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Treatment Options Report

Report Date 04 Nov 2022

What is this report?
This report provides a list of treatment options for you and your treating oncologist to review. This report does not constitute a medical treatment plan and is not a substitute for medical advice. However, it is intended to be actionable information for you to understand and discuss with your treating oncologist.

How was this report created?
This report was created by a Ph.D. scientist following review of your Care Summary. Your Care Summary (appended to this report) reflects our understanding of your case history at this treatment decision point. It is generated based on your medical records, including physician notes, test results, imaging scans, genomic sequencing, and/or molecular profiling. The list of treatment options presented is informed by the latest clinical evidence and clinical trial data, as well as by learnings from the actions and outcomes of other patients on our platform.

If your treating oncologist would like help with access to these treatment options, please contact us at medical-affairs@xcures.com.

Your Treatment Options

1 **Bevacizumab, Lomustine**

Access Mechanism
Standard of Care

Why
Continue on current treatment regimen of lomustine and bevacizumab as most recent scan shows treatment response.

2 **Everolimus, Osimertinib**

Access Mechanism
Off-Label

Note
Targets the EGFR mutation.

Why

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In case of disease progression, consider the combination of the Egfr inhibitor osimertinib and the mTOR inhibitor everolimus. Osimertinib has been reported to penetrate the blood-brain barrier and have efficacy against brain metastases in NSCLC, as well as activity in GBM (<Reference #1>, <Reference #2>). Osimertinib has also been shown to have activity against uncommon EGFR mutations, including S768I (<Reference #3>, <Reference #4>, <Reference #5>). Activation of the PI3K/AKT/mTOR pathway has been reported as a resistance mechanism to Egfr inhibitors, and preclinical studies in NSCLC have shown that everolimus restores sensitivity to the Egfr inhibitor gefitinib (<Reference #6>, <Reference #7>). In addition, the combination of everolimus and Egfr inhibitors has been shown to have antitumor activity in NSCLC Phase 1 trials (<Reference #8>, <Reference #9>).

References

1. Link to Reference #1
   https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6880297/
2. Link to Reference #2
   http://dukecancerinstitute.org/news/new-finding-efficacy-osimertinib-against-egfrviii-glioblastoma
3. Link to Reference #3
   https://ascopubs.org/doi/10.1200/JCO.19.00931
4. Link to Reference #4
   https://www.lungcancerjournal.info/article/S0169-5002(20)30346-9/fulltext
5. Link to Reference #5
   https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7273558/
6. Link to Reference #6
   https://pubmed.ncbi.nlm.nih.gov/19427302/
7. Link to Reference #7
   https://pubmed.ncbi.nlm.nih.gov/22941374/
8. Link to Reference #8
   https://pubmed.ncbi.nlm.nih.gov/17577220/
9. Link to Reference #9
   https://pubmed.ncbi.nlm.nih.gov/22968184/

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3 Afatinib, Temozolomide

Access Mechanism
Off-Label

Note
Targets the EGFR mutation.

Why
In case of disease progression, consider treatment with afatinib. Case studies of lung adenocarcinoma patients with the EGFR S768I mutation have reported efficacy of afatinib (<Reference #1>, <Reference #2>). In addition, studies analyzing uncommon EGFR exon 20 mutations, including EGFR S768I, have reported efficacy of afatinib in patients previously treated with an EGFR TKI and in EGFR TKI naive patients (<Reference #3>, <Reference #4>). Studies in GBM have also reported efficacy of afatinib and temozolomide and the ability of afatinib to penetrate the CNS (<Reference #5>, <Reference #6>, <Reference #7>).

References

1. Link to Reference #1
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5919859/
2. Link to Reference #2
https://pubmed.ncbi.nlm.nih.gov/32901897/
3. Link to Reference #3
https://www.sciencedirect.com/science/article/pii/S1556086420300149
4. Link to Reference #4
https://www.inoncology.com/sites/default/files/related_materials/wclc_uncommon_mutations_2013_yang_et_al.pdf
5. Link to Reference #5
https://jeccr.biomedcentral.com/articles/10.1186/s13046-019-1264-2
6. Link to Reference #6
https://academic.oup.com/neuro-oncology/article/17/3/430/2280697
7. Link to Reference #7
https://pubmed.ncbi.nlm.nih.gov/26423602/

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4 **Radiation, Bevacizumab, Pembrolizumab**

Access Mechanism
Off-Label

Why
In case of disease progression, consider re-irradiation to area(s) of most growth in combination with bevacizumab and the checkpoint inhibitor pembrolizumab. A Phase 1 study of radiation, bevacizumab, and pembrolizumab in 24 bevacizumab-naïve patients with recurrent high-grade glioma reported complete or partial responses in 20 patients and median progression-free and overall survival times of 7.92 and 13.45 months, respectively (<Reference #1>).

