WEB EXTRA MATERIAL

Table A1. Study-Specific Modifications to RANO Criteria *Online only*

| **Criteria** | **Study-Specific Modification** |
| --- | --- |
| **General** | Corticosteroid dose assessed as the average dose over the seven (7) days prior to the current scan, as compared to the average dose over the seven (7) days prior to the baseline scan |
| **Complete Response:** requires all of the following:* Complete disappearance of all enhancing measurable and non-measurable disease sustained for at least 4 weeks.
* No new lesions.
* Stable or improved non-enhancing (T2/FLAIR) lesions
* Patients must be off corticosteroids (or on physiologic replacement doses only)
* Stable or improved clinically.

Patients with non-measurable disease only cannot have a CR; the best response possible is SD. | Physiologic replacement doses of corticosteroids defined as: up to the equivalent of 20 mg/day of hydrocortisone  |
| **Partial Response:** requires all of the following:* ≥ 50% decrease compared with Baseline in the SPD of all measurable enhancing lesions sustained for at least 4 weeks.
* No progression of non-measurable disease.
* No new lesions.
* Stable or improved non-enhancing (T2/FLAIR) lesions on same or lower dose of corticosteroids compared with Baseline scan.
* The corticosteroids dose at the time of the scan evaluation should be no greater than the dose at the time of the baseline scan.
* Stable or improved clinically.

Patients with non-measurable disease only cannot have a PR; the best response possible is SD. | In order to qualify for Partial Response, subjects must be on a corticosteroid dose that is stable (< 10% increase) or decreased when compared with the dose at the time of the baseline scan. |
| **Stable Disease:** requires all of the following:* Does not qualify for CR, PR or PD.
* Stable non-enhancing (T2/FLAIR) lesions on same or lower dose of corticosteroids compared with baseline scan.
* In the event that the corticosteroid dose was increased for new symptoms and signs without confirmation of disease progression on neuroimaging, and subsequent follow-up imaging shows that this increase in corticosteroids was required because of disease progression, the last scan considered to show stable disease will be the scan obtained when the corticosteroid dose was equivalent to the baseline dose.
 | In order to qualify for Partial Response, subjects must be on a corticosteroid that is < 50% increased when compared with the dose at the time of the baseline scan.  |
| **Progressive Disease:** defined by any of the following:* ≥ 25% increase in SPD of enhancing lesions compared with the smallest (nadir) tumor measurement obtained either at baseline (if no decrease) or best response.
* On stable or increasing doses of corticosteroids.
* Significant increase in T2/FLAIR nonenhancing lesion on stable or increasing doses of corticosteroids compared with baseline scan or best response after initiation of therapy not caused by co-morbid events (e.g., radiation therapy, demyelination, ischemic injury, infection, seizures, post-operative changes, or other treatment effects)
* Any new lesion.
* Clear clinical deterioration not attributable to other causes apart from the tumor (e.g., seizures, medication adverse effects, complications of therapy, cerebrovascular events, infection and so on) or changes in corticosteroid dose.
* Failure to return for evaluation as a result of death or deteriorating condition.
* Clear progression of non-measurable disease.
 | For subjects with little to no residual disease, a 25% increase in area could reflect only imaging variance. As such, to be considered PD, a > 5 mm increase in SLD (of the target lesions) along with a ≥ 25% increase in SPD (of the target lesions) will be required to call PD. |

Table A2. Overall Survival Analyses Adjusted for Baseline Patient Characteristics *Online only*

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| --- | --- | --- |
| Factor | HR (95%CI) | P-value |
| Unadjusted  | 0.53 (0.32, 0.88) | 0.01 |
| Age  | 0.53 (0.32, 0.88) | 0.01 |
| Sex  | 0.54 (0.32, 0.89) | 0.02 |
| KPS  | 0.57 (0.34, 0.94) | 0.03 |
| Prior Relapses  | 0.50 (0.30, 0.83) | 0.007 |
| Surgery since relapse  | 0.51 (0.31, 0.85) | 0.01 |
| Steroid at baseline  | 0.52 (0.31, 0.87) | 0.01 |

The P value for the unadjusted analysis is based on logrank test. The adjusted analysis is based on Wald test from Cox model. Although potential imbalances in baseline patient characteristics existed between treatment arms with regard to the number of patients who underwent surgery at last relapse and number of relapses, this adjusted analysis indicates that these factors do not contribute to the survival advantage observed for the rindopepimut arm.

Figure A1. Duration of Response *Online only*

Patients experiencing complete response are indicated with dark bars, while patients who experienced a partial response are indicated by light gray bars. One patient remaining on treatment with ongoing response is indicated with an arrow. Patients who discontinued treatment in the absence of progression by expert review are indicated with ‘+’. A patient excluded from per-protocol population analyses is indicated with ‘\*’.

Figure A2. Disease Course for Long-Term Survivors. *Online only*

Time from diagnosis to first relapse, from first relapse to second relapse (when applicable), and from most recent relapse to study entry are shown in the left panel, while progression-free survival by central review and overall survival are shown in the right panel, for the patients who experienced survival of at least 18 months on study. Patients who remain alive at final analysis (as of the cut-off date of May 25, 2016) are indicated with ‘→’, while patients without progression by central review (as of the cut-off date of September 1, 2015) are indicated with ‘\*’.

Figure A3. Example of a radiographic response in a patient receiving rindopepimut *Online only*

This 60 year-old male patient previously underwent gross-total resection followed by standard radiation and temozolomide, with recurrence of disease less than five months after initial diagnosis. While receiving rindopepimut with bevacizumab on study, the patient experienced a partial response persisting more than 18 months, and remains alive without initiation of alternate therapies at 27 months.