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A phase II, multicenter trial of rindopepimut (CDX-110) in newly diagnosed glioblastoma: the ACT III study

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See the editorial by Lim, on pages 771–772.

Background. The epidermal growth factor receptor variant III deletion mutation, EGFRvIII, is expressed in ~30% of primary glioblastoma and linked to poor long-term survival. Rindopepimut consists of the unique EGFRvIII peptide sequence conjugated to keyhole limpet hemocyanin. In previous phase II trials (ACTIVATE/ACT II), rindopepimut was well tolerated with robust EGFRvIII-specific immune responses and promising progression-free and overall survival. This multicenter, single-arm phase II clinical trial (ACT III) was performed to confirm these results.

Methods. Rindopepimut and standard adjuvant temozolomide chemotherapy were administered to 65 patients with newly diagnosed EGFRvIII-expressing (EGFRvIII+) glioblastoma after gross total resection and chemoradiation.

Results. Progression-free survival at 5.5 months (~8.5 mo from diagnosis) was 66%. Relative to study entry, median overall survival was 21.8 months, and 36-month overall survival was 26%. Extended rindopepimut vaccination (up to 3.5+ years) was well tolerated. Grades 1–2 injection site reactions were frequent. Anti-EGFRvIII antibody titers increased ≥4-fold in 85% of patients, and increased with duration of treatment. EGFRvIII was eliminated in 4/6 (67%) tumor samples obtained after >3 months of therapy.

Conclusions. This study confirms, in a multicenter setting, the preliminary results seen in previous phase II trials of rindopepimut. A pivotal, double-blind, randomized, phase III trial ("ACT IV") is under way.

Keywords: ACT III, EGFRvIII, glioblastoma, glioma, rindopepimut.

The epidermal growth factor receptor variant III deletion mutation, EGFRvIII, results in a constitutively activated receptor with a novel, highly immunogenic extracelluar epitope. EGFRvIII is present in 25%–30% of glioblastomas[1] but is not significantly expressed in healthy tissue. Expression of EGFRvIII correlates with increased tumorigenicity in mouse models.[2] In glioblastoma, EGFRvIII has been associated with poor long-term survival, independent of other known significant prognostic factors, such as gross total resection (GTR).[3–6] EGFRvIII expression is often heterogeneous in glioblastoma specimens, but EGFRvIII+ cells may influence neighboring EGFRvIII–tumor cells through cytokines and microvesicles, providing a proliferative signal even to nonexpressing cells.[7–9] EGFRvIII is also frequently expressed in glioblastoma tumor stem cells.[10,11]

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EGFRvIII and isocitrate dehydrogenase (IDH) 1/2 mutations, the latter associated with long-term survival, rarely coexist in the same patient.[12,13]

Rindopepimut vaccine consists of the unique 13 amino acid sequence created by the in-frame deletion of EGFRvIII, chemically conjugated to keyhole limpet hemocyanin (KLH) as described by Heimberger and colleagues.[14] Rindopepimut is designed to generate a specific immune response against EGFRvIII+ tumor cells, an approach which may be particularly relevant for glioblastoma, where diffuse infiltration of tumor into healthy white matter presents a treatment challenge. Preclinical models have demonstrated that induction of humoral and cellular anti-EGFRvIII immune responses can be effective against EGFRvIII+ intracranial tumors.[14] In 2 small single-arm phase II trials conducted at MD Anderson and Duke University ("ACTIVATE" and "ACT II"),[6,15] rindopepimut was well tolerated in patients with resected, EGFRvIII+ glioblastoma with promising progression-free survival (PFS) and overall survival (OS) compared with a contemporary cohort of patients matched for major study eligibility. In addition, the vaccine elicited robust anti-EGFRvIII immune responses despite concurrent temozolomide chemotherapy, and EGFRvIII was routinely eliminated in posttreatment tumor samples obtained at recurrence. The current study ("ACT III") was performed to confirm these results in a larger, multicenter trial.

Methods

Study Design

The ACT III study (Protocol CDX110-003) was originally an open-label, randomized phase II/III trial to evaluate the clinical activity of rindopepimut in patients with newly diagnosed, resected glioblastoma. The phase II portion had a primary endpoint of PFS, and up to 90 patients were to be randomized in a 2:1 ratio to receive rindopepimut with standard adjuvant temozolomide, or temozolomide alone. However, the study was converted to an open-label, phase II, single-arm design following near-complete voluntary attrition of the first 16 patients randomized to receive temozolomide alone. The primary objective of the redesigned study was to evaluate PFS status at 5.5 months from study day 0 (PFS5.5), which coincided with the third disease assessment. Secondary study objectives were to assess OS, safety, and immune responses to rindopepimut vaccinations. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice Guidelines. Research ethics board approval was obtained prior to initiation of the study at each of the participating institutions, and all patients signed written informed consent prior to any protocol-specific procedures.

