Cost-Effectiveness of Temozolamide for Treatment of Glioblastoma Multiforme in India

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PURPOSE Glioblastoma multiforme (GBM) has poor outcomes following surgery and radiation. Adjuvant temozolamide along with radiation therapy has been shown to improve survival. In this paper, we evaluate the cost-effectiveness of concomitant temozolamide with radiation and maintenance temozolamide for 6 months of treatment for GBM in India.

MATERIALS AND METHODS We used a Markov model to evaluate the lifetime costs and consequences of treating GBM with radiation alone versus radiation with adjuvant temozolamide. The model was calibrated using the published evidence from European Organisation for Research and Treatment of Cancer-NCIC trial on progression-free survival and overall survival to estimate the life years (LYs) and quality-adjusted LYs (QALYs). Cost of treatment and management of complications were estimated using the data from the National Health System Cost Database and Indian studies. Future cost and consequences were discounted at 3%. Incremental cost per QALY gained with temozolamide was estimated to assess cost effectiveness.

RESULTS Temozolamide resulted in an increase of 0.59 (0.53-0.66) LY and 0.33 (0.29-0.40) QALY per person at an incremental cost of ₹75,120 in Indian national rupee (INR) (59,337-93,960). Overall, the use of temozolamide incurs an incremental cost of ₹212,020 INR (138,127-401,466) per QALY gained, which has a 4.7% probability to be cost-effective at 1-time per capita Gross Domestic Product (GDP) threshold. In case the current price of temozolamide could be decreased by 90%, the probability of its use for GBM being cost-effective increases to 80%.

CONCLUSION Temozolamide is not cost-effective for treatment of patients with GBM in India. This evidence should be used while framing guidelines for treatment and price regulation.

INTRODUCTION Glioblastoma multiforme (GBM) is the most common and the most aggressive brain tumor in adults.1 The standard of care for patients with newly diagnosed GBM includes maximum possible safe resection followed by adjuvant radiotherapy.2 However, the outcomes continued to be poor, and this led to the trial of various chemotherapeutic agents for patients with GBM in an attempt to improve survival.3 Among the various agents used, temozolamide has emerged superior because of the survival advantage offered.4,5 The addition of concomitant temozolamide to radiation followed by 6 months of maintenance temozolamide in patients with newly diagnosed GBM has been reported to improve the median overall survival (OS) by 2.5 months and the progression-free survival (PFS) by 1.9 months.3 Incorporating temozolamide as the standard treatment in the concomitant and maintenance setting as per the standard guidelines becomes expensive in a resource-limited country like India. As a result, assessment of its value for money becomes important. The drug has been shown to be cost-effective in developed countries like the United States,6 the United Kingdom,7 Mexico,8 and Canada,9 but at the same time, the drug has been shown to be cost-ineffective in China.9 There have been several methodological limitations in the above cost-effectiveness studies. For example, Lamers et al7 and Uyl-de Groot et al10 reported outcomes in terms of life years (LYs) and not quality-adjusted LYs (QALYs) gained. In the study by Wu et al,9 discounted rates were not applied in view of short survival associated with patients with GBM. Several cost-effectiveness analyses5,9 have estimated outcomes up to what has been reported in trials—either until 2 years or 5 years of onset of disease. Life-term consequences have not been assessed robustly.
In view of this, we undertook this study to estimate the incremental cost per QALY gained in patients with newly diagnosed GBM in India, who received temozolamide in addition to adjuvant radiotherapy as compared with radiotherapy alone.

### MATERIALS AND METHODS

A Markov model with three health states—PFS, progressive disease (PD), and death—was developed. Patients with newly diagnosed GBM entered the model at the age of 50 years, which is the most common age of presentation of GBM in India. A cycle length of 1 month was considered appropriate based on the maintenance treatment cycles. One thousand patients enter the model in the PFS state. A societal perspective that incorporates both the health system costs and out-of-pocket (OOP) expenditures was used, as most of the treatment costs in India are borne OOP. Health outcomes were calculated as LYs and QALYs gained. India’s per capita gross domestic product (GDP) in year 2019 was $2,169 USD and this was used as a cost-effectiveness threshold for the present analysis, which translates to approximately ₹150,000 in Indian national rupee (INR). The use of per capita GDP as cost-effectiveness threshold is recommended by Indian Government’s Health Technology Assessment (HTAIn) agency and used by many recent HTA studies conducted in Indian context. All future costs and consequences were discounted at 3%.

