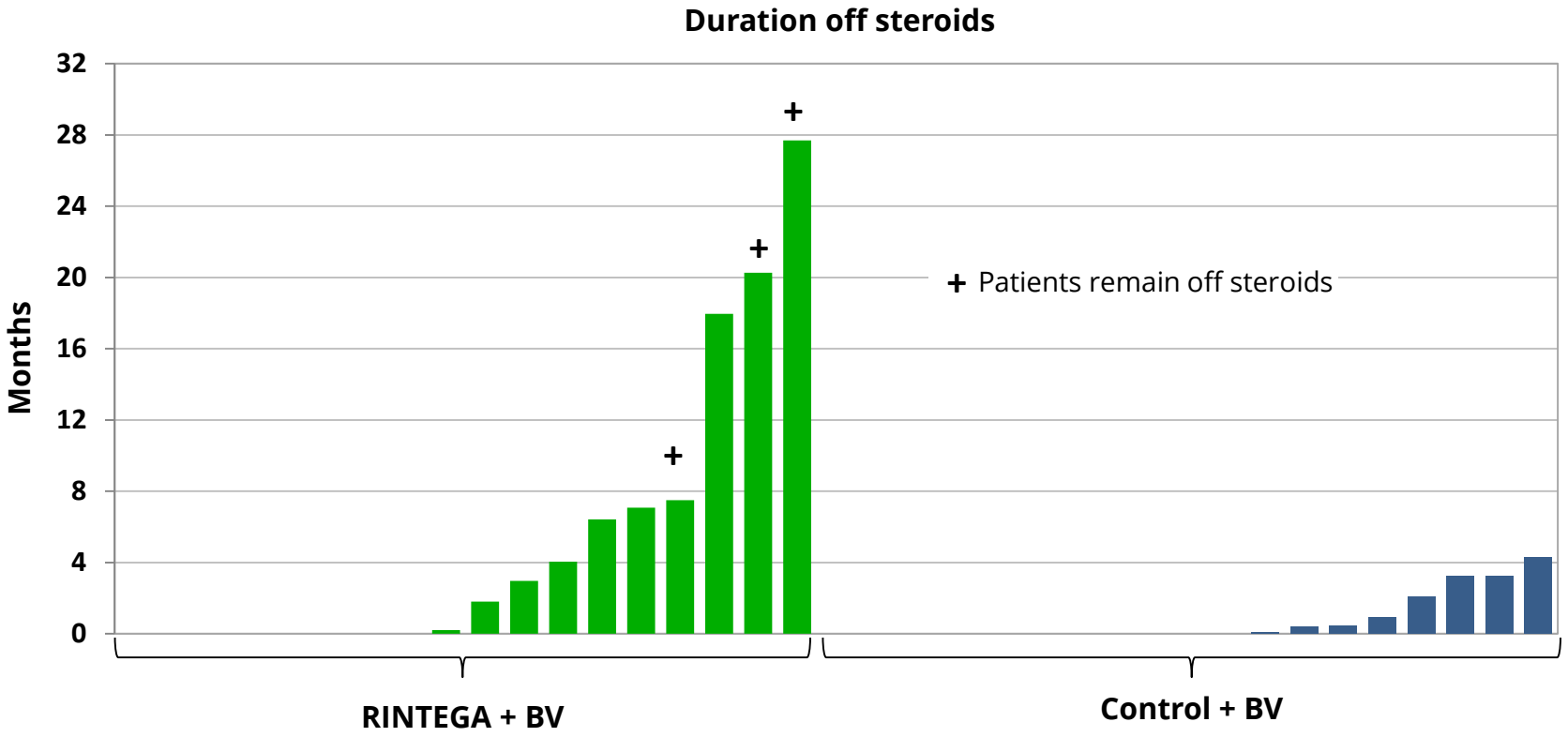
Response-evaluable patient subset with measurable disease. Data based on independent expert radiographic review.