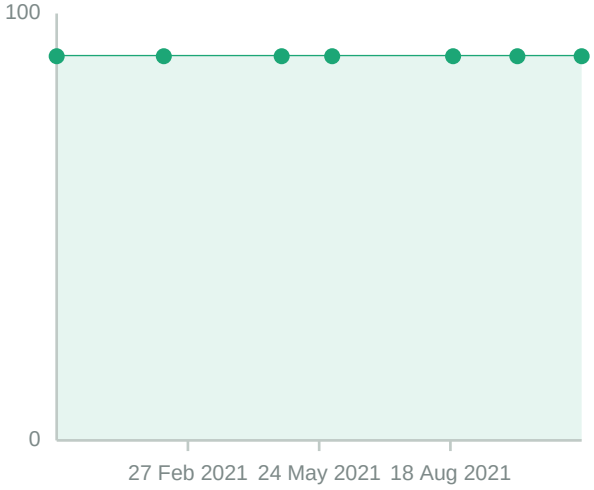
References
1. Link to Reference #1
https://pubmed.ncbi.nlm.nih.gov/33173935/

Care Summary

Last Modified 03 Dec 2021

My Health

90 KPS Score
12 Nov 2021



My Cancer

10 Sept 2019 (Latest)
Diagnosis (Current, Primary): Glioblastoma

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Stage/Grade: WHO Central Nervous System Grade 4
Location(s): Brain, Right frontoparietal lobe

Biomarkers

DATE	GENE	ALTERATION
06 Jul 2021	Tumor Mutational Burden	1.6 mutations/MB
06 Jul 2021	MGMT	Unmethylated
06 Jul 2021	Ki-67	14.8%
06 Jul 2021	GFAP	Positive
06 Jul 2021	EGFR	Positive
06 Jul 2021	p53	Nuclear staining in a few scattered cells
06 Jul 2021	EGFR	Ser768Ile
06 Jul 2021	TERT	C228T
06 Jul 2021	MSI	Negative
06 Jul 2021	IDH-1 R132H	Negative
10 Sept 2019	MGMT	Unmethylated
10 Sept 2019	EGFR	Missense mutation
10 Sept 2019	Ki-67	50%
10 Sept 2019	ATRX	Preserved in majority of tumor cells
10 Sept 2019	1p/19q co-deletion	Negative
10 Sept 2019	p53	<5%
10 Sept 2019	IDH2	Negative
10 Sept 2019	IDH1 R132H	Negative

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Current Treatments

Unspecified date
Cannabidiol

03 Oct 2021
Lomustine
200mg every 6 weeks

01 Oct 2021
Valacyclovir
500mg BID

01 Oct 2021
Bevacizumab
15 mg/kg every 3 weeks

15 May 2021
Metformin
500 mg

15 May 2021
Atorvastatin
40 mg

15 May 2021
Doxycycline
100mg QD 3 months on 30 days off

15 May 2021
Mebendazole
200mg QD

Historical Surgeries and Therapies

02 Sept 2021 - 06 Sept 2021
Temozolomide
150 mg/m2; cycle 13, stopped due to rapid tumor growth

09 Jul 2021 - 20 Jul 2021
Dexamethasone
2mg BID

06 Jul 2021 - 06 Jul 2021

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Resection
Right frontoparietal lobe

28 Jan 2020 - 12 Jan 2021
Temozolomide
150 mg/m2; 12 cycles

30 Oct 2019 - 11 Dec 2019
Radiation Therapy
Brain

30 Oct 2019 - 11 Dec 2019
Temozolomide

15 Oct 2019 - 17 Apr 2020
Bevacizumab
10 mg/kg; NCT01269853

12 Sept 2019 - 12 Oct 2019
Dexamethasone
2mg

10 Sept 2019 - 10 Sept 2019
Gross Total Resection
Right frontoparietal lobe