### Intervention and Control Arms

In the intervention arm, patients with newly diagnosed GBM after surgery were considered to have received temozolamide at 75 mg/m² once daily concomitant with radiation for a period of 6 weeks, followed by 4-weekly six cycles of maintenance temozolamide. During maintenance, temozolamide was given at a dose of 150 mg/m² once daily for 5 days in the first cycle, and subsequently, the dose was escalated to 200 mg/m² once daily for 5 days from the second to sixth cycles. The effective dose of temozolamide was calculated as per the body surface area (BSA). The BSA was derived using the weighted average height and weight for the average Indian patient considering the gender distribution of patients with GBM in India. The patients continued the prescribed dose and schedule unless they developed grade 3 or 4 hematological toxicity or other drug-related adverse reactions.

In the control arm, the patients were considered to have received only adjuvant radiation without concomitant or maintenance temozolamide. Once in the PD state, the patients were offered best supportive care, and no second-line chemotherapy was accounted.

### Valuation of Consequences

The data of OS and PFS as reported in the European Organisation for Research and Treatment of Cancer (EORTC)-NCIC trial at a 5-year follow-up were used for our analysis. The extent of toxicity, dose modification, and drug discontinuation rates were also obtained from the same trial results obtained at a 2-year follow-up. The findings from the EORTC-NCIC trial on effectiveness are representative of the Indian population as these are similar to what has been reported in various real-world single-arm Indian studies. However, in view of the longer follow-up reported in the EORTC NCIC trial, the findings from the latter were preferred for the present analysis.

The transition probabilities were calculated to calibrate the intervention and control arms with the median survival and PFS reported at 6, 12, 18, 24, 36, 48, and 60 months. After 5 years, the transition probabilities at 60 months were applied for each cycle over the lifetime. Age-specific all-cause mortality reported in the Sample Registration Survey report of India was used. Utility values for the GBM health states reported by Garside et al were used in our analysis (Table 1).

### Costing

In both the groups, costs for conformal adjuvant radiation with a radiation dose of 60 Gy in 30 fractions delivered over 6 weeks, as reported in a recent Indian study, were included. In addition, the cost for temozolamide at a...
TABLE 1. Key Parameters Used in the Cost-Effectiveness Model