Reduction in Steroid Use

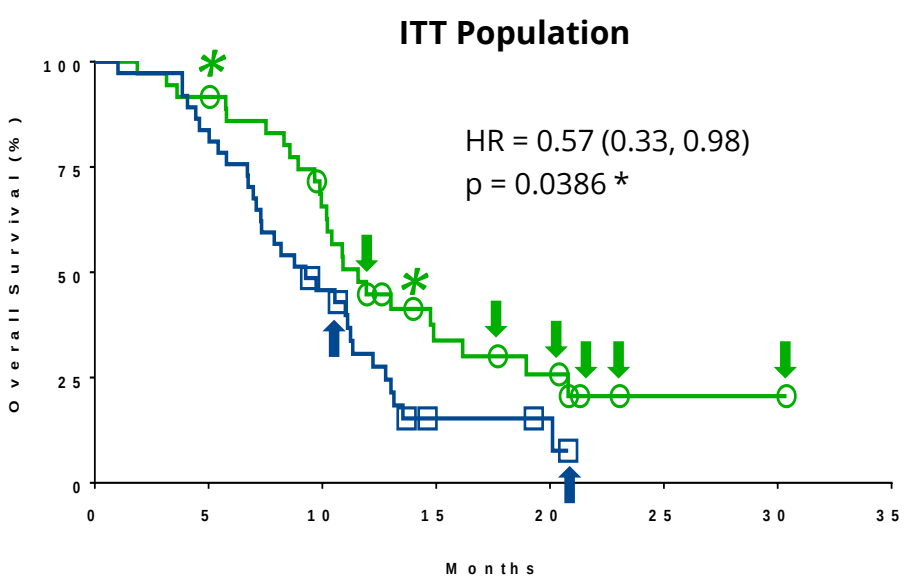
	RINTEGA + BV	Control + BV
Able to stop steroids for any duration*	10/18 (56%)	8/19 (42%)
Able to stop steroids for ≥2 months*	8/18 (44%)	4/19 (21%)

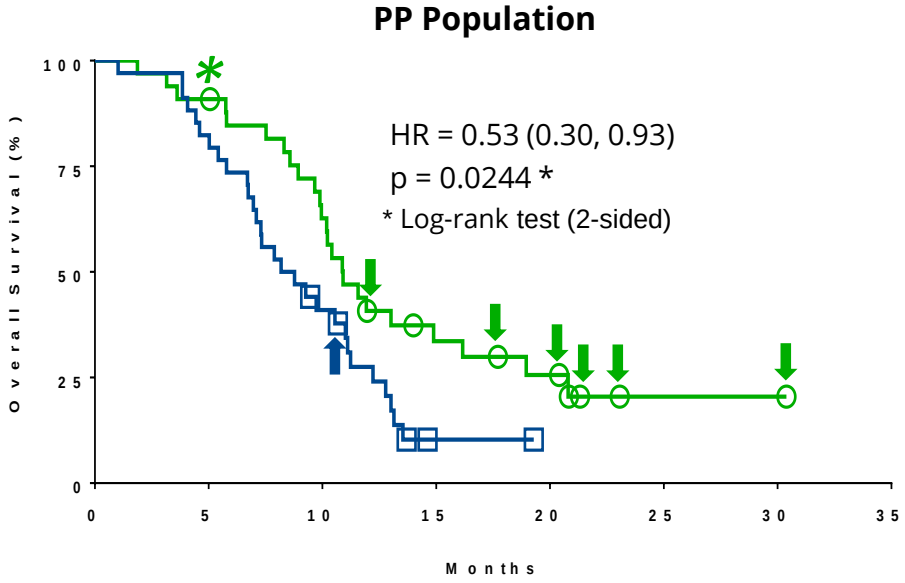
**Subset on steroids at study entry*



Overall Survival

	ITT Population			PP Population		
	Median (95% CI)	OS 12	OS 18	Median (95% CI)	OS 12	OS 18
RINTEGA + BV	11.6 (10.0, 16.2)	45%	30%	10.9 (9.7, 16.2)	41%	30%
Control + BV	9.3 (7.1, 11.3)	31%	15%	8.5 (6.8, 11.1)	28%	10%

