Title: Efficacy and safety of nivolumab in Japanese patients with first recurrence of glioblastoma: an open-label, non-comparative study

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Using the expected 1-year survival rate ($p^*$) and threshold 1-year survival rate ($p_0$), the sample size was determined based on $\Pr(p > p_0 \mid \text{data})$, the posterior probability that the 1-year survival rate estimated from the results of the study ($p$) exceeds $p_0$, and on $\Pr(p < p^* \mid \text{data})$, the posterior probability that $p$ does not exceed $p^*$

$$\Pr(p > p_0 \mid \text{data}) = \frac{1}{B(a + S, b + F)} \int_{p_0}^{1} p^{a+S-1} (1 - p)^{b+F-1} \, dp$$

$$\Pr(p < p^* \mid \text{data}) = \frac{1}{B(a + S, b + F)} \int_{0}^{p^*} p^{a+S-1} (1 - p)^{b+F-1} \, dp$$

- $S$: Number of patients alive at 1 year
- $F$: Number of deaths at 1 year
- $p \sim Beta(a, b)$ (Prior probability)

$Beta(a, b) = \int_{0}^{1} t^{a-1} (1 - t)^{b-1} \, dt$
Online Resource 2  Baseline characteristics and efficacy in the current study of nivolumab, the JO22506 [1] study of bevacizumab, and the CheckMate 143 study [2]

|                                | This study (Nivolumab) (N = 44) | JO22506 study (Bevacizumab) (N = 29) | CheckMate 143 study Nivolumab (N = 184) | Bevacizumab (N = 185) |
|--------------------------------|---------------------------------|-------------------------------------|----------------------------------------|-----------------------|
| Sex                            |                                 |                                     |                                        |                       |
| Male                           | 31 (70.5)                       | 14 (48.3)                           | 116 (63.0)                             | 119 (64.3)            |
| Female                         | 13 (29.5)                       | 15 (51.7)                           | 68 (37.0)                              | 66 (35.7)             |
| Age, years                     |                                 |                                     |                                        |                       |
| < 65                           | 32 (72.7)                       | 19 (65.5)                           | 142 (77.2)                             | 156 (84.3)            |
| ≥ 65                           | 12 (27.3)                       | 10 (34.5)                           | 42 (22.8)                              | 29 (15.7)             |
| Karnofsky Performance Status   |                                 |                                     |                                        |                       |
| 90–100%                        | 21 (47.7)                       | 17 (58.6)                           | 113 (61.4)                             | 103 (55.7)            |
| 70–80%                         | 23 (52.3)                       | 12 (41.4)                           | 69 (37.5)                              | 81 (43.8)             |
| Corticosteroid use at baseline |                                 |                                     |                                        |                       |
| Yes                            | 4 (9.1)                         | 10 (34.5)                           | 73 (39.7)                              | 79 (42.7)             |
| No                             | 40 (90.9)                       | 19 (65.5)                           | 111 (60.3)                             | 106 (57.3)            |
| Recurrence status              |                                 |                                     |                                        |                       |
| First                          | 100 (100.0)                     | 17 (58.6)                           | NA                                     | NA                    |
| Second                         | 0                               | 12 (41.4)                           | NA                                     | NA                    |
| MGMT promoter methylation status|                                 |                                     |                                        |                       |
| Unmethylated                   | 7 (15.9)                        | NA                                  | 59 (32.1)                              | 67 (36.2)             |
| Methylated                     | 11 (25.0)                       | NA                                  | 43 (23.4)                              | 42 (22.7)             |
| Not reported/unknown           | 26 (59.1)                       | NA                                  | 82 (44.6)                              | 76 (41.1)             |
| 1-year survival rate, %        | 54.5                            | 34.5                                | 41.8<sup>a</sup>                       | 42.0<sup>b</sup>      |
| mOS, months                    |                                 |                                     |                                        |                       |
| All                            | 13.1                            | 10.5                                | 9.8<sup>a</sup>                        | 10.0<sup>b</sup>      |
| No corticosteroid use at baseline | 13.1<sup>c</sup>             | NA                                  | 12.6<sup>d</sup>                       | 11.8<sup>e</sup>      |
| mPFS, months<sup>f</sup>       | 1.5                             | 3.3                                 | 1.5<sup>g</sup>                        | 3.5<sup>h</sup>       |
| ORR<sup>i,j</sup>              | 1 (3.8)<sup>i</sup>            | 8 (27.6)                            | 12 (7.8)<sup>k</sup>                   | 36 (23.1)<sup>i</sup> |

Values are n (%), unless otherwise stated

<sup>a</sup>N = 154
\(N = 147\)
\(N = 40\)
\(N = 111\)
\(N = 106\)

For mPFS and ORR, RANO criteria were used in the current study, whereas MacDonald criteria were used in the JO22506 study.

\(N = 171\)
\(N = 146\)

ORR was in patients with measurable lesion.

\(N = 26\)
\(N = 153\)
\(N = 156\)

\(\text{MGMT} O^6\)-methylguanine-DNA methyltransferase, \(mOS\) median overall survival, \(mPFS\) median progression-free survival, \(NA\) not available, \(ORR\) objective response rate, \(RANO\) Radiologic Assessment in Neuro-Oncology

References

1. Nagane M, Nishikawa R, Narita Y, et al (2012) Phase II study of single-agent bevacizumab in Japanese patients with recurrent malignant glioma. Jpn J Clin Oncol 42(10):887–895. https://doi.org/10.1093/jjco/hys121

2. Reardon DA, Brandes AA, Omuro A, et al (2020) Effect of nivolumab vs bevacizumab in patients with recurrent glioblastoma: the CheckMate 143 phase 3 randomized clinical trial. JAMA Oncol 6(7):1003–1010. https://doi.org/10.1001/jamaoncol.2020.1024