| Parameters                  | Base Case | LL  | UL  | Source |
|-----------------------------|-----------|-----|-----|--------|
| **Transition probabilities: no temozolamide** |           |     |     |        |
| PFS to PD                   |           |     |     |        |
| 0-6 cycles                  | 0.15      | 0.12| 0.18|        |
| 6-12 cycles                 | 0.20      | 0.16| 0.25|        |
| 12-18 cycles                | 0.13      | 0.11| 0.16| 4,5    |
| 18-24 cycles                | 0.14      | 0.11| 0.17|        |
| 24-36 cycles                | 0.01      | 0.01| 0.01|        |
| 36-48 cycles                | 0.00      | 0.00| 0.01|        |
| 48 and above                | 0.00      | 0.00| 0.01|        |
| PD to death                 |           |     |     |        |
| 0-6 cycles                  | 0.09      | 0.07| 0.11|        |
| 6-12 cycles                 | 0.12      | 0.10| 0.14|        |
| 12-18 cycles                | 0.17      | 0.14| 0.20|        |
| 18-24 cycles                | 0.12      | 0.10| 0.15| 4,5    |
| 24-36 cycles                | 0.09      | 0.07| 0.11|        |
| 36-48 cycles                | 0.03      | 0.02| 0.03|        |
| 48-60 cycles                | 0.09      | 0.07| 0.11|        |
| 60 and above                | 0.11      | 0.09| 0.14|        |
| **Transition probabilities: temozolamide** |           |     |     |        |
| PFS to PD                   |           |     |     |        |
| 0-6 cycles                  | 0.099     | 0.079| 0.119|        |
| 6-12 cycles                 | 0.108     | 0.086| 0.129|        |
| 12-18 cycles                | 0.056     | 0.045| 0.068| 4,5    |
| 18-24 cycles                | 0.096     | 0.077| 0.115|        |
| 24-36 cycles                | 0.037     | 0.030| 0.045|        |
| 36-48 cycles                | 0.009     | 0.007| 0.010|        |
| 48 and above                | 0.026     | 0.021| 0.031|        |
| PD to death                 |           |     |     |        |
| 0-6 cycles                  | 0.124     | 0.099| 0.149|        |
| 6-12 cycles                 | 0.115     | 0.092| 0.138|        |
| 12-18 cycles                | 0.128     | 0.102| 0.153|        |
| 18-24 cycles                | 0.111     | 0.088| 0.133| 4,5    |
| 24-36 cycles                | 0.065     | 0.052| 0.078|        |
| 36-48 cycles                | 0.034     | 0.027| 0.041|        |
| 48-60 cycles                | 0.040     | 0.032| 0.048|        |
| 60 and above                | 0.093     | 0.074| 0.111|        |
| All-cause mortality: 50-55 years | 0.001   | 0.001| 0.001| 23     |
| All-cause mortality: 55-60 years  | 0.001   | 0.001| 0.001|        |
| **Utility**                 |           |     |     |        |
| PFS                         | 0.887     | 0.710| 1.000|        |
| PFS RT                      | 0.824     | 0.659| 0.989|        |
| PFS RT with temozolamide    | 0.743     | 0.594| 0.891| 24     |
| PFS with temozolamide       | 0.733     | 0.586| 0.880|        |
| PD                          | 0.731     | 0.585| 0.878|        |

(Continued on following page)
A dose of 75 mg/m² (120 mg) once daily for 6 weeks and for Pneumocystis Carinii Pneumonia (PCP) prophylaxis and adverse effect management were included in the intervention arm. Both groups accounted for the cost for a weekly physician visit during radiation therapy. In addition, cost of day care management for radiotherapy was obtained from a recently published Indian study. The cost of laboratory investigations as per standard protocols was also included in both intervention and control arms. Both the groups included costs for hospitalization for 10% of patients for management of raised intracranial tension during the course of radiation therapy. One month after completion of radiotherapy, both the arms included costs of magnetic resonance imaging (MRI) of brain for response assessment. Subsequently, patients in the control arm were assumed to be on regular follow-up with physician visits and radiological examination at a frequency as recommended by standard guidelines until disease progression when patients moved to the PD state (Table 1).

In the intervention arm, 1 month after completion of radiotherapy, cost of temozolamide was estimated at a dose of 150 mg/m² once a day for 5 days (1250 mg) for the first

| Parameters | Base Case | LL | UL | Source |
|------------|-----------|----|----|--------|
| Cost parameters (INR) | | | | |
| Drug prices | | | | |
| Phenytoin 100 mg | 0.45 | 0.36 | 0.9 | 34 |
| Ondansetron 4 mg | 2.47 | 1.976 | 4.94 | 45 |
| Syp. Cremaf | 47 | 37.6 | 94 | 34 |
| Cotrimoxazole DS | 0.33 | 0.26 | 0.66 | |
| Dexamethasone tablet 4 mg | 3.48 | 2.78 | 6.96 | |
| Ranitidine 150 mg | 0.62 | 0.50 | 1.24 | 45 |
| Ciprofloxacin 500 mg | 1.9 | 1.52 | 3.8 | |
| Augmentin 625 mg | 4.33 | 3.46 | 8.66 | |
| Becosule tablet (B-complex) | 0.73 | 0.58 | 1.46 | |
| Injection GCSF | 350 | 280 | 700 | |
| Tablet temozolamide 250 mg | 600 | 480 | 1,200 | 32 |
| Tablet temozolamide 100 mg | 240 | 192 | 480 | |
| Tablet temozolamide 20 mg | 185 | 148 | 370 | |
| Diagnostic prices | | | | |
| CBC | 155 | 124 | 310 | |
| RFT | 259 | 207 | 518 | |
| LFT | 259 | 207 | 518 | |
| Contrast-enhanced MRI | 2,257 | 1806 | 4,514 | 47 |
| Serum electrolyte | 100 | 80 | 200 | 46 |
| Chest X-ray | 236 | 189 | 472 | 47 |
| Blood culture | 433 | 346 | 866 | |
| Sputum for gram stain | 149 | 119 | 258 | |
| Services (neurosurgery/radiotherapy/medical oncology/neurology department) | | | | |
| Per outpatient visit | 538 | 430 | 646 | |
| Per bed day hospitalization | 3,096 | 2,477 | 3,715 | |
| Radiotherapy 3D-CRT | 81,594 | 65,275 | 97,913 | |
| Cost of per day care visit | 1,032 | 826 | 1,238 | 26 |
| LOS in days | | | | |
| Mean LOS for hospitalization among patients with PFS | 3.00 | 2.40 | 3.60 | |
| Mean LOS for hospitalization among patients with PD | 8.75 | 7.00 | 10.50 | |