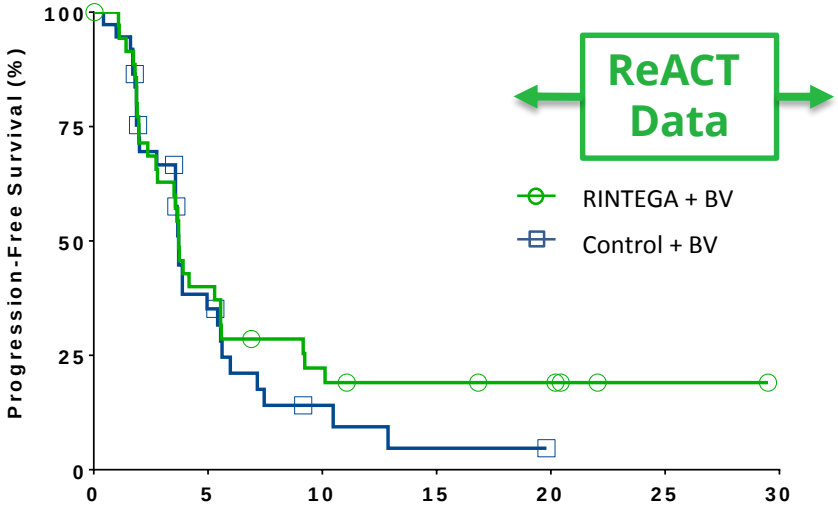


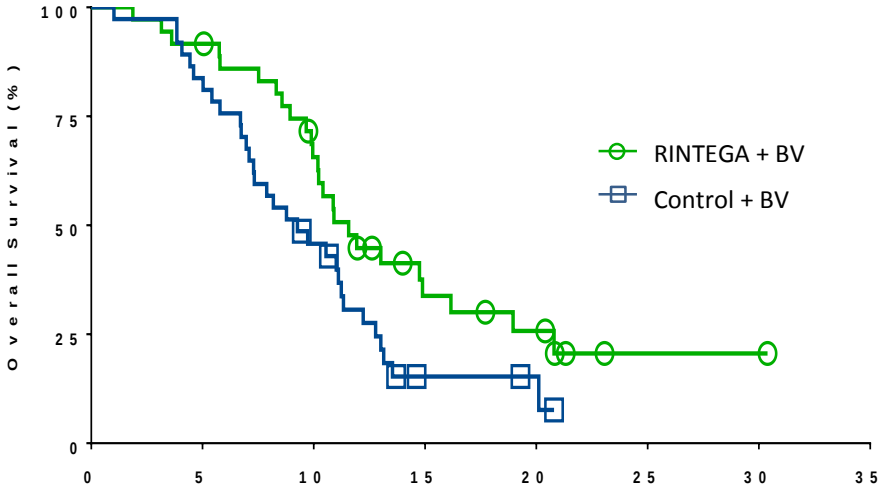


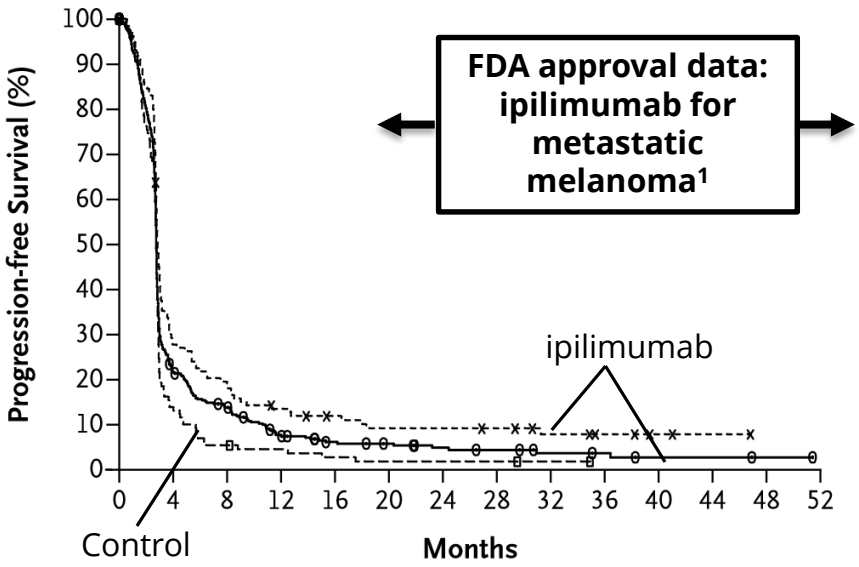
Patients have not yet experienced progression of disease on study treatment

