Prolonged Survival In Patients With Recurrent Glioblastoma Multiforme Who Are Treated With Tumor Lysate-Pulsed Autologous Dendritic Cells

Marnix L. Bosch[1], Robert Prins[2] and Linda Liau[2]
[1]Northwest Biotherapeutics, Inc, and [2]University of California, Los Angeles, USA

ABSTRACT

Background: Recurrent Glioblastoma multiforme (rGBM) is a life threatening condition, with a mortality rate approaching 100%. Overall survival (OS) in rGBM patients has not materially changed in the past several decades.

We treated 55 rGBM patients with autologous dendritic cells pulsed with autologous tumor cell lysate (DCVax®-L) in an "Information Arm" outside of our Phase III clinical trial. 51 of these 55 patients were not eligible for the trial because they had actual or apparent early progression (recurrence) at a Baseline Visit at the end of 6 weeks of daily radiotherapy and chemotherapy after surgical resection of their brain tumor. 4 of the patients were not eligible for the trial for other reasons (e.g., insufficient doses of DCVax-L).

These rGBM patients received the same DCVax-L product, on the same treatment schedule, in the same medical centers, in the same time period as the Phase III clinical trial, and the data have been collected and maintained by the same CRO managing the Phase III trial.

Aim: To provide compassionate use treatment and to determine OS of these rGBM patients treated with DCVax-L.

Methods: Disease progression (recurrence) was determined through MRI imaging at the Baseline Visit and at Month 2 thereafter. All images were reviewed and analyzed by an independent specialized medical imaging company. Each image was reviewed separately by two independent reviewers, and any material differences were resolved by a third independent reviewer. Reviews were conducted using both RANO and McDonald criteria.

OS data is available for all 51 patients. Baseline and Month 2 images are available so far for 46 of the 51 patients.

Based on comparison of the Baseline and Month 2 images, the independent medical imaging company classified the 46 patients into the following 3 groups. The other 5 patients were unclassified, due to lack of available images.

- **20 Rapid-Progressor Patients**: A new lesion ≥ 1 cm or tumor growth ≥25% at Baseline and at Month 2
- **25 Indeterminate Patients**: Stable disease, modest progression and/or regression, or measurements still unclear
- **1 Pseudo-Progressor**: Month 2 image showed resolution of most of the prior appearance of tumor growth

Information Arm

51 patients had evidence of apparent disease progression in imaging at Baseline Visit following 6 weeks' chemo-radiation

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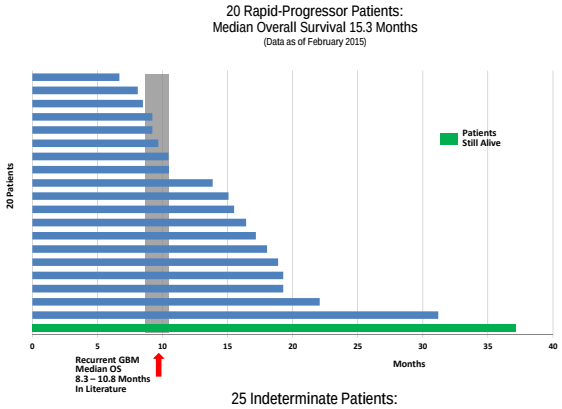
Patients re-imaged at Month 2 after Baseline Visit to confirm either actual disease progression or pseudo-progression

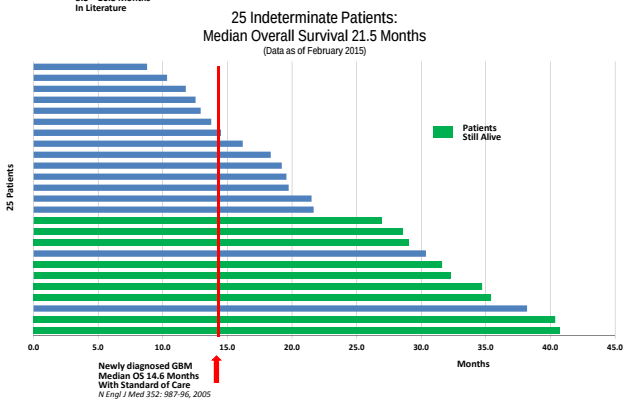
(patients categorized by independent medical imaging company)