Abbreviations: CBC, complete blood count; CRT, conformal external beam radiation therapy; GCSF, granulocyte colony stimulating factor; INR, Indian national rupee; LOS, length of stay; LFT, liver function test; LL, lower limit; MRI, magnetic resonance imaging; PD, progressive disease; PFS, progression-free survival; RFT, renal function test; RT, radiotherapy; UL, upper limit.
cycle. For the next five cycles, the cost of temozolomide each month was estimated at a dose of 200 mg/m² once a day for 5 days (1650 mg). Cost of monthly physician visits and laboratory investigations was added to each cycle. Costs for MRI brain were added after 3 cycles of maintenance temozolomide and 1 month after completion of the maintenance therapy. The extent of grade 3 and 4 hematological adverse effects, which led to drug discontinuation, was assumed to be 10% in the concomitant phase and 8% in the maintenance phase. Another 9% of the patients could not be escalated from 150 mg/m² to 200 mg/m² during the monthly cycles 2-6 of maintenance temozolomide, as reported in the EORTC NCIC trial. Corresponding dose modification for these patients was done for the purpose of costing in our model. Costs for management of adverse effects such as nausea, emesis, constipation, seizure prophylaxis, PCP prophylaxis, raised intracranial tension, and neutropenia or severe infections were also included. The incidence of hematological adverse effects including neutropenia and severe infections, as reported in the EORTC-NCIC trial, was considered as 7% in the concomitant phase and 9% in the maintenance phase. All adverse effects, except high-risk neutropenia or severe infection, were assumed to be treated using drugs in outpatient setting based on standard treatment guidelines. Ten percent of patients in both intervention and control arms with raised Intra Cranial Tension (ICT) during treatment were assumed to be managed in inpatient setting using steroids, osmotic diuretics, and antiepileptic and antiemetic drugs. Average cost of management in inpatient setting, routine or intensive care, was obtained from the National Health System Cost Database and analysis of recently conducted nationally representative hospital costing study. A range of temozolomide prices by multiple brands were available through this website, and therefore, a mean price was considered appropriate for the current analysis. In addition, we accounted for the uncertainty in price variation in sensitivity analysis. The drugs used for the management of side effects, along with their prices, are mentioned in the parameters shown in Table 1. Similarly, low-risk neutropenia was also assumed to be managed in outpatient setting with antibiotics and growth factors (Table 1). Patients with high-risk febrile neutropenia were assumed to be hospitalized and managed with intravenous antibiotics as per culture sensitivity, growth factors, and supportive care. The prices of each of these drugs were accessed from the website of the Department of Pharmaceuticals, Government of India. The cost of hospitalization was derived from published studies and Indian National Health System Cost Database. Table 1 also shows prices for the drugs used in management of adverse effects.

Once the patients in both the groups entered the PD state, costs were included for best supportive care (antiepileptics and steroids) and hospitalization for life-threatening episodes in 37% patients with an average hospital stay of 8.75 days. For both intervention and control group patients in the PFS state, costs for 3 monthly physician visit and brain imaging were included for the first 2 years, which extended to 6 monthly visits until 4 years and annually thereafter. All costs are reported in INR and converted to USD using an exchange rate of ₹71.66 INR = $1 USD.