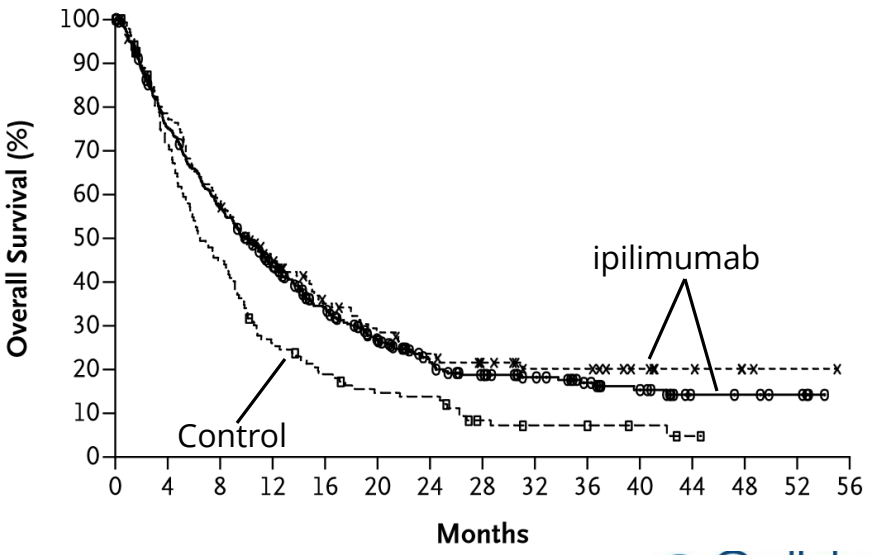
Patients discontinued study follow-up

ReACT Results are Consistent with Immunotherapy Experience







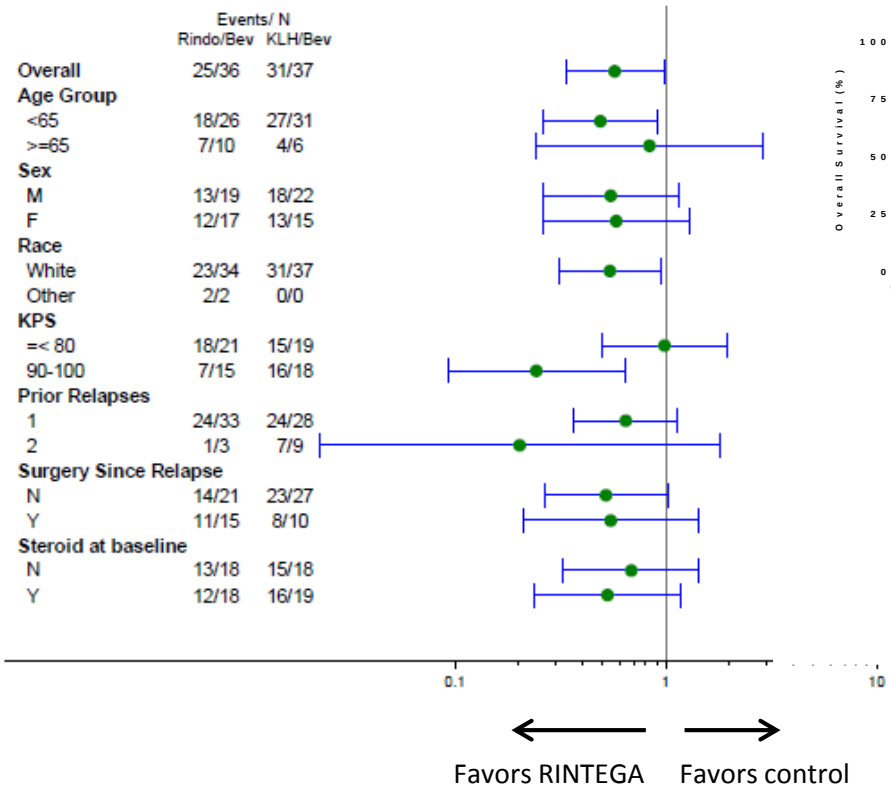


1. Hodi NEJM 2010

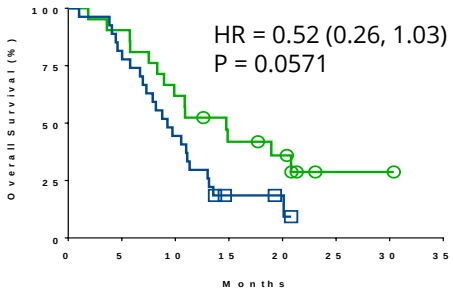
Celldex therapeutics

Overall Survival: Sub-group Analysis

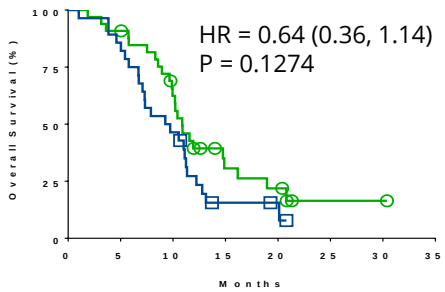
ITT Population



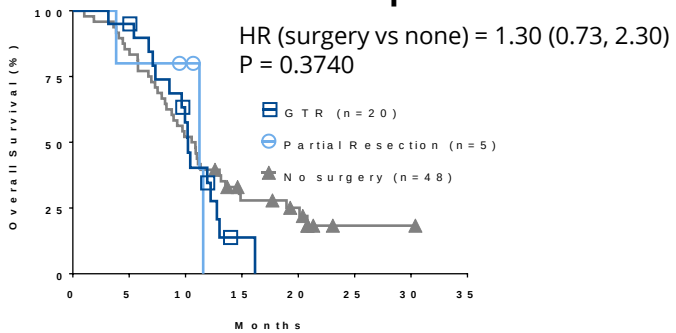
No surgery after last relapse



One prior relapse



All patients, by whether surgery after last relapse



Prior surgery did not portend a better outcome in this population.

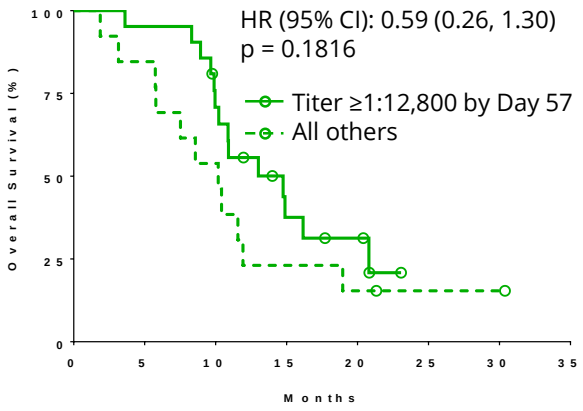
Anti-EGFRvIII Immune Response

Robust Anti-EGFRvIII Immunity Induced by RINTEGA + BV

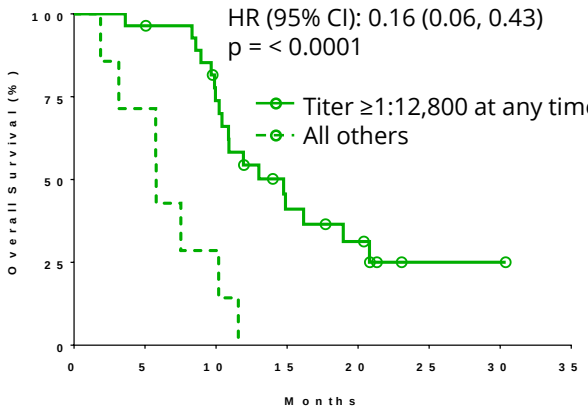
- 4-fold increase in anti-EGFRvIII Ab titers in 89% of patients (nearly all remaining patients treated for < 1-2 months)