Patients

Men and women ≥18 years of age with newly diagnosed, de novo glioblastoma confirmed EGFRvIII+ by central immunohistochemistry (IHC) were enrolled. Eligible patients had prior GTR (residual disease ≤1 cm^2), followed by standard chemoradiation consisting of at least 90% of the standard planned radiotherapy dose (typically 60 Gy) and at least 80% of the planned dose density of continuous daily temozolomide (typically 75 mg/m^2 body surface area per day from the start to end of radiotherapy).

Patients were excluded if they had progression of disease prior to enrollment, Karnofsky performance status (KPS) <70%, or systemic corticosteroid doses >2 mg of dexamethasone (or equivalent) per day; received an experimental drug within 60 days prior to enrollment; or had undergone stereotactic radiosurgery or placement of carmustine wafers. Exclusionary conditions included diffuse leptomeningeal disease, gliomatosis cerebri, active systemic infection requiring treatment, known immunosuppressive disease, concurrent neurodegenerative disease, pregnancy or lactation, hypersensitivity to any vaccine components, and history of anaphylactic reactions to shellfish proteins.

Treatment

Rindopepimut vaccinations consisted of 500 μg rindopepimut admixed with 150 μg granulocyte-macrophage colony-stimulating factor (Leukine, Bayer/Sanofi-Aventis) in 0.8 mL volume, administered as 4–8 separate intradermal injections within an area of 3–5 cm in diameter in the groin.

Study treatment began 14–20 days after completion of standard chemoradiation. Rindopepimut was administered in an initial vaccine priming phase (days 0, 14, and 28), and then monthly, concurrent with standard adjuvant temozolomide chemotherapy (targeted dose of 200 mg/m^2; days 1–5 of repeated 28-day cycles). As prior studies have shown that potent cellular and humoral immune responses can be generated when patients are immunized during recovery from temozolomide-induced lymphopenia,[15] rindopepimut was administered on approximately the 21st day of each temozolomide cycle. Chemotherapy continued for at least 6 cycles, with additional cycles permitted when consistent with local standards of care. Rindopepimut vaccination continued until intolerance or disease progression.

On-Study Evaluation

Physical examination, vital signs, and routine hematology, blood chemistry, and urinalysis were performed throughout study participation. Brain MRI was conducted prior to enrollment (within 20 days after completion of chemoradiation) and every 8 weeks until documented progression of disease. Tumor response was assessed by the investigator in accordance with the Macdonald response criteria for malignant glioma,[16] with one modification: in these patients with minimal residual disease, the total area of the progressing lesion(s) needed to exceed 1 cm^2 to constitute radiographic progression. Following progression of disease, all patients were followed for survival.

Statistical Methodology

The null hypothesis (H_0) for the primary endpoint of the redesigned, single-arm phase II study was that PFS5.5 would be ≤53%, while the alternative hypothesis (H_A) was that PFS5.5 would be ≥73%. H_0 was estimated from published results for standard of care radiation and temozolomide in which 45% of patients were alive and progression free at 8.5 months from diagnosis (roughly equivalent to 5.5 mo from study entry).[17] With up to 60 patients receiving rindopepimut, the study had ~90% power to reject H_0 in favor of H_A based on a one-sample exact binomial test and a one-sided significance level of .05.

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The durations of PFS and OS were summarized descriptively using the Kaplan–Meier method. For PFS analysis, patients last known alive without progression or who did not have progression within 28 days after initiation of an alternate anticancer therapy were censored as of the last evaluable disease assessment. Patients without on-study disease assessments or death prior to the first scheduled disease assessment were censored as of study day 0. For OS, patients last known alive were censored as of the last contact date. Subgroup analysis by O^6-methylguanine–DNA methyltransferase (MGMT) promoter methylation status was performed using the Cox proportional hazards model. PFS and OS outcomes were compared in an exploratory manner to earlier rindopepimut studies and matched historical controls.

Data for the patients randomized to receive rindopepimut prior to the study redesign were included in all analyses.