**Sensitivity Analysis**

A probabilistic sensitivity analysis (PSA) was carried out to ascertain the effect of variation in parameter uncertainty. A variation of 20% was assumed on upper and lower sides for transition probabilities and utility weights. As the cost parameters are generally positively skewed in nature, we assumed 20% and 100% variation for lower and upper limits, respectively. In PSA, appropriate probabilistic distributions were used for different parameters such as gamma distribution for cost parameters; beta distribution for transmission, transition, and utility parameters; and uniform distribution for other parameters. Probabilistic model was simulated 1,000 times, and 2.5th and 97.5th percentile values were used to generate the confidence limits for base results. A univariate sensitivity analysis was also undertaken to assess the likelihood of temozolomide to be cost-effective with variation in its price.

**RESULTS**

**Costs**

The lifetime cost of treating a patient with newly diagnosed GBM with adjuvant radiation and temozolomide was ₹181,235 INR ($2,529 USD) (Table 2). The cost of temozolomide was 15.3% of the total lifetime cost in the intervention arm. Similarly, the lifetime cost of treating the patient with GBM without temozolomide was ₹105,502 INR ($1,472 USD). More than half (51.4%) of the incremental cost of INR ₹75,120 ($1,048 USD) per patient was on account of introduction of temozolomide. The predominant cost in both the arms (52% in the intervention arm and 79% in the control arm) was that of conformal adjuvant radiation.

**Outcomes and Cost-Effectiveness**

Life years lived per patient in temozolomide and control arm were 1.85 (1.67-2.08) years and 1.26 (1.15-1.42) years, respectively. The number of QALYs lived per patient in the temozolomide arm was 1.45 (1.21-1.73) years versus 1.12 (0.92-1.33) years in the control arm. The incremental health benefit of temozolomide was 0.59 (0.53-0.66) LY and 0.33 (0.29-0.40) QALY per person. Finally, the incremental cost per QALY gained was ₹212,354 INR (138,347-401,466) ($2,963 USD; 95% CI, 1,927 to 5,602) (Table 2).
TABLE 2. Costs, Health Benefits, and Cost-Effectiveness of Temozolamide Compared With Treatment Without Temozolamide

| Parameters                                      | Temozolamide | No Temozolamide |
|------------------------------------------------|--------------|-----------------|
| Lifetime costs per patient, INR (USD)           | Median       | 181,235 (2,529) | 105,502 (1,472) |
|                                                 | 2.5th        | 156,274 (2,180) | 88,762 (1,239)  |
|                                                 | 97.5th       | 210,458 (2,937) | 122,978 (1,716) |
| Health outcomes per patient                     |              |                 |                 |
| LYs                                            | 1.85         | 1.67            | 2.08            |
| QALYs                                          | 1.45         | 1.21            | 1.73            |
| Incremental costs, INR (USD)                   | Median       | 75,120 (1,048)  | —               |
|                                                 | 2.5th        | 59,337 (828)    | —               |
|                                                 | 97.5th       | 93,960 (1,311)  | —               |
| Incremental benefits per patient                |              |                 |                 |
| LYs                                            | 0.59         | 0.53            | 0.66            |
| QALYs                                          | 0.33         | 0.29            | 0.40            |
| Incremental cost-effectiveness ratio, societal perspective |
| INR (USD) per life year gained                  | Median       | 119,289 (1,665) | —               |
|                                                 | 2.5th        | 84,743 (1,183)  | —               |
|                                                 | 97.5th       | 195,727 (2,731) | —               |
| INR (USD) per QALY gained                      | Median       | 212,354 (2,963) | —               |
|                                                 | 2.5th        | 138,127 (1,927) | —               |
|                                                 | 97.5th       | 401,466 (5,602) | —               |

Abbreviations: 2.5th, 2.5th percentile; 97.5th, 97.5th percentile; INR, Indian national rupee; LYs, life years; QALYs, quality-adjusted life years; USD, US dollar.

