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**Motexafin Gadolinium Combined with Prompt Whole Brain Radiotherapy Prolongs Time to Neurologic Progression in Non–Small-Cell Lung Cancer Patients with Brain Metastases: Results of a Phase III Trial**

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**Purpose**

To determine the efficacy of motexafin gadolinium (MGd) in combination with whole brain radiotherapy (WBRT) for the treatment of brain metastases from non–small-cell lung cancer.

**Methods and Materials**

In an international, randomized, Phase III study, patients with brain metastases from non–small-cell lung cancer were randomized to WBRT with or without MGd. The primary endpoint was the interval to neurologic progression, determined by a centralized Events Review Committee who was unaware of the treatment the patients had received.

**Results**

Of 554 patients, 275 were randomized to WBRT and 279 to WBRT+MGd. Treatment with MGd was well tolerated, and 92% of the intended doses were administered. The most common MGd-related Grade 3+ adverse events included liver function abnormalities (5.5%), asthenia (4.0%), and hypertension (4%). MGd improved the interval to neurologic progression compared with WBRT alone (15 vs. 10 months;  $p = 0.12$ , hazard ratio [HR] = 0.78) and the interval to neurocognitive progression ( $p = 0.057$ , HR = 0.78). The WBRT patients required more salvage brain surgery or radiosurgery than did the WBRT+MGd patients (54 vs. 25 salvage procedures,  $p < 0.001$ ). A statistically significant interaction between the geographic region and MGd treatment effect (which was in the prespecified analysis plan) and between treatment delay and MGd treatment effect was found. In North American patients, where treatment was more prompt, a statistically significant prolongation of the interval to neurologic progression, from 8.8 months for WBRT to 24.2 months for WBRT+MGd ( $p = 0.004$ , HR = 0.53), and the interval to neurocognitive progression ( $p = 0.06$ , HR = 0.73) were observed.

**Conclusion**

In the intent-to-treat analysis, MGd exhibited a favorable trend in neurologic outcomes. MGd significantly prolonged the interval to neurologic progression in non–small-cell lung cancer patients with brain metastases receiving prompt WBRT. The toxicity was acceptable.

[Brain metastases, Non–small-cell lung cancer, Whole brain radiotherapy, Motexafin gadolinium, Neurologic progression, Neurocognitive function](#)


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