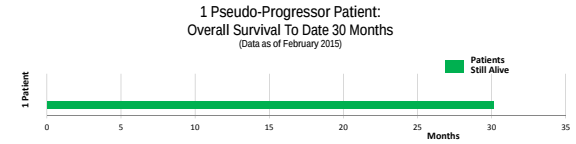
20 patients had further progression at Month 2: Rapid-Progressors	25 patients had stable disease or modest progression/regression or measurements unclear at Month 2: Indeterminate	1 patient had resolution at Month 2: Pseudo-progressor	5 patients Unclassified due to lack of images

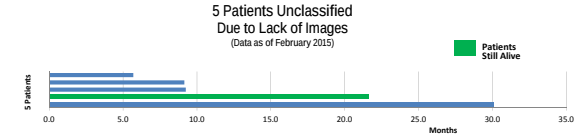
Median Overall Survival (OS) in Rapid-Progressor Patients

Reference	Population	Median OS
DCVax-L (20 patients)	Progressive disease (PD) post RT+chemo, and additional PD (>25%) 2 months later	**15.3 months**
Brandes et al. 2008 (18 patients)	PD at 4 weeks post RT+chemo, confirmed after 2 more tmz cycles	10.2 months
Roldan et al. 2009 (10 patients)	PD at 4-6 weeks post RT+chemo, confirmed after ≥1 more tmz cycle(s)	9.1 months
Kang et al. 2010 (10 patients)	PD at 2 consecutive scans post RT+chemo	10.8
Sanghera et al. 2010 (29 patients)	PD at 2 consecutive scans within 8 weeks post RT+chemo	8.3 months
Gunjur et al. 2011 (27 patients)	PD at 2 consecutive scans within 3 months post RT+chemo, or clinical deterioration	10.4 months
Linhares et al. 2013 (13)	PD at 2 consecutive scans within 3 months post RT+chemo	9.0 months









Results

Overall: The median OS is 18.3 months. 15 of the 51 patients who were ineligible for the Phase III trial due to apparent early recurrence lived beyond 2 years, and 12 of the 15 remain alive.

20 Rapid-Progressors: The median OS is 15.3 months (95% Confidence Interval: 10.5 – 17.2) and the range is 6.7 to 37.1 months. A literature search revealed 6 publications with comparable populations of patients (listed at left), which reported median OS of 8.3 to 10.8 months.

12 of the 20 DCVax-L treated Rapid-Progressors lived beyond 13 months; 10 of the 20 DCVax-L treated Rapid-Progressors lived beyond 15 months; and 7 of the 20 DCVax-L treated Rapid Progressors lived beyond 18 months.

25 Indeterminate Patients: The median OS is 21.5 months, and the range is 8.8 to 40.7 months. 9 of these 25 patients remain alive today at more than 24 months, 6 of these 9 patients remain alive at more than 30 months, and 4 of these 9 patients remain alive at 35-40+ months.

1 Pseudo-Progressor: This patient is still alive. OS is 30.1 months to date.

5 Unclassified Patients: 1 patient is still alive. The median OS is 9.2 months, and the range is 5.7 to 30.1 months.

Conclusions

- Patients with evidence of disease recurrence immediately following 6 weeks of daily radiotherapy and chemotherapy after surgical resection of their brain tumor appear to survive longer than would be expected based on data in the literature, when treated with DCVax-L.
- The apparent extended survival of these patients is seen in both Rapid Progressor Patients and Indeterminate Patients (as well as the Pseudo-Progressor Patient).
- The combined data suggest a possible survival benefit for patients with recurrent GBM conferred by the DCVax-L treatment.
- The ~30% of survivors who have lived beyond 2 years may reflect long term tumor control.
- DCVax-L treatment (vaccination of patients with autologous dendritic cells loaded with autologous tumor lysate antigens) also continues to have an excellent safety profile.