Sensitivity Analysis

The findings of sensitivity analysis show that cost-effectiveness is highly sensitive to progression rates from PFS to PD, quality of life scores, cost of temozolamide, cost of diagnostics, proportion of patients completing temozolamide course despite toxicity, etc. There is a 4.7% probability for temozolamide to be cost-effective at the willingness-to-pay threshold equally to the per capita GDP (Fig 1). However, decreasing the price of temozolamide by 90% increases the probability of temozolamide to be cost-effective to 80% (Fig 2).

DISCUSSION

Overall, our analysis found that the addition of temozolamide is not a cost-effective option in India at a willingness to pay equally to the per capita GDP. Most of the previous cost-effectiveness analyses have shown temozolamide to be a cost-effective option. However, several of these studies have based their conclusion for cost-effectiveness not on the basis of any country-specific threshold but on the basis of several other drugs being used in clinical practice with similar cost-effectiveness ratios. Second, most of these previous analyses have reported the estimate in terms of...
cost per LY gained, rather than cost per QALY gained. As shown in our analysis, as well as in previous analyses, the gain in QALY per patient is almost half of the gain in LY per patient. Hence, the estimate of incremental cost-effectiveness ratio (ICER) is likely to be sensitive to the measure of outcome valuation—LY or QALY. Given the international and national guidelines, incremental cost per QALY estimate should be used to judge cost-effectiveness and to make decisions on resource allocation, as has been done in our analysis.

Our analysis methods are in line with the recommendations of India’s HTAIn. The Health Technology Assessment of Board was set up in India in 2017, with its Secretariat (HTAIn) institutionalized in the Department of Health Research. The HTAIn maintains a hub-and-spoke structure for receiving topics from various policymakers and commissioning these topics for conducting research to technical agencies. The present analysis is part of one such broader study evaluating value-based pricing of anticancer drugs.

A major difference between our study and previous analyses is the extent of gain in health outcomes. Most of the previous model-based evaluations have reported a gain in LY ranging from 0.1 year to 0.25 year per person. We found gains in LY and QALY per person to be 0.58 and 0.3, respectively. We calibrated our model based on the EORTC NCIC findings. The estimated proportion of GBM survivors on temozolamide at 12, 24, 36, 48, and 60 months as per our modeled analysis was 61.3%, 26.6%, 16.2%, 12.6%, and 9.6%, respectively, which is very similar to what has been reported by Stupp et al (Table 3). Similarly, our estimated survivors for the nontemozolamide arm (10.8%, 4.43%, 3.6%, and 1.9% at 2, 3, 4, and 5 years, respectively) closely match the previous trial (Table 3). Despite this, the differences in outcomes from other model-based cost-effectiveness analyses could be due to the truncated time horizon of 5 years in previous studies. On the other hand, we used a lifetime study horizon. After 5 years, we used an exponential distribution to model survival benefits. In one study that undertook a sensitivity analysis to report outcomes with a lifetime study horizon, a gain of 0.53 LY was reported, which is similar to our study findings. Based on the finding of the EORTC-NCIC trial, there was right censoring at the completion of the trial, which was disproportionately higher among the intervention arm. Hence, our approach of a lifetime study horizon seems more justified to value the full benefits. Nonetheless, it is important to highlight that even with higher health benefits, our overall conclusion is that the use of temozolamide is not cost-effective at the current price.

Unlike some of the previous analyses, which use a single value of hazard ratio based on the median OS or median PFS, we used the reported outcomes at different time intervals (6, 12, 18, 24, 36, 48, and 60 months) to estimate transition probabilities for intervention and control arms. Various published Indian studies report similar PFS and OS, as well as the corresponding drug discontinuation and adverse effects among Indian population. All costing parameters were derived from Indian studies, including price of the drug and cost of toxicity management.