Correlative Studies

EGFRvIII expression

Formalin fixed paraffin embedded (FFPE) tumor tissue was analyzed centrally by IHC and polymerase chain reaction (PCR) methods. Study eligibility was based solely on IHC, with a positive result defined by EGFRvIII expression in ≥10% of cells. IHC was performed on slides using affinity purified rabbit anti-EGFRvIII antibody and detection with Envision+ (Dako). For PCR, RNA was extracted following macro-dissection of hematoxylin-and-eosin stained sections of tumor tissue using the Stratagene Absolute RNA FFPE Tissue Kit. The real-time reverse transcription PCR assay employs the use of forward primer 5′ ggc tct gga gga aaa gaa agg ta and reverse primer 5′ ccg tct tcc tcc atc tca tag c to selectively amplify the EGFRvIII transcript. A fluorescent-labeled nucleic acid probe (5′ FAM-att atg tgg tga cag atc a) was used as the means of detecting the EGFRvIII transcript.

MGMT promoter methylation

FFPE tumor samples were analyzed centrally (MDx Health) by methylation-specific PCR.

Humoral responses to the vaccine

Antibody titers were measured by an enzyme-linked immunosorbent assay using microtiter plates directly coated with EGFRvIII peptide or KLH. Dilutions of patient plasma were incubated in the plates, and the anti-EGFRvIII antibodies were detected with an Fc fragment specific goat anti-human IgG antibody conjugated to horseradish peroxidase (Jackson ImmunoResearch Labs) followed by tetra-methylbenzidine substrate. Absorbance was measured at a wavelength 450 nm. The antibody titer for patient samples was calculated as the highest dilution with a value greater than twice the background.

Human leukocyte antigen analysis

Typing of human leukocyte antigen (HLA) class I alleles (A and B loci) and HLA class II alleles (–DR locus) by serology or DNA-PCR was performed at a laboratory accredited by the American Society for Histocompatibility and Immunogenetics (ClinImmune Labs) using fresh blood samples.

Generation of Contemporary EGFRvIII+ Glioblastoma Cohort

To provide a contemporary assessment of the prognosis for patients with EGFRvIII+ glioblastoma receiving current standard of care, a retrospective analysis of the Radiation Therapy Oncology Group (RTOG) 0525 trial was performed. As previously described, RTOG 0525 was a randomized phase III trial comparing standard adjuvant temozolomide with a dose-dense schedule in 833 patients with newly diagnosed glioblastoma.[18] PCR for EGFRvIII (as described above) was performed at MD Anderson for the 494 patients from RTOG 0525 with available archived tumor samples. Analysis of OS and PFS by EGFRvIII expression status was performed by RTOG statisticians. To identify a population similar to that enrolled in ACT III, additional subset analyses were performed for patients with GTR, initiation of adjuvant temozolomide (ie, without progression during chemoradiation), and baseline KPS of ≥70.

Results

Patients

Archived tumor specimens for 637 screened patients were submitted from 33 study centers. Of the 617 patients analyzable by IHC, 162 (26%) had >10% of tumor cells expressing EGFRvIII. Eighty-one EGFRvIII+ patients were not enrolled; reasons included residual tumor >1 cm^2 (23%), incomplete/inadequate chemoradiation (15%), progression of disease (14%), and patient choice (10%).

Eighty-one patients were enrolled at 24 centers from August 2007 to November 2009. Prior to the study redesign, 16 patients were randomized to the concurrent control arm, consisting of standard adjuvant temozolomide. However, the majority of these patients withdrew consent for participation after learning of the assigned open-label study treatment. Consequently, the data for these patients are limited and not described further within this report. The pretreatment characteristics of the 65 patients who received rindopepimut are summarized in Table 1.

Dosing and Toxicity

The median duration of temozolomide treatment was 6.6 months (range, 0.1–21.3). Forty-four patients (68%) received ≥6 cycles, including 21 (32%) who received ≥12 cycles. The median duration of treatment with rindopepimut was 7.4 months (range, 0.5–42.3+). Ten patients received rindopepimut for 1.6 to 3.5+ years. The majority (90%) continued rindopepimut until progression.

Rindopepimut was well tolerated with no indication of cumulative toxicity over time. Mild to moderate injection site reactions (ISR), chiefly erythema and pruritus, occurred in nearly all patients. Nearly all resolved without intervention. ISR occurred throughout the duration of long-term treatment, although not all patients experienced ISR with the first few administrations of rindopepimut, or consistently with each injection of

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Table 1. Baseline demographic and clinical characteristics

	All Treated Patients ($N = 65$)
Age, y, median (range)	56 (30–83)
≥50 y, *n* (%)	52 (80)
Male, *n* (%)	33 (51)
KPS, *n* (%)	
100	22 (34)
90	26 (40)
80	11 (17)
70	6 (9)
Time from diagnosis to study entry, mo, median (range)	3.0 (2.4–4.4)
MGMT methylation status, *n* (%)	
Methylated	25 (38)
Unmethylated	40 (62)
EGFRvIII expression, *n* (%)	
By IHC (≥10% of tumor cells)	64 (98)[a]
By PCR	63 (97)[b]

[a]One patient considered negative by IHC (5%, 3+) but positive by PCR was allowed on study.
[b]Two patients were positive by IHC but negative by PCR.

