投稿 ▶原著

膠芽腫を対象とした第II相試験で設定される有効性エンドポイントの近年の傾向に関する調査研究

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Fact-finding Research on Efficacy Endpoints in Recent Phase II Clinical Trials Targeting Glioblastoma

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Summary

Background: Setting appropriate efficacy endpoint(s) in Phase II clinical trials is important for success in subsequent Phase III trials or for conditional approval based on Phase II findings. However, there is no consensus about efficacy endpoints in Phase II trials targeting glioblastoma.

Objective: To compare endpoints used in recent Phase II clinical trials of glioblastoma treatments.

Method: 117 clinical trials involving glioblastoma were identified on the ClinicalTrials.gov website. The main efficacy endpoints used in them were examined.

Results: Seventeen trials had no efficacy endpoint and were excluded. Efficacy endpoints in the remaining 100 trials were OS in 33 trials (29%), response rate in 23 (20%), PFS in 20 (17%), OS rate in 11 (10%), PFS rate in 10 (9%), and others in 16 (14%) (note that multiple endpoints were used in some trials). Response rates ranged from 2 cases of 45 (4%) for newly diagnosed glioblastoma to 20 of 51 (39%) for recurrent glioblastoma ($p = 0.0004$). Response rate evaluation was done using RANO criteria in 9 trials, iRANO in 2 trials, RECIST in 2 trials, and unknown in 9 trials. In 20 trials that employed OS rate or PFS rate as an efficacy endpoint, the timing of the efficacy evaluation was 12.0 months (median value) [range: 12.0 to 12.0 months] for OS and 6.0 [6.0 to 12.0] months for PFS in cases of newly diagnosed glioblastoma, and 12.0 [6.0 to 24.0] months for OS and 6.0 [6.0 to 12.0] months for PFS in recurrent glioblastoma. The timing of efficacy evaluation appears to be earlier than the median in pivotal studies of previously approved products.

Conclusions: Various efficacy endpoints have been set in Phase II clinical trials targeting glioblastoma, and there is no consensus as to which endpoint should be preferred. In trials using time-to-event endpoints, some of the study designs make it difficult to interpret the results.

Key words

Efficacy endpoint, Phase II, Glioblastoma, Clinical trial, Response rate