Our study has a few limitations. First, in the absence of country-specific evidence on quality of life of patients with GBM, we
used the utility values for GBM health states reported in a published study from the United Kingdom. Second, we did not incorporate the indirect costs because of lost productivity as a result of morbidity or premature mortality. However, this was in view of Indian HTA guideline recommendations that do not support inclusion of productivity costs. Third, cost for management of certain adverse effect of prophylaxis was assumed to be constant and continuous during the treatment to facilitate the model parameters. Although this may not be representative of real-life situation, but as it does not add much to the cost and was found to be insensitive in the sensitivity analysis, this assumption does not affect the results. Fourth, we acknowledge that the cost of care in the public and private sectors can vary significantly, which may alter the ICER values. We primarily used the estimates for cost of care from the studies undertaken in the public sector. Since the cost of care in the private sector is relatively high, using private-sector costs would have only increased the ICER value. Our analysis using the public-sector cost estimates shows that temozolamide is not cost-effective. An analysis from a private-sector perspective would have made the use of temozolamide even lesser cost-effective. Hence, using private-sector costs would not have altered the conclusion of our analysis. Finally, we did not evaluate the cost-effectiveness of temozolamide in the patients with O6-methylguanine–DNA methyltransferase (MGMT) promoter methylated tumors versus MGMT promoter unmethylated tumors where in the former condition, temozolamide results in improved survival. In India, currently, MGMT promoter methylation status is not routinely checked because of both nonavailability of test at all centers and additional cost associated with it. However, we find this as relevant research question, which should be evaluated in future studies.

Overall, we found that the use of adjuvant temozolamide along with radiation is not cost-effective in India as compared to radiation alone for the treatment of GBM. Reduction in price of temozolamide by 90% is likely to increase its probability to be cost-effective to 80%. Indian standard treatment guidelines and reimbursement protocols under the Ayushman Bharat Prime Minister Jan Arogya Yojana should consider our findings for formulation of evidence-based guidelines and policies.

**TABLE 3.** Comparison of Model Estimates for Survival With Existing Studies

| Therapy          | PFS | OS |
|------------------|-----|----|
|                  | Duration of Follow-Up (Months) | Model Estimate | Stupp et al (2005)⁵ | Julka et al (2013)¹¹ | Goda et al (2015)¹⁰ | Jalali et al (2007)²² | Model Estimate | Stupp et al (2005)⁵ | Julka et al (2013)¹¹ | Goda et al (2015)¹⁰ | Jalali et al (2007)²² |
| Temozolamide     | 12  | 26.7 | 26.9 | 34 | 48.6 | NR | 61.3 | NR | 44 | 66 | 66.8 |
|                  | 18  | 18.8 | 18.4 | NR | NR | NR | 39.5 | NR | NR | NR | NR |
|                  | 24  | 10.2 | 11.2 | (7.9 to 15.1) | 12 | NR | NR | 26.6 | 27.2 | (22.2 to 32.5) | NR | 34 | 29.8 |
|                  | 36  | 6.4  | 6.0 | (3.6 to 9.2) | NR | NR | NR | 16.2 | 16.0 | (12.0 to 20.6) | NR | NR | NR |
|                  | 48  | 5.7  | 5.2 | (3.3 to 8.7) | NR | NR | NR | 12.6 | 12.1 | (8.5 to 16.4) | NR | NR | NR |
|                  | 60  | 4.1  | 4.1 | (2.1 to 7.1) | NR | NR | NR | 9.6 | 9.8 | (6.4 to 14.0) | NR | 7 | NR |
| No temozolamide  | 12  | 9.2  | 9.1 | NR | NR | NR | 50.1 | NR | NR | NR | NR |
|                  | 18  | 3.9  | 3.9 | NR | NR | NR | 20.5 | NR | NR | NR | NR |
|                  | 24  | 15.2 | 1.8 | (0.7 to 3.8) | NR | NR | NR | 10.8 | 10.9 | (7.6 to 14.8) | NR | NR | NR |
|                  | 36  | 1.36 | 1.3 | (0.4 to 3.3) | NR | NR | NR | 4.43 | 4.4 | (2.4 to 7.2) | NR | NR | NR |
|                  | 48  | 1.3  | 1.3 | (0.4 to 3.3) | NR | NR | NR | 3.6 | 3.0 | (1.4 to 5.7) | NR | NR | NR |
|                  | 60  | 1.2  | 1.3 | (0.4 to 3.3) | NR | NR | NR | 1.9 | 1.9 | (0.6 to 4.4) | NR | NR | NR |

Abbreviations: NR, not reported; OS, overall survival; PFS, progression-free survival.

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Accountable for all aspects of the work: All authors

AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST
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Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

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