Table 2. Treatment-related toxicity

	CTCAE Grades 3–4, *n* (%)		Any Severity, *n* (%)	
Alanine aminotransferase increased	1	(2)	2	(3)
Angioedema	1	(2)	1	(2)
Asthenia	1	(2)	1	(2)
Blood lactate dehydrogenase increased	1	(2)	2	(3)
Fatigue	1	(2)	17	(26)
Gamma-glutamyl transferase increased	1	(2)	2	(3)
Headache	1	(2)	5	(8)
Hypokalemia	1	(2)	4	(6)
Hypophosphatemia	1	(2)	2	(3)
Injection site bruising	0	(0)	9	(14)
Injection site erythema	0	(0)	56	(86)
Injection site induration	0	(0)	10	(15)
Injection site pain	0	(0)	13	(20)
Injection site pruritus	0	(0)	40	(62)
Injection site rash	0	(0)	12	(18)
Injection site swelling	0	(0)	19	(29)
Injection site urticaria	0	(0)	7	(11)
Leukopenia	1	(2)	2	(3)
Lymphopenia	1	(2)	4	(6)
Nausea	0	(0)	8	(12)
Rash	0	(0)	11	(17)
Toxic epidermal necrolysis	1	(2)	1	(2)
Urticaria	1	(2)	1	(2)

Abbreviation: CTCAE, Common Terminology Criteria for Adverse Events. Table includes events assessed as related to rindopepimut by the investigator and occurring in >10% of patients overall, or in any patients at CTCAE severity grades 3–4. There were no grade 5 treatment-related adverse events.

rindopepimut. Additional treatment-related toxicity included fatigue, rash, nausea, pruritus, and headache (Table 2). Grade 3 or 4 events were relatively rare and limited to single patients. No fatal adverse events were reported.

Three serious adverse events were considered potentially related to rindopepimut. A 60-year-old Asian patient developed toxic epidermal necrolysis, which began as a rash after the first dose of rindopepimut and then worsened after the second dose with associated fever, angioedema, and increased liver function tests. The patient had received prophylactic dapsone for 2.5 months in addition to traditional herbal remedies. The event resolved soon after discontinuation of dapsone and within 12 days of hospital admission. Although the event was consistent with dapsone hypersensitivity syndrome, it is unclear to what degree rindopepimut contributed to the event. A second patient experienced a transient grade 2 hypersensitivity reaction (pruritus, erythema, flushing, and mild shortness of breath) within 10 min of the seventh vaccination, which fully resolved within 1 h of antihistamine and corticosteroid treatment. Study treatment was subsequently discontinued for these 2 patients. A third patient experienced a grade 3 urticarial rash 3 days after the first vaccination, but subsequently received 32 additional monthly vaccinations without recurrence of generalized rash. No additional patients discontinued treatment due to toxicity.

EGFRvIII Expression and Immune Monitoring

The eligibility criterion for positivity (≥10% of cells EGFRvIII+) was met in 162/617 (26%) samples screened by IHC. However, any EGFRvIII expression was detected in 192/617 (31%). Of the 627 samples analyzed by PCR, 196 (31%) were positive. IHC and PCR were concordant for detection of any EGFRvIII expression in 573/609 (94%) samples assessed by both methods.

Tumor samples were obtained at recurrence (at a range of 0.1–2.6 mo after the last rindopepimut vaccination) for 10 patients. Of 6 patients who received rindopepimut vaccine for more than 3 months, 4 (67%) no longer expressed EGFRvIII by IHC, and 3 were also negative by PCR. Maximum anti-EGFRvIII antibody titers achieved within the first 6 months of treatment were 1:6400, 1:51 200, 1:204 800, and 1:409 600 for patients with elimination of EGFRvIII compared with 1:1600 and 1:25 600 for those without. Four additional patients who received limited therapy (treatment durations of 0.5, 0.9, 1.8, and 2.8 mo) had persistent EGFRvIII expression at recurrence. Three had humoral response assessed, and posttreatment peak titers were <1:100, 1:800, and 1:12 800.

