COST-EFFECTIVENESS OF VISMODEGIB VS STANDARD-OF-CARE THERAPY IN THE TREATMENT OF LOCALLY ADVANCED OR SYMPTOMATIC METASTATIC BASAL CELL CARCINOMA IN HUNGARY – AN ADAPTATION TO THE GLOBAL COST-EFFECTIVENESS MODEL

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BACKGROUND

Basal cell carcinoma (BCC) is a slow-growing, locally invasive, malignant epidermal skin tumor. Cumulative sun exposure promotes tumor development. Consequently, although BCC can appear on any part of the body surface, it is found usually on the surfaces exposed to sunlight, including the face, and head-neck area. Most BCCs are small and are typically treated successfully by dermatologists using various surgical methods, photodynamic therapy, and approved topical treatments. Cure rates are generally high. A very small proportion of BCCs may progress to an advanced state (aBCC) that is locally advanced (laBCC) or metastatic (mBCC). Treatment options for aBCC are limited.
In general the epidemiology of aBCC has been poorly described and the survival rates for patients with aBCC are not well established. The ratio of locally advanced or metastatic BCC is lower than 0.1% of cases of BCC.

The Hedgehog signaling pathway is a key driver in the pathogenesis of BCC. Vismodegib is a first-in-class small-molecule inhibitor of the Hedgehog pathway. It is indicated for the treatment of adult patients with symptomatic metastatic basal cell carcinoma (mBCC) and locally advanced basal cell carcinoma (laBCC) inappropriate for surgery or radiotherapy. [1]

Primary analysis of the pivotal, multicenter, nonrandomized ERIVANCE BCC trial of vismodegib demonstrated an objective response rate (by independent review) of 30% and 43% in mBCC and laBCC patients, respectively, with a median duration of response of 7.6 months [2]. Median overall survival (OS) could not be estimated at the time of primary analysis.

Model adaptation

A global Markov model (area under the curve [AUC]) was developed to compare the cost-effectiveness of vismodegib vs standard of care (SOC) in patients with laBCC or mBCC. The efficacy inputs were based on the ERIVANCE BCC study [2]. As the pivotal trial was designed as a single-arm study, an assumption was made allowing the cost-effectiveness model to incorporate a comparator arm, SOC.
Due to lack of specific data and literature in laBCC and mBCC, the SOC arm of the global model used mortality data from the general population.

AIM

In order to adapt the model locally and generate pharmacoeconomic data, it was necessary to define more accurately the disease-specific survival parameters of patients with laBCC and mBCC
A physician-based panel was assembled to develop such disease specific survival assumptions. These data were then used as base-case assumptions for adapting the global model locally.

METHODS

Based on a literature review, no relevant data were available to clarify the survival rates of patients with laBCC or mBCC. The small patient number, and heterogeneity of relevant physicians treating patients with aBCC (oncologists, dermatologists, otolaryngologists, plastic surgeons) could have influenced the methodology of the research. A local questionnaire was used, and it resulted in a wide range of data end points, potentially increasing the uncertainty of the right estimates to be used in the model. Therefore, a Delphi-panel survey was conducted to estimate the overall survival (OS) of patients with laBCC and mBCC who were treated with SOC.

Our Delphi-panel survey was a multi-round, online survey, in which 5 professionals determined the local survival data of the examined patient group.

Due to lack of available evidence, initial baseline data were extrapolated from research conducted with a dermato-oncologist. These data served as a baseline for the rest of the Delphi panel.
Involved physicians (dermato-oncologist, oncologist, otolaryngologist-oncologist) were asked in several rounds to answer a survey. At the end of each round, results were evaluated and only considered if 80% consensus was reached amongst the experts. When inconsistent answers appeared, then the median value was set as the intermediate result. In case of disagreements, the specialists had to give concrete values to the given questions. The results were presented to the experts in the next questionnaire, and they had to review their former opinion by either changing it or confirming it with further justification. This exercise was repeated several times until the answers were increasingly grouped around a mean. Through feedback on the results of each round, the responders were able to refine their estimations. The final prediction evolved from the aggregation of estimations and the reduction of deviations through subsequent steps.
The data, which derived from the questionnaire, were stored, managed, processed, and assessed by an independent company. The answers to the questionnaires were recorded on a Web site. The results of the survey are only presented in an aggregated form. The specialist' participation in the survey was voluntary, and they could only see their own answers.

RESULTS

The questionnaire process took place between June 6, 2014, and September 1, 2014, and the survey resulted in 3 rounds. The consensus (80%) was made

- In the 1st round, laBCC median OS (48 months)
- In the 2nd round, mBCC median OS (23 months)
- In the 3rd round, mBCC overall OS (58 months)

Since there was no consensus at 80% for overall OS in laBCC, the arithmetic mean of the answers became the outcome (102 months).
According to our Delphi-panel survey, the median OS for patients with laBCC and mBCC was 48 months and 23 months, respectively. In the SOC arm, the total OS for patients with laBCC and mBCC was 102 and 58 months, respectively.

	laBCC Median OS	laBCC Overall OS	mBCC Median OS	mBCC Overall OS
Baseline	48	180	24	87,6
Result	48	102	23	58
Consensus	1st round		2nd round	3rd round

Table 1. The Summary of Baseline and the End Result (months)

CONCLUSIONS

Vismodegib represents a safe and effective treatment for patients with aBCC. In the development of a model to compare the cost-effectiveness of vismodegib vs. SOC in this area of high unmet clinical need, Delphi-panel surveys were used to generate a consensus statement and facilitate survival estimates in patients treated with SOC.
Delphi panel appears to be a good methodologic choice for health-economic analysis if the therapeutic area is not very well understood and significant heterogeneity is observed.

REFERENCES

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