- High-titer response (1:12,800 to 1:6,553,600) in 80% of patients
- Robust humoral response similar to that seen in studies of newly diagnosed patients, despite advanced disease, use of steroids, presence of bulky tumor
- The prominent isotype is IgG1
- Titer correlates with binding to EGFRvIII+ glioma cells
- Antibodies can mediate tumor cell killing via ADCC and CDC

Anti-EGFRvIII Response Associated with Prolonged Survival

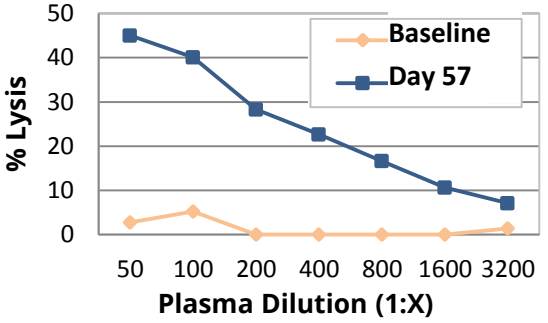
Early (Day 57) Antibody Response



Overall Antibody Response



Tumor Cell Killing by Anti-EGFRvIII Antibodies From RINTEGA Treated Patients



Data from representative patient
Target cells: EGFRvIII transfected U87 glioma cells
Effector cells: Peripheral blood mononuclear cells