Anti-EGFRvIII antibody titers increased ≥4-fold over baseline levels in 46/54 (85%) patients with a baseline and at least one follow-up sample (Fig. 1). Some patients developed high titers following the priming doses of rindopepimut (month 1), whereas the majority of patients developed high-titer responses by 4 months. On average the magnitude of the response plateaued at ~1:50 000 between months 8 and 12; however, a number of patients reached titers well above 1:100 000. Attempts to analyze cellular responses to

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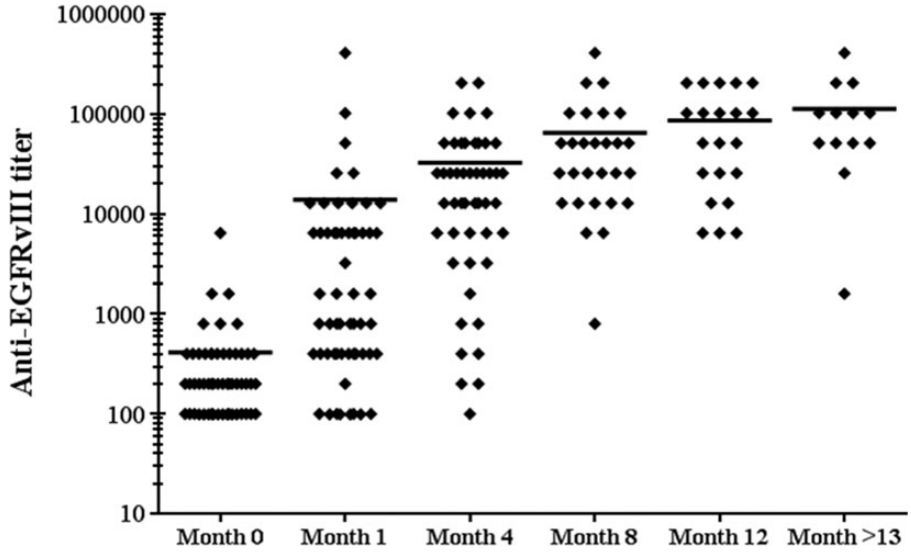

Fig. 1. Anti-EGFRvIII antibody titers. Antibody titers to EGFRvIII were measured by enzyme-linked immunosorbent assay as described under Methods. Each point represents an individual patient titer, while horizontal lines delineate the mean for that time point.

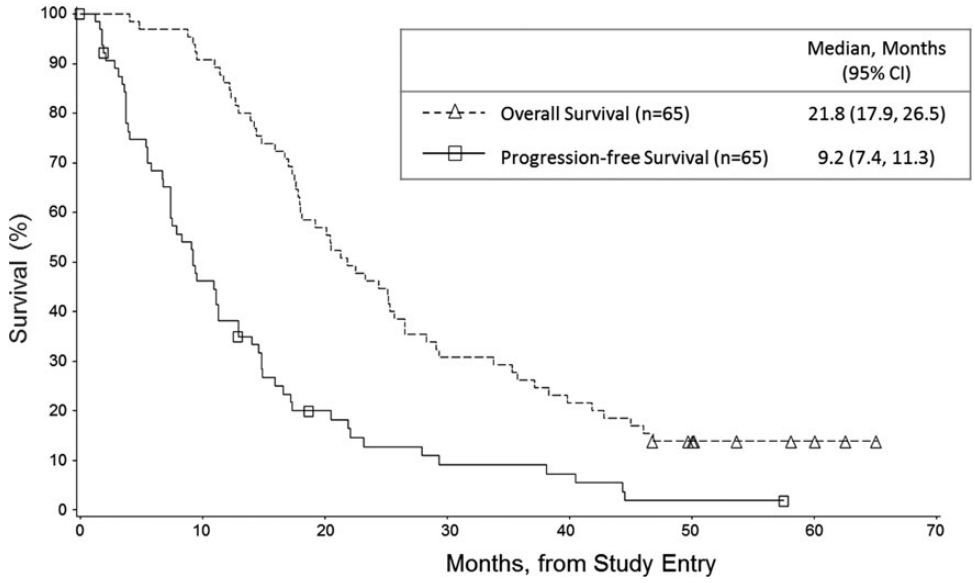

Fig. 2. Kaplan–Meier estimates of PFS and OS. Survival durations are calculated from study entry, representing a median of 3.0 (range, 2.4–4.4) months from diagnosis (as shown in Table 1). Line markers represent censored data.

rindopepimut vaccination by interferon-gamma enzyme-linked immunosorbent spot were unsuccessful in providing clear results, primarily due to the low number of viable and functional T cells from these patients due to temozolomide therapy.

HLA typing was performed for 60 patients. For each HLA type with ≥5 patients available for analysis, PFS and OS were estimated using Kaplan–Meier methods. In this relatively small group of patients, no specific HLA subtypes were associated with significantly prolonged PFS or OS compared with the remaining study population.

Activity

The primary endpoint for promising activity was met. PFS5.5 (equivalent to ~8.5 mo from diagnosis) was 66% (95% CI: 55%–76%), and H_0 was rejected ($P = .0168$). Figure 2 displays OS and PFS measured from study entry, which was generally equivalent to 3 months postdiagnosis. Median PFS was 9.2 months (95% CI: 7.4–11.3) and median OS was 21.8 months (95% CI: 17.9–26.5) from study entry. For patients with methylated MGMT promoter, median PFS was 14.7 months (95% CI: 7.4–20.5) and median OS was 29.3 months (95% CI: 21.8 to [upper limit not estimated]). Patients lacking

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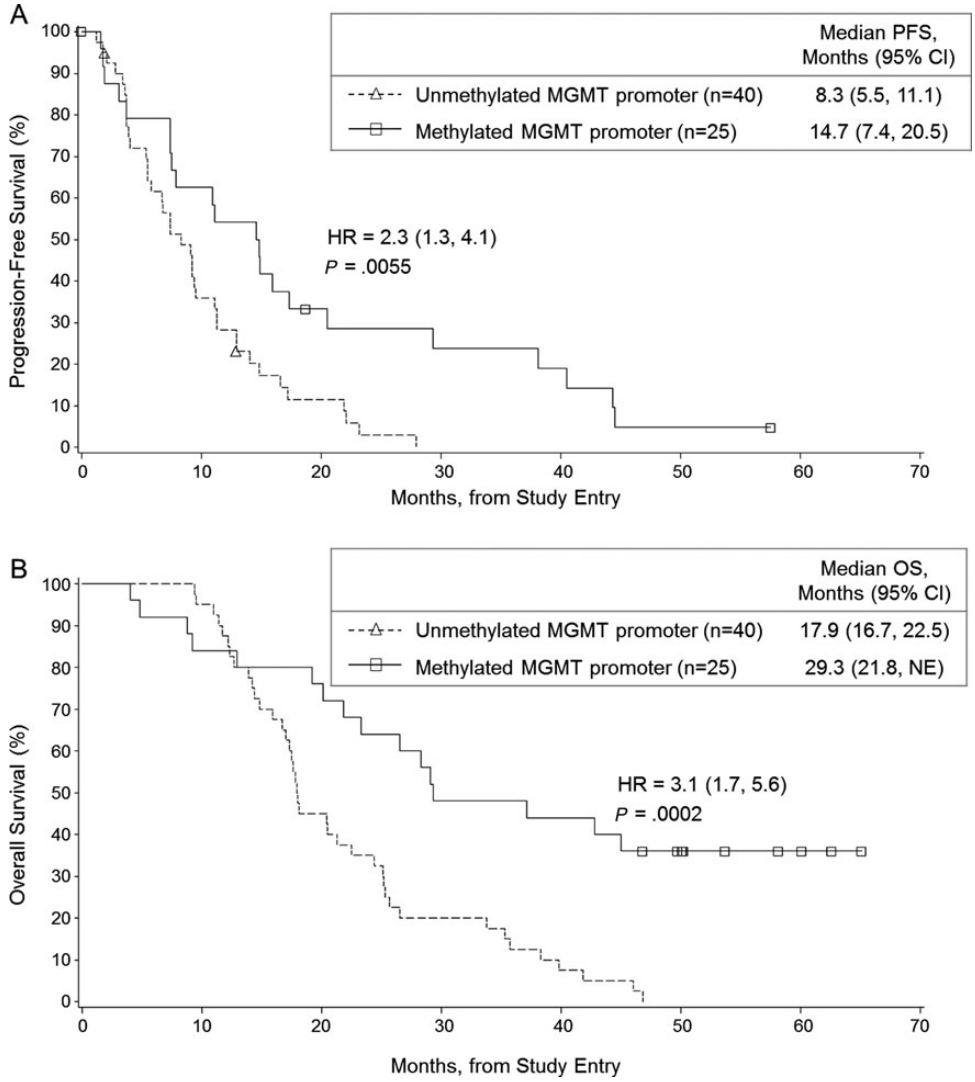

Fig. 3. Kaplan–Meier estimates of PFS and OS, by MGMT promoter methylation status. (A) PFS and (B) OS are calculated from study entry, representing a median of 3.0 (range, 2.4–4.4) months from diagnosis (as shown in Table 1). Line markers represent censored data. HR, hazard ratio; NE, not estimated.