Celldex therapeutics

Conclusions

- RINTEGA was very well tolerated without additive toxicity to bevacizumab
- Bevacizumab-naïve patients
  - The randomized Phase 2 study met its primary endpoint of PFS6:
  - 28% vs. 16% (p = 0.1163)
  - Overall survival advantage (HR=0.57, p=0.0386) with apparent long-term survival benefit
  - Advantage to RINTEGA therapy across multiple endpoints including long-term progression-free survival, objective response rate and steroid requirement
- Bevacizumab-refractory patients: Evidence of rare and prominent tumor regression
  - Up to 11% objective response rate
- Activity profile consistent with prior immunotherapy experience[1]
- Remarkable frequency and level of anti-EGFRvIII immune responses despite prior chemotherapy and growing tumor
  - Development of anti-EGFRvIII titer may be a biomarker of improved outcome
- The Phase 3 trial in newly diagnosed patients (ACT IV) has completed accrual and the first interim analysis is to be performed this summer

1. Hodi, NEJM 2010

Acknowledgements

The ReACT patients and their families

The ReACT Study Investigators and Coordinators

Ron Steis & Kathy Frank
Lynn Ashby & Andrea Ralph
Karen Fink & Sara Gonzales
David Peereboom & Marci Ciolfi
David Reardon & Karly Griffin
Laszlo Mechtler & Olga Ananina
Annick DesJardins & Shelly Dutton
Samual Goldlust & Lori Cappello
John Trusheim & Meghan Hultman
Michael Lim & Susan Zhen
Richard Green & Sandra Baker-Bolden
Tara Morrison & Yasmin Candelo
J. Paul Duic & R. Kimberly Prabhu
Jorg Dietrich & Tucker Cushing
Atif Hussein & Norma Cuervo
Joseph Landolfi & Charles Probeni
Ryan Merrell & Nancy Miedzianowski
Nicholas Avgeropoulos & Mollie Geismer
Jeff Chen & Susan Staat
Erin Dunbar & Michelle Humphreys
Heinrich Elinzano & Wendy Turchetti
Nina Paleologos & Amanda Begley
Gordon Skralovic & Vivki Gilreath
Gordon Li & Sophie Bertrand
Agnieszka Kowalska & Susan Fiore
Tara Benkers & Nathan Hansen
Lawrence Berk &Sharon Porth
Morris Groves & Marlena Griffin
Nicholas Butowski & Thelma Munoz
Andrew Sloan & Gina Cascone
Louis Nabors & Thiru Pillay
Daniela Bota & Jinah Chung
Maciej Lesniak, Lucas Rimas, Kelly Nicholas &
Christina Amidei
Richard Curry & Suzanne Sifri
Denise Damek & Monica Robischon
Larry Junck & Adam Booth
James Schuster & Chau Nguyen
Jan Drappatz & Melinda Vargas-Jaffe
Nimish Mohile & Jennifer Serventi
Sigmund Hsu & Greg Lu
Maciej Mrugala & Ashley Waldie
Naveed Wagle & Aida Lozada
Nitin Chandramouli & Robbyn Oliver
Reid Thompson & Tom Leonard-Martin
Glenn Lesser & Jennifer MacLean
David Tran & Madelyn Kissel

Independent Expert Radiographic Review Panel

Raymond Y. Huang, MD, PhD
Associate Radiologist, Dept. of Radiology/Neuroradiology
Brigham and Women's Hospital

Whitney Pope, MD, PhD
Associate Professor, Radiology
Director, UCLA Brain Tumor Imaging
David Geffen School of Medicine at UCLA

John deGroot, MD (adjudication)
Associate Professor, Department of Neuro-Oncology
Director, Neuro-Oncology Fellowship Program
Director, Clinical Research, Department of Neuro-Oncology
University of Texas MD Anderson Cancer Center

Celldex Therapeutics, Inc.
The ReACT study team

For his pioneering work and continued collaboration in the development of RINTEGA:
John H. Sampson, MD, PhD
Professor of Neurosurgery and Chief of the Division of Neurosurgery at Duke University Medical Center

Celldex therapeutics

Celldex
therapeutics