MGMT promoter methylation had median PFS of 8.3 months (95% CI: 5.5–11.1) and median OS of 17.9 months (95% CI: 16.7–22.5) (Fig. 3). Figure 4 displays OS and PFS measured from diagnosis, along with updated outcomes for the prior rindopepimut studies in the same population (ACTIVATE and ACT II).[6,15]

Contemporary EGFRvIII+ Glioblastoma Cohort

Of the 494 patients from study RTOG 0525 with available archived tumor sample, 142 (29%) were determined to have EGFRvIII+ tumor by PCR. Median OS from study registration was 15.1 months for all patients with EGFRvIII+ tumors ($n = 142$) and 17.0 months for those whose tumors did not express EGFRvIII ($n = 352$). For the subset of patients who were matched for ACT III eligibility (including GTR and standard chemoradiation without disease progression), median OS from study randomization was 16.0 months for patients with EGFRvIII+ tumors ($n = 29$) and 22.2 months for those without ($n = 74$).

Discussion

This study confirms, in a multicenter setting, the promising results seen in the 2 previous phase II trials of rindopepimut. All 3 trials resulted in median PFS of 12.3 to 15.3 months from diagnosis, and median OS of ~24 months from diagnosis.

Standard therapy of surgery, chemoradiation, and adjuvant temozolomide has been reported to result in a median PFS of ~8 months and a median OS of ~16–19 months from diagnosis.[17,18] Compared with the patient population enrolled in these studies, the ACT III patients are similar with regard to age and MGMT promoter methylation. However, the ACT III patients were selected for additional favorable prognostic factors,

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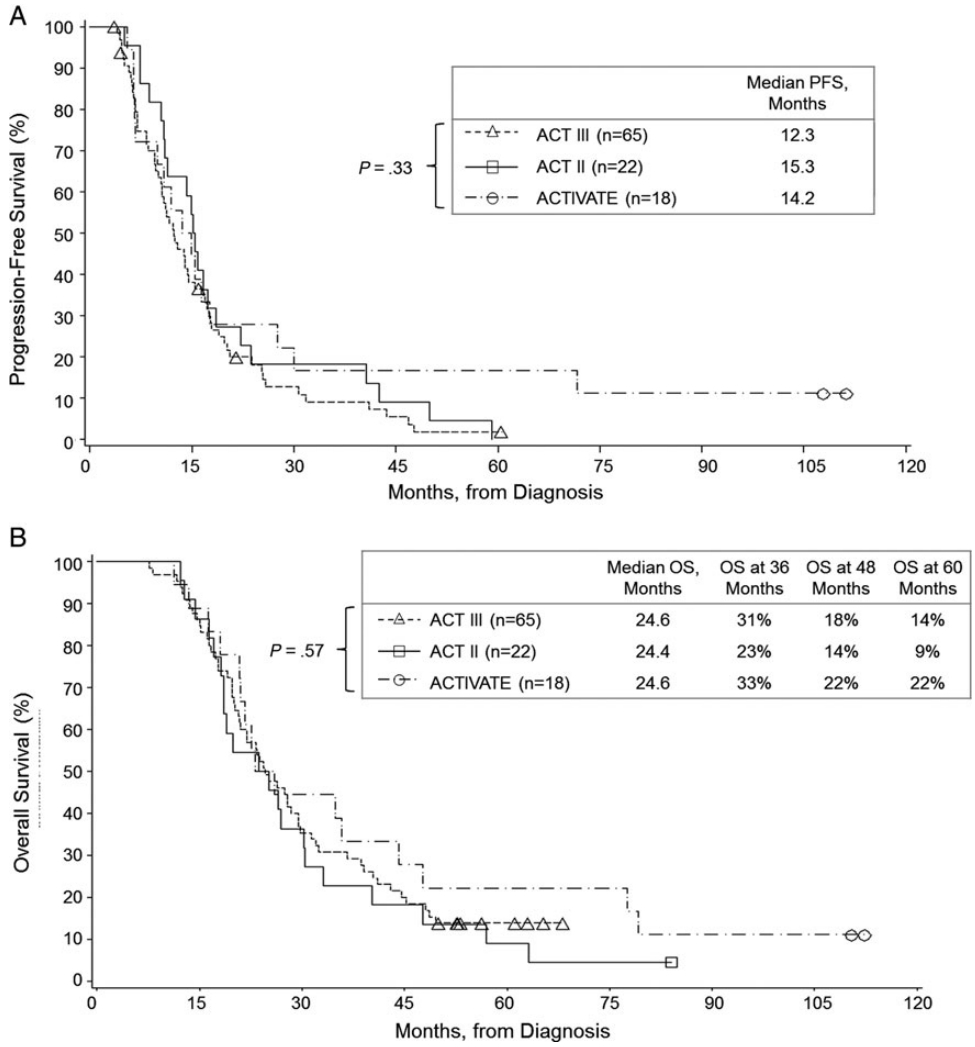

Fig. 4. Kaplan–Meier estimates of PFS and OS for phase II rindopepimut studies. (A) PFS and (B) OS are calculated from diagnosis. Line markers represent censored data. In the 3 rindopepimut studies (ACTIVATE, ACT II, and ACT III), rindopepimut vaccinations began ~3 mo after diagnosis.

including GTR and completion of chemoradiation without progression. Conversely, these patients also had EGFRvIII+ tumors, which has been associated with poor long-term survival independent of other known significant prognostic factors, including GTR.[3] A median survival of 15 months from diagnosis (~12 mo from study entry) was previously reported for a small cohort of patients ($n = 17$) treated at MD Anderson contemporaneously to the ACTIVATE study and matched for eligibility (EGFRvIII+, GTR, radiation/temozolomide, no progression through ~3 mo postdiagnosis).[6] More recently, in a preliminary retrospective analysis of study RTOG 0525 that examined a subset of patients who were matched for ACT III eligibility (including GTR and standard chemoradiation without disease progression), median OS from study randomization was 16.0 months for patients with EGFRvIII+ tumors ($n = 29$) and 22.2 months for those without ($n = 74$). Although these results do suggest a modest improvement over previously reported datasets, the RTOG 0525 data continue to demonstrate that patients with EGFRvIII+ glioblastoma fare worse than the general glioblastoma patient population.

Most patients in all 3 rindopepimut trials produced robust, specific, and durable immune responses, despite concurrent temozolomide therapy. These responses were remarkable for an antigen-specific vaccine, supporting the utility of EGFRvIII as a target. Evidence of EGFRvIII-specific cellular response was noted in some patients, but the quality of lymphocytes from these chemotherapy-treated patients significantly compromises the ability to evaluate peripheral cellular responses to the vaccine. Although the importance of a CD8+ T-cell mediated effect cannot be ruled out, the lack of a clear correlation between HLA type and clinical benefit suggests that this is not the dominant mechanism of response. Preclinical models have shown that humoral immune responses induced by rindopepimut are sufficient to mediate an antitumor effect.[14]

In the ACTIVATE and ACT II studies, loss of EGFRvIII expression was seen in 21/23 (91%) patients with posttreatment assessment of recurrent tumor.[6,15] Similarly, in ACT III, EGFRvIII expression was eliminated in 4/6 (67%) patients with samples of recurrent tumor after >3 months of treatment, and this was

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generally associated with more rapid and robust humoral immune responses. Taken together, these results suggest that immune-mediated eradication of tumor cells bearing EGFRvIII, a "driver" mutation shown to promote tumor growth and proliferation, contributes to prolonged PFS and OS in patients receiving rindopepimut.

The consistent results from the ACT III, ACT II, and ACTIVATE studies are encouraging but associated with the uncertainty inherent to small, open-label, single-arm studies. A pivotal, double-blind, phase III trial ("ACT IV"), randomizing patients with resected, EGFRvIII+ glioblastoma to receive either rindopepimut or a control injection of KLH, is under way. Rindopepimut is also under evaluation in recurrent glioblastoma (the "ReACT" study) and pediatric pontine glioma.

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- 2011 Annual Meeting of the Society for Neuro-Oncology (SNO): Abstract ID: IM-03/Platform Presentation.
- 2010 Annual Meeting of the Society for Neuro-Oncology (SNO): Abstract ID: OT-31/Poster.
- 2010 Annual Meeting of the American Society of Clinical Oncology (ASCO): Abstract ID: 2014/Poster.

Conflict of interest statement. J.A.G., T.K., and T.A.D. are employees of and hold stock options in Celldex. D.D.B. holds equity interest in Celldex. J.H.S. receives funding from license fees paid to Duke University by Celldex. T.K. and T.A.D. are officers of Celldex. S.C. and J.H.S. are paid consultants to Celldex. D.D.B. and A.B.H. hold patents on subject matter related to the research.

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